3D printed implant structure for breast reconstruction and systematic drug delivery for preventing the reoccurrence of cancer

C. Ludusan[1], D. Ojados González[2], R. Pacurar[1], J. F. Roca González[3], M. García Fuentes[2], L. Martínez Abellán[2]

[1] Industrial Engineering Department, Technical University of Cluj-Napoca, Cluj-Napoca, Romania, cristinna.ludusan@yahoo.com, razvan.pacurar@tcm.utcluj.ro

[2] Technological Research Support Service (SAIT), Polytechnic University of Cartagena, Cartagena, Spain, {lola.ojados, marta.garcia, lucia.mabellan}@upct.es

[3]Department of Automation, Electrical Engineering and Electronic Technology, Polytechnic University of Cartagena, Cartagena, Spain, jroca.gonzalez@upct.es

Abstract

Breast cancer is one of the most common and deadly cancers among women worldwide. The treatment of breast cancer often involves mastectomy, which can cause physical and psychological distress to the patients, affecting their quality of life and self-esteem [1]. Therefore, the surgical intervention of breast cancer should not include only the removal of a tumor, but also psychological support by restoring the natural shape of the breast and achieving proper aesthetic for each patient. Conventional breast reconstruction techniques have several limitations, such as donor site morbidity, implant failure, infection, and poor cosmetic outcome. Moreover, breast cancer patients often require systemic chemotherapy or hormone therapy after surgery, which can cause severe side effects and complications.

In this article, it is proposed a novel implant based 3d printed structure for breast reconstruction and systematic drug delivery. The implant consists of a biodegradable scaffold that is 3d printed with a customized shape, coated with Polydopamine and Alginate, and sized to fit the patient's chest. The implant provides mechanical support, aesthetic improvement and can also enhance the efficacy and safety of chemotherapy or hormone therapy by delivering treatment directly to the target site through a channel system. The aim of the article presented here is a proposed process protocol for obtaining this prosthesis.

1. Introduction

Due to tissue engineering, breast reconstruction surgeries and clinical treatment strategies gain an encouraging perspective when it comes to overcoming the limitations of their development and innovation [2]. Using scaffolds to guide the formation of adipose tissue offers an optimistic view regarding the control of regeneration of soft tissue and a new tactic for obtaining the desired shape and surface features for each patient. The implant opens the possibility for the scaffold to be seeded with adipose-derived stem cells(ADSCs) that can differentiate into adipocytes and form new fat tissue [3]. Moreover, choosing the right unit cell, density and distribution in the scaffold, an efficient system for delivering targeted treatment could be obtained. The goal is to design a framework that can withstand the above-mentioned requirements and provide resistance to mechanical forces, stresses and strains and offer comfort and aesthetic satisfaction to the patient.

2. Objectives

The main objective of this study is to develop a protocol for the design of this type of prosthesis, which is a biodegradable implant with a customized shape for each patient. This implant must provide a structure where new fat tissue is generated. This also requires the choice of a material suitable for this purpose.

3. Methodology

3.1. Model

In order to obtain the desired protocol, this study follows the case of a patient who will undergo a tumor removal surgery as a support to elaborate a guide of steps to follow in this process set as an objective.

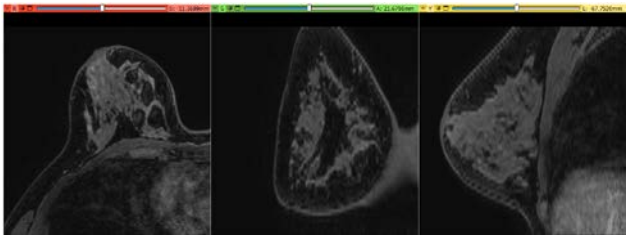

Figure 1. *DICOM images*

For this purpose, the image used from this particular case is a specific MRI (Figure 1) of a patient whose 3D model and geometry were generated using Slicer 5.2.2. (Figure 2) which is a free, open source software for visualization, processing, segmentation, registration, and analysis of medical, biomedical, and other 3D images [4]. In this case, the images have been obtained from the radiology repository "*cancerimagingarchive.net*" [5].

ISBN: 978-84-17853-76-1

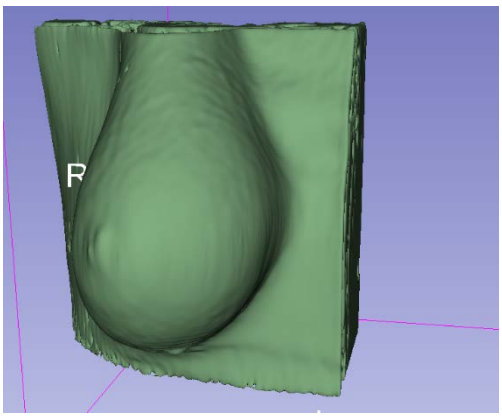

Figure 2. *Example of a 3D model generated from a specific MRI scan*

Then, the surface mesh (.STL model) (Figure 3) was imported into SolidWorks 2022-2023, where the model was converted into a solid and therefore used as a template for the design of the following structures. In the preliminary state, a prototype of the implant was designed, to represent the layout of the scaffold's architecture and the channel in the structure. The pre-designed model is then customized to the patient's breast parameters and needs (Figure 4), being able to withstand the sequelae required for tumor removal. This opens the possibility to regulate the topology of the model and apply different patterns with variable mesh density in each section. The final CAD design(Figure 5) will then be used for finite element analysis (FEA) and finally exported for fused deposition modeling (FDM).

Therefore, the protocol steps can be extracted from the methodology used in this specific case.

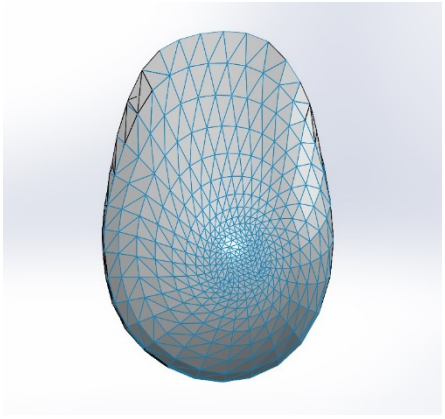

Figure 3. *Surface mesh*

Figure 4. *Example of distribution channels*

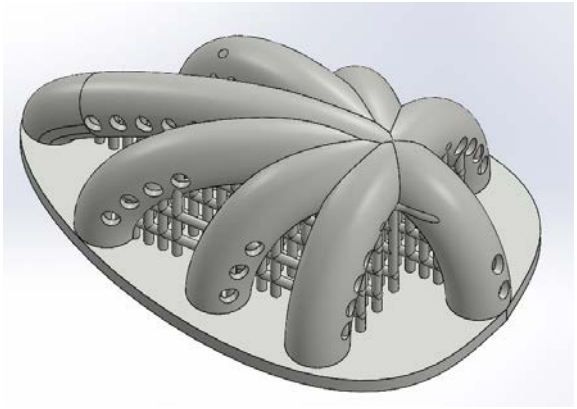

Figure 5. *Example of final implant structure*

3.2. Materials

The materials required to make this type of prosthesis can be estimated after the completion of this study, in which it is proposed that the scaffold consists of three materials: a base made of polycaprolactone, coated with polydopamine and alginate (Figure 6).

Coating PCL with a PDA layer followed by an alginate layer can be a multi-step process and has various purposes: PCL is often used as a scaffold material in tissue engineering. Coating it with PDA and alginate can enhance cell adhesion [6], proliferation, and tissue integration, making them more suitable for cell attachment and growth [7]. Also, PCL can be used as a drug delivery vehicle, and PDA and alginate coating can further control pharmacokinetics and improve drug-loading capacity.

PDA and alginate/gelatine coatings can also be used to immobilize bioactive molecules, growth factors, or signaling molecules onto the PCL surface, further enhancing its functionality. The addition of alginate can also introduce some viscoelastic behavior to the composite material [8], which can be relevant for simulating the mechanical behavior of natural tissues.

ISBN: 978-84-17853-76-1

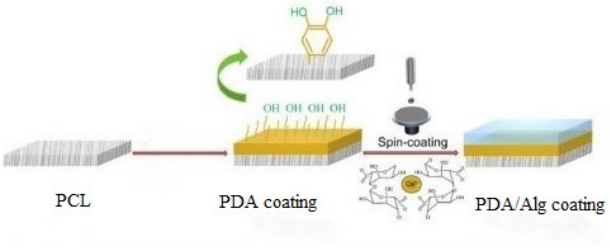

Figure 6. *PCL scaffold with PDA and alginates coatings*

3.3. Scaffolds

The scaffold (Figure 7) should enable the formation of tissue that closely resembles the patient's natural tissue in terms of its biological, physical, and chemical characteristics. It should offer three-dimensional structural stability, exhibit a low elastic modulus and include proliferation [9]. The construction and distribution of the unit cell is vital.

As for the printing parameters, the pattern should be zig zag with a 45 degrees infill direction 0.2 mm layer height and 70% infill density. These parameters would assure an ideal environment for cell growth [8].

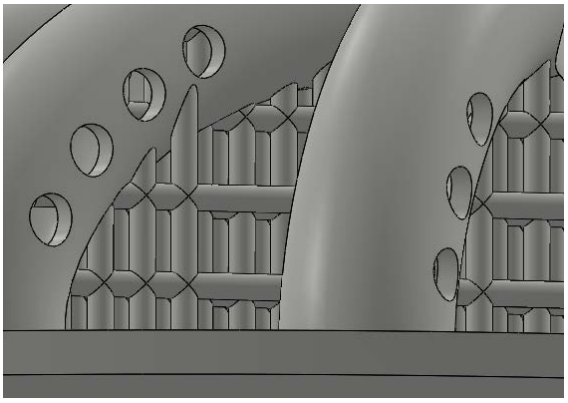

Figure 7. *Close up of an example of the scaffold*

3.4. Finite element analysis

The finite element analysis is done in Solidworks 2022-2023 Simulation by applying mechanical loads on the external part of the structure (Figure 8).

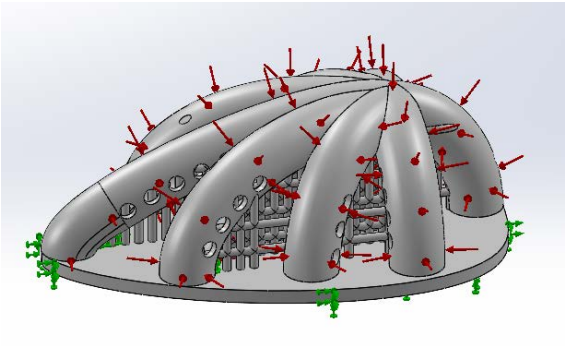

Figure 8. *FEA of the structure*

The stresses and strains that appear during the analysis are in correlation with the volume, structure and figure of the scaffold, as well as the patient's habits and amount of physical activities.

The first step is to set a static analysis. After that, the properties of the material are introduced and a mesh control is projected on the whole model. The parameters and mechanical forces are applied to obtain visual results of the strains that occur in the solid model, as following: a normal force of 5 N that comes in contact with the implant, the tensile strength and Young's modulus of 59 ± 11.3 KPa, respectively 0.53 ± 0.24MPa [9].

3.5. Optimization

Further studies are required in order to obtain realistic outcomes of the influence of the above-mentioned parameters.

Optimization in this case would constitute modifying the unit cell of the scaffold, diameter, density and their distribution and topography. Moreover, it could also imply a change in the number of channels or their volume. One important mention is that the mechanical properties of the PCL-PDA/Alg scaffolds could be tailored by the thickness of the PDA coatings and the density infill.

4. Results

The result to be obtained from this article is the following protocol for the development of this type of prosthesis:

- Firstly, the .stl will be extracted from a DICOM image of a patient by using specific software for this purpose.
- The mesh will be obtained through a CAD software.
- The mesh will be used as a template to obtain a 3D model of the prosthesis that is the target of this article.
- Once the 3D model is obtained, a finite element analysis is carried out.
- Finally, it will go through the usual FDM printing process.

5. Conclusion

Breast scaffolds with distinct structures have been created to meet the complex biomechanical demands of large-volume and long-term tissue regeneration. Furthermore, a channel structure is included to enable precise drug delivery to prevent the reoccurrence of cancer. The process including MRI scans and producing patient-specific model, adapting the dimensions and overall form of the implant would solve the aesthetic and comfortability problems mentioned in the beginning of his article.

Depending on the viscosity of the fat, a gradient of pore sizes can be applied to minimize fat displacement and prevent leakage effectively. Therefore, these scaffolds should be capable of topical stimulus-responsive treatment, long-term drug delivery and overall encouraging the fat distribution inside the structure.

The study examined in this context illustrates the potential of 3D printing for breast reconstruction but, nevertheless,

ISBN: 978-84-17853-76-1

significant efforts are still required to validate this technique and facilitate its broader clinical application.

Aknowledgements

The author would like to express their gratitude to the organizing committee of CASEIB for the permission to use their style guides as a reference for the realization of this document and also thank the staff of SEDIC (Industrial Design and Scientific Calculation Service) of the Technical University of Cartagena for their support in the development of this work and for the possibility of having scientific-technical equipment.

.

References

[1] Fernández-Delgado, J., López-Pedraza, M. J., Blasco, J. A., Andradas-Aragones, E., Sánchez-Méndez, J. I., Sordo-Miralles, G., & Reza, M. M. (2008a). Satisfaction with and psychological impact of immediate and Deferred Breast Reconstruction. *Annals of Oncology*, *19*(8), 1430–1434. doi:10.1093/annonc/mdn153

[2] Dang, W., Wu, J., Wang, G., Zhen, Y., & An, Y. (2023). Role of adipose-derived stem cells in breast cancer. Chinese Journal of Plastic and Reconstructive Surgery, 5(2), 73–79.doi:10.1016/j.cjprs.2023.02.002

[3] Teixeira, A. M., & Martins, P. (2023). A review of bioengineering techniques applied to breast tissue: Mechanical properties, tissue engineering and finite element analysis. *Frontiers in Bioengineering and Biotechnology*, *11*. doi:10.3389/fbioe.2023.1161815

[4] Web 3D Slicer (2022). URL: *https://www.slicer.org/* (Visited September 2023)

[5] Web cancerimagearchive (2022). URL: *https://www.cancerimagingarchive.net/* (Visited: September 2023)

[6] Khan, Ziyauddin & Shanker, Ravi & Um, Doo-Seung & Jaiswal, Amit & Ko, Hyunhyub. (2018). Bioinspired Polydopamine and Composites for Biomedical Applications. 10.1002/9783527807918.ch1.

[7] Mu X, Zhang J and Jiang Y, 3D Printing in Breast Reconstruction: From Bench to Bed. Front. Surg. 8:641370. doi: 10.3389/fsurg.2021.641370

[8] Mina Mohseni, Onur Bas, Nathan J. Castro, Beat Schmutz, Dietmar W. Hutmacher, Additive biomanufacturing of scaffolds for breast reconstruction, Additive Manufacturing, Volume 30, 2019, 100845, pp 4, (ISSN 2214-8604).

[9] Rabionet M, Polonio E, Guerra AJ, Martin J, Puig T, Ciurana J. Design of a Scaffold Parameter Selection System with Additive Manufacturing for a Biomedical Cell Culture. Materials (Basel). 2018 Aug 14;11(8):1427. doi: 10.3390/ma11081427. PMID: 30110889; PMCID: PMC6119890.

[10] Chunyang Liu, Zhiyong Wang, Xiaoyue Wei, Birui Chen, Yongxiang Luo, 3D printed hydrogel/PCL core/shell fiber scaffolds with NIR-triggered drug release for cancer therapy and wound healing, Acta Biomaterialia, Volume 131, 2021, Pages 314-325, ISSN 1742-7061, https://doi.org/10.1016/j.actbio.2021.07.011.