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BIOCERAMICS AND THE FUTURE

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The Beginnings

Bioceramics is the newest commercial field of ceramics with sales of orthopedic and dental implants beginning only about 20 years ago. (Hench,1991) However it is the area that has the closest social relevance to people because bioceramics are used to repair, replace or augment the human musculo-skeletal system. Bones, teeth and joints deteriorate with age and disease or are damaged by accident. Replacement is necessary if quality of life is to be maintained. Metals and polymers or plastics were the first materials used for replacement body parts, termed prostheses or implants. However, metals corrode and polymers degrade in the harsh environment of living tissues. The emphasis for many years in biomaterials research was the development of implants that were more chemically resistant. Special medical grades of stainless steels, cobalt-chrome alloys, titanium and titanium alloys were produced and medical grades of polymers such as silicones and polymethylmethacrylate(PMMA) were developed and are now widely used for forty or more different types of prostheses (Hench and Ethridge,1982).

The first use of ceramics for implants was largely motivated by the desire to have a material that resisted change in the physiological environment (Hulbert et al, 1987). Alumina is an excellent material for certain orthopedic applications, such as the ball in an artificial hip joint, because of its chemical stability, low friction, high wear resistance, and high strength, as established by ceramic engineers, such as Dorre(1980) and Heimke(1981). A thin non-adherant fibrous capsule is formed adjacent to an alumina implant. This type of interfacial response is termed bio-inactive or bio-inert (see Table 1) and the implants must be held in place by mechanical means, such as screw threads, or by use of polymerizing cements.

To improve the fixation of implants in bone without the use of polymer cements, ceramic scientists such as Hulbert and co-workers (1972) and White and colleagues(1975), studied the use of porous ceramics as implants. They discovered that bone would grow into pores of >100 micrometers diameter and would remain healthy. This type of interfacial response is termed Biological Fixation in Table 1.

Table I

TYPES OF BIOCERAMICS-TISSUE INTERFACE AND BIOCERAMIC CLASSIFICATION

Type of Bioceramic	Type of Attachment	Example
BIO-INACTIVE	Dense, nonporous nearly inert ceramics attach by bone growth into surface irregularities by cementing the device into the tissues, or by press-fitting into a defect. (Termed Morphological Fixation)	Al_2O_3 (Single Crystal and Polycrystalline) ZrO_2 (Stabilized)
POROUS	For porous inert implants bone ingrowth occurs, which mechanically attaches the bone to the material. (Termed Biological Fixation)	Al_2O_3 (Porous Polycrystalline) Hydroxyapatite coated Porous Metals Porous Hydroxyapatite (HA)
BIOACTIVE	Dense, nonporous surface-reactive ceramics, glasses, and glass-ceramics attach directly by chemical bonding with the bone. (Termed Bioactive Fixation)	Bioactive glasses Bioactive glass-ceramics Hydroxyapatite
RESORBABLE	Dense, nonporous (or porous) resorbable ceramics are designed to be slowly replace by bone.	Calcium Sulphate (Plaster of Paris) Tricalcium Phosphate Calcium-Phosphate Salts

A third type of interfacial response is a tissue to implant bond by means of an hydroxyapatite layer formed on the material after implantation. This type of bonding is called Bioactive Fixation in Table 1. It was first discovered by the author and colleagues in 1969 (Hench et al,1972) and later expanded to include bioactive glass-ceramics, developed by Broemer, Deutcher and Gross (Gross et al 1988) and Yamamuro and Kokubo (Kokubo et al,1982), and dense hydroxyapatite materials, developed by Jarcho and co-workers (Jarcho,1981) and deGroot and colleagues (deGroot,1983).

The fourth type of interfacial response to an implant listed in Table 1 is dissolution, or resorption, with the implant being replaced by the host tissues. This is the ideal since tissues have the capacity to repair themselves in response to applied stresses. However, it is extremely difficult to design a material that can meet the requirements of a load bearing prosthesis and then resorb with time as new tissues replace it.

Several reviews document the historical evolution of bioceramics, including Hulbert et al (1987), Hench and Ethridge (1982), Gross et al (1988), Hench (1991), and books edited by Ducheyne and Lemons (1988), Yamamuro, Hench and Wilson (1990), Davies (1991), and Hench and Wilson (1993).

Growth

The science of bioceramics began in the early '70s with a series of interdisciplinary research conferences organized by Professor Hulbert at Clemson University. In 1980 the first World Congress on Biomaterials was held in Vienna and Congresses have followed in Washington D.C.(1984), Kyoto(1988), and Berlin(1992). Dr. June Wilson has analyzed the distribution of papers presented at the four Congresses. Figure 1 compares the total number of papers with the papers given on bioactive ceramics. In 1980, of the 281 papers presented there were only 6% devoted to the new field of bioactive ceramics. By 1992, the field of biomaterials had expanded enormously with 693 papers presented. The interest in bioceramics, and especially bioactive ceramics, had increased even more dramatically with 160 papers presented, now 23% of the total. The large increase in papers reflects the rapid expansion of interest in the field of bioactive ceramics worldwide. In 1980 there were only 5 countries and 12 research centers studying various types of bioactive ceramics. By 1992 the number of countries with research programs in this field had increased to 21 with 88 research centers involved (Fig. 2) (Wilson,1992).

The expanded research has led to a clear understanding of the various types of tissue response to bioceramics and the limitations associated with each.The microstructural requirements for long term stability of load bearing alumina implants have been identified and international standards specified (ISO Standard 6474). The compositional range for bioactive implants has been established and related to the surface reactions that create the interfacial bond with tissues (Hench,1988). Differences between hard tissue (bone) bonding and soft connective tissue bonding have been discovered (Wilson et al, 1981) and related

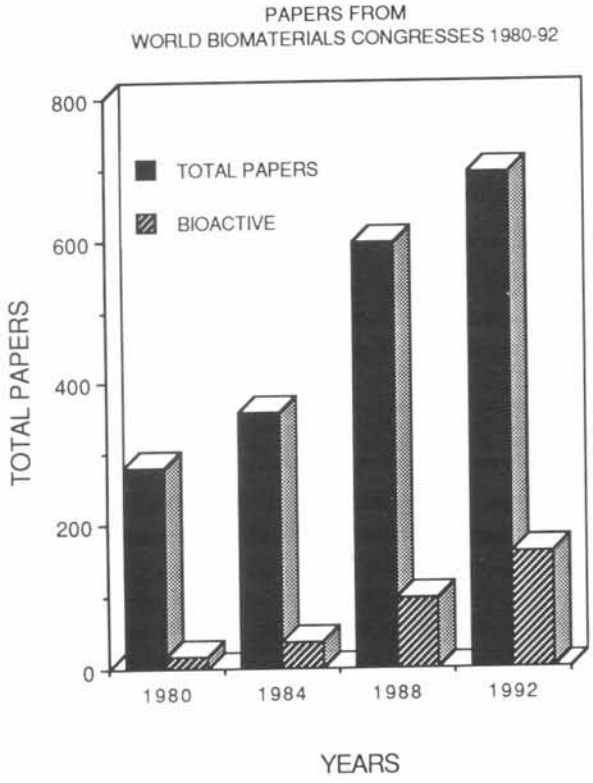

Figure 1. Comparison of total number of papers from World Biomaterials Congresses vs number of papers on bioactive ceramics.

to differences in surface reaction kinetics. Design of new bioceramics can now be based upon scientific principles rather than simply on trial and error. This is a major step forward within the short 20 year history of the field.

Applications

The rapid growth of the science of bioceramics has permitted a rapid increase in clinical applications (Hulbert et al,1987). A summary of the present uses of bioceramics in medicine and dentistry is given in Table 2. The primary areas of application are in the repair or replacement of hard tissues, such as bones, joints, or teeth. However, novel compositions of glasses and glass-ceramics have also been developed for therapeutic use in medicine, especially the use of radioactive glass beads for the treatment of tumors, pioneered by Prof. Day and colleagues (Day,1992), and the use of magnetic bioactive glass-ceramics by Profs. Yamamuro and Kokubo's groups.

Limitations: Bomechanical performance

Limitations on the future use of bioceramics generally fall into two categories: 1)

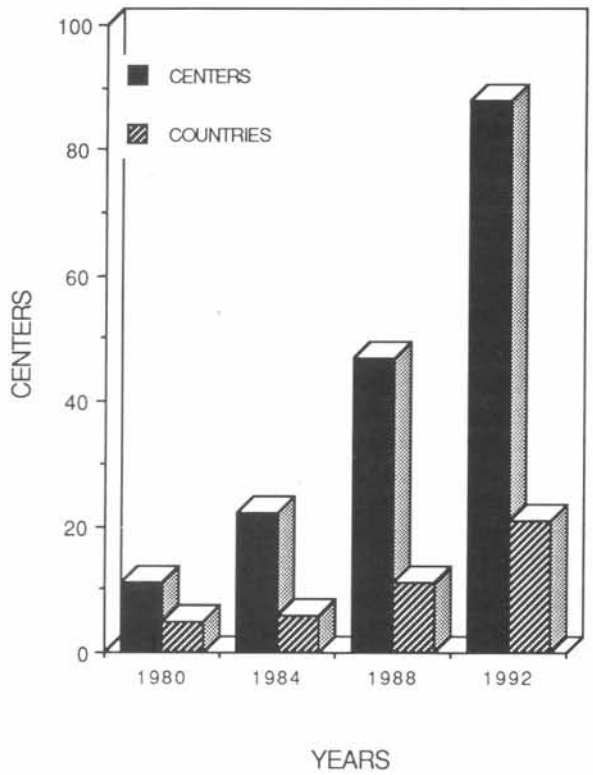

Figure 2. Number of research centers and countries presenting studies on bioactive ceramics in the World Biomaterials Congresses.

biomechanics and 2) biochemistry. The present generation of bioceramics, regardless of type, have problems with respect to their biomechanical performance over the long term (>10 years). The phenomena of slow crack growth, static and cyclic fatigue, low toughness, stress corrosion, deterioration of toughness with time and sensitivity to tensile stresses are all of serious concern in loadbearing applications. For these reasons, alumina bioceramics are largely restricted to use in the ball of total hip replacements whereas the loadbearing stem of the device is metallic (Boutin,1987)(Christel,1988)(Oonishi,1981).

Bioactive ceramics generally lack the strength for load bearing orthopedic applications. However, the A/W glass-ceramics described by Prof. Kokubo in this Forum do have sufficient strength for use as replacement vertebrae and repair of the iliac crest and are now in clinical suse for these applications (Yamamuro,1991). Bioactive glass-ceramic composites that contain transformation toughened zirconia particles may have sufficient strength for load bearing applications (>400 MPa) as does partially stabilized zirconia (1200 MPa), however, long term fatigue studies that demonstrate reliabilty of the multiphase interfaces under physiological conditions are yet to be reported. Concern about radioactivity of zirconias has also not been resolved.

Table 2

PRESENT USES OF BIOCERAMICS

ORTHOPEDIC LOAD BEARING APPLICATIONS
Al_2O_3
Stabilized Zirconia
Polyethylene HA Composite

COATINGS FOR CHEMICAL BONDING
(Orthopedic, Dental & Maxillofacial Prosthetics)
HA
Bioactive Glasses
Bioactive Glass Ceramics

DENTAL IMPLANTS
Al_2O_3
HA
Bioactive Glasses

ALVEOLAR RIDGE AUGMENTATIONS
Al_2O_3
HA
HA - Autogenous Bone Composite
HA - PLA Composite
Bioactive Glasses

OTOLARYNGOLOGICAL
Al_2O_3
HA
Bioactive Glasses
Bioactive Glass Ceramics

ARTIFICIAL TENDON AND LIGAMENT
PLA - Carbon Fiber Composite

ARTIFICIAL HEART VALVES
Pyrolytic Carbon Coatings

COATINGS FOR TISSUE INGROWTH
(Cardiovascular, Orthopedic, Dental & Maxillofacial Prosthetics)
Al_2O_3

TEMPORARY BONE SPACE FILLERS
Tricalcium Phosphate (TCP
Calcium and Phosphate Salts

PERIODONTAL POCKET OBLITERATION
HA
HA - PLA Composite
Tricalcium Phosphate (TCP)
Calcium and Phosphate Salts
Bioactive Glasses

MAXILLOFACIAL RECONSTRUCTION
Al_2O_3
HA
HA - PLA Composite
Bioactive Glasses

PERCUTANEOUS ACCESS DEVICES
Bioactive Glass-Ceramics
Bioactive Glasses
HA

ORTHOPEDIC FIXATION DEVICES
PLA - Carbon Fibers
PLA - Calcium/Phosphorous-Base Glass Fibers

SPINAL SURGERY
Bioactive Glass-Ceramic
HA

The limited range of elastic modulus of the present generation of bioceramics is also a limitation on their use in the body. The Young's modulus (in GPa) of cancellous bone has a range from 0.05 to 0.5 depending on location and age; cortical bone ranges from 7-25 (Bonfield,1984). In contrast, medical grade alumina (>99.8%Al_2O_3) has a Young's modulus of 380 GPa and partially stabilized zirconia has a value of 200 GPa. Thus, there is a modulus mismatch between cortical bone and an alumina implant in the range of 15-55X. The mismatch with cancellous bone is enormous, 760X to 7600X (Hench,1991).

A consequence of a mismatch in elastic modulus is that a bioceramic implant will shield a bone from mechanical loading. Nearly all the mechanical load will be carried by the implant. This is undesirable because living bone must be under a certain amount of load in order to remain healthy. Bone that is unloaded or is loaded in compression will undergo a biological change which leads to resorption and weakening of the bone and deterioration of the implant-bone interface. Loosening and/or fracture of the bone, the interface, or even the implant can result.

The rate and type of fixation of bioceramics to the skeletal system is also of concern. Bio-inactive ceramics offer no advantage in fixation over metallic prostheses which are cemented into bone. The bone-cement interface deteriorates with time causing loosening, pain, and fracture. An important alternative is the use of bioactive fixation since stress is transferred more naturally across the chemically bonded interface of bone mineral, hydroxyl carbonate apatite, bonded to collagen fibers and bone matrix.

However, the rate of bonding of a bioactive implant is very slow compared with the almost immediate interfacial fixation obtained with PMMA cement. Several weeks may be required for bioactive materials to develop sufficient interfacial strength to withstand full weight on the implant (Gross,1988). Many months are required for a bioactive interfacial bond to develop the strength of a cemented interface. Consequently, the short term loading of an implant needed for rapid recovery from surgery and healthy bone repair is not so good for bioactive ceramic implants even though the long term prognosis may be better than cemented prostheses.

Limitations: Biochemical Understanding

The response of a living body to an implant is a complicated series of biochemical and cellular reactions (Hench and Ethridge,1982). In addition, an implant may also change during its exposure to living tissues. Bioactive fixation is due to an appropriate match of the changes of the implant surface with the biochemical changes. Figure 3 summarizes the sequence of changes at the interface of a bioactive glass and bone. Much is known about reaction stages 1-5 (Hench et al, 1992). Gross et al (1988) summarize the extensive knowledge regarding bone growth on bioactive implants, stages 10-11. However, there is very little information about the early biochemical and cellular reactions at an implant interface, stages 6-9 (Davies 1991).

A further limitation is the lack of data on the effects of age, metabolic state, disease states, and infection on the behavior of bioceramics of all types. Most investigations reported involve short term tests on healthy animals. Most mechanical tests are performed on unloaded or nonfunctional devices for short terms of one year or less. In shocking contrast, the human need is for long term (>15 years) mechanical stability of the device and interface under loaded conditions in aged and often arthritic or osteoporotic bone or in recurrently

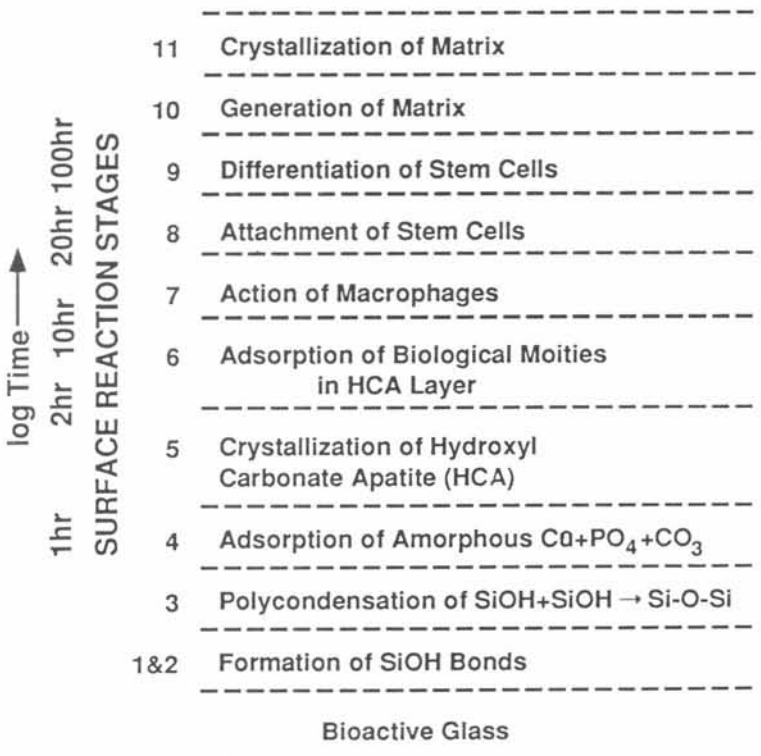

Figure 3. Stages of surface reactions at the tissue interface of a 45S5 bioactive glass.

infected sites. The changes in biochemical factors with age, disease, and load are not known.

There is also an enormous contrast between the testing conditions and the use conditions for bioceramics. The consequence of this disparity has been the failure of some ceramic implants in certain applications after only a few years of clinical use. Such failures give rise to ethical concerns, discussed below. Such failures also provide the incentive for new research and development opportunities.

R&D Opportunities:Short Term

1) Advanced Composites: Composites with a low elastic modulus that matches cortical bone, with high toughness and fatique resistance, and rapid rates of interfacial bonding are needed for orthopedic applications, as described by Bonfield (1988). Gradient modulus structures need to be developed that apply loads unformly across a bioactive interface in order to eliminate stress shielding. Methods are needed for applying bioactive coatings capable of rapid interfacial bonding to composite substrates with optimized elastic moduli and toughness.

2) Bioactive Cements: An in-situ polymerizing cement is the best means of achieving rapid short term fixation of orthopedic prostheses. A bioactive cement that develops strength rapidly, both within the cement and between the cement and bone, appears to be the ideal solution. Efforts in Bonfield's IRC in Biomaterials in London and Yamamuro and Kokubo's groups in Kyoto show early promise in achieving a new generation of bioactive ceramic cements. However, tests under simulated physiological loading conditions are still underway. It is too early to know whether the bioactive ceramic cements will be superior to PMMA which now has many years of clinical success in the range of 80%-95% after 5-15 years use in fixation of total hip prostheses (Hench,1987).

3) Predictive in-vitro and in-vivo tests: Introduction of a new medical material or device into the clinic requires a reasonable expectation that it will be superior to a previously used material or device. Standardized tests of mechanical and biological performance are needed to compare new biomaterials. At present there are almost no standardized tests for bioceramics. It is therefore nearly impossible to compare quantitatively new materials from laboratory to laboratory. Effects of composition, structure, phase state, surface conditions, and microstructure on properties and reliability cannot be compared without standardized tests that specify simulated physiological conditions, type of loading, etc.

Standardized in-vivo test models are also needed. Because of the absence of standardized animal tests it is impossible to compare interfacial bonding strengths of various bioactive ceramics and bioactive cements as a function of time to establish their relative merits compared with PMMA bone cement, the accepted surgical standard. Standardized tests are also needed to produce and compare lifetime prediction diagrams for bioceramics. Methods exist for determining probabilities of failure under realistic implant loading conditions, as described by Ritter et al (1979). However, the methods are seldom used and the test conditions have never been standardized.

R and D Opportunities: Long Term

1) Augmentation of autogeneous bone: The ideal use of a biomaterial is to use it to help diseased or damaged tissues repair themselves. Bioactive glasses show promise for use in this manner,e.g, to augment the natural repair of the patient's own (autogeneous) bone. A mixture of bioactive glass in particulate form combined with autogeneous bone chips produces a larger quantity of new bone (and cartilage), in a dog rib model, than bone alone or bioactive glass alone (Wilson,Yu, and Beale,1992). If the biochemical mechanisms responsible for this accelerated repair can be identified it may be possible to design the molecular composition of bioactive glasses or ceramics to augment the growth of various types of tissues.

This approach has the enormous advantage that the newly created structure has the necessary blood supply and natural repair processes to achieve a revitalization of the tissue that was previously damaged or removed along with a tumor. Consequently, augmentation of tissues, instead of replacing them, circumvents

most biomechanical problems. Augmented tissues will grow in thickness and strength in response to the stresses applied to them throughout their lifetime.

2) Resurfacing of Joints: A natural consequence of the above concept of augmentation of natural repair processes is to resurface joints instead of replacing them. An understanding of the potential for regeneration and repair of the articulating cartilage in joints is needed. Presently it is assumed that damaged joint surfaces cannot be repaired naturally and therefore must be replaced by inorganic non-living mating surfaces. Patients >65 years old can often obtain the 15-20 years of potential useful life of a total joint replacement using existing materials and methods. However, patients in the 30-65 year range must presently expect to undergo at least one repair surgery if they have a total joint replacement. Younger patients, however, also have the greatest potential for regeneration of tissues if the biochemical processes to stimulate them can be identified and incorporated within the molecular design of the surface of bioactive ceramics.

3) Kinetics of Interfacial Reactions: a critical step in developing the means to stimulate natural physiological repair processes is to understand the mechanisms of interfacial reactions of bioceramics at a molecular level. Rates of inorganic reactions must be measured, rate constants determined and effects of composition and solution concentration of interfacial fluids established. The selective adsorption of metabolic constituents on the surface of the implants must be measured and related to effects on cell membranes, attachment of cells to the implant surface followed by differentiation of cells capable of repair of the tissues.

Compositional effects on interfacial reaction rates must be related to rates of tissue response. Figure 4 shows such a relationship for a number of bioactive glasses composed of SiO_2-Na_2O-P_2O_5-SiO_2. Compositions with silica content less than 53+/- 1 mole% form a hydroxy-carbonate apatite(HCA) layer on the glass in test solutions within 2-3 hours. All of these glasses bond rapidly to bone *and* bond to soft connective tissues as well. Compositions with silica content between 53 and 60 mole % silica require 1-3 days to form a hydroxyapatite layer and bond *only* to bone. Glasses with more than 60% silica do not form a HCA layer even after several weeks and do *not* bond to either bone or soft tissues,i.e. they are bioinactive.

4) Biological Factors in Inorganic-Organic Reactions: The biochemical reasons for the correlation between the in-vitro reaction kinetics and in-vivo biological responses shown in Figure 4 are not known. In general, the role of inorganic trace elements in biomineralization is poorly understood. For example, the function of protein templates in heterogeneous nucleation of inorganic crystal phases and vice versa is proposed but the mechanisms are largely conjecture. Even after two decades it is still unclear why trace quantities of hydrated silicon are required for bone to mineralize(Evered and O,Conner,1986) . The presence and origin of dislocations in biological apatite crystals is just beginning to be

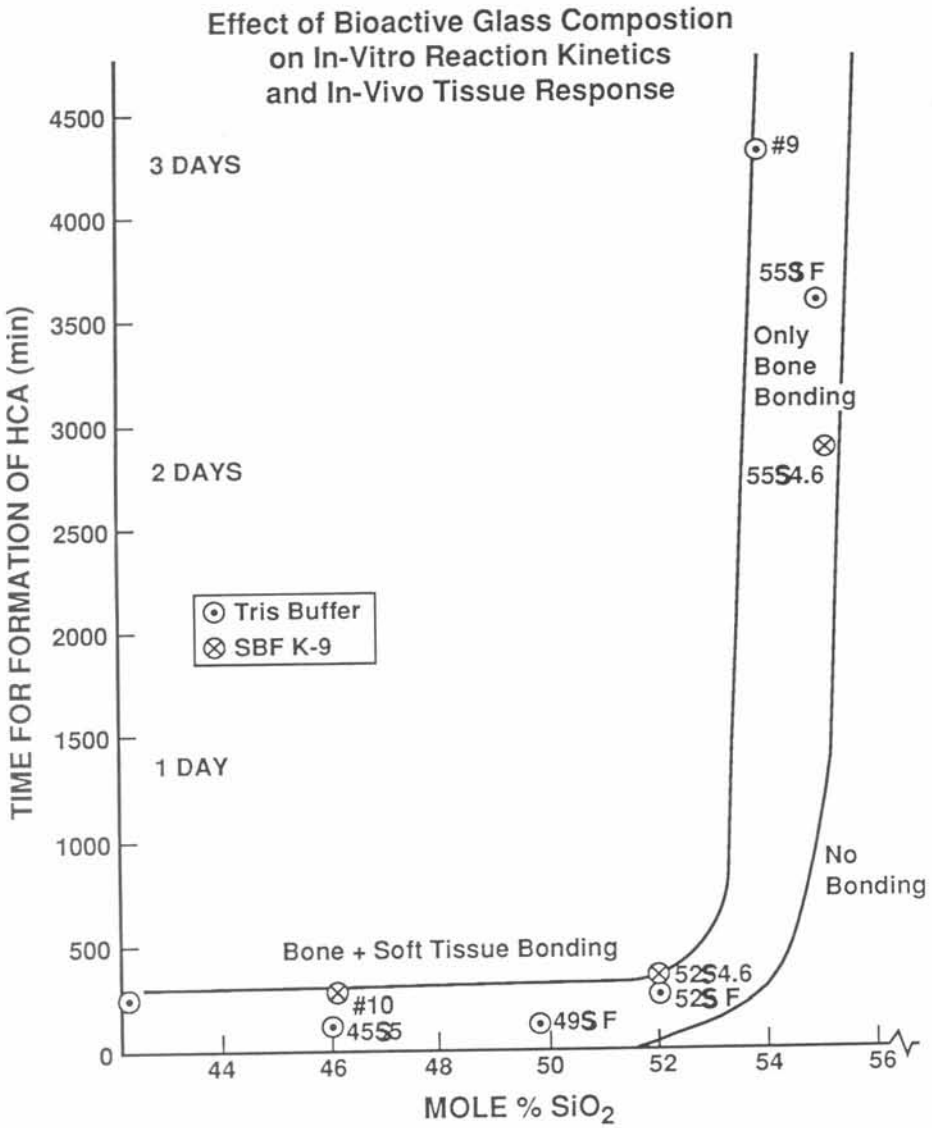

Figure 4. Effect of bioactive glass composition on in-vitro kinetics and in-vivo tissue response (Hench et al., 1992).

studied with high reolution TEM and the consequence of dislocations on their bonding to collagen or other biological constituents is still unknown (Bonfield,1992).

5) Genetic Coding of Biomineralization and Repair Processes: In order to design bioceramics at a molecular level to stimulate physiological repair processes it will

be necessary to know more about the genetic coding involved in biomineralization and formation of natural bone-cartilage, bone-tendon and bone-ligament interfacial structures. The human genome project underway worldwide (Shapiro,1991) may eventually provide this understanding. It is essential that the bioceramics field keep abreast of these developments and use the results in the experimental design of new materials. At present, most of the papers illustrated in Figure 1 are still based upon trial and error experiments.

6) Molecular Orbital Modeling and Molecular Design of Bioceramics: Recently developed semi-empirical methods for quantum mechanics calculations (Dewar etal, 1985,87 and Zerner et al, 1980) make it possible to model the interfacial reactions that occur on bioactive ceramics (West and Hench,1992). Results show that a condensation reaction between neighboring silanol groups (Stage 3 in Fig. 3) can provide an energetically favorable pathway for adsorption of calcium and phosphate groups and possible nucleation of a hydroxapatite crystal by means of a screw dislocation. The favored structure is shown in Figure 5. If experiment confirms this prediction then it will reinforce the potential for calculating the preferential adsorption of alternative biological moities on active inorganic surface sites. The cluster size involved in this type of calculation is in the range of 40-60 atoms and therefore is a reasonable approximation of a real surface. Because of the complexity of analyzing experimentally these inorganic-organic interactions, there is great need for a calculational approach that can identify specific experimental objectives to test. The calculations can then be used to predict the effects of changes in composition of the surface of the material and molecular design of new materials for specific biological functions.

Ethical Issues

There are 5-10,000,000 implants per year worldwide, a 10-fold increase over the last 20 years. This huge increase is in part because of the much larger number of people living to an age of >60 years (BMA,1990). It is also due to the many more types of spare parts available (Cauwels,1986). It is also, in part, because there are fewer ethical concerns when artificial materials are used rather than living transplants. Donor consent is not needed for an implant. Source of an artificial material is not an ethical issue. However, informed patient consent, patient/risk ratios, cost/benefit ratios, reliability, and incidence of revision surgery are moral and ethical issues as important for implants as for transplants. Boundaries for use of implants and introduction of new materials and devices need to be established that take into consideration complex ethical conflicts.

A major difficulty in establishing ethical guidelines for bioceramics and prosthetic devices is the existence of a fundamental problem in ethical theory. The theoretical foundations for physical sciences and biological sciences have been well developed with many decades of experimental verification. In contrast, there is no agreement in the theoretical foundation for analysing ethical issues. The utilitarianism view of John Stuart Mill and followers is that an action is "right" if it leads to the greatest possible good, i.e., "right is relative" to circumstances. In fundamental contrast, the ethical theory developed by Immanuel Kant and

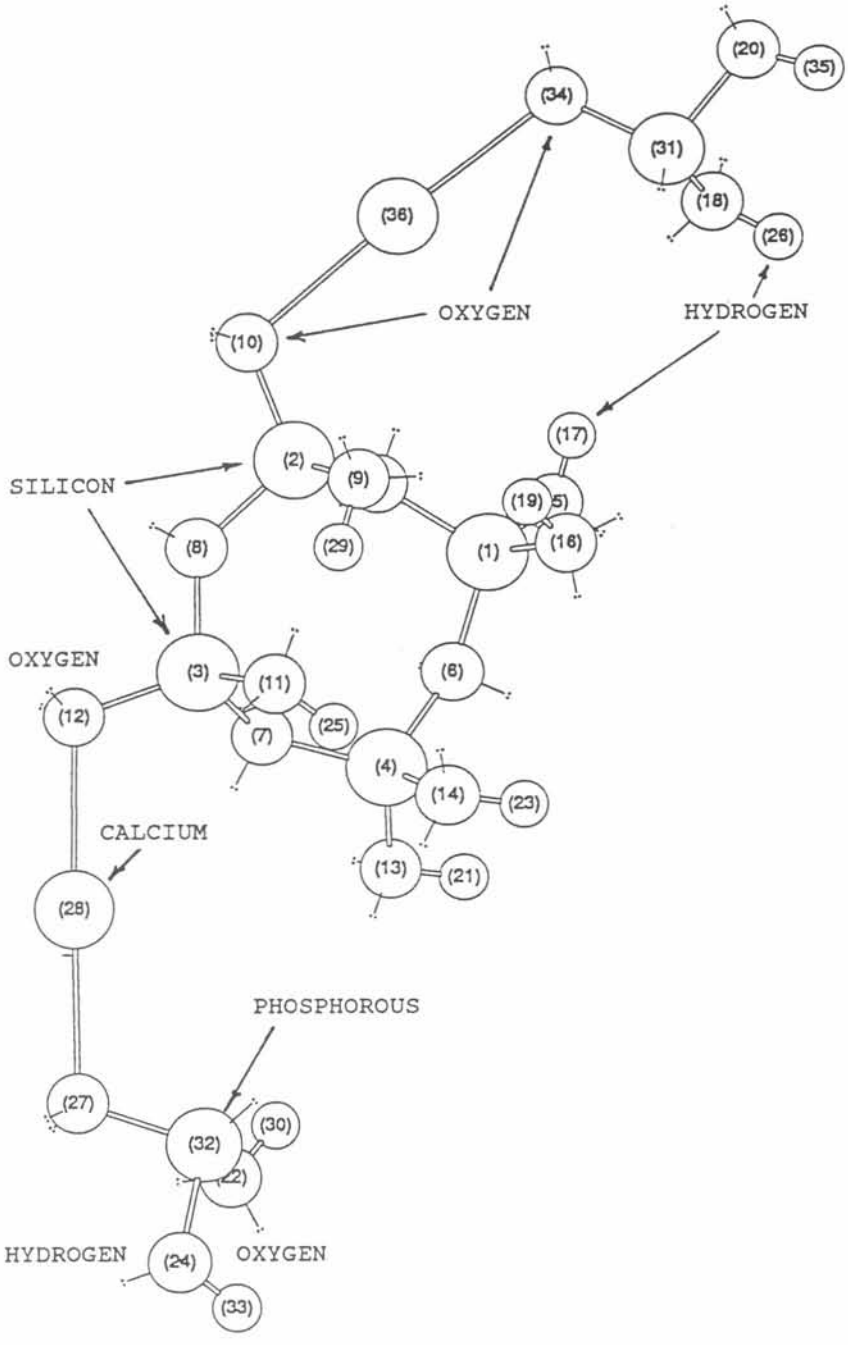

Figure 5. Calcium phosphate molecules nucleating on a siloxane ring, as calculated using an AM-1 semi-empirical molecular orbital method (West and Hench, 1992).

successors, such as W. D. Ross, maintains that moral standards exist independent of utilitarian ends. Thus, an act is "right" because it satisfies the demands of an overriding obligation, i.e., "right is revealed".

In spite of this difficulty there is a consensus among moral philosophers, according to Beauchamp and Walters (1989), that three general principles exist for making ethical decisions. They are: Respect for Autonomy, Principle of Beneficence, and Principle of Justice. Features of all three principles are summarized in Table 3. Respect for Autonomy, the concept that each person has the right to decide what is best for himself, is considered to rank highest in any hierarchy of ethical principles and take precedence in a medical situation. Difficulties arise, however, when it is unclear whether an individual is capable of making a "rational" decision, such as often occurs in medical emergencies or fatal illnesses.

Table 3

THREE GENERAL PRINCIPLES FOR MAKING ETHICAL DECISIONS

-RESPECT FOR AUTONOMY
(The concept of personal self-governance. The principle of a person's right to choose. It assumes that individuals have an intrinsic value and have the right to determine their own destiny. It is the opposite of slavery.)

-THE PRINCIPLE OF BENEFICENCE
(The concept that an action or decision should not inflict harm on another, should prevent or remove harm, or promote good to another.)

-THE PRINCIPLE OF JUSTICE
(The concept that like cases should be treated alike. This principle is difficult to use because individuals are not alike and often do not desire to be treated alike.)

The Principle of Beneficence, i.e. do no harm or create no risks, also should be considered inviolate in medical situations. However, there can be conflict between this principle and the respect for autonomy if a patient is incapable of expressing his choices or cannot understand the options. Also, a person may desire to have an implant for personal reasons, such as silicone breast implants or cosmetic facial injections of collagen, even though there is evidence that doing so involves risk and may not be "harmless". The assessment of risk is a statistical concept (BMA,1990) and thus the perceived risk for an individual is likely to be different for a manufacturer, surgeon, engineer, or patient.

The Principle of Justice leads to the most uncertainty and ethical conflicts. The

theoretical ideal of complete equality is impossible to achieve because individuals are not alike and often do not want to be treated alike. Consequently, the formal principle of justice is usually implemented in terms of what are called "The Material Principles of Justice". Table 4, based upon Beauchamp and Walters, 1989), summarizes alternatives for making decisions regarding distribution of material goods and health care resources. Decisions usually involve a complex mixtures of these options. The rapidly accelerating cost of health care in all countries (Callahan,1990, JAMA,1991) is leading towards an unwritten policy where health care depends upon personal finances rather than being based upon any principle of justice or fairness.

Table 4

MATERIAL PRINCIPLES OF JUSTICE

Which include as alternatives:

1) To each person an equal share.
2) To each person according to individual need.
3) To each person according to acquisition in a free market
4) To each person according to individual effort
5) To each person according to societal contribution
6) To each person according to merit
7) To each person according to age

Ref: T. L. Beauchamp and L. Walters, Contemporary Issues in BioEthics (3rd edition), Wadsworth Publishing Co., Belmont, CA (1989)

There is no theoretical foundation for resolving conflicts betwen the Principles of Autonomy, Beneficence, and Justice. Beauchamp and Walters summarize the present dilemma facing moral philosophers, and each of us as well: **"The problem of how to value or weigh different moral principles remains unresolved in contemporary moral theory".**

The important, practical consequence of this theoretical problem is that there is no basis for resolving ethical conflicts between individuals and between individuals and society. Laws are written but do not solve the moral dilemma.

When an implant fails, and they are at a rate of hundreds of thousands per year, conflict can arise between the patient, surgeon, and manufacturer. Why? The patient has given informed consent thereby honoring the principle of autonomy. The operation was chosen because the patient needed it to alleviate pain and statistics indicated a probability of success, so the principle of beneficence was respected. The problem? The patient perceives that the principle of justice has been violated. This because in our present day overemphasis of the successes of technology the patient not only expects *equal treatment* but also expects *equal*

results. The patient and his/her family do not care about statistics. They care only that their implant failed.

The ethical conflict is due to an unjustified expectations of *equal consequences* of an act instead of *equal performance* of an act. The principle of justice requires only that "like cases be treated alike". However, because individuals are different the results can be different even when the treatment is the same. The difference can be perceived, wrongly, as unjust.Technology and greed have amplified this problem, as discussed by the author in a recent paper (Hench, 1992). Rapid changes in technology lead to the impression that the "latest is best". This leads to a proliferation of choices with often no advantages offered other than sales promotion. The statistical basis for risk assessment and beneficence becomes progressively more uncertain the greater the options.

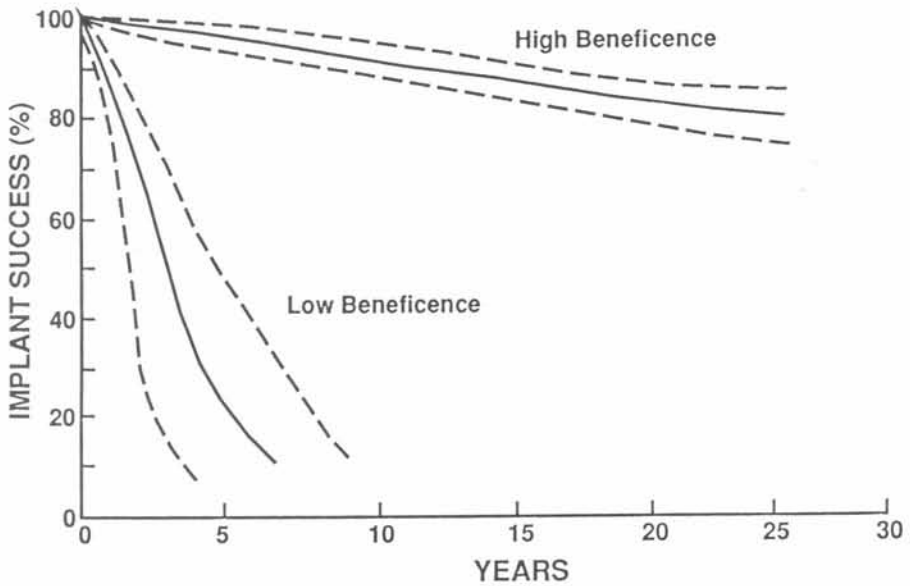

Figure 6. Comparison of implant failures as a function of time for high vs low beneficence to the patients.

Economic pressures lead to the allocation of corporate resources and introduction of implant products with only minimal standards of testing in order to have something "new" to offer. Research to obtain solutions to long term reliability problems are avoided because to do so is to admit that long term reliability is a problem. Thus, the implant field grows in volume but not necessarily proportionally in beneficence to the larger number of patients.

What should be done? The field of bioceramics must take steps to ensure that all new implants introduced into clinical use offer high standards of beneficence to the patient. Figure 6 illustrates the type of failure analysis that needs to be done for all implants in use or propoased for use clinically. Clinical results show that implants can be separted into two classes, High Beneficence (top curves) or Low Beneficence (bottom curves).

Ethics require that an implant meet the harsh standard of the upper curve because otherwise the principle of "do no harm" will be violated. Any implant that performs in limited clinical trials as indicated in the lower curve should not be put into general use. Many examples exist where this criterion has been violated in the past (Hench,1992). It is the responsibility of each of us in the field of bioceramics to ensure that it is not violated in the future.

The time has arrived for the field of bioceramics to move from trial-and- error product development into the future where molecular design of new ceramics for specific physiological requirements will be achieved. Steps along this new path have been taken. We must make certain that short cuts and ethical conflicts are avoided.

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