# HOW SCAFFOLD DESIGN INFLUENCES BONE REGENERATION

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## Introduction

Bone is a complex natural composite material composed of both, an organic matrix and an inorganic mineral phase, giving it a unique combination of flexibility and mechanical strength. However, the natural ability of bone to regenerate is insufficient when a critical-sized bone defect occurs, such as following trauma or surgical resection, necessitating the use of synthetic scaffolds to restore functioning [1].

A solution is bone scaffolds, which are three-dimensional structures designed to facilitate tissue regeneration by enabling cells to attach, proliferate and differentiate. In most cases, scaffolds for hard tissue healing are permanent and need to maintain their shape, strength, and biological integrity during bone healing. They must be biocompatible, non-toxic, strong, stable over time, and osteoconductive to promote bone growth and integration. Generally, we use 3D printed scaffolds that provide a structural model for new bone formation. Because of its superior osseointegration qualities, high strength-to-weight ratio, and resistance to corrosion, titanium alloys (Ti-6Al-4V) is generally employed as a material for implants [2]. Microarchitecture and porosity can be precisely controlled by Selective Laser Melting (SLM). However, designing an optimal metallic scaffold is challenging, we seek to determine how variability in scaffold design influences mechanical performance and osteointegration. Our objective is to identify the most suitable scaffold design for clinical use and propose potential improvements for the alternative design. The goal of this work is to improve the continuous development of more efficient and patient-specific bone implants.

## Methods

This study analyzed two different metallic bone scaffold designs manufactured using Selective Laser Melting with Ti-6Al-4V, a titanium alloy. For manufacturing variability, three scaffolds per design were produced and analyzed using X-ray micro-computed tomography at a 6.67 µm resolution. The objective is to quantitatively compare key structural parameters like bone volume fraction (BV/TV), pore size, strut thickness, and surface-to-volume ratio. One of each scaffold design was assigned to a different student group for individual analysis using CTAn software. To obtain the most accurate estimation of each parameter, results from multiple students were compiled. Outliers and erroneous values were identified and removed using GraphPad Prism. For each scaffold, the mean value of each structural parameter was calculated across all student results for each printed scaffold. A t-test was performed to compare the two scaffold designs and assess significant differences in their structural properties. Additionally, CTVox and DataViewer were used to generate 3D reconstructions of each scaffold, providing a visual assessment of their internal architecture.

## Results and Discussion

As we can see in the figures below, scaffold 1 has a very high porous architecture with large and interconnected pores, that’s mean it has also a low volume fraction (% BV/TV). Thanks to this high porosity, the scaffold will improve vascularization, cell migration, and nutrient diffusion, which are essential for rapid bone growth. Research suggests an optimal pore size between 100 µm and 500 µm [1]. However, in this case, the pore size exceeds 600 µm, which may be too large and compromise cell attachment and tissue formation. Also, as the stiffness is lower, this will reduce the resistance to stresses, thus allowing better load transfer to the surrounding bone and therefore preventing bone resorption over time [1]. However, its lower mechanical strength makes it less suitable for load-bearing applications. Finally, this type of scaffold is particularly useful where rapid tissue integration is a priority. Scaffold 2 has a denser structure with smaller pores, that’s mean it has also a higher volume fraction and a high mechanical stability. That makes it more suitable for bones such as the femur or tibia, where structural integrity is essential. However, the reduced pore size can reduced vascularization and slow bone regeneration. Despite this, the increased surface area in contact with bone tissue can promote osseointegration and improve implant fixation over time. Finally, as we can see in the table below. The very low p-values for the t-test show that the structural differences between the two scaffolds are statistically significant and unlikely due to chance. We also see that we have good repeatability of the prints, except for the S/V parameter of scaffold 2.

## Conclusion

In conclusion, both scaffolds are viable, but designed for different applications. Scaffold 2 has very low repeatability, while Scaffold 1 has excessively large pore sizes. A hybrid scaffold combines the advantages of both designs and maybe incorporating surface treatments that improve osseointegration, vascularization, and overall bone regeneration could give a more optimal solution in terms of load-bearing and biological performance. Bioactive coatings or composites could also further improve the scaffold's functionality, promoting faster and more efficient bone healing.

## References

[1] Alvarez K, Nakajima H. Metallic Scaffolds for Bone Regeneration. Materials (Basel). 2009 Jul 23;2(3):790–832. doi: 10.3390/ma2030790. PMCID: PMC5445750.

[2] Fan L, Chen S, Yang M, Liu Y, Liu J. Metallic Materials for Bone Repair. Adv Healthc Mater. 2024 Jan;13(3):e2302132. doi: 10.1002/adhm.202302132. Epub 2023 Nov 12. PMID: 37883735

[3] Alabbad FA, Alslameen AAH, Alwaif MA, Alswar AS, Alfandi NHJ, Alenazi SS, Al Ruwaili AN, Alharbi BSO, Al Dosari SS, Alaqil FA. Metallic scaffolds for tissue and bone engineering: applications in radiology, pharmacy, nursing, emergency services, and laboratory sciences. Metall Mater.

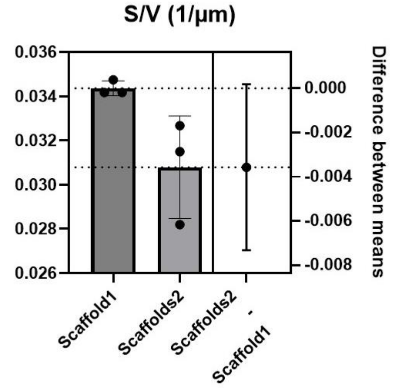


*Figure 1: Surface to Volume ratio comparison for the two types of scaffolds*

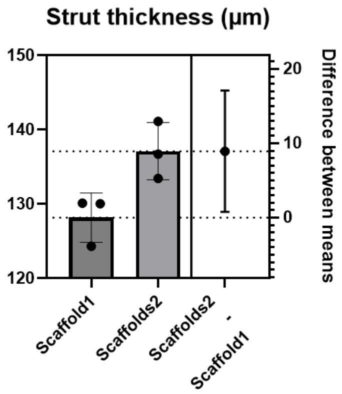


*Figure 2: Structure thickness comparison for the two types of scaffolds*

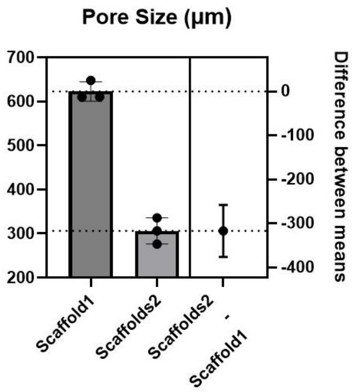


*Figure 3: Pore size comparison for the two types of scaffolds*

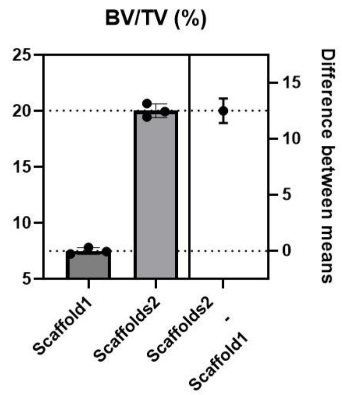


*Figure 4: Volume fraction comparison for the two types of scaffolds*

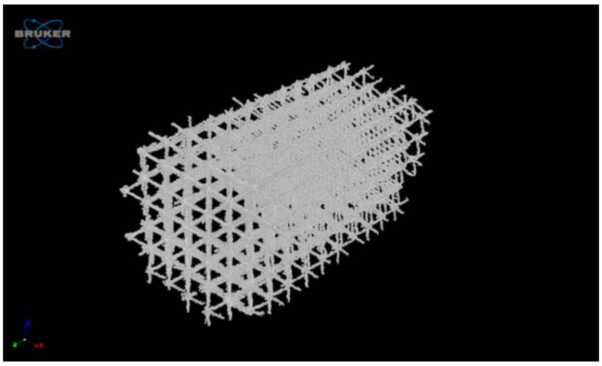


*Figure 5: 3D representation of the Scaffold n°1*

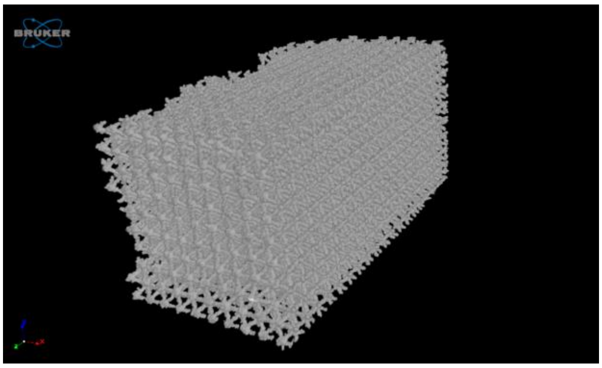


*Figure 5: 3D representation of the Scaffold n°2*

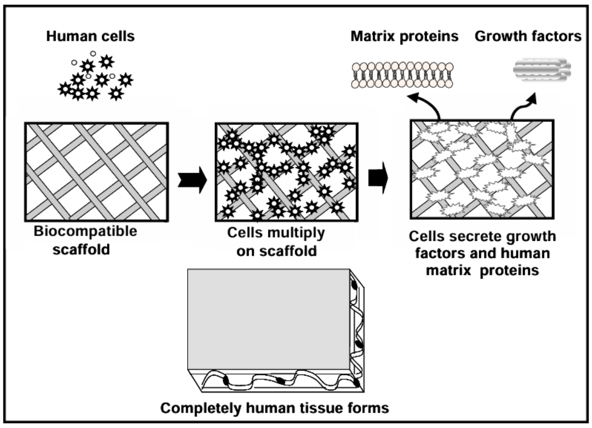


*Figure 5: Cell-based tissue regeneration approach for the repair of bone defects.[1]*

| | P_value t-test | P_value F-test |
|---|---|---|
| S/V | 0.0574 | 0.0409 |
| Strut thickness | 0.0385 | 0.8497 |
| Pore Size | 0.0001 | 0.7028 |
| BV/TV | <0.0001 | 0.3857 |

*Table 1: Table of statistical results (p-value)*