

BIOCERAMICS FOR TISSUE ENGINEERING APPLICATIONS

Abstract

This chapter mainly introduces the classification of bioceramics and their biomedical applications. Zirconia and alumina composite bio-inert ceramics are currently used as femoral head, dental implants and hip replacement acetabular cups. Nanostructured, bio-inert ceramics have significantly improved toughness and stability, making them ideal for future clinical needs. Bioactive glass and calcium phosphate are being studied as scaffolds for bone cement, bone fillers, coatings and tissue regeneration and bone repair. These natural and synthetic materials, designed to have a strong binding force with bone, appear as alternatives to metal implants. These biomaterials are divided into bio-inert ceramics such as zirconia and alumina, bioactive glass and glass ceramics, and bioabsorbable calcium phosphate-based materials. Bioceramics include calcium phosphate, bioglass and hydroxyapatite, which are used as scaffolds, bone fillers and coating agents due to their mineral composition similar to hard tissues.

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I. INTRODUCTION

Many millennia ago, humans discovered that fire irreversibly converted clay into pottery, which eventually led to a huge improvement in agricultural society and quality of life and time [1]. Another revolution in the use of ceramics to enhance quality of life has occurred over the previous 40 years. This revolution involves the creative use of uniquely created ceramics to reconstruct and mend diseased or injured body parts. Bioceramics are used for this purpose.

Ceramics, considered the oldest material used by humans, have been increasingly used in medical applications, energy-related, optical and electronic applications. The use of ceramics in tissue engineering has advanced significantly during the past few decades [2]. Ceramics, biocolloids, and glass ceramics are typically included in bioceramic materials. Advances in a variety of specialised bioceramics, including tricalcium phosphate, hydroxyapatite, zircona, alumina and bioactive glass, have significantly influenced the growth of the modern medical business over the past 50 years and enhanced the standard of living for people [3]. These ceramics are able to replace or restore various damaged bone tissue systems because their composition is similar to the minerals of bone. At present, bioceramics are mainly used in the tooth root, elbow joint, knee joint, hip joint, elbow joint and skull. Numerous ceramic materials have been tried, but few have found success in clinical use on people [4]. It is now known that clinical success requires simultaneous implementation of a stable interface with connective tissue, as well as matching the mechanical behavior of the implant with the replaced tissue.

In general, we divide bioceramics into two series: bio-inert ceramics and bioactive ceramics. Their classification is based on whether the ceramic can integrate directly at the bone/ceramic interface [5]. When biologically inert material is implanted in the body, soft-tissue interactions occur, preventing the growth and formation of new bone. The germination of new bones can, however, frequently be achieved with bioactive ceramics [6]. In order to improve form integration and stop sterile implants from becoming loose, "bio-inert" ceramics for hip prostheses or knee replacements are frequently coated with bioactive ceramics [7]. At present, it is reported that CaP ceramics such as hydroxyapatite (HA) produced by corals have been used for bone defect reconstruction in orthopedics. These porous coral hydroxyapatite scaffolds have been reported to exhibit hydrothermal exchange reactions that convert the porous coral skeleton material into HA (hydroxyapatite) with a microstructure similar to that of the starting carbonate skeleton material [8].

II. CLASSIFICATION OF BIOCERAMICS

Based on their interaction with bone tissue, bioceramics are divided into three series: bioinert, bioactive, and bioresorbable ceramics (Figure 1). Ceramic materials having consistent physicochemical characteristics and strong biocompatibility are referred to as near-inert bioceramics. Alumina and zirconia with high densities and strengths are commonly referred to as bio-inert ceramics. [9].

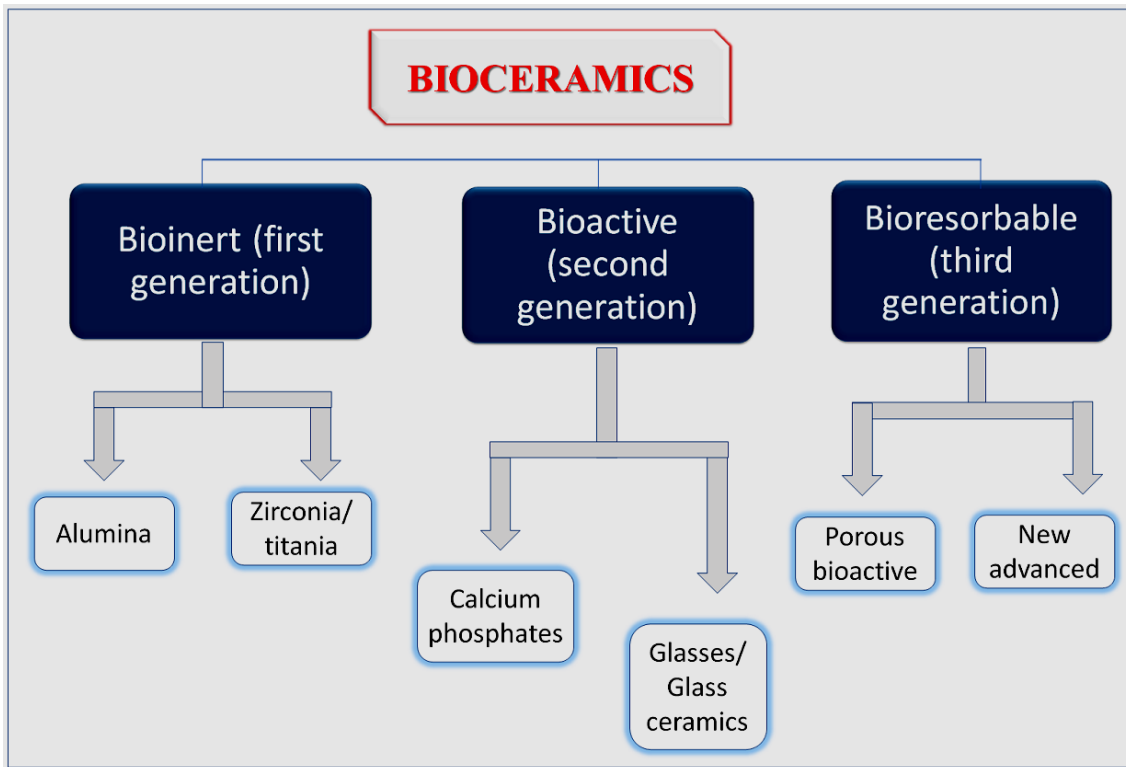


Figure 1: Classification of Bioceramics

- 1. Bioceramic for tissue regeneration:** The technique in which tissue attaches to an implant is strongly tied to the nature of tissue reaction there. None of the materials is considered inert because all materials are able to obtain reactions/response from living tissue. **Table 1** shows four types of bioceramic-tissue response.

Table 1: Types of Materials and Tissue Response at Implant.

Type of material	Tissue response
<i>Toxic</i>	<i>Death of the surrounding tissue</i>
<i>Non – toxic, biologically inactive (bioinert)</i>	<i>Formation of a fibrous tissue</i>
<i>Non – toxic, biologically active (bioactive)</i>	<i>Formation of fibrous tissue</i>
<i>Non – toxic, resorbable or degrades (biodegradable)</i>	<i>Replacement of the surrounding tissue</i>

- 2. Bioinert ceramics:** The biologically inert material does not interact with the surrounding tissues after implantation. They are resistant to corrosion and wear and offer a respectable fracture toughness. These ceramics are frequently utilized as structural support implants,

including femoral heads and bone devices. Alumina and zirconia are two types of ceramics that are bio-inert [10]. The principle uses of alumina or zirconia are in total hip and knee replacement due to its superior good biocompatibility, high wear resistance and corrosion resistance.

- **Alumina (Al₂O₃):** The biological inertness of alumina has been proven since 1975. Alumina-based bioceramics were commercially used for the first time for dental implants and acetabular cup replacements for total hip prostheses. The crystalline nature of alumina makes it insoluble in conventional chemical reagents at room temperature [11]. It was used in the manufacture of many artificial implants when alumina was introduced into the artificial femoral head. Due to the surface energy and smooth surface of alumina, it has good properties such as low wear, coefficient of friction and good corrosion resistance. Aluminum ions occupy gap sites in the hexagonal structure of Al₂O₃ [12]. Properties such as chemical inertness of alumina, strength and abrasion resistance increase its application in hard microstructure engineering. Thus, this bioceramic has been used as a synthetic bone graft or porous repair device to provide a stable binding to host tissues by using a biomimetic coating on alumina [13]. Due to good mechanical properties, alumina implants can lead to long-term survival predictions. Alumina prostheses are also used in dental implants, bone screws, jaw replacements, corneal replacements, middle ear bone replacements, and blades and screws.

- **Zirconia (ZrO₂):** Zirconia was used as a ceramic pigment for a very long time after it was discovered for the first time by Martin Heinrich Klaproth in 1789. At room temperature, zirconia is monoclinic, whereas at higher temperatures, it is cubic and tetragonal. Because monoclinic is a stable phase at low temperatures, the phase change from tetragonal to monoclinic increases toughness [14]. Phase transitions deteriorate mechanical characteristics, which can cause cracking. Therefore, manufacture of medical implants can use partially stable zirconia with normal mechanical strength. Zirconia's stability is increased by nonmetallic substances including MgO, CaO, and Y₂O₃ [15]. It has many advantages that have led to interest in other ceramic materials because its phase transition mechanism enhances toughness, which manifests itself in the parts made from them. The good mechanical behavior and wear properties of zirconia make it a superior ceramic material over alumina. It has good mechanical properties and appropriate biocompatibility. **Table 2** below shows the types of bioceramics and their advantages.

Table 2: Properties of Bioceramic Materials with Applications.

Bioceramics	Artificial Implants	Application	Advantages
<i>Alumina</i>	<i>Knee, Hip, Shoulder</i>	<i>Reconstruction of fractured part</i>	<i>High hardness low friction</i>
<i>Zirconia</i>	<i>Hip, Tooth</i>	<i>Reconstruction of fractured part</i>	<i>Corrosion resistant, hard, less friction</i>

3. **Bioactive ceramics:** It is widely acknowledged that no foreign substance introduced into a live body is entirely compatible. Ceramics that interact with surrounding bone and/or

soft tissue after being implanted within the human body are referred to as bioactive ceramics. Following implantation, bioactive materials form a direct link with live tissues in a manner similar to how bones grow together [16]. These fragile ceramics have been used to fill up periodontal abnormalities and small-bone flaws. Bioglasses and glass-ceramics are two examples. Calcium phosphate ceramics, bioactive glasses, and glass-ceramics are a few of the key families of bioactive ceramics.

- **Calcium phosphate ceramics:** Calcium phosphate ceramic is a bioactive ceramic, which is extensively used due to the fact of its high biocompatibility, low system toxicity and bone growth promoting properties [17]. Although calcium phosphate ceramics produce minimal immune and external body reactions, they additionally act as bone conductors and bone integrators, so that after implantation, the ceramic create a layer of hydroxyapatite and stubbornly bind via cell activity. The required calcium and phosphate ions come from the bones and the implants themselves. Calcium phosphate ceramics are additionally chemically stable, light in weight, chemically and morphologically comparable to bone minerals. Calcium phosphate ceramics are characterized through the composition of calcium and phosphate ions, the presence of impurities, pH, part of the pressure of water, the temperature of preparation or sintering, and the synthesis method [18]. They are resistant to microbial attacks, pH modifications and solvent conditions, but are hard to sinter. Calcium phosphate ceramic support, etc. increases lattice gaps and grips in the complicated stress state of the performance of poor mechanical strength, and then, its resistance to fatigue reduces [19]. This technique makes calcium phosphate ceramics which are incapable in load bearing applications. But, a material can be regarded as a viable choice for artificial bone grafts.

Although calcium phosphate ceramics are usually chemically stable, stability depends mostly on the temperature and the presence of water, such as water in body fluids [20]. The imbalance in the ratio of calcium to phosphate ions leads to the formation of unrelated phases, which prevents their use as organic materials. For example, it has been suggested that compound contained calcium phosphate ratio less than one has a greater degradation rate and is not appropriate for biological implantation. However, there are many sorts of calcium phosphate that are commercially used, and the two most usually used materials for tissue regeneration are hydroxyapatite (HA) and triamcinolone phosphate (TCP) [21].

- **Bioactive glasses:** Bioactive glasses are the most promising biological material that exhibits excellent bioactivity and biocompatibility by forming HAp layers on the material interface in interaction with bones and tissues [22]. Bioglass was invented by University of Florida professor Larry Hench in the early 1970s. According to Hench recommendation, wt% 45S5 bioglass compositions include 45% SiO₂, 24.5% Na₂O, 24.5% CaO, and 6% P₂O₅. There are different types of BGs: traditional silicates, such as bioglass 45S5; phosphate glasses; and borate glasses. Glasses are composed of network formation, modification and intermediate oxides [23]. They exhibit an amorphous feature, reflecting structural disorders. The composition, texture, density, and porosity of BG, among other characteristics, all have an impact on its biological activity. [24]. Recent studies of different CaO-SiO₂-P₂O₅ have shown good *in-vitro* biological activity and

biocompatibility. Bioactive glasses which related to Class A bioactive materials, can be easily bind to bones and soft tissues and accelerate the stimulation of bone growth. The bone bonding capability of the glasses is associate to their ability to form hydroxycarbonate surface layers (HCA) [25]. A series of chemical reactions occur during BG implantation, resulting in the formation of a layer of crystal HA on its surface that explains its biological activity.

However, recent studies have shown that the role of BGs is basically to release critical concentrations of bioactive ions at the rate required for cell proliferation and differentiation. The tuning of all new concepts and great possible components of bioglass bioactivity has inspired many research efforts to discover and test new formulations, add new elements to their structures, and produce composite bioglass-polymer/metal/ceramics in search of superior bionic behavior. In view of this, the size dependence of spectacles is thought to improve the production of effective bioactive substances through nanotechnology. **Table.3** below shows the role of bioglass and calcium phosphate ceramics in tissue regeneration.

Table 3: Role of Bioglass and Calcium Phosphate Ceramics in Tissue Regeneration.

Bioceramics	Artificial Implants	Application
<i>Bioglass</i>	<i>Spinal Fusion</i>	<i>Protect Spinla Cord</i>
<i>Calcium phosphate, Hydrocyapatite</i>	<i>Tooth, bone</i>	<i>Replacement of damaged teeth</i>

4. Bioresorbable ceramics: The *In-vivo*, bioresorbable materials are gradually absorbed and then replaced by bone. Several examples include calcium phosphates, calcium phosphate cements, calcium carbonates, and calcium silicates [26]. Second generation bioactive ceramics are progressively being replaced by third generation bioresorbable ceramics, either through modifications to existing materials or the development of entirely new materials that incorporate biological agents [27].

- Mesoporous bioactive glass:** It has been universally accepted that the mesoporous material has a large surface area, and well-mannered mesoporous structure, an adaptable pore size and volume, a clear surface characteristic, and attractive features to be modified. Mesoporous materials have so been carefully considered for a wide range of application such as adsorption/separation, catalysis and the production of nanomaterials. In recent times, research on the application of mesoporous porous materials has been extended to the area of biomaterials science, one of which is drug delivery systems, and various studies on controlled drug delivery systems based on mesoporous porous materials have been published in the past few years. The other direction of the mesoporous material in the study is for bone tissue regeneration. So far, a number of research groups have studied studies related to the mesoporous porous material of bone regeneration. For example, Vallet-Regi systematically studied the *in-vitro* biological activity of different types of mesoporous porous materials and determine that phosphate-like layers can be formed on MCM-48, SBA-15 [28]. Zhao et al. successfully prepared a highly ordered hexagonal MBG (SiO₂-CaO-P₂O₅) powder with different chemical compositions, and demonstrated that MBG has

superior bone-forming bioactivity *in-vitro* compared to ordinary bioactive glasses [29]. The development of biomaterials for use in bone tissue regeneration has shown a current tendency toward the development of engineering structures that will provide the essential assistance for the management and rebuilding of human systems.

- **Nanobioactive Glasses:** Nanomaterials have unique physical and chemical properties (e.g. small size, high surface area/volume ratio) and form a wide range of applications, from high-quality consumer design to effective disease diagnosis and treatment. When tissues such as bones or teeth come into contact with nanoparticles, they can be deposited or mineralized more quickly when they come into contact with micron-scale particles [30]. In addition, the bone structure shows nanoscale features consisting of a custom mixture of collagen fibers and HAP nanocrystals. The Nanobioglasses with higher specific area not only allows for faster release of ions, but also allows for higher protein adsorption, so bioactivity can be expected to be enhanced [31]. In order to improve the properties of biological materials such as biological activity or bio-absorption or regeneration, bioactive materials such as glass and glass ceramics are converted into nanostructure materials [32]. The transition from bulk BG to NBG is used to increase the formation rate and thickness of the HAp layer.

Engineered mesoporous bioactive glass (MBG) shows the possibility of highly ordered mesoporous channel structure with pore sizes ranging from a few nanometers. A major feature of MBG is its increased specific surface area and pore volume, with higher biological activity compared to non-porous BG materials [33]. The advantage of BGs with other bioceramics (i.e. HAp) is that they exhibit faster formation of apatite in physiological fluids and on the surface of scaffolds *in- vivo* study [34]. Studies have also shown that BG can improve cell adhesion and increase bone proliferation and differentiation [35]. BG components containing CaO-SiO₂-P₂O₅ can be bonded to soft and hard tissue without involving the fiber layer. Currently, it is considered that nanobioglass particles are very fruitful in regenerating bone defects, but the compositions that have regulatory approval as particulate synthetic bone grafts are not convenient for making fibres, scaffolds or coatings. Novel bioglass compositions are expected to obtain regulatory approval by meeting the characteristics required for biomedical applications.

III. CONCLUSIONS AND FUTURE TRENDS

This chapter provides a brief description of traditional and existing synthetic bioceramic materials for tissue regeneration. These materials improve the compatibility, suitability and longevity of implants. Bioceramics have been widely used in the biomedical field as orthopedic and dental implants and porous stent implants. While ceramics and bioactive glass have the ability to produce osteoconduction and osteoinduction, bio-inert ceramics, such as zirconia and alumina, have excellent mechanical qualities and can be employed for load-bearing applications. These materials require further research to improve the quality and stability of implants in patients. Future developments will involve tailoring the composition, molecular surface and microstructure chemistry of various bioceramic materials to the unique biological and metabolic needs of tissues or disease states. Millions of people's quality of life as they age should be improved by this strategy. In addition, in the

future trend, two ways to treat cancer have been proposed; treatment is carried out by hyperthermia, as well as radiation therapy. High-temperature treatment involves implantation of bioceramic materials containing ferrites or other magnetic materials. The implant and surrounding area are then heated by an alternating magnetic field that is applied to this region. The chemistry, composition, and micro- and nanostructures of materials are now being researched to increase their biocompatibility.

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