

# Bio-Ceramics — An Introduction to Bone Repair Materials

**Kirubanandan Shanmugam\***

Independent Research Professional, Chennai, India

\**Corresponding author:* Kirubanandan Shanmugam, ksh1005@yahoo.com

**Copyright:** © 2024 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

**Abstract:** The realm of biomaterials, particularly ceramics, continues to revolutionize the fields of medicine and dentistry through their diverse applications and groundbreaking capabilities. From dental restorations to orthopedic implants and beyond, the biocompatibility, mechanical strength, and durability of ceramics have made them indispensable in the pursuit of enhancing patient care and outcomes. As research progresses, the potential of ceramics in supporting tissue regeneration, promoting bone healing, and creating more effective medical devices and implants is boundless. The ongoing development of bioactive, bio-reactive, and re-absorbable ceramics, along with advancements in nanotechnology and composite materials, promises to further expand the horizons of medical engineering. The journey of ceramics from traditional applications to their pivotal role in regenerative medicine and tissue engineering underscores the transformative power of biomaterials in shaping the future of healthcare. As researchers continue to explore and innovate, the promise of ceramics as a cornerstone of medical and dental advancements remains as robust as the materials themselves, paving the way for a future where the integration of biology and engineering fosters unprecedented healing and restoration possibilities.

**Keywords:** Re-absorbable ceramics; Bio-reactive ceramics; Bio-inert ceramics; Bio-composites; Bioactive glass

**Online publication:** August 23, 2024

## 1. Introduction

Ceramics have been widely used as biomaterials in the field of medicine and dentistry due to their biocompatibility, mechanical strength, and durability. Some common applications of ceramics as biomaterials include the following. Dental ceramics: Dental crowns, bridges, and veneers are commonly made from ceramics due to their natural appearance, biocompatibility, and resistance to staining and wear. Orthopedic ceramics: Ceramics such as alumina and zirconia are used in orthopedic implants, such as hip and knee replacements, due to their high strength, low wear rates, and biocompatibility. Bioactive ceramics: Bioactive ceramics, such as hydroxyapatite and tricalcium phosphate, can bond directly to bone tissue and are used in bone grafts, dental implants, and other applications where bone regeneration is needed. Porous ceramics: Porous ceramics are used in tissue engineering applications, such as scaffolds for cell growth and drug delivery systems, due

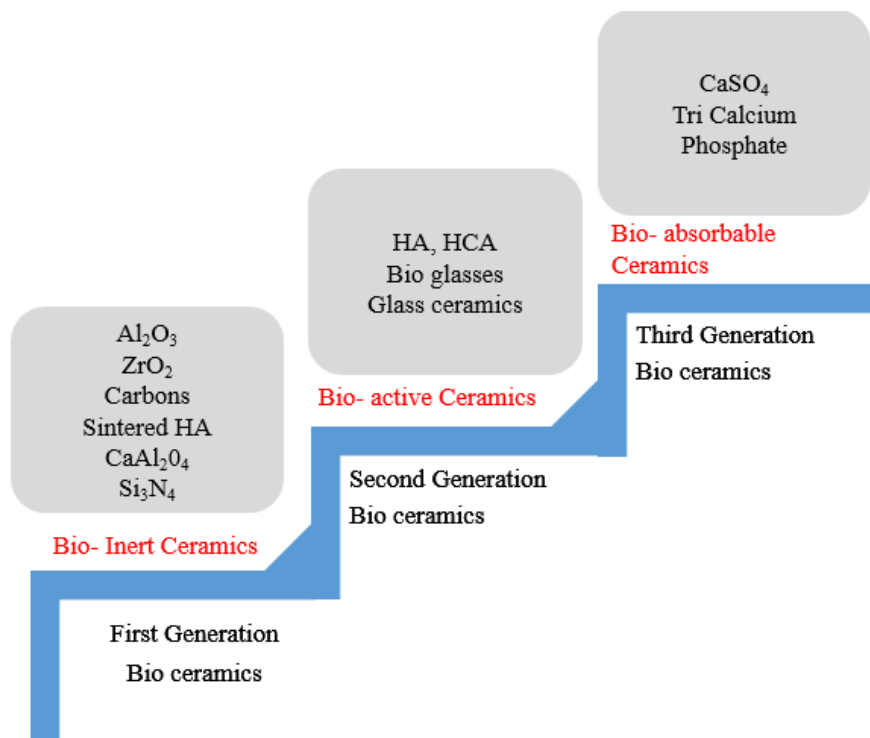
to their ability to support cell growth and promote tissue regeneration. Overall, ceramics offer a wide range of properties that make them suitable for use as biomaterials in various medical and dental applications. Ongoing research is focused on developing new ceramic materials with improved biocompatibility, mechanical properties, and functionality for use in regenerative medicine and other advanced healthcare applications.

Biomaterials are materials that are derived from natural sources, such as plants, animals, or microorganisms, and are used in the field of medicine and healthcare. These materials are often used in the development of medical devices, implants, and tissue engineering applications. Biomaterials are designed to interact with biological systems safely and effectively and can be used to replace or repair damaged tissues and organs in the body. Examples of biomaterials include collagen, alginate, and chitosan. Hydroxyapatite: A natural mineral form of calcium apatite that is commonly used in bone grafting procedures due to its similarity to the mineral component of human bone. Calcium phosphate ceramics: Bioceramic materials that have shown excellent biocompatibility and bone regeneration properties. They can be used in the form of porous scaffolds or coatings on implants. Collagen: A natural protein found in connective tissues that can be used as a scaffold for cell growth and tissue regeneration. Collagen-based materials are often used in combination with other biomaterials for bone regeneration. Polymers: Synthetic materials such as polylactic acid (PLA), polyglycolic acid (PGA), and polycaprolactone (PCL) can be used to create scaffolds for tissue engineering applications. These polymers can be tailored to have specific mechanical and degradation properties. Bioactive glasses: Glasses that can interact with biological tissues and promote tissue regeneration. Bioactive glasses release ions that can stimulate bone growth and integrate with surrounding tissue. Silk fibroin: A protein derived from silk fibers that have been used in tissue engineering for its biocompatibility and mechanical properties. Silk fibroin scaffolds can support cell growth and promote tissue regeneration. Composite materials: A combination of different biomaterials, such as ceramics and polymers, can be used to create scaffolds with enhanced properties for hard tissue regeneration. Composite materials can provide a balance of mechanical strength, biocompatibility, and bioactivity. Nanomaterials: Nanotechnology has enabled the development of nanomaterials with unique properties for tissue regeneration. Nanoparticles, nanofibers, and nanocomposites can be used to enhance the performance of biomaterials for hard tissue regeneration.

This paper deals with the scope of bio-ceramics for hard tissue repair and their types for clinical applications.

## 2. Ceramics as biomaterials

Ceramics is a biomaterial used for both soft and hard tissue repair. Because of their superior biological inertness and higher compressive strength, ceramics are inorganic composites and non-metallic materials that are useful for developing scaffolds for tissue engineering and regenerative biomaterials for hard tissue repair. Silicates, metallic oxides, carbides, sulphides, refractory hydrides, selenides, and carbon structures like diamond and graphite are the most often utilized ceramics in biomedical applications. Ceramics have very few drawbacks because of their great hardness, including brittleness and poor mechanical characteristics. The poor electrical conductivity, low thermal conductivity, and high melting point of ceramics are all highly beneficial properties. Owing to the swift advancements in materials science, ceramics are now utilized in medical engineering as possible bio-ceramics and bio-composites. **Figure 1** displays the categorization and examples of ceramic materials. Three primary categories comprise the biological applications of ceramics, including re-absorbable ceramics, bio-reactive ceramics, and bio-inert ceramics.



**Figure 1.** Classification of ceramics as biomaterials

## 2.1. Re-absorbable ceramics

Re-absorbable ceramics are substances that, through physiological medium and related biochemical/biological interactions within the body, can chemically break down into particle fragments or inorganic chemical species, which can subsequently decay and be reabsorbed by the endogenous tissue. The body does not suffer any negative effects from the broken pieces of ceramics as they go through the metabolic route. When utilized as implant or tissue engineering structures in orthopedic applications, it breaks down over time and is replaced by endogenous tissues, which leads to the regeneration and repair of normal, functioning bone. The breakdown process of calcium phosphate implants is examined in **Figure 2**.

The capacity of these materials to produce osteoid, to be osteoconductive, or to permit osteoblast integration of the materials with bone, is their primary characteristic. The most often used substances are calcium phosphates, hydroxyapatite, and plaster of Paris, or calcium sulfate dihydrate. The rates of osteoid development and degradation differ depending on the kind of material. These materials usually undergo a considerable reduction in their mechanical properties throughout the reabsorption process, which causes a major change in their load-bearing capacity during the integration period. Tissue engineering has made use of re-absorbable scaffolds seeded with cells, which can function as a synthetic extracellular matrix. It is also broadly classified into synthetic re-absorbable ceramics and natural ceramics. The artificial bio-reabsorbed ceramics consist of hydroxyapatite and calcium phosphate. It may crystallize into salts, like the primary building block of teeth and bones, hydroxyapatite. Outstanding biocompatibility and the ability to directly bind with hard tissue, such as bone, are two qualities of hydroxyapatite. The naturally occurring bioresorbable ceramics are made of coral, which is converted into hydroxyapatite, which is biocompatible with the body's environment, promotes bone formation, and is utilized to heal broken or damaged bone. According to Paramsothy and Ramakrishna, the scaffold made of these materials is employed as a template for replacing bone abnormalities and diseases <sup>[1]</sup>.

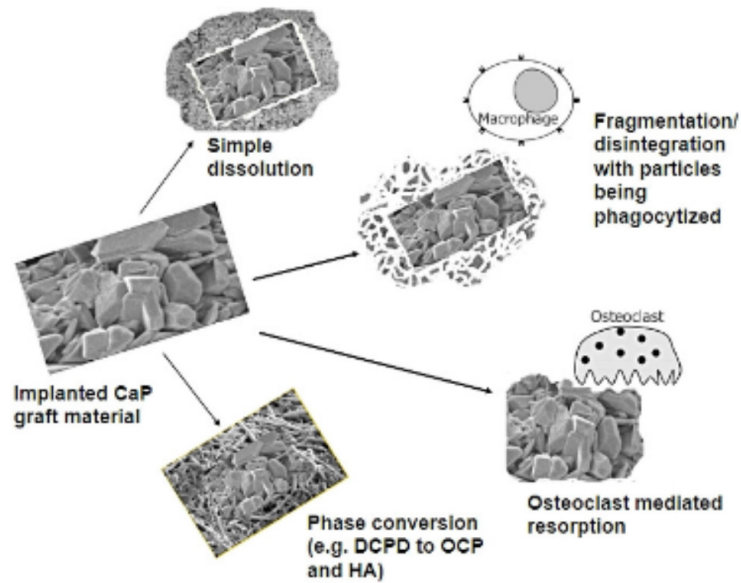


Figure 2. Mechanism of degradation of calcium phosphate implants <sup>[2]</sup>

## 2.2. Bio-reactive or bioactive ceramics

These ceramic materials can interact chemically with hard tissue, forming bonds at the contact. Bioglass and Ceravital, which are utilized as fillers in bone cement, as well as composites for hard tissue restoration and implant interfacial coatings, are appropriate examples of these materials. These materials are coated on the implants to improve their biocompatibility and capacity to respond to a physiological environment. Furthermore, under the impact of the physiological environment and reduced stress at the interface between implants and tissues, the covering of the implant made of these materials encourages osteointegration with the surrounding tissue. Implants with bioactive ceramic coatings have increased surface activity to support the tissue regeneration process <sup>[3]</sup>. **Figure 3** depicts the development of a layer of bioactive ceramics that interacts with cells to initiate the process of repair and regeneration.

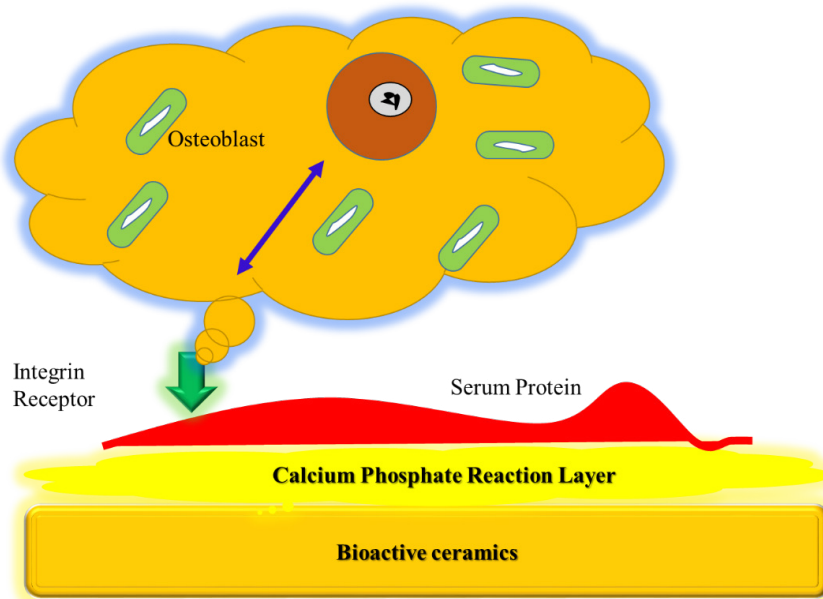


Figure 3. Contact of the ceramic with biological fluids leads to the cell signaling process <sup>[4]</sup>

## 2.3. Bio-inert ceramics

Biocompatible materials that retain their mechanical and physical characteristics after implantation are known as bio-inert ceramics. The lack of a biological reaction and non-carcinogenicity to surrounding tissue are the intriguing features. Bioinert ceramics are often utilized in orthopedic repair as an excellent biostructure support. Owing to their superior wear characteristics, these materials are helpful for sliding applications. Alumina (aluminum oxide;  $\text{Al}_2\text{O}_3$ ), zirconia (zirconium oxide;  $\text{ZrO}_2$ ), pyrolytic carbon, and silicon nitrides are the most often occurring minerals in this group<sup>[3]</sup>. Carbon as a bio-inert ceramic material offers superior biocompatibility, high strength, and adjustable lubricity and conductivity.

### 2.3.1. Ceramics biocomposites as biomaterials

Composites are the macroscale mixtures of two or more different materials, such as metals, ceramics, polymers, or any other synthetic material. These materials offer the appropriate physical and mechanical characteristics for each to be utilized. When designing composites, a continuous phase known as the matrix is often sandwiched between a discontinuous phase for immobilization or embedding. The forces that are transferred at the contact between the composite materials determine how the components behave. The volume percentage, shape, and orientation of the constituents all affect the composites' characteristics. Particulate and fibrous composites are the two types of composites. Small particles are incorporated into a continuous matrix as part of a particulate composite. These materials are usually isotropic, meaning that they lose some flexibility or stiffness in exchange for greater toughness in all directions. These materials include, for example, ceramic matrices containing silica particles used as dental composites and rubber catheters reinforced with silica ( $\text{SiO}_2$ ) particles. One particular kind of particle composite is a porous material, in which the air serves as the inclusion phase. It has been applied to both soft and hard tissue healing, particularly in regenerative medicine and tissue engineering projects where porous composites encourage tissue ingrowth. Fibers immobilized in a matrix are called fibrous composites. One use of a fibrous composite is joint replacement with carbon-reinforced polyethylene. For a variety of uses in tissue engineering and regenerative medicine, a unique class of fibrous composites is laminated, consisting of multiple stacked fiber composite laminate.

### 2.3.2. Ceramics as biomimetic materials

A synthetic material that mimics or resembles naturally occurring materials while maintaining functioning is called a biomimetic substance. "A synthesized or fabricated material via biomimetic processes based on the structure found in biological systems" is what is meant to be understood as the biomimetic material. The materials have to have a synthetic origin, replicate physiological functions, create a link with natural structures, and not cause any biological reaction at the regeneration site. Certain materials can be combined with other bioactive materials because they exhibit bioactivity in the physiological environment. Bentonite, synthetic hydroxyapatite, and Mineral Trioxide Aggregate (MTA) are the prevalent materials. When it comes to creating scaffolds and other structures for tissue engineering, where cells may be implanted to promote improved tissue regeneration, ceramics are thought of as biomimetic materials. The complex ceramic materials that have been synthesized using natural structures resemble the biological scaffold that exists naturally and may be used to seed cells of interest. These models provide a new structure of hard tissue and an analogy for bone<sup>[5]</sup>. The most significant materials in these categories are bioceramics made of calcium phosphate, which are synthesized using a structure called coralline that mimics bone. As a result, these materials are utilized in implants for bone formation in orthopedic applications. Another intriguing substance is calcium orthophosphate, which is employed as a replacement for bone because of its remarkable biocompatibility with a physiological environment and osteointegration due to its chemical resemblance to mammalian teeth and bone. Furthermore,

calcium orthophosphate functions as an osteoconductive, or scaffold to promote the growth of new bone at the site of injury as well as an environment that is favorable for osteoblast adhesion and proliferation. It would be impractical to employ these materials to repair significant osseous flaws since they may be used only as coatings and fillers. These materials are very porous and exhibit poor mechanical behavior. The proportion of phosphate to calcium might regulate the characteristics of these materials. Because of the high solubility and acidity of the components, calcium orthophosphate is not appropriate for implantation into the body when the ratio of calcium to phosphate is less than 1 [6].

Dental ceramics, dental composite material, and glass ionomer cement are some other examples of these types. Glass ionomers are materials composed of an acid and base component of polyelectrolyte, which is a copolymer or homopolymer of alkanolic acids, an unsaturated carboxylic acid class. Calcium aluminosilicate, a glass-containing fluoride biomimetic substance with strong adhesion to the tooth structure, minimal shrinkage and microleakage, and dimensional stability at high humidity, is the component of glass ionomer cement. Glass ionomer cement is also referred to as man-made dentin, synthetic dentin, or dentin replacement since it can replace dentin with a biomaterial. As a dentin replacement, glass ionomer cement may be utilized to patch up perforations made during root canal therapy. Dental composite material is utilized in endodontics, conservative dentistry, and other dental problems. Dentin is made up of 70% inorganic materials, 20% organic materials, and 10% water. The dentin contains the following inorganic compounds: calcium (26.9%), phosphorus (13.2%), carbonate (4.6%), sodium (0.6%), and magnesium (0.8%). Collagen, proteins, and lipids make up about 90% of the dentin's organic content. The inorganic fillers used in endodontics include quartz and glass particles with sizes ranging from 0.1 to 100  $\mu\text{m}$ , as well as colors like titanium oxides and coupling agents like organosilanes. In contrast to hybrid resins, which are less aesthetically pleasing, aesthetics, microfilled, and nanofiller composites contain tiny filler particles that scatter light. Fillers exert an impact on them.

The tooth's glossy surface is influenced by the filler's size and form. The form of the fillers affects how light scatters on the tooth's surface, and composites packed with nanoparticles transmit light more efficiently than composites without nanoparticles. Excellent aesthetics, extended color stability, high compressive strength and hardness, superior chemical inertness, and exceptional biocompatibility are all possible with dental ceramics. Based on the silica structure, it has two phases: a glass phase and a crystal phase. The counterparts of the dental prism rods found in porcelain are leucite and lithium disilicate crystals. Four to eight micrometers is the diameter of the enamel rod or prism. The hydroxyapatite crystals are arranged into a compact agglomeration. Its cross-section features a recognizable keyhole form. In addition to having superior strength and abrasiveness, dental ceramics can absorb compressive stresses. Dental ceramics have the same hardness coefficient as dental enamel in teeth.

### **3. Bioceramics in the human body and its applications**

Every year, biomaterials increase people's survival rates and significantly raise the level of living quality of people. Biomaterials have a wide range of applications, such as dental implants, vascular grafts for tissue engineering, corneal bandages for corneal repair, wound dressings for soft tissue repair, and scaffolds for tissue engineering that can be used for hard tissue and skin replacement. Biomaterials based on ceramics are important to biomedical science and technology. Novel biomaterials have several advantages over conventional grafts, including decreased morbidity, cost-effectiveness, repeatability, sterility, and safety. The creation of novel biomaterials made possible by developments in material science and engineering greatly enhances patients' quality of life and overall health.

The functionality and structure of organs and tissue serve as a common basis for the development of novel biomaterials. Therefore, to develop new biomaterials and designs for scaffolds for tissue engineering, it is vital to understand the structure and function of the human body. From smallest to biggest, the human body is a single, well-organized organization with several complicated levels: chemical, cellular, tissue, organ, system, and organ. The section that follows addresses the levels of the human body in a hierarchy. **Figure 4** depicts the normal human body structure. Specifically, the finest examples of ceramics found in the human body are found in bone and teeth. Joints, tendons, cartilage, and other calcified tissues resemble ceramic composites with additional extracellular proteins.

The 26 distinct types of elements that make up the human body are necessary for life. Of these, the four most prevalent elements—oxygen (O) (65.0%), carbon (C) (18.5%), hydrogen (H) (9.5%), and nitrogen (N) (3%)—account for 96% of the body weight. Proteins, fats, carbohydrates, and DNA are common examples of substances that consist of these four components. These components are also found in bodily fluids, water (H<sub>2</sub>O), and carbon dioxide (CO<sub>2</sub>). In addition to these, the metallic elements that make up 3.8% of body weight are calcium (Ca) (1.5%), phosphorous (P) (1.0%), potassium (K) (0.4%), sulfur (S) (0.3%), sodium (Na) (0.2%), chloride (Cl) (0.2%), magnesium (Mg) (0.1%), and iron (Fe) (0.1%). Potassium (K) is a major element that maintains the heartbeat at a normal rhythm. Calcium (Ca) is a major element of hard tissues and other calcified tissues like bones and teeth. Iron (Fe) is a major element required for oxygen transport by red blood cells. Sulphur (S) is a major element present in most proteins that maintain the strength of various tissues by forming sulfur “tie-bars” (also called sulfhydryl bonds) between connective tissue proteins. The minor elements include silicon (Si), tin (Sn), vanadium (V), zinc (Zn), aluminum (Al), boron (Br), chromium (Cr), cobalt (Co), copper (Cu), fluorine (F), manganese (Mn), iodine (I), molybdenum (Mo), and selenium (Se).

It makes up 0.2% of the human body weight and is involved in hormone release, enzyme activity, and homeostasis. Anything made up of two or more elements joined by chemical bonds is called a molecule. Numerous chemical molecules and substances found in the human body may be roughly classified as either organic or inorganic. An inorganic compound is one that does not include carbon, such as water or calcium phosphates, whereas an organic substance contains carbon, such as proteins and carbohydrates.

The next level of structural organization, known as the cellular level, is where molecules come together to create the body’s fundamental functioning structures or cells. It is the smallest unit that can split, multiply, and replenish itself on its own. The human body is made up of billions of distinct cell kinds, such as muscle, neuron, and blood cells, each of which is in charge of performing a single task. Despite the wide range of sizes, shapes, and functions that cells might have, most of their fundamental characteristics remain the same. The human body’s cells are primarily made up of three parts: the cell membrane, the cytoplasm, and the nucleus.

A collection of related cells and surrounding materials are arranged to carry out a certain function at the tissue level. Compared to cells, tissues are a little more complicated. Based on their mechanical and structural characteristics, tissues can be generically categorized as soft or hard from an engineering perspective. As an illustration, bone and teeth belong to the hard tissue category, which is stronger (tensile strength) and stiffer (elastic modulus) than soft tissue. Prominent examples of the latter category are skin and cartilage. Strength and elastic modulus are two characteristics that have been used to distinguish between soft. **Table 1** illustrates the primary mechanical property differences between soft and hard tissues, which may assist readers in determining the sort of material best suited for a certain application. The human body is composed of four different types of tissue: muscle, nerve, connective, and epithelial tissue. Connective tissue is typically utilized to study how ceramic biomaterials interact with different kinds of tissue.

**Table 1.** Mechanical properties of tissues

Tissue	Modulus (MPa)	Tensile Strength (MPa)	Strain at break in %
Soft Tissues			
Smooth Muscle, Relaxed	0.006	-	300
Smooth Muscle, Contracted	0.01	-	300
Pericardium	20.4 ± 1.9	-	34.9 ± 1.1
Patellar tendon (29–50 years old)	660 ± 266	64.7 ± 15	14 ± 6
ACL ligament (21–40 years old)	345 ± 22.4	36.4 ± 2.5	15 ± 0.8
Hard tissues			
Cortical bone	17000–24000	90–130	1–3
Cancellous bone	0.1–4.5	10–20	5–7
Cartilage	0.001–0.01	10–40	15–20

Different tissue types are arranged together at the organ level to create the body's structure and carry out a single purpose. Organs are more intricately designed and functioned than tissues. The body is made up of several organ systems. The skin, bones, liver, kidneys, lungs, brain, eye, stomach, and heart are a few examples. The biggest organ in the human body is the skin, which is followed by bone. This paper goes into great depth on the composition and purpose of the skin and bones in the upcoming part.

There are two main classifications for the characteristics of human bodily tissues. These are the soft and firm tissues that are typically damaged and injured. Normal bones and teeth are examples of hard tissue, which is distinguished by its strength, hardness, and elastic modulus. Since it is the fundamental load-bearing component of the human body, it serves a distinct purpose and, as is evident, has a high strength and elastic modulus. Ceramic materials are often appropriate for replacing hard tissue. Since there is significant elastic deformation but no plastic deformation. As this paper will discuss later, it is essentially a composite structure—rather than a straightforward monolithic structure—which explains why it contains so many elastic modules. Because ceramics are brittle and lack flexibility, they are especially well-suited for hard tissues. Thus, it is evidently not the soft tissues, but rather the rigid tissues. It is possible to replace soft tissues or find a better material to do so, so polymers and other composite materials are obvious choices. Therefore, it stands to reason that the body's hard tissues are of interest to us.

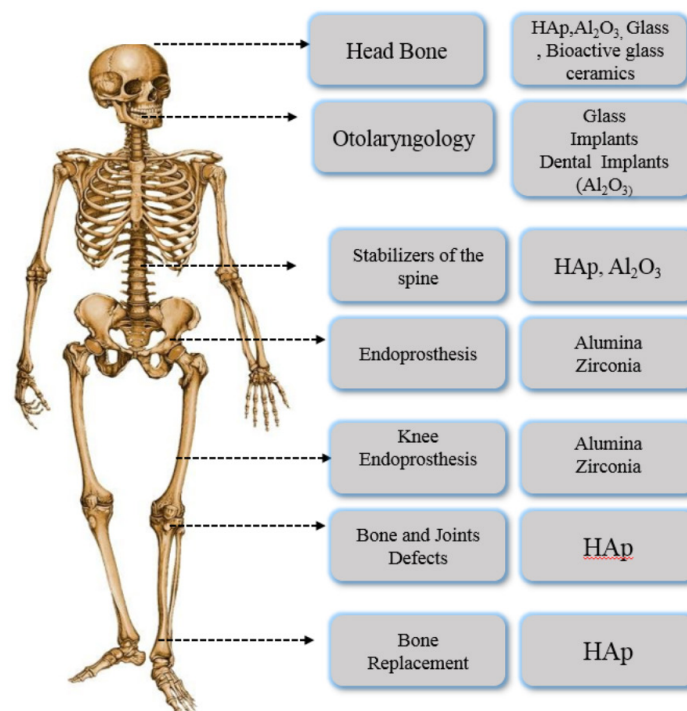
There are at least two different kinds of bones: cortical bones, which have a highly anisotropic microstructure and a much-increased strength in the loading direction; and cancellous, trabecular, or spongy bones, which are porous. The optimal balance of strength and modulus can be found in the cortical bones. Enamel, dentine, and cancellous bone come next. However, bone properties vary according to where in the body they are located. Hard tissue type 1 is primarily composed of four components: 16.5% collagen fibers, 60% hydroxyapatite, 2% other organics, and 23.5% water. The components of hard tissue (II) consist of 95% hydroxyapatite, which is found in tooth enamel.

Natural bones are thought to be natural nanocomposites, with collagen serving as the fiber bundle, proteins, polysaccharides, and so on. functioning as the cement, and HAp nanoparticles dispersed throughout. It is a highly intricate structure, and the way that nature created this specific substance is amazing. The mechanical characteristics, or similar, average values for the human system, or around 18 GPa. The cortical and cancellous bones have a density of around thirteen GPa, a dentin of roughly eleven, and an enamel of only 0.4, which is only a layer on the dentin. Therefore, the value for the elastic module is often in the range of 10 to 20 GPa.



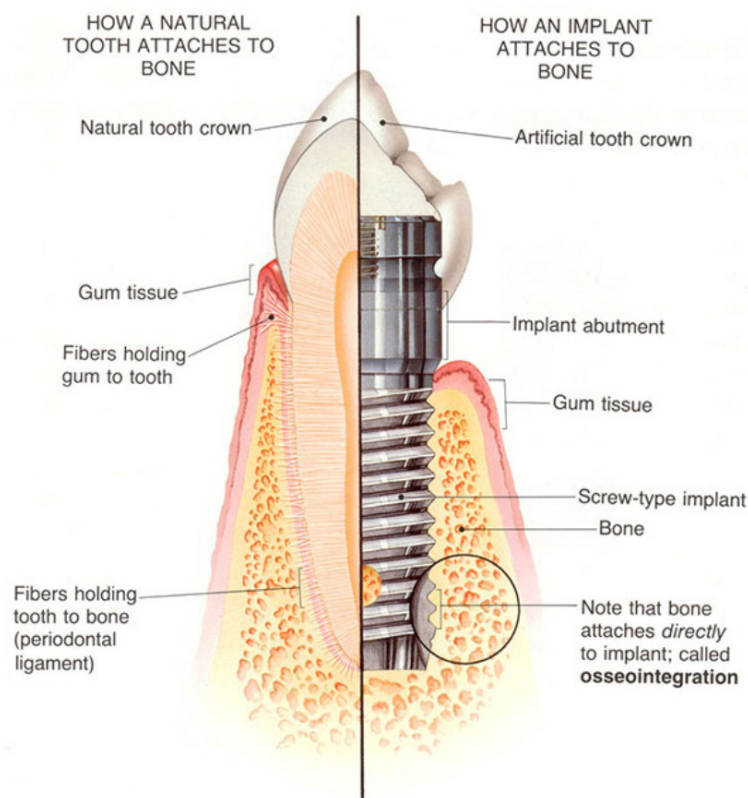
The cortical bone has a tensile strength of 135 MPa, compared to 52 MPa for cancellous bone, which is less than half that of cortical bone, much less for dentine, and much less for enamel. Thus, this is essentially the mechanical characteristic of the many kinds of human bones.

In the human body, ceramics constitute the basis of both bone and teeth. Bone is regarded as a major supporting organ since it is a hard, stiff kind of connective tissue that is involved in the creation of the skeletal system. Not only does bone give an organism mechanical support, but it also stores minerals, especially phosphate and calcium. Bone is thought to be a collection of sophisticatedly constructed hierarchical structural components at different length scales. Macroscopically, adult lamellar bone may be divided into two types: compact bone and spongy bone. They are arranged with macro-to nanoscale multilayer holes to create various activities, such as the movement of bodily fluids, nutrients, and oxygen. About 20% of the total bone is made up of spongy bone. It is also frequently referred to as cancellous or trabecular bone. Compared to compact bone, it is less thick and lighter. Compared to compact bone, it has a larger concentration of blood veins and a higher porosity. If the pores are particularly big, the porous architecture may be seen with ease with lower power microscopes or even the unaided eye. The pores' diameter ranges from a few micrometers to millimeters. Conversely, compact bone has a far higher density than spongy bone. Another name for it is a dense or cortical bone. It makes up around 80% of the whole bone. Because of its reduced porosity, there are fewer blood vessels concentrated there. Because of its lower porosity, its porous architecture is not evident to the unaided eye. The pores have a diameter of around 10–20  $\mu\text{m}$  and are mostly spaced 200–300  $\mu\text{m}$  apart. While spongy bone primarily acts in compression, compact bone functions mechanically in tension, compression, and torsion. The Haversian system, or osteon, is the primary structural unit of compact bone at the microstructural level. These units serve as weight-bearing pillars. In contrast, spongy bone is composed of an interconnected structure of trabeculae rather than such osteon units. There are three different cellular structure types seen in trabeculae: plate/plate-like, plate/bar-like, and bar/bar-like. According to studies conducted on the nanoscale, bone is mostly composed of collagen fibers and hydroxyapatite (HA) nanocrystals. The interactions between the mineral matrix determine the mechanical behavior of the bone.



**Figure 4.** Structure of human body and ceramics as biomaterials in replacement

The restoration of teeth is a significant additional use for biomaterials based on ceramics (**Figure 5**). The creation of ceramic-based materials for dental tissue engineering and regeneration requires an understanding of the structure and function of teeth. Mammalian teeth are used for chewing and food dissolution. The enamel organ, dental papilla, and dental follicle are the three components that make up the tooth. The hardest and most mineralized material is tooth enamel, which is made of hydroxyapatite, a crystalline calcium phosphate. Dentin is found between the pulp chamber and enamel or cementum and is composed of 70% inorganic components, 20% organic materials, and 10% water by weight. A unique kind of bone called cementum is similar to the substance that covers a tooth's roots. It is mostly composed of hydroxyapatite (45%), collagen (33%), and water (22%). The core of teeth, known as the dental pulp, is mostly made of soft connective tissue [7].



**Figure 5.** Structure of teeth and surrounding calcified tissues [8]

Zirconia ceramics are substituted for metallic implants in dental applications and are utilized as dental implants. The human body has several calcified tissues, in addition to bones and teeth, that need to be treated and restored with ceramic materials. Other areas of calcified tissue include the hips and joints.

#### 4. Synopsis of ceramics biomaterials

The most exceptional qualities for creating implants that effectively replace and regenerate both soft and hard tissues are found in bioceramics. Any potential tissue/implant reaction and its interactions in a physiological environment might be addressed by these materials. There are four different kinds of biological interactions: bioactive—tissue forms a chemical bond with the implant surface; toxic—tissue dies as a result of chemical leaching from the ceramics; biologically inert—tissue forms a non-adherent fibrous capsule around the implant surface; and dissolution of the implant—the implant surface dissolves, allowing tissues to fill the space left by

the implant.

Based on the biological response of ceramics to the human body, bioceramics can be classified into nearly inert ceramics, porous bio-ceramics, bioactive ceramics, and re-absorbable ceramics (**Table 2**). In the fields of tissue engineering and regenerative medicine, this categorization of bio-ceramics as implants and scaffolds is crucial.

#### 4.1. Nearly inert ceramics

The host attempts to separate itself from the foreign body by covering the implant in non-adherent fibrous tissue, and this form of bioceramics shows very little significant contact with the host tissues. Morphological fixation is the process of securing the implant and the tissue together only by mechanical engagement. Bio-inert ceramics can withstand wear and corrosion in physiological conditions, as well as with the body's hard tissues and joints. Yet, it offers the human body good biocompatibility. The most prevalent are single-phase calcium aluminum silicates, zirconium oxide, and aluminum oxide. In addition to these substances, carbon is employed as fibers in reinforced composites or as coatings in situations where blood contact is required. Bio-inert materials, including metallic and polymeric materials, cause a foreign body response because of their bioinert nature. Even if the material is biocompatible with the physiological environment, the body may nevertheless react with its surface through several biochemical reactions, including those involving collagen fibers, macrophages, giant cells, and cytokines. Consequently, an acellular collagen capsule covers the material surface, isolating it from the body. At the material surface, a non-adherent capsule of fibrous tissue forms. This causes interfacial micro motions, which worsen with time and ultimately lead to the failure of some types of prostheses. Nonetheless, the foreign body response is not a problem for almost bio-inert ceramic applications like bearing surfaces and blood contact.

**Table 2.** Clinical application of bio-inert ceramics

Bio inert ceramics	Clinical applications
Alumina Al <sub>2</sub> O <sub>3</sub> & Zirconia ZrO <sub>2</sub>	Bearing-surface total joint arthroplasty components: hip implants (ball and cup), knee prosthesis
Carbons-based bio-inert ceramics	Bone screws
	Maxillofacial and alveolar ridge reconstruction
	Dental implants, crowns, brackets, and inlay
	Ossicular bone substitutes, cochlear replacement
	Ophthalmology
	Heart valve coatings
	Orthopedic implants

#### 4.2. Alumina oxide (Al<sub>2</sub>O<sub>3</sub>)

Drug delivery systems, sterilization tools, and ventilation tubes are all made of alumina oxide. According to ASTM Standard (ASTM F603-78), the high-purity alumina derived from bauxite ore, which is utilized as a biomedical material for scaffold construction and medical grade alumina, includes more than 99.5% Al<sub>2</sub>O<sub>3</sub>, with silica and alkali oxide impurities less than 0.1%. Dental implants are made from a single naturally occurring crystal of sapphire or alumina. Nevertheless, new materials like fiber-reinforced composite materials are currently taking the place of conventional materials. The mechanical strength of alumina implants is determined by the porosity and grain size of the polycrystalline alumina used to create the alumina-based implants. Generally speaking, the materials have a high mechanical strength because the grain size is very tiny and low

porosity. The alumina is very finely grained, with a grain size of less than 4 microns and an elastic modulus of 380 GPa. The most popular technique for creating alumina-based materials for biomedical purposes at a temperature between 1600 and 1700 °C is sintering. This technique uses a modest quantity of magnesia (MgO, < 0.5%) as a sintering assist material, and it is crucial in controlling the alumina material's grain size.

Alumina materials' mechanical and physical characteristics are listed in **Table 3** and **Table 4** [9]. For the past 20 years, hip prosthesis applications have benefited from alumina materials' exceptional wear surface qualities and high hardness. However, in older individuals with osteoporosis or rheumatoid arthritis, the stress shielding resulting from alumina's high elastic modulus may promote bone atrophy and loosening of the acetabular cup. The attempt to increase the alumina material's grain size may cause the implants' mechanical qualities to deteriorate quickly. The age joint disease type determines how precise quality control of alumina implants is therefore essential, and the biomechanics of the repair is crucial to the success of alumina prostheses. The majority of alumina is utilized in dentistry for pine-type dental implants, endosteal screws, blades, and root analogs [10]. However, after many years, the blade and root of dental alumina implants have become a feature. The mechanical strength of the implant decreases with prolonged use of alumina. Other dental uses for alumina include the production of ceramic crowns. Note that only materials in contact with soft tissue and bone are referred to as dental implants. Alumina ceramics have also been utilized in single-crystal alumina bone screws, middle ear implants, complete knee prosthesis, and ophthalmology [11].

**Table 3.** Mechanical properties of alumina ceramics

Properties	Alumina ISO 6474	Alumina ASTM F603
Content (%)	≥ 99.5%	≥ 99.5%
Density (g/m3)	> 3.90	> 3.94
Average grain size (µm)	< 7	≤ 4.5
Vickers hardness (GPa)	> 2000 (106 psi)	18
Compressive strength (MPa)	-	4000
Flexural strength (MPa)	400	45,000
Elastic modulus (GPa)	380	380
Fracture toughness (K1c) MPa	5–6	-
Weibull modulus	-	8

**Table 4.** Standard specification for alumina materials

Chemical Requirements	Al <sub>2</sub> O <sub>3</sub> ≥ 99.5 (wt%) MgO ≤ 0.5 (wt%) Other oxides ≤ 0.1 (wt%)
Physical Requirements	Minimum density should be 3.94±0.01 g/cm3 The median grain size should be 4.5 µm or less
Mechanical Requirements	Flexural strength ≥ 400 MPa (58 KPsi) Vickers hardness ≥ 18 GPa (measured at 1 kg load) The Weibull modulus should be ≥ 8

### 4.3. Zirconia bioceramics

Outstandingly biocompatible biomaterial is found in zirconia (ZrO<sub>2</sub>) bioceramics. This material is employed as the articulating ball in hip prostheses because of its strong tribological qualities. At high temperatures, zirconia

often experiences a significant volumetric shift during phase changeover. Implant construction uses partially stabilized zirconia (PSZ) as a biomaterial substitute for alumina. The mechanical characteristics of PSZ are superior to those of alumina. Furthermore, zirconia-based dental implants have a mechanical strength that is comparable to that of teeth, a high degree of fracture toughness, and a lower production cost than single-crystalline alumina.

A dopant oxide, such as yttria ( $Y_2O_3$ , about 6 mol.%), is present in the PSZ and is utilized to stabilize the high-temperature phase. Higher strength and a reduced elastic modulus are two of zirconia's possible benefits in load-bearing applications. Temperature influences the three polymorphisms of zirconia ( $ZrO_2$ ): symmetry, monoclinic below 1170°C, tetragonal between 1170°C and 2370°C, and cubic beyond 2370°C, which includes a high-pressure orthorhombic phase.

Zirconia undergoes a significant 5% change from tetragonal to monoclinic. It causes zirconia ceramics to become less elastic and to crack and shatter. In the process of production, zirconia minerals are combined with yttria ( $Y_2O_3$ ), calcium oxide (CaO), or magnesia (MgO) to stabilize them in tetragonal or cubic phases. The zirconia phases that make up partially stabilized zirconia (PSZ) are cubic, tetragonal, and monoclinic. When compared to other phases, tetragonal zirconia polycrystals, or TZP, are the clearest version of the tetragonal phase. For the creation of the scaffolds and biomedical device, PSZ and TZP are taken into consideration. Zirconia ceramics' mechanical characteristics are summed up in **Table 5** and **Table 6**.

Yttria-TZP ceramics have significant strength and fracture toughness, nearly twice that of alumina. As a result, when zirconia heads come into touch with metal cones, they are less vulnerable to stress. The majority of PSZ tetragonal zirconia, which is medical-grade zirconia, is being taken into consideration for medical device development. Compared to alumina, it exhibits less microhardness, an elastic modulus, high strength, and fracture toughness. Due to its better mechanical strength and minimum, zirconia may be used to develop ceramic ball heads smaller than 32 mm.

Zirconia is limited in terms of radiation and deterioration, though. Degradation is mostly caused by a phase transition that occurs in the physiological medium of the human body. It appears that the phase change has little effect on the surface deterioration of zirconia balls. All ceramic components' mechanical performance is reliant on manufacturing quality standards. Even at high concentrations, ceramic particle debris generally elicits unfavorable biological reactions and is chemically stable and biocompatible. The creation of alumina/zirconia composites may yield more advancements in these almost bioinert ceramics <sup>[11]</sup>.

**Table 5.** Mechanical properties of zirconia ceramics

Properties	Yttria-Stabilized Zirconia ASTM F1873	ZrO2	ZrO <sub>2</sub> (MgO-stabilized)
Content (%)	≥ 93.2% + yttria	-	-
Density (g/m <sup>3</sup> )	> 6.0	6.1	-
Average grain size (μm)	≤ 0.6		-
Vickers hardness (Gpa)	1200	12	-
Compressive strength (MPa)	1200	1074	-
Flexural strength (MPa)	800	-	-
Ultimate strength (MPa)	900	7500c/420t	634
Elastic modulus (GPa)	200	201	200
Fracture toughness (K1c) MPa	15	6–15	-
Weibull modulus	10	-	-

**Table 6.** Standard specification of zirconia with magnesia material

Chemical Requirements	ZrO <sub>2</sub> +HfO <sub>2</sub> +MgO ≥ 99.8 (wt%) MgO 3.1–3.4 (wt%) HfO <sub>2</sub> ≤ 2.0 (wt%) Total other oxides <0.20 (wt%) Other oxides Fe <sub>2</sub> O <sub>3</sub> < 0.01 (wt%) SiO <sub>2</sub> < 0.05 (wt%) CaO < 0.02 (wt%) Al <sub>2</sub> O <sub>3</sub> < 0.05 (wt%)
Physical Requirements	Minimum density should be 5.800 g/cm <sup>3</sup> Total porosity should be <1.0 vol% of which open porosity must be <0.1 vol% The monoclinic phase in the PSZ should be <15% as determined by ASTM F2393-12
Mechanical requirements	Flexural strength ≥600 Mpa (87 Kpsi) Vicker's hardness ≥ 1000 HV (measured at 1 kg load with a dwell time of 15 s) Room temperature elastic modulus should be ≥180 Gpa

## 5. Carbon materials

Carbon exhibits exceptional biocompatibility with the body's surrounding tissue and is utilized as a bioinert material in the development of implants and biomedical devices. Three kinds of carbon materials are available for use in biomedical applications: pyrolytic carbon (also known as low-temperature isotropic carbon, or LTI), vapor-deposited carbon (also known as ultralow-temperature isotropic carbon, or ULTI), and glossy carbon (also known as vitreous carbon), as shown in **Table 7**. Petroleum hydrocarbons like propane and methane are thermally broken down or pyrolyzed in the absence of oxygen to produce pyrolytic carbon, which is a key component of prosthetic heart valves.

**Table 7.** Mechanical properties of the carbon materials

Properties	LTI PyC+ 5–12% Si	Pure PyC	Si-alloyed PyC	Glass carbons
Content (%)	5–12% Si	0 Si%		
Density (g/m <sup>3</sup> )	-	1.5–2.2		1.5
Average grain size (μm)	-	3–4 nm		
Vickers hardness (GPa)	-	150–250		
Compressive strength (MPa)	600	517	494	171
Flexural strength (MPa)	-	-		
Ultimate Strength (MPa)	-			
Elastic modulus (GPa)	30	18–28	30.5	21
Fracture toughness (K1c) MPa	-	4.8		
Weibull modulus	-	-		

The carbon exhibits high durability, strength, and resistance to wear. It is well suited for biomaterials fabrications because of its exceptional qualities. The resistance of carbon to blood coagulation or clotting at the interface between material surface and tissue is another intriguing property of carbon. For minor orthopedic joints, including fingers and spinal inserts, pyrolytic carbon is used <sup>[12]</sup>. The allotropic forms of carbon that are utilized as bio-inert materials include pyrolyzed carbon, diamond, graphite, and nanocrystalline glassy carbon. Biomedical composites with reinforcement are made of carbon fibers. Clinical uses for carbon nanotubes and buckyballs are possible <sup>[11]</sup>. There are two types of pyrolyzed carbon: LTI and ULTI. Excellent strength,

resilience to fatigue, and durability are displayed by the LTI pyrolyzed carbon. As a result, it is utilized in the development of mechanical heart valve prostheses as well as coatings made of silicon alloyed as monolithic or polycrystalline substrates. ULTI pyrolyzed carbon is used to improve the more complex form and mechanical qualities of various substrates by producing an impermeable layer by vapor deposition. The dense layers of glassy carbons are applied to the substrate due to the fragility and low density of glassy carbons.

## 6. Porous bioceramics materials

Perforated bioceramics are biomaterials that can promote tissue self-regeneration by acting as scaffolds and reservoirs for cells and signaling molecules like growth factors. Porosity added to bioceramics has a greater positive effect on tissue regeneration. Aptite scaffolds with varying pore sizes and interconnectivity have been shown to be appropriate for biological microenvironments. Currently, one of the most difficult tasks in tissue engineering and regenerative medicine is the creation of porous ceramics that might stimulate the response of the cells involved and cause the regeneration of osseous tissues.

The development of bioactive tissue engineering scaffolds for efficient regeneration and the encapsulation of cells or medications for the regeneration of injured tissue are both accomplished by the porous ceramic scaffold. The porous ceramic scaffold's mechanical strength is poor, though. As the scaffold's porosity rises, its mechanical strength falls. The process of cell destiny and the transfer of nutrients for tissue regeneration may be significantly influenced by the holes in the scaffold. In general, for bone development to retain its vascularity and long-term cell survival, pores larger than 100  $\mu\text{m}$  are required.

By replicating the porous biomimetic structure of natural ceramics like corals, the replamine form technique has produced porous materials of alumina, titania, and calcium phosphates. As an alternative, soluble metals and salts are combined with ceramic materials to create a porous structure, or calcium carbonate, which is employed as a foaming agent, evolves gases upon heating. The shape and size of soluble particles dictate the pores' size and structure.

The mechanical strength of the ceramic material sharply declines with increasing scaffold porosity. Furthermore, a large surface area is exposed, and the significance of environmental influences increases. Thus, low-strength porous ceramics can only be used in very limited, non-load-bearing applications. Porous ceramics may serve as a useful implant if load bearing is not taken into account. In cases when illness requires the removal of portions of the bone, porous alumina has also been employed as a bone spacer.

The preferred biomaterial for non-load-bearing bone implants is porous bioceramics. Because calcium phosphates have great biocompatibility, they are commonly used for these particular purposes. The primary purpose of porous ceramics is to fill up flaws in the bone. This scaffold has the potential to be employed as both a medication delivery system and a scaffold for tissue engineering in the context of this particular bone-filling activity. A certain microporosity is required if the porous bioceramic implant is to be employed as a medication delivery system. The linked macroporous network of a bone tissue engineering scaffold should have pore sizes bigger than 100  $\mu\text{m}$  to facilitate efficient bone tissue growth within the implant and promote quicker regeneration.

The following three processing techniques were examined to produce macroporous calcium phosphate ceramics: forming of ceramic slip (65% to 75%; non-uniform pore size; very brittle); infiltration of ceramic slip into polymeric pore precursor (65% to 75%; uniform pore size); and pressing of ceramic powder with burn-out additives (open porosity 25%; non-uniform pore size). Research was done on the potential use of calcium phosphate glass as a sintering aid for porous calcium phosphate ceramics. Tricalcium phosphate-hydroxyapatite ceramic material may be made from hydroxyapatite and calcium metaphosphate glass.

The forerunner of biomorphic SiC ceramics utilized in the production of biomaterials. Scaffolds for tissue

engineering can be created from obtained SiC ceramics. Drugs were loaded into obtained porous hydroxyapatite bioceramics by vacuum impregnation with a drug-water solution. Both in vitro and in vivo studies were conducted on drug-loaded bioceramics. Due to the structural flaws caused by micropores and macropores that encourage cracking, high-porosity bioceramics are extremely brittle. To increase the mechanical characteristics of porous bioceramics, it is crucial to select appropriate processing conditions in addition to achieving high porosity levels. In biomedical applications, mesoporous materials based on silica are employed as drug delivery systems. These substances have recently shown promise as bioceramics. These materials are synthesized using surfactants, and this process allows for customization of the material's size, pore walls, and porosity. Recently, mesoporous microspheres have been created for use in biomedicine. Accordingly, magnetic silica microspheres for drug targeting and bioactive glass microspheres with faster HCA deposition rates and hemostatic effectiveness have been described [13-14].

Porosity calcium phosphate ceramics have been employed as scaffolds for tissue engineering; these scaffolds replicate the porosity structure of hard and calcified tissue and offer an environment conducive to the ingrowth of bone cells. One typical issue with bone abnormalities is bone infections, which call for the carefully directed administration of medications to the affected area. To manage infections and provide a regulated supply of antibiotics like gentamicin for bone defects, the porous CaP scaffold functions as a drug reservoir [13].

Porous ceramic implants are made with hydroxyapatite to promote osteogenesis. High-temperature sintering of the ceramic powder is the standard manufacturing method. For instance, blocks with strongly interconnected 500 µm holes, 77% porosity, 17.4 and 7.2 MPa compressive and three-point bending strengths, and 0.12 GPa Young's modulus were created using sintered hydroxyapatite powder. In vivo experiments using HAp scaffolds for bone regeneration revealed induced ectopic bone growth [15].

Similarly, rats' femoral lesions healed after receiving cylinder-shaped synthetic porous hydroxyapatite implants with 80% porosity and 400–600 µm pores [16]. Porous ceramics' porosities and pore diameters are listed in **Table 8**. In general, porous ceramic biomaterials can osseointegrate by forming carbonate hydroxyapatite or a substance resembling bone apatite on their surfaces; nevertheless, their sluggish rates of degradation and brittleness make them unsuitable for long-term usage [17].

**Table 8** Porosities and pore sizes of crystalline ceramic scaffolds for bone regeneration [19]

Ceramics materials	Fabrication technique	Morphology of the scaffold	Pore size (µm)	Application
Hydroxyapatite	Sintering	Scaffolds with honeycomb pores	90–120 and 350	BMP-2 delivery and ectopic bone formation in rats
Hydroxyapatite	Sintering	Scaffolds with honeycomb pores	100–200	BMP-2 delivery and ectopic bone formation in rats
Hydroxyapatite	Sintering	Scaffolds	366 and 444	Mandible defects
Hydroxyapatite	Sintering	Scaffolds	400 and 800	Goat bone marrow stromal cells ex vivo and ectopic bone formation in goats
Tricalcium phosphate cement	Salt-leaching	Pellets	0.2 and 8.7 31 and 62	-
Calcium metaphosphate	Sintering	Blocks	200	Rat bone marrow stromal cells ex vivo and ectopic bone formation in mice
Natural coral	Sintering	Human mandibular condyle	150–200	Rabbit marrow mesenchymal cells ex vivo and ectopic bone formation in mice
Hydroxyapatite/tricalcium phosphate	Sintering	Blocks	100–150	Femoral defect in dogs



Although it is stated that a scaffold's increasing porosity and pores encourage positive bone ingrowth, the scaffold's porous design negatively affects its mechanical qualities, making it less durable. For instance, the CaP scaffold exhibits reduced compressive strength (37000–430 kPa), compressive (2900–37 MPa), and Weibull (4.2–2.0) modulus due to its median pore size (0.2–8.7  $\mu\text{m}$ ) and low % of pores less than 100 nm<sup>[18]</sup>.

## 7. Bioactive bioceramics

Due to their strong binding to bone, glass, ceramics, and glass-ceramics have formed unique compositions. When inserted into the body, bioactive ceramics can change their surface kinetically and in response to time. The material's surface is covered in layers of hydroxycarbonate apatite (HCA), which may interact with surrounding tissues and physiological conditions. The materials' HCA phase forms an interfacial connection with hard tissue like bone because it resembles the chemical and structural elements of bone. In the same vein, bioactive ceramics are also created for soft tissue therapeutic bonding.

The index of bioactivity, which measures how long it takes for more than 50% of the interface between an implant and a hard tissue, such as bone, to chemically bind, has been used to assess the bonding capability of bioactive ceramics. The bioactive ceramics may be divided into two primary categories, such as "Class A" and "Class B," based on the bioactivity index. Materials of class A bioactivity have an index of bioactivity higher than 8, and they include bioactive materials like bioactive glasses that both accelerate the proliferation of bone cells and serve as a matrix for bone cell development (osteoconductive process).

A Class A bioactive substance near the interface causes an additional, intracellular reaction. These substances are referred to as osteoproliferative. Materials classified as class B bioactive are those that have an Ib value of more than 0 but less than 8, such as synthesized HA that is only osteoconductive. As a result, the substance only reacts extracellularly at the interface. When compared to Class B Bioactive material, Class A Bioactive material shows a higher rate of bonding with hard tissue and a faster rate of protective layer creation, such as the precipitation of the hydroxycarbonate-apatite layer in 20 hours.

The ability of Class A bioactive materials to create bonds with soft tissue is another noteworthy benefit. However, Class B bioactive compounds can only develop in hard tissues like bone. The BMP and other growth factors should be given materials to promote the production of bone for them to qualify as Class B Bioactive Materials that are osteoconductive. Precursor cells are stimulated by BMP to become osteogenic cells,

resulting in the proliferation of bone cells and an acceleration of the creation of bone matrix. The osteoproliferative materials boost the pace at which preexisting osteoprogenitor cells proliferate and accelerate the production of a matrix by the bone cells, but they do not induce the osteogenic transformation of precursor cells.

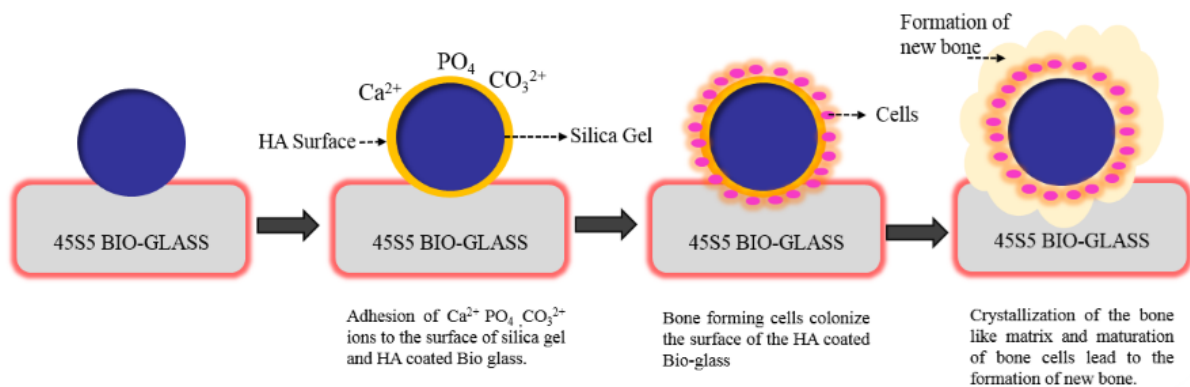
These biomaterials can interact with physiological fluids to generate biological-type apatite, which can stimulate the production of new bone at the site of injury. This apatite is the result of a chemical reaction that occurs in the presence of live cells. The most prevalent examples of this type of glass are calcium phosphates and various glass compositions, including ceramic glasses. The aforementioned materials are produced as powder, dense, porous, injectable mixes, and coatings for substrates. They have relatively weak mechanical qualities, yet they have good bioactivity and biocompatibility.

### 7.1. Bioactive glasses

Biomedical applications employ ceramics in a variety of shapes and compositions. Silicate ceramics are often used when the SiO<sub>2</sub> content is more than 65% weight. Silica ceramics is another name for glass. Glasses made of silica with a 65-weight percent SiO<sub>2</sub> concentration are incredibly bioinert. Less than 60 mol% SiO<sub>2</sub>, a high

concentration of  $\text{Na}_2\text{O}$  and  $\text{CaO}$ , and a high  $\text{CaO}/\text{P}_2\text{O}_5$  ratio are the three main compositional characteristics of these glasses that set them apart from conventional soda-lime-silica glasses. The formula “45S5”, which stands for 45 weight percent  $\text{SiO}_2$  (S = the network former) and a 5:1 molar ratio of Ca to P, is the foundation for the majority of bioactive silica glasses. Glasses with significantly lower molar ratios of Ca to P do not connect with bone because  $\text{P}_2\text{O}_5$  adds a large amount of bioactivity to the  $\text{SiO}_2\text{-Na}_2\text{O-CaO}$  matrix. Furthermore, bonding is inhibited by adding as low as 3 weight percent  $\text{Al}_2\text{O}_3$  to the 45S5 formula (**Figure 6**).

Polycrystalline ceramics called glass ceramics are created when glasses crystallize under regulated conditions [20]. The formation class ceramics is influenced by the nucleation, growth, and dispersion of tiny crystals (<1 micron). Bone was found to be attached to a kind of low-alkali (0–5 wt.%) bioactive silica glass-ceramics known as “Ceravital.” Bone bonding is inhibited when tiny quantities of  $\text{Al}_2\text{O}_3$ ,  $\text{Ta}_2\text{O}_5$ ,  $\text{TiO}_2$ ,  $\text{Sb}_2\text{O}_3$ , or  $\text{ZrO}_2$  are added to Ceravital for nucleation and growth. Designed for bone regeneration, the alumina-containing multiphase bioactive glass with phlogopite  $[(\text{Na}, \text{K}) \text{Mg}_3[\text{AlSi}_3\text{O}_{10}] [\text{F}, \text{OH}]_2]$ , mica, and apatite crystals may establish a link from one bone to another. Multiphase glass ceramic’s brittleness and compositional limitations to increase mechanical strength are drawbacks. Thus, they find applications as fillers in coating materials, dental restorative composites, and bone cement.



**Figure 6.** Bio-glass 45S5 and bone growth promotion from implant and tissue interactions. (Modified and reproduced from Figure by Jon Velenz) [21]

## 7.2. Bioactive glass-ceramics

Glasses may serve as starting points for the creation of bioactive glass ceramics. In actuality, the glass may be heat-treated to create glass ceramic, which has improved mechanical qualities among other benefits. Porosity would not be taken into account at this time, and the conversation will only be on thick materials. If the bioactivity investigation is now carried out with glass ceramics, taking into consideration, for example, a sample of composition: 70%  $\text{SiO}_2$ , 26%  $\text{CaO}$ , and 4%  $\text{P}_2\text{O}_5$ , it can be seen that the bioactivity process begins at the more soluble portions since the sample is composed by distinct phases, some of which are more soluble than others. The mechanical qualities of the entire object are strengthened by the unique microstructure of glass ceramics. As a result, bioactive glass ceramics with mechanical characteristics that are now substantially more similar to those of genuine bone may be produced. These types of materials could be classified into organic-inorganic composite, magnetic glasses and glass ceramics mixtures, calcium phosphate cement, and ordered mesoporous silica materials.

### 7.2.1. Organic-inorganic composite:

In therapeutic settings, the organic-inorganic composite is utilized. The content or proposal of mixed oxide

systems, such as inorganic phases like SiO<sub>2</sub>, CaO, and TiO<sub>2</sub> with siloxanes produced by osmosis, acrylic polymers, caprolactones, and so on, is the basis for the development of these materials. These components are used to replace missing bones. The materials' mechanical strength might be increased by the organic and inorganic combination, making them comparable to bone.

### **7.2.2. Magnetic glasses and glass ceramics mixtures**

By treating osseous tumors with hyperthermia, the glass that has magnetic components added to it can meet the needs of both bone regeneration and the treatment of cancer cells in bone tissues. The temperature at which tumors might be heated in this method is 47° C. Malignant cells are eliminated on a selective basis at this temperature, whereas normal cells only sustain little or temporary harm. For this purpose, magnetite (Fe<sub>3</sub>O<sub>4</sub>) and maghemite ( $\gamma$ -Fe<sub>2</sub>O<sub>3</sub>) are the most often used magnetic minerals.

### **7.2.3. Calcium phosphate cement**

When calcium phosphate cement is injected into the osseous cavity, simultaneous regeneration and a very rapid reaction to bone attachment occur. The creation of a scaffold made of calcium phosphate cement that encases osteoblast cells to promote bone regeneration is the subject of ongoing research on these materials. Ongoing efforts are being made to lessen the high levels of bioactivity and reactivity with the physiological media. Research is also needed since these materials emit phosphates, which lowers PH levels.

### **7.2.4. Ordered mesoporous silica materials**

Mesoporous materials based on silica have distinct structural properties. The walls of the well-organized system of pores and cavities are made of an amorphous silica network. These materials are synthesized using the surfactant as a template. Both the generated micelle and the material's pore size are greater in this procedure. Put another way, mesoporous materials may be produced with a chemical composition that is very comparable to that of bioactive glasses. Such structures ought to behave in a bioactive manner akin to that previously reported in glasses when in contact with physiological fluids. It is possible to get another ceramic that can regenerate bone tissue if parallel research is conducted, like the one that was done with glasses, and if the mesoporous material is bioactive.

## **7.3. Bioresorbable ceramics**

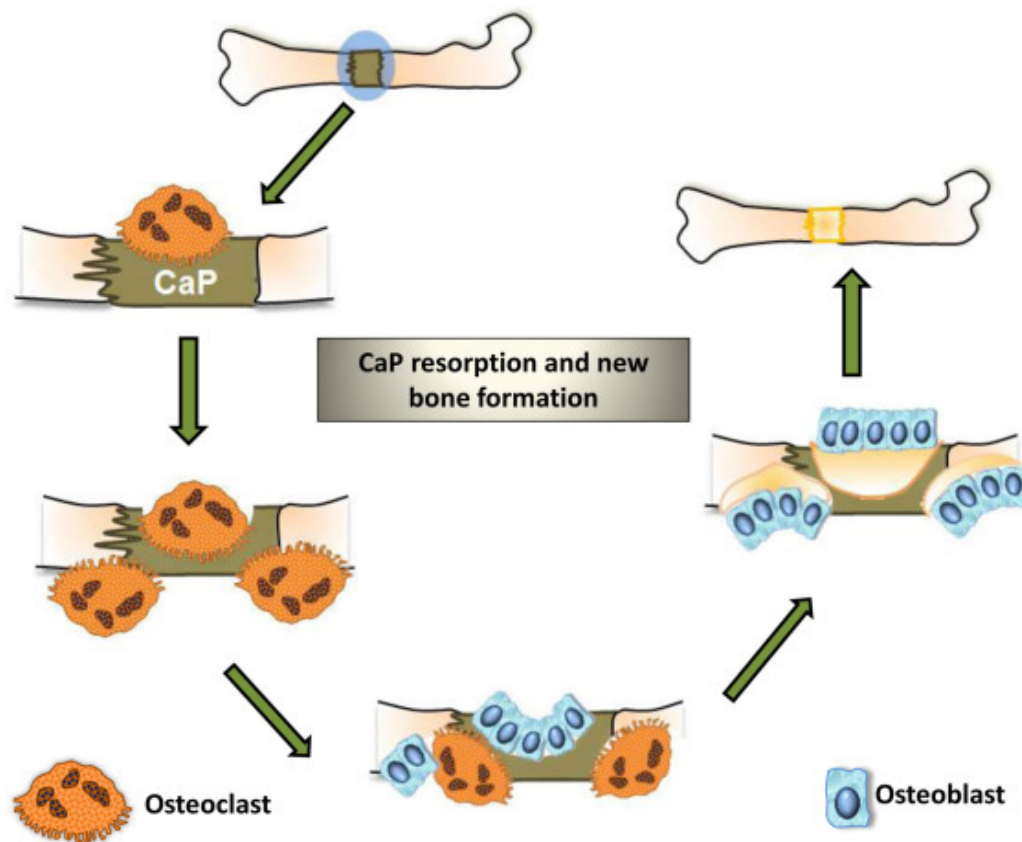
The human body's primary function is the resorption or biodegradation of materials and/or chemicals. Similar to this, biochemical or metabolic activity in the human body has the potential to cause bioceramics to break down or resorb into the physiological system. The materials' physical characteristics, such as their porosity, density, particle matter, or block structure, as well as their chemical makeup all influence how quickly they degrade. The process of biodegradation involves three stages: physical disintegration of the material into small particles through biochemical reaction or metabolic processes; physiochemical dissolution of the product, which depends on the solubility and local pH of the material; and biological factors, such as phagocytosis, which lowers the local pH.

The propensity for deterioration differs throughout bioceramic kinds. When subjected to physiological conditions, the majority of calcium phosphate ceramics are resorbable or biodegradable, and the rate of resorption rises as the Ca/P ratio falls. The reabsorbed ceramics are utilized to regenerate injured tissue. The choice of bioceramics is determined by the correlation between the bioceramic resorption rate and the bone tissue regeneration rate. Tricalcium phosphate, hydroxyapatite, and biphasic calcium phosphate are the most widely used resorbable ceramics. Biphasic calcium phosphates (BCP) ceramics are HA and TCP phase

composites that are utilized to promote quicker bone regeneration and a better-forming connection with bone <sup>[22]</sup>.

Because the BCP releases calcium and phosphate ions into the biological media, it is soluble and progressively dissolves in the body, serving as a substrate for the production of new bone. Beyond biocompatibility and osteoconductivity, BCP has also been suggested as a viable matrix for a bioactive drug delivery system where the resorption of the TCP ceramics facilitates the in situ release of a medicinal substance.

Through physical and cell-mediated mechanisms, bioresorbable calcium phosphate breaks down in the physiological environment to promote the growth of new bone (**Figure 7**). In the physiological medium, the majority of calcium phosphate is soluble, and its solubility is influenced by the Ca/P ratio. As the Ca/P ratio decreased, the solubility of CaP rose. Furthermore, HA becomes more soluble when additional metallic ions like Sr<sup>2+</sup> and Mg<sup>2+</sup> are added. Reducing crystallinity, particle size, and density might be used to customize solubility <sup>[23]</sup>.



**Figure 7.** Tissue engineering approach of osteoclastic resorption of bone; with permission from Roy et al. <sup>[23]</sup>

## 8. Conclusion

Ceramics are widely used as biomaterials in medicine and dentistry due to their biocompatibility, mechanical strength, and durability. Common applications include dental crowns, bridges, veneers, orthopedic implants, bioactive ceramics, and porous ceramics. Ceramics offer a wide range of properties, making them suitable for use in various medical and dental applications. Biomaterials, derived from natural sources, are used in medical devices, implants, and tissue engineering applications. Examples include hydroxyapatite, calcium phosphate ceramics, collagen, polymers, bioactive glasses, silk fibroin, composite materials, and nanomaterials.

Bioactive ceramics, such as hydroxyapatite and tricalcium phosphate, bond directly to bone tissue,

promoting tissue regeneration in bone grafts and dental implants. Porous ceramics are used in tissue engineering applications, supporting cell growth and promoting tissue regeneration. Synthetic materials like polylactic acid, polyglycolic acid, and polycaprolactone can be used to create scaffolds for tissue engineering applications. Nanotechnology has also enabled the development of nanomaterials with unique properties for tissue regeneration.

Ceramics are biomaterials used for soft and hard tissue repair due to their superior biological inertness and higher compressive strength. They are inorganic composites and non-metallic materials used in tissue engineering and regenerative biomaterials for hard tissue repair. Ceramics have few drawbacks due to their great hardness, poor mechanical characteristics, poor electrical conductivity, low thermal conductivity, and high melting point. They are now used in medical engineering as bio-ceramics and bio-composites. Three primary biological applications of ceramics are re-absorbable ceramics, bio-reactive ceramics, and bio-inert ceramics.

Re-absorbable ceramics can break down into particle fragments or inorganic chemical species, which can be reabsorbed by endogenous tissue. They are used in implant and tissue engineering structures in orthopedic applications, promoting bone regeneration and repair. Bio-reactive ceramics, such as bioglass and Ceravital, interact chemically with hard tissue, forming bonds at the contact. These materials are coated on implants to improve their biocompatibility and capacity to respond to a physiological environment. Bioactive ceramic coatings have increased surface activity to support tissue regeneration.

## Disclosure statement

The author declares no conflict of interest.

## Reference

- [1] Paramsothy M, Ramakrishna S, 2015, Biodegradable Materials for Clinical Applications: A Review. *Reviews in Advanced Sciences and Engineering*, 4(3): 221–238.
- [2] Sheikh Z, Abdallah MN, Hanafi A, et al., 2015, Mechanisms of in Vivo Degradation and Resorption of Calcium Phosphate Based Biomaterials. *Materials*, 8(11): 5430
- [3] Myer K, 2003, Bioceramics, in *Standard Handbook of Biomedical Engineering & Design*. McGraw Hill Professional, New York.
- [4] Ducheyne P, Mauck RL, Smith DH, 2012, Biomaterials in the Repair of Sports Injuries. *Nature Materials*, 11(8): 652–654.
- [5] Ben-Nissan B, 2005, Biomimetics and Bioceramics, in *Learning from Nature How to Design New Implantable Biomaterials: From Biomineralization Fundamentals to Biomimetic Materials and Processing Routes*. Proceedings of the NATO Advanced Study Institute, Portugal, 13–24 October 2003, Springer Netherlands, Dordrecht, 89–103.
- [6] Dorozhkin SV, 2010, Bioceramics of Calcium Orthophosphates. *Biomaterials*, 31(7): 1465–1485. <https://doi.org/10.1016/j.biomaterials.2009.11.050>
- [7] Plum F, 1987, *Anatomy: A Regional Atlas of the Human Body*, Third Edition. By Carmine D. Clemente Baltimore, Urban & Schwarzenberg, 1987 439 pp, Illustrated, \$42.50. *Annals of Neurology*, 22(4), 560–560. <https://doi.org/10.1002/ana.410220431>
- [8] Jayesh R, Dhinakarsamy V, 2015, Osseointegration. *Journal of Pharmacy and Bioallied Sciences*, 7(5): 226–229. <https://doi.org/10.4103/0975-7406.155917>
- [9] *Ceramic Biomaterials*, 2010, Biomaterials. CRC Press, Florida, 187–215.
- [10] Li J, Hastings GW, 1998, Oxide Bioceramics: Inert Ceramic Materials in Medicine and Dentistry, in *Handbook of*

Biomaterial Properties. Springer US, Boston, 340–354.

- [11] Vallet-Regi M, Salinas AJ, 2009, Ceramics as Bone Repair Materials, in Bone Repair Biomaterials. Woodhead Publishing, Sawston, 194–230.
- [12] Park JB, Lakes RS, 2007, Hard Tissue Replacement — II: Joints and Teeth, in Biomaterials. Springer, New York, 395–458.
- [13] Dagnija L, Janis L, Kristine S, 2011, Porous Hydroxyapatite Bioceramic Scaffolds for Drug Delivery and Bone Regeneration. IOP Conference Series: Materials Science and Engineering, 18(19): 192019.
- [14] Locs J, Berzina-Cimdina L, Zhurinsh A, 2008, Development of Biomorphic SiC Ceramics for Biomaterial Purposes, in 14th Nordic-Baltic Conference on Biomedical Engineering and Medical Physics: NBC 2008 16–20 June 2008 Riga, Latvia. Springer Berlin, Heidelberg, 48–51.
- [15] Dong J, Kojima H, Uemura T, et al., 2001, In Vivo Evaluation of a Novel Porous Hydroxyapatite to Sustain Osteogenesis of Transplanted Bone Marrow-derived Osteoblastic Cells. Journal of Biomedical Materials Research, 57(2): 208–216.
- [16] Damien E, Hing K, Saeed S, et al., 2003, A Preliminary Study on the Enhancement of the Osteointegration of a Novel Synthetic Hydroxyapatite Scaffold in Vivo. Journal of Biomedical Materials Research Part A, 66A(2): 241–246. <https://doi.org/10.1002/jbm.a.10564>
- [17] LeGeros RZ, 2002, Properties of Osteoconductive Biomaterials: Calcium Phosphates. Clinical Orthopaedics and Related Research, 395(2002): 81–98.
- [18] Barralet JE, Grover L, Gaunt T, 2002, Preparation of Macroporous Calcium Phosphate Cement Tissue Engineering Scaffold. Biomaterials, 23(15): 3063–3072. [http://dx.doi.org/10.1016/S0142-9612\(01\)00401-X](http://dx.doi.org/10.1016/S0142-9612(01)00401-X)
- [19] Karageorgiou V, Kaplan D, 2005, Porosity of 3D Biomaterial Scaffolds and Osteogenesis. Biomaterials, 26(27): 5474–5491. <http://dx.doi.org/10.1016/j.biomaterials.2005.02.002>
- [20] Sakamoto A, Yamamoto S, 2010, Glass-ceramics: Engineering Principles and Applications. International Journal of Applied Glass Science, 1(3): 237–247.
- [21] Jon Velez, 2016, Ceramic Biomaterials, [https://openwetware.org/wiki/Ceramic\\_Biomaterials,\\_by\\_Jon\\_Velez](https://openwetware.org/wiki/Ceramic_Biomaterials,_by_Jon_Velez)
- [22] Lobo SE, Arinze TL, 2010, Biphasic Calcium Phosphate Ceramics for Bone Regeneration and Tissue Engineering Applications. Materials, 3(2): 815–826.
- [23] Roy M, Bandyopadhyay A, Bose S, 2017, Chapter 6: Ceramics in Bone Grafts and Coated Implants, in Materials for Bone Disorders. Academic Press, Cambridge, 265–314.

**Publisher's note**

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.