Design and Characterization of a Microfluidic Biological System for Bone Tissue

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Abstract. Tissue engineering has managed to revolutionize the transplantation and regenerative medicine, it is responsible for developing biomaterials to generate a promising approach for studying complex physiological processes in vitro. The design and application of biological systems evaluate a microfluidic platform based on organs physiology, modeling the nutrient distribution, and testing potential implants.

The present investigation aims to design and characterize a biological system to simulate the microfluidic environment of the bone tissue. The system must provide the conditions for adequate cell regulation, to achieve this, adhesion, migration, proliferation, and differentiation are used, as well as the adequate delivery of bioactive factors such as growth and adhesion.

A novel hydraulic circuit with radial flow and their components were designed in SolidWorks, then the pieces were calculated with the Navier-Stokes equations using ANSYS and COMSOL software, to have a laminar environment and their behavior using microfluidics and cells mimicking the bone structure. The components were generated by 3D printing and the additive stereolithography resin technique.

According to the CFD simulations, it was found that the system had a media flow of 18.56 nl/s with the smallest pressure of 146.32 mPa our chamber is the optimum model for the bone cells.

Our microfluidic system's design shows the flow change can be used to follow the bone anatomy, which indicates an appropriate irrigation of nutrients for the cells. The proposed biological system has confirmed to be an adequate model for the bone tissue with a continuous irrigation of the media.

Keywords: biomaterials · bone tissue · tissue engineering · biological system · microfluidic simulation

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1 Introduction

Bone tissue engineering seeks to develop innovative approaches to regenerate and repair bone defects. The biological system technology provides a platform to mimic the complex microenvironment and microfluidic of bone tissue and study its cellular interactions and physiological processes in function of the structural and functional aspects of the bone tissue. The key components such as microchannels, cell culture chambers, and perfusion systems are discussed, emphasizing their role in creating dynamic and biomimetic bone tissue models [1].

The aging of the population leads to an increased incidence of bone fractures due to osteoporosis. Understanding the mechanisms of bone physiology is essential to design advanced treatments. Bone is a dynamic tissue in continuous formation and resorption through coordinated communication between osteoblasts (Ob) and osteoclasts (Oc). Mechanical loads modulate bone architecture and cell physiology and play an important role in bone tissue homeostasis. Although many in vitro models of Ob/Oc cultures exist for material analysis, little is known about cell communication under mechanical stimulation in this system [2].

Around 115 million animals were used in experiments around the world last year, with most tests being carried out without anesthesia or painkillers, and the toxic substances cause long-term pain, according to the report. European Coalition to End Animal Experiments (ECEAE). Mexico spends 10 million on animals for experimentation. Worldwide, more than 500,000 animals suffer and die each year because of laboratory tests [3].

The development and characteristics of biological models, explores the integration of relevant cell types, such as Ob, Oc, and mesenchymal stem cells, within the designed platforms, to avoid the animal experimentation in every experiment. The platform includes the incorporation of mechanical properties, such as fluid flow, share stress and strain, and the importance of extracellular matrix components in creating physiologically relevant bone tissue microenvironments [4].

The strategies employed in design biological models' considerate aspects of the bone tissue microenvironment. This includes the integration of vascular networks, the introduction of biochemical gradients, and the simulation of bone remodeling processes. It discusses the ability of the systems to mimic bone-related pathologies, such as osteoporosis, bone metastasis, and bone infections. The use of this platforms for high-throughput drug screening, assessment of drug efficacy, and personalized medicine approaches is also addressed [5].

The challenges associated with bone tissue models, including the need for improved complexity and scalability, the incorporation of other tissue interfaces like muscle-bone interfaces, and the integration of patient-specific cells. It also discusses potential future directions, such as combining biological system models with advanced imaging techniques, multi-organ systems, and the use of bioinks for 3D printing of bone tissues [6].

For the design of the Bioreactor, the COMSOL Multiphysics software was used based on the Solidworks design and the ANSYS mesh, The combination of those tools allowed us to solve the physics problems necessary to carry out the fluid simulation and control. In the simulation process it is considered the geometry of the Bioreactor, the fluid

physics with their respective boundary conditions and domains, define the simulation parameters and define and simulate the control strategy of the device [7].

This research presents a design of bone tissue biological system. The models were designed using SolidWorks, and hydrodynamic simulations were done in ANSYS and COMSOL afterward. The flow behavior in the irrigation system's channels were studied to determine which configuration of pressure and stress were the optimum values to imitate the anatomy and irrigation of bone microenvironment.

2 Methodology

2.1 Biological System Design

The blood flow in bone tissue, circulates trough a closed cavity where the pressure must stay constant in the vessels and above the veins. This circulation allows the interchange of nutrients and minerals among the blood and bone tissue. In other hand, the capillaries within bone structure have the same anatomic assembly as those located elsewhere in the body [7].

We design a platform based on bone circulation with two tubes of 2 mm of diameter for the input and output media, the base is an octagon of 30 mm side and 3 mm wide, the circular base is 25 mm long and 3 mm wide. The base of the test system is circular because it refers to an internal part of a bone, the two external parts are for introducing the cells and in the same way they can be introduced by lifting the lid. The in vitro test system was designed in an octagon shape with 1 tube at each end using SolidWorks CAD software to observe cell flow. It has 1 removable lid that prevents the cells from coming out as shown in Fig. 1), inside it has a tube with holes that allow the cells to flow.

2.2 System Flow Simulation

The objectives of the flow simulation were to see in which zones of zero flow within the in vitro test system, the assembled system was exported to the ANSYS software to obtain the optime mesh for the model and then it was used in COMSOL Multiphysics to resolve the Navier-Stokes equations to determine the flow fields, speed, and tension alongside bone tissue.

The simulation carried out allowed us to study the behavior of the fluid, such as the pressure profiles and velocity in the chamber, with these values it was possible to define a qualitative range of stresses present in the chamber for different flow values. With the variable control of flow and stress, it was possible to establish a range in which the simulation converges. For the validation of the Bioreactor simulation, it was proposed to design an object with specific characteristics and like that of a human bone tissue.

Once imported the model we can generate their mesh, a volume to represent the fluid in the channels had to be created. This volumetric body meshed with hexagonal hexahedral volumetric elements. The elements were refined at the channels. Working pressure at 1 atm, and a viscous-laminar model to describe the fluid as Newtonian, therefore, viscosity is considered constant. The working fluid was set with a characteristic

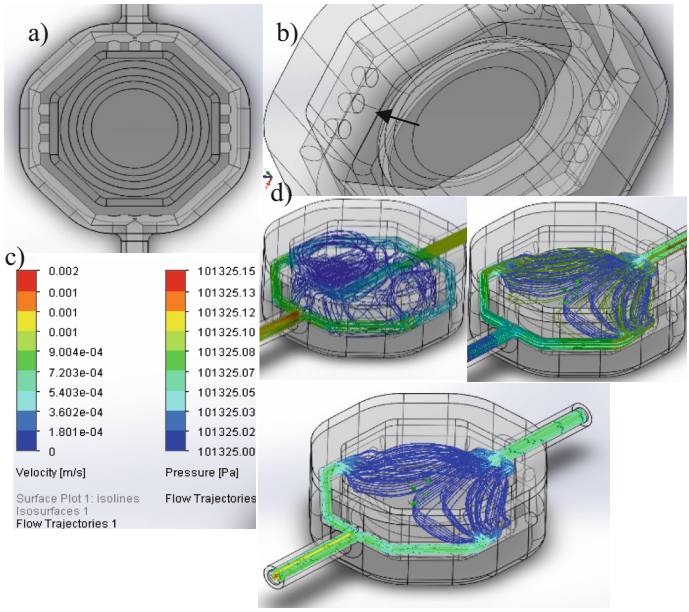

Fig. 1. Components of the microfluidic biological system. a) Top view of the system. b) The pipes and holes of the in vitro test system. c) The top view of the pipes of the in vitro test system. d) preliminary Flow simulation with inlet velocity of 8.3×10^{-5} m/s, value referred to a peristaltic pump; and outlet condition at 1 atm.

Pr = 4.34. The boundary conditions were set as: inlet velocity 8.3×10^{-5} m/s. Solver algorithm was set to *Simple*, with a *Green-Gauss Cell* gradient, and residuals were set to 1×10^{-06}. Set was started at the inlet, and 500 iterations as shown in Fig. 2.

2.3 Platform 3D Print

The parts of the biological system were 3D printed on a photolithography additive printer (Creality LR-002) using a photosensitive resin to generate the complex figures in one piece to fabricate the final test. To complete this, Creality® Chitubox V2.2® slicing software was used to print the resin parts with the following parameters used for resin printing:

Layer Height 0.4 mm Bottom/Top, Thickness 0.2 mm Print Speed (mm/s) 6 s, Print Temp 27 °C, Fan Enable, Cut Bottom of Object 0.0 mm, Overlap 0.15 mm, supports along the structure 5 mm.

3 Results

The results of the flow simulation are shown in Fig. 3. a) at the entrance and exit is constant 9×10^{-4} m/s. b) the simulation shows that the flow decreases as it passes through the pipes. c) top view of the simulation and it is observed how the flow changes

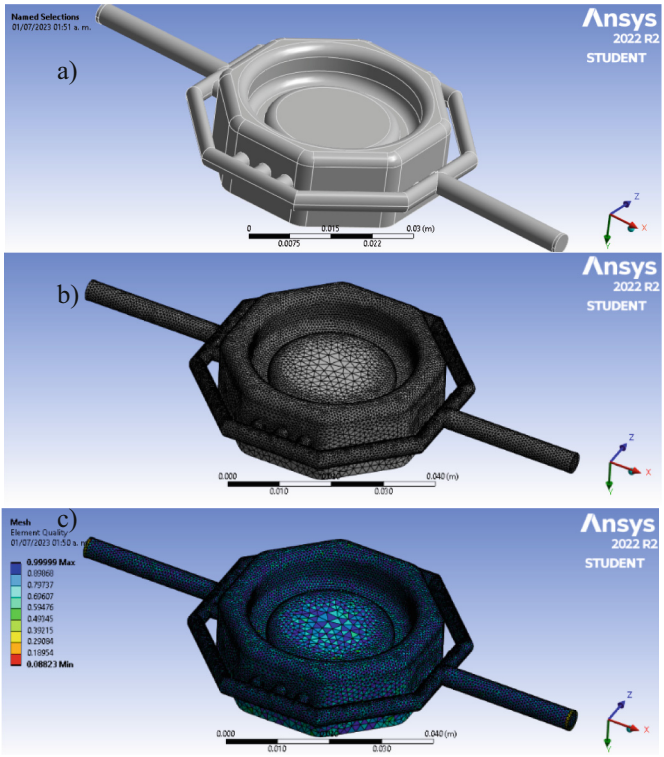

Fig. 2. Components of the microfluidic biological system meshed, Fluid volume: 1.009169×10^{-08} m^3, Solid volume: 2.716106×10^{-06} m^3. a) Volume of the system. b) Generic mesh. c) Element quality and functional cells.

color. The spiral lines are continuous colors, without turbulent flow, it is observed as is, ensuring that the cells will not have shear stress. The simulation values were Fluid volume: 1.009169×10^{-06} m^3, Solid volume: 2.716106×10^{-06} m^3, Total cells: 11,913, fluid cells: 11,913, Fluid cells in contact with solids: 7,132.

3.1 Printed Model

Finally, the images of the printed model are shown in Fig. 4. This prototype could be probed with a colored liquid to demonstrate the computational results. The system with the bone cell culture will be on a CO_2 incubator to control the gases temperature and measure the density of living cells and biomass, it allows to monitor critical parameters continuously and automatically to the changing conditions of the process.

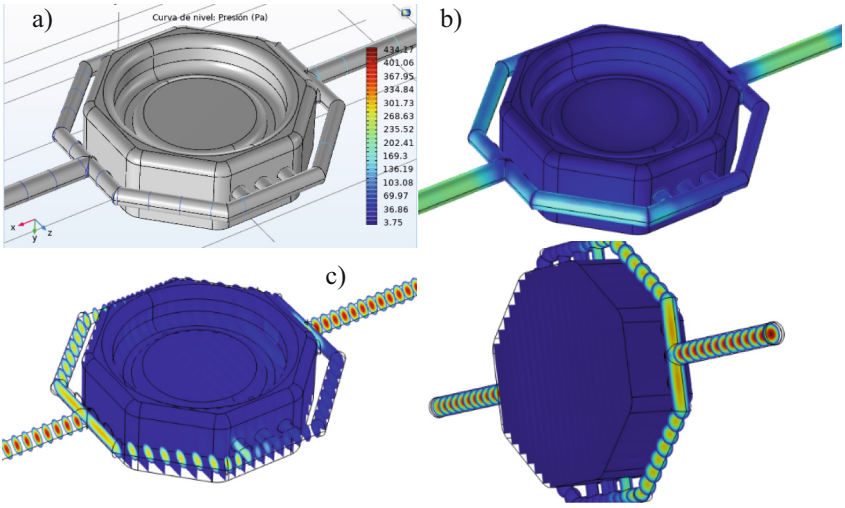

Fig. 3. Navier-Stokes COMSOL solver of the microfluidic biological system. Flow simulation components. a) System Volume with conditions. b) Chamber flow fields and their distribution. c) Vectors fields through the support in the form of the chamber.

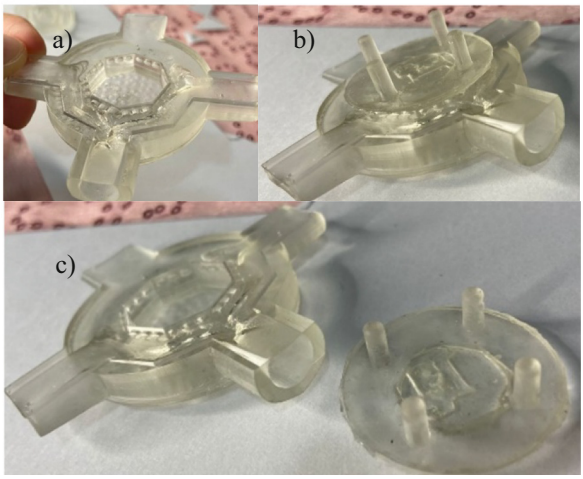

Fig. 4. Final prototype printed model of the in vitro test system. The clear resin was selected to facilitate the visual inspection of the flow and culture.

4 Conclusion

The biological system was designed and manufactured, it will provide a constant laminar flow, since in the flow lines it can be observed that there were no regions with zero flow, since a good fluid exchange was carried out, and the cells will not be affected.

The microfluidic technology holds immense potential for advancing bone tissue engineering and regenerative medicine. The ability to create biomimetic bone tissue models in a controlled and dynamic microenvironment allows for better understanding of bone biology, disease mechanisms, and drug responses. With continued advancements and interdisciplinary collaborations, bone tissue models have the potential to revolutionize personalized medicine, accelerate drug discovery, and improve patient outcomes in the field of bone health.

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