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Review

The Perspectives of Sapphire Implants Use in Bone Reconstruction Surgery

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Abstract: Background: Despite the fact that bone reconstructive surgeries are widely practiced worldwide, the search for an ideal bone replacement matetrial is still an open issue. We aimed to provide an overview of the current status of research and developments in this field with a focus on sapphire materials; Methods: A literature search and review was conducted using the PubMed, Scopus, and Embase databases. We searched for literature using the following keywords: bone implants; biocompatible materials; bone replacement material; sapphire implants; Results: Sapphire has a unique combination of mechanical, physical and chemical characteristics thanks to wich it has an excelent biocompatability and biointegrity.Unlike other materials it is incredibly strong and has a high endurance. The successful experience of using this material in medical instrument engineering, dentistry and cardiac surgery shows its benefits; Conclusions: We consider that sapphire is a perspective material for bone replacement implants and researchers should look in this direction.

Keywords: bone implants; bioprinting; biocompatible material; bone replacement material; sapphire implants

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1. Introduction

According to the literature data, bone augmentation remains at the leading position among other reconstructive surgeries [1–3].

The following methods are currently represented in the reconstructive surgeons' armory: autografting, allografting, as well as the use of the artificial materials. At the same time, the use of bone autografts has a number of disadvantages such as traumatization of the donor area [4], technical complexity of the operation, significant increase in the duration of the operation and recovery period, and often the inability to achieve the desired aesthetic result [5,6] due to the lack of a personalized approach to the production of the graft. In relation to the aforesaid, the problem of choosing bone reconstructive materials requires to look for new solutions, and especially in terms of the additive technologies and tissue engineering progress. Nowadays, the issue of using of the artificial implants made by 3D bioprinting is being actively examined [7,8]. Metal, ceramic, or composite materials can be used for bone-replacement constructions [7].

This article aim is to provide an overview of the current status of biocompatible bone implants, their advantages and disadvantages, and the prospects for the use of innovative materials. By exploring the current state of research and developments in this field, the present review will show the current progress and the potential of these advanced bioinert materials in artificial bone implants such as sapphire implants.

2. Which materials are currently being used for bone replacement constructions?

2.1. Metal materials.

Titanium implants are the most frequently used nowadays - it is considered that this particular metal is classified as a bioinert metal [9,10] and is corrosion-proof [11,22]. However, many scientists agree that these features are variable and, like other metals, titanium can be exposed to

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microcorrosion due to the influence of the biological fluids pH and deterioration of the superficial layer [12,14]. It is essential to note the fact that titanium is likely to cause hypersensitivity and inflammatory reactions of tissues in the peri-implant zone [14,28,29].

Numerous efforts have been made to improve the strength and osseointegrative parameters of titanium implants by adding a number of different metals to its alloy [15–18]. However, besides improving the mechanical parameters, these implants have demonstrated not only local reactogenicity [12], but also generalized citotoxic [15], carcinogenic [16], and neurotoxic effects as well [17].

Zheng Liu. et al. proposed to improve titanium structures and to use porous titanium alloy with VEGF/BMP-2 microspheres, which promoted osteogenic differentiation and osseointegration due to the consistent release of the microspheres [10]. Nevertheless, this project remains on the experimental model phase and requires further investigation.

2.2. Ceramic and composite constructions.

Ceramic and biopolymer materials, despite having their benefits such as biocompatibility - stronger than titanium [19–22] and the possibility of creating bioactive constructions [20,21], are currently also flawed: their most important disadvantage is their insufficient toughness for bone tissue [11,18,20].

The ability to create an implant which is appropriate for sternum grafting is a matter of particular interest for reconstructive surgeons. The weak points of all titanium constructions have been described above - the main one is represented by reactogenicity, tendency to microcorrosion and insufficient wear resistance. The biopolymeric materials that are currently used for this task also require searching for an alternative, as they are prone to cardiorespiratory complications [23–25] due to their insufficient stiffness [11,20,23–25].

3. The criteria for bone implants.

The implant should follow the general requirements for all bioimplantable materials, the most essential of them is biocompatibility [26,28,34]. This feature, primarily, is characterized by the absence of toxic influence on the organism and the absence of chemical reactions with biological fluids, areactogenicity and corrosion stability [26,28,29,34].

Besides, this biomaterial should fulfill the requirements based on the anatomical field of application and possess the features of substituting structures [26,31]. Thus, the specific characteristics of bone substitutes are the adequate toughness, elasticity, the required porosity for osseointegration [27,30–32], and a specific surface topography [31,33].

Considering the aforesaid, we may conclude that not a single material that has been demonstrated so far has all the necessary qualities at he same time.

Thus, porous metal scaffolds meet the mechanical parameters [11,22] of bone tissue, but do not provide the required implant integration due to insufficient biocompatibility, tendency to microcorrosion [12,14,53] and reactogenicity [12,14,15].

Bioactive ceramic structures, especially the ones with hydroxyapatite, demonstrate an outstanding compatibility with bone tissue and provide the necessary osseointegration conditions, but they do not meet the requirements for bone implant rigidity. [20,23,25].

4. Sapphire implants.

4.1. The history of discovery and application.

The studies on the evaluation of sapphire materials biocompatibility in order to improve bone implants quality date back to the end of the last century [35–39].

For instance, in 1980 the scientists from Japan under the supervision of Kawahara H. And T. Shikita discovered the unique features of sapphire [35]. According to the results of their study, sapphire perfectly showed itself as an alternative material for dental implants: the consolidation was observed in all cases, there were no inflammatory changes in the peri-implant zone.

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Later, T.Shikita has described a successful experience of peripheral osteosynthesis with sapphire pins [36]. The results of experimental use of the material on animals have demonstrated chemical areactogenicity and biomechanical stability of sapphire pins. Clinical observation and evaluation of radiologic parameters have also demonstrated complete consolidation and absence of reactogenicity of this material.

Based on the obtained results, the authors concluded that sapphire materials, with their corrosion resistance and better biocompatibility, are as resistant as metal implants in their resistance.

7 years later, in 1987 T. Iizuka et al. during the experimental use of the sapphire pins for the mandibular fixation confirmed the results of the previous studies testifying in favor of the excellent biocompatibility and mechanical characteristics of sapphire [37].

Thus, when X-rays were evaluated one year after the implantation, the consolidation was observed in all cases, and there was no need in pin replacement and removal.

Later, the biocompatibility of sapphire implants was evaluated at the histologic (M. Hashimoto et al., 1988) and ultrastructural (M. Hashimoto et al., 1989) levels. The authors, as well as the previous researchers, have described the absence of inflammatory changes in the peri-implant region [38,39].

In 1990, a team from Washington under the supervision of A. Sclaroff conducted a clinical evaluation of sapphire dental implants, which results also testify in favor of the areactogenicity of sapphire materials.

According to the obtained results, sufficient neovascularization and formation of a thin fibrous capsule in the peri-implant zone were registered, osteolysis, implant loosening and inflammatory changes were no more present, which demonstrates a high level of such features of sapphire materials as osteoconductivity, osteointegration and biocompatibility [40].

It is well known that biointegration requires the absence of perception of the biomaterial as foreign, while the degree of implant reactogenicity is defined by the thickness of the capsule formed around it [28,29,32,55].

K.Arvidson conducted a study to estimate the biocompatibility of sapphire materials in vivo: no inflammatory changes were observed during subcutaneous implantation, a thin fibrous capsule was found in the peri-implant zone, which confirms a high degree of biocompatibility of sapphire implants [41].

In 1991, M.Ishizuki published the experience of using sapphire pins in upper limb fractures. The study sample consisted of 22 patients and only one case showed delayed bone fusion, while osteolysis and inflammatory changes were not observed in all subjects, which allowed the author to conclude that sapphire constructions are very promising as a material for internal fixation in limb fractures [42].

Sapphire implants also showed some encouraging results in larger-scale long-term studies. In 1997, K. Arvidson published the results of a 10-year evaluation of the effectiveness and safety of sapphire implants in upper and lower jaw adentia. The authors evaluated the degree of biointegration and the presence of complications 3, 5 and 10 years after the implant placement. The absence of complications on the lower jaw side was found in the whole group of patients and in 92.6% of cases - on the upper jaw part [43].

In 2008, T. Takahashi et al. published the results of long-term follow-up of patients who had undergone the installation of dental sapphire implants and confirmed the results of previous studies [44].

4.2. Physicochemical features of sapphire. Medical application.

Sapphire is a single crystal form of the α-isomer of aluminum oxide [54] and has a unique combination of mechanical, physical and chemical characteristics. The latter are represented by absolute inertness, areactogenicity and resistance to changes in the pH [52–54,56].

As it was discovered later on, the aforementioned features are accounted by the unique crystallographic structure of sapphire and anisotropy [48,54]. The theory that the structure and functional features of sapphire are correlated is supported by the results of numerous applied studies [46,48–52].

The possibility of growing shaped sapphire crystals enables to set its porosity, surface topography and structure depending on the characteristics of the potential donor area [47,50,56,58].

The technology of crystal growth with an edge foil of EGF (epidermal growth factor) allows to create constructions of unique shape and structure [48,60], which is especially important for creating anatomically advanced bone structures of the maxillofacial region.

As of today, due to the advantages described above, sapphire is successfully used in medical instrument engineering [49–53,60].

Thus, due to its excellent optical properties and ability to transmit laser radiation, as well as its physicochemical neutrality, electrolytic passivity and high temperature resistance, sapphire is successfully used in medical instrument engineering for the manufacture of tips for laser scalpels, microsurgical instruments [49,50,52,60], neuroprobes and substrates for neurodetectors [51,53].

In 2020, scientists from Germany conducted the first research to evaluate the hemocompatibility of sapphire, the results of which led to the discovery of the unique atrombogenicity of this material [54]. V.Parlak et al. in their in vitro experiment paid a particular attention to the aspects of cell adhesion to sapphire and discovered an amazing "selectivity" of atrombogenic and anti-inflammatory factors in relation to the sapphire surface, which may explain the excellent stability of this material in the biological environments of the body.

The fact that polycrystalline aluminum oxide having the same chemical formula has not demonstrated similar results, testifies in favor of the theory that sapphire physical characteristics, peculiarities of its crystallographic structure and anisotropy correspond with its unique features, bio- and, especially, hemocompatibility.

The results of studies have shown the absence of generalized toxicity in sapphire materials [53,54,57], sapphire does not demonstrate chemical instability when the pH of the environment changes [54], it is corrosion proof and completely inert, which leads to the conclusion that this material meets the main requirement for all biomaterials - biocompatibility.

Besides excellent biocompatibility, sapphire implants also meet specific requirements for bone substitute constructions.

Thus, sapphire implants, unlike metal implants, do not lead to bone tissue demineralization [53,55,58], along with ceramic constructions they possess absolute corrosion stability, while sapphire has no ceramic disadvantage such as low durability [20,22].

As it was mentioned earlier, high durability of sapphire structures can be achieved by using the high-temperature processing. It allows to set the necessary porosity with no loss of mechanical features.

Meanwhile, according to fundamental sources [30,31], the bone-substitute construction should have a porosity of at least 100 microns in order to achieve sufficient osseointegration. Fulfillment of this requirement when manufacturing sapphire constructs, as opposed to ceramic ones, does not lead to a decrease in durability parameters [31].

Sufficient cell adhesion and connection of the biomaterial surface layer with integrins are also fundamental for the implant biointegration and overcoming the rejection reaction [28,30–32,59]. This characteristic significantly depends on the physicochemical characteristics of the implant surface, which include both topographic parameters, represented by different degrees of roughness and porosity, and also the charge, electrical conductivity and chemical properties. As it was mentioned above, sapphire exhibits "selective" adhesion and chemical stability under the influence of pH of biological fluids of the organism [54], and the possibility of profiled cultivation of sapphire crystals allows to manufacture implants with specified physico-mechanical parameters.

In accordance with the results of fundamental researches the hardness index of sapphire is ~23 Gpa, which corresponds to the parameters of bone tissue [33], and the crystallographic orientation of this material is close to the structure of hydroxyapatite of bone structures, which also provides conditions for osteointegration [33,46,48].

Because of anisotropy, sapphire also has excellent tribological properties, and this is an undoubted advantage for the use of sapphire prostheses in orthopedics [55].

The fact that absolute inertness, especially magnetoresistance [51,52,54], allows sapphire materials to be used without interfering further dynamic MRI monitoring. This is an extra advantage, especially since a large number of oncological patients are the candidates for bone reconstructive surgeries.

5. Conclusion.

Due to the increasing demand for the bone tissue reconstruction surgeries and the existing disadvantages of autografts, the question of searching for a material for manufacturing bone-replacement structures that meets all the requirements to the " optimum" remains urgent.

Considering the results of fundamental research on the excellent biocompatibility and unique physical qualities of sapphire, as well as the successful experience of using this material in medical instrument engineering and the existing experience of implementation in clinical practice, we believe that consideration of sapphire as an alternative to the materials currently available for bone substitute materials is an up-to-date task standing at the crossroads of reconstructive surgery and tissue engineering.

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