

Research Article

Development of Parametric Voronoi-Based Scaffolds for Trabecular Bone Tissue Replacement Using Additive Manufacturing

Gabriel de Souza Vieira Bié ¹, Zilda de Castro Silveira ², Rafael Vidal Aroca ³, Marcia Cristina Branciforti ^{1, *}

1. Department of Materials Engineering, Sao Carlos School of Engineering, University of Sao Paulo, Avenida Trabalhador San-carlense, 400, Sao Carlos - SP, CEP13562-590, Brazil; E-Mails: gabrielvieira10@gmail.com; marciacb@sc.usp.br
2. Department of Mechanical Engineering, Sao Carlos School of Engineering, University of Sao Paulo, Avenida Trabalhador San-carlense, 400, Sao Carlos - SP, CEP13562-590, Brazil; E-Mail: silveira@sc.usp.br
3. Department of Mechanical Engineering, Federal University of Sao Carlos, Rodovia Washington Luis, Km235, Sao Carlos – SP, CEP15565-905, Brazil; E-Mail: rafaelaroca@gmail.com

* **Correspondence:** Marcia Cristina Branciforti; E-Mail: marciacb@sc.usp.br

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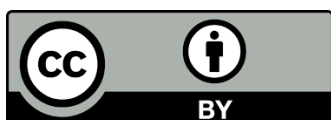
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Abstract

Tissue engineering is a technique for regenerating living tissue using portions of the patient's tissue, which are dissociated into cells and cultured on biological or synthetic supports before being transferred to the patient. In this context, the present study seeks to develop implant models (scaffolds) for replacing trabecular bone tissue, with requirements such as porosity and interconnected pores. All design development was aimed at the manufacturing of scaffolds using the material extrusion additive manufacturing process. For the development of this study, the Grasshopper program was utilized, an extension of Rhino that facilitates the creation of structures easily modifiable by parameters. The model developed involves applying the Voronoi 2D diagram in two perpendicular planes to generate extruded structures



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along a vector perpendicular to the plane of the respective diagram. This approach aims to create a Voronoi-based pore structure interconnected in two directions. Prototypes have been produced that fulfil the requirements for pore structure interconnection and porosity calculation, which are essential properties for a scaffold intended to replace trabecular bone tissue. In addition, the geometry of the prototypes was very close to the original model, even using low-resolution 3D printers.

Keywords

Tissue engineering; scaffolds; additive manufacturing; parametric design

1. Introduction

Scaffolds are implanted in a living body, and as such, they need to adhere to a series of principles for proper functioning. The following topics are listed as the main properties required for these scaffolds. The three main biological properties that scaffolds need are biocompatibility, biodegradability, bioreabsorption, and bioactivity. Biocompatibility refers to the material's capability not to be rejected by the biological environment in which it is implanted. In other words, the material should induce minimal biological response [1]. Scaffolds and their by-products generated by degradation must be biocompatible to avoid immunologically damaging responses, such as infections, which can impair their functioning and the biological system in which they are implanted. Biodegradability can be understood as the capacity of the material to degrade in the environment where it is placed, through bacteria, fungi, or other means, reducing it to non-toxic substances. In the context of implants, this means that the material must be able to deteriorate through biological means inherent to the implanted site without causing damage elsewhere. Since scaffolds are non-permanent transplants in bones, intended to restructure them, their biodegradability is fundamental so that surgical removal of the implanted material is not necessary. In addition to being non-toxic, the by-products must be adequately absorbed by the environment through bioreabsorption. Bioactivity refers to a beneficial reaction of the material with the biological system. In the case of osseous implants, this is achieved through osseointegration, which is defined as a structural bond between the implant and the bone, involving tissue growth in the region, resulting in a firm, direct, and lasting connection between the bone and the scaffold [2]. This aspect is necessary for the bone to regenerate itself through times that it does not need scaffold presence permanently, in addition to creating a structure that favors the mechanical properties of the injured site.

During the implantation period, the scaffold must withstand the loads imposed by the body under normal conditions, thus requiring proper mechanical resistance. If the mechanical resistance is too low, several problems may occur, such as mechanical failure during use or surgery. Conversely, if the mechanical strength is too high, the cells adhered to the material may not be subjected to the necessary conditions for healthy development, as exposure to loads is essential for their growth. A material with high mechanical strength acts as a barrier preventing loads from reaching the cells, but this scenario is rare due to the high porosity of the produced scaffolds [3-5].

For complete integration of the bone and scaffold, precise control of scaffold pores is necessary, as they serve as pathways for distributing nutrients to the surrounding bone tissue. Therefore, the porosity should closely match that of the bone structure. The ideal porosity for a scaffold is around 90% to maximize cell infiltration and nutrient diffusion; however, samples with porosity ranging between 55% and 74% are generally used due to the lower mechanical resistance of the material compared to bone, while still supporting biological functions. Additionally, the pores must be interconnected to facilitate better diffusion of substances throughout the organ [3, 6]. Regarding pore size, the requirement is closely related to the type of bone being replaced. In the present study, trabecular bones were examined, where the pore size typically ranges from 75 to 200 μm [7], which will therefore be the range of ideal size of the scaffolding pores to be modeled.

In addition to the basic structural requirements, producing scaffolds for bone implants that are increasingly efficient requires understanding the tissue and its components. By comprehending their functions, processes, and components, it becomes possible to mimic or stimulate them using the scaffold's structure or components. The ultimate goal is to accelerate the regeneration and calcification of bone tissue [8].

Scaffold research has grown exponentially in recent decades; the number of results for the word "scaffold" in 2023 was 16,460, almost ten times greater than in 2003, which was only 1,631 according to the Web of Science® database. This size growth demonstrates that this is still a developing area, with a large open margin for evolution. Understanding the requirements of a scaffold is fundamental to the present study because, in developing new models, it is crucial to consider everything necessary or unnecessary for the project. This ensures there are no unnecessary problems of incompatibility with the main objectives of the application.

The integration of scaffolds and additive manufacturing has revolutionized biomedical engineering by enabling the fabrication of highly controlled, patient-specific, and biomimetic structures that enhance tissue regeneration and repair. Used in the last couple of decades and significantly boosted in recent years, additive manufacturing is defined by ASTM as a process of joining materials to create objects through 3D model data, typically layer by layer. It stands in contrast to subtractive manufacturing methodologies, as it involves adding material to a structure instead of removing material from it. This definition, solely focused on the process, applies to any material [9].

Material extrusion is currently the most common additive manufacturing process used in universities and industries due to its relatively low cost and simple process reproducibility. The machine consists of a head fed by a filament, which is melted at its tip, and then deposited at the designated location. This is a constant process where the filament is consumed and feeds the head regularly. As with the previous processes, the process also occurs in layers divided by the machine software. In each layer, the head passes the marked path, depositing molten material, which adheres to the previous layers and is rapidly solidified, forming the base layer for the next ones [10].

Among the various limitations of the material extrusion process, one is the necessity to use only thermoplastic polymers due to the requirement of melting the material. Additionally, because the process is gravity-dependent, the range of possible geometries is relatively limited. Parts that increase in height horizontally, akin to oblique prisms, must have angles greater than 45° to allow proper structuring of the material during deposition. Parts with smaller angles require temporary supports to prevent material leakage or collapse during the process [11]. Another issue stemming from the characteristics of the molten material is the potential formation of unwanted small wires

between material spans. This occurs due to either the lack of adhesion between the molten material and the base or when dealing with tiny spans.

Understanding additive manufacturing processes is crucial because it determines how the scaffold will be produced, significantly influencing its properties. Additionally, it helps identify limitations in part geometry, pore size, porosity, interconnection size, structural sections, deterministic/stochastic models, etc., and the reasons behind them, making the choice of the manufacturing process very important. Authors [12] studied random Voronoi-type geometries of materials with isotropic and anisotropic porous structures, which are 3D-printed. The materials exhibit strong hardening behavior under compressive loads due to the smoothness and randomness of the void geometries, as well as the non-uniformity of the intervoid ligaments. Dimartino et al. [13] fabricated customized 3D printed supports using digital lighting processing, additive manufacturing, and polymeric formulation based on monomers and crosslinkers to create the polymeric network. They obtained 3D supports with a complex, ordered morphology and tunable properties for different bioengineering applications.

Regarding the pore geometry, the honeycomb format is used in several research studies, with square or hexagonal pores with 400 to 800 μm in size, ideally ranging from 50 to 710 μm , and total porosity ranging from 50 to 70%, ideally greater than 90% [14, 15]. Thavornytikarn et al. [16] modeled using several types of pores in the form of repetitive cells. The authors concluded that the format that generated better mechanical properties was the diamond format. The porosity obtained was 60%, with pore diameters ranging from 700 to 400 μm and with compressive strengths of 3.5 and 6.7 MPa, respectively.

In fields such as biomaterials, geomechanics, and materials science, where understanding and controlling pore structures are crucial, the Voronoi method has been widely used to model and analyze pore geometry, particularly in scaffolds, foams, and other porous materials [17, 18]. The valuable Voronoi tool provides a mathematical framework for analyzing pore geometry, including size, distribution, interconnectivity, and porosity.

Voronoi is a method of portioning a region into cells based on a discrete set of points, known as seed points, which are scattered within the region randomly or in a specific pattern. Each cell contains all the points closest to the seed point from which the cell originates. There is also research using, as in the present study, the Voronoi function of Grasshopper to make a scaffold model, but in cubic form, obtaining comparative graphs of elastic modulus, porosity and specific surface area for scaffolds with different amounts of pores, which can be changed freely using the program [19].

Voronoi-based scaffolds outperform honeycomb and randomized pore models in bone regeneration due to their natural bone-mimicking architecture, which leads to more homogeneous load transfer, improved fatigue resistance, and consequently superior mechanical adaptability. Additionally, they exhibit enhanced biological performance, resulting from highly interconnected pores that facilitate better mass transport of oxygen, nutrients, and waste removal, thereby improving cell viability and tissue integration. Furthermore, Voronoi structures are well-suited for 3D printing techniques, allowing fine-tuning of mechanical and biological properties through computational modeling [17-21]. These advantages make Voronoi-based scaffolds ideal candidates for patient-specific bone implants and tissue engineering applications.

Herat et al. [22] used the Voronoi approach to design a biodegradable bone scaffold with macropores (>4 mm) for the surgical treatment of bone defects. The study demonstrated the potential of Voronoi-based designs for patient-specific bone scaffolds, with macropore sizes that

mimic the geometry of trabecular bone. It concluded that polymer extrusion additive manufacturing is a suitable fabrication method for these scaffolds. Han et al. [20] proposed a lattice-inspired design for Voronoi-based metamaterials (LIVMs) to enhance their mechanical and permeability for bone implants. Using laser powder bed fusion, the authors fabricate LIVMs with varying topologies, demonstrating yield strengths of 3.35 to 17.59 MPa and permeability values similar to trabecular bone. The study shows how the unit cell topology affects printability, mechanical performance, and mass transport, offering a method to balance strength and permeability in bone implant applications.

To the best of the authors' knowledge, there are few studies to date on using polymer extrusion additive manufacturing to fabricate Voronoi-based bone scaffolds. Therefore, this study aims to establish the foundation for a design platform that enables the creation of implant models for trabecular bone tissue replacement, considering key requirements such as porosity and interconnected pores, based on Voronoi modeling. The methodology is presented educationally and straightforwardly, with a step-by-step explanation of each stage of scaffold generation. Customizable Voronoi-based scaffolds for trabecular bone replacement were developed using parametric design and low-resolution 3D printing, ensuring clarity and accessibility for researchers and practitioners in the field.

2. Materials and Methods

2.1 Materials

Filaments of polylactic acid (PLA), with and without pigment, 1.75 mm thickness and 210°C melting temperature were supplied by GTMax Company, Brazil.

2.2 Rhino Program

As the base platform for the present study, the Rhino5 program was used, a 3D modeler similar to AutoCAD, but with great support for file types that can be manipulated and saved, besides having plug-ins that complement its usefulness. Mathematically, Rhino5 is based on non-uniform Rational B-Splines (NURBS), mathematical representations of a 3D geometry that can describe solids or 3D surfaces through 2D lines, being a very flexible and precise model [23]. Rhino5 is the latest version and can be purchased at <https://www.rhino3d.com/>, but there is also a 90-day free trial version of the tools that can be downloaded from the same site.

2.3 Grasshopper

The modeling in the present study mainly used Grasshopper, a plug-in of the program Rhino5 that allows the creation of objects in CAD using design by parameters. These parameters can be modified to change the model from the outset, providing from a single project, which takes longer to be done, numerous combinations of structures and designs. This type of design allows great flexibility of work, because changes in the design can be made by modifying only one or two parameters. Grasshopper is essentially a block programming platform, where each block is an operation that receives data, changes it and passes it to other blocks or the Rhino interface. To program using Grasshopper, it is unnecessary to know programming in advance, since the interface is concise and straightforward. However, scripts are also supported using Python, Visual Basic, or C

#. This tool is widely used by architects. Still, it has a fantastic potential for engineering, especially in the field of 3D printing, as used in this study. Grasshopper is a free tool and can be downloaded from its official website: <http://www.grasshopper3d.com/page/download-1>. In addition, the site also has a forum dedicated to supporting the tool, in the following link: <http://www.grasshopper3d.com/forum>, also with the help of the tool creator, Scott Daivison.

Rhino and Grasshopper tools were chosen explicitly over other design software because Rhino offers robust capabilities for modelling complex 3D geometries. Grasshopper provides a flexible, parametric design environment that allows for rapid design iterations and easy modification of parameters. These features are particularly valuable in tissue engineering scaffold design [19]; where precise control over microstructural details and the ability to quickly adapt designs to meet specific requirements are crucial.

It is worth mentioning that the Grasshopper's resolution limits and time complexity depend on the number of elements, the complexity of geometries, and hardware capabilities. Initially, there are no strict resolution limits. Still, as the number of seed points and geometrical operations increases, the software may become significantly slower due to its parametric and iterative nature. Generating dense Voronoi patterns or highly detailed scaffold models can result in high memory usage and long computation times. These computational challenges are discussed in forums like the McNeel Forum and Grasshopper3D.com.

2.4 Weaverbird Modeler

Weaverbird is a complement to Grasshopper used for modeling topologies through meshes. Instead of doing the study through complicated scripts, the plug-in reconstructs the model made, subdivides any present mesh, and prepares the design for manufacturing [24]. This add-on is free and can be downloaded at: <http://www.giuliopiacentino.com/weaverbird/>.

2.5 Methods

In this work, the Voronoi approach was implemented on two perpendicular planes instead of a full 3D Voronoi, primarily to simplify the control of pore geometry and improve the printability of the Voronoi-based model. Applying patterns on two 2D planes offers advantages, such as better control over pore size, orientation, and interconnectivity. This approach can also reduce the occurrence of complex or unsupported geometries, making the structures more compatible with additive manufacturing processes and enabling better mechanical predictability.

2.5.1 Building the Box

First, a box was created through two points using the commands Box 2Pt, Construct Point, XY Plane, Number Slider and Negative. Box 2Pt will construct a box based on two points with X, Y and Z coordinates, which will be defined by Construct Point. This box will be in the XY plane, defined by the XY Plane command and will have zero height, essentially forming a plane. The coordinates of the points are then defined by the Number Slider command. The Negative operation will also be used, all arranged as shown in Figure 1(a). The desired figure is a square with center at the origin and side 20 mm, so the points used are (10,10,0) and (-10,-10,0). The square formed was then filled by dots using the command Populate2D and Number Slider, and in parallel, a prism was formed

based on this square using the commands Box Rectangle, Unit Z and Number Slider, all arranged as shown in Figure 1(b). The parameter used in Populate2D is the number of points that the square will fill. Unit Z indicates that the prism will grow in the Z direction, and the parameter indicates the height of the prism formed. The prism formed will be the basis for the other transformation.

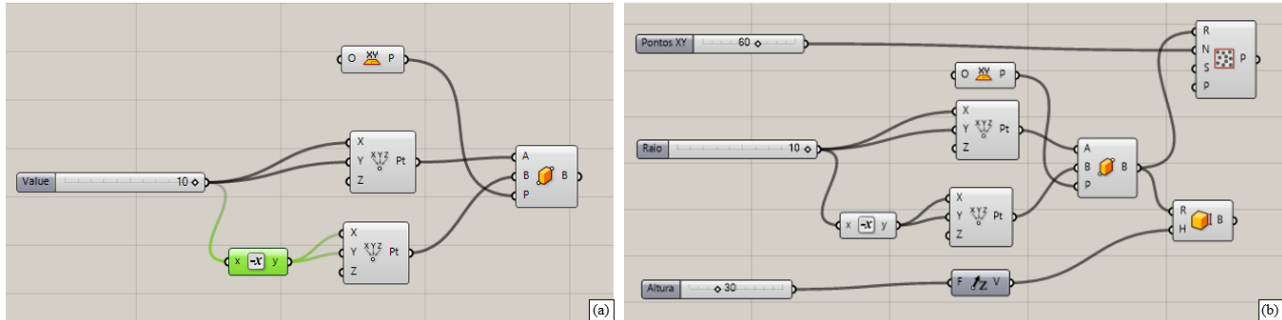


Figure 1 (a) Building the box. (b) Filling with dots and creating a prism.

2.5.2 Creation of Voronoi Function

The Voronoi function was then made of the points that fill the square, which was previously placed in a collection of points for better understanding. The Voronoi and Point commands, arranged as shown in Figure 2(a), were used. The connection between the prism and the Voronoi function was made to define the limits of the function. For the walls of the Voronoi to be thick, the Offset command connected to a new parameter was used. Then the walls and Voronoi were extruded using the Extrude command. The elements formed then had their voids closed by the CapHoles command, and then the subtraction between the solids was made using the Solid Difference command, all arranged according to Figure 2(b).

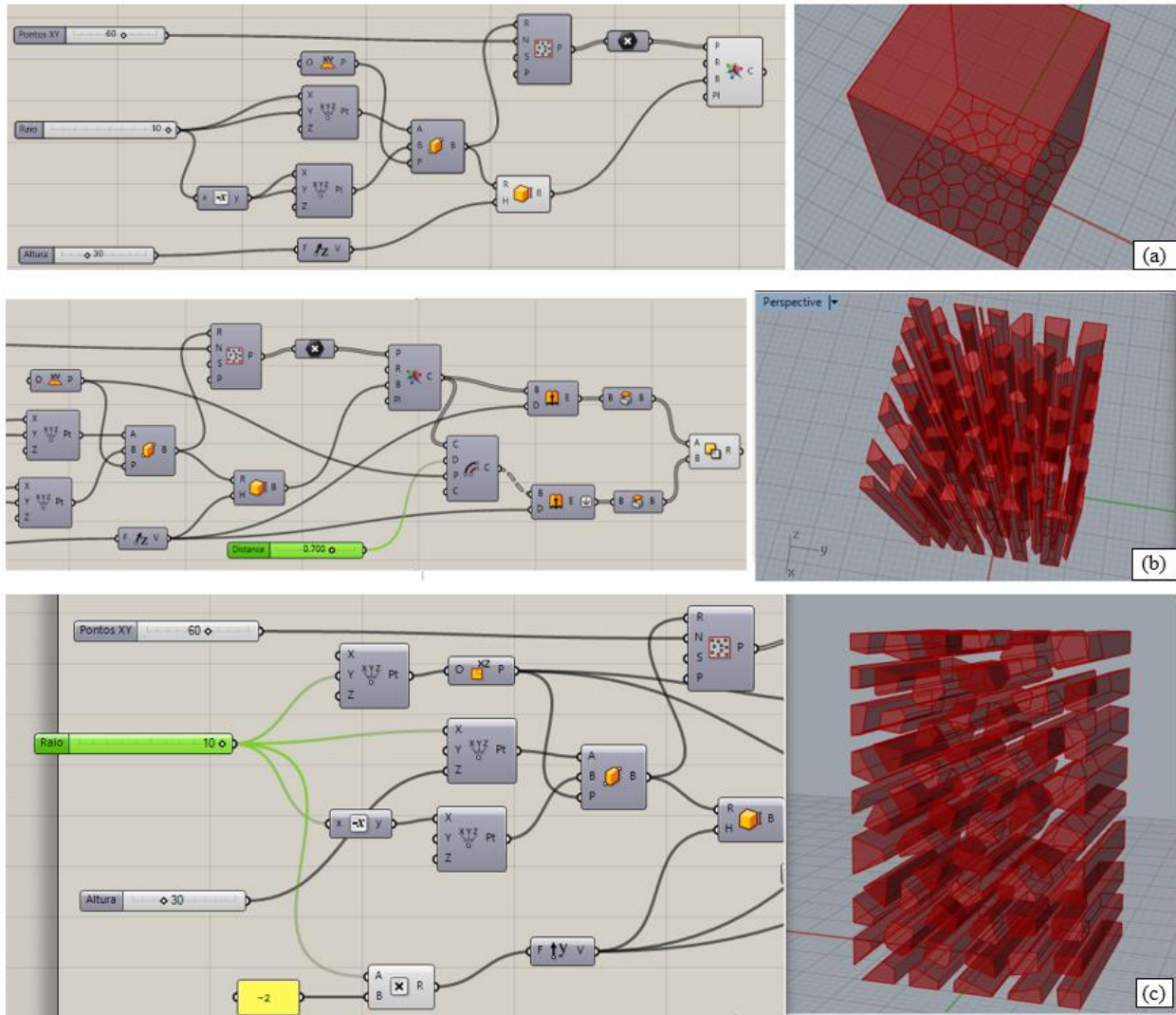


Figure 2 (a) Creation of Voronoi function and its representation in Rhino. (b) Extrusion of Voronoi and Offset and subtraction between them. (c) Adaptations to the XZ plane and result.

The extrusions were made on the Z axis, so they were joined with the same. In the extrusion formed by the Offset each solid formed is counted as an object in a list of its own, to enter all in the same list was used the command Flatten by right-clicking in the box of extrusion and selecting the command, in the image this change is indicated by the arrow facing down inside the control. It was then repeated, all the structure made so far, adapting to the XZ axis instead of the XY axis. To adapt to the XZ plane first, the XY plane was changed to the XZ plane, which, unlike the previous one, receives a start point (0,10,0) so that the extrusion occurs in the correct plane. The points of the box are also replaced by the points (10,0,30) and (-10,0,0). Finally, the height of the new prism was changed from the Z-axis to the Y-axis, with the size equal to the side of the prism made at the beginning and the negative direction, i.e., -20. This was done using the Multiplication command, connected to a panel, a structure that can be used to define a constant to be used. Three solid subtractions were then made, the first using the first prism and set of columns made, so that the negative of the columns, which is the box with voids, is formed; one using the two results obtained;

and finally, using the form received in the previous subtraction and the first prism created, to create the union of the columns, as shown in Figure 2(c).

The number of points in the planes was then modified, since the subtraction with the prism can lead to the exclusion of specific columns, because there is no processing power to do it with many columns. Because the XZ plane side was larger, 100 points were used; 50 points were used for the XY plane. In addition, to facilitate parameterization, the Offset distance has been equalized in both Voronoi diagrams. Other parameters will be joined later to have as few parameters as possible, so the final structure is easily modifiable.

2.5.3 Cylindrical Structure Generation

To achieve the final cylindrical structure, a cylinder was created in the XY plane with a radius equal to half of the prism's side and a height matching that of the prism. This cylinder will then subtract its structure from the object made so far. The Cylinder command was used, followed by the capping of the voids as shown in Figure 3(a). Using the Weaverbird extension commands, the mesh created with the Weaverbird's Join Meshes and Weld command was made, so the mesh was smoothed using the Weaverbird's Catmull-Clark Subdivision command, as shown in Figure 3(b). The constant used represents the number of iterations of subdivision for each face of the mesh, with a default of two. The mesh resulting from the method used in the last command is always quadrilateral.

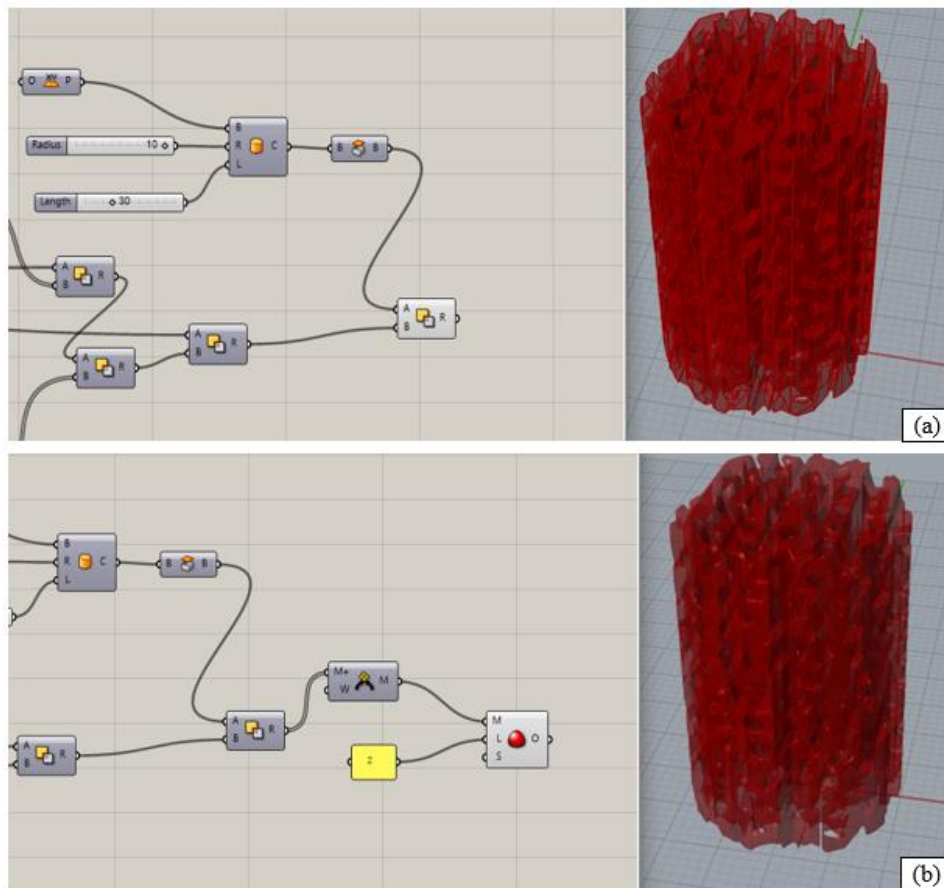


Figure 3 (a) Transformation to cylindrical shape and result. (b) Mesh and result application.

As it already represents the final structure desired for this project, it was exported to Rhino by clicking on the last command with the right mouse button and selecting Bake. After that, the file was saved in the ".stl" format so it can be printed to a 3D printer.

2.5.4 Porosity Calculation and Final Structure of the Grasshopper Program

In addition to making the model, the porosity of the model was also calculated by calculating the volume of the structure created using the Volume command. This volume was then divided by the total volume (of the cylinder) and then multiplied by 100 to obtain the relative volume in percentage, and then subtracted by 100 to find the porosity in percentage. The structure of the program is described in Figure 4(a).

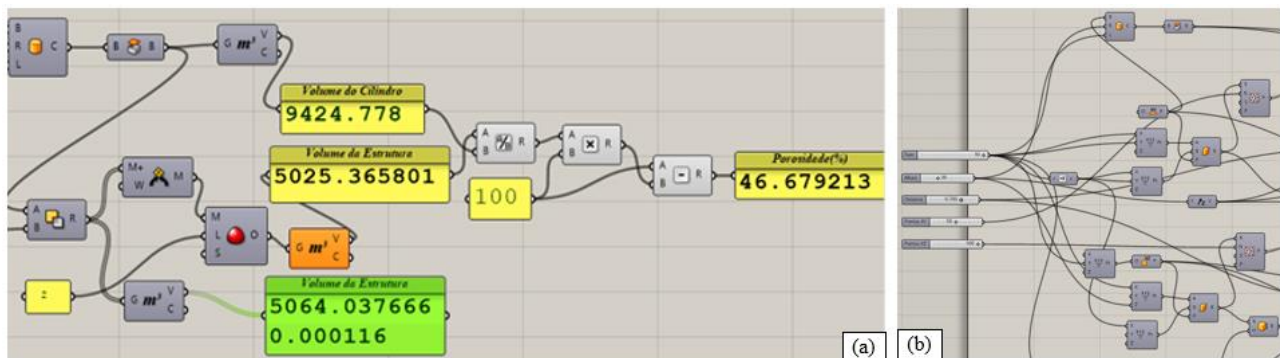


Figure 4 (a) Calculated porosity. (b) Final structure of the parameters.

As shown in the orange warning, Figure 4(a), the calculated volume of the structure after the mesh smoothing may not be 100% correct because the structure is not entirely closed. However, a comparison was made with the previous structure and found to be very similar and is therefore considered a reasonable estimate. In the volume of the structure calculated before the mesh transformation, two volumes appeared, which indicates that the subtraction formed two solids, one being very small. But the mesh transformation solved this problem. Then the program structure was modified so that all the repeated parameters disappeared and were organized so that they could be easily found and modified in the program structure. The structure of the parameters is shown in Figure 4(b). Finally, the final structure of the Grasshopper program is shown in Figure 5.

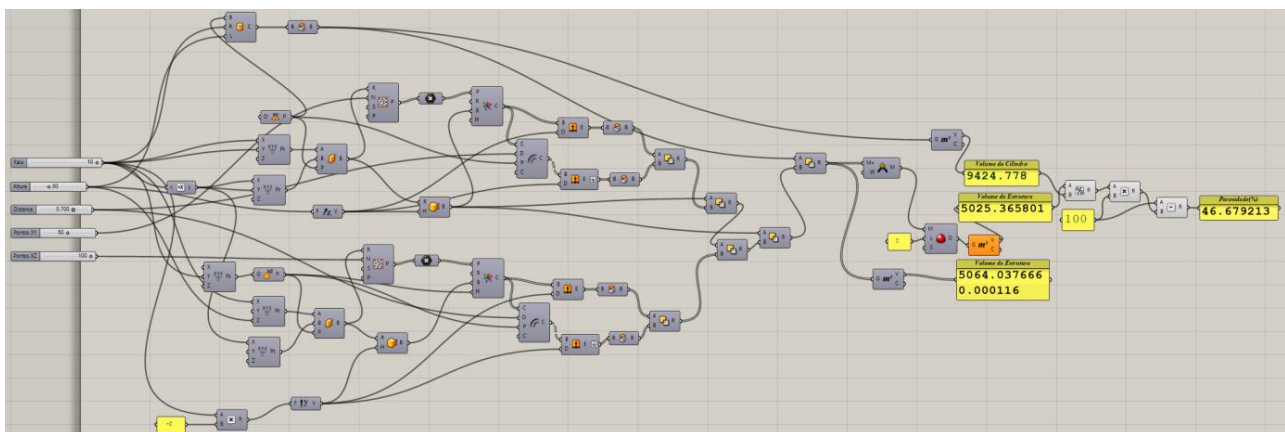


Figure 5 Final structure of the Grasshopper program.

2.6 Experimental Setup

Below is a structured overview of the experimental setup for this study. It covers the materials, software tools, scaffold-design workflow, printing parameters, and post-processing steps.

Commercially sourced PLA filaments were used to fabricate Voronoi-based porous scaffolds via fused filament fabrication (FFF). Scaffold geometries were generated in Rhino5/Grasshopper (with the Weaverbird plug-in) by applying 2D Voronoi patterns on orthogonal planes, extruding and subtracting them from a prism, mapping the result onto a cylinder, and then smoothing the mesh. Porosity was estimated via volume measurements. Cylindrical prototypes (50 mm height × 30 mm diameter) were printed on two desktop FFF printers (ClonerDH 3D and Sethi3D 3S) using a 0.1 mm layer height, ~ 210°C nozzle temperature, and two target porosity levels (50% and 60%), with both pigmented and unpigmented PLA. Pore sizes of the fabricated prototypes were measured by 2D images obtained through conventional optical microscopy (Carl Zeiss® Axiolab A1).

3. Results and Discussions

Towards manufacturing the scaffolds, initially, a wall made of hexagons was made. Because the format, besides being very simple, also does not have interconnected pores, it was done with the primary purpose of learning basic Grasshopper functions. After learning how the program worked, an attempt was made to study tasks that generated non-regular pores, such as the polygons of the first structure made. The Voronoi function (R_k) was then found, which produces contours from points defined on a surface. The Voronoi function consists of the application of the Voronoi diagram, which is governed by the equation:

$$R_k = \{x \in X | d(x, P_k) \leq d(x, P_j) \text{ to all } j \neq k\}$$

Where x is a metric space with distance function of d and $P_1, P_2, \dots, P_n$ are the given points. Thus, the diagram indicates that the area of the given point k (P_k) consists of all points whose distance from it (P_j) to point k is less than or equal to the distance between it and any other of the given points; j is any index different from k .

Because it is a non-regular function, whose contours fit according to the given points, this seemed an appropriate way to be considered for the project. The Voronoi function is represented in Figure 6(a). Through the procedure of subtraction of a prism by an extension of the Voronoi function, a Voronoi-based 3D structure was created, which is shown in Figure 6(b).

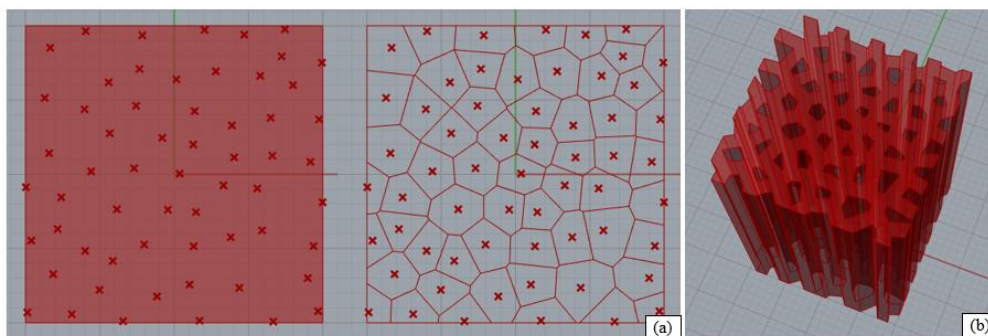


Figure 6 (a) Set of points on a surface and the Voronoi function. (b) 3D structure created by Voronoi.

Despite having irregular pores, this structure still did not have interconnectivity between them. To solve this, it was proposed to subtract Voronoi cells in the three planes: XY, XZ, and ZY. However, this caused a structure with many empty spaces, which generated components not connected to the main structure, causing problems for the 3D printing process. Therefore, the idea was discarded. In substitution, the subtraction was done in only two planes, XY and XZ, generating more consistent results, mainly with relatively low porosity. The top, perspective, front, and right views of the porous structure made with Voronoi subtraction in two planes are presented in Figure 7.

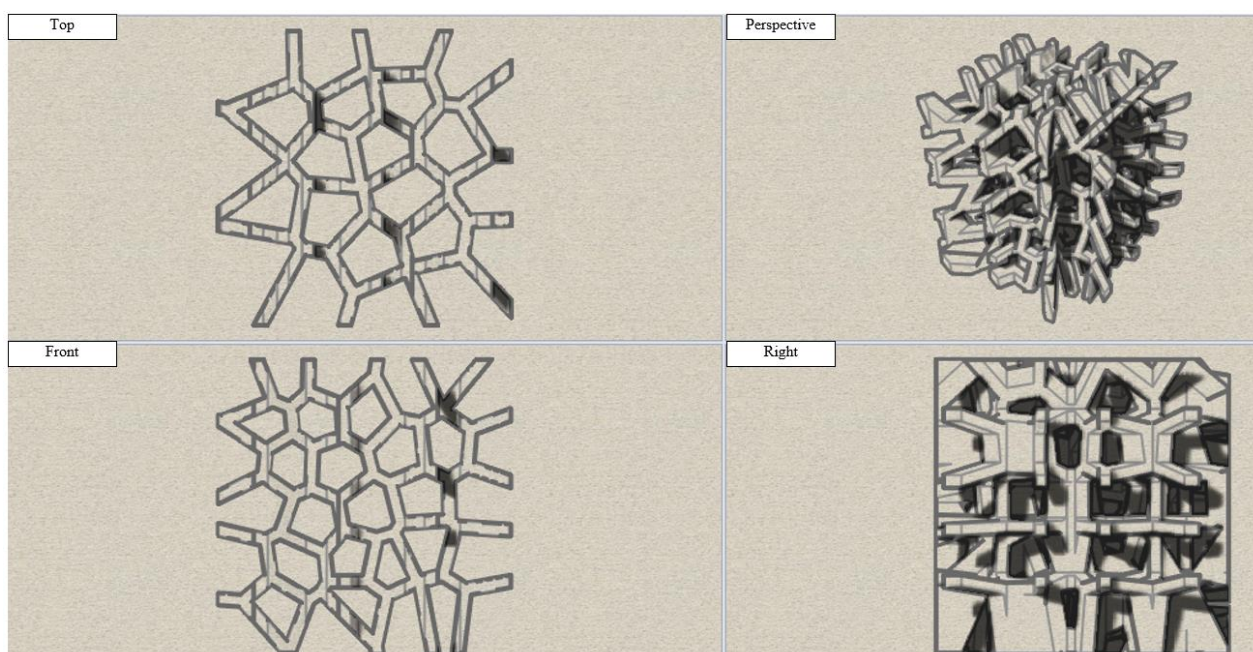


Figure 7 Top, perspective, front, and right views of the porous structure made with Voronoi subtraction in two planes.

Finally, this structure was then subjected to a series of changes aimed at improving both the 3D printing process and future mechanical tests. For this, the porosity was decreased, the pores were rounded, the geometry was changed to cylindrical and the dimensions, which were very small before, were altered. The result is the final porous structure design developed in this study. Figure 8 shows the top, perspective, front, and right views of the developed porous structure.

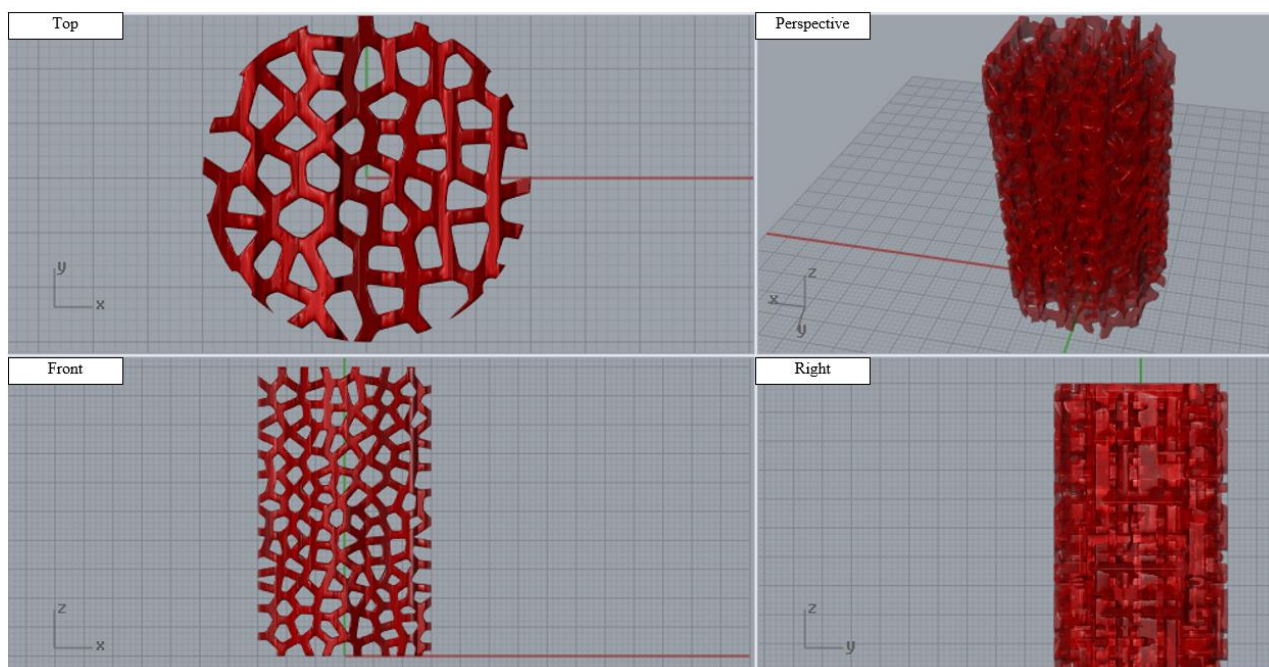


Figure 8 Top, perspective, front, and right views of the developed Voronoi-based porous scaffolds.

Prototypes of the final Voronoi-based porous scaffolds were manufactured using the ClonerDH 3D and the Sethi3D model 3S printers, both with material extrusion technology. The cylindrical prototypes, measuring 50 mm in height and 30 mm in diameter, were made of polylactic acid (PLA), with and without pigment, using two representative porosity values (50 and 60%), a layer thickness of 0.1 mm – all model walls are assumed to have uniform thickness, and a working temperature of approximately 210°C. Table 1 summarizes the printer models, materials, porosity, and key parameters used for prototype fabrication in the “first” and “second” prints. It is essential to highlight that the prototypes in this study were not fabricated or tested under sterile conditions or simulated physiological environments, as the focus was on design and fabrication process.

Table 1 Printer model, material, porosity, and print settings used for prototype fabrication.

	ClonerDH 3D printer		Sethi3D 3S printer	
	First print	Second print	First print	Second print
Material	PLA with pigment	PLA with pigment	PLA without pigment	PLA without pigment
Porosity (%)	60	50	60	50
Layers thickness (mm)	0.1	0.1	0.1	0.1
Working temperature (°C)	~210	~210	~210	~210
Offset distance (mm)	0.900	0.700	0.900	0.700
Points in the XY plane	60	50	60	50
Points in the XZ plane	130	100	130	100

Figure 9 shows the side, top and bottom views of the printed representative Voronoi-based scaffold structures from the first and second prints, respectively. These prototypes were fabricated using the ClonerDH 3D printer.

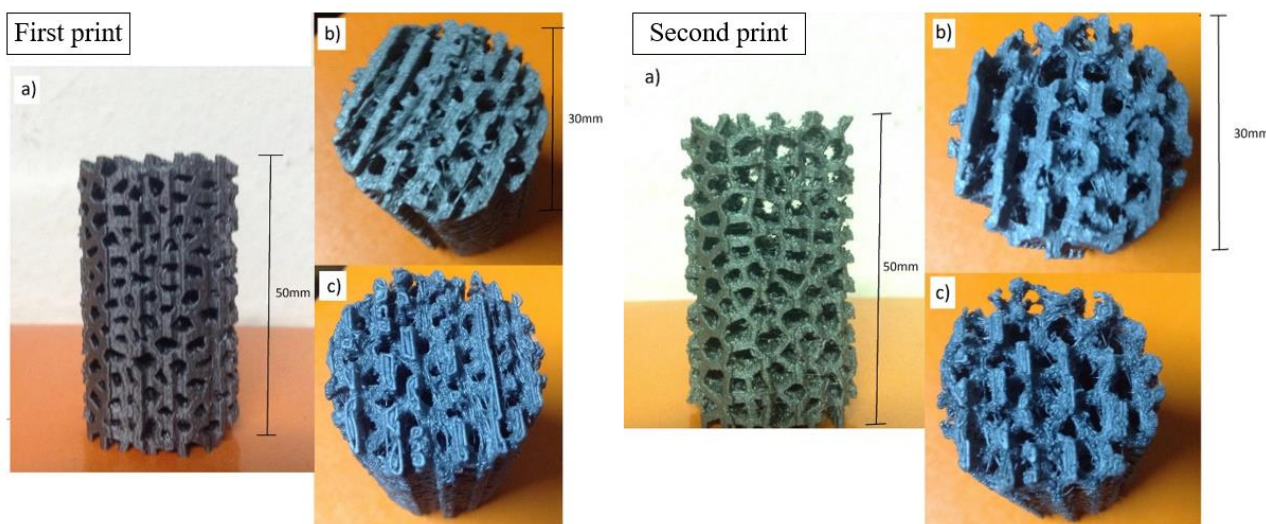


Figure 9 (a) Side, (b) top and (c) bottom views of the first and second printed representative Voronoi-based scaffolds fabricated using the ClonerDH 3D printer.

In the scenario depicted in Figure 9, the initial impression was generally satisfactory. Notably, the base exhibited a coarse texture, typically generated to support parts with minimal surface area. Moreover, small strands of residual material were visible between the pores of the structure. These strands commonly result from high printing speeds and low operating temperatures. The second print displayed even more favorable morphology, attributed to wider pores. Consequently, this led to an increase in the accumulation of threads between the pores of the structure. Additionally, the vertical voids became slightly more discernible along their entire length. However, owing to the model's thinner walls and greater inclination, a heightened presence of excess material was observed in the corners of the structure.

Figure 10 presents the side, top, and bottom views of the printed representative Voronoi-based scaffold structures from the first and second prints, respectively. These scaffold structures were fabricated using the Sethi3D 3S printer.

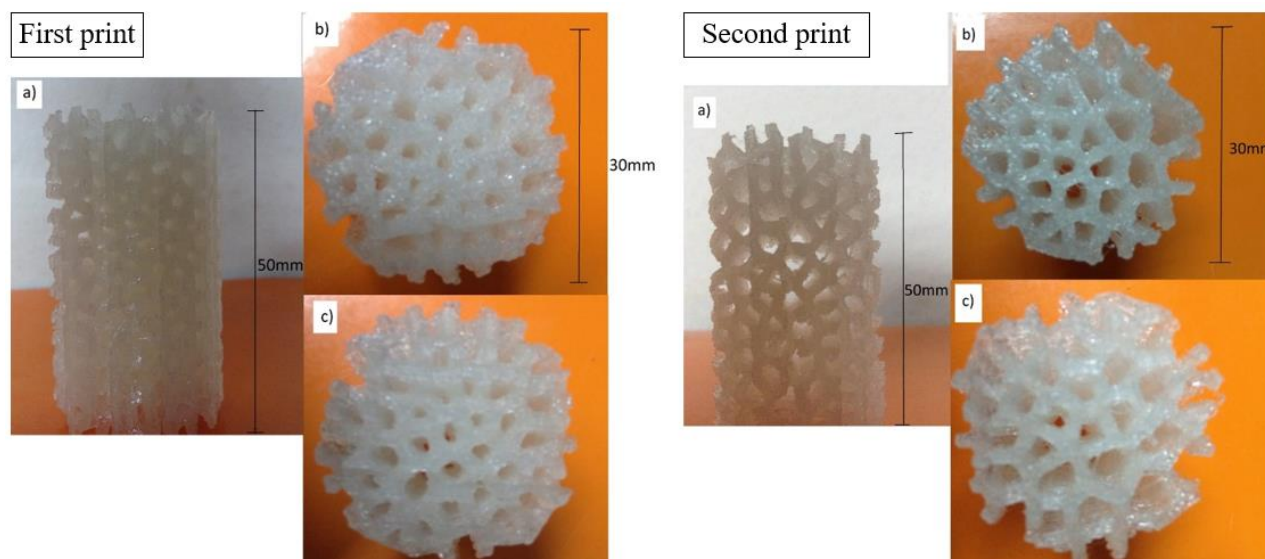


Figure 10 (a) Side, (b) top and (c) bottom views of the first and second printed representative Voronoi-based scaffolds fabricated using the Sethi3D 3S printer.

Figure 10 illustrates that both prototypes produced by the Sethi3D 3S printer exhibited significantly higher precision than those from the ClonerDH 3D printer. These prototypes boasted numerous advantages, including a notable reduction in excess material, diminished presence of wires within voids, apparently more cohesive structure, improved visibility of vertical pores with greater extension, and eliminating the necessity for a removable base in the model, which typically requires subsequent removal.

In general, the pore sizes of the fabricated prototypes ranged from 1 to 4 mm, which is considerably larger than the ideal range of 75 to 200 μm . This result reflects the lack of accuracy of the model in achieving the intended porous structure. However, this discrepancy presents an opportunity for substantial improvement through Voronoi model refinement and the utilization of high-resolution 3D printers. Low-resolution 3D printers can reduce the effectiveness of Voronoi-based models by producing larger-than-intended pore sizes, thicker walls, and a loss of intricate geometric details. By optimizing the print setting like reducing layer height and nozzle diameters, or adjusting infill density and support structures to preserve intricate pore geometries, allows for finer structural details. In summary, the literature [18-21] describes that increasing the density of seed points and adopting a more uniform seed placement in the Voronoi-based structure leads to smaller and more refined pores. Thinner walls in the Voronoi-based structure also allow for smaller pores while maintaining overall porosity. Additionally, combining Voronoi structures with lattice reinforcements can help refine pore architecture while preserving structural integrity.

Aiming to qualitatively demonstrate how the present work compares with previously published studies, Table 2 summarizes the methods used, porosity values, and pore size reported in similar works from the literature and this study. It can be concluded that the present study demonstrated competitive porosity levels (50% and 60%) within the optimal range for tissue engineering applications. The pore size achieved (1-4 mm) is suitable for enhanced vascularization and bone ingrowth, offering a structurally heterogeneous scaffold design through Voronoi-based modeling. In addition, using a cost-effective FFF printing process provides an accessible alternative to more complex fabrication techniques reported in the literature.

Table 2 Comparison of methods, porosity, and pore size between similar studies reported in the literature and the present study.

Reference	Method	Porosity (%)	Pore Size (μm or mm)
[12]	Computational design of mechanical growth + 3D printing	Very low to moderate (not exactly specified)	Variable (circular, Voronoi, hexagonal)
[13]	3D printing (DLP) with customized polymer formulations	Controllable via formulation	$\sim 50 \mu\text{m}$ (typical printing resolution)
[14]	Extrusion to fabricate β -TCP scaffolds	60–70%	400–800 μm
[15]	3D printing of sacrificial mold + cold isostatic pressing	High (not exactly specified)	Not specified
[16]	Stereolithography (SLA) + partial pre-sintering	$\sim 60\%$	400–700 μm
[19]	Voronoi structure design via CAD + 3D printing	Variable, mimicking trabecular bone	20–1000 μm
[20]	3D printing LPBF of lattice-inspired Voronoi metamaterials	Controllable (exact value not specified)	Adjustable via unit cell (~ 100 –500 μm)
[22]	FFF printing of customized Voronoi scaffolds	71%	4.0–11.8 mm
This study	FFF printing of Voronoi scaffolds using Rhino5/Grasshopper	50% and 60%	1–4 mm

As the prototypes in this study do not meet the required pore size specifications for complete mechanical and biological evaluations, we were not encouraged to conduct mechanical and biological validations at this stage. Literature [19–22] emphasizes that an ideal bone scaffold should mimic natural bone in mechanical, biological, mass transport, and microstructural properties to prevent stress shielding and to ensure cell penetration, nutrient diffusion, and proper biodegradation. The mechanical and fluid properties of Voronoi-based scaffold models, made through 3D printing, are directly influenced by the microstructural characteristics of the porous structure. Key factors to control include total porosity and bone surface area, which can be easily controlled at the initial stages of the Voronoi design methodology. Mechanical strength and mass transport properties in Voronoi implants can be balanced, with mechanical strength increasing at the expense of porosity reduction. In contrast, permeability increases when the specific bone surface area is decreased. For instance, increasing the number of seed points generally produces a finer distribution of smaller pores, improving overall porosity. However, this often results in reduced mechanical strength due to lower material density in the structure. Moreover, a lattice-inspired design methodology effectively achieves a favorable combination of superior printability, mechanical properties, and tunable permeability in Voronoi-based scaffold models. These findings provide valuable theoretical guidance for developing Voronoi-based scaffolds for bone implant applications using additive manufacturing.

4. Conclusions

This study aimed to develop scaffolds for replacing trabecular bone tissue, meeting specific requirements such as porosity and interconnected pores. All design efforts were geared toward manufacturing scaffolds using material extrusion additive manufacturing techniques. Through the use of Grasshopper, we introduced novel scaffold models by a parameterized design approach. To support accessibility, detailed step-by-step explanations of Grasshopper's basic functions were provided, allowing individuals with limited programming experience to use the tool for model development in tissue engineering effectively. Despite these advances, limitations posed by Grasshopper, Weaverbird, and the available computational resources resulted in models with pore sizes larger than initially desired. Nonetheless, this study provides an educational framework for scaffold generation and a solid foundation for further research. Future iterations will focus on refining the models to meet all necessary specifications for practical application in tissue engineering applications, ensuring the scaffolds are optimized for functional and biological performance.

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Author Contributions

Eng. Bié was responsible for conceptualization, methodology, formal analysis, and writing-original draft preparation. Drs. Silveira and Aroca assisted with laboratory facilities, resources and writing-review and editing. Dr. Branciforti oversaw the work, provided technical direction, resources, data curation, and writing-review and editing.

Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the study reported in this paper.

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