Developing Novel Biomaterials for New Challenges

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Abstract

The use in the medical field of materials such as stainless steel, alumina and polyethylene that were originally developed for general engineering applications rather than for tissue replacement in human bodies has obviously been successful and it is certain that most of these proven materials will be continuously used in the healthcare industry. However, there are also shortcomings of these materials for their intended medical applications. With the advances in materials science and engineering, some currently available implant materials are being modified with regard to their surface and bulk properties so that their performance in the biological environment can be enhanced. Using natural tissues as templates, novel, “designer” biomaterials are being developed for tissue replacement and regeneration. Furthermore, with the emergence of tissue engineering, new scaffolding materials are under active development. In this paper, some of our efforts in developing new biomaterials as well as in modifying existing biomaterials are briefly reviewed.

1. Introduction

Gold was first used in dentistry by the Romans, Chinese and Aztecs more than 2000 years ago. Ever since plaster of Paris was tried for bone repair in the 19th century, numerous materials have been used for bone substitution. Nowadays, a variety of materials including metals, polymers, ceramics and composites are being used in orthopaedics, plastic surgery, etc. [1]. As it has been well recognised since the middle of the last century that biocompatibility is the paramount criterion for using a material in the human body environment [2], surface modifications have been made to some engineering materials so that they can be suitable for medical applications. Moreover, new biomaterials that meet the biocompatibility requirement have been specifically developed for various clinical uses. Having satisfied other criteria such as bioactivity and mechanical compatibility, a host of new biomaterials can interact with biological systems and are successful in replacing damaged or diseased tissues and restore body functions.

<table>
<thead>
<tr>
<th>Material</th>
<th>E (GPa)</th>
<th>σ (MPa)</th>
<th>ε (%)</th>
<th>KIC (MN m$^{-3/2}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-Cr alloy</td>
<td>230</td>
<td>900-1540</td>
<td>10-30</td>
<td>~100</td>
</tr>
<tr>
<td>316L stainless steel</td>
<td>200</td>
<td>540-950</td>
<td>6-70</td>
<td>~100</td>
</tr>
<tr>
<td>Ti-6Al-4V alloy</td>
<td>106</td>
<td>900</td>
<td>12.5</td>
<td>~80</td>
</tr>
<tr>
<td>Alumina</td>
<td>400</td>
<td>450</td>
<td>~0.5</td>
<td>~3</td>
</tr>
<tr>
<td>Zirconia (Mg-PSZ)</td>
<td>200</td>
<td>450-700</td>
<td></td>
<td>7-15</td>
</tr>
<tr>
<td>Hydroxyapatite</td>
<td>45-116</td>
<td>60-190</td>
<td></td>
<td>~1</td>
</tr>
<tr>
<td>Polyethylene (high density)</td>
<td>1</td>
<td>30</td>
<td>&gt;300</td>
<td></td>
</tr>
<tr>
<td>Cortical bone</td>
<td>7-30</td>
<td>50-150</td>
<td>1-3</td>
<td>2-12</td>
</tr>
</tbody>
</table>

E : Young’s modulus σ : tensile strength ε : elongation at fracture KIC : fracture toughness
Active research is currently conducted on developing new orthopaedic materials. As shown in Table 1, current implant materials such as Co-Cr alloys and alumina are much stiffer than human cortical bone. The modulus mismatch between an implant material and the host tissue can cause bone to resorb at the implant-bone interface, leading to implant instability and hence its eventual failure. Seeking biological as well as mechanical compatibility with host tissues has provided the impetus in developing new composite materials that mimic the structure and match the properties of natural tissues.

2. Developing Novel Biomaterials

**Bioceramics**

Ceramics, glasses and glass-ceramics for use in the medical field are grouped together and termed “bioceramics”. They have gradually gained their recognition and some of them are now accepted as viable biomaterials for tissue substitution [3]. Bioceramics have the advantage of being compatible with the human body environment. Their biocompatibility is a direct result of their chemical compositions which contain ions commonly found in the physiological environment (such as Ca$^{2+}$, K$^+$, Mg$^{2+}$, Na$^+$, etc.) and of other ions showing very limited toxicity to body tissues (such as Al$^{3+}$ and Ti$^{2+}$). One remarkable success of bioceramics as implant materials over the last two decades is perhaps the emergence and clinical use of bioactive ceramics which include calcium phosphates (with hydroxyapatite being the prominent family member), Bioglass®, A-W glass-ceramic, and other bioactive glasses and glass-ceramics that elicit a specific biological response at the interface of the material resulting in the formation of a strong bond between the tissue and the material.

Calcium phosphate-based bioceramics have been in use in medicine and dentistry for more than 20 years now. The interest in one group member, hydroxyapatite, arises from its similarity to bone apatite, the major component of the inorganic phase of bone, which plays a key role in the calcification and resorption processes of bone. Different phases of calcium phosphate ceramics can be used in medicine, depending on whether a bioactive or a resorbable material is desired. However, the low strength of calcium phosphate bioceramics such as hydroxyapatite (HA, Ca$_{10}$(PO$_4$)$_6$(OH)$_2$) have limited their scope of clinical applications and hence more research needs to be conducted to improve their mechanical properties. Our interest in this group of materials is for their use as a porous structure [4, 5], as the bioactive phase in composites [6, 7], as a bioactive coating on metallic implants [8, 9], and as the bioactive matrix of composites [10]. Figure 1 illustrates the use of HA in various situations.

![Image](a) dense HA  (b) porous HA  (c) HA/HDPE composite  (d) HA coating

*Figure 1  Hydroxyapatite used in various forms*

HA in the particulate form can be produced using a variety of methods: wet method, dry method, and hydrothermal method. The wet method is commonly used for the mass production of crystalline HA or noncrystalline calcium phosphate powder. Characteristics of HA powders have significant effects on the subsequent products, with HA being in the form
of dense or porous structure, in coatings, or in composites. During HA production, the reaction temperature, reactant concentrations and other production parameters should be carefully controlled in order to obtain high purity, good quality HA powder. The particle size, particle size distribution and particle morphology of HA powders must be optimized for their use as the secondary, bioactive phase in various composites and for their use as the feedstock for bioactive coatings.

**Bioactive Composites**

Bone supports the body and its movement. Bone serves as the template for making new materials for hard tissue replacement. Bone is a natural composite material, having a complex structure in which several levels of organisation, from macro- to micro-scale, can be identified [1]. Two levels of composite structure are considered when developing bone substitutes (Figure 2): first, the bone apatite reinforced collagen forming individual lamella at the nm to µm scale and, second, osteon reinforced interstitial bone at the µm to mm scale. It is the apatite-collagen composite at the microscopic level that provides the basis for producing bioactive ceramic-polymer composites as analogue biomaterials for bone replacement [11]. Mechanical properties of bones have been well documented, which serve as the benchmark upon which the mechanical performance of bone analogue materials is evaluated. As an anisotropic material, cortical bone has a range of associated properties rather than a set of unique values (Table 1).

In order to overcome the problem of modulus-mismatch between existing implant materials and bone and promote the formation of a secure bond between the implant and host tissue, the concept of analogue biomaterials was introduced by Bonfield et al in the 1980s [12]. Since then, a variety of bioactive composite materials have been produced and investigated [11]. These materials (i.e., the composites which consist of more than one type of materials (metallic, ceramic, or polymeric)), unlike the first-generation biomaterials which extended their use in engineering to medicine, are specifically designed for medical applications and hence truly “designer biomaterials”. Due to the presence of particulate bioactive bioceramics such as HA, Bioglass® and A-W glass-ceramic in these composites, implants made of these composites can form a strong bond with the host tissue resulting in their integration into the biological system.

**Table 2** Mechanical properties of various bioactive composites

<table>
<thead>
<tr>
<th>Volume of reinforcement (%)</th>
<th>Young’s modulus (GPa)</th>
<th>Tensile strength (MPa)</th>
<th>Elongation at fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>0.00</td>
<td>0.65</td>
<td>0.65</td>
<td>0.85</td>
</tr>
<tr>
<td>1.00</td>
<td>0.98</td>
<td>1.60</td>
<td>1.34</td>
</tr>
<tr>
<td>10</td>
<td>1.40</td>
<td>1.21</td>
<td>1.34</td>
</tr>
<tr>
<td>20</td>
<td>2.73</td>
<td>–</td>
<td>1.33</td>
</tr>
<tr>
<td>30</td>
<td>2.26</td>
<td>2.54</td>
<td>2.14</td>
</tr>
</tbody>
</table>

(1) HAP/PE11; (2) Bioglass®/HDPE; (3) A-W Glass-ceramic/HDPE.
By judiciously choosing constituent materials of composites and carefully controlling processing parameters, the biological and mechanical performance of bioactive composites can be tailored in order to meet various clinical requirements [6, 7, 13, 14]. Table 2 lists mechanical properties of some composites that have been developed for hard tissue replacement [15]. Advanced processing techniques can enhance the mechanical performance of bioactive composites [16].

**Surface Modification of Implantable Metals**

The use of metals in human bodies has a long history. Implants made of metallic materials provide the strength and toughness that are required in load-bearing parts of the body and due to these advantages, metals will continue to play an important role as orthopaedic biomaterials in the future. However, there are concerns with regard to the release of certain ions from and corrosion products of metallic implants [2]. Research has been continuing on modifying the compositions of metals [17] or, more recently and perhaps more importantly, changing surface properties of metals [18] for their biomedical applications.

One of the most publicised success of bioceramics as well as surface modification of implantable metals is the use of HA as a bioactive coating on total hip prostheses [19]. However, the manufacturing process in industry of depositing the HA coating on metal substrates using the plasma spray technique has been found to cause decomposition of HA due to high temperatures used. Using a low temperature process, HA and other bioactive ceramic coatings can be form on metals and the decomposition problem thus avoided [9]. This low temperature process needs to be optimized in order to produce good quality implants for clinical uses.

It has been found that after they had undergone chemical and heat treatments, a few metals could induce the formation of bone-like apatite on their surfaces [20, 21] (Figure 3). The formation of bone-like apatite on implant materials is believed to play an important role in the formation of direct bone bonding between implants and the tissue. Therefore, surface modification of implantable metals through the *in vitro* apatite formation process appears to be a promising method for improving the use of these metals in the medical field. Mechanisms of apatite formation on metal surfaces are being studied using a variety of analytical techniques [21, 22].

**3. Outlook**

Materials have played an important role in our lives and it is no wonder that historians classify the early ages of mankind according to the main materials used. When we embrace the new millennium, we may ask ourselves about the types of materials that we shall use for further improving our lives and realising our dreams.

Biomaterials of the first generation are engineering materials which extend their applications into the medical field. Due to their distinctive characteristics and proven record, they have remained in service and may continue to be used in the medical field in the foreseeable future.
Designer biomaterials are specially developed materials according to clinical requirements and they are increasingly used to solve various medical problems. With the emergence of tissue engineering, new materials/scaffolds are being developed for in vitro or in vivo tissue formation.

It is unequivocal that materials science and engineering is playing a pivotal role in the technological revolution that is taking place. We, materials scientists and engineers, shall take up challenges and make our own contributions to the advancement of our society. For those of us who are enthusiastically engaged in materials research and development, our pursuit for newer and better materials may never end.

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References


