Final Degree Project

Biomedical Engineering Degree

"AR application for sentinel lymph node detection in breast cancer "

Barcelona, 8th of June of 2022

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Acknowledgments

This project would not have been possible without the help and guidance of various people. I would like to express my biggest gratitude to them for investing their time in helping me learn and grow through this process.

First of all, I would like to sincerely thank my tutor, Dra. Aida Niñerola, for being an outstanding professional that has helped me tremendously when developing this project and has made the whole process much more nurturing.

Also, I would like to thank my director, Dr. Eduardo Soudah, and Mr. Óscar de Cross for giving me the idea and the opportunity to work on this project and for all the support given throughout the whole development.

Abstract

With the growing relevance of breast cancer in worldwide health reports, its treatment techniques are constantly assessed for improvement. Most of breast cancer patient face surgery at some point of the disease and one of the most typical interventions they may undergo is sentinel node lymph biopsy, a radio-guided surgery in which the patient's sentinel lymph nodes are extracted to be analyzed in order to assess further treatment. In order to perform an accurate and minimally invasive resection of lymph nodes, it is necessary to have a clear localization of the element and for this reason, new visualization systems like the one proposed in this project are emerging.

The aim of this project is to create an AR application to improve nuclear image data visualization in sentinel node biopsies, this way the burden on nuclear physicians will lessen. Accordingly, two different AR 3D models based on nuclear images were built to assess its performance for advanced image visualization in sentinel nodes biopsies. While the first approach was performed on a breast phantom, the second one was based on a real patient nuclear images, both provided by the Nuclear Medicine Department of Hospital Clinic.

The final AR application was developed in Unity and, while the results obtained were limited, they were satisfactory and encouraging for further development in the emerging field of AR in healthcare.

Keywords: Augmented Reality · Sentinel lymph node biopsy · Breast cancer

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Glossary

- **WHO:** World Health Organization
- **ECIS:** European Cancer Information System
- **SEOM:** Spanish Society of Medical Oncology
- **SLNB:** Sentinel Lymph Node Biopsy
- **SPECT/CT:** Single Positron Emission Computed Tomography/Computerized Tomography
- **AR:** Augmented Reality
- **VR:** Virtual Reality
- **HMD:** Head-Mounted Device
- **PET:** Positron Emission Tomography
- **Tc99m:** Technetium-99m
- **I-125:** Iodine-125
- **CAS:** Computed-Assisted Surgery

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1. Introduction
1.1 Motivation

Cancer is the one of the most common causes of death and one of the leading obstacles in the increment of life expectancy everywhere in the world. In 2020, the GLOBOCAN report by the Agency for Research of Cancer, which estimates cancer incidence and mortality, reported that approximately 19.3 million new cancer cases (18.1 million excluding nonmelanoma skin cancer) and almost 10 million cancer deaths (9.9 million excluding nonmelanoma skin cancer) occurred. Particularly, female breast cancer surpassed lung cancer as the most commonly diagnosed one, with an estimated 2.3 million new cases (11.7%), followed by lung (11.4%), colorectal (10.0 %), prostate (7.3%), and stomach (5.6%) cancers. Nonetheless, lung cancer remained the leading cause of cancer death, with an estimated 1.8 million deaths (18%), followed by colorectal (9.4%), liver (8.3%), stomach (7.7%), and female breast (6.9%) cancers. In addition, it is expected that by 2040, the global cancer burden will be of 28.4 million cases, a 47% rise compared to 2020 [1].
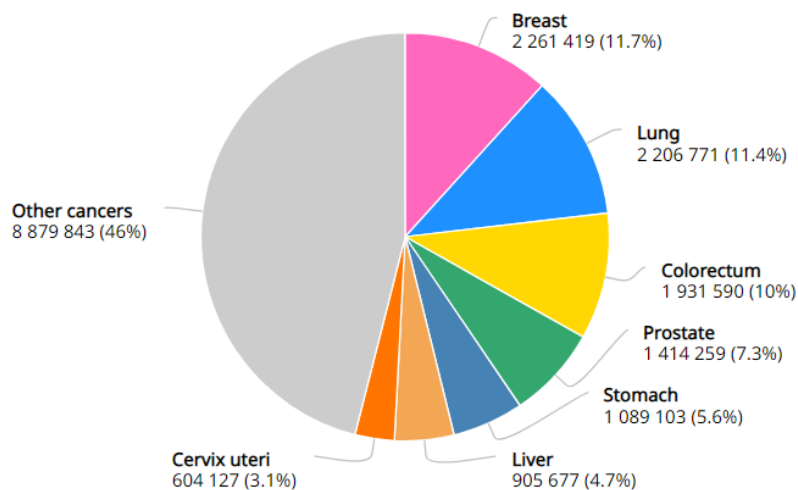
Fig. 1 Estimated number of new cases of cancer worldwide [2]

Given the statistical relevance of breast cancer in our society, different strategies have been developed to combat this problem. One of the major contributors to breast cancer treatment is nuclear medicine, a specialized area of radiology that uses small amounts of radioactive materials to examine a patient's organ function and structure [3].

After breast cancer has been diagnosed and staged by physicians, most patients undergo surgery and the most prominent use of nuclear medicine imaging in breast cancer surgery is in Sentinel Lymph Node Biopsy (SLNB), a surgical procedure in which sentinel nodes are removed and analyzed to determine whether cancer has spread beyond a primary tumor [4]. In this type of intervention, radiologists prepare a guide map of the localization of sentinel nodes using SPECT/CT imaging for surgeons to use [5].

On the other hand, important technological innovations have prompted new opportunities for clinician-as-user applications related to Augmented Reality. While "Virtual Reality" (VR) and "Augmented Reality" (AR) are typically confused, both VR and AR differ in the way they incorporate real-world elements to its visualization [6]. Regarding its role in medicine, the main application is 3D data visualization. For instance, accurate localization and description of the shape of lymph nodes is crucial when performing SLNB so, image-guided interventions enhance the precision of the resection. Besides, 3D reconstructed images of nuclear imaging techniques such as PET and SPECT can be powerful tools not only in clinical applications, but also for student training [7].

1.2 Objectives

The aim of this project is to continue the Final Degree Project conducted by Silvana Gràcia – a former Biomedical Engineering Student in UB – and take one step further in the implementation of AR in surgeries. While the former's main goal was to create an artificial phantom to improve the accuracy in the location of the tumor in breast cancer and assess the performance of an AR model with numerical methods [8], this project aims to improve the localization of sentinel lymph nodes in SLNB using AR.

The principal idea is to increase the accuracy and minimize the overall costs and resources invested in SLNB through the implementation of AR. Thanks to this hypothetical application, a nuclear medicine physician will not have the obligation to be physically in the surgery room during the intervention as they will be able to previously assess the localization of the sentinel node. The following specific objectives were set to achieve the main goal:

A. **3D model based on nuclear images of a breast phantom:** The author will develop a 3D model based on SPECT/CT scan images from a previously prepared breast phantom with radioactive activity to simulate hypothetical results.

B. **3D model based on nuclear images of a real patient:** The author will build a 3D model based on SPECT/CT scan images from a real breast cancer patient.

C. **Assessment of 3D models in AR:** The author will visualize the resulting AR 3D models in an AR tool.

1.3 Methodology

The steps to follow in this project can be separated in two different sections. The first section will be focused on creating a manual where it is explained what is necessary and how to build a 3D Model from a nuclear medicine image for an AR application. First, we will collect nuclear images from a breast phantom, those image reconstructions will be segmented and processed and after that, the virtual objects created will be placed in an AR scenario.

Once the results based on the breast phantom images are satisfactory, the second part will be conducted. Segmentation, processing, and AR implementation will be applied to nuclear images from a breast cancer patient but, the result will be a more complex model that features more virtual objects such as skin, bones, or lungs.

AR 3D model based on breast phantom	AR 3D model based on real patient
Breast phantom acquisition	Real patient acquisition
Segmentation and post-processing	Segmentation and post-processing

Virtual 3D models in AR
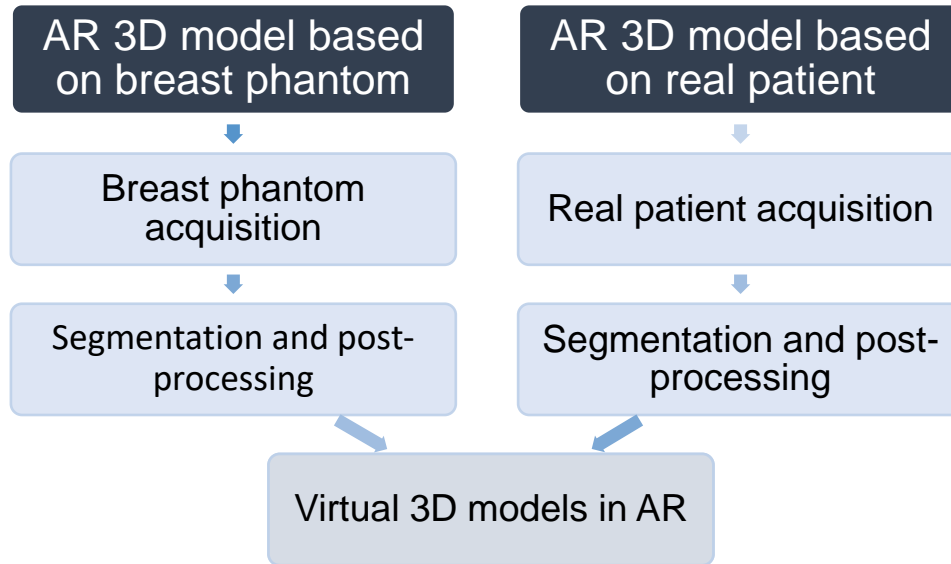
Fig. 2 Diagram of the project's methodology

1.4 Scope and span

The main interest of this project is to improve SLNBs by implementing AR technology. To do so, the scope of the project includes:

- Bibliographic research of recent AR innovations and improvements made in the SLNB field.
- Recreation of a patient's radioactive activity when prepared for a SLNB through a breast phantom.
- Building of a breast phantom 3D model, including the simulated radioactive activity.
- Creation of an AR application to visualize the whole 3D model.
- Assessment of the breast phantom holographic results.
- Building of a 3D model based on a real patient's anatomy and acquisitions.
- Validation of the complex human model in AR technology.

On the other hand, the span of this project goes from February 2022 until June 2022, the last semester of 4th year of Biomedical Engineering. The author must fulfill all previous objectives without missing the timing given that the real patient acquisition should be done only one time. Furthermore, the author chose to work on the project from distance so, communication with tutors was done mostly in a telematic way.

1.5 Location

The project presented was carried out with the aid of the Nuclear Medicine Department at the Hospital Clínic of Barcelona, located at the floor 0 – stairs 9 – Door 9A. Also, the author was helped by CIMNE (International Center for Numerical Methods in Engineering) located at the Campus Nord of the UPC (Polytechnical University of Catalonia). As stated before, the majority of the meetings to discuss the development of the project happened online periodically with Dra. Niñerola, Dr. Soudah, and Óscar de Cross.

2. Background

2.1 General concepts

In order to have a better understanding of the motivation of the project and the areas it covers, this section will give insight about treatment of breast cancer and more specifically, SLNB.

2.1.1 Treatment of breast cancer

Different therapeutic approaches employed for breast cancer management include cytoreductive surgery, radiation treatment, targeted endocrine/molecular therapy, and chemotherapy. Due to the heterogeneity of the disease, the treatment protocol requires rationalized therapy in individual cases according to the characterization and stage of the disease [9]. Nonetheless, most women with early-stage breast cancer are candidates for breast-conserving surgery with radiotherapy or mastectomy. According to Cancer Research UK, the world's largest independent cancer research organization, 81% of breast cancer treatment requires surgery of some kind [10].

There are different types of breast cancer surgeries that can be performed depending on the situation arisen. Operations to treat breast cancer include [4]:

Fig. 3 Sentinel node biopsy [4]

- **Lumpectomy**: The surgeon resection the carcinoma and small part of surrounding healthy tissue. It is recommended for removing smaller tumors.
- **Mastectomy:** The surgeon removes the entire breast, including lobules, ducts, fatty tissue, and some skin (nipple and areola).
- **SLNB:** The surgeon extracts a limited number of lymph nodes to analyze and evaluate if cancer has spread outside the breast.
- **Auxiliary lymph node dissection:** After assessing that cancer has been found in sentinel lymph nodes, the surgeon can remove additional lymph nodes.
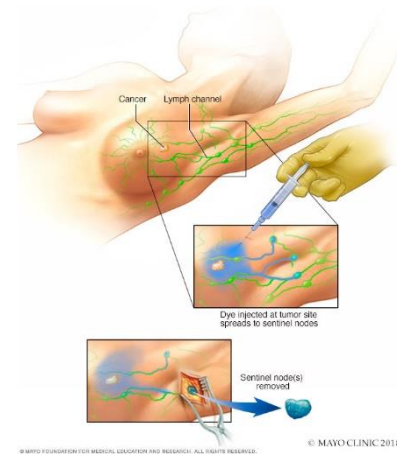
2.1.2 Sentinel lymph node biopsy in breast cancer

To understand better the importance of lymph node in cancer diagnosis and treatment, it is necessary to understand what the lymphatic system and sentinel node is. The lymphatic system is a part of the circulatory system that helps maintain fluid balance in the body by collecting excessive fluid and its particulate matter from tissues and depositing them in the bloodstream [11]. Lymph nodes are small organs part of the lymphatic system. These structures filter substances that travel through the lymphatic fluid, and they contain lymphocytes that help the body's immune system [12].
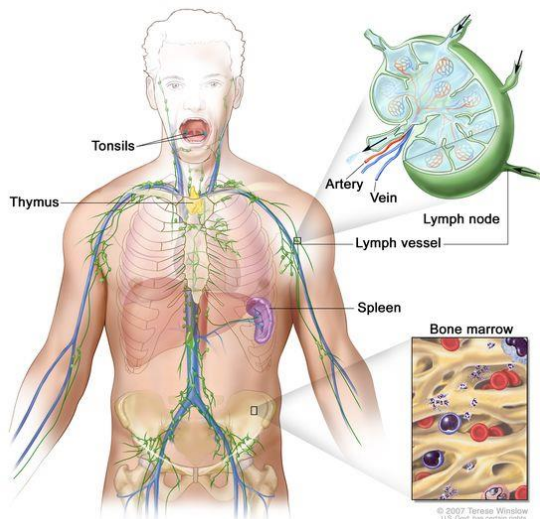
Fig. 4 Anatomy of the lymph system [12]

There are many lymph nodes throughout the body and the reason why they are so relevant is because sentinel nodes are the first lymph nodes where cancer cells might drain from a tumor. For breast cancer, they are usually located in the armpit and if there's no sign of cancer in the sentinel nodes, it is unlikely that cancer has spread to other lymph nodes. Thus, sentinel lymph node biopsy is crucial in the accurate staging of cancer and reducing side effects of the surgery [13].

Sentinel node biopsy is used for axillary staging, and individualized approaches are minimizing the need for axillary dissection in women with positive sentinel nodes. Administration of hormone therapy or chemotherapy after primary surgery is used in most women based on proven survival benefit so, the relevancy of SLNB for the future patient's treatment is clear. Staging helps decide the adequate dose of chemicals for therapy [14].

The procedure of a sentinel lymph node biopsy (SLNB) starts with nuclear imaging. Before the surgery, a nuclear medicine clinician injects a radioactive tracer, typically technetium-99m (Tc99m) as it bonds with cancerous cells, near the tumor to observe where it drains in the lymph system. After that, a SPECT/CT is performed in the patient to detect where the sentinel lymph nodes are [15]. Once the location is known, another radiotracer can be placed inside the patient for better structure detection. For example, Iodine-125 (I-125) can be placed inside the patient's desired location through echography and it will not move. Then, another SPECT/CT will be performed in order to have more information.
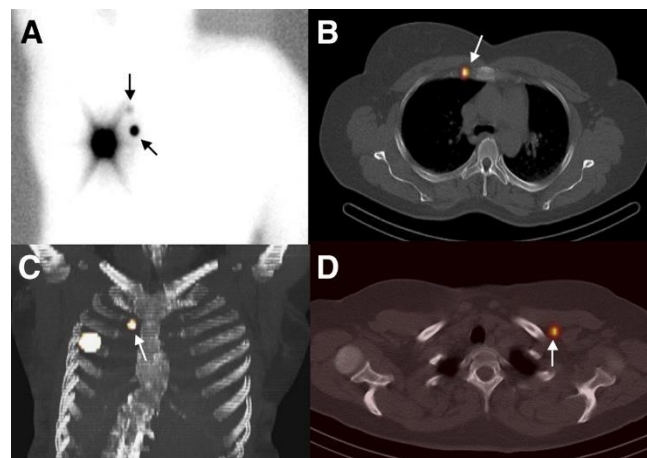
Fig. 5 Tc99m SPECT/CT results for lymphatic mapping [16]

After that, the nuclear medicine professional gathers the results and assesses an optimal guiding plan for the surgeon to follow. The following day, the patient still has the radiotracers inside their body and during the intervention the surgeon will use a device to detect lymph nodes with radioactive activity. Once the sentinel lymph node is located, the surgeon makes a small incision and removes the node. If cancer is found, the surgeon may remove additional lymph nodes, either during the same biopsy procedure or during a follow-up surgical procedure. SLNB is usually done at the same time the primary tumor is removed. In some cases, the procedure can also be done before or even after (depending on how much the lymphatic vessels have been disrupted) removal of the tumor [15].

2.2 State-of-art

Computer-assisted surgery (CAS) is the new cutting-edge technology transforming the field. This technique was introduced more than 20 years ago but the necessity of more operative accuracy and improved safety regarding the surgery has brought new elements to the already revolutionizing method. Different augmented reality systems have been proposed and tested positively for different types of surgeries, mainly orthopedic surgery and craniomaxillofacial surgery. However, limitations such as the cost of the devices or the lack of prospective comparative studies have created a big gap between research and wide application [17]. Current studies state that while AR is still in an evolving state where clinical applications are limited, it will soon become part of standard of care in surgeries [18].

AR techniques have been introduced to better able to pre-operatively plan the surgery, intra-operatively navigate through reconstructions of patient imaging and discuss remotely with other colleagues outside the operating room. To further analyze the role of AR in sentinel node mapping, the author presents a literature review to assess the studies related to AR in sentinel node-related procedures. The author has performed a PubMed search using the keywords "Augmented Reality" AND "sentinel node", where 15 articles were shown. After reading the abstract of each one, 7 articles were chosen given their relevance related to the topic.

Ref.	Type of cancer	Purpose	Data Source	Segmentation Software	AR display system
[19]	Head and neck melanoma	Show that AR SPECT/ CT data visualization in 3D can be used to accurately localize targets for head and neck melanomas.	SPECT/CT	Horos Software	Microsoft HoloLens

[20]	Cervical cancer	Usage of a drop-in gamma probe for intra-operative SPECT imaging through AR in the scope of minimally invasive robot-assisted interventions.	SPECT	Not mentioned	Da Vinci's vision cart
[21]	Breast cancer	Show that integrated use of freehandSPECT-mobile gamma camera combines better than the individual radio guidance.	SPECT	Declipse SPECT system	Declipse SPECT system
[22]	Penile cancer	Investigate magnetic particle imaging and navigation modality (fhMPI) for intraoperative localization, along with a hybrid approach.	SPECT	Declipse SPECT system	Declipse SPECT system
[23]	Head and neck melanoma	Assess gamma-camera based freehandSPECT for intraoperative sentinel node identification	SPECT/CT	Declipse SPECT system	Declipse SPECT system
[24]	Skin melanoma	Introduction to an AR coaxial projection imaging technique to directly observe the surgical area with the naked eye.	ICG imaging	AR-CPI system (NIRF-2H, Sino-medic)	AR-CPI system (NIRF-2H, Sino-medic)

[25]	Head and neck cancer	Describe an innovative SLN guidance approach using a radionuclide tracer, 3D augmented reality-guided imaging, and near infrared (NIR) fluorescence over-lay imaging.	SPECT/CT	Surgic Eye 3D system	Surgic Eye 3D system

Table 1 Literature review of AR approaches in SLNB

The most recent AR study in sentinel lymph node visualization during surgeries was carried out by the Department of Radiology of Stanford University in California, USA. The team built eight head and neck phantoms to show how AR visualization of SPECT/CT could help accurately localize targets in the head and neck region. For all evaluations, using the AR wearable reduced the time to detect targets compared to using the gamma probe alone.

During the study, the phantoms were painted with a mix of radioactive Tc-99m, which can be detected with a handheld gamma probe, and a fluorescent liquid visible under ultraviolet light to simulate lymph nodes on their surface. After scanning the phantoms for acquisition, the group sent the SPECT/CT data to Horos Project, a software to view and reconstruct medical images. After segmenting the images, the resulting mesh files were simplified and later manipulated in Unity to create the AR application.
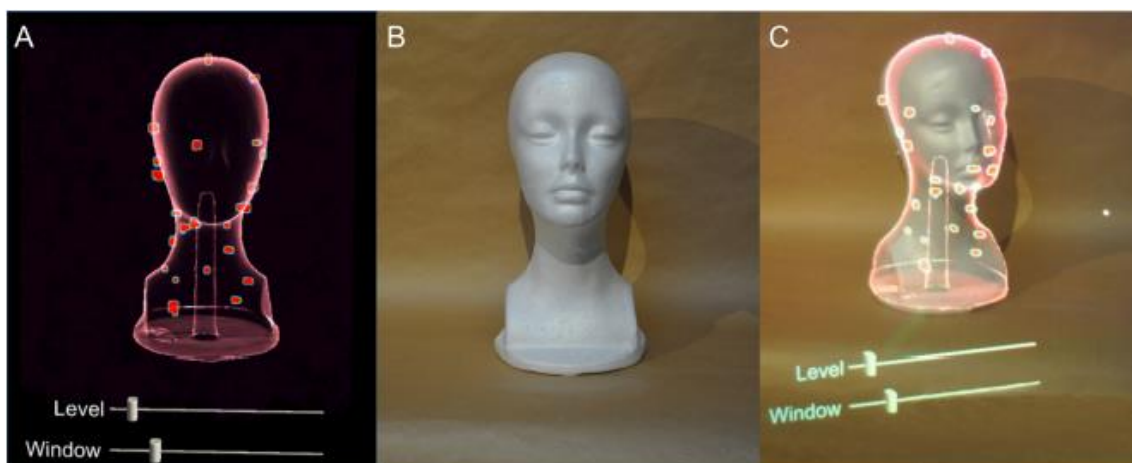
Fig. 6 3D virtual rendering superimposed in physical model [19]

The operator wearing Microsoft HoloLens could accurately superimpose the 3D virtual rendering to the mannequin thanks to previously implemented voice commands. After comparing the detection time per node with or without the AR headset, it was demonstrated that using the AR system could lessen the time to localize the simulated nodes. Furthermore, the average misregistration was less than 9mm.

Even though AR tools seem to be the future standard in sentinel node-related interventions, the alignment accuracy of the models in real-time must be improved to be used more widely. The error in identifying the site correctly may be caused by various causes. Some of the problems include: The professionals have to manually align 3D virtual renderings to phantoms, the fact that the software used to build the application is an open-source renderer not optimized for HoloLens and that the spatial resolution of SPECT is limited [19].

While most literature focuses on sentinel node in skin cancer, this project aims to take this application one step further and perform better and quicker registration of sentinel lymph nodes in SLNB.

It is important to acknowledge that this final studies project is a follow up project of three other UB Biomedical Engineering final degree projects. First of all, O. Palomares project studied the use of AR in lamb liver surgery. To do so, the author created and printed a 3D model of the liver, which was later tried on by the AR system [26]. Secondly, M. Puigferrat created personalized AR models of liver and breast to improve oncosurgeries [27]. Finally, S. Gràcia developed a Mixed Reality system to improve breast cancer interventions using an AR headset [8].

3. Marketing Study
3.1 AR in healthcare

AR has grown within the healthcare industry and many different companies have shown interest in taking part of it. Medical applications with AR are various and they range from augmented surgery, to augmented diagnosis and augmented practice etc. To exemplify this fact, a research of the most important AR medical companies has been performed.

Company	Product
MediVis	SurgicalAR is an FDA-cleared medical software using Microsoft HoloLens 2 to view medical images in 3D real-time. It is not intended for diagnosis but for informational purposes. AnatomyX is a medical software used for learning and educational purposes [28].

echopixel	Echopixel is a software platform that enables physicians to use a digital twin of the patient thanks to their medical images and view it as a hologram. The product is FDA-cleared so, it can be used for surgical planning and operative guidance solutions [29].
HELP LIGHTNING	Software service that specializes in remote assistance. They use augmented reality features to let surgeons remotely project their hands into the AR device of a surgeon on site and guide during the procedure [30].
AccuVein	Medical device that uses projection-based AR to find veins. They combine a laser-based scanner, processing system and digital laser projection to let users view a virtual real-time image of the vascularity of the patient on their skins' surface [31].
sentiar	CommandEP creates interactive augmented reality images real-time from catheters and 3D electroanatomic mapping systems to reflect the anatomy of the inner heart surface [32].
TOUCHSURGERY	They have a platform to train surgical students through AR technology. Allows users to practice surgery anywhere and consequently, improve the student's skills [33].
ImmersiveTouch	ImmersiveView is FDA-cleared platform that converts 2D medical images to 3D spatial models, improving surgical interventions. Advanced visualization helps physician study better the patient's anatomy [34].

Table 2 Emerging AR in healthcare companies

3.2 Future perspectives

As time goes by, Augmented Reality has started to be more present in the healthcare industry, not only as a diagnosis tool but also, a learning and treatment tool. Augmented Reality devices allow professionals to overlay digital information into the real world, which can result in important improvements in clinical practice, so the incorporation of such technique has been broadly studied so far [35].

In fact, according to Gartner's hype cycle, a methodology used by companies to assess whether a technology has already "matured", AR is no longer an "emerging technology" and is entering the phase where it is productive in the enterprise space. In 2020, Gartner's hype cycle report completely removed the technology as they considered that the innovation in this field has already started to move fast towards maturation [36].
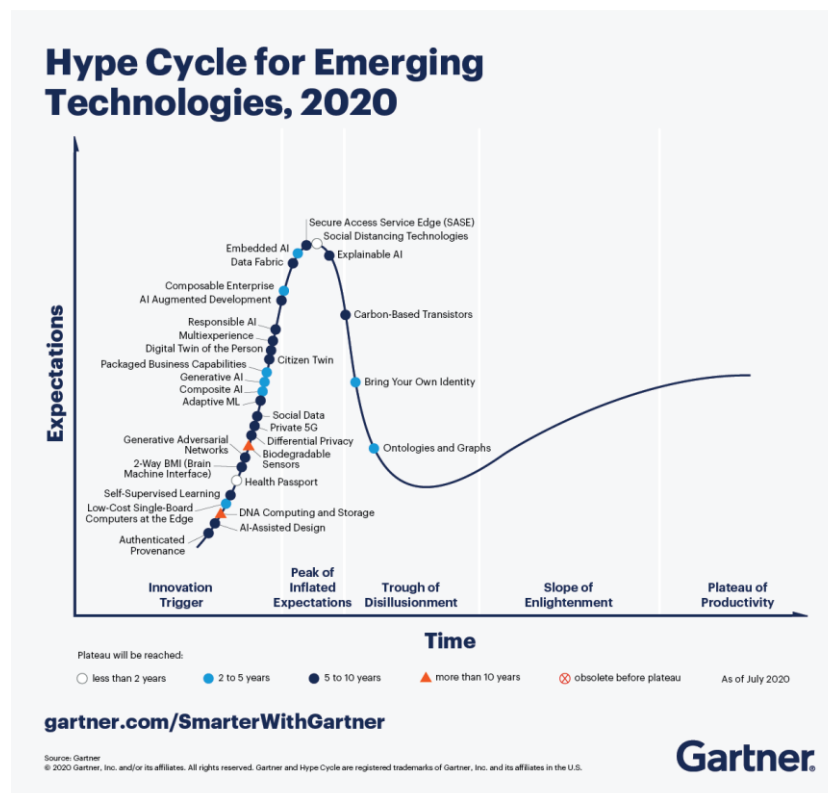
Fig. 7 Gartner Hype Cycle of 2020 [37]

While there are still some concerns related to bringing new technologies into existing workflows, privacy and regulatory affairs, costs etc. it is clear that the future of AR in healthcare is going to be a widely spread reality. Specifically, we will see proliferation in the following fields:

- Medical Education: Different universities such as NYU have started to use augmented reality tools for doctors and nurses in training. This way, they can access to more detailed learning materials and understand human anatomy with more precision. Furthermore, AR videos that show how to perform certain interventions and such can make the students reach a deeper understanding of the process [38].

- Operation Room: AR in surgeries is thought to be the future standard of care as more precision means better treatment and less recovery time for the patient. For instance, it can allow the surgeon to project CT or X-rays onto the body, to see both of them aligned at the same time. Technology like this can act as a navigator for the professionals to follow and help them maneuver with more ease [38].

- Clinical Practice: The potential of Augmented Reality in medicine is wide. AR could be useful in vastly different settings such a primary care center, an emergency room, or a dental office. Not only it can help physician to proceed with protocols faster, but also with more precision. Thanks to this advantage, diagnosis and treatment can improve logistic-wise [39].

According to Crunchbase, a platform to find business information about different companies, during the last quarter of 2021 almost $1.9 billion of venture capital was invested in startups in the virtual and augmented reality soft and hardware market [40]. Furthermore, it is expected that Augmented Reality Software World Market size will be worth $137.14 billion by 2028, growing at a CAGR (compound annual growth rate) of 57.21% from 2021 to 2028 [41].

Fig. 8 VR/AR Venture Capital Funding Numbers per year [40]

4. Legal aspects and normative

The whole project has taken place in Barcelona, Spain. For this reason, all legal requirements are subjected to the Spanish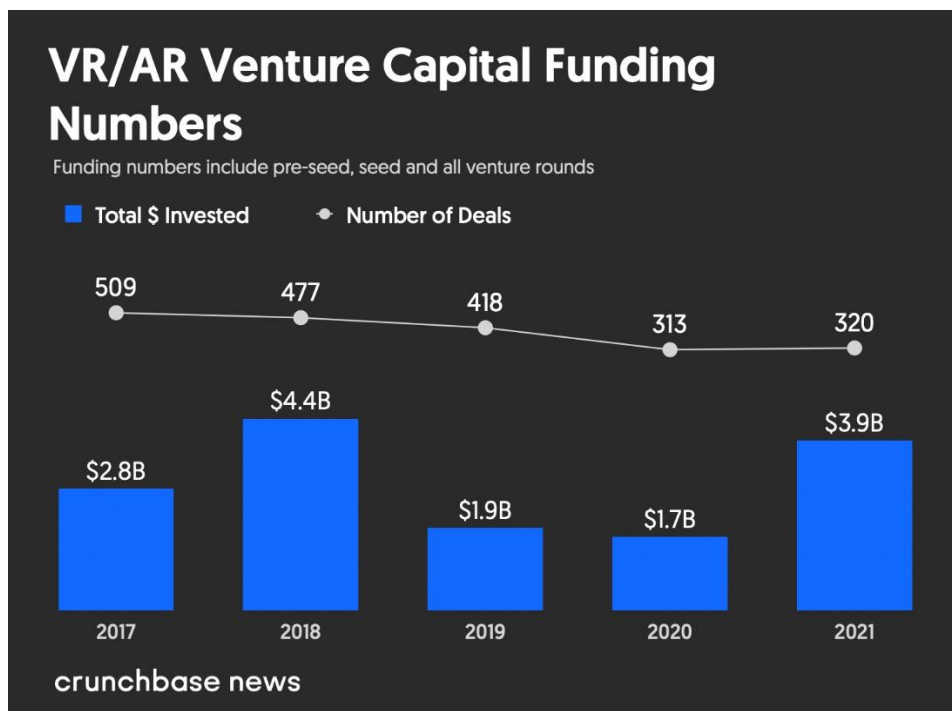 law. Precisely, this project functions under the regulations established by the University of Barcelona *"Normes generals reguladores dels treballs de fi de grau de la Universitat de Barcelona"* [42], the college where the author is affiliated. Specifically, this final project is regulated by *"Normes reguladores dels treballs de fi de grau d'enginyeria biomèdica"* [43], which is the regulation for final degree projects carried out by biomedical engineering students.

The Medical Device Regulation 2017/745/EU defines "medical device" in Article 1, p.2 as [44]: *Any instrument, apparatus, appliance, software, implant, reagent, material, or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:*

- *Diagnosis, prevention, monitoring, prediction, prognosis, treatment, or alleviation of disease,*
- *Diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability*
- *Investigation, replacement, or modification of the anatomy or of a physiological or pathological process or state,*
- *Providing information by means of in vitro examination of specimens derived from the human body, including organ, blood, and tissue donations,*

and which does not achieve its principal intended action by pharmacological, immunological, or metabolic means, in or on the human body, but which may be assisted in its function by such means. The following products shall also be deemed to be medical devices:

- *Devices for the control or support of conception.*
- *Products specifically intended for the cleaning, disinfection or sterilization of devices as referred to in Article 1(4) and of those referred to in the first paragraph of this point.*

It is important to point out that most of the devices (HoloLens 2 and Kinect) and tools (3D Slicer, MeshLab, and Unity) used for the project are not considered medical devices so, they are not required to follow European medical devices' regulations.

Moreover, this project uses real patient data, therefore the *"Ley Orgánica de Protección de Datos y Garantía de Derechos Digitales 3/2018"* must be followed. The aim of this law is to protect the intimacy, privacy, and integrity of the individual, in compliance with Article 18.4 of the Spanish Constitution. Similarly, it regulates the obligations of the individual throughout the data transfer process to ensure the security of the exchange [45].

5. Concept engineering

5.1 Solutions studied

The aim of this section is to evaluate different solutions to fulfill the tasks specified before:

	Possible solutions
3D Segmentation software	• 3D Slicer [46] • ITK-SNAP [47] • Syngo.via by Siemens [48]
Optimization of the model	• MeshLab [49] • Gmsh [50]
Post-processing	• MeshLab [49] • Blender [51] • Wings 3D [52]
Display AR	• HoloLens [53] • HoloLens 2 [54] • Intel AR headset [55] • Google ARCore[56]

Table 3 Possible solutions for every project task

5.1.1 3D Segmentation software

The three candidates to be the 3D segmentation software for this project were chosen based on the previous final projects. 3D Slicer, which was used by S. Gràcia [8], is a free and open-source software used for image analysis and scientific visualization. Given that the development of the platform is made by users, developers, partners etc., its features are various, and the results can be exported in different formats. Segmentation is a prominent feature of the application and even though it is not intended for clinical data, it supports a wide range of DICOM information objects [46].

Because 3D Slicer was not meant for clinical data, the author searched for a license-free segmentation software that was specialized in medical images and found ITK-SNAP. ITK-SNAP is a multi-platform image analysis tool focused on the problem of segmentation of 3D structures in medical images. The tool provides semi-automatic segmentation while also including the functions of manual segmentation, support of many 3D formats, tutorials etc. [47]

Finally, Syngo.via was evaluated as this was the segmentation software of choice in the final project of T. Puigferrat [27]. Syngo.via is a multimodality software created by Siemens with the aim of offering a complete solution for imaging applications for oncology, cardiology, and neurology. The diagnostic tool supports all the workflow from processing to diagnosis and sharing. It is possible to use advanced PET and CT segmentation and quantification tools and achieve fast and accurate results in 3D models [48]. Nonetheless, this option was discarded because, as of today, the software's license is still closed, and it is not possible to export the results.

5.1.2 Optimization and post-processing of the 3D model

MeshLab is an open-source software used for processing and editing 3D triangular meshes. Its features include aligning, visualization and presentation, reconstruction, hollowing and closing, cleaning 3D models, analysis and measurement, color mapping and texturing, simplification, refinement and remeshing etc. [49]

Gmsh is an open-source 3D finite element mesh generator prepared with a pre- and post-processing features. The aim of this software is to provide a user-friendly meshing tool with advanced visualization capabilities [50].

Blender is a free and open-source software used for 3D creation. It supports the whole process from modelling, rigging, simulating to rendering and compositing. It runs in Linux, Windows, and Macintosh computers. Even so, Blender is not meant for clinical data and is more focused on the artistic aspect of 3D modelling [51].

Wings 3D is a free and open-source software used as a 3D polygon modeler. It features a user-friendly interface where you have wide range of modelling and meshing tools. Said interface is configurable for further commodity and the resulting model can be exported to common 3D file formats [52].

5.1.3 Display AR

HoloLens is wearable VR headset with transparent lenses for an augmented reality experience. HoloLens allow users to experience holographic images as if they were part of the real world. The device runs the Windows Mixed Reality platform and two models have been developed by Microsoft, one in 2016 and another in 2019 [53]. To compare both devices more accurately, the following table compares relevant characteristics to consider when choosing the solution:

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	HoloLens (2016) [53]	HoloLens 2 (2019) [54]
Processor	Intel 32-bit (1GHz)	Qualcomm Snapdragon 850
Design and fit	579g and bulkier	566g and more stylish
Memory	2GB RAM	8GB RAM
Field Of View	30 degrees	52 degrees
Hand and eye tracking	One hand and no eye tracking	Two hands and eye tracking
Camera	2.4MP, HD video	8MP, 1080 video
Resolution (in pixels)	1280 x 720 (per eye)	2048 x 1080 (per eye)
Price	$3,000	$3,500

Table 4 HoloLens vs. HoloLens 2 comparison

On the other hand, other devices outside HoloLens were also considered. Oculus Quest 2 is a VR display headset by Facebook Reality Labs that allows the visualization of elements in AR. Some of its features include a new processor called New Qualcomm Snapdragon XR2 Platform, a hand tracking system, a field of view of 100 degrees, a resolution of 1832x1920 (per eye) and a reasonable price ($399) [55].

Another possible solution is using the Magic Leap One, a head-mounted display that can support complex 3D visualization through sophisticated sensors. If we compare this device with the others mentioned above, the features that stand out are its lightweight (316g), its tracking and control that includes haptic feedback and 6DoF, and its price which is $2,295 [56].

5.2 Solutions proposed

The following table shows the result of the options picked after carefully evaluating every section of the solutions studied:

	Solutions proposed
3D Segmentation Software	3D Slicer
Optimization of the model	MeshLab
Post-processing	MeshLab
Display AR	HoloLens 2

Table 5 Solutions proposed for every project task

Referring to the 3D segmentation software, the author chose 3D Slicer given that the software was open source, which meant that it had many features, and free to use. Also, the author was familiar with the application while the other options required some training and previous tutorials. Furthermore, 3D Slicer had the option of exporting the resulting file in different formats, making it compatible with many platforms.

Regarding the optimization and post-processing of the mesh, MeshLab was chosen for both as the best option. The reason why MeshLab was considered the most suitable solution was because its performance was the easiest to learn in comparison to the other candidates. Given that MeshLab was a candidate for both optimization and post-processing of the model, choosing it would mean that the author would have to spend less time learning how to use software. Also, some of them did not export the final models into compatible file formats for the next tasks.

Finally, the AR display the author will use is HoloLens 2. Even though the other solutions studied had similar qualities to the chosen one while being cheaper, CIMNE – the investigation center where the research team is based – had both models of HoloLens. Given that HoloLens 2 is an upgraded version of HoloLens, and the team was already familiar with its workflow and specifications, the headset was the best option.

6. Detailed engineering

6.1 Image acquisition of breast phantom

The first task to do is the nuclear image acquisition of the breast phantom. This part of the project was done in the Nuclear Medicine Department with the help of Dra. Niñerola. The breast phantom was chosen because first trials need to be performed in mannequins in order to be assessed. Once the procedure is validated, trials are performed in patients. Also, since first trials in mannequins are mandatory, the department has different breast phantoms available to perform nuclear imaging tests.

The first step was introducing the radioactive materials necessary inside the breast phantom to simulate the activity of the radiotracer when reaching the sentinel lymph node. As explained previously, before SLNB, Technetium 99 sulfur colloid (Tc99m) is injected near the patient's tumor. By doing so, the substance is drained in lymph nodes near the carcinoma and a physician can use a device to detect its exact location. In our case, Tc99m material will be placed in three locations with different acquisition dose percentages compared to the hypothetical initial dose that would be injected in one single place.
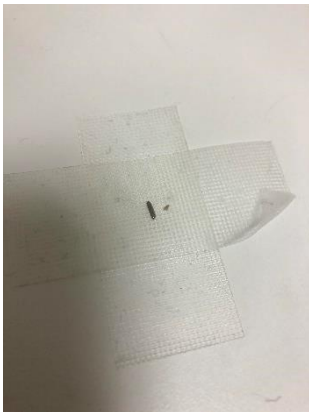
Fig. 9 I-125 radioactive seed

After that, we will introduce 2 different radioactive seeds of Iodine-125 in the areas of interest. This radioactive material is typically used to mark the sentinel node or tumor location. The reason why another marker is needed is because Tc99m is bound with tumoral cells, which means that the material circulates along the lymphatic system. In contrast, I-125 is placed through echography and there is no risk of it moving since its placement. The following picture is an example of the Iodine seeds used in this project. As it can be seen in Fig. 9, the material is extremely small, and it must be manipulated carefully by a professional.

*Fig. 10 Location of radioactive material in breast phantom.
Green: Injecting site; Red: I-125; Blue: Tc99m*

Fig.10 shows the location in which the radioactive material was inserted. The green circle tells where the hypothetical injecting site is. Next, the three blue circles mark where Tc99m was placed to simulate the presence of sentinel nodes. Number 1 corresponds to 2% acquisition while number 2 corresponds to 5% and number 3 to 10%, which makes sense given the location of the injecting site. Finally, the two red circles point where the Iodine-125 was placed.

After that, a physical marker was placed above the breast phantom in order to have a reference when overlapping the different elements in the future. This object is necessary for the alignment of the different elements in the 3D model later. The first placement of the marker is shown in Fig. 11 but, after observing its instability when placed in the SPECT/CT machine, the location changed to the clavicle area.

Fig. 11 Physical marker for breast phantom

Both the CT and SPECT scan were performed in a hybrid SPECT/CT scan (Symbia Intevo, Siemens) which is located in the Hospital Clinic. First, the SPECT scan was performed on the phantom and the result was a nuclear image with the Tc99m window (technetium reconstruction) and another one with the Iodine-125 window (iodine reconstruction). This was possible because the photopeak energy of both radioactive materials is far from each other, with Tc99m at 140keV while I-125 is at 35keV. Next, a CT scan was performed to register a cross-sectional image of its simulated tissue and the physical marker. After performing the acquisitions, the resulting DICOM files were imported into the segmentation software.

6.2 Segmentation of SPECT/CT results

With the aim of performing the segmentation on 3D Slicer, the author used the previous final project by S. Gràcia to learn [8]. Furthermore, an extension for the software called Segmentation Editor Extra Effects was added to have more options when segmenting and improve the accuracy. The following steps can be applied generically for the breast phantom and both the CT and SPECT acquisitions:
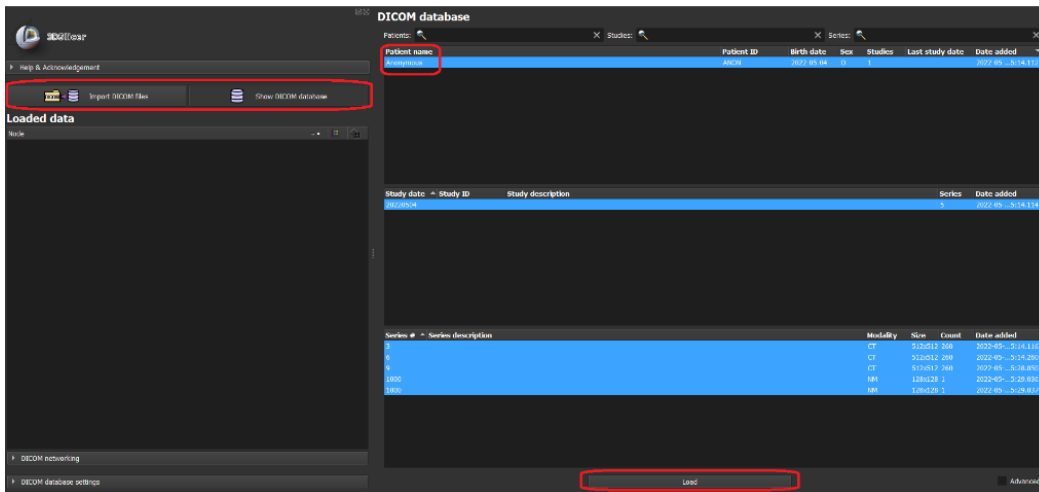
6.2.1 Loading of DICOM data

Fig. 12 View of 3D Slicer menu after loading data

The first step is loading the DICOM data correctly. After opening the platform, the "Load DICOM Data" option is chosen. When importing DICOM files, it is important to select the folder that contains all images (CT and SPECT included). If there is no error, data is shown in the DICOM database on the right of the screen. Then, it is necessary to select the patient and load the data through the "Load" option below. Finally, the result of the image acquisition should be shown like in the following figures (make sure show/hide branch or node is enabled). The results can be seen from all planes (transverse in red, sagittal in green and coronal in yellow) in 3D Slicer.

While Fig. 13 shows a SPECT scan with the Tc99m window and Fig. 14 shows a SPECT scan with the I-125 window, Fig. 15 shows a CT scan of the breast phantom and the physical marker (these parts appear in white).
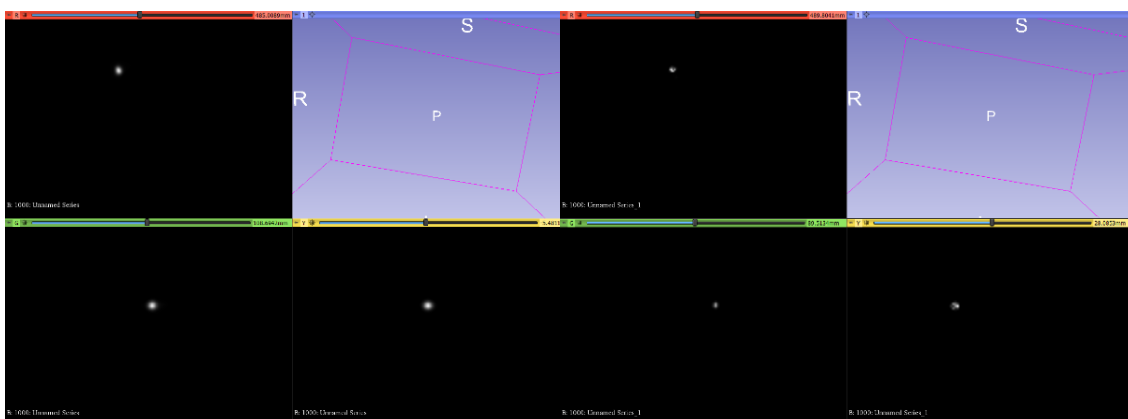

Fig. 13 SPECT scans of breast phantom with Tc99m window and with I-125 window
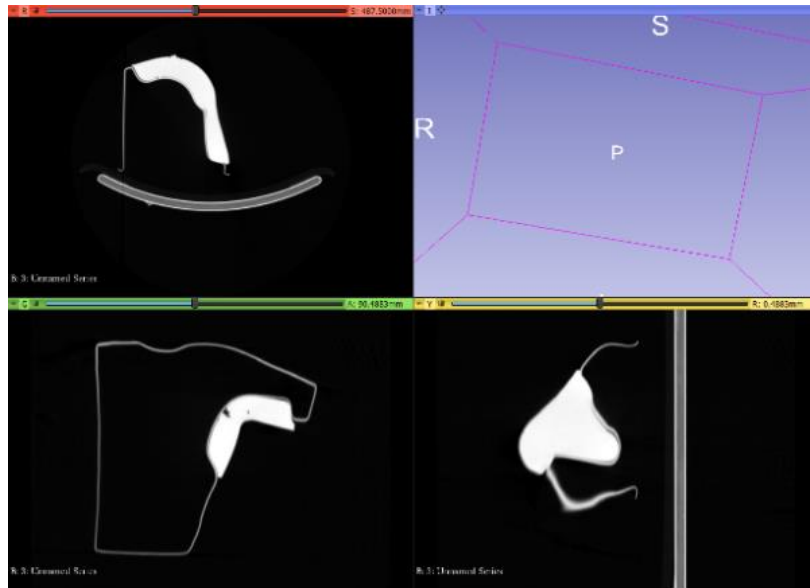
Fig. 14 CT scan of breast phantom

6.2.2 Thresholding of the segmentation

Fig. 15 Threshold of the CT scan segmentation

The aim of this step is to limit the breast phantom image in the most accurate way. To segment the CT, the "Segment Editor" in the upper options bar is needed. The "Master volume" option presents all the volumes that can be edited and after choosing the desired one, the "Add" button will create a new segmentation. Next, the "Threshold" option in the menu is chosen and a threshold minimum and maximum value has to be chosen so that only the desired part to be segmented is colored (and as little white as possible).

In this case, the threshold range goes from 99 to 3071 and the result is shown when pressing "Apply" and then, "Show 3D" (the model can be off-center). A result resembling the one shown in Fig. 16 should appear.
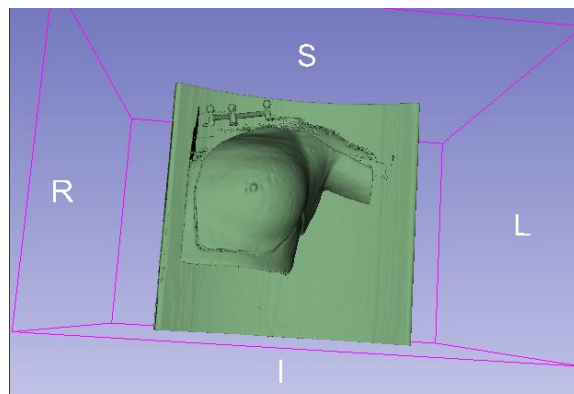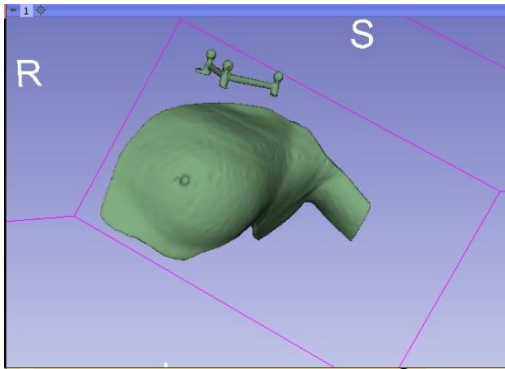

Fig. 16 Result of breast phantom CT scan thresholding

6.2.3 Manual slicing of the model

Fig. 17 Breast phantom model after applying "Scissors"

As shown in Fig. 16, the result needs some modifications. Thanks to the "Scissors" option in the "Effects" menu, it is possible to delete manually the undesired parts of the model created, especially the obvious ones like the table behind the breast phantom's model. After removing the unnecessary parts of the segmentation, the result should be just the phantom and the marker, as shown in Fig. 17.

6.2.4 Smoothing

The "Smoothing" option from the "Effects" menu is a powerful tool that can remove extrusions and fill possible undesired small holes within the model. Furthermore, it is possible to apply "Median" and "Gaussian" filters to smooth its surface by flattening irregularities and have a more polished segmentation result like in Fig. 18. After retouching the model until its final shape, the result must be exported to a STL file format so that post-processing and optimization can be performed.
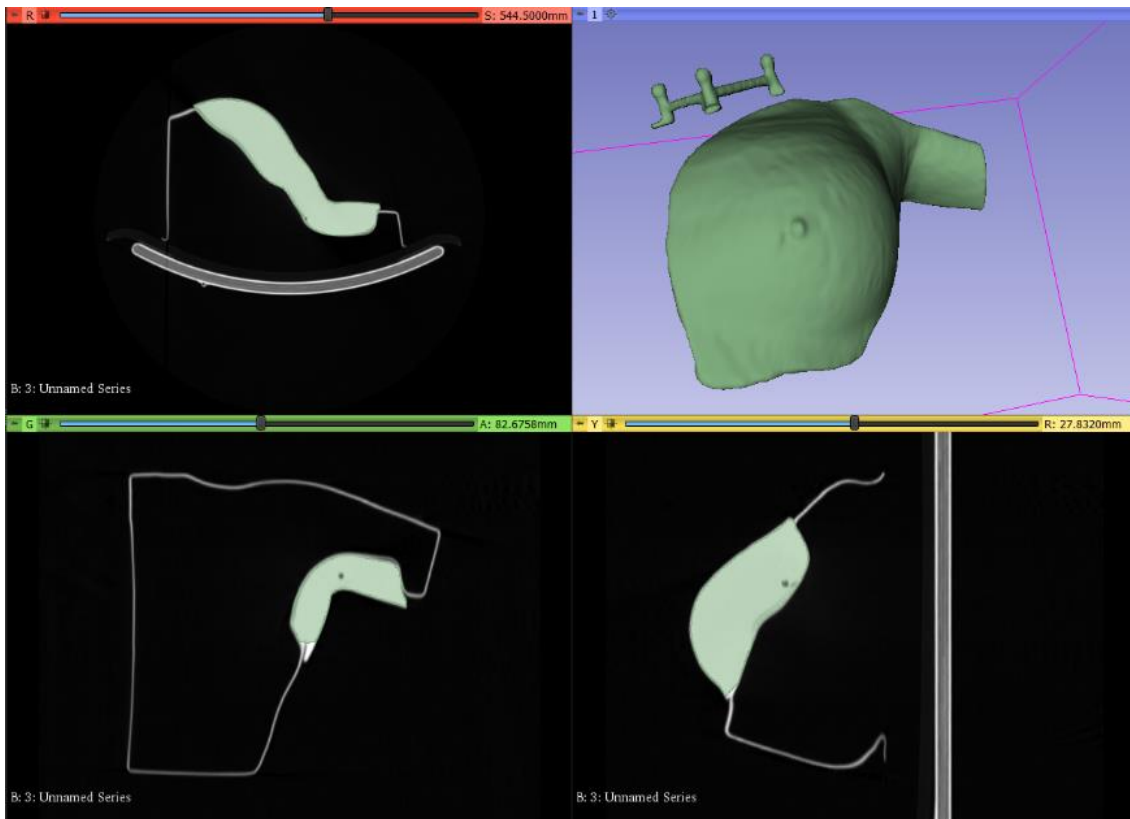

Fig. 18 Final breast phantom model in 3D Slicer

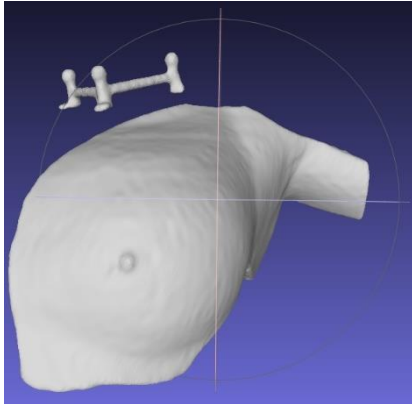## 6.3 Optimization and post-processing of the breast phantom's mesh

Fig. 19 Breast phantom model in MeshLab

The purpose of this objective is to improve the shape of the model so it can be implemented in the AR application in the best condition possible. MeshLab is the chosen software to fulfill the task and the previous STL file must be imported with the "Import Mesh" option in the tool bar. The visualization of the mesh should look similar to the one in Fig. 19. The following steps were followed for both the mannequin model, Tc and I acquisitions.

6.3.1   Filter application

The "Filters" options in the upper bar offer various techniques to filter the model we are working with. First of all, a smoothing filter is applied to correct different imperfections. While the most typical smoothing filters are the Laplacian and the Taubin one, the latter is chosen as it is desirable to preserve the original shape of the input model and the Laplacian filter has more shrinkage.

In this case, the default parameters are changed into lambda = 1 and smoothing steps = 20 for a better result. The resulting smoothed model can be seen in Fig. 20.
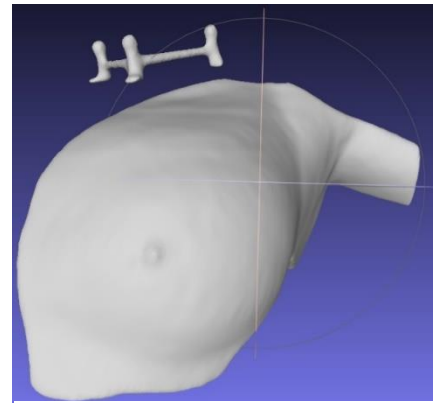
Fig. 20 Breast phantom model after smoothing

6.3.2   Simplification of objects
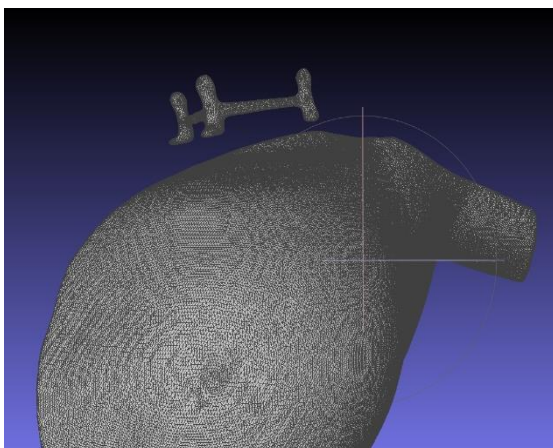
Fig. 21 Breast phantom mesh before simplification

Fig. 21 shows the complexity of a triangular mesh that the breast phantom model is. This high number of shapes is not efficient when talking about computational time so, a simplification of the model must be performed.

The objective is not to lose accuracy when simplifying the model, and for that reason the "Simplification: Quadratic Edge Collapse Decimation" is chosen among other options.

The number of triangles is reduced from 130410 to just 5000 while preserving the boundaries of the mesh. Thanks to this option, the limits of the models stay the same while the inner area of the mesh is simplified. The result of this reduction is shown in Fig 22.

In addition, Fig. 23 shows the final model of the SPECT showing the radioactive activity of I-125 radiotracers while Fig. 24 shows the final model of SPECT showing the radioactive activity of Tc99m.
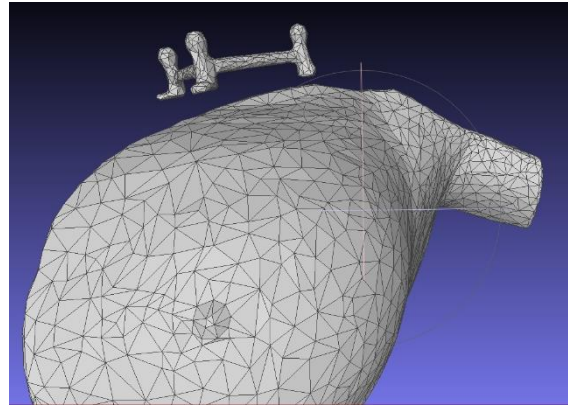
Fig. 22 Final breast phantom model after simplification
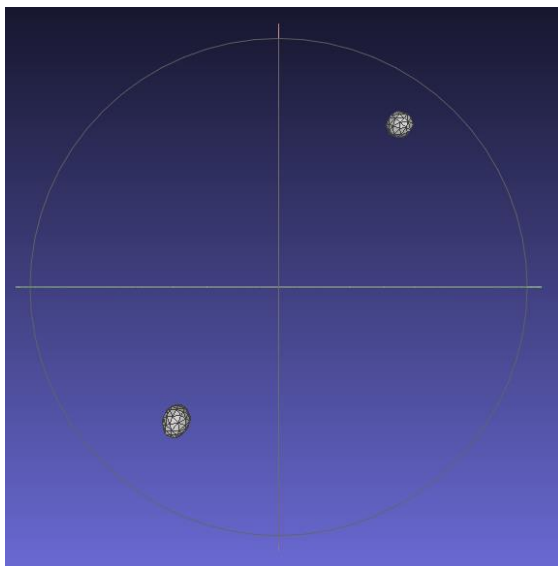
Fig. 23 Final model of I-125 window SPECT

Fig. 24 Final model of Tc99m SPECT

6.4 Segmentation of CT and SPECT scans of a real patient

After assessing the AR application for the breast phantom, the next step is following the same procedure again but with a real patient.
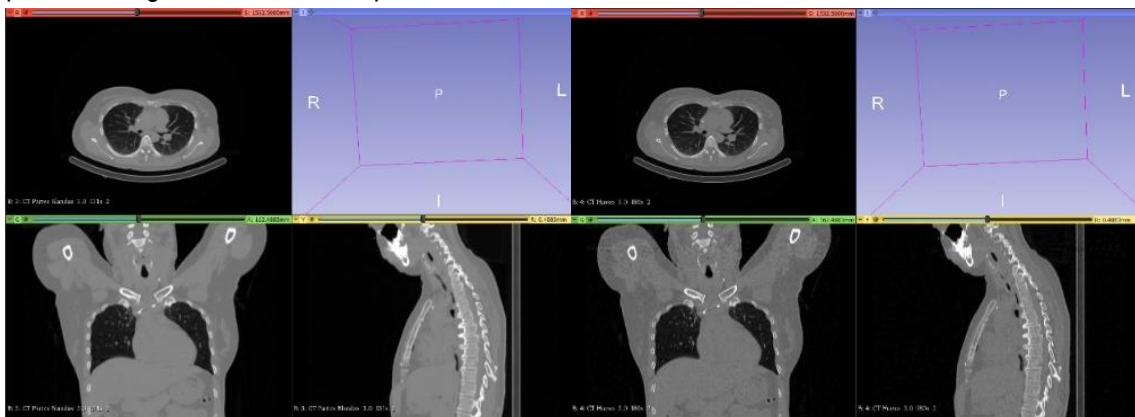
Fig. 25 CT scans of the patient's soft tissue and bones

This patient has been scanned in a SPECT/CT scan in the Nuclear Medicine Department and they have: 2 Iodine-125 radioactive seeds and a sentinel node that was previously localized through the injection of Tc99m. DICOM data was uploaded in 3D Slicer for its visualization as shown in Fig. 25.

The patient's images contain two CT scans, one for bones and another one for soft tissue. Also, there is a reconstruction in the Iodine-125 window, another reconstruction in the Tc99m window and a copy of the previous one but with a mask in the injecting point to erase it because it had too much activity.

The steps to follow are the same as the previous section (6.2), by using the "Threshold" option it is possible to separate the volume of interest from the rest of the model. Since this is an actual patient's data, 5 different elements have been segmented: Skin, bones, lungs, sentinel node (Tc99m activity) and I-125.
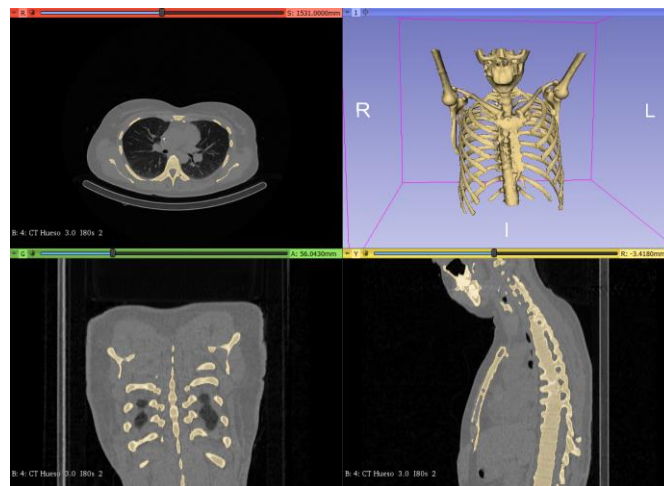
Fig. 26 Segmentation of the patient's skeleton

Fig. 26 shows how a CT scan of bones from the patient was transformed into a model. Even though majority of bones are recognized in the model, there are some parts missing that are not registered by the software.
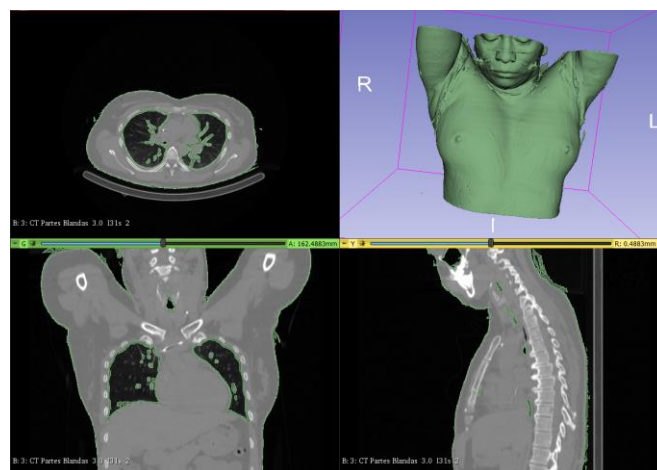
Fig. 27 Segmentation of the patient's skin

Fig. 27 shows how a CT scan of soft tissue was turned into a skin model of the patient. Given how thin skin is, it was not possible to segment it without registering the lungs' skin too. Furthermore, majority of smoothing filters were not applicable because they would erase the outer skin of the model.
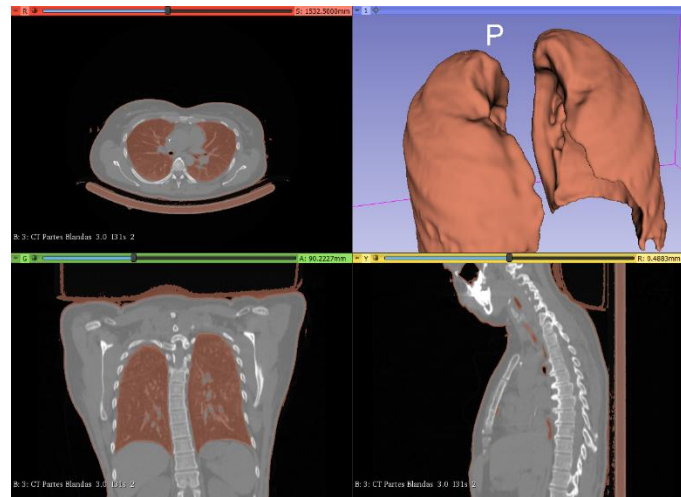
Fig. 28 Segmentation of the patient's lungs

Fig. 28 shows how a CT scan of soft tissue was turned into a lung model of the patient by changing some of the parameters mentioned in the previous section. The main shape of the lungs is conserved but the inside of it has some holes that cannot be filled without changing the whole model.
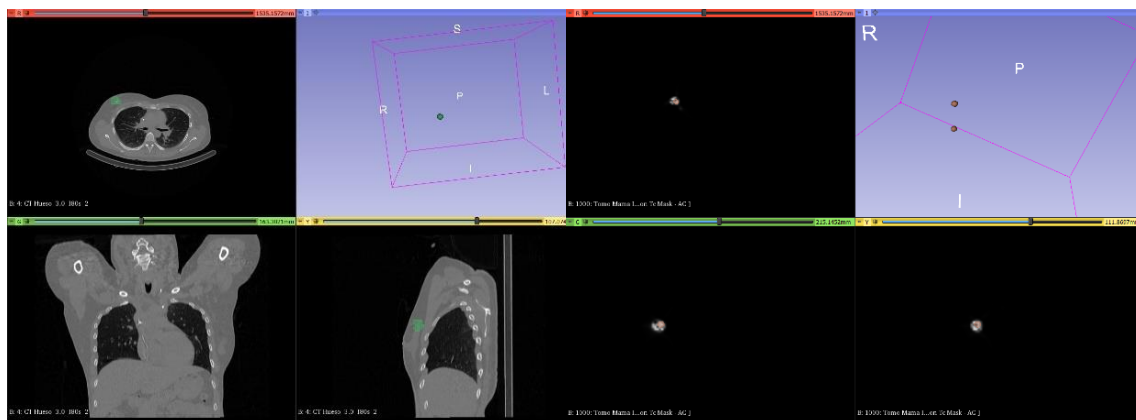
Fig. 29 Segmentation of Tc99m activity and I-125 activity SPECTs

Fig. 29 shows the result of modelling the activity of Iodine-125 and Tc99m. Tc99m is injected near the patient's tumor to identify where is the sentinel node in which tumoral cells drain. A mask was applied because the injecting point gave too much radioactive activity. More so, two Iodine seeds are placed close to where Tc99m activity is to mark where to intervene.

6.5 Optimization and post-processing of the patient's mesh

In this part the steps are the same as stated in the previous section (6.3). By loading the exported STL files from 3D Slicer in MeshLab it is possible to improve the model with more accuracy. Every element was modified and exported to OBJ separately.
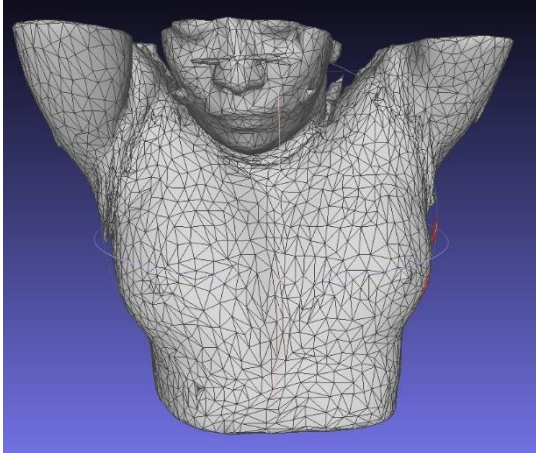
Fig. 30 Final 3D model of the patient's skin

Fig. 30 shows the result after processing the skin 3D model. Thanks to the "Select Vertex Cluster" from the tool bar it was possible to select only the inner parts of the model and erase them (ctrl+del).

The mesh of triangles was simplified from more than 500,000 faces to just 20,000 triangles.

Fig. 31 shows the final optimized model of the patient's skeleton. While it was not possible to elongate the shortened ribs until the sternum, most of the inconsistencies and holes were fixed. Taubin smoothing filter was applied with the previously mentioned parameters.

The model was simplified from more than 1,000,000 triangles to a simpler mesh of 20,000 geometric faces.
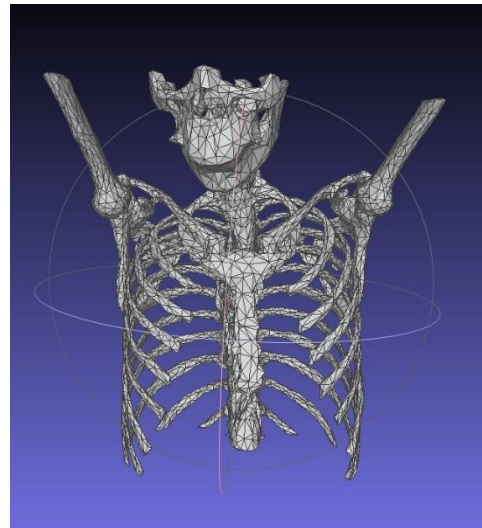
Fig. 31 Final 3D model of the patient's skeleton
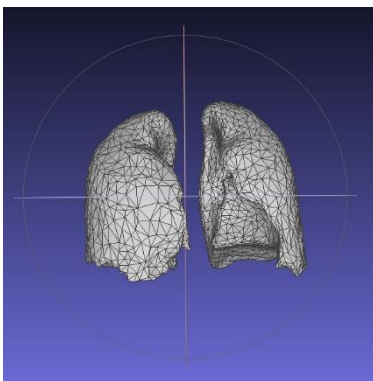
Fig. 32 Final 3D model of the patient's lungs

Fig. 32 shows the resulting lungs model of the patient. This element was particularly hard to optimize because its segmentation did not have great quality. There were many irregularities towards the limits of the model, but they were mostly fixed by applying the Taubin smoothing filter three times in a row.

It is worth mentioning that the model did shrink a bit after the filtering and the simplification of the model was until approximately 200 triangles in the mesh.

Finally, Fig. 33 show the modelling of the Tc99m and Iodine-125 activity inside the patient. Both models were processed the same way. Taubin smoothing was applied and after that, a simplification was performed to lessen the burden of computing time for the model. The reduction ended with both meshes at approximately 50 triangles each.
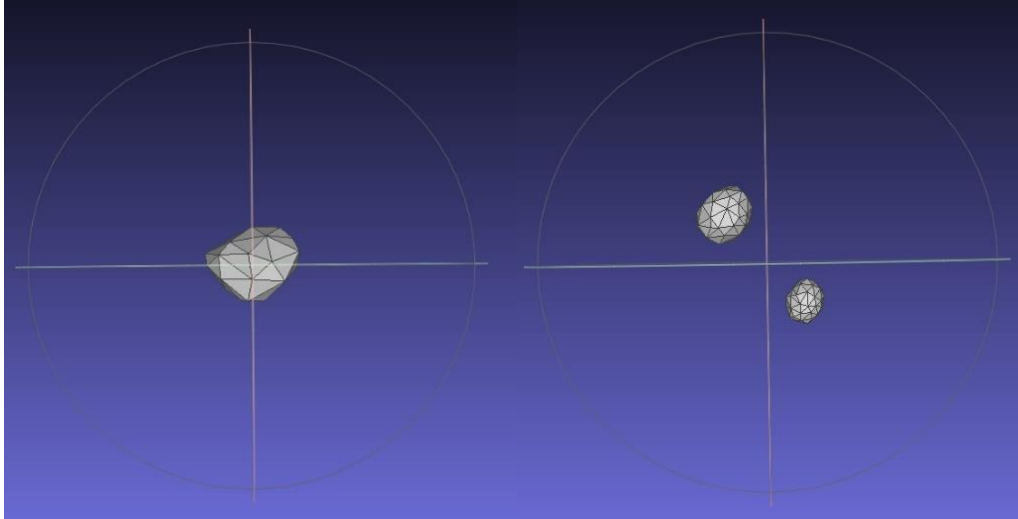
Fig. 33 Final model of the Tc99m and I-125 activity of the patient

6.6   3D model in AR

6.6.1   AR application of breast phantom model

The aim of this section is to create a 3D model of the breast phantom that can be separated into its different elements and be ready to be visualized by the AR headset. In order to complete this objective, it is necessary to download Unity Hub, a free application that helps you create and manage Unity Projects. Unity is a real-time open-source development platform that provides an environment to create AR applications [57]. In addition, it is also necessary to import Vuforia, a software development kit that contributes to the visualization of the holograms. This engine offers a simple way of tracking and recognizing 3D objects in real-time for AR scenarios. Thanks to Vuforia it is possible to place and orientate virtual objects with a system based on target markers [58].

6.6.1.1 Environment setup

The first step is creating an AR (core) project where the model will be built. To import Vuforia is it necessary to import it from the Asset Store where further instructions are explained. In order to get the Vuforia License Key, it mandatory to register in their webpage. Once the license key is activated correctly, it is possible to set up the AR camera that will simulate how the model will be visualized in the AR device.

Another important aspect is the creation of the target in which we will reference our model. In this case the target is the "skin" of the breast phantom along with the physical marker. The model target is imported from the .obj file from MeshLab and we can change its color/texture by creating a new material.

6.6.1.2 Creating the 3D model

The next part aims to create the 3D model manually by inserting each element and moving them, so they fit the same way they were visualized in the scans. It is necessary to upload the .obj models created in MeshLab separately in a folder. When the breast phantom is uploaded, it should be placed above the plane to make it easier to operate with. Fig. 34 exemplifies how the breast phantom model should look.

Fig. 34 Breast phantom 3D model in Unity AR

Hereafter, the other elements are added by following the same steps. First, iodine-125 activity is added. It is important to manually make it fit with as much precision as possible so that it resembles the previous scans. Also, Tc99m activity should also be added to the model fitting its location with where I-125 is. Finally, the project should be exported so it can be uploaded into the AR glasses.

6.6.2 AR application of the real patient model

In order to complete this section, the same steps as the previous AR application were followed. Nevertheless, since the patient did not have a physical marker to reference the whole model, an image target was chosen. The image target is a generic one from the Vuforia samples folder. In this case, the result will be visualized if the AR device detects said image with the same size as the model in real life.

Fig. 35 Folder containing the models and colors created

Fig. 36 shows the result of uploading the skeleton on the patient in the scenario. It is recommended that the localization of the model is within the sight of the AR camera. Furthermore, a color can be applied to the bones by creating a material in the folder where the desired .obj files are.

Fig. 36 Patient's skeleton 3D model in Unity

Fig. 37 shows how the lungs model fit inside the skeleton model of the patient. In order to place the lungs correctly, the element will be manipulated through the "Move" and "Rotate" tools. To have better visualization, lungs were colored so they stand out in the torso.

Also, the radioactive activity should be represented in the model like in Fig.38 and Fig. 39. Different colored balls should represent the activity of Iodine-125 (red) and the sentinel lymph node in Tc99m (green). Both elements are placed manually by comparing its position in the CT/SPECT scans and copying it in the Unity project. Only
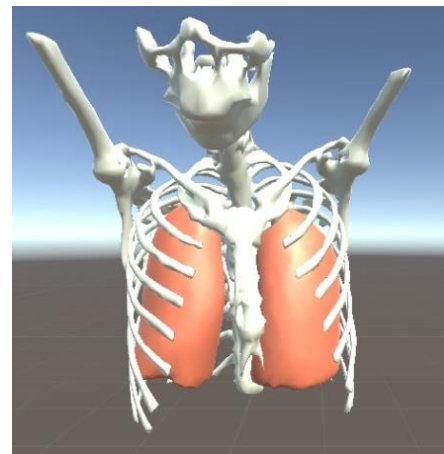
Fig. 37 Patient's skeleton and lungs 3D model in Unity

one of the two seeds of iodine should be visible because the sentinel node activity is bigger and is superimposed.
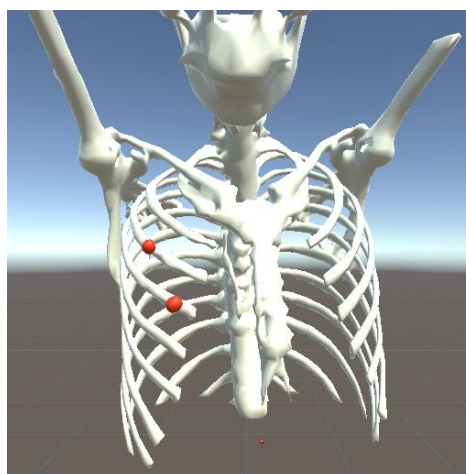
Fig. 38 Final 3D model of the patient's I-125 activity in Unity
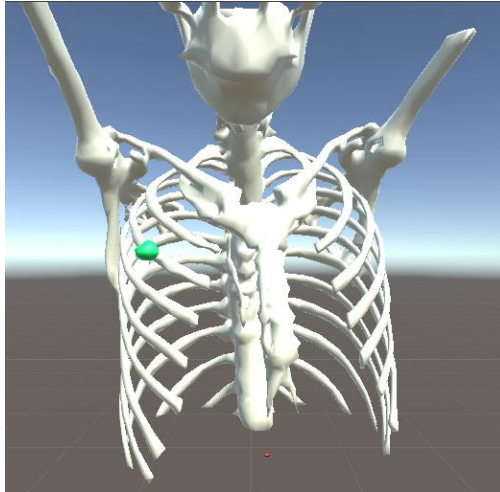
Fig. 39 Final 3D model of the patient's Tc99m activity

7. Results

It is important to mention that the following results are visualized from a Unity AR scenery. They are supposed to be visualized from AR glasses but, because of a conflict in schedules, it was not possible. Even so, the model is completely prepared for visualization and the following figures simulate how it should be seen.

7.1 Breast phantom model results

First of all, there is the breast phantom model. This first approach was to create a model capable of representing the location of sentinel nodes with Tc99m and Iodine-125 for a more exact location. It is possible to view the model in 3D and navigate through the different layers. While the segmentation and processing part was not difficult to carry out, the assembly of the model in Unity was a more complex process. Furthermore, given that the placement has to be done manually, the location is not completely accurate.
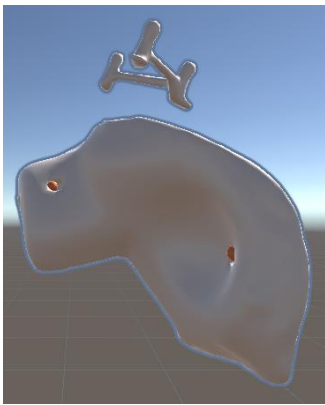
Fig. 40 Final 3D model of breast phantom in AR environment
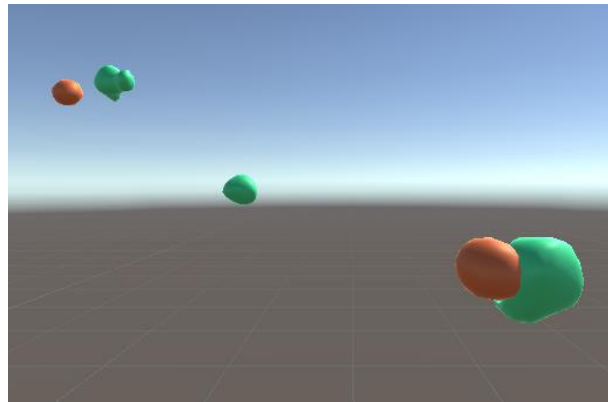
Fig. 41 Final 3D model of the breast phantom's radioactive activity in AR environment

If we compare the primary model made in 3D Slicer where it is placed exactly where the SPECT/CT scans mark and the final model after all the optimizing and manual placing process, the results are similar. In fact, the model in Unity has a much more polished result where its shape resembles more to the physical breast phantom.
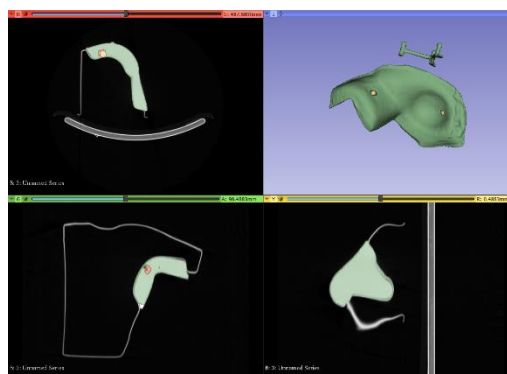
Fig. 42 Breast phantom primary segmentation

7.2 Real patient model results

The results of the real patient 3D model are also visualized in an AR environment simulation in Unity. In this case, the results are more complex and difficult to assess. Also, given that there are no physical markers in the patient's scans, the target for the hypothetical hologram is a generic image.
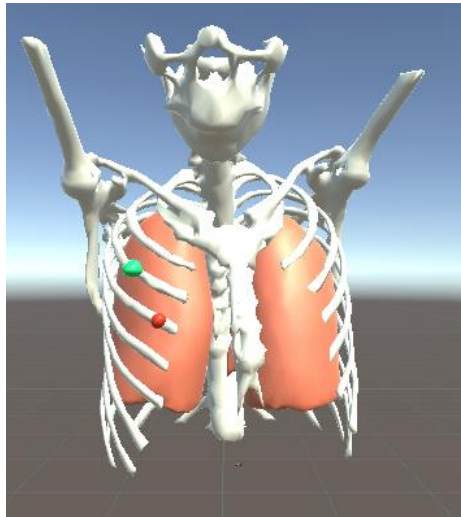
Fig. 44 Final 3D model of the patient without skin in AR environment

Fig. 43 Final 3D model of the patient with skin in AR environment

Fig.43 and 44 show the final 3D model of the real patient which features 2 Iodine-125 radioactive seeds in red and a sentinel node that was previously localized through the injection of Tc99m in green. It is possible to navigate through the different elements of the model (skin, bones, lungs, Tc99m and I-125). Since it was not possible to isolate this organ without including most of the other soft tissue, the patient's heart was not segmented. Also, as skin is superimposed in all previous elements, only the patient's outer layer is visible.
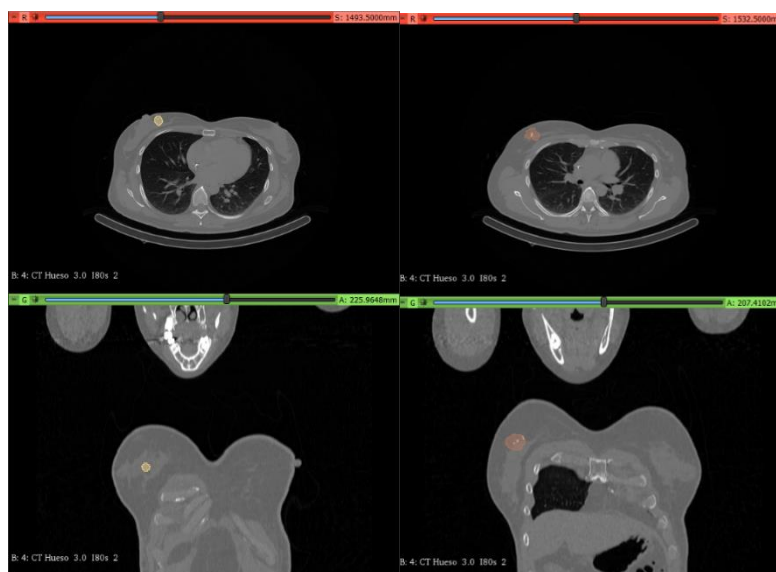
Fig. 45 CT scans of the patient with Tc99m and I-125 activity segmented respectively

The previous figures show the location of the radioactive activity injected in the patient, according to the CT scan. Once again, red balls represent the activity of Iodine-125 while the green one represents the sentinel lymph node in Tc99m. Only one of the two red balls are visible because the green one is bigger and is superimposed. Both elements were placed manually by comparing its position in the CT/SPECT scans and copying it in the Unity project. As it can be seen, the location of the final model elements is not exactly the same as the scan image. Besides, there is a noticeable difference between the first model in 3D Slicer and the final one in Unity. The latter has a more polished finishing, but the size is smaller than intended due to processing.

8. Discussion and future improvements

8.1 Discussion

The aim of this section is to discuss whether the different objectives were achieved or not.

The first objective that was the development of a 3D model of a previously prepared breast phantom has been achieved. The model was created based on a CT scan and two SPECTs. It is worth mentioning that this part required previous planning and research to fully understand the process. Also, the action happened in the Nuclear Medicine Department of Hospital Clinic of Barcelona so, a previous appointment had to be arranged with Dra. Niñerola. Thanks to her help, it was possible to prepare the breast phantom accordingly to what a typical SPECT/CT scan of a breast cancer patient should look like.

The most crucial part of the project was the correct segmentation of the images, which was successfully completed correctly. Thanks to 3D Slicer, a free-source software to visualize and segmentate images, it was possible for the author to work from home and build a triangle mesh. While segmenting a SPECT scan does not require a lot of accuracy, segmenting a CT scan does. In fact, the main challenge is being capable of creating a model that resembles reality enough. Furthermore, it is important to segment separately every element of the model. After optimizing and post-processing the STL files, the resulting virtual objects were similar to the physical ones in shape and size so, it was a success.

The second objective that was creating a 3D model based on scans from a real patient with breast cancer was also completed successfully. Segmenting and post-processing the medical images of a breast cancer patient was vastly different from carrying it out with the breast phantom's images. Some differences between the two processes were noticed. The segmentation of a real patient anatomy was harder than expected and it showed the weaknesses of 3D Slicer, especially because the software was not as accurate as the author thought it would. Also, shrinkage of the models during post-processing was more noticeable but, it was unavoidable if a certain polished result was to be reached. At the end, the final virtual objects were similar enough to the ones shown in the SPECT/CT scans and they performed well.

The third and final objective was to create the virtual 3D models in a platform that could support AR in order to visualize it in an AR headset. This part of the project was fulfilled partially. Unity was difficult to understand as the author had no previous notions and there were not many sources where tutorials for the specific application of this project could be found. Nonetheless, it was possible to create the two 3D models containing all the desired elements placed in their respective location and navigate among them. But, since the author created the final model in AR behind schedule, it was not possible to assess if the model could be visualized in real-life like in Unity's simulation.

All in all, majority of the objectives were clearly achieved with positive results, especially the ones regarding the building of a 3D model with 3D Slicer, MeshLab, and Unity for AR. It is clear that using AR technology for viewing purposes would improve the current workflow of SLNB by reducing the time to localize the sentinel node(s). However, there are several aspects to be discussed related to what should improve in this project to achieve better results to solidify the presence AR tools in SLNB.

8.2 Future improvements

This section will discuss different improvements to be made in this project in order to obtain clearer results and take a step further into the main goal.

First of all, it would be important to test the AR 3D models in a real environment. Assessing if the model is clearly visible and navigable using an AR headset should be the first step to take to move the project forward. In addition, testing the application in real patients would also benefit the project. Being able to discuss how positive is the response of the 3D model to an actual patient would bring the project closer to its principal objective, which is improving sentinel node detection in SLNB logistically. The first approach should be with a person that will have markers drawn or superimposed onto their skin to project the holograms while the final one would be testing the application in a clinical case.

It is worth mentioning that future 3D models will be more complex as they will feature the whole patient's relevant anatomy, including for instance blood or lymphatic vessels. While the first approach of the AR application went smooth and was successful, it was partly due to the simplicity of the breast phantom. The main challenge of this project was related to segmenting accurately the patient's human's anatomy. In order to sort out this problem, it would be advisable to invest in a more complex and clinical data-focused segmentation tool.

Furthermore, once the resulting AR 3D model is ready to be used as a tool to help for the detection of sentinel nodes in a patient, European legislation for medical devices will be applied.

9. Technical feasibility

To analyze the technical feasibility of this project, a SWOT was conducted. SWOT is a tool that allows the entrepreneur to analyze the reality of their company, brand, or product in order to make decisions for the future [59]. The SWOT analysis is divided into two parts: Internal analysis (Strengths and Weaknesses) where a picture of the situation of the company or business project is made considering its strengths and weaknesses. The second part is the external analysis (Threats and Opportunities); Both threats and opportunities belong to the world outside the company but should be considered either to overcome them, in the case of threats, or to take advantage of the opportunities offered by the market.

Strengths	Weaknesses
Internal analysis	
• Follow-up project • Previously well-documented • Facilitate SLNB • Added value • Help of experts and useful tools	• Not frequent in clinical use • Model was not tested on physical models • Result is not polished and ready-to-use
Opportunities	**Threats**
External analysis	
• Emerging market • Application is in demand • Possibilities to innovate • Different possible target groups	• Wide variety of devices in the market • Price is out of range • Human distrust to new technology • AR systems have a learning curve

Table 6 SWOT analysis of the project

9.1 Strengths

Commenting on the strengths of the project, the main advantage is that it is a follow-up of a previous final degree project. This means that previous processes to follow are well-documented and that offers flexibility with the schedule. Also, the main objective is to facilitate SLNB, a typical procedure when someone is diagnosed with breast cancer. This type of cancer is one of the most common ones so, an improvement in the treatment is very relevant. The implementation of AR has an added value as it can be used on medical education to help train students. Furthermore, the development of the project was done with the help of CIMNE and the Nuclear Medicine Department so, the author had access to useful tools and expert advisors.

9.2 Weaknesses

One of the main weaknesses of the project is that AR applications are still not frequent in clinical use and thus, it is difficult to establish a complete and functional application without precedent. Also, the models were not superimposed in any of the physical models so we cannot assess how effective the solution could be. In addition, all models were built with free and open-source programs so, the result is not very polished and is not suitable for clinical use.

9.3 Opportunities

When analyzing the opportunities that the market offers, it can be concluded that the AR in healthcare market is clearly emerging. Given the prevalence of breast cancer, new improvements in diagnosis and treatment are in demand. AR is still growing in its earlier phases of development and innovative solutions can be revolutionary. Besides, there are many possible applications for AR so even if the target group is not convinced with the solution, other investors and clients can pick it up.

9.4 Threats

Regarding threats for the project, it is clear that there is a wide variety of devices currently on the market. The AR market has a lot of competitors, and it may be difficult to stand out among other solutions. Also, the current price of AR technology is out of range and its results are not drastically improved so, many clinics and institutions can distrust its performance. More so, clinical protocols are strictly supervised, and the implementation of radically new technology may be hard as they normally have a learning curve.

10. Economic feasibility

This section will highlight the theoretical costs of this project. Four types of costs are classified depending on where they were invested. First, there is human resources costs (Table 7) in which a salary should be paid to every person who intervened in the project according to the hours they invested. The total amounts to 4,250 euros.

	Salary per hour	Hours invested	Total salary
Biomedical engineering student	10 euros	300 hours	3,000 euros
Expert in AR technology (advisor)	35	10	350 euros
Expert in imaging techniques (advisor)	35	20	700 euros
Senior research engineer (advisor)	20	10	200 euros

Table 7 Human resources cost

Second, there is software costs (Table 8). As it shows, there is no software investment as all platforms chosen were free.

Software	Price
3D Slicer	Free source
MeshLab	Free source
Unity	Free source

Table 8 Software cost

Thirdly, there is hardware costs which represent the price of every device that was used during this project. The only device used in this project was a laptop that the author already had so, no investment was made in this part.

Finally, there is material costs that amount to the money needed to buy all materials used during the project. Nevertheless, the price of the material is unknown as all the materials necessary were provided by the Nuclear Medicine Department.

All in all, the total cost of the project was just the human resources cost, which is 4,250 euros.

11. Execution chronogram

The purpose of this section is to describe the tasks completed for this project and how they were organized. To manage the project correctly, a schedule of tasks to be completed for the project was created. Furthermore, a GANTT chart was created to illustrate the calendar better. In order to have a better understanding of the project, the tasks needed to fulfill it were divided into three stages:

The planning stage was about doing all the tasks necessary to be prepared for the developmental stage. The tasks included designing the project structure (Objectives, scope and span, tasks etc…), carrying out a literature review and learning how to use the different platforms chosen to create the 3D model by looking up different tutorials. The most important task of this stage was the literature review as having knowledge of relevant data related to breast cancer would give the author a better insight of what should be included in this project. Also, this included a study on the current state of AR in healthcare at the clinical level and in the market.

The developmental stage was about the building of the AR 3D model of the breast phantom and the real patient. This part not only included the segmentation, processing and building of the desired 3D models, but also required continuous communication with the final project tutors for guidance.

Finally, the writing stage was about documenting the whole process of the project in a report. This section was carried out during most part of the project and it went through several changes with the aid of the project tutors. In addition, it was necessary to do an oral presentation that highlighted the most important parts of the project.
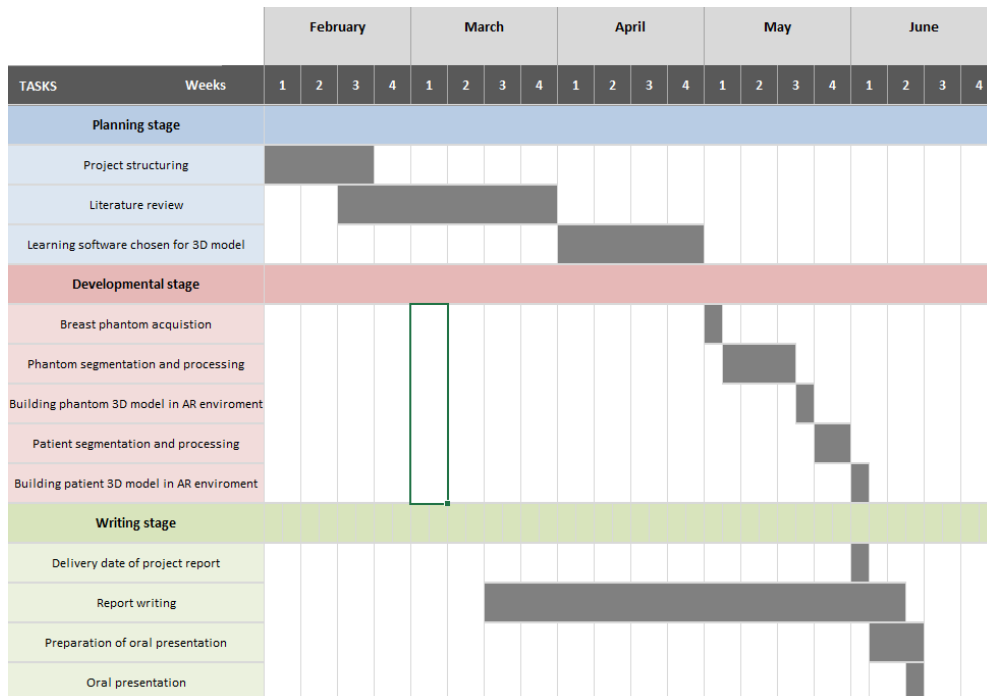

Fig. 46 GANTT chart of the project

12. Conclusions

All in all, this project reaffirmed the potential that AR has as another tool in healthcare, especially as an advanced technique of data visualization. The results of the project suggested that using AR models of nuclear image scans is valid and that the application can be used to improve processes like radio-guided surgeries logistically. Also, it is worth mentioning that this technique could also be used as an educational tool for students and not only in the nuclear medicine-related field, but for almost all medicine branches.

In order to implement this method in clinical practice as an auxiliary tool for nuclear medicine specialists to use when assessing nuclear image scans, some improvements must be carried out. First of all, the resulting 3D model should be more detailed as it is going to be used as medical data hypothetically, which means that segmentation and post-processing methods should be evaluated again. Secondly, as the 3D models may be superimposed on the patient, the AR model should be prepared for the environment's instability.

Thus, AR technologies have started to gain traction in the healthcare market and given the current results, it is only a matter of time until it becomes the standard of medical care. AR applications offer a non-invasive and ergonomic option for advanced visualization of 3D data, and it is expected that the number of healthcare-related companies involved in AR will continue increasing in the next years.

To wrap it up, even though the project has different shortcomings and needs further development, this approach seems to be on the right track in the development of AR tools in medical data visualization.

13. References

[1] Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians*, 71(3), 209–249. https://doi.org/10.3322/CAAC.21660

[2] *Global Cancer Observatory*. (n.d.). Retrieved June 8, 2022, from https://gco.iarc.fr/

[3] *Nuclear Medicine | Johns Hopkins Medicine*. (n.d.). Retrieved June 8, 2022, from https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/nuclear-medicine

[4] *Breast cancer - Diagnosis and treatment - Mayo Clinic*. (n.d.). Retrieved June 8, 2022, from https://www.mayoclinic.org/diseases-conditions/breast-cancer/diagnosis-treatment/drc-20352475

[5] Greene, L. R., & Wilkinson, D. (2015). The role of general nuclear medicine in breast cancer. *Journal of Medical Radiation Sciences*, 62(1), 54. https://doi.org/10.1002/JMRS.97

[6] Sutherland, J., Belec, J., Sheikh, A., Chepelev, L., Althobaity, W., Chow, B. J. W., Mitsouras, D., Christensen, A., Rybicki, F. J., & La Russa, D. J. (2019). Applying Modern Virtual and Augmented Reality Technologies to Medical Images and Models. *Journal of Digital Imaging*, 32(1), 38–53. https://doi.org/10.1007/S10278-018-0122-7/FIGURES/12

[7] Venkatesan, M., Mohan, H., Ryan, J. R., Schürch, C. M., Nolan, G. P., Frakes, D. H., & Coskun, A. F. (2021). Virtual and augmented reality for biomedical applications. *Cell Reports Medicine*, 2(7), 100348. https://doi.org/10.1016/J.XCRM.2021.100348/ATTACHMENT/CE8D0DC4-C819-459B-A4DC-6D4AB2952DA8/MMC1.PDF

[8] S. Gràcia, E. Soudah, O. de Cross & A. Niñerola. (2021) "Mixed Reality System to study deformable objects: Breast Cancer application". Final Degree Project. Biomedical Engineering Degree

[9] Fahad Ullah, M. (2019). Breast Cancer: Current Perspectives on the Disease Status. *Advances in Experimental Medicine and Biology, 1152*, 51–64. https://doi.org/10.1007/978-3-030-20301-6_4/FIGURES/5

[10] *Breast cancer treatment statistics | Cancer Research UK*. (n.d.). Retrieved June 8, 2022, from https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/diagnosis-and-treatment

[11] *lymphatic system | Structure, Function, & Facts | Britannica*. (n.d.). Retrieved June 8, 2022, from https://www.britannica.com/science/lymphatic-system

[12] *Definition of lymph node - NCI Dictionary of Cancer Terms - NCI*. (n.d.). Retrieved June 8, 2022, from https://www.cancer.gov/publications/dictionaries/cancer-terms/def/lymph-node

[13] *Sentinel Node Biopsy: Definition & Recovery*. (n.d.). Retrieved June 8, 2022, from https://my.clevelandclinic.org/health/diagnostics/9192-sentinel-node-biopsy

[14] *Sentinel Lymph Node Biopsy - NCI*. (n.d.). Retrieved June 8, 2022, from https://www.cancer.gov/about-cancer/diagnosis-staging/staging/sentinel-node-biopsy-fact-sheet

[15] Mok, C. W., Tan, S. M., Zheng, Q., & Shi, L. (2019). Network meta-analysis of novel and conventional sentinel lymph node biopsy techniques in breast cancer. *BJS Open*, *3*(4), 445–452. https://doi.org/10.1002/BJS5.50157

[16] Van Der Ploeg, I. M. C., Valdés Olmos, R. A., Nieweg, O. E., Rutgers, E. J. T., Kroon, B. B. R., & Hoefnagel, C. A. (2007). The Additional Value of SPECT/CT in Lymphatic Mapping in Breast Cancer and Melanoma. *Journal of Nuclear Medicine*, *48*(11), 1756–1760. https://doi.org/10.2967/JNUMED.107.043372

[17] Verhey, J. T., Haglin, J. M., Verhey, E. M., & Hartigan, D. E. (2020). Virtual, augmented, and mixed reality applications in orthopedic surgery. *The International Journal of Medical Robotics + Computer Assisted Surgery : MRCAS*, *16*(2). https://doi.org/10.1002/RCS.2067

[18] Ghaednia, H., Fourman, M. S., Lans, A., Detels, K., Dijkstra, H., Lloyd, S., Sweeney, A., Oosterhoff, J. H. F., & Schwab, J. H. (2021). Augmented and virtual reality in spine surgery, current applications and future potentials. *The Spine Journal*, *21*(10), 1617–1625. https://doi.org/10.1016/J.SPINEE.2021.03.018

[19] Nakamoto, R., Zhuo, J., Guja, K. E., Duan, H., Perkins, S. L., Leuze, C., Daniel, B. L., & Franc, B. L. (2022). Phantom study of SPECT/CT augmented reality for intraoperative localization of sentinel lymph nodes in head and neck melanoma. *Oral Oncology*, *125*, 105702. https://doi.org/10.1016/J.ORALONCOLOGY.2021.105702

[20] Fuerst, B., Sprung, J., Pinto, F., Frisch, B., Wendler, T., Simon, H., Mengus, L., Van Den Berg, N. S., Van Der Poel, H. G., Van Leeuwen, F. W. B., & Navab, N. (2016). First Robotic SPECT for Minimally Invasive Sentinel Lymph Node Mapping. *IEEE Transactions on Medical Imaging*, *35*(3), 830–838. https://doi.org/10.1109/TMI.2015.2498125

[21] Engelen, T., Winkel, B. M., Rietbergen, D. D., KleinJan, G. H., Vidal-Sicart, S., Olmos, R. A. V., Berg, N. S. van den, & Leeuwen, F. W. van. (2015). The next evolution in radioguided surgery: breast cancer related sentinel node localization using a freehandSPECT-mobile gamma camera combination. *American Journal of Nuclear Medicine and Molecular Imaging*, *5*(3), 233. /pmc/articles/PMC4446392/

[22] Azargoshasb, S., Molenaar, L., Rosiello, G., Buckle, T., van Willigen, D. M., van de Loosdrecht, M. M., Welling, M. M., Alic, L., van Leeuwen, F. W. B., Winter, A., & van Oosterom, M. N. (2022). Advancing intraoperative magnetic tracing using 3D freehand magnetic particle imaging. *International Journal of Computer Assisted Radiology and Surgery*, *17*(1), 211–218. https://doi.org/10.1007/S11548-021-02458-2/FIGURES/5

[23] KleinJan, G. H., Karakullukçu, B., Klop, W. M. C., Engelen, T., van den Berg, N. S., & van Leeuwen, F. W. B. (2017). Introducing navigation during melanoma-related sentinel lymph node procedures in the head-and-neck region. *EJNMMI Research*, 7(1), 1–8. https://doi.org/10.1186/S13550-017-0312-1/FIGURES/2

[24] Zhang, R., Yang, R., Lang, Z., Wu, B., Shao, P., Liu, P., Zhong, X., Contreras, C. M., & Xu, R. X. (2021). Coaxial projective imaging for sentinel lymph node mapping in melanoma. *JAAD Case Reports*, 15, 46–50. https://doi.org/10.1016/J.JDCR.2021.06.023/ATTACHMENT/5AF2A314-D854-4426-A8F3-2BC829D35712/MMC1.MP4

[25] Chand, M., Keller, D. S., Devoto, L., & McGurk, M. (2018). Furthering Precision in Sentinel Node Navigational Surgery for Oral Cancer: a Novel Triple Targeting System. *Journal of Fluorescence*, 28(2), 483–486. https://doi.org/10.1007/S10895-018-2211-X/FIGURES/5

[26] *On the usage of augmented reality in hepatic oncosurgery - Palomares et al 2019a - Scipedia*. (n.d.). Retrieved June 8, 2022, from https://www.scipedia.com/public/Palomares_et_al_2019a

[27] M.Puigferrat, E.Soudah, O.de Coss & A. Niñerola. (2020) "On the usage of augmented/virtual reality for surgical clinical applications", Final Degree Project. Biomedical Engineering Degree.

[28] *Microsoft Azure Marketplace*. (n.d.). Retrieved June 8, 2022, from https://azuremarketplace.microsoft.com/en-us/marketplace/apps/medivis.surgicalar?tab=overview

[29] *EchoPixel, Inc.* (n.d.). Retrieved June 8, 2022, from https://echopixeltech.com/

[30] *(61) Vipaar: Acerca de | LinkedIn*. (n.d.). Retrieved June 8, 2022, from https://www.linkedin.com/company/vipaar-inc-/about/

[31] *Augmented Reality | AccuVein*. (n.d.). Retrieved June 8, 2022, from https://www.accuvein.com/why-accuvein/ar/

[32] *SentiAR – Realtime Clinical AR*. (n.d.). Retrieved June 8, 2022, from htps://sentiar.com/

[33] *Touch Surgery brings surgery training to augmented reality | TechCrunch*. (n.d.). Retrieved June 8, 2022, from https://techcrunch.com/2017/01/06/touch-surgery-ar/

[34] *ImmersiveTouch® — Medical VR Solutions*. (n.d.). Retrieved June 8, 2022, from https://www.immersivetouch.com/

[35] *The future of augmented reality in healthcare - HealthManagement.org*. (n.d.). Retrieved June 8, 2022, from https://healthmanagement.org/c/healthmanagement/issuearticle/the-future-of-augmented-reality-in-healthcare

[36] *(61) AUGMENTED REALITY | LinkedIn*. (n.d.). Retrieved June 8, 2022, from https://www.linkedin.com/pulse/augmented-reality-ayushi-shrivastava/

[37] *5 Trends Drive the Gartner Hype Cycle for Emerging Technologies, 2020*. (n.d.). Retrieved June 8, 2022, from https://www.gartner.com/smarterwithgartner/5-trends-drive-the-gartner-hype-cycle-for-emerging-technologies-2020

[38] *Augmented Reality to Revolutionize the Health Care*. (n.d.). Retrieved June 8, 2022, from https://aabme.asme.org/posts/novel-augmented-reality-technology-to-revolutionize-the-health-care-industry

[39] *The Role of Augmented Reality in Medicine*. (n.d.). Retrieved June 8, 2022, from https://www.webmd.com/a-to-z-guides/features/augmented-reality-medicine

[40] *VR/AR Investments Increase Just As Metaverse Talk Heats Up—But That May Not Be The Only Reason*. (n.d.). Retrieved June 8, 2022, from https://news.crunchbase.com/startups/metaverse-augmented-reality-virtual-reality-investment/

[41] *Augmented Reality Software Market size worth $ 137.14 Billion, Globally, by 2028 at 57.21% CAGR: Verified Market Research®*. (n.d.). Retrieved June 8, 2022, from https://www.prnewswire.com/news-releases/augmented-reality-software-market-size-worth--137-14-billion-globally-by-2028-at-57-21-cagr-verified-market-research-301524850.html

[42] Universitat de Barcelona. (n.d). Retrieved June 8, 2022, from http://www2.giga.ub.edu/acad/gdoc/fitxers/pdf/normes_TFG.pdf

[43] *Grau en Enginyeria Biomèdica - Facultat de Medicina i Ciències de la Salut - Universitat de Barcelona*. (n.d.). Retrieved June 8, 2022, from https://www.ub.edu/portal/web/medicina-ciencies-salut/grau/-/ensenyament/detallEnsenyament/4917593/10

[44] *Definition of Medical Device*. (n.d.). Retrieved June 8, 2022, from https://www.obelis.net/definition-of-medical-device/

[45] *Ley Orgánica de Protección de Datos - LOPDGDD 3/2018 | Grupo Atico34*. (n.d.). Retrieved June 8, 2022, from https://protecciondatos-lopd.com/empresas/nueva-ley-proteccion-datos-2018/#Que_es_la_Ley_Organica_de_Proteccion_de_Datos_y_Garantia_de_Derechos_Digitales_LOPD-GDD

[46] *3D Slicer image computing platform | 3D Slicer*. (n.d.). Retrieved June 8, 2022, from https://www.slicer.org/

[47] *ITK-SNAP Home*. (n.d.). Retrieved June 8, 2022, from http://www.itksnap.org/pmwiki/pmwiki.php

[48] *syngo.via*. (n.d.). Retrieved June 8, 2022, from https://www.siemens-healthineers.com/en-us/molecular-imaging/pet-ct/syngo-via

[49] Corsini, M., Cignoni, P., & Scopigno, R. (2012). Efficient and flexible sampling with blue noise properties of triangular meshes. *IEEE Transactions on Visualization and Computer Graphics*, *18*(6), 914–924. https://doi.org/10.1109/TVCG.2012.34

[50] *Gmsh: a three-dimensional finite element mesh generator with built-in pre- and post-processing facilities*. (n.d.). Retrieved June 8, 2022, from https://gmsh.info/

[51] *Features — blender.org*. (n.d.). Retrieved June 8, 2022, from https://www.blender.org/features/

[52] *Wings 3D*. (n.d.). Retrieved June 8, 2022, from http://www.wings3d.com/

[53] *Microsoft HoloLens 2 review - mixed reality smartglasses (holographic)*. (n.d.). Retrieved June 8, 2022, from https://www.aniwaa.com/product/vr-ar/microsoft-hololens-2/

[54] *HoloLens 2—Pricing and Options | Microsoft HoloLens*. (n.d.). Retrieved June 8, 2022, from https://www.microsoft.com/en-us/hololens/buy

[55] *10 BEST Augmented Reality Glasses (Smart Glasses) In 2022*. (n.d.). Retrieved June 8, 2022, from https://www.softwaretestinghelp.com/best-augmented-reality-glasses/

[56] *Magic Leap 1 AR information and pricing | Magic Leap*. (n.d.). Retrieved June 8, 2022, from https://www.magicleap.com/magic-leap-1

[57] *Unity Real-Time Development Platform | 3D, 2D VR & AR Engine*. (n.d.). Retrieved June 8, 2022, from https://unity.com/

[58] *Getting Started with Vuforia Engine in Unity | VuforiaLibrary*. (n.d.). Retrieved June 8, 2022, from https://library.vuforia.com/getting-started/getting-started-vuforia-engine-unity

[59] *Herramienta DAFO*. (n.d.). Retrieved June 8, 2022, from https://dafo.ipyme.org/Home