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Technological Adoption and Trends in Health Sciences Teaching, Learning, and Practice

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Table of Contents

Preface	xvi

Chapter 1

Skin Tribology: Overview and Insights on Frictional Properties of Human Skin.....	1
<i>Roberto D'Amato, Universidad Politécnica de Madrid, Spain</i>	
<i>Alessandro Ruggiero, University of Salerno, Italy</i>	

Chapter 2

Tridimensional Vectorial Modeling of the Human Body From Anatomical Slices: A New VR Learning Tool for Students	26
<i>Jean François Uhl, Paris University, France</i>	
<i>Vincent Delmas, Paris University, France</i>	
<i>Rodolphe Burgade, Université François Rabelais, France</i>	
<i>Guillermo Daniel Prat, Universidad Nacional de La Plata, Argentina</i>	
<i>Barbara Constanza Lorea, Universidad Nacional de La Plata, Argentina</i>	
<i>Camillo Ruiz, Universidad Nacional de La Plata, Argentina</i>	
<i>Joaquim Armando Jorge, Technic Superior Institute, Lisboa University, Portugal</i>	

Chapter 3

Healthcare E-Learning Ecosystem for the Use of Ultrasound in Interventional Procedures: Sharing the Keynotes on a Real Experience	49
<i>Belen Curto, University of Salamanca, Spain</i>	
<i>Vidal Moreno, University of Salamanca, Spain</i>	
<i>Francisco Javier Serrano, University of Salamanca, Spain</i>	
<i>Felipe Hernández, Salamanca University Hospital, Spain</i>	
<i>Pablo Alonso, Salamanca University Hospital, Spain</i>	
<i>Francisco Javier Blanco, University of Salamanca, Spain</i>	
<i>Juan Alberto Garcia-Esteban, University of Salamanca, Spain</i>	

Chapter 4

Magnetic Resonance Imaging Simulator: From a Proof of Concept to a Useful Tool in the Education of Radiographers.....	66

Rodrigo de Luis-García, Universidad de Valladolid, Spain

Daniel Treceño-Fernández, Giveme5D Ltd., Spain

Juan Calabia-del-Campo, Hospital Clínico Universitario, Spain

Félix Jesús de Paz-Fernández, Universidad de Valladolid, Spain

Carlos Alberola-López, Universidad de Valladolid, Spain

Chapter 5

Smart Splint Development: New Technologies for Diagnosis During Initial Stages of Treatment Applied to Splints – New Therapy Possibilities	94

Jose María de Agustín, University of Salamanca, Spain

Chapter 6

Anatomical Variability and Biomedical Imaging for Spinal Anesthesia Individualization: How 3D Tools Enhance Understanding	126

Anna Puigdemívol-Sánchez, University of Barcelona, Spain & University of Vic-Central

University of Catalonia, Spain & Terrassa Health Consortium, Spain

Xavier Sala-Blanch, Hospital Clínic of Barcelona, Spain & University of Barcelona, Spain

Miguel A. Reina, College of Medicine, University of Florida, USA & School of Medicine,

CEU-San-Pablo University, Spain

Alberto Prats-Galino, University of Barcelona, Spain

Chapter 7

An ETL Approach to the Generation of Educational Resources From Digital Radiology Medical Collections	147

Felix Buendia, Universitat Politècnica de València, Spain

Joaquín Gayoso-Cabada, Universidad Politécnica de Madrid, Spain

José-Luis Sierra, Universidad Complutense de Madrid, Spain

Chapter 8

From Anatomic Lab to Operating Theatre: Technological Tools for Continuing Learning and Education	164

Giulia Guizzardi, Universitat de Barcelona, Spain

Alberto Di Somma, Hospital Clinic de Barcelona, Spain

Jorge Torales, Hospital Clínic de Barcelona, Spain

Pedro Roldan, Hospital Clínic de Barcelona, Spain

Federico Varriano, Universitat de Barcelona, Spain

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Jose Juan Gonzalez Sanchez, Hospital Clínic de Barcelona, Spain

Joaquim Enseñat, Hospital Clínic de Barcelona, Spain

Alberto Prats-Galino, University of Barcelona, Spain

Chapter 9

Technological Environments of Anatomical-Radiological Vision in 3D for the Study of Pelvic Structures	190

Lourdes Asensio-Romero, Hospital Virgen de la Concha of Zamora, Spain

Manuel Asensio-Gómez, School of Medicine, University of Salamanca, Spain

Alberto Prats-Galino, University of Barcelona, Spain

Chapter 10

Mangement of a 3D Visualization Program From Radiological Images in Neuroradiology.....	215

Roberto Domingo Tabernero-Rico, Hospital Virgen de la Concha, Zamora, Spain

Sonia-Francisca Pozo-González, Hospital Virgen de la Concha, Zamora, Spain

Alberto Prats-Galino, University of Barcelona, Spain

Chapter 11

3D Printing in Bone Tissue Engineering: Bibliographic Review of Current Advances and Future Potential	245

Israel Barrutia Barreto, Innova Scientific, Peru

Lucio Arnulfo Ferrer Peñaranda, National University of Callao, Peru

Fabrizio Del Carpio Delgado, National University of Moquegua, Peru

Renzo Antonio Seminario Córdova, Innova Scientific, Peru

Brian Alberto Chero Arana, Innova Scientific, Peru

Chapter 12

Medical Learning Through Simulations With Immersive Virtual Reality and Augmented Reality Devices.....	265

Juan Antonio Juanes-Méndez, University of Salamanca, Spain

Samuel Marcos-Pablos, University of Salamanca, Spain

M Auxiliadora Velasco-Marcos, Sanidad de Castilla y León, Spain

Santiago González Izard, ARSOFT, Spain

Chapter 13

The Role of Data in Health Sciences Ecosystems: Experiences Within a Psychoeducation-Oriented IT Platform.....	283

Samuel Marcos-Pablos, University of Salamanca, Spain

Juan Antonio Juanes-Méndez, University of Salamanca, Spain

Francisco José García-Peñalvo, Universidad de Salamanca, Spain

Chapter 14

Computational Study of In-Vivo CT-Based FEM Application in Bone Tissue Engineering	300

Ranjit Barua, OmDayal Group of Institutions, India

Sudipto Datta, Indian Institute of Engineering Science and Technology, Shibpur, India

Debasish Banerjee, OmDayal Group of Institutions, India

Chapter 15

Artificial Intelligence in the Era of Clinical Imaging: How Training Models Could Be a Challenge
for New Upcoming Physicians in Radiology – Learner Needs of Radiology Residents Regarding

AI 317

Georgios Kolostoumpis, Stelar Security Technology Law Research UG, Germany

Olga Vasila-Vakhnina, SUS, Sweden

Nikolaos Vasilas, Medical University of Gdansk, Poland

Compilation of References 326

About the Contributors 377

Index..... 385

Detailed Table of Contents

Preface	xvi

Chapter 1

Skin Tribology: Overview and Insights on Frictional Properties of Human Skin.....	1

Roberto D'Amato, Universidad Politécnica de Madrid, Spain

Alessandro Ruggiero, University of Salerno, Italy

The purpose of this chapter is to give an outline and interpretation of the experimental findings for the in vivo and in laboratory experiments about frictional behavior of human skin. The scientific literature framework will be illustrated, and the different factors affecting human skin's friction behavior will be explored considering the theoretical aspects which were summarized and discussed connected to the friction mechanisms, with an emphasis on the analysis of the adhesion and deformation component in different skin conditions. Moreover, the chapter highlighted some technical concepts considering different techniques and measurement parameters used to investigate the friction of human skin in different human body parts and in different contact conditions.

Chapter 2

Tridimensional Vectorial Modeling of the Human Body From Anatomical Slices: A New VR	

Learning Tool for Students	26

Jean François Uhl, Paris University, France

Vincent Delmas, Paris University, France

Rodolphe Burgade, Université François Rabelais, France

Guillermo Daniel Prat, Universidad Nacional de La Plata, Argentina

Barbara Constanza Lorea, Universidad Nacional de La Plata, Argentina

Camillo Ruiz, Universidad Nacional de La Plata, Argentina

Joaquim Armando Jorge, Technic Superior Institute, Lisboa University, Portugal

Digital anatomy has emerged as an essential subfield of anatomy that processes the human body with the help of a computer. 3D reconstruction tools have been developed over the years, being always complementary to cadaver dissection. Teachers' main goal is to provide a greater understanding of the spatial structures of the body and its internal organs thanks to 3D reconstruction techniques. Manual segmentation and creation of 3D vectorial models is probably the best anatomy learning tool for beginners and students. The aim of this chapter is to show how to create vectorial models from anatomical slices with Winsurf® software, highlighting their educational value. Resulting 3D models could also be used through the interface of virtual dissection, which has been proven to be immensely valuable for anatomy education, particularly by using immersive reality techniques. It could also be the basis of future simulation tools for surgeon training.

Chapter 3

Healthcare E-Learning Ecosystem for the Use of Ultrasound in Interventional Procedures: Sharing the Keynotes on a Real Experience	49

Belen Curto, University of Salamanca, Spain
Vidal Moreno, University of Salamanca, Spain
Francisco Javier Serrano, University of Salamanca, Spain
Felipe Hernández, Salamanca University Hospital, Spain
Pablo Alonso, Salamanca University Hospital, Spain
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Ultrasound imaging (USI) has become a disruptive element in medicine. To achieve a safer USI application, professionals need sound practical training. This chapter presents the keynotes in the development of a teaching-learning ecosystem, where students (future specialist physicians) and teachers participate, with the concrete educational contents. The ecosystem is supported by a LMS that includes recourses and activities for collaboration, implemented by a multidisciplinary team of health and ICT experts. Practical skills are acquired through a computer-based simulator for the training of the USI-based interventional procedures that the student can handle autonomously at any time and is highly realistic. As a main result, the ecosystem is applied to a real experience, focusing on the treatment of spasticity by botulinum toxin infiltration. Learning outcomes have been evaluated through academic grades and a survey of students who have participated in a specialist course.

Chapter 4

Magnetic Resonance Imaging Simulator: From a Proof of Concept to a Useful Tool in the Education of Radiographers.....	66

Rodrigo de Luis-García, Universidad de Valladolid, Spain
Daniel Treceño-Fernández, Giveme5D Ltd., Spain
Juan Calabia-del-Campo, Hospital Clínico Universitario, Spain
Félix Jesús de Paz-Fernández, Universidad de Valladolid, Spain
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Magnetic resonance imaging (MRI) is one of the most powerful medical imaging modalities available. From an educational perspective, MRI faces a difficult challenge. Operating an MRI scanner is a complicated task due to the fact that it is based on advanced concepts borrowed from physics. A large number of parameters are involved and hands-on training for practitioners is usually scarce due to the high costs of the equipment and the increasing clinical demands, which make MRI scanners intensively exploited facilities. In this context, the development of computerized simulations for MRI seems a natural alternative. This chapter reports an actual experience on the creation and evolution of an MRI simulator for educational purposes, thus obtaining an increasingly refined set of functional and usability requirements that such a system must fulfill in order to make an impact in MRI education, quantifying the usefulness of the simulator in realistic settings and providing technological solutions and strategies to overcome its limitations.

Chapter 5

Smart Splint Development: New Technologies for Diagnosis During Initial Stages of Treatment Applied to Splints – New Therapy Possibilities	94

Jose María de Agustín, University of Salamanca, Spain

After suffering a fracture in an upper or lower limb, a plaster cast is placed on the affected limb. It is a very old and efficient technique for recovery from an injury that has not had significant changes since its origin. This project aims to develop a new, low-cost smart 3D-printed splint concept by using new sensing techniques. Two rapidly evolving advanced manufacturing (AM) technologies will be used: 3D scanning and 3D printing. This is possible thanks to the application of engineering on additive manufacturing techniques and the use of biocompatible materials available in the market. This study proposes the use of these materials and techniques, including sensor integration inside the splints. The main parameters considered to be studied are pressure, humidity, skin colour, and temperature. These aspects are combined and analyzed to determine any kind of unexpected evolution of the treatment. The goal of this study is to generate a smart splint by using biomaterials and engineering techniques based on the advanced manufacturing and sensor system for clinical purposes.

Chapter 6

Anatomical Variability and Biomedical Imaging for Spinal Anesthesia Individualization: How 3D Tools Enhance Understanding 126

*Anna Puigdemívol-Sánchez, University of Barcelona, Spain & University of Vic-Central
University of Catalonia, Spain & Terrassa Health Consortium, Spain*

Xavier Sala-Blanch, Hospital Clínic of Barcelona, Spain & University of Barcelona, Spain

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Spinal anesthesia can be affected by gaps in the ligamentum flavum that may confuse epidural needle placement; cause Quincke needle deformation if the vertebral bone is hit, expanding the dural sac hole and leading to cerebrospinal fluid (CSF) leakage and post-dural puncture headache; and variability in CSF volume, altering intrathecal drug dilution and anesthetic efficacy. Paramedian approaches with previously calculated optimal angles can be adopted, and CSF volumes may be estimated using threshold selection within the grayscale range following anatomical criteria. Angles can be determined by previously quantifying the skin-dural sac distance using ultrasound. Here, the relevant anatomical structures are illustrated (ligaments, the ligamentum flavum gap, vertebrae, meninges, cauda equina roots) using a freely available 3D PDF tool (<http://hdl.handle.net/2445/55225>), the additional inconvenience of variability in vertebra rotation is quantified, a free guide for optimizing spinal puncture is presented (<http://hdl.handle.net/2445/179594>), and the possibility of individualizing intrathecal drug dosages is discussed.

Chapter 7

An ETL Approach to the Generation of Educational Resources From Digital Radiology Medical Collections 147

Felix Buendia, Universitat Politècnica de València, Spain

Joaquín Gayoso-Cabada, Universidad Politécnica de Madrid, Spain

José-Luis Sierra, Universidad Complutense de Madrid, Spain

This chapter describes an ETL (extract, transform, load) approach for the generation of instructional resources from pre-existing collections of clinical data, in particular in the field of radiology. The approach advocates, on the one hand, the extraction of information from such sources and its representation in a unified and machine-processable format. On the other hand, the extracted information can be transformed to fit different instructional needs. This transformation process can involve both automatic transformations and transformations carried out by experts using specialized editors. Finally, the information resulting

from the transformation process can be exported in standard formats in order to load it to learning management platforms (e.g., Moodle or Canvas). The chapter illustrates, with the help of a radiology clinical case collection, how this approach can be supported by a flexible digital collection management tool called Clavy.

Chapter 8

From Anatomic Lab to Operating Theatre: Technological Tools for Continuing Learning and

Education 164

Giulia Guizzardi, Universitat de Barcelona, Spain

Alberto Di Somma, Hospital Clinic de Barcelona, Spain

Jorge Torales, Hospital Clínic de Barcelona, Spain

Pedro Roldan, Hospital Clínic de Barcelona, Spain

Federico Varriano, Universitat de Barcelona, Spain

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Alberto Prats-Galino, University of Barcelona, Spain

The neurosurgical practice is always evolving, achieving new technologies and new techniques every day. From the beginning in the anatomic laboratory, the neurosurgeon could visualize on specimens all the structures and all the areas of the brain. When facing a lesion, the treatment must be carefully planned, and all the information collected by each study and investigation performed must be organized and summarized. This complex work of planning will make the surgery much more efficient, and every technology will perform its precise role. Moreover, the patient management is multidisciplinary and requires a precise teamwork: the follow-up usually is a lifelong course. When a case finishes, it's time for the neurosurgeon to go back to the anatomical lab and start again to study the possible perspectives for the next case.

Chapter 9

Technological Environments of Anatomical-Radiological Vision in 3D for the Study of Pelvic

Structures 190

Lourdes Asensio-Romero, Hospital Virgen de la Concha of Zamora, Spain

Manuel Asensio-Gómez, School of Medicine, University of Salamanca, Spain

Alberto Prats-Galino, University of Barcelona, Spain

Computer applications have been incorporated as valuable elements in teaching, thanks to the innovation of new technologies in recent decades. The implementation of these computer developments in the field of medical education has been a true revolution. The authors present a computer development designed for PC environments that allows visualizing and interacting in a virtual environment with the main anatomical structures (bone, muscle, vascular, and visceral) of the female pelvis in three dimensions (3D) integrated with cadaveric sections and serial sections of magnetic resonance imaging. The consequence of the application of 3D environments for training and the integration of all these technological innovations in clinical medicine, together with the rapid evolution of information and communication technologies,

is the emergence of a new teaching methodology with new opportunities for the development of the teaching-learning process.

Chapter 10

Management of a 3D Visualization Program From Radiological Images in Neuroradiology..... 215

Roberto Domingo Tabernero-Rico, Hospital Virgen de la Concha, Zamora, Spain

Sonia-Francisca Pozo-González, Hospital Virgen de la Concha, Zamora, Spain

Alberto Prats-Galino, University of Barcelona, Spain

The latest technological advances in postprocessing of images have made possible the generation of three-dimensional (3D) models from 2D radiological images. The use of these models in PDF file allows interaction, providing useful visualization tools and management that facilitate the work and understanding of the anatomical region of the study area. All this is possible from a personal computer without the requirement of a professional workstation. In this chapter, the authors present the characteristics of 3D PDF software with anatomical models of the skull base. Therefore, through the management and development of these new educational contents, introduced as complementary didactic material for the study of anatomy in complex regions, the ability to understand is improved and learning is expedited. This is very important not only in the field of teaching but also in other applications, such as clinical practice and the scientific field, since it allows the use of these contents without the need to compromise patient safety.

Chapter 11

3D Printing in Bone Tissue Engineering: Bibliographic Review of Current Advances and Future

Potential 245

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This chapter seeks to explore the current state of 3D printing technology in bone tissue engineering from the reflectibility approach, analyzing in more detail what this field consists of, as well as the materials and techniques mainly used nowadays in 3D printing. Likewise, the potential of this technique in the future is analyzed with the possibilities of improvement in the short and long terms. The research methodology used was non-experimental, documentary, and descriptive. The information was collected from indexed journals and web platforms using keywords such as “bone tissue engineering” and “3D printing” in search engines. Therefore, this chapter represents a very important and necessary source of bibliographic information to be able to carry out new research in this field.

Chapter 12

Medical Learning Through Simulations With Immersive Virtual Reality and Augmented Reality

Devices..... 265

Juan Antonio Juanes-Méndez, University of Salamanca, Spain

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Different examples of the use of recent technologies, based on virtual reality and augmented reality techniques, for the learning of medical students are presented. The use of different glasses, both virtual reality and augmented reality, as well as gloves with movement sensors, allow the user to enter a scenario very close to the real one, resulting in an improvement and optimisation of their learning. The use of these resources in different areas of medicine facilitates the acquisition of skills, for example in cardiac auscultation training in more dynamic learning of human anatomy, with three-dimensional images, or learning protocols for virtual surgical approaches, among many other possibilities. The satisfaction of the users who handled these devices was excellent, acquiring, in very short periods of time, practical skills in many of the actions carried out with these technologies.

Chapter 13

The Role of Data in Health Sciences Ecosystems: Experiences Within a Psychoeducation-Oriented IT Platform..... 283

Samuel Marcos-Pablos, University of Salamanca, Spain

Juan Antonio Juanes-Méndez, University of Salamanca, Spain

Francisco José García-Peñalvo, Universidad de Salamanca, Spain

This chapter aims to provide an overview of the importance of data governance in digital ecosystems in the province of healthcare and to place special emphasis on the significance of taking business processes into account from the early stages of development of this type of solution. It should be borne in mind that business processes are not only those that produce economic benefits, but also those that provide added value for the entire ecosystem and make it sustainable over time. The chapter ends by exemplifying the above discussed approach in a specific use case of a platform initially conceived for the psychoeducation of formal and informal caregivers. Said platform has been conceived using a business process modelling approach focused on data exploitation from the early stages of development, which has allowed services, stakeholders, and potential users of the ecosystem to be extended far beyond the initial ecosystem goal.

Chapter 14

Computational Study of In-Vivo CT-Based FEM Application in Bone Tissue Engineering 300

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At present, computational methods are highly utilized by modern healthcare science. This modern technology gradually solves the complex area of healthcare science, and therefore, the upcoming treatments become more effective. Presently, in bone tissue engineering, the mechanism and different features of bone tissue are being discussed. The finite element method (FEM) gave the extra threshold to the study of bone tissue engineering. FEM method is basically a computer method of structural or mechanical stress investigation advanced in mechanics. The development of upgraded features of FEM applied with the help of the CT (computed tomography) model has enlightened a new hope in the study of biomedical and tissue engineering. The healthcare staff is provided with useful data by CT-based FEM which helps in taking further steps in medical treatment. The motive of this study is to show the improvement in the use of FEM in bone biomechanics in the last few years and also to help the medical specialists for improving the modern treatment and upcoming growth of new bone fracture fixation design.

Chapter 15

Artificial Intelligence in the Era of Clinical Imaging: How Training Models Could Be a Challenge for New Upcoming Physicians in Radiology – Learner Needs of Radiology Residents Regarding

AI 317

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Artificial intelligence technology is a marked change in the imaging field. Clinical imaging and operations applications are metamorphosed as new methods and tools, and algorithms are being brought into radiology's daily practice. Looking forward, further attempts could prove quite beneficial to the literature. Modern technologies like AI technology, particularly deep learning, clearly show evidence of development. AI technology can be exceptionally good at identifying. The authors outline how to interact with and methods to effectively, safely, and efficiency use these tools and technologies.

Compilation of References 326

About the Contributors 377

Index..... 385

Preface

The use of technology in health sciences has a direct impact on health outcomes, as well as on the quality and the safety of healthcare processes. However, bringing in new technologies into the health sector is a complex task. Different actors such as health and care practitioners, technological solution providers, health organizations and regulators and governing bodies, may be involved with the provision of a single service. However, many existing health providers still manage health issues in a disconnected and fragmented way, and there is still a lack of coordination across health ecosystem actors. Thus, from the point of view of the technological research and development community it is important to have a comprehensive vision of the health sciences ecosystem, encompassing many different areas of research.

In this sense, although recent advances in technologies have spurred the health field, expanding the possibilities of providing better and more reliable technological solutions for assisting people, many of the current developments still have not evolved from an end user-centric perspective. There is a clear need to change this approach towards a broader perspective in the development of technology for health and care provision, considering the different stakeholders, application goals, business models, etc. in the design, development, and implementation process of not only care provision management, but also the different related technological components involved in providing care and assistance services (hardware, software, platforms, protocols, ontologies, etc.).

During the last decade, there has been an increasing interest in the development of different types of solutions that allow the interaction between the different actors in the health and care sector (mainly pure health practitioners and technology developers), to deliver integrated and user-friendly health and care services. This interest has been spurred by governing authorities, as the development of such ecosystems is beneficiary due to three main factors: affordability, as health services tend to be expensive; regulatory, searching for regional, national, and international standard compliance in order to provide safe health and care services; and availability, in order to provide specialized services in remote regions within a particular country.

Thus, the current trend in IT solution providers for the health sector is to move from fragmented services to progressively more integrated ones, which are likely to be provided by multiple stakeholders through well-elaborated collaboration mechanisms. This means that together with the necessary development of techno-centric and/or isolated technological solutions for health, the importance of the role of communities and other forms of collaborative networks involving all stakeholders, operating as an ecosystem, is being recognized during the last years.

In addition, the use of new technological developments in medical education has proven to be greatly effective, as it allows to create realistic learning environments to experience with procedures and devices that will become common in medical practice. Transmission of knowledge using teaching innovation

Preface

technologies and computer systems is, nowadays, one of the great scientific-technical and cultural revolutions in our society, where the field of biomedical and health sciences has been able to obtain excellent developments and applications.

Technology, applied to training in health sciences, has undergone great changes over time, always parallel to the technological evolution of society. For that reason, technological advances have modified the teaching and learning methods of university students in the experimental and health sciences. The relationship between the current context of the information society, medicine and health systems is especially important given that information and knowledge are especially relevant in this field.

The application of computer technologies in training in experimental sciences and health, expands the possibilities of action and intercommunication between teachers and students, also allowing access to new means of exploration and representation of information, along with new ways of access to knowledge, through very diverse resources, such as computer simulations, stereoscopic visualization systems with augmented reality glasses, computer platforms for managing and using resources and documents, etc.

Taking the above into account, the aim of this book is twofold. From the point of view of the health technological research and development community it is important to have a comprehensive vision of the whole health ecosystem (encompassing many different areas of research), in order to obtain an overview of the needs and existing technological solutions, and identify the strengths and weaknesses of the research presented to date, which in turn will point out the possible future research directions along with their potential applications, stakeholders and market.

Furthermore, it aims to collect some of the most innovative computer based technological developments applied to both the contexts of medical training and clinical practice, as well as in other fields related to health sciences training, providing an excellent opportunity for the promotion and exchange of innovative teaching experiences in the health field, especially those based on the use of state-of-the-art technology.

Target audience includes all health sciences fields (such as medicine, dentistry, nursing, physiotherapy, podiatry, ophthalmology, optician, or occupational therapy). Additionally, the rest of health ecosystem actors such as health organizations, health and care workers, regulators and governing bodies, and medical technological solution providers (medical engineering, informatics, or robotics) should find valuable information in order to incorporate added value to their health-related activities.

The book consists of 15 chapters that show different aspects of the technological adoption and trends in health sciences teaching, learning, and practice.

The chapter entitled “Skin Tribology: Overview and Insights on Frictional Properties of Human Skin” outlines the experimental findings for in vivo and in laboratory experiments focused on the frictional behavior of human skin. Authors describe the different factors affecting human skin’s friction behavior, considering the theoretical aspects connected to the friction mechanisms, with an emphasis on the analysis of the adhesion and deformation component in different skin conditions. Additionally, the chapter highlights some technical concepts considering different techniques and measurement parameters used to investigate the friction of human skin in different human body parts and in different contact conditions.

The next chapter, “Tridimensional Vectorial Modeling of the Human Body From Anatomical Slices: A New VR Learning Tool for Students,” shows how digital anatomy has emerged as an essential subfield of anatomy that processes the human body with the help of a computer. An overview of 3D reconstruction tools is presented as a teachers’ tool to provide students with a greater understanding of the spatial structures of the body and its internal organs. Authors state that the creation of 3D vectorial models along with segmentation is one of the best anatomy learning tools for beginners and students. They show how

to create vectorial models from anatomical slices with available software, highlighting their educational value, particularly by using immersive reality techniques.

In “Healthcare E-Learning Ecosystem for the Use of Ultrasound in Interventional Procedures: Sharing the Keynotes on a Real Experience,” the importance of providing professionals with ultrasound practical training is presented. Authors provide some keynotes in the development of a teaching-learning ecosystem, where students (future specialist physicians) and teachers participate. Their solution is supported by a LMS that includes recourses and activities for collaboration, implemented by a multidisciplinary team of health and ICT experts. Practical skills are acquired through a computer-based simulator for the training of ultrasound imaging-based interventional procedures that the student can handle autonomously. Particularly they present a real application which focuses on the treatment of spasticity by botulinum toxin infiltration. Learning outcomes are evaluated through academic grades and a survey of students.

“Magnetic Resonance Imaging Simulator: From a Proof of Concept to a Useful Tool in the Education of Radiographers” outlines how Magnetic Resonance Imaging (MRI) is one of the most powerful medical imaging modalities available but faces difficult challenges from an educational perspective. As MRI operation is based on advanced concepts borrowed from physics, a large number of parameters are involved and hands-on training for practitioners is usually scarce, due to the high costs of the equipment and the increasing clinical demands, which make MRI scanners intensively exploited facilities. In this context, the development of computerized simulations for MRI seems a natural alternative, and the chapter reports an actual experience on the creation and evolution of an MRI simulator for educational purposes.

The chapter “Smart Splints Development: New Technologies for Diagnosis During Initial Stages of the Treatment Applied to Splints – New Therapi Possibilities” describes a project aimed to develop a new low-cost smart 3d printed splint by using new sensing techniques. Two advanced manufacturing (am) technologies are used to develop a plaster cast for upper or lower limbs: 3d scanning and 3d printing, by applying additive manufacturing techniques and the use of biocompatible materials available in the market. In addition, sensors are integrated inside the splints, providing with pressure, humidity, skin color and temperature. These aspects are combined and analyzed to determine any kind of unexpected evolution of the treatment.

Next, in “Anatomical Variability and Biomedical Imaging for Spinal Anesthesia Individualization: How 3D Tools Enhance Understanding,” the authors describe how spinal anesthesia can be affected by different setbacks, such as gaps in the ligamentum flavum that may confuse epidural needle placement; Quincke needle deformation if the vertebral bone is hit, expanding the dural sac hole and leading to cerebrospinal fluid (CSF) leakage and post-dural puncture headache; and variability in CSF volume, altering intrathecal drug dilution and anesthetic efficacy. To overcome these problems, a free guide for optimizing spinal puncture is presented, where the relevant anatomical structures are illustrated (ligaments, the ligamentum flavum gap, vertebrae, meninges, cauda equina roots) using a freely available 3D PDF tool, and the additional inconvenience of variability in vertebra rotation is quantified.

The next chapter, entitled “An ETL Approach to the Generation of Educational Resources From Digital Radiology Medical Collections,” describes an ETL (Extract, Transform, Load) approach for the generation of instructional resources from pre-existing collections of clinical data in the field of radiology. The approach shows the extraction of information from such sources and its representation in a unified and machine-processable format, and how this information can be transformed to fit different instructional needs. This transformation process can involve both automatic transformations and transformations carried out by experts using specialized editors. Finally, the information resulting from

Preface

the transformation process can be exported in standard formats to be loaded into conventional learning management platforms.

In “From Anatomic Lab to Operating Theatre: Technological Tools for Continuing Learning and Education,” the authors claim that the complex work of planning neurosurgical procedures the treatment must be carefully planned, and all the information collected by each study and investigation performed must be organized and summarized. As so, the chapter presents different technological tools for continuing learning and education, as well as neurosurgical planning, which will rend the surgery much more efficient, and allow the different technologies employed to be correctly and proficiently used.

The chapter entitled “Technological Environments of Anatomical-Radiological Vision in 3D for the Study of Pelvic Structures” describes the use of 3D visualization for interacting in a virtual environment with the main anatomical structures (bone, muscle, vascular and visceral) of the female pelvis in three dimensions, integrated with cadaveric sections and serial sections of magnetic resonance imaging. The application of 3D environments for training and the integration of these technological innovations in clinical medicine, allows a new teaching methodology with new opportunities for the development of the teaching-learning process.

In “Management of a 3D Visualization Program From Radiological Images in Neuroradiology,” the authors present the use of 3D PDF software for the visualization of anatomical models of the skull base. Its introduction as complementary didactic material for the study of anatomy in complex regions allows the development of new educational contents which improve the ability to understand the teaching material and foster learning. The importance of their approach resides not only in the development of innovative teaching/learning contents, but also in avoiding the need of compromising patient safety.

In “3D Printing in Bone Tissue Engineering: Bibliographic Review of Current Advances and Future Potential,” the authors explore the current state of 3D printing technology in bone tissue engineering from the reflectivity approach, as well as the materials and techniques mainly used nowadays in 3D printing. Likewise, the future use of this technique is explored along with the possibilities of improvement in the short and long term. The research methodology employed is non-experimental, documentary, and descriptive. The information was collected from indexed journals and web platforms using keywords such as “bone tissue engineering” and “3D printing” in search engines. Therefore, this chapter represents a very important and necessary source of bibliographic information to be able to carry out new research in this field.

The next chapter, “Medical Learning Through Simulations With Immersive Virtual Reality and Augmented Reality Devices: Learning With Immersive Devices,” conveys different examples of the use of virtual reality and augmented reality techniques, for the education of medical students. The use of different technological resources, such as glasses, gloves or movement sensors facilitates the acquisition of skills, for example in cardiac auscultation training; in dynamic learning of human anatomy with three-dimensional images; or learning protocols for virtual surgical approaches, among others. The evaluated user satisfaction was excellent, and they were able to rapidly acquire practical skills in many of the actions carried out with these technologies.

In “The Role of Data in Health Sciences Ecosystems: Experiences Within a Psychoeducation-Oriented IT Platform,” the authors provide an overview of the importance of data governance in digital ecosystems in the province of healthcare, and to place special emphasis on the significance of taking business processes into account from the early stages of development of this type of solutions. The authors state show how business processes are not only those that produce economic benefits, but also those that provide added value for the entire health ecosystem and make it sustainable over time. The chapter ends

by exemplifying the above discussed approach in a specific use case of a platform initially conceived for the psychoeducation of formal and informal caregivers. Said platform had been conceived using a business process modelling approach focused on data exploitation from the early stages of development, which allows services, stakeholders, and potential users of the ecosystem to be extended far beyond the initial ecosystem goal.

The chapter “Computational Study of In-Vivo CT-Based FEM Application in Bone Tissue Engineering” explores the benefits of using finite element methods (FEM) in bone biomechanics. FEM provides a computerized method for structural and mechanical stress investigation used in mechanics, but which can be extrapolated for bone tissue investigation. The FEM is applied with the help of computed tomography for the study of biomedical and tissue engineering. The study contained in the chapter shows the improvements in the use of FEM in bone biomechanics during the last few years. The purpose is to encourage medical specialists to adopt these modern approaches that allow new bone fracture fixation designs.

Finally, in “Artificial Intelligence in the Era of Clinical Imaging: How Training Models Could Be a Challenge for New Upcoming Physicians in Radiology,” the authors outline and explore the future of Artificial Intelligence technology, with special emphasis in the clinical imaging field. The authors try to show the benefits of recent advances, such as deep learning techniques to assessing radiographic features. The chapter also describes that, as clinical imaging and AI algorithms are incorporated into radiology’s daily practice, new teaching and learning approaches should be taken in order to incorporate these technologies into the radiologists’ curricula.

The above chapters show how healthcare technologies are a highly valued tool for improving and transforming healthcare. As they are being adopted by the health community, there has been a reduction in the number of cases of human error, an improvement in clinical outcomes, easier coordination, and more efficient clinical practices. The objective of this book is to obtain an overview of the technological trends within the health sciences ecosystem, identifying the strengths and weaknesses of the research presented to date and depicting the possible future research directions within education and practice.

This publication is expected to impact on the different levels of the health sciences ecosystem. It and may allow, on the one hand, developers of medical technologies to broaden their perspective for the creation of future medical technologies and applications, and on the other hand, practitioners, and medical educators to gain insight into emerging technological research within the health sciences.

Chapter 1

Skin Tribology: Overview and Insights on Frictional Properties of Human Skin

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ABSTRACT

The purpose of this chapter is to give an outline and interpretation of the experimental findings for the in vivo and in laboratory experiments about frictional behavior of human skin. The scientific literature framework will be illustrated, and the different factors affecting human skin's friction behavior will be explored considering the theoretical aspects which were summarized and discussed connected to the friction mechanisms, with an emphasis on the analysis of the adhesion and deformation component in different skin conditions. Moreover, the chapter highlighted some technical concepts considering different techniques and measurement parameters used to investigate the friction of human skin in different human body parts and in different contact conditions.

INTRODUCTION

Human skin tribology is an exploration subject which has been at the focal point of a branch of the bio-tribological investigations in the last years. In most of the reported tribological studies, skin conditions were correlated with the use of skin care products or dealt with dermatological or cosmetic questions affecting and being affected by skin condition, maturing, skin wounds, skin healing and so on... (Cua et al., 1990). Another class of studies was identified with the role of skin contact on the finger cushion, regarding the feeling of touch (Dinç et al., 1991; Skedung et al., 2011; Tomlinson et al., 2007). Furthermore, different materials are being created, considering human factors, for example: skin similarity, fabric perception, touch properties and ergonomics (Li et al., 2012). In this overview is shown how much is important the knowledge of the tribological behavior and of the contact mechanic between the human

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skin and other materials including materials touching the skin also for clinical and sports applications (Chen et al., 2009; Vilhena & Ramalho, 2016).

Nowadays, thanks to instrumental tribological measurements that provide objective and reproducible results, the evaluation of friction and tactile properties is not directly tested using the human body. The humidity present in the stratum corneum as well as in the interface between the skin and a contact surface are determining factors for the evaluation of the friction of the skin, as will be explained later (Johnson et al., 1993).

André et al. (Chen et al., 2009) state that during the object's manipulation, the humidity of the fingertip is modulated by the human body to significantly reduce the forces required to grasp that object. On the contrary, the results of Warman and Ennos (Warman & Ennos, 2009) suggest that the primary function of fingerprints is to improve tactile perception and not to influence friction. Dowson (Dowson, 2009) described the practical aspects of skin tribology during bathing and washing, shaving and so on. Other subjects correlated with the perception of walking barefoot versus sliding on a wet floor. Last two topics are more focused on the subjectivity of the experience of human skin, which is not the main theme of this chapter but it's worth mentioning them. Other factors that are decisive for the tribological study of human skin and which have been the subject of experimental studies are: the friction between the feet and the socks, the contacts between the fingertips and rough surfaces, aging and wrinkles of human skin. In fact, injuries such as abrasions and bedsores are due to the reduced thickness of the skin and the low viscoelastic recovery (Chen et al., 2009) of the aged skin. This means that frictional and shear forces are known as significant risk factors.

Due to various factors, such as the complex anatomical structure of human skin, which makes it a soft biomaterial and therefore characterized by a non-linear viscoelastic behavior (Chen et al., 2009), the friction of the skin strongly depends on the contact conditions. This means that all experimental studies are not uniform and are very difficult to standardize, even if this issue should constitute a challenge for the future.

HUMAN SKIN: ANATOMY AND FRICTION PROPERTIES

The skin represents the largest organ of the human body and is the protective envelope that can reach the extension, in an adult, between 1.6 and 2 m². It accounts for about 16% of an individual's weight. Human skin can be seen as a multi-layered composite material. In concrete there are three functional layers: upper cellular avascular layer (epidermis), intermediate layer (dermis) and subcutaneous adipose layer (subcutis). Blood vessels and sensory receptors can be located within the numerous layers of the skin, hair and skin appendages.

The dermis is composed of a network of collagen and elastin fibers immersed in gelatinous interstitial fluids such as hyaluronic acid, fibroblasts, proteoglycans and water. All these components provide it with high elasticity, high resilience and high tensile and tear resistance.

One of the main characteristics of the connective tissue of human skin is that it is capable, under the action of an external pressure, of expelling water and incorporating it, again when the external pressure applied vanishes, exactly as happens with a sponge. The adipose tissue of the subcutis is in contact with and is intertwined with the loose connective tissue through solid fibers that connect the skin to the surrounding and underlying muscle or bony structures (e.g., fascia and periosteum).

Skin Tribology

Human skin is characterized by nonlinear, viscoelastic material properties (Silver et al., 2001). When a surface comes into contact with human skin, by creating a relative motion between the two surfaces, the most important measured tribological parameter is the friction coefficient (COF) which is defined as the relationship between the frictional force F_f and the normal force N :

$$\mu = \frac{F_f}{N} \quad (1)$$

According to Amontons' friction model, in the case of dry sliding contacts between solid bodies with limited elastic properties, μ is inversely proportional to the applied normal load and remains unchanged regardless of the apparent area of contact between the surfaces. As reported by the studies of El-Shimi (EL-SHIMI & F., 1977) and Comaish and Bottoms (Koudine et al., 2000) the increasing variability of the COF of the skin strongly depends on its viscoelastic nature which causes non-linear deformation, even with reduced normal loads. Furthermore, due to various factors, such as, the type of contact conditions, the presence of fluids acting as lubricants (such as sweat, water and sebum) and the thickness of the film in relation to the surface roughness of the contact materials in contact soft elastohydrodynamic lubrication modes could arise (Adams et al., 2007).

Wolfram (WOLFRAM & J., 1983) provided a theoretical analysis where dynamic skin friction should be related to normal load such as:

$$\mu \propto N^{-\frac{1}{3}} \quad (2)$$

Koudine et al. (Koudine et al., 2000), in their study, found experimentally that this dependence can be expressed as:

$$\mu \propto N^{-0.28} \quad (3)$$

As seen, human skin is one of the most complex, protective, and largest organ of the integumentary system. The skin itself is the surface of the human body, for this reason is useful to exam and define it in terms of surface characteristics, such as friction. Skin tribological studies provide knowledge about how the skin interacts with other surfaces and how it can vary within different conditions (hydration, sebum level) and also how friction is influenced by mechanical contact parameters, mainly normal load and contact pressure.

Surface Properties of Human Skin

Skin Surface Roughness

Human skin's surface topography depends on the body zone, which is formed of localized ridges (finger pads) or furrows (e.g., forearm) that delimit regions of different scale. Typical surface roughness values R_a and R_z lie in the range (10–30) μm and (30–140) μm (Table 1) (Derler & Gerhardt, 2011). Skin roughness, as well as furrow spacing, and anisotropy have been reported to increase with age (Sivamani

Table 1. Different skin sites surface roughness values

Skin region	Ra [μm]	Rz [μm]
Index finger	26.1 ± 6.1	87.3 ± 17.1
Edge of hand	14.9 ± 6.7	54.1 ± 21.2
Back of hand	(23–28)	(138–144)
Volar forearm	(17–20)	(119–125)
Volar forearm	(12–13)	(82–92)
Forehead (temple)	(12–15)	(84–95)

& Maibach, 2006). Until now, only few research has been accessible that offer still an imperfect and ambiguous description of skin topography 's effect on friction.

One of the fundamental aspects to be taken into consideration for the study of the tribological properties of human skin derives from studies on the grip properties of engineering surfaces. An analysis of the experimental studies shows that the COF, between a hard surface and a naturally dry skin of the hand, decreases with increasing surface roughness, especially when R_a varied in the range $0.03\text{--}11.5\text{ }\mu\text{m}$ and $R_z 0.05\text{--}45\text{ }\mu\text{m}$. Subsequent studies have highlighted how the roughness of the probe surface can greatly influence the friction behavior. In fact, in the case of surfaces with a high roughness, the COF increases with the increase of the surface roughness due to the interaction with the friction ridges and ploughing (Tomlinson et al., 2007). On the contrary, as demonstrated in Masen's study (Masen, 2011), in the case of hydrated leather, there is a bell-shaped relationship between the roughness coefficients ($R_q = 0.004\text{--}2\text{ }\mu\text{m}$) and the friction (variable from 0.9 to 1.7) with maximum values at intermediate roughness.

On the basis of these experimental results, it is possible to distinguish two cases. One for moisturizing skin and one for dry skin. In the first case, the high COF value depends on the average roughness of the surfaces in contact and on the ratio between the adhesion and deformation components. In the second case, however, it can be assumed that the COF, which depends on the roughness of the probe, in the initial phases decreases with the increase of the roughness due to the phenomenon of adhesion which is predominant, and which generates a high real contact area, to then assume a minimum value and subsequently increase to a plateau value.

This value is characteristic of a lubrication regime in which the deformation phenomenon is predominant and is characterized by hysteresis, ploughing and interlocking (Derler & Gerhardt, 2011; Masen, 2011; Tomlinson et al., 2007). In fact, according to Moore's theory for elastomers, the COF of materials on rough surfaces increases with a high amplitude of surface roughness.

Superficial Sebum

The skin surface is normally covered by an acid hydrolipid film, which regulates skin flora, avoids pathogenic species from colonizing the skin, and acts as a barrier against invasive microorganisms. The hydrolipid film consists of sweat and sebum water, which coats the skin as an emulsion of water and oil. The function and importance of sebum lipids has been controversially debated in relation to skin tribology. Due to capillary phenomena the skin surface lipid film has shown to influence the skin adhesion properties. In fact, a significant adhesion force could be measured on normal skin, while the adherence force decreased after elimination of the lipid film. Gupta et al. (Gupta et al., 2021), found a

moderate positive linear relationship between sebum level and forearm skin friction measured against steel, but Cua et al. observed no correlation for nine other anatomical skin regions and suggested that surface lipids play a limited role for skin friction (Cua et al., 1990). The available literature suggests that the features of skin surface lipid film should be considered in case of sliding friction. Still not a well-known subject, though.

Relationship Between Skin Moisture and COF

The study on the factors of the multidimensional problem of hydration of human skin has been carried out considering both intrinsic factors, such as age or the part of the body studied, and extrinsic factors, such as environmental humidity or the chemistry of the individual. Studies on the increase and decrease of skin hydration with relative variations in the coefficient of friction show that dry skin has less friction than hydrated skin (Sivamani & Maibach, 2006; Zhang & Mak, 1999). However, the skin's response is more complicated, as very wet skin also has a lower coefficient of friction similar to the characteristics of dry skin (Sivamani & Maibach, 2006).

One of the most studied cases is that of an intermediate state of hydration in which the skin is considered moistened in the subcutaneous layers without the formation of a “slippery” water film on the external surface. In these cases, the values of the COF of the skin vary in a range between 1.5-7 between wet and dry conditions (Derler & Gerhardt, 2011). Among the factors that produce this variability in the results are the different test methods, materials and experimental parameters used. The time interval between a friction calculation and application of moisturizer or skin exposure to water is potentially one of the most significant causes. Previous studies have reported linear, power-law, exponential and bell-shaped relationships between skin hydration and friction. Luís Vilhena varied the skin hydration status of the volar forearm in 22 subjects and found a highly positive linear correlation between skin moisture and COF values during tribological skin-textile tests (Vilhena & Ramalho, 2016).

In other studies (Zhang & Mak, 1999) on fingers it has been shown that the COF value initially increases with the increase of humidity up to a limit value and then undergoes a strong decrease. This type of behavior was previously described as bell-shaped behavior and clearly shows a transition from boundary to mixed lubrication if the skin is sufficiently wet. In other words, this behavior can be explained by considering that the addition of water increases the coefficient of friction temporarily before the skin returns to its ‘natural’ state due to the evaporation of the water. The water softens the skin and this causes the roughness of the skin to be smoothed out forming a greater real contact area (RCA). During the tribological tests, adhesive forces were observed between the water and the probe, with a consequent increase in the resistance to friction, between the skin and the probe, and therefore in the COF (Zhang & Mak, 1999). Dry skin becomes less soft due to evaporation, so the probe does not reach the same contact area and this allows the sample to move more easily on the skin surface.

Physical Friction Mechanisms in Wet Skin Conditions

Johnson and Adams et al. (Johnson et al., 1993) discussed the lubrication of the skin by water in detail. If skin becomes soaked with water, and excess water accumulates in the interface, hydrodynamic lubrication, characterized by a liquid layer that completely separates the sliding surfaces, takes place. Under these conditions, a contribution due to viscous friction is replaced by the adhesion component of the friction. Both mixed lubrication or boundary lubrication can take place (Derler et al., 2009) depending on the

contact conditions, film thickness and skin roughness. For finger pads that slide on a wet, smooth glass surface (Derler et al., 2009), significantly lower friction coefficients have been observed if compared to those found on a rough, wet glass surface; analytical results have shown that hydrodynamic lubrication has come into play (Derler et al., 2009), but to completely describe the friction behavior of wet skin on rough glass, we must say that skin's surface roughness was much greater than the minimum film thickness needed for EHL, it was believed that water films were only developed locally between skin and glass, while dry contact zones coexisted in other regions (mixed lubrication) (Derler et al., 2009).

Lubricants/Emollients/Moisturizers

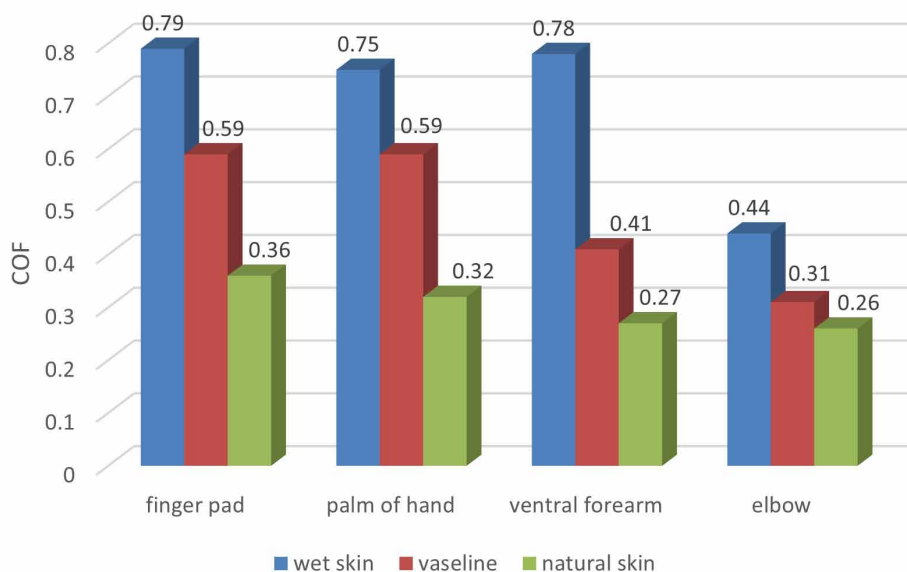
The amount of moisture between the human skin and textiles was the topic of many studies (Cua et al., 1990; Vilhena & Ramalho, 2016).

According to the anatomical body region investigated, the effect of Vaseline on the COF values is different as shown in Figure 1. However, if compared with the natural skin conditions, the COF value always increases with the increase of Vaseline.

Vaseline spread on the skin can create a barrier to reduce moisture in the skin and, as a consequence, increase in the COF value. In addition, it was shown in the early 1980s by Nacht et al. (Nacht et al., 1981) that a mixed effect would occur with the use of occlusive agents, including Vaseline. The COF initially decreases due to the Vaseline's lubricant properties, while later the coefficient increases due to the increased hydration caused by the occlusion.

The significant rise in COF values when skin is wet is attributed to the moisture-dependent mechanical properties of the stratum corneum. Water decreases the elastic module of the last one (plasticizing effect) leading to smoothening of skin roughness asperities and thus increasing the real contact area, resulting in improved adhesion in the friction component. Contrary to hydrated skin, though, the completely wet skin surface can induce hydrodynamic lubrication, resulting in much lower COF values.

Figure 1. Comparison of coefficient of friction for different types of lubricant, measured on different body regions



The significant rise in COF values when skin is wet is attributed to the moisture-dependent mechanical properties of the stratum corneum. Water decreases the elastic module of the last one (plasticizing effect) leading to smoothening of skin roughness asperities and thus increasing the real contact area, resulting in improved adhesion in the friction component. Contrary to hydrated skin, though, the completely wet skin surface can induce hydrodynamic lubrication, resulting in much lower COF values.

No major variations in skin tension over ethnicity were observed in previous studies (Gitis & Sivamani, 2008). Some research analyzing skin tension on different anatomical sites find no variations with regard to gender and age. Sivamani et al. (Gitis & Sivamani, 2008; Sivamani & Maibach, 2006) found that the stiffness of the volar forearm against a PTFE wheel or a metal wire did not improve with age. Cua et al. (Cua et al., 1990) found no substantial age- and gender-related skin friction variations for eleven areas of the body. Female skin tension in contact with textiles was, however, more sensitive / susceptible to changes in moisture (Deleau et al., 2009); this effect was due to increased skin softening and the creation of a greater actual contact area for women.

With respect to the influence of various body regions, certain experiments were carried out under specific lubricating conditions in four separate skin regions. Figure 1 indicates that there are major differences in the COF value around the human body. For example, The COF value in the elbow region is considerably lower than in other parts of the body (e.g., finger pad). As previously stated, the variability of the experimental COF values was attributed primarily to differences in skin hydration. Briefly, it was noted that the pressure on the finger pad, hand palm, neck, and vulva was higher than on the edge of the hand, belly, hips, legs, and lower back. Hairs on the men's dorsal forearm is presumably the cause for the lower COF measured on the volar forearm (Li et al., 2012). The specific physical (RCA reduction) and/or chemical (hair cuticula lubricants) reasons why hairs with reduced skin friction are unclear. The influence of hairs on human skin's friction behavior remains an interesting subject of future research.

The variations in skin hydration and body area suggest that monitoring of skin friction measurements at the anatomical site of interest is essential, as the effects of skin friction at one anatomical location are not generally descriptive for those at other anatomical sites.

Measurement Techniques

The skin friction coefficient values are influenced also by the adopted measurement technique. With reference to a pin on disk-based experiments, for different contact materials Zhang and Mak (Zhang & Mak, 1999) observed slightly increasing COF values as disk rotation speed increased from 25 rpm (~.7 mm/s) to 62.5 rpm (~.2 mm/s). On the other hand, with increasing speed (1–8 mm / s) of a steel sphere, Adams (Briscoe & Adams, 1987) found no change to the COF. Johnson et al. (Johnson et al., 1993) used power-law expressions to define friction coefficients which increase with sliding velocity (0.25–33 mm / s). The precise physical processes contributing to increased velocity skin friction are still unclear and it needs to be investigated. It can be expected that the presence or absence of fluid in the contact will greatly influence the effect of the sliding speed by determining whether soft EHL effects can occur physically.

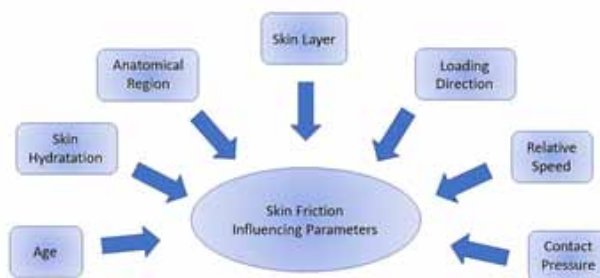
The friction coefficient increases linearly with increased contact pressure on the skin. One possible reason is that the probe's elevated contact pressure raises sweating in the skin region being examined, resulting in greater friction. That is why using a spinning probe does not seem appropriate to calculate an accurate human skin friction coefficient. The device with a rotary probe is mobile, so it is useful to compare various areas of the skin, but it is not clear whether the friction contact conditions are reliable.

Because human skin's frictional behavior largely depends on the skin's hydration state, it is recommended that the friction measurement value be combined with skin's hydration measurement value.

By comparing the friction coefficients, the values produced by rotational movements are greater than those produced by linear motions. This could be due to the fact that the contact surface continuously deforms a new region of the skin with linear motion, while only a small area of the skin at the beginning of the process is deformed in the mentioned rotational motion. This can be better understood considering deformation and adhesion phenomena.

The research from the last several decades on skin tribology has constantly indicated the surface roughness of the materials in contact with the skin, but it would also be useful to specify the surface roughness of the skin areas tested in experiments to provide further microscopic-level contact information. A drawback of a lot of studies presented in the literature is that only the skin of a sample was examined. Additionally, calculating normal load (to approximate contact pressure) would help to increase comparability between the different experiments. Since the results of tribological measurement on the skin depend on different parameters (Figure 2), in order to study specific cases or applications, it is often important to reproduce the actual contact conditions as much as possible.

Figure 2. Influencing skin friction factors



IN VIVO TESTS

COF values of human skin in vivo were measured by several researchers by using different experimental setups and test conditions. The In Vivo Tests can be summarized into two primary categories:

- Tribological tests in which probe materials are rubbed against skin.
- Tribological tests in which human subjects rub their skin against surfaces and materials.

Comparison of experimental results across studies is not easy due to the variability of the test conditions. This may be one explanation why most of the skin tribology reports concentrated mainly on a very general discussion of the spectrum of calculated COFs and factors that affect skin friction. Derler (Derler & Gerhardt, 2011) stated that if the apparent contact pressure between human skin and the test material is investigated, the information on skin tribology can be essentially improved, yet in a large portion of the examinations looked into, no skin contact pressure was estimated or determined. However, if the normal contact force is known, the Hertz contact model (Landau & Lifšic, n.d.) may provide a

reasonable basis for determining the contact pressure (Johnson et al., 1993) if friction measurements are carried out on a flat skin surface by the spherical probe. The Hertz model is appropriate for linear elastic activity and is restricted to minor deformations, but nonlinear mechanical behavior characterizes the skin and underlying soft tissues (Fung, 1993; Silver et al., 2003) and major deformations of the skin and tissues are typically found in tribological experiments (Kwiatkowska et al., 2009).

Xydas and Kao (Xydas & Kao, 2016) applied the Ramberg-Osgood model, developed to describe the behavior of elastoplastic materials, to study the contact of bearings against a flat substratum. In the case of convex anatomical regions in connection with rigid structures, this procedure could be reasonable to measure the effective pressure in contact with the skin up to broad tissue deformations. *In several experiments, large laboratory environments are used to measure the friction between skin and other materials.* The benefit of this measuring instrument is that the invention of modern equipment is not required, but traditional tribological instruments may be used to measure the human skin. The primary drawback of estimating skin friction in a research facility arrangement is that all materials must be estimated in that laboratory and that has diminished individuals' readiness to coordinate. A solid technique is needed to decide the factors that impact the friction of human skin in contact with different materials, without the test subject having to make too much effort.

Many experimental designs and measurement instruments emerged in recent decades as the basic concepts used for calculating friction by rubbing the probe substance on human skin with linear sliding motion and rotation (Cua et al., 1990). Recently a portable wireless device built on the concept of spinning probes was developed to measure the friction between the human skin and different materials. Portability enables researchers to take measurements wherever they wish. It can be easily transported to the subject without taking it to the measuring instrument.

The main drawback of this device is that it is not very typical to have frictional contact between the skin and the small rotating disc or ring. In the other side, the measurement tool cantered on the linear movement of the probe material is fixed and is only suitable for anatomical areas that have a relatively uniform surface and can be placed on the platform. Following paragraphs will report some experiments conducted in Vivo to investigate some aspects.

Tests with Spherical Probes

The spherical probe is used primarily to measure the skin's COF under sliding conditions, and the inner forearm is the most frequently studied anatomical area. Mean COF values of skin are calculated taking in account the apparent skin contact pressures. They are calculated for the elastic interaction between spherical and planal surfaces based on the Hertz model which relates the geometrical parameters, the contact force N and the composite elastic modulus E_c according to the equations (4-6):

$$a = \left(\frac{3RN}{4E_c} \right)^{\frac{1}{3}} \quad (4)$$

$$d = \frac{a^2}{R} = \left(\frac{9N^2}{16RE_c^2} \right)^{\frac{1}{3}} \quad (5)$$

$$E_c = \left(\frac{1 - \nu_1^2}{E_1} + \frac{1 - \nu_2^2}{E_2} \right)^{-1} \cong \frac{E_{skin}}{1 - \nu_{skin}^2} \quad (6)$$

The E_c parameter is calculated taking in account the elastic moduli E_1 , E_2 and the Poisson ratios ν_1 , ν_2 of the materials forming the tribological contact. If one material is considerably softer than the other, E_c can be approximated as soft material.

Adams and Johnson et al. used an elastic modulus of 40 kPa with an estimated Poisson ratio of 0.49 to measure the contact pressures between forearm skin and spherical probes. Thus, to evaluate the literature results calculated using spherical probes, these values were used to establish mean apparent touch pressures $p = \frac{N}{(\pi * a^2)}$. Although the results were strongly dispersed, the typical range of dry skin fric-

tion coefficients is about 0.5 and above 1 for wet skin. We can see that damp or moist skin's average friction coefficients are a factor between 2 or more than 3 higher than dry skin ones. The important effect of moisture on skin friction is based on literature data, although in the studies analyzed no details on skin hydration were found. For measurements in dry conditions, the skin has not been treated or cleaned. On the other hand, to create wet skin conditions, the skin has been wet with water or caused by sweat.

These tests would definitely suggest an increase in skin hydration rates during friction measurements. Most data from the literature were measured on the inner forearm. The results are arranged within the same data range for other anatomical areas examined with spherical probes. The elastic properties of the skin and subcutaneous tissue vary according to the thickness and anatomical differences of the tissue. The probe material is not as important as the skin because of its roughness on the surface, according to Hendriks and Franklin (Kwiatkowska et al., 2009). However, spherical probes have not been used to specify surface roughness in any study. The test materials are mostly made of steel and glass, but ruby probes are also used. The highest COF value can be obtained by measuring with steel balls. In vivo measurement results are expected to vary from individual to individual and various repeated experiments on the same subject will vary too.

Derler et al. (Derler & Gerhardt, 2011) used a power-law of the form $\mu(p)=apb$ to indicate a dependence on the pressure of the COFs of wet skin. Assuming the skin's elastic contact nature in keeping with the Hertz model and assuming the friction force to be measured by adhesion forces relative to the surface contact field, the COF value is predicted to decrease to -1/3 with enhanced normal pressure. In this case the Hertz model is only valid for small deformations $d/R < 0.10$ (Dintwa et al., 2007).

Tests with Rotating Probes

The experiments are based on the calculation of the torque required to sustain a steady angular velocity of the device. A 12 mm disc or ring-shaped probe is used in most cases. PTFE, PA, and aluminum are the most popular probe products. The contact pressure with the skin is defined or can be calculated on the basis of the probe configuration and the usual load. The contact pressure was measured based on a Hertz model.

Since the method appears flexible and it can be used on relatively small areas of the skin, many different areas of the skin were examined together with the inner forearm. For example, Zhang and Mak (Zhang & Mak, 1999) and Cua et al (Cua et al., 1990). They studied six and eleven different anatomical regions. For these two studies, the average friction coefficients for all anatomical areas were calculated and analyzed. The range of skin friction coefficients measured using rotating probes is similar to the one found in previous paragraph. The literature values for dry skin fluctuate within 0.5 (mean $\pm$ SD: 0.53 ± 0.39 , median: 0.42). Moist skin COF values are even higher but the skin under this condition has been studied only few times. Based on cheek measurement data (Kwiatkowska et al., 2009), factor 1.6 can be roughly estimated for the difference between dry and wet conditions, but, in the case of the inner forearm, the results indicate factors between about 3 and 6 (Kwiatkowska et al., 2009). Instead, in the case of rotating probes on dry skin, the results show an upward trend with contact pressure. This behavior means that mechanisms of deformation are involved, or that moisture in the skin increases friction at high pressure. In fact, thermal impacts in the contact region cannot be phased out due to local skin heating. The COF values that increase with pressure would be qualitatively in line with the expectations of the elastomers for which viscoelastic hysteresis is considered an important friction mechanism. If the touch pressure rises, proximity to deeper layers of skin is gained and neighboring skin weakening and swelling guarantees better communication and a higher working surface, resulting in further bending and wrinkling. In contrast, a linear increase in the measured friction coefficients can also be associated with skin hydration effects (Derler et al., 2009). High skin moisture can be caused by an occlusion that causes sweating or water build-up. Data from the entire revolving probe literature reveal that there is no apparent impact due to the probe material. Hendriks and Franklin (Kwiatkowska et al., 2009) observed that skin tension (forearm and cheek) was decreased by about 25 percent relative to other materials (such as aluminum) by using PTFE as a probe medium. In their study, due to skin hydration, the transition from dry to wet in the laboratory doubled skin friction.

Experimental effects on human finger stiffness and touch actions can be derived from research on surface tactile properties, and from research on material handling. Human fingertips and high intensity sweat glands describe the smooth surface of human fingers, all important for frictional behavior. Recent research has shown that the key function of the epidermis' superficial ridges is not to affect friction but to activate the receptors found in the tissues on the underground soil surface, thus enhancing contact.

Dynamic Friction

As regards the friction between fingers and objects, a number of recent experimental tests on this subject have been published. Skin touch pressure information is normally not accessible, as additional skin contact area measurements are needed. The contact area (A) between the finger and the flat surface as a function of normal load (N) is assessed with optical techniques, fingerprints and pressure sensitive films (Derler et al., 2009). The result of the measurement of A (N) shows a nonlinear curve, which is

characterized by a strong initial increase when the normal force is as high as 2-5 N and a moderate increase, thus stabilizing the value under a greater force.

For a contact force of about 10 N, the apparent contact area of the index finger is usually between 2 and 3.5 cm² (Derler et al., 2009). The contact area of the finger will vary due to individual differences and measured parameters (such as the angle between the finger and the contact surface). In testing the subject, Warman and Ennos (Warman & Ennos, 2009) found the index finger contact region to be slightly larger than that of the other fingers. Xydas and Kao (Xydas & Kao, 2016) have used the type $A(N)=aN^b$ functions to examine the fingertips' evident contact region after rubbing against a flat surface. Their method was focused on the definition of nonlinear mechanical behavior using the Ramberg-Osgood model stress-deformation relationship, which was originally designed to study the uniaxial stress deformation curves of elastoplastic materials (metals). The Ramberg-Osgood model has also been used to characterize tissue and fiber mechanical behavior, as well as biomaterials such as bones and heart valve implants. Nonlinear shear-stress activity is common for skin and other sensitive biologic tissues. The human fingertip experiences a force / deformation-like behavior when squeezed, defined by forces that increase roughly linearly with deformations of less than 1 mm and develop in a non-linear fashion, with deformations of more than 1.5 mm (Serina et al., 1997).

For dry fingers, the COF value is generally between 0.2 and 1 (0.60 ± 0.38 , median: 0.45). Some studies have studied wet or damp index fingers and have usually found that the friction coefficient is greater than 1 (1.28 ± 0.67 , median: 1.25). The middle finger search results (Serina et al., 1997; Tomlinson et al., 2007) correspond with the index results. Warman and Ennos (Warman & Ennos, 2009) have observed that all finger rubbing behavior was similar. There is little question that the different materials examined (including glass, metals, plastics, elastomers, paper and fabrics with broad surface properties) would induce a major difference in the COF. Obviously, the humidity condition of the skin is essential for the rubbing of the fingers. Tomlinson et al. (Tomlinson et al., 2007) under dry conditions investigated the frictional behavior of the patient's fingertip. *"They noticed mean COF values that ranged for twelve materials (metals, plastics, and elastomers) in a fairly small range (0.14-0.83). In comparison, the calculated COFs showed no high dependency on normal forces of up to 40 N."* In this case, the frictional force is proportional to the real contact area between the surfaces. *"Since for solids with rough surfaces the effective contact surface is proportional to the normal load (Greenwood & Williamson, 1966), the corresponding COF is independent of the load"*. Under dry conditions, the COF value in the pressure spectrum being measured were virtually independent of the load. On the other side, in wet environments, the COF value increased with declining pressure (Derler & Gerhardt, 2011). This is primarily attributed to skin hydration and softening, resulting in a greater overall contact region with rough glass. The differences between dry and wet finger friction were particularly pronounced for contact pressures of less than 20 kPa. Interestingly, a similar discrepancy between wet and dry friction can also be observed in the results of other anatomical areas of the skin examined using sliding probes (Derler & Gerhardt, 2011). Despite of the usage of hydrodynamic lubrication the friction coefficient is very small in damp environments. Comparison show that the rubbing behavior of the fingers is generally consistent with the rubbing behavior of other areas of the skin. A peculiar finding in the finger-friction experiment is that liquid fluids (sweat and sebum) vaporize, resulting in a small reduction in the regularly tested friction coefficient (Derler & Gerhardt, 2011).

Static Friction

In a typical gripping experiment, the measuring body with the sample brought by the subject is held by two fingers. Normal clamping force and tangential force components are measured by an integrated force sensor. The results of studies show that the static COF value of human skin is in the range of 10-40% higher than the dynamic friction coefficient. The static COF determined by the grip experiment is in the same range of the dynamic COF measured for the finger and it shows a similar reduction with the increase of the contact pressure. Most of the styling experiments analyzed relate to conditions of dry skin. In order to evaluate the contact pressure of the fingertip in the gripping procedure, it is presumed that the gripping force is uniformly distributed over all the fingers. Most of the studies investigated the situation of a grasp with precision that keeps the item between the index and the thumb. Few research, however, have used alternate positions for grasp, such as two-finger grasp, three-finger grip, five-finger grip, or full hand grip. In several experiments, O'Meara and Smith found average static COF values of 0.98 to 1.72 between the hand and five handle materials in dry and wet conditions. The COF value of the palm were found higher than those of the fingers, suggesting an effect of the region of the skin and the strength of skin touch. Most tests on grip have been related to dry skin conditions. But Andre 'et al. (Chen et al., 2009) reported higher coefficients of static friction for wet skin compared with dry, normal and very wet skin.

Main Friction Influencing Phenomena: Deformation and Adhesion

The friction coefficient can be divided into two components, one originating from deformation of the skin and one from adhesion between the skin and surface. To be noted is that deformation and adhesion interfere with each other in different ways

This friction coefficient can be said in case of skin friction, to be the sum of two components: the experimental results are explained using a commonly used two-term non-interacting model for unlubricated contacts (Johnson et al., 1993) but with small differences. In this case, in order to calculate the value of the friction force the adhesion and deformation friction components would be taking in account:

$$\mu = \mu_{def} + \mu_{adh} \quad (8)$$

The adhesion friction is the result of shear stress due to relative motion between surfaces. Instead, and the deformation friction is the result of energy dissipated by subsurface viscoelastic deformation at the front of the probe, like in the case of rolling friction. The deformation friction is the result of an incomplete recovery of the skin after the pressure made by the contact with the probe. Both Adhesion and deformation paragraph consider the most common situation: a spherical probe against volar forearm, this particular contact is used to explain all the skin behavior.

The surface component (adhesion) is the energy dissipated in the breaking of irregular junctions formed between the two sliding surfaces due to attractive molecular short-range forces, such as Van der Waals connection. Other research mentioned in this analysis often support the popular belief that adhesion is the key friction mechanism of human skin. According to (Bowden & Tabor, 1986), the friction force is given by $F = \tau \cdot A_r$ where τ is the interfacial shear strength and A_r the real area of contact. In the case of the presence of organic lubricated film, it has been found that the interfacial shear strength is a

linear function of the mean contact pressure p as follows: $\tau = \tau_0 + a \cdot p$ where τ_0 is the intrinsic shear strength, a is a pressure coefficient and $p_r = \frac{N}{A_r}$ the real contact pressure.

The friction coefficient can then be written as:

$$\mu(p_r) = \frac{\tau \cdot A_r}{N} = \frac{\tau_0}{p_r} + \alpha \quad (9)$$

Taking in account the relation between apparent and real contact areas and contact pressures: $A \cdot p = A_r \cdot p_r$ the COF as a function of the apparent contact pressure $p_r = \frac{N}{A_r}$ is given by:

$$\mu(p_r) = \frac{A_r}{A} \cdot \frac{\tau_0}{p} + \alpha \quad (10)$$

If the real area and the apparent one overlap, the disparity between apparent and real contact pressure vanishes. That's the case of soft materials where the contact surface is fully compatible. This case appears reasonable for the skin, which is weakened by hydration and adheres to the opposite side thanks to a small quantity of interface water which acts as an adhesive bridge. Dry skin friction contrasts strongly with wet skin friction, defined by a lower friction coefficient. For certain tests, it has been found on forearms or fingers as seen in Chapter 2, that the dry skin friction coefficient is independent of the normal load (Greenwood & Williamson, 1966).

A complete examination of the published experimental results on human skin friction recently showed that damp or wet skin friction coefficients are always higher than 1 and displayed a marked decrease with increasing contact pressure. In contrary, dry skin values are essentially independent of load, and are typically around 0.5. The surface relief of the skin (epidermal ridges and wrinkles) enables the water films to penetrate to a certain degree even on smooth skin. Skin is never completely dry. It means that the corresponding COF value is not exactly known. The dependence of the contact area (A) on the normal load (N) and it may be described using the Hertz equation in the following form:

$$A = \pi \left(\frac{3NR}{4E^*} \right)^{\frac{2}{3}} \quad (11)$$

where R is the radius of the sphere and E is Young's modulus.

The following relationship may be written for the frictional force from equations (9), (10) and (11):

$$F_{int} = \pi \tau_0 \left(\frac{3R}{4E^*} \right)^{\frac{2}{3}} N^{\frac{2}{3}} + \alpha N \quad (12)$$

So:

$$\mu = \frac{F_{int}}{N} = \pi\tau_0 \left(\frac{3R}{4E^*} \right)^{\frac{2}{3}} \frac{1}{N^{\frac{1}{3}}} + \alpha \quad (13)$$

This relationship is valid only for non-compressible materials, such as carbon fiber (Adams et al., 2001). It has been noted (Briscoe & Adams, 1987) that equation (12) is an expression of the friction force with two load terms powered to 2/3 and 1. It is a particular case of the general equation $F=k*N^n$ where F is the frictional force, N is the total normal load, k is a load-dependent coefficient of friction and n is the load index) where 2/3 and 1 representing the lower and upper limits for n . Coefficients n and k are defined as follow:

$$n = \frac{2 + 3b\underline{N}^{\frac{1}{3}}}{3 + 3b\underline{N}^{\frac{1}{3}}} \quad \frac{2}{3} \leq n \leq 1 \quad (14)$$

and

$$k = \left(\frac{c}{\underline{N}^{\frac{1}{3}}} + \alpha \right) \underline{N}^{1-n} \quad (15)$$

where $c = \pi\tau_0 \left(\frac{3R}{4E^*} \right)^{\frac{2}{3}}$ and $b = \frac{\alpha}{c}$. the quantity $\underline{N} = \left(\sqrt{N_{min} \cdot N_{max}} \right)$ is the geometric mean of the range of normal loads over which equation $F=k \cdot kN^n$. is applied, such that N_{min} and N_{max} are the minimum and maximum values of this load range. It may be noted that $n=n(\underline{N})$ and $k=k(\underline{N})$ so that these parameters will vary depending on the load range being considered.

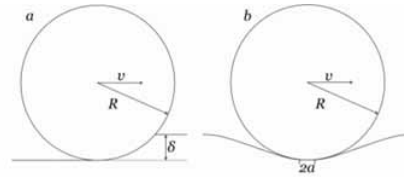
Therefore, the topographical elements of wet skin are distorted under typical sliding contact pressures, so that the skin acts as a smooth body. The increment of the contact area, rather than the reduction of the interfacial shear strength, is the guiding factor that causes the friction of the skin to increase the presence of water.

The friction of dry skin can be compared with that of a solid material with a rough surface (Derler et al., 2014) and the real contact area of rough solid surfaces linearly increases with the normal load, i.e., $A_r/N = \text{const.}$ and thus $\mu(p) = \text{const}$ (Greenwood & Williamson, 1966).

Deformation Friction

Deformation component has usually proved to play only a small role in assessing the overall intensity of skin friction for the experimental conditions. When subjected to an external force, the skin can be classified, in lateral and vertical directions, as a viscoelastic material with different mechanical properties that depend on the loading conditions and on penetration depth. When rubbing a spherical probe against human skin, deformation component can be calculated in various ways. Bhushan (Wolfram & J., 1983),

Figure 3 a/b. Representation of a sliding probe on a surface, realizing a ploughing effect(a) where the material is plastically deformed, and viscoelastic effect(b) where the material is not permanently deformed



suggest that the probe plastically deform the skin like a plough (Figure 3a), Greenwood (Greenwood & Williamson, 1966) (Figure 3b), instead, proposed a viscoelastic deformation model; in both cases the work of deformation generate augmented friction coefficient. Also, Dowson (Dowson, 2009) reported that skin and subsurface of soft tissue deformation during friction contacts will contribute to a grow of coefficient of friction in the form of viscoelastic hysteresis or plugging.

For small deformations and with the soft skin, μ is defined in dependence the radius of the probe R and ploughing depth δ , for the first case:

$$\mu_{plastic} = \sqrt{\frac{1}{2\left(\frac{R}{\delta}\right) - 1}} \quad (16)$$

Since the skin is not plastically deformed a better model would be a *viscoelastic* one in which work is dissipated due to the viscoelasticity or hysteresis of the skin. By increasing normal load and contact pressure a contribution due to hysteresis is expected to increase too, while ploughing would lead to a load-independent contribution for the friction coefficient.

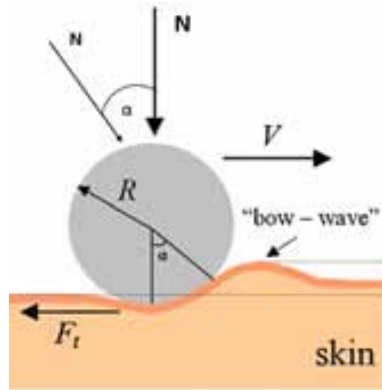
Just a few of the studies published specific articles on the deformation aspect of skin friction: Johnson et al. (Johnson et al., 1993) and Adams et al. (Dowson, 2009) studied skin friction in contact with spherical probes on the volar forearm, thus applying Greenwood's approach (Greenwood & Williamson, 1966). They find that hysteresis contribution to the coefficient of friction is about 5%. Kwiatkowska et al. (Kwiatkowska et al., 2009) have published findings within the same range (4-6%).

Often, components extremely deformed are possibly caused by the combination of effects of hysteresis and ploughing of the skin by rough surface asperities. Tomlinson et al. (Tomlinson et al., 2007) recorded significant contributions of interlocking effects (50 percent of ploughing and measurable contributions of hysteresis (~10 percent), for the friction between finger and small, ridged surfaces. In addition, aged skin was characterized by decreased viscoelastic regeneration and skin turgor, along with more significant displacements of skin tissue and increased frictional interaction.

Kwiatkowska found that when a spherical probe is used, the skin is deformed, and formed a “bow-wave”, and stretching behind because of friction (Kwiatkowska et al., 2009).

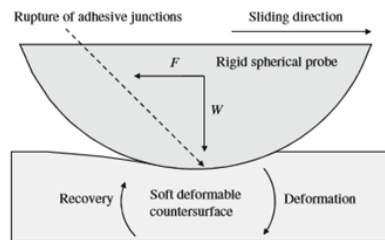
Particularly when a small rigid body is moved with a reciprocating motion on soft skin the material surrounding the contact area is cyclically deformed and relaxed (Subhi et al., 2017); friction and lateral skin displacement cause the skin to become compressed in front of the probe, forming this “bow-wave”, and stretching the skin behind (Figure 4). The formation of bow-waves results in skin wrapping over the probe. This tends to cause the normal force vector rotation and leads to extra resistance in the slid-

Figure 4. Schematic representation the bow effect, caused by a sliding probe on the skin, that also causes a rotation of the Normal loading



ing direction which depends, among other factors, on the wrapping angle α . While the action of skin friction in sliding has been thoroughly studied, there is little knowledge in the literature regarding the “bow-wave” effect.

Figure 5. Zoomed representation of the effect of a rotating probe, on a soft deformable surface, where the mechanism of deformation is underlined



The deformation component is usually due to the incomplete recovery of dissipated energy (Figure 5) by viscoelastic deformation of the skin/material subsurface under the front of the probe. It should be noted that the process of energy dissipation for a rolling or sliding sphere are comparable. Greenwood and Tabor (1958) suggested an expression for the frictional force of such a contact (Chen et al., 2009) that has been validated by Adams et al. (Johnson et al., 1993):

$$F_{def} = \beta \left(\frac{9}{128R} \right)^{\frac{2}{3}} \left(\frac{1 - \nu^2}{E} \right)^{\frac{1}{3}} N^{\frac{4}{3}} \quad (17)$$

where β is viscoelastic hysteresis loss fraction, R is the probe radius, ν is the Poisson's ratio, E is the effective Young's modulus of the skin and N is the normal force. The parameters β and E must be measured at a deformation rate that is comparable to the speed of sliding contact. They may be convenient-

ly measured using this formula $\beta = \pi \tan \delta$. where $\tan \delta$ is the viscoelastic loss tangent. It may be seen that equation (17) is in the form of equation $F_{def} = k F_n^{\frac{4}{3}}$ with a load index of 4/3. In the case of skin, an additional viscoelastic stretching due to plane contribution, and even hysteresis could occur which are not accounted for by this relationship. In order to estimate effective Young's Modulus, Hertz equation for spherical probes presented by Johnson was used (Johnson et al., 1993). The following equation has been already presented in Chapter 2 where a is the contact radius:

$$a = \left(\frac{3RN}{4E^*} \right)^{\frac{1}{3}} \quad (18)$$

where the reduced elastic modulus E^* is given by the following expression:

$$E^* = \left(\frac{1 - \nu_p^2}{E_p} + \frac{1 - \nu^2}{E} \right)^{-1} \quad (19)$$

The index p refers to the probe; the non-index parameters are referred to the skin. The contribution of the elastic properties of the probe is negligible for a rigid sphere that is in contact with human skin, so Eq. (19) reduced to:

$$E = E^* (1 - \nu^2) \quad (20)$$

In order to evaluate the skin modulus E of Young effectively from the experimental results, eq. (18) is reformulated using Eq. (20)

$$E = \frac{3}{4} \frac{NR}{(1 - \nu^2) a^3} \quad (21)$$

When the skin is exposed to a cyclic load, the deformation friction is the consequence of viscoelastic hysteresis whereby, based on the product's speed, the strain energy will be only partly restored, resulting in an additional loss of friction.

It is known that the obtained stress-strain curves form hysteresis loops when soft tissue is subjected to cyclic uniaxial tensile tests, continuously decrease and then stabilize, so another contribution to the deformation force is due to the hysteresis. Tang et al. (Tang et al., 2008) reported that when the sliding speed of a spherical probe on the forearm was increased, the friction coefficients increased and “stick-slip” phenomena became more pronounced, indicating that hysteresis contributed to the friction. The equation (17) does not take into account hysteresis contribution, so to evaluate Hysteresis contribution, the Voigt rheological model of behavior material properties it is applied to calculate the equivalent Young

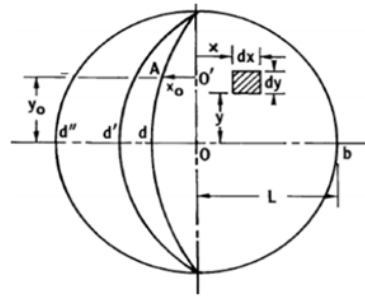
modulus, as the skin is considered a Voigt material (a viscoelastic material having the properties both of elasticity and viscosity).

$$E_p = \frac{E_1 E_2^2 + \omega^2 (E_1 + E_2) \nu^2}{E_2^2 + \omega^2 \nu^2}; \quad (22)$$

$$\nu_p = \frac{\nu E_2^2}{E_2^2 + \omega^2 \nu^2} \quad (23)$$

where ω is angular frequency in dynamic model, E_1 and E_2 Young Modulus of materials and ν is the viscosity

Figure 6. Spherical probe with a non-constant pressure configuration



Since the pressure is not constant over the sphere, the mechanical equilibrium and boundary condition are (Figure 6):

$$N = \int_{x_0}^L \int_{y_0}^L p(x, y) dx dy \quad (24)$$

$$p(x_0, y_0) = 0 \quad (25)$$

In the moving sphere in x direction occurs the moment (M_p) of all pressure force in the center O of the sphere. Therefore, the hysteresis force in rolling direction is:

$$F_{hyst} = \frac{M_f}{R_r} = \frac{\int_{x_0}^L \int_{y_0}^L x p(x, y) dx dy}{R_r} \quad (26)$$

The contribution of hysteresis (μ_h) can be obtained by dividing the force with the normal load:

$$\mu_h = \frac{F_{hyst}}{N} = \frac{F_{hyst_a}}{N_a} \quad (27)$$

In order to calculate this relationship without using the double integral, an experimental dimensionless formula can be used:

$$N_a = \frac{2NL}{E_p R_r^3}; F_{hyst_a} = \frac{2F_{hyst}L}{E_p R_r^3}; x_1 = \frac{x_0}{L}; y_1 = \frac{y_0}{L}; \quad (28)$$

$$L_a = \frac{L}{R_r}, \gamma_v = \frac{\beta_v}{L_a} \text{ with } \beta_v = \frac{\nu_p}{E_p}$$

$$N_a = L_a^3 (1 - x_1)(1 - y_1) \left[1 + \frac{\beta_v}{L_a} (1 + x_1) - \frac{1}{3} (1 + x_1 + x_1^2) + \frac{1}{4} (1 + x_1 + x_1^2 + x_1^3) \right] \quad (29)$$

$$F_{hyst_a} = L_a^3 (1 - x_1)(1 - y_1) \left\{ (1 + x_1) \left[\frac{1}{2} - \frac{1}{6} (1 + y_1 + y_1^2) \right] + \frac{L_a}{8} (1 + y_1 + y_1^2 + y_1^3) + \frac{2\beta_v}{L_a} (1 + x_1 + x_1^2) + \frac{\beta_v L_a}{5} (1 + x_1 + x_1^2 + x_1^3 + x_1^4 + x_1^5) \right\} \quad (30)$$

From the boundary condition, $x_1 = \left(1 + \gamma_v^2 - \gamma_1^2\right)^{\frac{1}{2}} - \gamma_v$. Now, from the knowledge of F_{hyst_a} and N_a by substituting them in the Eq. (27) it is possible to calculate μ_h . The medium hysteresis friction coefficient from circular contact will be obtained by:

$$\mu_{hm} = \frac{1}{L_a} \int_0^{L_a} \mu_h dy_1 \quad (31)$$

It has to be noticed that the hysteresis friction component increases nonlinearly with the normal load, evaluated by Stribeck dimensionless contact pressure:

$$p_{s_a} = \frac{N}{\pi R_r^2 E_p} \quad (32)$$

The deformation component of friction is usually small if particularly in comparison to adhesion one, but that there are specific cases in which deformation mechanisms become relevant, so it is worth considering them.

OPEN RESEARCH

The scientific community assumes that the secret to a deeper understanding of skin's macroscopic friction behavior will be studies examining the behavior of human skin on a microscopic scale. High-priority research questions relate to four key topics:

1. *The friction adhesion component:* In order to define the friction adhesion component accurately, both effective contact area (microscopic) and contact shear stress must be measured with precision. To do those measurements, however, in vivo measurements on the skin, the application of modern instruments (such as micro-tribometers and atomic force microscopes) seems to be minimal. Furthermore, the optical methods used to measure the microscopic area of contact between the fingers and the smooth glass are not suitable for raw surfaces and without transparent material, for which there are no current measure methods.
2. *Two-term skin friction model:* Until now it is unknown under what circumstances mechanisms of deformation become important (viscoelastic hysteresis, ploughing, interlocking). Another problem is whether the friction components of adhesion and deformation are two non-interacting concepts as stated in the two-term model.
3. *Skin hydration:* It tends to be unmistakably observed from the writing information that skin hydration and interfacial water impact the skin's rubbing coefficient, yet no methodical investigations have been directed so far on the change from dry to wet skin. The impacts of hydration and mellowing of the skin on its micromechanical properties and the related changes in the geometry of the small-scale contact are to a great extent obscure. Furthermore, it is not clear the role of a small amount of water in the interface between the skin and the counter-surface (capillary bridges, filling of empty spaces and the effect of hydrophilicity / hydrophobicity) and the effect of skin substances such as lipids (to sebum).
4. *Correct theoretical models for human skin touch:* Theoretical principles for solids such as the Greenwood and Williamson models (Greenwood & Williamson, 1966) were used to explain qualitatively some aspects of dry skin's contact and friction behavior. In connection with the complex surface topography of human skin the shortcomings of these models are still unclear. Another question still unanswered is, to what degree theoretical principles are suitable to the hydrated skin case. In addition, there are many unresolved issues related to skin tribology on a macroscopic and phenomenological level:
5. *Tactile friction and haptics:* In comparison to skin tribology, tactile awareness is mostly unstudied and little known. This research focus is important not only for the design of surfaces with predefined tactile feel (smooth, soft), which improve consumer service, but also for robotics technologies and applications.
6. *Skin lesions and ageing:* Advanced statistical and numerical skin models (e.g., finite element models incorporating the structure of the related body parts and taking into consideration the effect of subsurface soft tissues and bones) are projected to greatly improve skin tribology awareness

and understanding skin deformation, processes for injury, wound and blister formation, wrinkling processes and skin ageing.

7. *Effects of hair, abrasion and skin peeling:* Tribological human skin experiments have so far concentrated on glabrous (hairless) and shaved bodies. The influence of hairs on skin friction, however, is sometimes ignored and significant in connection with applications such as sport textiles or clothing comfort generally.

CONCLUSION

In this chapter, some results from published research on experimental skin tribology were reported and discussed in order to better interpret the results of the human skin tribosystems in terms of COFs and factors influencing skin friction behavior. In general, the measured COF values are characterized by high variations. All the experiments were carried out with different measurement techniques, and, for this reason, it was difficult to find common points between various studies, but there is no doubt that the main influencing variable is the hydration. Wet, moist and dry skin behaves very differently one with another: dry skin friction is characterized by relatively small COF values and independent by the pressure similar as in the case of friction under dry conditions of rough solid, while damp or naturally moist skin has high COF values that rise dramatically with lower contact pressure and are basically due by the increased contact area; but totally wet skin behaves as a lubricated tribological system where friction coefficients drops again. In the case of in-vivo experiments was found out that probably one of the most important parameters for the comparison of results is the contact pressure. As it could be seen in all the experiments, for wet or for dry skin, for smooth and even for rough materials the common point in all the graphs is always the pressure. The skin friction range is wide, and not all the trends are well known. But most of the dependence of the COF with any other parameter could be explained and interpreted based on the adhesion-deformation model. The total coefficient of friction so it's made of these two terms, even if adhesion influence is much bigger than deformation one.

On the basis of the considered scientific literature, it was clear that, while the adhesion component has been well studied and its mechanisms are well understood, for both dry and wet condition, the deformation component, on the other hand, is still not totally eviscerated. For this reason, the deformation contribution to the overall COF, is not always neglectable, so it is always important to study both mechanism, case by case.

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Skin Tribology

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Chapter 2

Tridimensional Vectorial Modeling of the Human Body From Anatomical Slices: A New VR Learning Tool for Students

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ABSTRACT

Digital anatomy has emerged as an essential subfield of anatomy that processes the human body with the help of a computer. 3D reconstruction tools have been developed over the years, being always complementary to cadaver dissection. Teachers' main goal is to provide a greater understanding of the spatial structures of the body and its internal organs thanks to 3D reconstruction techniques. Manual segmentation and creation of 3D vectorial models is probably the best anatomy learning tool for beginners and students. The aim of this chapter is to show how to create vectorial models from anatomical slices with Winsurf® software, highlighting their educational value. Resulting 3D models could also be used through the interface of virtual dissection, which has been proven to be immensely valuable for anatomy education, particularly by using immersive reality techniques. It could also be the basis of future simulation tools for surgeon training.

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INTRODUCTION

The advent of digital technologies has imposed itself in recent years in all fields, particularly in anatomy. The 3D reconstruction of human anatomical structures has proven to be a real revolution for teaching and learning morphology.

It opens the way to virtual anatomical dissection and to all surgical applications: surgical planning, simulation, training and augmented reality.

The objectives of this paper are to describe the methodology, to show the interest of this manual segmentation process done with the Winsurf® software version 3.5 and to assess the educational value of this technique with a group of students.

BACKGROUND

Cadaver dissection has long been an essential step in human anatomy, being the gold standard for education (Sugand 2010). Anatomy is one of the core courses in medical education, a morphological discipline that requires a large amount of human material. Increasing student enrollments and decreasing numbers of cadavers have made it more difficult for medical students to access and manipulate cadavers within their less available laboratory training time (Older 2004). Improvement and deepening of knowledge by using anatomical specimens and practical anatomy can obtain the best teaching results (Chapman, 2013; McMenamin, 2018).

Digital anatomy is a technology that can computerize the anatomical structures in order to virtually observe, measure, and manipulate them (Zhang 2005). Its main goal is to provide a greater understanding of the human body's internal organs, helping student's ability to recall spatial relationships between structures, both in two-dimensions (2D) and three-dimensions (3D). Virtual reality techniques enable the user to combine digital input and real-world objects. Thus, it is a true revolution in anatomy using virtual anatomy education systems (Preim 2018).

Otherwise, there is an increased demand from radiology and endoscopy imaging and other invasive and non-invasive medical techniques. Currently, the use of radiological imaging (CT and MRI) is an integral part of teaching. The use of virtual reality (VR) technology using a virtual anatomy teaching system could therefore provide real, reusable teaching resources to the learning process (Yammine, 2015; Wilson, 2018). It could also be used for surgical education and simulation.

Sectioned images of the visible human projects are of considerable interest due to their high resolution to build 3D atlases of the human body based on vectorial modeling. It is also the best way to provide the reconstruction of the nerves, not visible when using angio-CT reconstructions.

The authors explain here their process of 3D modeling of the body from the slices of Korean Visible human (KVH) data. The structures are precisely segmented manually using 2D images, then reconstructed and displayed as 3D images. The volume models can thus display an arbitrary section of the model and provide a virtual dissection function. A new networked teaching system using this technique with a 3D atlas of the body can be read remotely, displayed locally, and manipulated interactively.

This manual segmentation of anatomical slices process has been achieved with the Winsurf® software (Moody 1997) producing an interactive 3D vectorial model of the whole body.

This is slightly different for the digital data from CT angiograms. Here, the segmentation process is fully automated by dedicated software. (see chapter 5.2)

The process using Winsurf from anatomical slices has two main advantages:

Firstly, to train the students to identify the anatomical structures on the 2D slices, and to help them visualize each structure in the 3D space. This 2D manual segmentation of each anatomical element could be considered as a computerized dissection. It can be followed and improved by the interactive display of the 3D object during the 2D segmentation process, enabling the representation of anatomical structures in the 3D space.

Secondly, it provides a 3D atlas of the whole body that can be used as a dissection learning tool.

For this, the different anatomical elements are gathered into a 3D vectorial model and exported in Acrobat® 3Dpdf format, producing a 3D atlas of the whole body.

Here, the human-computer interface plays an important role, thanks to the advance of new technology trends, in particular graphic processors and availability of multi-touch technology, enabling quick, easy and intuitive interaction.

Anatomical structures can be individually and interactively manipulated with a touch screen: you can swipe, scroll, zoom, rotate and navigate inside the model as well as remove layers of skin and muscle and take measurements. In addition, 3D labels with the name of each anatomical element are available in four languages (English, French, Spanish, Latin). This new computerized Diva3d® virtual dissection table (Uhl 2021) is a simple and powerful learning tool for students. It could also be the basis of future simulation tools for surgeons training.

MATERIAL AND METHODS

Material

Our database is the series of anatomical slices of the visible human projects.

The first set of anatomical slices was the US Visible Human Project (VHP; male and female) conducted in the United States (Ackerman, 1999). Since, several projects were set up: visible Korean; male & female whole body, male head, and female pelvis (Park, 2005a, 2006; Shin, 2011a; Chung, 2015) Chinese Visible Human [Zhang, 2005; Fang, 2017; Zhang, 2019], Virtual Chinese Human (VCH; male and female) (Yuan, 2008)

Each model has its advantages and disadvantages.

Here, the authors use the slices of the Korean man & woman visible human projects.

Methodology for Building the 3D Models

The anatomical slices datasets were used with the 5 following steps (Uhl, 2021)

- Segmentation and 3D vectorial modeling of anatomical elements with Winsurf® software version 3.5 (PC windows).
- Exportation of the Winsurf® mesh into a cad format
- Mesh refinement, cleaning and arrangement with Blender®
- Ranking of 1206 anatomical elements with Acrobat 3D toolkit®
- Building the final user interface with Acrobat pro®.

Segmentation and 3D Reconstruction of Mesh Models

Instead of performing a segmentation with Photoshop first like Park (2005b) the authors directly achieved the segmentation on the anatomical slices of the KVV dataset by manually outlining it with the Winsurf® software.

Creation of New 3D Object: Each 3D object representing an anatomical structure was built separately, identified by manually placing chains of points around the object edges, this way each distinct anatomical structure was segmented by mapping. Figure 1 shows the Winsurf interface window, with the available tools on the left upper side of the left window to edit or modify the contours. Here, the boundaries of the left upper limb's veins were drawn.

Scale Measurement of the 3D Model: The scale parameters were measured on a slice as well as the slice thickness by a special function of the software. The resulting value was $5650/2/x$ for the man, and $6000/1/x$ for the woman, where x represents the jump between slices during display. The same scale parameters are to be used for all anatomical objects of the same body.

Creation of 3D Anatomical Objects: It is achieved by outlining them slice by slice: it is a manual thorough segmentation of the objects. This step can seem long and tedious, but it is an essential part of the process of learning anatomy.

Once the contours had been assigned to each serial slice containing the object, vertices were connected using a surfacing routine developed especially for Winsurf® software (Moody, 1997). This routine computes and refines a best-fit solution for assembling the vertices into a volumetrically optimized 3D object.

Figure 1 shows how to use the several color channels to build the arborescence of the upper limb's veins. This option is very useful for the user to localize a mistake or missing information on one of the colored channels. When finished, all objects could be gathered by using the "add surface file" option of the software, in order to obtain the final 3D model. In addition, textures could be applied on the objects to obtain a more realistic 3D reconstruction.

Educational Interest of This Segmentation Technique

This methodology of manual segmentation slice by slice to create the 3D objects is of high educational value because the outlining process can be followed step by step in real time with display of the resulting 3D object.

Errors in segmentation and outlining can be corrected this way. In the same way, the confrontation of the different segmented objects makes it possible to correct the mistakes in the anatomical relation between different organs.

Exportation of the 3D Mesh Model

The 3D Mesh are produced by manual outlining with the pen tool of Winsurf® software version 3.5. In fact, Winsurf® is an old software working well with the windows® xp Operating system, very easy to use. Before this exportation, it is important to ensure that every anatomical object has a different RGB color, in order to import it as a separate anatomical element under the Acrobat format. The format conversion was achieved by using a simple function of Adobe Acrobat® 3D version 9, in the menu option of the software: "create a pdf file by 3D capture". It could be then exported in .wrl file format and exported to Blender software.

Mesh Refinement with a Powerful Free Modeler: Blender® v 2.79b

Improvement of the mesh models and correction of some anatomical issues were done with Blender®, as well as the embedding of a series of 100 anatomical slices into the 3D model. This step is very important to improve the quality of the models and the anatomical accuracy, as well as to improve the student's understanding of anatomical relationships in the 3D space. Regarding the vessels, the nerves and the tendons, the irregular 3D meshes of Winsurf® were replaced by “skins” (with the skin modifier of Blender®), to produce more realistic anatomical structures. (Figure 2)

Exportation of the 3D Model into Acrobat3D Toolkit®.

After exportation of the whole Blender 3D model and slices into .obj or .3Ds format, Acrobat 3D toolkit® software was used to produce a “.u3d” compatible file and to set up the hierarchical list of the anatomical elements, displaying them in the model tree window located on the left side of the Acrobat window.

3D Interactive Display with Acrobat® 3D PDF Interface

The pdf interface is very versatile with the command panel on the right, giving access to the different anatomical regions of interest. 3D handling of the interactive model is user-friendly, being possible:

- By system (bone, muscles, ligaments, arteries, veins, nerves)
- By anatomical region of interest (head, neck, thorax, abdomen, pelvis, upper & lower limbs)
- By anatomical element: For any of these options, by clicking the color boxes of this list of anatomical structures (on the right) the user can make any element visible, hidden or transparent. It is also possible to select and display the horizontal slices together with the 3D models, which makes the relationship between the 2D image and the 3D anatomical volume more understandable.

Other functions of the Acrobat® interface are also available by using the 3D toolbar located at the top of the display window. Menu of interactive handling functions of the 3D model, choice of lighting effects, background color, 3D rendering options (solid, wireframe, shaded wireframe, transparent wireframe, illustration...), 3D labels, cross section in any plane and “menu” memorizing the display view together with the whole parameters of the 3D anatomical model.

The authors created a user-friendly interface with JavaScript® programming with the help of our colleagues of Amsterdam University who created an outstanding 3D tool dedicated to the human embryo development (De Bakker, 2016) available at: <https://www.3dembryoatlas.com>.

By clicking on a structure, the 3D object is highlighted and its name is displayed in 4 languages inside the blue window.

As a result, all these functionalities are available through the simplified interface of the Diva3D® virtual dissection table represented by a big touch screen working with only 3 fingers (Figure 3).

A demonstration of this tool is available on the website <https://en.diva3d.net>, extended to the whole female and male bodies.

Virtual Reality and 3D Printing of the Model

The same 3D model could also be integrated into a Unity® interface with an immersive reality environment. (Figure 4) see also chapter 5.6 the “anatomy studio” project.

In addition to the interactive display of the 3D models with several devices or interfaces, materialization of the anatomical parts of the models is possible with a 3D printer.

It requires an arrangement and improvement of the mesh models with the Meshmixer® software. (<http://www.meshmixer.com>)

Then Cura® software is used to create a file in “gcode” format to be sent to the 3D printer (<http://www.cura.com>).

The interface window of Cura® software is shown with the head on figure 5.

The inexpensive solution is to use an ENDER® pro 3 printer with PLA material.

Figure 6 shows the final result of the 3D printing with the supports, after a delay of 2 days.

The final step is to colorize the model with acrylic painting to make it more realistic (Figure 7)

RESULTS

The **Virtual Dissection Table** (Uhl, 2021) is provided by DIVA3D® company (<https://en.diva3d.net>)

1205 anatomical structures were reconstructed separately as 3D objects (Table I): 230 bones, 370 muscles & tendons, 82 ligaments, 55 nerves, 91 arteries, 150 veins (lymphatics were not reconstructed), heart (6), brain (52), respiratory system (18), alimentary system (25), urinary system (22) genital man (8) genital woman (10), glands (10), skin (1) and anatomical slices (100)

Anatomical elements are then arranged into systems and areas of interest by the use of menus provided by Acrobat pro®, directly available from buttons on the touch screen. Terminology of all anatomical structures is available in 4 languages: French, English, Latin and Spanish by clicking the object in the 3D window. Figure 3 shows the interface of the Diva3D® virtual dissection table.

This tool is also provided with other educational solutions:

Virtual dissection tools:

- DIVA3D® atlas of man and woman from Korean visible project
- Embryo’s atlas (De Bakker, 2016)
- DIVA3D® atlas version 2 (also compatible with tablets)
- MRICro® GL by Chris Rordens (<https://www.nitrc.org/projects/mricrogl>)
- Open anatomy® project (<http://www.openanatomy.org>) 3d atlases using 3dslicer®

Other applications:

- Horos® library (<http://horosproject.com>)
- Paperboard®, software replacing the classical blackboard for anatomical drawings
- 3Dslicer® (<http://www.slicer.org>)
- Sketchfab® (http://sketchfab.com/chair_digital_anatomy)
- NIH 3D print® (<https://3dprint.nih.gov>)

- Terminology (<http://anatomicalterms.info>)

Youtube courses and dissection movies are also available.

All these educational tools can be used either by teachers to give a course or by the students for workshops, training sessions and revision. The same atlas 3D model (with simplified functions) will be also available on tablets for individual use.

EVALUATION OF LEARNING VALUE IN ANATOMY

The authors performed an evaluation study involving four Argentinean medical universities. 86 medical students or physicians were included. They were divided into three groups according to the duration of their basic training in digital anatomy (1, 2 and 3 days respectively). All participants learned how to use the Mesh tool and how to model 3D structures from anatomical sections with Winsurf software. At the end of the training, they were given a survey form (Table II). Participants were also asked to rate the training (Poor; Average; Good; Very Good; Excellent).

Student's evaluation of a workshop and training program of digital anatomy.

The workshops were done during the Sixth international congress of clinical anatomy hold in Santiago del Estero, Argentina (18th to 20th of September 2018)

The aim was to build 3D models from anatomical slices by using the Winsurf software. The average age of the participants was 23.5 (+/- 9.5 years). They were in 71% of cases, 5th or 6th year medical students (n=61). Twenty participants (23%) were medical graduates. Of these, 11 were doctors of anatomy.

This was the first contact with the digital anatomy in 43% of cases. The participants' opinion was satisfactory, the majority being rated as "excellent" (n=81). 6% of participants rated the training as very good. No negative feedback was received from participants.

The main criticism of the training is its duration, which was considered too short by 10 participants, 6 of whom were in the 1-Day group. All participants found an interest in using the software and intended to use it in their daily practice in the future.

The results are summarized table II.

DISCUSSION

Limits of This Virtual Dissection Tool (3DPDF Atlas from Slices)

Although working well, the segmentation with Winsurf® software does not produce perfect mesh models with complex structures like vertebrae, sacrum and cranial bones. Here, a refinement with a CAD editor is needed. The export of the mesh is also difficult.

The applicability of the teaching tool also depends on the quality of the anatomical slices. It also depends on the pathological abnormalities of the sliced body (in this case, the man has a huge splenomegaly due to a lymphoma).

However, the 3D reconstruction of the body from the manual segmentation of anatomical slices gives complete and accurate 3D models which offers a remarkable learning tool in anatomy.

This technique is probably the best to make a 3D reconstruction of the nerves, which are lacking when using angio-CT investigation.

Free Software Tools for 3D Reconstruction from DICOM Angiograms

Two free and open-source powerful tools are available for automatic or semi-automatic anatomical segmentation, that is extraction of the geometric information necessary to reconstruct the anatomical structures by identification of their boundaries.

They enable the creation of 3D educational atlases from CT or MRI exams, working locally or remotely.

ITKSNAP® (<https://www.itksnap.org>)

This software is an open-source collaborative project between the University of Pennsylvania and the University of Utah. It enables segmentation and annotation of 3D medical images, using deep learning object detection algorithms.

3dSLICER® (<https://www.slicer.org>)

3D Slicer is open-source software dedicated to medical image processing as well as three-dimensional visualization. It is complex but extremely powerful for anatomical segmentation using several algorithms provided by dedicated plugins.

The Open Anatomy Browser (Halle, 2017) is a Collaborative Web-Based Viewer for Interoperable Anatomy Atlases, working under the 3D slicer license.

Inside OABrowser, anatomical structures can be inspected as 2D cross sections (in the slice panel or in the 3D view), as 3D models, or as entries in the hierarchy view. When a structure is selected, its name is displayed in the bottom status window, along with a “breadcrumb” list of parent and ancestor structures all the way up to the root of the atlas. Each ancestor name is a hyperlink that selects the respective containing structure.

A user can manipulate the slices and 3D views in OABrowser by panning, zooming and selecting structures. Structures appear in similar colors in the 3D view and in color overlays in the slices. Individual structures and trees of substructures can be turned on and off. Optional crosshairs indicate the location of cross-sectional slices in each view. The window and level of the volumetric data can be changed to improve image contrast. Ranges of voxel values can be rendered transparent to improve model visibility.

Several 3D atlases are available with 3D slicer®: Neuroanatomy, head and neck, abdomen, thorax, inner ear. (<http://www.openanatomy.org>)

Other 3D Virtual Atlases (Table III)

Several open access 3D virtual tools are available on the web free of charge, mainly for tablets or smartphones.

It should be underlined that the origin of the dataset is slightly different from the previous tools. The 3D models were NOT constructed from real patients (anatomical slices, CT) but created by computer designers, so it should be considered as theoretical and not REAL anatomical models.

Moreover, these models most often suffer from lack of verification and validation by experts in morphology.

A wider database of anatomy tools is available at: <https://anatomytool.org/>

Educational Value of the New Virtual Anatomy Education Tools

Despite their limitations, the educational tools using 3D PDF files remain a powerful learning technique in the field of morphology. For students, these tools have a double interest:

- First, to learn by performing virtual dissection with the labeled 3D atlases, which palliates to the lack of cadavers for real dissection.
- Second, to build themselves manually the 3D models from the 2D slices, hence to better understand the arrangement and relationship between the anatomical structures in the 3D space. This second aspect is an innovative *learning technique*, using virtual reality, probably the most powerful to keep in mind the complex anatomy of the human body.

In practice, in a field as difficult as anatomy, these computer virtual tools are changing the way students engage and interact with learning material: The manual creation of 3D anatomical objects by 2D slices segmentation is a meaningful experience and a gain in deep knowledge.

In this regard, several papers were published using the Korean data:

Several regions or anatomical systems were reconstructed: urogenital tract (Uhl 2006), coronary vessels (Uhl, 2017), cervical spine, (Kante, 2020a), brain (Kante, 2020b), Lumbosacral anatomy (Shin, 2011b), female pelvis (Shin, 2013) hand anatomy (Chung BS, 2017) Whole body (Chung, BS 2019b), head of KVH (Chung B.S, 2020).

Other source of data than the visible human projects were also used to create educational models:

Birt (2017) used the mixed reality to improve paramedic distance education through mobile simulation; Jain (2017) promoted an AR learning tool working on mobiles;

Guimarães (2018) highlights the new trends in anatomy education, with the use of VR, AR and simulation; Kurniawana (2018) offered a mobile application using AR to help the students to switch from 2D to 3D anatomy; Asensio Romero (2018) created 3D models of female pelvis structures represented in combination with anatomical and radiological sections.

Erolin (2019) showed in a pilot study the usefulness of VR for anatomy education.

Bork (2019) showed the benefits of the Augmented Reality Magic Mirror System for integrated radiology teaching in gross anatomy.

Wheeler (2020) showed that simulation is an efficient teaching modality to educate and train paramedics.

Rosmansyah (2021) published a systematic review to describe the landscape and trajectory of development for the use of VR technology in anatomy education.

New Educational Tools Using Augmented Reality (AR) and Immersive Reality

Recent progress in AR and VR hardware enables a wide range of educational applications in anatomy. They provide the students with a better understanding of the special relations of the anatomical structures, and of their complex variations, hence improving the learning process. They also improve memory retention, especially long-time memorization.

As highlighted by B. Preim (2018) the revolution with the user's interface plays a central role in this evolution of touch interface, speed, interactivity and labeling in real time.

The starting point was the new technology trends combining several factors:

- Rapid development of new imaging modalities
- Availability of graphic processing units supporting direct volume rendering
- High resolution with multi-touch surfaces enabling intuitive interaction with complex 3D environments

For this reason, more and more anatomy teachers agree that virtual dissection is now a major tool for the students, as showed by meta-analysis published since several years (table IV)

Several works were done with the *objective of VR anatomy learning*:

Yammine (2015) published a meta-analysis on the educational effectiveness of 3D visualization technologies in teaching anatomy.

Paech (2017) showed that Contrast-enhanced cadaver-specific computed tomography improved student's learning in gross anatomy teaching.

An augmented reality tool to learn on mobile devices was evaluated by Jain (2017)

Bork (2019) assessed the benefits of an augmented reality Magic Mirror System for Integrated radiology teaching in gross anatomy.

Darras (2019) proposed an Integrated virtual and cadaveric dissection laboratory for anatomy beginners.

In parallel with education, augmented reality techniques were also set up *for surgical applications and simulation* (table V)

3D models from MRI to train on the lumbar spine were built by Prats-Galino (2014)

Moro (2017) showed that VR and AR promote intrinsic benefits such as increased learner immersion and engagement and significantly enhance anatomy learning.

Soler (2015) demonstrated the interest of the concept of image-guided hepatic surgery, and suggested a webservice for surgeons (Visible patient®) providing a 3D model of the patient for simulation and surgical planning.

In orthopedic open surgery, Condino (2018) used mixed reality with the Microsoft Hololens® system.

Prats-Galino (2018) built a training virtual model of the endoscopy approach to anterior communicating complex.

The main limitation today is the price of these devices for education, particularly for immersive reality glasses, limited to an individual use.

3D Printing of Anatomical Objects

Similarly, to the new techniques using virtual reality (VR) and augmented reality (AR), **3D printing of anatomical models** is now commonly used for teaching (AbouHashem, 2015; Wu, 2018; Mogali, 2018; Tripodi 2020)

Printing of 3D models can be done using open-source software Cura® (<http://www.cura.org>) with intuitive interfaces and Fused Deposition Modeling technology, an inexpensive and easy way to materialize the models.

3D modelling and printing seems a promising tool to complement the traditional way of teaching anatomy by using dissected cadavers. It has the advantage of showing structures in the way they are disposed of in a living human being, the relationships they have. It also offers the possibility of scaling anatomical structures.

Many anatomical variations and pathological structures that can be reconstructed and 3D printed as another tool for improvement of the learning process.

Moreover, 3D printing of patient anatomy has been broadly used in the surgical field.

This new technique is mainly used for implant creation and shaping, selection of patients, surgical planning, molds for prosthetics, surgical guides and postgraduate pedagogical applications. These models are required to be highly precise, if not they may interfere with the accurate development of the procedure. Digital models can potentially be a powerful tool in surgeries, an example of this is the research regarding the use of augmented and virtual reality in the operating room providing information regarding the anatomy of the region the surgeon is working on (Soler 2015).

Future Collaborative Projects

The new “Anatomy studio” virtual reality project [32] using immersive reality is a new collaborative educational tool. This project enriches the VR tool by displaying the 3D models with the new Oculus® glasses using immersive reality.

It is a work in progress in collaboration with DIVA3D® company and school of Engineering, University of Lisboa (Professor Joaquim Jorge)

The authors are about to create a new software “anatomy studio 2” in order to replace the Winsurf® software. It uses virtual reality and a network methodology based on a dedicated web server. Two different data are stored on the server: the whole set of anatomical slices, and the reconstructed 3D vectorial models.

Anatomy Studio takes place at a drafting table, where users are seated and equipped with Oculus see-through displays, tablets and styli. Our approach adopts a familiar drawing board metaphor since tablets are used as sketch-based interfaces to trace anatomical structures, while simple hand gestures are employed for 3D navigation on top of a table (Figure 4). By using hand gestures combined with mobile touchscreens, the anatomists can easily access any cryosection or 2D contour and follow each user’s contribution towards the overall 3D reconstructed model.

The outlining is done on the slices with a tablet connected to the server, and the resulting 3D models are displayed on the Oculus® quest 2 64GB device.

It works with a network of students working on the same body, under the supervision of a teacher showing how to achieve the segmentation.

This is a kind of collaborative virtual dissection school for teaching human anatomy.

This allows collaborative teamwork of students and teachers around the world in real time. The results indicate that our system encourages closely-coupled collaborations, teaching and group discussions.

FUTURE RESEARCH DIRECTIONS

The aim of the UNESCO Chair is to promote all these new educational tools for anatomy. It is also to set up a worldwide network of experts in morphology willing to develop these digital tools, and a huge 3D vectorial database in anatomy. A worldwide partnership is the best way to establish a huge databank of accurate 3D vectorial models validated by experts. These educational tools could be used in different situations: Self-directed study, classroom teaching, workshops. They also could be available on web servers. Specimen replacement is also necessary to study the anatomical variations of the human body.

The DIVA3D company (<http://www.diva3D.net>) created in 2018 is an official sponsor of the Unesco Chair of digital anatomy (Professor V. Delmas, Paris University).

Both are dedicated to developing educational VR solutions for anatomy teachers on the basis of these new tools, including the 3D printing of anatomical objects.

These techniques are the subject of collaborative workshops around the world to train students in the use of these new tools.

Due to the recent spread of coronavirus disease since 2019, medical colleges are increasingly using virtual learning to make up for a lack of available practice in medical institutions. Therefore, more precise evaluation of the effects of the virtual learning system is highly desired.

Another important question to be solved is how teachers check for new and deeper learning when integrating virtual reality in the anatomy classroom and workshops: it is imperative that we study the value these tools can bring to schools from the perspective of both educators and students.

Finally, 3 important questions need more precise answers: (Castadena, 2021)

1. What challenges do teachers encounter as they seek to assess student learning from VR experiences?
2. After using VR in their classroom, how do teachers perceive the efficacy of the assessment strategy they used?
3. What are students' perceptions about the assessments' ability to evaluate their learning from VR?

Future studies should bring answers to these relevant questions.

CONCLUSION

To compensate for the growing demand from students and the lack of corpses for dissection, digital tools based on 3D modeling and virtual anatomy are widely used in educational anatomy around the world.

The technique of *digital dissection* by computerized segmentation shown here by the authors offers a remarkable learning tool in anatomy. By producing these 3D models from 2D anatomical high-resolution slices, the students gain a real anatomical knowledge of the human body: the segmentation process done by outlining the anatomical slices to build vectorial model is one of the most powerful training methods to memorize the 3D anatomical volumes inside the student's brain, since it is providing a greater understanding of the spatial structure of the body and its internal organs.

The progressive and interactive building of the 3D model slice by slice is indeed the best way for an accurate and sustainable learning of relationships between anatomical structures.

The student evaluation in a workshop and training program confirms this viewpoint.

Finally, virtual reality and augmented reality techniques have a promising value for teaching anatomy in addition to a positive economic impact on universities.

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APPENDIX 1

Table 1. 1205 structures in the male body were segmented and reconstructed by the Winsurf® software to build separate anatomical 3D objects

Systems	N	polygons	Names of anatomical elements reconstructed
		(thousand)	
Integumentary	1	20	Skin
Skeleton	230	443	Head & spine, ribs pelvis and limbs
Muscles & tendons	370	410	Head & neck, thorax, abdomen pelvis and 4 limbs
Ligaments	82	16	Spine pelvis and 4 limbs
Respiratory	18	190	Right & left lungs with segments, trachea, bronchi pulmonary arteries, pulmonary veins
Heart	6		Left & right atrium & ventricles - valves
Arteries	91	131	Head & neck, thorax, abdomen pelvis and 4 limbs
Veins	150	354	Sup. & inf. Vena cava, Azygos and Portal systems
Nerves	55	77	thorax, abdomen pelvis and 4 limbs
Brain	52	87	7 cortex lobes, central grey nuclei, ventricles, pituitary gland, eyes, cranial nerves
Alimentary	25	51	Oesophagus, Gaster, duodenum, ileum, jejunum, ascending colon, transverse colon, descending colon, sigmoid, rectum, pancreas, Liver with VIII segments, Gallbladder, biliary tract
Urinary	6	22	Bladder, Right & left kydneyes urethra & Ureters
Genital (man)	10	15	Prostatis, testis, deferents, vesicules seminales,
Glands	10	9	Thyroid, Surrenals, Parotids, submaxillar, sublingual
Anat. slices	(100)	0	selected original anatomical slices
TOTAL	1205	1825	

Table 2. End-training survey form and results

	Total*	Group 1	Group 2	Group 3
N=	86	34	19	33
Was this your first experience in digital anatomy? (Yes/No)	37/49 (43%)	12/22	11/8	14/19
Do you feel that the training time was sufficient? (Yes/No)	76/10 (88%)	28/6	18/1	30/3
Do you think you are able to use the software independently? (Yes/No)	85/1 (99%)	33/1	19/0	33/0
Do you think the Mesh software is easy to use? (Yes/No)	85/1 (99%)	34/0	19/0	32/1
Do you think the result obtained is usable in your clinical practice? (Yes/No)	86/0 100%	34/0	19/0	33/0

*yes (%)

Tridimensional Vectorial Modeling of the Human Body From Anatomical Slices

Table 3. Available 3D software tools or models with open access on the internet. More informations at: <https://anatomytool.org/content/investigation-anatomy-learning-resources-which-are-open>

Name	Internet link	Description	A/B*
AnatomyLearning.com	https://anatomylearning.com/	3D models that you can use freely to create imagery with. Showing the logo is required. By Dr. Blanco Salado, Valencia. Has quiz tools.	B
Anatronica (CHI)	https://anatomy-3d-anatronica.soft112.com/	Free 3D Web app on human skeletal and muscular anatomy.	A
Audilab	http://audilab.bme.mcgill.ca/~funnell/davis3d/	3D models of head, trunk and foot	B
Biodigital	https://www.biodigital.com/	3D rotatable model. You can hide or show systems or structures. Click on a structure to get its name. An explanation is provided	A
BodyParts 3D	https://dbarchive.biosciencedbc.jp/en/bodyparts3d/desc.html	3D model data that can be used to create applications	A
Anatomography	http://lifesciencedb.jp/bp3d/	3D models of individual structure (parts) in BodyPart 3D model	A
SketchFab, UMCg	https://sketchfab.com/eLearningUMCG	Mainly heart & organs	B
SketchFab, Intervoke	https://sketchfab.com/intervoke	16 interactive models	B
SketchFab, Univ Dundee	https://sketchfab.com/anatomy_dundee/models	171 models bones, kidney	B
SketchFab, Unesco chair	https://sketchfab.com/Chair_Digital_Anatomy	42 models collection of 110 models	B
TeamLabBody	http://www.teamlabbody.com	Bone 3D motion included Tablet or smartphone version only	B
Visible body (USA)	https://www.visiblebody.com/	Not free but 23\$ per year	A
Zygote Body (USA)	https://www.zygotebody.com/	Light version free	A

*A= application B= works on browser

Table 4. Studies using virtual reality, AR, MR tools in anatomy learning and simulation

Author	Year	Tool*	study	device
Birt	2017	MR	Paramedic web education	mobile
Jain	2017	AR	Medical education	mobile
Guimarães	2018	AR/VR	Trends in anatomy learning	computer
Kurniawana	2018	AR	3D space recognition	mobile
Asensio Romero	2018	VR	Female pelvis 3D model	computer
Erolin	2019	VR	Pilot study	computer
Bork	2019	AR	Magic mirror system	computer
Wheeler	2020	VR	Training paramedics	computer
Rosmansyah	2021	VR	review	computer

*VR= virtual reality MR= mixed reality AR= augmented reality

Table 5. Studies using virtual reality tools in education or surgery

Author	Year	Tool*	study	E/S**
Peach#	2020	-	Comparison 3 groupes of 50	E
Yammine#	2015	-	Review of meta-analysis	E
Jain	2017	AR	Mobile device	E
Moro	2017	AR	AR versus tablet	E
Darras	2019	VR	Virtual versus cadaver	E
Bork	2019	AR	Magic mirror system	E
Prats Galino	2015	VR	Lumbar spine simulation	S
Soler	2015	AR	Liver specific anatomy	S
Moro	2017	AR	Benefit for learning	E
Condino	2018	MR	Hololens - orthopedics	S
Preim#	2018	-	Review of digital tools	S
Prats Galino	2019	VR	Simulation of neuro-surgical Approach	S

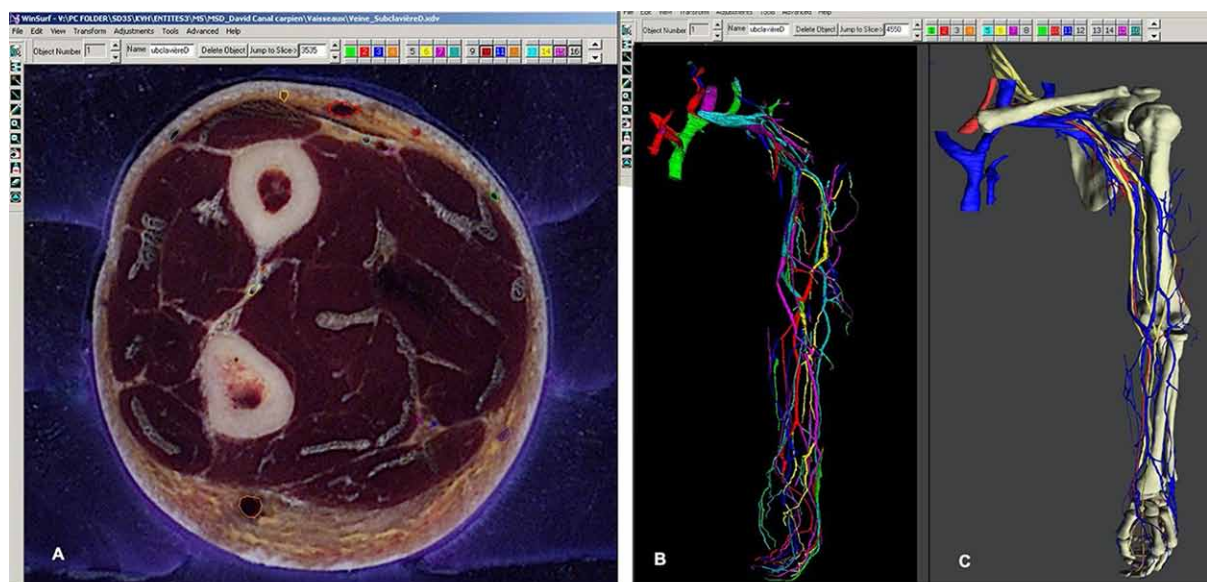
meta-analysis and reviews

*VR= virtual reality MR= mixed reality AR= augmented reality

**E= Education S= simulation

APPENDIX 2

Figure 1. Creation of 3D mesh of the upper limb's veins with Winsurf® software



Tridimensional Vectorial Modeling of the Human Body From Anatomical Slices

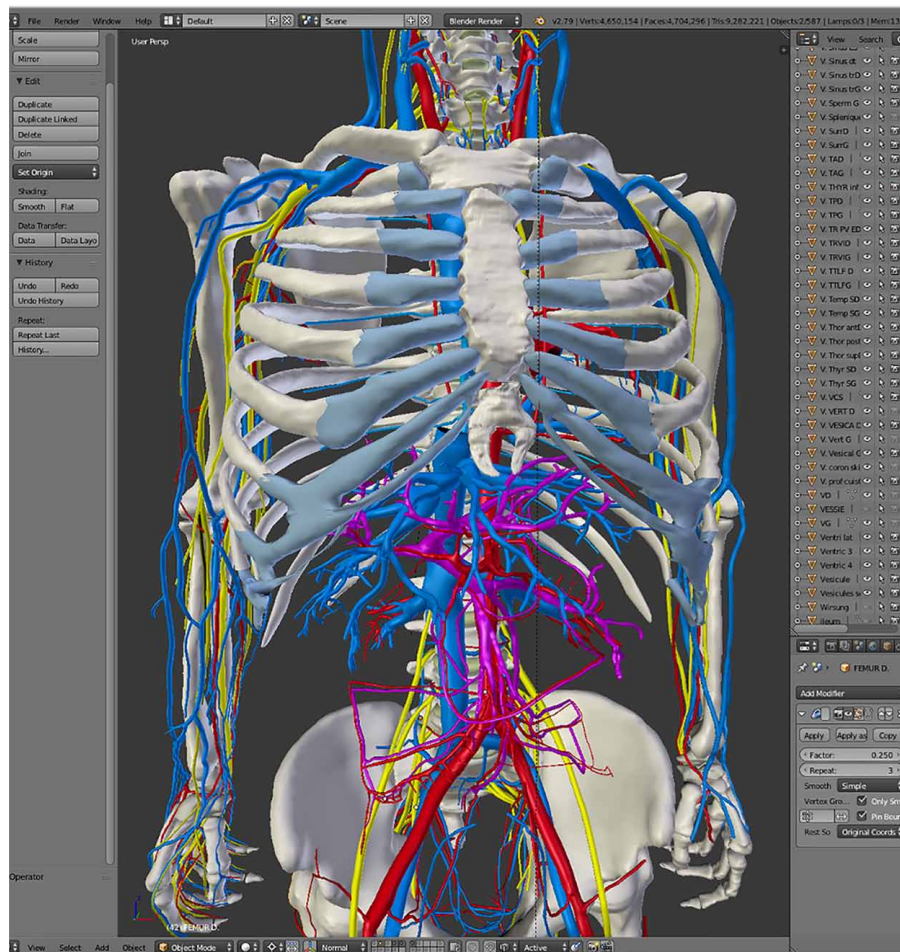
Interface of the Winsurf® software with the available 2D tools on the left upper side of the window to edit or modify the contours, navigate through the slices and choose the color channels. On the right, the whole 3D model of the left upper limb.

4A: Outline of the 2D slice of veins of the upper limb by using several colored channels

4B Resulting 3D model with the colored 3D mesh in “wireframe” mode.

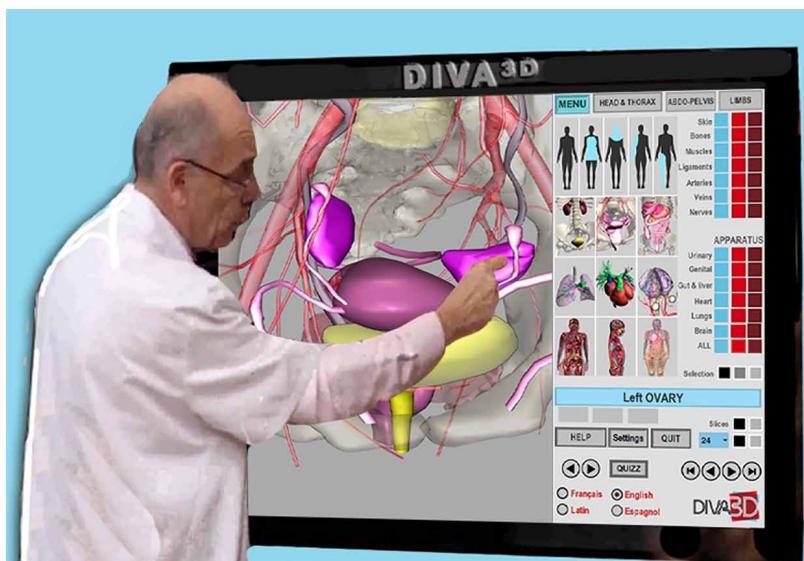
4C Resulting modeling of the bones, nerves, arteries and veins displayed inside the 3D window.

Figure 2. Interface of the Blender® screen with bones, vascular and nervous structures built from the anatomical slices of the Korean visible human project



Tridimensional Vectorial Modeling of the Human Body From Anatomical Slices

Figure 3. Interface window of diva3D® virtual dissection table displayed with the 55 inches touch screen with a female pelvis model



On the left, the 3D model is handled with 3 fingers. On the right, the menu with the command buttons gives access to regions, systems and possibility to display/ hide/ make transparent the anatomical structures. The name of the selected element is shown in the blue window in 4 languages (French, English, Spanish, Latin). A 3D quiz is also available.

Figure 4. Overview of Anatomy Studio, a collaborative MR dissection table approach where one or more anatomists can explore anatomical data sets and carryout manual 3D reconstructions using tablets and styli. Each anatomical structure is outlined on the tablet connected to a server. The resulting 3D model can be displayed in real time with an Oculus Rift 2 system of immersive reality provided by the server

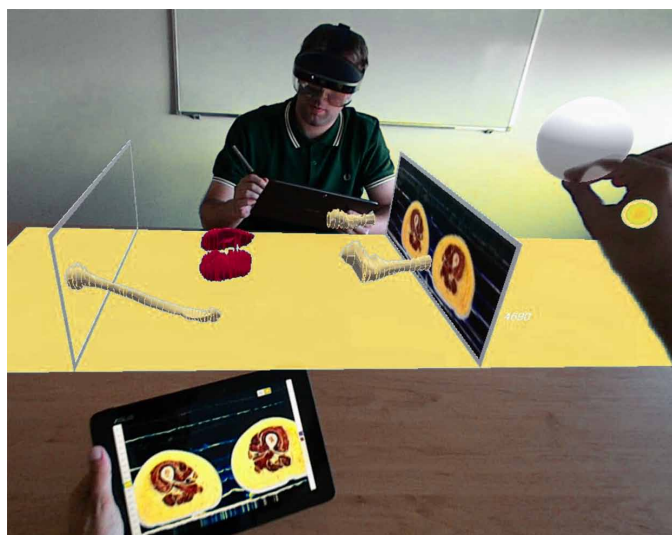
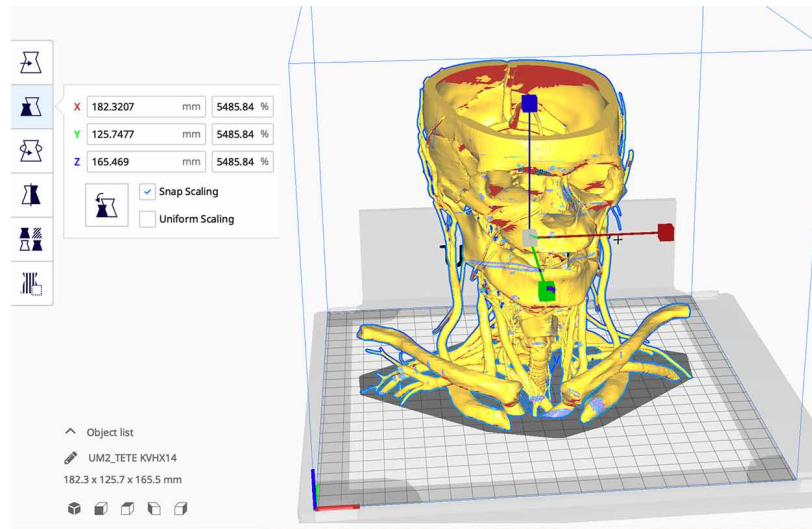


Figure 5. Interface window of Cura® software showing the preparation of the 3D printing of the head



On the left, the main commands to handle the 3D printed object. From top displacement, scaling, rotation, section.

Figure 6. Ender® pro 3D printer with the printed head in PLA with supports

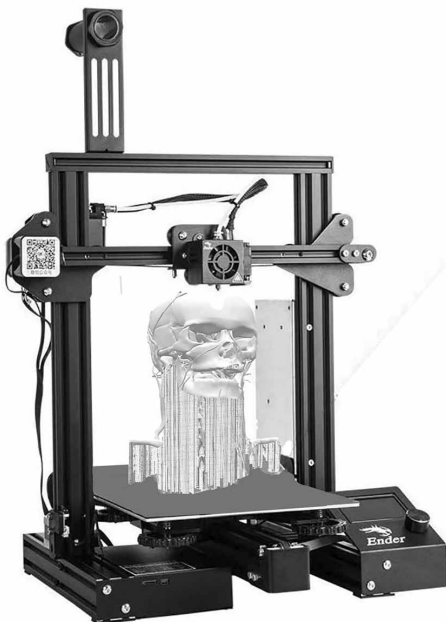
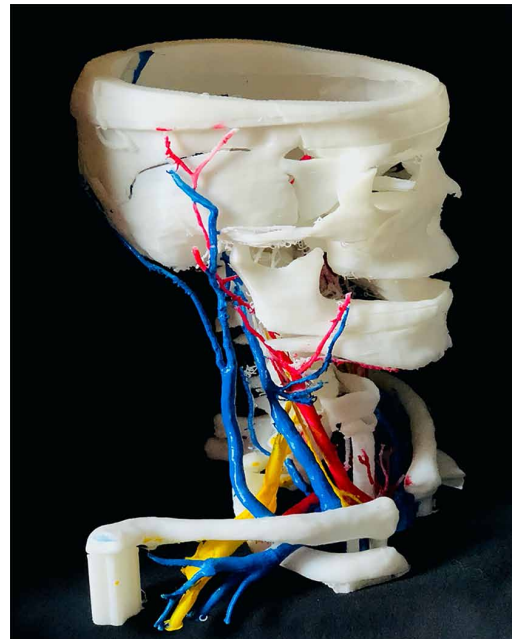


Figure 7. 3D printed head and neck of the Korean visible human with vessels and nerves (life size)



After printing (duration 3 days) and removal of the supports, the vessels and nerves were color-painted manually.

Chapter 3

Healthcare E-Learning Ecosystem for the Use of Ultrasound in Interventional Procedures: Sharing the Keynotes on a Real Experience

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ABSTRACT

Ultrasound imaging (USI) has become a disruptive element in medicine. To achieve a safer USI application, professionals need sound practical training. This chapter presents the keynotes in the development of a teaching-learning ecosystem, where students (future specialist physicians) and teachers participate, with the concrete educational contents. The ecosystem is supported by a LMS that includes recourses and activities for collaboration, implemented by a multidisciplinary team of health and ICT experts. Practical skills are acquired through a computer-based simulator for the training of the USI-based interventional procedures that the student can handle autonomously at any time and is highly realistic. As a main result, the ecosystem is applied to a real experience, focusing on the treatment of spasticity by botulinum toxin infiltration. Learning outcomes have been evaluated through academic grades and a survey of students who have participated in a specialist course.

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INTRODUCTION

Medical imaging is not only a useful tool in diagnostics and interventional procedures, in fact it has become a disruptive element in Medicine. From all the kinds of imaging techniques, ultrasound (US) has a lot of advantages when it is compared to other techniques like basic radiography (X-rays), Computed Tomography (CT), Magnetic Resonance Imaging (MRI). Thus, in US imaging patients have no need for radiation exposure, US is convenient, inexpensive, and repeatable. Moreover, as it can provide dynamic and comparative images in real time, it now has a primary role in the diagnostic protocol for a wide spectrum of diseases at physical medicine and rehabilitation tasks (Özçakar et al., 2012). Ultrasound is used at a face-to-face and interactive (in situ) exploration, which allows the practitioner to use high-resolution images of human soft tissues in real time way. It can be easily performed by physicians and is readily accepted by patients as it does not cause any injuries. Another US important advantage in clinical practice comes from the fact that it is suitable for guiding diagnostic and therapeutic interventions. US could be used to aid needle positioning and to facilitate invasive procedures such as fluid aspiration, abscess drainage, tissue biopsy and local injection of therapeutic agents. Ultrasound-guided interventional procedures are especially useful when fluid concentrations are very small or when the needle trajectory can be very close to vital structures (e.g., nerves and arteries) that could be severely damaged during the procedure.

Its main limitation comes from the fact that it is highly operator dependent (Romero-Morales et al., 2020). Therefore, experience, within a typically complex training procedure, is mandatory before being able to reliably perform an imaging assessment of various pathologies or an interventional procedure. However, due to certain barriers, such as a real US device availability in most clinics and the lack of training at real health facilities, have limited its use. Originally, ultrasound scanners were expensive, difficult to move and only available to specialized medical centers. Thanks to technological advances in the electronic device miniaturization, portable scanners (Rykkje et al., 2019) have recently become available, with reduced cost and sufficient image quality. As a result, their use is spreading to all specialties, which has a particular impact on the need for training (Bhagra et al., 2016).

One of the most effective and safer strategies for medical training for the necessary skills acquisition for interventional US is given by simulation resources (Blum et al., 2009; García-Esteban et al., 2019). First, training and learning through simulators avoids causing injuries to patients when they are due to lack of experience. Other advantages are that it enables unlimited training, so it allows the construction of a wide variety of case studies where the most interesting characteristics (Moreno-Guerrero et al., 2020; Zhang et al., 2021) appear.

At the same time, for a continuous actualization, specialized training at advanced techniques and daily work must be compatible (Aljawarneh, 2020). In this way, for the last decades, distance learning has been revealed as an important tool to the knowledge transmission (Moreno-Guerrero et al., 2020) for people that cannot leave the work and aspects like high accessibility, availability, and autonomy (Ashwin & Guddeti, 2020) are significant. Supported by Web technologies, considering actual LMS (Learning Management System), the e-learning makes it possible to acquire it, in addition to self-training, a greater student participation (V. Moreno et al., 2019) at the educational process both in synchronous and asynchronous activities.

In this chapter the authors present the keynotes on the development of a teaching-learning ecosystem where professionals in training will be able to acquire all the theoretical knowledge and they will also be able to practice US interventionism. The ecosystem proposed is based on a learning management tool,

where students and teachers participate actively together sharing educational contents and activities. Two virtual simulators will be the strategic tools that will help the professional being trained to practice the knowledge acquired on case studies. To show the capabilities of the system based on ultrasound images of a specific muscular pathway, and with the only help of the mouse, the trainee will be able to proceed to inject a fictitious drug in a correct localization.

MATERIAL AND METHODS

The ecosystem proposed for learning management is based on a platform that integrates all the elements that constitutes it, including tools for collaboration and communication with teaching experts, ICT (Information and Communications Technology) professionals, training activities, incorporation of didactic materials, etc. Later ones include theoretical contents and real cases on the subject, supported by graphics, real US images and videos, as well as a three-dimensional anatomical viewer with all the components of human body.

In addition, in the e-learning ecosystem proposed, the practical training is based on an US exploration simulator for musculoskeletal (MSK) localization that replicates, with great realism, the lineal movement of a virtual probe along a muscular pathway. Also, in order to practice US interventionism, a simulator with a virtual syringe and needle is included to replicate the syringe inclination and the needle penetration movements.

Customized LMS

The ecosystem has been built on a customized LMS of the University of Salamanca based on Moodle (Modular Object-Oriented Dynamic Learning Environment), where several didactic elements (Sáiz-Manzanares et al., 2020) shown in Figure 1 are available. Resources such as “File”, “URL”, “Video”, etc. can be used by the teacher as an aid in the teaching-learning process. Activities such as “Assignment”, “Quiz”, etc., are tasks that the student can develop alone or in interaction with other classmates. The tasks can be evaluated, and the teacher will have feedback both on the outcome and on the problem-solving processes of a student or students group. Both elements, resources, and activities, provide the interaction between the teacher and the learners and the learners themselves.

Profile of Teaching Team and Students

The teaching team is made up of experts in two fields of knowledge: on the one hand, specialists in Anesthesiology, Reanimation and Pain Therapy, Physical Medicine, Rehabilitation, Radiodiagnosis, Traumatology and Surgery, among others; and on the other hand, specialists in Information Technology, Simulation, Robotics and Artificial Intelligence are needed to technical development and support.

The first group will be responsible for the technical direction and coordination, design and development of specific activities and materials, as well as acting as tutors for academic, orientation and planning tutorials through asynchronous and synchronous means. The second group will carry out functions like construction of multimedia materials, management, and configuration of the LMS and related databases, and construction of the virtual interactive simulators, as well as providing support in their installation.

Figure 1. “Resources” and “Activities” included at the personalized LMS environment



When the student's group is considered, they are professionals already graduated in the field of Health, such as Rehabilitation Doctors, Physiotherapists, Rheumatologists, Traumatologists, Neurologists, Specialists in Pain Treatment and in the rest of the specialties related to techniques where US-guided diagnostic or therapeutic interventionism is required.

Resource Repository

The resources repository will include human model photographs, real US images, thematic videos, 2D anatomical images and sections, a 3D anatomical model, among others. The theoretical contents will be elaborated by means of Microsoft PowerPoint presentations, including the typical audiovisual elements.

The team of US specialists was responsible for capturing the ultrasound images and photographs of the right side of an informed and consenting 46-year-old male. The actual US images were obtained using ESAOTE's MyLab 25 with a variable-band linear array probe, model L4 523, which operates in the frequency range of 5 to 12 MHz. US videos were also recorded where a path over the muscle to be treated is shown, as well as the movement or contraction of the muscle performed voluntarily by the patient. Doppler ultrasound videos were also recorded and focused on the treatment area. These videos allow the detection of the blood flow and show it on the screen using colors and they serve to identify the existing blood vessels in the area, whose puncture should be avoided.

Using the anatomical viewer, students will be able to visualize the neuromuscular systems (NMS) of the human body in 3D. An intuitive interface allows to perform typical actions as zoom in, zoom out, rotate, and pan the 3D model with the computer mouse to efficiently visualize all the anatomical

structures of the locomotor apparatus. In addition, the NMS are included in textual form following a tree structure. A specific NMS or a specific structure of a NMS can be selected/deselected interactively in the textual tree and the corresponding structure can be displayed or hidden in the 3D model.

Defining the Virtual Simulator: Ultrasound-Based Exploration and Intervention

The virtual simulator allows students to practice with case studies that has been designed by experts in the field of Medicine on the subject matter of the ecosystem and will be implemented by experts in Technology.

In the US exploration simulator, a virtual probe is represented on a photo of a human model in the same plane. As the virtual probe moves over the model with the mouse, a real set of previously recorded frames of the scanning area is displayed. The synchronization between the image visualization from a real scanner and the mouse movement is performed by choosing, from the pre-recorded image repository, the frame corresponding to the position of the virtual probe on the model. Each of the practices has a path assigned to it in which the set of frames that make up the video is uniformly distributed. Each path can have one or more exploration zones. When the virtual probe is in an examination zone, the playback of a video simulating the active exploration with the US scanner starts.

The interventional US software simulator includes a virtual syringe represented on the anatomical slice in a plane perpendicular to the model represented at the computer screen. By moving the ultrasound probe, as in the exploration simulator, the ideal puncture point is determined for a specific practice. When the correct point and orientation has been reached, the anatomical slice and the corresponding ultrasound image are displayed. The student can now start practicing with the virtual syringe. By clicking on the syringe with the mouse, you can change its inclination with respect to the probe in a plane approach with the probe. As the virtual needle is introduced over the anatomical slice by means of the mouse, the needle is displayed superimposed on the ultrasound images, in the same way that a real operation. The length and inclination correspond to the distance and orientation that the virtual syringe is moved.

As a learning aid tool, this virtual simulator interactively shows the outline of the different anatomical structures as the needle reaches them by moving the virtual syringe with the mouse. If a critical structure is reached by mistake, the needle can be extracted to a certain distance where the attitude of the virtual syringe can be modified to orient it again towards the correct target.

The simulation software has been implemented using the C++ programming language and Qt, a cross-platform framework that has the necessary tools to build GUIs (Graphical User Interface) that works on the most important operating systems (Microsoft Windows 10, Mac OS, Linux, ...)

RESULTS

Targeting the Proposed Ecosystem

Among all the possible applications of the proposed ecosystem in a real e-learning experience, the authors have chosen the training of professionals using botulinum toxin (BT) for the treatment of spasticity. BT infiltration is considered by experts (Picelli et al., 2012, 2014) as one of the most effective and best performing methods for the focal treatment of spasticity, as it guarantees a high efficacy and a low probability of occurrence of complications. One of the most important aspects for the success of

this treatment is the correct infiltration of BT, choosing the right dose, the correct infiltration site and localization techniques (Walker et al., 2015).

There exist different guidance techniques to locate and identify the muscle to be infiltrated by the specialist. The most commonly ones used by health personnel are palpation or localization by anatomical references, electromyography, and ultrasound imaging. Currently, the most recommended is ultrasound scanning (Chan et al., 2017), since it is a safe, effective, and well-tolerated technique. It allows real-time visualization of the aforementioned infiltration area, localization and identification of structures such as veins, arteries, nerves, muscles, bones, etc. In addition, it allows the visualization of the needle tip, facilitating its guidance towards the muscle belly to be infiltrated and avoiding affecting other structures. Through ultrasound images, it is also possible to visualize the movement of the target muscle, either actively performed by the patient or passively by the specialist, which makes it possible to ensure that it is the right place. Among the existing techniques, ultrasound imaging is the only one that makes it possible to observe the amount of drug injected (Blum et al., 2009).

However, the use of US as a guidance technique for BT infiltration is highly dependent on the experience of healthcare specialists. It has a high learning curve and requires prior training before the professionals in training can implement it in patients. Thus, it is important to position and orient the US probe correctly in order to obtain a quality image. Likewise, it is essential to interpret the acquired images and identify in them the muscle bellies, blood vessels, nerves, bones, etc., with the aim to not affect any other structure that may cause any damage or injury to the patient.

The proposed ecosystem e-learning objective is that the medical specialist, in his professional work with different health teams, can carry out a correct infiltration of BT using US. Therefore, it is important to realize that students participating on the ecosystem should receive training, both from a theoretical and practical point of view, for an integral approach to spasticity. Focused on achieving this design objective, the teaching team has designed the theoretical contents, case studies and activities. The technology expert team oversaw configuring and making teaching and technical materials available to the students through the resources offered by the LMS (Figure 2).

With the theoretical contents the students will assimilate the necessary knowledge to start practicing the BT infiltration treatment by means of US imaging. Using the typical resources, such as “File”, “Folder” among others, the theoretical topics have been made available to the students by means of PowerPoint presentations in pdf (Portable Document Format), which include real images and videos of patients focused on the study of spasticity patterns, real and US images of a healthy person to show the different BT infiltration techniques, images captured from the 3D anatomical model and 2D anatomical sections made by graphic designers for the in-depth study of the anatomy of the locomotor apparatus.

With a wide range of practices included on virtual simulators, students will learn, in a visual and interactive way, how to position a virtual ultrasound probe to visualize the correct image. In addition, they will be able to practice with a virtual syringe to learn, aided by the ultrasound image, where to inject BT without causing injury to patients. Its inclusion within the LMS has been done through the resource “Url”, where participants will access links from where they can download the app that supports the two simulators for Windows and MacOs operating systems. The technology group has enabled the following resources in the LMS (Figure 3) for the resolution of technical issues:

- “File” for app installation help manuals.
- “Video” for a video tutorial explaining in detail how the app works from the end user’s point of view.

Figure 2. LMS aspect for the theoretical contents of the course and its presentation



- “Page” for a FAQs (Frequently Asked Questions) section.

Also, a forum related with all the topics has been installed, where the technology group can participate actively. Nevertheless, an email direction has been enabled to give personal technical support over punctual questions.

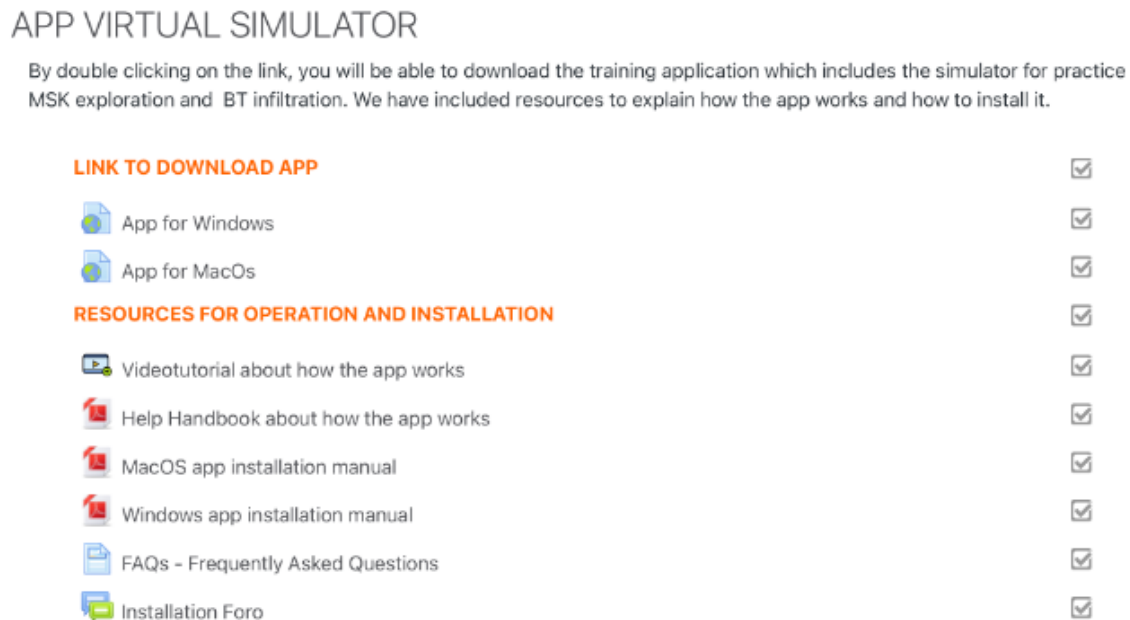
Regarding the activities, the teaching team has developed tests to monitor the students’ learning in all the theoretical topics, which have been included in the LMS through the “Quiz” activity. The student must complete and pass the tests for each topic before he/she can access the next topic. With these tests the teaching team monitors and evaluates the student’s progress in the course.

In addition, to complete the course, each student must prepare a final project on a real clinical case that presents a specific pattern of spasticity, but there can be several patterns in the same patient. For this clinical case the student will have to provide as treatment a BT infiltration. A report must be made, which must be accompanied by iconography (image and/or video format), showing the performance of the technique guided by ultrasound by the author of the report. An “Assignment” will be enabled in the LMS where each student will upload the report and material, he/she considers appropriate. An evaluation panel will assess the student’s skill in performing the US-guided technique.

Theoretical Contents

In the course of treatment of spasticity by means of ultrasound-guided toxin infiltration, the theoretical contents are organized into modules and topics. The first module deals with the anatomy of the locomotor system, focusing on the body’s joints and its neuromuscular systems. The second focuses on the physiology of spasticity and its treatment with BT. The third one is dedicated to the practical use of electrostimulation techniques related with BT infiltration. The fourth is addressed to US imaging and

Figure 3. Habilitated resources at the LMS for the practitioners



its applicability for clinical practice (Figure 4). The following modules describe the spasticity patterns in the lower and upper limbs, respectively, and how to treat a spastic patient. Finally, the last modules deal with clinical cases and examples of US-guided BT infiltration.

Practical Cases for US-Based MSK Exploration

Within the modules dedicated to the study of spasticity patterns, the teaching team has designed a set of cases aimed at enabling the student to visualize and recognize a 3D anatomical structure in a 2D ultrasound image. Specifically, the cases designed have focused on the different muscles involved in spasticity patterns affecting the upper and lower limb. To facilitate the student to develop practical skills regarding anatomical-ultrasound correspondences, the proposed e-learning ecosystem includes a powerful US-guided MSK exploration simulator.

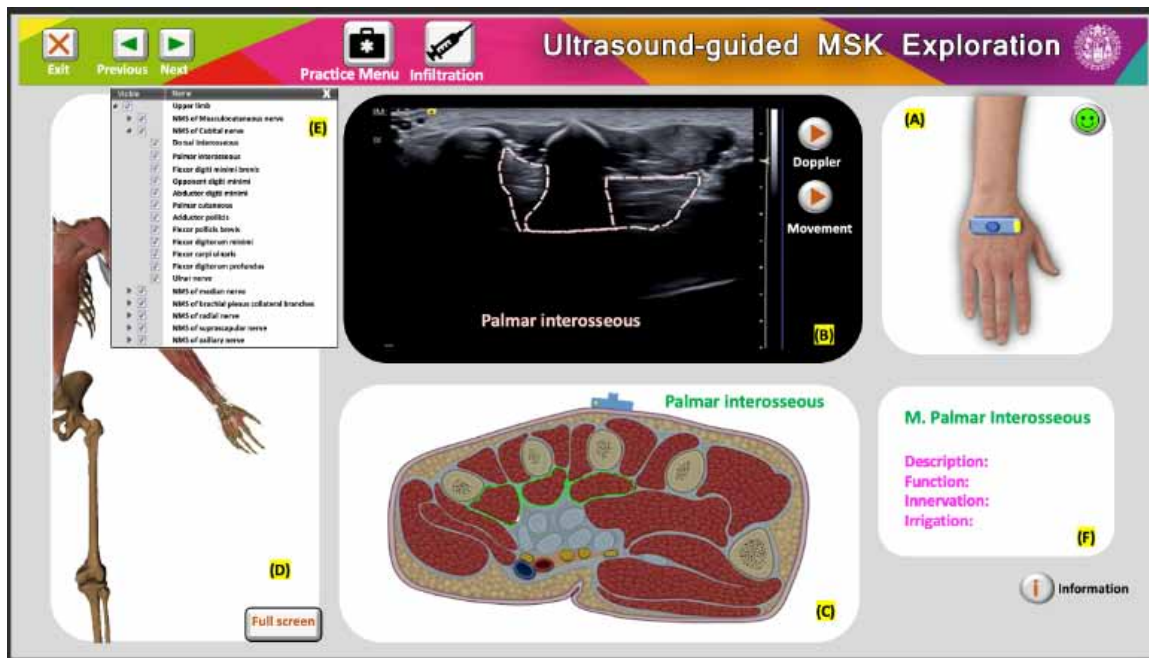
In the design, the GUI of the MSK exploration simulator (Figure 5) was distributed into five main sections:

- Upper right section includes a real photo of the human model corresponding to the practice being performed and a virtual probe (Figure 5A).
- Upper central section includes an US viewer (Figure 5B) showing real US images and buttons to switch to video mode.
- Lower central section includes a real anatomical slice viewer (Figure 5C).
- Left section includes a three-dimensional anatomical viewer (Figure 5D).
- Lower right section includes a window with anatomical information (Figure 5F).

Figure 4- Module 4 with topics and quizzes

Module 4.- Sonography concepts	
RESPONSIBLE PROFESSORS	
F. Hernández Zaballos	P. Alonso Hernández
PRESENTATIONS WITH THEORETICAL CONTENTS	
Theme 1 - Physical basis of ultrasound	☒
Theme 2 - Practical notion of ultrasound exploration	☒
Theme 3 - Ultrasound artefacts	☒
Theme 4 - Ultrasound-guided intervention	☒
Theme 5 - Ultrasound muscular anatomy. Spastic muscle	☒
TEST FOR ULTRASOUND MODULE	
M3 - TEST THEMES 1, 2, 3	☒
M3 - TEST THEMES 4, 5	☒

Figure 5. GUI of the proposed ultrasound-guided MSK exploration simulator



To facilitate the app's navigability, the upper part of the GUI includes a set of icons to go to the previous and next practice, to access the global menu with all the available practices and the infiltration simulator.

As a case study, Figure 5 shows the practice corresponding to the claw hand spasticity pattern, whose description, the muscles involved, and possible infiltration techniques have been studied in the theoretical contents. Among the muscles involved in this pattern are the palmar interosseous muscles. From a didactical point of view, it is proposed that the student should locate the most effective point of the BT by means of US scanning (Figure 5A) in the treatment of the claw hand spasticity pattern. To reach this, using de computer mouse, the student can move the virtual probe over the photo of the hand of the human model following a defined anatomical path. Above the probe there exists a yellow marking as a reference for the orientation of the probe. As a learning aid, a face-based icon has been included that changes color according to the proximity to the US region of interest: red, yellow and green indicate whether it is far away, near or over the exploration area.

When the student has placed the virtual probe in an area close to the target location, he can view actual ultrasound scans (Figure 5B) of the working muscle bundle on the viewer. By switching to Doppler mode video, he can identify the veins and arteries in the area of interest. He can also identify the muscle belly where he has to inject the BT by switching to motion video mode, where the patient's movement or contraction of the muscle to be infiltrated is shown.

When the probe is over the correct exploration location, an anatomical illustration (Figure 5C) related with the corresponding axial cut appears. So that the student can identify the muscles, veins, arteries, nerves, bones, and tendons on the correct localization, when the mouse passes over the ultrasound image (Figure 5B), these anatomical structures appear surrounded by a dashed line in both images together with a help text. Similarly, when the student moves the mouse over the image of the anatomical slice (Figure 5C), the MSK structures involved are highlighted. In this way he will be able to relate them and learn how to visualize the anatomical sectional information at the model. The information button provides a theoretical description (Figure 5F) of the muscles, nerves and other significant structures that the student selects with the mouse. These utilities constitute a valuable learning aid together with the 3D anatomical model. This model is configured to visualize the structures corresponding to the upper and lower limb NMSs, depending on the practice selected. To facilitate the relationship between the visual aspect, the location, the NMS to which it belongs and the name, a hierarchical tree of the different NMSs has been included to the right of the 3D model (Figure 5E). Students will be able to hide or show each of the structures or the complete NMSs. They can also do the opposite process, i.e., students can select on the 3D model, with the mouse pointer, the muscles and nerves and the label will be highlighted in red in the tree. So, it is a solid tool to understand the structure of human body and the role of its elements at diagnostic and treatment of the patients.

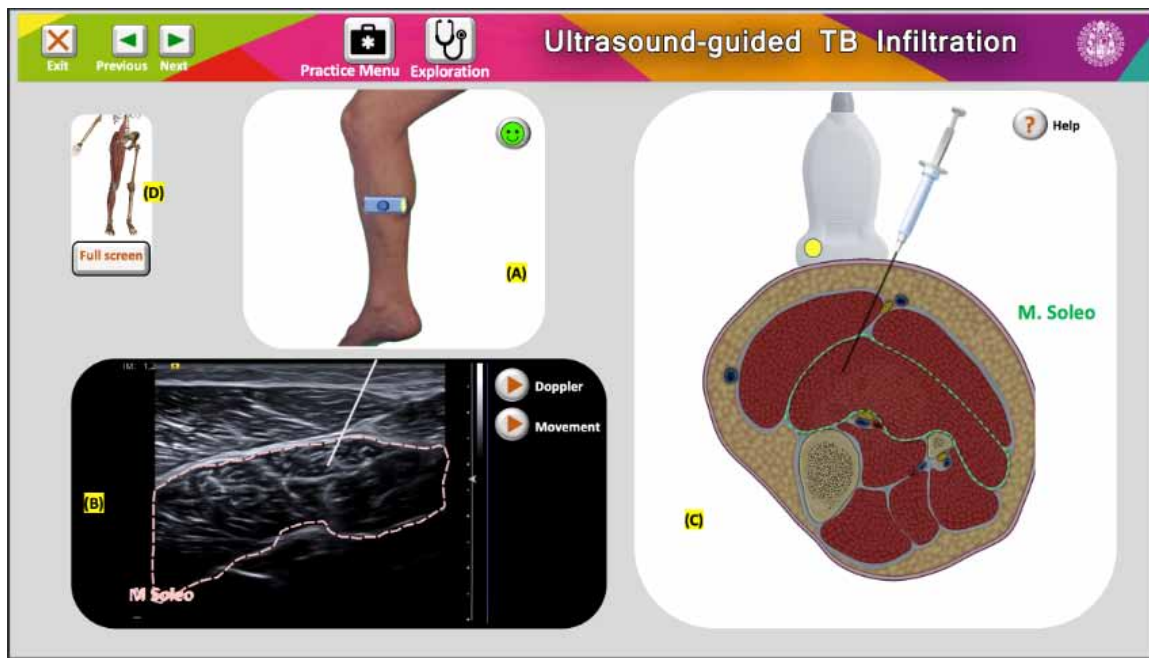
Practical Cases for US-Based Infiltration

Each of the practical exercises includes a BT infiltration simulator. Through a virtual syringe, the student will be able to perform infiltrations guided by an ultrasound image. In this way, the student will learn, in each exploration area, which is the muscle belly or bellies where the puncture and infiltration of BT would be performed and which are the veins, arteries and nerves whose puncture should be avoided.

When designing the training window, it was divided into three main sections:

- Upper left section includes a photo of the real model corresponding to the practice to be performed and the probe positioned on it (Figure 6A).
- Lower left section includes the ultrasound image viewer (Figure 6B).

Figure 6. GUI of the ultrasound guided infiltration simulator



- At the right section a virtual syringe (Figure 6C) is displayed over the axial anatomical section to perform an in-plane approach.
- At the left upper corner (Figure 6D) a link for the anatomical 3D viewer can be found.

As an example of one case study, the practice corresponding to the equines foot spasticity pattern is presented, whose description, the muscles involved, and the possible infiltration techniques have been studied in the theoretical contents (available at the ecosystem). Among the muscles involved in this pattern is the soleus. Figure 6 illustrates the infiltration technique of the soleus using ultrasound.

The upper right section (Figure 6A) shows the posterior aspect of the thigh and the virtual probe on the thigh. The student must move the probe with the mouse over the path until the correct infiltration location is reached. When moving the probe, the US images corresponding to the probe path over the model are displayed on the ultrasound viewer (Figure 6B). When the infiltration zone is reached, a video is played that simulates an active exploration like when using a real ultrasound scanner: dynamic effects as pulse can be observed. By hovering the mouse pointer over the image, the student will be able to identify muscle bellies, veins, arteries, nerves, or bones, which will be highlighted with green, blue, red, yellow or white dashed line polygons, respectively. In addition, you can see an explanatory text with the same colors. Figure 6B shows an example where the soleus is highlighted.

In the upper left section (Figure 2C), the student can move the syringe, its orientation (taking the probe as a reference) can be changed before the puncture is performed using the computer mouse. Subsequently, the student can move the syringe with the mouse, while maintaining the orientation, to simulate the puncture. In this way, the virtual needle will be introduced so it will be shown at the axial slice. As the needle reaches the anatomical structures, the highlighted contours of these structures are interactively displayed as an aid in the practice of the infiltration.

At the same time the needle on the ultrasound video is shown (Figure 2B). The trainee will be able to direct it towards the target point at the muscle to infiltrate the drug. Every time the needle should be prevented from passing through or touching a vein, artery, nerve, or bone (as in real patients). During the puncture, the students will be informed on the ultrasound itself, with green color and a text that the procedure is being performed correctly, when it is a muscular area; or on the contrary, with red color if it is a vein, an artery, a nerve, or a bone.

The simulator will allow the puncture to be performed on the right or left side of the virtual probe, depending on the type of area of the human body in which the puncture is to be performed. In those cases, in which it can be performed on both sides, the student can choose the preferred one. Once the spastic muscle to be infiltrated is reached, the infiltrating the BT gesture is recreated by double-clicking with the right mouse button on the syringe. A halo like the one that would be observed in a real procedure is shown over the ultrasound image.

Ecosystem Efficiency Estimation

The course has been held for 6 editions with a course load of 60 ECTS (European Credit Transfer and Accumulation System) in 1 year and has been attended by a total of, approximately, 240 students.

The designed ecosystem's formative capacity is assessed through a series of multiple-choice tests in each module (Figure 4). These tests assess whether students have acquired the necessary knowledge to successfully pass the module and, indirectly, whether the resources set, and activities designed let reach the expected results.

To ensure a reliable evaluation system, the faculty has built a repository of questions in Aiken format. Each questionnaire consists of 20-30 multiple-choice questions. A limit of 3 attempts per quiz has been set and time is limited to ensure that the student is prepared to pass the quiz. For each test, for each student and each attempt, the questions are randomized from the question bank. Each attempt is graded automatically, where all questions are scored equally, and each wrong answer subtracts a quarter of the score of a successful question. The final grade is the highest grade of the 3 attempts.

When considering the total amount of enrolled students, 92% completed the questionnaires, of which 100% successfully passed the questionnaires. Out of a maximum score of 10 points, the distribution of scores (Figure 7) was 46% with a score above 9 points, 37% between 7 and 9 points and 9% between 5 and 7 points. As an indication of performance, the average mark for the final coursework was 8.5 out of 10 points.

At the end of each of the editions, the students were asked for their opinion on the progress of the course by means of a survey designed by the teaching and technology support team. Five sections related to the student profile, previous experience in an interventional procedure using US imaging, the technical quality of the provided theoretical documentation, technical aspects of the simulation application in terms of installation and usability, and the practical skills developed using the simulators were evaluated.

Regarding the student profile, it should be noted that 85% of the medical specialty is Rehabilitation, 5% Neurology and 10% other health care degrees. Regarding previous experience with an US-based procedure, 93% had experience in US imaging and 35% of them had used it in an interventional procedure.

The second section related to the technical quality of the theoretical documentation available in the LMS and whether it is up to date, the majority opinion of the students is "highly satisfactory" with 76% and "satisfactory" with 24%, while the rest of the answers ("indifferent", "not very satisfactory" and "not at all satisfactory") were not indicated by any of the students.

Figure 7. Distribution of marks obtained by students in the course



Regarding the technical aspects of the simulation app, in terms of ease of downloading, installation and help material, in total, the students considered it to be “high” with 68% and “normal” with 32%, while “low” was not mentioned by any of them. As for the usability of the app and the quality of the GUI, 76% considered it to be “indifferent”, 16% “satisfactory” and 8% “highly satisfactory”, while the other two options “not very satisfactory” and “not at all satisfactory” were not marked. It is not a satisfactory situation, but it was clear that the improvements at this aspect would be desirable.

When the virtual simulator, regarding the 3D anatomical viewer, the students consider that its visual qualities and help in the assimilation of theoretical concepts are “satisfactory” (47%), “indifferent” (42%) and “highly satisfactory” (11%). Concerning the acquisition of practical skills, the majority (94%) rated as “highly satisfactory” the realism in learning experience and an improvement in training in exploration and infiltration by means of US imaging is assessed, and the rest of the students considered it as “indifferent”.

To conclude the survey, the overall rating of the e-learning ecosystem is “high” with 92%, “medium” with 8% and “low” was not indicated, in such a way the satisfaction rating has a clearly positive assessment.

DISCUSSION AND CONCLUSION

In view of the scores obtained by the students on the test and the opinions reflected in the survey, the teaching team considers that the resources that have been made available to the students and the activities proposed have fulfilled the main goals of this e-learning ecosystem, that the medical specialist can carry out a correct infiltration of TB using US. With the offered e-learning ecosystem, students can perform autonomous learning in this specialty from anywhere, without the need to travel, at any time, with great realism and with an unlimited number of attempts.

The teaching team, composed by 6 medical specialists, has carried out an enormous effort, developing more than 50 theoretical chapters and 35 practical scenarios that include an exploration phase and an infiltration phase. It can be seen as an intensive work in capturing real and US photographs, images and videos, and in the elaboration stage for the rest of the theoretical and practical materials for each module. Two professors responsible for each module were appointed as tutors to attend to technical issues. However, student communication with the teaching team through forums and email has been not very high, so it can be desirable a better communication between the students and the teaching team.

In addition, the work of the technical support team, made up of 4 ICT professionals, has been intense. The configuration and management of the LMS, the development of the two simulators, the app to build case studies and the support for the installation of these apps have been the main responsibilities carried out by this team. The simulation apps required an activation code to control the installation of registered users for our ecosystem, which has been mostly respected and few (Picelli et al., 2012) unauthorized installation attempts have been detected. The forum enabled for students to express their doubts or problems in the installation of the supplementary apps (the exception has been related with the US simulator) has a poor participation of students (2 questions in 6 years), which could indicate that the usability of the computing components is very high.

However, numerous queries (more than 100 in the first edition) have been produced through email related to the two main supported operating systems (Windows and Mac-OS). As a corrective action, the ICT team developed videos and help manuals, as well as FAQs, on the installation and operation of the simulator. These made installation easier and significantly reduced (by 90%) the number of student e-mail queries in subsequent editions. Thanks to the obtained feedback through the open questions of the survey and the suggestions of the teachers, the ICT team has been updating the simulator with new versions to improve the visualization of the US images and the navigability and adding new functionalities in the infiltration simulation. In that sense, the app for editing practices has been a success because it has meant an enormous saving of work, both from the point of view of the programming of the simulation software and the practical exercises construction by the teaching staff. The provided ecosystem, especially with the virtual simulator, the application to edit the case studies and the LMS, has a high flexibility and can be easily adapted to training in other types of treatment where an interventional procedure guided by US imaging is performed.

Regarding the course management and organization, the students have mostly raised organizational issues, in terms of timing of activities, grading, presentation of the final master's thesis, certificate awarding, etc. However, as a channel of communication with the course director they have again chosen email. In general, forums have been used minimally and students have preferred to resolve their questions through an individualized channel such as email and have completely discarded the synchronous means that had been established within the LMS, such as videoconferences ("Meeting"). Nevertheless, the recent pandemic scenarios have change the communication channels usability (Martín-Cuadrado et al., 2021).

Considering the use made by the students of the forums and "Meeting", it can be considered that the LMS has not been used to develop collaborative learning, between teachers and students and among the students themselves. It is possible that this lack of collaboration is since students have a high capacity for autonomy in learning and the target capabilities are related with dexterous and, personal, skills.

Thanks to the provided US scanning simulator design and the included 3D anatomical viewer, students can visually and interactively relate the anatomical structures that appear in the US image with those of a cross-sectional anatomical section of the same area and with three-dimensional images. This aspect will accelerate the acquisition of practical skills in ultrasound exploration.

Regarding the infiltration simulator, it recreates with great realism the positioning of the needle inside human tissues as the syringe attitude is modified. In this way, the simulator helps professionals being trained to build a mental model that allows them to direct the needle to correctly apply the corresponding dose of BT on the muscle bellies, without collateral effects on other anatomical structures present in the approach zone.

Although it can be considered unnecessary to use a real ultrasound machine in the described approach, it is important to notice that the training of professionals should always require to practice with an US machine with real patients. In this way, the developed system has a series of possible limitations, such as: it does not include the use of a real probe and syringe; the working environment is two-dimensional, so it is not practiced with a 3D positioning of the real world; when performing the puncture, the professional in training does not perceive a sensation of resistance of the human tissues. The resolution of these aspects will constitute the goal of future research activities. However, as the aim of the training is to learn how to perform a puncture on a patient, with the developed training simulator, the professional would already have many practical skills before facing an infiltration on a person. The professional has been immersed in a safe virtual experience where he/she can make mistakes and thus learn from these ones.

The developed ecosystem has been able to allow that more than 240 professionals from different geographical areas, mainly in Spain and Latin America, have completed a highly specialized training without moving house and without leaving their workplace. The first two editions were financed by companies in the health sector, specifically companies in the pharmaceutical sector. In the following editions, the number of students enrolled was drastically reduced, as each student had to support the cost of enrollment. Therefore, having regard to this enrollment trend, and given the importance of the training provided, it would be essential that the institutions or organizations where professionals work should finance these specialization courses in advanced techniques. The main result of this will be the implementation of these techniques in daily clinical practice and, therefore, an improvement in the quality of the service offered by the health organization (public or private) to its patients. Therefore, the well-being and health of the people will be particularly benefited.

Nowadays, the team works are related with the construction of Human-Machine Interaction (HMI) devices that let the user to reach a more realistic immersion at the simulation activities that can be seen as a key element of the presented ecosystem (Vidal Moreno et al., 2018). More concisely, a real replica of a US probe has been designed to record the human movements at the exploration, especially the ones that are related with the rotations and displacements that define the attitude and position of a real probe at 3D scenario. Several kinds of advanced sensors will be used, and real time restrictions will be met. Thus, in the US-guided MSK exploration simulator, the virtual probe will be replaced by a physical and realistic probe that is built using a 3D printer. In addition, the “Robotics and Society” research group is working on a real needle that incorporates integrated sensors to follow the movements made by the specialist in US-guided infiltration tasks. Instead of the movements of a virtual syringe with the desktop mouse, the user can get the best practice with real needles, i.e., the same ones used in infiltration procedures. The device will have several on-board sensors that will detect the hand movements made by the healthcare professional. However, both devices, i.e., the probe and the needle, must be fully integrated in the simulation procedure of the developed ecosystem.

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Chapter 4

Magnetic Resonance Imaging Simulator: From a Proof of Concept to a Useful Tool in the Education of Radiographers

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ABSTRACT

Magnetic resonance imaging (MRI) is one of the most powerful medical imaging modalities available. From an educational perspective, MRI faces a difficult challenge. Operating an MRI scanner is a complicated task due to the fact that it is based on advanced concepts borrowed from physics. A large number of parameters are involved and hands-on training for practitioners is usually scarce due to the high costs of the equipment and the increasing clinical demands, which make MRI scanners intensively exploited facilities. In this context, the development of computerized simulations for MRI seems a natural alternative. This chapter reports an actual experience on the creation and evolution of an MRI simulator for educational purposes, thus obtaining an increasingly refined set of functional and usability requirements that such a system must fulfill in order to make an impact in MRI education, quantifying the usefulness of the simulator in realistic settings and providing technological solutions and strategies to overcome its limitations.

INTRODUCTION

Magnetic Resonance (MR) Imaging (MRI) is the medical imaging modality of choice for many clini-

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cal applications. Its advantages include the use of non-ionizing radiation, the good contrast that it can provide (specially in soft tissues), the capability of acquiring information in any anatomical plane (and also 3D volumes), the flexibility due to the enormous amount of sequences that can be employed, and its capacity to obtain not only anatomical information but also functional details.

However, all these advantages pay a price. Some of the most important disadvantages are the high cost, the relatively long acquisition times and the qualitative nature of the images that are obtained (at least when using conventional sequences).

From an educational perspective, MRI also faces a difficult challenge. Operating an MRI scanner is a complicated task, due to several reasons. First, MRI is based on advanced concepts from different scientific fields, such as nuclear physics, electromagnetism and signal processing. All of them can be hard to grasp for technicians during their training. Secondly, a high number of parameters are involved in the acquisition process, and their choice can have a big impact on the quality of the resulting images, the duration of the acquisition process and the possible presence of imaging artifacts. On top of that, each manufacturer employs its own console and nomenclature, which has shown to be a problem also for radiologists (Jorritsma, 2016). Finally, hands-on training for students is usually very scarce, due to the high cost of the equipment and the clinical demand on the scanners, which make MRI scanners intensively exploited facilities.

In this context, creating computerized simulations for MRI seems a natural alternative, similarly to flight simulators that have been developed for pilot training, for instance. This type of simulators has the potential to provide unlimited training time, and also make it possible to acquire a deeper understanding of the physical and technological foundations of MRI. Hence, several MRI simulators have been proposed in the literature. Most of them, however, were not designed for educational purposes, but for other goals such as sequence prototyping and optimization, artifact simulation or the analysis of the effects of patient motion, among others.

In this chapter we describe an actual experience on the creation and evolution of an MRI simulator for educational purposes. Our objective is to identify a set of functional and usability requirements that such a system should fulfill in order to make an impact in MRI education, together with its implementation. Since sequential educational experiences have been conducted, requirements have been progressively identified. Each step along the way in the creation of the simulator is referred to as *Version*, which is labelled with a number. Each version, whenever possible, is accompanied with a quantification of its usefulness in realistic settings as well as the provision of technological solutions and strategies to overcome its limitations.

BACKGROUND

The Internet, its and Education in Medicine

It is currently indubitable that the Internet has brought a revolutionary impact in many aspects of our societies (Leiner 2009). Almost every activity in our personal and social lives has been changed by this phenomenon, and education is not an exception. A first consequence in this context has been the democratization of the access to information, which is now easily available everywhere and every moment. As a result, younger generations have developed an increased interest in a personalized, practical and delocalized education. Web-Based-Education is a natural response to this interest (Papachristos

2011, Peredo 2011), and there are nowadays multiple platforms (some of them have been created from traditional academic institutions, while others are independent from them) offering every sort of courses and educational resources via web. MOOCs (Massive Open Online Courses) are a good example of this, and they have proliferated to the point of being part of the academic portfolio of every academic institution of higher education.

In Medicine, web-based education is also present. However, although this technology can successfully address many of the educational needs in theoretical situations, limitations arise when this training incorporates a higher practical component. This is the case, for instance, when learning surgical techniques, where it is clear that specific technological solutions are needed to cope with the interaction of the trainee with a complex environment. One technological response to this challenge is the development of surgical simulators, which try to reproduce the complexity of surgical situations, sometimes also making use of physical devices for user interaction.

When acquiring practical skills in web environments or using simulators, guiding the student through the operation of these (inherently complex) systems or through the learning process becomes a problem. In this context, the first Computer-Assisted Instruction (CAI), Intelligent Computer-Assisted Learning (ICAL) or Intelligent Tutoring Systems (ITS) appeared in the early 70s of last century.

The term ITS was however coined in the 80s, and refers to the application of Artificial Intelligence techniques to the adaptive execution of tutoring and learning activities (Sleeman 82). Since then, such systems have been proposed in different areas, such as military training (Hill 2006, Mulgund 1998, Stottler2006), teaching children how to read (Mostow 2001) and applications in mathematics, physics or even microbiology (Pane 2014, Arroyo 2014, Schulze 2000, Sabourin 2012).

A recent review on the use of ITSs in education (Mousavinasab 2018) showed that a high number of such systems have been developed for applications related to Medicine and Health Sciences. Also, these systems have shown to be effective, obtaining results comparable, or even superior, to those of human tutors (VanLehn 2011, Ma 2014).

Some examples of ITSs applied to this field include a virtual simulator for anesthesia (Jeon 2007) or a system that helps develop diagnostic skills in clinical situations (Kazi 2012).

Regarding MRI, however, no simulator has ever incorporated an ITS, to the best of our knowledge.

MAGNETIC RESONANCE IMAGING SIMULATORS

As stated before, MRI is a very powerful and versatile imaging technique, as well as complex. Thus, many simulators have been developed in the last years, designed for different purposes such as education or sequence development. Next, we review the most relevant MRI simulators describe in the literature.

Among those simulators designed for educational applications, we can highlight the following:

- Bloch Simulator (Hanson 2007). It is focused on the basic physical concepts in magnetic resonance, as well as the Bloch equations (Bloch 1946). It allows the user to work on concepts such as magnetic resonance as a physical phenomenon, or spin dephasing and rephasing. It is possible to modify different parameters and observe their influence on the behaviour of the system through graphical plots. With regard to the technology employed, it was implemented using Adobe Flash Player, which may cause compatibility problems in modern browsers. This simulator can be reached at <https://www.drcmr.dk/BlochSimulator/>

Magnetic Resonance Imaging Simulator

- Simplified MRI (McKagan 2008). It is part of a broader system for training in quantum mechanics, and generates graphical descriptions of the behaviour of the nuclear magnetic moment in presence of an external magnetic field or a radiofrequency pulse. The simulator works on a Java virtual machine, which makes it portable but not very easy to use. It can be reached at <https://phet.colorado.edu/en/simulation/mri>
- Virtual MRI (Hackländer 2005). This system emulates some of the main elements of the acquisition process in an actual MRI scanner. The user can choose among several acquisition sequences, and modify some parameters such as echo time or repetition time. The result of the acquisition can be visualized in the k-space, and some basic artifacts, such as motion, can be simulated. However, only one axial brain slice can be acquired, and no 3D geometrical planning is included. As the system described earlier, it was developed using Java, and it is available at <http://www.iftm.de/index.php/e-learning/virtual-mri/downloads>
- Torheim simulator (Torheim 1994). Similar to VirtualMRI, it was however developed several years earlier. It also allows the addition of simulated lesions to the model, and it was developed in C++.

Among those MRI simulators developed for non-educational purposes, the following are especially relevant:

- MRILab (Liu2013). It was created to support the development of new MRI techniques, and has kept evolving after its initial version (Liu 2017). It is based on the simulation of the evolution of the magnetization vector using the Bloch equation, which implies a high computational cost even though it allows the use of GPUs (Graphic Processor Units). The system works on Matlab, but the simulation kernel runs on code developed in C/C++ or CUDA. This last option requires code configuration and compilation, which makes the system unsuitable for users who are not experts in informatics. The system is available at <http://mrilab.sourceforge.net/>
- JEMRIS (Jülich Extensible MRI Simulator) (Stöcker 2010). It is focused on sequence development. Using Bloch equations, different gradients or coil configurations can be simulated, as well as the effect of magnetic field inhomogeneities or the computation of the chemical shift. Like MRILab, it works on Matlab but the simulation kernel was coded in C++, so compilation is needed. This simulator can be reached at https://www.jemris.org/ug_downl.html
- POSSUM (Physics-Oriented Simulated Scanner for Understanding MRI) (Drobnjak 2006). It was designed for research on some MRI artifacts, such as motion, field inhomogeneities or chemical shift. Among other purposes, it has been employed for the quantitative comparison among different postprocessing methods for diffusion MRI (Graham 2016). It is available at <https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSL>
- SpinBench (Overall 2007). It simulates pulse sequences, and its graphical interface allows their design and creation without the need to program them. This simulator, however, does not generate MRI images, and is available at <https://en.freownloadmanager.org/Mac-OS/SpinBench-FREE.html>
- PSUdoMRI (Cao 2010). Again, this tool is oriented to the realistic simulation of magnetic fields for the computation of the signal and noise in magnetic resonance. It allows the generation of contrast images, noise maps and magnitude and phase images for each coil, and the result of the

reconstruction, including the k-space. It also works on Matlab but with a simulation kernel in C/C++.

Beyond these simulators, other similar tools include MRISIMUL (Xanthis 2013), BlochSolver (Kose 2017) and ODIN (Jochimsen 2004).

Several important conclusions can be extracted from the review of the existing MRI simulators. First, most of the research-oriented simulators use a simulation kernel based on solving the Bloch equations. Even though this approach allows more realistic simulations and incorporating some artifacts such as those related to field inhomogeneities, its high computational cost makes it unfeasible for educational simulators, where short response times are critical in order to allow a smooth learning activity.

On the other hand, most educational simulators focus in the physical foundation of magnetic resonance, but not in the acquisition process (with the notable exceptions of (Hackländer 2005) y (Torheim 1994)). Even in these two cases, however, geometrical planning is not considered, at least from a 3D perspective.

With regard to implementation and availability, research-oriented simulators are usually desktop applications, or even code that needs to be compiled, making them impossible to use for non-expert users. Education-oriented simulators, on the other hand, usually offer easier distribution. However, we are not aware of any MRI simulator that emulates the acquisition process and that works as a web application.

DECISIONS ON HOW TO SIMULATE IMAGES IN EDUCATIONAL MAGNETIC RESONANCE

From a mathematical point of view, simulating magnetic resonance images, depending of the type of acquisition sequence and the parameters employed, essentially requires two groups of ingredients: the availability of maps with the physical properties of the tissue (relaxation times T1 and T2 and proton density, PD, these maps are usually referred to as relaxometry maps), and the use of a physical model that allows the computation of the resulting image from those data.

With regard to the relaxometry maps, we must realize that the result of an MRI acquisition is an image where every pixel depends, on the one hand, of these three parameters, and on the other hand, on the acquisition sequence and other acquisition parameters such as TR (repetition time) and TE (echo time). Relaxometry can be performed following different approaches, the most common involving the use of specific acquisition sequences that provide several images from which a physical model is applied to estimate the desired parameters.

This strategy, however, suffers from several drawbacks. The first is that the acquisitions needed for relaxometry are in general very long, especially the one needed for the estimation of the T2 map. Since the maximum resolution that can be simulated is limited by the resolution of these relaxometry maps, they must be acquired at the higher possible resolution. As an example, the acquisition needed for the computation of relaxometry maps for the brain, at a resolution of 1x1x1 mm³, took more than 90 minutes. This problem limits the number of relaxometry maps from different subjects and anatomical areas that can be acquired, and makes it almost impossible to obtain maps in cases with pathology, due to evident ethical reasons.

Some technological alternatives have appeared in the last few years for the estimation of relaxometry maps. One of them is known as MRI Fingerprinting (Ma 2013), and employs special acquisition sequences that afterward allow the identification of the physical parameters of the tissue. These sequences,

however, are not available in commercial scanners. A different possibility is the application of Artificial Intelligence algorithms for the obtention of relaxometry maps from conventional sequences (Moya 2020, Moya 2021).

With regard to the physical model for the simulation of the resulting images, there are essentially two alternatives. The first one consists in solving the Bloch equations, which describe the magnetic resonance phenomenon. Their iterative resolution allows to follow the magnetization of spins at each voxel, and this way the resulting signal intensity can be computed depending on the type of sequence and the parameters involved. The main advantage of this approach is the high realism that can be achieved in the simulated images, and the possibility to naturally simulate some artifacts such as those related to magnetic field inhomogeneities. However, the main disadvantage is the high computational cost that this simulation implies, due to the series of complex mathematical operations that are needed for each voxel that is simulated. A parallel implementation of this procedure provides a great acceleration (Moya 2017), but requires the use of GPUs, a hardware resource which is costly and not available in most personal computers. Most research-oriented simulators employ this kind of approach.

Alternatively, many of the most common sequences in MRI are described by closed-form mathematical expressions for the image intensity at each point. For instance, the mathematical expressions for Spin Echo and Gradient Echo sequences are the following [Liang2000]:

$$A = M_z^0 \left(1 - e^{-TR/T1}\right) e^{-TE/T2}$$

$$A = M_z^0 \frac{\sin \alpha \left(1 - e^{-TR/T1}\right)}{1 - \cos \alpha e^{-TR/T1}} e^{-\frac{TE}{T2^*}}$$

where A is the resulting intensity signal, M_z^0 is the magnetization at the initial time, TR and TE are the repetition and echo times, respectively, α is the flip angle, and T1 and T2* are the longitudinal and transversal relaxation times (the latter is affected by field inhomogeneities), respectively.

The main advantage of this strategy is its simplicity and low computational cost. However, these simulations lack the realism that can be achieved using the former approach, and besides native simulations of some artifacts cannot be performed.

OUR PROPOSAL

Overall System Conception and Requirement Setting

Starting from the general goal of developing and deploying a MRI simulator that can be used as an educational tool, before proceeding further it is necessary to decide an initial specification of the requirements this simulator must fulfill.

This definition is the result of the analysis of the MRI simulators found in the literature, several meetings and informal discussions with radiologists and technologists who are experts in MRI as well as in software engineering.

The requirements an MRI simulator must fulfill in order to address the desired goals are the following:

- The system must have a user interface similar to the one found in a real MRI scanner. However, particular details of any specific manufacturer must be avoided, as well as employing commercial names.
- The system must include as many steps as possible from those that comprise the MRI acquisition process, and allow the user to carry out these steps in a sequential order, the same way as in a real scanner.
- The system must allow the user to enter personal data for a simulated patient, as well as to select patient position, coil and other details that must be taken into account in the simulation.
- The system must be able to generate simulated MRI images that are the result of the application of common acquisition sequences such as Gradient Echo, Spin Echo, Fast Gradient Echo, etc.
- It must be possible to modify basic parameters of the acquisition process, such as repetition time, echo time, inversion time, ETL (Echo Train Length), etc. Some of these parameters are present in all sequences, while other are specific for only some particular sequences.
- Other parameters that also affect the resulting image must also be editable, such as the number of excitations (NEX) or other options related to k-space (Partial Fourier or Scan Percentage).
- The system must be able to simulate common artifacts in MRI, such as fold over, the presence of noise, motion artifacts, etc. It must be noticed that in a real system deactivating these artifacts is not possible, which makes this a unique feature of an MRI simulator.
- If possible, the system must simulate parallel acquisition techniques, such as SENSE or GRAPPA.
- The system must allow the activation of some imaging options that are common in commercial scanners, such as NPW (No Phase Wrap) or the application of saturation bands.
- Some relevant acquisition parameters, such as acquisition time, signal to noise ratio or SAR (Specific Absorption Rate) must be displayed.
- The images generated by the simulator must have the usual format of medical images (DICOM), and it must be possible to download them.
- The system must allow a 3D geometrical planning of the acquisition, by means of a graphical interface that allows the positioning of the slices, FOV (field of view) selection, as well as the determination of the slice thickness and voxel size.
- The system must allow the application of imaging protocols, defined as temporal sequences of acquisition sequences.
- It must be possible to select some general properties of the scanner, such as the strength of the magnetic field or the value of the field inhomogeneity.
- To the best possible extent, the system must be able to simulate acquisitions with non-conventional MRI techniques, such as diffusion MRI or susceptibility imaging.
- Simulations must be generated in a short time, so as to allow a smooth learning experience by the user.
- The system must include access control and the definition of different roles, such as instructor and student.
- The system must be easy to install and to execute, and must run on different computational platforms.

Version 1

Conception and Design Decisions

Two main strategic decisions had to be made for this first version. Specifically, we had to decide the simulation methodology itself, as well as whether a desktop application or a web-based application was to be developed.

As for the simulation strategy, the approach of using closed-form mathematical expressions was chosen to approximate the image intensity at each point. The reasons that support this decision are:

- Iterative simulations that solve the Bloch equations have a high computational demand, which gives rise to a several minute delay per slice in high resolution images, a fact that hinders the use of such a simulator as an education-oriented instrument. Although this means a realism loss with respect to physics-based procedures, speed seems mandatory to the purposes sought.
- A number of artifacts cannot be natively simulated with this approach (this would be the case of field inhomogeneity) but these artifacts can be approximated ex-post by using, for instance, geometrical transformations on the resulting images.
- The number of sequences that can be simulated with this approach is somewhat limited but we understand this number suffices for a first version of a simulator in which basic sequences are targeted.

About the type of application to develop, a web-based application was chosen with the following motivation:

- A web application does not require any sort of installation in the local computer, which makes simulator distribution quite straightforward.
- Similarly, a web application should be platform agnostic, i.e., Windows, MacOS or Linux users should be capable of using the application “as is”. Such a solution should also work on tablets and cellular phones, although these devices are not considered our priority since geometrical planning would be somewhat intricate on them.
- Updates are immediate to deploy on web applications. This is of paramount importance for an evolving project.
- User access control and user role definition are very simple to implement. Moreover, this makes resource selective access (i.e., access to parametric maps) and privacy issues easy to handle.
- A web application allows the programmer to decide whether highly demanding calculations will be carried out on the client or on the server side. For the latter case, all users may have access to powerful hardware regardless of their local equipment. In addition, flexibility to access massively parallel devices is granted in the case that the simulation strategy is changed to a Bloch-solver solution.

Functionality and Implementation

Functionality of version 1 is, loosely speaking, that enumerated at the beginning of section “Overall System Conception and Requirement Setting”. This simulator was carried out by means of a collabora-

tion between the research group “Laboratorio de Procesado de Imagen” of the University of Valladolid, Spain, and the company GIVEME5D S.L.

The user interface has been developed by following the Model-View-Controller paradigm and was implemented using AngularJS. The server side was programmed in Python using Django. The simulation kernel is coded in C++ and makes use of ITK.

Figure 1 shows an overview of the simulator user interface. Its components are now listed (using the same numbers than those shown in the Figure):

1. Administration panel, which provides access to general simulator controls as well as to the library of protocols.
2. Patient information panel, to enter the expected data.
3. A graphical representation of the patient position within the magnet, which is read from the data in letter d.
4. Patient position panel, where both patient position and coil type are selected.
5. Image main parameters panel.
6. Protocol selection panel.
7. Visualization panel. It is designed to show a pre-visualization of the latest acquisition.
8. Access button to advanced visualization (see Figure 2).
9. Sequence panel. The panel includes the sequence that the selected protocol comprises. Each sequence can be selected for execution.
10. Scanner times panel. Sequence relevant times can be adjusted (TR and TE among others). Some of the parameters may be active according to the specificities of the selected sequence.
11. Advanced additional parameters. Several additional graphical interfaces can be launched for advanced settings. Specifically, access is provided to the geometrical planning interface (ver Figure 3).
12. Acquisition times panel: this panel provides information about additional features of the sequence and it also expects the input of the number of excitations (NEX).
13. Scanner range. It shows numerical values of parameters related to acquisition geometry and K-space extension. Some parameters can be edited.
14. Sequence execution information panel. This panel provides information on acquisition duration, estimated signal to noise ratio and SAR. The “Scan” button (for sequence launch) is located in this panel.

Evaluation: Methods

In this section we describe the experimental work carried out on the first version of the simulator in which we evaluated the user satisfaction after using the simulator. To this end, two experiences were carried out:

Experience I: On-Line Course SERAM-2018

Thanks to the fact that the simulator was developed as a web application, it was used as a learning tool in the on-line course entitled “Principles and Acquisition of Magnetic Resonance” organized by the Spanish Society of Medical Radiology (SERAM). The course took place in 2018, from May through July. 179

Magnetic Resonance Imaging Simulator

Figure 1. Simulator main user interface



Figure 2. Advanced visualization panel. Images can be visualized in detail and acquisitions can be downloaded for local use

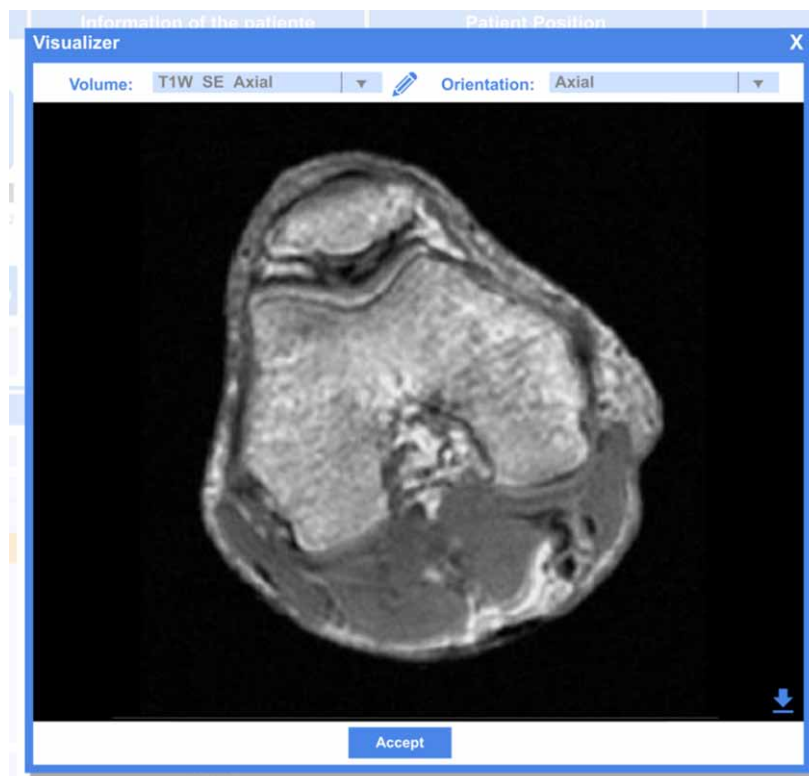
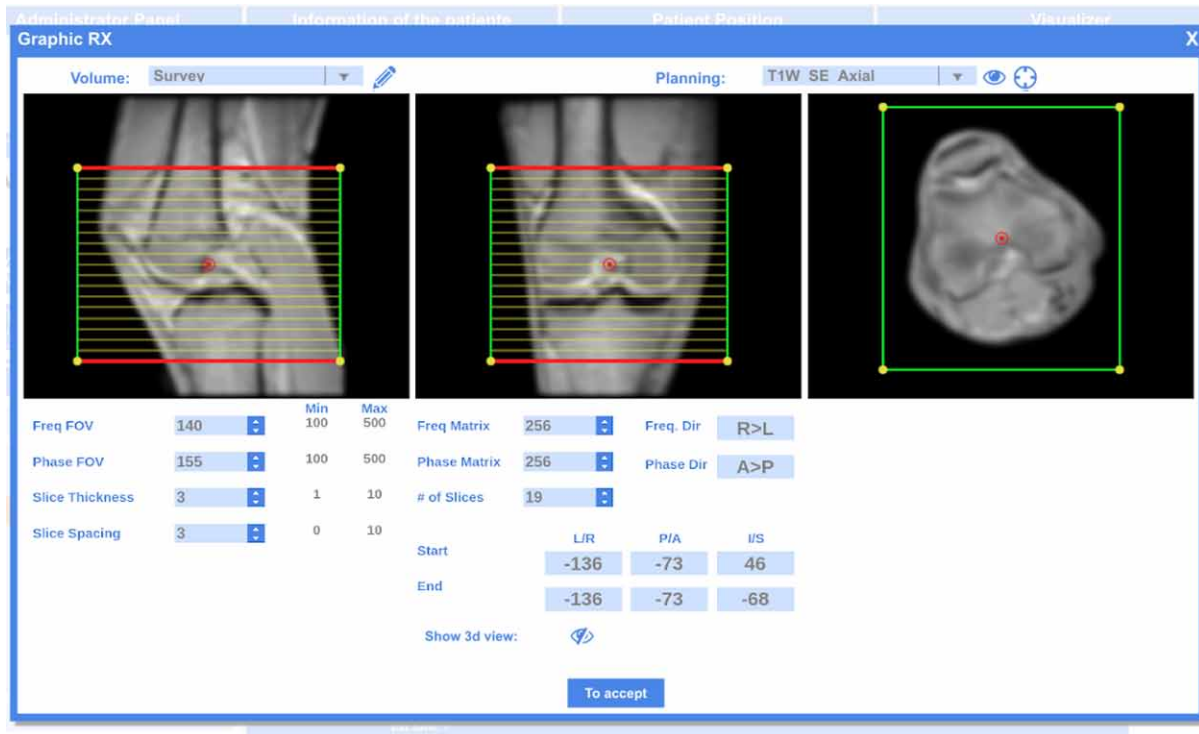


Figure 3. Geometrical planning interface. It is designed to allow the user to adjust the position and angulation of the slices and it shows the planning result on slices in different planes obtained from previously executed sequences. Numerical adjustments are also allowed



students were enrolled in the course and all of them had access to the simulator. Students were provided with a brief videotutorial about the use of the simulator as well as a number of exercises.

For user satisfaction evaluation, a questionnaire known as System Usability Scale (SUS) was used. The questionnaire consists of 10 questions with answers from the 5-point Likert scale and it provides a usability score ranging between 0 and 100 points. Students were asked to fill in this questionnaire at the end of the on-line course. The specific questions were the following (translated here into English):

1. I would like to use the MR simulator frequently
2. I find the MR simulator unnecessarily complex
3. I think the MR simulator is easy to use.
4. I think I need technical support to use the simulator
5. I find the MR simulator functionality well integrated
6. I found too much inconsistency in the MR simulator
7. I think most of the users would quickly learn how to use the simulator
8. I found the MR simulator quite unfriendly and cumbersome to use.
9. I found myself comfortable using the MR simulator
10. I needed to learn a lot of things before being in the position to use the MR simulator

Magnetic Resonance Imaging Simulator

Additionally, students were asked to provide their “Likelihood to Recommend” (LTR), which is another parameter also frequently used in these scenarios. Finally, two more questions were provided to find out about the perceived utility by the students, namely:

11. The MR simulator was useful to me to learn concepts about MR principles.
12. The MR simulator was useful to me to learn concepts about MR acquisition.

Both LRT and the two final questions made use of the same 5-point Likert scale as SUS (for the sake of specificity, the answers were: “strongly disagree”, “disagree”, “neutral”, “agree” and “strongly agree”). In all the measurements, higher is better. Results were then summarized in average values and standard deviation.

Experience II: Presential Session in the School of Radiographers

The second experiment was a (presential) classroom experience. The experience took place in October 2018 at the Hospital Clínico San Carlos, Madrid, with students from its Radiographers School. Participants were recruited from both the first and the second year students of that school; 64 (out of 80 students) agreed to participate in the experiment. Those students had no background on MR technology but for 30 of them who had received a 4-hour introduction to this topic in the past. In this case we meant to measure both student satisfaction and the impact of the simulator in the learning process.

The experience began by giving an exam to the students (say, a pre-test). Grades were ordered and following this ordering pairs of students were randomly assigned to either group 1 or group 2. Group 1 would be selected for a simulator-guided experience while group 2 would not use the simulator. Hereinafter, group 1 will be referred to as “Case” group while group 2 will be “Control” group.

The 64-student group received an introductory 90-minute session about MR principles. Then students were split into the two groups, and both of them were given a second lecture; the difference lay on the methodology. While the Case group received this lecture by means of a hands-on guided tour with the simulator, the Control group received a, say, traditional slide-based presentation. Then the two groups received a second test, the content of which was exactly equal as the pre-test. This second test will be referred to as post-test. Finally, the Case group filled in the same questionnaires as those described for the on-line course, i.e., questions 1 through 12 and the LTR.

Evaluation: Results

116 questionnaires were received (out of 179) from the on-line course students. As for the classroom experience, 29 out of 32 participants from the Case group provided their answers. Table 1 shows average and standard deviation values of both SUS (values between 0 and 100, higher is better) and LTR (ranging from 1 to 5, higher is better).

About perceived utility (questions 11 and 12) in the on-line experience, Table 2 shows the percentage of responses that were either “agree” and “strongly agree” for both questions (rows) and for the two experiences (columns).

As for the on-line course, approximately 25% of the responses to both questions were either “strongly disagree” or “disagree”. As for the classroom experience, no “strongly disagree” responses were found

Table 1. SUS and LTR overall results from the two educational experiences with version 1 (higher is better)

	SERAM on-line course 2018	Classroom Experience (Hospital Clínico San Carlos)
SUS	55,86 $\pm$ 20,56	63,02 $\pm$ 13,39
LTR	3,65 $\pm$ 1,23	4,45 $\pm$ 0,63

in any of the two questions; in addition, question 11 received no “disagree” responses (the remaining 11% were “neutral”) while question 12 received less than 10% disagreements.

As for the impact of the simulator in the learning process, statistical differences were found between the Control and the Case groups in the post-test results ($p=0.036$), while these differences did not exist in the pre-test.

Discussion

The design, implementation and evaluation of the first version of our MR simulator gives rise to some interesting conclusions.

First, a MR web-based simulator satisfied most of the requirements previously stated. To the best of our knowledge, this is the first web-based simulator that is capable of emulating the overall acquisition process as a radiographer would do in daily practice. In addition, the simulator seems to have a significant impact in the learning process according to the Case-Control experiment carried out within the context of the classroom experience.

The design decision consisting in making use of closed-form mathematical expressions, as an alternative to rigorously solving the Bloch equations, provided reasonable simulation times for an educational application. The execution time depends on the selection of the parameters involved (space resolution, slice number etc.) but, loosely speaking, it remained under 30 seconds, so the user observes an acceptable interaction degree. Artifacts can also be included after the ideal image is obtained by adding the appropriate effects, typically on k-space.

The possibility of carrying out the geometrical planning procedure is one of the main ingredients in our simulator. This utility allows the student to gain dexterity in one of the main issues in the acquisition process as well as to observe the effects of an incorrect planning.

As for numerical results concerning user satisfaction, values from both SUS, LTR and perceived utility obtained in the 2018 edition were somewhat modest and showed clear differences with respect to the classroom experience. This may be due to two factors:

Table 2. Percentage of responses “agree” and “strongly agree” for questions 11 (Q11) and 12 (Q12)

	SERAM on-line course 2018	Classroom Experience (Hospital Clínico San Carlos)
Q11	56	89
Q12	59	92

Magnetic Resonance Imaging Simulator

- MR acquisition is a complex task. Hence, a MR simulator cannot be expected to be simple since it should reflect the intrinsic complexity of both the overall acquisition procedure as well as the user interface one will encounter in daily practice. This is parallel to the fact that flight simulators are not simple either since the process they mimic is inherently complex. Therefore, a parameter such as SUS may not be the most adequate for complex simulation programs. However, we are not aware of other measurement instruments specifically designed for this sort of applications.
- In the classroom experience the simulator exercises were guided by the instructor by posing specific tasks to carry out and solving doubts that arose during the execution. This was not the case for the on-line experience, in which the only guidance was a videotutorial.

These conclusions led us to pose the hypothesis that the simulator would substantially improve by incorporating a tool that would guide the student throughout their learning process, which would give rise to a higher user satisfaction and higher perceived utility. Verification of this hypothesis is the purpose of Version 2, which we describe next.

Version 2

Conception and Design Decisions

The main objective of the second MR simulator version is the inclusion of a system that guides the student through the learning process. In order to achieve this goal, we decided to include an Intelligent Tutoring System (ITS); specifically, we chose to use one based on the CTAT technology (Aleven 2016). The system consists of a number of tools that allow the designer to implement and deploy an ITS that stems from a rule-based cognitive model. Put another way, CTAT is based on a number of ordered steps that the student should take to accomplish a specific task. The tool is constantly monitoring the interaction between the student and the simulator and, after evaluating the degree of accomplishment of the rules set beforehand, the tool is able either to suggest the next step, to show a small tutorial on how to proceed or to provide some additional feedback. This strategy seems to fit the MR acquisition process, in which a number of ordered actions have to be carried out in order to complete the acquisition.

Functionality and Implementation

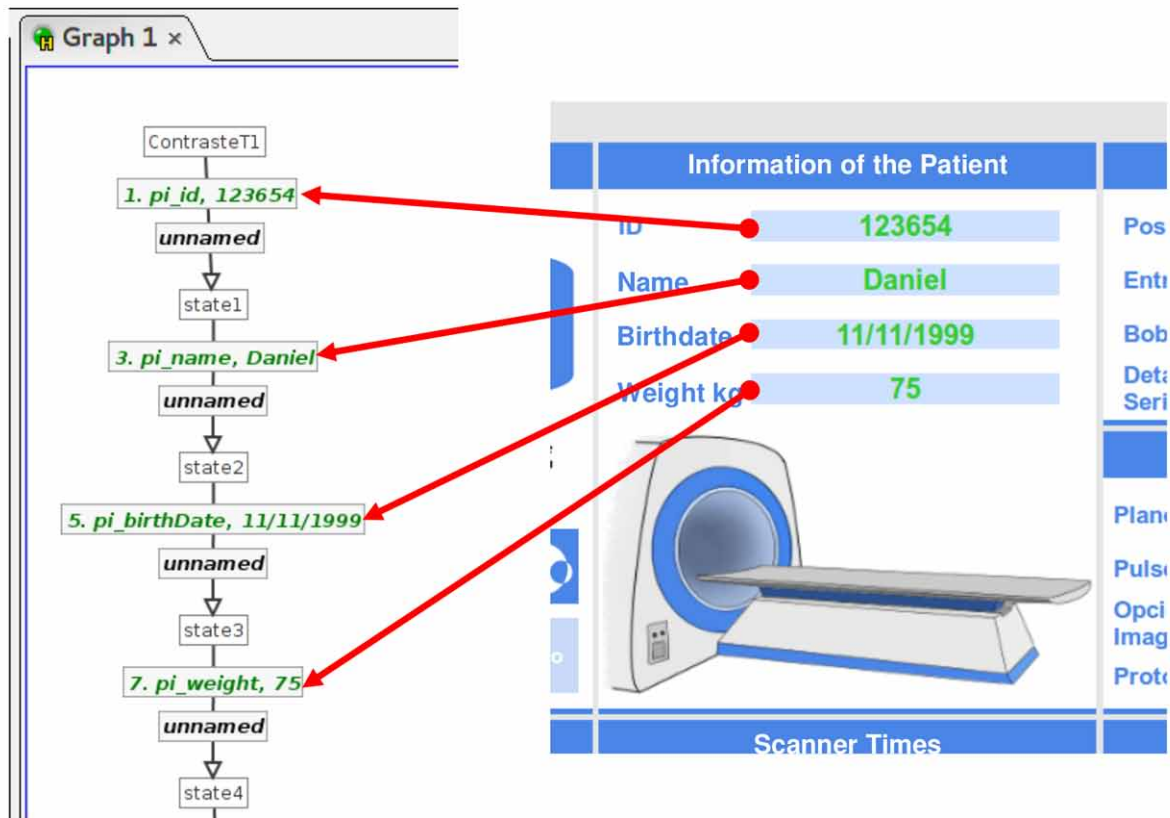
Departing from the functionality described in the first version, the second version includes an ITS that is capable of guiding the student through their learning process.

With respect to implementation, the ITS integration must comply with a number of requirements. First, the ITS should not interfere with the regular simulator behavior, nor should it have an impact on its performance. Moreover, future developments of ITS and simulator should be independent of each other.

Accordingly, the ITS can be chosen to be active only when required. Specifically, the ITS is limited to be active on the number of exercises that have been specifically designed by an expert to be solved with the ITS guidance. The designer has to choose a subset of the parameters available in the simulator about which the ITS will provide feedback along the exercise execution. Figures 4 and 5 show graphical information concerning two instants of the ITS operation. Figure 4 shows the expected student behavior with respect to inserting the information related to the patient (panel b in Figure 1); rules are defined by means of a graphical user interface. Then (Figure 5, left) feedback can be provided either to indicate

the need of modification of some step (red color) or to indicate that the step was correctly taken (green color). Feedback from the ITS can also be provided by mean of an informative message (right).

Figure 4. An example of how to define, by means of a graphical interface, the expected student behavior to insert patient information into the simulator



Evaluation: Methods

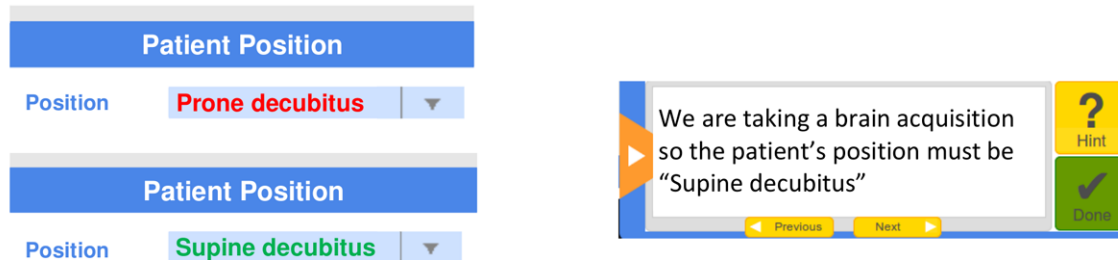
In this section the experimental work carried out on the second version of the simulator is described; specifically, the user satisfaction after using the simulator with the integrated ITS was evaluated.

Experience: On-Line Course SERAM-2019

Approximately one year after the celebration of the 2018 SERAM on-line course, described in the first version of the simulator, the second edition of the on-line course was celebrated. The course started on May 2019.

The MR simulator was used in this second edition as a complementary tool in the course and the ITS was made available as an additional help for some specifically-designed exercises. The ITS was set

Figure 5. Examples of feedback provided to the student by the ITS; (left) by means of a color code or (right) with an informative panel



as optional for the course participants and all of them were informed that the intention was to evaluate the tool for research purposes.

The same measurement instruments used in the first version (i.e., SUS, LTR and perceived utility) were also used here, so that results could be compared between the three editions. In this case, questions 1 through 12 described above were slightly modified so that they explicitly mentioned the presence of the ITS with the MR simulation tool.

Evaluation: Results

27 students chose to fill the questionnaire out of 176 enrolled in the course. The number may seem somewhat low but we recall that the activity was set as optional in the course. Anyway, SUS results are considered stable when participants are above 12 (Tullis 2004).

Table 3 shows average values and their standard deviations for the SUS scale (within the interval 0 through 100), LTR (scale from 1 through 5). Remember that higher is better. The three experiences described so far (the two leftmost columns correspond to experiences with version 1 and the rightmost column with version 2) have been gathered together for easier reading.

About perceived utility (questions 11 and 12) in the on-line experience, Table 4 shows the percentage of responses that were either “agree” and “strongly agree” for both questions (rows) and for the three educative experiences (columns).

As for the 2019 on-line course, approximately 11% of the responses to both questions were either “strongly disagree” or “disagree”. Question 12 received only a few “strongly disagree” responses, on the approximate amount of 3%.

Table 3. SUS and LTR overall results from the three educational experiences (higher is better). The rightmost column includes the ITS in the simulation tool

	SERAM 2018 online course	Classroom experience. San Carlos Clinical Hospital	SERAM 2019 online course
SUS	55,86 ± 20,56	63,02 ± 13,39	68,33 ± 20,87
LTR	3,65 ± 1,23	4,45 ± 0,63	4,15 ± 1,17

Table 4. Percentage of responses “agree” and “strongly agree” for questions 11 (Q11) and 12 (Q12)

	SERAM 2018 online course	Classroom experience. San Carlos Clinical Hospital	SERAM 2019 online course
Q11	56	89	88
Q12	59	92	88

Overall, results seem to indicate that the inclusion of an ITS improves both SUS and LTR in equivalent scenarios (i.e., when the 2018 and 2019 on-line courses are compared). Results are not as high as those obtained in the presential experience, since the ITS seems not to be able to completely replace the guidance of an expert in the simulator. Similar comments apply for perceived utility.

Discussion

Inclusion of an ITS in the MR simulator showed that it is technically feasible to use CTAT technology with an existing web tool without modifying its behavior and with a reasonable student satisfaction. The ITS seems not to overload the MR simulator so its performance remains acceptable for students, according to the figures we have described above. The ITS seems to increase user satisfaction, when measured in comparable situations, although human interaction for receiving feedback seems preferred.

Although technically speaking the overall goal seems achieved, room for improvement exists so that the tool may have a leading role in the curriculum of radiographer schools. To this end, different conversations with radiographers, radiologists, teachers of those schools and the simulator development team were conducted. This process let identify several limitations that hindered the adoption of the tool as the main learning instrument:

- The number of regions that we are able to simulate is somewhat reduced (currently: brain, knee, angle and shoulder). In addition, no pathological cases are available for simulation. This limitation stems from the difficulty in obtaining parametric maps, which are needed for simulation. As previously stated, sequences are quite long and they are even longer if some sort of synchronism is needed, as it would be the case of abdominal imaging. Volunteers may be targeted (without synchronism) but recruiting patients to this end is out of the question.
- Physical phenomena involved in magnetic resonance imaging are intrinsically complicated and its profound comprehension is not easily achieved even though a simulation tool is used. The effects of many of these physical phenomena are somewhat indirect and subtle so as to be easily perceived.
- Similarly, the details of the sequences involved are difficult to understand, even the most basic of them. This is due to the fact that, with both a real scanner and the simulator, students can only observe the effects of the complete and correctly designed sequence so the effects of each its components cannot be analyzed in isolation.

These limitations are the starting point for the conception and development of the next simulator version, which will be described in next section.

Version 3

Conception and Design Decisions

The limitations identified in the previous section after the conversations with experts in the field led the designers to define the following priorities as for the third version:

- To integrate the simulator in a learning management system (LMS) that gives room to specifically-targeted simulators (STS). These STSs should be designed to help understand a particular concept related to MR imaging.
- To extend the number of anatomical regions for which simulations could be possible.
- To incorporate in the simulator images with pathology despite the simulation itself cannot be fully accomplished (i.e., parameters cannot be changed but geometrical planning and some artifacts could be available).

Functionality and Implementation

The functionality available up to version 2 has been extended within the context of an LMS to include the following functionality:

- A number of STS have been included. Specifically:
 - Rectangular filtering in K-space (see Figure 6). K-space acquisition is allowed to be limited by means of a rectangular adjustable window and its impact on the images is immediately observed. It is specifically targeted to ease comprehension of spatial frequencies and their impact on imaging.
 - K-space subsampling (Figure 7): in this case one line out of M ($M=1,2,3$) are retained and (folded) results are presented. This STS illustrates that K-space line separation cannot be arbitrary for a specific FOV.
 - Non-periodic motion (Figure 8). This STS shows the effect of simulated motion of the patient during the acquisition. Both motion intensity and direction are adjustable.
 - Cartesian acquisition in K-space (Figure 9). This is an animation that illustrates how K-space is sequentially populated and what the effect on the image is.
 - Sequence editor (Figure 10). This is a basic sequence editor in which several building blocks (gradients, radiofrequency pulses etc.) can be placed with some ordering and a number of parameters can be set. It allows the student to create a sequence and to see its effects.
- Partial simulations are allowed. In these cases, we depart from conventional weighted images (as opposed to parametric maps). The simulator, in this case, provides the capacity to carry out geometrical planning and to modify its associated parameters. Contrast, however, is not changeable. These partial simulations allow the user to deal with pathology in the simulation as well as to re-slice the available volumes.
- Viewer of interesting cases: An additional viewer is incorporated in the LMS. Specific question on the cases can be posed and markers can be added for easier guidance.

Figure 6. Two snapshots of the STS related to rectangular filtering in K -space. In the upper figure K -space is complete. In the lower, vertical frequencies are limited and the effect on the image is shown on the right hand side; F.V. and F.H. stand, respectively, for vertical and horizontal frequencies and the sliders adjust a percentage of the frequencies allowed for image reconstruction

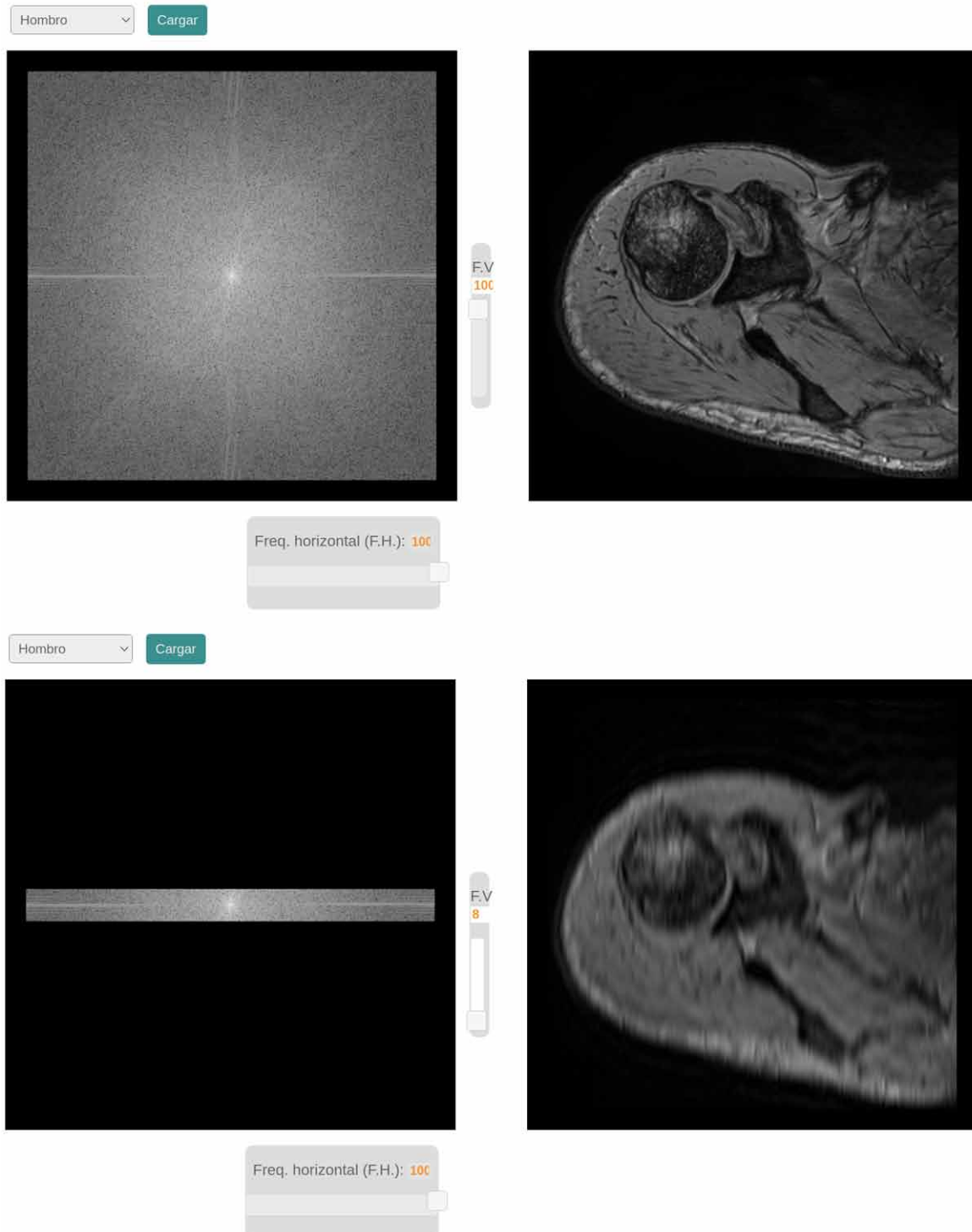
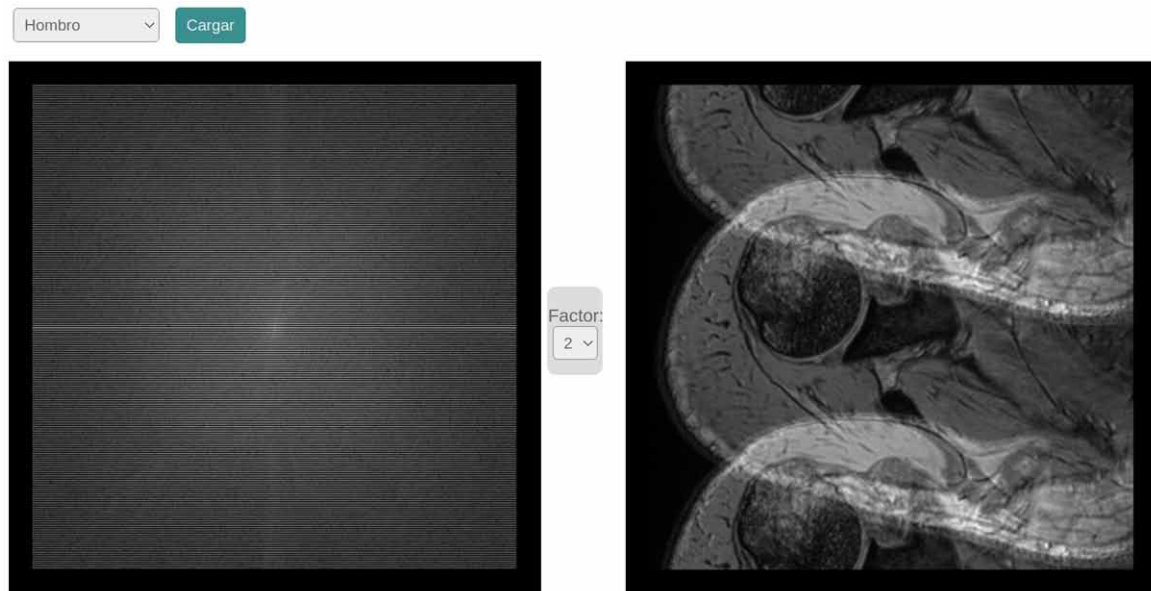


Figure 7. Snapshot of “K-space subsampling” STS



Evaluation

Implementation of version 3 was finalized on the spring of 2021 so no evaluation in an actual educational context has been carried out so far. However, a new edition of the on-line SERAM course is scheduled for the fall of this year. In this new edition a similar methodology to that used in the previous experiences may be followed to measure SUS, LTR and perceived utility for comparative purposes.

FUTURE RESEARCH DIRECTIONS

In the short term, and as previously stated, the impact of version 3 in terms of student satisfaction should be measured and compared to the previous version. The improvements made, together with a number of exercises that fully exploit the potential of the new functionality give room for optimism with respect to the impact the new version may cause in the students. Remember that not only functionality in the main simulator has been included, but an overall LMS –that can be specifically tuned to the learning needs of different and diverse audiences– has been provided. In addition, the fact that pathology is now available to students by means of partial simulations, together with a viewer of interesting cases, extends the breadth of possibilities for advanced learning.

Including pathology in the main simulator is a mandatory step and reported results (Moya 2020, Moya 2021) concerning Synthetic MRI provide some degree of optimism. The capabilities of a convolutional neural network (CNN) to generate parametric maps out of conventional weighted sequences has been described; indeed, satisfactory results are achievable when a network is trained on the basis of synthetic images. Specifically, by making use of synthetic maps obtained directly from BrainWeb (Cocosco 97) and creating weighted images from closed-form expressions, the CNN is trained with a fully synthetic

Figure 8. Snapshot of the “Non-periodic motion” STS

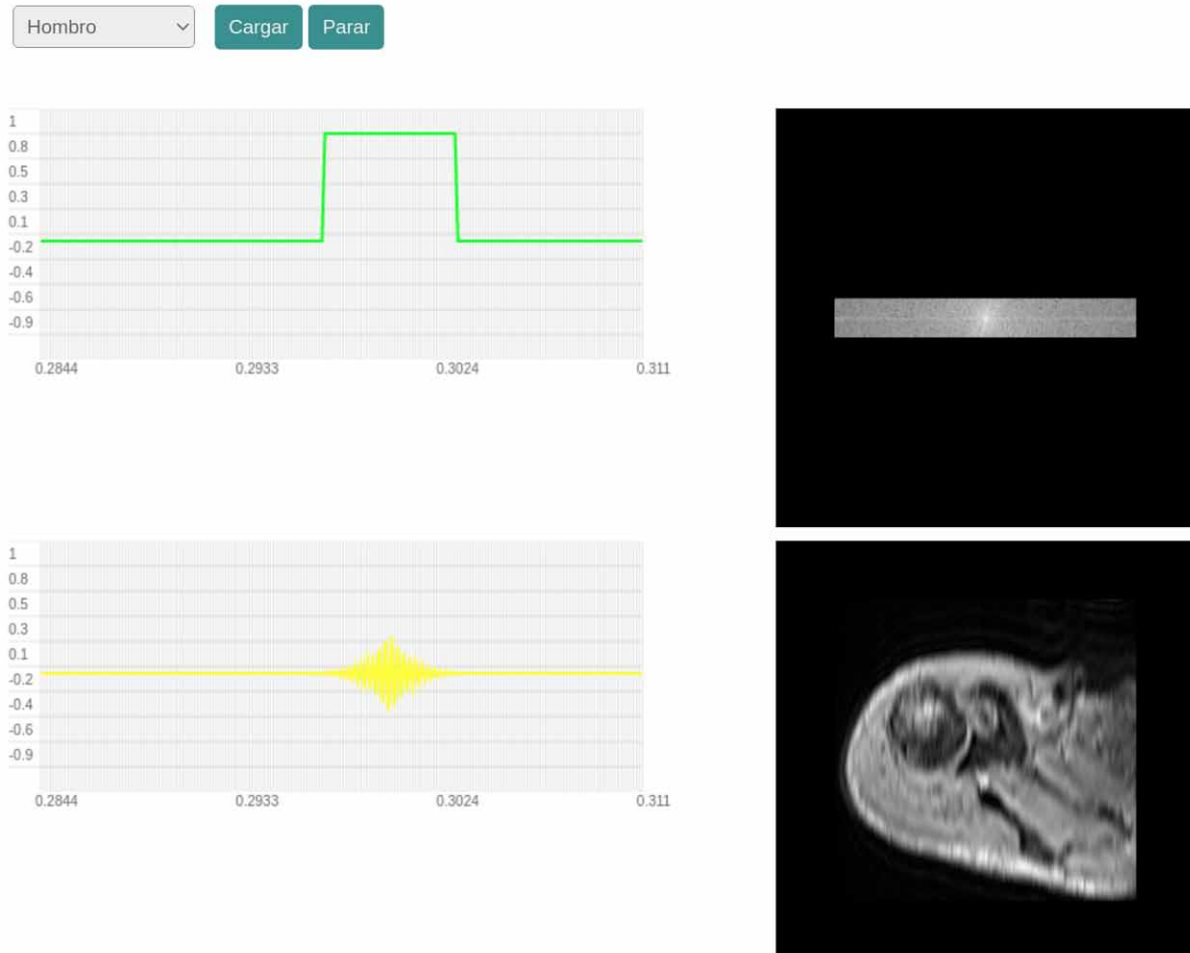


database; the inputs to the network are two customary weighted images (with T1 and T2 weighting) and outputs are the three parametric maps that need for MRI simulation. Once the network is trained, if conventional weighted images are used as input, the parametric maps obtained at the output have a nice resemblance with the actual maps obtained from specifically-designed sequences. A simple refinement with a few pathological cases is expected to provide useful results as for pathological maps.

On the other side, one of the design decisions made was to use a simple simulation engine based on closed-form expressions. This *per-se* gives rise to a limitation in simulation capabilities. Hence, more involved simulation procedures seem a natural extension for the simulator. This has the immediate consequence of requiring higher computational capabilities. In order for this requirement to be satisfied but, simultaneously, being able to run both in multithreaded CPUs, GPUs or any other device, we understand that a language such as OpenCL is a nice candidate to explore. OpenCL is an open standard for parallel computing, similar in its objectives to the nVidia-exclusive CUDA language, but it covers a much wider set of computing devices (including nVidia GPUs) while ensuring that source code and data are unique, thus avoiding the need for code and data replication among prospectively supported devices. However, it is generally regarded as more complicated and less mature than CUDA. As a matter of fact, OpenCL programmers must deal on their own with device selection and initialization, memory management, kernel loading and compilation, host-device interaction and administration overload. The framework OpenCliper (<http://opencliper.lpi.tel.uva.es>) has been designed to manage the OpenCL complexity just mentioned and to offer developers direct interaction with device kernels, host processes and data so that they can focus on algorithm development exclusively. This seems the natural choice for the new endeavor.

Magnetic Resonance Imaging Simulator

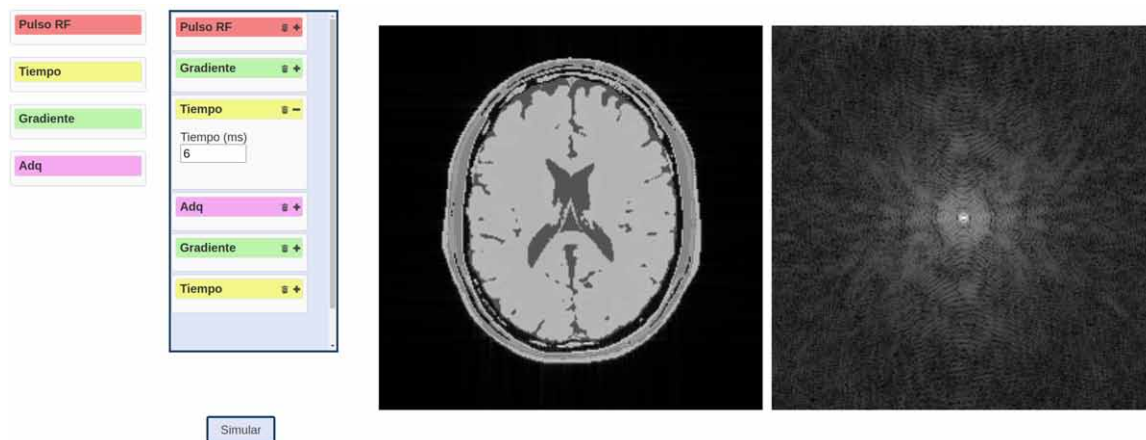
Figure 9. Snapshot of the “Cartesian acquisition in K-space” STS. The green signal represents the activation of the frequency encoding gradient while the yellow signal represents the echo. The acquired image is represented on the right hand side, both directly in K-space (upper) and in the image space (lower)



CONCLUSION

This chapter describes the authors experience in the design, implementation and testing of a magnetic resonance imaging simulator intended to ease the radiographers learning process. To this end several discussions with the involved stakeholders have been conducted, the results of which have been structured in three versions. Version 1 consisted in the core of the simulator; the main decisions concerning the simulator were made at this point, specifically, to develop a web application and to use a somewhat simple simulation engine but with minimal delays to guarantee fast user interaction. This version was used in two academic experiences in 2018, one of them on-line while the second one was a presential classroom experience. Lessons learnt from this experience, specially from the former, led the authors to include an intelligent tutoring system in the simulator. To this end, the appropriate technology was identified so that such a tool could be included without compromising either simulator functionality

Figure 10. Snapshot of the “Sequence editor” STS. On the leftmost panel the building block menu is displayed. These blocks can be dragged into the blue-filled rectangle to create the sequence. One of the blocks has been opened to show the adjustable parameter. Once the sequence is built it can be launched by pressing the button labelled as “Simular”. The images on the right hand side represent the acquisition both in image space (left) and on K-space (right)



or its performance. The simulator with the ITS has been referred to in the chapter as Version 2. This release was used in a second on-line experience, in this case, starting in the spring of 2019. Finally, additional conversations with other schools helped the authors to conceive the tool as a part of a learning broader ecosystem in which additional tools should be made available to students. These tools include both specifically-targeted simulators as well as additional facilities for dealing with pathological cases. This comprehensive tool has been referred to as Version 3.

In this effort the authors have also pursued to quantify the impact of their tool in the students that have made use of it. Quantification has been twofold. On one hand, the authors have measured student satisfaction, in terms of three parameters, namely, usability (SUS), likelihood to recommend (LTR) and perceived utility. On the other, the authors have also quantified whether an MR simulator gives rise to a significant effect on the student learning process. For this second point a simple, yet methodologically rigorous, Case-Control study with a pre-test and a post-test was designed. Results for the student satisfaction analysis indicate that the progressive refinement described had an impact on satisfaction as for the on-line courses. As for the impact of the learning process, the Case group showed higher grades than the control group, with a significative difference. Finally, version 3 has not been so far tested, although this is something to accomplish immediately.

Hence, the authors have identified a number of requirements that an educationally-oriented MR simulator should satisfy to have a measurable impact, for which the authors have acted accordingly. It is expected that the ideas described for further improvement will let the simulator move forward in the educational path the authors have traced.

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Magnetic Resonance Imaging Simulator

Treceño-Fernández, D., Calabia-del-Campo, J., Bote-Lorenzo, M. L., Gómez-Sánchez, E., de Luis-García, R., & Alberola-López, C. (2020). Integration of an intelligent tutoring system in a magnetic resonance simulator for education: Technical feasibility and user experience. *Computer Methods and Programs in Biomedicine*, 195, 105634. doi:10.1016/j.cmpb.2020.105634 PMID:32645627

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Chapter 5

Smart Splint Development: New Technologies for Diagnosis During Initial Stages of Treatment Applied to Splints – New Therapy Possibilities

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ABSTRACT

After suffering a fracture in an upper or lower limb, a plaster cast is placed on the affected limb. It is a very old and efficient technique for recovery from an injury that has not had significant changes since its origin. This project aims to develop a new, low-cost smart 3D-printed splint concept by using new sensing techniques. Two rapidly evolving advanced manufacturing (AM) technologies will be used: 3D scanning and 3D printing. This is possible thanks to the application of engineering on additive manufacturing techniques and the use of biocompatible materials available in the market. This study proposes the use of these materials and techniques, including sensor integration inside the splints. The main parameters considered to be studied are pressure, humidity, skin colour, and temperature. These aspects are combined and analyzed to determine any kind of unexpected evolution of the treatment. The goal of this study is to generate a smart splint by using biomaterials and engineering techniques based on the advanced manufacturing and sensor system for clinical purposes.

INTRODUCTION

Currently, 3D technology with biocompatible materials is being used for many applications (Miravete et al., n.d.) such as in dental reconstruction, by using the Selective laser fusion technique (SLM) (Gebhardt et al., n.d.; Scholz et al., n.d.); or the manufacture of orthopedic prostheses (Bandyopadhyay et al., 2015; Chia & Wu, 2015b) by using Fusion Deposition Modelling (FDM). In both cases, the process consists of scanning the patient's teeth or limb and after the corresponding processing, it is possible to manufacture a custom piece (Fernando Blaya et al., 2019). Moreover, in recent years, many studies have shown that 3D printing techniques make it possible to engineer anatomical parts of the human body

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Smart Splint Development

such as tissues and organs (Fernando Blaya et al., 2018; Chia & Wu, 2015a; Melchels et al., 2012). The advantages offered by 3D technology applied to health science are of fundamental importance for the patient's recovery. Especially for people with injuries whose only therapy is the immobilization of a part of the body. Furthermore, the digitalization and 3D prototyping of medical artifacts for immobilization, allows during the design phase, to create a solid product with non-continuous surfaces, while maintaining rigidity and resistance. It also ensures a level of hygiene that cannot be attained with conventional immobilization techniques, thanks to the use of bio-plastic materials compatible with humid environments (Ambu et al., 2020; Ugidos Lozano et al., 2018, 2019).

In addition, there is another great advantage of using new splints instead of traditional ones. These new splints allow the design of dedicated therapeutic windows (material-free areas) to apply treatments that must be applied directly to the skin, and therefore, cannot be applied otherwise. A simple window will allow cures for the case of wounds, dermatological pathologies or surgeries. The generation of windows on the splint, also allows for periodic visual medical inspection during the immobilization phase and rapid decisions on the evolution of the lesions.

This project focuses on the development and prototyping of an immobilization smart splint for a leg using a 3D scanner, processed from the obtained file, and its subsequent printing with biocompatible material. Taking advantage of new manufacturing techniques and novel technologies in sensors and electronics, it is proposed to bring the reinterpretation of this technique from the 10th century to our present time, by using new sensing and electronic technologies (Lozano et al., 2017; McAuliffe et al., 2015) and the use of the Internet of Things (Dimitrov, 2016; YIN et al., 2016), applied in medical applications. It will be possible to develop intelligent splints designed according to the lesion and morphology of the patient.

The splint will be designed exclusively for each individual, and it may be possible to have splints prepared prior to injury, especially in high-level athletes. This would make it possible to modify the rehabilitation treatments with the data acquired by the sensors during the process (Fan et al., 2014). In this study, the steps to manufacture a smart splint with AM technology starting from the digitalization of the leg to immobilization will be presented.

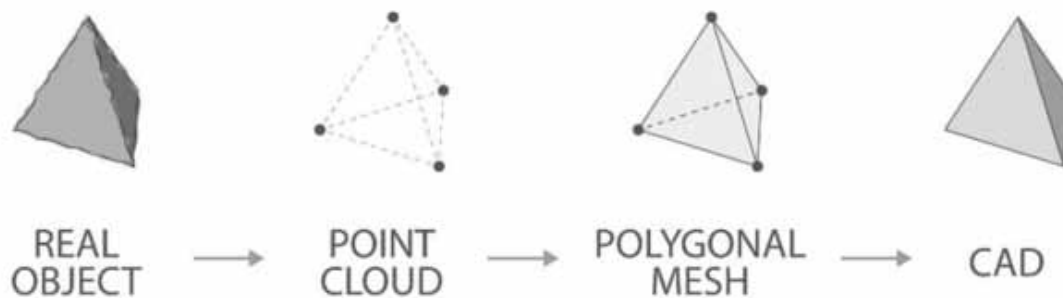
The sensing technologies will be presented for data acquisition in the IoT-based healthcare system. The parameters that will be monitored are temperature, humidity, pressure and skin colour. The combination of these, can indicate different problems that the patients may be suffering (Ju et al., 2005; Schlereth et al., 2014), such as inflammation. In order to obtain the prototype of the splint, the windows for the accommodation of the rehabilitation therapies and the type of treatment will be considered. In fact, the application of treatments in the immobilization phase has a substantial influence on the evolution of the injury and on mobility rehabilitation of the limb. Moreover, the splint will allow visual access through windows and direct contact with the skin.

The process is called reverse engineering (Figure 1). Firstly, it will be obtained the 3D scanning model using a 3D scanner, as well as the verification of the obtained data. After this, the file provided by the scanner will be modified using a CAD Software to obtain a final model. This model will incorporate the sensors holes and windows to apply the different treatments. Finally, the model will be produced and the Software and electronics will be integrated.

As part of the process, objectives that will be considered are:

- development of the protocol for scanning, meshing, designing and producing the splint.
- development of mobile application for sensor monitoring.

Figure 1. Reverse engineering methodology (hire freelance point cloud modeling services for your company | Cad Crowd, n.d.)



- implementation of an algorithm to detect inflammation through changes in pressure, temperature or colour of the affected area.
- study on the measurement of humidity on the internal face of the splint, according to the discussion of convenience that will be done later in the article.

The full process will include obtaining the 3d scanning model using a 3dscanner first, as well as the verification of the data obtained. After this, the file provided by the scanner will be modified using cad software to obtain a final model. This model will incorporate the sensors windows to apply the different treatments. Finally, the model will be produced and the software and electronics will be integrated.

BACKGROUND

The new industry is experiencing an enormous growth, thanks to the use of techniques that include advanced manufacturing and industrial design. Moreover, the optimization of the process (Bandyopadhyay et al., 2015; Jammalamadaka & Tappa, 2018; Tappa & Jammalamadaka, 2018), the development of new materials by manufacturers (Chia & Wu, 2015a; Guvendiren et al., 2016; Valášek et al., 2018), or the decrease of environmental costs (Affatato et al., 2016) are some achievements that make it possible to expand these technics further than the industrial area. Nowadays, these techniques are being transferred to medicine areas, by applications known as bioengineering (Affatato et al., 2016). Among all emerging technologies in the area of bioengineering, the implementation of additive manufacturing (AM) in the healthcare industry has led to several benefits. The design freedom allows customization of surgical equipment, medical devices, and implants. In fact, anatomy for pedagogical objectives (Ugidos Lozano et al., 2018, 2019), craniomaxillofacial surgery (Lozano et al., 2017), oral appliance therapy for snoring and obstructive sleep apnea (OSA) (Ghai et al., 2018; Montesdeoca et al., 2019), orthopedics surgery (Montesdeoca et al., 2019), and rehabilitation (Mulford et al., 2016) are some examples in which the benefits of fused filament fabrication (FFF) technology could improve the clinical course of patients. These new techniques allow to improve wearing comfort and better hygiene due to the bio-compatible and sterilizable properties (Lunsford et al., 2016). Over this fields, many developments have been carried out in recent years, like exoskeletons (P Fitzpatrick, 2017), prosthesis, or assistive devices. These

specialties are in demand in developed countries (Cernohorsky & Cadek, 2017), but a level of maturity and technological development is necessary to promote a change in the actual model. Moreover, both orthopedics and rehabilitation are specialties of medicine very conducive and receptive to all kinds of technological developments or applications in the field of research, development, and innovation (R&D&I).

Thanks to the use of different methods of industrial three-dimensional digitization and reverse engineering, advanced manufacturing has generated a recent emergence of solutions. Based on additive manufacturing it has allowed a great advance in products of mass use such as splints, braces, prostheses, or assistive devices (Evill & Evill, 2013). Moreover, these techniques, combined with new sensors and actuators, have revolutionized the applications of exoskeletons by the hand of robotics (Robin et al., 2020). Products such as splints made by additive manufacturing offer great advantages over classical methods of permanent and splinting (splinting) or commercial immobilization (braces, corsets, etc.). Some of these advantages are adaptation, personalization, hygiene, materials used, or environmental impact, among others. The incursion of these new 3D techniques in medical processes allows to include smart systems to analyze different states of the medical evolution process (Goncu-Berk & Topcuoglu, 2017). This study proposes to combine 3D techniques with electronic systems to develop a new era of splints that have not been achieved before. The use of these kind of systems, which include small electronic boards, programming systems, and data communication, would make possible to monitor parameters as temperature and pressure. These parameters would be sent to an application running on a portable device and compared in a database with other similar treatments data or sent to the doctor to see if the process is evolving correctly. This way, it is possible to include the smart splints into the use of big data in healthcare and the Internet of Things (IoT) movement (Chiu et al., 2018; Dimitrov, 2016). In fact, it has been shown that the use of the IoT, allows data exchange through network connectivity and devices integrated with hardware, software, and sensors (YIN et al., 2016). This, applied to medicine, will lead to a reduction in costs and inefficiencies and better patient satisfaction in terms of medical care. One of the factors for the use of IoT in medicine and in rehabilitation (Zanella et al., 2014) are medical devices (things) integrated with a detection technology for the continuous acquisition of physiological data from patients. For these reasons, the purpose of this study is to present how to design and manufacture a smart and functional splint in order to monitor different physiological parameters of the patient and of the device (skin temperature, humidity, pressure, and color changes on the skin). In this manner, it is possible to have a continuous data acquisition that allows to improve the treatment outcomes and to reduce recovery times and healthcare costs.

DEVELOPMENT OF THE SMART SPLINT

Considered Therapies During the Design Process

Lymph Drainage

The lymphatic system has been identified late in history. This is probably because of it is not possible to see it with the naked eye. However, manual techniques for the lymphatic system have been used since the end of the 19th century. Therapist Emil Vodder, developed an innovative approach that allowed manually enhance lymph flow of the body. Today, manual therapists, use Combined Decongestive Physiotherapy for lymphedema. CDP is one of the non-invasive treatments that are chosen for lymphedema, and it is

recognized and reimbursed by insurance companies (Society et al., 2017). CDP consists of many components as hands-on, skin care, manual lymph drainage therapy (MLDT), external compressions, etc. The basis of MLDT is to create different pathways through which lymph can flow (Chikly et al., 2014; Wei et al., 2019).

Iontophoresis

Iontophoresis is one of the most used during rehabilitation treatment for delivery of anti-inflammatory and painkiller medication in the parts of the human body affected by inflammatory processes of the musculoskeletal system (Costello & Jeske, 1995; Hamann et al., 2006; Rigby, Mortensen, et al., 2015). This way, some medications are able to pass through the skin and produce their effect, circumventing the digestive tract and without the need to have them administered by injection (Hao, 2014; Neeter et al., 2003; Taskaynatan et al., 2007). The explanation of the working mode is that ionic substances have an electric charge, so because of this, tend to move to the pole of the opposite sign. It is in that point where they are absorbed through the skin. This way, some medications are able to pass through the skin and have their effect, avoiding to go through the digestive tract and without the necessity of administering them by injection.

Ultrasound

Therapeutic Ultrasound technique is considered an effective treatment for rehabilitating musculoskeletal conditions due to joint contracture, pain and muscle spasm or injuries. It improves the elasticity of tissues, and it has mechanical, analgesic and circulatory (Baker et al., 2001; Robertson & Baker, 2001). This treatment promotes the release of heat to tissues such as tendons, muscles and joints, reducing the symptoms of inflammation and promoting tissue regeneration (J. M. ; Bjordal et al., 2006; Ebenbichler et al., 1999). This treatment is not painful, has no side effects and is carried out by means of a transducer capable of generating alternating frequency electrical currents and capable of penetrating the tissue and stimulating blood flow in the area. Ultrasound can also be used in underwater mode or with gel.

The sound waves released through the transducer penetrate the tissue according to the type of medium used, that is, gel or lotion, quality of the transducer, treatment surface and the type of lesion to be treated. Normally the bones and the tendon connection area have low absorption capacity, being recommended to carry out another type of treatment or to use a lower frequency of ultrasound. (Mitragotri, 2005; Rigby, Taggart, et al., 2015).

Laser

Laser therapy accelerates the metabolism energy and tissue synthesis. There are many studies that concluded that therapeutic laser can potentially be effective in treating tendinopathy when recommended dosages are used. (J. M. Bjordal et al., 2010; Kneebone, 2010; Tumilty et al., 2010)

Low-level laser therapy is considered to act through light absorption by photoreceptors, that stimulate the cells and modulates inflammatory processes (Gao & Xing, 2009; Karu, 2008; Moriyama et al., 2009). Different studies performed in a variety of pathological conditions as injured tendons and using LLLT. The tendons, were treated daily for 3 to 21 days. It was observed histopathological changes in tendons that were receiving LLLT as an increment of collagen production, improved collagen bundle organiza-

Smart Splint Development

tion, and also an increment of the number of small blood vessels (J. M; Bjordal et al., 2006; Fillipin et al., 2005; Ng & Fung, 2008; Reddy et al., 1998). Moreover, some studies have investigated the effect of Laser therapy within the first 24h after an acute inflammation. It was found that after inflammation followed by just three or four LLLT sessions, the concentrations of inflammatory markers and cells had been reduced compared to no-treatment controls (Aimbire et al., 2006; Joensen et al., 2012).

Electrostimulation

The application of electricity for the treatment of pain dates back to thousands of years BC. The Ancient Egyptians and later the Greeks and Romans recognized that electrical fishes are capable of generating electric shocks for relief of pain (management & 2003, n.d.). The modern electrotherapy therapies for neuromuscular-skeletal from mild to moderate pain is based on transcutaneous electrical nerve stimulation (TENS) and percutaneous electrical nerve stimulation (PENS) (Heidland et al., n.d.). There are also different studies about the effects of electrostimulation on pain, muscular strength and functional capacity in patients with osteoarthritis of the knee (Rosemffet et al., 2004).

For the electrostimulation therapy a simple device having at least one circuit with a pair of electrodes is required. Different curves and frequencies may be selected. Muscular electrostimulation electrotherapy TENS in gastrocnemius muscle has antalgic and anti-inflammatory effect, low frequency analgesic currents and faradic currents produces retardation of muscle atrophy in calf muscle, and stimulating currents in gastrocnemius and intrinsic muscles of the sole produces motor responses, avoiding Subdeck processes (Martín, 2014).

These techniques are only some examples considered in this study, that may for instance be applied to injuries or lesions in arms (Johansson et al., 1999), knees (Aiyejusunle et al., 2007), elbows (Stasinopoulos & Johnson, 2005) or Achilles tendons (Kaplan et al., 2019). However, by using 3D splints, it could also be possible to apply other therapies, considered by a specialist (Moein et al., 2017).

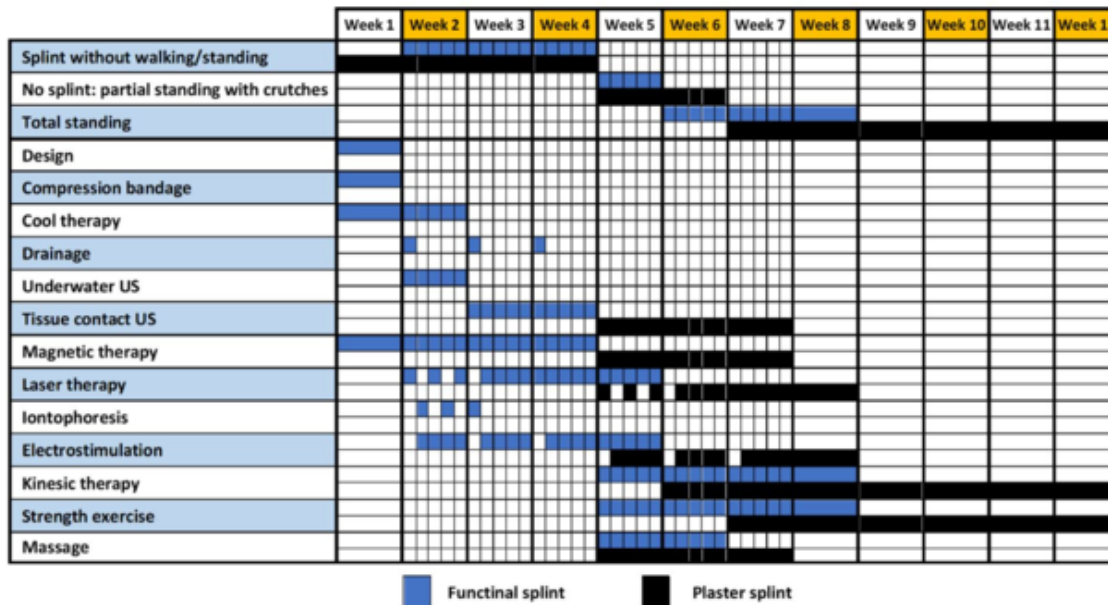
According to the previous study (Fernando Blaya et al., 2019), the treatment programming is shown in black colour in Figure 2. Traditional splints do not allow the application of physiotherapy techniques until the device is removed. However, by using new smart splints, it is possible to apply the treatments as soon as the injury occurs. It is possible to see the new timing possibilities in blue colour in Figure 2.

This reduction involves at least 30% of the treatment period. Moreover, the application of physiotherapy techniques during the immobilization phase contributes to the prevention of joint, muscular and vascular complications, derived from the application of retention devices in the initial phase of the treatment.

Sensors

For this study, the parameters that will be monitored are temperature, humidity, pressure and skin colour. The information recorded by these sensors is combined to determine if there is any kind of unexpected evolution of the treatment. In total, the implemented sensors are: two temperature sensors DS18B20 (Dallas DS18B20 Temperature Sensors Semiconductor, 2002) in contact with the skin, one temperature and humidity sensor between the skin and the splint (DHT22) (Aosong Electronics Co., 2015), two pressure sensors DF9-40 (*Film Pressure Sensor DF9-40@10kg V2.0*, n.d.) placed in two different axes of the splint (X, Y), and one colour sensor TCS34725 (*TCS3472 COLOR LIGHT-TO-DIGITAL CONVERTER with IR FILTER*, n.d.). The shocks and vibrations that may be produced by the human body are not critical to the performance and durability of these sensors. Moreover, when an injury of these

Figure 2. Chronogram of rehabilitation when new techniques are applied (Fernando Blaya et al., 2019)



characteristics is being treated, it is due to the re-quirement of immobilization. Therefore, the shock and vibrations are controlled. In addition, some of these sensors have been tested in a previous study, where it is detailed that accuracy of the selected sensors is enough for the purpose. Details of these sensors are shown in Table 1.

The DS18B20 sensors (Dallas Semiconductor™ Maxim Integrated Products, Inc., Dallas, TX, USA) are 1-Wire digital temperature sensor. It reports degrees in Celsius, with a precision of 9 to 12-bit. Each sensor has a unique 64-Bit serial number etched into it, which allows a huge number of sensors to be used on one data bus. The DHT22 sensor (Aosong Electronics Co., Ltd., Guangzhou, China) utilizes exclusive digital-signal-collecting-technique and humidity sensing technology, its sensing elements is connected with 8-bit single-chip computer.

The DF9-40 sensor (Zhengzhou Winsen Electronics Technology Co., Ltd., Zhengzhou, China) is a film pressure based on flexible pressure sensing technology. In order to measure the applied force with an Arduino, it will be necessary to build a voltage divider circuit with a pull-down resistor. This circuit creates a variable voltage output that can be read by the ADC (analog to digital converter) input of the microcontroller. It means that for a simple force-to-voltage conversion, the force sensing resistor

Table 1. Technical specifications of the sensors

Sensor Serial Number	DS18B20	DHT22	DF9-40	TCS34725
Dimensions (mm)	6 x 6 x 50	15 x 7.7 x 20	40 x 20 x 0.25	25 x 20 x 1.5
Power voltage (V)	3.0 – 5.5	3.3 – 6	5	5
Working range	-55°C to 125°C	-40°C to 80°C	0 to 100% RH	0-500 g
Resolution	± 0.0625°C	0.1°C	0.1% RH	14.5 g

(RFSR) device is tied to a measuring resistor (RM) in a voltage divider. In this case, a 10kΩ resistor will be used. The output voltage (Vout) which is possible to measure with the Arduino is described by the following equation:

$$V_{out} = V_{cc} \cdot \frac{R_M}{R_M + R_{FSR}}. \quad (1)$$

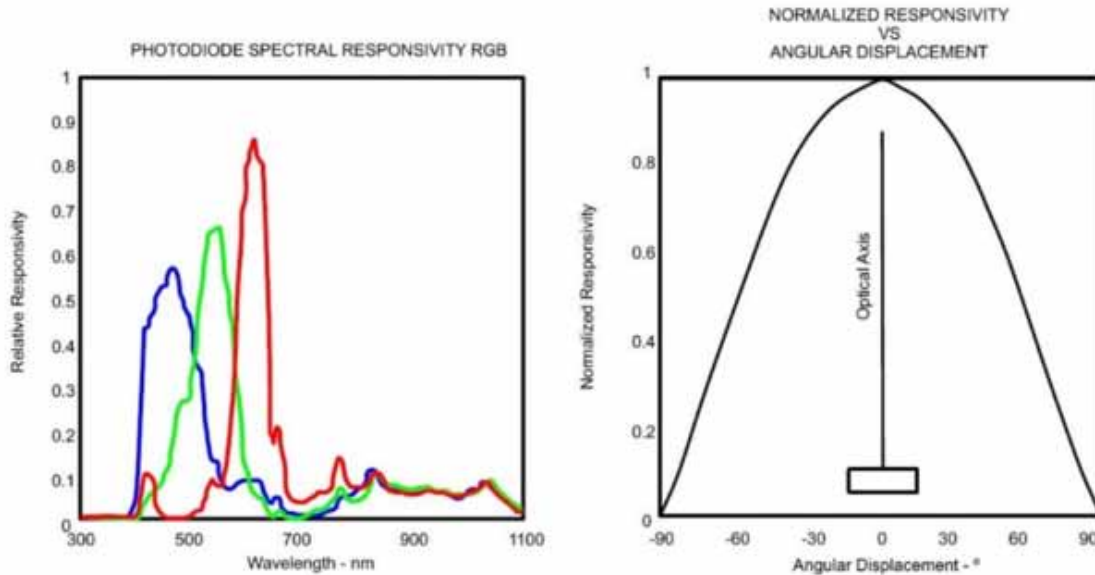
Note that the output voltage measure is the voltage drop across the pull-down resistor. When no force is applied, the FSR resistance will be really high, for example, 10 MΩ. Using a 10 kΩ pull-down resistor and a VCC of 5 V, results in the following output when no force is applied $V_{OUT} = 0.005$ V. When the FSR is pressed, the resistance goes down to roughly 200 Ω. This results in the following output voltage $V_{OUT} = 4.9$. Similar developments have been carried out in other studies for other medical applications (Society et al., 2017).

During the healing process, a bruise will usually go through different colours. It often starts red because fresh, oxygen-rich blood has newly pooled underneath the skin. After around 1–2 days, the blood begins to lose oxygen and change color. A bruise that is a few days old will often appear blue, purple, or even black. In about 5–10 days, it turns a yellow or green color. These colors come from compounds called biliverdin and bilirubin that the body produces when it breaks down hemoglobin. After 10–14 days, it will turn to a shade of yellowish-brown or light brown (*Bruise Colors: Causes, Timescale, and When to See a Doctor*, n.d.; *Tell-Tale Color Changes: Camera Can Find Age of a Bruise | Features | Oct 2012 | BioPhotonics*, n.d.).

The TCS3472 sensor provides a digital return value of three components of the light (red, green and blue), and it also clears the light detection values. It includes an IR blocking filter, which minimizes the IR spectral component of the light, allowing for accurate colour measurements over the skin, where there is not external light. Figure 3 shows graphs of the specific response from this sensor to the light. As Figure 3a shows, the sensor is able to detect different wavelengths by using a spectral photodiode. In this way, it comprises the amount of light of each wavelength that bounces off a surface. Figure 3b illustrates that the highest responsivity of the sensor is in the perpendicular direction of the photodiode surface. This must be considered when the housing of the sensor is designed. This sensor is an ideal solution for varying lighting conditions and materials, due to its sensitivity, the wide dynamic range, and the IR blocking filter. The data is transferred via an I2C bus, using the SDA and SCL contacts.

Previous studies show the suitability of different RGB channels and their differences for detection of hematomas or ecchymosis (Al Ghozali et al., 2017; Patašius et al., 2016). The colour sensor detects changing colours of the skin, during the initial inflammation stage, due to ecchymosis (*Automatización de La Datación de Equimosis En El Peritaje Médico Legal Peruano Mediante Redes Neuronales Artificiales y Procesamiento de Imágenes*, n.d.), which occurs around approximately the first six days (Ghavimi et al., 2018; Gurlek et al., 2006). The main purpose of using an RGB sensor, is to detect the variation in red, green and blue components of the light. The device, incorporates an emitter of white light, that bounces off the skin, and goes back to the receiver. The sensor reads the variation of the three components, in comparison to the original white light. This way it is possible to know what component is absorbed, and therefore, the colour of the skin. It is not necessary to modify the gain value or other parameters, as the sensor is already configured. Moreover, as the initial stage of the lesion that must be monitored has a duration of one week, the durability is not a critical parameter. The sensor reads the values in terms of RGB (red, green and blue) between 0 and 255.

Figure 3. TCS3472 sensor responsivity graphs (a), (b) (TCS3472 color light-to-digital converter with IR filter, n.d.)



3D Model and Design

As reported in other previous studies, the first step was to get the 3D model of the injured part (Fernando Blaya et al., 2019).

From that point, the splint is modeled over this part, considering the areas where the sensors are placed. A commercial scanner (Sense™ 3D scanner, 3D Systems Inc., Rock Hill, SC, USA) was used for the digitalization of the arm at a distance of 40 cm according to the manufacturer's instructions.

The technical specifications of the scanner are shown in Table 2.

It is possible to scan the entire area, at once or in several times if necessary due to limitations produced by a possible injury. Later, the software joins the points cloud. Figure 4 shows the scan process, and the 3D point cloud obtained the total time for the scanning process is 6 min.

Once the 3D point cloud is obtained post-processing has been carried out by using a 3D CAD software Geomagic FreeForm (3D Systems, Inc., United States). The 3D scanned models are shown in figure 5.

Table 2. Technical specifications of the Sense™ 3D scanner

Maximum Scan Volume	2 × 2 × 2 (m)
Minimum Scan Volume	0.2 × 0.2 × 0.2 (m)
Working Distance	0.2–1.6 (m)
Number of Cameras	2
Resolution at 0.5 m	1mm

Figure 4. Scanning process of the arm to get the digital model (a) and points cloud (b)



With this software it was possible to clean the point cloud by filling the holes due to noise appears during the scanning process and by correcting with a smoothing algorithm any minor anomalies due to misplaced of some points of the cloud or due to surfacing process. With this procedure it was possible to obtain a simpler mesh of the arm by limiting the area of the interest started from a point cloud. Starting from this mesh and creating an offset of 0.5mm, it is created the solid which will be the basis of the splint. Figure 6 shows the mesh of the scanned arm and the solid digital model obtained.

The solid digital model shown in the figure 7b represents the first step of the design of the splint. In fact, the solid surface created represents the internal face of the splint in direct contact with the skin of the patient's arm. Once this reference surface of the splint has been created a 5 mm thickness solid has been generated as shown in figure 7.

Once the body of the splint has been created, it was necessary to divide it in two parts to make the mounting possible, that will be later joined with a mechanical closure (figure 8a). Also, the places for the sensors are designed and some holes are introduced as shown in the figures 8b and 8c. The function of these holes and windows is manifold. In fact, they allow, on the one hand, direct medical inspection of the injured part, aeration of the skin in contact with the splint and, on the other, the possibility of

Figure 5. 3D model of the arm obtained after the scanning process: top side (a) and bottom side (b)

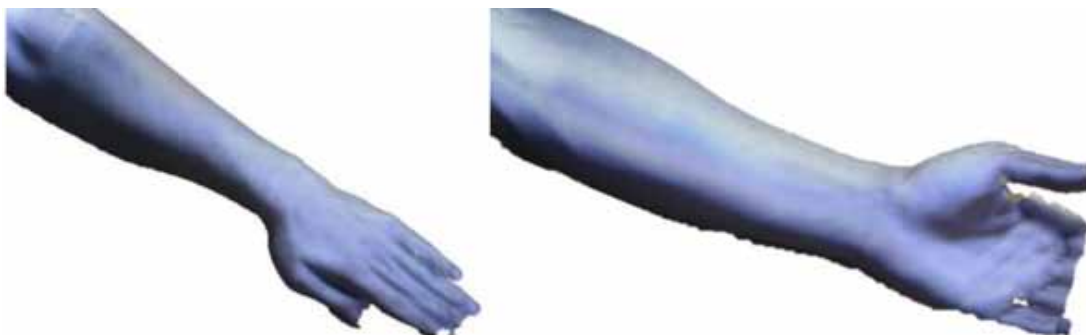
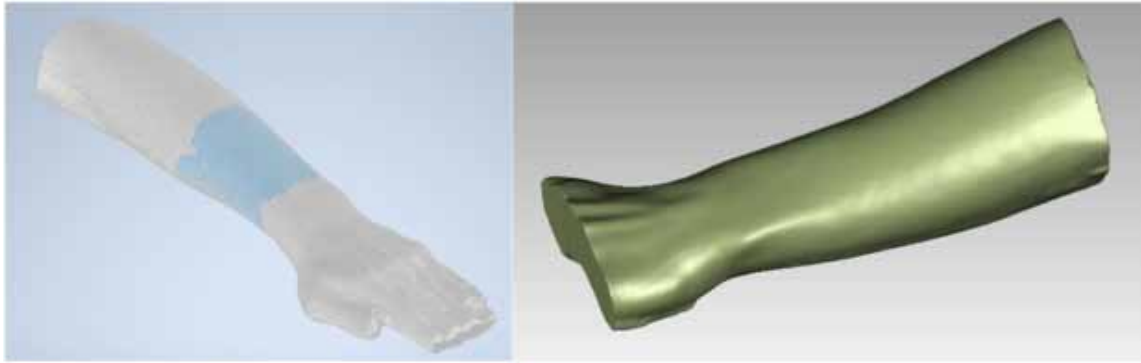


Figure 6. Post processed: mesh of the scanned arm (a) and solid digital model obtained from the clean mesh (b)



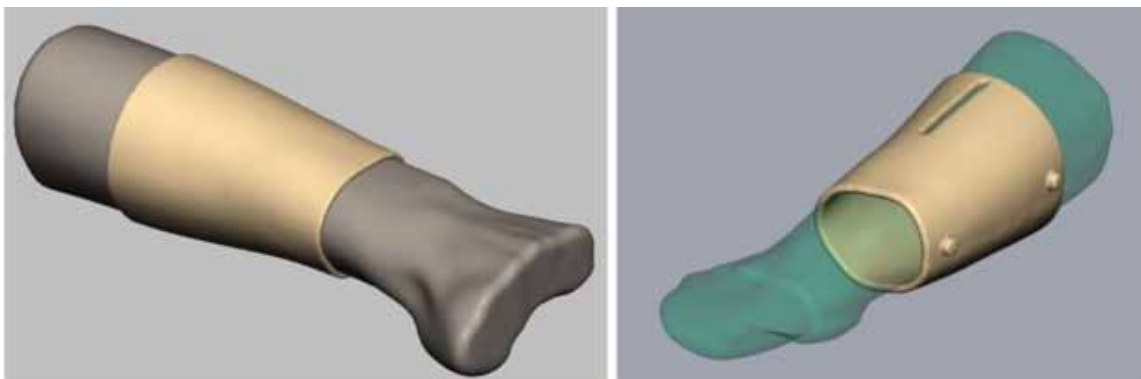
using electromedical devices for rehabilitation during immobilization of the limb. Figure 9 shows the final modelled splint over the initial 3d model.

This process may be also applied to other limbs (see Figure 10 and 11):

Additive Manufacturing

After the digital modeling and design process, the file obtained is sent to a slicer that prepares the part to be produced by using the additive manufacturing process (Figure 12). The splint was manufactured by using a fusion deposition modeling (FDM) 3D printer “TotalPrinter” machine (Figure 12a). This 3D printer was designed, developed, and manufactured in the Additive Manufacturing and Rapid Prototype Laboratory of the Escuela Técnica Superior de Ingeniería y Diseño Industrial at Universidad Politécnica de Madrid. This 3D printer allows continuous temperature and humidity control of the printing chamber and of extruder temperature with the aim of optimizing the process and obtaining an homogeneous splint in terms of adhesion of the various printing layers, density of the material, and mechanical characteristics. In addition, this 3D printing machine allows continuous monitoring of the thickness of the PLA

Figure 7. Initial solid obtained from the points cloud (a) and initial stage of the design, including the hole for the temperature sensor and closing buttons (b)



Smart Splint Development

Figure 8. Different steps during the modelling of the splint: division of the splint (a), design of different sensor holes (b) and final top side splint (c)

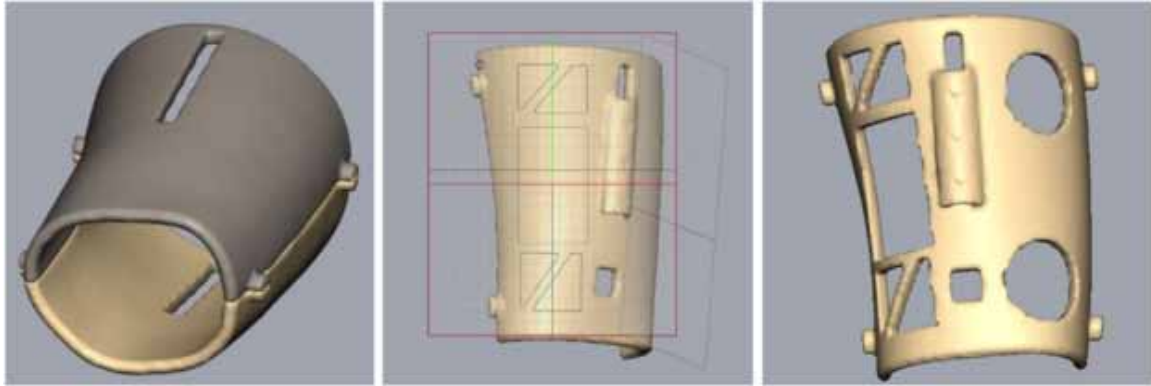


Figure 9. Final result of the modelled splint over the patient arm

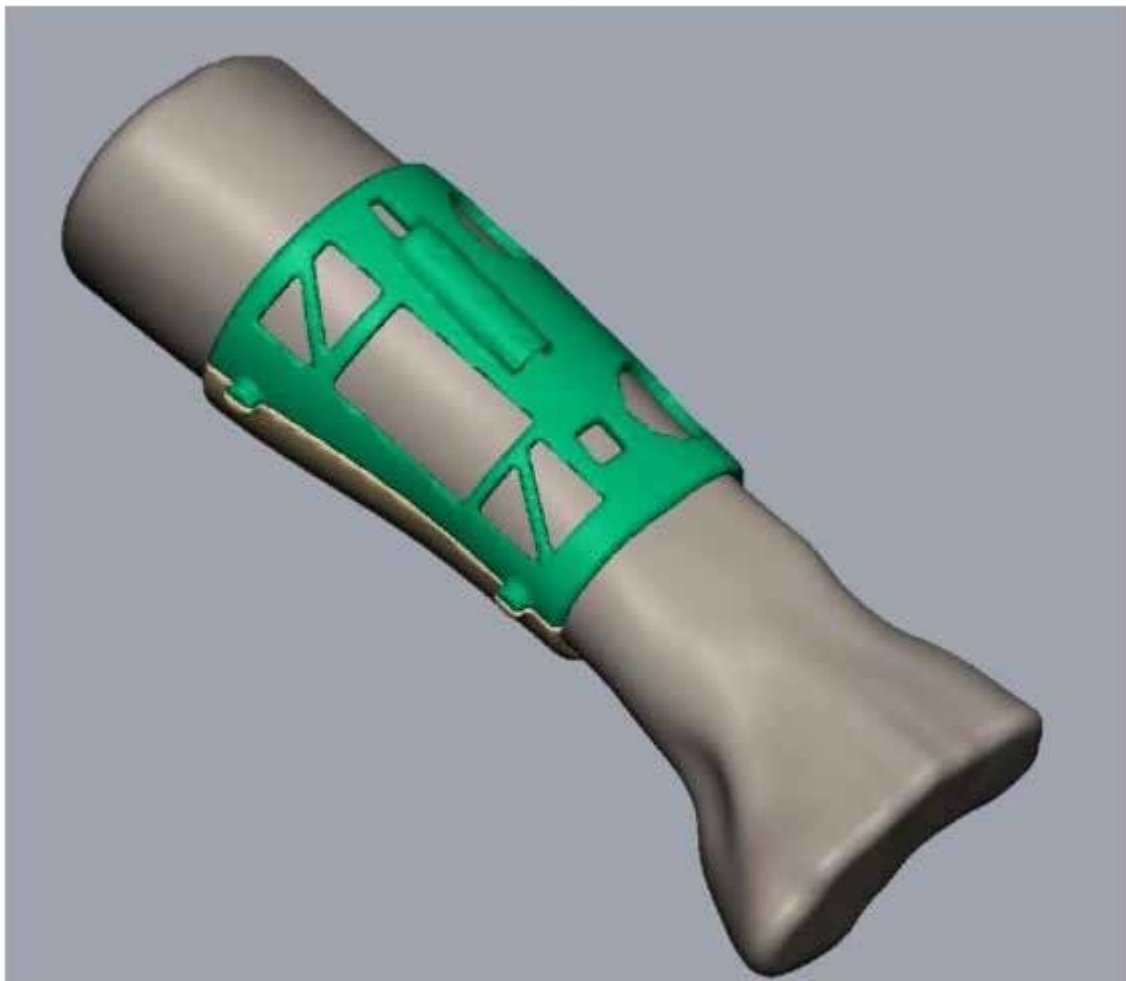
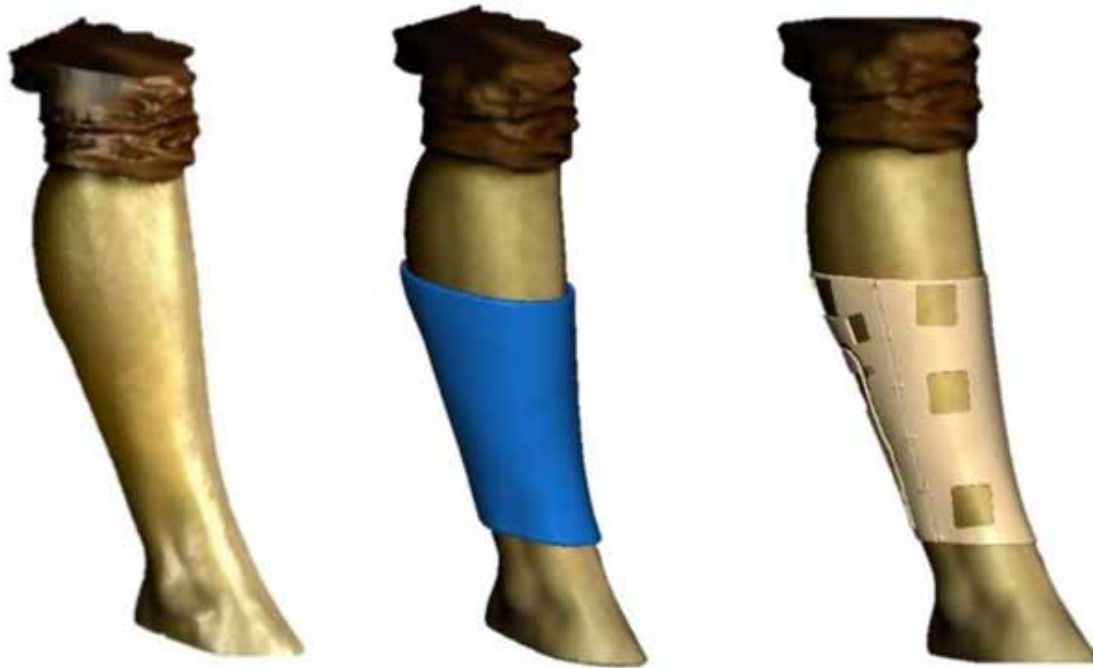


Figure 10. Final result of the modelled splint over the patient leg



filament used as reported in the study of Soriano et al. (2019) and in the study of J. M. D. A. Del Burgo et al. (2018) (Haro et al., 2019, 2018).

For producing the splint, PLA filament (see table 3 for mechanical properties) with a diameter of 1.75mm was chosen. The material and process should be followed carefully in order to avoid biocompatibility issues (Del Burgo et al., 2019; Salentijn et al., 2017; Vladescu et al., n.d.). The vertical position for printing was chosen as shown in Figure 12, taking into account the volume chamber of this machine (200mm x 200mm x 400 mm). In Table 4, it is possible to see the printing parameters set in the manufacturing process, following the material manufacturer's recommendations to obtain a quality and structure rigid enough.

Assembly of the Real Model

In order to correctly detect the data from the sensors, it is necessary to develop an electronic board for connecting everything easily. It is important to focus on a durable design, with low weight and dimensions. By focusing on these main purposes, a board that will be installed directly to the TTGO OLED Display and Battery Board is designed, shown in Point 2.2 of this study. This board has two analog to digital converters (ADC1 and ADC2). The resolution of these converters is 12 bits. A 12 bits ADC means that is able to read 2^{12} values between 0 and 5v. This is 4096 values, so it detects changes of 1.22mv, which is enough for what is required by the selected sensors. ADC1 is used for the sensors, whilst ADC2 is used for the communication between the microprocessor and the Wi-Fi module, which is used to create the web server (*ESP32 Series Datasheet Including*, 2020).

Smart Splint Development

Figure 11. Final modelled splint

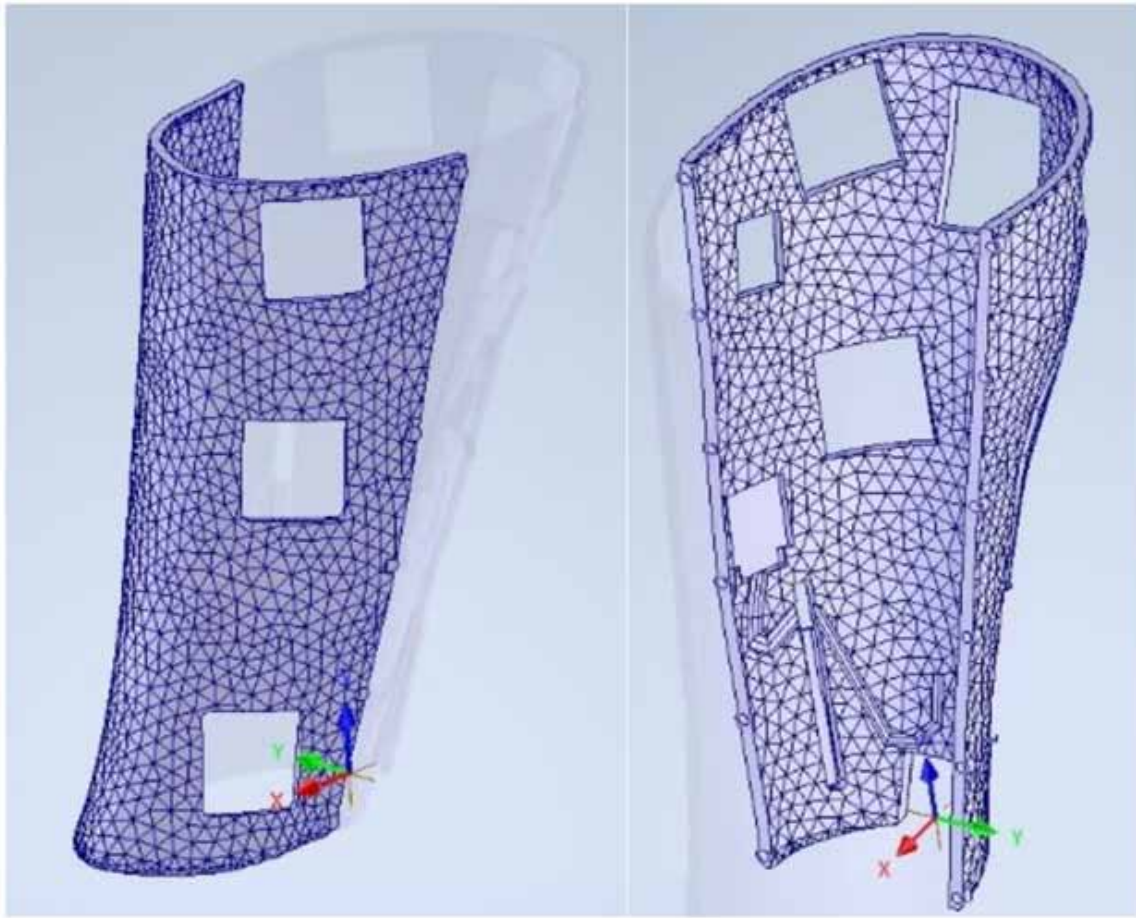


Figure 12. TotalPrinter machine developed to work with biomaterials (a). G-Code process generation

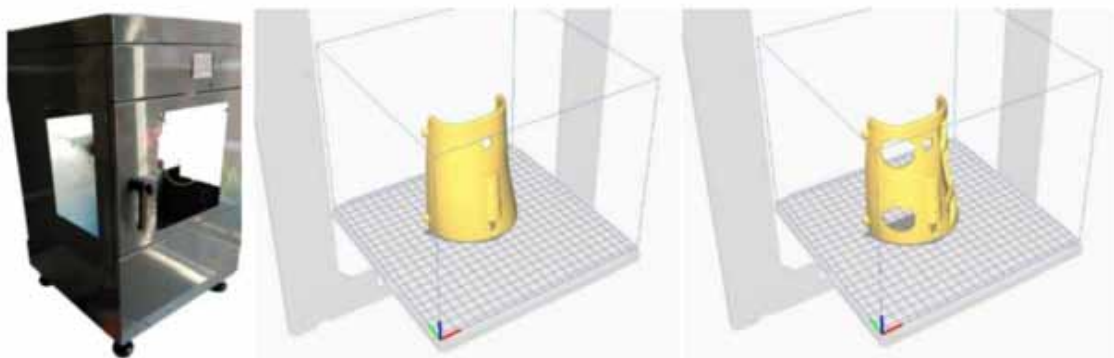


Table 3. Mechanical properties (Farah et al., 2016)

Properties	Units	PLA
ρ (Polymer density)	g/cm ³	1.21–1.25
σ (tensile strength)	MPa	21.0–60.0
E (tensile modulus)	GPa	0.35–3.50
ε (ultimate strain)	%	2.50–6.00
σ^* (specific tensile strength)	Nm/g	16.8–48.0
E* (specific tensile modulus)	kNm/g	0.28–2.80
T _g (glass transition temperature)	°C	45–60
T _m (melting temperature)	°C	150–162

The chosen board, as explained before, can be accessed from other devices through different ways and protocols. It has an OLED display that may show the acquired data (pressures, temperatures, humidity and colour change detection). Also, it is possible to create a Bluetooth connection with a mobile phone or similar device. However, in this case, the option of creating a web server is selected. This way, the information may be consulted from any device connected to the internet, anywhere in the world. The great benefit of this, is that a doctor can see the data and follow the treatment in real time from their place of work.

The total real consumption of the electronic board and sensing system is 84.66mA. Due to the battery has a capacity of 12210mAh, the autonomy of the system is around 144h. This means that the system is able to collect data during six days without charging the battery, what is very significant because the first week after occurring the lesion is the most important period to be analyzed (*Bruise Colors: Causes, Timescale, and When to See a Doctor*, n.d.; *Tell-Tale Color Changes: Camera Can Find Age of a Bruise | Features | Oct 2012 | BioPhotonics*, n.d.). After that, it is possible to replace or charge the battery.

Figure 13 shows the splint prototype obtained with the wiring and sensors fully assembled. In Figure 14 it is possible to see the interior of the splint with the housing for the sensors.

To test the fully assembled leg splint on a real leg, the splint was fixed to a healthy volunteer for 1.5h (Figure 15). The volunteer was placed in seated position for the tests. However, this new “smart splint” is capable of obtaining data in a continuous way, so the patient does not need to adopt particular positions during the data acquisition. The main purpose of this test, was to collect data so that it could be analyzed if the sensors were able to acquire information correctly. The data collected by the sensors

Table 4. Different parameters used for the manufacturing of the leg splint

Layer height [mm]	0.2
Extruder [mm]	0.4
Density [%]	40
Thickness perimeter each layer [mm]	1
Print speed [mm/s]	60
Temperature [°C]	220

Smart Splint Development

were treated with ESP32 micro and sent to a computer every 3 seconds by using the serial monitor of the Arduino platform. In the following sections the acquired data will be explained.

Figure 13. Real arm splint assembled with the sensors

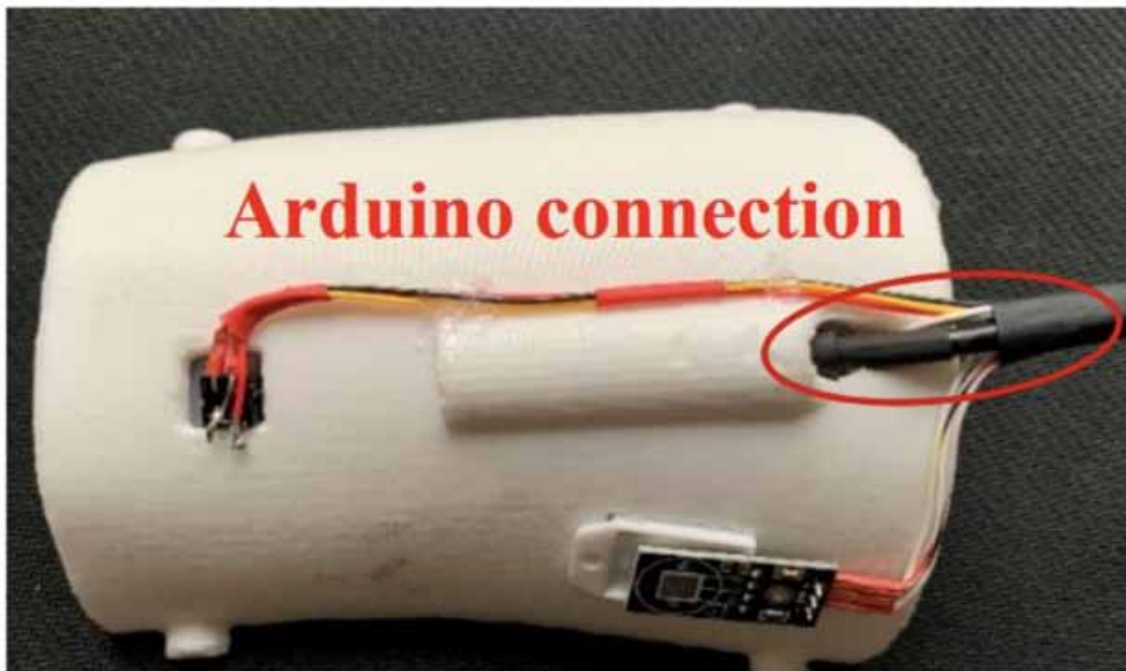


Figure 14. Real leg splint assembled with the sensors (a) and interior view (b)



Figure 15. Real model over the leg



Temperatures and Humidity

Two temperature sensors in contact with the skin were placed in two different zones. Moreover, a third sensor not in direct contact with the skin, read the temperature and humidity. The mean temperature of the first two sensors is shown in the colour orange, whereas the internal temperature is shown in the colour blue (Figure 16). The graph shows that the registered temperature by the sensor is slightly lower than 36°C. This occurs because the exterior area of the sensor surface is not in real contact with the skin, and this produces a gradient of temperature between the environment and the body. However, what the authors are looking for in this study, is to detect an increment or decrement of the temperature of the located area of the skin, compared with the historical. It is perfectly possible to detect an increase or decrease of the registered temperature, in comparison with the historical data.

Monitoring the humidity inside the splint and its fluctuations allows us to know if the injured area is in a healthy environment and unsuitable for the proliferation of bacteria, especially in cases of surgery or injury. Furthermore, some physiological events that can occur following a trauma have been shown to include changes in skin colour due to edema, changes in temperature and an increase in sweating in the area affected by the lesion (Birklein et al., 2001). In fact, a change in the sudomotor function of the injured part implies central disturbances of thermoregulation (Jänig, 1990; Ju et al., 2005). Figure 17 shows the percentage of humidity that was registered during the test inside the splint (in orange colour) and outside the splint (in blue colour).

Pressure

Two sensors for reading pressure are placed. One is placed on the “X” axis and the second on the “Y” axis (Figure 18). The sensors have been placed on these positions for the tests, and the data are collected with the leg in vertical position and weightlessly. However, the potential of these kinds of 3D techniques makes it possible for other medical requirements to also be considered and included during the design process, according specialist dictated requirements.

Figure 16. Temperature's graph

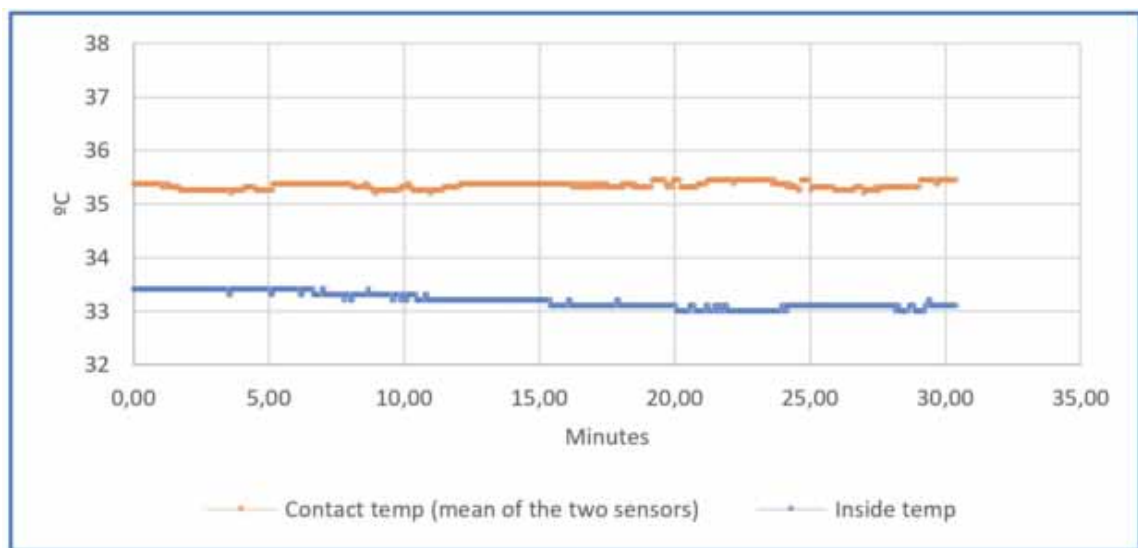


Figure 17. Humidity graph

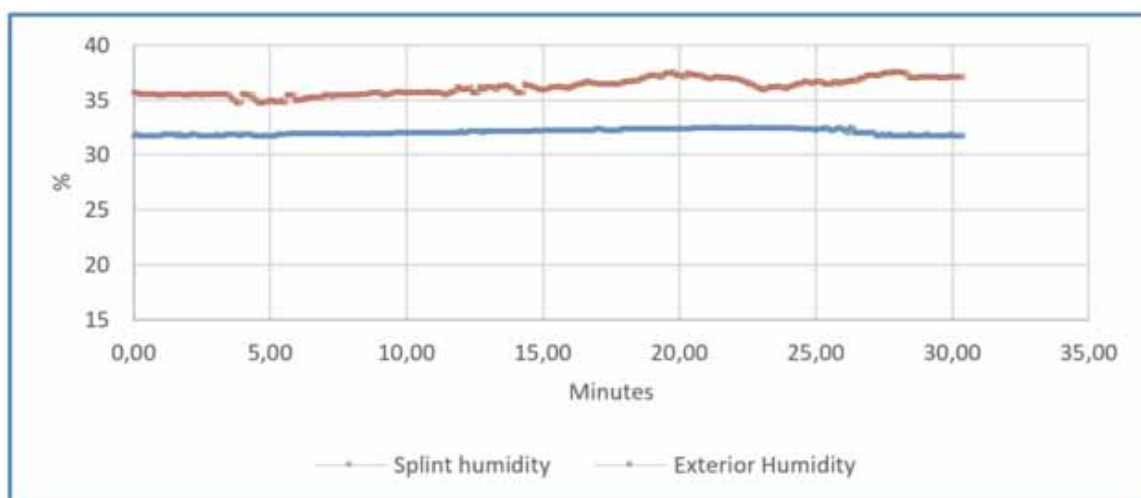


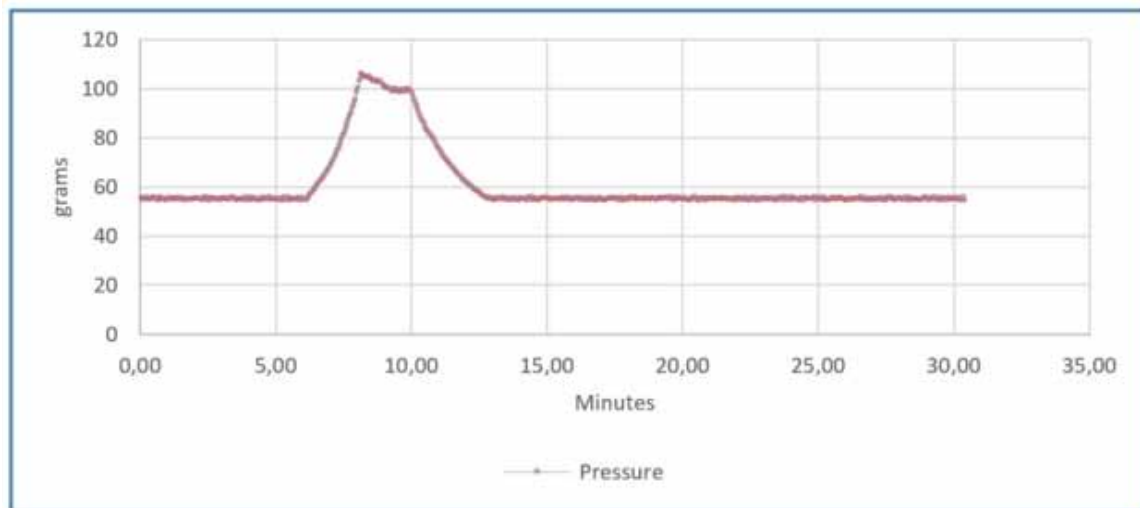
Figure 18. Pressure sensors on the “X” and “Y” axis



The surface of the pressure sensor during the limb immobilization phase is 1 cm^2 , according to $1\text{N}=1\text{Kg/s}^2$ the pressure values read by the sensor will have the dimensions of gf/cm^2 . Figure 19 shows the detected mean pressure. As illustrated, during the normal state, the value of the pressure is constant and is equal to 60 gf/cm^2 . However, when a slight pressure is produced due to an inflammatory process, the sensors are able to perfectly detect an increment of this pressure. In order to simulate what occurs in an inflammatory process, a force over the splint was applied between minutes 7 and 10. This varia-

Smart Splint Development

Figure 19. Pressure graph



tion was detected by the sensors, reading a pressure that rose from 60 gf/cm^2 to 100 gf/cm^2 . Therefore, when the pressure was increased due to the inflammation of the area, the sensors perfectly detected the increment of the mass inside the splint (De Agustín Del Burgo et al., 2020). The graph shows the actual and historical pressure. Real-time monitoring and the collection of historical data on the pressure variation of the injured area during the immobilization period allows the specialist to control inflammatory phenomena.

Colour

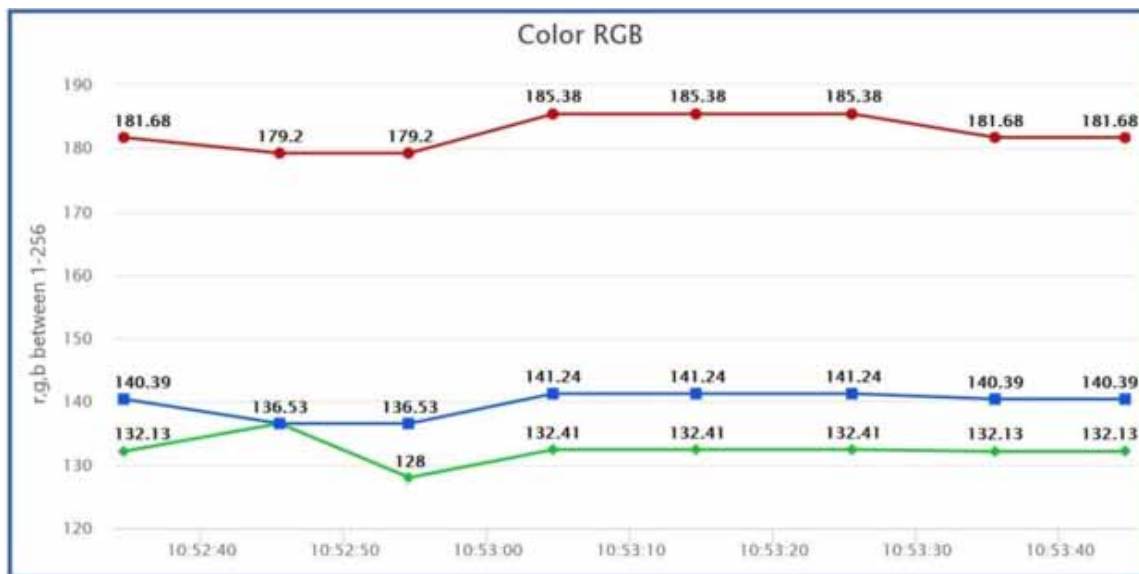
The test was done on the skin of a volunteer that had a hematoma, and was compared to another part of his body, that had no signs of hematoma. The sampling of the test was carried out with a frequency of 10 seconds. It is possible to see in Figure 19 that the sensor is capable of detecting a colour change in the skin. In Figure 20a, the skin has a normal colour with no signs of hematoma, whilst in Figure 20b the sensor detects an increment in the RGB values due to the signs of hematoma. Due to this, it will be possible to check the evolution of the colour during the very initial stages of the treatment, but also during posterior stages. It is possible to see that the three values are incremented, but it is specifically the 38% increment of the red value that makes it possible to detect the hematoma.

Diagnostic

The knowledge of these data makes it possible to identify temperature, humidity, pressure or skin colour changes. Combining them, makes it possible to identify signs of inflammation and detect possible problems during the treatment.

To accomplish this, an algorithm that can be configured to consider temperature and pressure changes during a period of time was programmed, to consider these data to be produced by an inflammation process but not by a position of the limb over a specific object. The considered parameters are showed

Figure 20. Colour RGB sensor lectures without hematoma (a)



in Table 5. However, these parameters are showed as an example of the possibilities of the system, with no real medical considerations in this case. The timing would be the necessary to distinguish a value due to inflammation from a collision or resting state position. Moreover, to avoid a wrong measure of the pressure sensors, it may be considered to add a third sensor in opposite position. An inflammation process will produce an increment volume inside the splint, and an increment of the pressure in all the

Figure 21. With hematoma (b)

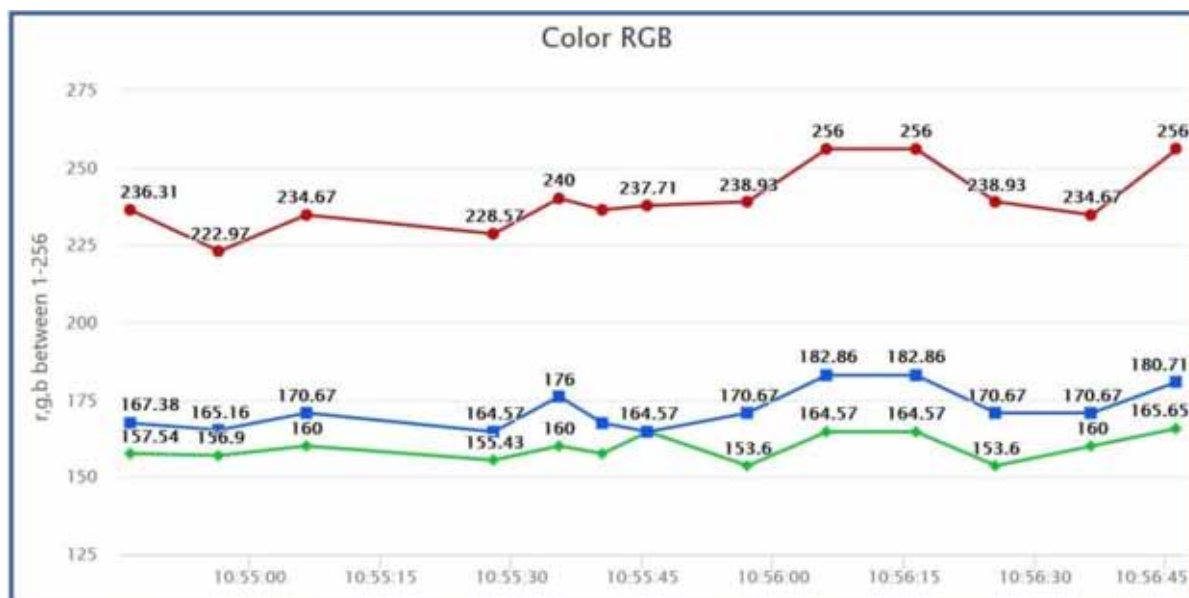


Table 5. Algorithm configuration to detect inflammation

Temperature increment	1.5 °C
Pressure increment	60 gf/cm ²
Time during temperature increment	60 m
Time during pressure increment	60 m

sensors, in a simultaneous and coterporally way. About the range, it is proposed a 5-10% change of the value due to the acquired data during the tests.

Moreover, the combination of this information with colour and humidity that can also be consulted remotely by a specialist will result in a complete diagnosis.

SOLUTIONS AND RECOMMENDATIONS

This study shows the combination of traditional immobilization techniques with new 3D modelling and prototyping techniques. This new system allows us to follow the evolution of the injured part in a very detailed way. Moreover, it is possible to apply treatments that improve not only the timing but also the quality of the rehabilitation. As previously explained, in this study electrostimulation, drainage, iontophoresis, laser and ultrasound have been considered as treatments. However, the potential of these kinds of 3D techniques makes it possible for other medical therapies to also be considered and included during the design process, according specialist dictated requirements.

These treatment possibilities are combined with the acquired data to even improve the treatment. Adding sensors to these splints, makes it possible to analyze in real time how the therapy is functioning and new steps to get the most progress.

Also, the vast capacities that remote monitoring allows would simplify the revisions that must be carried out by a specialist. This allows doctors to follow the progress of more patients, by using objective data. These data may be collected into a database, in order to compare different evolutions of different treatments in similar injuries.

For this study, the use of ruggedized sensors was not considered, as the main purpose of the study is to show the new possibilities of using sensors in splints, and the benefits of using new technologies in this kind of treatment. The performance and resolution of the implemented sensors, were correct for the tests, as it is possible to see in the different figures. Humidity sensor DHT22 has an error due to hysteresis of $\pm 0.3\%$. The sensor is looking for an increment of the internal humidity in comparison with the external humidity. The value will be around 3-5% higher when a sweating process is produced. Due to this, the error is not significant and will not interfere in the correct detection of a sweating process. In this case, it is completely functional.

From a medical point of view, there is no necessity to know the absolute value, or trying to get an optimal value, as this will depend on the patient and lesion. This is why the main focus of the study is to analyze the new capabilities by detecting the variations on the acquired data.

The design of the different windows includes round edges to avoid any kind of chafing or similar. In no case the design of these windows may cause injury to the affected limb or by edge effect since the additive manufacturing design allows smoothing all the edges in contact with the patient, nor by suction

effect on the skin (Lowe, 2017) as the splint is not indicated for support in load nor produce its own vacuum because it is an open design. Also, it is mandatory to use biocompatible materials (Hernández et al., 2020; Kim et al., 2016) to avoid any kind of irritation, eschar or ulcer.

The design of the splint is made according to the affected anatomic area of each patient. The design includes an offset to suit perfectly over the area. The design and the position of the windows must be supervised by a medical specialist, according to the lesion. These windows allow a visual control of the treatment, what is especially critical in the initial stages. However, the windows do not intervene in the treatment. In cases where the use of splints indicated for support and gait of the lower limb is required, the corresponding structural study would be carried out, and accessible windows should be generated only at the time of use through the design of a closure. Moreover, this kind of modules would allow to take off the splint to clean the skin if needed, something not possible with traditional splints.

For nearly half a century research has been conducted on humans (LAWSON, 1956) and animals (Ströberg, 1974; Wang et al., 2016) showing the correlation between temperature patterns and medical conditions. The temperature variation of an area of the body is produced by cell metabolism and local blood flow. The increments in temperature are normally the result of an increase of these factors, although it is true that blood flow plays the most important role. Moreover, with some disease processes or during the different bone formation stages and fractures repair, it may occur a reduction in blood flow to the affected areas (Rundle et al., 2006). This will also produce some alterations in surface temperature.

In the case of using a conventional arm splint, the weight of the material may produce pain in the neck. Also, the lack of ventilation and the difficulty of bathing could produce allergies and itching due to the poor hygiene of the skin and the device. Another negative point of traditional cast implants is the difficulty of handling it in some daily activities by patients (F. Blaya et al., 2018).

This study proposes the implementation of a series of sensors to detect possible problems during the whole time of the treatment. The duration of the treatment does not interfere with the data collection and interpretation. In fact, the collection may be carried out periodically, depending on the specialized doctor necessities and on the injury evolution. For this reason, the data collection is carried out as a sign that the system works.

As it is possible to see in the charts obtained from the sensors, it is perfectly possible to detect temperature variations, pressure increment and humidity inside the splint. Besides, if more temperature sensors are situated in the splint, it would be possible to create a digital mapping of the different areas under the splint. This information to quantify temperature changes in skin surface indicates both hot and cold responses which may co-exist if the pain associate with an inflammatory focus excites an increase in sympathetic activity (Ju et al., 2005). Continuous monitoring of these parameters allows to know the progression of area at any time of the treatment. This allows early detection of possible vascular, muscular or joint complications that are difficult to observe without the removal of the immobilization splint or through severe symptoms caused by often irreparable damage.

The temperature registered by the sensor in contact with the skin, is slightly lower than the normal temperature. this is due to the temperature gradient that occurs on the sensor surface. The sensor surface in contact with the skin is about a 40%. The rest of the surface is covered by the splint but not in contact with the skin. This fact produces a difference of temperature between different points of the sensor. The metallic surface tends to get an equilibrium due to thermal conductivity (Horai & Shankland, 1987). The sensor gets a final temperature that is not the real skin temperature. However, this fact does not interfere with the main purpose of this sensor, which is to detect incremental temperature changes.

Temperature, humidity and pressure are correctly detected by the sensors. Also, the presence sensor detects perfectly whereas the splint is correctly fixed. However, the presence sensor cannot be used for its second propose, detecting colour changes by the variations of the reflection due to the skin colour. This sensor has not enough sensibility to detect so light variations. Moreover, it does not include an RGB sensor to detect different wavelengths, making it really difficult to use the sensor for this purpose. Therefore, the use of such a sensor for the proposed purpose is not estimated.

CONCLUSION

The main objective of this work was the study, design and manufacture of a smart and immobilization splint to monitor different parameters about the real evolution of an injury. This makes it possible to have real time data to diagnostic any kind of problems that are not possible to detect with traditional splints. The current state of the technology allows the realization of particular and individualized immobilization splints by using Advanced Manufacturing, based on fused deposition modelling, 3D digitalization and reverse engineering. Moreover, the knowledge of these parameters, might reduce the curing time as some treatments can be applied in this kind of splints but not in traditional splints.

In this study it is shown an interesting and really possible evolution of the traditional splints, to provide them with the term “intelligent”. The great possibilities that it is offered by this kind of splints, is fully demonstrated. However, there are some improvements that are proposed to be carried out in future studies:

- Implementation of a sensor to detect colour changes of the skin: This would make it possible to detect bruising and redness, that would allow to get more data for the diagnostic.
- Sending these data to a Bluetooth device that allows remote medical monitoring of the treatment applied and the application of an alarm system in the event of complications, as well as the generation of the data dump in a database for study.
- Integration into functional splints based on rehabilitation techniques in the immobilization phase. This would make necessary to incorporate a battery to get a full autonomous system.

To finish this study, the main objective is considered to have been achieved, by the incorporation of these sensors and demonstrated that it is possible to detect complications in the treatment of injuries using immobilization splints.

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Chapter 6

Anatomical Variability and Biomedical Imaging for Spinal Anesthesia Individualization: How 3D Tools Enhance Understanding

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ABSTRACT

Spinal anesthesia can be affected by gaps in the ligamentum flavum that may confuse epidural needle placement; cause Quincke needle deformation if the vertebral bone is hit, expanding the dural sac hole and leading to cerebrospinal fluid (CSF) leakage and post-dural puncture headache; and variability in CSF volume, altering intrathecal drug dilution and anesthetic efficacy. Paramedian approaches with previously calculated optimal angles can be adopted, and CSF volumes may be estimated using threshold selection within the grayscale range following anatomical criteria. Angles can be determined by previously quantifying the skin-dural sac distance using ultrasound. Here, the relevant anatomical structures are illustrated (ligaments, the ligamentum flavum gap, vertebrae, meninges, cauda equina roots) using a freely available 3D PDF tool (<http://hdl.handle.net/2445/55225>), the additional inconvenience of variability in vertebra rotation is quantified, a free guide for optimizing spinal puncture is presented (<http://hdl.handle.net/2445/179594>), and the possibility of individualizing intrathecal drug dosages is discussed.

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INTRODUCTION

When attempting epidural or spinal anesthesia the different anatomical structures to be traversed by the needle must be considered. An important concern is the possibility of touching bone structures with the needle when attempting to reach the spinal canal. When this occurs, the needle tip becomes deformed and may create a larger hole in the dural sac in spinal anaesthesia procedures, with subsequent leakage of cerebrospinal fluid (CSF) through the dural disruption. Furthermore, risk of accidental intrathecal puncture when trying an epidural procedure may happen. Epidural needles have a greater diameter (1.4mm, compared to spinal needles of 0.5 mm or less) and may produce a greater dural hole and CSF leakage. Another concern is the variability in the anesthetic effect due to the variability in CSF volume.

In this chapter, the anatomical structures involved in spinal anesthesia are illustrated by means of a freely available 3D PDF tool (ligaments, bones, meninges, cauda equina roots), the possibility of individualizing intrathecal drug dosages is discussed, the additional inconvenience of variability in vertebral rotation is quantified, and the development of a guide to optimize spinal puncture is detailed.

BACKGROUND

The deformation of the tip of the needles when touching bone during a spinal puncture is of special relevance when Quincke needles are used (Reina et al., 2002) which will cause a larger dural disruption after redirection of the needle and a new attempt of dural puncture. The leakage of cerebrospinal fluid (CSF) through the dural disruption can produce a post-dural puncture headache (PDPH) (Buddeberg et al., 2019). The hole size is known to be related to the needle type (Reina et al., 2017). Furthermore, accidental dural puncture when performing epidural analgesia during labour occurs in as many as 1.5% of cases (Maranhao et al., 2020) and PDPH may last for months. Given that intrathecal or epidural procedures are performed thousands of times a day worldwide, PDPH affects thousands of patients every year. In the other hand, the variability in dilution volume due to the variability in CSF volume per segment (Prats-Galino et al., 2012; Puigdel·lívol-Sánchez et al., 2015a, 2015b), might also produce a variability in the anesthetic effect.

Medial and paramedian epidural / spinal approaches will be analyzed. In the medial approach, the needle must traverse either the supraspinous ligament, the interspinous ligament and the ligamentum flavum before arriving to the epidural space and dural sac. However, sometimes a gap is present at the midline of the ligamentum flavum (Lirk et al., 2004; 2005; Hermanides et al., 2012), removing the usual midline resistance that is felt, and introducing the potential to misinterpret the dural sac as being at the ligamentum flavum level (Reina et al., 2016). A paramedian approach avoids this, ensuring that the ligamentum flavum is identified first and that the needle is located in the epidural space, after traversing the ligamentum flavum, either in epidural procedures or in spinal procedures, before penetrating the dural sac. This approach is limited by the choice of the correct angle to avoid hitting the articular process. Freely available 3D PDF tools can help to understand the needle trajectory and the ligamentum flavum gap inconvenience. In this chapter, illustrative images have been prepared to show those anatomical aspects.

Skin–dural sac distance by means of ultrasound evaluation can be used to calculate the optimal angles of the needle for paramedian approaches by means of an easy formula to avoid a touching bone structures (Puigdel·lívol-Sánchez et al., 2016). An additional issue is the frequent vertebral body rotation, which may also affect the final angle of incidence to vertebral canal. The rotation of vertebral bodies

in a sample of patients will be calculated in this chapter. Axial rotation of vertebral bodies may affect the optimal angle of incidence, even if the skin-sac distance is calculated. Rotations have extensively been assessed for scoliosis studies, but axial rotation is frequently mistaken (Illés et al., 2019) and no detailed studies relating rotations and anesthesia exist. Furthermore, given that additional rotation may appear when punctures are performed in a lateral decubitus position, quantification of that rotation will be presented in an illustrative case.

Another consideration is correct vertebral level selection. The end of conus medullaris is located at L1–L2 in most adults (Ellis & Feldman, 1997; Boon et al., 2004; Prats-Galino et al., 2012). However, several studies have shown that anesthesiologists may be confused by one or two vertebral levels (Furness et al., 2002, Boon et al., 2004). Indeed, Furness (2002) showed a 30% of accuracy in identifying the L4–L5 intervertebral space by palpation of the Tuffier's line, between both iliac crista, with confusion of one level in 29% of cases and up to two spaces above in 9% and below in 18%. Thus, when trying to puncture at L3–L4, the final level could be L1–L2 in 9% of cases, increasing the potential to affect the conus medullaris at the end of the spinal cord with the needle and cause potentially neuronal damage. Correct selection of the vertebral level is of extreme importance and may be facilitated by tools such as ultrasound, but its widespread use is still limited in most departments.

Finally, variability in lumbosacral CSF volumes may underpin the observed variability in anesthetic effects (Sullivan et al., 2006). Our group has previously proposed anatomical criteria to select thresholds in the grayscale range on magnetic resonance imaging (MRI) to allow quick and easy semiautomatic quantification of the CSF volume (Puigdemívol-Sánchez et al., 2015a, 2015b). This CSF volume will likely be related to the dilution volume of the injected drug. Here, the CSF volume around the L3–L4 interspace, the most commonly used in intrathecal anesthesia, will be quantified to assess such variability in the segments where an intrathecal drug is likely to diffuse.

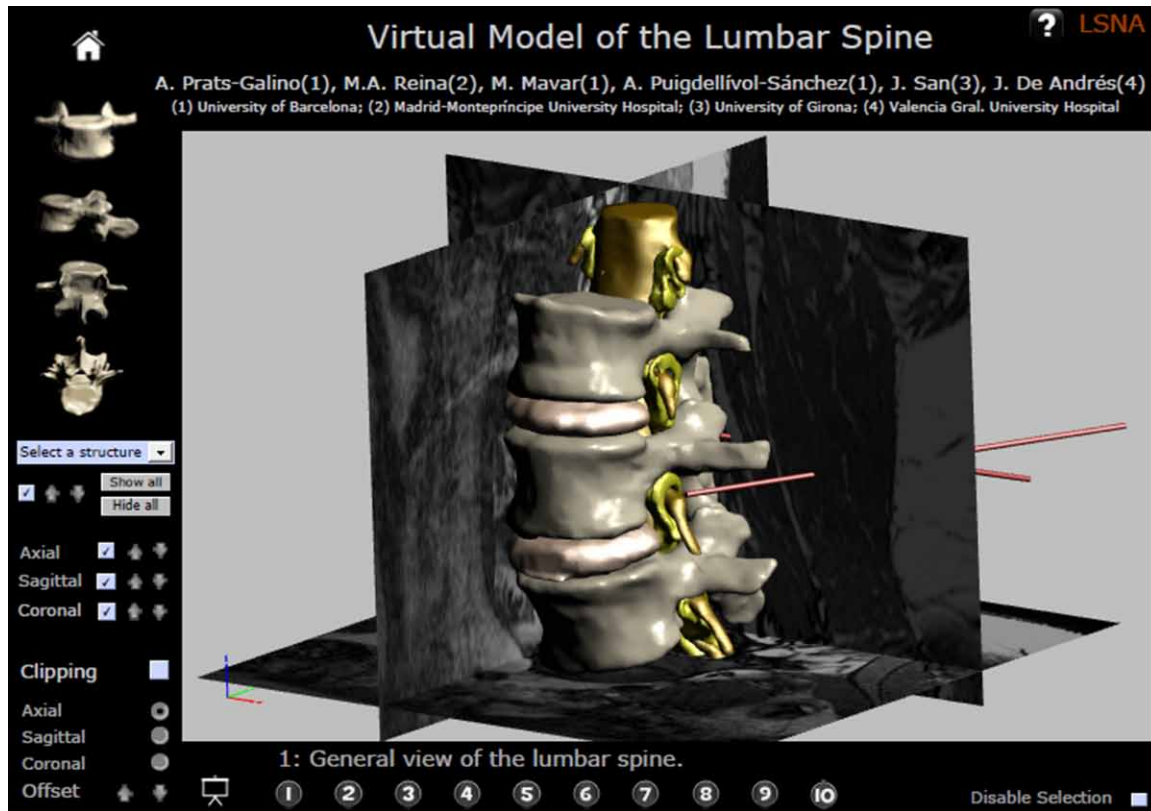
ANATOMICAL STRUCTURES INVOLVED IN SPINAL ANESTHESIA AND 3D PDF TOOLS

3D-PDF Tools

A 3D PDF tool was developed to enhance the understanding of the structures involved in spinal anesthesia (Prats-Galino et al., 2014) (Figure 1). The development of this tool has been described previously (Prats-Galino et al., 2015). It runs on desktop computers, and it is freely available at <http://diposit.ub.edu/dspace/handle/2445/44844?locale=en>. As seen in Figures 1–6, the model can be oriented and rotated in the three axes of space. Each reconstructed structure may be selected by clicking on it, and transparency may be adjusted (Figures 2 and 4) or hidden (Figure 3) with the arrows below the drop-down menu of the structure list (Figure 1). Detailed instructions are available at the same website.

Figure 1. Commands to orientate the model, select the structures, change transparency, visualize the original radiologic images in three axes, and clip the model are on the left of the screen, while a pre-defined sequence of ten illustrative preselected images is available below.

Figure 1.



Anatomical Structures Involved in Spinal / Epidural Anesthesia

For epidural procedures, the anesthesiologists must reach the epidural space and inject the drug into epidural fat (e.g., epidural anesthesia during delivery), while in spinal anesthesia, intrathecal punctures must be performed, penetrating the dural sac. The anatomical structures involved in these punctures, illustrated from behind the patient (the common approach for both punctures from the anesthetist's perspective) are presented in Figure 2.

Figure 2. Structures involved in spinal anesthesia. A. L3, L4 and L5 vertebrae are reconstructed. L2 vertebra and L2–L3 ligamentum flavum (fl) are hidden to improve visualization of the dural sac (ds) and epidural fat (epf). Needles must avoid the upper (uap) and lower (lap) articular process to penetrate the interlaminar space (arrows), between vertebral lamina (vl). The ligamentum flavum covers the interlaminar space. B. The ligamentum flavum is hidden and the dural sac is transparent to allow visualization of Cauda Equina roots (cer).

The epidural fat of the lumbar spine, where the anesthetic drug is aimed to be injected in epidural procedures, is mainly located at midline, dorsally to the dural sac in the epidural space, and also surrounding nerve cuffs (Figure 3). The anesthetic drug is expected to diffuse circumferentially surrounding the dural sac and also cranially and caudally, reaching thus the cauda equina roots. The negative thoracic pressure will predispose to a cranial extension of the drug. Part of the liquid will also diffuse towards the paravertebral space, when exiting the spinal canal through the vertebral foramina.

Figure 2.

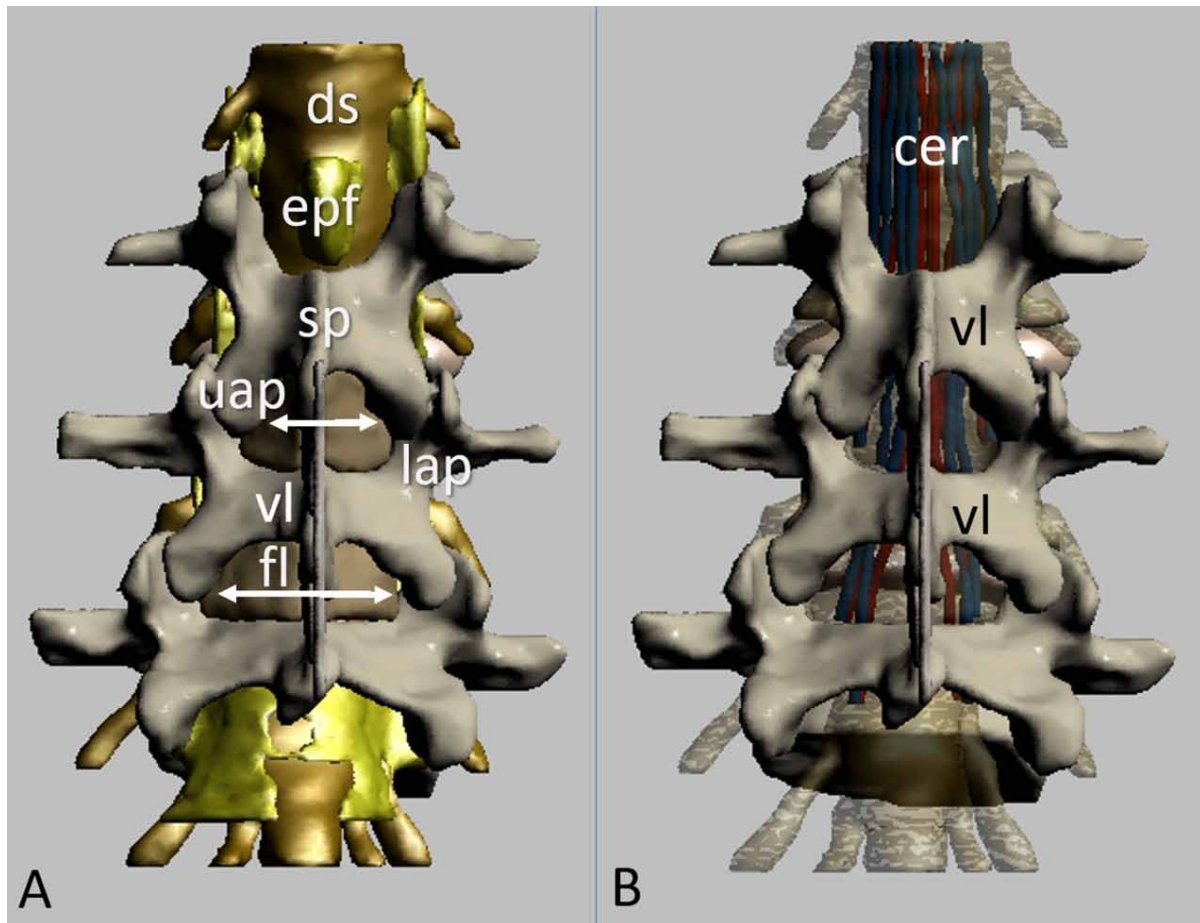
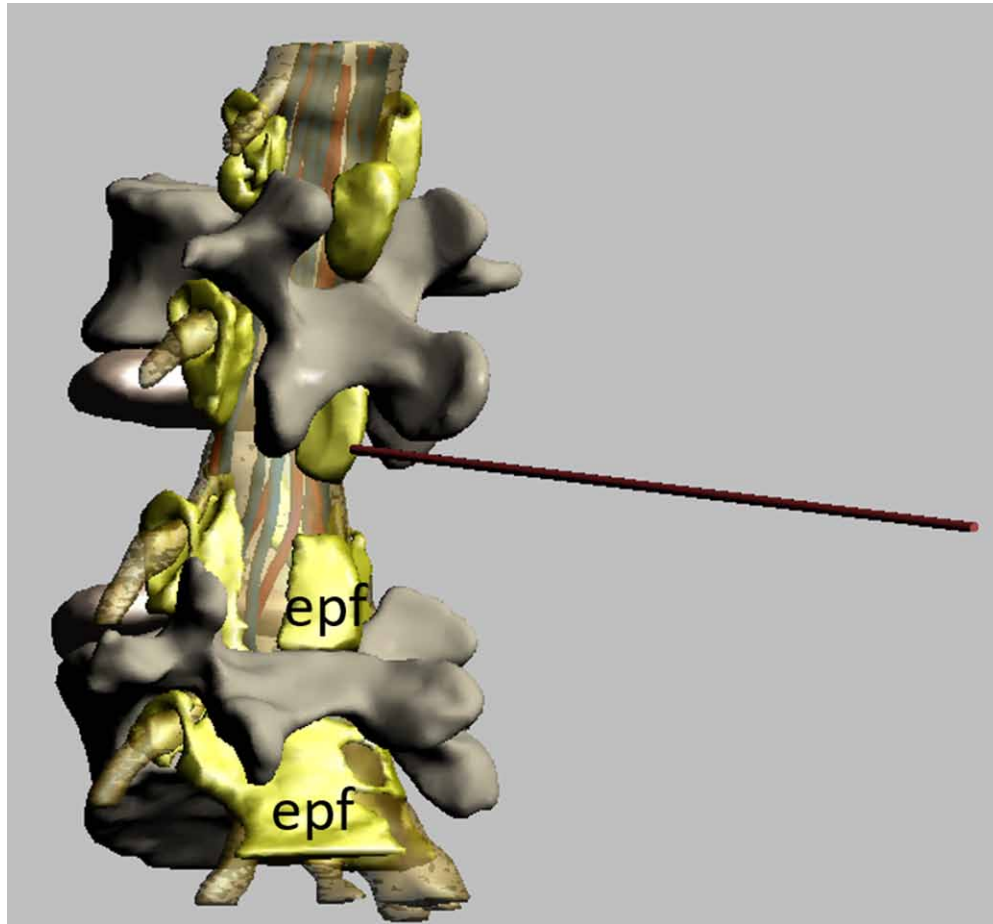


Figure 3. The L4 vertebra is removed to enhance visualization of the epidural fat (epf) distribution surrounding the dural sac, which has been made partly transparent to help visualize the cauda equina location.

Undesired hitting the vertebral laminae or the upper or inferior articular process during spinal anesthesia attempts would deform the needle tip and may result in a larger hole than desired in the dural sac.

The supraspinous ligament, the most dorsal of the ligaments and the first to be traversed, is allocated between the edges of the spinous process. The interspinous ligament is in the midline, adherent over the spinous process and extending from the lower part of the upper spinous process to the upper part of the lower spinous process of every interspinous space. Finally, the ligamentum flavum is adherent to the upper and lower vertebral lamina from the midline and extending laterally towards the upper and lower articular processes, connecting vertebral laminae and covering the full interlaminar space. In cases where a midline gap exists, the “loss of resistance” sensation when arrived to epidural space is not perceived (Figure 4).

Figure 3.

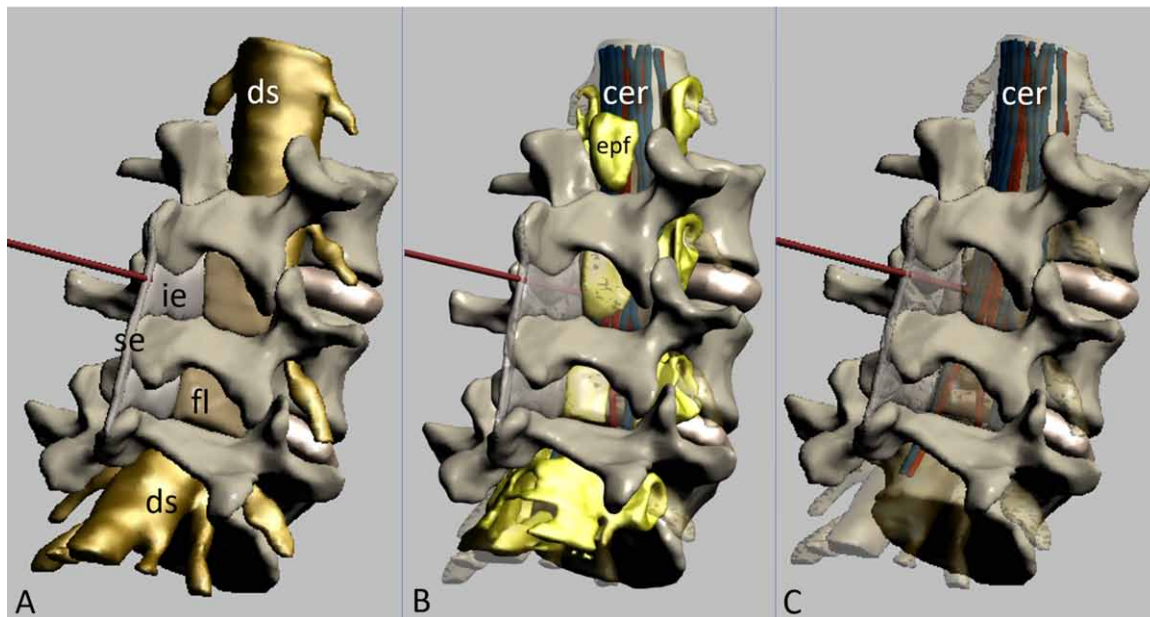


Medial Approaches and Ligamentum Flavum Gaps vs. Paramedian Approaches and Optimal Angles

For the medial epidural approach, the most common, the needle must traverse the supraspinous, interspinous, and flavum ligaments before reaching the epidural space (Figure 4). The epidural space is classically localized using the ‘loss-of-resistance’ technique (Blomberg et al., 1989) with either air or saline solution (Antibas et al., 2014; Brogly et al. 2018).

Figure 4. Ligaments of the spine and needle path in the epidural medial approach. A: Supraspinous (sp), interspinous (ie) and flavum ligaments (fl) must be traversed before the puncture of the dural sac (ds). B: Ligaments and dural sac have been made partly transparent to allow the visualization of the needle path until the epidural space, to apply the anesthetic drug into the epidural fat (epf). Dural sac, containing cauda equina roots (cer), must not be traversed in epidural punctures. C: The epidural fat has been removed to allow the visualization of the close relationship between the epidural space and the cauda equina roots.

Figure 4.



Resistance to injection of air or saline solution is felt when traversing these ligaments, which is lost when reaching the epidural space (“loss of resistance” technique for epidural anesthesia/analgesia). However, Ligamentum flavum midline gaps has been described (Figure 5B) in up to 11% of people at lumbar levels (Lirk et al., 2004, Reina et al., 2016). In these cases, the “loss of resistance” may appear before reaching the epidural space and confuse the identification of the epidural space. In that case, the anesthetic drug could diffuse through the space of Okada (1981), posterior to the ligamentum flavum and anterior to the vertebral lamina (Reina et al., 2020; Riquelme et al. 2021). Also, the confusion of the identification of the epidural space may lead to combined spinal epidural failure, unblocked segments or accidental subarachnoid catheter placement, if the anesthesiologist continues much further, among other complications (Antibas et al., 2014). Some authors have proposed a “test dose” to detect unintentional subarachnoid injections when performing an epidural anesthesia technique to avoid spinal anesthesia risk if the total epidural volume of drug was injected (Colonna-Romano et al., 1994; Pratt et al., 2013, among others).

Figure 5. Ligamentum Flavum gaps. A. Axial view of the 3D PDF model, clipped at the level of puncture for the medial approach, visualized with the corresponding radiological axial plane. Ligamentum flavum (arrows) delimit a triangular epidural space where the tip of the needle is located. A. White curved line delimits the dorsal dural sac. B. Dorsal 3D PDF view. Ligamentum Flavum (arrows) with a midline gap (circle) are illustrated, traversed by the needle. The epidural space is reached by the needle without resistance from the ligamentum flavum.

To avoid the problem of the precise localization of the epidural space, associated to the existence of the ligamentum flavum gaps at midline, the paramedian approach may be performed (Figure 6). However, a disadvantage of this approach is that the correct angle must be chosen to avoid hitting the bone structures, with special consideration to the articular process.

Figure 5.

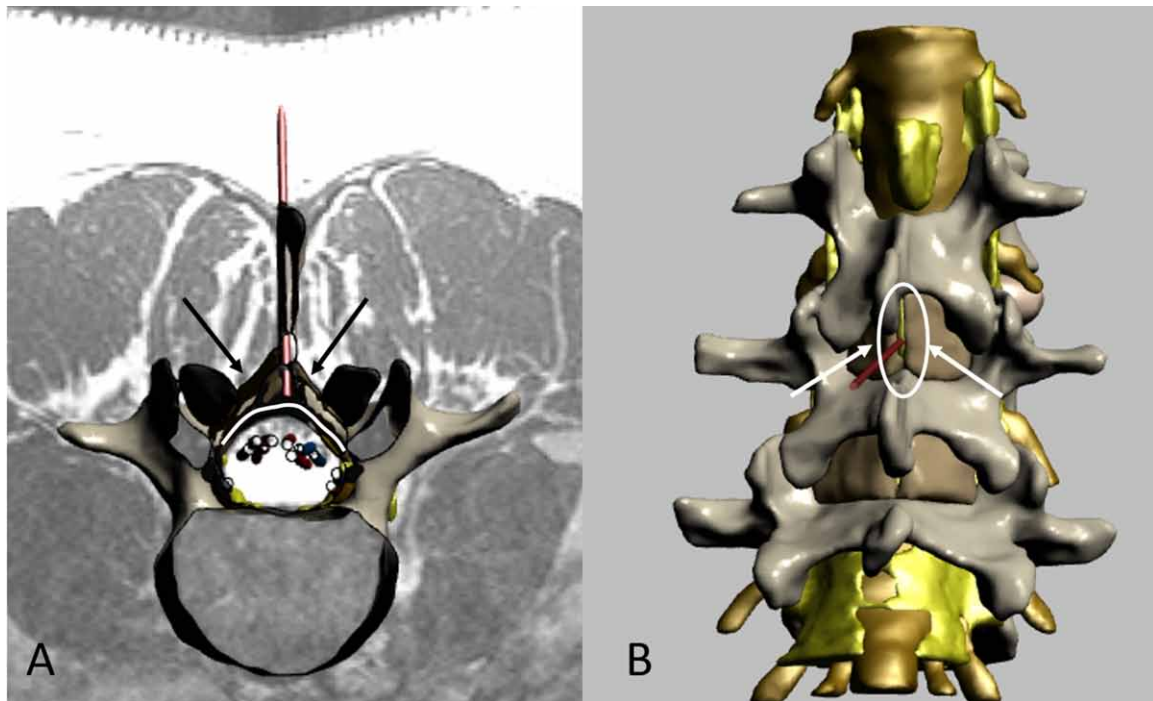


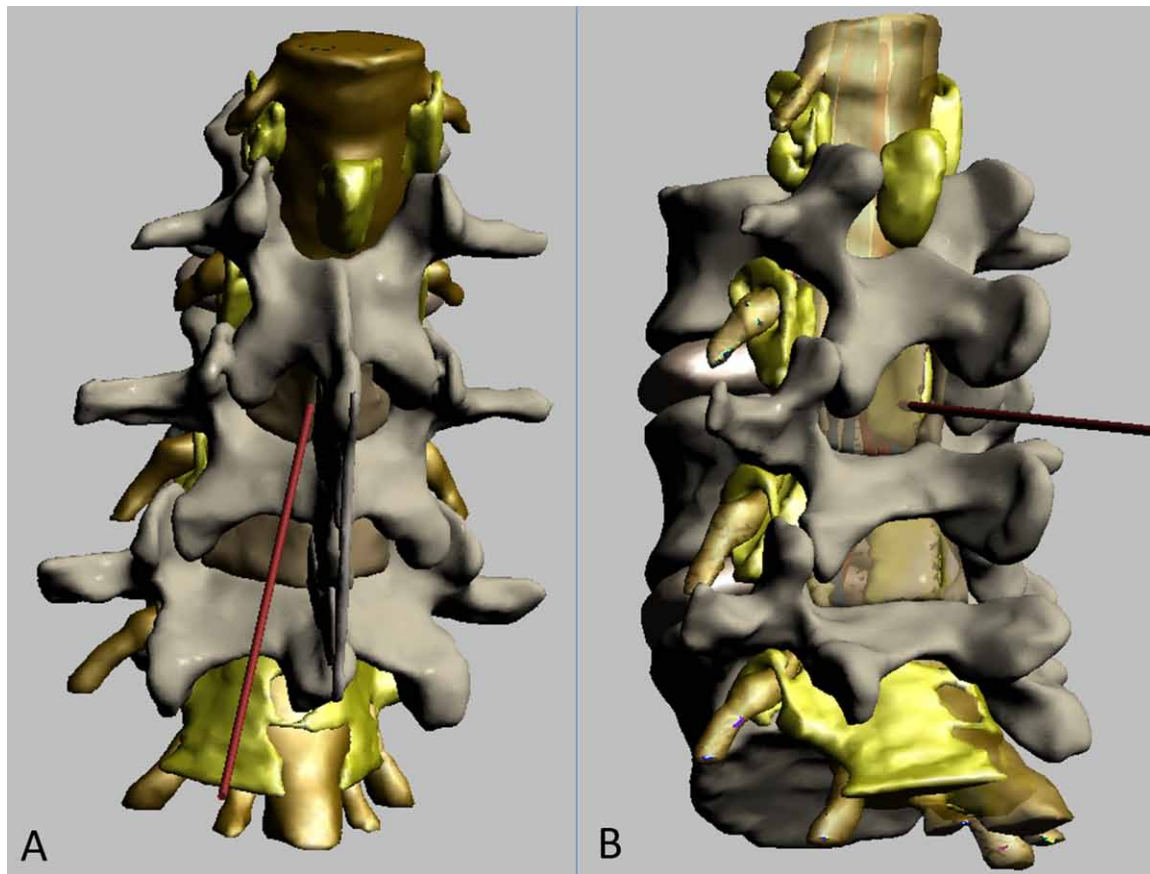
Figure 6. Paramedian approach. A Dorsal view of the 3D PDF model. B. Left dorsolateral view. Supraspinous and interspinous ligaments have been hidden and the ligamentum flavum and dural sac have been made partly transparent to enhance the visualization of the needle reaching the epidural fat, close to the cauda equina roots, after penetrating the ligamentum flavum, avoiding the midline gap.

Most authors recommend needle insertion from 1 cm lateral to the midline at an angle of 15° medial and cephalad (Boon et al., 2004, Jane & Wray, 2020). However, to reach the dural sac, at least five attempts may be needed in >40% of cases, while up to ten attempts may be needed in 20%, according to some reports (Kampitak et al., 2018). When assessed by MRI, there may be great variability in optimal angles among cases and between intervertebral levels in the same case. Furthermore, the range of possible angles that will allow any dural puncture, even if suboptimal, is <10°. Thus, slight variation in needle orientation will likely produce bone contact and needle deformation. The good news is that the angle may be calculated by an easy formula if the skin–duralsac distance (d) is estimated. Then, the optimal angle (α), when the needle is inserted x cm paramedially, would be:

$$\alpha = \arccosine \sqrt{x^2 + d^2}$$

Consequently, the angle should be individualized based on the skin–dural sac distance, which may be quantified by ultrasound, X-ray, or MRI before the anesthetic procedure (Puigdemívol-Sánchez et al., 2016). Other studies have proposed a complementary formula based on the inverse of the tangent between the paramedian distance and the skin–dural sac distance. With this pre-injection estimation, 100% of cases need three attempts at most to achieve successful dural puncture (Kampitak et al., 2018).

Figure 6.



Additional Threats: Rotation of the Vertebral Bodies

An additional consideration when choosing the right incidence angle is the rotation of the vertebral body, which relates to the angulation of the spinous process. The angle of the spinous process regarding the sagittal plane at the level of the dorsal part of the dural sac (Figure 7) has been recorded in seven subjects in MRI to assess the incidence of vertebral rotation. This angle is a modification of the common ϕ angle in other methods for quantifying axial vertebral rotation -Cobb, Nash and Moe and Stokes- (Il-lés et al. 2019), that relate the angle of the spinous process to the axis of the sagittal plane at the level of the center of the vertebral body. Patient characteristics, such as age, weight, height, and body mass index have been described previously (Puigdemívol-Sánchez et al, 2011). Vertebral body rotation was present in all subjects, even when no pathology was described in medical records. Some subjects had vertebral bodies rotated towards the left and also towards the right. The detail of vertebral rotations is presented in Table 1.

In supine position a subject may show rotation toward the left or right at adjacent levels (Figure 7), and the associated spinal process angulation may confound anesthesiologists in the absence of X-ray or MRI. Indeed, even if the medial approach is chosen, straight puncture from the middle of the spinous process may not always find the dural sac within the spinal canal (e.g., L1 and T12 in Figure 7).

Table 1. Degrees of the angle of rotation of vertebral bodies following the spinal process per level at supine position regarding the sagittal plane. The angulation (A) towards the right (R) or left (L) is indicated

Case	L5	(A)	L4	(A)	L3	(A)	L2	(A)	L1	(A)	T12	(A)	T11	(A)
1	2.5°	L	4.1°	L	4.7°	L								
2	7.8°	L	2.1°	R	3.9°	R	3.4°	R						
3	1.8°	R	3.0°	R	4.0°	R	3.9°	R	4.6°	R	3.0°	R	0.0°	
4	2.6°	R	4.0°	L	4.2°	L	8.4°	L	5.4°	R	0.0°		2.5°	R
5	3.5°	L	3.6°	R	2.3°	R	4.0°	R	6.2°	R	10.0°	R	0.0°	
6	2.4°	R	2.7°	R	1.5°	R	3.2°	L	7.4°	L	5.9°	L	6.3°	L
7	2.8°	L	2.8°	R	2.4°	L	3.6°	L	0.0°		3.4°	L	4.0°	L

Figure 7.

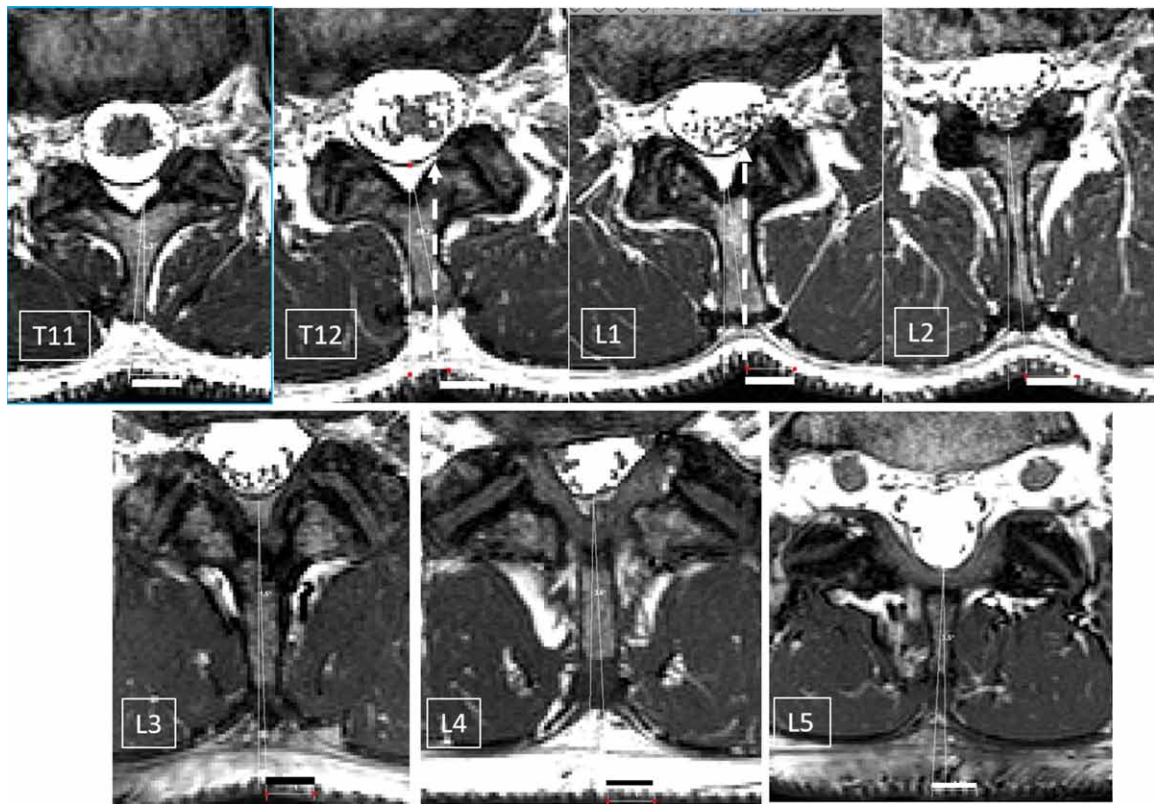
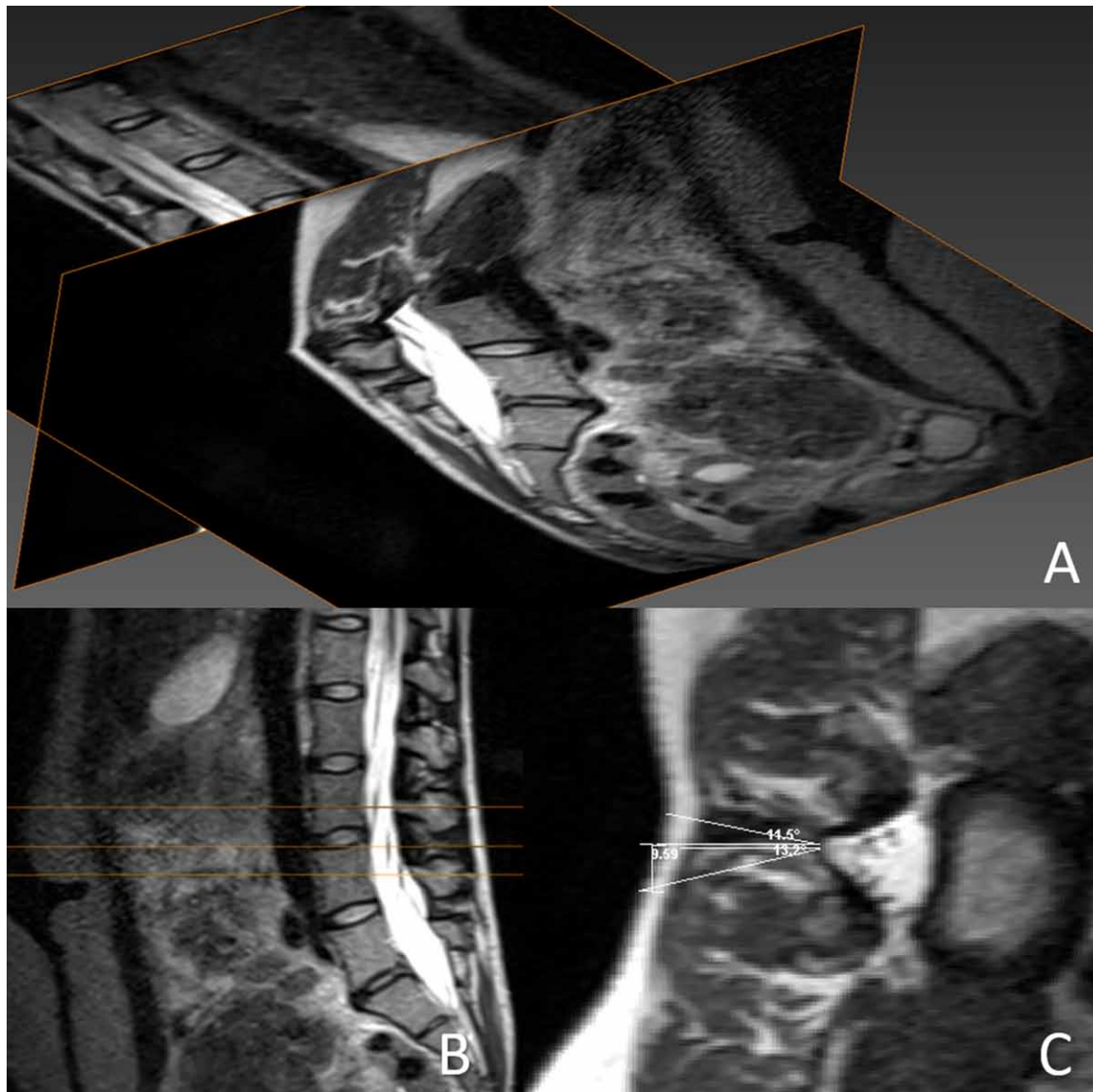


Figure 7. Spinal process angulations in case 5. Adjacent levels, such as T11 and T12, can be oriented differently, towards the left or right, respectively, in the same patient. Depending on the degree of angulation, even straight entry at the center of the spinous process will not always allow an optimal dural sac puncture (discontinuous arrows at T12 and L1). Scale bar: 1 cm.

Figure 8.



Angles have been also estimated in the MRI of an additional healthy volunteer (female; height 158 cm; weight 57.5 kg). MRI images were acquired in the supine and lateral fetal positions in which many spinal anesthesia is performed (Puigdemívol-Sánchez et al., 2016). Rotation was quantified in both positions, with additional rotation appearing with regards the axial plane. Such angulation may exceed 17° (Table 2). Notice the additional inclination of the different vertebral bodies regarding the horizontal plane in the fetal position (Figure 8C). Such inclination toward the inferior side of the body is probably due to natural inclination of the body and legs towards a relatively prone position to maintain the lateral position.

Figure 8. Angle of rotation of the L3–L4 interspace in a volunteer by MRI in fetal lateral decubitus. A: Dorsolateral view of the middle sagittal plane and of the axial planes. B: The flexed spine produces a rectification of the lumbar vertebral bodies. C: Lateral view of the axial plane. Notice the dorsal posi-

Table 2. Rotational angulation (A) of vertebral bodies by vertebral level on MRI. Results are shown for the supine together with the lateral flexed (fetal) position for a volunteer. Rotation in the supine position is related to the sagittal plane, while the rotation in the lateral position is related to the axial plane

Volunteer position	L5	(A)	L4	(A)	L3	(A)	L2	(A)	L1	(A)	D12	(A)	D11
Supine	4.2°	R	1.8°	R	1.1°	R	4.3°	L	3.4°	R	2.8°	R	0
Lateral	13.8°		11.5°		17.8°		14.6°		14.3°		17.5°		15.6°

tion of cauda equina roots, even in a flexed position, as well as the angle of the spinous process to the horizontal plane.

In the L3–L4 interspace, typically preferred for anesthesiologists, the Cauda Equina roots are located rather dorsally in this case, even in fetal position (Figure 8C). Although some authors have described that roots are located at the most ventral part within the spinal canal at that position (Takiguchi et al., 2004, 2009), this shows that roots may still be present dorsally in some patients.

Ultrasound will specially allow rotation to be estimated in a patient in the lateral decubitus position in which anesthesia will be performed, helping to avoid hitting the spinous process. If a medial approach is used, such angulation will affect the correct needle pathway. In a flexed and lateral decubitus fetal position, only ultrasound can assess rotation accurately. More research is needed to assess if rotation is also modified in the flexed seated position.

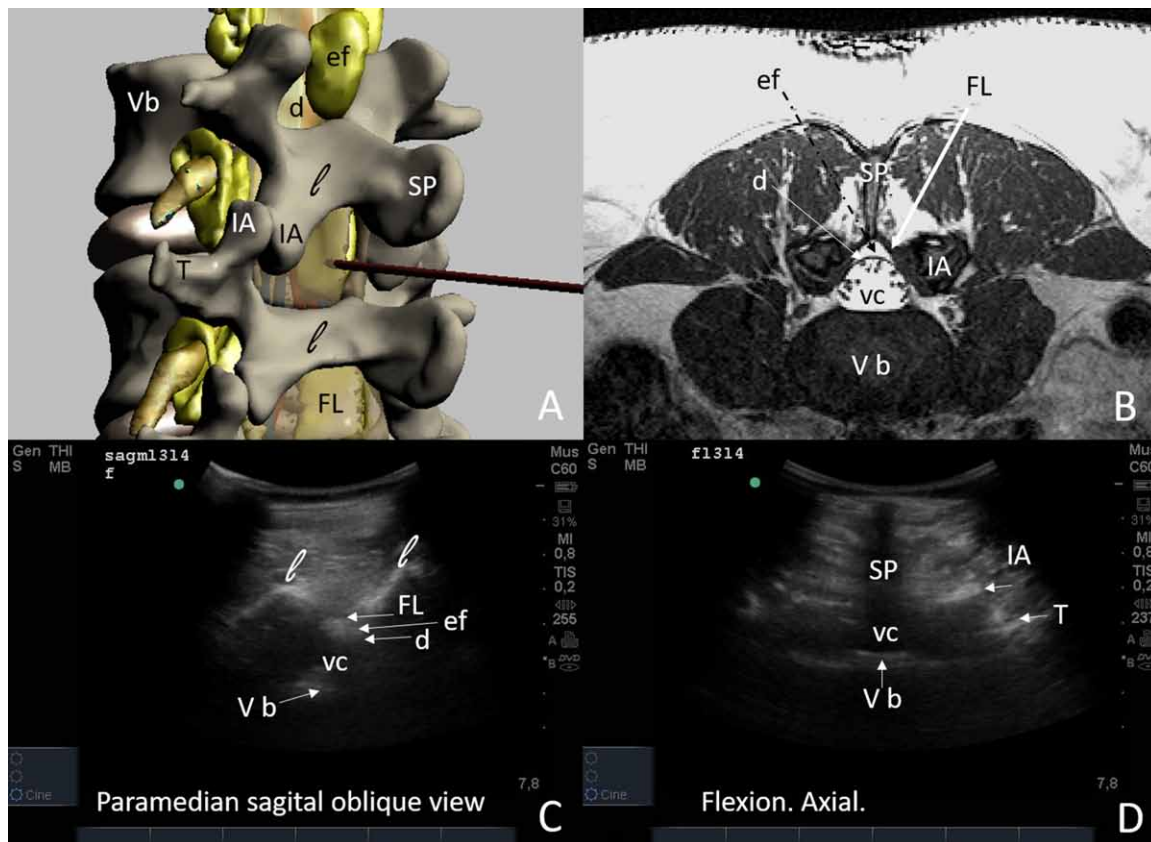
Finally, any angle estimated by ultrasound will be slightly increased compared with that calculated by MRI because there is slight compression of subcutaneous fat and consequent reduction of the skin–sac distance by application of the ultrasound transducer. Further research is needed to assess how to correct this bias.

Neuroimaging: How MRI and Ultrasound May be Used to Estimate the Skin–Dural Sac Distance

The skin–dural sac distance may be calculated using MRI slices before delivery in pregnant. If MRI is not available, ultrasound can be used to examine the spine. Either axial, sagittal, or oblique planes may be taken. Correct interpretation of the 3D anatomical structures involved in spinal anesthesia is important when comparing MRI and ultrasound (Figure 9).

Figure 9. A. Oblique view of the 3D model. Vertebral lamina (l) relates the spinous process (SP), palpable at the middle sagittal line of the back, with the interapophyseal joints (IA) and the transverse process (T), which is also related to the vertebral body (Vb). Epidural fat (ef) is mainly located at the dorsal part of the dural sac (d). The ligamentum flavum (FL) must be traversed by the needle before reaching the epidural space. B. MRI. Axial view. The usual view has been rotated 180° to enhance the comparison with the ultrasound image and its understanding. C. Ultrasound. Paramedian Sagittal Oblique View. D. Ultrasound. Axial plane in the flexed seated position. The interapophyseal joint (IA) and transverse (T) process appear denser while the most dorsal part of the vertebral body (V b), indicating the ventral limit of the vertebral canal (vc), appears as a white line at the bottom.

Figure 9.

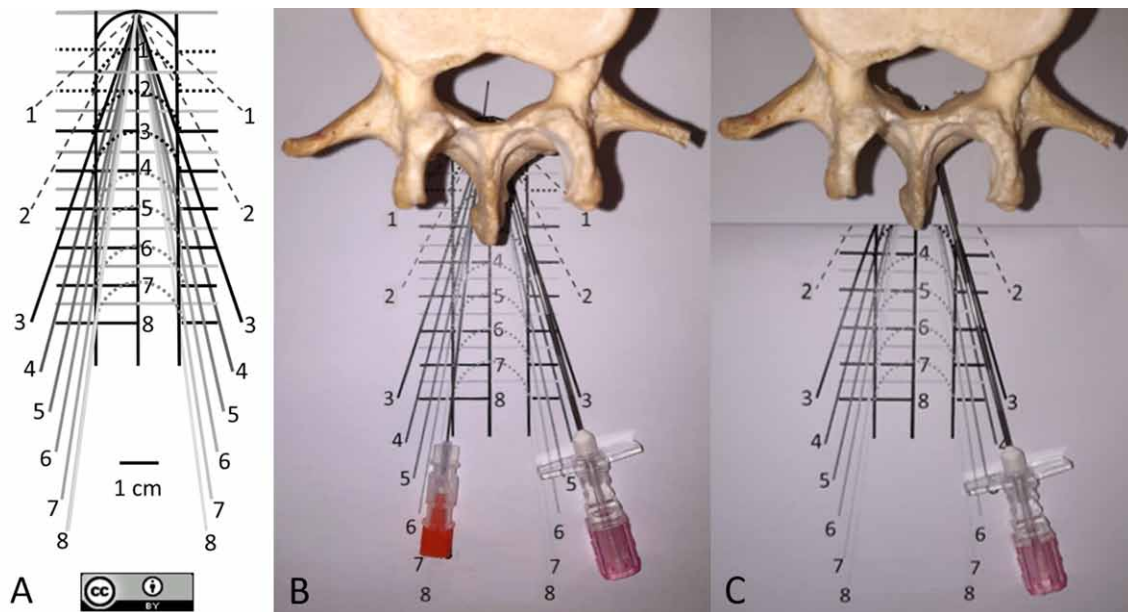


A Visual Guide for Optimal Angles in Spinal Punctures

After determining the skin–dural sac distance and spinous process rotation by ultrasound to individualize the puncture angle, anesthesiologists could use a guide to ensure that the estimated angle is used. A table of the required angles based on determined skin–dural sac distances has previously been published (Puigdemívol-Sánchez et al., 2016, Table 1). However, this did not show how to implement a determined angle (e.g., 12.5°) for an estimated distance (e.g., 4.5cm) with a given vertebral rotation (e.g., 3°). Furthermore, notice that the lower the distance, the higher the needed angle. Below 3.5 cm, the distance for people with a height <1.60 m and IMC <25, all angles are above the commonly recommended 15°. Thus, special care must be taken when individualizing angles in pediatric and small patients.

We propose a visual guide (Figure 10) that can be applied to the skin of the patient to show the needle trajectories by specified skin–dural sac distances. Once the distance is known, the guide may be flexed or cut, covered with any sterile transparent surface, and apposed to the skin at the level of the patient's spine. The anesthesiologist then simply follows visually the required angle. A guide based on the published calculated angles at 1cm paramedian may be found in the Public Repository of the University of Barcelona at the following link: <http://diposit.ub.edu/dspace/handle/2445/179594>. It's offered under a CC-BY Creative Commons license, that allows any free use given that authors are cited.

Figure 10.



In Figure 10, the optimal angles are shown for reduced skin–dural sac distances of 3.5 cm, that corresponded with those quantified in our volunteer by MRI in the flexed fetal position, and also for the average 6–7 cm in the studied cases. The volunteer was only 158 cm in height (Puigdemívol-Sánchez et al., 2016).

Figure 10. A. Visual guide. Angles are illustrated bilaterally to facilitate use by right- and left-handed anesthesiologists. B. Spinal and epidural needles. Spinal needle (25G, Quincke) at the left of the image with the corresponding angle for an average distance of 7 cm. Epidural needle (18G, Tuohy), directed to the epidural space of a hypothetical small patient with a short skin–dural sac distance of 3.5 cm. A puncture for a theoretical 3.5 cm of skin–dural sac distance is illustrated. C. Puncture can be aided by flexing the visual guide to the required distance and apposing it to the skin (in this case, hypothetically at the tip of the spinous process) once the skin–dural sac distance is known.

The visual guide could also be rotated with the vertebra. It includes a discontinuous curved line at centimeter intervals to allow adaptation of the guide to vertebral bodies angulations. Vertebral rotation may also be determined by ultrasound, using the angle of the spinous process to the angle perpendicular to midline. Thus, an anesthesiologist would just need to adapt the guide to the rotation of the spine, choose the corresponding skin–dural sac distance, and corresponding angle on the guide, following its inclination with the needle in the axial plane. Notice the variability of vertebral angulation in the axial position (Figure 7) and the lateral decubitus fetal position (Figure 8).

Regarding the vertical plane, it has been shown that a perpendicular angle below the upper vertical process may allow the interlaminar window to be reached (Puigdemívol-Sánchez et al., 2016), where more epidural fat is present (Figure 9B). Further studies are needed to confirm if this perpendicular angulation allows for successful puncture. If confirmed, it is easily reproducible and would reduce the risk of hitting the vertebral lamina.

3D VOLUMETRIC ESTIMATIONS OF CSF VARIABILITY

Variability in CSF volumes is also of interest (Lee et al., 2001, Sullivan et al., 2006, Puigdemívol-Sánchez et al., 2015b), since it could affect the dilution volume of intrathecal drugs. Experimental studies suggest that the higher concentrations of the intrathecal drug are found few centimeters around the injection (Bernards, 2006).

To calculate the dilution volumes of the anesthetic intrathecal drug within the dural sac, anatomical criteria for threshold selection ranges in MRI have been proposed to individualize dosages, which could be of particular interest in pediatrics and oncology. Variability of up to 120% in CSF volumes has been detected among cases for determined MRI distances (50 MRI slices from L5–S1), while variability in threshold selection does not exceed a 30% when selecting maximal or minimal possible threshold values (Puigdemívol-Sánchez et al., 2015b). Threshold selection may therefore help to estimate root and CSF volumes. The relationship between root volume and dural sac in a specific interspace will be related to the vulnerability ratio, the possibility of contact with a root during an intrathecal puncture (Prats-Galino et al., 2012). Dural sac volume is the sum of the root volume and the CSF volume.

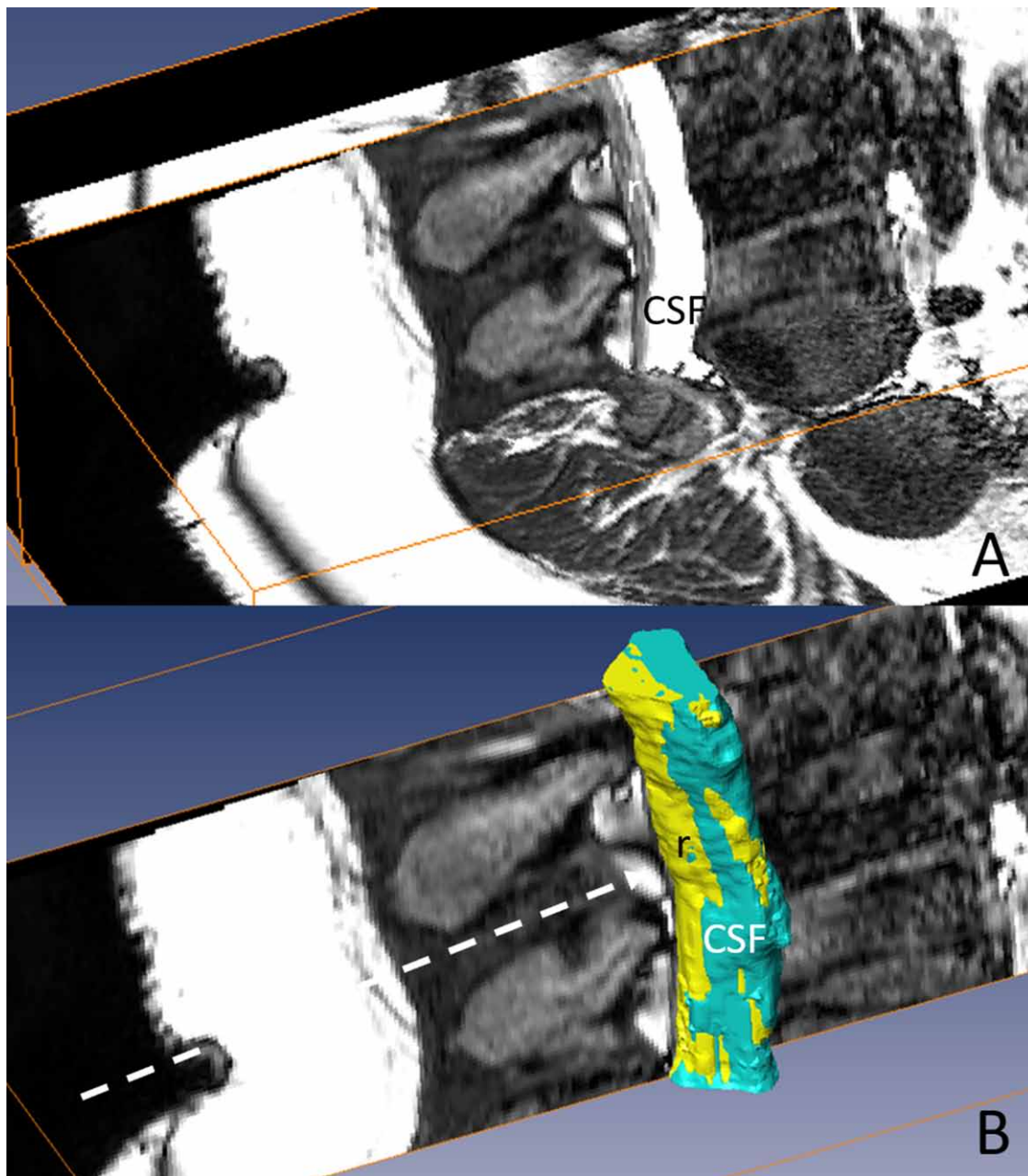
Differential threshold selection was also behind the differences in estimated volumes of lumbar blocks when the estimations of different research groups were compared. One group selected thresholds close to the root thresholds and excluded them from the dural sac volume, while another group selected thresholds that allowed direct semiautomatic CSF selection (Puigdemívol-Sánchez et al., 2011). However, differences in CSF volume were <3 mL between whole lumbar blocs between both teams.

The specific anesthetic effect will also depend on the anatomical segments where the drug may diffuse and, possibly, on its final dilution, which may be related to the total CSF volume of those segments. Previous experimental evidence has shown that drug concentration in CSF and spinal cord decreases rapidly as a function of distance, with most drug found within a few centimetres from the site of administration (Bernards, 2006). Here, the CSF volume per case, one segment above and below the L3–L4 intervertebral space, one of the most often chosen for spinal anesthesia, has been quantified. The previously reconstructed lumbar blocks (Puigdemívol-Sánchez et al., 2011) have been segmented to select only the L3 and L4 vertebral segments, where a drug injected in the L3–L4 interspace will initially be diluted. The reconstructed 3D volume of the CSF and roots at the L3 and L4 vertebral segments are shown for an illustrative case in Figure 11. In addition, the full CSF volumes at the L3 and L4 vertebral levels are shown in Table 3 together with the corresponding root volumes, vulnerability ratios, and vertebral L3–L4 heights.

Figure 11. Reconstructed CSF and root volumes around the L3–L4 interspace. This is a typical puncture site (arrow). A. Axial and Sagittal MRI planes of an illustrative case. B. The 3D reconstructed root (r) and CSF volumes.

Notice that vertebral heights between two segments are quite homogenous among cases (6.6–7.7 cm), but that the root and CSF volumes are much more variable (2.7–4.8 mL for roots, 6.5–13 mL for CSF). The relationship between root volume and CSF may also affect the risk of contacting roots with the needle during an intrathecal approach, producing undesired paresthesia. Indeed, the lower vulnerability ratio is >20% and may reach 42.6%. Furthermore, although previous studies have shown that nerve roots are displaced toward the anterior dural sac in a flexed position (Takigushi et al., 2004–2009), even with fully flexed legs, some roots may lie caudally (Takigushi et al., 2009, Fig 2 D), close to the dorsal part, which may be reached by a lower paramedian approach. In the flexed volunteer (Figure 8C),

Figure 11.



the roots may still be present in the dorsal part of the dural sac and can be easily contacted by lower or upper paramedian approaches.

Another concern is the relationship between the minimal and maximal CSF volumes. Height variability at vertebral levels L3–L4 is minimal for available cases, being 1.1 cm different between smaller (6.6 cm) and larger (7.7 cm) vertebrae, although height among cases ranged from 1.60 to 1.84 (Puigdemívol-Sánchez et al., 2011). However, even for a similar L3–L4 vertebral height of 6.6 cm, the CSF volume

Table 3. CSF and root volumes in L3 and L4 vertebral levels. These volumes help to calculate the vulnerability ratio (the probability of contacting a root when attempting intrathecal puncture in the L3–L4 interspace). * Root volume/Dural sac volume

Case	CSF volume (mL)	Root volume (mL)	Vulnerability ratio (%)*	Vertebral L3 and L4 height (cm)
1	13.0	2.8	21.2%	6.6
2	11.6	4.8	42.6%	7.0
3	10.5	3.5	33.5%	7.7
4	11.7	2.7	22.7%	7.2
5	10.9	2.4	22.1%	7.0
6	6.5	2.5	38.2%	6.6
7	8.9	3.2	35.8%	6.6

ranged from 6.5 mL in case 6 to 13 mL in case 1. This 100% variability may affect the dilution volume of intrathecal drugs and explain the differences in anesthetic response among patients by CSF variability (Lee et al., 2001; Sullivan et al., 2006; Puigdemívol-Sánchez et al., 2015b).

FUTURE RESEARCH DIRECTIONS

Systematic comparison of optimal angles in flexed seated or lateral decubitus positions, the possibility of upper approaches in the lateral position, changes in vertebral rotations depending on the position and angle correction due to subcutaneous fat compression during ultrasound positioning are other aspects that require more precise exploration. Epidural punctures during delivery may benefit from precise location of the epidural space, avoiding the confusion with the intrathecal space, to avoid complications.

Ongoing research includes the assessment of needle puncture attempts in an anesthesiology unit and its improvement using visual guides. The easiest and cheapest procedure may be to use the proposed visual guide, above, covered by a transparent sterilized material, apposed to the back of the patient according to a measured dural sac distance. Alternative devices may need to be developed, simulating the guide, to help follow the desired inclination of puncture. These may be prepared using sterilizable materials.

Different guides may be prepared for different distances or one single flexible device could be designed, that should also be adaptable to the vertebral rotations. Alternatively, digital devices based on augmented reality, adaptable to individualized patient dimensions and anesthetist eye-puncture distances, could also be considered in the early future.

Finally, intrathecal procedures may benefit from developing a generalized semiautomatic CSF volume calculation, because variability in those volumes is likely to generate differences in anesthetic effect. When intrathecal drugs are to be administered in oncologic patients, where drugs may have considerable side effects, dosage precision is of special interest.

CONCLUSION

The understanding of Anatomical aspects involved in Spinal Anesthesia can be enhanced by the freely available 3D PDF tool, VSL-v2, which has been made freely available at the Public Repository of the University of Barcelona (<http://diposit.ub.edu/dspace/handle/2445/44844?locale=en>). Gaps in the middle of the ligamentum flavum may confuse the identification of the epidural space if the medial approach is chosen for spinal anesthesia. However, when the paramedian approach is chosen, hitting the vertebral bones with the needle can cause Quincke needle tip deformation that can lead to larger dural holes, CSF leakage and subsequent post-dural puncture. Great variability exists in the distances between skin, epidural space, and dural sac, while vertebral body rotation is also common and often unpredictable, especially in the lateral decubitus position. Spinal anesthesia may be facilitated if optimal angles are estimated before puncture, using ultrasound to measure the skin–dural sac distance and to identify the right vertebral level and rotation. A free visual guide may help anesthesiologists to follow the calculated angle and it's also available in the same Public Repository (<http://hdl.handle.net/2445/179594>). CSF volume might also be estimated before intrathecal procedures to reduce the drug dosages, that could be adapted to the wide variability in CSF volumes in the future. These considerations are of interest when seeking to individualize spinal anesthesia, epidural procedures, and intrathecal treatments, especially in small or pediatric cases.

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Chapter 7

An ETL Approach to the Generation of Educational Resources From Digital Radiology Medical Collections

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ABSTRACT

This chapter describes an ETL (extract, transform, load) approach for the generation of instructional resources from pre-existing collections of clinical data, in particular in the field of radiology. The approach advocates, on the one hand, the extraction of information from such sources and its representation in a unified and machine-processable format. On the other hand, the extracted information can be transformed to fit different instructional needs. This transformation process can involve both automatic transformations and transformations carried out by experts using specialized editors. Finally, the information resulting from the transformation process can be exported in standard formats in order to load it to learning management platforms (e.g., Moodle or Canvas). The chapter illustrates, with the help of a radiology clinical case collection, how this approach can be supported by a flexible digital collection management tool called Clavy.

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INTRODUCTION

Data sources in healthcare have been growing in an exponential way over the last years. The variety and volume of data sources coming from different health systems and clinical environments have boosted new technological platforms and tools based on AI (Artificial Intelligence) to processing this huge amount of information. This situation is particularly critical in the current pandemic context due to the increasing number of digital medical collections which are composed by myriads of radiology images, clinical reports, and text annotations over them. These multiple and heterogeneous data sources must be collected and processed by means of AI tools and they can also be used as instructional resources for training future healthcare students and practitioners. Therefore, there is a real educational demand for novel platforms and mechanisms to support the collection and processing of these multiple types of healthcare data and the current work proposes an ETL (Extraction-Transform-Load) approach (Ong et al, 2017) to cope with such a demand. The proposed ETL approach is based on a tool called *Clavy* (Gayoso-Cabada et al, 2016, Buendía et al. 2020, 2021), specialized in the management of data collections, and it is addressed to deal with the three stages of Extraction, Transformation and final Load of instructional resources which can be generated from existing digital medical collections.

The first challenge in the extraction of healthcare data sources is the high number of locations in which such data items can be found. That is particularly true in the radiology domain that uses public imaging repositories, publishing databases, specialized Web sites or dataset archives holding data associated to this domain. Moreover, these data sources can store different multimedia formats ranging from clinical text reports written in natural language, electronic health database records, spreadsheets measuring several biomarker values or images gathered by means of imaging techniques such as X-Ray, MR, CT or ultrasound. Their access and extraction require a wide range of mechanisms depending on the data source location, the structure of the collected data or the semantics associated to them.

Once this myriad of data sources has been extracted, the second challenge lies in obtaining an information model that provides a homogeneous schema of the required data structure. The aim of this global information model is to show the multiplicity of features and attributes characterizing the considered radiology data sources. A first transformation process will populate this model with the information gathered from all these information sources. Afterwards, other transformation processes should be able to convert this raw information in the integrative model to fit in more specific schemata according to the selected educational purposes which can range from merely expositive presentations to advanced interactive products (e.g., including questions or simulation exercises). These transformations can be supervised by experts who decide which data attributes will be integrated into the final instructional resources or the multimedia items attached to them. Moreover, cleaning or curation processes should be incorporated to guarantee the quality or safety of the data used during this transformation stage.

The final challenge of the ETL approach consists in generating the instructional resources from the schemata used during the previous transformation processes and loading them into platforms or environments which allow for the different healthcare agents their actual application. In particular, we have experimented with the generation of resources for the educational domain (Buendía et al. 2020, 2021). In this point, the use of standard educational specifications is crucial to enable the upload of these resources to the most popular e-learning platforms as well as improving their reusability and interoperability. In summary, the main objectives of the current work consist in providing a global framework that enables the extraction and transformation from medical digital collections to finally generate and load educational resources, which can be deployed in different kinds of e-learning platforms.

BACKGROUND

As mentioned in the Introduction section, there is a high number and variety of data sources, which can be used in several healthcare areas, including their collection to be processed in IA applications (Lateef, 2016) or as a support for generating instructional resources addressed to healthcare students and practitioners (Buendía et al. 2020, 2021). The current work is focused on the instructional perspective given the potential of digital medical collections in this context. Recent studies (Wynter et al, 2019) wondered about the type of resources used by medical students. Their authors mention the high number of resources available when studying a degree in medicine and they remark the use of traditional textbooks together with a growing attention to e-learning tools such as online question banks or video recordings. In this sense, Shultz & Berryman (2020) surveyed the impact of “non-traditional” online resources by asking Academic Health Sciences Libraries directors who confirmed the demand for many of these resources among students although they also detected economical barriers to access this kind of resources. So, open health collections as those provided by the Michigan University (<https://open.umich.edu/find/find-open-content-you-can-use/open-health-collections>) seem to be a good alternative to commercial or access-limited resources. They include many materials such as textbooks, courses, audio-videos, journals, images, datasets, software, or other mixed content which are free to be used in for health sciences or even shared with some conditions. From this huge number of resources, the main challenge addressed in the current work consists in how to extract the information stored through multiple locations and formats, transform it in a unified organization model and enable its loading in different e-learning platforms under standard specifications.

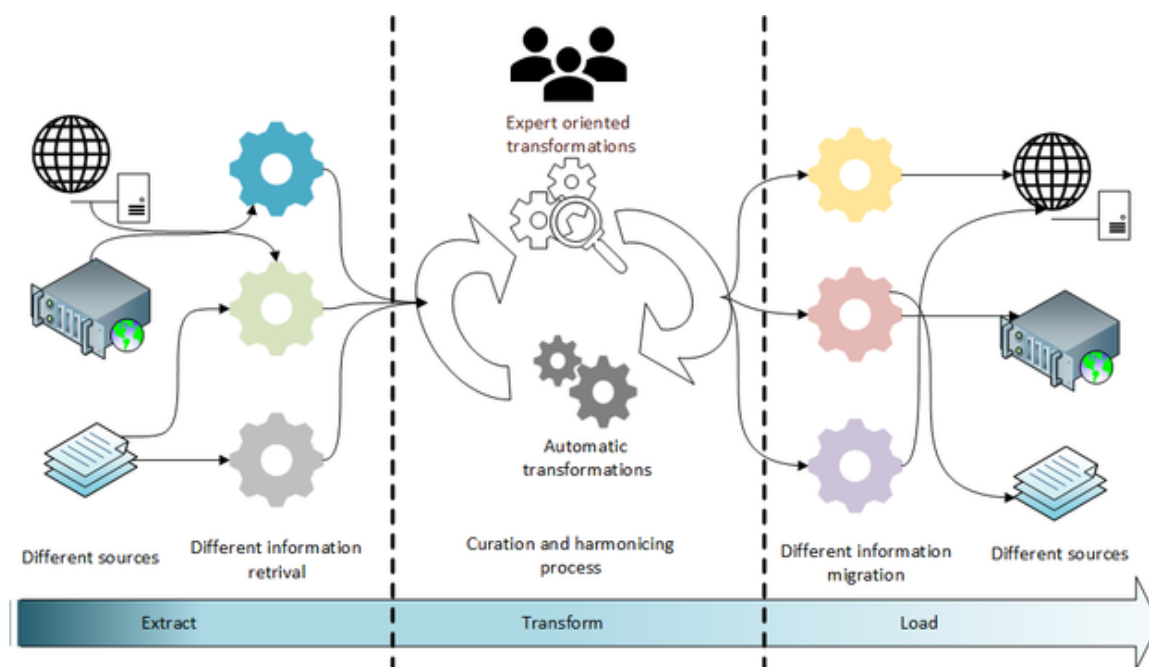
There have been several initiatives dealing with the challenge of obtaining “standard” instructional resources. For example, the Open Osmosis project (DeFilippis et al, 2015) developed a platform to create an “easily accessible repository of curated clinical educational resources” given the fragmentation of content available for graduate and undergraduate medical education.

PiHPES (Precision in Health Professions Education Scholarship) is a similar project addressed to the collection of OERs (Open Educational Repositories) as a way to getting an educational value from this kind of repositories (Topps et al, 2019). A central question is how to build these repositories and ETL processes can provide a suitable approach to take advantage of the huge amount of existing healthcare data. ETL tools have been used to feed a data warehouse based on electronic healthcare records (Pecoraro et al, 2015) and clinical data warehousing can also be benefited from their application (Tute & Steiner, 2015). At the end, an ETL dynamic approach (Ong et al, 2017) can be considered as a suitable way to collect the wide diversity of healthcare data sources and it is one of the most relevant references for the current work. Moreover, the proposed approach takes advantage of the benefits that authors such Lateef (2016) or Ellway et al (2019) observed in the use of big data techniques for education purposes in healthcare areas. In this sense, this work is close to the proposal of building a medical education outcomes center (Rosenberg et al, 2019) or the “Development and maintenance of a medical education research registry” (Wilhite et al, 2020). For the sake of simplicity, the ETL approach has been focused on the radiology domain in order to show how it can manage the multiple data sources (medical images, written reports, lab observations...) which are deployed in this domain. Next sections describe the basics of the proposed ETL approach and its applications in the radiology context.

PROPOSED APPROACH

The current section describes the proposed approach to extract, transform and load educational resources from existing healthcare data sources. It is divided into these three steps which characterize an ETL based strategy: (i) the extraction of the target data sources and the preservation of the ingested information; (ii) the transformation of this information according to the specific rules of the healthcare domain to be considered; and finally, (iii) loading the obtained resources into an educational platform. Figure 1 shows a global view of the proposed ETL approach and the processes described in the next sections.

Figure 1. Overview of the ETL approach



Extraction of Data

As mentioned before, one of the main challenges in the extraction of healthcare data sources is the high number of locations in which such data items can be found. So, every data source must be identified and located, providing the most suitable mechanism to introspect into them and extract their items. While some of these data sources are based on conventional formats such as database records, structured text documents or standard notations, others require more sophisticated tools such as an API (Application Programming Interface) mechanism, a specific point of access or a combination of input data sources to allow their extraction. This problem is even more complex if data sources can store information in a personalized semantic format with a structure, or even lacking it in case of unstructured data (e.g. free text documents), or they have different data schemata than are only readable by means of a legacy-based software. Therefore, many extraction scenarios can come out since every healthcare data system intends to address a certain context, facing different objectives and requiring specific retrieval methods to adapt

the application of the multiple types of data to be used. Moreover, these retrieval methods must be tuned in order to fit them collecting the target data sources in the most suitable way.

Even in a specific healthcare context as the one corresponding to the radiology domain, the extraction of data sources usually requires the management of multiple formats. This problem can be mitigated by using medical standard specifications or controlled vocabularies that enable a more organized or structured data representation. However, radiology staff usually writes diagnostic reports or clinical cases using natural language that makes the standardization of the generated data difficult. An additional complication arises when combining these text documents with images obtained through several techniques such as X-Ray, MR, CT or ultrasound, and other multimedia resources. In this sense, one of the most important issues in radiology or medical training, in general, is the retrieval of real clinical cases and their instructional application. So, those systems and mechanisms addressed to extract multimedia data have to deal with reading and managing multiple types of information in a wide variety of formats. The radiology context provides a myriad of medical collections many of them publicly available, which offer the possibility to extract their multimedia data sources, represented by clinical cases composed by text documents and a set of resources associated with the different explorations results of the patient such as images, video recordings, spreadsheets observations (e.g., blood pressure or sugar levels), ECG signals or biomarkers items. These clinical cases can be also linked with EHR (Electronic Health Records) or genomic databases that complement the available healthcare information. Therefore, the central point in this approach step is extracting clinical cases from existing medical collections, which can contribute with a remarkable instructional value. As commented, each clinical case has a text data part that stores specific information about patients such as their age or gender, a general description of the condition or sickness they have alongside with the diagnosis observations or annotations about their treatment. This text can be structured according to a given template but, in many cases, radiologists write it in a free natural language and using acronyms that make difficult their processing from a data computing perspective. The multimedia resources that are attached to clinical cases are also based in a wide range of formats and even, some specific resources such as radiology images can be stored in very different ways, from vector or raster formats (e.g., JPG or PNG) or medical specification as DICOM (Mildenberger et al, 2002). Moreover, these images can be annotated with certain terms that add special information to the clinical cases and they are usually supported by controlled vocabularies such as RadLex (Langlotz, 2006) or Snomed-CT (Stearns et al, 2001). At the end of this extraction step, the set of selected clinical cases must be ingested in data warehouses regardless the type of multimedia formats or the complexity of their information semantic structure, and ready for their further management. In this sense, it is important to remark that agnostic retrieval methods are required to support this multiplicity of formats and resource complexity with the goal of harmonizing different structures obtained by every source entailed in the data extraction. Another critical factor consists in getting the maximum amount of original information, not only coming from raw data, but also, being able to maintain the semantic of the information and the relationship among their elements. In that point, the intervention of experts to monitor and supervise the extraction of medical collections and tracking the importation of their available items deem crucial.

Transforming Data

Once available data sources have been extracted, there is a lot of work to do until the information can become meaningful within an ETL context. A first challenge consists in the analysis of the semantic structure of ingested data. It requires the importation system can be able to process structures in a batch

process applying those transformation actions to regenerate a harmonized clinical case structure that represents all the available information items. One of the main problems when data sources are extracted directly from original medical collections is the huge amount of information related to the internal organization of the data sources, for example, those identifiers which are local to the imported system or some timing and personal information when authoring the clinical case. Another process supervised by experts is recommended to be performed over the collection of medical data and also supported by tools that enable the different transformation actions in this process to harmonize the collected information items and redefine them in a given healthcare context. Moreover, these tools should be simple to allow experts to apply them by reducing their learning curve and simplifying the transformation process.

In this sense, transformation process includes operations which are shown on Table 1 and addressed to creating, renaming, or deleting the different data items which will be the result of this process. Data items can be also organized in hierarchical levels which can be updated by upgrading or downgrading them. These basic actions will allow to reorganize the inner schema of the collected clinical cases to obtain the relevant information that is equivalent for any collection and fit all the data items that contain it. At this point, specific data structures will merge in a unique master schema. Other important aspects in this transformation process are related to the capability to aggregate additional collections in the future and the scalability to apply these actions in a reasonable time that can be assumed by experts in charge of their supervision.

Table 1. Transformation operations

Name	Description
Creating	Create a new data item.
Renaming	Change the name of the data item.
Upgrading	Update the level of a data items regarding another one by increasing their hierarchy level.
Downgrading	Update the level of a data items regarding another one by decreasing their hierarchy level.
Deleting	Remove a data item and its subordinate items

Data Curation

A typical situation when working with data items edited by a set of experts, consists in the lack of coherency of those vocabulary terms (e.g., acronyms to represent patient conditions) selected by each expert. Such a situation demands an agreement among the experts to edit the transformed data collection and an additional curation process to allow them to standardize the clinical case description by using a common vocabulary and the replacement of specific terms and acronyms by a more controlled vocabulary in form of ontology semantic formats. This task requires a process like the one described in the aforementioned data transformations to provide experts with tools to review the set of medical terms deployed in the clinical reports and other related data sources. Moreover, experts can improve the description of clinical cases by aggregating quizzes, input forms, or other data items with an educational purpose. Curation and transformation processes can be performed in a cyclic or iterative way to obtain successive version of the data collection until the expert decides that a certain level of quality has been reached. Before

this collection can be exported, experts can annotate the items of the collection and edit them to adapt their format to the selected target.

Loading Transformed and Curated Data into Instructional Platforms

After the application of the transformation and curation actions, obtained outcomes must be loaded and stored on data warehouses which enable their further exploitation. The current work follows an instructional perspective, and the transformed data will be used in the context of e-learning platforms addressed to the area of healthcare education. Therefore, a selection of these platforms and the format they can be able to load those items coming from the previous stage become critical. In order to facilitate this loading process, the use of interoperable data formats is highly recommended, and standard specifications such as IMS-CP or SCORM (Kurilovas, 2009) help healthcare education managers to integrate them in widely used platforms such as Moodle or Canvas (Gros & García-Peñalvo, 2016).

As same as extraction, this loading process can be performed under a systematic way but, in this case, the final target is less complex since the control of the data was done in the origin. Also, there are simple methods to transform data collections if they have a controlled structured and the outcome to be obtained is based on a well-known standard specification. If the collection data or the target system is too much complex, is possible to have a better solution by implementing direct transformation in the loading process.

APPLICATION OF THE APROACH

To face all mentioned challenges in the generation of instructional or educational resources from medical collections, an application of the proposed ETL-based approach is described in this section. Such an application is supported by a data collection management tool called *Clavy* (Gayoso-Cabada et al, 2016) that provides users with mechanisms to obtain and integrate information from different data sources using plug-in components which can be adapted to different data schemata/structures. *Clavy* is an experimental software tool developed within the ILSA (Implementation of Language-driven Software and Applications) research group at Complutense University of Madrid, whose main objectives are addressed to the integral management of digital data collections. This tool has been used to extract, transform and load instructional resources generated from several medical collections in the radiology field: the *MedPix* (2016) repository, which represents a web repository of clinical cases which can be explored and retrieved through an API (Application Programming Interface) mechanism based on REST services and returning JSON data, the *PadChest* dataset (Bustos et al, 2020), a large chest x-ray image dataset with multi-label annotated reports, or the *EuroRad* network (Vorwerk, 2002), the largest database for peer-reviewed radiological case reports, operated by the European Society of Radiology (ESR). As described in (Gayoso et al. 2016, Buendía et al. 2020, 2021), *Clavy* is a reconfigurable data management tool that is able to get pieces of content that are usually poorly structured in external sources and arrange them in highly specialized digital collections. For this purpose, the current release of *Clavy* fully supports the operational part of the approach described in the previous section. More specifically:

- *Clavy* enables the aggregation of content from multiple external sources using *import plug-ins*, which makes it possible to import data from standard platforms and formats (XML, JSON, re-

lational databases or NoSQL databases, etc.). Therefore, importation plug-ins in *Clavy* provide support for the *extraction* stage of the ETL approach.

- *Clavy* also supports the addition of different *transformation plug-ins*, which makes it possible to enrich data with domain-specific semantics. In addition, *Clavy* supports powerful edition capabilities, allowing domain experts (physicians, in our case) both edit and enrich individual information items and also to reorganize the overall structure of the digital collection. These capabilities can, in turn, be specialized using suitable *edition plug-ins*. Transformation and edition plug-ins partially supports the *transformation* stage of the ETL approach (as indicated below, this stage can also be supported by the edition of the collection schemata).
- Finally, *Clavy* can be extended with suitable *export plug-ins*, which can be used to convert the transformed and edited collections to different standard formats, which can be loaded in platforms supporting these standards. Thus, this kind of plug-ins supports the *load* stage of the approach.

In order to harmonize all these elements, *Clavy* provides a unified digital collection model inspired in generalized markup languages like SGML and XML (Coombs et al., 1987). Indeed, a digital collection in *Clavy* integrates a set of *documents* conforming to a set of *document schemata*. Documents in *Clavy* allow for aggregating and organizing resources in terms of *element-value* pairs. These elements can be of four types:

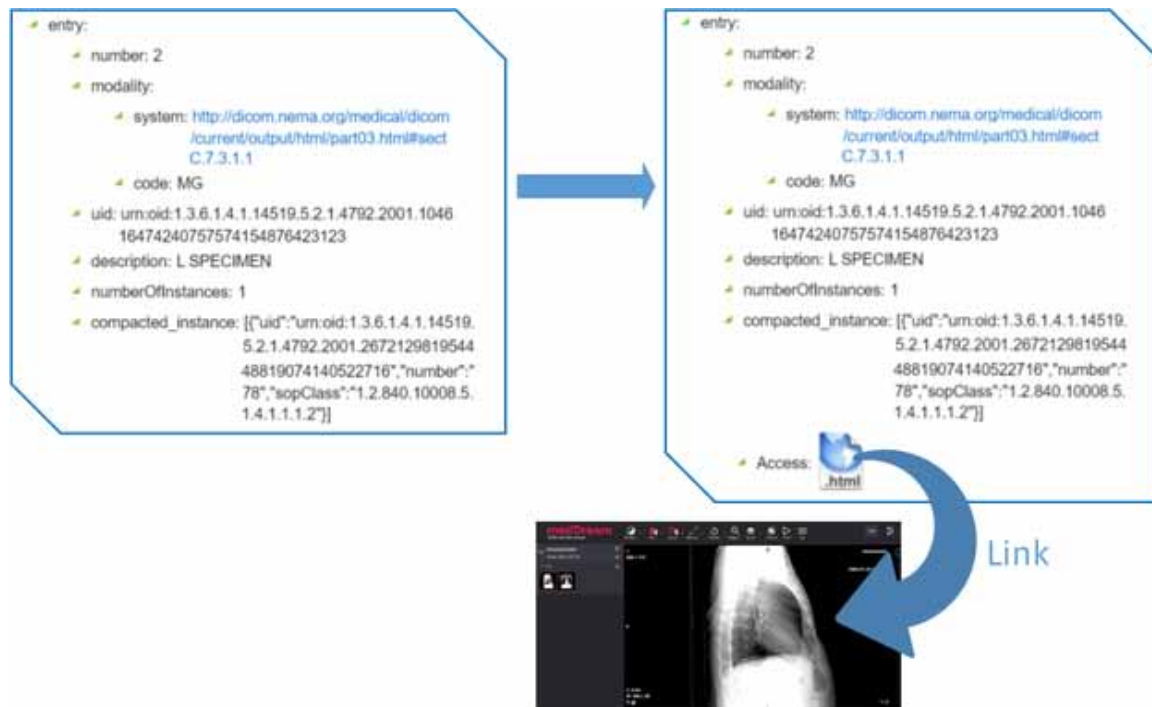
- *Descriptive* elements, which delimit textual descriptions concerning all the information aggregated in the document.
- *Resource* elements, which refer to *resources* in the collection. These resources include both local digital files (image, audio, video, etc.) as well as external resources represented by URLs.
- *Link* elements, which makes it possible to refer to other documents in the collection. These elements enable the representation of semantic relationships among documents.
- *Structural* elements, whose only purpose is to enhance document organization and readability.

In addition, a document schema describes the hierarchical organization of the elements in the documents that conforms this schema. Using the edition facilities of *Clavy*, it is possible to *reconfigure* schemata by adding new element types, by renaming and erasing existing elements, and by reorganizing the hierarchical relationships among all the elements in the schemata. As a consequence, these changes in the schemata are automatically mirrored in the collection documents. This feature lets domain experts reorganize the whole collection by solely editing the collection's document schema. In addition, they can use the document editing facilities of the tool to make more fine-grained adjustments in the content, as well as to enrich this content with new information items, for example, text and image synchronized annotations, like those described in (Buendía et al. 2020b).

Therefore, a distinctive feature of *Clavy* is to actively involve domain experts during the *transformation* stage in the ETL approach. Indeed, besides automatic transformations, experts can reconfigure the overall structure of the collection by using the *edition schema* facility of *Clavy*. In addition, they can use the document edition functionalities of the *Clavy* tool to enable more fine-grained adjustments in the content and enrich it with new data using ad-hoc editors or displaying part of the document. Figure 2 shows an example of visualization capability in *Clavy* that displays an image set based on a DICOM format.

Next subsections will illustrate the whole process of extracting data using the *Clavy* tool from radiology repositories to generate an education package using the interoperable standard specifications IMS-

Figure 2. Structure enrichment to access a DICOM visualization for medical image series



CP which can be used in educational platforms such Moodle or Canvas. *Figure 3* shows the different stages that configure this process starting with the data extraction from the aforementioned repositories.

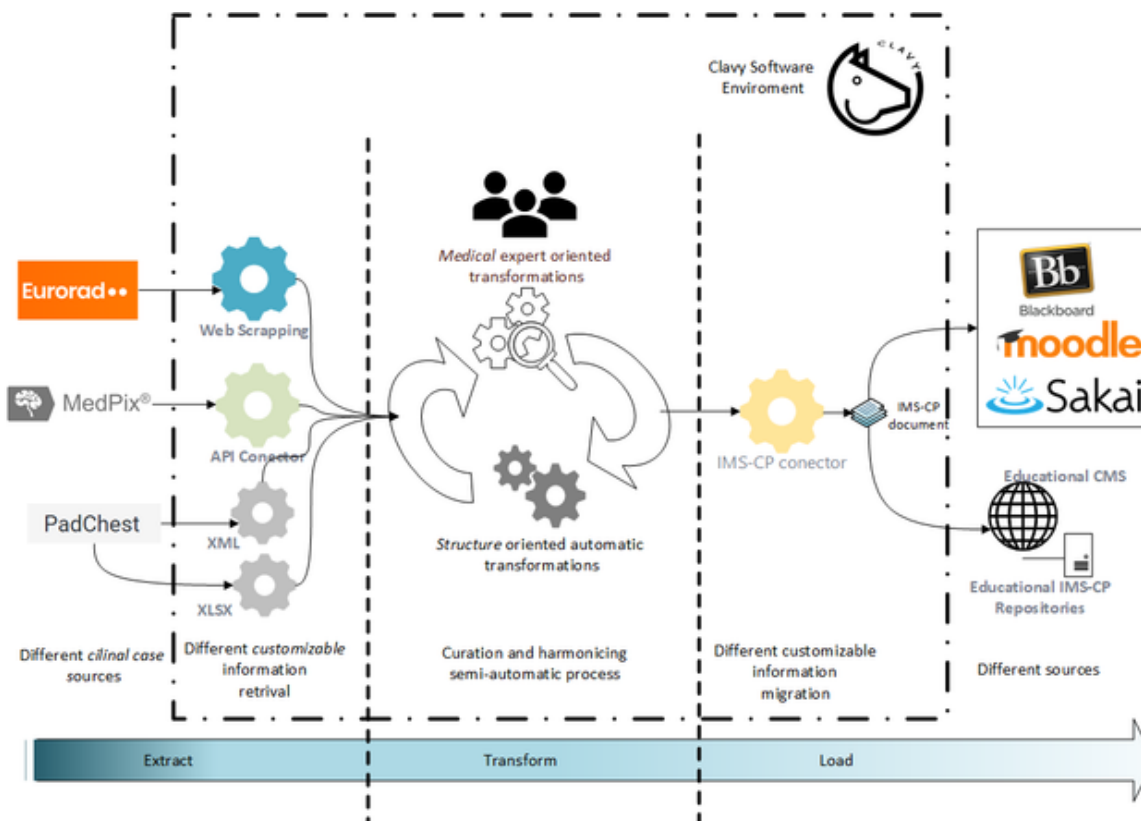
From Radiology Repositories to Clavy Data Models

In the case of *MedPix*, the approach application starts with a set of selected clinical cases and their associated topics, which will be used to show the *Clavy*'s capabilities to extract healthcare data sources from the *MedPix* API. In a similar way, other data sources can be imported using alternative mechanisms such as Web scrapping techniques in the case of *EuroRad* or processing XML notations, image files or Excel spreadsheets for the *PadChest* dataset. *Figure 4* shows some samples of these input data sources.

In order to exemplify these processes, we will focus on the case of *MedPix*. In this case, the extraction stage is based on a cyclic process based on a collection-specific *plug-in*. For this purpose, the *plug-in* accepts indications on one or several clinical cases to be ingested, and, driven by the collection-specific organization, recovers all the relevant information. In *MedPix*, *clinical cases* (comprising clinical images and additional descriptive information) cover different *clinical topics*, being both types of elements cross-referenced. Therefore, once the clinical cases to be ingested are specified, the next steps are performed:

- The *plug-in* uses the *MedPix* REST API to recover the URLs in *MedPix* for these clinical cases.

Figure 3. Application of the Clavy tool



In its turn, each case can be recovered by using the REST API again. Then, by scrapping each case, the plug-in it is able to discover the set of related topics. The actual information for the topics can be retrieved using the REST API a third time.

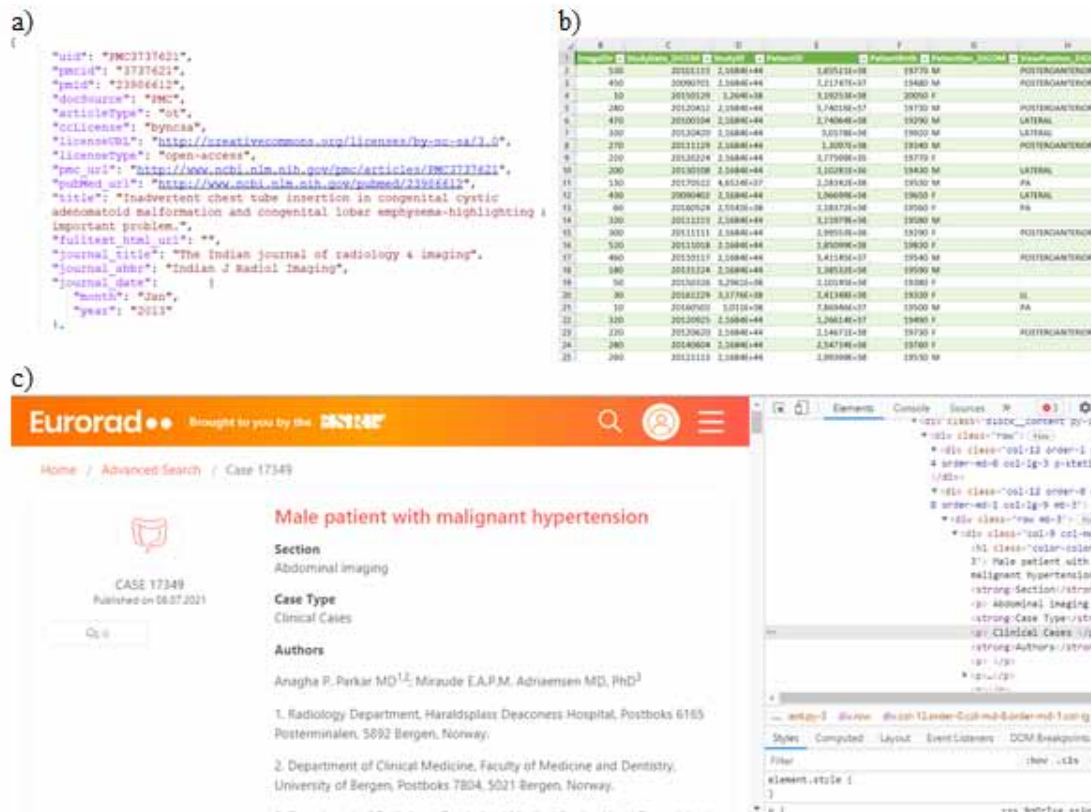
Topics are in their turn scrapped to retrieve additional related cases, which, in their turn, are ingested and analyzed until all the relevant information has been retrieved.

Harmonizing the collection structure

Once data items have been extracted, they can be stored as a *Clavy* collection of documents that mimic the structure of the retrieved items. To exemplify these aspects, we will focus again on *MedPix*. In this case, the retrieved data items are encoded in a JSON format, so the *Clavy* collection produced mirrors the original JSON data. Screenshot in the left of *Figure 5* shows the original structure of the retrieved clinical cases. The resulting documents have an intrinsic organization that can be altered or edited during the transformation stage to enable an educational purpose as described below:

Next steps will be addressed to apply transformation processes which will provide with the required instruments to create links connecting the document elements to multimedia resources (e.g. radiological images, medical text findings, topic-related questions or clinical scenario simulations). Besides these transformation tasks, it is also possible to link the medical or clinical terms which are stored in the *Clavy*

Figure 4. Different sources of the information. a) JSON data from MedPix; b) XLSX from PadChest; c) EuroRad website with HTML format



documents with controlled vocabularies and ontologies such as Snomed-CT or Radlex that enable the normalization of these terms.

Furthermore, experts can assume a more specialized role in the transformation process by removing structural elements in the collection that are not relevant for the final instructional purpose. For example, the information identifiers gathered from the *MedPix* repository are useless for the final instructional platform. In addition, they can re-organize the collection to yield a better structure. For instance, all the information concerning the patient of a clinical case can be grouped behind a *Personal Data* structural element, elements can be renamed to more descriptive names, etc. In order to carry out all these recon-figurations, they can use *Clavy*'s edition capabilities for collection schemata. The screenshot in the right of *Figure 5* shows a view of the transformed structure.

Finally, if the experts consider it necessary, they can access into individual documents and edit them to remove typos, modify field names or complete required information. For this purpose, they can use *Clavy*'s document edition features. Moreover, these experts can add annotations to the text of the clinical reports, which can be linked with specific terms in controlled vocabularies and multimedia resources associated to these reports. Figure 6 shows two screenshots displaying several aspects related to the mentioned advanced edition features. The first one (right part of the figure) displays a screenshot of the

Clavy editor that allows users to modify or alter text items in the data collection while the second one (right part) shows a *Clavy* plug-in in action, which enables the linking of text in the original case with terms coded using a UMLS (Bodenreider, 2004) notation and image locations.

Figure 5. Schema transformation example in MedPix a) Initial document schema from MedPix collection b) Final document schema after transformations

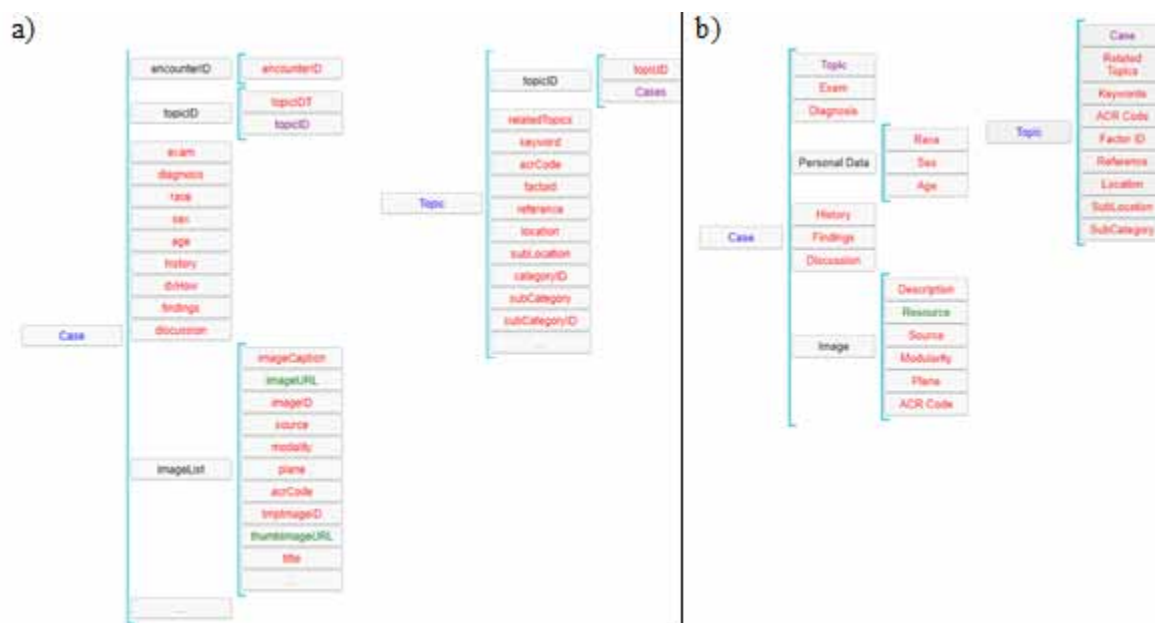


Figure 6. Example of expert edition in a Document. a) Generic text-based editor for documents; b) Expert editor for a set of elements creating annotations of described images with a medical vocabulary

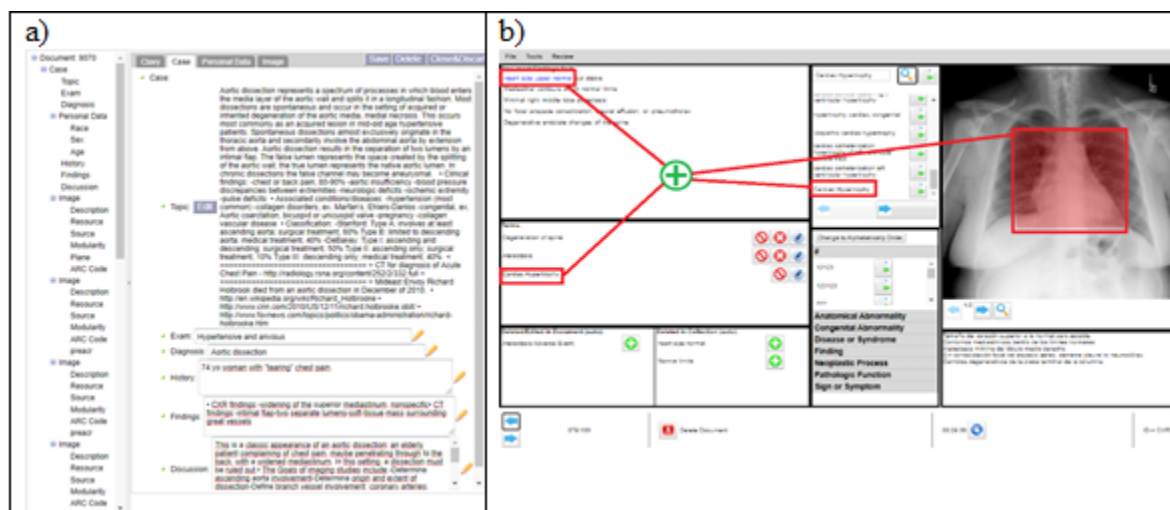


Figure 7. Export results in IMS-CP. a) IMS-CP structure of package and manifest; b) Result of exported packages into a Moodle platform



Data Standardization into Educational Packages

Finally, the transformed documents obtained in the previous stages must be loaded into external e-learning platforms and environments (e.g., Moodle or Canvas). In this context, the use of standard educational specifications such as IMS-CP, SCORM or Xapi is vital since they allow instructors to manage and interact with didactic contents regardless the selected learning platform. *Clavy* has proven to be an effective tool in the generation/exportation of instructional resources using IMS-CP or SCORM packages. Thus, the application of the proposed approach will facilitate the extraction and management of a huge variety of available healthcare data sources that usually are outside the academic realm. This fact together with the generation of reusable standard educational contents will contribute to improving not only the instruction or training in radiology disciplines but in general, the quality of an integral medical education. During this stage, experts can play again an essential role by selecting data items from the *Clavy* collection and by generating a standard package according with the chosen educational goals. This item selection uses annotations in the semantic tree and item relationships to determine the final set of elements as well as temporal transformations to adapt in a fine-grained detail the collection to the expected scenario. Figure 7 shows an example of package through two screenshots that display, first, the standard package encoding produced during the generation stage and secondly, on the right part of the figure, how the package is displayed in a Moodle platform. In this example, the final package format is based on IMS-CP a well-known standard specification (Kurilovas, 2009). For this purpose, *Clavy* includes a *plug-in* able to export in IMS CP. This *plug-in* accepts a set of documents to be exported as input and recursively follows the structure imposed by link elements to recreate these contents in IMS CP terms. For doing it so, it uses additional attributes attachable with elements to decide where represent descriptive elements as organization items or as additional IMS CP resources. It also controls and breaks potential cycles in the link structure, since the IMS CP information model is primarily tree-shaped.

DISCUSSION AND FUTURE RESEARCH DIRECTIONS

The growth of healthcare information either considering the number of available data sources or the huge volume of clinical knowledge associated to them has boosted the need to manage and process this myriad of medical data sources. The current work has focused on the wide spectrum of digital medical collections which are spread through the Web and, more specifically, in the radiology area and their instructional applications. Therefore, technologies and tools are required dealing with the extraction, transformation and further processing of these collections in order to generate educational resources that can be finally loaded into e-learning platforms with an instructional purpose in a medical context. The proposed ETL approach has proven to be very useful when extracting and processing multiple types of multimedia contents which are stored on these medical collections. The use of the *Clavy* tool has contributed to facilitate the development of these extraction and transformation processes by providing mechanisms to automatically implement them together with its flexibility to allow experts the supervision of the whole process. Such a contribution addresses a key issue when processing these multiple and heterogeneous resources which are present in electronic health records (EHRs), clinical observation registries, medical images or reports written in natural language. Surely, in a near future new formats and types of healthcare data sources will arise such as 3D images, high-resolution video recordings or VR/AR (Virtual/Augmented Reality) contents, which will have to be considered and linked with existing clinical resources. Another emerging trend consists in the possibility to connect the digital collections in a healthcare context with those controlled vocabularies and ontology notations able to code condition or clinical issues. The current work has shown the potential of the *Clavy*-based approach to link this kind of vocabularies such as RadLex or UMLS, and it is prepared to consider alternative notations. Additionally, new lines of research will address the semantic annotation of this set of resources by adding links with multimedia resources (e.g., a DICOM image) or those controlled vocabularies that can be connected with a specific healthcare domain. Moreover, the exchange of health information among different systems entails research challenges oriented towards the use of interoperable formats. In this context, the HL7 FHIR (Fast Healthcare Interoperability Resources) standard format can help to provide users with powerful mechanisms in the management of digital health collections that can easily be exchanged in different healthcare domains (Buendía et al. 2021). So, a promising line of research will consist in linking these healthcare interoperable formats with other notations used in the interoperability of educational platforms such as those addressed in the current work.

CONCLUSION

The current work has presented an ETL approach to generate educational resources from digital radiology medical collections. This approach has been applied in a radiology context although it could be addressed to other clinical areas since generic stages dealing with the extraction, transformation and loading of medical data have been defined. The proposed approach has also taken advantage of the *Clavy* tool which provides users with such mechanisms to obtain and integrate information from different data sources using *plug-in* components which can be adapted to different data schemata. The potential of *Clavy* to process and manage digital medical collections has been tested with several well-known radiology repositories (*MedPix*, *PadChest*, *Eurorad*), whose information items have been extracted and transformed into documents ready to be reviewed by experts. In this point, it is important to highlight the

role of experts who can contribute to better supervise the transformation of the collected data sources and the combination with the use of automatic extraction mechanisms that complement their intervention. The *Clavy* tool has proven its ability to retrieve and organize multiple types of multimedia information sources coming from medical collections such as the aforementioned radiology repositories and others. Moreover, the generation of educational resources compliant with some of the most popular standard specifications and their further loading in a Moodle e-learning platform has also shown the potential of the addressed approach. As mentioned in the previous section, several lines of research are planned in the future, including the instructional application of the educational resources produced by this approach and their testing with healthcare professionals and practitioners.

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Chapter 8

From Anatomic Lab to Operating Theatre: Technological Tools for Continuing Learning and Education

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ABSTRACT

The neurosurgical practice is always evolving, achieving new technologies and new techniques every day. From the beginning in the anatomic laboratory, the neurosurgeon could visualize on specimens all the structures and all the areas of the brain. When facing a lesion, the treatment must be carefully planned, and all the information collected by each study and investigation performed must be organized and summarized. This complex work of planning will make the surgery much more efficient, and every

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technology will perform its precise role. Moreover, the patient management is multidisciplinary and requires a precise teamwork: the follow-up usually is a lifelong course. When a case finishes, it's time for the neurosurgeon to go back to the anatomical lab and start again to study the possible perspectives for the next case.

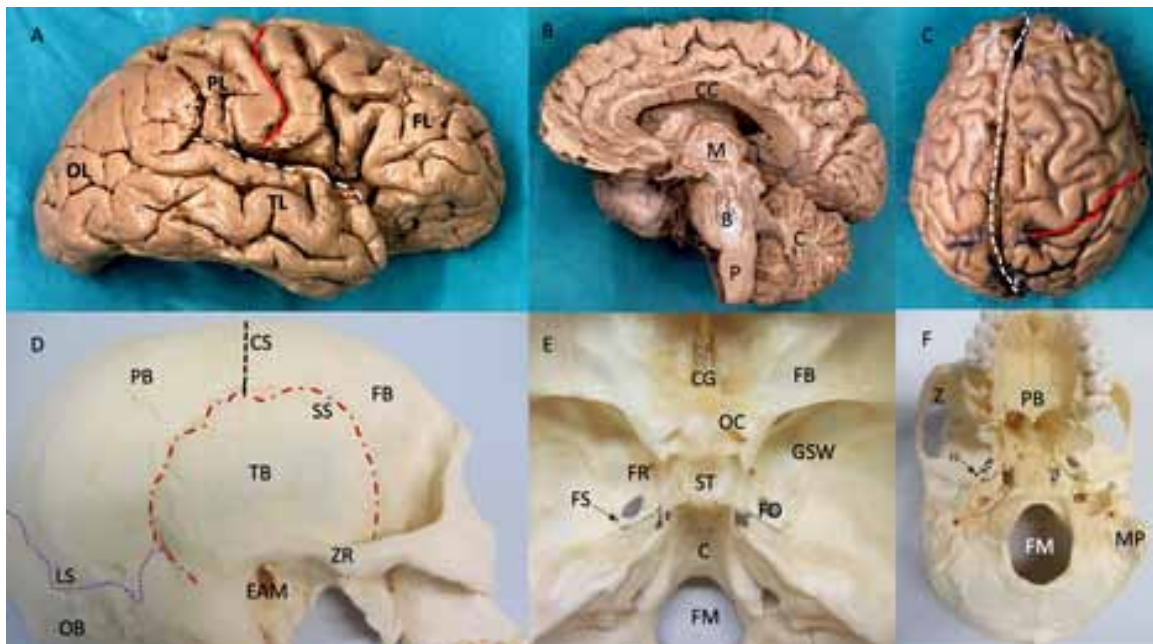
INTRODUCTION AND BACKGROUND

Introduction: The Study of Anatomy

The deep knowledge of human body and central nervous system anatomy is essential for neurosurgical practice (de Divitiis et al., 2019; Farhadi et al., 2020). Right from the beginning of medical and surgical practice, the anatomic dissection represents the starting point for every kind of innovation: to assess the feasibility and the safety of new tools, new approaches, new treatments the anatomic lab step is mandatory.

The anatomy could be directly visualized on specimen and all the theory learned from books become real and tridimensional. The tangible relationships between different brain structures could be clearly seen, and dissection to reach deep areas could be performed (Cappabianca & Magro, 2009; de Divitiis et al., 2019) (Figure 1).

Figure 1.



Further, nowadays we can rely on new tools that help us to optimize the entire process. Microscopic or endoscopic surgical procedures are modified and improved everyday: when developing innovative techniques or new ideas for surgical treatments the starting point to assess their feasibility is the anatomical lab. Here is where research arises, and ideas can be experimented. With the use of neuroradiological

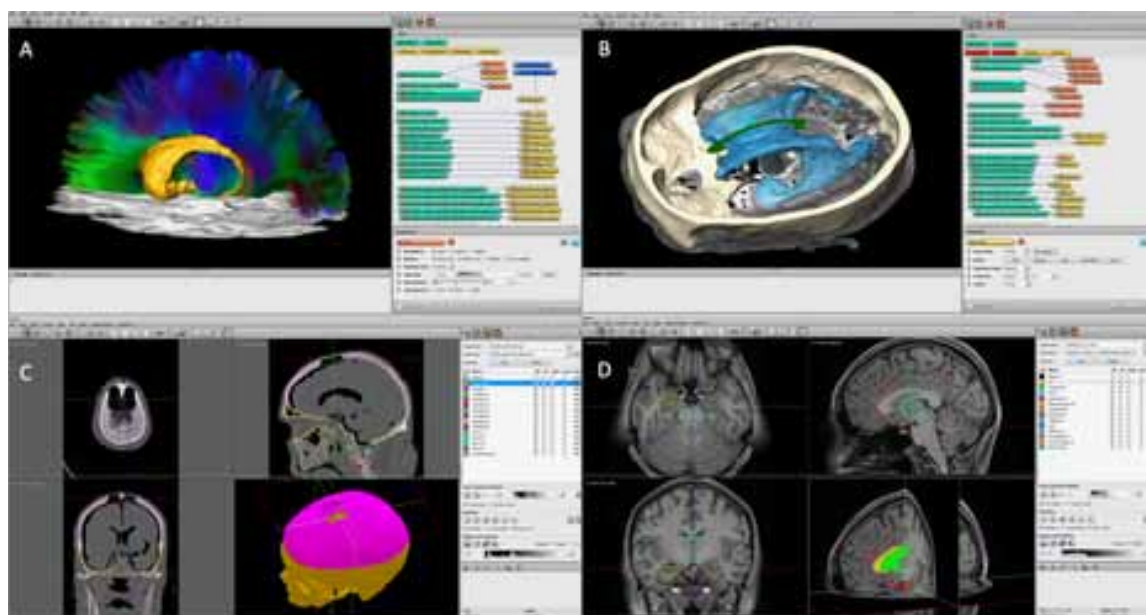
images and the software for data elaboration, the efficacy of different approaches accessing a specific target (e.g. middle cerebral artery) could be compared; moreover the obtained visualization of the anatomic structures and the real feasibility of the surgical route, considering the working area exposure and instruments maneuverability (the so-called “surgical freedom”), could be numerically quantify (de Notaris & Prats-Galino, 2014; Noiphithak et al., 2018).

Background: The Starting Instruments

Amira Visage Imaging Software – Detailed 3D Representation of the Anatomy

Anatomical research has encountered an incredible technological evolution: from the standard cadaveric dissections of the past, now can praise some of the most complex and modern computer softwares for qualitative and quantitative data elaboration. After their realization on the specimens, techniques’ efficacy and results could be assessed with specific software: a virtual 3D model could be created using Amira Visage Imaging (Amira Visage Imaging Inc., San Diego, California, USA). AMIRA software, using neuroradiological exams based on the specimens (computed tomography or magnetic resonance imaging), realizes 3D reconstruction and graphical images of the technique performed; moreover, produces numerical values to assess its efficacy on the surgical target (e.g. quantity of bone removal to access skull base structures, percentage of epileptogenic neural fibers disconnected with an endoscopic approach). The final multimodal image that could be obtained is a **3D-volume-rendered representation of the brain**, with volume or surface-rendered clusters representing different modalities. The user can manipulate the final multimodal image in a number of ways, including alteration of the transparency of the brain and different modalities, rotation of the image in any plane, and changing the scaling of the image (Nowell et al., 2015). Modalities are color coded: every single different structure could be

Figure 2.

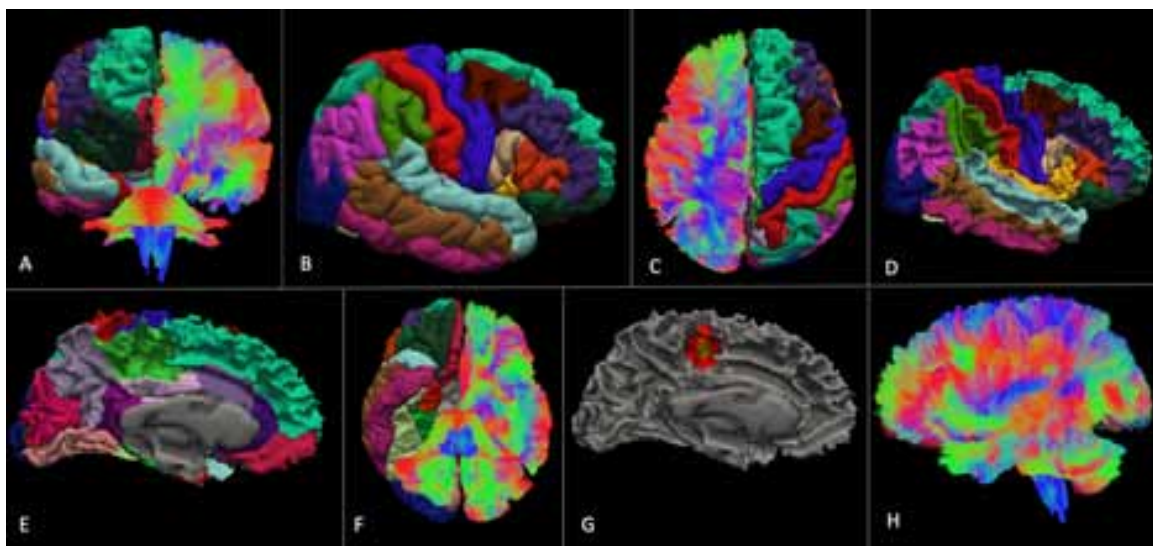


underlying and represented with different colors (e.g. the lateral ventricles, the arterial or venous patterns, the fibers' tracks, the basal ganglia) (Figure 2). A new technique could be tested and recreated in the software to assess its feasibility and efficacy. The software could reproduce a surgical technique and estimate the access to the target and practical results: theorized resection planes could be simulated, or the resection volume could be calculated after and before tests on specimens. However, the real efficacy and feasibility of a potentially new technique could be revealed only in-vivo.

Human Connectome Project – Look at the White Matter

To ameliorate and to provide a major accuracy to a new surgical technique test, the next step is to simulate the procedure on a real brain. The introduction of diffusion MRI tractography towards the end of the 1990s represented another revolution in neuroimaging as it permitted in vivo visualization of white matter fascicular architecture (Panesar et al., 2019). This complex anatomy could be resumed simplify by dividing in three groups of fibers: projection fibers, that connect the cortical areas with the deep gray nuclei, brainstem, cerebellum, and spinal cord or vice versa, association fibers, that connect different cortical areas within the same hemisphere and commissural fibers that realize connection between the two hemispheres. All these information, coming from DTI, could be add to AMIRA software: with this software we can elaborate a diffusion MRI tractography realizing a 3D model of white matter tracts with a high precision and resolution, where surgical procedures or lesions effects could be simulated (Figure 3).

Figure 3.



To implement the quantity of this type of data, and to give accessibility to high resolution MRI images worldwide, a database of the healthy young adults' brains has been created: the Human Connectome Project. This is an international project for data storing: the goal of the Human Connectome Project is to build a “network map” (connectome) that will shed light on the anatomical and **functional connectivity** within the healthy human brain, as well as to produce a body of data that will facilitate research into

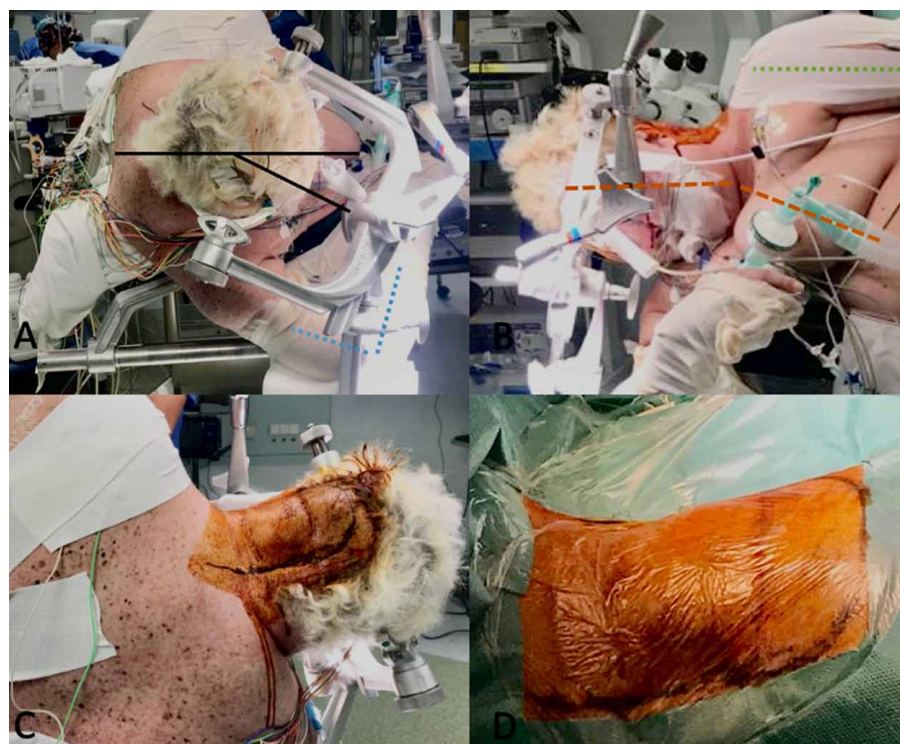
brain disorders. It contains a database of 1200 mapped brains using 3T MR, 7T MR, MEG and diffusion sequences, which permits to identify white matter fibers and eloquent areas. All these data are available for all the researchers for free. This project represents a starting point for multiple research and advances in anatomical and functional knowledge of brain connections (Briggs et al., 2021; Palejwala et al., 2021; Richard et al., 2021). Based on these brain models, with AMIRA software we can simulate and test our technique with a higher grade of accuracy than the tests on specimens. Moreover, the quantitative results extracted from these simulations would be more reliable.

BEFORE THE OR: SURGICAL PLANNING AND 3D-SIMULATION

Patient Positioning and Additional Instrumentation

Before entering the operating room, every surgeon needs to plan and evaluate all the aspects of the neurosurgical procedure that will be performed. **Patient positioning** is the first step that should be carefully planned and depends on the lesions' characteristics and patients' conditions (Figure 4). A frontal lobe lesion could be approached with a supine position, a posterior fossa lesion will be performed in a lateral decubitus or prone position. Some particular areas, as the cerebello-pontine angle, could be approached with a semisitting position: some patients, with a cardiac condition known as FOP (forame ovale pervio) absolutely cannot afford this position and the intervention should be planned differently. Moreover, the

Figure 4.



correct positioning of the patient is fundamental: the wrong angle of head rotation or inclination could prejudicated the entire approach. Any possible additional instrumentation that could be required during the intervention, according to pathology localization, anatomical characteristics and patient's conditions must be evaluated. Another important aspect of the preoperative planning is to predict every important anatomic structure encountered: every possible complication must be considered, and a possible **quick solution** should be planned. For example, sometimes the location of the craniotomy could be close to important huge venous structures: the dural sinuses. The rupture of one of these veins could sometimes be fatal. Hence dural sealants should be ready to use in case of venous damage.

Preoperative Images Evaluation

The study of the neuroradiological images is the starting essential point: due to its excellent soft tissue visualization, magnetic resonance imaging (MRI) has already been established as the noninvasive diagnostic modality of choice and as an essential part of routine clinical work up in the diagnosis and evaluation of brain tumors. Together with classical sequences of images, specific acquisition could be performed, to assess different tumor characteristics (Conti Nibali et al., 2019).

First of all, post-contrast images give us a lot of details: the post-contrast enhancing pattern permits to distinguish the most common brain lesions (high grade VS low-grade glioma VS metastasis). Many other MRI sequences could be performed to obtain further and more precise information. For example, in a **spectroscopy** sequence, instead of using the frequency information (provided by the read-out or frequency gradient) to provide spatial or positional information, the frequency information is used to identify different chemical compounds of a determined lesion. Tumor metabolites that could be investigated are multiples: N-Acetyl-Aspartate, Choline, creatine, lipids, glutamate, lactate and many others. In brain malignancies, (e.g. glioblastomas) increased level of choline and decreased level of NAA are pathognomonic (Nakae et al., 2021) (Figure 5). These new imaging biomarkers enable noninvasive quantitative measurement of tissue hypoxia, microvascular vessel diameter, and neovascularization activity, thereby providing precise insight into the heterogeneously structured tumor microenvironment (Stadlbauer et al., 2017), (Heynold et al., 2021).

Other important information was given by the **tractography** study made with the diffusion-weighted imaging (DWI) MRI (Wende et al., 2020). This sequence is based on the measurement of thermal Brownian motion of water molecules. Within cerebral white matter, water molecules tend to diffuse more freely along the direction of axonal fascicles rather than across them. Such directional dependence of diffusivity is termed anisotropy. This direction of maximum diffusivity along the white-matter fibers is projected in the final image. In fiber tractography imaging, the convention for color coding is as follows: red for transverse fibers, green for anteroposterior fibers and blue for craniocaudal fibers.

Moreover, with peculiar protocols, a study of determined brain function could be performed. **Functional MRI** is based on the vascular response to functional activation of the brain: the most common fMRI method uses blood oxygenation level-dependent (BOLD) contrast. Neural activation in the brain induces an increase of local cerebral blood flow (CBF). The increased CBF boosts the oxygen supply to an extent greater than that required to meet local metabolic needs. This results in a decreased concentration of deoxyhemoglobin in the capillaries and venous blood vessels (Ogawa & Sung, 2019). The most used method to testing the patient is a repeated block of activities (paradigm) separated by blocks of inactivity or alternative activity. Each paradigm is designed to elicit a specific cortical response. Numerous paradigms have been developed of various complexity. The cortical functions most indagated are

Figure 5.

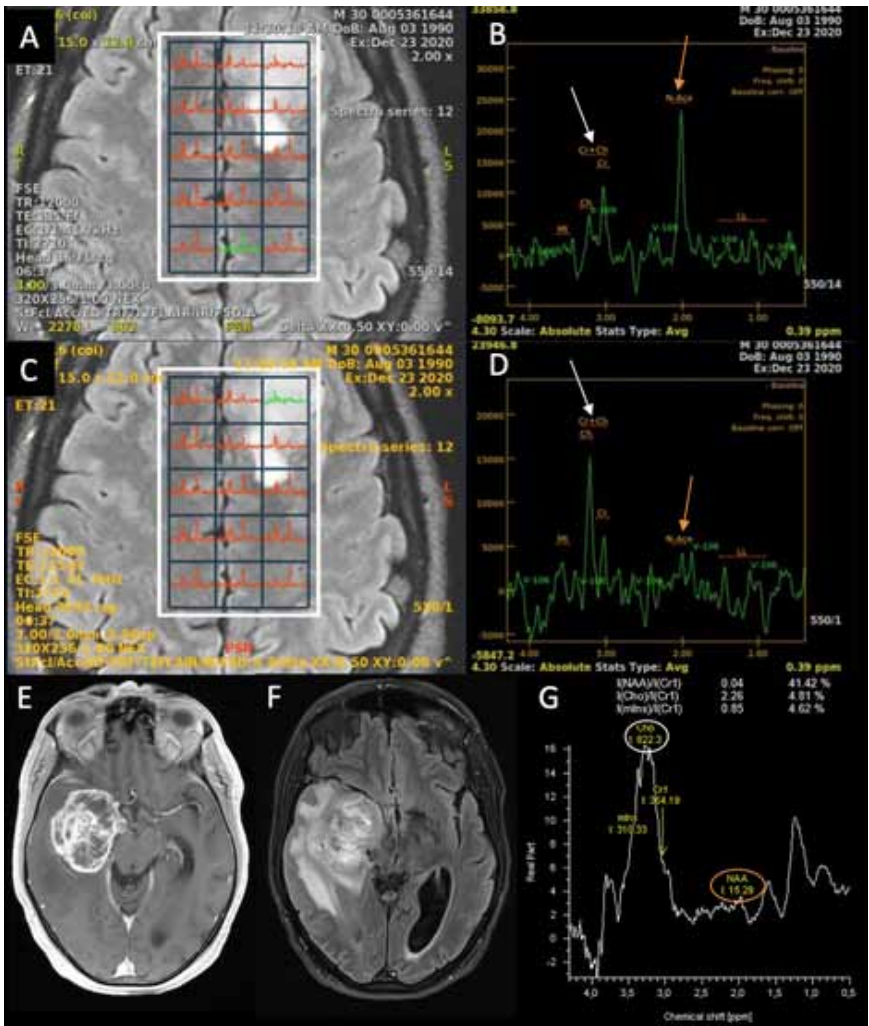
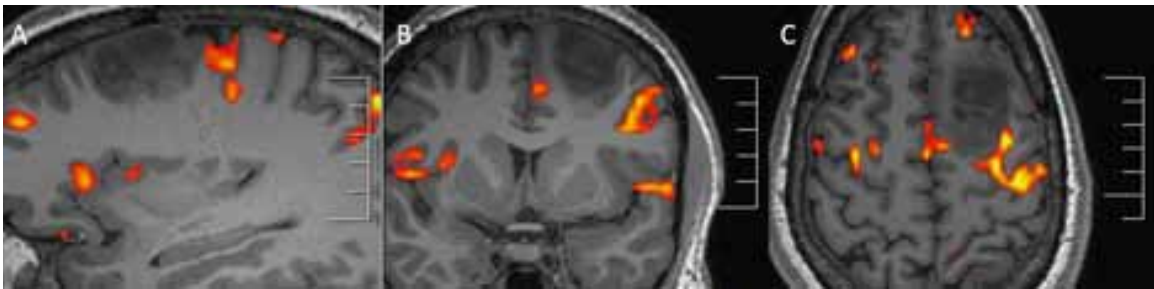


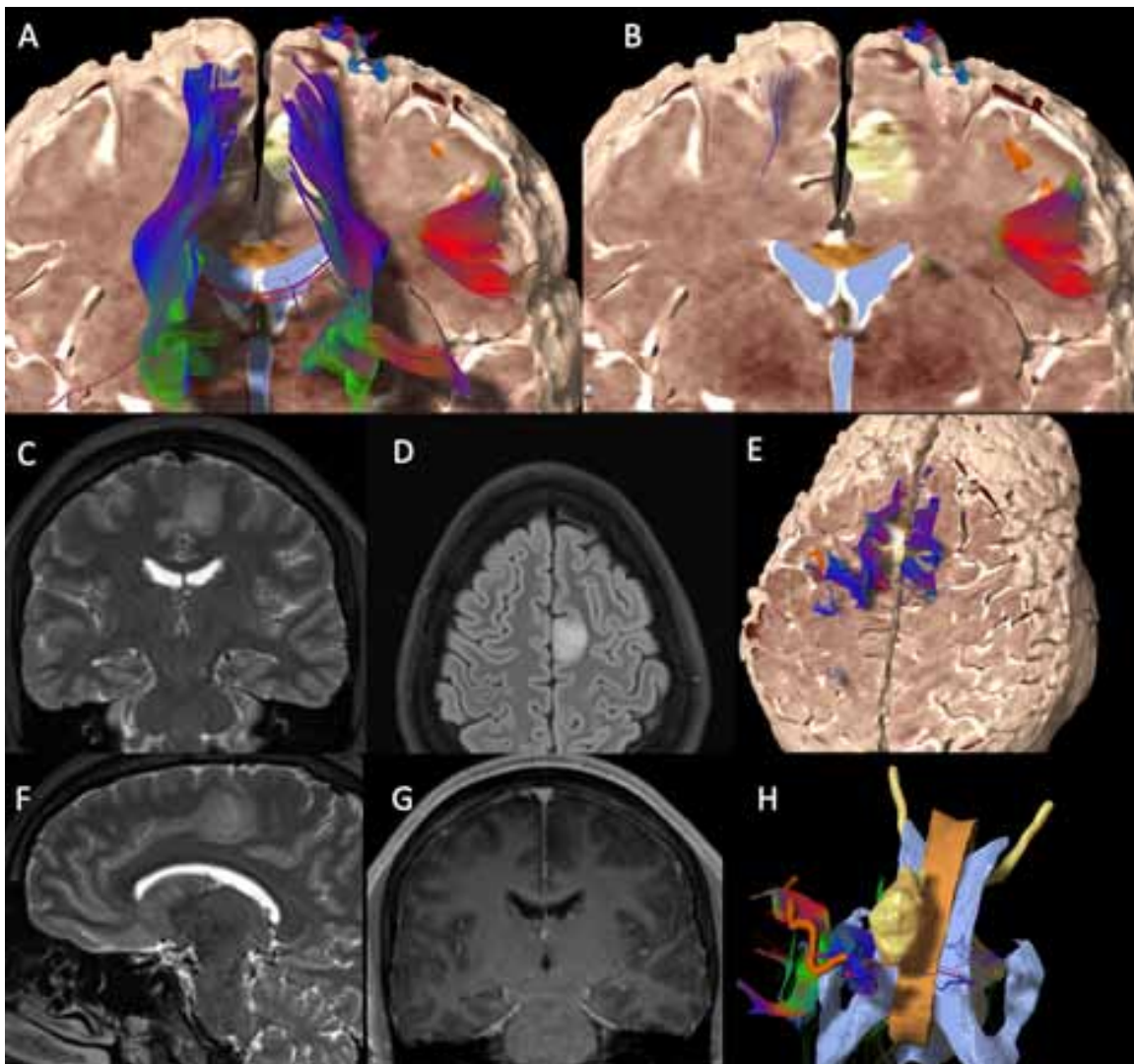
Figure 6.



movement, language, visual capability and memory. After processing the images obtained, each cortical area responsible for the function indagated could be localized (Peck et al., 2021) (Figure 6).

All this data from neuroradiological imaging at this point are collected and added to the Brainlab station (Brainlab, Westchester, Illinois, USA) or to StealthStation navigation system (Medtronic, Dublin, Ireland). With this **neuronavigators**, the images from contrast enhanced sequences, tractography and functional MRI are processed and fused in a 3D model (Figure 7). Furthermore, the surgeon could highlight every important structure in the working area, to protect it and to help intraoperative orientation (e.g. carotid artery, optic chiasm, basal ganglia). The software creates a 3D image of patient brain which permits to simulate all the relevant surgical step: the presence of a venous vessel just behind the posterior margin of a tumor, a cerebral sulcus that could be used as access route or to easily localize a lesion, the proximity or the infiltration of motor fibers tract. With this information the neurosurgeon

Figure 7.

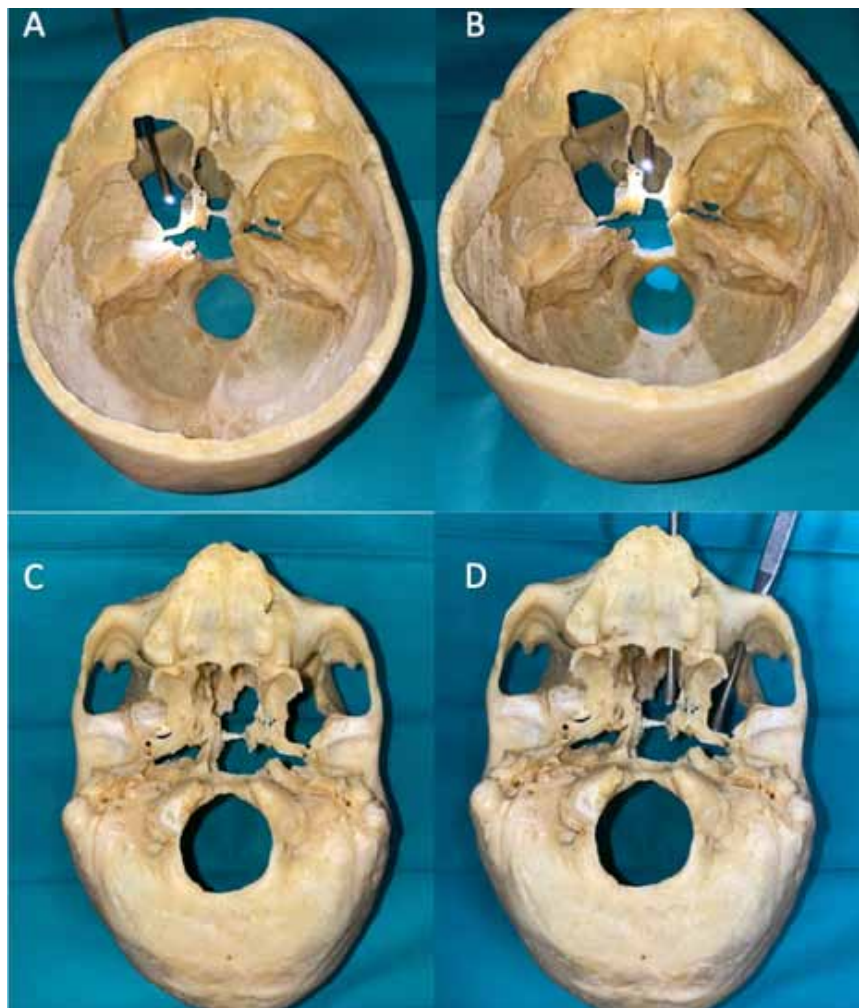


could decide more easily its pre-surgical planning: to administer the 5-ALA to patient, to use neurophysiological monitoring of the motor pathway, to perform surgery in awake to control language function.

Complex Skull Base Lesions

In case of skull base pathology an important challenge has always been represented by the type of surgical approach. Nowadays many different **minimally invasive strategies** have been developed during the last decades as alternative to standard transcranial approaches: first of all, the endoscopic endonasal approach, with its extended variants, is used worldwide to approach midline and paramedian lesions of the skull base, located from the ethmoidal planum to the lower clivus (Cappabianca et al., 2000; Cappabianca et al., 1998; Cavallo, Frank, et al., 2014; Cavallo et al., 2020; de Lara et al., 2014; Kassam et al., 2005a, 2005b; Schwartz et al., 2008; Solari et al., 2019; Wang et al., 2019). This approach permits to access skull base lesions with a minimal craniectomy, avoiding brain and nervous structures retrac-

Figure 8.



tion. The wider panoramic view offered by the endoscope increased the versatility of the transphenoidal approach and permitted it to be expanded to different parts of the skull base (Cavallo, Solari, et al., 2014) (Figure 8). Moreover, many efficient techniques for reconstruction have been developed and the patient's postoperative recovery is faster, and the hospital stay is shorter (Cavallo et al., 2019; Hadad et al., 2006; Kassam et al., 2008). For skull base lesions located more laterally an old technique has nowadays regained popularity (Houlihan et al., 2021): used in the past for psychiatric diseases management, nowadays the transorbital neuroendoscopic approach could be used to manage lateral speno-orbital region tumors, middle and posterior fossa lesions (De Rosa et al., 2019; Moe et al., 2010; Yoo et al., 2021). The transorbital route allows a multi-portal, multi-angled approach to lesions of the skull base that are extremely difficult through even expanded transnasal endoscopic procedures (Doglietto et al., 2009). Moreover, surgical morbidity and cosmetic deformity are minimized compared to standard open, craniofacial approaches (Ramakrishna et al., 2016).

THE MODERN NEUROSURGEON'S IN THE OR: STRAIGHT TO THE TARGET, FROM DIFFERENT PERSPECTIVES

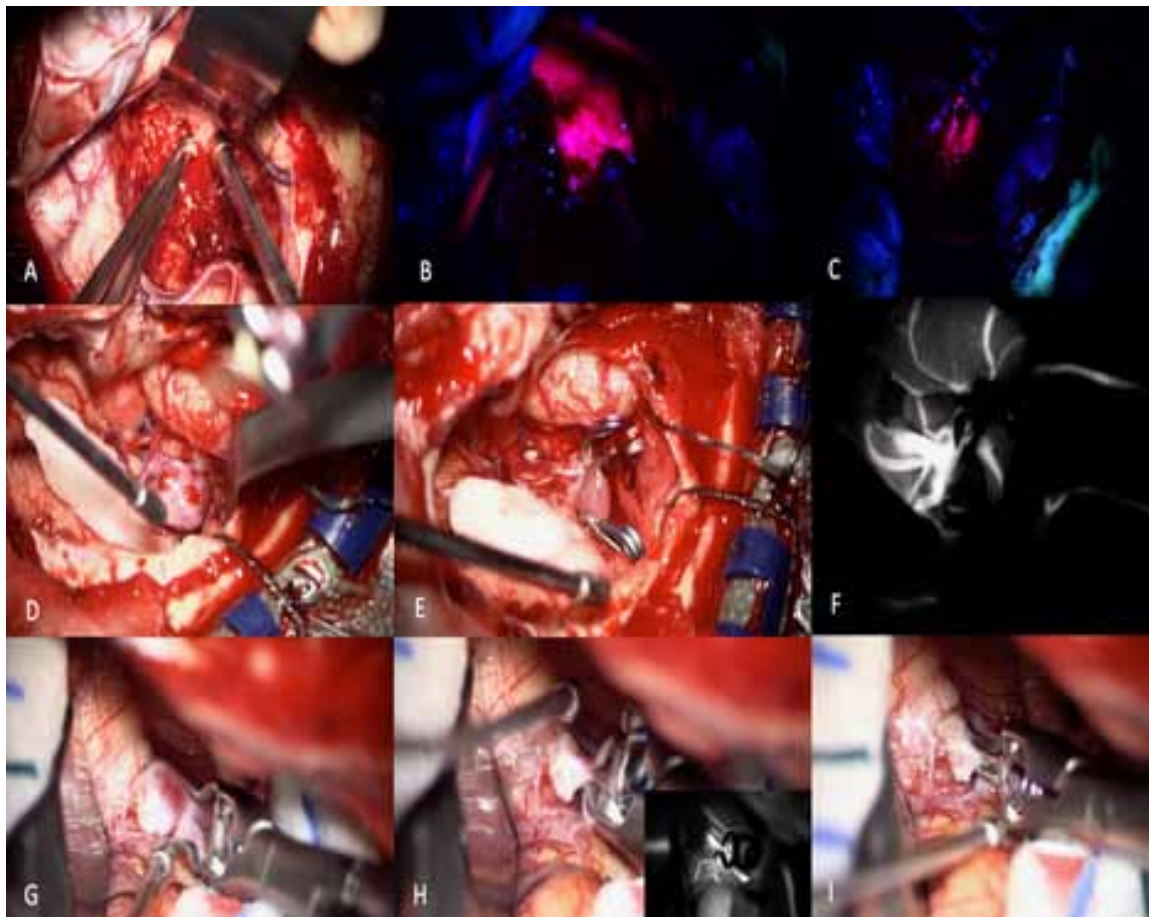
The **modern operating rooms** are designed to host and combine all the tools and instruments necessary for a certain surgical procedure. All these techniques are useful for the neurosurgeon and permit to highly improve the efficacy and the safeness of the intervention. In malignant tumors brain surgery, research and protocols are evolving continuously: the goal of this surgery is to remove as much as tumor as possible, preserving patient's neurological functions (Fujii et al., 2021; Hervey-Jumper & Berger, 2019; Wang et al., 2021). The postoperative **quality of life** of a patient, his capacity to tolerate adjuvant treatments are strictly related with the preservation of his functions. To realize this, the neurosurgeon must be extremely careful when manipulating the brain and needs to be sure that the tissue that he's removing is actually tumor. To help the neurosurgeon with this issue, new technologies have been added to his armamentarium.

Fluorescence-Guided Vision

The oral administration of **5-Aminolevulinic acid** to the patient, 3 hours before surgery, has become a vital tool in the intraoperative identification and differentiation of high-grade glioma: the malignant cells, because of their augmented metabolism, process the 5-ALA more than normal tissue, and this provides a fluorescent effect when observed under blue light. This facilitates to distinguish tumoral area from normal brain tissue and permits an intraoperative "diagnostic orientation": low-grade glioma and metastasis in the majority of cases, do not provide this fluorescent effect (Dadario et al., 2021) (Figure 9).

In cranial vascular surgery, whether clipping an aneurysm, removing an AVM, performing a microvascular decompression or a bypass, the possibility to clearly view and assess cerebral anatomy and blood flow is critical for an optimal outcome. The intravenous administration of **fluorescein and indocyanine green** allows direct visualization of blood flow after aneurysmal sac occlusion, enabling the observation of vessel permeability and the effectiveness of aneurysmal obliteration (Figure 9) (Kakucs et al., 2017).

Figure 9.



Intraoperative Ultrasounds

Together with the neuronavigation system (Figure 10), another important resource is the **intraoperative ultrasonography**. This effective and cost-less instrument used world-wide in many different surgical specialties, during the last decade, has regained popularity in neurosurgery too (Ivanov et al., 2010)(Quadri et al., 2018). It permits to quickly identify, with high precision, the location of a brain lesion, and extremely help intraoperative orientation, recognizing other important anatomical landmarks: the falx, the tentorium, lateral ventricles. Moreover, instead of the neuronavigator, which is based on preoperative imaging, the echography provides a real time image; this is especially useful in particular cases, where the step of the surgical approach, could modify the brain set up: in case of particularly edematous lesions, after the dura mater opening the brain swelling could modify the spatial relationships acquired by the preoperative magnetic resonance and decrease neuronavigation accuracy (Mahboob et al., 2016; Marcus et al., 2017). In other cases, for example with multilobulated complex lesions, the removal of the more superficial portion could modify the spatial organization of the latter mass component, making more difficult a complete resection. In both these cases the use of intraoperative echography could clarify all the doubts (Figure 11, 12). Moreover, in case of deep cystic lesions, an echography guided needle

Figure 10.

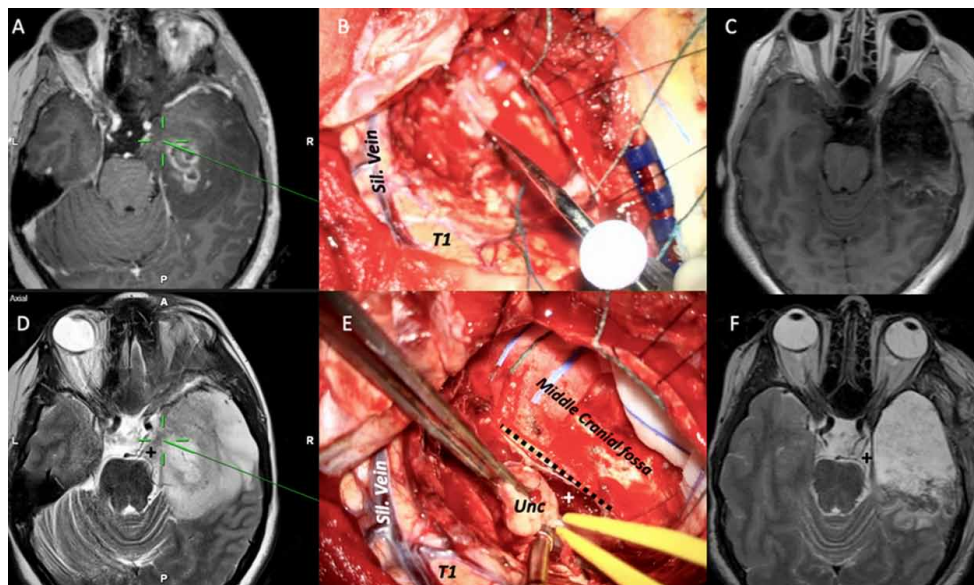


Figure 11.

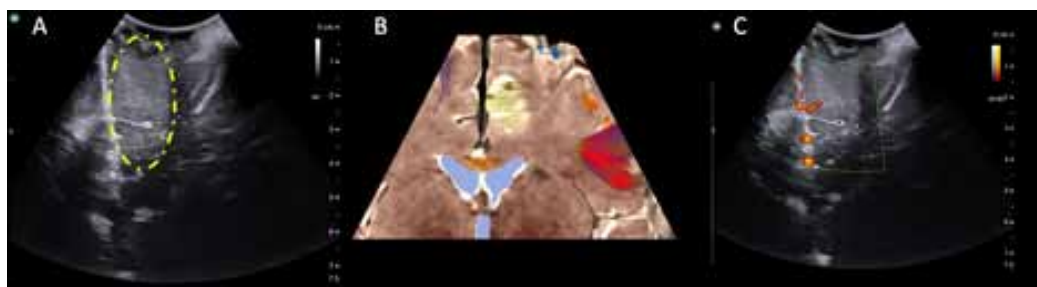
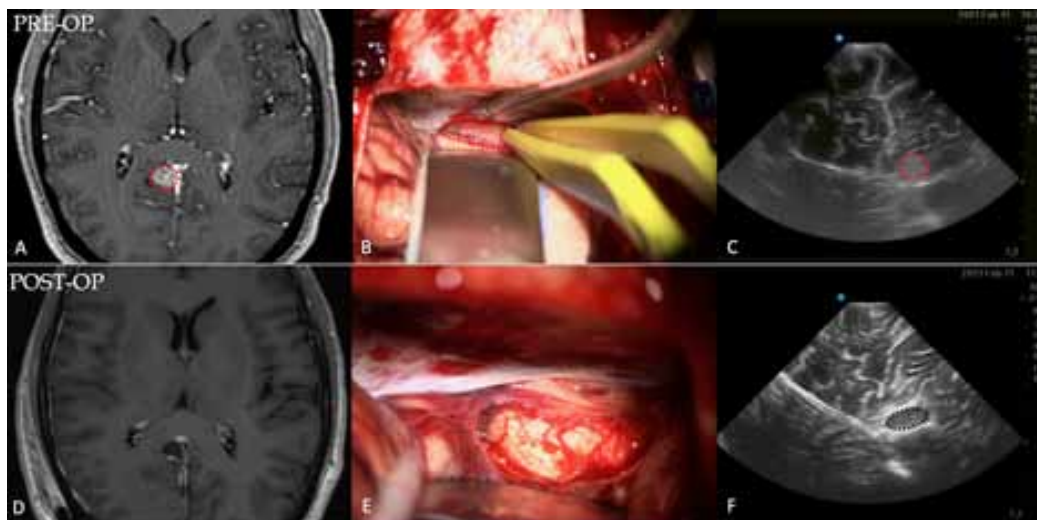


Figure 12.

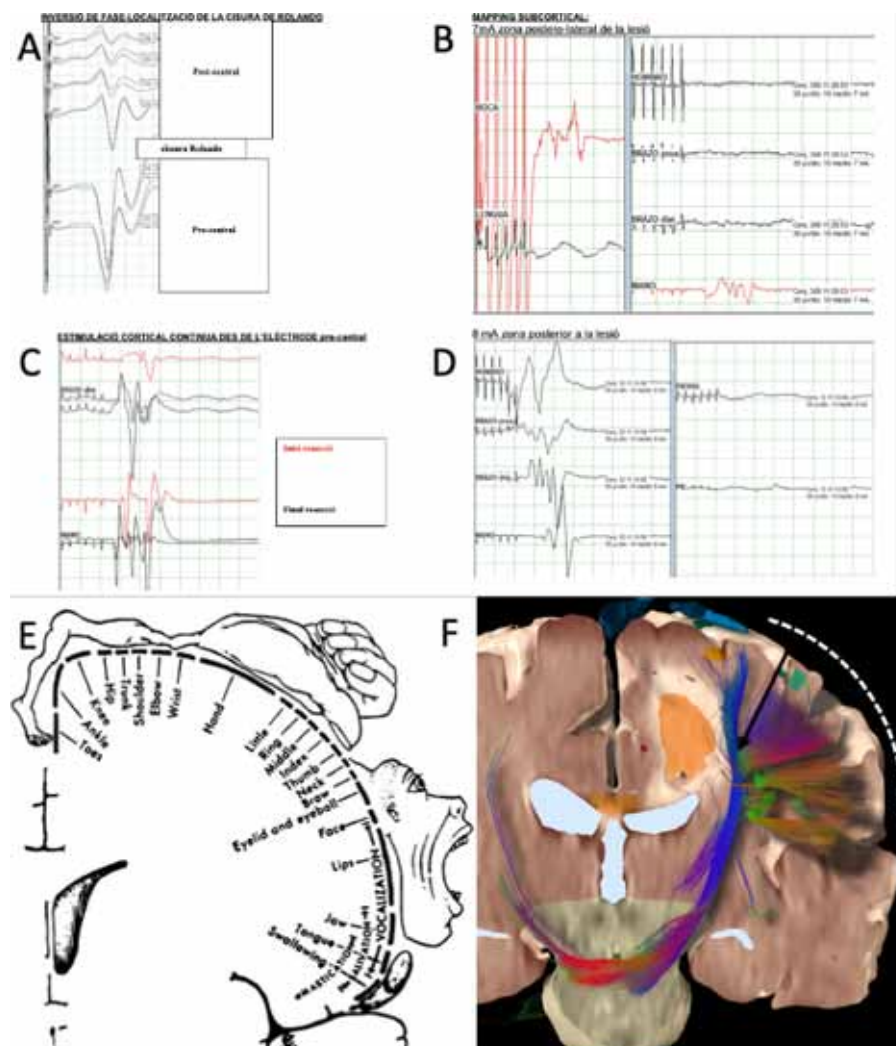


biopsy could be performed. In the most modern models of echograph, a fusion and integration with the neuronavigation system is possible, permitting to fuse preoperative images with real time ultrasounds.

Neurophysiological Monitoring

Moreover, to identify and protect eloquent areas of the brain the neurophysiologist plays an important role in the operating room. When required, and tailored to patient lesion site and preoperative deficits, the neurophysiologist could control the functions of cranial nerves, motor cortex and motor pathways with a cortical and subcortical mapping respectively (Gogos, Young, Morshed, Avalos, et al., 2020). For lesion located in proximity of the motor cortex and motor pathway, with a **direct stimulation**, permits to **localize motor cortex** in order to respect it. Moreover, with continue stimulation during tumor removal, allows to localize motor fibers in advance in every moment: in this way, tumor removal could be stopped before disrupting motor fibers, preserving patient movements (Ghimire et al., 2021) (Figure 13).

Figure 13.



In some patients, tumors are localized in eloquent areas responsible for speaking comprehension and production (Gogos, Young, Morshed, Hervey-Jumper, et al., 2020). To control and preserve these functions there's the possibility, in selected patients, to perform “**awake**” surgery. In fact, after the initial approach, and dura mater opening, while the patient is mildly sedated, the patient is gradually awakened completely, and its speaking capability, with the aid of a neuropsychologist, is constantly monitored during tumor removal.

Intraoperative Imaging

Nowadays modern OR are equipped with an imaging armamentarium to perform intraoperative real-time imaging.

To assess the real extent of resection, a 0,2 Tesla PoleStar® N30 ioMRI system (Medtronic Inc.) with the StealthStation® S7® navigation system could be used to evaluate intraoperative extent of resection. Intraoperative imaging protocol included T1 and T2-weighted imaging, and, if necessary, Gadolinium enhanced T1-weighted imaging. Images obtained were fused with preoperative MRI using StealthStation® S7® navigation system and further tumor resection could be performed as needed. If resection was amplified, another ioMRI was obtained to ensure that the final surgical goal was achieved according to preoperative planification (Figure 14 C, D).

In stereotactic procedures, as tumor biopsy, deep brain stimulation, spinal pedicle screws placement, intraoperative CT scan could be performed to confirm with high grade of precision the correct positioning of the instruments in real time (Figure 14 A, B).

Figure 14.



AFTER THE OR: MEDICAL ADJUVANT TREATMENTS

Neuro-oncology treatment is made of several different steps, and a multidisciplinary team is required to follow these patients. After the surgical intervention, the information that will guide all the patient course is the anatomopathological result. Based on this and on patients general and neurological status, the appropriate medical adjuvant treatment protocol will be started. Nowadays histological diagnosis has changed a lot from the past: as we can see from the new WHO classification of central nervous system tumors of 2016 (Louis et al., 2016), for the first time, molecular parameters are used in addition to histology to define many tumor entities, thus formulating a concept for how CNS tumor diagnoses should be structured. As the matter of fact, these molecular parameters, are also prognostic factors (Wesseling & Capper, 2018): a particular mutation could predict the tumor behavior and its response to adjuvant chemotherapy. Following this tendency, also chemotherapy and radiotherapy are evolving to patient-tailored treatments according to tumor molecular and radiological characteristics. Every case is discussed in a **multispecialists' session** where the entire course of the patient is revised, and further treatments are decided. Every tumor, every patient, has its own protocol, its treatment and its follow-up schedule. Together with the neurosurgeon, in case of lesions operated by endoscopic endonasal or transorbital approaches, the patients are followed from the ENT and ophthalmology teams, respectively.

A STEP FORWARD: INNOVATION AND FUTURE PERSPECTIVES

Neuro-oncology is a continuous evolving and complex subspecialty: however, the treatment of malignant primary or metastatic CNS tumors is still limited and the prognosis remains poor. An interdisciplinary team is required to meet the challenges, in clinical patient cure but also in updated research activities. A strict communication network between clinicians, surgeons and data scientists is required to ensure that emerging data from basic, translational and clinical research can be used for improving the sometimes extremely limited and prognostically poor treatment options (Tabatabai & Weller, 2019). The development of massively parallel (next-generation) sequencing technologies in the 2000s facilitated genome-wide mutational profiling of tumors. As a matter of fact, according to the recent Society for Neuro-Oncology (SNO) and European Association of Neuro-Oncology (EANO) consensus (Schiff et al., 2019), comprehensive genomics and integrative bioinformatics studies from 2008–2015 radically changed the diagnostic landscape for gliomas, culminating in the new WHO classification of central nervous system tumors of 2016 (Wesseling & Capper, 2018).

For this reason, all the efforts are looking for other therapeutic and more efficient treatments. There are many different studies on possible future treatments running at the moment.

Future Medical Therapies

One of the major limitations for medical therapy of central nervous system tumors is that pharmaceutical compounds are not able to access the brain while circulating in blood due to the presence of the BBB that limits entry into the brain and protects it from infections or harmful substances. The barrier prevents the diffusion of even small molecules. Despite the shield imparted by the BBB, its integrity can be disrupted by several pathologic conditions, including glioma. In the clinic, BBB disruption in malignant gliomas has been observed by accumulation of gadolinium-based magnetic resonance imaging (MRI) contrast

agents within tumor regions. However, any drug delivery enhancement that results from BBB leakage is not enough to cure GBM. Hence, while many essential molecules are able to diffuse across this barrier, it often excludes therapeutic compounds.

The essential need for novel therapies has led to the development of nanoparticles as anticancer drug delivery carriers. One of the most important issues in nanotechnology is the transfer of anticancer agents through the BBB for the treatment of CNS tumors, depending on cancer type, as well as tumor characteristics, stage, and location (Yu et al., 2016). In fact, nanoparticles combined with polymer coatings can overcome BBB and facilitate the delivery of drugs to CNS: the NPs penetrate through the tight junctions between the endothelial cells of the vessels and enable the drug to pass through the BBB. Endocytosis and transcytosis of NPs can also facilitate drug transfer through the endothelial cell layer.

A variety of strategies have been suggested to overcome the BBB, thus improving drug delivery in treating glioma; however, non-selective opening of the BBB induced by mannitol can also result in various complications including epilepsy and brain edema (Marchi et al., 2007). Thus, selective and efficient opening of the tumor BBB at the site of glioma would be beneficial for the targeting of cytotoxic therapies and minimization of side effects. To date, two main treatment strategies have been explored to exploit tumor BBB leakiness in the tumor core: one that relies on passive drug accumulation at sites of tumor BBB disruption and another that leverages specific targeting of glioma regions with disrupted tumor BBB (Luo & Shusta, 2020). Another option is to use an alternative route to CNS which is not obstructed by BBB: in this scenario, drugs intranasal delivery provides an exciting route for topical and systemic applications. For example, intranasal drug delivery of Central Nervous System (CNS) drugs can be designed to pass the BBB barrier via the nose-to-brain pathways. It is known that absorption of molecules takes place at the olfactory and respiratory epithelia. The routes of compound transfer through the olfactory area, of the nares, to the olfactory bulb are transcellular through either the sustentacular cells or the exposed olfactory sensory neurons (Kanazawa et al., 2020). The route of compounds' transfer through the nasal respiratory epithelium to the brain is via the trigeminal nerve (Li et al., 2019).

The Future Neurosurgical Armamentarium

The research of extreme accuracy and efficacy is the constant aim that is moving all the medical practices. In neurosurgery many tools are being developed to improve neurosurgeons' visualization and skull base access: one of these new trends, which is gaining an increasing popularity is augmented reality. For pre-surgical planning and intraoperative orientation, the neuronavigation systems are nowadays a useful and essential instrument. However, neurosurgeons, are required to create a three-dimensional (3D) mental image of the MRI/CT views to match the surgical field. In addition, they must frequently alternate their gaze between the surgical field and the personal computer (PC) monitor. To overcome this difficulty, several navigation systems have been developed using augmented reality techniques (Deng et al., 2014; Gavaghan et al., 2011; Maurer et al., January 2015): new guiding systems enable surgeons to see intracranial structures virtually overlaid on the patient's head as if they were looking directly into the head; It is especially useful at the initial stages of brain surgery, for example in connection with skin incision, craniotomy, or corticotomy (Watanabe et al., 2016). Without the need of use many different tools, which could require a loss of time, all the data coming from different instruments could be fused and superimposed onto the surgeon's visual field, thus enhancing intra-operative visualization. An extraordinary example of these new technology are the Stereoscopic Integrated Imaging Goggles (Mela et al., 2015), which consists in a wearable stereoscopic fluorescence imaging system for wide-field intraoperative

image guidance, to present both depth perception and lateral spatial information to the surgeon: both color reflectance and near infrared fluorescence information and handheld microscopic imaging are offered simultaneously to the user in real time. The goggles can be integrated with non-optical imaging modalities such as ultrasound, providing multimodal image guidance to the surgeon and mitigating the optical imaging limitation of penetration depth; moreover, enables wireless goggle-to-goggle stereoscopic view sharing, where the remote collaborator can visualize the same data that the local goggles wearer sees. In the OR of the future, these goggles could be completed with a special sterile sensory glove which could permit to modify parameters and switch to a different imaging visualization modality, using a projected tactile screen. Moreover this kind of smart gloves could be used in the case of remote manipulation (Caeiro-Rodríguez et al., 2021): its application could be related to teach the fundamental skills of robotic surgery to novice and experienced surgeons (usually through simulations) and that of performing complex or new surgeries on real patients which requires a remote expert supervision.

Another kind of innovation could be a peculiar and dedicated smart surgical instrumentation to optimize surgery efficacy and efficiency: bioengineering plays a fundamental word for the development of futuristic intraoperative multiparametric instruments that could be used to ameliorate surgeons' comfort, reduce the risk of neurological damage, and increase patients' safety.

As the matter of facts, an actual issue in neurosurgery is the reduction of training and education: many of the most successful programs have been disrupted by the travel restrictions of the COVID-19 pandemic. There is therefore a pressing need for creative virtual solutions. Also in this case, virtual reality (VR) and augmented reality (AR), can be used for remote tele-proctoring, whereby an experienced surgeon can virtually assist with a procedure regardless of geographical location (Higginbotham, 2021). Expert guidance can therefore be given to both neurosurgical trainees and non-neurosurgical practitioners: a remote neurosurgical training, with the potential to reduce the learning curve of complex procedures, could be really useful, particularly in low-resource settings.

CONCLUSION

The neurosurgical practice is always evolving, achieving new technologies and new techniques every day.

From the beginning in the anatomic laboratory, the neurosurgeon **could visualize on specimens** all the structures and all the areas of the brain. Every idea, every doubt could be tested, could be investigated. When facing with a lesion, the **treatment must be carefully planned**, and all the information collected by each study and investigation performed must be organized and summarized.

Only at this point, the correct approach could be planned: all the steps could be simulated, and all the tools required could be estimated. This complex work of **planning will rend the surgery much more efficient**, and every technology will perform its precise role, adding a particular information. Moreover, the patient management is multidisciplinary, and required a precise teamwork: the follow-up usually is lifelong course.

When a case terminates, it's time for the neurosurgeon to go back to the anatomical lab and starts again to study the possible perspectives for the next case. We know that it could sound like a **never-ending story**: but actually, it is just an ordinary day of a **modern neurosurgeon**.

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APPENDIX: LEGEND FOR FIGURES

Figure 1. Formaline-fixed cadaver brains: in the anatomy lab, brain structures could be directly visualized. The anatomic details, including the natural colors, are so well preserved that they give a real picture of the morphologic details, such as preservation of anatomic landmarks and pathologic alterations. The specimen can be observed from different angles, enhancing the student's opportunity for visual examination. (A) Lateral view of a cerebral hemisphere: the red line marks the central sulcus, the white dotted line represents the Sylvian scissure, FL: frontal lobe, PL: parietal lobe, TL: temporal lobe, OL: occipital lobe. (B) Sagittal cut of a cerebral hemisphere, brain stem and cerebellum, CC: corpus callosum, M: midbrain, B: bulb, P: pons. (C) Superior view of cerebral hemispheres, the red line marks the central sulcus, the white dotted line the interhemispheric scissure. (D) Lateral view of a dry skull, the black dotted line represents the coronal suture (CS), the red dotted line marks the squamous suture (SS) and the violet dotted line underlines the lambdoid suture (LS), FB: frontal bone, PB: parietal bone, OB: occipital bone, TB: temporal bone, ZR: zygomatic root, EAM: external acoustic meatus. (E) Superior view of a dry skull base: CG: crista galli, FB: frontal bone, OC: optic canal, GSW: greater sphenoid wing, ST: sella turcica; FR: foramen rotundum; FO: foramen ovale; FS: foramen spinoso; FL: foramen lacero; C: clivus; FM: foramen magno. (F) Inferior view of a dry skull: MP: mastoid process; FM: foramen magno; CC: carotid canal; FL: foramen lacero; PB: palatine bone; FO: foramen ovale; FS: foramen spinoso; Z: zygoma.

Figure 2. 3D-volume-rendered representations created using Amira Visage Imaging. From tractography image a 3D model of striatum (yellow structures) could be realized and a simulation transection plane through the corpus callosum could be realized (A). Skull base bone and lateral ventricles (blue) 3D model reconstruction from T2 MRI (B), and a simulation of corpus callosotomy (green). Screenshot capture of 3D editor for skull base reconstruction based on CT images (C). Screenshot capture of 3D editor for brain components reconstruction based on a T1 MRI (D).

Figure 3. Advanced 3D-modeling: visualization and automatic segmentation obtained with FreeSurfer software. Tractography images has been elaborated with TractSeg program and the projected values on surfaces have been calculated with a script using FSL. Images highlighting the contrast between pial (A) and white matter surface (B), Desikan-Killiany segmentation. Tractography could be added in the models (C, E, F, H, I). Moreover, there is the possibility to evidence areas of interests in the segmented images (D, G).

Figure 4. Example of patient positioning in the OR: straight lateral position for a foramen magnum meningioma resection. The head is flexed downwards and turned to the floor about 10 to 15 degrees (A, B) as well as elevated above to the level of the thorax (C). The bottom arm is placed off the bed in an arm sling; the other arm is fixed to the thorax and abdomen and it was minimally stretched downward. A linear skin incision is planned (D) and sterile draping is placed.

Figure 5. MRI spectroscopy sequences: in these images the tissue metabolites could be investigated. The volume examined is highlighted by the green squared, initially is centered on a normal tissue area (A): the spectroscopy result is normal, with a high concentration of the N-Acetyl-aspartate (NAA, orange arrow) and a lower concentration of choline (CHO, white arrow). In the next sequence (C) the volume examined is centered on the pathological area: the spectroscopy result is abnormal (D) with the inversion of NAA (orange arrow)/CHO (white arrow) rate, pathognomonic characteristic of high-grade

glioma. Post-contrast (E) and FLAIR (F) axial images of a temporo-parietal mass: also in this case, the spectroscopy result is abnormal (G) with the inversion of NAA (orange circle)/CHO (white circle) rate. Figure 6. Sagittal (A), coronal (B) and axial (C) images of a functional MRI, mapping the language function, which appeared to be close to the postero-lateral portion of the tumor. In this case, basing on the MRI results, the surgery was performed in “awake”, for a better control of the language function.

Figure 7. Neuroradiological imaging added to the Brainlab station (Brainlab, Westchester, Illinois, USA) where could be processed and fused in a 3D model (A, B). This is a case of a left frontal parasagittal lesion (C, D, F) without contrast enhancement (G). Moreover, is possible every important structure in the working area (E), to protect it and to help intraoperative orientation (e.g. carotid artery, optic chiasm, basal ganglia, corpus callosum); with this software is possible to high light the motor cortex (H, orange curvilinear line) and the cortico-spinal tract of fibers.

Figure 8. Superior views of a dry skull base: the endoscope is demonstrating the access gained with a transorbital approach (A), and with an endonasal approach (B) with the respective craniectomies. Inferior view of a dry skull (C): the endonasal and transorbital routes are highlighted by the dissectors (D).

Figure 9: Fluorescence-guided vision. After the administration of 5-ALA, in case of a high-grade glioma (A), the tumor illuminated with UV 800 light assumes this characteristic bright pink fluorescence (B, C). Microsurgical aneurysm clipping (D, E, G, I): the intravenous administration of fluorescein and indocyanine green allows direct visualization of blood flow after aneurysmal sac occlusion, enabling the observation of vessel permeability and the effectiveness of aneurysmal obliteration (F, H).

Figure 10. Intraoperative use of the neuronavigator. During intratumoral resection, the pointer could be used to ameliorate surgeon orientation (B): in this case of a large temporal mass, the further objective was to remove the uncus, which appeared to be herniated in the prepontine cistern (D, black cross). The pointer confirm that we reached the uncus (A), that was removed safely (E, prepontine cistern demonstrated by the white cross). In the postoperative MRI (the images have been rotated on the horizontal plane for educational purposes) a complete resection was achieved (C) and a decompression of the middle fossa and of the prepontine cistern (D, black cross).

Figure 11. The intraoperative ultrasonography permits to ameliorate surgeon orientation and to confirm data in real time: as planned with the neuronavigator (B) the echograph confirm that we reached the location of a parasagittal mass (A); with the eco-color-doppler function (C) is possible to accurately visualize arterial and venous vessels which could be encountered during dissection.

Figure 12. This is the case of a deep seated parasagittal parieto-occipital lesion (A, red dotted circle). The lesion was reached through a posterior interhemispheric approach (B, lesion in red dotted line), as confirmed with the echograph (red dotted line C). After the resection the removal of the lesion was confirmed intraoperatively (E) and with the echograph (black dotted line); the postoperative MRI showed a complete removal of the tumor (D).

Figure 13. Intraoperative neurophysiological monitoring of motor function. After electrodes positioning, the location of the motor cortex was identified by the “phase reversal” sign (A) and stimulated during all the surgery (C). At this point the safe site of corticectomy was chosen and further resection was performed with continuous subcortical stimulation (B, D): the resection was stopped when the stimulation revealed the presence of motor fibers for mouth-tongue and hand. These intraoperative findings were expected by the Penfield homunculus representation of the motor cortex and by the presurgical planning (motor cortex of mouth, tongue and hand marked with white dotted line, surgical access trajectory represented by the black arrow, F).

Figure 14. Intraoperative imaging systems. The intraoperative CT scan, O-arm (Medtronic, Dublin, Ireland), permits to realize stereotactic procedures and implant collocation with high precision and maximal safeness (A, B). The 0,2 Tesla PoleStar® N30 ioMRI system (C) (Medtronic, Dublin, Ireland) with the StealthStation® S7® navigation system could be used to evaluate intraoperative extent of resection: T1 post-contrast images could be obtained to evaluate extent of resection (D).

Chapter 9

Technological Environments of Anatomical–Radiological Vision in 3D for the Study of Pelvic Structures

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ABSTRACT

Computer applications have been incorporated as valuable elements in teaching, thanks to the innovation of new technologies in recent decades. The implementation of these computer developments in the field of medical education has been a true revolution. The authors present a computer development designed for PC environments that allows visualizing and interacting in a virtual environment with the main anatomical structures (bone, muscle, vascular, and visceral) of the female pelvis in three dimensions (3D) integrated with cadaveric sections and serial sections of magnetic resonance imaging. The consequence of the application of 3D environments for training and the integration of all these technological innovations in clinical medicine, together with the rapid evolution of information and communication technologies, is the emergence of a new teaching methodology with new opportunities for the development of the teaching-learning process.

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INTRODUCTION

We live in the era of globalization, in the so-called “knowledge society”, in which the rapid development of information and communication technologies (ICT) has brought about changes in all areas of human activity.

In the field of education, the arrival of ICT and the advantages they offer in teaching have led to questioning of the pedagogical models traditionally used. The objectives of the new educational model lie mainly in placing students as the protagonists of the teaching-learning process and introducing digital teaching methods accessible to all, free of spatiotemporal restrictions, which motivate and promote a type of learning that is autonomous, active, constructive, participatory, interactive, responsible and permanent.

This educational trend, determined to take advantage of the potential of ICT in teaching, together with the advances achieved by imaging techniques for diagnosis and medical clinic, have also driven the need to implement new teaching methods in the discipline of Human Anatomy, whose objective throughout history has been to teach students to observe, analyze, interpret and learn anatomy, with a view to clinical practice, diagnosis and treatment of diseases.

The introduction of digital models that allow the representation of three-dimensional anatomical images from those obtained from cadavers or diagnostic techniques such as magnetic resonance imaging (MRI), has provided a new way of understanding anatomy. Three-dimensional vision is a crucial tool for understanding many complex anatomical structures and regions, especially those that require greater spatial ability.

In medicine, the reconstruction of body structures in three dimensions (3D) will allow not only a better knowledge and understanding of their morphology and the spatial relationships established between them, but also a better approach to the diagnostic data of pathologies and their possible subsequent surgical treatment.

The generation of this type of digital resources, of 3D vision, independent of software or hardware platforms, which allows the manipulation of the anatomical models at will, surpasses the visualization obtained with the classic anatomical atlases.

For all these reasons, the possibility arises of generating and putting at the service of medical training an interactive computerized teaching tool that allows visualization, analysis and interaction with 3D models of the anatomical structures of the female pelvis, with simultaneous cadaver and MRI slices, in the three planes of space, with the intention of facilitating the study and understanding of the structures that make up this complex body region. This tool can serve as an aid and complement to the traditional anatomical training that is usually performed under static flat image formats in the different classic anatomical atlases.

It is intended that users can easily, quickly and dynamically experiment with means adapted to the current technological reality in the areas of medical sciences.

To achieve the proposed objectives, we proceeded to the analysis of the different anatomical sections, both cadaveric and radiological, with the support of experts in the disciplines of anatomy, radiology and gynecology, in order to accurately identify the different anatomical structures for their segmentation. In addition, we have also had the help and advice of experts in computer science for the proposed technological development.

Logically, we also want to evaluate the degree of satisfaction of the technological tool, by means of a questionnaire carried out to a group of students, to obtain information on the degree of practical usefulness in the teaching of this anatomical region.

BACKGROUND

“Anatomy”, defined as the science that studies the structure of the human organism, is a fundamental discipline in health education, which not only provides knowledge about the structure of the human body, but also contributes to enhance the development of skills and attitudes essential for the exercise of health professions, as many authors believe, including Rodriguez-Herrera et al. (2019).

Etymologically, the word “anatomy” derives from Greek and means “to cut again”, which already indicates that the preferred methodology for learning anatomy since ancient times has been the dissection of cadavers. Although cadaver dissection allows direct visualization and subsequent manipulation of anatomical structures, images have also been great allies for teaching this discipline. However, establishing the spatial relationship between the different anatomical structures from the two-dimensional and flat representation in drawings, illustrations or photographs of three-dimensional physical models or real bodies is difficult and requires a high mental effort.

ICT, which authors such as Bringman -Rodenbarger and Hortsch (2020), defined as those technologies related to the storage, processing, retrieval and communication of information through the use of electronic and computerized devices, have transformed the teaching-learning system.

ICTs foster an active attitude in the student, making him/her the protagonist and actor of his/her own learning. They reinforce visual memory, which facilitates both the comprehension of content and its recall. They also provide flexibility, versatility, interactivity and connectivity to the student, so that they can complement, enrich and transform their training in the opinion of several authors such as Moro et al. (2020) among others.

The introduction of teaching associated with technology in educational institutions, and especially in universities, is nowadays mandatory, especially when the current generation of students is accustomed to using digital devices in their daily lives, which allows them to access a large amount of information, with unprecedented ease, speed and depth, anytime, anywhere.

The possibility of constructing three-dimensional images from those obtained with current technology, and allowing user interaction with them, has led to the learning of a new type of anatomy, more dynamic, in which the student directs his own training and sets his own pace of learning.

The application of 3D environments for training is a new source of opportunities for the teaching-learning process. They offer a three-dimensional representation of organs and structures, allowing their visualization from different angles and distances, facilitating the understanding of complex and abstract concepts. They are intuitive and attractive to students, providing extra motivation for learning as described in their papers by authors O’Rourke et al. (2020), Triepels et al. (2019) and Ugidos Lozano et al. (2019).

It is evident that the conformation of the organs and anatomical structures of the female pelvis in the three planes of space is complex and difficult to represent. For this reason, the authors consider that the application of three-dimensional interactive digital anatomical models facilitates their visualization and, above all, the perception of the spatial relationships established between them, something that not all students achieve with 2D images.

The aim of this work is to offer an interactive 3D methodology that is attractive for learning female pelvic anatomy, so that it can serve as a guide for both the anatomy student and the health professional in their daily clinical practice.

MATERIAL AND METHODS

Acquisition of Sectional Images

For the acquisition of ultrasound and MR images, a 59-year-old woman, voluntary, nulliparous and with no known history of gynecological pathology, was scanned.

The radiological examination was carried out, with prior informed consent and without economic remuneration for her participation, in the radiodiagnostic services of the Hospital Clínico Universitario of Salamanca.

The MR images selected for the software were high-resolution, 0.5 mm spaced, proton density-enhanced images of the pelvic region. Specifically, three orthogonal MRIs were obtained, each in a different spatial plane, using a 1.5 Tesla scanner (Signa General & Electric).

Siemens Acuson Antares and Voluson E6 ultrasound scanners were used to obtain the ultrasound images required for computational development.

In addition, multiple 0.33 mm thick, high-resolution axial sections from the cadaver of a 59-year-old woman, obtained from the Visible Human Project (VHP) of the US National Library of Medicine under license number HW1-020645 for teaching and research purposes, were used.

The different images obtained from these three resources were used for the subsequent reconstruction of the anatomical structures of the pelvis.

Segmentation of Anatomical Structures, Delimitation of Regions of Interest (ROIs) and Reconstruction of Three-Dimensional Models

The segmentation and delimitation of ROIs consisted of the subdivision of each acquired anatomical image into homogeneous regions.

The greatest difficulty was in the 3D reconstruction of nerves and blood vessels, due to their small caliber, for which a tool was created to simulate nerve and vascular pathways.

Segmentation was based on manual delimitation using Autodesk Maya and supervision by expert observers (anatomists, radiologists and gynecologists), making it more robust than other automatic segmentation methods. The detection of the edges relative to the different anatomical structures was performed according to their shape, size and location. Manual segmentation strategies were used since the change in intensity or edge between many of the pelvic structures is difficult to detect due to the lack of sharpness of their boundaries. The segmentation process was very laborious and time-consuming, as it was performed individually for each dataset. The different components were identified in the serial VHP and MR images, for subsequent manual labeling with different color codes using Maya software.

Moreover, the ROIs were realigned in the three reference planes. Alignment involved the incorporation of the different original data sets, acquired from different orientations, into a common coordinate system. A surface model composed of a mesh was obtained from each of the resulting ROIs. Decimation algorithms were applied to the models to simplify and smooth them and finally they were exported to DirectX format.

The selected sectional images from the VHP, as well as the MRI slices and all the 3D surface models obtained in the previous phase, were designed for a viewer specifically developed for this software application, programmed in Visual C++ and including DirectX controls.

Evaluation Surveys

Satisfaction surveys were carried out with health sciences students (n=35), in order to assess and determine the degree of educational usefulness of this computer tool. The limitation of the number of users was due to the availability of technological equipment to validate the computer development, considering a sufficiently representative number to obtain an indicative sample of student satisfaction with the technological development presented. All the students had previous knowledge of the subject, and all of them had passed the human anatomy course on splacnology prior to the satisfaction survey.

Before carrying out the satisfaction survey on the technological procedure, another survey was conducted to determine the degree of usability of the portable devices by the same students who had carried out the evaluation test of the software generated. This survey sought to know the types of portable devices they use on a regular basis and their degree of handling them.

The second survey focused exclusively on the computer development itself, trying to assess the effectiveness and satisfaction of the users who handled the teaching program.

The data were processed with Excel, which allowed us to analyze and process all the survey results.

RESULTS

Sectional Images

The software development consists of a collection of sectional images (axial, sagittal and axial) from cadaver and MRI, as a reference to perform a comprehensive three-dimensional assessment of the anatomy of the female pelvis, being able to visualize together the sections of the different planes of space and in any spatial position.

In addition, this software application allows anatomical correlation with another imaging technique such as ultrasound, which allows a parallel anatomical analysis between MRI sections and ultrasound images. There are anatomical-radiological differences between the evaluation of static ultrasound images and MR sections, so the authors considered it interesting to focus this software development on helping to correlate and interpret the anatomy shown in these two very different imaging techniques.

Sectional anatomical images make it possible to analyze the structure of the human body by making slices in the three planes of space, and enhance the knowledge of the spatial relationships between various organs and tissues, offering a realistic view of them, since they faithfully reflect their shape and relative position by preserving the spatial relationships that exist naturally between them.

It is very important in any anatomical application for teaching, whether with three-dimensional models or not, to have an abundant number of anatomical illustrations, which reinforces the importance of the collection of serial cadaver sectional images used as an anatomical reference for this computer development.

It is true that anatomical slices can be unintuitive and extremely complex, as they require the observer to have anatomical knowledge and the ability to orient themselves with 2D images that are a representation of 3D structures, especially in unversed subjects. Once these difficulties are overcome, sectional anatomy images provide a wealth of information about anatomical structures.

Serial sectional anatomy of MRI and cadaver allowed the authors to determine the structures (bony, muscular, visceral and vascular) that make up the female pelvis and pelvic floor, by providing a clear

and precise anatomical map of the elements that comprise them, which facilitated their identification, location and delimitation.

Three-Dimensional Anatomical Models

3D anatomical models of the structures that make up the female pelvis, both of its continent (bones and muscles) and its content (organs, vessels and nerves) were elaborated with the sectional cadaver and MRI images. These three-dimensional models can be seen isolated or embedded within the sectional images of cadaver and MRI.

Bone 3D Models of the Female Pelvis

The bony structures were easy to identify in the sectional slices, which allowed the authors to reconstruct the entire bony substratum of the female pelvis (sacrum, coccyx, coccyx).

3D Muscular Models of the Female Pelvis

The muscles of the pelvis were reconstructed from the sectional images, including those that make up the perineum, and that constitute the pelvic diaphragm (superficial cervical, coccygeal, levator ani (along with its fascicles), obturator internus and externus, pyramidal or piriformis, iliacus and psoas-iliacus, among others). Figure 1 is an example of 3D model of the bones and muscles.

3D Reconstructions of Nerve Structures of the Female Pelvis

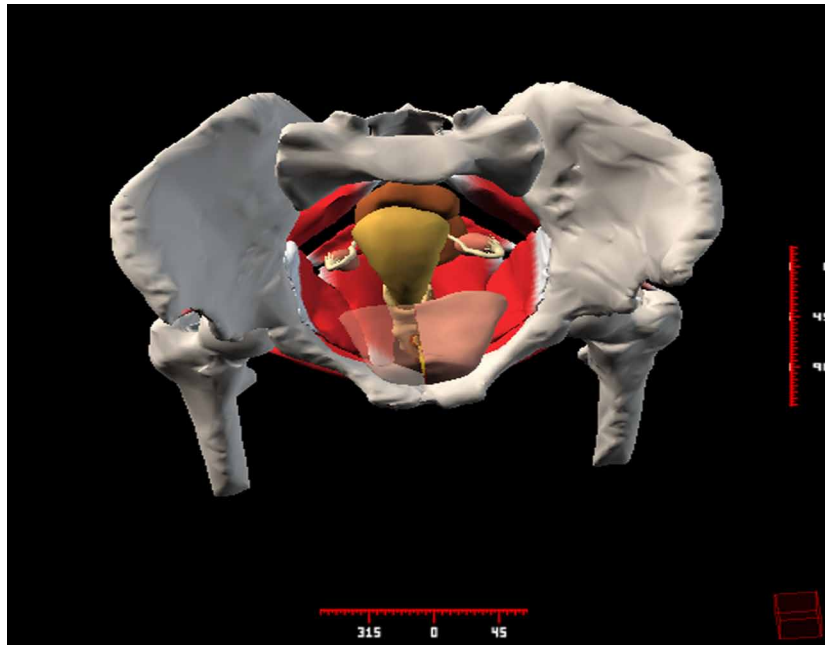
The nervous system was the most complicated and difficult to solve, since sectional images do not provide very accurate information to follow the path of the nerves, so the authors had to resort to anatomical knowledge to differentiate these entities and intuit their tracing. With this in mind, the lumbar plexus (which includes, among other nerves, the obturator nerve and the femoral nerve), the sacral plexus, the sacro-coccygeal plexus, the innervation of the genital apparatus, the ano-rectal innervation and the innervation of the lower urinary apparatus were reconstructed in a didactic manner.

3D Models of the Vascularization (Arteries and Veins)

The irrigation of the pelvis was, within its complexity, more accessible in terms of following its course than the innervation, since the information on these structures provided by MRI and cadaver sections is greater. It was possible to reconstruct large caliber arteries and veins without problem, and with a higher degree of difficulty those of smaller caliber, taking into account how difficult it is to delimit the capillaries, especially around areas of great vascularization, such as organs and muscles. These include:

- Arteries: abdominal aorta, femoral, iliac (common, external and internal with their posterior and anterior trunks), inferior mesenteric, perineal, pudendal (external and internal), rectal (inferior, middle and superior), middle sacral, uterine, vaginal and vesical (inferior and superior).

Figure 1. 3D model of the bones and muscles of the pelvis. Uterus, ovaries, tubes, bladder and rectum are included. Half of the bladder is displayed with a certain degree of transparency (as desired by the user) so that the structures behind the bladder can be seen



- Veins: vaginal azygos, inferior cava, femoral, iliac (common, external and internal), inferior mesenteric, perineal, pudendal (external and internal), rectal (inferior, middle and superior), middle sacral, great saphenous, uterine, vaginal, and vesical (superior and inferior).

Three-Dimensional Models of the Viscera

The female pelvic organs were much easier to reconstruct from the sectional images available to the authors, with some exception due to their tortuosity and spatial arrangement, as is the case of the fallopian tube, for example.

Three-dimensional models of the internal (vagina, uterus, fallopian tubes and ovaries) and external genital organs, lower urinary tract (bladder and urethra), and terminal digestive tract (rectum and anal canal) have been reconstructed. An example of the 3D models of the uterus, fallopian tubes and ovaries can be seen in figure 2.

Functionality of the Computer Application: User Interface

The possibilities of combination and variation of the two modules available in the program (sectional images and 3D models) are multiple, allowing the representation of different anatomical areas of the female pelvis from different angles and positions in space.

The graphical interface generated for this software application is very simple and easy to use, as it clearly shows the different options that allow the user to interact with the anatomical viewer. It exhibits

Figure 2. 3D model of the uterus, ovaries, fallopian tubes, vagina



the use of floating windows that can be relocated, whose display may or may not be selected, and which are shown in the anatomical viewer. Also included was the use of icons and not only text in the different sections of the interface, so that they would be identifiable and allow convenient access to the different functions.

The user interface is divided into four parts: anatomical viewer, visualization control, plane control and model control.

To begin with, the main function of this program is “to allow to observe the anatomical structures of the female pelvis in 3D, having as reference pattern the cadaver or MRI sections, in the three planes of space”, although it admits other functions at the user’s request.

Anatomical Viewer

All interactions with the elements of the visual scene (rotations, translations, zoom and selection) are performed by placing the cursor on the viewer, using the computer mouse. Figures 3 and 4 show a screenshot of the anatomical application viewer.

Visualization Control

There are three perspectives predefined by the program to observe the composition represented in the anatomical viewer, which can be selected using the buttons that appear in the display control (as shown in figure 5). These perspectives are sagittal (focuses the image of the anatomical viewer from the side), axial (we see it from above) and coronal (presents a frontal view), which can be subsequently modified by the user by moving the 3D model, the sectional image or the set of both with the mouse.

Figure 3. Screenshot of the application's anatomical viewer showing the uterus, fallopian tubes and ovaries combined with an axial cadaver section of the VHP

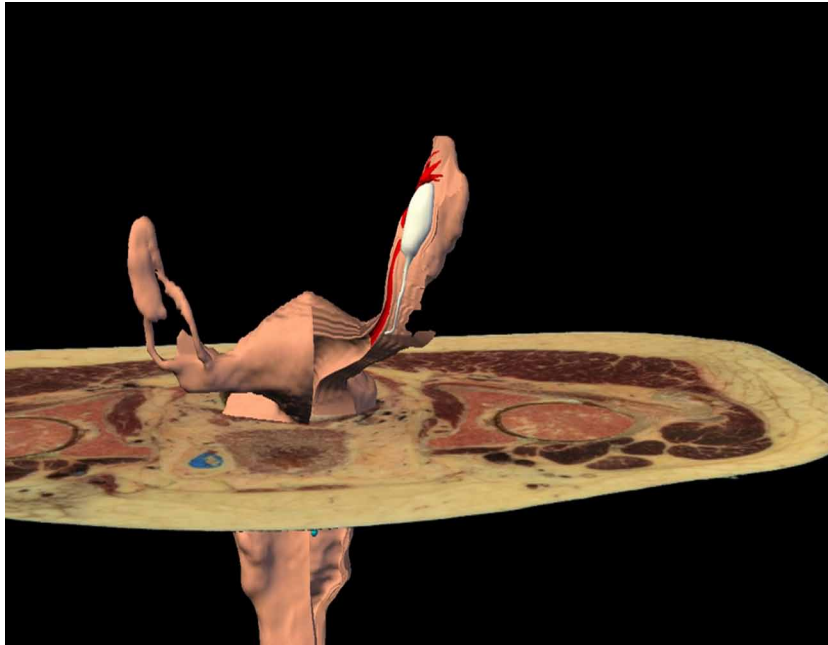
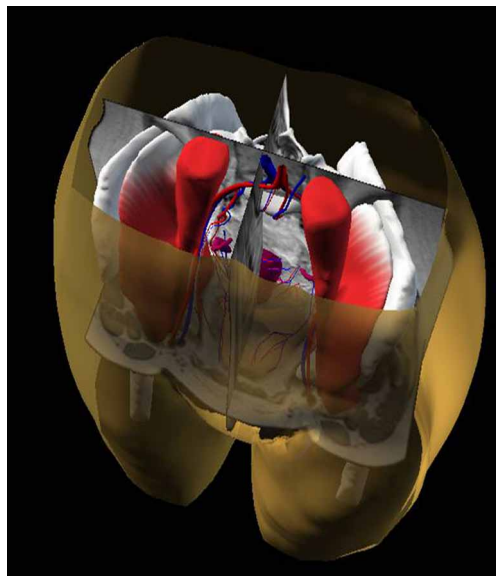
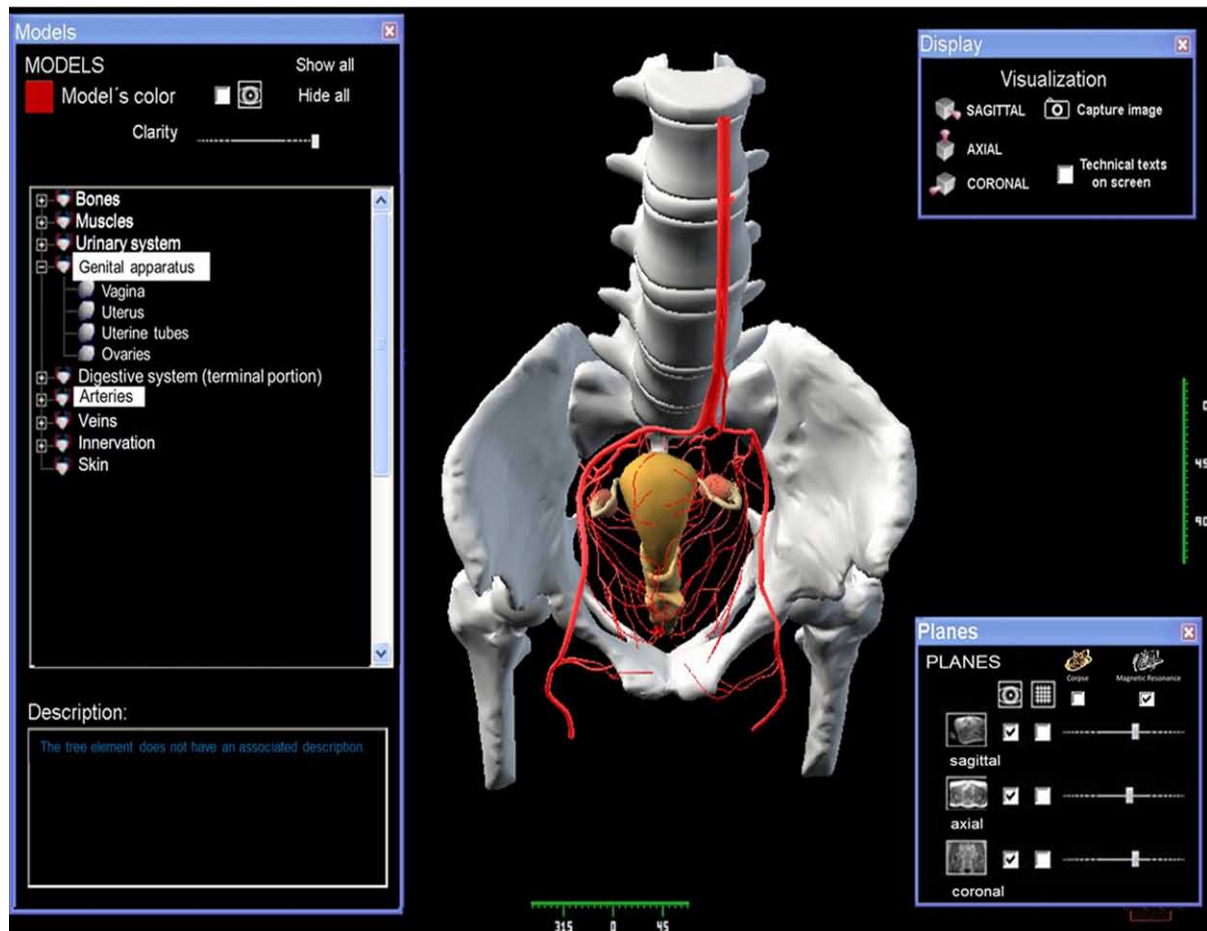


Figure 4. Screenshot of the anatomical viewer of the application showing various pelvic structures with MRI sections in the 3 planes of space as reference. The skin can be seen represented with transparency



The scene represented in the anatomical viewer, after making the modifications desired by the user, can be stored as an image in a bitmap (.bmp) format file, by means of the “capture image” option.

Figure 5. Screenshot of the application in which we can see at the top right “the visualization control”



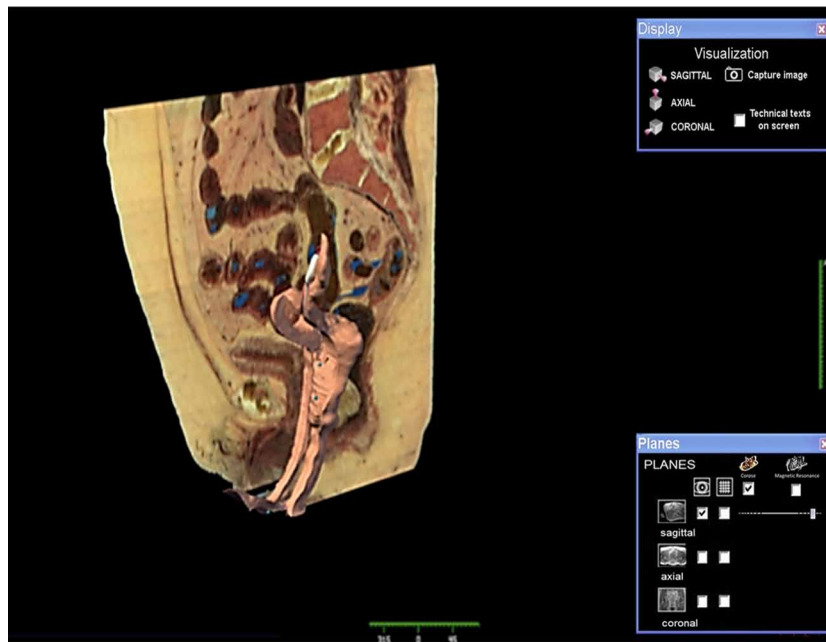
Planes Control

Contains the controls necessary to manage the MRI and cadaver sections of the female pelvis presented in the viewer. In the upper right part of the plane control window, there are two boxes where you can select which images you want to use: cadaver or MRI.

There are three orientation planes: axial (horizontal), sagittal (lateral) and coronal (frontal). Each plane, when activating its visualization, has a scroll bar that allows to change the height of the slice in the specific plane that we are manipulating and a selection control to activate or deactivate its visibility, as it appears in figure 6. You can also change the position of the selected plane by moving the cursor horizontally on the viewer while pressing Shift, without holding down any mouse button.

The icon simulating a grid allows the appearance of 1-10 mm squares (whichever the user wishes to apply), in order to measure structures, since the 3D models are made to scale.

Figure 6. Screenshot of the application in which we can see at the bottom right “the plane control”



Models Control

The “Models” section controls the anatomical structures represented by 3D models.

By selecting on the color it is possible to modify and assign the color that the user likes the most.

The visible selection box allows you to activate or deactivate the visibility of the selected model. You can also activate or deactivate the visibility of the 3D models as a whole.

The cross bar next to the “Transparency” label facilitates the visualization of the set of structures by being able to determine the degree of translucency (whether or not we want to see through that 3D model).

In the “Tree” window the models are selected/deselected independently, opening the different branches to see the available 3D structures and their hierarchical relationship. Figure 7 shows the “tree” window of the pelvic innervation as an example.

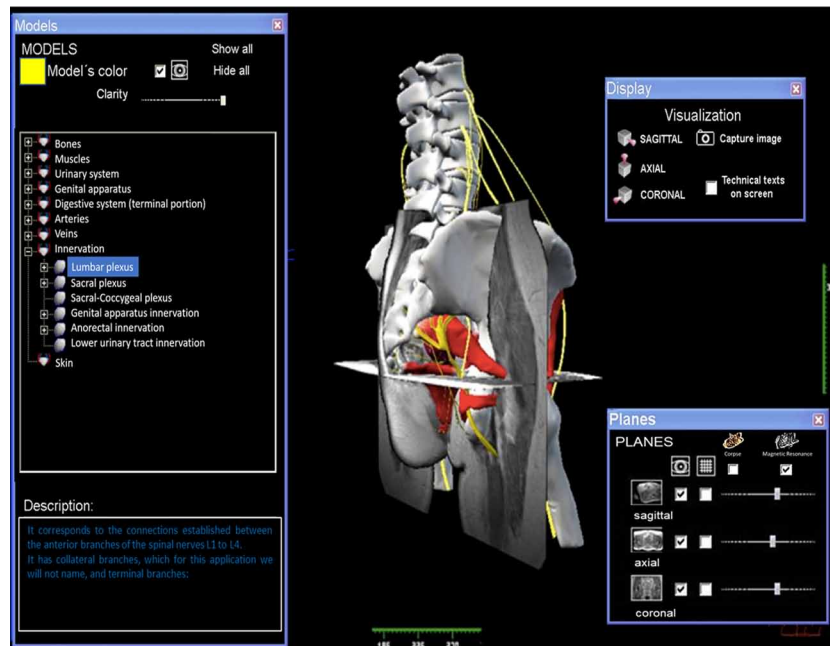
The lower text box shows a small anatomical description of each selected structure, otherwise it appears devoid of information.

Correlation between MR Images and Ultrasound Images

Faced with the need to correlate MR images with those obtained by ultrasound, the authors developed another application, which can be seen in figure 8, that allowed the integration of the anatomical information provided by both imaging studies.

This complementary section has serial sectional MR images and different ultrasound images obtained by different ultrasound modes.

Figure 7. Screenshot of the application in which we can see on the left “the control 3D models”



The computer application has been designed in such a way that all the options it offers can be handled at will, which translates into a real interaction with the program, preventing the user from becoming a mere spectator.

It is a teaching tool, carefully designed and elaborated, which aims to facilitate the knowledge and understanding of this body region, enabling the analysis of the anatomical structures that compose it in three dimensions and from any spatial position.

User Evaluation Survey

The authors conducted two different surveys with the students, one more focused on the application and their evaluation after using it, and another more generic one on the use of the technology at present.

In the context of the use of technological devices by the student population, the following considerations drawn from the survey can be reflected.

It is no longer surprising that the highest percentage of students in any of the health science careers is female. In surveys of a group of student volunteers, the result is 77% female and 23% male.

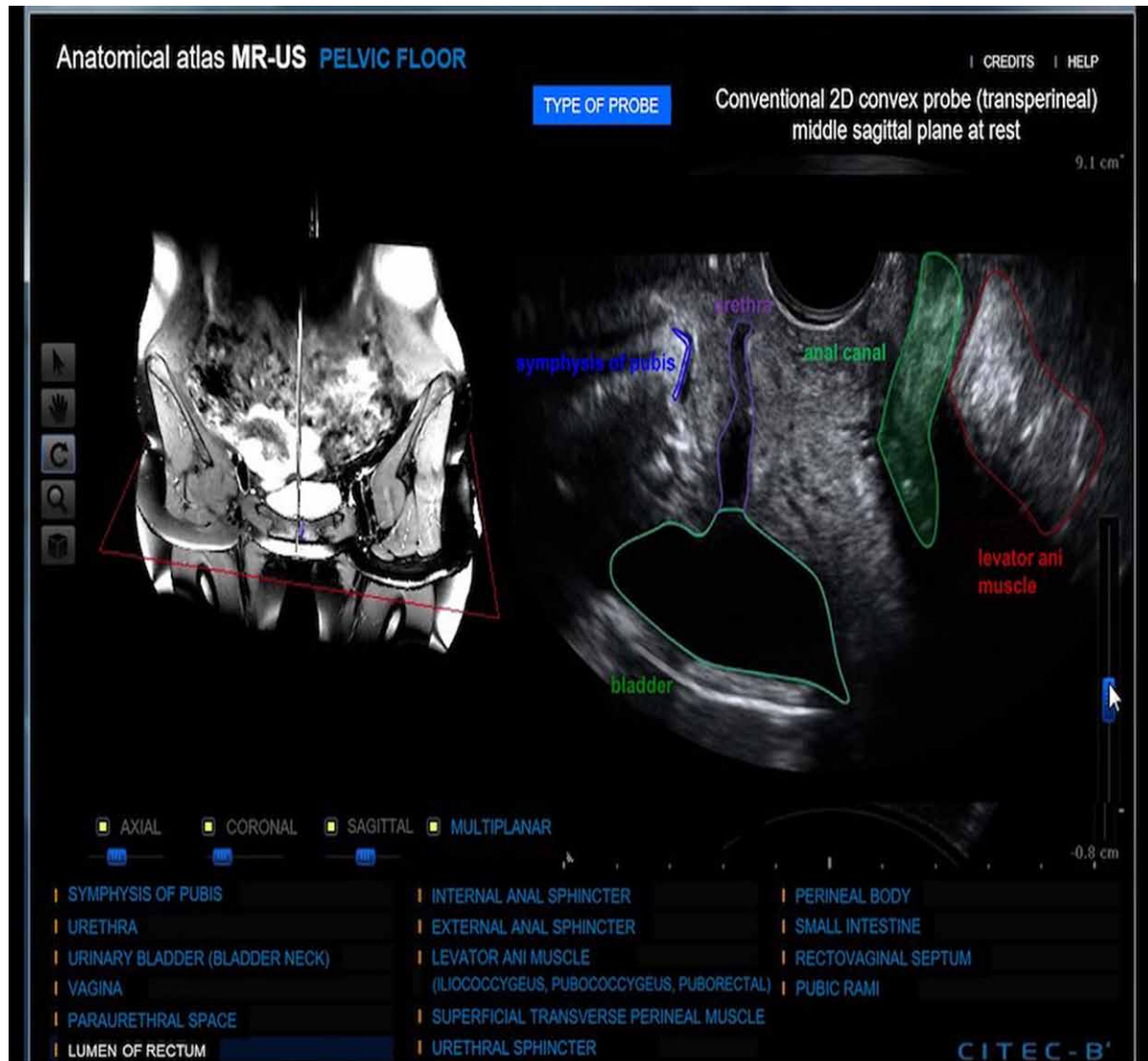
The average age of the students surveyed was between 18 and 19 years.

In relation to the operating system most used in their mobile devices, Android was the most prominent, followed by iOS. The most widespread cell phone brands were Samsung, Huawei and Xiaomi.

Although all the students have a smartphone with Touch and 4G technology, not all of them have a Tablet, with those with the Android operating system standing out.

The main use of the cell phone is for personal calls and social networks, and it is not very often used in the teaching environment, although it is consulted occasionally.

Figure 8. Screenshot of the application developed by the authors for the correlation of ultrasound and MR images



The time dedicated to the use of the portable device stands out very significantly, reaching three hours a day for some, and exceeding five hours a day for a large majority. In addition, most of this time is spent on entertainment, followed by information management and news reading.

Most of them have good skills in installing or uninstalling different applications for these devices. However, the use of these applications for their academic training is only used sporadically. Only a small group uses them frequently, and others hardly ever.

In all cases there is unanimous agreement that the use of multimedia resources facilitates a better understanding and knowledge of the subjects consulted.

In relation to knowledge and experimentation with virtual reality stereoscopic vision techniques, there is a predominance (63%) of those who have not used these technologies. The lack of experimentation with these technological devices is also reflected by the scarcity of students who have virtual reality glasses, only 20% of them.

However, despite the scarce use and handling of these virtual reality technological procedures, the vast majority considers that it can be a good teaching resource if properly applied.

The results obtained in the survey carried out on the evaluation of the software of radiological anatomy of the female pelvis show very positive data in terms of satisfaction and learning through the use of this technological tool.

Overall, the appreciation of the users who used the software has been very satisfactory, exceeding the level of 4 (out of a maximum of 5) in practically all the situations formulated, except in the question related to the theoretical content of what is described, which dropped to 3.11.

What does stand out in its overall assessment is the software, with 88% of respondents saying that it is easy to install and practically 100% of users saying that the application never or almost never crashes. Navigation through the program is very intuitive, the brief explanatory comments on the anatomical structures displayed are well appreciated, and the program interface is very intuitive and easy to use, a response given by almost 100% of the users.

In relation to the users' considerations on what this technological development contributes to the teaching-learning process, there is also a high degree of satisfaction.

From the teaching point of view, the evaluation as a good complementary didactic resource to the study stands out. In addition, the three-dimensional view of the anatomical structures is highly valued by users, with a high degree of satisfaction. On the other hand, a good group of respondents pointed out that this tool surpasses many anatomo-radiological atlases that are static. The visual presentation of the contents is very attractive, being therefore highly valued by the students. The whole development is very beneficial, being recommendable for other colleagues or students, according to the users.

DISCUSSION

In recent decades, ICT have revolutionized all social spheres and have strongly burst into the educational system, evidencing the need to establish changes in traditional pedagogical models in order to adapt them more in line with the demands of today's society and the characteristics of a student body accustomed to coexist with technology on a daily basis.

In this line, it can be seen that the students who were offered the study of pelvic anatomy with this application were quite familiar with technological tools, most of them having the latest generation of cell phones with powerful operating systems, which they used for several hours a day, mainly for social relations and entertainment, being occasionally used to obtain information or consult news and very rarely for subjects related to the teaching field. Most of them had good skills in installing or uninstalling different applications for these mobile devices, but only used them sporadically for academic training, although they recognized that the use of multimedia resources facilitated knowledge and understanding of the subjects consulted and that other technological procedures, such as virtual reality, properly implemented, could be a good teaching resource.

The familiarity of these new generations of students with digital media, the realization that traditional teaching based on the teacher's master class and evaluation by means of a final examination of the

students, has proved to be an ineffective tool in the teaching-learning process, the enormous potential offered by technology for the transmission of knowledge and the predisposition of current students to incorporate in their studies more innovative methodologies based on technological advances, are the fundamental issues that have led to consider the application of ICT in the teaching of the 21st century.

The methodology presented by the authors promotes autonomous learning and makes the student the direct protagonist of his or her learning process. The continuous interaction with the computer application, besides stimulating the development of skills to improve computer and audiovisual training, awakens interest and motivation in the study of pelvic anatomy and reduces the time required for learning it, as pointed out by the students after the implementation of this didactic resource, which also allowed an involvement in the task free of spatial-temporal barriers. The authors agree with the views of Papadopoulou et al. (2019) and Pickering and Swinnerton (2018) and Hampton and Shung (2010) that the application of technological methodologies can help students improve learning outcomes by increasing student participation and involvement in the study activity. However, for Golenhofen et al. (2020) the success of these technological applications on learning depends solely on students' motivation or predisposition for their use, which also seems to be higher in those who show better overall academic performance.

The authors' interactive didactic resource, provides a complementary methodology to traditional teaching, focused on exploration and inquiry processes, stimulating critical thinking, unlike most of the applications studied by Martínez et al. (2017), which in their opinion, are based solely on providing new information but without enhancing skills that favor the construction of knowledge in students, which for Svirko and Mellanby (2017) is fundamental in the teaching and learning process and is mainly achieved through observation, research, experience, reflection and reasoning.

The use of image-based technologies, especially those based on 3D representation, as the didactic tool that the authors have developed, reflect what is being taught in theory, but with a three-dimensional view of the structures, which allows a more meaningful understanding and assimilation of the content being studied. With these media, a level of visualization impossible to achieve with 2D teaching methods is obtained, since they provide a view of the structures with a more realistic depth of field, making it possible to illustrate concepts and principles that would otherwise be very difficult for students to understand, especially those that require spatial ability. In addition, they have an interesting clinical medical application, since the knowledge of anatomical structures in the healthy individual facilitates the diagnosis of pathologies and can serve as a basis for planning a surgical approach as reflected in the work of Weiss et al. (2021).

Today there are a multitude of 3D applications, such as the one developed by the authors in this work, which can be used for learning anatomy and other disciplines related to the area of health.

The applications listed below are a small representation of the numerous 3D digital resources that have been provided for the teaching-learning of anatomy.

- Human Anatomy (<https://human-anatomy-atlas-2018-complete-3d-human-body.softonic.com/>):

Virtual atlas of human anatomy in 3D that offers a complete anatomy model with visualization of structures of all anatomical systems in man and woman. The program has a large library of models. It presents a larger collection of three-dimensional models and supplementary text, covering a wider field of anatomical knowledge, unlike the authors' application, focused only on the female pelvis. Because of this some anatomical details may not be overly concise. Different from the computer tool under analysis, it does not offer the possibility of viewing MRI or cadaver sectional images, since the sectional images

that can be evaluated are obtained only from the 3D models developed. Another drawback, stated as a “contra” by the developers, is that getting familiar with the integral application can be intimidating, so its handling will not be as intuitive and easy as with the authors’ application.

- Visible Body (<https://www.visiblebody.com/es/anatomy-and-physiology-apps/human-anatomy-atlas>):

Paid application of 3D models of the entire human body quite complete, presents sectional images and CT cadaver images, 3D models are not shown embedded within the sectional images, they appear next to them to compare them. It can be installed on computers and mobile devices, unlike the authors’ application which is for computer.

- Virtual Medical Vision (VMV) 3D (<https://visionmedicavirtual.com/es>):

On-line 3D tool for the presentation and study of human anatomy, with a lot of information available in addition to anatomical models. Its main difference lies in its online access, as an obstacle, it requires an annual subscription to be able to use it. Although it has an important compilation of radiological images, it does not allow their comparison, nor the joint visualization with the 3D models as the 3D application of the authors makes possible.

- 3D Human Anatomy (<http://anatomiahumana3d.com/>):

Project consisting of the digitization of anatomical structures of the human body in three-dimensional models (real), which allows the visualization of the same from different angles, and with the possibility of using augmented reality, reproducible through a mobile or tablet. Access is free and provides anatomical classes in pdf. An important handicap compared to the development of the authors is that it does not refer to the pelvis and its structures. It only allows the assessment of isolated structures and without support of sectional images.

- Zygote body (<https://www.zygotebody.com/>):

Virtual application that offers 3D anatomy models of the human body for pedagogical purposes. It presents a complex 3D anatomical model, in which you can see its components as a whole and select one in particular, allowing you to visualize its position and path in the case of vessels and nerves. It has functions that can only be accessed for a fee. It lacks real sectional images. Its use is not intuitive. It is difficult to discern the function of each button and how to operate the application. The free version contains disabled functionalities. The authors’ application seems superior in terms of the incorporation of sectional images and that the use of the application is more understandable and easier for the user.

- Bio TK (<https://www.biotk.co/site/index.php?lang=es>):

3D anatomy atlas generated from cadaver slices, making it accurate and realistic. It allows the evaluation of cadaver sectional images (not MRI) and the 3D models embedded in it, as well as the authors’ application. It allows to simulate a cadaver dissection, extracting organs and analyzing them indepen-

dently. Compositions can be stored and shared, as with the authors' application. It is compatible with virtually all hardware platforms and integrates easily with e-learning platforms, allows partial access for free and has premium paid versions.

- Human Dissection Models Project (<https://www.proyectoohdm.com/>):

Based on the creation of models with three-dimensional vision technology (they are not reconstructed 3D models) from organs or structures dissected from human bodies, which provides their assessment in isolation and through augmented reality. The authors' application is more complete in terms of usability and contribution to medical training.

- Sectra 3D Dissection Table (<https://www.simulat.com.ar/productos/mesa-sectra>) (<https://www.medicaexpo.es/prod/touch-of-life-technologies-toltech/product-81270-644641.html>):

Digitized representation of human body structures in different planes, using images of cadaver slices from the VHP and MRI database. The images were processed using the VH Dissector program installed on a SECTRA digital 3D touch screen visualization table. The fact that this specific visualization table is required for its use means that it is only possible to use it in universities or large centers, which greatly limits its availability compared to the authors' application, which only requires a computer for its use.

- Human Body (male) (https://play.google.com/store/apps/details?id=com.rendernet.humanmale&hl=en_US):

Only male human anatomy is available. It covers several biological systems and 3D models of organs (it has narrations and animations), but in a simple way, without going into too much detail or realism. It does not make use of sectional images. It is an application whose purpose is not to promote the anatomical knowledge of medical students, which falls short in the provision of information. The development of the authors requires an anatomical base and skills in the interpretation of previous sectional images. It can be used on portable devices.

- Anatomy Learning (<https://anatomylearning.com/>):

Offers a wide range of human anatomy with various biological systems (male and female), along with 3D models of different body parts and organs. It is based on very schematic 3D models, for use on mobiles, tablets and computers via online. It does not relate anatomy with sectional images, so it does not collaborate in anatomical learning like the authors' computer application. It allows to navigate and find the contents you are looking for, but the way to use the content (interface) is not always intuitive and instructions for use are needed.

- Complete Anatomy by 3D 4 MEDICAL (Elsevier) (<https://3d4medical.com/>):

Editorial platform for education with 3D anatomy to interact with the smallest details of the human body. It is a paid application, with many possibilities, including fostering interest in anatomy in students thanks to its augmented reality features. Its three-dimensional models are very realistic, allowing

animations and representations of certain functionalities of the human body. It does not have sectional anatomy like the authors' software.

- 3D model for the study of the female pelvis (Balaya et al., 2016):

Special mention to this application since it is very similar to the development made by the authors, but more rudimentary in terms of its interface and visualization. The reconstruction of the 3D models is of cadaver sections, but the sectional slices cannot be visualized along with the 3D models. Some structures are not represented, especially those of smaller caliber and size, probably because of the difficulty of their identification during segmentation and subsequent reconstruction.

- 3D application for the study of the male urogenital tract (Uhl et al., 2006):

Three-dimensional reconstruction of the male urogenital tract from cadaver sectional images, but does not employ MR sectional images. The model does not include muscles related to the urogenital system such as the pelvic diaphragm and perineal muscles, and only shows 3D models, but not sectional images unlike the authors' application. It includes a special viewing mode to provide a stereoscopic effect by using green and red glasses.

- 3D model for the study of the female pelvic floor (Hampton and Sung, 2010):

Shows pelvic organs and their supporting structures, but does not include vascular or nerve structures, so it has less anatomical detail than the authors' application. In addition, the tour of the pelvis follows a guided itinerary, not at the user's will. It shows 3D models, but not sectional images. It has voice-over, animations and video clips. It combines 3D models with teaching modules on pelvic floor pathologies.

- 3D resource for the study of cranial muscles and nerves of the oculomotor system (Allen et al., 2015):

Employs sections of the VHP for reconstruction, but only shows models, not sectional images. As a difference with the authors' application, it is accompanied by narration, employing what they call personalization effect (personal and welcoming voice), they refer that by receiving the information through two sensory channels, such as sight and hearing, the cognitive load is reduced and learning is improved.

- 3D application for the study of the ventricular system of the brain (Gonzalo Domínguez et al., 2016):

Assesses the morphology of the ventricular system of the brain as a whole and from any spatial position. Displays 3D models and sectional MR images, but not cadaver images. Allows interaction with the models and has an intuitive interface.

We outline below the issues that we consider most significant in the interactive 3D development of this work. They are, mainly, the anatomical fidelity that it reflects, among other reasons thanks to the quality of the sectional images used, the didactic/practical utility and the functionality, basically determined by the user interface.

A study by Zilverschoon et al. (2018), after the analysis of several 3D tools concludes that applications using sectional images are more complete and provide greater anatomical realism by allowing the inclusion of small biological structures. In addition, those using images obtained by diagnostic techniques such as MRI allow observing the existence of anatomical differences between different individuals. Those for commercial purposes tend to have better functionality as they are designed by “experts”, but are more complex, can be applied to any operating system in general, including mobile devices, and show greater anatomical extension but less structural detail. In their opinion, applications with a mainly didactic purpose, as is the case of the pelvic resource developed by the authors of this work, are usually restricted to specific anatomical areas and generally have greater anatomical detail, allowing a better understanding of structurally complex regions.

In reference to anatomical detail, Kraima et al. (2013) highlight that, in order to perform a reliable anatomical reconstruction, with the inclusion of small anatomical structures, it is preferable to use cadaver sectional images and sectional images provided by diagnostic techniques such as MRI.

The models of some authors, with applications similar to the one developed by the authors of this work, such as Balaya et al. (2016), could not show small caliber nerve structures, even though the first of them, also performed manual segmentation of the pelvic sectional images. For the image segmentation process, it should be taken into account that, although automatic and semi-automatic segmentations are clearly faster and more convenient, they do not allow in many occasions to differentiate small structures with similar density or contrast as opined by Erolin (2019) and An et al. (2017).

In recent years, there has been much research on automatic segmentation systems of anatomical structures from sectional images and other methods for their three-dimensional reconstruction, due to the difficulty in 3D reconstruction of these small caliber nerve and vascular structures as explained by Uhl and Chahim (2021). However fully automatic applications still offer some shortcomings, especially in fields as complicated as 3D medical imaging and especially in areas as anatomically complex as the female pelvis. For this reason, in the computational procedure of the authors, they opted for manual segmentation, which provides greater robustness and reliability in the generation of three-dimensional images.

The authors’ development provides an iconographic collection of high-quality cadaver, MRI and ultrasound sectional images and can be applied to different functions such as instructing students in radiological image interpretation, as also pointed out by Drapkin et al. (2015), or as a teaching support tool for future projects and applications involving anatomical interpretations or descriptions.

An important feature of the authors’ computer development is the possibility of correlating two imaging techniques so important in the study of the pelvis, especially the female pelvis, such as MRI and ultrasound. Most students are intimidated the first time they have contact with ultrasound images. Unlike MR images, which can be easily interpreted by anyone with sufficient anatomical knowledge and basic notions of these imaging techniques, ultrasound images are operator-dependent for interpretation. This makes it a difficult diagnostic test to analyze by people untrained in its routine use. Therefore, the authors’ application contributes to the students’ better understanding of pelvic ultrasound images thanks to the possibility of selecting the same structure in the MR image and in the ultrasound image.

The interactive 3D pelvic development is considered as a dynamic regional anatomical anatomy atlas, which is positioned as an appropriate and useful tool for descriptive teaching of anatomy, especially for the understanding of concepts that require spatial ability, as confirmed by Jamil et al. (2019) and Guimarães et al. (2018) after the didactic use of this type of resources. In fact, the volumetric vision of

the authors' 3D resource was highly valued by the students, stating that the application facilitated their understanding and comprehension of the anatomical structures that constitute the female pelvic region.

It is also estimated that it represents an attractive tool for residents and professionals of different medical specialties to take advantage of it as an auxiliary means for the planning of a surgical scenario in some body regions, as Mavar-Haramija et al. (2015) believe with their work, although according to Kostusiak et al. (2017) rigorous studies are needed to certify the usefulness of these applications for surgical training.

It is a learning technology of great value to complement traditional methods, as expressed by most students, and very effective for the teaching and learning process, as supported by the results of studies conducted by Bogomolova et al. (2021), Mai et al. (2020), Triepels et al. (2019), Wilson et al. (2019), among others. However, for O'Rourke et al. (2020) and another authors, this methodology does not outperform traditional static anatomical-radiological atlases (a view shared by some of our students) and even for others such as Yammine and Violato (2016), it is outperformed by didactic tools such as physical models. For Estai and Bunt (2016), who defend the multimodal approach to teaching, the greatest effectiveness of these didactic models is obtained by combining them with various pedagogical resources.

Although, as can be appreciated, there are different views on the best learning model, all the authors mentioned suggest that interactive 3D applications facilitate learning and increase student satisfaction, as the results of the authors' work also reflected. The students who used the application considered it to be a very beneficial tool for supporting and complementing traditional teaching, with quite complete and illustrative contents of pelvic anatomy and with a 3D view of the structures that provides a better understanding and analysis of them, increasing motivation for the study of this anatomical region and increasing the perceived satisfaction with its use, so that they would recommend it to other colleagues for the study of the anatomy and radiology of the pelvis, pelvic floor and its contents.

To optimize learning with educational software, it is important to pay attention to the design of the user interface. The authors believe that the way or arrangement in which the elements are distributed influences the response of the users, making them keep their attention on the software development and arousing their interest in the didactic content. The attractive aesthetics stimulates the student to stay longer on the contents of the program and, therefore, to better retain the concepts conveyed with the application. A good functionality that allows to explore the software application in a simple way and without spending excessive time for its operation will also be more attractive and dynamic for the users. The interface design must ensure that the interaction process is easy and intuitive so that the user can perform the desired actions in the simplest possible way.

The interface design of the authors' software development makes it attractive, easy to understand and very simple to operate, allowing users to navigate through the application quickly and efficiently. According to Bringman-Rodenbarger and Hortsch (2020) many users select for study those applications that have an attractive interface, ignoring other aspects, such as their didactic or formative importance.

For O'Rourke et al. (2020), on the contrary, the implementation of these resources requires previous knowledge in the handling of this type of computer technology.

The quality of this didactic resource was subjected to the assessment of the students and reflected that the installation and operation (it never or almost never blocked) and the handling of the application are simple, the navigation through the program is easy and intuitive and the visual presentation of the contents is attractive. In addition, the application is accessible to students, since the availability of computer equipment compatible with the needs of running this teaching software is practically generalized nowadays.

It is no longer striking that the highest percentage of students in any of the health sciences are female, although it seems that the sex of the students does not influence the results obtained after the use of educational software in teaching, as seen in some study conducted in this regard by Guimarães et al. (2018). However, for Jamil et al. (2019), spatial perception offered better results in male students.

It is clear that in the educational environment, and especially in medical training, technology and education will evolve in parallel, so that educational needs will drive technological progress and this in turn will induce changes in educational models, which ultimately confirms that the education-technology binomial will be one of the basic pillars for the development, growth and progress of society.

FUTURE RESEARCH DIRECTIONS

As we commented at the beginning of the discussion, the familiarity of students with technological resources, poses new challenges, such as the possibility of adapting the application in the future for use on mobile devices.

In the same way, the dynamic and continuously evolving nature of medical and health education and the ever-increasing possibilities offered by technology have led the authors to think about a possible development of the work towards augmented reality and non-immersive and immersive virtual reality, currently booming.

CONCLUSION

After developing and analyzing an interactive teaching computer tool fully user-controlled, for the 3D visualization of the anatomical structures of the female pelvis, it can be concluded that axial sectional cadaver images and high-resolution MRI slices have been excellent resources for manual identification and segmentation of the anatomical structures. The students who have used the tool have considered that it is an innovative computer design, which facilitates the study, understanding and learning of the anatomy of the female pelvis. The incorporation and use of 3D visualization computer resources open new perspectives for teaching anatomy, closer to the anatomical reality of the human body, and in accordance with today's technological society.

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KEY TERMS AND DEFINITIONS

Anatomical 3D Models: Representation of an anatomical structure in three magnitudes (dimensions of space) of a set that allow defining a phenomenon.

Information and Communication Technologies: Any tool or technological development that serves to transmit knowledge in the field of education.

Pelvic Floor: Set of muscles and ligaments located in the lower part of the abdominal cavity, whose function is to support the pelvic organs.

Regions of Interest: Delimited area of an image on which a certain action is to be performed or a parameter is to be evaluated.

Serial Anatomical Sections: Term used in medicine and radiology for flat images obtained by imaging techniques that perform very fine ordered cuts of anatomical areas of an individual allowing a better correlation with the three-dimensional anatomical reality represented in two dimensions.

Three-Dimensional Computer Application: Computer program with the technical capacity to reproduce three-dimensional visual information, creating an illusion of depth in an image.

User Interface: Set of controls and sensory channels through which a human being can communicate with a machine.

Visible Human Project: Initiative to create an iconographic collection of sectional images of real human cadavers.

Chapter 10

Mangement of a 3D Visualization Program From Radiological Images in Neuroradiology

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ABSTRACT

The latest technological advances in postprocessing of images have made possible the generation of three-dimensional (3D) models from 2D radiological images. The use of these models in PDF file allows interaction, providing useful visualization tools and management that facilitate the work and understanding of the anatomical region of the study area. All this is possible from a personal computer without the requirement of a professional workstation. In this chapter, the authors present the characteristics of 3D PDF software with anatomical models of the skull base. Therefore, through the management and development of these new educational contents, introduced as complementary didactic material for the study of anatomy in complex regions, the ability to understand is improved and learning is expedited. This is very important not only in the field of teaching but also in other applications, such as clinical practice and the scientific field, since it allows the use of these contents without the need to compromise patient safety.

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INTRODUCTION

Visual material transcends language barriers and does not present the difficulties of technical terminology. It allows attention to be focused and interest to be drawn to a particular element, which might otherwise go unnoticed.

Images, and in particular those used in the healthcare field, have come a long way during their development, from the early days of their appearance as illustrative tools to support learning and medical practice.

Three-dimensional formulations are currently gaining ground over traditional two-dimensional images in many fields, including the biomedical field because, as has been evaluated in a multitude of works, structures are represented in greater detail and in a more reliable way (Erten & Yılmaz, 2018a; Jyothikiran et al., 2014; Yarboro et al., 2017).

The progress of computer science has and will continue to have a great influence on the application of medical imaging. In 1972, the first computerised tomography, in which the image is digital, was presented in London by Briton Hounsfield.

Gradually with the continuous innovations in computing and informatics, the digitisation of the image, as well as the continuous increase in machine power and network speed, have brought about enormous development and improvements in image quality and greatly reduced image production times.

Any anatomical region can be assessed with three-dimensional images; however, it is most useful in those regions with the greatest number of details and complex spatial relationships, which are the most difficult for students. Also, those that are difficult to access, where the direct study is not possible. The present study focuses on the region of the base of the skull, as it is an anatomical area where a multitude of structures and details are concentrated and whose learning is usually difficult.

Interactive three-dimensional models of human anatomy have evolved over the last decade with advances in computer technology. New curricula for web-based training (online education) are also becoming more common. These digital models can be used within the classical teaching environment in a blended learning approach as well as in non-face-to-face education schemes (Abulrub et al., 2011; Faria et al., 2016; Johnson et al., 2012; Mayfield et al., 2013; Pereira et al., 2013).

BACKGROUND

In the biomedical field, three-dimensional (3D) formulations are represented in a multitude of structures (pharmacological chemistry molecules, orthopaedic insoles, biomechanical and anatomical structures, prostheses, brain mapping, tractography...) (Kumar et al., 2008). However, the data has generally been represented in a two-dimensional format, or by projecting 3D images onto a two-dimensional (2.5D) plane. This brings with it an inherent loss of visual information. The main reasons for this are technical problems and lack of experience in handling 3D formulas (Erten & Yılmaz, 2018b; Jyothikiran et al., 2014).

3D technology is often thought of as recent or modern, but it is a technology that is more than 100 years old. However, a few years ago, with the advent of 3D films, interest in it has grown significantly.

From very early on, man has wanted to represent movement in images, achieving it through frames. This is how cinema was born.

Another obsession was that images should be able to represent the three dimensions that make up a real image.

The 3D visualisation techniques applied in medicine are different from the techniques used in photographic or cinematographic imaging. They rely on the ability of powerful computers to create three-dimensional “photographs” from a given set of medical images. By taking multiple consecutive images of a region, sufficient information is obtained about the voxels that make up the image, filling in the “gaps” with algorithms based on information obtained from adjacent images. In such a way that they give a surface image from the sectional images obtained in the radiological studies.

With this data, we can create three-dimensional models that can be managed by different computer programs, such as PDF, which is the most widely used file format to transmit information on the network.

The Portable Document Format (PDF) is the most widely used file format for the exchange of electronic documents. It allows documents to be read while retaining their original accuracy. It does this regardless of the device or operating system used to create or read the document. It is the standard file format for communicating biomedical information over the Internet and for electronic scholarly publications.

PDF software was created by Adobe in 1992 and the tools for creating and viewing PDF files (Acrobat) were released in 1993. Since then, improvements and add-ons have been added to each version. In 2008, PDF became an international ISO standard (ISO 32000-1: 2008) and is the electronic standard for most private and business documents.

Nowadays, the latest versions of Adobe PDF offer more features, little known to the general public. PDF can support additional resources (e.g. text, images or multimedia files) and open them easily with the free Acrobat Reader software. They also offer the possibility to be electronically signed (‘Taking Documents to the Next Level with PDF 2.0’, 2017).

The latest versions of Adobe’s PDF format allow the incorporation of three-dimensional (3D) surface mesh models, thus enabling interactive viewing (e.g. zooming, panorama, rotating and component selection) of these objects with qualified reading software.

The software that enabled a more efficient use for working with 3D models in PDF was Acrobat 8, released in early 2006. This version provides tools for the import and conversion of many 3D formats and a 3D editor (History of PDF - Rgbcmkyk, n.d.).

MAIN FOCUS OF THE CHAPTER

Nowadays, modern radiological techniques make it possible to obtain images with complex data sets, which subsequently allow the use of post-processing techniques, obtaining models in three dimensions, with a high resolution and very high quality (Juanes et al., 2014; Neue & Ganslandt, 2013; Ruisoto Palomera et al., 2014).

This has enabled the development of crucial tools for teaching and learning in different sciences (Hoyek et al., 2014; Jang et al., 2018). Previously, in some topographical and spatial science and engineering disciplines (such as architecture), three-dimensional formulas were used that represented reality in proportion, made to scale, (so-called “mock-ups”). In this way, they were able to present the information in a quicker, more direct and more graphic way. Currently, new techniques have emerged and are progressively being implemented in classrooms; such as augmented reality, telematic visualisation, holograms, 3D images, and three-dimensional models, which in addition to visualisation, allow interaction with them and represent a new form of interactive and agile learning (Colucci et al., 2015;

Johnson et al., 2012; Mitrousias et al., 2018; Pereira et al., 2013; Preece et al., 2013; Pujol et al., 2016; Triepels et al., 2020).

Accordingly, 3D technology has spread to all scientific disciplines, which use different three-dimensional resources to present information in a more accurate way (Newe & Becker, 2018). This technology is gradually being implemented in training (undergraduate and postgraduate), as it allows students to be introduced to the use of complex anatomical models, from engineering, computer science, biology... etc., and particularly in the biomedical field (Abulrub et al., 2011; J. Cong et al., 2006; Jason Cong et al., 2006; Eslahpazir et al., 2014; Sampaio et al., 2010; Singh et al., 2014; Wang et al., 2012; Waran et al., 2014).

This chapter, therefore, aims to present the main characteristics and the potential use of PDF with 3D models for the study of anatomy, especially in complex anatomical regions such as the base of the skull. It also aims to extend the diffusion and functionality of three-dimensional models, from the visualisation of a structure from any angle, with a wide range of detail, to various forms of interaction with it, adding dynamism and creating a deeper level of experience.

New viewpoints are exposed, and different sections, cuts and transparencies of (parts of) the different 3D models can be applied to assess their neighbourhood relationships more easily. It is also possible to visualise parts of the model independently and with different visual characteristics. There is also the possibility of configuring and customising the model itself, from the texture, colour, size... and its environment, modifying the atmosphere, lights, shadows... etc.

The ease and speed with which reliable three-dimensional models of the anatomy of patients can be produced will be demonstrated, without the need for professional workstations or expensive software, so that any user can make use of this technology from their personal computer. The aim is to bring this technology closer to the users.

We will also examine the usefulness of 3D models in different fields, not only in education. It is intended to describe uses in professional clinical practice and even in the scientific field.

Volume representation techniques have been developed to enable CT, MRI and sonogram software to produce 3D images (Fujita et al., 2008; Lauterbur, 1973).

However, one of the main challenges of 3D approaches is to share complex datasets effectively and intuitively among colleagues from different fields for discussion, and finally present them in a publishable format.

In general, 3D datasets needed special software for visualisation, so in the past, they were reduced to 2D images. However, there is also free software available on the web, such as the PDF format, to handle these images. This is a digital document storage format, independent of software or hardware platforms, that allows the user to handle the models only by using a freely available programme (Adobe Reader), thus avoiding the need for expensive and complex 3D viewers on the market (Phelps et al., 2012; Ruthensteiner & Heß, 2008).

CREATION 3D PDF MODELS

Three-dimensional models of the anatomical region under study are generated from computed tomography images obtained from radiological studies (Fig 1).

Several methods are currently available for the creation of the models. From free or paid software packages, as well as complex programmes for users with high knowledge in 3D modelling with various construction and reformatting processes.

Figure 1. TC Philips



The latest updates of CT machine software include compatible packages for the creation of 3D images and models. This has facilitated the creation of models in recent years and has considerably reduced the time spent on model creation (Grauer et al., 2009; Schendel & Jacobson, 2009).

In this chapter, the models have been created with free software obtained from the web (3D Slicer © Version 5.4.0-1 software), to show a free and open method available to the general public, and also using the licensed software package included in the CT machine (InterlIISpace Portal).

The images obtained are stored in DICOM format for embedding in the 3D Slicer © programme; Version 5.4.0-1, obtained free of charge from the network (fig 2).

Once the images are loaded, they are analysed, reformatted and processed (segmented) to obtain three-dimensional models, representative of the area of interest, in this document, the base of the skull.

Finally, the 3D models are created and the key images of the region are saved by selecting the storage format of interest.

3D PDF MAGEMENT

Once the 3D models were obtained, they were managed using Adobe Acrobat Document Cloud (version 2019.010.20064) (figure 3), a free standard downloaded from the web, from the Adobe website: <https://get.adobe.com/es/reader/>.

After enabling the 3D content (we can do it once, or for as long as we open the document), the 3D toolbar is activated, to manage and manipulate the document.

Figure 2. Software 3D slicer

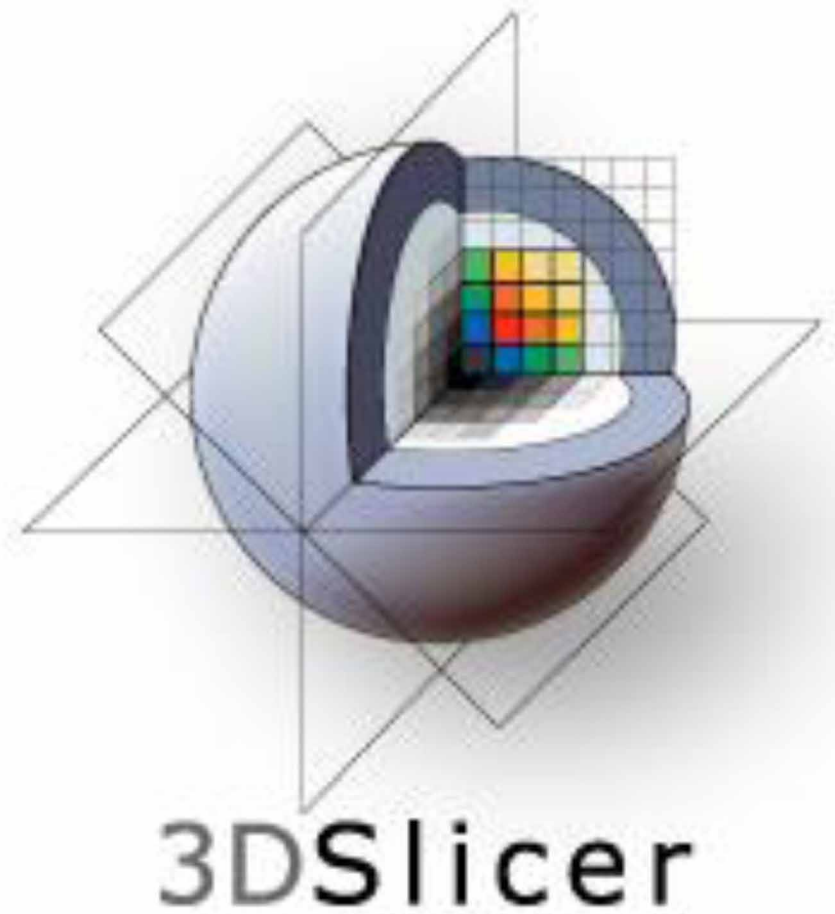
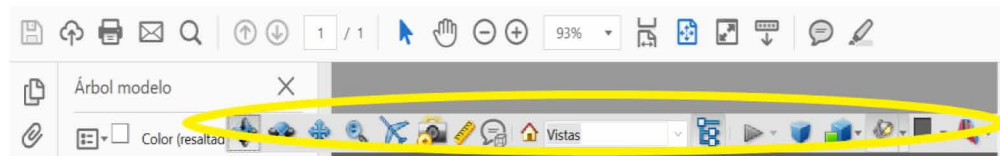


Figure 3. Adobe PDF



Adobe Document Cloud

Figure 4. Toolbar3d. PDF



Even if you are working with a three-dimensional document, the PDF file allows you to make use of its general tools, common to all PDF documents (“file”, “edit”, “view”), to share or apply the view preferences of interest. Once the 3D content is activated, the 3D content toolbar appears, allowing interaction with the model (figure 4).

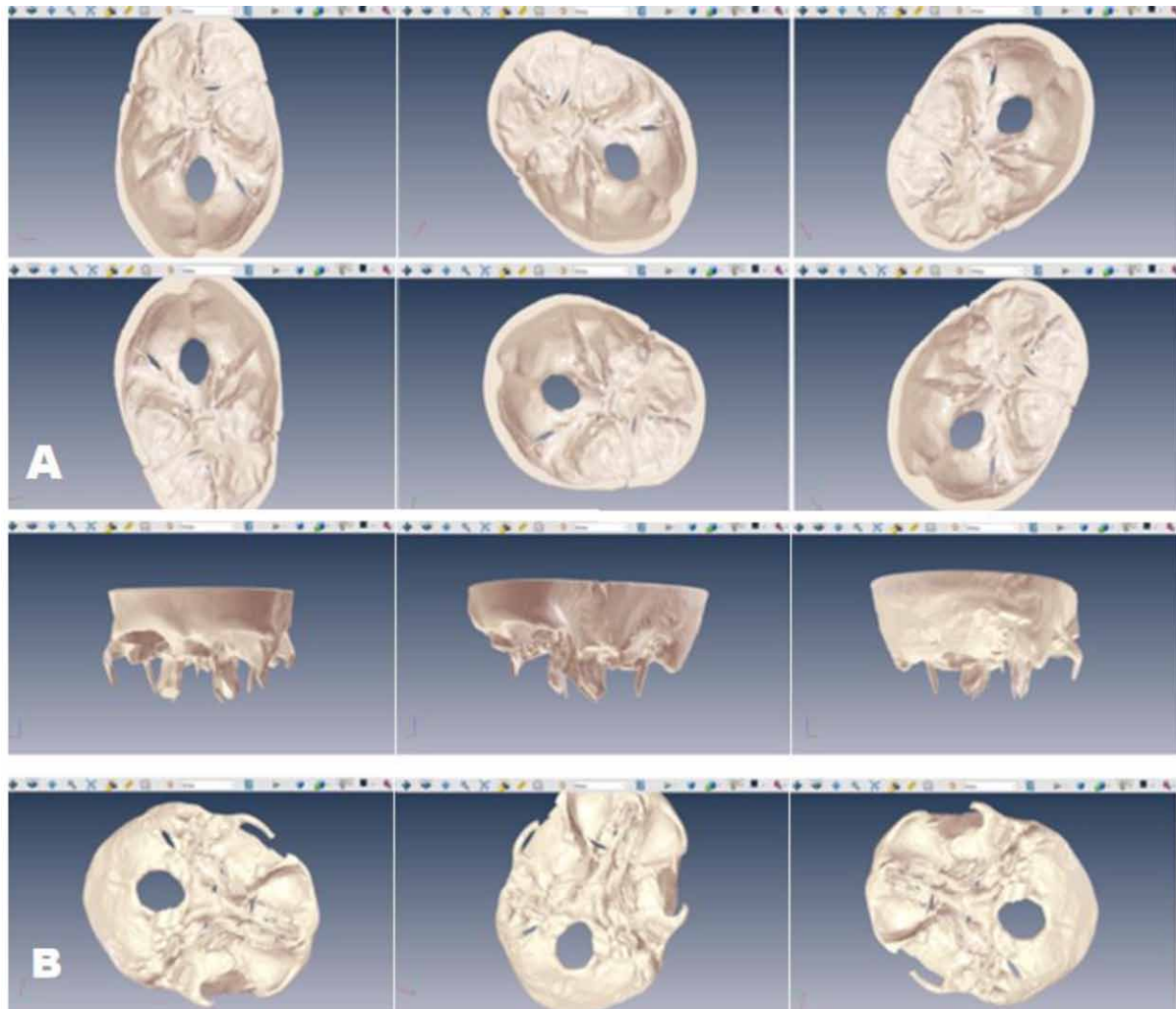
You can use the 3D toolbar to zoom in and out, rotate and pan the object.

The Tree Model allows you to hide or isolate parts, or to make parts transparent.

A 3D model is manipulated by selecting and dragging with various 3D navigation tools.

- **3D navigation tools:**
 - Rotate (figure 5)
 - Turn (figure 5)
 - Pan
 - Zoom in/out (figure 6)
 - Walk
 - Fly
 - Camera properties
 - Measurement tool (figure 7)
 - 3D adjustment to endpoints.
 - 3D adjustment to linear edges
 - 3D adjustment to radial edges.
 - 3D adjustment to silhouettes.
 - 3D adjustment to flat faces.
 - 3D point-to-point measurement.
 - Perpendicular 3D dimensioning.
 - 3D radial dimension.
 - 3D measurement angle.
 - Add comment.
- **View controls: view menu.**
 - Default view.
 - Alternate tree model.
 - Play/Stop animation.
 - Use orthographic projection.
 - Model representation mode menu (figure 8).
 - Activate additional illumination menu (figure 9).
 - Background colour.
 - Alternate cross-section (figure 10).

Figure 5. Model 3D-PDF



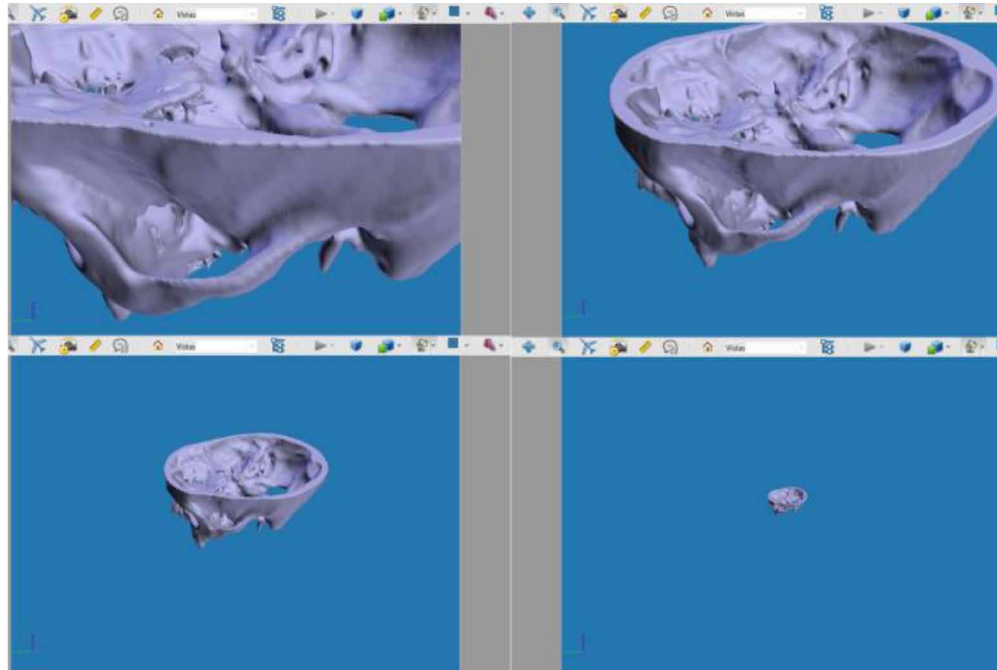
- Add 3D multimedia/comment (figure 11).

The use of this programme with 3D content allows for a very detailed analysis of anatomical details as well as their neighbourhood relationships. It also allows measurements and calculations, which would be impossible with classical anatomical images and even very complicated with anatomical dissection models. Complex volumetric calculations can be performed on an entire part or internal structures (fig 12, 13, 14 y 15).

SOLUTIONS AND RECOMMENDATIONS

The mental representation of the shape, details and organisation of different anatomical structures is a crucial step in the learning process of any anatomical region.

Figure 6. Models 3D expand and decrease



Complex computer processes applied in medical imaging make it possible to obtain multiple data from the organs or regions under study, which can be used for the creation of new forms of information representation in novel formats. This has made it possible to represent structures that were previously only studied by means of drawings or diagrams, such as nerve bundles (Borges, 2009; Parmar et al., 2009; Raut et al., 2012).

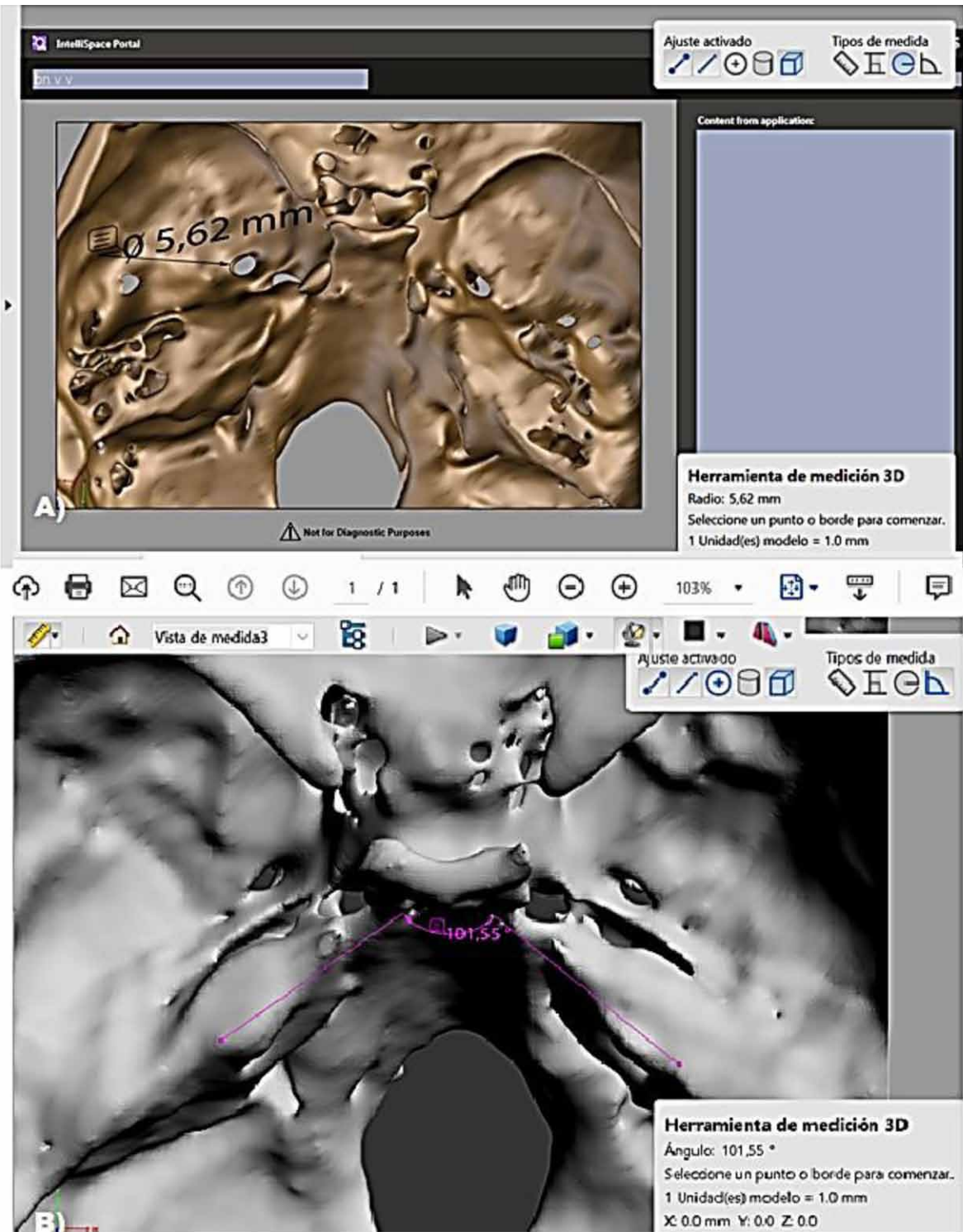
The three-dimensional models presented in this work, since they contain more information, represent more anatomical details than traditional models. Therefore, these tools are considered to facilitate anatomical teaching, speeding up the process and improving understanding skills (Colucci et al., 2015; Hoyek et al., 2014; Preece et al., 2013; Pujol et al., 2016; Ruisoto et al., 2012). For this purpose, 3D images and models must be of high quality and be able to correctly represent the information and detail of the depicted region (Harrell et al., 2002).

With new 3D image representation techniques, spatial perception and anatomical understanding are improved and it is possible to develop teaching content from complex visual models, embedding them in simple portable storage documents or PDFs (Newe, 2015; Phelps et al., 2012).

Users (students or healthcare professionals) now have the opportunity to access new angles, accesses and details, which offer a better understanding of the object under study and enable the planning and implementation of novel, hard-to-reach approach techniques. Modern medicine relies entirely on 3D visualisation (Jyothikiran et al., 2014; Yarboro et al., 2017).

Three-dimensional imaging resources can be effectively integrated alongside traditional methods of drawings and diagrams, in addition to descriptive models, efficiently facilitating the learning of anatomy in order to enhance the anatomy teaching process (Caswell et al., 2015; Ruisoto et al., 2012; Wiecha et al., 2002).

Figure 7. Measurement 3D model



Mangement of a 3D Visualization Program From Radiological Images in Neuroradiology

Figure 8. Examples surface model 3D-PDF

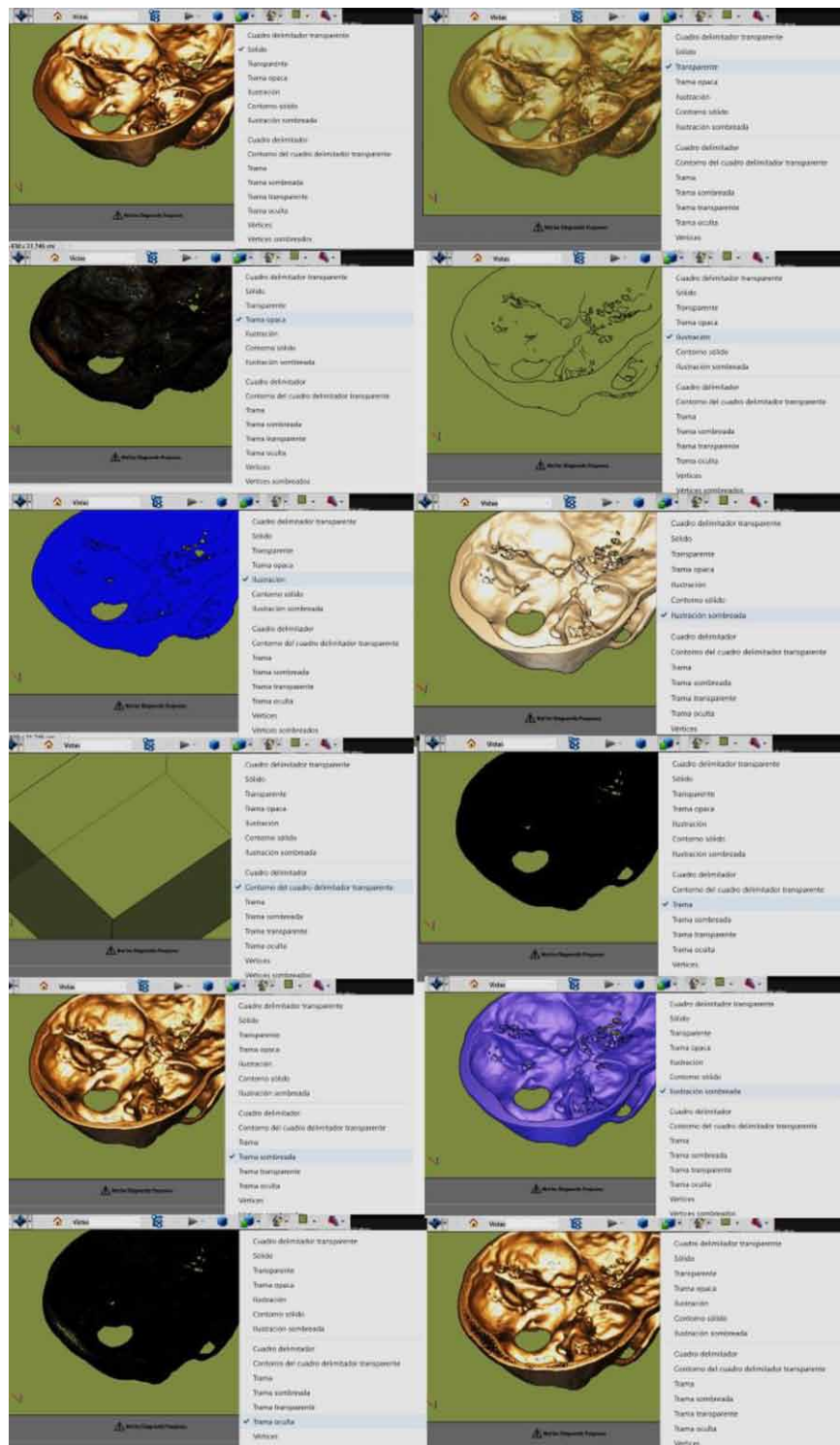
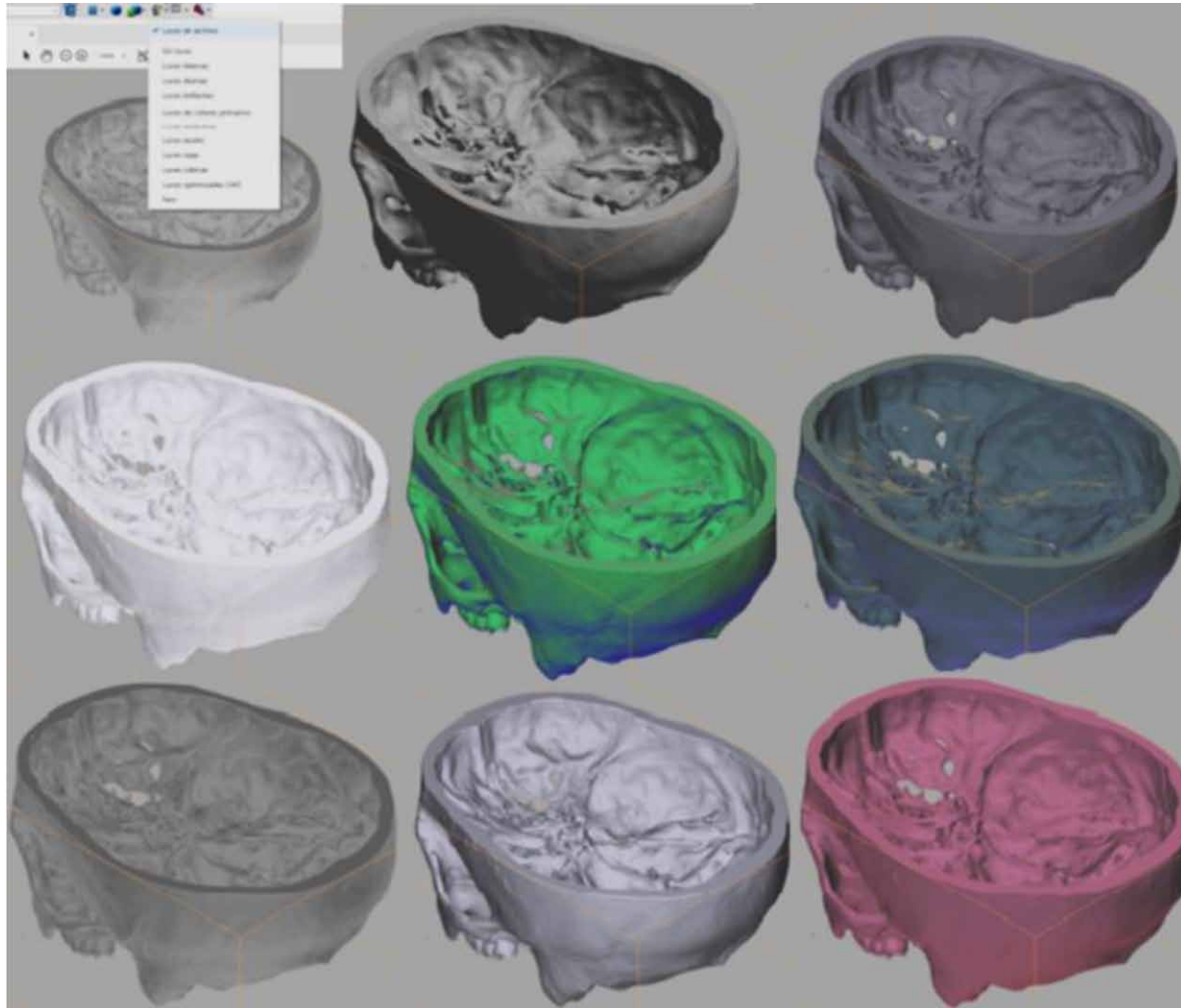


Figure 9. Lighting effects 3D-PDF

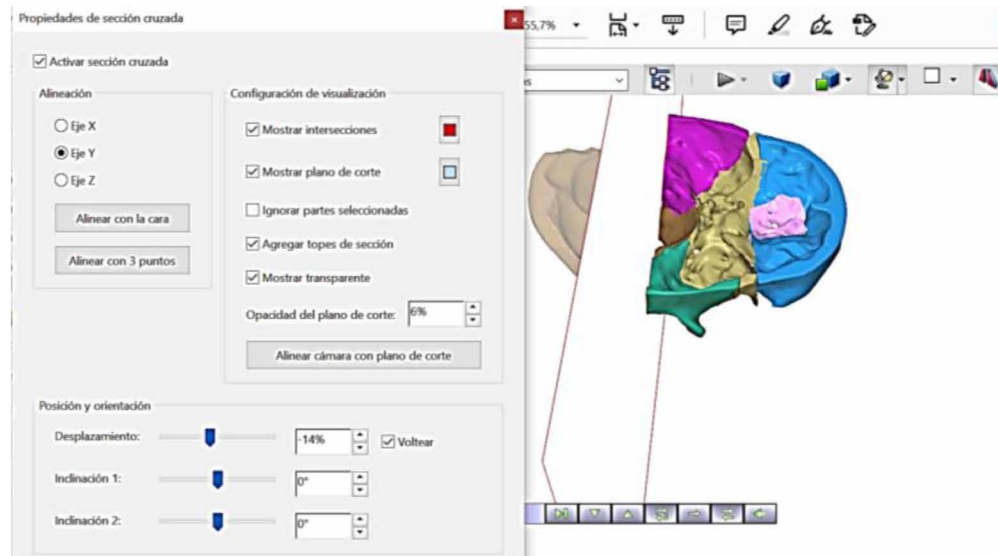


The PDF programme with these 3D anatomical contents is very useful for measurements and annotations, with great simplicity. In such a way, we can obtain various useful parameters in a simple and very fast way (obtaining diameters and lengths of structures; foramen, apophysis, etc.). We highlight the possibility of combining different tools (measurement and partial section) to optimise the measurements and diameters of, for example, the central regions of the holes at the base of the skull, or the internal ducts.

The authors also consider it a very interesting tool for volumetric data, such as the surface and volume occupied by each bone in the conformation of the skull base. By using these 3D models, it is possible to easily and directly obtain complex data that are very difficult to calculate using classic images.

These volumetric calculations performed by the PDF READER DC software have been analysed and refuted with the same analyses using the 3D slicer software, obtaining similar results. Therefore, the authors are in a position to affirm that the volumetric calculations carried out on the three-dimensional models by the PDF Reader DC software are reliable and provide identical results to other programmes using the same anatomical model.

Figure 10. Cross-section model 3D-PDF



An important advantage of these models stored in PDF format is the ease with which this information can be shared and transmitted to other users quickly and easily. This is very interesting in the current environment, where work is generally carried out by groups of people, who are not necessarily physically together (in the implementation of remote work or “teleworking”). The format itself among its features offers several possibilities to share the document: an invitation to users, or uploading the file to the cloud, after sending a password for greater security, or simply as an e-mail attachment. This makes it possible for each user to access the content from their personal computer or any other electronic device capable of reading PDF files.

In recent years, a multitude of programmes or methods for processing and segmenting digital images have been created, the so-called “CADs” (Computer-aided design) (Bernardini et al., 1999; Bosche & Haas, 2008; Tiede et al., 1990; Toriya & Chiyokura, 2012). Some of them are more focused on fields such as architecture or engineering, and others more in the biomedical field (Fujita et al., 2008; Lucie Gaget, 2017; Starly et al., 2005; W. Sun et al., 2005; Viceconti et al., 1998).

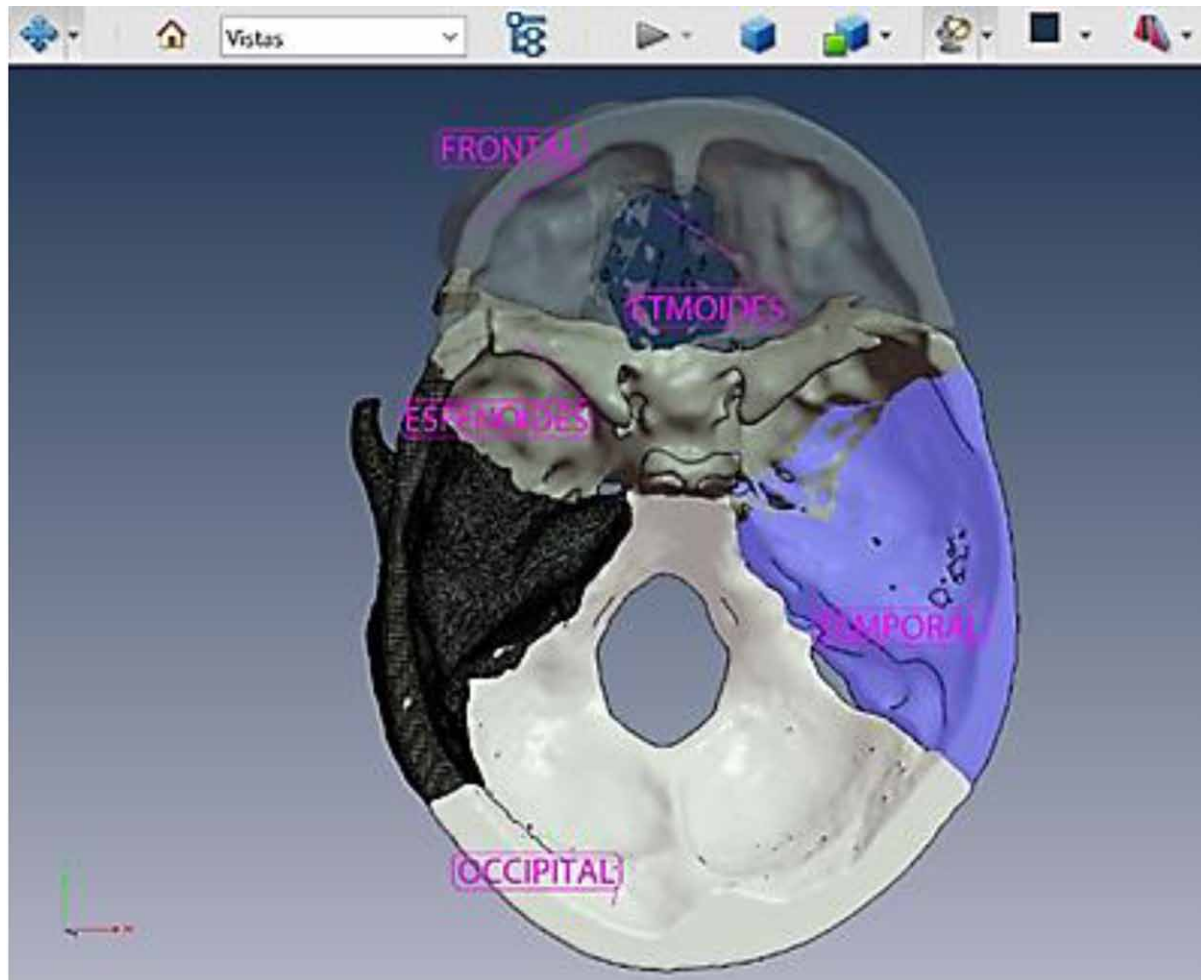
In general, they are programmes designed and oriented to make 3D printing meshes. They are provided upon payment, except for some versions with a free DEMO version. In general, they are not very difficult to use and are not very different in terms of use and interface.

These 3D-PDF models are being implemented in different areas, from education to the workplace and science.

Regarding the Educational Field

Students, in addition to the identification of structures of a human body, must develop new skills, such as a three-dimensional understanding, particularly useful in the handling of these models, as it allows to assess in a high degree of detail the characteristics of some region, organ or complex structure, as well

Figure 11. 3D-PDF comments



as their neighbourhood relationships (Erolin, 2019; Khayruddeen et al., 2019; K. P. Murphy et al., 2014; Petersson et al., 2009; Phillips et al., 2012; Smith et al., 2018; Tory & Moller, 2004).

This can be achieved through supervised cadaver dissection or examination of processed specimens, supported by visual aids such as atlases with 2D images. However, cadaver dissection has several limitations, including specimen availability, cost and the need for a substantial time commitment (Faria et al., 2016). In conjunction with traditional learning techniques, the use of new 3D handling techniques is implemented. 3D “atlas” have been proposed in various fields (de Bakker et al., 2012, 2016). Other formulas, which some authors have called “digital dissections” have been tested, without the drawbacks of traditional cadaveric dissections (Bangeas et al., 2019; Erolin, 2019; Miranda-Merchak et al., 2018; Mitrousias et al., 2018; Older, 2004; Richardson-Hatcher et al., 2014).

The possibility of interactive manipulation can encourage the user to explore the “image” in great detail on an individual basis. In addition to the new information gained, this stimulating action can also support curiosity and long-term memorisation (Caswell et al., 2015; Chen et al., 2017; Park et al., 2019; Petersson et al., 2009; Triepels et al., 2020).

Figure 12. Measurements esfenoid bone

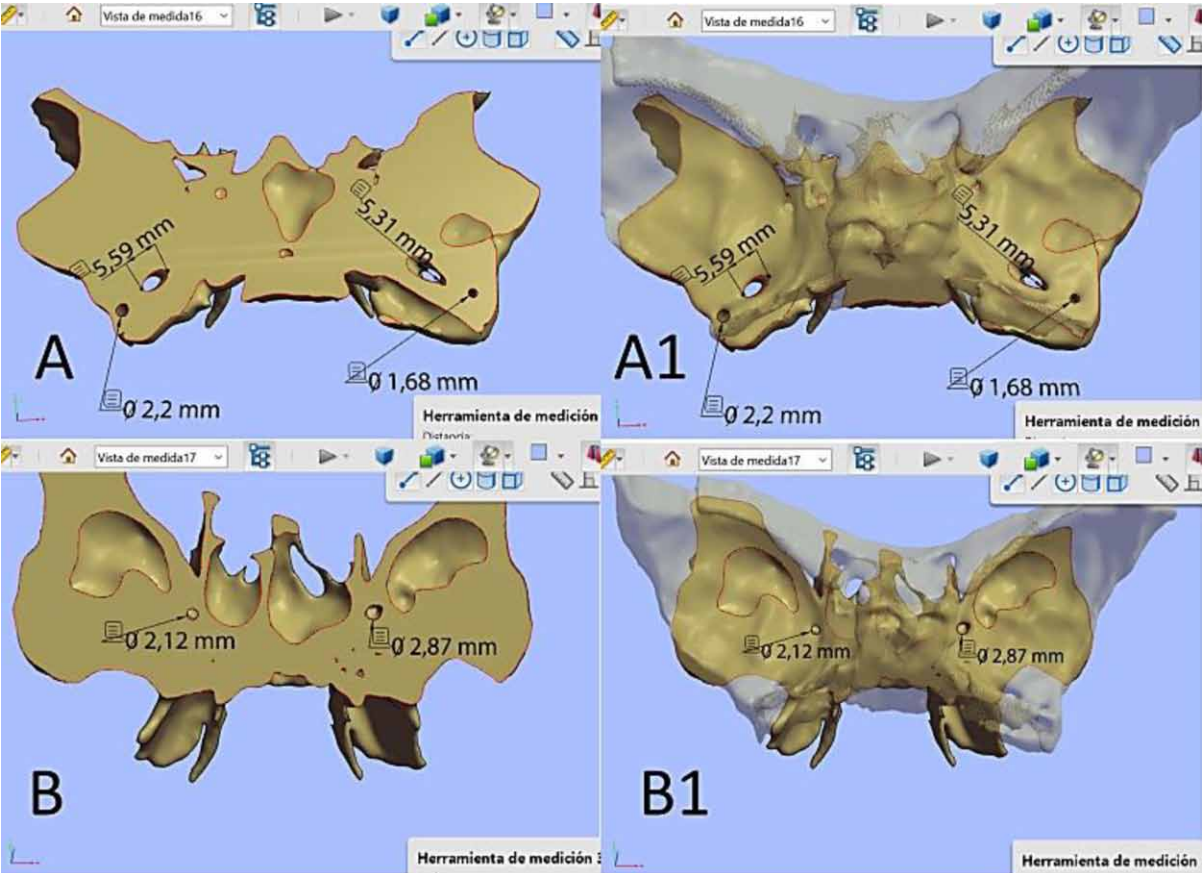


Figure 13. Volumetry esfenoid bone

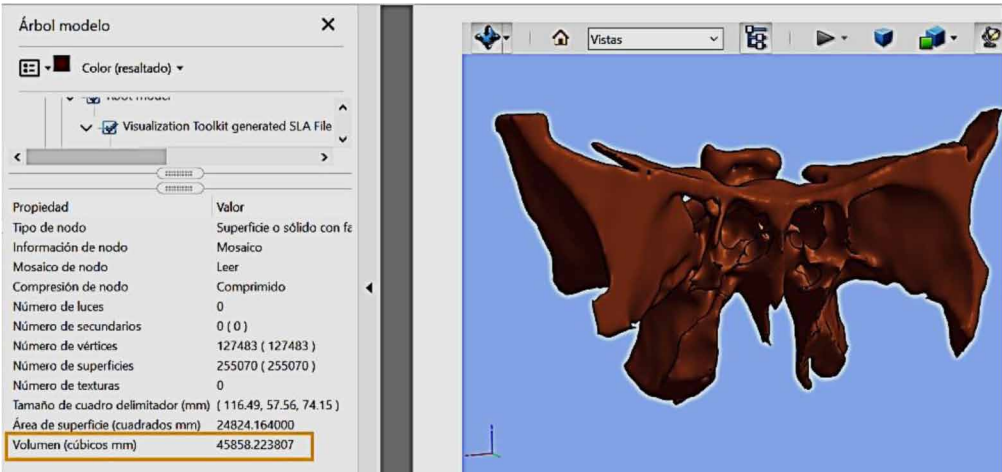


Figure 14 Internal structures temporal bone

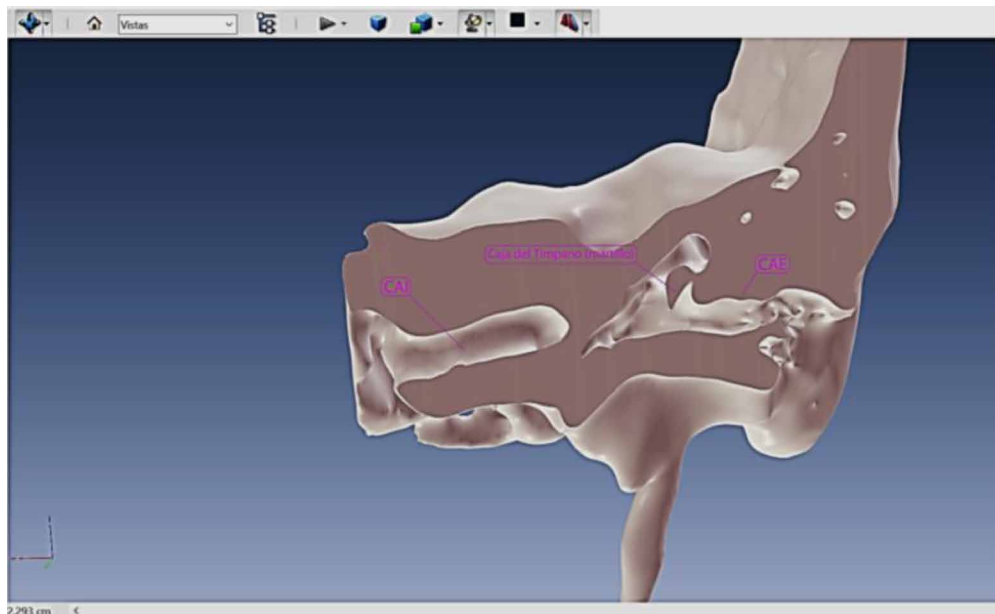
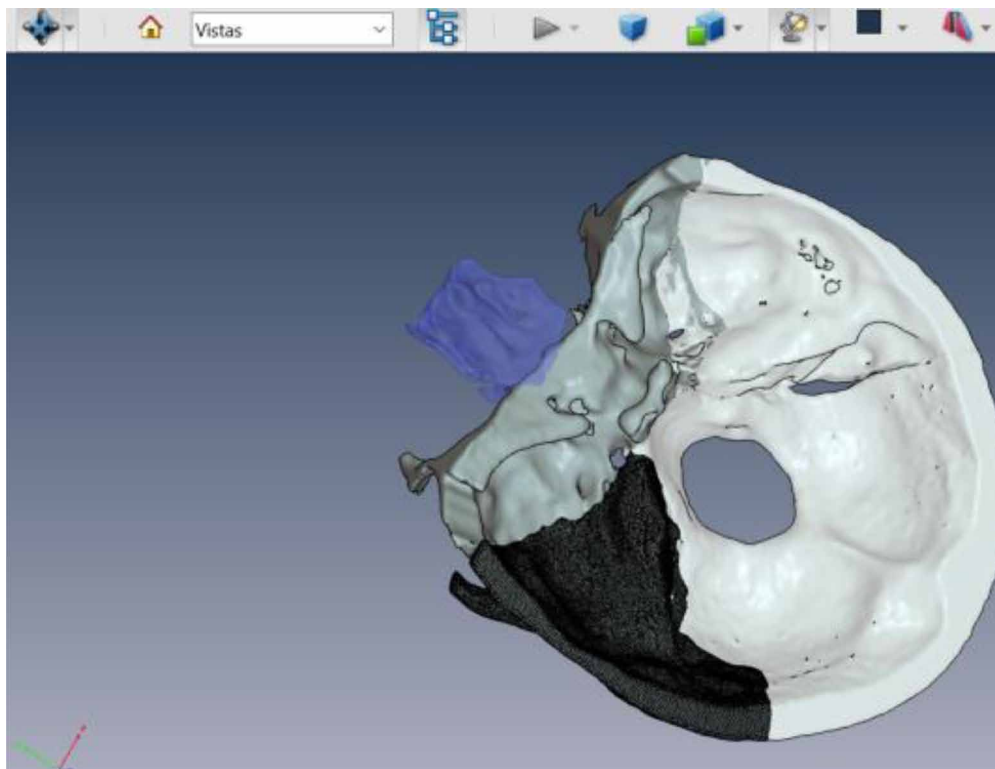


Figure 15. Bone component skull base



Regarding the Scientific Domain

Three-dimensional formulae in biomedicine are present in a multitude of structures, from biomolecules, protein and DNA sequences, pharmacological formulations or viral or cellular conformations, histological studies...

In general, there is no support for interaction with the 3D image in the online version of congresses or scientific journals, nor is there any support in the submission forms and publication forms for scientific articles. Lately, this is in the process of changing. In the current scenario, existing technology today allows handling 3D models from a simple PDF file, where virtual objects with real 3D qualities can be manipulated. This increases the realism and information offered to end-users (Newe, 2015, 2016; Newe & Becker, 2018; Rydmark et al., 2001; van de Kamp et al., 2014).

Finally, it should be added in this scientific section, that these models stored in PDF, each user can access the contents from the personal computer at home in a more personal and dynamic way.

Healthcare Work Environment: Medical and Surgical

With 3D medical imaging, healthcare professionals can now access new views, angles, resolutions and details that offer a better understanding of the body part in question. Using this visualisation technique, virtual environments can be recreated and new access and medical techniques can be assessed for application on patients safely and without risk (Boccardi et al., 2011; Lorenzo Alvarez, 2018; Usón et al., 2014). New contingencies and difficulties of novel techniques can be assessed.

Modern medicine relies entirely on 3D visualisation (Aimar et al., 2019; Hong et al., 2018; Starly et al., 2005; Udupa & Herman, 1999). Its use has been established in organs such as the liver (Kong et al., 2016), kidneys (Coll et al., 2000; Wragg et al., 2019), cardiovascular system (Kaye et al., 1997; Luboz et al., 2005; Trunk et al., 2007), the lungs (Javan et al., 2016; Kuhnigk et al., 2003; Zrimec et al., 2004), the brain (Giesel et al., 2009; Li et al., 2006; Qiyu et al., 2005) or muscle (Tesařová et al., 2018).

Another point that has been discussed in some publications is the importance of these files to improve communication between professionals or with patients (Bernhard et al., 2016; Biglino et al., 2015). Communication is of vital importance for physicians and patients, however, there are challenges in traditional communication, such as issues related to language clarity, specialised medical nomenclature, interpersonal skills or situations where shared knowledge is highly technical and difficult to communicate verbally or with traditional means. These three-dimensional tools, as complementary support, facilitate and bring the information closer to the users.

In surgical specialities, extensive knowledge of the anatomical structures of organs and tissues is even more important (Kong et al., 2016).

The essential steps for surgical planning with computer-aided design are analysis, planning, virtual surgery, implant design and production, and finally post-operative analysis (Erten & Yilmaz, 2018b; Markiewicz & Bell, 2011).

Using simulation CAD tools, several different methods and strategies can be improvised to determine the most optimal surgical approach. Potential unintended consequences, complications and intraoperative problems can be recognised long before performing the actual procedure on the patient (Greenberg, 2018; Mavar-Haramija et al., 2015; S. B. Murphy et al., 1986; Schendel & Jacobson, 2009; Westermarck et al., 2005).

In general, the application of 3D technology in surgical planning can be summarised as follows:

- **Diagnostics.** Since the 3D image allows a better understanding of the anatomy.
- **Quantitative measurement and analysis.** It allows structures to be measured and volumetric parameters to be obtained directly. It permits the comparison of results with the theoretical ideal (Schendel & Jacobson, 2009).
- **Virtual surgical simulation.** This offers the great advantage of unlimited trial and error. Explore possible unexpected complications, identify and resolve them.
- **Fabrication of surgical approach guides and templates.** Osteotomies approaches can be modified to take into account anatomical details with greater precision (Caloss et al., 2007; Prats-Galino et al., 2015; Puigdemívol-Sánchez et al., 2011; Swennen et al., 2009).
- **Comparison of postoperative outcomes and outcome prediction.** Using these 3D modelling techniques, it is possible to assess the possible final results, even before the start of the procedure or surgery.

Finally, by manipulating and handling these documents, models can be generated from the printout. This format allows for suitable printing properties and wide compatibility with 3D printers on the market because it is a standardised file format.

3D printing is an ideal partner for medical 3D imaging due to the uniqueness of the individual patient and the new therapeutic challenges. In this way, biomodels “tailored” to patient characteristics are being used, e.g. prostheses, but also specific neonatal devices, or even “fabricating” artificial tissues for short-term care (figure 16).

From 3D data, physical printed models can be obtained. The main challenge with 3D printing remains speed, and this is what has so far limited its implementation. It can take hours, or even days, to create a printed model from real 3D medical imaging data (Aimar et al., 2019).

The various medical applications of 3D printing in medicine can be broadly grouped into 3 categories (Rengier et al., 2010; Valverde, 2017).

- **Anatomical models**

3D models can be used for educational purposes, both for students, medical trainees and surgeons (Garcia-Valadez et al., 2017).

- **Preoperative planning**

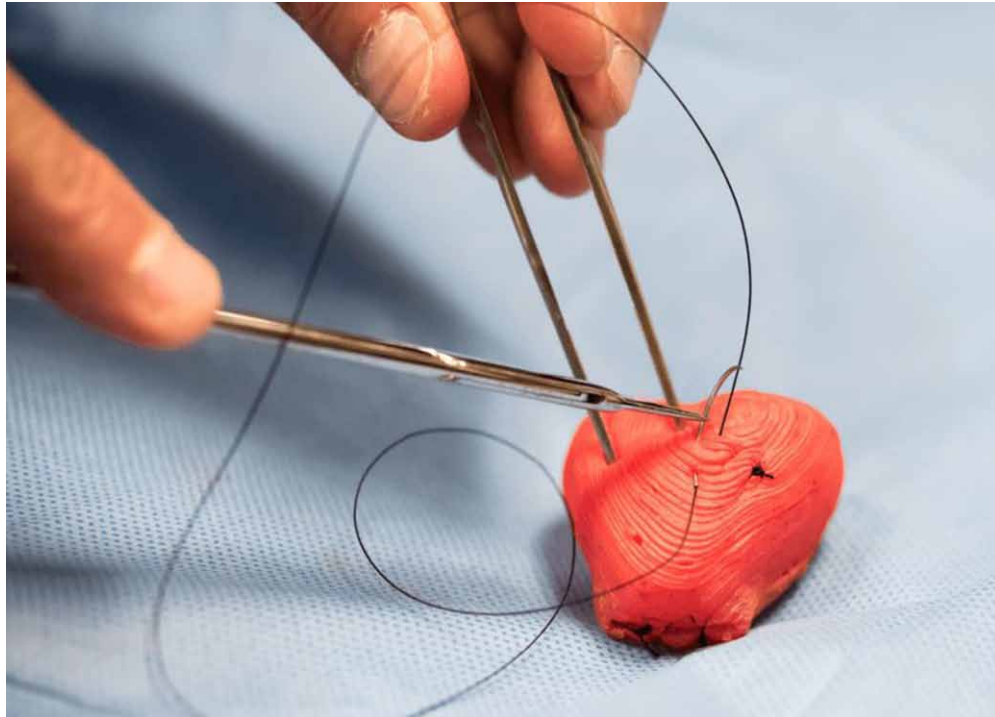
3D printing has also been introduced to the surgical field as a tool for a better understanding of any complex underlying anomaly.

Once the virtual surgical planning is done, designs for individualised treatment guides and implants can be made (Kohli et al., 2018; Mavar-Haramija et al., 2015; Newe et al., 2014; Singhal et al., 2016; X. Sun et al., 2018; Yao & Lin, 2018).

Simulating surgery and potential complications in advance using prototype models can help to predict intraoperative and postoperative complications. Results have been reported regarding a reduction of surgery time, which allows for more cost-effective use of the wards (D’Urso et al., 1999; Rengier et al., 2010).

- **Medical research**

Figure 16. 3-D printed prostate model. It can be equipped with pressure sensors that allow surgeons to practice on material with a realistic feel while rehearsing procedures. Taken from: K. QIU ET AL / ADVANCED MATERIALS TECHNOLOGIES 2018



3D printing opens up new opportunities for scientific research activities and can help elucidate physiological processes that are not yet fully understood. Haemodynamics can be investigated, for example, by coded velocity MRI or by optical flow measurements in transparent models (César-Juárez et al., 2018; de Zélicourt et al., 2005, p.).

FUTURE RESEARCH DIRECTIONS

Currently, 3D technology is being implemented in everyday use, which has improved clinical care, providing new visions to employ novel surgical approaches or even in the relationship with colleagues or patients, conveying information more explicitly and clearly (Harrell et al., 2002; Markiewicz & Bell, 2011; Westermarck et al., 2005). Also, in the scientific field, the current poster format used in many courses or conferences could be improved by adding 3D models to the scenario where virtual objects with real 3D qualities can be manipulated. This would increase the realism and information offered to end-users (Newe & Becker, 2018; Newe & Ganslandt, 2013).

We believe that future research should primarily focus on the development of software tools that can be easily used by all and at no cost. Furthermore, we consider that the degree of awareness of 3D PDF software in the scientific community, in particular in the biomedical and clinical fields, should be investigated (e.g. through surveys).

In addition, simple instruction manuals for existing tools are needed and should be further disseminated. Also, the routine use of 3D PDF in clinical and scientific applications should be further promoted and evaluated for disciplines other than those outlined in this paper. Finally, future research could also consider domains other than biomedical.

CONCLUSION

Three-dimensional models embedded in PDF format (Adobe) combine the advantages of a three-dimensional visualisation with the advantages of handling a PDF document, which we are used to, as it is the most widely used file format for file exchange on the web.

3D models embedded in PDF format are a useful medium used more and more frequently in the healthcare field, both for teaching purposes and for the precise transmission of information, as well as for programming and carrying out new techniques and approaches in medicine and surgery. The characteristics and security of the PDF format for the reliable exchange and preservation of digital information (biomedical models) are also highlighted.

This tool (three-dimensional models saved in PDF format) offers a multitude of advantages already discussed in previous sections.

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KEY TERMS AND DEFINITIONS

DICOM: Digital imaging and communication on medicine.

Digitization: Convert a physical quantity, a text, or an analog signal into a digital representation.

Interactive: That allows an interaction, by way of dialogue, between the machine and the user.

Postprocessing: Post, behind; process, processing or set of operations to which a thing is subjected to elaborate or transform it.

Reformatting: Re- Back to; format, organize a disk or other media according to a specific format of sectors, tracks, etc., so that it is operational.

Segment: Separate or divide a thing into segments.

Tractography: MRI imaging technique to reveal neural bundles.

Voxel: Minimum processable unit of a three-dimensional matrix. Pixel equivalent in a 2D image.

Chapter 11

3D Printing in Bone Tissue Engineering: Bibliographic Review of Current Advances and Future Potential

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ABSTRACT

This chapter seeks to explore the current state of 3D printing technology in bone tissue engineering from the reflectibility approach, analyzing in more detail what this field consists of, as well as the materials and techniques mainly used nowadays in 3D printing. Likewise, the potential of this technique in the future is analyzed with the possibilities of improvement in the short and long terms. The research methodology used was non-experimental, documentary, and descriptive. The information was collected from indexed journals and web platforms using keywords such as “bone tissue engineering” and “3D printing” in search engines. Therefore, this chapter represents a very important and necessary source of bibliographic information to be able to carry out new research in this field.

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INTRODUCTION

The bone structure of the human being is one of the most important as it is the main support of the body; however, although they are resistant elements, any type of severe damage to some of their elements can seriously affect people (Koons et al., 2020). The natural self-repair capacity of bones may be enough to heal minor damages such as fractures and small cracks, but it turns out to be insufficient when dealing with severe damage caused by traumatic injuries, tumor removal or even natural degeneration due to advanced age (Black et al., 2015).

In these situations where the body is not able to achieve complete regeneration, specialized clinical care is required to achieve full recovery of the patient (Koons et al., 2020). For this reason, doctors initially used elements such as biologically inert metallic devices, autografts (bone tissue from the same patient) or allografts (bone tissue from an external donor), which became the most used methods to repair severe damage to some element of the bone structure (Bez et al., 2017).

However, the insertion of these elements into the human body involves a certain degree of complexity and may entail several risks to the patient's health, mainly the risk of infection caused by the placed grafts in case they come from an external donor (Koons et al., 2020). Likewise, autografts carry risks such as chronic postoperative pain, hypersensitivity and infections, in addition to requiring additional intervention for their extraction; at the same time, there is a limit to the amount that can be cultivated, and most likely some cells may not be able to survive transplantation (Delloye et al., 2007).

On the other hand, allografts require initial processing by techniques such as irradiation, freeze-drying or lyophilization to eliminate most immunogenic factors, among other factors that negatively affect their mechanical and biological properties. There is also a small chance that an allograft is rejected by the body (Nazirkar et al., 2014). In this context, bone tissue engineering appears, which focuses on the repair of severe bone damage with new technologies that do not require autografts or allografts; that is, they do not put the patient's integrity at risk.

Therefore, the aim of the present study is to explore, from the reflexivity approach, the progress of bone tissue engineering, the application of 3D printing technology in this field and its recent progress, as well as the current challenges faced by these novel techniques and their sustainability in the future.

BACKGROUND

Bone Tissue Engineering

Bone tissue engineering was born from the clinical need to develop alternatives to methods involving bone tissue autografts and allografts which achieve the same results, but without their negative aspects (Roseti et al., 2017). This initiative eventually produced a large number of strategies that combined regenerative medicine with tissue engineering to develop solutions that promote bone regeneration (Farokhi et al., 2016). In this way, using knowledge on bone physiology and technological advances on materials, bone tissue engineering presents innovative techniques that integrate biology and engineering to address problems concerning bone defects. However, and despite experimental progress, it still needs to be further developed to achieve optimal results (Li et al., 2018).

Thus, the main advances in bone tissue engineering techniques include the cultivation and use of stem cells, the development of vascular networks, and bone regeneration (Black et al., 2015). Similarly, some

3D Printing in Bone Tissue Engineering

studies focus on investigating the regenerative properties of human bone, specifically on the existence of a stem cell population that performs these repairs, and how they can be harnessed (Dawson & Oreffo, 2008). Other studies have focused on studying the vascular network inside bones, as well as its relationship with bone stem cells and how blood vessels could harbor undifferentiated skeletal progenitors that promote bone tissue repair in affected areas (Mercado-Pagán, 2015).

Furthermore, the fabrication and application of specialized scaffolds that, by implementing an extracellular microenvironment, stimulate the *in vivo* cellular regeneration of bone tissue in the affected area was studied (Kondiah et al., 2020). These scaffolds mechanically stabilize the affected area for the necessary time until it is replaced by new bone tissue, using osteogenic and angiogenic stem cells (Söhling et al., 2020). The present book chapter focuses on these specialized scaffolds and their evolution in recent years.

3D Printing in Scaffold Manufacturing

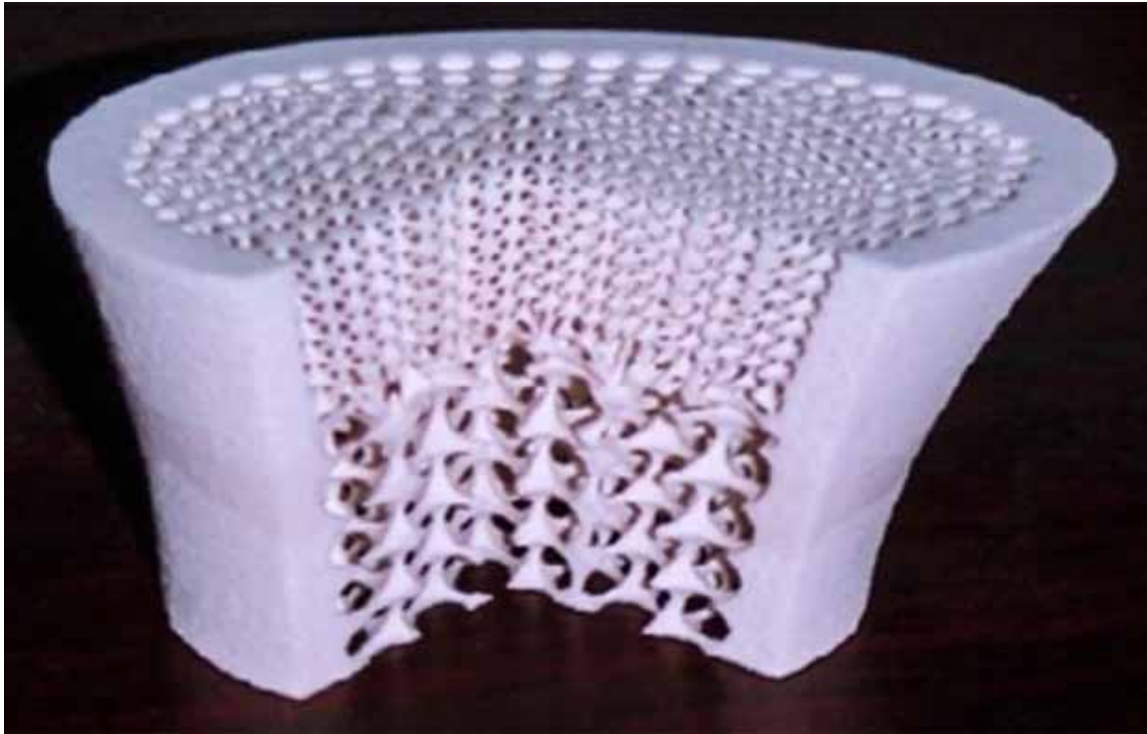
In bone tissue engineering, bone scaffolds are three-dimensional, biocompatible structures that mimic the properties of extracellular matrices and allow for the stimulation of bone tissue formation. One of the ways to fabricate these specialized scaffolds involves the application of 3D printing, a fabrication method that allows a wide range of geometries to be generated precisely with several materials (Haleem et al., 2020). Bone scaffolds being an important element in bone tissue engineering, this technology possesses great potential in this field due to its ability to print porous scaffolds with defined shapes, interconnected porosity, controlled chemistry, among other characteristics, whose high versatility gives a wide range of applications in the treatment of bone problems (Bose et al., 2013).

To fulfill their objective, the scaffolds manufactured by this method require specific properties due to the complexity involved in bone regeneration at the molecular, cellular, biochemical and mechanical levels (Haleem et al., 2020). Among these macro- and micro-molecular properties are shape, porosity and pore size, degradability, biocompatibility, mechanical properties and desired cellular response, so that the scaffolds can correctly induce bone regeneration (Wang et al., 2020). As these scaffolds must support the body to be able to regenerate the required tissues, they must be produced using a variety of biomaterials with properties similar to those of real human bone, and customized depending on the characteristics of the recipient body (Wu et al., 2014). A bone scaffold fabricated by 3D printing can be seen in Fig. 1.

Likewise, a scaffold must have a resistant structure and be manufactured with specific dimensions and a highly porous structure that can serve as an extracellular matrix and allow cell penetration. In addition, it must count with adequate biological and chemical properties, since a scaffold with the correct properties is capable of improving cell attachment and promoting their development and reproduction in new matrices, producing a complete regeneration of bone tissue (Kondiah et al., 2020). These scaffolds are also intended to be biodegradable, as the body produces its own extracellular matrix from them, which in turn renders any additional extraction process unnecessary (Haleem et al., 2020).

Figure 1. Bone scaffold fabricated by 3D printing

Source: Cai et al., 2012.



MAIN FOCUS OF THE CHAPTER

Current Situation in 3D Printing Materials

In order to manufacture bone scaffolds, biomaterials are used, the most commonly used being bioceramics, natural or synthetic biodegradable polymers, metals and composites (Wubneh et al., 2018). The importance of these materials lies in the fact that they are able to mimic the organic and inorganic characteristics of the extracellular matrix of bone, and are coupled with biologically active cells or molecules, which will be in charge of bone regeneration (Koons et al., 2020). Bioceramic scaffolds can be produced at micro, macro and nano scales, since they are designed with a hierarchical structure (Ma et al., 2018).

Conventional 3D printing technology can fabricate objects with a wide variety of materials, including thermoplastics, ceramics, graphene-based materials and metals (Shahrubudin et al., 2019). Thus, the most commonly used bioactive ceramics in bone tissue engineering are hydroxyapatite (HA), bioactive glasses and tricalcium phosphates ($\text{Ca}_3(\text{PO}_4)_2$) (Zhou et al., 2020), which can be seen in Fig. 2. Similarly, natural polymers have also been proposed as alternatives; however, their limited structural integrity and low mechanical properties were found to limit their use in scaffold manufacturing (Madrid et al., 2019).

Hydroxyapatite

It is one of the most widely used materials in the manufacture of bone scaffolds and is present in the composition of human bones (65% w/w), which makes it an ideal material, due to its resemblance to natural bone tissue and its high biocompatibility (Zafar et al., 2019). This composite is able to activate osteoblast proliferation and promote stem cell growth and differentiation by local addition of calcium ion (Ca^{2+}) (Zhao et al., 2017). To improve their properties, several materials with hydroxyapatite as the base element were developed for use in bone tissue engineering. In addition, ion-doped hydroxyapatite, hydroxyapatite composites with polymers, and surface-modified hydroxyapatite have been developed, each with its own advantages that improve the original properties of the composite (Shi et al., 2021). As a result, hydroxyapatite has become a very important material for the manufacturing of bone scaffolds, which is why it has been widely used in this field.

Tricalcium Phosphates $\text{Ca}_3(\text{PO}_4)_2$

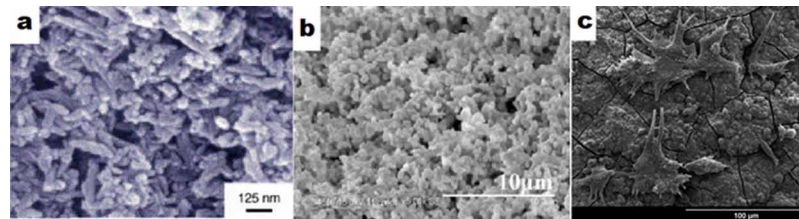
These materials present good biocompatibility and degradation, but they withstand a lower compressive force (Zafar et al., 2019); likewise, they are suitable for use in bone tissue engineering since they are already naturally found in the bone composition, and are used as an independent biomaterial in bone implant coating, or as reinforcement in a composite scaffold, which is why it is considered with the potential to become the biomaterial of the future (Lowe et al., 2019). However, scaffolds manufactured with this material present a slow release of osteogenic ions, therefore, a low regenerative capacity is generated. For this reason, tricalcium phosphates (TCP) require the addition of dopants to improve their structural, topographical, physical and biological properties (Evis & Webster, 2011). Studies have focused on investigating the addition of trace elements such as zinc, magnesium, copper or boron to tricalcium phosphates to achieve the desired osteogenic properties, with positive results (Pazarçeviren et al., 2021).

Bioactive Glass

It is a type of bioceramic existing in non-porous and solid form, composed of silica dioxide, silica oxide, calcium oxide and phosphorus. This material is important in bone tissue engineering for possessing enhanced in vitro biocompatibility of bone tissue growth (Zafar et al., 2019). The ultimate bioactive glass is known as 45S5 Bioglass, due to the strong chemical bond that can be created with the host bone tissue (Figure 1), which cannot be separated without fragmenting the bone (Brauer, 2015). This powerful bonding occurs through the release of sodium and calcium ions, before depositing a layer of carbonate hydroxyapatite on the surface of the glass (Kong et al., 2018). Since this form of glass does not have microporous structures, it depends on a low amount of silica to achieve good bioactivity (<60%), and thus, if it exceeds the percentage, it may not be able to stimulate the formation of the apatite layer or achieve the bonding with the host tissue, since glasses with high percentages in silica have a more stable structure that does not allow the release of sodium and calcium ions (Arcos & Vallet-Regí, 2010).

It should be noted that bone scaffolds made from these materials usually require post-processing techniques to improve their initial mechanical properties. For example, sintering is applied to produce shrinkage in the scaffold, which generates the formation of fracture distortions that are used to add the biological molecules more easily (Madrid et al., 2019).

Figure 2. (a) Scanning electron micrograph (SEM) of Hydroxyapatite powders. Source: Zafar et al., 2019, (b) SEM of β -TCP porous scaffolds. Source: Yang et al., 2015, (c) SEM showing osteoblasts in apatite layer formed on bioactive glass Source: Brauer, 2015.



Current Status of 3D Printing Methods

Among the main conventional 3D printing methodologies, Kondiah et al. (2020) stated three:

1. **Selective laser sintering**, which uses a laser to synthesize powders and bond materials that form solid structures; thus, bioactive ceramic or tricalcium phosphate scaffolds manufactured by laser sintering have good mechanical properties, similar to those of authentic trabecular bone tissue.
2. **Stereolithography**, which allows complex designs of micrometer-scale architectures to be processed and precisely fabricated using extrusion techniques; however, by printing with limited viscosity and stability, it greatly reduces the list of materials suitable for processing.
3. **Fused deposition modeling**, which uses melt extrusion techniques in order to fabricate intricate dimensional geometries. Mainly thermoplastic polymers are used, which can be extruded through a nozzle and then solidified to form solid structures.

The typical extrusion manufacturing process consists of preparing the material for scaffolds using raw materials such as ceramics, metals, plastics, and gypsum. These are applied in layers during the 3D printing process, and then consolidated by selective injection of a liquid binder, this sequence is repeated as many times as necessary until the desired 3D shape is obtained (Wang et al., 2020). Likewise, 3D printing technology has experienced great growth in recent years, until it became possible to use it in bone tissue engineering, specifically in the fabrication of bone scaffolds (Haleem et al., 2020).

Among the main current 3D printing techniques for bone scaffolds, there are: printing of ceramic scaffolds, printing of hydrogel scaffolds, high temperature printing of polyester scaffolds and post-treatment, cryogenic printing of scaffolds, and printing of synthetic or natural polymer scaffolds (Wang et al., 2020). Among these techniques, 3D printing of biomaterial-based scaffolds stands out, which are nowadays the most widely used in bone tissue engineering due to their ability to emulate the structure and chemical composition of bone extracellular matrices present in natural bone (Kondiah et al., 2020).

Scaffold manufacturing through bone tissue engineering and 3D printing, as explained by Qu (2020), involves three important steps: design, fabrication and evaluation. First, in order to develop the design, it is important to capture detailed images of the structure (macro and micro) of the patient's affected bones using computed tomography or magnetic resonance imaging. With these images, the defects in the bone to be repaired are identified, as well as the size of pores, the type of cellular unit, etc.; then, the three-dimensional model of the scaffold is developed with computer-aided design software (CAD)

with the patient's personalized specifications. After that, the appropriate biomaterials and techniques are chosen to manufacture the final product. Before the manufactured scaffold can be worked with, usually in experimental investigations, structural analysis and testing of its mechanical and biological properties are performed to ensure its quality.

Once this initial shape is obtained, the scaffold must undergo a process known as 3D bioprinting, in which biomaterials are introduced to the bone scaffold in order to promote osteoblast formation, in other words, to promote bone regeneration (Zhou et al., 2020). There are mainly three conventional methods to perform 3D bioprinting: either by injection, extrusion or laser (Adepu et al., 2017). The injection method being the fastest and cheapest, the extrusion method the slowest, and the laser method the most expensive. Also, this process requires precise control of the resolution, speed and concentration of cells in the impression, so that the correct spacing of the cells is achieved and the material is adequate to allow the creation of a living cell microenvironment (Zhou et al., 2020).

In order to achieve these goals, it is necessary to use an additional component known as bioink, a special mixture that is embedded in the bone scaffold (Pavek et al., 2021). The elaboration of these special inks requires great care when working with fluids that contain a mixture of nutrients, matrix components and cells, as well as regulatory factors and proteins. For this reason, the ideal materials for making an efficient bioink must have characteristics such as good plasticity, adequate porosity and pore size, good mechanical properties, biocompatibility and surface activity (Zhou et al., 2020), and for this reason, the aim is to promote this technology and obtain novel inks made with new materials (Adepu et al., 2017).

Nowadays the development of new techniques and biomaterials for use in bone tissue engineering are hampered mainly by the high costs involved and stringent regulatory requirements imposed by the Food and Drug Administration (FDA) (Koons et al., 2020), which include compliance with standards such as Good Manufacturing Practices (GMP) for implementing these products in clinics (Codrea et al., 2020). Although this entity has not been efficient in adjusting its requirements to new technologies over the past few years, proposed updates seek to streamline this process and achieve full approval of new materials and techniques by demonstrating their safety and efficacy over a period of 7 years (Hoffman et al., 2019). Due to the great interest in these topics, they are being heavily researched nowadays despite these constraints.

Recent Advances in Bone Tissue Engineering

Scaffold Materials for 3D Printing

Chitosan

It is a material widely studied in bone tissue engineering due to its biocompatibility and its osteogenic and antimicrobial properties. However, for chitosan to be used in bone scaffold manufacturing, it requires the addition of polymers and inorganic materials that greatly improve its original properties (LogithKumar et al., 2016). Among these elements, silver is among the most recently studied for fabricating chitosan bone scaffolds with silver nitrate (CS-Ag), as it has been shown to have good properties (Vaidhyanathan et al. 2021).

Silica

It is a new material studied due to the advantages of its use in bone tissue engineering, due to its ability to promote the viability of osteoblastic cells, and to provide a guide for cell distribution (Shadjou & Hasanazadeh, 2015). Additionally, an important advantage of silica is that it can be extracted from natural sources such as diatomite, which is a low-cost and abundant source. Although it requires purification processes to remove contaminants, it results easy to process (Eivazzadeh-Keihan et al., 2019).

Bacterial Cellulose

Another novel material investigated for use in bone tissue engineering is bacterial nanocellulose, which is produced extracellularly by microorganisms (Torgbo & Sukyai, 2018). This compound is currently used in the pharmaceutical industry and has generated great interest about its application in biomedicine, this due to its high degree of purity, flexibility, porosity and biocompatibility, in addition to unique properties such as its ability to store water, mechanical stability, crystallinity, and not requiring costly purification processes (Picheth et al., 2017).

Hydroxyapatite

It is one of the most widely used materials in this field, and the feasibility of using natural sources for its extraction has been studied. Hydroxyapatite is currently synthesized by chemical precipitation, hydrothermal, microwave irradiation, electrospinning and microemulsion processes (Haider et al., 2016); however, these are costly operations that can generate impurities in the material (Sharifianjazi et al., 2021). Hydroxyapatite, moreover, can be found naturally in the composition of human bones, and also in the bones of some species, such as bovine, shrimp or fish, and other natural sources such as biological waste (Szcześ et al., 2017).

Boron Nitride

Boron nitride is considered a good candidate material due to its high chemical, mechanical and thermal stability, as well as its electrical insulation (Belaid et al. 2020). Also, when biodegradable synthetic materials were studied, the possibility of integrating boron nitride with cubic or hexagonal shaped structures in various compositions in the form of graphene was considered in the composition of some of these to improve their compatibility with the biological tissue of patients (Ozbek et al., 2018).

Calcium Peroxide

In recent years, oxygen-releasing scaffolds have gained importance, useful for working on tissues, such as bones and muscles, that demand large quantities of this element. These scaffolds use peroxide components that produce oxygen through chemical reactions, of which calcium peroxide has attracted the interest of researchers for its ability to produce oxygen in a more controlled manner than other components such as magnesium or hydrogen peroxide (Khorshidi et al., 2020).

Gold

This metal has been found useful for biologic therapies. Gold nanoparticles have to be modified and recombined in order to improve some characteristics and allow their use in bone tissue engineering appli-

Table 1. Summary of recent research and experiments on materials in bone tissue engineering

Material	Investigation	Results	Reference
Chitosan	Sintering of CS-Ag scaffolds at various concentrations (0.5M, 1M, 1.5M), and subsequent experimentation.	• Better control over swelling and degradation rate found in 1.5M solution. • Improved antibacterial activity and matrix mineralization, with differentiation in osteoblasts.	Vaidhyathan <i>et al.</i> , (2021)
Silica	Research on the performance of bone scaffolds manufactured with silica nanomaterials.	• Improved mechanical pressure distribution throughout the scaffold's structure. • Investigated possibility of scaffolds to contain and distribute medicine to the body.	Eivazzadeh-Keihan <i>et al.</i> (2019)
Bacterial cellulose	Research on the potential of bacterial cellulose as a material for bone scaffolds.	• Bacterial cellulose induces bone cell generation. • The aim is to modify the added value of bacterial cellulose and its physicochemical properties. • Addition of components investigated in order to promote bone regeneration.	Pang <i>et al.</i> , (2019)
Hydroxyapatite	Extraction of natural hydroxyapatite, derived from pigeon bone waste.	• Natural hydroxyapatite has a better metabolic activity, bioactivity and calcium/phosphorus ratio than synthetic version. • Extracted hydroxyapatite shows higher cell viability and alkaline phosphatase activity than synthetic version.	Sharifianjazi <i>et al.</i> (2021)
Boron Nitride	Development of porous scaffold, reinforced with exfoliated boron nitride.	• Improved structural roughness, thermal stability and bioactivity of the polymer. • Reduced hydrophobicity and crystallinity in the polymer. • No changes in the scaffold's mechanical properties were observed.	Belaid <i>et al.</i> , (2020)
Calcium Peroxide	Development of a scaffold with calcium peroxide in its nanofibers.	• Scaffold with calcium peroxide for a controllable oxygen release. • Oxygen levels similar to those found in natural bone tissue, in the range of 30-94 mmHg. • Maximum oxygen production time in 14 days to achieve blood vessel formation (angiogenesis).	Khorshidi <i>et al.</i> , (2020)
Gold	Research on the applications of gold nanoparticles in bone tissue engineering	• Mechanical strength, antioxidant activity, promote cell proliferation and differentiation. • Potential for use in delivery systems, due to ability to penetrate cell membranes and promote wound healing. • Toxicity, efficacy and clinical safety tests are required to be standardized for further use.	Li <i>et al.</i> , (2020).

cations (Li *et al.*, 2020). This material counts with high conductivity, high catalytic activities, biocompatibility, low toxicity, anti-microbial activity, among other characteristics (Nezhad-Mokhtari *et al.*, 2020).

Table 1 briefly explores research and experiments for each of the materials previously mentioned, seeking to lay the foundations for future research applications, and to innovate in their use or method of obtaining them.

Applications of Bone Scaffolds

Craniofacial Defects

The possibility of treating craniofacial bone defects by means of bone tissue engineering has been analyzed, in which complex geometries need to be developed according to their relationship with local structures.

In order to work on craniofacial bone tissue, bone tissue engineering could make use of materials based on natural polymers, such as collagen or hyaluronic acid (Shen et al., 2020).

Dentistry

Bone tissue engineering is also receiving attention in the field of dentistry, due to the potential offered by teeth stem cells as an alternative material to increase the regenerative potential of bone scaffolds (Salgado et al., 2020). On the other hand, there is one material known as graphene oxide, which is known for its antibacterial properties and low cytotoxicity and is attracting the attention of researchers for its application in dentistry (Nizami et al., 2020).

Clinical Treatments

The bioelectrical phenomenon present in natural bone has been recognized as an important factor in bone development and fracture regeneration (Khare et al., 2020). In recent years, the potential of electrical stimulations (EStim) in bone tissue engineering treatments has been highlighted. It is known that these practices stimulate bone tissue regeneration by stimulating stem cells and osteoblasts, which is why the aim is to take advantage of their potential and optimize the performance of bone tissue engineering techniques (Leppik et al., 2020).

4D Bioprinting

In 2014, a laboratory at the Massachusetts Institute of Technology (MIT) succeeded in developing for the first time what came to be known as 4D printing, taking the conventional properties of 3D technology and adding time as a fourth dimension. This involves the use of different materials known as smart polymers during the manufacturing process. Although this technology is still in its infancy, its future potential for use in bone tissue engineering is already recognized (Wan et al., 2020).

Table 2 briefly explores research and experiments carried out for the new applications mentioned above, seeking to lay the groundwork for future experiments by providing preliminary information on possible solutions to specific problems.

SOLUTIONS AND RECOMMENDATIONS

The methodology of experimentation with newly fabricated bone substrates will be discussed generally below, so that an initial idea of these procedures can be provided to future researchers interested in developing and testing bone substrates manufactured with new biomaterials. Through a brief review of the section on experimental research related to the analysis of scaffolds made of polymers with boron nitride and hydroxyapatite composites with bacterial cellulose and polycaprolactone, some guidelines for analyzing the quality of bone scaffolds will be presented (Belaïd et al., 2020; Cakmak et al., 2020).

Among the required analyses to verify the quality of the manufactured scaffold, an analysis of the structure and morphology of the scaffold must be performed by means of optical microscopes or electronic scanners. The physicochemical composition of the scaffold must be analyzed by means of a Fourier transform spectrophotometer. The thermal properties of the material should also be analyzed using a differential calorimetry scanner. In addition, the mechanical properties of the material should be

Table 2. Summary of research and experiments on recent applications in bone tissue engineering

Field	Investigation	Conclusions	References
Craniofacial surgery	Study of TGF- β superfamily of bioactive molecules for scaffold fabrication.	- TGF- β molecules are actively involved in bone and vascular homeostasis. - The fabricated scaffold tested on the skeleton of an adult rabbit was able to form new bone tissue in 8 weeks.	(Shen <i>et al.</i> , 2020).
	Development of an alternative hydrogel for craniofacial bone tissue and testing in mice.	- This hydrogel showed favorable mechanical properties and desirable degradation speed in bone repair. - The biodegradability, biocompatibility and osteoconductivity of the hydrogel was proved by subcutaneous implantation in mice.	Hasani-Sadrabadi <i>et al.</i> , (2020)
Dentistry	Development of bone scaffolds made with stem cells extracted from teeth.	- Stem cells are easier to extract from this source compared to other ones. - Demonstrated high cell viability and osteogenic differentiation in fabricated bone scaffold.	Salgado <i>et al.</i> (2020)
	Compilation of potential uses of graphene oxide in dentistry.	- Combining graphene oxide with hydroxyapatite in dental and orthopedic bone regeneration. - Combining graphene oxide with zinc as a coating for dental implants. - Combining dental stem cells with fibroin scaffolds and graphene oxide for therapeutic use.	Nizami <i>et al.</i> (2020)
Clinical treatments	Compilation of recent research on electrical stimulation to stimulate bone regeneration.	- Although experiments with EStim have good results, there is nothing conclusive due to lack of standardization in models and protocols. - There is the possibility of combining bone scaffolds with EStim by using electroactive smart polymeric biomaterials.	Leppik <i>et al.</i> , (2020)
4D bioprinting	Research on recent advances on 4D bioprinting.	- Development of materials that change shape and size over time in response to stimuli such as temperature, moisture, electricity, etc. - Creation of more complex structures with dynamically controlled forms and functions. - Development of microvascular systems and nerve networks within bone scaffolds.	Wan <i>et al.</i> , (2020)

analyzed by means of stress tests to determine the maximum loads that can be withstood, as well as the viability of the cells cultivated on the manufactured scaffold by means of sterilization under ultraviolet light and subsequent incubation of the cells of interest.

FUTURE RESEARCH DIRECTIONS

As previously mentioned, biomaterials are a crucial element in the manufacture of bone scaffolds by 3D printing. Existing biomaterials still have to be studied so their properties like their mechanical properties or durability are well characterized and documented (Poomathi *et al.*, 2020). Although a large number of new biomaterials have been developed during the last few years, it is expected that the trend of systematic research on biomaterials will continue in the future. In this way, new knowledge about their mechanisms of action and their corresponding cellular response can be expanded in order to further develop new biomaterials able to carry out conflicting requirements (Koons *et al.*, 2020).

It is also expected that the study of scaffolds made with nanomaterials will be more in-depth, since they show better performance than the ones made with conventional materials (Zhang *et al.*, 2020).

However, properties such as their localized concentrations or surface topography still need to be rigorously studied before they can have clinical applications. Therefore, future research should focus on analyzing the mechanisms of nanomaterials that promote bone regeneration and exploit them to develop multifunctional scaffolds. This future research should particularly focus on promoting regeneration of blood vessels and nerves, for this has been reported to be important for the bone regeneration process (Ye et al., 2020).

3D printing technology has made progress in the past decades and has consolidated its position in the biomedical industry, but there are still many challenges to be addressed in the future in order to exploit its full potential, and they are mentioned below (Wang et al., 2020):

- Improve the ability of 3D printing to copy the multilevel hierarchical structure of real bones by designing nozzles with micro extrusion, so that greater accuracy can be achieved in such copies.
- Improve 3D printing techniques to be able to mimic the heterogeneous structure of bone with its varied mechanical properties, so that customized scaffolds with complex characteristics can be produced.
- Improve the ability of 3D printing to enable the development of vascular-like channels and the controlled release of angiogenic agents into the body, so that scaffolds with improved regenerative capacity and enhanced vascularization can be produced.
- Achieve cell incorporation simultaneously with substrate fabrication during 3D printing to avoid uneven cell distribution and limited cell density in substrates with post-fabrication cell incorporation.
- Achieve the use of 3D printing in the production of anti-bacterial or anti-cancer bone scaffolds to treat problems with bone tumors or infections.

CONCLUSION

This book chapter demonstrates the rapid progress of bone tissue engineering in the development of bone scaffolds by 3D printing, based on the extensive knowledge acquired about bone biology and advances in material synthesis in recent years. For this reason, research aimed at identifying a better use of current materials, sintering of novel composites or completely new materials is of vital importance to further advance the development of this technology in the fabrication of bone scaffolds. It is also apparent that 3D-printed scaffolds are at an important stage in their development, having incorporated a variety of biological materials with beneficial properties to allow said element to better adapt to the recipient body and promote bone healing in it.

Biomaterials have proven to be very useful elements in this field due to their wide range of properties that in different ways promote bone tissue regeneration. For this reason, a trend in research can be seen, which has been strongly focused on the study and development of biomaterials, such as hydroxyapatite or tricalcium phosphates to be used with 3D techniques. In the present work we have seen the most used materials in bone tissue engineering, and how this trend has led to produce a great variety of biomaterials with new components of all kinds, such as ceramics, metals, polymers, etc., with properties that can enhance many characteristics of the original biomaterial. In this way, the number of biomaterials and composites continue to increase, always seeking to improve their properties in contrast to their predecessors.

Everything indicates that the short-term future of 3D printing in bone tissue engineering will continue to focus strongly on extending the development of biomaterials, as their impact in the field and their potential is well recognized by researchers. For this reason, and as we have seen, research is already being carried out in this direction to allow these techniques to have novel applications as a result of the latest technological advances in bone tissue engineering. For this reason, this field promises to continue to greatly expand the number of biomaterials available in different ways, either by synthesizing completely new ones, creating composites with novel combinations, finding new ways to obtain conventional materials (e.g., hydroxyapatite), etc.

This trend, together with the advancement of 3D printing technology and other techniques such as the novel 4D bioprinting, are factors that will eventually push the manufacturing of a new generation of bone scaffolds. In this way, they will be able to be manufactured with greater precision and better performance to treat a greater number of bone problems of different sizes and in a customized way. Having demonstrated the great importance of this field in medicine, it can be concluded that it is likely to continue to expand, developing new technologies and attracting the interest of new scientists, who will contribute to further explore and exploit the potential of these techniques for the benefit of people.

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KEY TERMS AND DEFINITIONS

3D Printing: A manufacturing process capable of producing a three-dimensional model through the addition of layered material. This process can be used to create a wide range of complex geometries in an efficient manner, being able to use almost any material.

Bioink: A special liquid containing living cells, a structural material and growth factors, which allow the material to be transformed into pure biological tissue by cell reproduction. These special inks can be used in the same way as other materials in 3D printing, being extruded from the nozzle of a 3D printer.

Bioprinting: The combination of cells and biological materials with 3D printing techniques to produce three-dimensional biomedical developments with properties similar to living tissue. The main bioprinting techniques include extrusion, laser-assisted, acoustic wave, and SWIFT techniques.

Bone Scaffold: Three-dimensional scaffolds with porous structures, in charge of guiding the formation of new organs and tissues. Bone scaffolds manufactured by 3D printing allow a better integration with the host bone tissue and allow vascularization and bone development.

Bone Structure: Also called bones, which are the osseous tissue responsible for giving shape and support to the body, allowing its mobility, serving as storage for various minerals, and even protecting internal organs from trauma. The human bone structure is composed of 206 bones.

Osteogenesis: The process by which bone tissue is formed and even regenerated to some degree after bone injury.

Scaffold-Assisted Regeneration: The use of bone scaffolds manufactured by 3D printing and applied to a bone defect to promote complete regeneration of the affected area.

Tissue Engineering: A branch of bioengineering capable of improving or replacing biological functions by combining knowledge in materials engineering with biochemistry and physiochemistry. In practice, it refers more to applications aimed at partial or total tissue repair or replacement.

Chapter 12

Medical Learning Through Simulations With Immersive Virtual Reality and Augmented Reality Devices

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ABSTRACT

Different examples of the use of recent technologies, based on virtual reality and augmented reality techniques, for the learning of medical students are presented. The use of different glasses, both virtual reality and augmented reality, as well as gloves with movement sensors, allow the user to enter a scenario very close to the real one, resulting in an improvement and optimisation of their learning. The use of these resources in different areas of medicine facilitates the acquisition of skills, for example in cardiac auscultation training in more dynamic learning of human anatomy, with three-dimensional images, or learning protocols for virtual surgical approaches, among many other possibilities. The satisfaction of the users who handled these devices was excellent, acquiring, in very short periods of time, practical skills in many of the actions carried out with these technologies.

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INTRODUCTION

Research into applications of Virtual Reality (VR) and Augmented Reality (AR) techniques in medicine began more than 20 years ago. However, their use did not begin to be democratised until the hardware was powerful enough to provide good quality results and cheap enough to reach a larger audience.

So far, VR has been evolving and advancing along its own independent path, within a world with a strong tendency to display data, images, videos, etc., in a virtual format. This tendency to represent the real world in a virtual format has generated the need to develop increasingly more sophisticated software and hardware. The enormous realism achieved by current video games or movies, are good examples. On the other hand, the aim sought with AR is precisely the opposite: to represent virtual information in a real environment. In other words, augmented reality is a technology that has advanced, so to speak, against the tide compared to other technologies. The most interesting thing about augmented reality is that the virtual information reaches the user in as simple and as natural way as possible. That is, AR is aimed to facilitate the user to perform any activity for which this enlargement of reality is necessary without distractions or interruptions.

The devices employed in VR and AR range from smartphones and tablets to a variety of glasses, stereoscopic vision goggles and gloves with hand movement sensors. All these different types of devices can be broadly grouped into five categories: fixed outdoor systems, fixed indoor systems, mobile outdoor systems, mobile indoor systems, and mobile indoor and outdoor systems. Of these possible devices, the ones that are currently receiving the greatest attention from developers are the mobile systems (both indoor and outdoor). The main reason is that mobile devices are already owned by a great number of users, so there is a greater demand of VR and AR solutions from the average non-specialised user.

Currently, the devices with the highest expectations are VR and AR glasses, as they allow the user to be hands-free while performing different interactive activities. These glasses need nothing more than a specific software application to operate them, which can be easily installed in a smartphone. In the mobile applications market, there are many virtual and augmented reality applications intended for entertainment such as video games or movies, although new entertainment focused applications appear each day. All these applications, from the simplest to the most cutting-edge, offer innovative solutions for medical training and other areas of health sciences.

BACKGROUND

A quality medical education is one that responds to social needs, which have an impact on the individual skills development in all educational environments. Universities are beginning to introduce changes in education procedures that lead teaching professionals to assume new responsibilities, based on the use of emerging technologies (Curran & Fleet, 2005; Alvarez & Edwards, 2006; Beux & Fieschi, 2007; Briz-Ponce et al, 2016; Briz-Ponce et al, 2017). The integration of Information and Communication Technologies (ICT) and society has been one of the most recurrent lines of research in recent decades. In recent years, university education systems have sought a series of alternatives and proposals for education, using the Internet as a means of communication and trying to displace a high percentage of face-to-face classes. Likewise, the challenge for universities lies in redesigning their training guidelines around professional competences rather than around traditional subjects, to promote the development of didactic proposals that involve the students in collaborative environments. to the objective is to fos-

ter significant learning and a progressive increase of the use of electronic educational resources in the teaching/learning activity. One of these technologies that currently plays an important role in medical training is virtual reality (VR), making use of simulated environments, and allowing the end user to interact in three-dimensional environments in a realistic way. In addition, augmented reality (AR) is another technology that offers numerous educational possibilities in the university environment, and an immense potential to improve the learning and teaching in medicine. AR merges the virtual and the real world, so that virtual elements are superimposed on the physical world and can be visualised by means of electronic devices (Kuntze et al., 2001; Garg et al., 2002; Henn, 2002; Nichols & Patel, 2002; Burdea & Coiffet, 2003; Grigore & Coiffet, 2003; Levinson et al., 2007; Häfner et al., 2013; González Izard et al., 2017; Lim et al., 2017; Hanna et al., 2018; Escalada-Hernández, 2019; González Izard et al., 2019; González Izard et al., 2020; Mariscal et al., 2020). In a world where technological advances are happening at breakneck speed, virtual reality and augmented reality techniques are beginning to be widely incorporated into the teaching process of many universities around the world.

The acceptance of new technology in the teaching-learning province is achieving an excellent impact on students' performance in the field of medicine and other areas of health sciences. Virtual and augmented technological media and devices constitute a new paradigm that makes it possible to complement non-classroom teaching in some topics and subjects of different medical specialities, where students take responsibility for their learning and thus play a more active and decisive role in their medical training and learning process (Nikou et al., 2000; Scalese et al., 2008; Stadie, 2008; Ullrich et al., 2008; Okuda et al., 2009; Ruthenbeck, 2013; Pensieri & Pennacchini, 2016; Wang et al., 2016; Lim et al., 2017). Over the years, these technologies are being incorporated and used in teaching and learning processes. Many universities around the world are beginning to use technological developments based on virtual simulations in their teaching activities using different devices, such as stereoscopic vision glasses, gloves, or movement sensors. The uses of virtual and augmented reality in medicine are very broad, ranging from the training of doctors, through the treatment of different diseases to providing support to surgeons during operations. All these new technologies have positioned themselves as real working tools for the health sector (Nikou et al., 2000; Nichols & Patel, 2002; Stadie, 2008; Nakamoto et al., 2012; Ruthenbeck, 2013; Monkman & Kushniruk, 2015; Wang et al., 2016; Lim et al., 2017; Ullrich et al., 2018).

Experts claim that these tools help students increase their study productivity minimizing the effort needed, as lessons are based on creating new enjoyable immersive learning experiences. It is known that the human brain retains 10% of what it reads and 20% of what it hears but remembers 90% of what it experiences. Therefore, immersive learning, driven by new technologies, becomes a very useful teaching approach. Studies have shown that the use of these technologies improves learning and classroom interactions. Moreover, they can help students to enhance their digital and communicative skills (Lin et al., 2013; Liu et al., 2003; Mariscal et al., 2020).

The aim with this chapter is to show different virtual and augmented reality practical examples in health sciences, which have been developed and programmed by the authors. The examples showcase the use of different augmented and virtual technologies in health sciences teaching-learning scenarios. The objective is to increase the users' interest by creating virtual environments which are similar to their medical activity, by simulating situations of daily clinical practice under virtual learning environments.

METHODOLOGY AND TECHNOLOGICAL SET UP

Nowadays, technological advances have allowed the experience of virtual and augmented reality both on personal computers and smartphones. However, to obtain an immersive sensation, it is convenient to use resources that blur the line between the physical world and the digital or simulated world, generating a sense of reality in the user. For this reason, the authors have made use of different technological procedures, such as virtual and augmented reality glasses, for the development of the systems shown in this chapter. In addition, other alternative devices such as gloves with hand movement capture sensors have also been employed.

The range of employed glasses vary from simple and inexpensive cardboard glasses, on which the users need to insert their smartphone to experience stereoscopic vision in immersive experiences; to more sophisticated glasses with better features.

As an example, one of the glasses used in the developed technological applications for medical training has been the Oculus Go (see Figure 1), which incorporates its own screen and processor, providing an acceptable quality of visualisation and user experience for such a low-cost device.

Another device that has been tested is the Lenovo Explorer glasses, which supports Windows Mixed Reality and offers good quality viewing and virtual interaction at an affordable price. These glasses incorporate controls (see Figure 2) that allow six degrees of freedom, which facilitated the simulation of surgical approach protocols such as a lumbar transpedicular fixation operation.

The HTC Vive Pro goggles were also employed. They are a high-powered, high-quality device that incorporates external sensors that are placed around the user, which triangulate the user's position within a space delimited by these sensors.

For developments based on augmented reality techniques, other models of Epson Moverio BT300 and Vuzix M300 glasses were utilized. These glasses were not used for any 3D visualisation development, as they do not have sufficient rendering capacity. In such cases, the Magic Leap One glasses were chosen in order to achieve high quality visualisation experiences, as they have a powerful processing core, thus easily allowing the rendering of 3D models with higher polygonal load and higher quality textures. In addition, these glasses include sensors to analyze the user's environment, allowing the placement and fixation of objects around them.

Besides, VR gloves such as the Senso model shown in Figure 3 have also been employed. These gloves replace the controls which are commonly located in the glasses, allowing to design more realistic and user-friendly simulations. These gloves also incorporate vibration devices, thus offering a haptic response to the user when interacting with virtual elements. In other words, the user feels that he is touching a virtual object.

The Samsung Gear 360 camera has been employed as a low-cost alternative for recording rooms such as operating theatres, doctors' surgeries, etc. Those recordings of the operating environments are subsequently set up as immersive virtual reality backgrounds, providing the scene with a great level of realism.

Unity3D has been the chosen software for the design and set up of the 3D virtual environments due to its powerful 3D rendering engine, its support for virtual reality and augmented reality technologies and its integrated multiplatform system. In addition, Vuforia's SDK (software development kit) tool has been used to carry out the projections of the 3D models over the camera captured images. To achieve this feature Vuforia makes use of the native libraries Arcore and Arkit.

Arcore is a library that provides a low-level framework for the implementation of augmented reality solutions for both Android and iOS devices. This library is able to create a point cloud of the space

Figure 1. Group of students at the University of Salamanca, experimenting in the classroom with the Oculus Go glasses



surrounding the device based exclusively on the images obtained from the camera, without the need to include depth sensors. It's counterpart, Arkit, is the most powerful augmented reality library available. This may be due to the fact that it is only available for iOS devices and their associated hardware, so the library is developed under a tightly controlled hardware environment, dealing with a limited and well-known set of sensors such as cameras, accelerometers or gyroscopes.

Above the abovementioned libraries, AR Foundation is a high-level framework implemented by Unity that provides an abstraction layer for the use of Arcore and Arkit libraries. AR Foundation permits the development of cross-platform applications that internally use these two native libraries in a transparent way for the programmer. Thanks to AR Foundation developers can implement augmented reality applications that use the advanced capabilities of Arcore and Arkit, using Arcore in case of running the developed application on compatible Android devices and Arkit for compatible iOS devices.

The programming language mainly used for the implementation of the augmented reality and virtual reality systems has been C++.

In all cases, high-powered, high-capacity processing and rendering equipment has been used. This equipment includes state-of-the-art processors and the NVIDIA RTX 2080 Ti graphics card.

Figure 2. A professor at the University of Salamanca experimenting with the Lenovo Explorer glasses and controls, inside a clinical simulation room with a mannequin



Figure 3. Visualisation experience with VR goggles and Senso gloves with hand movement sensors



Figure 4. Group of students experimenting and visualising the anatomy of the skull, with different virtual reality glasses, which incorporate a Smartphone inside



RESULTS

In this section, three technological developments built by the authors' research and development group will be described, to showcase some of the many possibilities offered by virtual and augmented technologies for the medical training of students. The use of these technologies allows students to go from being simple passive content receivers to more proactive and creative participants in permanent communication and interaction within their learning process.

The use of virtual reality glasses, through stereoscopic vision, and the creation of specific software for the study of anatomy, facilitates an approach to body morphology in a way that is closer to reality, which leads to a better understanding of the structures that make up the human body. Figure 4 shows an example of a group of students using a developed augmented reality application for the study of the bones that comprise the skull. This bone structure was reconstructed from serial sections in DICOM (Digital Imaging and Communication On Medicine) computed tomography format.

The system makes it possible to analyse the skull structure in three dimensions from any spatial position. In addition, the user can navigate through the interior of the skull and assess the different cerebral fossae, their limits and the orifices they contain. The whole visualisation is very dynamic and interactive, which involves the active participation of the students who experiment with the immersive glasses (Fig.5). Three-dimensionality is one of the fundamental characteristics that define virtual reality, achieving the immersive sensation through the projection of stereoscopic graphics, generating different images for the user's right and left eye. Through binocular vision the user can appreciate the different distances and volumes in the environment that conform the skull.

Figure 5. Experience of visualisation and navigation inside the skull, under a virtual reality environment, with stereoscopic vision glasses



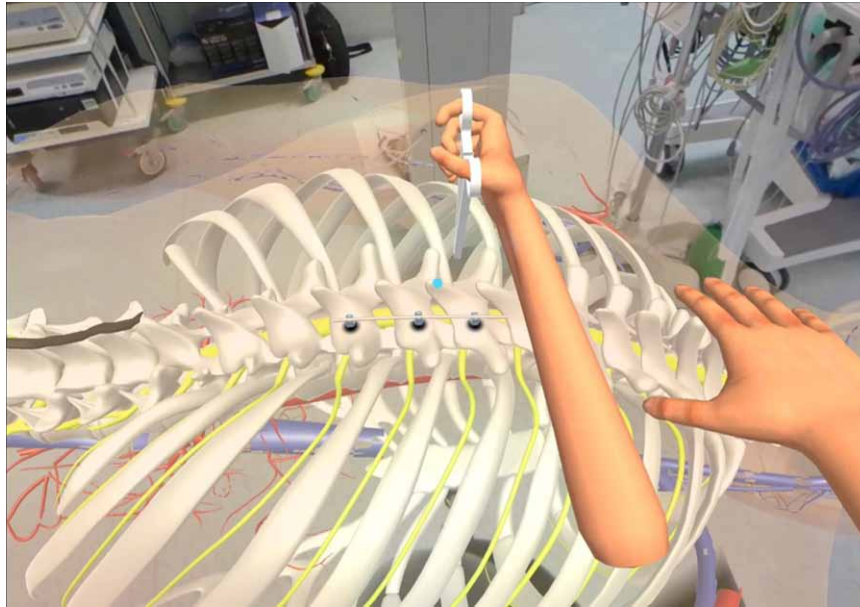
These technological experiences have shown that the use of collaborative and proactive work during university classes, which involves the sharing and confrontation of opinions while interacting with the virtual environment, contributes to enhance the learning process. In addition, the use and incorporation of these technologies in the teaching-learning process of various health science disciplines leads to an increase in the attention and motivation of students in the activities they carry out virtually. In this way, both virtual reality and augmented reality can help to increase the value of other technologies in the development of the professional and academic skills of university students in the areas of health sciences.

Augmented reality can improve the training of medical students and residents, allowing them to practice surgery and protocols as many times as needed without the need to manipulate medical material or real patients. In this sense, Figure 6 shows the simulation of a surgical procedure in the lumbar spine. All the action takes place in a real operating theatre, recorded with a 360° camera, which makes the scene more realistic. Therefore, the users never lose contact with the real world as they are inside a real operating theatre, and at the same time can interact with the superimposed virtual information, in this case a virtual patient on the operating table.

The use of these technological resources as complementary medical training materials is very useful for medical students' learning and for the acquisition of practical skills. The students show a high level of satisfaction when incorporating these technological tools into their educational practice and perceive them to be really useful.

As a final example of the role played by these techniques in medical training, Figure 7 shows a developed learning system in cardiac auscultation, under augmented reality environments. The environment recreated using mannequins along with the Epson's Moverio BT300 AR glasses, which allowed the user

Figure 6. Virtual surgical approach experience, inside a real operating theatre recorded in 360 degrees. The user practises a whole protocol that is carried out in this type of surgical intervention



to locate the usual auscultation points and listen to the noise of the specific auscultation focus (mitral, tricuspid, aortic and pulmonary). This technological procedure is very useful for users (students) to learn how to find the specific auscultation foci and how to recognise normal and abnormal sounds associated with different heart diseases for each possible auscultation focus. In addition, users can practice this situation as many times as they want and at any time, without causing any discomfort to the patient.

Figure 7. Experience of cardiac auscultation under augmented reality environments with Epson's Moverio BT300 glasses. The system allows to see through transparency the intercostal spaces where to place the stethoscope for the analysis of the different cardiac sounds



It has to be noted, however, that the immersive glasses have caused slight subjective discomfort in some users, such as dizziness or tiredness, loss of balance users, as well as visual disturbances. It is therefore advisable to limit their use to short sessions to improve the adaptation of user to the device.

The students of medicine and other health science degrees who used these learning technologies welcomed these immersive teaching contents with great interest. In many cases, students improved their academic results, not only because the technology allowed them to assimilate the contents more easily, but also because they felt more motivated to study (González et al. 2017, 2019, 2020).

These virtual and augmented reality technologies are applicable to any medical speciality (anatomy, radiology, cardiology, surgery, etc...) as has been shown in the presented examples; they are therefore good complementary resources in medical training and in daily clinical practice. The possibility of carrying out clinical simulations based on these virtual and augmented reality technologies undoubtedly improves the training process and increases the acquisition of skills necessary for subsequent clinical practice. Many of the applications developed and applied to medical education have been considered by students to stimulate their attention, concentration, immediate memory and reasoning.

CONCLUSION

Augmented and virtual reality technologies have a long way to go, offering great opportunities for medical education. In this chapter, different ways of applying these technologies in the medical field have been presented: from medical learning procedures focused on the teaching of human anatomy, as well as other more complex developments based on technological tools for medical-surgical practice, both for exploration and surgical approaches. Several authors have developed and applied technological procedures based on virtual reality and augmented reality techniques in the field of medicine (Konishi et al., 2005; Levinson et al., 2007; Stadie, 2008; Ferrari et al., 2009; Blum et al., 2012; Nakamoto et al., 2012; Albrecht et al., 2013; Bressler & Bodzin, 2013; Kilby et al., 2013; Ruthenbeck, 2013; Bifulco et al., 2014; Kramers et al., 2014; Monkman & Kushniruk, 2015; Wang et al., 2016).

In the province of health sciences, these technologies can become useful tools for daily clinical practice, as well as providing information that allows a better understanding of the clinical activities, reduce risks and, most importantly, provide healthcare professionals with new approaches for clinical practice. For example, the adoption of these technologies can lead to a reduction in surgery time, minimize risks to patients, or revolutionise diagnostic imaging tests by providing information in real time.

A well-trained student will undoubtedly perform better clinical and healthcare work, reducing risks, and thus improving patient satisfaction. For this reason, the use of VR and AR techniques as clinical training mechanisms turns out a promising approach in the field of health sciences. The recreation of virtual clinical scenarios, close to reality, opens the door to more precise practices with fewer associated complications, as well as more practical and dynamic learning (González Izard et al., 2017; Escalada-Hernández, 2019; González Izard et al., 2019; González Izard et al., 2020).

Most of the applications currently being developed with these technologies are aimed towards the basic training of healthcare professionals, using different technological systems and devices. These applications are focused on visual learning of the insides of the human body, practising basic clinical explorations with three-dimensional images, as well as visual learning of different types of wounds, among others. Using these techniques in medical education for learning of human anatomy allows medical students to

improve their academic results, not only because the technology makes it easier to assimilate the content, but also because they feel more motivated to study (Briz-Ponce et al., 2016; Briz-Ponce et al., 2017).

These technologies respond perfectly to the training needs in the field of medicine. Thanks to these technological procedures, students of medicine or other health sciences can repeat the training of a clinical situation as many times as necessary, put into practice different exploratory tests, different surgical protocols and methods, analyse different pathologies, and visualise the different body organs in three dimensions and from different angles, thus avoiding the initial practice with real patients. In this way, the student is training and acquiring the necessary skills for the practice of their profession, for when they have to face real patients.

As virtual reality and augmented reality techniques gain maturity, the health sciences field has made use of such advances (Nikou et al., 2000; Henn, 2002; Konishi et al., 2005; Ullrich et al., 2008; Stadie, 2008; Scalese et al., 2008; Lamounier et al., 2010; Kramers et al., 2014; Soeiro et al., 2015; Kilgus et al., 2015; Pensieri & Pennacchini, 2016; Lim et al., 2017; Hanna et al., 2018). However, in most cases, these are pilot applications that have had a lot of media coverage. (Escalada-Hernández, 2019).

It seems clear that these technologies are obviously promising in terms of their foreseeable results, as shown by several authors (Greenhalgh, 2001; Griswold et al., 2002; Van Dam et al., 2002; Sung et al., 2005; Albrecht et al., 2013; Chang et al., 2013; Cuendet et al., 2013; Häfner et al., 2013; Chiang et al., 2014; Escalada-Hernández, 2019).

Among the main benefits of employing virtual and augmented reality in health sciences are: the reduction of experimentation costs during learning and practicing; practice with real patients would also be avoided; any test or clinical exploration could be repeated as many times as desired so that the user would have good clinical training; greater experience would be offered in the management and control of the different pathologies and complications; and the risk of the operation and post-operative treatment would be analysed with greater accuracy. In addition, as the field of virtual and augmented reality gains maturity, more useful applications are available for low-cost devices, for example using mobile phones for learning how to perform electrocardiogram (ECG) tests or ultrasound scans (Erkoyuncu, et al., 2013; Bifulco et al., 2014).

These technological environments of virtual and augmented reality, applied to medical training and clinical practice, will undoubtedly evolve in parallel with society, so that the teaching needs in medicine will drive technological progress and this will in turn lead to changes in educational models. The education-technology binomial will be one of the basic pillars for the development, growth, and progress of the health sciences field.

Although the technology is mature enough to be useful in training environments in the field of medical sciences and other health science disciplines, new developments in virtual reality and augmented reality technologies will lead to a new generation of applications and students, who will complement their learning with the use of these training and clinical practicing devices.

FUTURE RESEARCH DIRECTIONS

Virtual and augmented reality resources enrich and facilitate the transmission of didactic content, favouring medical training. The use of these mobile and immersive approaches allow students to manage their knowledge, developing new forms of teaching/learning innovation. These applications encourage student learning, promoting a more participatory approach. The use of virtual and augmented reality in

the university is beginning to change learning habits, opening new paths in medical training. The very characteristics of these technological developments encourage student involvement in learning through direct interaction with teaching content, making them excellent resources for medical training and for the acquisition of practical skills.

The use of these technologies provides with learning scenarios that are more motivating, collaborative, interactive, and help to make medical training more open and creative. These technological resources allow teaching content to be presented in a more dynamic and realistic way, thus making training more attractive, innovative, and motivating for students. In this sense, the technological applications under these virtual reality and augmented reality procedures, aimed at medical training, facilitate the performance and learning of many techniques and clinical explorations, as they bring the theory closer to the student and future professional in the areas of health sciences, allowing interaction with these technologies in a more practical and visual way. Therefore, students of any area of health sciences can be trained as if they were in direct contact with patients.

In the authors humble opinion, it turns out necessary to incorporate these technologies and their use in university classrooms, since, in addition to serving as new means of conveying learning, they make it easier for students to acquire the necessary skills for their correct and appropriate professional development. In this sense, universities should play an important role as promoters of the new technological competences and curricula that future professionals will have to acquire through in their academic, personal, and professional development.

The aim of this work is to provide a current overview of the use of VR and AR techniques in the training of students in the different areas of the health sciences, and to present some practical examples developed by the authors' working group. By showing healthcare professionals some very useful teaching tools that facilitate and improve learning and university training, the main objective is that these VR and AR technologies will be incorporated more widely in university environments, favouring the training of future health professionals, and also benefiting the patients. However, there is still work to be done in the research and incorporation of these new technologies in medical training, as the wide variety of techniques used in the different specialities of the health sciences constitute a broad field of work, where VR and AR techniques can offer very interesting and useful possibilities in the training of university students.

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Chapter 13

The Role of Data in Health Sciences Ecosystems: Experiences Within a Psychoeducation– Oriented IT Platform

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ABSTRACT

This chapter aims to provide an overview of the importance of data governance in digital ecosystems in the province of healthcare and to place special emphasis on the significance of taking business processes into account from the early stages of development of this type of solution. It should be borne in mind that business processes are not only those that produce economic benefits, but also those that provide added value for the entire ecosystem and make it sustainable over time. The chapter ends by exemplifying the above discussed approach in a specific use case of a platform initially conceived for the psychoeducation of formal and informal caregivers. Said platform has been conceived using a business process modelling approach focused on data exploitation from the early stages of development, which has allowed services, stakeholders, and potential users of the ecosystem to be extended far beyond the initial ecosystem goal.

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INTRODUCTION

In the digital transformation that most organizations and countries are undergoing, data plays a key role. In fact, the technological revolution brought about by the new digital era pursues an adaptation to the new way of doing business that, both at a technical level and in terms of organizational culture, poses great challenges to companies and administrations.

As a strategic asset of any kind of organization, data are essential in this massive digital transformation effort. Information systems in complex environments, such as health, have a data-intensive component that requires merging, synthesizing, representing and visualizing data with interfaces so users can interact and employ data for high-impact decision making. All data management processes, from acquisition to visualization, should be carefully considered for exploiting health ecosystems strategic value.

Far from offering a partial view of the end user, when launching digital transformation processes they should be oriented towards a more complete view of the end user. It is not so much a matter of enriching information from a traditional point of view, but of broadening the vision by applying a sociological perspective. The goal is to know their needs in a personalized way, transcending the typical segments to provide appropriate responses to the reality of each one of them. At this point, data management requires strategies that target a people-oriented vision, leaving the product in the background.

Within this approach, optimal data management requires an integration of information that strikes a balance between the internal and external spheres of the health ecosystem. A well-known fact within the business province is that the success of tactical actions depends to a large extent on their implementation from a global vision. However, this approach is generally omitted when developing ecosystems in the health sector domain, as they are usually focused on providing services for the patient end user but forget the rest of the stakeholders when it comes to ecosystem exploitation. In addition, health ecosystems commonly start from small projects with a view to scaling up, but technology decisions are not aligned with a defined IT strategy. Ultimately, this strategy should be framed by data governance in line with the ecosystem goals, with a strong end user focus.

Within health ecosystems, aligning organizational objectives with technological capabilities is the big challenge. Fundamentally, it is essential to adapt processes accordingly, as well as to guarantee data quality, integration, adaptation to the digital ecosystem security and strategic use. This is a complex process that requires a great deal of effort and involvement from the entire ecosystem actors. Striving for it is the key to developing health ecosystems that success after deployment. Among other advantages, it not only allows to drive research initiatives more efficiently, but also to use analytics to respond quickly and accurately not only to end users but to all ecosystem actors' needs.

Within the health sciences environment, it is important to effectively carry out the necessary transformation to change the business model by taking advantage of the benefits offered by technology.

BACKGROUND

Digital health is one of the most important challenges in the province of healthcare. Major international bodies such as the World Health Organization are strongly committed to the potential of data and digital technologies to solve health problems. The Organization's Global Digital Health Strategy (2020 - 2024) promotes improving people's health through the incorporation of digital solutions as to involve and engage the participation of all stakeholders in digital health. As an example, during the last decade the

European Union has invested heavily in R&D by funding several proposals for platforms focused on the healthcare sector that has given rise to some open source solutions: LinkSmart (Lamprinakos et al., 2015), OpenAAL (Wolf et al., 2010), UniversAAL (Hanke et al., 2011), Net4Care (Christensen & Hansen, 2012). However, these early developed solutions were mainly focused on providing software media and ontologies for the integration of different telehealth medical devices following standards.

Taking the private sector into account, digital health is a very promising market, using existing resources and developments available in the cloud. Thus, large companies such as Microsoft (Microsoft, 2021) or Philips (Philips, 2021) have been developing their health service platforms in recent years. Other examples of commercial platforms are: Salesforce Health Cloud (Salesforce, 2021), OpenTeleHealth (OTH, 2021) or DXC Open Health Connect (DXC, 2021). As a concrete example of the opportunities that arise in the exploitation of data and digital technologies in the health sector, the latter solution from DXC has recently (April 2021) been sold to the privately held Dedalus Group for about \$450 million.

Information systems in complex environments, such as health, have a data-intensive component that requires merging, synthesizing, representing, and visualizing into interfaces with which users interact for high-impact decision making. All data management processes, from acquisition to visualization, therefore take on an essential role in exploiting their strategic value.

In recent years, technological ecosystems (Kapoor et al., 2021) (Senyo et al., 2019) (Marcos-Pablos & García-Peñalvo, 2019) have emerged as an evolution of traditional ICT technology platforms. The concept of technological ecosystems is based on biological ecosystems, promoting the interaction of a set of actors on a common technological platform that results in a series of solutions or services. Based on this biological foundation, one of the fundamental characteristics of technological ecosystems is their ability to evolve, allowing for the rapid development of new capabilities and fostering innovations that may be unforeseeable by the original platform design. The evolutionary nature of technological ecosystems allows to evolve from simple or fragmented, patient-centric services into highly complex integrated services provided by multiple stakeholders through well-elaborated collaboration mechanisms.

A recent systematic review focused in Technological Ecosystems in the province of Care and Assistance (Marcos-Pablos & García-Peñalvo, 2019) identifies the following opportunities of delivering health through technological ecosystems: remote access to the relevant care records, more effective and assisted clinical decision making, real-time monitoring of structured patient care delivery and opportunity for patient, family and informal caregivers participation in health and care processes. In addition, all the data that could be extracted from the ecosystem information exchange (considering privacy and security issues) allows the establishment of new business models that could attract other stakeholders even not directly related to the health and care provision.

However, the same review shows that there are still many challenges and gaps that need to be fulfilled for providing the above opportunities in a consistent way, as the maturity of many technological ecosystems in the health sector are far from their relatives in other areas. In general terms, the main ecosystem architectures employed in the health sector are cornerstone and infrastructure-based ecosystems. This means that these ecosystems are generally built around a central IT platform, where the governance of the ecosystem and the ecosystem's data is highly centralized. This often results in a lack of means to model the inclusion of new software and hardware developments that do not follow the templates provided by the ecosystem software orchestrator, hindering the incorporation of new potential stakeholders.

The beforementioned gaps have a negative impact on the ecosystem business model. In these types of ecosystems, the business structure is generally omitted and merely relies on existing business models developed for other fields such as software-based ecosystems. The business processes are only oriented

towards providing health services to the patient, causing a lack of involvement of additional stakeholders in the ecosystem development, which in turn hinders data exploitation capabilities. This final-user-centric model, rather than stakeholder-centric, makes it complicated to develop business models once the platform has been implemented and to attract other ecosystem actors. Thus, business processes are reduced to patients and families care providers (individuals or organizations) using the ecosystem services. However, scarce attention is given to other business processes such as: IT support and maintenance; providing training for end users, health professionals or health-technology developers; develop ecosystem data and analysis tools (such as dashboards) for health managers; or even allowing third parties to incorporate non-health specific added services.

As the key for information systems no longer resides in their internal infrastructures, but in extracting insights from the data, it is increasingly necessary to actively being able to adapt health ecosystems' business processes and services to allow exploiting digital health (Mahajan et al., 2021). This includes facing two fundamental challenges: the immense variety of data sources available, and the wide variety of types of data to be integrated (from the most structured, such as clinical data, to the most unstructured, such as social networks) (Vo et al., 2021). Exploiting health data requires a well established data governance, which in turn relies on a good organizational ecosystem structure. However, as for many health ecosystems, there is also a lack of an organizational structure to govern the ecosystem data, which has a negative impact when it comes to attracting stakeholders such as health authorities and governmental organizations (Christensen et al., 2014). Although the process of delivering health and care is quite generic, complex digital health services are difficult to generalize due to different factors such as geography, legislation, demographics, patients' health, or social conditions, etc. Health ecosystems rarely consider this variability from an organizational perspective. They do not provide the necessary links between the software and business structures, and lack of an adequate organizational structure to govern the exchanged data. To mitigate these issues, health ecosystems should feature a high degree of modularity while using established standards, and consider other aspects such as data ownership, security, privacy etc. (Kanwal et al., 2021).

The above gaps can be seen as opportunities for enhancing current health ecosystems and data exploitation models, applying big data paradigms to capture a more realistic view of digital health. Links between health provision, software and business should be established from the very beginning of ecosystem development, incorporating the organizational and business structures during meta-modelling the ecosystem software structure and taking them into account in the data health specific ontologies could help to reduce these gaps.

In addition, further research is needed to develop tools that allow the evaluation of the ecosystems' performance with metrics conceived for the health sciences data monitoring (Marsch, 2021). Furthermore, means to make this data available for third parties should be studied (considering interoperability, security and privacy) so that they can exploit them and increase the business model and the value chain. Finally, incorporating and standardizing training actions for care provision, adding new services into the ecosystem, new devices, new software and instructions on how to use all the available tools, should be approached in order to attract not only end users but also third-party developers.

DIGITAL HEALTH ECOSYSTEM IN A NUTSHELL

The adoption of digital health by the traditional actors in the health sector clearly depends on being able to show the value of managing and exploiting data within the health ecosystem. To this end, ecosystem stakeholders need to attain an understanding of the health ecosystem. A good definition of health ecosystem is given by Iyawa et al.:

A network of digital health communities consisting of interconnected, interrelated and interdependent digital health species, including healthcare stakeholders, healthcare institutions and digital healthcare devices situated in a digital health environment, who adopt the best-demonstrated practices that have been proven to be successful, and implementation of those practices through the use of information and communication technologies to monitor and improve the wellbeing and health of patients, to empower patients in the management of their health and that of their families. (Iyawa et al., 2016)

To adopt and implement the best-demonstrated practices that have been proven to be successful in other fields, it is necessary to clearly define what the different components of the ecosystem are, how these components interact with each other, and the ontology and semantics of the data that originate from this interaction. The following sections summarize the main characteristics of health ecosystems.

Health Ecosystem Types

In general terms a digital ecosystem is a widespread type of ubiquitous computing environment comprised of different actors, technologies, and services. Digital health ecosystems can be conceived as a subdomain of digital ecosystems, and since it exhibits the same features as those in the digital ecosystems, we can classify health ecosystems adapting classifications employed in other domains, such as the one of digital software ecosystems given by (Knodel & Manikas, 2015). As such, we can distinguish between four types of ecosystems:

- **Cornerstone Ecosystems:** where actors interact on top of a common software platform and usually extend the platform's functionality. Thus, the existence of a technological platform is of central importance for an ecosystem of this type. The structure and governance of this type of ecosystem is usually centralized.
- **Standard-based Ecosystems:** where instead of a common platform, the compliance to standards is the key requirement for contributing to the ecosystem. Usually, compliance to standards is set above the functionalities and concrete realization of the contributions.
- **Protocol-based Ecosystems:** where a protocol API is shared among all actors, providing more flexibility over technical contributions to the ecosystem. Protocols are a less restrictive and more flexible than standards and are usually independent from technology. However, they provide the necessary predefined specification of interaction within actors (e.g., exchange of data, call to software services, etc.).
- **Infrastructure-based Ecosystems:** where a common technology is shared among all actors, providing tools at development time but at the same time maintaining independence on the contributions. Usually, the interaction among actors is on a social level.

Health Ecosystem Structures

Three main structures can be distinguished within digital ecosystems (Christensen et al., 2014) are:

- **Software structure or technological structure:** the structure of software elements and devices that form the core of an ecosystem.
- **Business structure:** how ecosystem actors create value (in a for-profit or nonprofit manner).
- **Organizational structure:** how the interaction and organization of actors and software are governed, which is in turn related and dependent on the ecosystem architecture (e.g., for an actor to provide care services in the ecosystem).

At first glance it may seem that these structures are completely decoupled. Therefore, these structures are often developed by different departments or even different organizations and then integrated into a complete solution. However, it can be intuited how exploiting data in a health ecosystem depends on the three structures simultaneously. The software structure will determine the capabilities to extract, store, share and analyze the data in the ecosystem. The organizational structure will oversee data governance, which in turn will depend on the capabilities that the technology and software structure can offer. Finally, the business structure will determine what data is of interest to the different stakeholders in the ecosystem, and what processes of interaction between the actors will be in place to deliver the desired services to obtain a final system that is both profitable and attractive to the different stakeholders.

Health Ecosystem Actors

One of the main distinctions of digital ecosystems resides in the strong involvement of the different ecosystem actors in value cocreation. For that reason, data exploitation in digital health ecosystems needs the correct classification of stakeholders so to identify the ecosystem's relevant data subject to exploitation.

Ecosystem stakeholders' clustering into different groups and their nomenclature has been revisited over the years in different fields. The business environment was the first to worry about the correct typology and classification of stakeholders. Within business, stakeholders' clustering into different groups and their nomenclature has been revisited over the years (Sirgy, 2002), but has generally described three fundamental groups:

- **Primary stakeholders:** have direct involvement in the business activities (i.e. production, management and processes).
- **Secondary stakeholders:** are groups of beneficiaries that influence the success of the activities of primary stakeholders.
- **Tertiary stakeholders:** whose interest arises from indirect benefits from the business. Among tertiary users two subgroups are generally particularly considered: public and government entities. Public entities provide a critical insight into the activities of a business, based on the benefits or risks of its processes on the community. Government entities have the mission to protect and promote the generated value.

Parting from this classification, other stakeholders clustering proposals have been made in the field of health and care ecosystems. For example, in the province of AAL (Ambien Assisted Living), which

focuses on making senior users' lives easier and more independent through AI (Ambient Intelligence) based solutions and computing environments and systems, three fundamental types of stakeholders can be distinguished (Nedopil et al., 2013):

- **Primary end-users:** person who is using a product or health service.
- **Secondary users:** people or organizations that are accessing or using the ecosystem solutions for the benefit of primary end-users. This group benefits directly from AAL products or services by they use, and indirectly when primary end-users' needs for care are reduced (e.g. (in) formal caregivers, family members, care organizations).
- **Tertiary final users:** institutions and private or public organizations that are not directly in contact with the AAL solution, but that in some way contribute and benefit from their organization, budging or assessment (e.g. organizers of public sector services, social security systems, insurance companies, etc).

If considering the ecosystem technological infrastructure, the stakeholder clustering should incorporate additional groups or subgroups of stakeholders. If considering software ecosystems as a reference, five main stakeholder roles can be distinguished (Suortti, 2017):

- **End User:** Person, company, an entity that either purchases or obtains a complete or partial product of the ecosystem or a niche player.
- **Support Service Provider:** help and enable other ecosystem actors to achieve their goals (e.g. internet service providers, research and consulting companies and hardware suppliers).
- **Orchestrator (keystone):** responsible of the ecosystem governance (e.g. software platform management, actor relationship management and ecosystem health monitoring)
- **Third-party organization:** use the central technology as a platform for producing related solutions or services. They can be sub-based on:
 - Niche Player: responsible for ecosystem innovation and value creation. They develop specialized extensions to the platform and are motivated by business opportunities.
 - External Developer: provides indirect value to the ecosystem through its usage.

Health Ecosystem Data

Digital health systems have evolved from only putting patients at the center of the system to meet their needs, to including technologies that facilitate the recording and exchanging of information in interoperable systems, so that data can be shared between all ecosystem stakeholders. In fact, the strength and future of such solutions lies in developing new means of exploiting the potential of big data, that is, the use of large and wide-ranging amounts of data to enable knowledge discovery and better decision making (Mayer-Schnberger and Cukier 2013). Working with big data involves making use of technologies and tools from a wide variety of disciplines, such as those from text analytics, business intelligence, data visualization and statistical analysis (LHeureux et al. 2017). However, in many cases improving traditional methodologies or creating them from scratch is needed to get the most out of such data.

From a strictly health and care perspective, the strength of digital health lies in exploiting the interaction of data in order to understand how their interactions might be used to both prevent and treat diseases.

The goal is to explore how combinations of these data might be used to early diagnose the disease and monitor its prevalence within populations. Health data can be classified into:

- Biological
- Clinical/medical
- Social/environmental

Examples of biological data include: RNA and protein expression profiles (Catalina et al., 2020) (Wu et al., 2020), genetic information about healthy and disease-affected individuals (Whelan et al., 2020) (Aguir de Sousa Diana & Katan Mira, 2021), epigenetic data (Karađuzović-Hadžiabdić & Peters, 2021) (Sarno et al., 2021). These data can be acquired from different sources, such as cellular or animal models or human tissues, in which case is often linked to pseudonymized clinical data.

Clinical or medical data typically contain information about symptoms; diagnostic; rates of disease progression (Mahajan et al., 2021); types of treatment given for the disease of interest or for other diseases; the impact of that treatment; the presence of other illnesses and factors. In fact, clinical data are complex multimodal data by nature, and need to be acquired for a large number of cases and controls (Marsch, 2021). Population-based clinical data is generally accessible on much larger numbers of individuals than biological data, such as datasets of medical records or population-based epidemiological studies. However, these data are usually not integrated with a deep biological characterization, and therefore methods for inferring important data must be developed.

In addition, new efforts for correlating social and environmental data with clinical and biological data need to be developed. Some of these items such as socio-economic status, exposure to various environmental risks, diet, smoking, occupation, cognitive engagement, or exercise are already known to impact risk and/or progression of diseases. As so, the information content of social and environmental datasets is starting to being coupled with clinical and biological data, to explore the correlation between factors in disease prevention, diagnosis, and treatment. Potential sources of data are already available and extensively used for other purposes, such as mobile phone, Internet, or social media usage. These data likely contain information about lifestyle (e.g., diet, alcohol and cigarette consumption, exercise, etc.). In addition, changes over time in the complexity of some parameters such as social engagement can reflect changes in physical and cognitive activity that might describe the early stages of different diseases.

Linking biological and medical data to population-based data provides several benefits and opportunities in health and care provision. These benefits have a direct impact into primary and secondary ecosystem end-users:

- The development of a deeper and better understanding of the broad disease categories and patient population subsets.
- Specific understanding of the correlation between diagnostic criteria and patient subsets.
- Specific and better understanding of risk factors for disease development, potentially accelerating the development of preventive therapies.

In addition, data exploitation through digital health provides other benefits that could be exploited by other stakeholders, such as tertiary end-users:

The Role of Data in Health Sciences Ecosystems

- Optimizing the use of approved symptomatic therapies, as well accelerating the discovery and development of disease modifying agents for the indication.
- Better understanding of the health economic impact by disease category and patient sub-type, which would provide additional incentives to public and private sectors to invest in research.
- Create new business opportunities for non-pharmaceutical-based approaches to risk factor modification.

Apart from data strictly related to health and care provision, several other non-health-related data that arises from the ecosystem can be of use to other third-parties organizations and service providers. In fact, as digital health relies on a software infrastructure, software business models and approaches to data exploitation can be considered in order to enhance the ecosystem revenue and attract additional stakeholders. For example, in cornerstone ecosystems software providers will be interested in obtaining relevant data on the use of the digital platform for monitoring system performance. Furthermore, as primary and secondary users will seek data that can be easily consumed, they would likely need service providers or data intermediaries. This necessity attracts specialized roles related to data provision, such as data analyzers or data visualizers to help nonspecialized in the data consumption process. Also, as software and technology providers help to promote the interoperability of data and services, developers of medical hardware and software solutions (e.g., orthopedics, biomedical measuring systems etc.), can benefit from data on the evolution of patients as a result of the use of their devices or services.

A PRACTICAL APPROACH TO DIGITAL HEALTH DATA EXPLOITATION

In this section we present an example of the development of a technological ecosystem in the province of health, taking into account the business processes involved in the exploitation of data so that the ecosystem can be sustainable over time.

The starting point is an already developed generic framework of a technological ecosystem developed as support of services for the management of corporate knowledge. This framework has been set up in different environments (García-Peñalvo et al., 2018) (García-Holgado & García-Peñalvo, 2019), mainly in the province of e-learning. From a technological point of view, the framework allows the complete design and development of a technological ecosystem platform, in line with state of the art in software architectures. It has a strong evolutionary component whose architecture can be valid for different contexts, and that allows the integration of other software tools, as well as the development of new services that provide added value to the ecosystem.

Said framework has been successfully adapted to the care domain with the objective of providing comprehensive and remote support for the needs of formal and informal care providers (e.g., family members) of dependent older people with dementia. The aim was to provide a platform that allows (in) formal caregivers to develop and enhance their caregiving competences, as well as to mitigate the negative effects produced by caregiving activities such as physical and mental stress and social isolation.

The proposed framework adaptation has been incrementally developed, using a cornerstone architecture but considering the three main ecosystem structures, namely software, business and organizational. This approach proves the importance of modelling the business and organizational structures alongside the technological infrastructure during early stages of the ecosystem development. Thus, rather than a purely patient-centric approach looking for a “business-first” revenue (traditionally followed within health

ecosystems), the software structure is directed by the business structure, but the business processes are determined by the software components and the actors added value chain and organizational relationships. Software components build the technological infrastructure as the core of a software ecosystem. Second, the organizational structure governs the interaction and organization of actors and software, providing means to develop software-based services in the ecosystem. Finally, the business structure allows actors to create value within the ecosystem.

The initial framework's software structure is organized into four layers:

- Presentation layer: in charge of providing means for the use of ecosystem services by users inexperienced in the technology.
- Services layer: aims to provide different services to users. Initially considered services were a learning platform, a social network to exchange experiences and a dashboard for data visualization.
- Data Management layer: provides tools for storing and processing the data, a common ontology and semantics as well as mechanisms for data governance.
- Infrastructure layer: provides a set of services that are used by the software components from other layers.

In order to adapt the existing framework into a care ecosystem, the first step was to analyze the ecosystem's value propositions:

The motivation of actors to participate and engage within a medical ecosystem arises from the reciprocal benefits, namely the value propositions that variant types of actors within the ecosystem offer and seek (Litovuo et al., 2017)

To investigate the value propositions, the Business Model Canvas (BMC) developed by Osterwalder and Pigneur (Osterwalder & Pigneur, 2010) was employed. The BMC is a strategic management template used for developing new business models or documenting existing ones. It offers a visual chart for a global description value propositions, infrastructures, actors, and relationships. Osterwalder's approach has proven to be a valuable tool for describing not only commercial business models, but also in many other contexts including health-related ecosystems (León et al., 2016). Figure 1 shows the BMC of the ecosystem.

The second step was modelling the business processes that occur within the ecosystem, taking into account the expected actions that the main actors would carry out. The primary users are mainly (in) formal caregivers and patients. Caregivers sought value is to increase their caregiving competences. Although in this case patients are generally passive beneficiaries, they can contribute content within the social network, either directly or indirectly through their caregivers. A general use-case for a particular caregiver is shown in figure 2.

The definition of a generic use case as shown in Figure 2 allows identifying data that will be relevant for the exploitation of the ecosystem. The data mining is based on the interaction of users with the social network and the teaching-learning platform. The use case starts with an onboarding of new users (caregivers) into the platform. During this onboarding users are requested login data. The possible data requested during the onboarding includes:

The Role of Data in Health Sciences Ecosystems

Figure 1. Business model canvas of the ecosystem

Key Partners 	Key Activities 	Value Propositions 	Customer Relationships 	Customer Segments 
-Health and care authorities -Public & private hospitals / care institutions -Research institutions -Platform supplier -Platform operator	-Platform design, development, operation and maintenance -Psychoeducation eLearning content definition, development and update -Identification of relevant data from the application of care and psychological activities through the ecosystem -Ecosystem KPIs definition, analysis and visualization	-Improve quality of life of patients and (in)formal caregivers -Improve quality of care -Reduce care provision costs -(in)formal caregivers' accessibility to psychosocial programs and personalized learning itinerary -Social communication and support (relatives, informal caregivers, professional care networks) -Data and analysis for the evaluation of the different care or psychological action protocols -Psychological disorder evolution and trends analysis (personal, geographical, etc.) -Data and analysis of ecosystem usage, user needs and trends -Possibility of incorporate new services or modify existing ones through the ecosystem functionalities	-Psychoeducation training program -Professional medical and care contact -Training on platform usage -Platform content and services updates -Third-parties publishing of care-related services	-Patients/Families -Health & Care providers -Public health authorities
	Key Resources  -Ecosystem contents: social network, eLearning platform, mail, dashboard -Hosting infrastructure -Software development expertise -Expert personnel on data analysis / visualization -Expert personnel on psychoeducation and eLearning		Channels  -Regional/National health contacts -Care institutions & care networks contacts -Social Networks -Web	
Cost Structure 		Revenue Streams 		
-Communications infrastructure -Platform development and maintenance -Platform hosting -IT personnel -Health personnel		-Clients using ecosystem services -IT support and maintenance -Training for clients -Provide ecosystem data and analysis tools -Third parties publishing their care-related services		

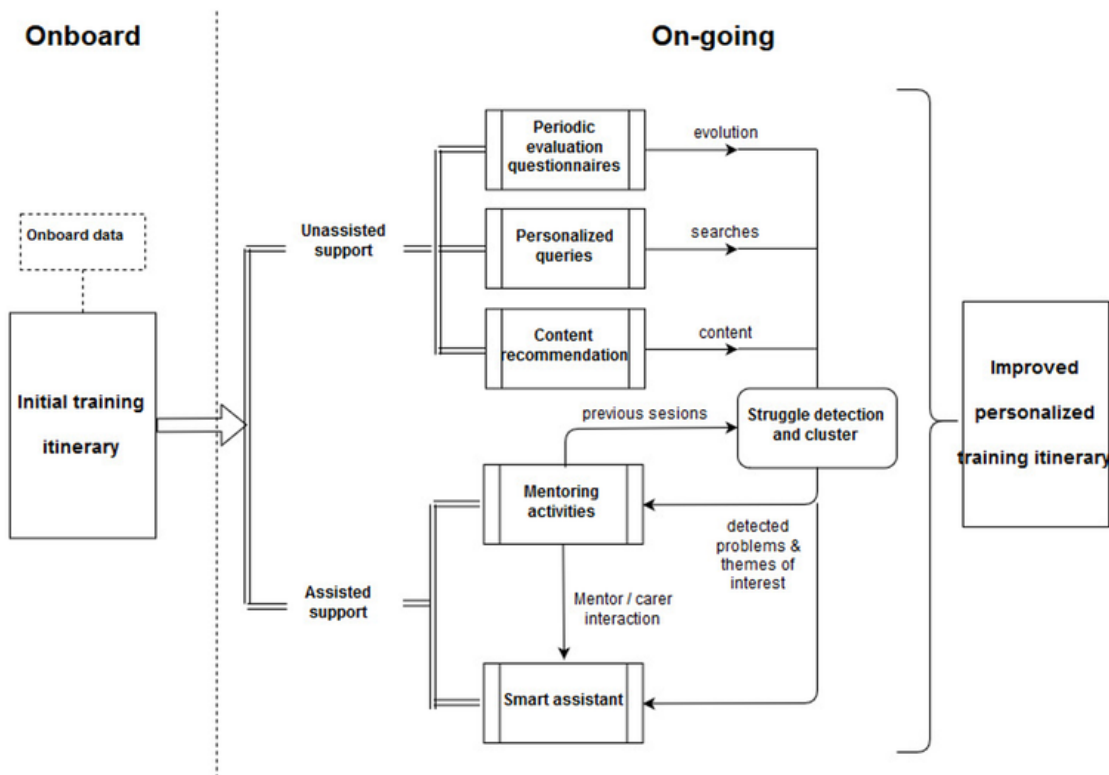
- Caregiver profile: ethnographic and geographic data (age, health status, geographic location), previous caregiving knowledge, family situation (e.g. number of hours spent per day on caregiving).
- Patient profile: ethnographic and geographic data, clinical data (based on the caregiver knowledge

During the ongoing stage, the caregiver can choose between two paths:

- Unassisted support: using tools that allow the user to follow his own learning path without mentoring: evaluation questionnaires, personalized searches, and content recommendation.
- Assisted Support: either provided by experts in the mentoring program that support the caregivers in scheduled sessions or through the social network, or through a Smart assistant that is nourished from the ecosystem interactions answers questions 24/7.

During the onboarding stage, data can be directly collected from the primary users, including ethnographical data and clinical and medical data. These data can be crossed with other patients' databases, provided that they are accessible. This set of data and their interaction with other sources (to a greater or lesser extent) is what generally takes place in developed health ecosystems.

Figure 2. Definition of a generic use case



However, greater utilization of the existing ecosystem data can be achieved by matching the activities of the primary users with the value sought by the secondary and tertiary users and vice versa. In this ecosystem, clinical and medical data can be directly combined with social and environmental data based on the primary users' interaction with the ecosystem services. These data can be extracted by combining different sources of information such as the questions, experiences and use cases shared by users in the social network, the type of teaching/learning contents sought or the training evolution of the caregiver, etc. Thus, the business model for exploiting data should focus on both the ability to extract data from the ecosystem software components usage as well as from the interaction between users:

- Health practitioners:** their main objective is to improve decision-making by identifying better treatments and discard the least efficient ones. They will seek to detect adherence to treatment, its effectiveness and finally to improve the quality of life of primary users (patients on the one hand and caregivers on the other). With this objective they may combine data obtained from the medical records, with additional knowledge of ethnographical or population-based data obtained from the social network. Although these two types of datasets are usually unlinked, the combination of medical records with other data such as socio-economic status, exposure to various environmental risks such as diet, smoking, occupation, and lifestyle factors such cognitive engagement, would result in better treatment decisions.

- **Research Networks:** their objective is to acquire new knowledge searching for new solutions to unresolved medical problems investigating the interaction of different factors within the data in order to understand: how they influence the risk for disease or disease expression; how combinations of these data might be used to diagnose the disease or monitor its prevalence within populations; and how these interactions might be exploited to both prevent and treat diseases.
- **Care managers:** care managers as secondary users will also seek to reduce costs and resource expenses. To do so they will seek to acquire data that helps them to improve learning contents, give better support in the training process and consequently improve the mentoring programs. The data of interest for this group will include the progress in the training programs, the churn rate, the number and type of questions raised during the training itinerary, the contents posted in the social network, etc.
- **Public administration and insurance companies:** they will seek for a better understanding of the health economic impact of dementia by disease category and patient sub-type, which would provide additional incentives to invest in dementia treatment and research and to look for preventive treatments. They will be interested in similar data as the health practitioners, but from a broader perspective. They will seek the effectiveness of the care and services provided, for instance from a geographical point of view, considering groups of patients rather than individuals.
- **Pharma:** in terms of drug treatment, some diseases as is the case of dementia are only susceptible of symptomatic treatment. In these cases, big data can provide a better understanding of how to best use the available therapies. The great majority of these patients discontinue therapy because of the benefit to an individual patient is not evident. Having a better understanding of how the patients respond to drug treatment would accelerate the development of novel treatments, providing means to analyze if there is a population-level benefit or a patient subset benefit to encourage the drug treatments and / or associated research.
- **Software and hardware providers:** include both service providers and the healthcare technology sector. Service providers will be interested in obtaining more relevant data on the use of the platform for monitoring system performance (time slots of maximum platform usage, technologies employed for accessing the system, etc.). From the point of view of developers of medical hardware and software solutions (e.g. orthopedics, biomedical measuring systems, etc.), data on the evolution of patients as a result of the use of their devices can be obtained from the social network (e.g., from activities carried out by certain patients with a prosthesis, questions formulated by caregivers about the use of their devices, etc.). On the other hand, they may be interested in including tutorials of their specific devices within the training itineraries.
- **Other:** given the evolutive nature of the ecosystem, the ability to extend its functionality and include new services, as well as the existence of the social network can lead to new business opportunities (e.g. specific advertising content for business focused on the elderly, such as travel agencies, etc.).

As can be seen, starting from an ecosystem in the field of health, although based on a teaching/learning environment, a broader digital health ecosystem capable of attracting a greater number of stakeholders can be achieved in a way that can be sustainable and healthy.

CONCLUSION

In this chapter we have shown an overview of the approach towards data exploitation in digital health ecosystems, so to obtain solutions which are not only focused on the patient but in other potential ecosystem actors. The importance of data and data governance in digital ecosystems in the province of healthcare is fundamental to achieving solutions that can be sustained over time, taking into account the business processes from the early stages of development of this type of solutions. To conclude the chapter, an example of an application of this approach in a health teaching-learning ecosystem has been shown.

FUTURE RESEARCH DIRECTIONS

It should be borne in mind that considering the different business processes and business model opportunities while developing the software structure, provides fundamental “constraints” or characteristics for the software structure, such as the data taxonomy & ontology, the data architecture and the data security and lifecycle, which in turn will determine the data governance and allow to establish the organizational structure. This means, however, that despite the recent interest in big data approaches, and their clear potential for providing insights into complex diseases, there are important data challenges when trying to apply the above approach for purely medical purposes. One is the uneven distribution of information content. For example, biological datasets usually have large amounts of intensely detailed quantitative information that has typically been acquired only on relatively small, often specialized, cohorts. In many instances, these subjects have been collected for specific reasons, which can make it difficult to cross-referencing information with social or environmental data. On the contrary, it may be difficult to access clinical or medical data for large population groups of ecosystem users that might more accurately reflect environmental or social data evolution.

Bigger limitations arise from the geographical scope of the ecosystem. For example, developing a cross-country or even cross-region ecosystem may produce a boost on data variability due to several factors, which include differences in the clinical data standards, treatment or diagnostic procedures applied, and even differences in the quality or reliability of data even when the same or similar measurement tools are used. They may also include differences in ethnicity, behavior, and environmental exposures. Last but not least, differences between the health and care provision policies may vary between regions, so differences in data availability, ethics and anonymization restrictions for obtaining and processing data makes data exploitation a more complex task than in conventional software platforms.

It can be seen that there are still several challenges to successfully addressing these limitations. However, digital health researchers and developers should overcome these limitations in order to transform current health provision and effectively carry out the necessary transformation to change the business model by taking advantage of the benefits offered by technology.

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Chapter 14

Computational Study of In-Vivo CT-Based FEM Application in Bone Tissue Engineering

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ABSTRACT

At present, computational methods are highly utilized by modern healthcare science. This modern technology gradually solves the complex area of healthcare science, and therefore, the upcoming treatments become more effective. Presently, in bone tissue engineering, the mechanism and different features of bone tissue are being discussed. The finite element method (FEM) gave the extra threshold to the study of bone tissue engineering. FEM method is basically a computer method of structural or mechanical stress investigation advanced in mechanics. The development of upgraded features of FEM applied with the help of the CT (computed tomography) model has enlightened a new hope in the study of biomedical and tissue engineering. The healthcare staff is provided with useful data by CT-based FEM which helps in taking further steps in medical treatment. The motive of this study is to show the improvement in the use of FEM in bone biomechanics in the last few years and also to help the medical specialists for improving the modern treatment and upcoming growth of new bone fracture fixation design.

INTRODUCTION

Currently, computational modeling methods have been playing an important role in the modern health-

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care sector, specifically bone-tissue engineering, modern regenerative medicine, etc. It can also help in analyzing the defective bone with the help of medical imaging, and also analysis of medical data, optimization, and planning of treatment, monitoring the response of the treatment (Izard et al., 2018). Different types of software like ANSYS-FEM, CAE, and ABAQUS, etc. are used to analyze the 3D image (Calderon et al., 2021) (Izard et al., 2020), stress-strain, and also important topological parameters. The mechano-regulation algorithms and FEM model helps in the simulation of different biological processes prominently, which results in further appropriate decision making. A computational method is one such method that is the junction of both engineering and medical science. Biomaterials of scaffold for bone tissue engineering can be created in various methods depending on the uses and the characteristics of the material. Maximum study into different biomaterials is based on an investigational trial-and-error method that confines the opportunity of creating differences to a particular material and studying its relations with its surroundings. As an alternative, computer-based simulation useful to bone tissue engineering can offer an additional comprehensive methodology to trial and remove the biomaterials. In the last few years in biomedical engineering system, the FEM or finite element method have been established as a functioning tool for displaying and simulation (Basafa et al., 2013). Several bone reconstructive surgery methods are mostly established on traditional, non-cell-based rehabilitations that depend on the usage of resilient materials from the external body of the patient. In contradiction of traditional resources, the area of bone tissue engineering is a multidisciplinary area that relates the codes of engineering or technology with life sciences to the progress of natural replacements that repair, sustain, or develop the function of bone tissue. The problems of biomedical and tissue engineering based on the concepts of continuum mechanics are solved by the FEM or finite element method of the computational technique (Huiskes et al., 1983). For the previous forty years, to put on the mechanical activities of bone tissue, the finite element method has been used. Though numerous validation techniques have been executed on certain anatomical spots and applying the load situations, this study focuses on the discussion of the probability of normal bone strong suit at the three core positions osteoporotic fracture measured in recent times concluded in vitro analysis (Anderson et al., 2010). Especially, the analysis of FEM is based on a technique which is known as clinical computer tomography or QCT, which is linked with another type of recent densitometry principles, areal BMD (aBMD), density, and contented of bone mineral (BMD). The clinical fractures were created in the distal radii of monotonic axial compression. Clinical computer tomography (QCT) oriented models of all these bones were prepared to simulate carefully, boundary conditions of each test (Basu et al., 1986). The finite element method displayed the minimum faults and the maximum connections in calculating the investigational strength of bone. The feature of the finite element method estimate in the bordering skeleton applying high-resolution outline CT was greater than that in the axial bones structure with whole-body QCT is because of the developed resolution of computer tomography image (Benca et al., 2019). Due to its scalar and projective nature, the execution of areal BMD correlates with the strength of bone which depends on active mode and was expressively lesser to finite element in normal compression of vertebral or radial zones which is not expressively lesser to finite element inside the active femur bone. At any of the three fracture sites, the most consistent surrogates of bone strength are offered by FE models. Generally, tissue engineering is an evolving part of biomedical engineering at the frontlines between biology and materials especially biomaterials. To design of scaffold for tissue engineering which includes various parameters that openly guidance the tissue restoration process on its microstructural apparent. To develop an effective scaffold, the growing importance is being motivated on the in-vivo and in-vitro investigation to gain the design of optimum scaffold prepared for exact use. Though, the assessment of the outcome of every particular scaffold fac-

tor on tissue restoration applying these methods needs expensive protocols or rules and long-standing investigates. A policy in recent times accepted to achieve the optimum design of scaffold contains in applying mechano-regulation and FEM or finite element method that mimic the load allocation from the microstructure of designed scaffold to the redevelop henceforward permitting the purpose of the analysis the mechano-biological impetus performing on the biological cells (Javaheri et al., 2020).

Bone is basically the most frequently studied biological matter and finite element analysis (FEA) is the computational technique that is most commonly applied for the investigation of bone biomechanical function (Bessho et al., 2007). For more than 30 years, FEA is used in the research work of bone which has a significant influence on our complex behavior of bone. Bones are organized in hierarchic order, protecting many distant scales. This study also reveals this hierarchic organization. Specifically, the main motive is on the uses of FEA, to know about the relation of the structure of bone and its mechanism at hierarchic levels (de Alcântara et al., 2019) (Poelert et al., 2013). Based distribution of the hierarchic levels, various problems have been examined with FEA, extending from medical issues connected with the quality of bone (for example – the risk of bone fracture and forecasting the strength of bone) to more major issues related to the mechanical features of biological procedure (for example – pressure and tension surrounding osteocyte lacunae). The scaffolds introduce biological practices which include vascularization and the construction of ECM (extra-cellular matrix); additionally, the mechanical loads on it is being resisted by the scaffold and then transmit to the nearby usual tissues (Sabet et al., 2016). A multidisciplinary method is required by the scaffold design for the directed restoration of thin tissue. To discover the optimum factors leading the act of bone scaffold, FEM or finite element method and mechano-biology can be applied in an incorporated method.

FEATURES OF FEM IN BONE TISSUE ENGINEERING

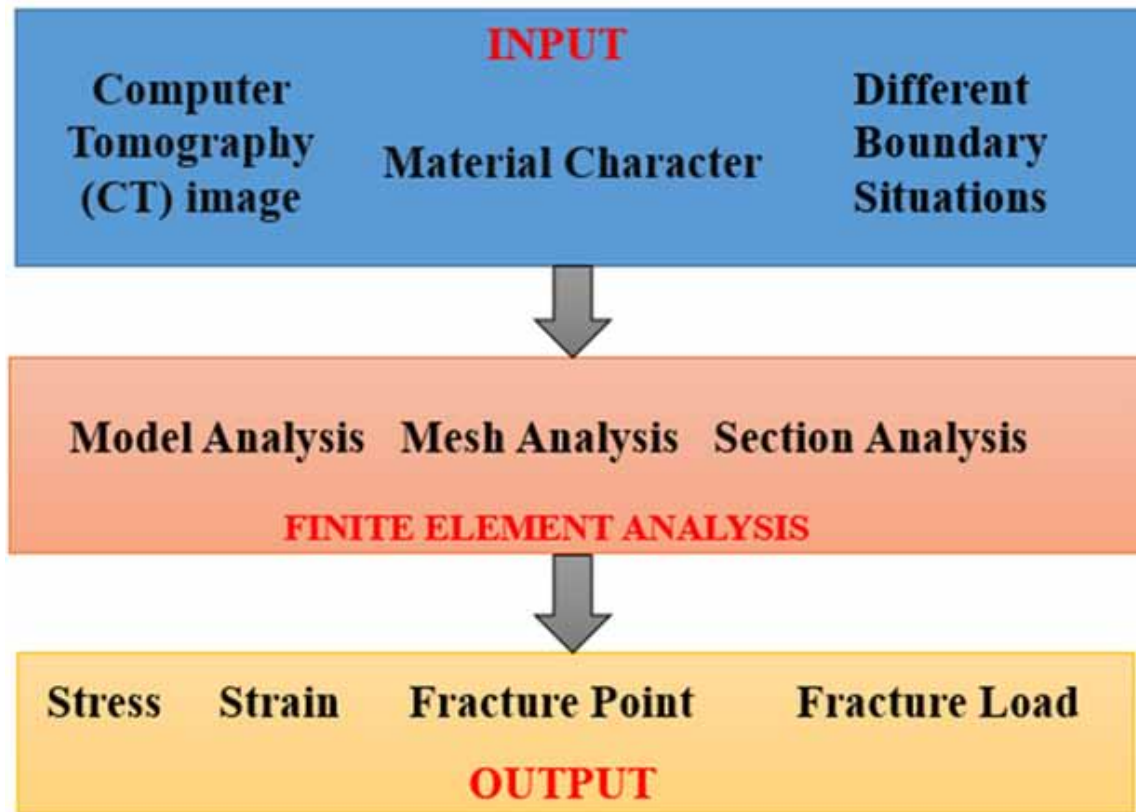
The study of tissue engineering, specifically bone tissue is a developing part of biomedical and tissue engineering at the boundaries between biomechanics and biomaterials (Brown et al., 2014). CT/FEM for human bones are categorized in three different steps, they are as follow, initial, resolution, and result (Poelert et al., 2013). In Figure 1, the stages are explained in brief. FEM or finite element technique is a mathematical method that provides imprecise explanations to PDE or partial differential equations that typical problems ascending in engineering and physics, in addition to integral equations form. The solution methodology is constructed either totally removing the differential equation for example steady-state problems, or interpretation the partial differential equations into an approaching method of ODE or the ordinary differential equations. FEM or finite element technique needs a problem distinct in the domain of geometrical shape to be divided into a predetermined number of minor sections in usual limited different structures. Due to this reason, the analyzed object should be isolated in many sub-areas which are represented as elements. The elements are typically designed as tetrahedral if the object's shape is complex. Every element that contains a specific amount of peaks is known as node. The finite element mesh is the summation of nodes and elements.

The finite element technique is created in the initial position and the complexity of the structure is explained by the FEM analyzer in the next resolution steps. The analyzed outcomes are examined in the further result. The initial phase of CT/FEM is to obtain computed tomography pictures of human bones; afterward, it conveys the data to the finite element modeling process (Zioupos et al., 2008). The region of interest (ROI) is sectioned and generation of mesh is continued, after the development of

computed tomography data. The feature and precision of the finite element model are extremely reliant on the region of interest (ROI) section and network group. A three-dimensional image is built with computed tomography scanning, which is known as a voxel. It is important to describe the anatomical bone profiles and section the region of interest precisely, to generate the good quality of finite element model (Shim et al., 2007). Before the mesh generation process can be prepared, the region of interest is sectioned and the three-dimensional bone geometry is achieved. There are numerous mesh generation methods (Boccaccio et al., 2008). Pre-described voxels make the computed tomography scanning which establishes component but there is no solid bodies or surface. Alternatively, in the structure-based mesh technique, the geometrical structure with surface areas is created. Also, this type of mesh can produce more intricate and shell-solid mesh. The section is analyzed with two types of components in the shell-solid mesh technique (Lengsfeld et al., 1998). Trabecular bone is demonstrated by the solid elements technique. Also, the exterior surface of the cortical bone or trabecular bone is analyzed by thin-plate shell components. Material characteristics of the individual component in the model are allotted after the finite element model is prepared (McCreadie et al., 2006). The density of the individual component is explained by the correspondences between the value of HU (Hounsfield unit) of the computed tomography and the ostensible density. Concerning finite element modeling of the bone, two problems have in there: i. the material characteristics spreading within the trabecular bone and the cortical bone is not similar; and ii. the material characteristics of dissimilar cortical and trabecular bone. An important process to explain the material characteristics in the finite element model contains adjusting the computed tomography density, involving the voxel value to the density of bone mineral (BMD), and precisely describing Young's modulus of the bone material (Peng et al., 2006). In computed tomography image acquirement, a calibration phantom is used which has determined the concentration of calcium hydroxyapatite. By standardizing the Hounsfield unit ranges with the familiar application of calcium hydroxyapatite, the equation of computed tomography density and bone mineral density of the bone is created. It is displayed that the deceptive density and the mechanical characteristics of the bones are connected with the power laws (Zioupou et al., 2008). The trabecular bone should display anisotropic mechanical character. Consequently, computed tomography and finite element model with anisotropic characters of the bones are presumed to be extra precise. In several studies, no major change was seen among the outcome by isotropic computed tomography and finite element models and by computed tomography and finite element orthotropic analysis. But different research shows an important change among the orthotropic computed tomography and finite element models and the isotropic computed tomography and finite element models (Cody et al., 1999).

In the last stage of the finite element model, the loads and boundary situations are applied. Boundary situations describe that allocated nodes of the components are restricted in their DOF (Degrees of Freedom) and which are measured. The controlled nodes are static or arranged to move in a stable amount (Gao et al., 2006) (Peng et al., 2006). The external force can deform the component and generate internal stress. The analyzer tries to explain the equilibrium between internal component stress and external loads; also the boundary situations. The position of the static component is described by making the given nodes of the component totally (Yang et al., 2010). It is important to utilize the boundary situations and exact loads to equally measure the mechanical characteristics in bone in regular events (Schileo et al., 2008).

Figure 1. FEM analysis of bone tissue engineering



Explanation and Biomedical Application of CT/FEM Analysis

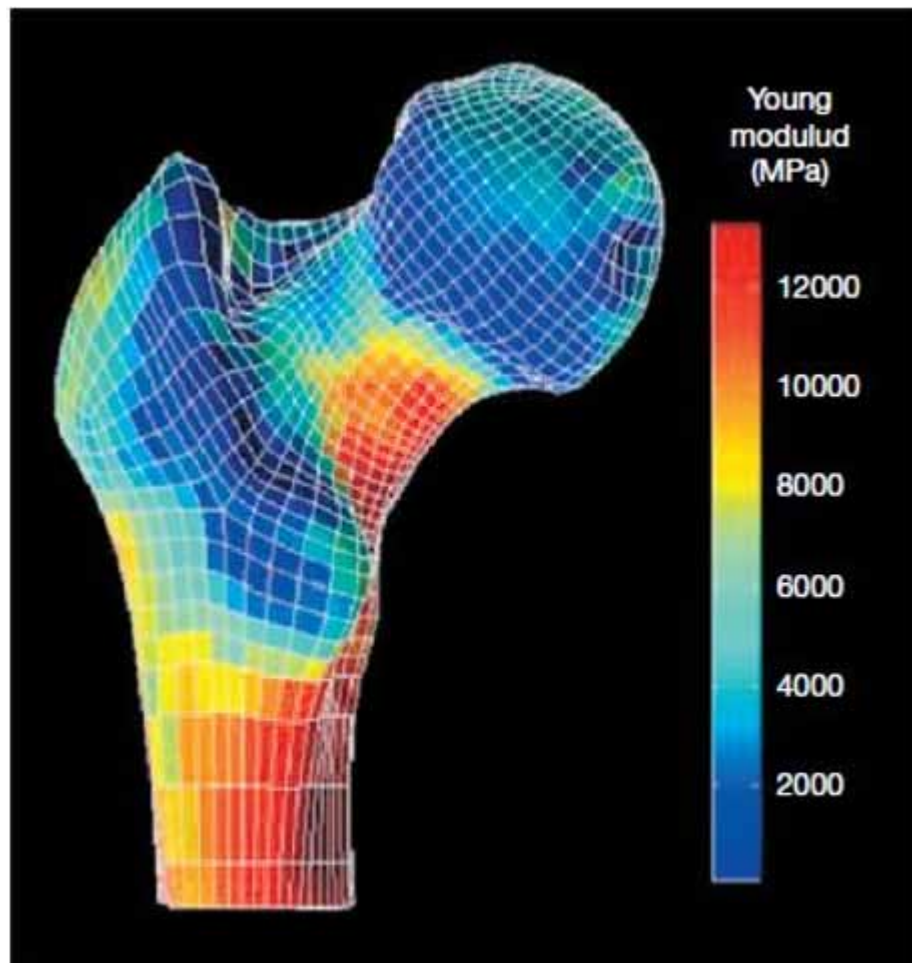
For commencing CT/FEA for the bones of the human body, the main two features should be taken into account first, failure of bone occurs due to low bone strength and overstress and the second one is remodeling and adapting by using applied stresses and loads also called Wolff's law (Prendergast et al., 1995). For these reasons i.e. the adaptation of bone tissue property the bone mechanical property is altered. In our present society, most aged people are having osteoporosis (Morgan et al., 2001). These patients have a high risk of a fracturing of bone because of inadequate strength of their bone. Bone fracture mostly happens in the forearm, spine, humerus, and hip (Griffith et al, 2011). Figure 2 shows the FEM analysis of the proximal femur. To conclude that whether a person needs any pharmacological intervention of osteoporosis, the assessment of the risk of accurate fracture is very helpful (Marco et al., 2015). Table 1 shows the different types of software used in spine analysis.

Conventionally, the BMD measurements applying dual-energy X-ray absorptiometry i.e. DXA is the main process of diagnosing osteoporosis. Moreover, this method is not reliable for the prediction of the actual fracture. Figure 3 shows the different boundary conditions of load on bone (Keyak et al, 2000). In many reports, it is found that most patients having BMD formed osteoporosis fractures (Yosibash et al., 2007) (Guldborg et al., 1998). The percentage of correlation between experimental fracture load and BMD was found out to be 45 to 57% (Dickinson et al., 2011). Currently, FRAX i.e. fracture risk assess-

Table 1. The different software used for analysis the spine

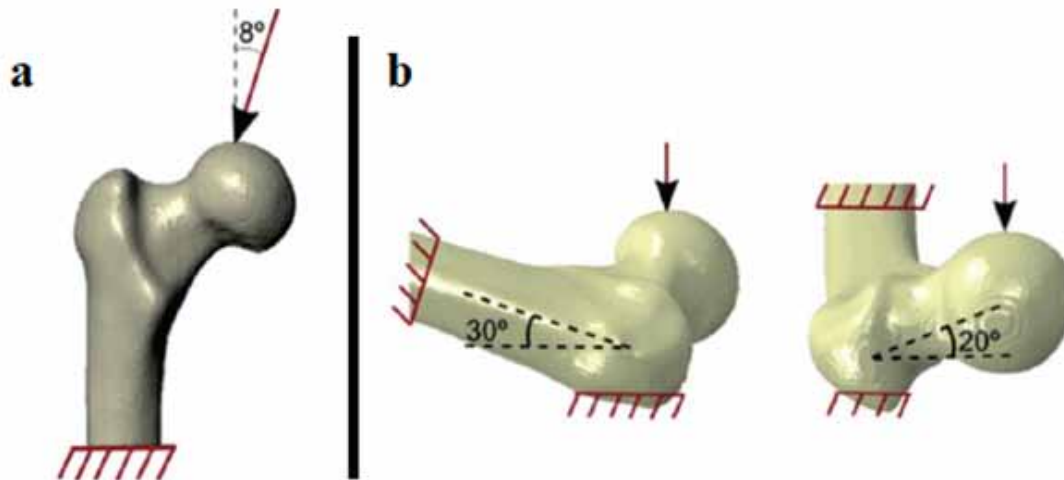
No.	Software Name	Variable	Slope
1	ADINA (Martin et al., 1998)	Failure load	0.57
2	ABAQUS (Kinzl et al 2013)	Specious strength	1.02
3	ABAQUS (Silva et al., 1998)	Thickness approx. 10 mm at vertebral area	0.86
4	Mechanical Finder (Imai et al., 2009)	Minimum principal strain	0.93

Figure 2. Finite element analysis of the proximal femur (Griffith et al, 2011)



ment tool is made for supporting the decisions in clinical treatments. World Health Organization (WHO) and Centre for Metabolic Bone Diseases first developed the FRAX and estimated 1-decade osteoporosis probability linked fractures (spine, hip, forearm, and humerus) (Lochmüller et al., 2000). For untreated

Figure 3. Boundary conditions of load a. normal position; b. fall lateral position (Keyak et al, 2000)



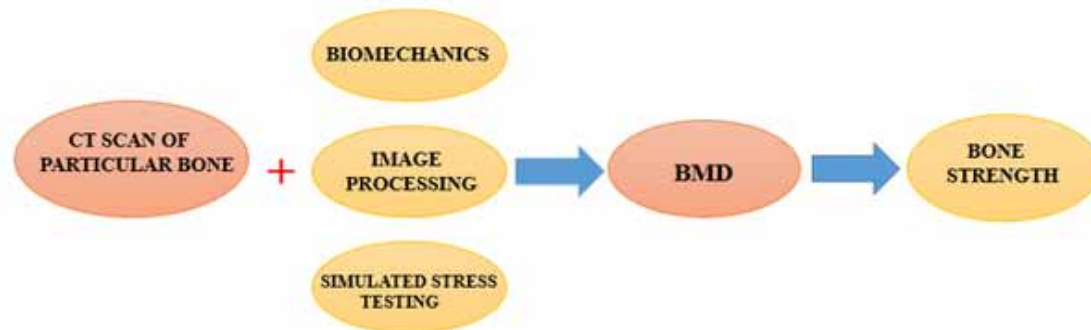
patients, FRAX can only be used. For osteoporosis-related fractures and primary osteoporosis screening, FRAX can be used but it cannot be used for measuring therapeutics effects (Hans et al., 2011).

The assessment of Strain and stress can be done by CT/FEA. In the post processing stage the fracture load, strain and stress are assessed (Feldkamp et al., 1989) (Marco et al., 2015). With fracture criterion, the fracture site and fracture load are predicted. For determining the biological and engineering materials strain-based or stress-based criteria are used. Drucker-Prager stress (Bessho et al., 2007), von Mises stress (Derikx et al., 2011), minimum principal strain (Yosibash et al., 2007), approx. the ultimate principal stress (Sandino et al., 2008) (Bessho et al., 2007), and ultimate principal strain (Imai et al., 2006) is the fracture criteria. Few studies showed regulation of bone fracture is done by stress and strain (Nalla et al., 2003) (Derikx et al., 2011).

Validation by CT/FEM Analysis

Fracture pattern, fracture load, and also fracture position are very suitable data for clinicians. In many ex-vivo studies, validations using CT/FEA analysis are there were measuring the fracture load and before measuring the performance mechanical testing accuracy by using cadaveric human specimens (Cody et al., 1999) (Uklejewski et al., 2021). The validation studies related to hips showed that CT/FEA can be used for the prediction of femoral strength much more than the quantitative DXA or CT (QCT) (Porter et al., 2007) which could able to find the site of the fracture in the proximal femur (Marco et al., 2015). A proximal femur nonlinear CT/FEA showed much precise fracture loads estimation at the proximal femur (Bessho et al., 2007). Nonlinear CT/FEA by applying shell-solid meshing can analyze the femoral bone surface principal strain and proximal femurs fracture loads more preciously (Keyak et al., 1998). CT/FEA can determine the fracture site as well as the von Mises yield criteria using Drucker-Prager yield criteria rather than the criteria von Mises yield (Sztefek et al., 2010). The hip sideways validation simulation study showed that CT/FEA can determine fracture patterns and fracture loads more accurately (Derikx et al., 2011). In the table, the proximal femur validation studies are shown (Porter et al., 2007).

Figure 4. Analyzing the CT image



CT/FEM Analysis of Osteoporosis Treatment

Based on cadaver studies verification and validation, CT/FEA is clinically applied for determining the treatment of osteoporosis and the risk of fracture (Yang et al., 2009). From the data of the clinic, the index of the risk of hip fracture possibility in the discrimination from the CT/FEM was meaningfully superior to structural engineering models based on DXA and total hip BMD (Porter et al., 2007). Figure 4 shows the procedure of analyzing the CT image. Depending on the specific force configuration the proximal femur strength changes.

The force direction and magnitude in the fall configuration are subjective to most biomechanical aspects like body height, position, and weight (Imai et al., 2009). Figure 5 shows the in-vivo volumetric x-ray for the reconstruction of the proximal femur (Ahmad et al., 2010). The assessment to find the relationship between the incident hip fracture in various loading cases and femoral bone strength using nonlinear CT/FEA, the posterior loading in the women and men were highly linked with the incident hip fracture (Fermor et al., 1998). For the case of vertical fracture, the power of nonlinear CT/FEA showed more discriminatory power than the DXA and BMD as well as volumetric QCT and BMD for vertical fracture (Porter et al., 2007). For the case of osteoporosis linked features QCT and DXA can be replaced by CT/FEA (Marco et al., 2015). The treatment related to osteoporosis can be done by CT/FEA for determining the alendronate and teriparatide effect of medication in the lumbar spine (Keaveny et al., 2007). Further study showed that nonlinear CT/FEA showed the vertical compressive strength was highly better determined for the vertebral fracture compared to BMD, as well as it can measure medication effect expressively earlier than the BMD (Marco et al., 2015) (Moerman et al., 2009).

BONE TISSUE ENGINEERING AND APPLICATION OF MECHANO-BIOLOGY

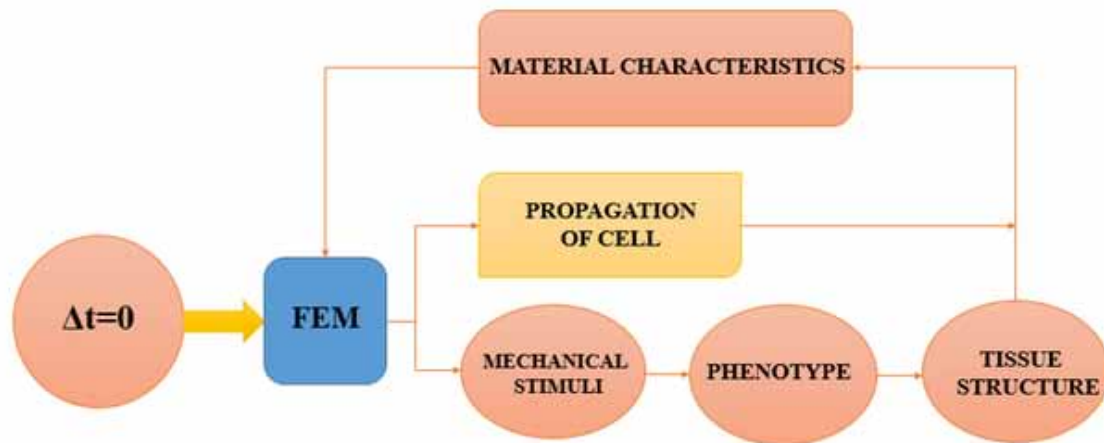
To enhance the scaffold morphology, mechano guideline structure can be used, precisely the pores dimension (shape and the size), the number of pores on an assumed area, and their three-dimensional circulation, etc. The geometry of scaffold which results in enhancing procedure can be very difficult and, generally, because of the technical boundaries, the conventional manufacturing methods have no capability of understanding like substances. The upcoming and developing manufacturing technologies presently

Figure 5. In-Vivo volumetric x-ray for the reconstruction of the proximal femur



used for the production of scaffolds for example SFF or solid free form and RP or rapid prototyping technology which allow solving these boundaries, therefore, permitting to understand each type of scaffolds has extra different shapes. Additional benefits that these methods can propose, is the opportunity of appreciating scaffolds with a modified peripheral profile in addition with constructions to rise the bulk transmission of nutrients and oxygen (Cheah et al., 2003) (Liebschner et al., 2003) (Sachlos et al., 2003). Mechano-biology guideline structure could be applied in the engineering of bone tissue analysis to enhance the morphology, the absorbency, the motorized elements of scaffolds along the situation of the surroundings. Recently, in various researches, such matters are examined. The different types of issues associated with physical reliability, artificial things, raising and cell development circumstances, and cell/biomaterial communications are included by the study of bone tissue for scaffold designing (Karande et al., 2004). The biophysical inducement transferred to the mesenchymal tissue is one of the prime features which have an impact on the molecular and cellular appliances (Schriefer et al., 2005). This incentive is related to the planning and the material characteristics of the scaffold that will assist as a lead to collect peripheral inducements for the construction of the matrix. The perfect scaffold has the capability of transporting the best promising stimulus on the redeveloping tissue, therefore, permitting the periods for the restoration to be concentrated and the optimum mechanical characteristics of the redevelopment to be attained (Geris et al., 2008). In research (Olivares et al., 2009), it was analyzed that the communications between the pore morphology of scaffold, at the level of cell microscopic phase,

Figure 6. Mechano-regulation algorithm



the development of mechanical stimuli, and culture situations utilized at the macroscopic phase on two usual constructions of the scaffold. In a finite element analysis (FEM), hexagonal and gyroid scaffolds of 70% and 55% absorbency were demonstrated and were given to a non-tensile strain or internal fluid flow. Thus, the difference procedure in the given constructions seems more delicate to internal fluid flow than the tensile strain of the scaffold is based on the mechano-regulation concept. Figure 6 displays the typical mechano-regulation algorithm. For tissue difference, to control the effect of the material characteristics of scaffold on chondrogenesis in a FEM of a problem of an osteochondral, a mechano-regulation algorithm was introduced (Kelly et al., 2006).

The algorithm forecasted that growing the scaffold stiffness grows the quantity of developing the cartilage and decreases the quantity of fibrous tissue construction in the fault. A computational mechano-guideline based structure was developed (Milan et al., 2009) to forecast the construction of bone tissue which is mechanically stimulated by complete dynamical compression contained by an absorbent scaffold (polymeric) concentrated by micro-CT. The consequence of the automatic stimuli and the construction of capillary linkage on cell distinction inside a morphology of uneven scaffold (Sandino et al., 2010), examined by FEM based on a micro CT. A glass-based calcium phosphate scaffold (porous) was replicated. A multi-scale model (Sanz-Herrera et al., 2009) clarified the consequence of scaffold absorbency, stiffness, the pore size of the pore, and kinetics reabsorption on regeneration of bone tissue. The structure projected growth of regeneration rate of bone tissue with growing stiffness of scaffold, size of pore, etc.

CONCLUSION

Because of the elderly population increment, the rate of vertebral and hip fractures is becoming a massive social issue. It is highly necessary to determine the risk of fracture, osteoporosis treatment, start medication, and fracture prevention. Bone tissue engineering has observed a remarkable development by new in vivo and in vitro experiments, with the advance of novel biomaterials that attempt to stimulate an exact response from the neighboring tissues. In this chapter, we have mentioned the CT/FEA

mechanism, human bones CT/FEA validation study, osteoporosis treatment, and fracture risk clinical application studies. Bone tissue engineering has managed to excessive prospects for several syndromes and medical surgery that are unable to resolve with conventional procedures. Such as serious bone defects or problems, whether made by trauma, initial tumor resection or careful surgical procedure have in various examples offered challenging tasks to the present benchmark treatment for repairing the bone tissue. The main determination of bone tissue analysis is to utilize the engineering ideas to stimulate and encourage normal bone healing procedures, which does not happen in serious bone defects. The upcoming CT/FEA-based computational models used in bone tissue engineering are very encouraging, with the creation of more controlling and accurate simulations that can mimic more exactly the natural progressions and the proposal of useful scaffolds. For accurately determining the fracture site, bone strength, as well as fracture risk and osteoporosis medication effect CT/FEA, is highly applied. Bone strength in daily living activities at various loading alignments CT/FEA can be used. By using the CT/FEA for the management and diagnosis of osteoporosis, clinicians, as well as the patients, can be able to adapt a plan of treatment as per the patient's exact clinical situation.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ADDITIONAL INFORMATION

Tissue engineering is broadly recognized as an actual way to treat serious size bone imperfections. Though, constructing the scaffold operative as an extracellular matrix (ECM) and responsible for the proliferation of cells with excellent material and design constraint to match carefully with the normal bone property is still a challenge. The scaffold has to support biological manners for example the fabrication of extra-cellular matrix (ECM) and vascularization, also the scaffold has to resist the mechanical loads performing on it and to transfer them to the normal tissues located in the neighborhood. The strategy of a scaffold for the guided regeneration of a bony tissue needs a multidisciplinary style. The finite element method (FEM) and mechanobiology can be applied in a combined method to find the optimum limits governing bone scaffold enactment.

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KEY TERMS AND DEFINITIONS

Bone Mineral Density: A bone mineral density is the volume of bone mineral with in-bone tissue.

Bone Tissue Engineering: A study which is focused in constructing implantable bone replacements for acute skeletal imperfections which can't restore normally.

Finite Element Analysis (FEA): A computational technique for calculating how a product act in response to practical different parameters like vibration, forces, fluid flow, heat, etc.

Mechanobiology: A study which basically emphases on how physical parameters like forces and changes in the mechanical characteristics of cells and tissues help in growth, physiology, cell difference, and infection.

QCT: A medical procedure that analyses the BMD (bone mineral density) by applying a standard X-ray CT scanner (Computed Tomography) with a standardization to transform the HU (Hounsfield Units) of the Computed Tomography image to BMD values.

Scaffold: Scaffolds are constituents that has been made to form required cellular interfaces to give the construction of new efficient tissues for remedial resolves.

Chapter 15

Artificial Intelligence in the Era of Clinical Imaging: How Training Models Could Be a Challenge for New Upcoming Physicians in Radiology – Learner Needs of Radiology Residents Regarding AI

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ABSTRACT

Artificial intelligence technology is a marked change in the imaging field. Clinical imaging and operations applications are metamorphosed as new methods and tools, and algorithms are being brought into radiology's daily practice. Looking forward, further attempts could prove quite beneficial to the literature. Modern technologies like AI technology, particularly deep learning, clearly show evidence of development. AI technology can be exceptionally good at identifying. The authors outline how to interact with and methods to effectively, safely, and efficiency use these tools and technologies.

INTRODUCTION

In the technological era AI has the power to significantly impact on a branch of medicine that uses imaging technology to diagnose and treat disease. In the field of radiology AI is quickly improving, while

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quickly adapting an essential role in all steps of medical imaging. It is an important interest, the acts of AI in radiology, which are increasingly accurate, showing better performance than trained radiologists for certain tasks. Shortly, radiologist residents will need to obtain the knowledge of AI tools, technology, how they increased time for consultation and development in imaging and extracting effective information and data from images.

Highlighting a significant strong effect on the different levels of radiologist residents and imaging to understanding the benefit and the limitations of AI to harness it is determine and integrate it effectively the capacity into their protocols and imaging workflows. Our chapter aim is to give a resident in radiology to adapt the types and the principles of AI technology, and the board areas of AI can applied in radiology.

we believe our findings compare well with AI methods come through automatically identifying consisting patterns in imaging data. At this point authors (Hosny, A., Parmar, C., Quackenbush, J., Schwartz, L. H., & Aerts, H., 2018) it makes adequate, qualitative, and quantitative assessments of techniques, methods, and characteristics. In our chapter, we will include several reasons and additional support for the data analysts, medical experts with the clinical context, how to frame the imaging questions, of the organization and integration of data collected, from various sources, outlining AI methods, algorithms performance.

STRENGTHENING THE LEARNING ENVIRONMENT IN RADIOLOGY

Highlighting and reviewing present teaching - centred methods and achievements as presented by authors (Sivarajah, R. T., Curci, N. E., Johnson, E. M., Lam, D. L., Lee, J. T., & Richardson, M. L., 2019), stating and justifying the acceptability of traditional didactic and effective methods of teaching, based on the recommendations of radiologists take part in many types of activities such as instructors and learners. We are focused on resident radiology performance, not instructor performance, and on behaviour, not subject matter; there should be only one learning outcome per objectives.

Despite the fact, that residents radiologists learn more and retain their knowledge longer if they acquire it in an active rather than a passive manner. However, flexibility is a great value for the optimal asset of knowledge, so in a way that deliberately avoids harm designed learning experiences. The greatest challenges in the radiology learning environment involve the engagement and contribution of the instructors, or faculty members, who must practice and innovative while teaching and mentoring the next generation.

The most well-known findings underlined by author (Collins, J., 2007), based on a learning expectations and experiences placed on that activity. At this point means that we are increasing the utilization of imaging examinations in clinical practice leads to increasing complexity and volumes of cases, requiring ever more knowledge, focus and time for interpretation. Merging healthcare system also tax existing workflow, as these systems may complicate already stretched systems.

In spite of the fact that adding to these stressors are radiologist-specific metrics such as turnaround times, peer review reporting and discordance rates. We are of the opinion that radiologists in a daily duty during the actual practice are affected not only by the vast amounts of imaging data they must review on a daily basis, as mentioned by authors (Collado-Mesa, F., Alvarez, E., & Arheart, K., 2018), have been clearly identified the time it takes them to search and find contextual clinical information regarding the imaging studies they read. Many interrelated challenges affect the radiology work environment, that means further evidence for every radiologist in worldwide view an every 3 second of every working day for the entire year.

Even more recent literature by authors (Slanetz, P. J., Reede, D., Ruchman, R. B., Catanzano, T., Oliveira, A., Ortiz, D., Whorms, D. S., Carrodeguas, E., & Deitte, L. A., 2018), suggest AI will include the development and sustainable of high-performance of teams. Thus, neural networks, robust machine learning algorithms, and concurrently cloud-based computational capabilities, are being applied to the large amounts of machine - readable digital data generated by radiology imaging studies. Regarding the interpretation of recent literature based on applications, implications on electronic health records (EHR), with goal of creating applications that, once clinically validated, are expected to be a promised way the specialty of diagnostic radiology is currently practiced.

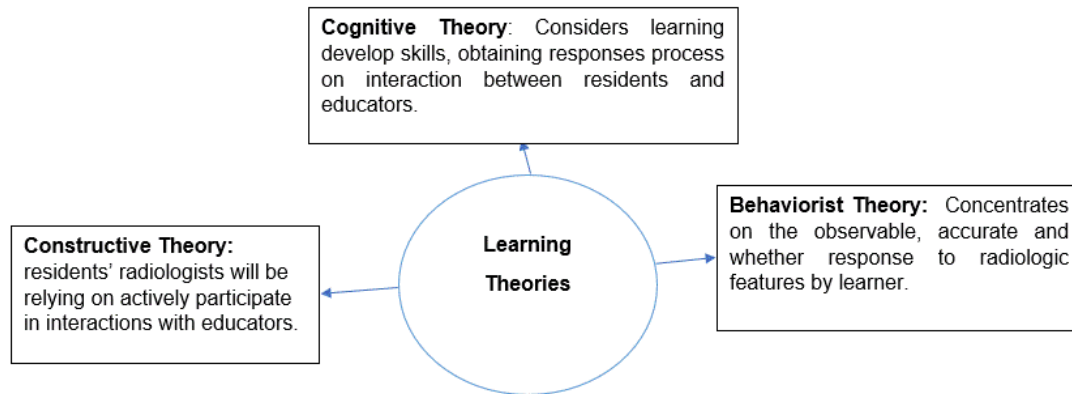
Due to the recent transformations in medical education, it follows that many efforts have been made to integrate technology and efficiently improve the clinical ability of residents including several studies as revealed by authors (Briz-Ponce, L., Juanes-Méndez, J. A., García-Peñalvo, F. J., & Pereira, A., 2016). Thus, radiology has often performed duties as the gateway for how technology has improved in the medical field, in spite of AI will likely be no different as the next wave in the digital revolution and persistent approach as a transformative technology for clinical imaging systems. Although, this approach is interesting, as most of the studies have tended to focus on medical image - learning experience teaches us how to learn us a several kinds of images to achieve on expert level. In spite of the fact that training expects for acquiring skills to analyse imaging features to identify patterns, generate a differential diagnosis that matches the patterns, and we have a mutual relationship and connection with the imaging aspects and differential with clinical findings to mark the most likely diagnosis as mentioned by authors (Cheng, C. T., Chen, C. C., Fu, C. Y., Chaou, C. H., Wu, Y. T., Hsu, C. P., Chang, C. C., Chung, I. F., Hsieh, C. H., Hsieh, M. J., & Liao, C. H., 2020).

EDUCATION FRAMED BY LEARNING THEORIES

As we can see by authors (Koçak, B., Durmaz, E. Ş., Ateş, E., & Kılıçkesmez, Ö., 2019), in order to address the maximum level of performance, it is accepted that we draw a distinction between approaches based on term “Radiology”, be created from words “*Radio*” and “*omics*”. Both terms are fully compliant with meaning medical images and we briefly mention the various fields like genomics that contribute to our understanding of various clinical conditions requires acquiring skills to analyse or extract imaging features.

With the above lines in our mind, we learn and develop trainers skills on learning theories such as behaviourism theory, cognitive theory, and constructivist theory. Therefore, learn and integrate various knowledge sources of how residents in radiology understand and addresses the differential diagnosis as we can see in (figure. 1), that are relevant to radiology residents and educators, observed by authors (Williamson, K. B., Gunderman, R. B., Cohen, M. D., & Frank, M. S., 2004), indicates digital technology adoption in relies on the future radiology education into the traditional apprenticeship educational model. Hence, from real human behaviour in teaching and training is challenged by ever-increasing workload demands by educators / medical trainees and can be increase the value of education by making it more useful for understanding relations between human and tools. We confirm our findings of the learning theories based on learning theories, that are relevant to radiology trainees as we outlined for the future work resident’s radiologist learn more and retain their knowledge longer if they acquire it in an active rather than passive manner. Furthermore, we believe that AI may offer potential improvements to current

Figure 1.



educational practice. It is a great significant for corresponding to any of the above perspectives to encourage our new upcoming radiologists to interacting with the human-machine interface utilizing the AI.

As other authors have highlighted (Bi, W. L., Hosny, A., Schabath, M. B., Giger, M. L., Birkbak, N. J., Mehrtash, A., Allison, T., Arnaout, O., Abbosh, C., Dunn, I. F., Mak, R. H., Tamimi, R. M., Tempany, C. M., Swanton, C., Hoffmann, U., Schwartz, L. H., Gillies, R. J., Huang, R. Y., & Aerts, H., 2019);, they are suggesting they are suggest us an intriguing area in the field of AI and how its implementation in radiology. will have a positive impact and attitude on a new upcoming residence physicians as the current technology is rapidly evolving, in the study of tumours and how it is affected by the application of these tools in the clinical learning environment.

On an alternative approach, we will. the challenges covering implementation with clinical outcomes and make adequate preparation for particular attitudes. This aims towards enhancing our understanding of how could be recently developed in the interpretation of medical images and workflow of detection and ensuring subsequent observation. In order to address issue and using the opinions of authors (Dembrower, K., Wählin, E., Liu, Y., Salim, M., Smith, K., Lindholm, P., & Strand, F., 2020), giving a general panorama how to examine how AI used in making suggestions to change a substance for radiologist workload.

Using state-of-art technology such as AI, in medical imagine marking out advances in tumor types like breast cancer to demonstrate how often occurring, clinical situation regarded. A significant advantage of AI is to adopt the effect of characterise medical procedures, but also artificial intelligence advanced methods for their performance as well. This chapter documents several key contributions made to the fields of how AI has been running rampant in radiology circles. We believe that our findings compare well mentioning positive aspects by authors (Prevedello, L. M., Erdal, B. S., Ryu, J. L., Little, K. J., Demirer, M., Qian, S., & White, R. D., 2017), explaining us how AI can will optimize radiologists workflows, facilitate quantitative radiology, methods and solutions transforming medical images. The results of AI provide further evidence for how could react in the experience to critically evaluate all the findings without becoming complacent and blindly accepting predictions produced by algorithms.

EDUCATION FOR MEDICAL IMAGES

Medical images can be a core “tool”, for teaching in diagnostic radiology as comprising a benefit component including information about clinical presentation, disease diagnosis or progression with imaging techniques for residences. In our view, current findings are based on a justified and satisfactory results might have been more interesting evidences based on medical imaging, which is a vast knowledge for radiologist, as dominated by diagnostic radiology. Authors (Suleiman, M. E., Rickard, M., & Brennan, P. C., 2020), who provide us much valuable approaches known about how radiologists’ image reading skills changes into variations in image interpretations, can the capacity to have an effect asses on the effectiveness of the early treatment of disease and may have important clinical implications. Based on radiological imaging exams performed daily, radiology be a part of the whole component of the information a radiologist utilizes to make diagnostic decisions more effectiveness.

In the process of our investigating researchers (Liu, Z., Wang, S., Dong, D., Wei, J., Fang, C., Zhou, X., Sun, K., Li, L., Li, B., Wang, M., & Tian, J., 2019) have addressed the progress in computational tools, especially in AI for medical image process and analysis, has converted these images into quantitative and minable data associated with clinical events in radiology management. It has been suggested by authors (Tajmir, S. H., & Alkasab, T. K., 2018) that AI tools, ML Techniques, and medical imaging predict that radiologists’ practice across the clinical, research and education domains perform segmentation, extraction, and classification of new biomarkers from raw image data.

More recent evidence by authors (Tajmir, S. H., & Alkasab, T. K., 2018), their introduction they mention, that AI tools can assist radiologists to improve their practice and be able to effectively supervise their use as most of curricula could acquire the knowledge to carry out new supervision offer new opportunities to bring learning into the on-going practice of attending as well.

In the field of imaging-based diagnosis (Liu, X., Faes, L., Kale, A. U., Wagner, S. K., Fu, D. J., Bruynseels, A., Mahendiran, T., Moraes, G., Shamdas, M., Kern, C., Ledsam, J. R., Schmid, M. K., Balaskas, K., Topol, E. J., Bachmann, L. M., Keane, P. A., & Denniston, A. K., 2019) the authors pointed that 99% of studies were found not to have a reliable design; furthermore, only one thousandth of the papers that were reviewed validated their results by having algorithms diagnose medical imaging coming from other source populations. As imaging AI products are developed and marketed, the role of the radiologist is to be an educated consumer about these tools. Being such an educated consumer requires the radiologist to (i) consider the clinical need for AI tools in specific clinical use cases, (ii) undertake formal evaluation of AI tools before adopting them in practice, and (iii) maintain his or her clinical Radiology expertise and guard against the pitfalls of over-reliance on technology.

CHALLENGES OFFERED BY AI

In the initial stage of the process, the application of AI could make time dependent tasks that can be performed facily. Afterward allowing radiologists more time and opportunities to engage in patient care via expanded time for consultation and development in imaging and extracting useful data from those images. Despite the fact that radiologists who use AI to their benefit, rather than to avoid it out or fear, might supersede those radiologists who do not. We are currently in the process of investigating authors (Gampala, S., Vankeshwaram, V., & Gadula, S., 2020), mentioned the practical implications of AI algorithm for residents’ curriculum and the benefits of AI in radiology. In the same way in oncology, AI

technologies have been integrated into the Computer Aided Diagnosis technologies such as detection and analysis of various parameters. AI field has a various sub-field, components, challenges that AI faces, biases that could take place during the suggestion, and ethical aspects of AI as already underway by authors (Mudgal, K. S., & Das, N., 2020). The radiologist will be well served by monitoring the benefit of AI in their practice on an ongoing basis. It is advisable for radiologists to become instructors, by author (Rubin D. L., 2019) have attempted to:

1. in of view of clinical needs matter their practices, and whether the AI technologies meet those needs,
2. evaluating AI technologies, as they are adopting utilizing case data from their own practices,
3. being knowledge of the potential hazards of over-reliance on technology and maintaining their clinical skills.

TEACHING AND LEARNING ACTIVITIES OF AI

Based on a learning activities in a clinical education are lectures often lack synergistic, and the learner is often a passive recipient of knowledge. We are support that author, (Collins J., 2007) are concentrate on a learning strategies include small group for problem solving, simulations, case studies. We confirm our residence response can be effectively used to allow vital active learning in an enormous lecture background. Other techniques for making a small group learning more interactive include:

1. using pre-tests and post-tests (with either slides or paper to present the materials to be covered),
2. asking questions (the audience is given questions about the content of the presentation before it begins and told to write down their answers),
3. using voting cards (with either true/false cards, numbered cards, or coloured paper strips),
4. reading (the audience receives a passage to read and is asked for comments),
5. implementing buzz groups (the audience is asked to discuss a problem with two to four neighbours for 3–10 minutes, and then some groups volunteer or one group is selected to present its consensus to the entire audience),
6. using a mini quiz (the audience members self-test their knowledge either before, after, or during the presentation),
7. posing a progressive problem (a patient scenario is presented in a progressive sequence; parts of the history are followed by questions about what is important or missing),
8. using discussion groups (panel members present mini-lectures or vignettes and solicit commentary from other panel members and the audience at large), holding debates (expert facilitators present opposing viewpoints and ask the audience to vote or discuss issues),
9. acting out a patient-related intervention (a patient relates the history of his or her disorder, which is often accompanied by role playing),
10. presenting video vignettes (questions about the video trigger discussion with a panel or the audience at large),
11. planting “standardized” patients in the group (standardized patients give the appropriate responses on cues from the audience; e.g., history, effects of therapy),

12. distributing question cards (cards are passed to the audience and attendees are asked to jot down any questions that arise during the presentation; at given pauses, the cards are collected and given to a moderator who establishes which will be of most value and asks the questions of the speaker). The above-mentioned activities generally take more time to conduct than do traditional lectures.

CONCLUSION

The AI technology coming to medical sector offer potentially exciting opportunities to meet the needs of radiologist, but excited about their intended to make a profit prospects and the competitive activity essential may push a flood of tools into the hands of radiologists with small in size understanding of whether and how to adopt them into their practices.

There is a rapid evolution of learning strategies and theories on the last few decades. Radiology educators are supposed to explore in order to benefit from them in their teaching tasks. There is a big difference between merely memorizing facts and routines and actually being able to function effectively as a clinical radiologist.

The art of learning theory has changed from teacher-directed approach to learner-cantered approach. A new concept in effective education that learner initiative is considered as essential ingredient, and new learning strategies aim to foster this concept. Likewise, a new trend has emerged, focusing on how learners approach complex situation rather than what each learner should know, this trend emphasizes component problems and playing down component skills.

Educators who have good knowledge about learning theories can create good learning environment for learners. The main reason of discussing these theories is to clarify the perspective of each theory about educational components. Every theory has its own point of view about education, which depends on the context of the educational process that is discussed.

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KEY TERMS AND DEFINITIONS

AI: Artificial intelligence.

EHR: Electronic health record.

ML: Machine learning.

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Index

3D Computer Application 190
 3D PDF 30, 34, 126-128, 132-133, 143, 215, 218-219, 233-234, 239, 242-244
 3D printing 31, 35-38, 48, 94, 104, 118-119, 121, 124, 227, 232-234, 237-238, 241, 243, 245-248, 250-251, 255-258, 260-264
 3D reconstruction 26-27, 29, 33, 41, 145, 166, 193, 208, 313

A

additive manufacturing 94, 96-97, 104, 115, 118-122, 260-262
 AI 148, 289, 317-323, 325
 Anatomical 3D Models 190, 214
 anatomical models 33, 35, 41, 191-192, 195, 205, 215, 218, 232, 236, 241
 anatomy of the female pelvis 190, 194, 203, 210
 angle 12, 17, 24, 71, 82, 127-128, 132-139, 142-143, 168-169, 218, 221
 Artificial Intelligence 51, 68, 71, 89, 91, 148, 297, 317, 320, 323-325
 augmented reality 27, 34-35, 37-41, 44-45, 64, 142-143, 160, 179-180, 182, 186, 205-206, 210, 212, 217, 265-269, 271-280, 282

B

bio-ink 245
 Bioink 251, 263
 Biomedical Sensor 94
 bioprinting 237, 245, 251, 254, 257, 260, 262, 264
 Bio-tribology 1
 Bloch equations 68-71, 73, 78
 bone mineral density 300, 303, 316
 bone scaffold 247-248, 251, 258, 264, 302, 310, 313
 bone structure 245-246, 264, 271
 bone tissue engineering 245-263, 300-302, 304, 307, 309-311, 315-316

business process 283

C

Cerebrospinal Fluid Variability 126
 Clavy 147-148, 153-161
 clinical imaging 244, 317, 319
 clinical practice 50, 56, 63, 122, 191-192, 215, 218, 235, 265, 267, 274-275, 312, 318
 clinical trainers 265

D

data exploitation 283, 286, 288, 290-291, 296
 data governance 283-284, 286, 288, 292, 296
 DICOM 33, 72, 151, 154-155, 160, 162, 219, 237, 244, 271
 didactic material 215
 digital anatomy 26-27, 32, 36, 41
 digital collections 147-148, 153, 160, 162
 digital health 160, 283-291, 295-298, 324
 digitization 97, 205, 244

E

ecosystem health 283, 289
 education 26-27, 34-35, 38-41, 45, 64, 66-68, 89, 91, 93, 149, 153-154, 159, 162-164, 180, 190-192, 206, 210-214, 216, 218, 227, 234-241, 243-244, 266, 274, 277-281, 317, 319, 321-323, 325
 educational application 78
 Educational Experience 64, 66
 EHR 151, 319, 325
 e-learning 49-51, 53-54, 56, 61, 64, 69, 90, 148-149, 153, 159-162, 206, 211, 213, 277, 279-281, 291
 e-learning platforms 148-149, 153, 159-160, 206
 Extract-Transform-Load (ETL) 147

F

Finite Element Analysis (FEA) 300, 302, 316
 framework 1, 53, 64, 86, 92, 148, 161, 243, 268-269,
 283, 291-292, 297, 299
 free software 33, 39, 215, 218-219
 friction 1-18, 20-25

G

grayscale range 126, 128
 guide 79, 126-127, 138-139, 142-143, 178, 183, 192,
 252, 277-278, 324

H

health information systems 280, 283
 health monitoring 94, 289

I

information and communication technologies 190-191,
 214, 266, 287
 Information management tools 147
 instructional resources 147-149, 153, 159
 intelligent tutoring system 66, 79, 87, 91-93
 interactive 27-28, 30-31, 37, 39-40, 50-51, 54, 91,
 145-146, 148, 191-192, 204, 207-212, 214-217,
 228, 236, 239-240, 242, 244, 266, 271, 276-277,
 279-281, 322
 interactive visualization 215
 Intraoperative Ultrasound 183-184
 IoT 94, 97

L

ligamentum flavum gap 126-127
 likelihood to recommend 77, 88
 LMS 49-52, 54-56, 60, 62, 83, 85

M

Measurement Techniques 1, 7, 22
 Mechanobiology 24, 300, 310-311, 316
 Medical Diagnostics 317
 medical imaging 40, 49-50, 66, 90, 92, 208, 216, 223,
 231-232, 238, 301, 318, 321, 324
 Medical knowledge 147
 medical training 49-50, 66, 151, 191, 206, 210, 265-
 268, 271-272, 274-276
 mL 140, 142, 321, 325

MRI 27, 33, 35, 50, 66-72, 85-86, 89-92, 128, 133-134,
 136-137, 139-140, 143-145, 167, 169, 171, 177-
 179, 183, 185, 187-188, 191, 193-195, 197-199,
 204-206, 208, 210-211, 218, 233, 237, 244

N

Neuro-Oncology 178, 183, 185
 neurosurgical anatomy 164
 neurosurgical practice 164-165, 180

O

osteogenesis 264, 314

P

pelvic floor 194, 207, 209, 211, 214
 perceived utility 77-79, 81-82, 85, 88
 Personalized Medicine 94
 porous scaffold 245
 post-dural puncture headache 126-127, 144-145
 postprocessing 69, 215, 244
 postprocessing images 215
 pre-operative planning 164

Q

QCT 300-301, 306-307, 311, 316

R

radiographers 66, 77, 82, 87
 radiology 27, 34-35, 38, 40, 65, 74, 89-90, 124, 147-149,
 151, 153-155, 159-163, 191, 209, 214, 235-237,
 239-241, 274, 279, 317-321, 323-325
 Reformatting 218, 244
 Regions of Interest 30, 193, 214
 Residency Training 317, 324

S

scaffold 245, 247-251, 254-255, 258, 260-261, 264,
 301-302, 307-311, 313-316
 Scaffold-Assisted Regeneration 264
 Segment 127, 140, 238, 244
 segmentation 26-29, 32-34, 36-37, 40, 42, 187, 191,
 193, 207-208, 210, 235, 238, 313, 321
 Serial Anatomical Sections 190, 214
 simulation 26-28, 34-35, 38, 41-42, 44-45, 50-51,
 53, 60-63, 66-67, 69-74, 78-79, 81-83, 86-87,

Index

90-91, 148, 187, 212, 231-232, 235, 238-239, 241, 243-244, 268, 270, 272, 279-282, 301, 306, 311, 315, 324
skin 1-19, 21-25, 28, 30-31, 94-95, 97-99, 101, 103, 110, 113, 116-117, 121-122, 127, 133, 137-139, 143, 179, 187, 198, 260
skull base 166, 172-173, 179, 181-182, 185, 187-188, 215, 226, 230, 235, 240
smart splint 94-95, 97, 108, 119
software 26-33, 35-36, 38-39, 41, 43-46, 48, 53, 62, 64, 71, 95-97, 102-103, 149-150, 153, 166-168, 171, 187-188, 191, 193-194, 196, 203, 207, 209-213, 215, 217-220, 226, 233, 237, 239, 250, 266, 268, 271, 278, 281, 285-289, 291-292, 294-299, 301, 304-305
surgical simulation 212, 232

T

Three-Dimensional Computer Application 214
three-dimensional images 62, 192, 208, 216, 265, 274
tissue engineering 121, 241, 245-264, 300-302, 304, 307, 309-311, 313-316

tractography 167, 169, 171, 181, 185-187, 216, 244
tridimensional images 215

U

ultrasound imaging 49, 54, 64, 144
Ultrasound-guided Infiltration 49
usability 60-62, 66-67, 76, 88-90, 92, 194, 206, 297
user interface 28, 53, 72, 74-75, 79, 196-197, 207, 209, 214

V

virtual dissection 26-28, 30-32, 34-36, 39-41, 47
virtual reality 27, 31, 34-39, 41, 44-45, 180, 203, 210, 234, 236, 244, 265-269, 271-272, 274-282, 312-313
virtual simulator 53, 61-62, 68
Visible Human Project 26, 28, 38, 42, 46, 214
voxel 33, 71-72, 244, 303