

Article

Synthesis and Evaluation of Porous Nanosynt Block (FGM[®]) as Synthetic Bone Substitute for Bone Tissue Engineering

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Abstract: Synthetic bone substitutes based on hydroxyapatite (HA) and β -tricalcium phosphate (β -TCP) are widely used in regenerative dentistry due to their favorable biocompatibility and osteoconductive properties. This study aimed to evaluate, through laboratory-based analyses, the porosity and surface characteristics of the Nanosynt Block (FGM Dental Group[®]) for bone regeneration applications. The Nanosynt Block, consisting of 60% HA and 40% β -TCP, was analyzed using scanning electron microscopy (SEM) for surface morphology characterization, micro-computed tomography (Micro-CT) for internal structure evaluation, and mercury intrusion porosimetry for porosity assessment. SEM imaging followed the ASTM E1829-02 standard, while Micro-CT and porosimetry provided detailed quantitative data. SEM analysis revealed a homogeneous pore distribution on the surface. Micro-CT indicated high structural stability and consistent volumetric porosity, ranging from 73.27% to 77.08%. Porosimetry indicated a total porosity of 94.9%, with a median pore diameter of 799 nm, characteristics suitable for promoting cellular adhesion and fluid infiltration. The structural and morphological properties of the Nanosynt Block highlight its potential to support initial bone formation and mechanical stability in clinical applications. These findings provide a robust basis for subsequent in vivo investigations to validate its clinical efficacy.

Keywords: bone substitute; hydroxyapatites; porosity



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1. Introduction

Bone regeneration is essential in rehabilitative dentistry, particularly in cases of structural losses resulting from extractions and trauma, which often lead to bone resorption, thereby compromising the stability of dental implants and aesthetic outcomes [1]. During the repair process, alveolar ridge resorption of 1 to 3 mm in height and 3 to 5 mm in width is commonly observed, which reduces the ridge’s capacity to adequately support prostheses and implants [2]. In this context, the use of bone grafts and substitutes is essential for restoring the lost volume, representing a key factor in the success of rehabilitative and reconstructive surgeries [1,2].

The selection of bone substitutes requires careful consideration of factors such as biocompatibility, resorption capacity, mechanical strength, and the capacity for integration with bone tissue [2]. While autogenous bone grafts are widely regarded as the “gold standard”, their limited availability and the morbidity associated with the procedure have driven the search for alternative options, including xenografts and synthetic materials [2,3]. Bone substitutes, such as calcium phosphate particulates and collagen–hydroxyapatite grafts, are widely used due to their inherent porosity and their ability to promote osteoinduction, providing a scaffold that facilitates cellular growth [1,4].

The biological processes of osteoconduction, osteoinduction, and angiogenesis are critical determinants in assessing the efficacy of bone substitutes. Osteoconduction relies on the material’s interconnected porosity, which facilitates cellular migration and adhesion [5,6]. Osteoinduction, in contrast, requires the stimulation of mesenchymal cells to differentiate into osteoblasts, a property that is generally limited in synthetic materials unless enhanced with bioactive agents [7]. Angiogenesis, which is critical for vascularization and long-term bone regeneration, is strongly influenced by pore size and connectivity, as these parameters regulate nutrient diffusion and blood vessel formation [7]. A comprehensive understanding of these biological mechanisms is essential for the designing of effective bone substitutes. Synthetic materials, such as hydroxyapatite (HA) and β -tricalcium phosphate (β -TCP), are engineered to replicate these processes while providing controlled composition and structural adaptability [3,4].

Among commercially available bone substitute options, Bio-Oss[®] (Geistlich Pharma AG, Wolhusen, Switzerland) is widely utilized due to its low resorption rate, providing prolonged structural support [8]. In contrast, β -TCP-based materials such as Cerasorb[®] (Curasan AG, Kleinostheim, Germany) exhibit controlled resorption, facilitating gradual replacement by native bone tissue [9]. Similarly, BoneCeramic[®] (Straumann Holding AG, Basel, Switzerland), a biphasic material composed of 60% HA and 40% β -TCP, integrates the prolonged structural stability of HA with the resorbable properties of β -TCP, making it an effective alternative for critical-sized bone defects [10]. The Nanosynt Block (FGM Dental Group[®], Joinville, Santa Catarina, Brazil), also composed of 60% HA and 40% β -TCP, offers a comparable balance between structural stability and controlled resorption. These characteristics position it as a promising material for addressing clinical challenges, particularly concerning volumetric stability and early bone formation [11].

Despite the widespread use of biphasic calcium phosphate ceramics, the influence of porous architecture on clinical performance remains inadequately understood. The porous matrix of these biomaterials, such as the Nanosynt Block, facilitates osteointegration and tissue regeneration. The interconnectivity of micro- and macropores optimizes cellular migration and proliferation, nutrient and oxygen transport, and vascularization, thereby creating a favorable environment for osteogenic cell colonization and bone matrix formation [12,13]. Although the composition of the Nanosynt Block is well established, a detailed characterization of its porosity is critical for linking its structural properties to clinical efficacy, thereby refining its application across different contexts. Previous studies have addressed its biocompatibility [14] and explored varying HA/ β -TCP ratios and bioactive coatings [15,16]; however, the direct relationship between porous architecture and clinical performance remains unclear. This knowledge gap, particularly regarding the Nanosynt Block—a relatively recent product in the Brazilian market—highlights the need for further studies on its structural properties.

This study aims to address this gap by comprehensively characterizing the structural and morphological properties of the Nanosynt Block. Using advanced techniques—including scanning electron microscopy (SEM), micro-computed tomography (Micro-CT), and mercury intrusion porosimetry—we will analyze its porosity, surface morphology, and

volumetric stability. This detailed analysis seeks to provide insights into the material's potential to support osteoconduction, angiogenesis, and ultimately bone regeneration, emphasizing the critical role of the structure–function relationship in the selection of bone substitutes to optimize the decision-making process.

2. Materials and Methods

2.1. Synthetic Bone Substitute

The Nanosynt Block is a synthetic biphasic bone substitute manufactured by FGM Dental Group[®] and commercially available in the Brazilian market. This study aimed to characterize the surface morphology and porosity of the Nanosynt Block. This biomaterial consists of porous, three-dimensional blocks fabricated from agglomerated Nanosynt microparticles [17,18] through a molding and sintering process (Figure 1).

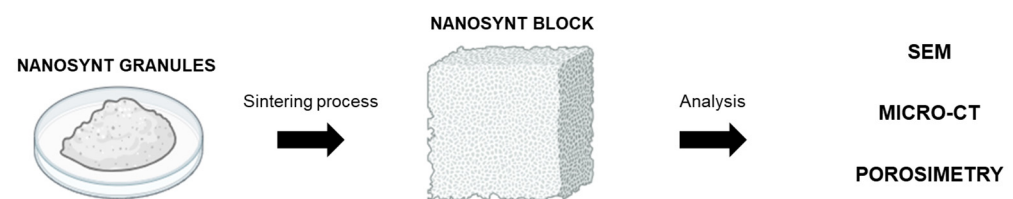


Figure 1. Schematic of the manufacturing process.

Nanosynt Granules, the precursor material, consist of 60% hydroxyapatite and 40% β -tricalcium phosphate and have been commercially available since 2016 through FGM Dental Group[®].

Commercially available Nanosynt Block samples were provided in three dimensions: $5 \times 10 \times 10$ mm, $10 \times 10 \times 10$ mm, and $8 \times 20 \times 20$ mm (Figure 2I). A comprehensive analysis was performed using multiple techniques. Scanning electron microscopy (SEM) was employed to evaluate surface morphology, while micro-computed tomography (Micro-CT) enabled a three-dimensional assessment of the internal structure. Both techniques are recommended by the ISO 13175-3:2012 standard for assessing the porosity of implantable materials with this composition [19]. Finally, mercury intrusion porosimetry was utilized to determine the total porosity and pore size distribution.

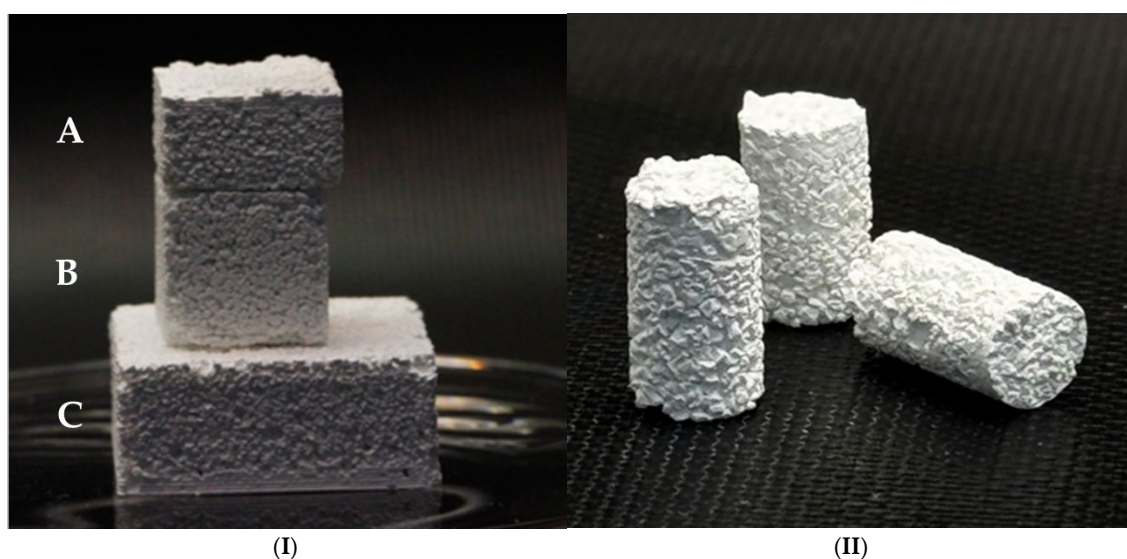


Figure 2. (I) Nanosynt Block in its three versions of dimensional forms. In A: $05 \times 10 \times 10$ mm, B: $10 \times 10 \times 10$ mm, and C: $08 \times 20 \times 20$ mm. (II) Samples for Micro-CT.

For Micro-CT analysis, cylindrical specimens (5 mm in diameter, 8 mm in height) were prepared from the blocks using a trephine (Figure 2II). These cylinders were subsequently positioned within the Micro-CT equipment's sample holder.

SEM analysis was performed without prior sample preparation, as the microscope operates under low-vacuum conditions. Samples of $05 \times 10 \times 10$ mm blocks were affixed to carbon tape and placed on the equipment stage for image acquisition.

For porosimetry analysis, five $5 \times 10 \times 10$ mm blocks were subjected to thermal treatment at $200\text{ }^{\circ}\text{C}$ in a stove for 2 h under vacuum conditions to remove moisture and then disposed of onto porosimeter equipment support to perform the evaluation.

2.2. SEM

The scanning electron microscopy (SEM) analysis was conducted in accordance with the ASTM E1829-02 standard guide for specimen handling prior to surface analysis. A field emission scanning electron microscope (FE-SEM, model FEI Magellan 400L[®], Thermo Fisher Scientific, Waltham, MA, USA) was used for the analysis. The imaging was performed at an accelerating voltage of 5 kV, utilizing the secondary electron (SE) mode for detailed surface morphology characterization.

2.3. Micro-CT

Three samples (blocks I to III) were analyzed using a SkyScan 1272 micro-computed tomography scanner (Bruker MicroCT, Aartselaar, Belgium) to characterize the porosity and internal structure of the bone substitute. Image acquisition was performed with a pixel resolution of $6\text{ }\mu\text{m}$, an accelerating voltage of 80 kV voltage, and a current of $125\text{ }\mu\text{A}$, using a 1 mm aluminum filter to enhance image quality. Scans were conducted with a rotation step of 0.4° , an exposure time of 2500 ms per capture, and the application of flat-field and geometric corrections to standardize intensity and minimize distortions. Image reconstruction was performed using NRecon software 2.2.0.6 (Bruker MicroCT, Aartselaar, Belgium), with Gaussian kernel smoothing, ring artifact correction set to intensity 8, and beam hardening correction at 40% to reduce artifacts and enhance visual quality. The three-dimensional reconstruction facilitated the identification and quantification of open and closed pores, which were classified and analyzed following the ISO 15901-1:2016 standard for porosity characterization. Porosity quantification was conducted using the CTAnalyzer software 1.14.4 (Bruker MicroCT, Aartselaar, Belgium), where regions of interest (ROI) were defined, and adaptive threshold segmentation was applied to differentiate the porous and solid phases of the sample. The analyzed parameters included total pore volume ($\text{Po.V}(\text{tot})$), open porosity ($\text{Po}(\text{op})$), and open pore volume ($\text{Po.V}(\text{op})$). A three-dimensional visualization of the porous structure was generated using CTVox software 2.0 (Bruker MicroCT, Aartselaar, Belgium).

2.4. Porosimetry

The porosity and pore size distribution were characterized using mercury intrusion porosimetry, performed with the AutoPore IV System (Micromeritics Instrument Corporation[®], Norcross, GA, USA) in accordance with ISO 15901-1:2005. The volume of mercury introduced into the sample was regulated by the applied hydrostatic pressure, and the pore diameter was determined using the Washburn equation ($d_p = -4 \cdot \gamma \cdot \cos\theta / P$). Measurements were conducted in a stepwise manner, with incremental readings recorded at each applied pressure level while maintaining the sample in its original condition.

3. Results

3.1. SEM

SEM images at various magnifications revealed the surface morphology of the Nanosynt Block. At low magnifications (Figure 3A–D), a uniform distribution of pores was observed, while at and high magnifications (Figure 3E–H), details of pore morphology and interconnection were visualized.

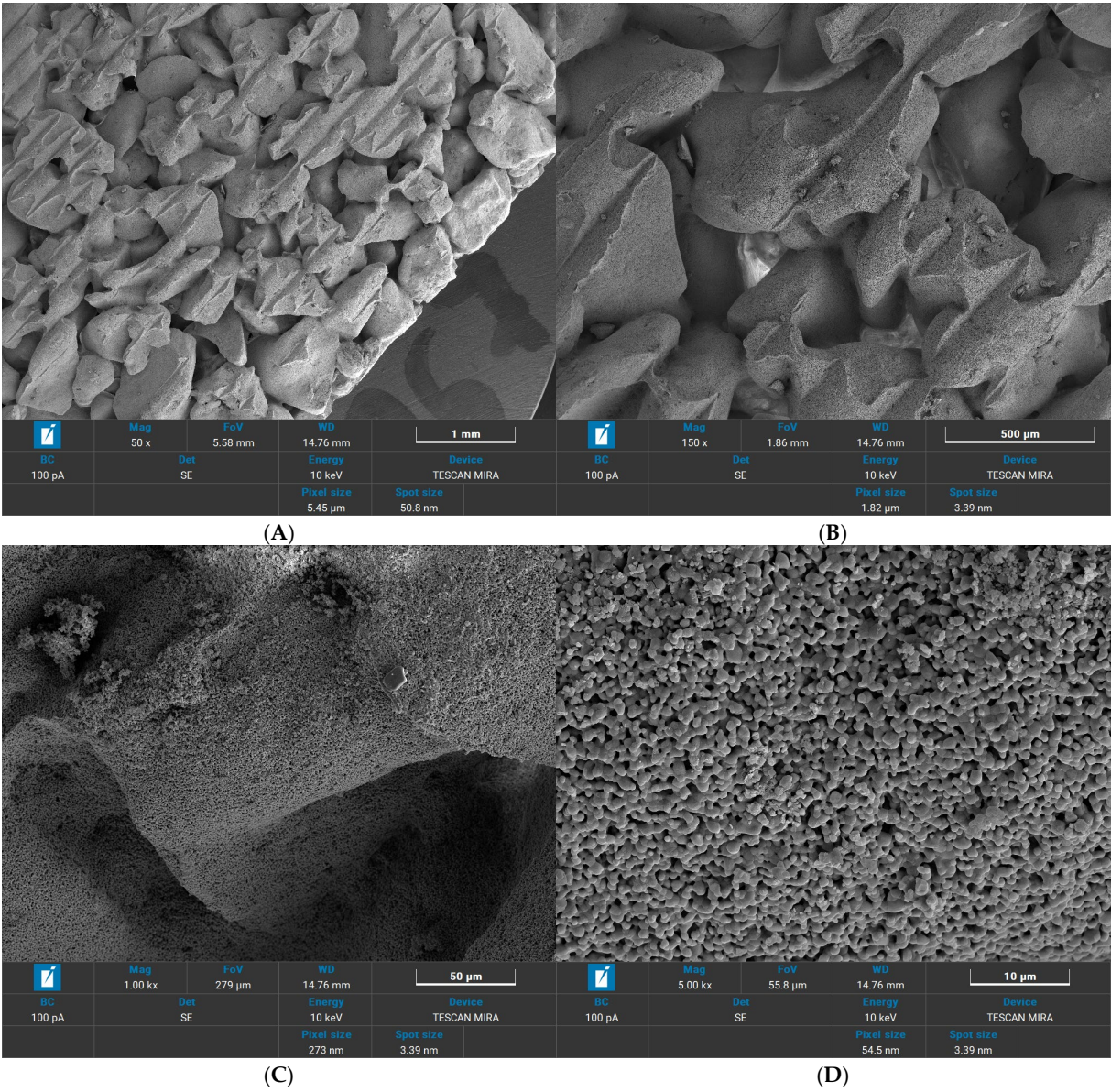


Figure 3. Cont.

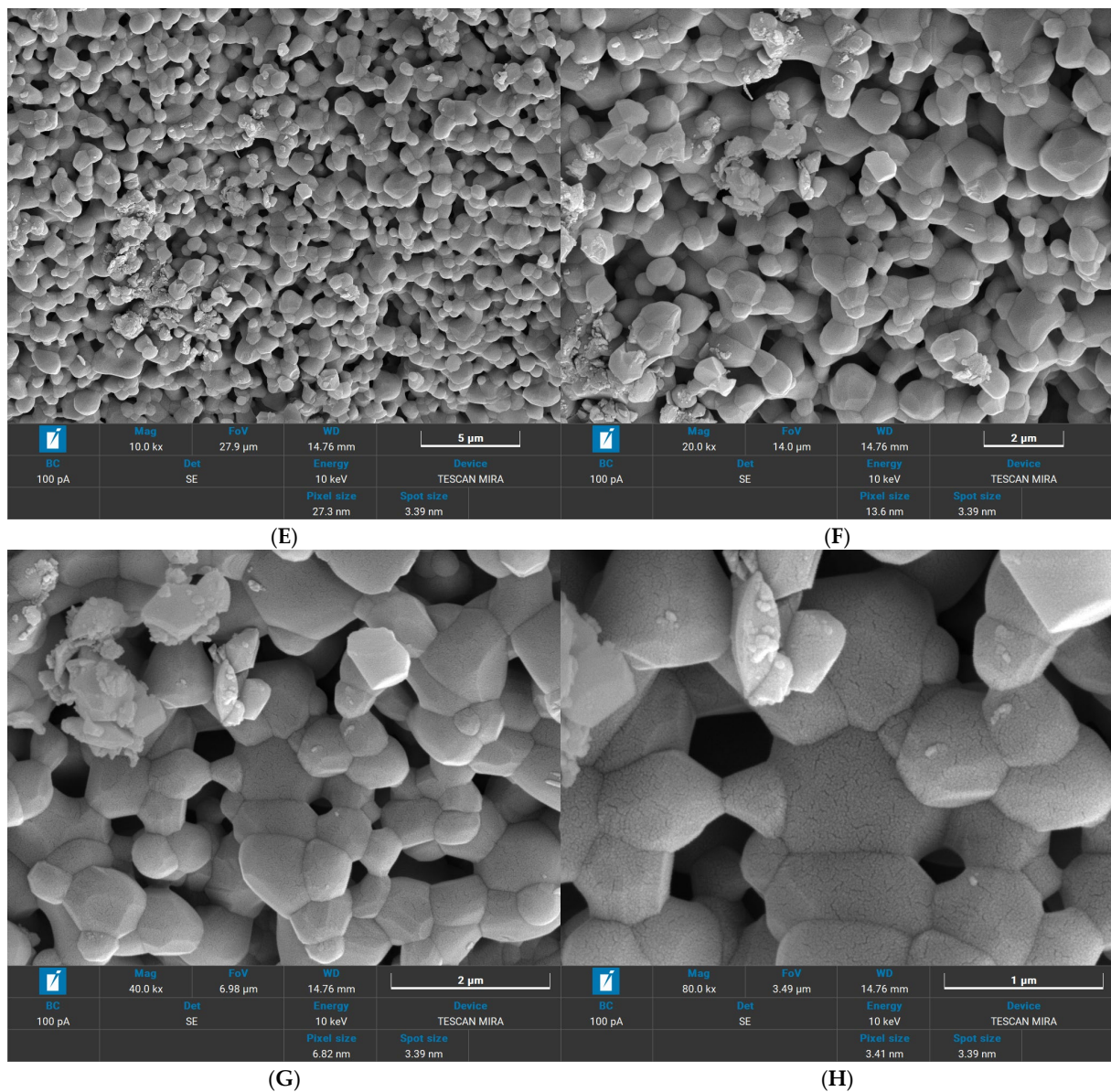


Figure 3. Magnified details of pore interconnections and morphology by SEM. (A): 50 $\times$, (B): 150 $\times$, (C): 1000 $\times$, (D): 5000 $\times$. (E): 10,000 $\times$, (F): 20,000 $\times$, (G): 40,000 $\times$, (H): 80,000 $\times$.

3.2. Micro-CT

Block I exhibited a total porosity of 77.08%, while Block II showed a porosity of 73.27% and Block III, 75.53%, indicating a predominantly porous internal structure of the Nanosynt Block (Table 1 and Figure 4).

Table 1. Parameters of Micro-CT analysis.

Block	Po.V (tot)	Po (op)	Po.V (op)
I	27.70	77.08	27.70
II	26.41	73.27	26.41
III	27.27	75.53	27.27

Po.V (tot): total pore volume, in percentage (%); Po (op): open porosity, in percentage (%); Po.V (op): open pore volume, in cubic millimeters (mm³).

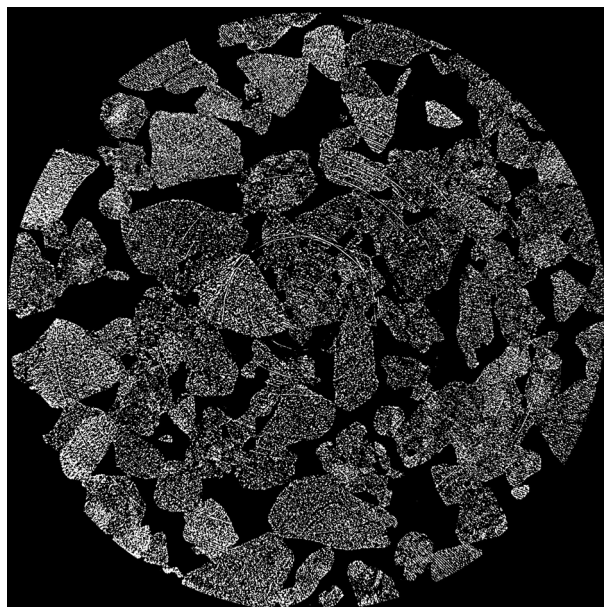


Figure 4. Three-dimensional reconstruction of Micro-CT analysis.

3.3. Porosimetry

Porosimetry analysis revealed a total porosity of 94.9%, indicating a well-distributed and interconnected pore network within the material. The median pore diameter was approximately 799 nm (Figure 5).

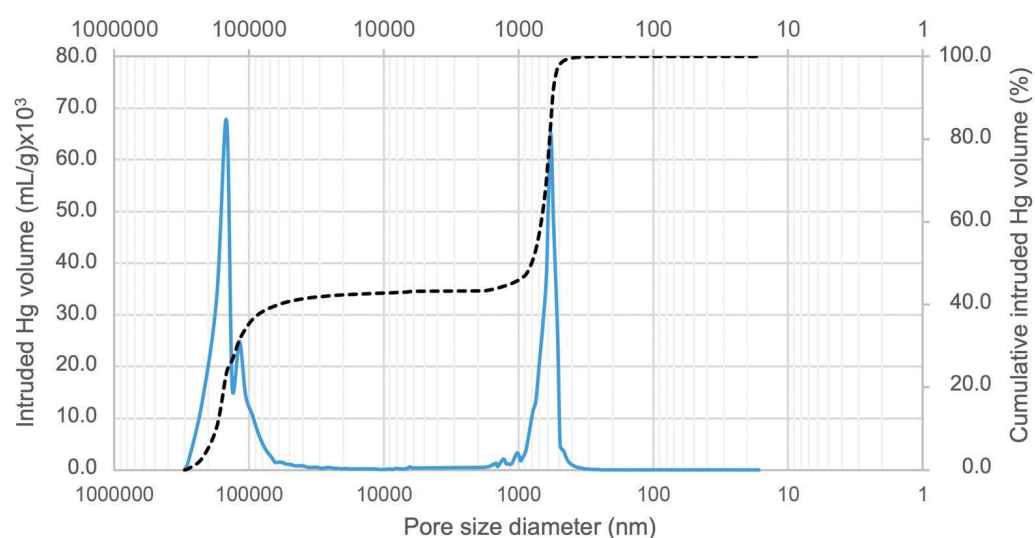


Figure 5. Mercure intrusion curve. The graph shows the volume of mercury intruded ($\text{mL/g} \times 10^3$) as a function of pore diameter (nm), representing the pore size distribution. The dashed line indicates the cumulative volume of mercury intrusion (%) relative to pore diameter.

4. Discussion

Bone substitute blocks are widely recognized as essential biomaterials for large-scale bone reconstruction due to their ability to provide three-dimensional support, mechanical stability, and volumetric maintenance [1–3]. In this study, the Nanosynt Block exhibited an average total porosity of 94.9%, with open porosity ranging from 73.27% to 77.08% and a median pore diameter of 799 nm, as determined by porosimetry. These structural characteristics facilitate cellular infiltration, nutrient diffusion, and initial adhesion of osteogenic cells, which are critical factors for the performance of bone substitutes [4,11,20]. These

properties are consistent with the findings of Pires et al. (2020) [5], who reported that hydroxyapatite (HA) and β -tricalcium phosphate (β -TCP) blocks support bone regeneration in critical-sized defects due to their interconnected and porous architecture.

Previous studies have investigated various types of biphasic HA/ β -TCP blocks; however, they have primarily focused on specific aspects, such as the proportion of components [15], the *in vivo* performance in relation to the material structure [14,18], or the application of bioactive coatings [16]. Nevertheless, a comprehensive analysis of porosity or internal connectivity remains lacking. The absence of preclinical studies in the literature that specifically characterize the structural properties of materials such as the Nanosynt Block limits direct comparisons with the findings of this study.

Micro-CT analysis in this study demonstrated dimensional uniformity among the tested blocks, with comparable total pore volumes (~27%), reinforcing their structural stability. This stability is critical for clinical applications requiring volumetric maintenance, particularly in the reconstruction of large bone defects [2,3]. Sawada et al. (2018) [6] reported that structured hydroxyapatite blocks preserve their shape and volume during bone regeneration, thereby reducing the risk of collapse in horizontal defects. This characteristic is especially relevant in cases where particulate materials may be prone to dispersion, a limitation that structured blocks effectively mitigate [6,21]. These findings emphasize the importance of manufacturing consistency in ensuring uniform structural properties, as even minor variations in porosity and pore volume can influence both the mechanical behavior and biological performance of the material [20,22].

The morphological analysis conducted via SEM complemented the quantitative data, revealing a surface with well-distributed pores and significant internal connectivity. This connectivity is crucial for facilitating fluid infiltration and enhancing interactions between the material and bone tissue [22]. Yazdanpanah et al. (2023) [23] demonstrated that high porosity improves material permeability, potentially enhancing nutrient and gas exchange within the bone microenvironment. Although macroporosity exceeding 100 μm is generally considered optimal for promoting cellular infiltration, it does not appear to have a direct correlation with the degree of osteoconduction [13,24]. Notably, while increased porosity enhances biological interactions, it also significantly affects the mechanical strength of the block, which tends to decrease as porosity increases, thereby posing challenges to handling and clinical application.

Montero et al. (2023) [24] reported that HA and β -TCP blocks with pore sizes ranging from 300 to 500 μm effectively promoted bone regeneration by facilitating angiogenesis, a process that requires larger pores to support blood vessel formation. In contrast, the Nanosynt Block exhibited microporosity, with a median diameter of 799 nm, which limits its direct capacity to promote angiogenesis. However, smaller pores offer advantages in other aspects, such as increasing surface area, thereby enhancing cell adhesion and fluid infiltration, both essential for the initial stages of bone regeneration [21]. Hassanajili et al. (2019) [25] investigated scaffolds composed of PLA/PCL/HA (70/30–35%), which exhibited a porosity of 77% and an average pore size of 160 μm , characteristics favorable for osteoconduction and bone regeneration in tissue engineering models. Thus, although the Nanosynt Block does not possess the optimal pore size for angiogenesis, as indicated by Montero et al. (2023) [24], its structural properties, particularly its high porosity and interconnectivity, remain sufficient to support early bone formation by promoting cell adhesion and differentiation, ensuring interaction between the biomaterial and bone tissue, and providing functional support in various clinical applications.

Although this study is based on laboratory analyses, its findings provide a promising foundation for future *in vivo* investigations. The high porosity, internal connectivity, and volumetric stability observed in the Nanosynt Block suggest its considerable potential

for the facilitation of early bone regeneration and supporting dental implant-associated rehabilitations.

5. Conclusions

The findings of this study, derived from laboratory-based analyses, highlight the Nanosynt Block as a promising material for bone regeneration applications. The combined use of Micro-CT, porosimetry, and SEM allowed for a comprehensive characterization, revealing key features such as high porosity, internal connectivity, and structural stability—characteristics that fulfill the biological requirements for mechanical support and initial bone formation. Although laboratory analyses have inherent limitations and may not fully replicate the biological environment, the data presented provide a strong foundation for future preclinical investigations.

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