TECHNICAL PROFILE

LINE

FGM

Nanosynt

BONE GRAFT



FGM DENTAL GROUP

CONTENT

1 . PRESENTATION 3

2 . BASIC COMPOSITION 3

3 . MAIN CHARACTERISTICS 3

4 . PRODUCT PRESENTATION FORMS 4

5 . PHYSICAL-CHEMICAL PROPERTIES 5

5.1 Characterization of biphasic calcium phosphate by x-ray diffraction 5

5.2 Porosity, specific density, and surface area analyzes 7

5.3 SEM characterization 8

5.4 Topographic Characterization 9

5.5 Controlled dissolution 10

5.6 Biocompatibility analyzes 11

6 . MECHANISM OF ACTION 11

7 . PRE-CLINICAL STUDY IN RABBITS 12

8 . CLINICAL EVALUATION IN HUMANS 16

9 . SUPPORT REFERENCES 21

1 . PRESENTATION

Nanosynt is a synthetic bone substitute material based on biphasic calcium phosphate (60% hydroxyapatite and 40% β-tricalcium phosphate, nominal values), to be used in filling bone defects, aiming for functional reconstruction and achieving natural esthetics in bone regeneration. It is a material available in the form of granules (particles of 200 to 500 µm, 500 to 1000 µm, 1000 to 2000 µm) and blocks (sizes 10 x 10 x 5 mm, 10 x 10 x 10 mm, and 20 x 20 x 8 mm, (length, width, and height), with a medical-grade purity (minimum purity of 95%), composed of nanostructured agglomerates containing interconnected pores. It has excellent osteoconductive action, being reabsorbed and replaced by living bone tissue during bone remodeling. In the composition of Nanosynt, whether in granules or blocks, hydroxyapatite, which has a lower resorption rate than β-tricalcium phosphate, helps prevent excessive resorption of the material, thus preserving the mechanical and dimensional stability of the grafted volume, contributing to both the esthetic and functional outcomes. Meanwhile, β-tricalcium phosphate stimulates the biological response during the early stages of bone formation creating an environment conducive to being replaced by natural bone (FGM DENTAL GROUP, 2020; FGM DENTAL GROUP, 2024).

When in contact with bone, Nanosynt acts as a support and conductor for bone tissue regeneration, allowing its growth within the structure of interconnected pores, which:

I). Enables the transport of nutrients to the bone tissue, accelerating its formation rate;
II). Allows the connection of forming and/or newly formed bone tissue with the surrounding bone tissue;
III). Prevents the excessive migration of connective tissue into the newly regenerated bone tissue.

2 . BASIC COMPOSITION

Active ingredients: Calcium phosphate in the form of hydroxyapatite (60%), calcium phosphate in the form of β-tricalcium phosphate (40%).

3 . MAIN CHARACTERISTICS

The **Nanosynt** materials, **in Granule and Block form**, are composed of agglomerates with porosity ranging from 80 to 95%. This morphological feature positively modulates the biological response of bone formation, influencing qualitative, quantitative, and chronological aspects. The optimized porosity promotes vascularization, osteoblast migration and bone deposition, as high porosity combined with a minimal amount of material, provides adequate space for the formation of new vital bone tissue. From a biochemical standpoint, this structure composed of micro and nanopores allows better permeability of the forming bone tissue, due to the presence of specific chemical groups at the interfaces of the biomaterial (FREITAS et al., 2014).

Additionally, besides stimulating greater bone formation, the differentiated (nanostructured) morphology of the Nanosynt family modulates the material's resorption rate, providing adequate amounts throughout the entire repair process.

Other advantages of **Nanosynt**:

- 100% synthetic, contributing to its biological safety (eliminates any risk of contamination);
- Gradually resorbed to preserve the framework (adequate composition of hydroxyapatite and β-tricalcium phosphate);
- Available in granules or blocks, both featuring the same structure (microparticles composed of nanostructured agglomerates), facilitating bonding and interconnection of the material at the recipient site and increasing mechanical stability between structures;
- High surface area and permeability (pore distribution + irregular granules);
- Low density and high porosity (less resorption and more space for new bone tissue);
- Safety and predictability in guiding bone growth (reproducible quality);
- Biocompatible (no toxicity and no allergic potential);
- Excellent wettability and handling: easy and safe mixing with sterile saline solutions, blood, or autogenous bone (high hydrophilicity, rapid fluid absorption), enabling particle agglutination and facilitating their application, in addition to increasing handling resistance and customization of the product in its block form;
- Fractionated and categorized presentation to enable simple and practical application in different surgical sites, resulting in low waste and better adaptation of the biomaterial;
- Radiopaque (for monitoring with radiographic and tomographic images during bone neoformation).

4 . PRODUCT PRESENTATION FORMS

Nanosynt Granules

Presentation in 02 or 04 ampoules of Nanosynt containing 0.27 cc or 0.53 cc, with the 0.53 cc option restricted to granulation between 1000 to 2000 µm. The product presents granule diameters of 200 to 500 µm (35 to 70 mesh) (Image 1A), 500 to 1000 µm (18 to 35 mesh)(Image 1B), or 1000 to 2000 µm (10 to 18 mesh)(Image 1C). Sterilized by gamma radiation.



Image 1 - Illustrates the available dimensions for commercialization of Nanosynt in Granule; (A) 200 to 500 µm; (B) 500 to 1000 µm; (C) 1000 to 2000 µm.
Source - Internal data, FGM Dental Products

Nanosynt Hospital Granules

Presentation in 02 or 04 ampoules of Nanosynt containing 3.2 cc or 6.4 cc per ampoule, with granule diameters of 1000 to 2000 µm (10 to 18 mesh)(Image 1C). Sterilized by gamma radiation.

Nanosynt Block

Packaging in a blister containing 01 unit. Dimensions: 10 x 10 x 5 mm, 10 x 10 x 10 mm, or 20 x 20 x 8 mm (Image 2A, 2B, and 2C). Sterilized by gamma radiation.

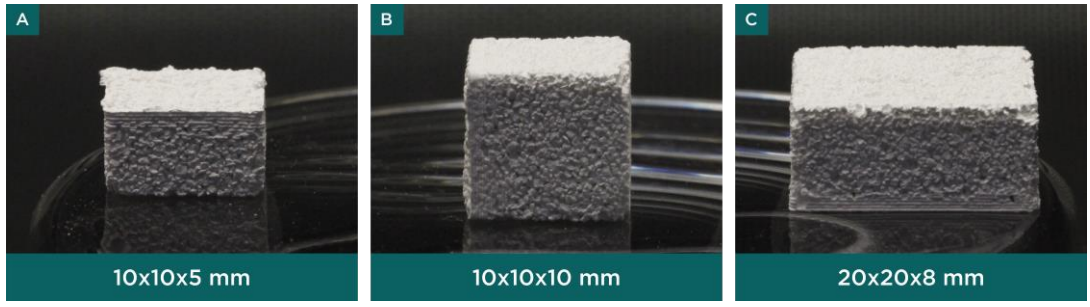
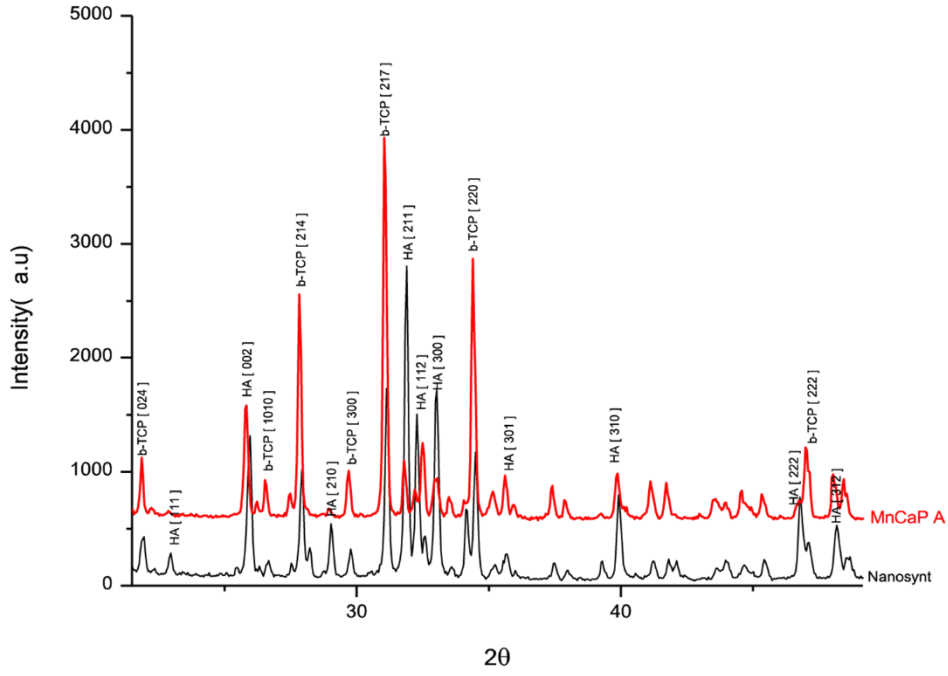


Image 2 - Available versions: (A) 10x10x5 mm; (B) 10x10x10 mm; (C) 20x20x8 mm.
Source - Internal data, FGM Dental Products

5 . PHYSICAL-CHEMICAL PROPERTIES

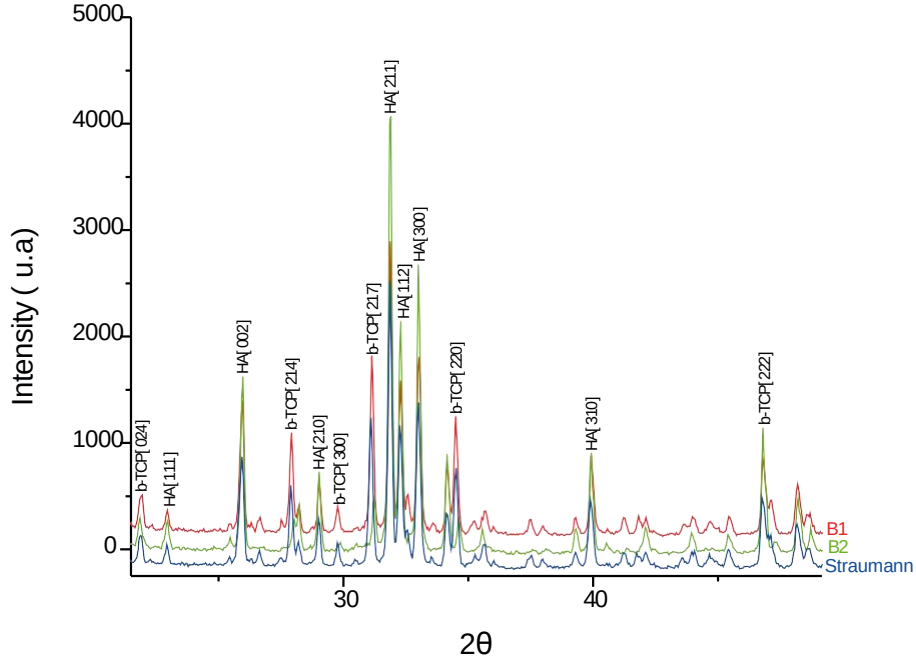
5.1 Characterization of biphasic calcium phosphate by X-ray diffraction

A test of the mineral phases of Nanosynt was performed, observing the phases of hydroxyapatite and β-tricalcium phosphate. These data were examined by X-ray diffraction. A Zeiss HZG4 diffractometer, operating at 30 kV and 15 mA, with CuKα radiation (λ = 1.542 Å), showed the XRD patterns collected in the 2θ range of 10 ◦ -100 ◦ . The samples were placed on the slide in powder form for subsequent analyzis in the device.
The typical patterns generated, according to PCPDFWIN 09.0432, indicated increasing and decreasing β-TCP peaks in the first period, which provides the rapid dissolution of the biomaterial in biological environments. When measured, hydroxyapatite showed fluctuation in the inflammatory peak, but after that it remained constant over time (Graph 1)(Nascimento et al., 2021).



Graph 1. X-ray diffraction (XRD) pattern of MnCaP and Nanosynt® samples, with a typical bifasic calcium phosphate pattern, predominantly with peaks of hydroxyapatite (HA) and beta-tricalcium phosphate (-TCP). MnCaP, red line; and Nanosynt®, black line.
Source: (NASCIMENTO et al., 2021b)

Another study by UZEDA et al., (2017) used the same methodology, comparing the release of minerals in group B1 (Nanosynt®) and BC (similar product). It was observed that there was partial decomposition of hydroxyapatite into β-tricalcium phosphate (β-TCP), which characterizes the production of a bifasic material with similar hydroxyapatite peaks (Graph 2).



Graph 2 — X-ray diffractogram of Nanosynt.
Source - (UZEDA et al., 2017)

A curve was created with the known percentage of hydroxyapatite and β-TCP, and the area of the peaks in the respective phases was calculated. Then, the same procedure was performed on the Nanosynt sample. The results showed that Nanosynt contains 60% hydroxyapatite and 40% β-TCP (nominal values), in accordance with the standards established by ISO 10993-18:2005 (INTERNATIONAL ORGANIZATION FOR STANDARDIZATION (ISO), 2018).

5.2 Porosity, specific density, and surface area analyzes.

The porosity of Nanosynt was evaluated using Helium pycnometry. The porosity analyzis of Nanosynt Block was performed using the Mercury intrusion method. The specific density of the products was also evaluated. The data are shown in Table 1 (INTERNATIONAL ORGANIZATION FOR STANDARDIZATION (ISO), 2012).

Table 1- Physical parameters of the biomaterials: Nanosynt, Nanosynt Hospital, and Nanosynt Block.
Source - Internal data, FGM Dental Products

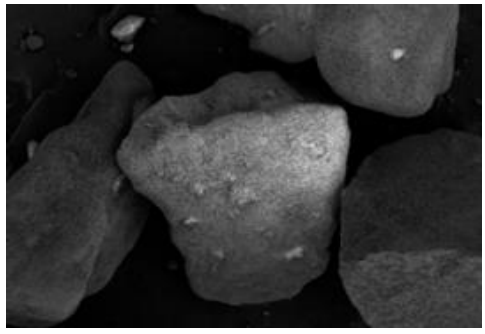
Product	Density (g/cc)	Porosity (%)	Surface Area (m^2/g)
Nanosynt	3,18	~80	1,9
Nanosynt Hospital	3,10	~80	1,9
Nanosynt Block	3,10	~95	8,7

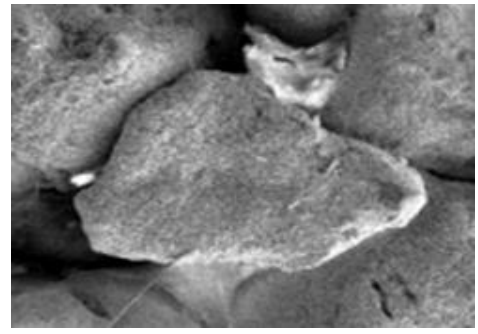
The optimized porosity of Nanosynt, Nanosynt Hospital, and Nanosynt Block promotes vascularization, osteoblast migration, and bone deposition. The low density of Nanosynt, combined with this high porosity, results in less material being resorbed during the bone repair process, while also leaving space for the formation of new vital bone. The high surface area of Nanosynt, Nanosynt Hospital, and Nanosynt Block promotes its wettability, which, combined with its nanostructured morphology, nano-textured surface and interconnected pores, favorably modulates its solubility in biological environments, contributing to an excellent biological response in bone formation (Tovar et al., 2014).

5.3 SEM characterization

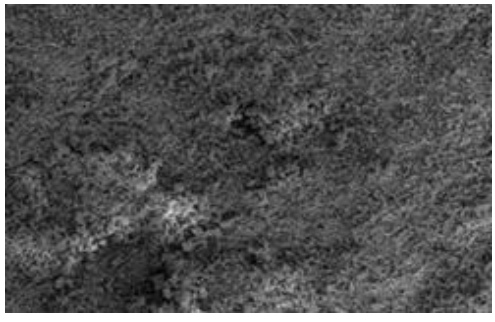
The morphological characterization of Nanosynt Granules (Images 3A, 3B, and 3C) and Block (Images 3D, 3E, and 3F) was performed using scanning electron microscopy (SEM) analyzis. In addition to other characteristics, the surface texture and its porosity (nano and micrometric) were evaluated, following the guidelines of the ("Biological evaluation of medical devices", 2006). Both were found to be composed of microparticulate agglomerates of nanostructured compounds, containing interconnected micro and nanostructured pores, exhibiting an identical structural appearance.

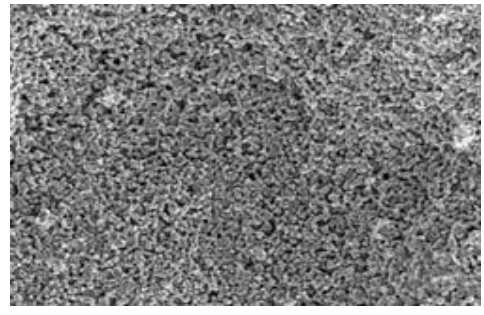
Granules **Block**



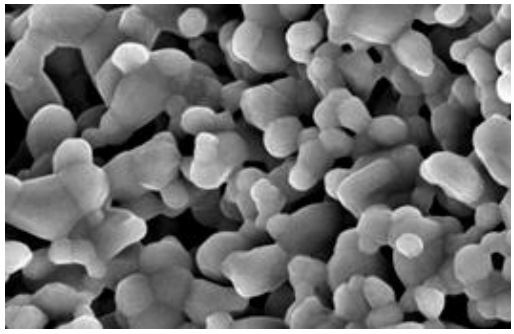


Granules **Image 3 (A and D)** **Block**





Granules **Image 3 (B and E)** **Block**



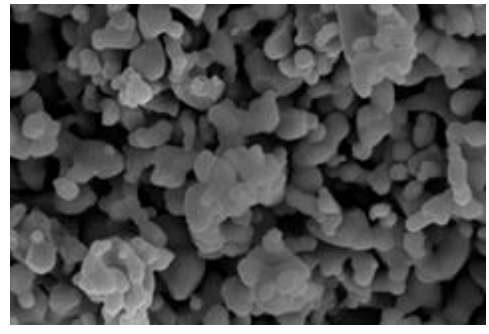


Image 3 (C and F)

Image 3 — Morphological pattern of Nanosynt Granules (Images 3A, 3B, and 3C) and Block (Images 3D, 3E, and 3F). Images obtained by scanning electron microscopy.
Source - Internal data, FGM Dental Products

5.4 Topographic Characterization

The surface of the bifasic materials is composed of interconnected nanostructured particles, interspersed with micro-sized pores (Image 4C). When comparing Nanosynt with a xenograft (DE OLIVEIRA JUNIOR et al., 2021), it was concluded that the contact surface was larger in the xenograft. However, the microporosity and coalescence between particles were considerably smaller than in Nanosynt, as explored in Table 2.

Table 2 - Mean (standard deviation), median (minimum and maximum values) of the total pore volume (cm3/g) of the materials studied (n=3)
Source - Adapted from Oliveira Junior et al.(2021)

Total Pore Volume (cm^3/g)		
Material	Mean (standard deviation)	Median (minimum and maximum values)
Nanosynt (G1 and G2)	7.72 (1.47)	7.50 (6.38-9.29)
Xenograft (G3)	0.48 (0.08)	0.44 (0.41-0.57)
p-value	p = 0.0134	

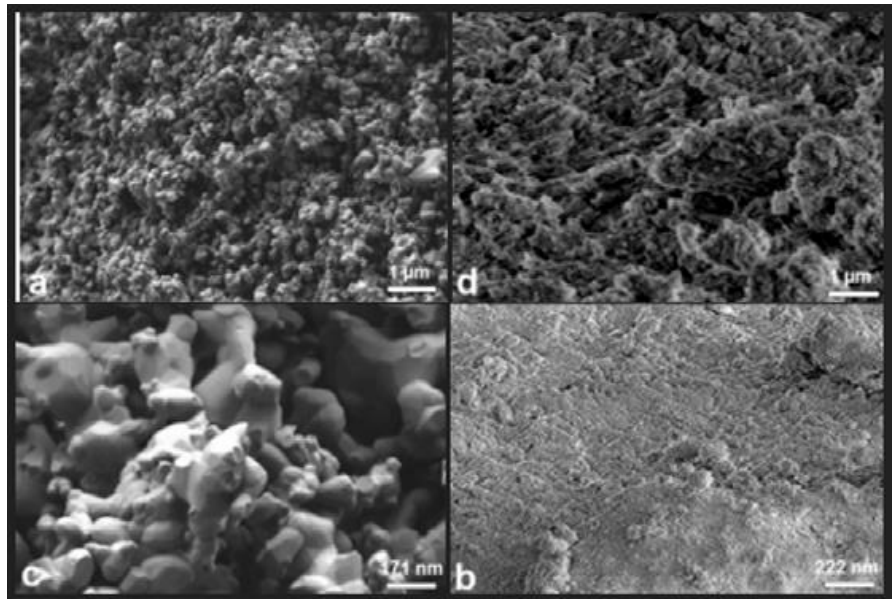


Image 4 - Representative images of scanning electron microscopy of the surface structures of the bifasic materials Nanosynt (a,c) and Xenograft (b,d).
Source - (DE OLIVEIRA JUNIOR et al., 2021)

The results of the study (DE OLIVEIRA JUNIOR et al., 2021) demonstrate that the bifasic ceramics exhibit a greater total pore volume, which allows their incorporation into the adjacent tissues through processes involving bone growth around and within the bifasic calcium phosphate structure.
Associated with another histological study and through visualization in SEM (SILVA et al., 2020), it was possible to observe the topography of the pores and the surface texture of Nanosynt, as well as its relationship with cell recruitment and anchorage. In the study, it was possible to observe cells interacting with the material's surface three months after regeneration, with an odontoblast noted adhering to the textured surface of the granule, as shown in Image 5.

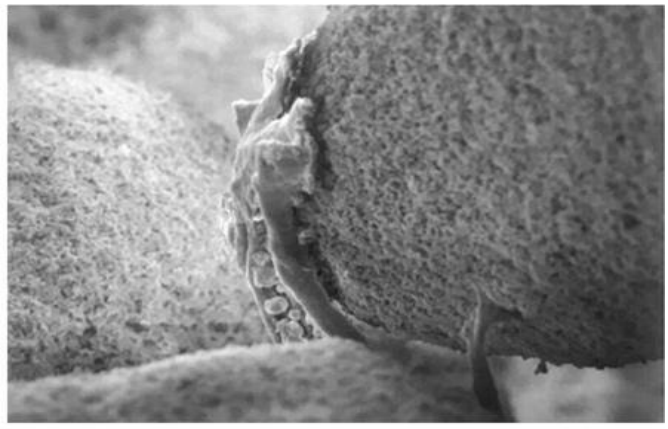


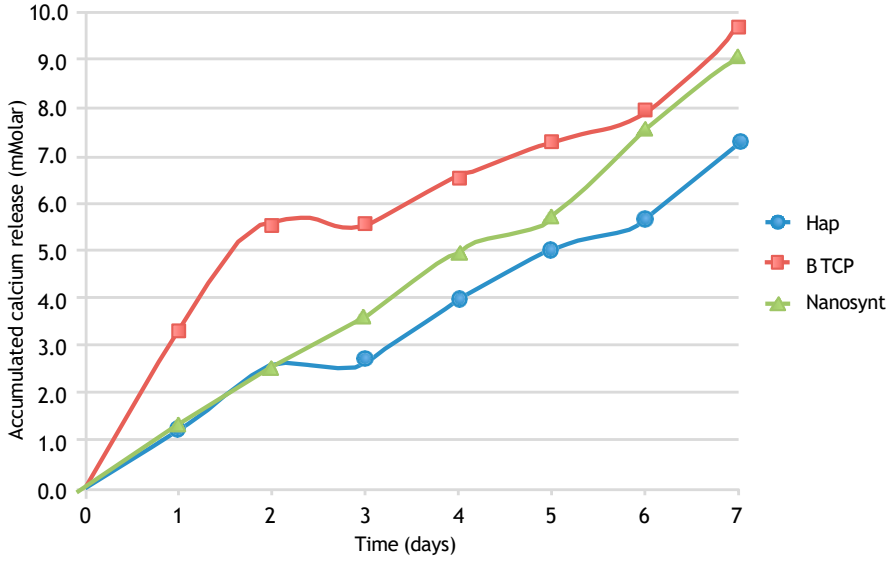
Image 5 - SEM-Surface/cell details (8000x).
Source - (COUTINHO, 2017)

Thus, it is highlighted the importance of having a surface with interconnected nanostructured particles, interspersed with micro-sized pores, which leads to improved cellular activation, adhesion, and migration (COUTINHO, 2017).

5.5 Controlled dissolution

To determine the short-term solubility pattern of bifasic calcium phosphate, calcium concentration (accumulated release) was assessed over a period of 7 days (Graph 3).

Nanosynt is gradually reabsorbed. Hydroxyapatite, which has a slower dissolution rate than β-tricalcium phosphate, acts by preventing excessive material resorption, thus preserving the mechanical and dimensional stability of the grafted volume and contributing to the preservation of the framework. Meanwhile, β-tricalcium phosphate stimulates the biological response in the early stages of bone formation, being replaced more rapidly by natural bone (TOVAR et al., 2014).



Graph 3 — Accumulated calcium release curve obtained for Nanosynt.
Source - (TOVAR et al, 2014b)

5.6 Biocompatibility analyzes

Cytotoxicity analyzes of Nanosynt samples (60% hydroxyapatite and 40% β-tricalcium phosphate, nominal values) were conducted at the Adolfo Lutz Institute, São Paulo, SP. The analyzes were performed in accordance with the INTERNATIONAL ORGANIZATION FOR STANDARDIZATION (ISO), 2018; "Test Method for Agar Diffusion Cell Culture Screening for Cytotoxicity", 2006) Nanosynt showed no toxic effect, **indicating its biocompatibility**.

6. MECHANISM OF ACTION

Since hydroxyapatite [$Ca^{10}(PO4)^6(OH)^2$] is the main constituent of the inorganic phase of bone tissue (about 65% by mass), products with similar chemical and structural characteristics, capable of providing calcium and phosphate ions at the appropriate concentrations and release rates, can repair or even promote bone tissue growth. The lower solubility of hydroxyapatite is compensated by the higher solubility of β-tricalcium phosphate [$Ca3(PO4)^2$], favoring new bone formation. Thus, during the early stages of the bone remodeling process, hydroxyapatite acts by preserving the volume, while β-tricalcium phosphate acts by releasing the calcium and phosphate ions necessary to drive bone tissue formation (GHANAATI et al., 2012).

Furthermore, regardless of the form of commercialization, Nanosynt has the advantage of possessing a nanostructured morphology, promoting rapid bone structure growth. The fact that the compounds are nanostructured facilitates the material's absorption and consequently increases the speed of the biological processes in which it participates. In addition, the great similarity between the composition of the biphasic calcium phosphate and that of the mineral bone tissue in the human body makes the biomaterial biocompatible, enabling the formation of bone tissue with characteristics similar to the bone matrix of the receptor bed.

Bone growth is dependent on the proximity of blood vessels, which are responsible for nourishing it. The high affinity of Nanosynt products for water promotes neovascularization, contributing to their osteoconductive action. This characteristic, along with its physiological pH, assists in the early stages of the regenerative process. Moreover, the product, obtained through processes free of chemical residues and capable of sterilization, features porosity and high surface area, characteristics that promote the reorganization of calcium and phosphate ions into hydroxyapatite by the body. This reorganization enables the reconstitution of bone tissue. Its 100% synthetic composition ensures biological safety.

Thus, when placed in contact with bone, the biphasic calcium phosphate acts as a support for bone tissue regeneration, allowing its growth within the structure of interconnected pores, which:

I) Accelerates Bone Formation: It facilitates the transport of essential nutrients to the bone tissue, stimulating its growth and development;

II) Integrates with Native Bone: It allows for direct and efficient connection between the new bone tissue and the existing bone, promoting faster and more complete repair;

III) Prevents Encapsulation: Prevents the formation of a connective tissue layer that could isolate the new bone and hinder its vascularization and integration;

IV) Absorbs and Remodels: It is gradually reabsorbed by the body and replaced by vital bone tissue, allowing for the natural remodeling of the bone and adaptation to mechanical forces.

7. PRE-CLINICAL STUDY IN RABBITS

Preclinical studies in rabbits (males, New Zealand lineage) were conducted by (TOVAR et al., 2014b), with the aim of determining the quality and quantity of bone tissue during healing in defects created in rabbit calvarias, and comparing it to 02 other materials available on the market, considered "gold standard" in the literature.

In this study, 04 critical defects were created in the calvaria of each animal, each with a diameter of 08 mm (Images 6A and 6B), which were filled with the following bone substitute materials:

1. Nanosynt® (FGM);
2. Bio-Oss® (Geistlich, material based on bovine-derived hydroxyapatite);
3. BoneCeramic® (Straumann, synthetic material based on biphasic calcium phosphate: hydroxyapatite + β-tricalcium phosphate);
4. Positive control, the critical defects were filled with blood clot;

The results show that Nanosynt exhibited superior performance compared to the others, promoting a greater amount of bone formation, a characteristic observed even in the early post-treatment phases.

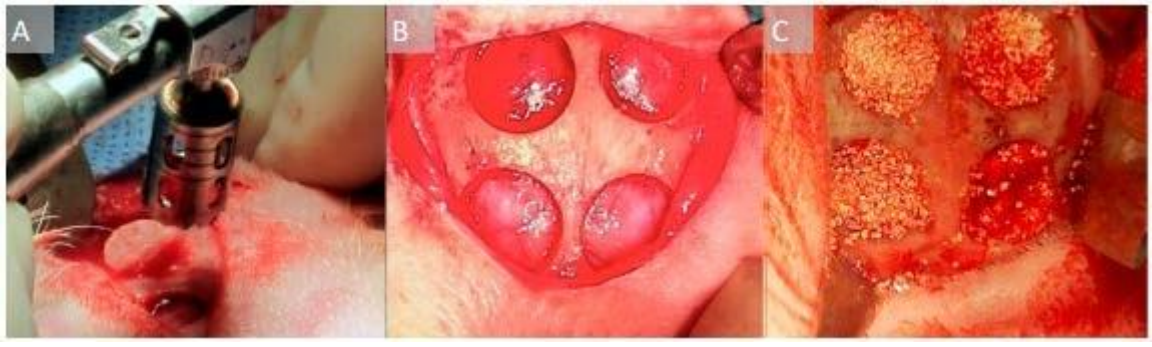
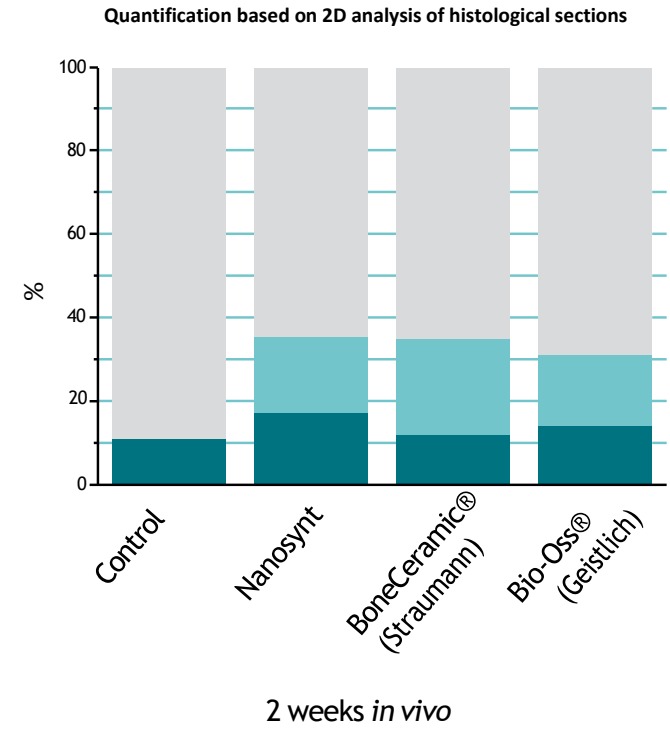
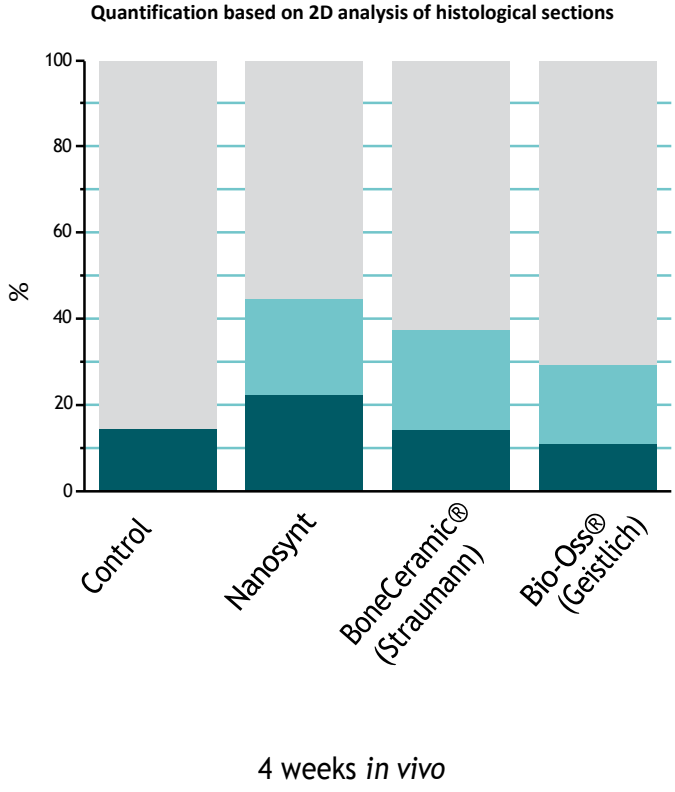


Image 6— Image of the rabbit calvaria prepared with surgical defects, which were filled with different bone substitution materials. (A) 8.0 mm trephine being used on the rabbit calvaria; (B) Bilateral 8.0 mm defects; (C) Surgical defects filled with bone graft material samples.
Source - (TOVAR et al., 2014b)

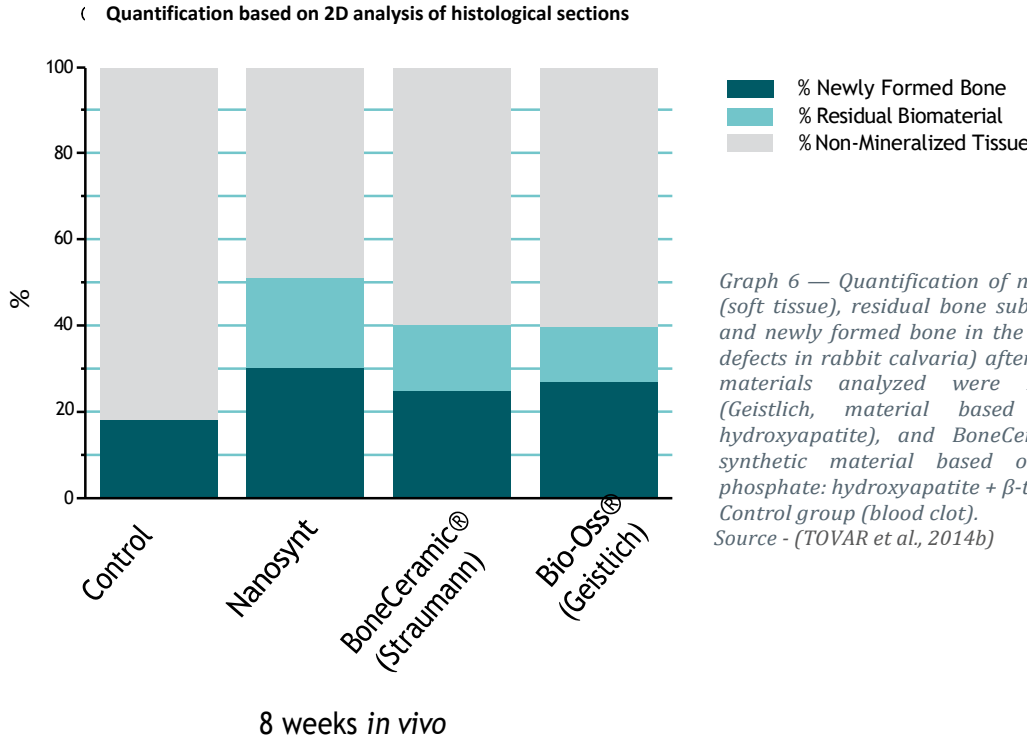
The biological response was evaluated after 2, 4, and 8 weeks in vivo.
Graphs 4, 5, and 6 show a summary of the quantification of histological sections for non-mineralized tissue (soft tissue), residual bone substitution biomaterial and newly formed bone in the repair areas for all the biomaterials analyzed after 2, 4, and 8 weeks in vivo, respectively. An increase in bone formation was observed over the course of the study. At all time points of analyzis, the clinical performance of Nanosynt was superior to that of the other commercial products, which are considered the gold standard in the global literature. When the sum of the percentages of bone and residual bone substitution material was evaluated, an increase was observed over the course of the study (2, 4, or 8 weeks in vivo), which is primarily attributed to the increase in the amount of newly formed bone (TOVAR et al., 2014).



Graph 4 — Quantification of non-mineralized tissue (soft tissue), residual bone substitution biomaterial, and newly formed bone in the repair areas (critical defects in rabbit calvaria) after 2 weeks in vivo. The materials analyzed were Nanosynt, Bio-Oss® (Geistlich, material based on bovine-derived hydroxyapatite), and BoneCeramic® (Straumann, synthetic material based on biphasic calcium phosphate: hydroxyapatite + β-tricalcium phosphate). Control group (blood clot).
Source - (TOVAR et al., 2014b)



Graph 5 — Quantification of non-mineralized tissue (soft tissue), residual bone substitution biomaterial, and newly formed bone in the repair areas (critical defects in rabbit calvaria) after 4 weeks in vivo. The materials analyzed were Nanosynt, Bio-Oss® (Geistlich, material based on bovine-derived hydroxyapatite), and BoneCeramic® (Straumann, synthetic material based on biphasic calcium phosphate: hydroxyapatite + β-tricalcium phosphate). Control group (blood clot).
Source - (TOVAR et al., 2014b)



Graph 6 — Quantification of non-mineralized tissue (soft tissue), residual bone substitution biomaterial, and newly formed bone in the repair areas (critical defects in rabbit calvaria) after 8 weeks in vivo. The materials analyzed were Nanosynt, Bio-Oss® (Geistlich, material based on bovine-derived hydroxyapatite), and BoneCeramic® (Straumann, synthetic material based on biphasic calcium phosphate: hydroxyapatite + β-tricalcium phosphate). Control group (blood clot).
Source - (TOVAR et al., 2014b)

"A better temporal healing pattern for the Nanosynt biomaterial was observed when compared to Bio-Oss® (Geistlich) and BoneCeramic® (Straumann). Throughout the investigated period, Nanosynt showed higher bone formation values within the defect and a greater capacity for preserving the defect, assessed by the sum of the amount of biomaterial within the defect and the amount of newly formed bone."(TOVAR et al., 2014b). Additional data related to the healing pattern (morphology and measurements of newly formed bone) of Nanosynt through the bone defect were also analyzed by light microscopy (Image 7).

The Nanosynt group showed a gradual increase in bone formation from the margins toward the center of the repair area, at different in vivo time points (2, 4, and 8 weeks). At 2 weeks the onset of bone formation between Nanosynt particles in the central region of the defect can be observed, along with the presence of a mild inflammatory infiltrate. Interestingly, a bone bridge connecting the edges of the defect along its entire length was already visible after 4 weeks in vivo, which was not observed for the competing biomaterials, demonstrating the superior clinical performance of Nanosynt. At 8 weeks in vivo, the statistical difference was not significant, although Nanosynt exhibited a higher amount of newly formed bone compared to the commercial products Bio-Oss® (Geistlich) and BoneCeramic® (Straumann). No inflammatory cell infiltrate was observed in the defect areas at 4 and 8 weeks in vivo.

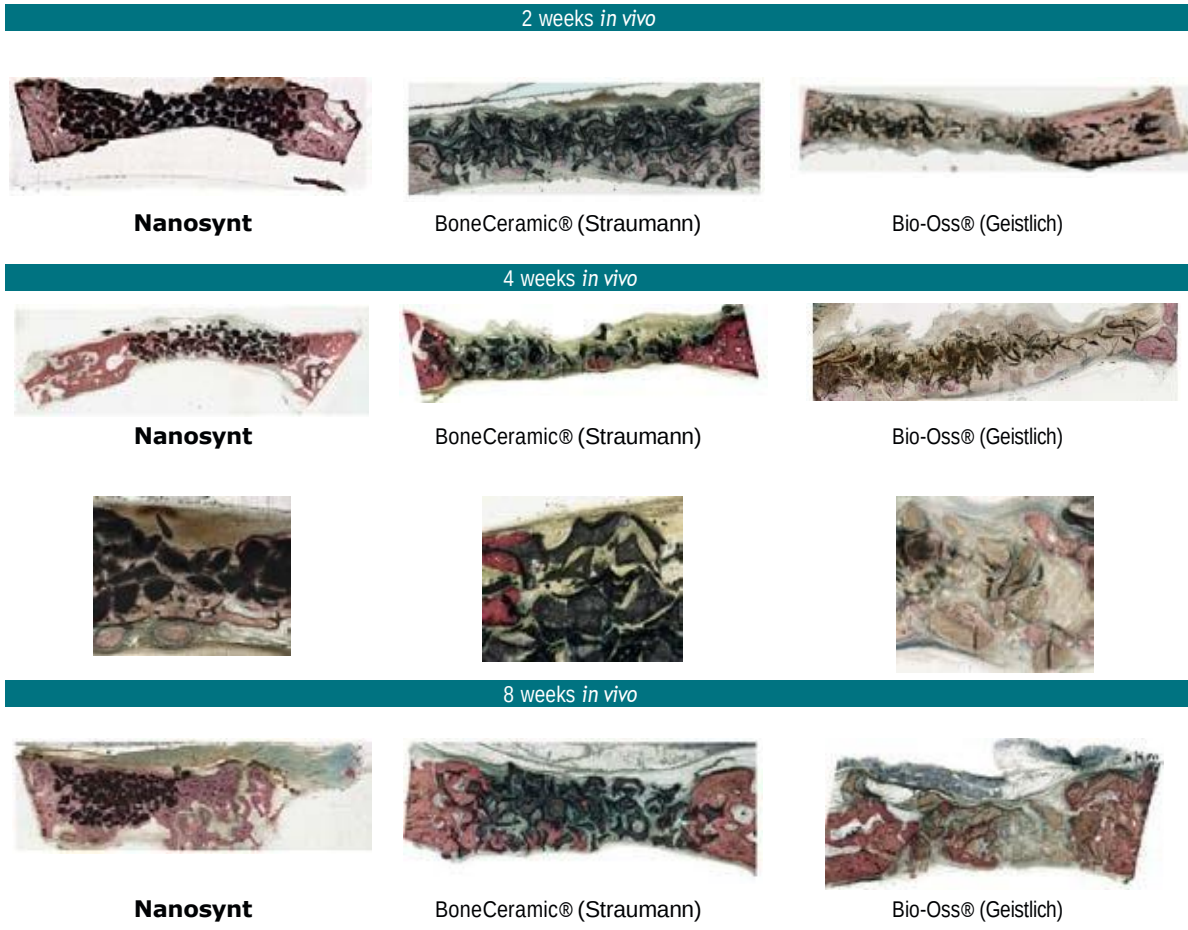
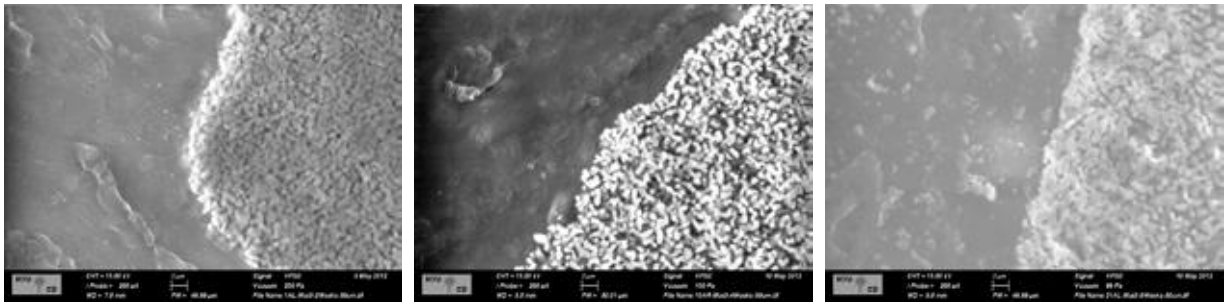


Image 7 — Image of the repair area after 2, 4, and 8 weeks in vivo. The images were obtained by light microscopy. The materials analyzed were Nanosynt, Bio-Oss® (Geistlich, material based on bovine-derived hydroxyapatite), and BoneCeramic® (Straumann, synthetic material based on biphasic calcium phosphate: hydroxyapatite + β-tricalcium phosphate). The pink markings indicate areas of bone formation. The black markings represent non-resorbed graft material. The green/beige markings indicate areas of soft tissue.
Source - (TOVAR et al., 2014b)

"The superior temporal healing pattern described for the Nanosynt biomaterial is attributed to its micro- and nanoscale pore configuration and the fraction of calcium-phosphate-based phases, which together resulted in a dimensional framework at both the macroscopic scale (overall defect space preservation) and the microscopic scale (due to its microtexture), more suitable for osteoconductivity, in addition to enhancing clot stabilization and subsequent interaction between this biomaterial and biological components during the in vivo periods analyzed"(TOVAR et al., 2014b).

Scanning electron microscopy images of the repair areas were also obtained after 2, 4, and 8 weeks in vivo. At all in vivo time points, Nanosynt showed an excellent interface of interaction with the newly formed bone tissue (Image 8).



2 weeks 4 weeks 8 weeks

Image 8 — Images of the repair areas with Nanosynt after 2, 4, and 8 weeks in vivo. The more radiopaque and granular area represents the non-resorbed bone substitution material. The flatter area represents bone tissue.
Source - (TOVAR et al., 2014b)

Together, these data demonstrate the bioactive (osteoconductive), biocompatible, non-toxic, and resorbable properties of Nanosynt.

8. CLINICAL EVALUATION IN HUMANS

The clinical evaluation in humans was conducted (MAIA, 2018), with the aim of histologically and histomorphometrically evaluating the biphasic calcium Phosphate that makes up Nanosynt in alveolar filling after immediate tooth extraction in comparison with another synthetic-origin bone substitute. This study included 36 volunteers, of both sexes, aged between 20 and 66 years, with teeth indicated for extraction, who were randomly divided into 3 experimental groups, according to the material that would fill the dental alveolus after extraction:

Group 01- blood clot (positive control 1);
Group 02- Nanosynt (FGM);
Group 03- BoneCeramic® (Straumann, synthetic material based on biphasic calcium phosphate: hydroxyapatite + β-tricalcium phosphate- positive control;

The volunteers were further subdivided into 2 groups according to the postoperative evaluation time: 3 and 6 months. In these periods (3 and 6 months), the grafted area was reopened, a trephination was performed for material collection, and a dental implant was placed for subsequent functional and aesthetic rehabilitation. The content obtained from the trephination was sent for histological processing and analyzis (MAIA, 2018).

Histological analyzis

Blood clot (positive control 1)

The photomicrography in Images 9A and 9B, referring to the positive control group 1 (blood clot) after the 6-month experimental period, shows almost entirely the presence of newly formed bone with small areas of connective tissue. This differs from the 3-month experimental period (Image 9A), which reveals the presence of bone trabeculae interspersed with loose connective tissue, with the latter being in greater quantity when compared to the 6-month period.

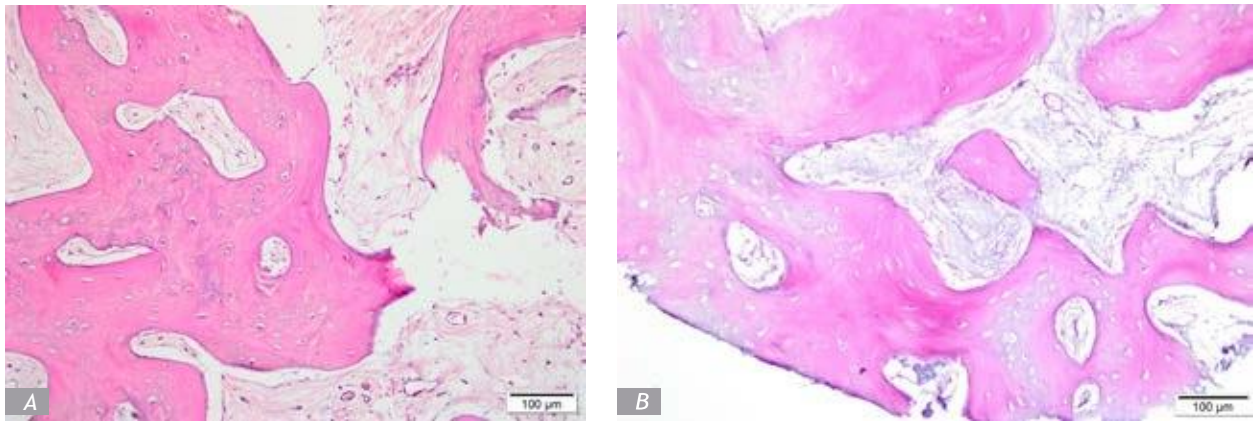


Image 9— Photomicrograph of a trephinated sample from the dental alveolus of the control group at the 3-month (A) and 6-month (B) experimental periods after tooth extraction.
A) Presence of newly formed bone interspersed with large areas of connective tissue, initial objective of 20X.
B) Presence of highly cellular newly formed bone interspersed with connective tissue, initial objective of 20X. Staining: Hematoxylin and Eosin.
Source - (MAIA, 2018)

Nanosynt

The trephinated sample of Nanosynt after 3 months of implantation (Image 10A) showed the presence of areas of newly formed bone in intimate contact with the biomaterial and areas of connective tissue. After 6 months of implantation (Image 10B), the newly formed bone appears in large quantity interspersing the biomaterial, and small areas of connective tissue are still present in small amounts.

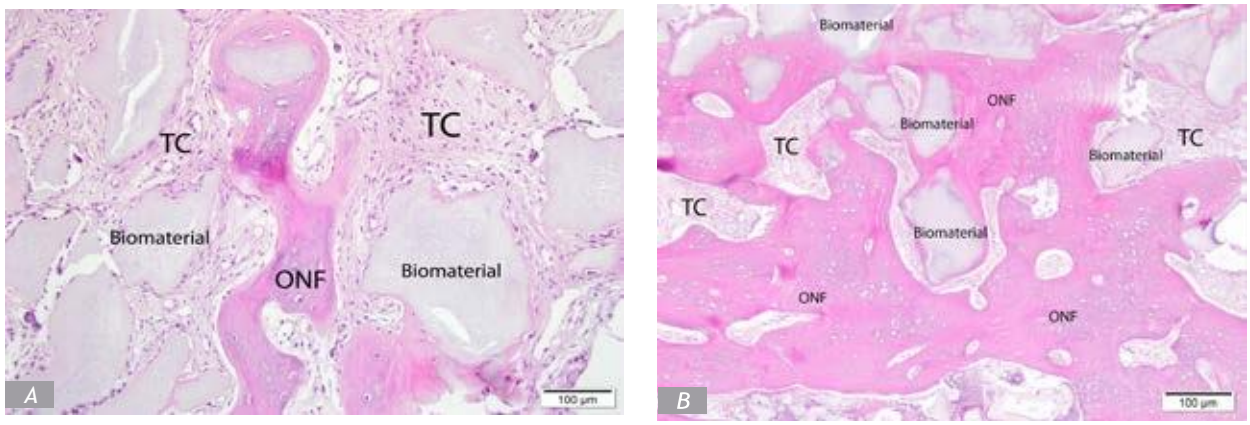


Image 10 — Photomicrograph of a trephinated sample from the dental alveolus of the control group at the 3-month (A) and 6-month (B) experimental periods after tooth extraction..
A) Presence of newly formed bone interspersed with large areas of connective tissue, initial objective of 20X.
B) Presence of highly cellular newly formed bone interspersed with connective tissue, initial objective of 20X. Staining: Hematoxylin and Eosin.
Source - (MAIA, 2018)

BoneCeramic®

After the 3-month experimental period a large amount of connective tissue was observed interspersed between the biomaterial with small areas of newly formed bone in the BoneCeramic group (Images 11A and 11B). After 6 months of implantation, bone trabeculae with osteoblastic paving were observed indicating bone neoformation activity.

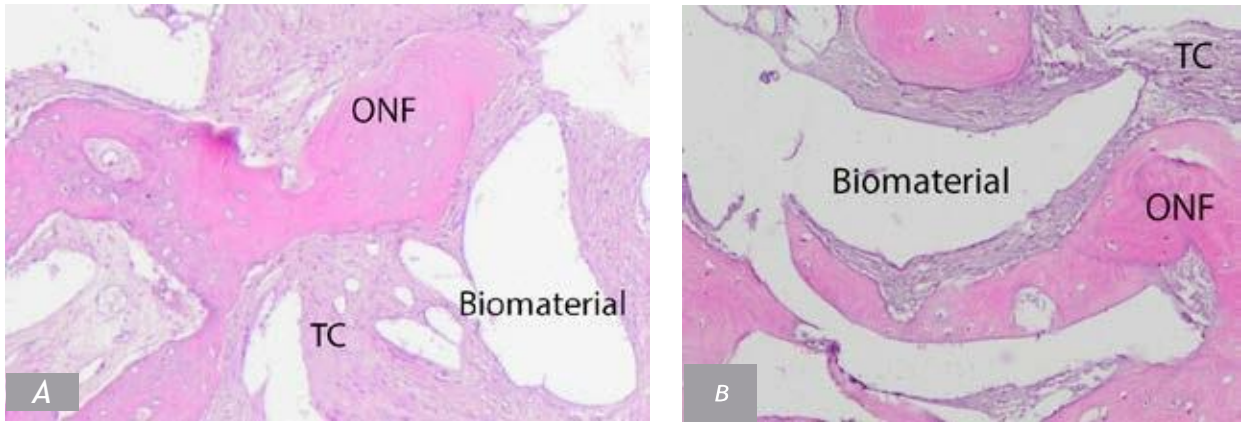
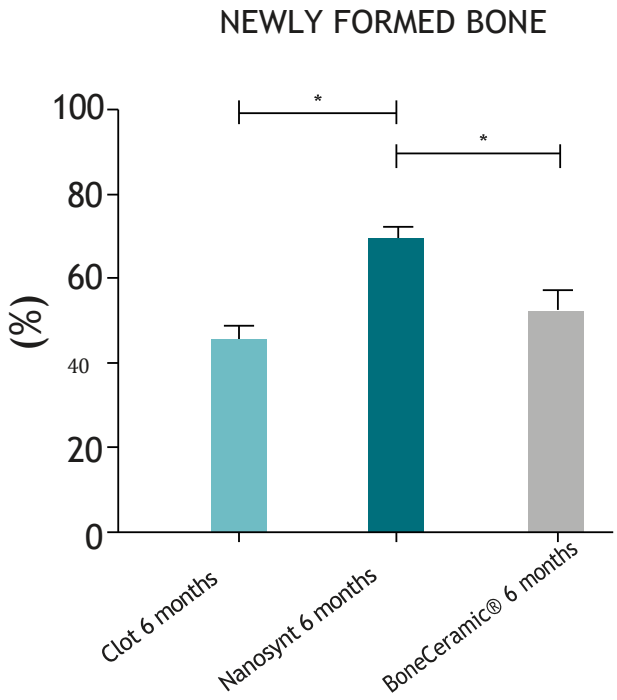


Image 11 — Photomicrographs of the trephinated samples with an initial magnification of 20X.
A) Presence of BoneCeramic® (Biom) surrounded by connective tissue (TC) and newly formed bone (ONF) after 3 months of implantation.
B) Small amount of BoneCeramic® (Biom) in areas of fibrous connective tissue (TC) interspersed with newly formed bone (ONF).
Source - (MAIA, 2018)

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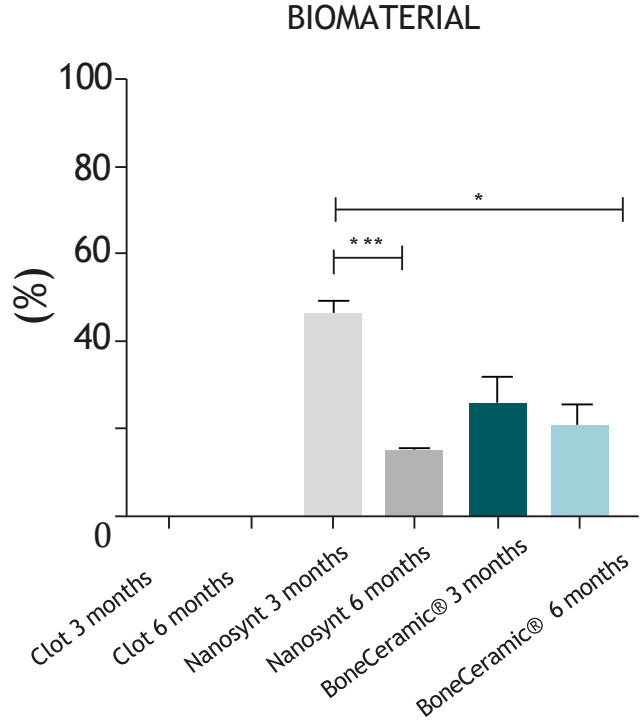
A greater amount of newly formed bone was observed in the samples that used Nanosynt (Image 10) compared to the clot (Image 9) or even BoneCeramic® (Image 11). In the 3-month period no statistical differences were observed between the experimental groups that used Biomaterial, regarding the area of newly formed bone. After 6 months of implantation, a statistical difference was observed between the group that used Nanosynt and the group that used the clot. After 6 months, a greater amount of newly formed bone was also observed in the Nanosynt group compared to the group that used BoneCeramic (Graph 7)(MAIA, 2018).



*Graph 7 — Histomorphometric evaluation of the experimental groups for newly formed bone after 6 months of implantation (n=5). * = p<0,05.*

Source – Adapted (MAIA, 2018)

A statistical difference was also observed between the Nanosynt and BoneCeramic groups regarding the presence of residual Biomaterial analyzed after 3 months of implantation (Graph 8). This residual biomaterial is extremely important for the preservation of the framework, as it preserves the volume at the site where the biomaterial was placed, allowing new bone cells to develop where this material is still deposited. This enables better quality of the bone formed at the end of the osteogenesis process.



*Graph 8 — Histomorphometric evaluation of the experimental groups for residual biomaterial assessment after 3 and 6 months of implantation (n=5). * = p<0,05, *** = p<0,001. Source-Adapted (MAIA, 2018)*

From a clinical standpoint, Nanosynt is easy to handle, offers excellent manipulation for alveolar filling and is radiopaque for monitoring through imaging exams. The reopening of areas grafted with Nanosynt, after 3 and 6 months, revealed areas completely filled with bone and biomaterial, allowing for the preservation of the alveolar architecture and the placement of dental implants. The use of Nanosynt in humans proves to be safe and effective. Together, these results show that Nanosynt is an excellent osteoconductive material, with outstanding performance throughout the entire repair process, offering new clinical treatment perspectives as early as the first postoperative quarter. These data show that Nanosynt is functional and exhibits optimized solubility in a biological environment due to its surface area, modulated by its nanostructured nature and its nano-textured morphology with interconnected pores (MAIA, 2018; UZEDA et al., 2017).

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