FGM

Nanosynt

BONE GRAFT

NANOTECHNOLOGY
BENEFITS BONE GRAFTING

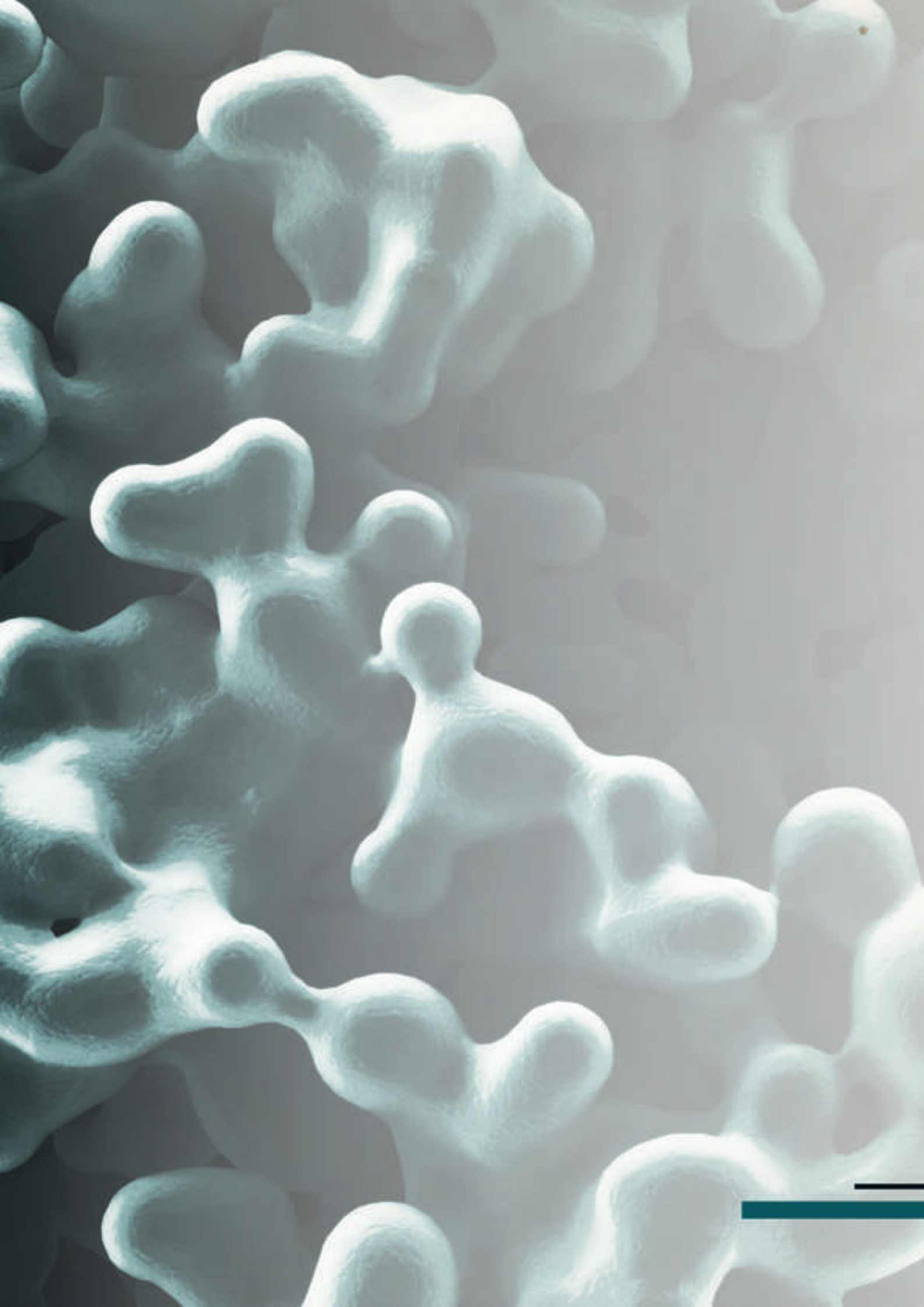
100% SAFE AND SYNTHETIC

20% MORE NEOFORMED BONE[1]

SMART PACKAGING

Practical ampoules in 4 or 2 portions of 0.27cc.

FGM DENTAL GROUP | 25 YEARS



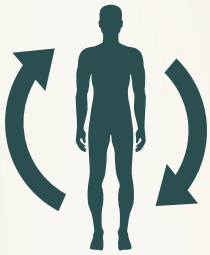
BIOMATERIALS:

What are they and how to choose the best?


FGM
Nanosynt
Material sintético de substituição óssea à base de fosfato de cálcio
Biphasic calcium phosphate synthetic bone substitute material

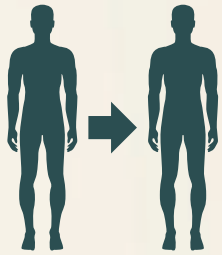
In bone healing of periodontal defects, fractures, vertical/horizontal reconstructions, post-extraction alveolar fillings, gaps in immediate implants, maxillary sinuses/nasal fossae and apicoectomy sites, bone grafts (autogenous) and/or bone graft substitutes (allogeneic, xenogeneic or synthetic) can be used.

In this context, it is worthwhile to discuss of the origin classification of materials (bone grafts) and biomaterials (bone graft substitutes) for bone reconstruction:



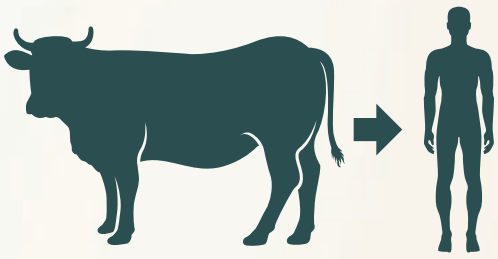
AUTOGENOUS

Donor is the individual.



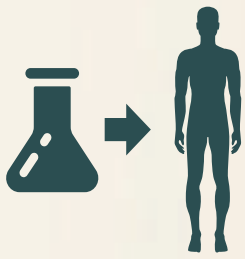
ALLOGENEIC

Donor is of the same species, but genetically different.



XENOGENEIC

Donor is of another species.

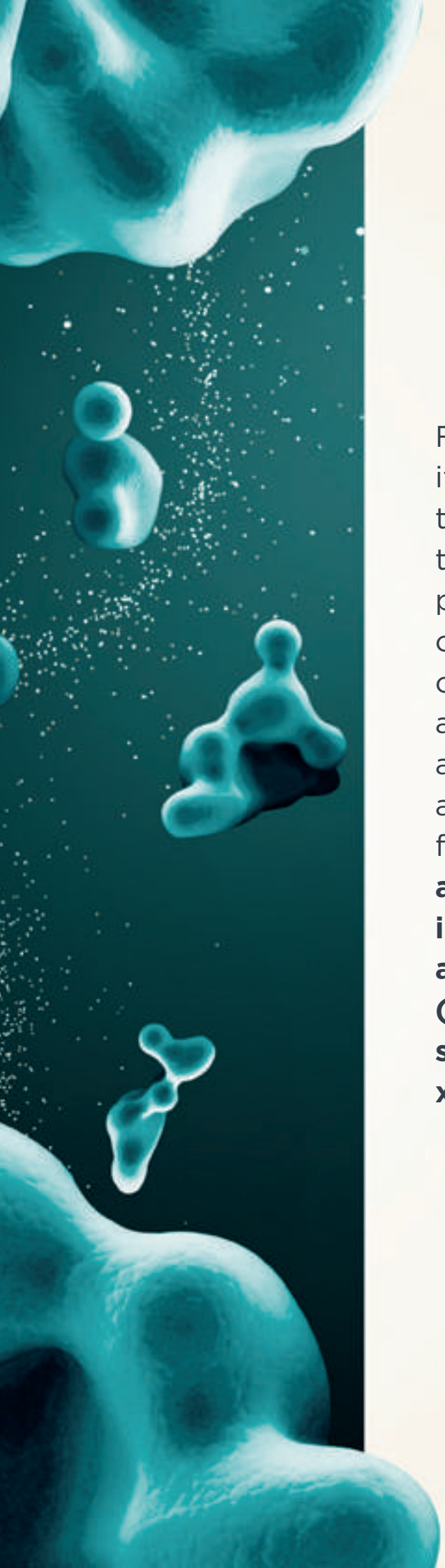


SYNTHETIC

Alloplastic

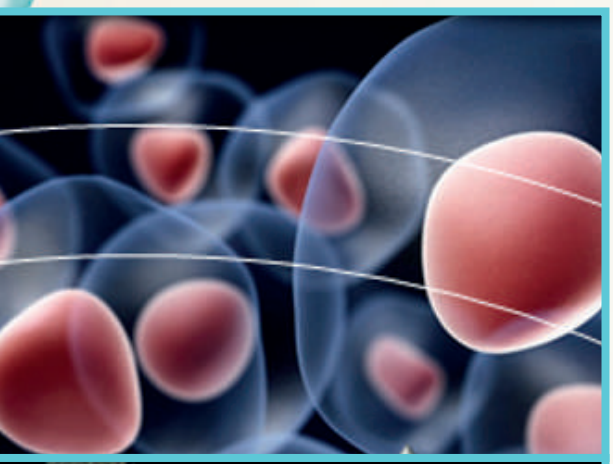
The selection of material or biomaterial for bone reconstruction is based on the following factors:*(Author unknown)

- **COMPLICATION RATES;**
- **AMOUNT OF BONE NEOFORMATION;**
- **MAINTENANCE OF BONE GAIN;**
- **PREDICTABILITY OF IMPLANTS;**
- **AVAILABILITY OF MATERIAL.**



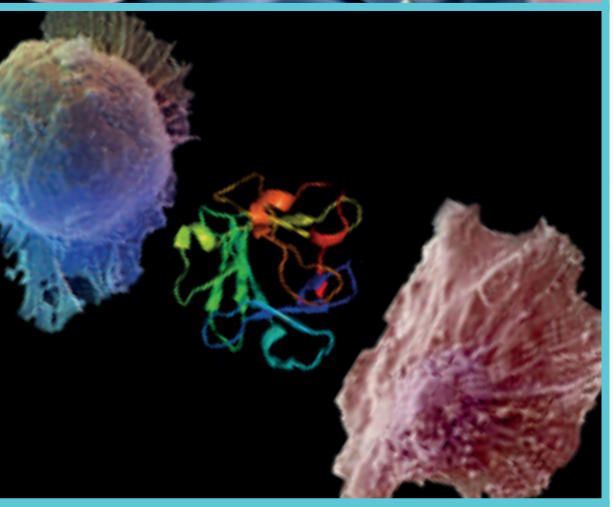
For decades, autogenous bone, in its various forms (scraped, crushed, trephined or block), was considered the Gold Standard, due to the possibility of the three mechanisms of bone formation (osteogenesis, osteoinduction and osteoconduction) and the absence of cross-infection and immune response. However, autogenous bone presents limiting factors such as the **need for a donor area, additional surgical procedure, increased morbidity, material availability, dimensional stability (maintaining bone gain) lower than some biomaterials (inorganic bovine xenogeneic and biphasic ceramics).**

Essential understanding of the bone formation mechanisms, in selecting the material or biomaterial used for bone reconstruction, is unquestionable. Briefly, the bone neoformation pathways are:



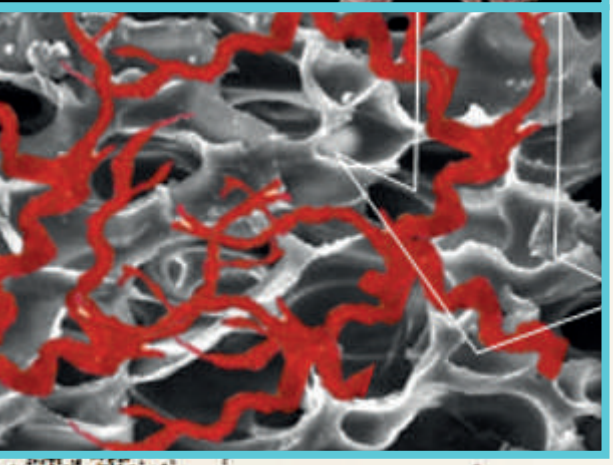
OSTEOGENESIS

Viable osteoblasts from the material promote bone neoformation.



OSTEOINDUCTION

Bone morphogenetic proteins -BMPs- present in the material or biomaterial induce stem cells from the receptor site to differentiate themselves into osteoblasts.



OSTEOCONDUCTION

Material or biomaterial architecture favors bone neoformation, regardless of the presence of viable osteoblasts or BMPs, in the bone graft or bone graft substitute.

Images: Drª. Mariane Beatriz Sordi

As discussed above, it is evident that only bone grafts have osteogenic potential. Regarding the osteoinductive capacity, besides autogenous materials, allogeneic and organic or mixed xenogeneic materials show the possibility of the presence of osteoinductive BMPs, but not all BMPs are morphogenic. Therefore, allogeneic and xenogeneic materials that have an organic matrix are generally only osteoconductive, like synthetic materials.

Note: All biomaterials (halogen, xenogeneic and synthetic) are osteoconductive.

Allogeneic materials, cryopreserved at -80ºC and demineralized lyophilized (DFDBA) or non-demineralized (FDBA), reveal the probability of cross-infection and immune response. Therefore, their use is questionable.

Xenogeneic materials have varied origins (bovine, equine, coral, chitosan, gusuibu and red algae). Those of bovine origin can be: organic (only organic matrix), inorganic (only inorganic component), mixed (organic and inorganic).

Organic bovine has osteoinductive potential. But routinely it's just osteoconductive. This biomaterial exhibits undesirable characteristics, such as low dimensional stability and the possibility of the presence of prion (infectious protein that can cause spongiform encephalopathies).

Inorganic bovine, only osteoconductive (inexistence of viable osteoblasts and BMPs), has high dimensional stability and absence of prion.

Inorganic bovines come in particulate and block forms. It is observed that the idea of isonomic biological behavior among all inorganic bovine is mistaken. Distinct processing methods generate different physicochemical properties and promote dissimilar biological and clinical responses.[01]

Note: The largest number of biomaterial studies have been carried out on inorganic bovine.

Mixed bovine, theoretically, intends to associate the inorganic's dimensional stability and to present the organic's osteoinductive potential. However, the risk of prion presence exists. Thus, organic and mixed bovines are not the preferred biomaterials.

With *inorganic equine*, only osteoconductive (absence of viable osteoblasts and BMPs), according to the manufacturer, the enzymatic process (digestive enzymes) at physiological temperature (37°C) favors similarity to human bone tissue.

Coral, demonstrates the following properties::

- Removal of organic content;
- Consisting of calcium carbonate;
- Low dimensional stability.

Chitosan, a product derived from a crustacean's skeleton, manifests the following particularities:

- Osteoinductive potential;
- May be associated with hydroxyapatite.

Gusuibu, a plant of Chinese flora origin, present the characteristics below:

- Osteoinductive capacity;
- Increased alkaline phosphatase activity (favoring mineralization).

Red alga has the following specificities:

- Increased alkaline phosphatase activity (favoring mineralization);
- Capability of chemical conversion to HA.

Note: Inorganic equine, coral, chitosan, gusuibu and red algae require further scientific evidence.

Synthetics, biocompatible, safe (no risk of cross infection/immune and prion response) with complete control of the synthesis pathway, can be:

POLYMERS AND COPOLYMERS

BIOGLASS (BIOACTIVE GLASS)

CERAMICS

Polymers, macromolecules generated by joining smaller molecules (monomers) by the chemical polymerization process, and copolymers (addition polymers from different monomers) are used in bone reconstruction due to their physical, chemical and mechanical properties that enable uses in Tissue Engineering. For example, the **poly lactic-co-glycolic acid (PLGA)** copolymer has several attributes:[02]

- **Biocompatible;**
- **Osteoconductive;**
- **Allows incorporation and release of substances;**
- **Interesting physicochemical properties;**
- **Degradation by hydrolysis;**
- **Non-toxic;**
- **Micro and macrostructure control.**

Bioactive glasses have the positive features:[03-05]

- **Outer layer rich in calcium phosphate and silica center;**
- **Ability to inhibit bacterial growth by releasing ions that raise the pH;**
- **Allow the incorporation of antimicrobial and antibiofilm agents in the chemical composition or physical structure;**
- **Stimulate bone neoformation and angiogenesis.**

Calcium phosphate-based ceramics are used in bone reconstruction due to the following characteristics:[02]

- **Biocompatibility;**
- **Biodegradability:**
- **Safety;**
- **Bioactivity;**
- **Osteoconductive ability;**
- **Favors osteoblast adhesion and proliferation;**
- **Possibility to add potentialities (controlled degradation) with biphasic materials.**

Calcium phosphate-based ceramics used in bone repair can be:

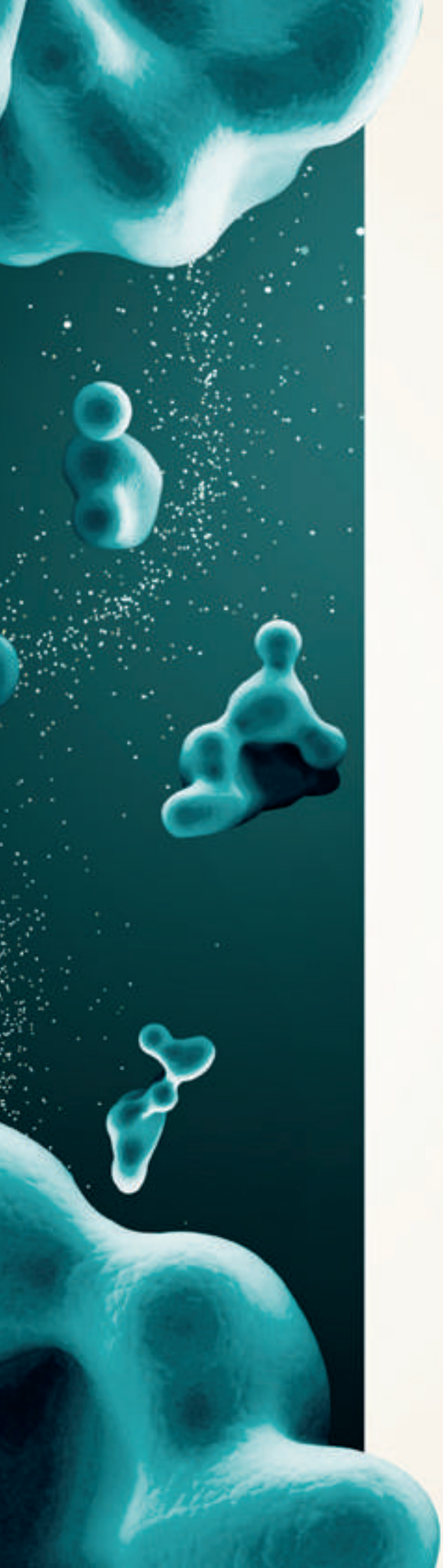
- **Hydroxyapatite (HA);**
- **β-tricalcium phosphate (β-TCP);**
- **Biphasic materials (HA and β-TCP association).**

Distinct calcium phosphate phases will give rise to differentiated levels of cell-mediated dissolution and/or resorption.[06] The ***hydroxyapatite*** phase (main inorganic component of bone tissue) exhibits slow degradation. Thus, the low resorption rate provides dimensional stability during bone neoformation (biomaterial particles can remain for long periods in situ without being replaced by neobone) and, in addition, it offers residual biomaterial that enhances late-stage bone healing.[07] However, the persistent existence of ***hydroxyapatite*** particles can hinder bone neoformation.[06] The surface adsorption potential of bioactive substances (ex. adhesive proteins) promotes cell adhesion to hydroxyapatite.[08] In ***β-tricalcium phosphate***, rapid reabsorption provides early-stage calcium and phosphate (ions needed to guide the mineralization of the organic matrix, that is, the conversion of calcium phosphate into ***hydroxyapatite***) and allows space for neoformation in the initial stages of bone repair.[08] Therefore, ***β-tricalcium phosphate***, which is more rapidly reabsorbed than ***hydroxyapatite***, promotes bone neoformation by the complete and gradual dissolution of its particles and concomitant replacement with bone tissue (osteoconduction).[09] Pure ***β-tricalcium phosphate***, presents an imbalance between the rates of biomaterial resorption and bone neoformation.

Note: The material's surface area, ion adsorption capacity and porosity influence the dissolution process of calcium phosphates.[08]

Note: The biomaterial's characteristics can affect the sequence of cell adhesion promotion events.[08]

The term ***biphasic calcium phosphate*** is used to describe the bioceramic materials resulting from the association of ***hydroxyapatite*** and ***β-tricalcium phosphate***.[10] The distinct proportions of these constituents control the biomaterial's bioactivity. A balance between ***hydroxyapatite*** (more stable) and ***β-tricalcium phosphate*** (more soluble) is postulated.[10] Isis Carvalho Encarnação asserted that "while ***hydroxyapatite*** is highly inert and considered relatively non-degradable, as it maintains biomaterial's volume for prolonged periods, the rapid resorption of ***β-tricalcium phosphate*** allows its replacement by new bone tissue more quickly". Additionally, the aforementioned researcher described that the environment rich in calcium and phosphate, due to the high solubilities and the high degradation rate of ***β-tricalcium phosphate***, favors bone



neoformation.[11] At the receptor site, with calcium phosphates in contact with the blood (interaction with the medium), the dissolution, solubility and precipitation properties are essential to initiate crystal degradation and bone neoformation.08 According to Paim, the dissolution of calcium phosphates is influenced by the following factors:[08]

- **Surface area of the biomaterial;**
- **Ion adsorption capacity,**
- **Porosity;**
- **Polarity.**

Note: Protein adsorption plays a significant role in the interactions between biomaterials and tissues (influencing cell migration, adhesion, proliferation and differentiation).[12]

Note: On the biomaterial's contact with tissue fluids, the adsorbed layer of proteins prepares the biomaterial-tissue interface for cell colonization.[12]

IN SUMMARY,

autogenous material is no longer considered the Gold Standard due to the complication rates, lack of bone gain maintenance and limited material availability. Currently, the biomaterials of choice, due to the predicates presented, are biphasic ceramics. The combination of 60% ***hydroxyapatite*** and 40% ***β-tricalcium phosphate*** has been shown to be effective in reconstructing bone defects, filling alveoli, maxillary sinuses/nasal fossae and immediate implant gaps. ***Hydroxyapatite's*** lower solubility is offset by the ***β-tricalcium phosphate's*** higher solubility, which benefits bone neoformation (via osteoconduction) with dimensional stability.[13] Therefore, in proportions lower than 60% ***hydroxyapatite,*** early-stage bone resorption to bone neoformation can promote less dimensional stability. A randomized clinical trial compared clinically, histologically and histomorphometrically the bone repair of post-tooth extraction alveolus filled with biphasic ceramics, after 3 and 6 months, with distinct proportions between ***hydroxyapatite*** and ***β-tricalcium phosphate***.[14] The group that used the proportion of 60.28% ***hydroxyapatite*** and 39,72% ***β-tricalcium phosphate*** had greater bone neoformation and less connective tissue and remaining biomaterial particles. However, it is suggested that all proportions evaluated are safe and effective for clinical use.[14]

In this scenario, ***Nanosynt*** is a biphasic ceramic (60% ***hydroxyapatite*** and 40% ***β-tricalcium phosphate***) that associates the dimensional stability of ***hydroxyapatite*** with the fast supply of space and the release of calcium ions from the ***β-tricalcium phosphate***. ***Nanosynt*** has a differentiated nanostructure, with superior geometry and porosity, favoring vascular growth and osteoconduction. These morphological characteristics significantly increase the biomaterial's surface area. Consequently, greater contact between particles and tissue fluids promotes increased adhesion of proteins and osteoprogenitor cells.[08]

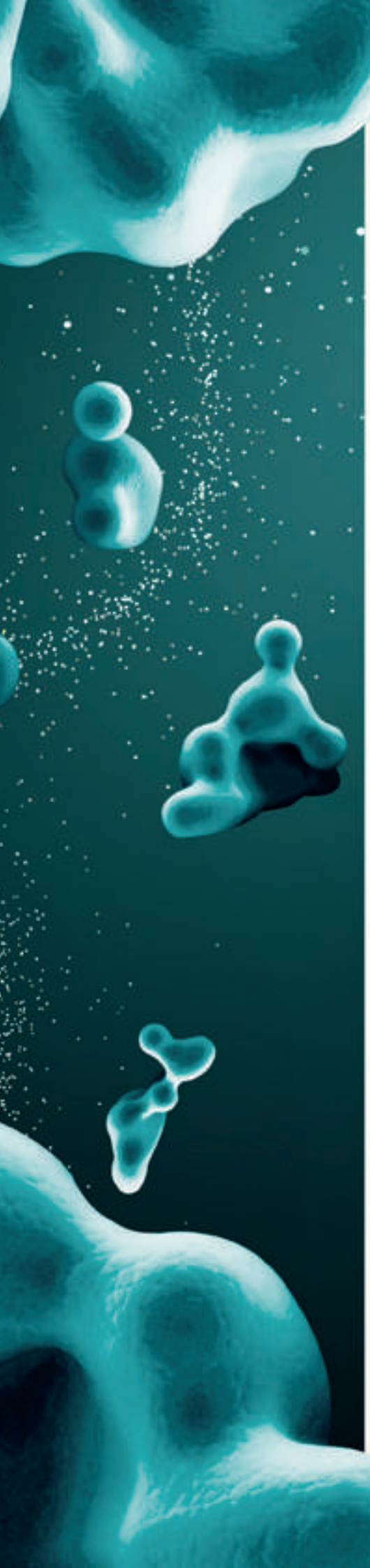
Note: Nanotechnology enables the manufacture of biomimetic biomaterials, which reproduce cell growth environments similar to tissue at a manometric scale favoring cellular and vascular interactions.[14]

Nanosynt boasts predicates that make it an effective biomaterial for bone neoformation, such as:

- **Biocompatibility;**
- **Non-toxic;**
- **Radiopaque;**
- **Safety (100% synthetic);**
- **High porosity (80 to 90%) favors vascularization, osteoprogenitor cell migration and bone deposition;**
- **Osteoconductive nanostructure allows vascularization and bone neoformation;**
- **Facilitated hydration (5 to 8 drops per 0.25g portion);**
- **Ease of handling;**
- **Convenience due to the availability in fractioned forms (2 or 4 ampoules of 0.27cc).**

Note: Nanosynt is extremely permeable, hydrophilic, with a cell adhesion-promoting surface.[08]

Note: Nanosynt has distinct forms of packaging:
200 to 500 µm – 4 portions of 0,27cc;
200 to 500 µm – 2 portions of 0,27cc;
500 to 1000 µm – 4 portions of 0,27cc;
500 to 1000 µm – 2 portions of 0,27cc.



CONCLUSION

The literature has demonstrated ***Nanosynt's*** effectiveness, a research carried out at New York University compared it with two other biomaterials (biphasic ceramic and inorganic bovine xenogeneic) used worldwide for bone reconstruction.[06] Histological results showed, after 4 weeks, a greater amount of bone neoformation in the ***Nanosynt*** group (23%) compared to biphasic ceramic (11%) and inorganic bovine (17%).[06] In conclusion, ***Nanosynt*** provides a safe, predictable and practical clinical performance due to structural specificities and an irrefutable cost-benefit ratio. Nanotechnology at your clinic's service!

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