Medical Journal of the
Islamic Republic of Iran

Volume 11
Number 3
Fall 1376
November 1997

Review Article

MEDICAL USE OF CERAMIC MATERIALS

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MJIRI, Vol. 11, No. 3, 267-273, 1997.

INTRODUCTION

Every surgeon dealing with hard tissues is confronted with the problem of repairing bony defects or reconstructing existing structures. To perform such work, the surgeon has several alternatives: autografting, allografting, and biomaterials.

Autogenous bone grafting (autografting) involves harvesting bone from another part of the body to utilize within the gap. This technique has a number of disadvantages,[1-3] including postoperative morbidity such as wound complications, increased operation time, and sometimes inadequate amount of bone to fill massive defects, particularly during childhood. Moreover, the patient's own bone always participates in remodelling processes, which might be a disadvantage if reconstruction is the goal. It is no use, for example, to reconstruct a congenital deformity with a remodelling material because the remodelling processes tend to restore the originally present deformity. Remodelling implants should be preferred only for filling defects due to disease or trauma. Finally, the patient's own bone cannot replace all functions in the body. For example, it is not possible to construct a hip joint with bone taken elsewhere from the patient.

Allografting, or using cadaver bone, has received a recent increase in popularity. There are several major disadvantages[2,4,5] with this technique. These include immune response (rejection by the recipient) in certain cases, possible acquisition of infectious diseases such as AIDS, and difficulty in obtaining the specimens due to religious beliefs or local customs.

The third alternative is using biomaterials. The use of certain materials as constituents of surgical implants is not new. Ever since the beginning of their profession, surgeons have sought a material that could replace missing parts of the human body. Substitutions of bone parts for repairing seriously damaged portions of the human skeleton have been reported since the pre-Christian era. Through the centuries many materials have been tried with varying degrees of success. At present, replacing damaged or diseased body parts is an increasingly important part of medicine, and biomaterials are playing a vital role in this field.

In general, a substance constituting an object able to substitute for an original living part of the body is called a "biomaterial". A comprehensive definition of this term was enunciated in 1982 at the National Institutes of Health (USA) Consensus Development Conference on the Clinical Applications of Biomaterials as follows:[6]

"A biomaterial is any substance, other than a drug, or combination of substances, synthetic or natural in origin, which can be used for any period of time, as a whole or as a part of a system which treats, augments, or replaces any tissue, organ or function of the body."

At the European Society for Biomaterials Consensus Conference held in Chester, UK, in 1986 there was significant disagreement with this definition and the following new simple definition was agreed: "Biomaterial is a non-viable material used in a medical device intended to interact with biological systems."[7] A synonymous term is "biomedical material."

Biomaterials that are employed in surgery cover a broad range of metals, polymers, ceramics, and composites. Among these materials, ceramics with biological applications (termed bioceramics) have received more attention during recent decades. This is mainly due to their compatibility with physiological environments.[3,8-10] The biocompatibility of certain ceramic materials is the result of the fact that they can be composed of ions commonly found in the body (calcium, potassium, magnesium, sodium, phosphorus, etc.) and of other ions such as aluminium and titanium which also show

very limited toxicity to body tissue.

Bioceramics made of calcium phosphate show an excellent compatibility with hard tissue. This can be understood from the structure of bone itself; it is a composite structure, consisting of a continuous phase (made of collagenous proteins and other biological polymers, and physiological fluid), in which small calcium phosphate crystals are dispersed.[11-12]

This article reviews the bioceramic materials, their classification, and their potential use in medicine and reconstructive surgery.

BIOCOMPATIBILITY

The human body has its own defence mechanisms designed to repel intruders.[13] A "foreigner" may be pushed back out through the skin, dissolved, or failing these, surrounded by a capsule of scar tissue, the thickness of which is inversely related to the severity of the body's reaction. This reaction depends upon the sterility of the intruder and the nature of the products of any chemical or physical breakdown. A severe local reaction can destroy physiological function and cause tissue damage. Examples are thrombus formation in blood vessels, calcification and gross fibrous encapsulation in heart valves, and gross fibrous encapsulation of silica or asbestos particles in the lung, leading eventually to a predisposition to malignant tumors. Immune reactions are also possible, especially from skin, bone or organ replacements from another person or species. After a few hours or days the foreign element stimulates an immune reaction that leads to loss of adherence and production of toxins. If drugs are given to reduce the

Table I. Types of implant-tissue response.[15]

If the material is toxic, the surrounding tissue dies.
If the material is nontoxic and biologically inactive (nearly inert), a fibrous tissue of variable thickness forms.
If the material is nontoxic and biologically active (bioactive), an interfacial bond forms.
If the material is nontoxic and dissolves, the surrounding tissue replaces it.

Table II. Applications of bioceramics in the medical field.[33]

Application	Material	Major exploited characteristics	Materials under investigation
Artificial tooth root	Alumina	High strength. High hardness Biological affinity (Does not adhere to bones)	Zirconia Composite of hydroxy-apatite and alumina
	Apatite	Biological affinity (Adheres to bones)	Carbon
Artificial bone (Cranial bone, jaw-bone, shoulder blade, humerus, backbone, thighbone) Auditory ossicle	Alumina	Biological affinity (Mechanical strength)	Calcium phosphate system crystallized glass Zirconia dispersion type crystallized glass Hydroxyapatite
Artifical joint (Hip joint, knee joint, leg joint, elbow joint)	Alumina	Biological affinity, Abrasion resistance, Self-lubrication, Low friction	Carbon
Artificial valve	Carbon	Resistance to thrombosis	
Bone fillers	Tricalcium phosphate (TCP)	Solubility	
	Apatite		

immune reaction, the patient becomes more susceptible to disease.

For solid materials to be useful in the body they must elicit a minimum of adverse reactions. These reactions result from several causes. There are the possibilites of direct toxicity of the implant materials to tissue and organs, and the toxicity of products from the implant that dissolve and migrate in body fluids and tissues. Metals such as chromium or nickel, fluorine, and certain organic molecules are examples of toxic materials. Any dissolution of these components into body fluids must be avoided.

The body is incredibly hard on materials used within its perimeters, eventually exacting its revenge on even the chemically inert materials.

Any material used in a medical or dental application is required to interface with viable living tissue, and whilst having a beneficial (or at worst no) effect on that tissue, should itself not suffer any ill-effects. Thus it can be seen that when testing or selecting a material, we must consider both the response of the host and of the materials.

In order to fulfill the requirements of biocompatibility, materials implanted within the body must have satisfactory properties in at least some of the following categories:[14]

–Implant materials should be resistant to corrosion and solution by body fluids. Any solutions formed should be non-toxic and non-carcinogenic.

–Where a material forms part of an articulating surface, either against natural tissue such as a partial denture, or another material such as an artificial joint, resistance to wear is required. It is undesirable, however, that natural tissue in contact with an artificial material should wear more quickly. This can occur where natural teeth contact hard denture or crown materials.

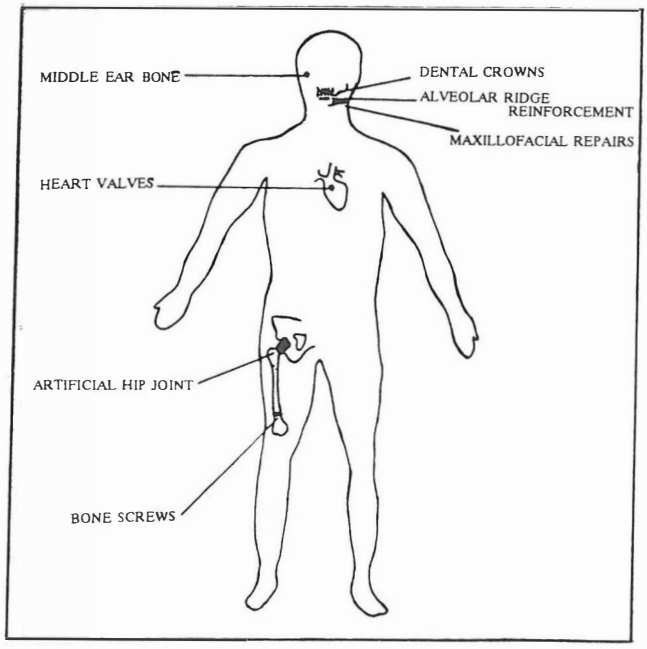

Fig 1. Prosthetic applications of bioceramics.[14]

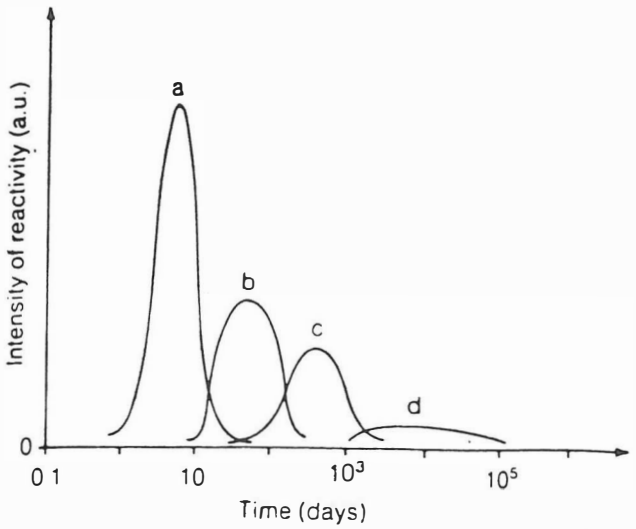

Fig 2. Indicative comparison of the times and the intensity of reactivity relative to the given classes of bioceramics: (a) resorbable, (b) bioactive, (c) porous, (d) nearly inert.[35]

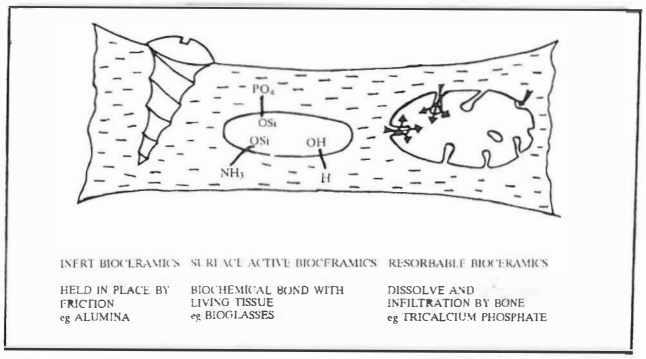

Fig 3. Schematic illustration of bioceramic-bone bonding.[15]

–If the material used is going to be in contact with blood, damage to blood cells causing thrombosis (clotting) is undesirable. Patients fitted with artificial heart valves often require administration of large quantities of anticoagulant drugs. This is turn can impair the healing of wounds.

Having fulfilled these criteria for biocompatibility, additional properties are required of a biomaterial.[14] Any material should be as strong as the tissue it replaces. A problem here, particularly when using ceramic bone replacements, is that their high flexural strength is accompanied by excessive stiffness. Where only part of a bone is replaced, or the bone is reinforced by a ceramic implant, this may result in relative movement of bone and ceramic during bending, resulting in loosening of the implant.

In order to reduce the possibility of post-operative infection, implant materials must be capable of surviving some form of sterilization by cold solution, dry or moist heat, gas or radiation, without degradation or loss of properties. Sterilization of porous materials may be particularly difficult due to their large internal surface.

Table III. Classification of bioceramics.[34]

Type of bioceramic	Type of fixation	Description of attachment	Materials
Nearly inert	Morphological	Bone grows into surface irregularities by cementing the device, or by press fitting into a defect	Single crystal and poly-crystalline alumina
Porous ingrowth	Biological	Bone ingrowth occurs, which mechanically attaches the bone to the material	Porous polycrystalline alumina, hydroxyapatite-coated metals
Surface reactive	Bioactive	Attaches directly by chemical bonding with the bone	Bioactive glasses or glass-ceramics, hydroxyapatite
Resorbable	Resorbable	Ceramics are slowly replaced by bone	Calcium sulfate, tricalcium phosphate, calcium phosphate salts

TYPES OF IMPLANT-TISSUE RESPONSE

No material implanted in living tissue is completely inert. All materials elicit some type of response from the body. Four types of response are possible:[15]

–If the material is toxic, the surrounding tissue dies. It is obvious that such a material cannot be used as an implant.

–If the material is non-toxic and biologically inactive (nearly inert) and dense, fibrous tissue of variable thickness occurs between the implant and the tissue. Because this tissue is not chemically or biologically bonded, it can easily move, leading to loosening of the implant and eventual failure.

–If the material is nearly inert and porous, an interfacial bond forms because of ingrowth of tissue into pores on the surface or throughout the implant. The increased interfacial area between the implant and the tissues results in an increased resistance to movement of the device in the tissue. Therefore, this implant can withstand more stress than the inert dense type.

–If the material is non-toxic and biologically active (bioactive), an interfacial bond forms between the tissues and the implant.

–If the material is non-toxic and dissolves, the surrounding tissue replaces it. These materials, known as resorbable biomaterials, are designed to degrade gradually over a period of time and be replaced by natural tissue.

The four types of implant-tissue response are summarized in Table I.

CERAMIC MATERIALS

Nowadays, engineering materials are classified into three major categories: metals (like iron, copper, and aluminium), organic polymers (like epoxy resins, rubber, and polyethylene), and ceramics (like porcelain, refractories, glass, and aluminium oxide).

The term "ceramic" comes from *keramos*, the ancient Greek word for objects made of fired clay.[16] While retaining this original meaning, now the word ceramic has also come to designate one of the three main materials' categories. It has taken on much of what was once included in traditional ceramics.

The broad term ceramic generally is defined as "an inorganic non-metallic material processed or consolidated at high temperatures."[17] Some scientists argue that ceramics are crystalline materials and, therefore, do not include glass. Most material scientists and engineers, however, regard glass as a ceramic.

Ceramic materials are complex chemical compounds of metallic and non-metallic elements. Calcium hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$, for example, is a ceramic composed of metallic (calcium) and non-metallic (phosphorus, oxygen, and hydrogen) atoms.

In their industrial meaning, ceramics are earthy materials processed in a furnace. But if this aspect of ceramic is emphasized, their importance will be misunderstood. Ceramics encompass a wide range of compounds, including silicates, oxides, carbides, nitrides, borides, hydrides, and sulfides. In fact, ceramics can be found everywhere: the abrasive grain that grinds steel parts,[18] the cutting tool that drills rocks,[19] the piezoelectric crystal that measures the thickness of thin films,[20] the single ruby crystal in a laser,[21] the pigments in paints,[22] the porcelain enamel on household appliances,[23] the thread guides in the textile industry,[24] the clay in paper,[25] the thermal sensors in electronic devices,[26] the calcium carbonate in toothpaste,[27] the uranium dioxide in nuclear reactor fuel,[28] and the hydroxyapatite in surgical implants.[29]

Because of their ionic or covalent bondings, ceramics are usually refractory (high melting point) materials. Apart from their ability to withstand elevated temperatures, ceramics have many other advantages.[17]

-Some ceramics are exceptionally hard. The hardest substances known, such as diamond, cubic boron nitride,

boron carbide, and silicon carbide, are ceramics.

-Many ceramics are highly resistant to oxidation and other chemical attack, as well as to erosion.

-Ceramics are usually lighter than metals. This is particularly important in aircraft, spacecraft, and gas turbine applications.

-Ceramics generally are made from abundant raw materials. Among the most common elements used in ceramics are silicon, which accounts for about 27% of the Earth's crust, and aluminium, which constitutes about 8%.

-Because of their low coefficient of friction, high compressive strength, and wear resistance, some ceramics can be used in bearings and other mechanical parts without requiring lubrication.

-Since ceramics have excellent compatibility with the living body, they can be used in medicine and surgery[9-11,14,30-32] for the repair and replacement of bones, tooth roots, and heart valves (Fig. 1) Table II gives the current applications of bioceramics in the medical field.

CLASSIFICATION OF BIOCERAMICS

The mechanism of tissue attachement is directly related to the type of tissue response at the implant interface. The four types of tissue response have alrealy been discussed. These responses depend on the type of material used. According to the different types of implant-tissue attachment,[34] bioceramics are classified into four types which are summarized in Table III with examples. An indicative comparison of the times and the relative chemical reactivity of different types of bioceramics is given in Fig. 2.

Nearly Inert Bioceramics

The tissue response to a biologically inactive, nearly inert implant is formation of a non-adherent fibrous capsule. The thickness of the fibrous layer depends on many factors, such as the conditions of the implant and host tissue, the conditions of motion and fit at the interface, and the mechanical load.

The mechanical stability of dense and inert bioceramic implants in bone is achieved by their geometry and by friction, bone growing into surface irregularities and remodelling around the implant to optimize stresses. This kind of attachment is called "morphological fixation"[15] (Fig. 3).

Nearly inert crystalline bioceramics such as high-purity, high-density alumina (Al_2O_3) are usually used in load-bearing prostheses and dental implants because of their combination of excellent corrosion resistance, good biocompatibility, high wear resistance, and high strength.

The success of these materials as implants depends on their mechanical properties which in turn are a function of grain size and purity.

Alumina has been used in orthopedic surgery for more than 25 years, motivated largely by its acceptance by the body and minimal scar formation which permits cementless fixation of prostheses, and in its exceptionally low coefficient of friction and wear rates.

The primary use of alumina is for the ball of the hip joint prosthesis.[36] Other clinical applications of alumina implants include knee prostheses, bone screws, jaw bone reconstruction, middle ear bone substitutes, corneal replacements, segmental bone replacements, and blade, screw, or post-type dental implants.

Other nearly inert bioceramics include zirconia (ZrO_2), titania (TiO_2), silicon nitride (Si_3N_4), sialons, and carbons.

Porous Bioceramics

The potential advantage offered by a porous ceramic implant is its inertness combined with the mechanical stability of the highly convoluted interface developed when bone grows into the ceramic. This attachment is called "biological fixation."[15] Mechanical requirements of prostheses, however, severely restrict the use of low-strength porous ceramics to low-load or non-load-bearing applications. Studies show that when load bearing is not a primary requirement, nearly inert porous ceramics can provide a functional implant.

When pore sizes exceed 100 μm, bone will grow within the interconnecting pore channels near the surface and maintain its vascularity and long-term viability. In this manner the implant serves as a structural bridge and model or scaffold for bone formation.

The microstructures of certain marine corals make an almost ideal casting material for obtaining structures with highly controlled pore sizes. Several types of coral are promising, with pore-size ranges of 140-160 μm and 200-1000 μm. After the coral shape is machined it is fired to drive off CO_2, or transformed directly into hydroxyapatite ceramic.

Porous ceramic surfaces can also be prepared by mixing soluble metal or salt particles onto the surfaces. The pore size and structure are determined by the size and shape of the soluble particles that are subsequently removed with a suitable etchant. The porous surface layer produced by this technique is an integral part of the underlying dense ceramic phase. Materials such as alumina may also be made porous by using a suitable foaming agent that evolves gases during heating.

Porosity has serious drawbacks in an implant. Porous materials are weaker than the equivalent bulk form. As the porosity increases, the strength of the material decreases rapidly. Much surface area is also exposed, making the implant more subject to corrosion and dissolution in comparison to dense, nonporous materials. Permeation of certain body fluids into the micropores of seemingly dense alumina has been shown to result in marked reductions in strength. More ominous is the inevitable residue of spaces

in the implant not filled by bone; these spaces are an invitation to bacterial infiltration and infection.

Bioactive Ceramics

The concept of bioactivity is defined as follows: "A bioactive material is one that elicits a specific biological response at the interface of the material which results in the formation of a bond between the tissues and the material". Bioactive is intermediate between resorbable and bioinert.

A bioactive material creates an environment compatible with osteogenesis (bone growth), with the mineralizing interface developing as a natural bonding junction between living and non-living materials.

Whilst the fixation of the implants made of the inert ceramics has to rely on their correct shape accounting for the remodelling ability of the adjacent bony tissue under the influence of the stress and strain field created by the insertion of such implants, the surface reactive ceramics possess chemical reactivity with the physiological environment. As healing of the wound site occurs, a simultaneous chemical bond between the tissue and the implant surface is stimulated. The interlocking of the two protects the implant from dislocation resulting from imposed stresses. This attachment is called "bioactive fixation"[15] (Fig. 3).

Surface reactive ceramics include dense hydroxyapatite, surface active glass, glass-ceramics, and composites. All these materials actively contribute to the bond formation, and therefore, they are called bioactive ceramics. For this reason, none of these ceramics are really stable in the body environment.

Resorbable Bioceramics

Resorbable ceramic materials are temporary space fillers or scaffolds for new tissue to develop (Fig. 3). Natural tissue reconstruction occurs simultaneously with resorption. Resorbable bioceramics are composed of materials which slowly dissolve releasing bone growth-stimulating ions. Eventually, resorbable implants become totally integrated with the living bone. The value of resorbable bioceramics is in the transient nature of their properties. The ingredients from which they are made should be either inert or easily processed through normal metabolic pathways.

Resorbable bioceramics have been used to treat maxillofacial defects, for obliterating periodontal pockets, as artificial tendons, and as composite bone plates. The tissue regeneration phenomenon relies on the natural dissolution tendencies of the bioceramic system and the ability of tissue to concomittantly replace it.

One of the unique advantages of a resorbable ceramic is that its initial pore size can be small, thereby possessing high mechanical strength compared to the strength of more porous substances. As the ceramic dissolves, it becomes more and more porous, allowing the ingrowth of more supporting tissue to occur. As a result, mechanical integrity is maintained and stress concentration is minimized.

Both fast-degrading and slow-degrading materials have their usefulness. The rapidly-degrading materials are often needed when tissue is to be replaced, such as for periodontal defects and open spaces in bone resulting from surgical procedures. Slowly degrading ceramics are important when tissue is to be augmented, such as filling of open spaces between vertebrae and spaces left by missing teeth or above resorbed alveolar ridges.

SUMMARY

Replacing of damaged or diseased parts of the body is an increasingly important part of medicine, and biomedical materials are playing a vital role in this field. Biomaterials that are employed in surgery cover a broad range of metals, polymers, and ceramics. Among these materials, ceramics possess the highest degree of biocompatibility with physiological environments. This is mainly because they can be composed of ions commonly found in the body and of other ions showing very limited toxicity to living tissues.

The mechanism of bioceramic-tissue attachment is directly related to the type of tissue response at the implant interface. The four types of body response to implants allow different means of achieving attachment of prostheses to the musculoskeletal system. According to the different types of implant-tissue attachment, bioceramics are classified into four types, namely nearly inert, porous, bioactive, and resorbable. Interest in bioceramics has grown dramatically during the past two decades and it is anticipated that their use in medicine will increase significantly in the coming years.

ACKNOWLEDGEMENT

The authors wish to thank Dr. S.A. Fazeli for editing this article and Mrs. F. Moradi for typing the manuscript.

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