Classes of Materials Used in Medicine:
Ceramics, Glasses, Glass-ceramics

INTRODUCTION

- Ceramics, glasses, and glass-ceramics include a broad range of inorganic/nonmetallic compositions.

- In the medical industry, these materials have been essential for

  - Eyeglasses
  - Diagnostic instruments
  - chemical ware
  - Thermometers
  - Tissue culture flasks
  - Fiber optics for endoscopy

- Insoluble porous glasses have been used as carriers for

  - Enzymes
  - Antibodies
  - Antigens

offering the advantages of resistance to microbial attack, pH changes, solvent conditions, temperature

- Insoluble glasses have also been developed as a microinjectable delivery system for radioactive isotopes for *in situ* treatment of tumors.
    - The glass microspheres go to the site of the tumor by way of the blood supply, and the radiation kills the cancer cells with very little damage to the other tissues, saving thousands of patients.

- Ceramics are also widely used in dentistry as restorative materials, such as in
    - gold–porcelain crowns
    - glass-filled ionomer cements
    - dentures

- Glass-ceramics are also widely used for dental restorations including
    - Inlays
    - Onlays
    - crowns
    - multi-unit bridges

- The main difference among inlays, onlays and overlays (crown) is in the size of damage and the area of the tooth being treated.

  - **Inlays cover** the central part of the tooth and are positioned within the hard tissues of the tooth. They do not cover the cusps or the pointed parts of the tooth.

  - **Onlays cover** a larger area. Besides replacing the internal part of the damaged tooth, they also cover one of the cusps. So, they are positioned inside the deep tissues of the tooth as well as cover part of the biting surface of the tooth.

TYPES OF BIOCERAMICS: TISSUE ATTACHMENT

- It is essential to recognize that **no one material is suitable for all biomaterial applications.**

- As a class of biomaterials, ceramics, glasses, and glass-ceramics are generally used to repair or replace skeletal hard connective tissues.

- Their success depends upon:

    1. achieving a stable attachment to connective tissue when used as bulk implants

    2. stimulating repair and regeneration of bone when used as particulates for bone grafting.

- **The mechanism of tissue attachment is directly related to the type of tissue response at the implant-tissue interface.**

- There are **four types of tissue response** and **four different means of attaching** prostheses to the skeletal system.

TABLE I.2.4.1 Types of Implant–Tissue Response

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 I.2.4.2 Types of Bioceramic Tissue Attachment and Their Classification

1. 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)
2. For porous inert implants, bone ingrowth occurs that mechanically attaches the bone to the material (termed "biological fixation").	Al_2O_3 (polycrystalline) Hydroxyapatite-coated porous metals
3. 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
4. Dense, nonporous (or porous) resorbable ceramics are designed to be slowly replaced by bone.	Calcium sulfate (Plaster of Paris) Tricalcium phosphate Calcium–phosphate salts

A comparison of the relative chemical activity of the different types of bioceramics, glasses, and glass-ceramics

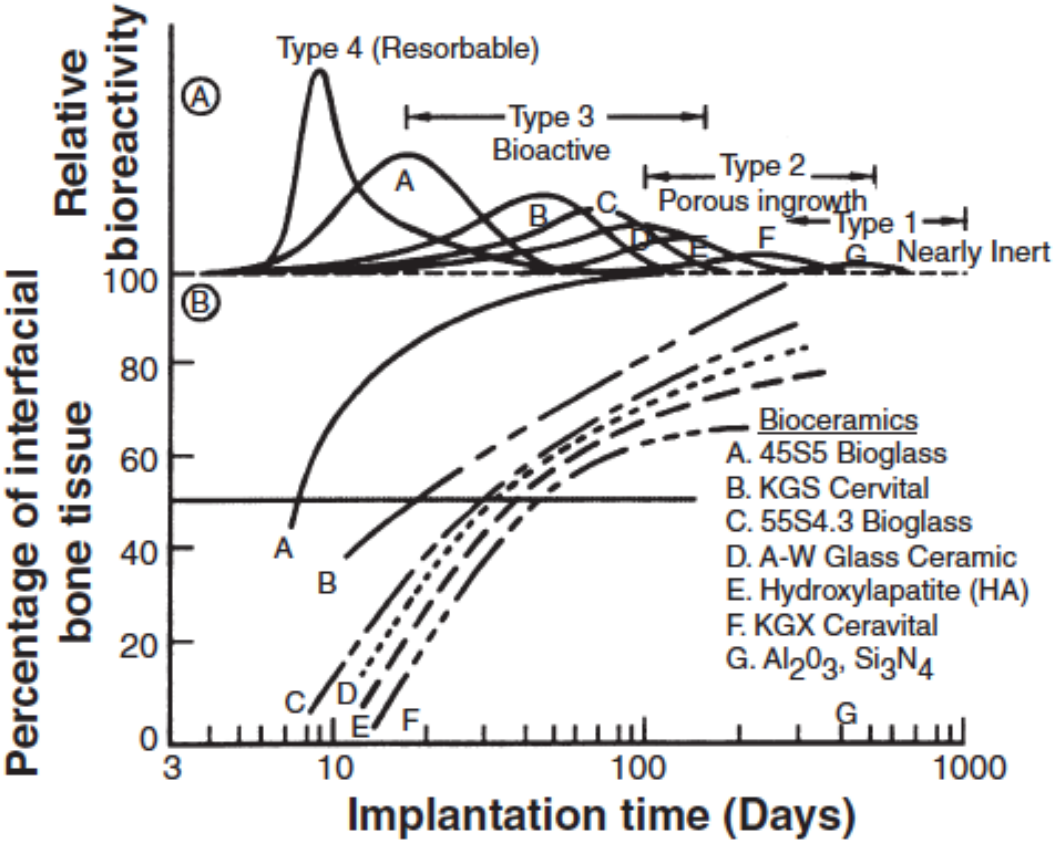


FIGURE I.2.4.1 Bioactivity spectra for various bioceramic implants: (A) Relative rate of bioreactivity; (B) Time-dependence of formation of bone bonding at an implant interface.

- The relative reactivity that is shown in Figure I.2.4.1A correlates very closely with the rate of formation of an interfacial bond of ceramic, glass or glass-ceramic implants with bone (Figure I.2.4.1B).

- The relative level of reactivity of an implant influences the thickness of the interfacial zone or layer between the material and tissue

- **Analyses of implant material failures often show failure originating at the biomaterial–tissue interface.**

    - When biomaterials are nearly inert and the interface is not chemically or biologically bonded, there is relative movement and progressive development of a fibrous capsule in soft and hard tissues.

    - The presence of movement at the biomaterial–tissue interface eventually leads to deterioration in function of the implant or the tissue at the interface, or both.

    - Wear particles can accelerate the deterioration of the tissue–implant interface.

- The thickness of the non-adherent capsule varies, depending upon both material (Figure I.2.4.2) and extent of relative motion.

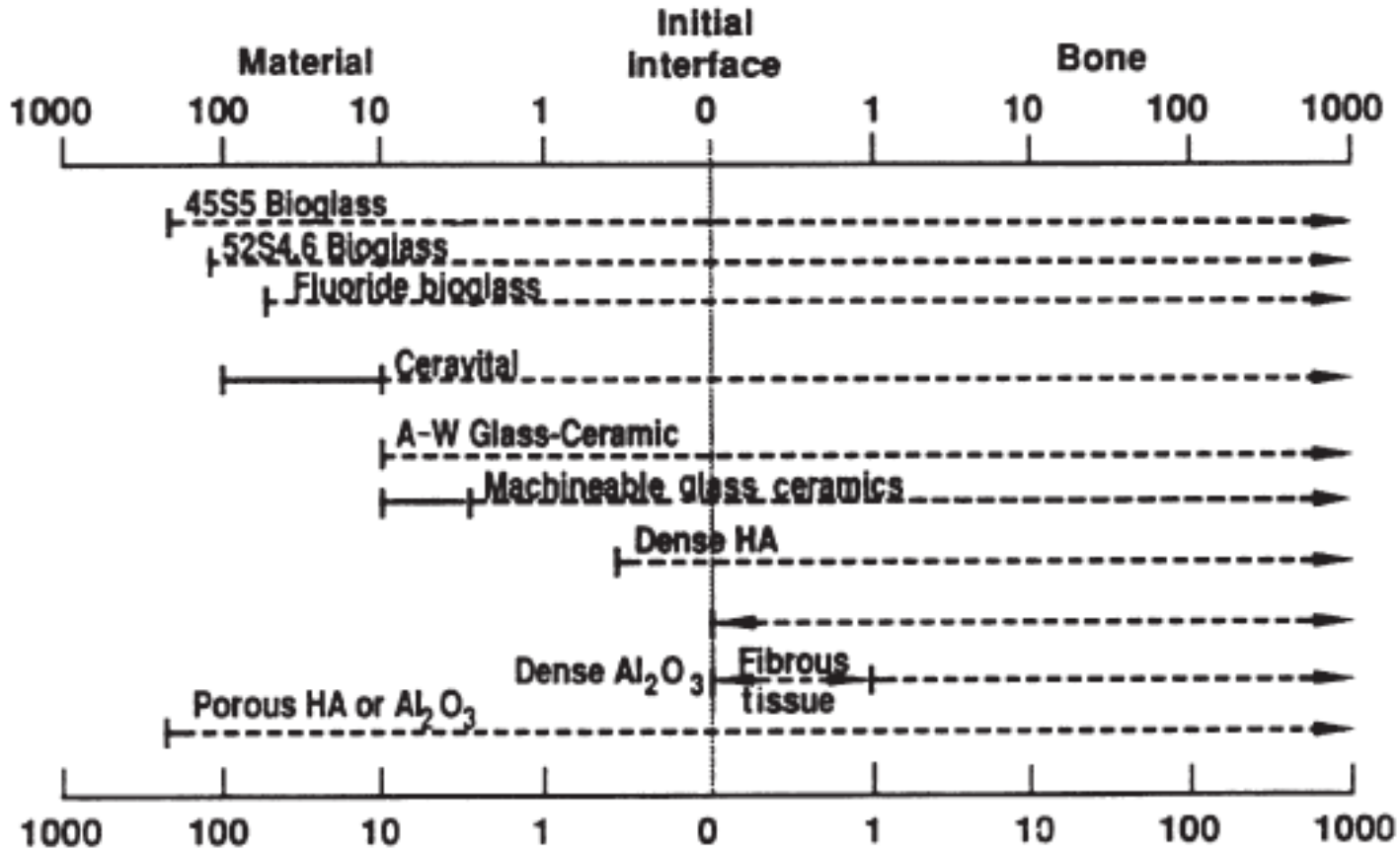


FIGURE I.2.4.2 Comparison of interfacial thickness (μm) of reaction layer of bioactive implants of fibrous tissue of inactive bioceramics in bone.

- The fibrous tissue at the interface of **dense Al_2O_3 (alumina)** implants is very thin. Consequently, if alumina devices are implanted with a very tight mechanical fit and are loaded primarily in compression, they are very successful.

- In contrast, **if a type 1 nearly inert implant is loaded so that interfacial movement can occur**, the fibrous capsule can become several hundred micrometers thick, and the implant can loosen very quickly.

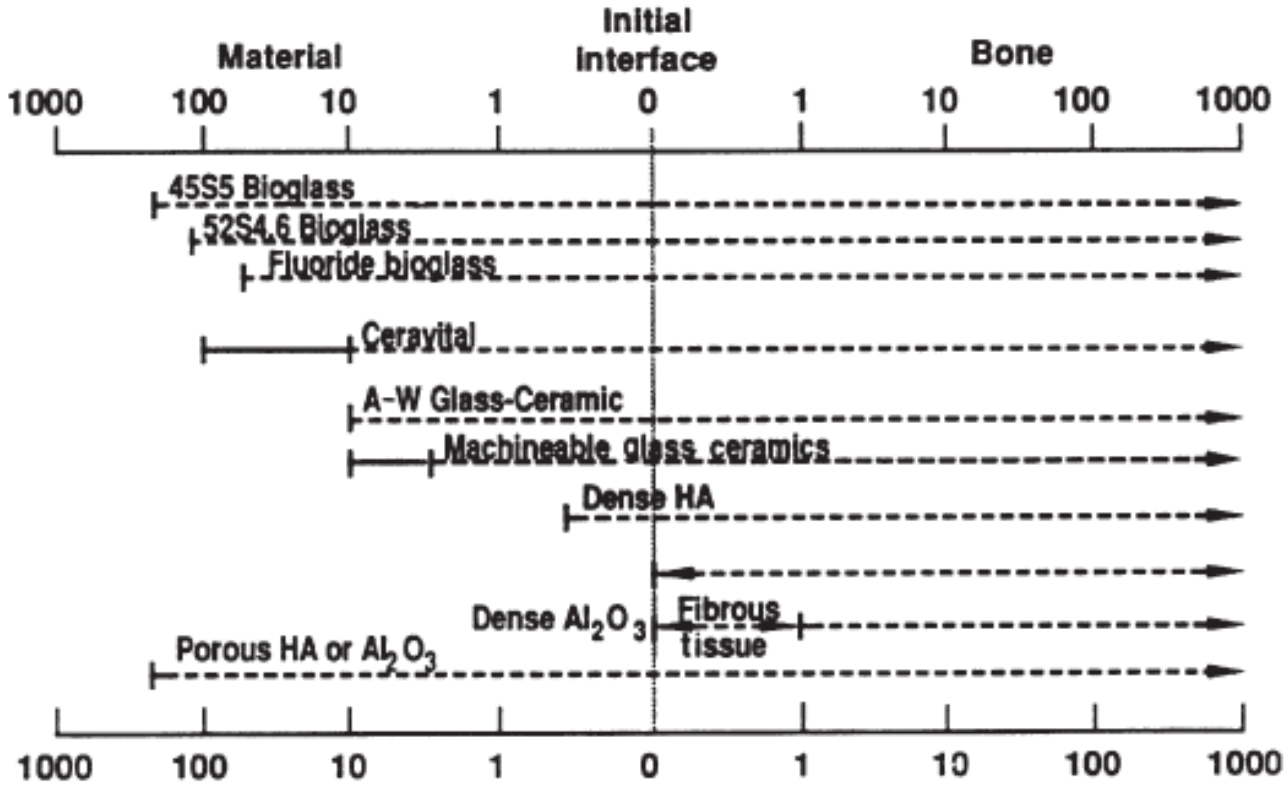


FIGURE I.2.4.2 Comparison of interfacial thickness (μm) of reaction layer of bioactive implants of fibrous tissue of inactive bioceramics in bone.

- **The mechanism behind the use of nearly inert microporous materials (type 2) is the 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. The interface is established by the living tissue in the pores.

  - This method of attachment is often termed **"biological fixation**." It is capable of withstanding more complex stress states than type 1 implants with "**morphological fixation**."

  - The **limitation with type 2 porous implants** is that for the tissue to remain viable and healthy, it is necessary for the **pores to be greater than 50 to 150 µm**

  - The large interfacial area required for porosity is due to the need to provide a blood supply to the ingrown connective tissue (**vascular tissue does not appear in pore sizes less than 100 µm**)

- When the material is a **porous metal**, the large increase in surface area can provide a focus for **corrosion of the implant and loss of metal** ions into the tissues.
    - This can be mediated by using a bioactive ceramic material such as hydroxyapatite (HA) as a coating on the metal.
- The **fraction of large porosity in any material also degrades the strength** of the material proportional to the volume fraction of porosity.
    - This approach works best when materials are used as **coatings or as unloaded space fillers in tissues** to **solve** interfacial stability

- **Resorbable biomaterials (type 4)** are designed to degrade gradually over a period of time, and to be replaced by the natural host tissue.

- Complications in the development of resorbable bioceramics are:

    1. **maintenance of strength and the stability of the interface** during the degradation period and replacement by the natural host tissue

    2. **matching resorption rates** to the repair rates of body tissues (e.g., some materials dissolve too rapidly and some too slowly).

    3. Because large quantities of material may be replaced, it is also essential that **a resorbable biomaterial consist only of metabolically acceptable substances.**

        - Successful examples of resorbable polymers include poly(lactic acid) and poly(glycolic acid) used for sutures, which are metabolized to CO_2 and H_2O and therefore are able to function for an appropriate time and then dissolve and disappear.

        - Porous or particulate calcium phosphate ceramic materials such as tricalcium phosphate (TCP) have proved successful for resorbable hard tissue replacements when low loads are applied to the material.

- **Bioactive materials are intermediate between resorbable and bioinert (type 3).**
    - A bioactive material is one that elicits a specific biological response at the interface of the material, resulting in the formation of a bond between the tissues and the material.
    - They include bioactive glasses such as 45S5 Bioglass; bioactive glass-ceramics such as A-W glass-ceramic; dense HA and bioactive composites such as HA-polyethylene.

- All of these materials (type1,2,3,4) form an interfacial bond with adjacent tissue. However, the time dependence of bonding, the strength of bond, the mechanism of bonding, and the thickness of the bonding zone differ for the various materials.

CHARACTERISTICS AND PROCESSING OF BIOCERAMICS

- The characteristics and properties of the materials differ greatly, depending upon the **processing method used.**

- The primary methods of processing ceramics, glasses, and glass-ceramics are summarized in Figure:

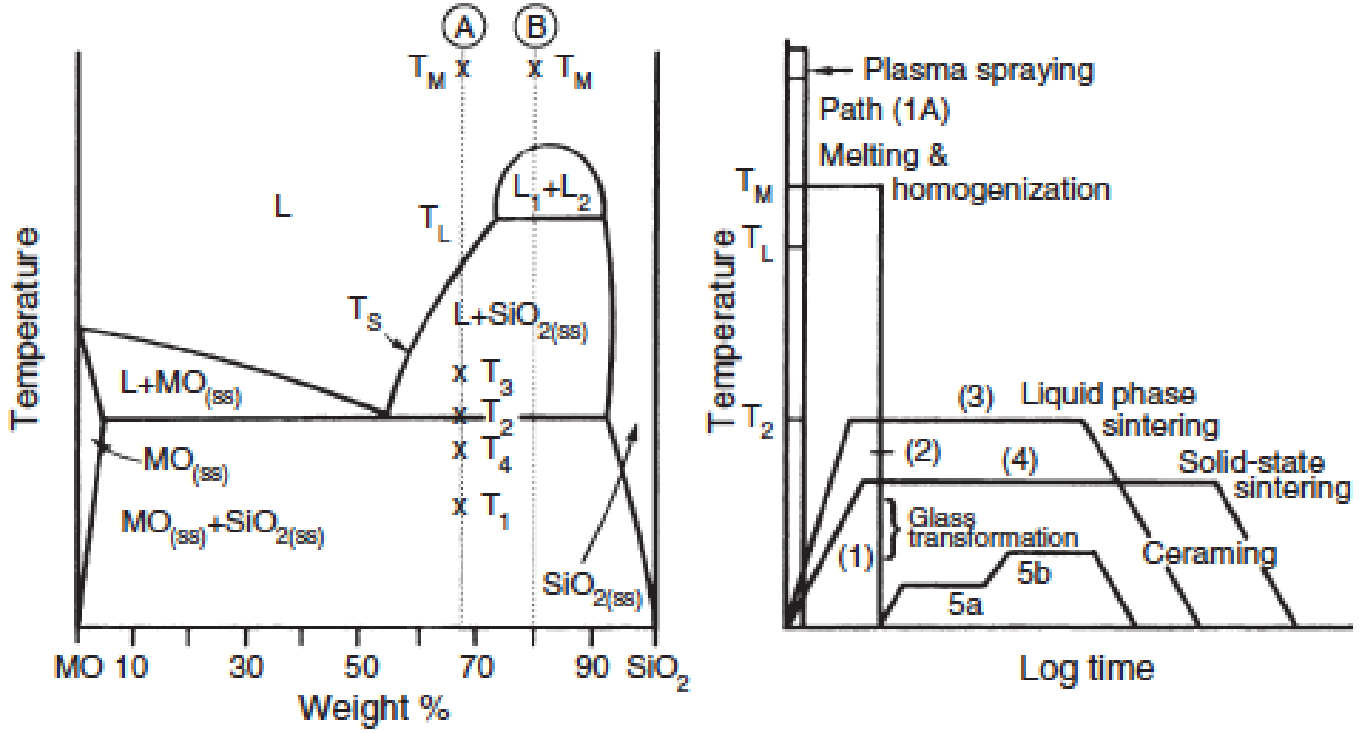


FIGURE I.2.4.3 Relation of thermal processing schedules of various bioceramics to equilibrium phase diagram.

- These methods yield five categories of microstructures:

    1. Glass
    2. Cast or plasma-sprayed polycrystalline ceramic
    3. Liquid-phase sintered (vitrified) ceramic;
    4. Solid-state sintered ceramic;
    5. Polycrystalline glass-ceramic.

- **Differences in the microstructures** of the five categories are primarily a result of the **different thermal processing steps** required to produce them.

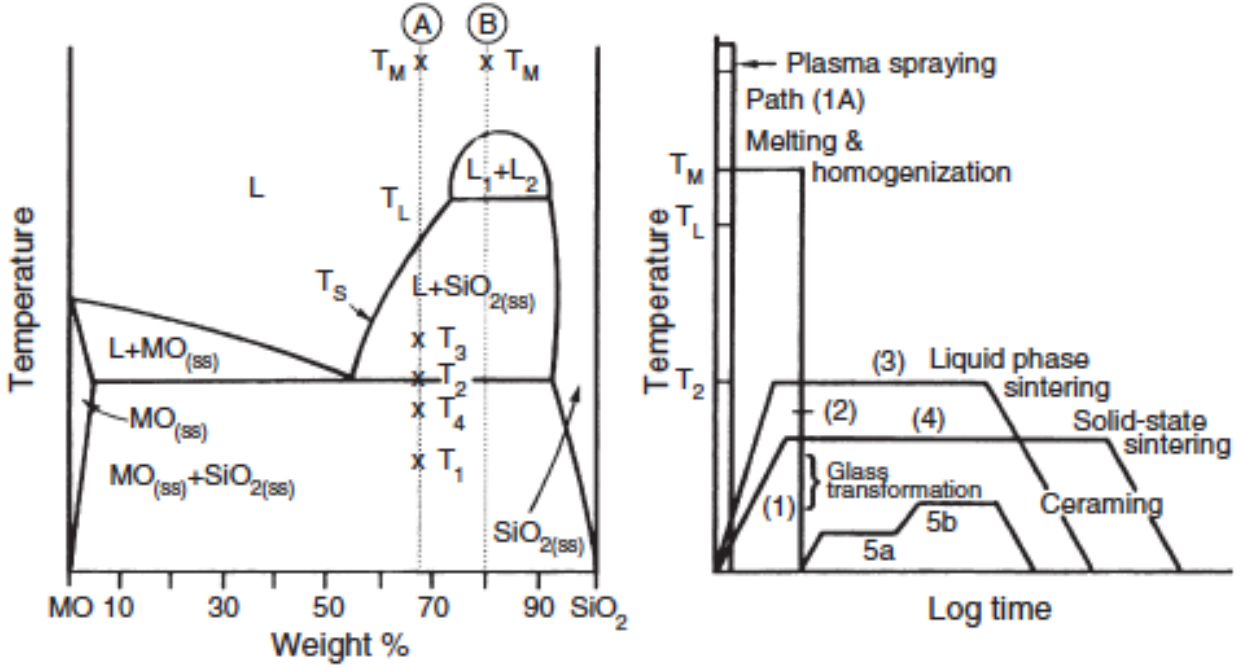
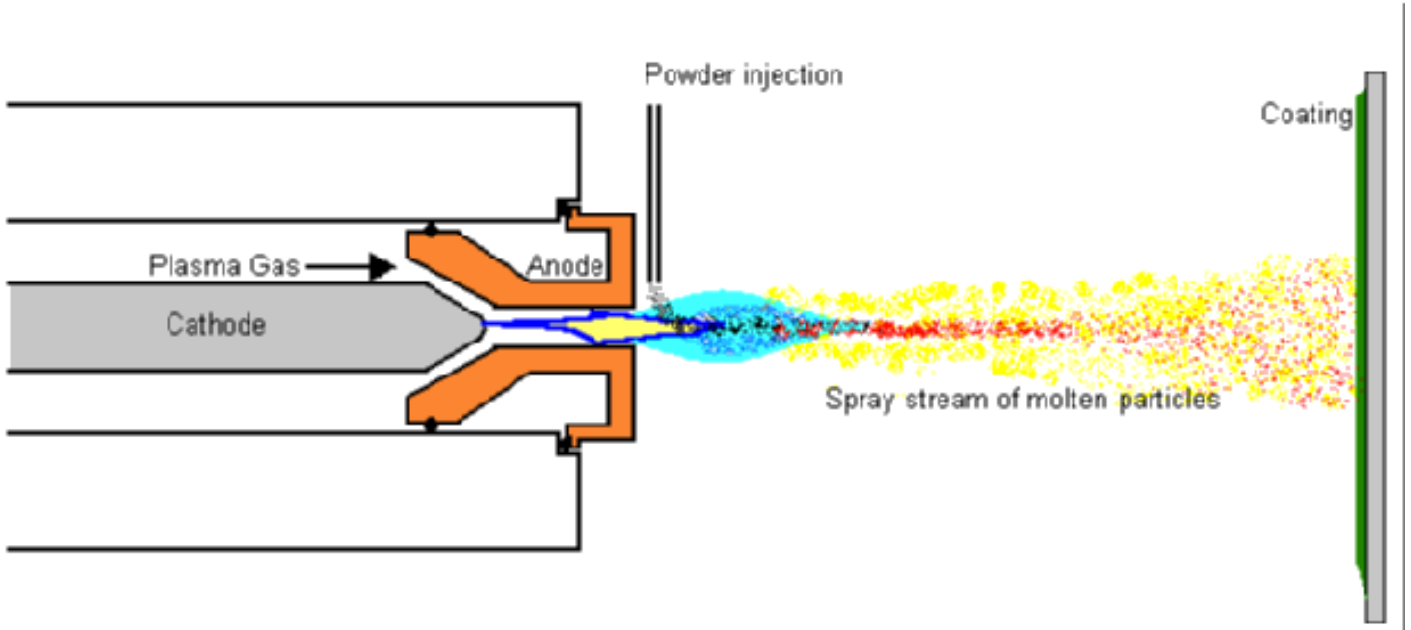
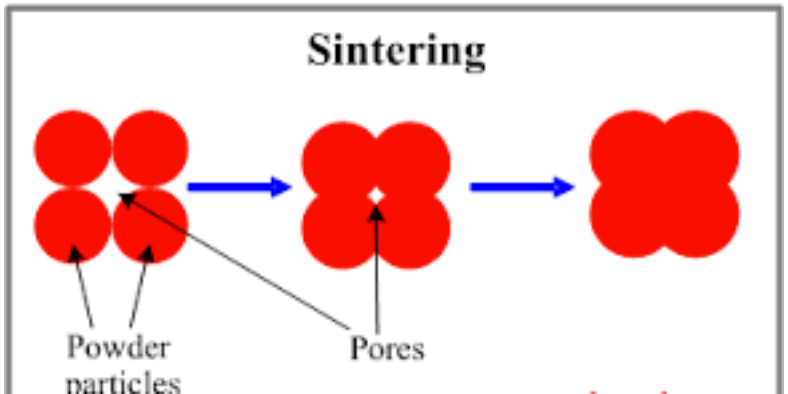


FIGURE I.2.4.3 Relation of thermal processing schedules of various bioceramics to equilibrium phase diagram.

- Basically the **spraying** of molten or heat softened material onto a surface to provide a coating.
- Material in the form of powder is injected into a very high temperature plasma flame, where it is rapidly heated and accelerated to a high velocity.



- **Sintering** is the process of compacting and forming a solid mass of material by heat or pressure without melting it to the point of liquefaction



videos

Nearly Inert Crystalline Ceramics

- High-density, high-purity (>99.5%) **alumina (Al_2O_3)** is used in the articulating surfaces of total joint prostheses because of its **excellent corrosion resistance**, good biocompatibility, **high wear resistance**, and high strength

- Al_2O_3 ceramics with an average grain size of <4 µm and >99.7% purity exhibit good flexural strength and excellent compressive strength.

- Physical properties are summarized in Table I.2.4.4, along with the International Standards Organization (ISO) requirements for alumina implants.

TABLE I.2.4.4 Physical Characteristics of Al_2O_3 Bioceramics

	High Alumina Ceramics	ISO Standard 6474
Alumina content (% by weight)	>99.8	≥99.50
Density (g/cm3)	>3.93	≥3.90
Average grain size (µm)	3–6	<7
Ra (µm)[a]	0.02	
Hardness(Vickers hardness number, VHN)	2300	>2000
Compressive strength (MPa)	4500	
Bending strength (MPa) (after testing in Ringer's solution)	550	400
Young's modulus (GPa)	380	
Fracture toughness (K_1C) (MPa^{12})	5–6	
Slow crack growth	10–52	

[a]Surface roughness value.

- super tribiologic properties (friction and wear)

- The **long-term coefficient of friction of an alumina–alumina joint decreases** with time and approaches the values of a normal joint.

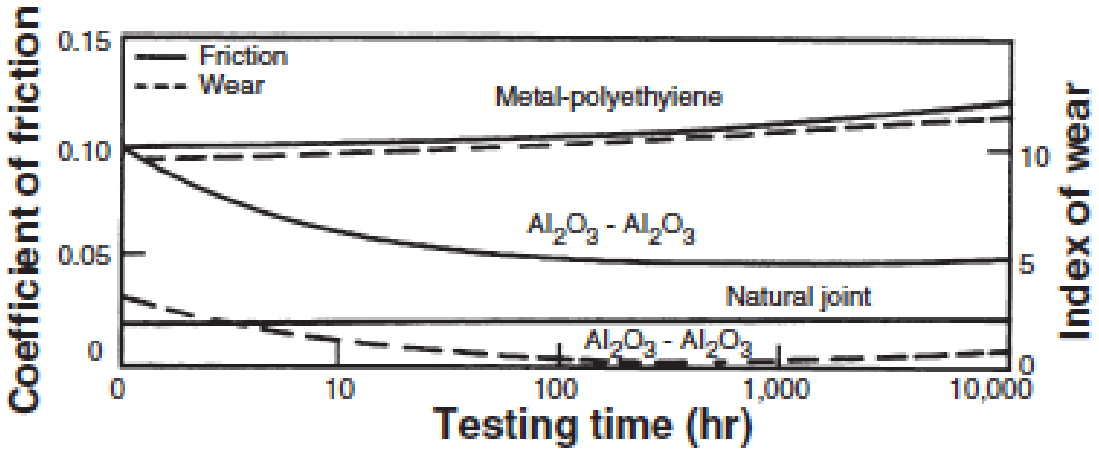


FIGURE I.2.4.4 Time dependence of coefficient of friction and wear of alumina–alumina versus metal–polyethylene hip joint (*in vitro* testing).

- This leads to wear on alumina-articulating surfaces being nearly 10 times lower than metal–polyethylene surfaces, and **eliminates formation of polyethylene wear particles** that are associated with loosening of total joint prostheses.

- Low wear rates have led to widespread use in Europe of alumina **noncemented cups press-fitted into the acetabulum of the hip**. The cups are stabilized by the growth of bone into grooves

- **Long-term results in general are good, especially for younger patients.**

- Christel et al. (1988) **caution** that stress shielding, owing to the high elastic modulus of alumina, may be responsible for **cancellous bone atrophy and loosening of the acetabular cup in old patients** with senile osteoporosis or rheumatoid arthritis.

    - Consequently, <u>it is essential that the age of the patient, nature of the disease of the joint, and biomechanics of the repair be considered carefully before any prosthesis is used, including alumina ceramics.</u>

- **zirconia** was also used in a similar way to alumina for articulating applications in hip and knee replacement

    - However a series of **implant failures around the year 2000**, resulted in the **withdrawal of zirconia** for these applications.

    - Today, there is **significant interest in the use of zirconia toughened alumina implants** due to the potential to **enhance strength and toughness properties** over those of alumina.

    - Zirconia is **used widely for dental applications** due to aesthetic and mechanical benefits the material offers.

- Other clinical applications of alumina prostheses include knee prostheses; bone screws; alveolar ridge and maxillofacial reconstruction; ossicular bone substitutes; keratoprostheses (corneal replacements); segmental bone replacements; and blade, screw, and post-dental implants.

Porous Ceramics

- The potential advantage offered by a porous ceramic implant is its **inertness combined with the mechanical stability** of the highly-convoluted interface that develops when bone grows into the pores of the ceramic.

- The mechanical requirements of prostheses, however, severely **restrict the use** of low-strength porous ceramics to **nonloadbearing** applications.

- when loadbearing is not a primary requirement, 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 or scaffold for bone formation.

- **Commercially available porous products** originate from two sources: hydroxyapatite converted from coral or animal bone.

- **Porous materials are weaker** than the equivalent bulk form in proportion to the percentage of porosity, so that as the porosity increases, the **strength** of the **material decreases rapidly**

Bioactive Glasses and Glass-ceramics

- Certain compositions of glasses, ceramics, glass-ceramics, and composites have been shown to bond to bone. These materials have become known as bioactive ceramics.

- Some specialized compositions of bioactive glasses will bond to soft tissues as well as bone

- The surface forms a **biologically-active carbonated HA** layer (HCA) that provides the bonding interface with tissues.

- Bonding to bone was **first demonstrated** for a compositional range of bioactive glasses that contained SiO_2, Na_2O, CaO, and P_2O_5 in specific proportions

TABLE I.2.4.5 Composition of Bioactive Glasses and Glass-Ceramics (In Weight Percent)

	45S5 Bioglass	45S5F Bioglass	45S5.4F Bioglass	40S5B5 Bioglass	52S4.6 Bioglass	55S4.3 Bioglass	KGC Ceravital	KGS Ceravital	KGy213 Ceravital	A-W GC	MB GC
SiO_2	45	45	45	40	52	55	46.2	46	38	34.2	19–52
P_2O_5	6	6	6	6	6	6				16.3	4–24
CaO	24.5	12.25	14.7	24.5	21	19.5	20.2	33	31	44.9	9–3
$Ca(PO_3)_2$							25.5	16	13.5		
CaF_2		12.25	9.8							0.5	
MgO							2.9			4.6	5–15
MgF_2											
Na_2O	24.5	24.5	24.5	24.5	21	19.5	4.8	5	4		3–5
K_2O							0.4				3–5
Al_2O_3									7		12–33
B_2O_3				5							
Ta_2O_5/TiO_2									6.5		
Structure	Glass	Glass	Glass	Glass	Glass		Glass-ceramic	Glass-ceramic		Glass-ceramic	Glass-ceramic
Reference	Hench et al. (1982)	Hench et al. (1982)	Hench et al. (1982)	Hench et al. (1982)	Hench et al. (1982)	Hench et al. (1982)	Gross et al. (1988)	Gross et al. (1988)		Nakamura et al. (1985)	Höeland and Vogel (1993)

- Surface reaction steps of silica glass in aqueous or physiological solutions

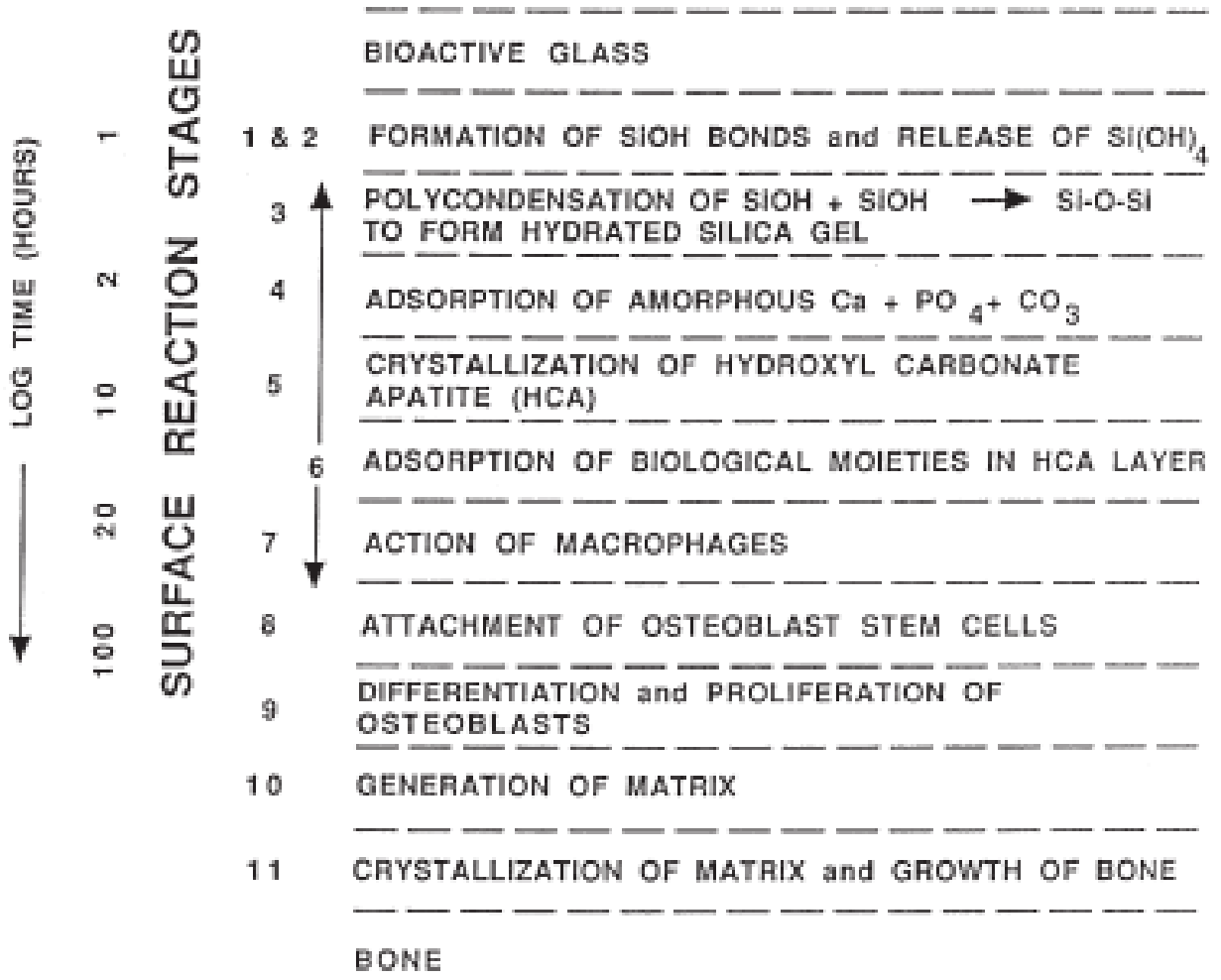


FIGURE I.2.4.6 Types of silicate glass interfaces with aqueous or physiological solutions.

➢ Bioactivity Reaction Stages

- There is a sequence of 11 reaction stages that occur at the surface of a Class A bioactive glass, as summarized in Figure I.2.4.6

- Controlled rates of dissolution of the glass provide the critical concentration of the biologically active ions to the cells via the interfacial solution.

- The families of genes that are upregulated and/or activated are shown in Table I.2.4.7

TABLE I.2.4.7	Families of Genes In Human Osteoblasts Activated or Up-Regulated by Ionic Dissolution Products of Bioactive Glasses
(1) Transcription Factors and Cell Cycle Regulators	
(2) DNA Synthesis, Repair and Recombination	
(3) Apoptosis Regulators	
(4) Growth Factors and Cytokines	
(5) Cell Surface Antigens and Receptors	
(6) Signal Transduction Molecules	
(7) Extracellular Matrix Compounds	

lists the clinical applications of 45S5 bioactive glass.

TABLE I.2.4.6	Typical Clinical Applications of Bioactive Ceramics, Glasses and Glass Ceramics (highlighting 45S5 and Hydroxyapatite as Examples)
Orthopedics	
Trauma:	
Long bone fracture (acute and/or comminuted); alone and with internal fixation	
Femoral non-union repair	
Tibial plateau fracture	
Arthroplasty	
Filler around implants (acetabular reconstruction)	
Impaction grafting	
General	
Filling of bone after cyst/tumor removal	
Spine Fusion	
Interbody fusion (cervical, thoracolumbar, lumbar)	
Posterolateral fusion	
Adolescent idiopathic scoliosis	
Cranial-Facial	
Cranioplasty	
Facial reconstruction	
General oral/dental defects	
Extraction sites	
Ridge Augmentation	
Sinus elevation	
Cystectomies	
Osteotomies	
Periodontal Repair	
Dental- Maxillofacial- ENT	
Toothpaste and treatments for dentinal hypersensitivity and inhibition of gingivitis	
Pulp capping	
Sinus obliteration	
Repair of orbital floor fracture	
Endosseous ridge maintenance implants	
Middle ear ossicular replacements (Douek MED)	

CALCIUM PHOSPHATE CERAMICS

- Bone typically consists by weight of 25% water, 15% organic materials, and 60% mineral phases.

- The mineral phase consists primarily of calcium and phosphate ions, with traces of magnesium, carbonate, hydroxyl, chloride, fluoride, and citrate ions.

- Hence, calcium phosphates occur naturally in the body, but they also occur within nature as mineral rocks, and certain compounds can be synthesized in the laboratory.

- Table I.2.4.8 summarizes the mineral name, chemical name, and composition of various phases of calcium phosphates.

TABLE I.2.4.8 Calcium Phosphates

Ca:P	Mineral Name	Formula	Chemical Name
1.0	Monetite	$CaHPO_4$	Dicalcium phosphate (DCP)
1.0	Brushite	$CaHPO_4 \cdot 2H_2O$	Dihydrate (DCPD) Dicalcium phosphate
1.33	—	$Ca_8(HPO_4)_2(PO_4)_4 \cdot 5H_2O$	Octocalcium phosphate (OCP)
1.43	Whitlockite	$Ca_{10}(HPO_4)(PO_4)_6$	
1.5	—	$Ca_3(PO_4)_2$	Tricalcium phosphate (TCP)
1.67	Hydroxyapatite	$Ca_{10}(PO_4)_6(OH)_2$	
2.0		$Ca_4P_2O_9$	Tetracalcium phosphate

- **interest has intensified in the use of calcium phosphates** as biomaterials, but **only certain compounds** are useful for implantation in the body, since both their **solubility** and speed of hydrolysis **increase with a decreasing calcium-to-phosphorus ratio**.
    - Driessens (1983) stated that those compounds with a Ca/P ratio of less than 1:1 are not suitable for biological implantation.

- A wide variety of methods have been investigated to produce synthetic hydroxyapatite.
    - The most commercially popular routes are based on **aqueous precipitation** or conversion from other calcium compounds.
    - **The stoichiometry of HA** is highly significant where thermal processing of the material is required.
    - **Slight imbalances** in the stoichiometric ratio of calcium and phosphorus in HA (from the standard molar ratio of 1.67) can lead to the **appearance of either α- or β-tricalcium phosphate**
    - **X-ray diffraction and infrared spectroscopy** should be used to reveal the phase purity of hydroxyapatite.(the standard molar ratio of calcium and phosphorus in HA: 1.67)

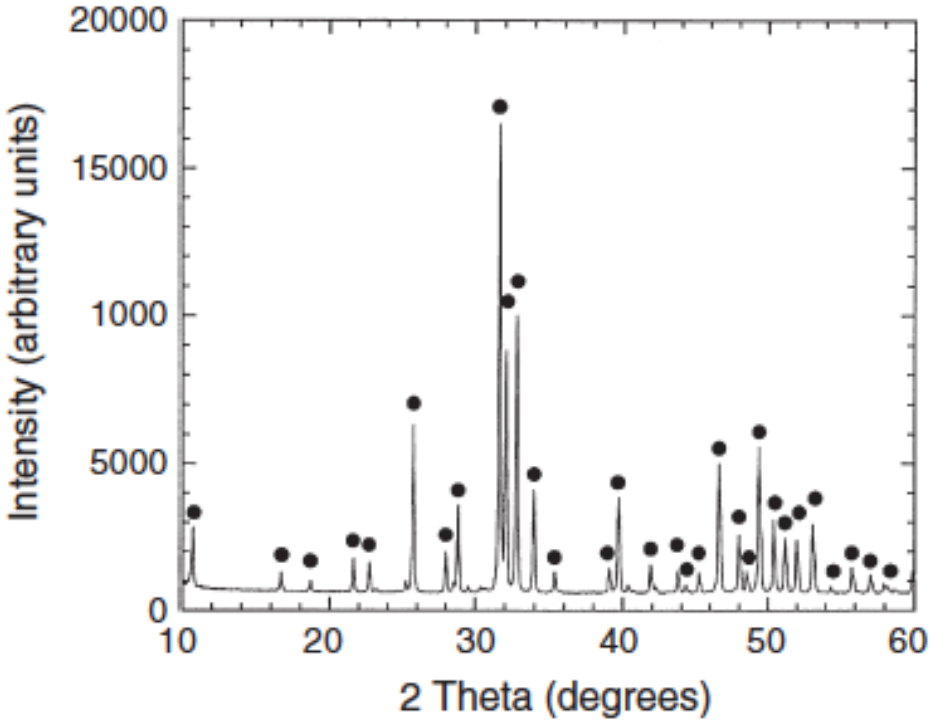


FIGURE I.2.4.9 X-ray diffraction of hydroxyapatite.

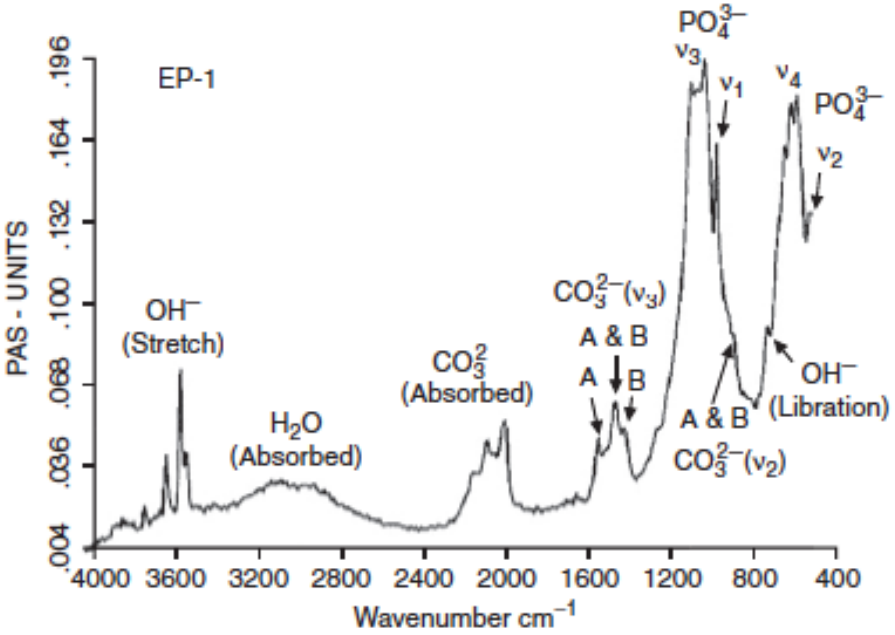


FIGURE I.2.4.10 Typical FT-IR spectrum for a bone mineral-derived hydroxyapatite.

- Typical data for one commercial hydroxyapatite powder are:

TABLE I.2.4.9 Trace Elements In a Commercial Hydroxyapatite

Trace Element	PPM
Al	600
Cu	1
Fe	1000
Ge	100
Mg	2000
Mn	300
Na	3000
Pb	4
Si	500
Ti	30

- Other ions which may be incorporated into the HA structure, either intentionally or unintentionally, include

  - carbonate ions (substituting for hydroxyl or phosphate groups)
  - fluoride ions (substituting for hydroxyl groups)
  - silicon or silicate ions (substituting for phosphorus or phosphate groups)
  - magnesium ions substituting for calcium

CALCIUM PHOSPHATE COATINGS

- The clinical application of calcium phosphate ceramics is largely **limited to bone grafting** applications or to **non-major loadbearing** parts of the skeleton.

- This is because of relatively poor mechanical strength and toughness, and inferior mechanical properties, and it was partly for this reason that interest was directed toward the use of calcium phosphate coatings on metallic implant subtrates.

- Many techniques are available for the deposition of hydroxyapatite coatings, including

    - Electrophoresis
    - sol–gel routes
    - electrochemical routes
    - biomimetic routes
    - sputter techniques

    but

    - the most popular commercial routes are those based on plasma spraying. Plasma sprayed coatings have been found to be highly successful, and are now widely used in hip joint replacement.

RESORBABLE CALCIUM PHOSPHATES

- Resorption or biodegradation of calcium phosphate ceramics is caused by three factors:

1. Physiochemical dissolution, which depends on the solubility product of the material and local pH of its environment.

2. Physical disintegration into small particles as a result of preferential chemical attack of grain boundaries.

3. Biological factors, such as phagocytosis, which causes a decrease in local pH concentrations.

- All calcium phosphate ceramics biodegrade to varying degrees; the rate of biodegradation increases as:

    1. Surface area increases (powders > porous solid > dense solid)
    2. Crystallinity decreases
    3. Crystal perfection decreases
    4. Crystal and grain size decrease
    5. There are ionic substitutions of CO_{-3}^{2}, Mg^{2+}, and Sr^{2+} in HA.

CALCIUM PHOSPHATE BONE CEMENTS

- These materials offer the potential for *in situ* molding and injectability.

- There are a variety of different combinations of calcium compounds (e.g., α-tricalcium phosphate and dicalcium phosphate) which are used in the formulation of these bone cements

- In the development and production of the bone cements a number of factors need to be considered, including

    - the processing parameters (such as solid and liquid component composition, particle size, and liquid-to-powder ratio)
    - setting properties
    - cohesion time
    - the injectability of the paste

- These will in turn significantly influence the microstructure and porosity, and hence mechanical behavior of the cement.