

## SYNTHETIC BONE in Practical Medicine, Maxillo-facial and Oral Surgery

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**Abstract.** Nanomedicine-trend in modern medicine, based on the use of the unique capabilities of nanomaterials and nano-objects for the selection, design, and changes in biological systems on human low-molecular level.

**Keywords:** Bioactive Ceramic Materials, Nanomaterial science, SYNTHETIC BONE, SYNTHETBONE, Modern Nanomedicine, Nanobiotechnology, Surgery, Cranio-Maxillo-Facial and Oral Surgery, Stomatology.

### Introduction

Bioactive Ceramic Materials SYNTHETIC (SYNTHETIC BONE, SYNTHETBONE) is a group of materials intended for the local repair of bone tissue after injury, removal of cysts, bone tumors, genetic and other defects. Such materials are widely known in the world market and are represented mainly by hydroxyapatite (HAP) in various structural states (or composites from HAP and organic additives – for example, COLLOPAN), by some other calcium orthophosphates:  $\alpha$ - or  $\beta$ -tricalcium phosphate (TKF), dicalcium phosphate dihydrate (mineral brusheit), as well as some silicate-phosphate-calcium glasses and sittals (45S5, 60S, Bioglass), calcium-phosphate cements based on bruschet, tetrakalcium phosphate (tetroxydate) usually offers single-phase material (consists of one of the phases listed), biphasic or three-phase compositions (GAP-TKF, GAP- $\alpha$ - and  $\beta$ -TKF) are less common. The peculiarity of the materials of the SINTHEBONE group is that it includes both the most popular single-phase materials (HAP,  $\alpha$ - and  $\beta$ -TKF, bioglass, biosital), and inorganic composites consisting of several (up to five) different phases (eg, bioglass, biosital,  $\beta$ -TKF, HAP) – this provides a synergistic effect due to the interaction of individual components, which improves the results of the clinical application of implants. In addition, alloyed variants of different materials of the SYNTHETBONE group containing a small amount of bioactive metals are studied and made, which provides a significant change in some of the biological properties of the implant – for example, bactericides (Ag, Cu), stimulates the synthesis of enzymes that promote

osteosynthesis, increase (Ln). This direction is quite perspective and constantly developing.

All the above materials are available in the form of powders, dense or porous granules of various sizes, as well as in the form of ceramic products – blocks or figured products (including individual models) with different structure and porosity.

The presence on the market of so many different materials of the same purpose (the number of which is constantly increasing) is explained by the fact that none of them yet solves completely (in all cases, unambiguously, in the required time) the task – complete restoration of bone tissue in the desired place of any volume.

A common feature of all bioactive ceramics is the property of bioactivity, which in this case means the ability to form direct biochemical bonds between bone tissue and a synthetic implant. In other words, such an implant is not perceived by the body as a foreign material, is not isolated from the body by a layer of connective tissue of any thickness, does not cause any allergenic or other negative immune reactions, is capable of adhesion between the surface of the implant and bone or soft tissue, is included in the processes of natural meta organism. However, even this common property is not always realized – due to poor planning and technique of surgery, as a result of the difference in the hardness of the ceramic implant and living tissue, micro-motility at the border of the implant and tissue, the presence of infection – these and other such factors can ensure rejection even by himself bioactive material.

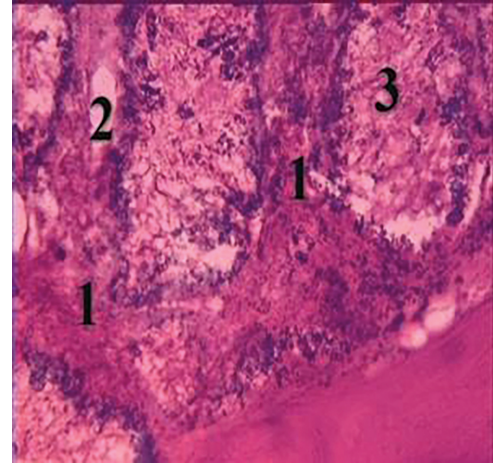
Other biological properties of bioactive ceramics are more specific, they are much more different for different ceramics, and this difference is the basis for the choice of

material in the planning of surgery, as well as the reason for the development and improvement of new materials of this type. Such properties include, first of all, adhesive bonding properties between ceramics and body tissues (strength, speed of establishment, etc.), the rate of absorption of material in a living organism (ie, degradation of the material due to the sum of all factors of the living organism), velocity and completeness of biotransformation of the material, i. absorption of its components of newly formed bone, Superposition of these basic properties is the basis of osteoconductivity – the rate of proliferation of new bone tissue on the surface and along the pores of bioceramics and the ability of the porous implant to be a framework for growing new bone. The osteoinductivity is also related to the basic properties – the ability of the implant material to stimulate the formation of new bone, including in places away from contact with bone tissue (ecotopic formation of new bone). It should be noted that the realization of all these properties depends to a large extent on the mentioned conditions of surgery – the place and volume of surgery, the patient's condition, the intensity of blood circulation in the given place, the local concentration of cells capable of differentiating into osteoblasts, the concentration of specific enzymes contributing to ostesynthesis. Therefore, it is more correct to speak not about the presence of the sum of certain properties in a given bioceramics, but about the ability to manifest them under optimal conditions (Figure 1).

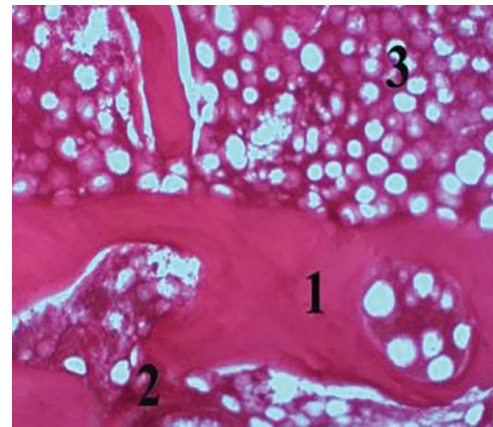
The bioactive glass used in SINTEKOST materials differs in maximum bioactivity, for a minimum time forms strong biochemical bonds not only with bone, but also with the soft tissues of the body. The glass is actively absorbed and biotransformed – for example, in the defect of the jaw bone of a volume of about 3 cm<sup>3</sup> filled with granules of fused bioglass, after 6 months coarse fibrous bone is observed and only a few percent of implanted granules, and even after the same period the structure of the porous intact is completely restored bone marrow (Figs. 2, 3). There are publications where they conclude



**Figure 1.** Bone-ceramic compo appearing at growing in of granules of GAP in a new bone.



**Figure 2.** Zone of implantation of granules of bioglass of term 6 mon SYNTHETBONE ths are bone trabeculas, 2 – is a remain of bioceramics (light color), 3 – is coarse fiber.



**Figure 3.** SYNTHETBONE bioglass granule implantation zone, period 12 months. 1 – bone trabeculae, 2 – coarse fibrous bone tissue, 3 – lamellar tissue and bone marrow.

on the osteoinductive properties of such glass. Among other candidates for osteoinductive bioceramics, octacal phosphate and  $\alpha$ -TKF can be mentioned, but both phases are not thermally stable. The disadvantages of bioactive glass can be attributed to the fact that its highest bioactivity is manifested only when the glass melt is quenched by rapid cooling. Otherwise, a crystalline phase occurs in the glass, i.e. it becomes a sittal with a slightly lower absorption rate, but still retains high adhesion strength and biotransformation rate. Recently, new types of bioactive glasses have been synthesized with a much larger specific surface area, whose biological properties are being studied. The bioactive sittal SINTECOST is characterized by the highest mechanical strength, well sintered, allowing to receive ceramics and granules of any porosity, capable of absorbing completely in a term close to the rate of glass absorption.

An important feature of SYNTHEBONE materials is the ability to make composites from several bioactive ceramics. Such implants show a synergistic effect and their bioactive properties are generally better than single-component ones.

The use of different synthesized materials (as already mentioned is determined by the type and objectives of surgery, the intensity of circulation and metabolic processes at the site of surgery, the patient's condition, concomitant diseases. For example, in dentistry most commonly used bioactive glass, similar in composition to 45  $\beta$ -TKF A similar glass containing ytterbium oxide is used to increase the X-ray contrast. The materials are used as porous granules of 0.3–0.5 mm and 0.5–1 mm in size.

Hydroxyapatite (HA,  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ) and  $\beta$ -tricalcium phosphate ( $\beta$ -TCP,  $\text{Ca}_3(\text{PO}_4)_2$ ) are of great interest since the chemical composition and structure of these substances resemble those of the biomineral, the inorganic component of bone tissue. In this regard, these substances have special biological properties and were identified several decades ago as most biocompatible of all known substances owing to their ability to form biochemical bonding with living tissues (in particular, with bone) and contribute to metabolic processes in the human body, while promoting the generation of new bone and gradually turning into it. Hence, HA and TCP, along with other bioactive ceramics, are widely used in implants, coatings, and components of composites for surgery. However, these substances have distinct biological properties: HA is much more stable in the human body than TCP. The complete biotransformation of implanted, well-crystallized HA takes quite long in the human body, more than 10 years. On the other hand, TCP, when implanted into areas with intensive blood supply, dissolves faster than new bone forms, thus leading to unfavorable result. Hence, it was decided to use two-phase HA–TCP composites in implants. To synthesize these composites, amorphous calcium phosphate (ACP) with the Ca/P ratio being from 1.5 to 1.67 is precipitated from solutions and then gradually heated; during heating, ACP gradually transforms into nonstoichiometric HA (at about 100°C) to further decompose (at 450–550°C) into the two-phase HA–TCP composite, whose ratio of components is determined by the Ca/P ratio in ACP. That nonstoichiometric HA shows up early in the process is attributed to its crystal lattice, which is largely isomorphic. Excess water, master/solution components, and other admixtures in ACP promote its crystallization in the form of nonstoichiometric HA stabilized by admixtures, which shows broad reflections in x-ray patterns and contains a great amount (to 30%) of admixtures that escape during further thermal treatment. It is the removal of these admixtures that leads to the decomposition of nonstoichiometric HA into a HA–TCP mixture, whose deviation from stoichiometry is commonly omitted and

assumed to be insignificant. X-ray diffraction patterns of stoichiometric HA and TCP remain unchanged up to 1300°C.

It is established that the starting phase composition changes when mechanical mixtures of thermally stable stoichiometric powders of hydroxyapatite and  $\beta$ -tricalcium phosphate are annealed:  $\beta$ -TCP addition causes HA to transform into secondary  $\beta$ -TCP, whose total amount increases to 100% in the composite in this way. The transformation of HA into  $\beta$ -TCP through the hydration reaction in mixtures is promoted by interphase activation in which the limiting nucleation stage disappears since the product phase ( $\beta$ -TCP) is in close contact with the hydrate phase and distributes its nuclei over the entire volume. Interfaces in the two-phase HA–TCP mixture have more defects than pure HA and thus are more permeable for water vapors and more effective for removal of gaseous reaction products.

Nanotechnology – an interdisciplinary field of fundamental and applied science and technology, which consists of a combination of theoretical study and practical research methods, analysis and synthesis, as well as methods of production and application products with a given atomic structure by controlled manipulation of individual atoms and molecules (Figure 4).

Nanomedicine-trend in modern medicine, based on the use of the unique capabilities of nanomaterials and nano-objects for the selection, design, and changes in biological systems on human low-molecular level.

Artificial bone (biocomposites), bioactive inorganic multiphase composite material (synthesized on the basis of nanocrystals hidroksilappatit, tricalcium – phosphate, bioactive glass, mixed oxides of metals and nonmetals), similar in composition to natural bone mineral and intended to restore it with different pathologies (Figure 5).

In the complement of biocomposit to be possibility to add antiseptic preparations (Figure 6).

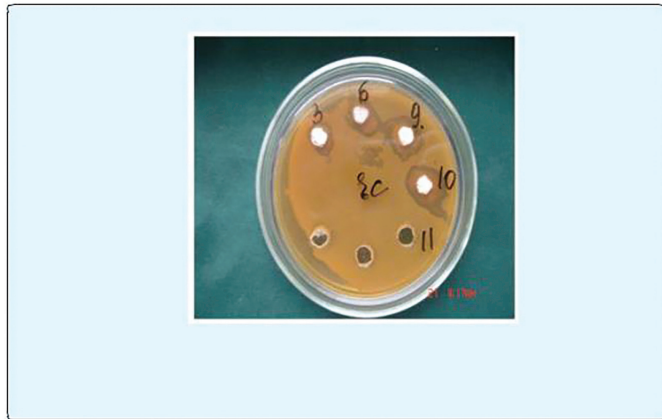
Due to the absence of organic components is possible multisterilization of reusable material. The using of autologous bone-may be replaced and supplemented by using of modern bioactive ceramics with the planned biological properties (Figure 6).



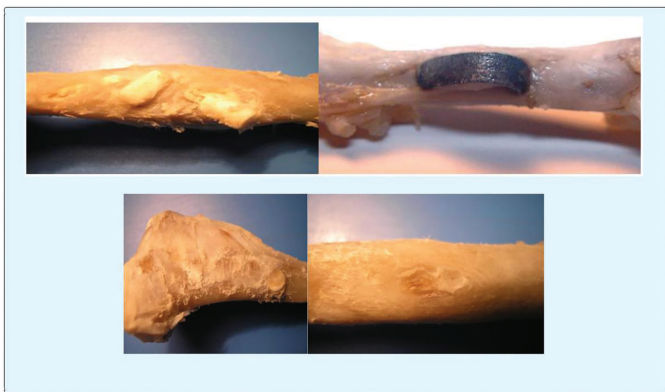
**Figure 4.** Cooperation of biocomposit with bone-osteointegration, dense fitting closely of bone.



**Figure 5.** Packages bioceramics in shape gidroxilapatit, threocalciumphosphatis and bioactive glass.



**Figure 6.** In the complement of biocomposit to be possibility to add antiseptic preparation.



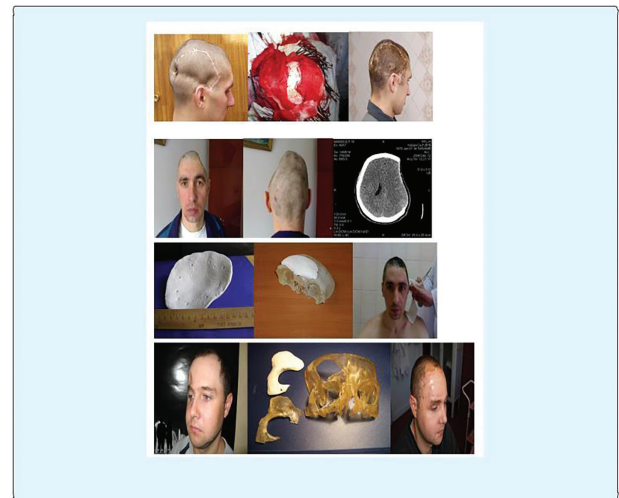
**Figure 7.** Osteointegration plates in a bone with bioceramics covering and witho.

System of artificial bone are multifunctional materials, as they have the ability to osseointegration, osteokonduktion, osteoinduktion, osteostimulyation and osteogenesis (Figure 7).

After the occurrence of bone-ceramic complex in the body material is partially or completely resorbed at the planned time-from 1,5-2 months – to several years, being replaced by bone tissue, which consists of products of resorbtion and synthesis.



**Figure 8.** Application of bioceramics in the defects of different bones.



**Figure 9.** Using of biocomposites in cranio-maxillo-facial surgery.

Mechanism, the nature and rate of resorbtion is planned and managed composition and structure of complex artificial bone (Figures 7, 8).

Selection of non-rezorbtion of the complex, which firmly holds the specified shape and volume, such asalveolar jaw. Biocompozit contains only the highest biocompatibility of inorganic constituents, which do not cause abnormal immune reactions, and inorganic baktericidus supplements, preobstruction inflammatory complications.

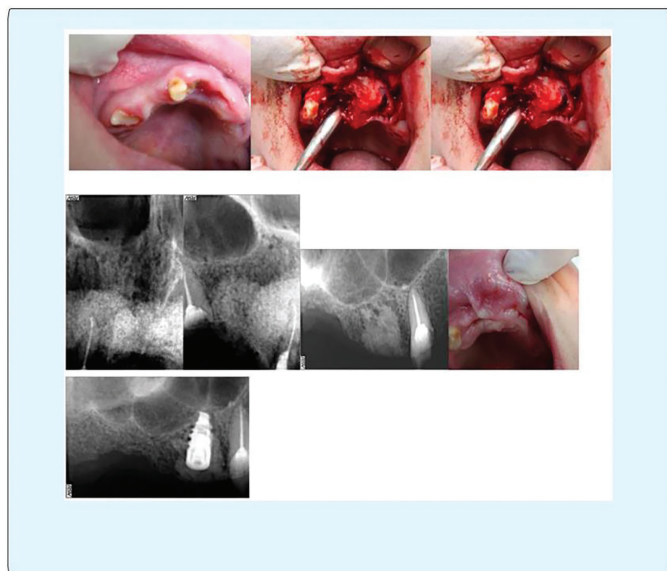
Using of biocomposites in oral and maxillo-facial surgery is possible (Figures 9–11):

Due to the absence of organic components is possible multisterilization of reusable material.

The using of autologous bone-may be replaced and supplemented by using of modern bioactive ceramics with the planned biological properties.

Using of biocomposites in oral and maxillo-facial surgery is possible:

- For replacement elements maxillo-facial bones and joints.
- To fill the bone cavities after capsulotomy and cystectomy, treatment of osteomyelitis.



**Figure 10.** In oral surgery – treatment defect of alveolar process with bioceramics to successive implantation.



**Figure 11.** Sinus-lifting left maxilla sinus and treatment chronic sinusitis with antiseptic bioceramics.

- To form the bone wall with perforated sinusitis.
- For bone grafting in plastic surgery.
- To fill bone defects (Figure 10).
- For a sinus-lift (Figure 11).
- At chronic sinusitis (Figure 11).

In stomatology:

- For the filling of periodontal defects.
- To fill the holes removed teeth.
- When you atrophy of alveolar bone in the jaw bone for augmentation.
- For obturating dentinal canals.
- In a deep root canal fillings, including extraapix therapy.

Thus, modern biocomposites represent the latest concept in the development of bioactive inorganic materials for reconstruction of bone tissue.

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