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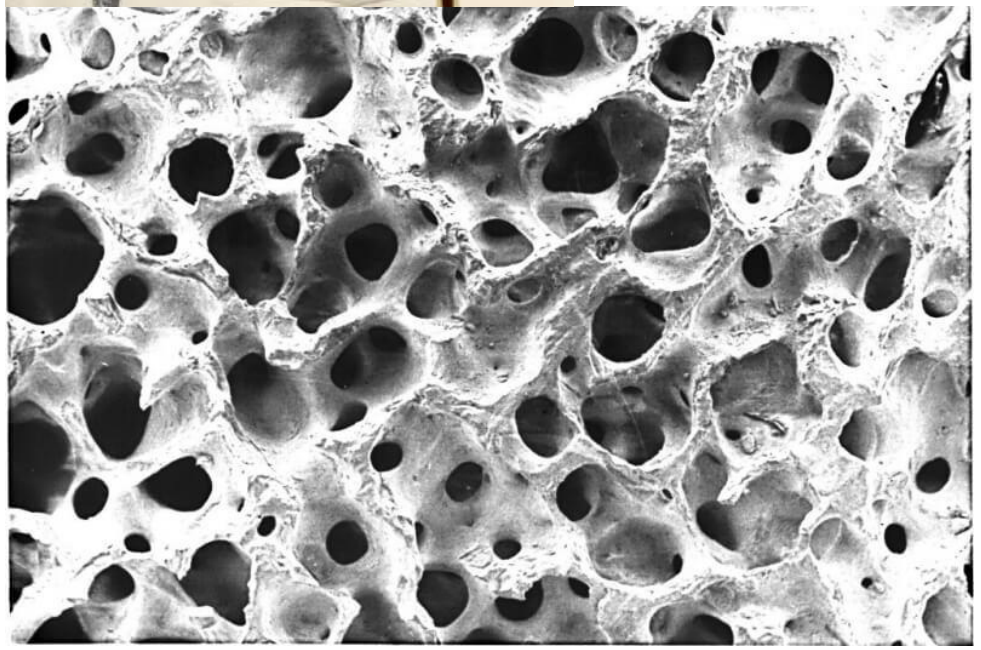
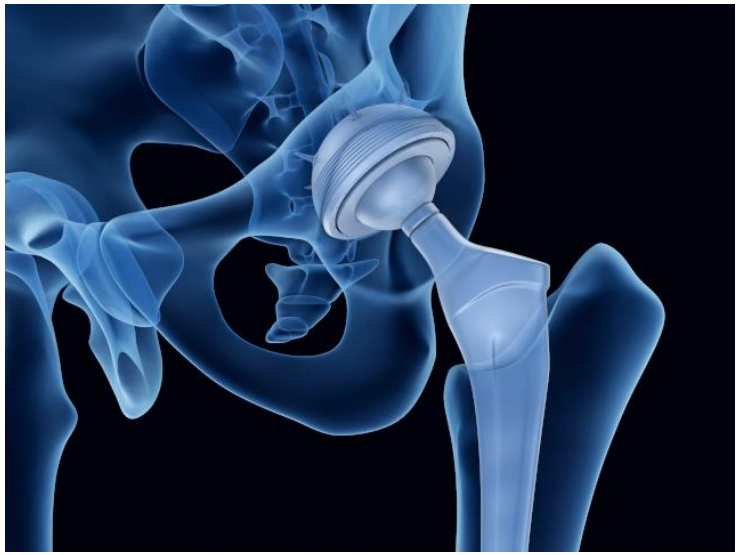


BIOCERAMICS – OBTAINING AND APPLICATION



«Modern European trends in biomedical higher education: Bionanomaterials.»
№ 620717-EPP-1-2020-1-UA-EPPJMO-MODULE

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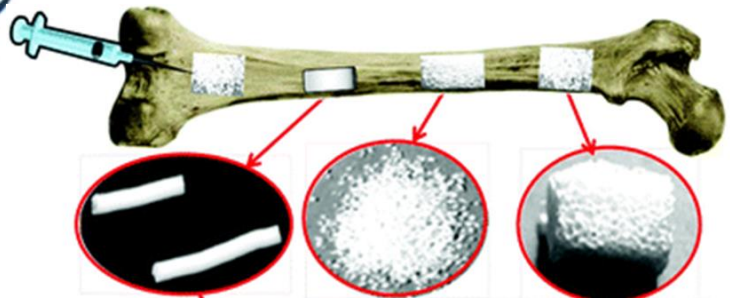
Ceramics is one of the most important classes of biomaterials



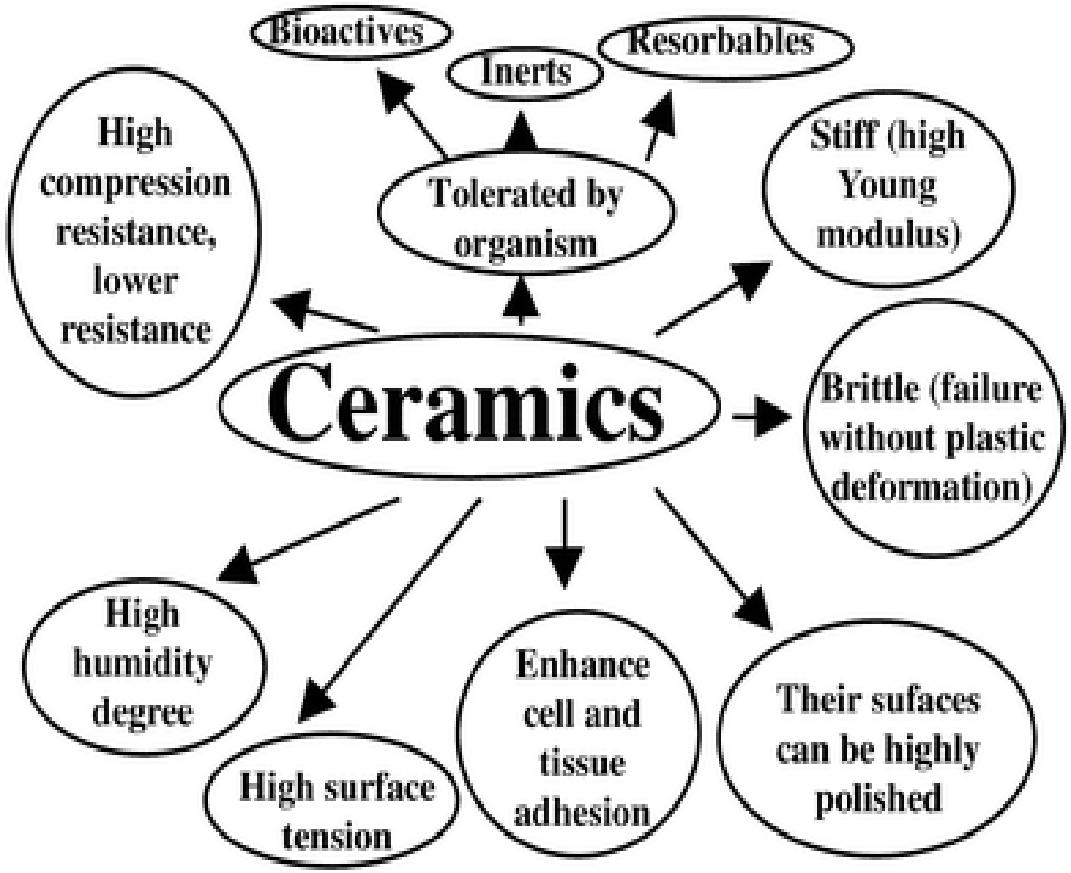
- **Biomaterials** must be distinguished from **biological materials** because the former are ***the materials that are accepted by living tissues and, therefore, they might be used for tissue replacements***, while the latter are the materials being produced by various biological systems.
  Further, **bioceramics (or biomedical ceramics) might be defined as biomaterials of the ceramic origin**. In general, bioceramics can have structural functions as ***joint or tissue replacements***, be used as ***coatings*** to improve the biocompatibility of metal implants, as well as function as ***resorbable lattices***, providing temporary structures and frameworks those are dissolved and/or replaced as the body rebuilds the damaged tissues [1]

- **Bioceramics** are a large class of specially designed crystalline, semicrystalline, or amorphous materials used for the repair and reconstruction of diseased or damaged parts of the body (Hench, 1991).

Bioceramics

inert	bioactive	biodegradable
Al_2O_3 ZrO_2 Carbons Sintered HA $CaAl_2O_4$ Si_3N_4 SiC	HA, HCA Biglasses Glass-ceramics: *A-W, Ceravital* *Particle size, crystallinity, porosity*	$CaSO_4$ Coral-$CaCO_3$: *aragonite* Ca-phosphates: α-TCP β-TCP OCP DCPA DCPD TetCP HA:10 μm also with: ZnO, Al_2O_3, Fe_2O_3,-

HA: hydroxyapatite
HCA: hydroxycarbonate apatite
A-W: apatite - wollastonite
TCP: tricalcium phosphate
OCP. octacalcium phosphate
DCPA: dicalcium phosphate anhydrous
DCPD: dicalcium phosphate dihydrate
TetCP: Tetracalcium phosphate monoxide



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Classification of bio ceramics

Bioceramics for bone replacement graft (BG)

Silicate bioceramics

Natural based
(e.g. marine sponges)

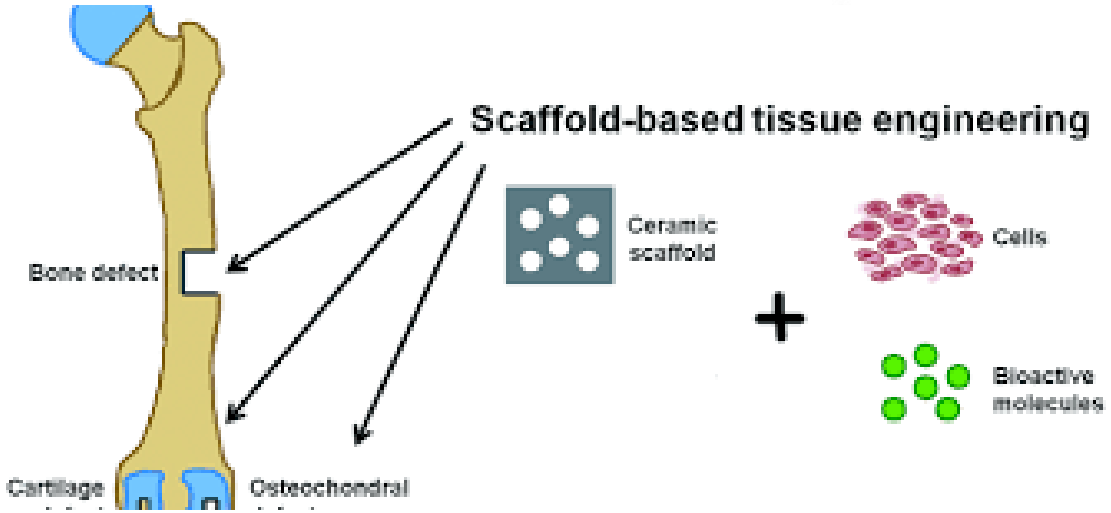
Glass based
(e.g. Bioglass 45S5, S53P4)

Non-silicate bioceramics

Oxide based
(e.g. TiO_2, ZrO_2)

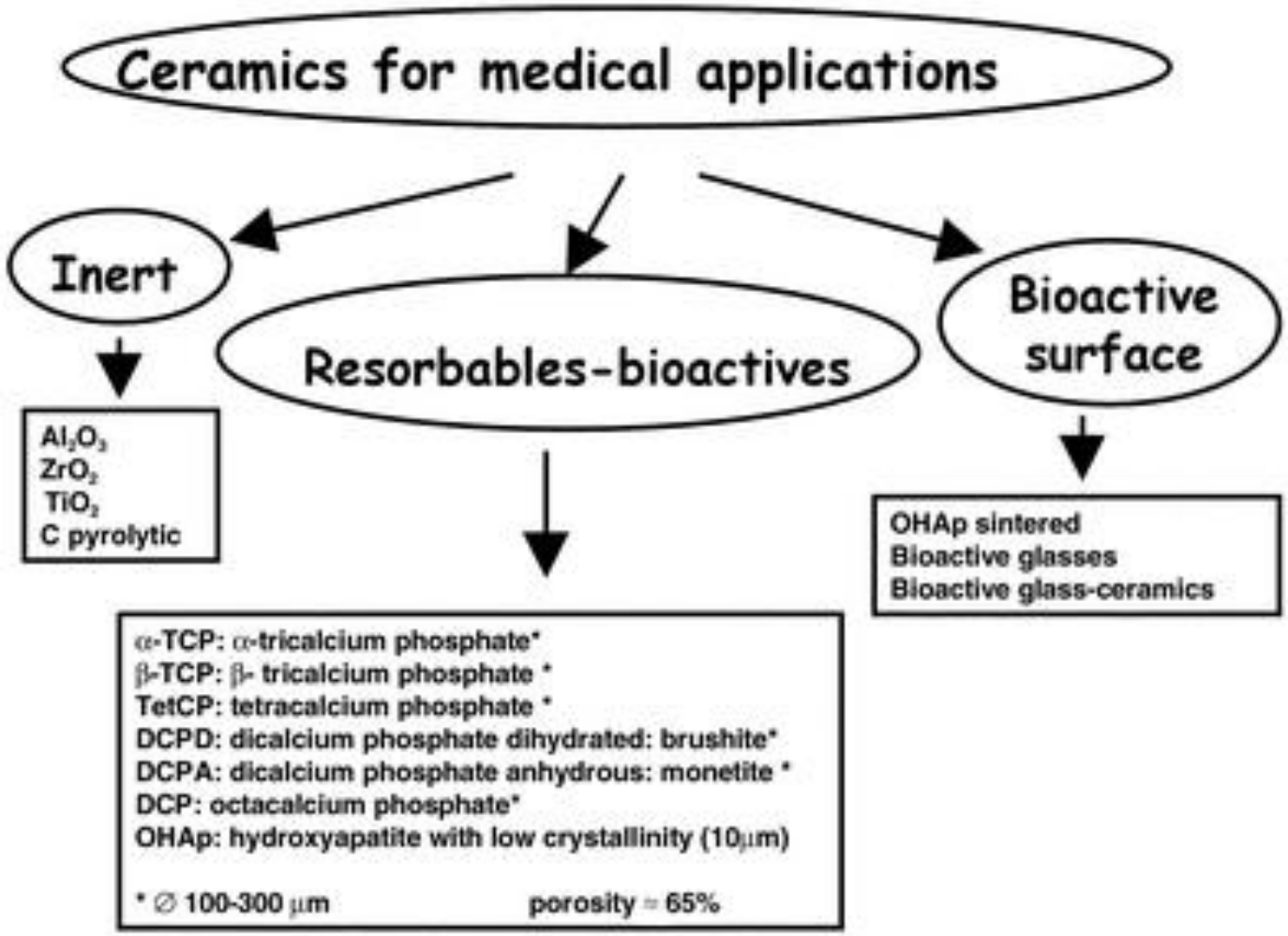
Non-oxide based
(e.g. CaPx, HA, α or βTCP)

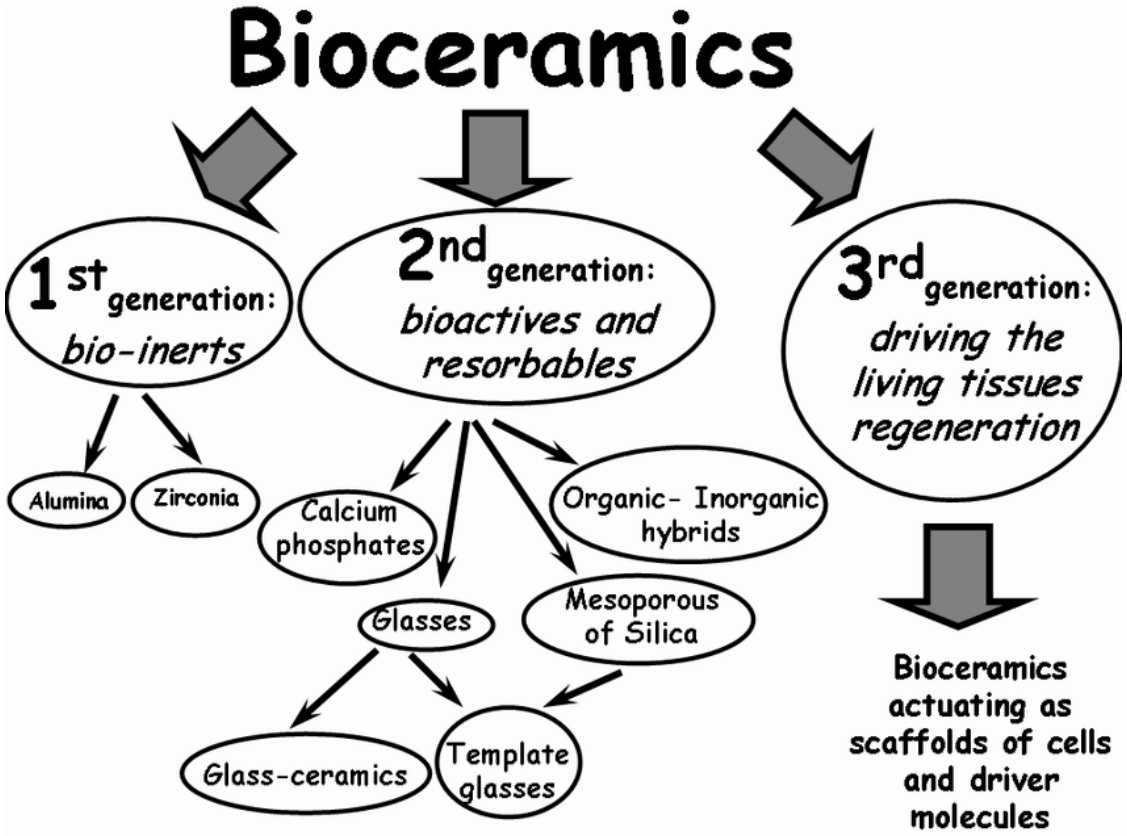
Natrual based
(e.g. corals, bovine human, equine bone)



- Calcium phosphate (CaP) bioceramics are widely used in the field of bone regeneration, both in orthopedics and in dentistry, due to their good biocompatibility, osseointegration and osteoconduction [1]

Classification of ceramics





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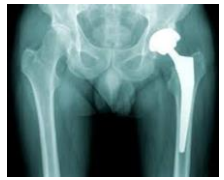
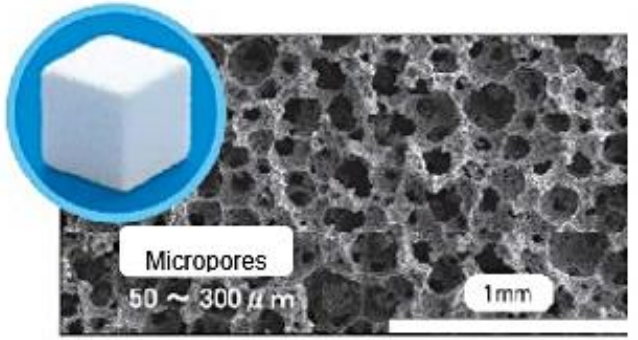
BIOMATERIALS

BIOCERAMICS BIOMETALS ORGANIC BIOMATERIALS



BIOCERAMICS

CHEMICALLY BONDED SINTERED CERAMICS GLASSES GLASS-CERAMICS

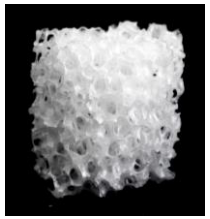


Porous artificial bones made of bioceramics

Figure 1: Example of products using bioceramics

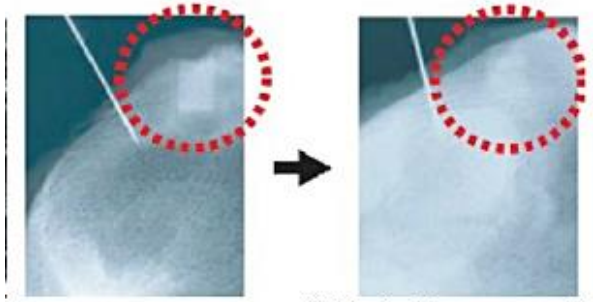
CHEMICALLY BONDED BIOCERAMICS (CBBCs)

BODY TEMPERATURE CBBCs HIGH TEMPERATURE CBBCs



BODY TEMPERATURE CBBCs

ACID-BASE REACTION WATER UP-TAKE POLYMERISATION REACTION

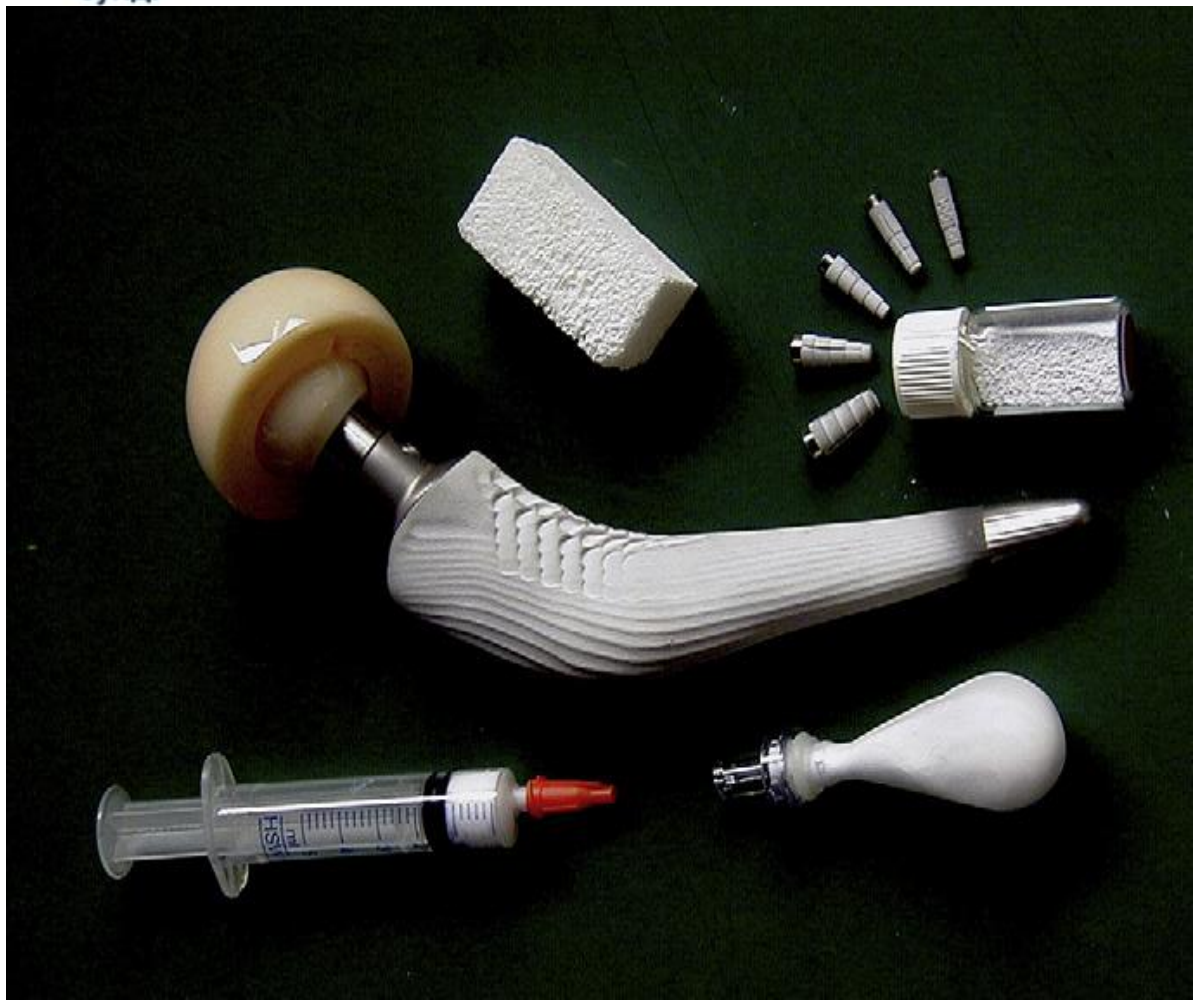


Subject before bone surgery operation

Subject with progress after the surgery operation

Figure 2: Pictures of bioceramics assimilating with operated-on bone

History of bioceramics



Several examples of commercial calcium orthophosphate-based bioceramics

- A strong interest in use of ceramics for biomedical applications appeared in the late 1960's. Used initially as alternatives to metals in order to ***increase a biocompatibility of implants***, bioceramics have become a diverse class of biomaterials, presently including ***three basic types: relatively bioinert ceramics, bioactive (or surface reactive) and bioresorbable ones***. Furthermore, any type of bioceramics could be porous to provide tissue ingrowth. During the past 30–40 years, there have been a number of major advances in this field. Namely, after the initial work on development of bioceramics that was tolerated in the physiological environment, emphasis was shifted towards the use of bioceramics that interacted with bones by forming a direct chemical bond.
  By the structural and compositional control, it became possible to choose whether the bioceramics of calcium orthophosphates was ***biologically stable*** once incorporated within the skeletal structure or whether it was ***resorbed over time***. Potential future applications of calcium orthophosphate bioceramics will include ***drug-delivery systems***, as well as they will become effective ***carriers of growth factors***, bioactive peptides and/or various types of cells for tissue engineering purposes.
  [2]

Types of ceramic materials

First generation:

Inerts

- Alumina
- Zirconia

Second generation:

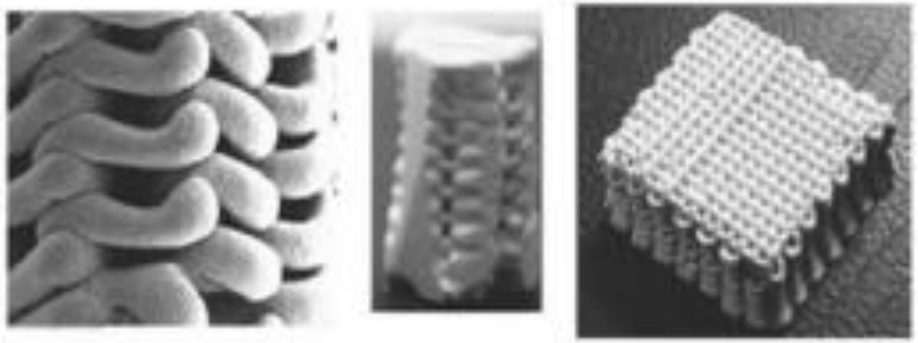
Bioactives and bioresorbables

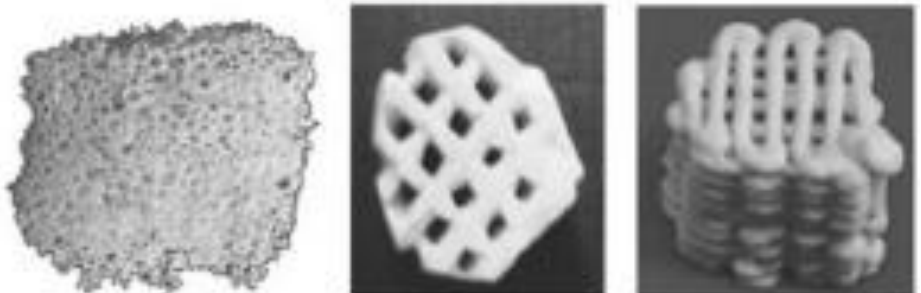
- Calcium phosphates
- Glasses
- Glass-ceramics

Third generation:

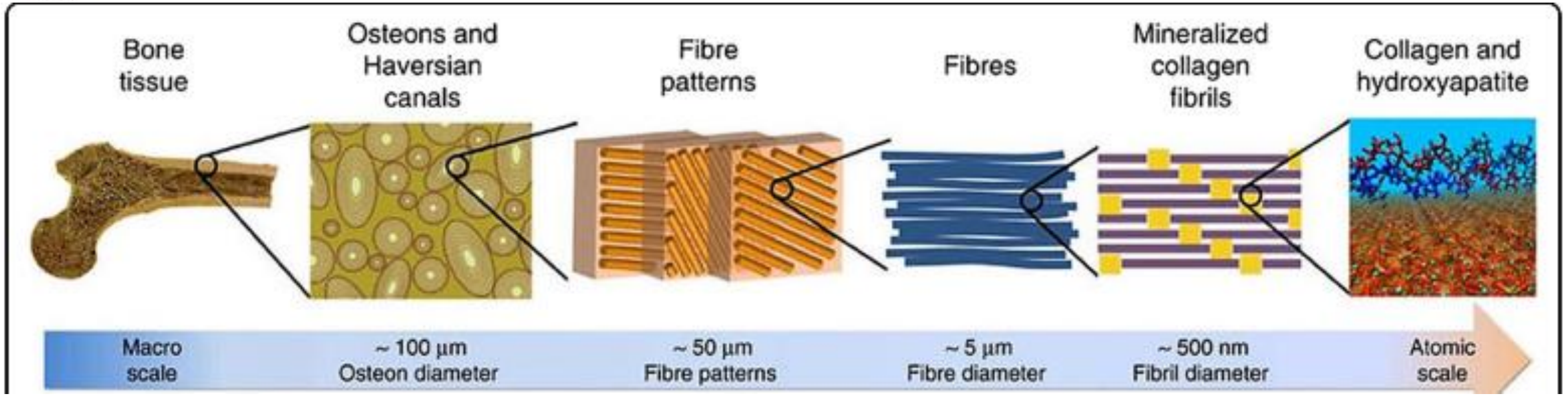
Tissue self-regeneration inducers

- Second generation porous bioceramics
- Novel advanced bioceramics
  - Mesoporous silica
  - Organic-inorganic hybrids
  - Templated glasses





Hierarchical structure of bone ranging from mesoscale skeleton collagen and HA [3]



The existence of calcium phosphates in bones was first discovered in 1769, and in the 1800s, calcium phosphates that exist in bones were subdivided into different categories. Since the 1900s, synthetic calcium phosphates have been actively studied for clinical use. Thereafter, bone regenerative applications such as bone cements, scaffolds, implants, and coating techniques using calcium phosphates have emerged, and some have been commercialized. Similar to these, the characteristics of calcium phosphates have been studied for bone regenerative applications [3].

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Typical compositional values of the inorganic phase of adult human calcified tissues [3]

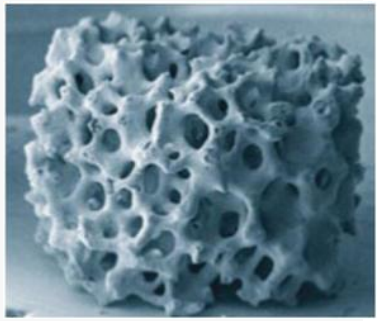
Composition	Enamel	Dentin	Bone	Hydroxyapatite
Calcium [wt.%]	36.5	35.1	34.8	39.6
Phosphorus [wt.%]	17.7	16.9	15.2	18.5
Ca/P (molar ratio)	1.63	1.61	1.71	1.67
Sodium [wt.%]	0.5	0.6	0.9	–
Magnesium [wt.%]	0.44	1.26	0.72	–
Potassium [wt.%]	0.08	0.05	0.03	–
Carbonate [wt.%]	3.5	5.6	7.4	–
Fluoride [wt.%]	0.01	0.06	0.03	–
Chloride [wt.%]	0.30	0.01	0.13	–
Pyrophosphate [wt.%]	0.022	0.10	0.07	–
Total inorganic [wt.%]	97	70	65	100
Total organic [wt.%]	1.5	20	25	–
Water [wt.%]	1.5	10	10	–
Ignition products (800 °C)	β-TCP + HAP	β-TCP + HAP	HAP + CaO	HAP

- The properties of calcium phosphates affect bioactivity, such as adhesion, proliferation, and new bone formation in osteoblasts. To exhibit these bioactive features, degradation and ion release in calcium phosphates are important
- First, calcium ions affect cells and living systems in several ways. Calcium is one of the ions that form the bone matrix, and it exists mostly in the form of calcium phosphates in bone tissues. These calcium ions cause bone formation and maturation through calcification. In addition, calcium ions affect bone regeneration and stimulate the osteoblastic bone synthesis.
- Over 80% of phosphorous ions are present in bone in the form of calcium phosphates along with calcium ions. Phosphorous mainly exists in the form of phosphate (PO_4^{3-}), which has great influence on tissue formation and growth
- Cell adhesion is strongly influenced by the ability to adsorb extracellular matrix proteins. It is influenced by the surface characteristics of calcium phosphates, such as surface roughness, crystallinity, solubility, phase content, porosity, and surface energy

Bioactive and bioresorbable ceramics

Biocompatible nanoceramics or nanostructured bioceramics used for hard tissue substitution in tissue engineering

Mineral	Name of compound	Abbreviation	Formula	Ca/P ratio
Bioinert oxide ceramics				
Alumina	Aluminum oxide		Al_20_3	
Zirconia	Zirconia oxide		ZrO_2	
Bioactive ceramics				
Glasses				
Bioglass	Silicium oxide		SiO_2 CaO Na_2O P_2O_5	
A/W glass ceramic	Oxyapatite and wollastonite		MgO CaO SiO_2 P_2O_5 CaF_2	
Calcium phosphates				
Whitelockite	Tricalcium phosphate	TCP	$Ca_3(PO_4)_2$	1.5
Hydroxyapatite	Pentacalcium-hydroxy-triphosphate	HA	$Ca_{10}(PO_4)_6(OH)_2$	1.67
Fluorapatite	Pentacalcium-fluoride-triphosphate	FA	$Ca_{10}(PO_4)_6F_2$	1.67
Hilgenstockite	Tetracalcium phosphate	TTCP	$CaO.Ca_3(PO_4)_2$	2.0



Existing calcium orthophosphates and their major properties [1,2]

Ca/P molar ratio	Compound	Formula	Solubility at 25 °C, -log(K_s)	Solubility at 25 °C, g/L	pH stability range in aqueous solutions at 25 °C
0.5	Monocalcium phosphate monohydrate (MCPM)	$Ca(H_2PO_4)_2 \cdot H_2O$	1.14	~18	0.0–2.0
0.5	Monocalcium phosphate anhydrous (MCPA)	$Ca(H_2PO_4)_2$	1.14	~17	[c]
1.0	Dicalcium phosphate dihydrate (DCPD), mineral brushite	$CaHPO_4 \cdot 2H_2O$	6.59	~0.088	2.0–6.0
1.0	Dicalcium phosphate anhydrous (DCPA), mineral monetite	$CaHPO_4$	6.90	~0.048	[c]
1.33	Octacalcium phosphate (OCP)	$Ca_8(HPO_4)_2(PO_4)_4 \cdot 5H_2O$	96.6	~0.0081	5.5–7.0
1.5	α-Tricalcium phosphate (α-TCP)	$\alpha\text{-}Ca_3(PO_4)_2$	25.5	~0.0025	[a]
1.5	β-Tricalcium phosphate (β-TCP)	$\beta\text{-}Ca_3(PO_4)_2$	28.9	~0.0005	[a]
1.2–2.2	Amorphous calcium phosphate (ACP)	$Ca_xH_y(PO_4)_z \cdot nH_2O$, $n = 3–4.5$; 15–20% H_2O	[b]	[b]	~5–12[d]
1.5–1.67	Calcium-deficient hydroxyapatite (CDHA)[e]	$Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x}$[f] $(0 < x < 1)$	~85.1	~0.0094	6.5–9.5
1.67	Hydroxyapatite (HA or OHAp)	$Ca_{10}(PO_4)_6(OH)_2$	116.8	~0.0003	9.5–12
1.67	Fluorapatite (FA or FAp)	$Ca_{10}(PO_4)_6F_2$	120.0	~0.0002	7–12
2.0	Tetracalcium phosphate (TTCP or TetCP), mineral hilgenstockite	$Ca_4(PO_4)_2O$	38–44	~0.0007	[a]

[a] These compounds cannot be precipitated from aqueous solutions.

[b] Cannot be measured precisely. However, the following values were found: 25.7 ± 0.1 (pH = 7.40), 29.9 ± 0.1 (pH = 6.00), 32.7 ± 0.1 (pH = 5.28). The comparative extent of dissolution in acidic buffer is: ACP >> α-TCP >> β-TCP > CDHA >> HA > FA.

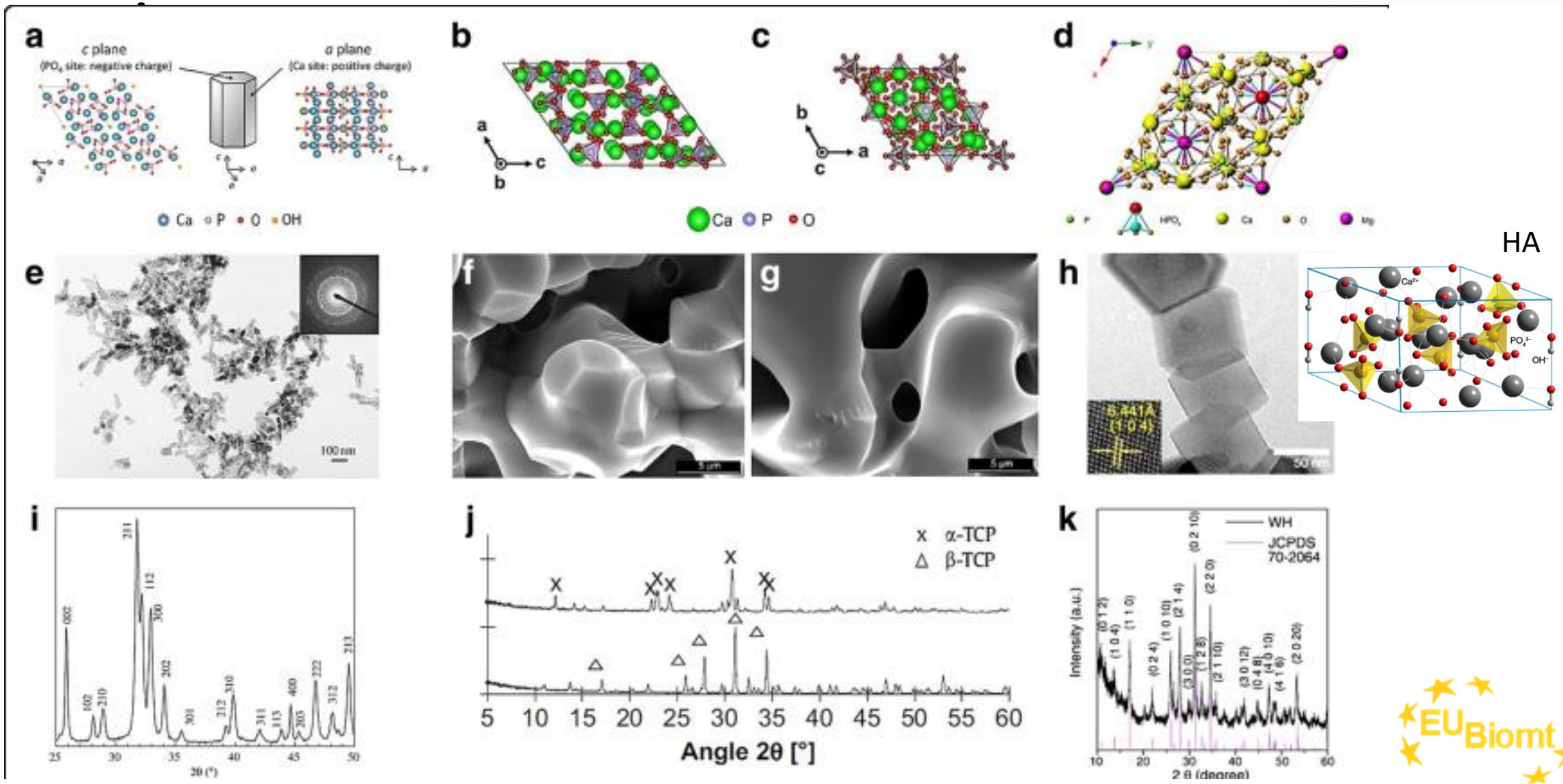
[c] Stable at temperatures above 100 °C.

[d] Always metastable.

[e] Occasionally, CDHA is named as precipitated HA.

[f] In the case $x = 1$ (the boundary condition with Ca/P = 1.5), the chemical formula of CDHA looks as follows: $Ca_9(HPO_4)(PO_4)_5(OH)$.

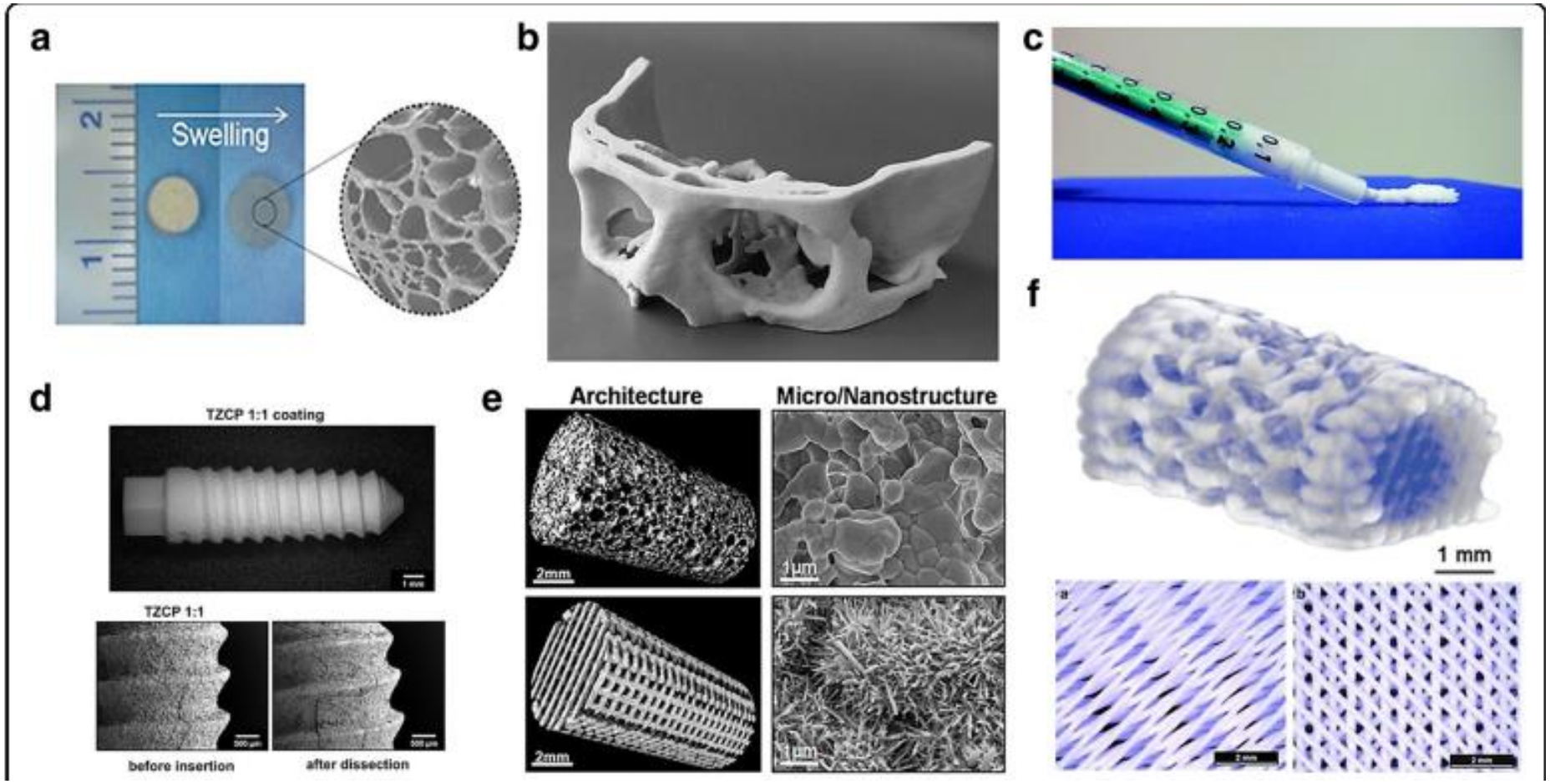
Illustration of the crystal structure of (a) HA , (b) α-TCP, (c) β-TCP, and (d) WH. Copyright 2013 American Chemical Society. TEM and SEM images of (e) HA, (f) α-TCP, (g) β-TCP, and (h) WH. XRD data of (i) HA, (j) α-TCP and β-TCP, and (k) WH [3]



Examples of the commercial calcium orthophosphate-based bioceramics and biomaterials

Calcium orthophosphate	Trade name and producer
CDHA	Cementek (Teknimed, France) Osteogen (Impladent, NY, USA)
HA	Apaceram (Pentax Corp., Japan) Calcitite (Zimmer, IN, USA) Bonefil (Mitsubishi Materials Corp., Japan) Bonetite (Mitsubishi Materials Corp., Japan) Boneceram (Sumitomo Osaka Cement Co., Japan) Ostegraf (Ceramed, CO, USA) Cerapatite (Ceraver, France) Synatite (SBM, France) Ostim (Heraeus Kulzer, Germany) Bioroc (Depuy-Bioland, France)
HA/polyethylene	HAPEX (Gyrus, TN, USA)
HA/$CaSO_4$	Hapset (LifeCore, MIN, USA)
Coralline HA	Interpore, ProOsteon (Interpore, CA, USA)
Algae-derived HA	Algipore (Dentsply Friadent, Germany)
Bovine bone apatite (unsintered)	Tutoplast (IOP, CA, USA) Lubboc (Ost-Developpement, France) Laddec (Ost-Developpement, France) Oxbone (Bioland biomateriaux, France) BioOss (Geitslich, Switzerland)
Bovine bone apatite (sintered)	Endobon (Merck, Germany) PepGen P-15 (Dentsply Friadent, Germany) BonAP Cerabone (aap Implantate, Germany) Osteograf (Ceramed, CO, USA)
β-TCP	Bioresorb (Sybron Implant Solutions, Germany) Biosorb (SBM S.A., France) Calciresorb (Ceraver, France) ChronOS (Synthes, PA, USA) Ceros (Thommen Medical, Switzerland) Cerasorb (Curasan, Germany) Conduit (DePuy Spine, USA) JAX (Smith and Nephew Orthopaedics, USA) Graftys BCP (Graftys, France) Osferion (Olympus Terumo Biomaterials, Japan)
BCP (HA + β-TCP)	MBCP (Biomatlante, France) Triosite (Zimmer, IN, USA) Ceraform (Teknimed, France) Biosel (Depuy Bioland, France) TCH (Kasios, France) Calciresorb (Ceraver, France) Osteosynt (Einco, Brazil) 4Bone (MIS, Israel) Kainos (Signus, Germany) SBS (Expanscience, France) Eurocer (FH Orthopedics, France) OptiMX (Exactech, USA) BCP (Medtronic, MN, USA) Hatric (Arthrex, Naples, FL, USA) Tribone (Stryker, Europe)
BCP (HA + α-TCP)	Skelite (Millennium Biologix, ON, Canada)
BCP/collagen	Allograft (Zimmer, IN, USA)
BCP/fibrin	TricOS (Baxter BioScience, France)
BCP/silicon	FlexHA (Xomed, FL, USA)
Carbonateapatite	Healos (Orquest, CA, USA)

Calcium phosphate based applications



(a) WH incorporated hydrogel scaffold [4]. (b) Cranial segment made of tetracalcium phosphate and β-TCP [5]. (c) The injectable paste included calcium phosphate nanoparticles [6]. (d) Mixed zirconia calcium phosphate deposited on dental implant [7]. (e) 3D printed calcium-deficient HAP scaffolds [8]. (f) 3D printed calcium phosphate cement [3-8]

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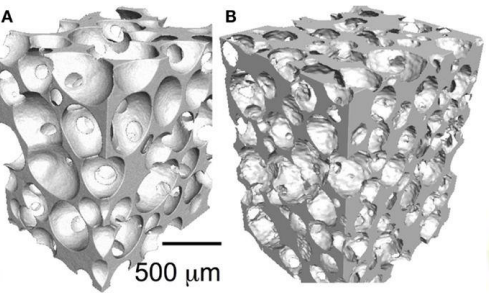
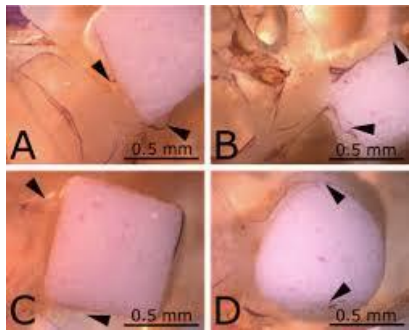


Bioactive glass - Alchetron

Cerabone

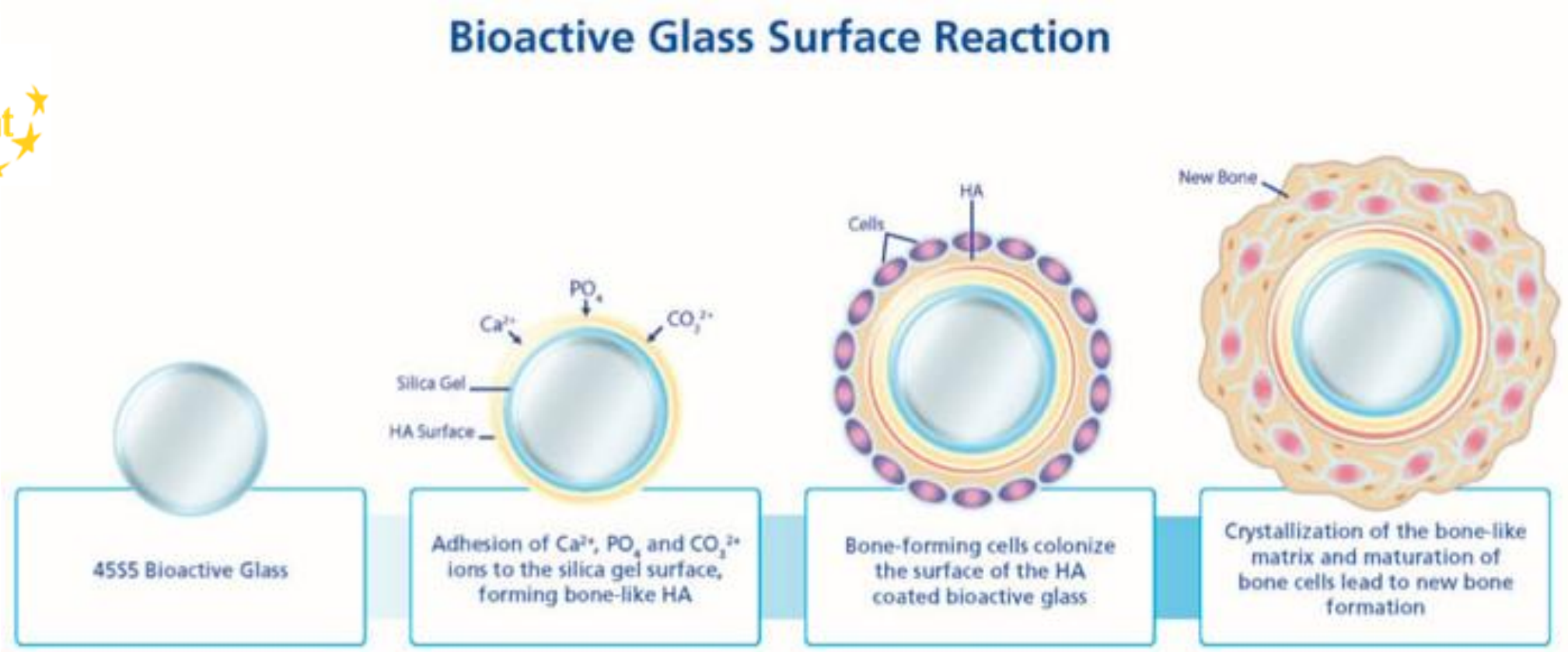


Bioverit

Bioactive Glass-ceramics

- **Commercialized glass-ceramics**
  - Cerabone ® — Developed by Kokubo *et al.*
  - Bioverit ® — Developed by Höland *et al.*
  - Biosilicate ® — Developed by Zanotto *et al.*
  - Ceravital ® — Developed by Brömer *et al.*
- **Further investigations are required**
  - Miscellaneous glass-ceramics
    - Apatite-mullite glass-ceramic — Developed by R.G. Hill *et al.*
    - Canasite-apatite glass-ceramic — Developed by C.C. Wolcott *et al.*
    - Rhenanite glass-ceramic — Developed by E. Apel *et al.*
    - Calcium pyrophosphate glass-ceramic — Developed by T. Kasuga *et al.*
    - Chlorapatite glass-ceramic — Developed by R.G. Hill *et al.*
    - K-fluorrichterite glass-ceramic — Developed by M. Mirsaneh *et al.*
    - Alkali-free glass-ceramic — Developed by J.M.F. Ferreira *et al.*
  - Coatings
    - On ceramic implants
    - On metallic implants
  - 3D porous scaffolds
  - Gel-derived & mesoporous
  - Composites
    - GC-reinforced polymer
    - Metal-reinforced glass-ceramic
  - Hyperthermia treatment

Bioactive Ceramics. Bioactive materials are those that chemically bond with bone or tissue of the hosts [1]. The most important applications of bioactive bioceramics has been metal coatings to provide bone-implant interfacing, this lowers the risk of rejection and transmission of diseases [2].



- Glass is made of Silica, Calcium oxide, and Sodium oxide (SiO_2-Na_2O-CaO), and bioglasses used for implantation are based on glass with at least 65 weight percent Silica. Bioglasses have high mechanical strength and are bioinert, but are also brittle and have poor tensile properties. They are normally used in bone plating, dental implants, spinal fusions, and more. In 1971 the first bioglass, 45S5 bioglass, was created. It was unusually weak with a composition of 45% Silica, 24.5% Calcium oxide, and 24.5% Sodium oxide. The high bioactivity of 45S5 is attributed to the later addition of 6% Phosphorus pentoxide (P_2O_5) by weight [1]

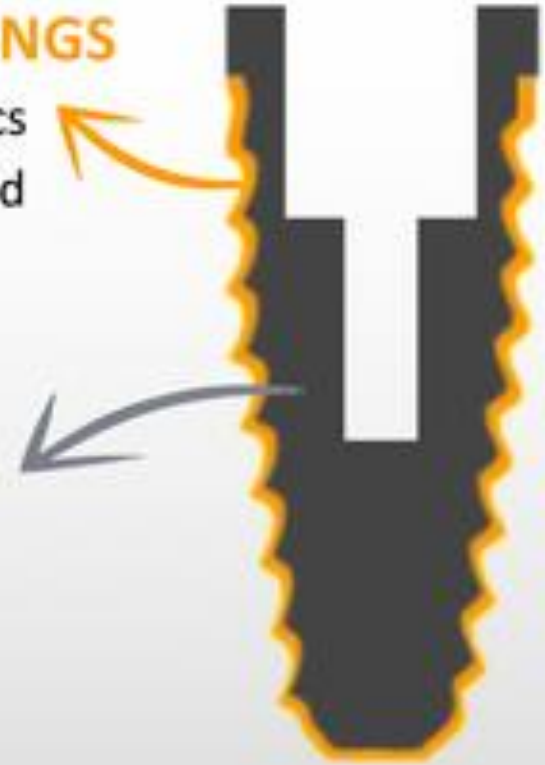
Ceramic coatings

BIOACTIVE COATINGS

- Silica-based ceramics
- Bioactive glasses and glass-ceramics

SUBSTRATES

- Ti-based
- Stainless Steel
- Mg-based

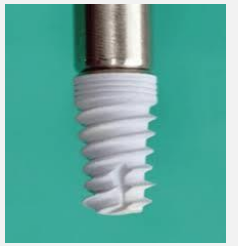


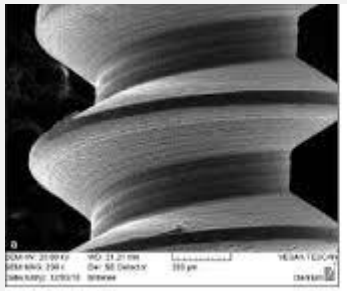
INVESTIGATED AREAS

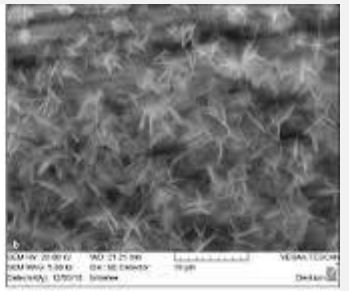
- Deposition methods
- Coating adhesion to substrates
- Immersion in SBF
- *In vitro* experiments
- *In vivo* experiments

Ceramic coatings The requirement for a sufficient mechanical stability necessitates the use of a metallic body for such devices to improve the contacts at the interface. The major way is to coat metals with calcium orthophosphate bioceramics that generally exhibit bone bonding ability between the metal and bone

Technique	Thickness	Advantages	Disadvantages
Thermal spraying	30–200 μm	High deposition rates; low cost	Line of sight technique; high temperatures induce decomposition; rapid cooling produces amorphous coatings
Sputter coating	0.5–3 μm	Uniform coating thickness on flat substrates; dense coating	Line of sight technique; expensive; time consuming; produces amorphous coatings
Pulsed laser deposition	0.05–5 μm	Coating by crystalline and amorphous phases; dense and porous coating	Line of sight technique
Dynamic mixing method	0.05–1.3 μm	High adhesive strength	Line of sight technique; expensive; produces amorphous coatings
Dip coating	0.05–0.5 mm	Inexpensive; coatings applied quickly; can coat complex substrates	Requires high sintering temperatures; thermal expansion mismatch
Sol–gel technique	<1 μm	Can coat complex shapes; low processing temperatures; relatively cheap as coatings are very thin	Some processes require controlled atmosphere processing; expensive raw materials
Electrophoretic deposition	0.1–2.0 mm	Uniform coating thickness; rapid deposition rates; can coat complex substrates	Difficult to produce crack-free coatings; requires high sintering temperatures
Biomimetic coating	<30 μm	Low processing temperatures; can form bonelike apatite; can coat complex shapes; can incorporate bone growth stimulating factors	Time consuming; requires replenishment and a pH constancy of simulated body fluid
Hot isostatic pressing	0.2–2.0 μm	Produces dense coatings	Cannot coat complex substrates; high temperature required; thermal expansion mismatch; elastic property differences; expensive; removal/interaction of encapsulation material
Electrochemical deposition	0.05–0.5 mm	Uniform coating thickness; rapid deposition rates; can coat complex substrates; moderate temperature, low cost	The coating/substrate bonding is not strong enough

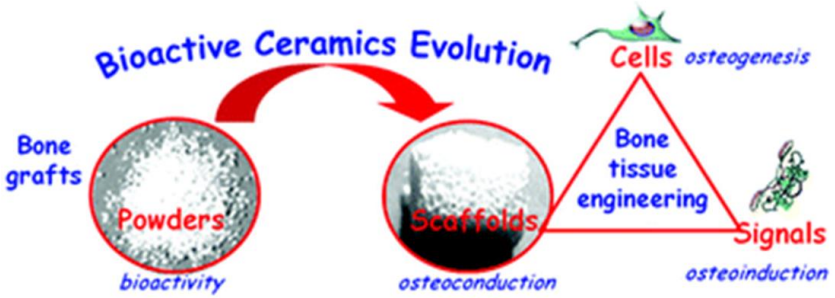






A number of factors influence the properties of calcium orthophosphate coatings including

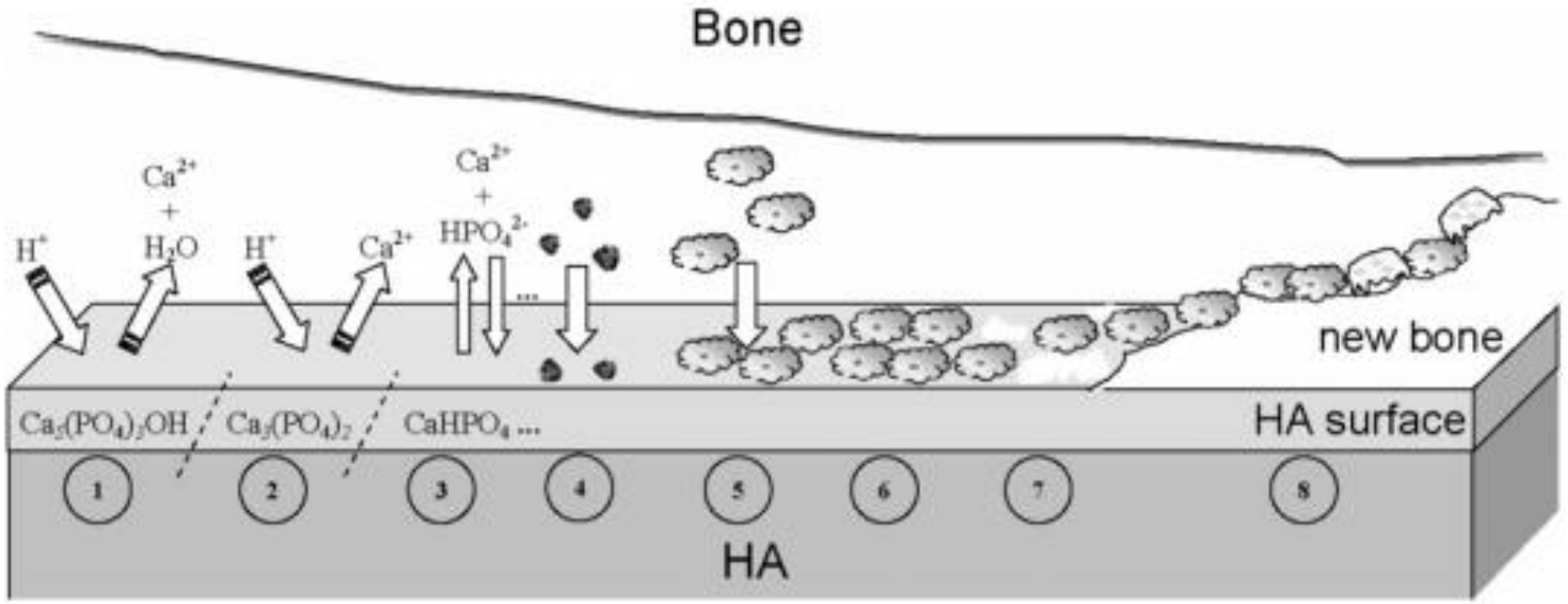
- coating thickness (this will influence coating adhesion and fixation – the agreed optimum now seems to be within 50–100 mm),
- crystallinity (this affects the dissolution and biological behavior), phase purity,
- chemical purity,
- porosity,
- Adhesion



HA coating as a system of fixation of hip implants was found to work well in the short to medium term (8 years, 10–15.5 years, 15 years, 17 years and 19 years). Similar data for HA-coated dental implants are also available. The longer-term clinical results are awaited with a great interest

With the support of the Erasmus+ Programme of the European Union

A schematic diagram representing the phenomena that occur on HA surface after implantation



(1) beginning of the implant procedure, where a solubilization of the HA surface starts;

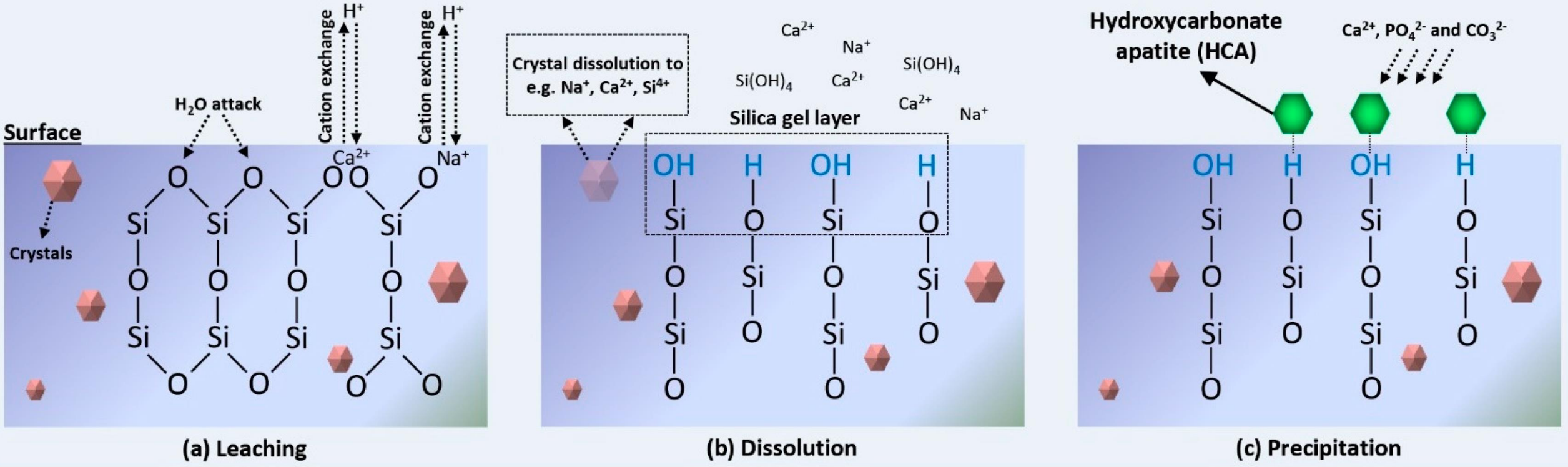
(2) continuation of the solubilization of the HA surface; (3) the equilibrium between the physiological solutions and the modified surface of HA has been achieved (changes in the surface composition of HA does not mean that a new phase of DCPA or DCPD forms on the surface); (4) adsorption of proteins and/or other bioorganic compounds; (5) cell adhesion; (6) cell proliferation; (7) beginning of a new bone formation; (8) new bone has been formed. Reprinted from Ref. [1].

Properties required from calcium phosphates for medical applications [11]

Property	Definition/Function
Bioactivity	The inherent ability of a material to participate in specific biological reactions or have an effect on living tissues
Biocompatibility	The ability of a material to perform with an appropriate host response in a specific application
Bioactive fixation	Reactive surfaces form chemical bonding with bone, thus minimizing the fibrous capsule formation
Biostability	The ability of a material to maintain its properties *in vivo*
Crystallinity	Higher level of crystallinity prevents fast resorption (dissolution) of the bioceramic in body fluids
Interfacial stability and good adhesion	Prevent mechanical failures under load-bearing conditions
Osseointegration	Direct anchorage of an implant by the formation of bony tissue around it without growth of fibrous tissue at the bone/implant interface
Osteoconduction	Ability to provide a scaffold for the formation of new bone
Osteoinduction	The process by which osteogenesis is induced. This term means that primitive, undifferentiated and pluripotent cells are somehow stimulated to develop into the bone-forming cell lineage
Resorption	Gradual degradation over time to replace the biomaterial with the natural host tissue
Therapeutic capabilities	Templates for the in situ delivery of drugs and growth factors at required times
Wettability	The property that indicates a material's ability to attract/repel water molecules

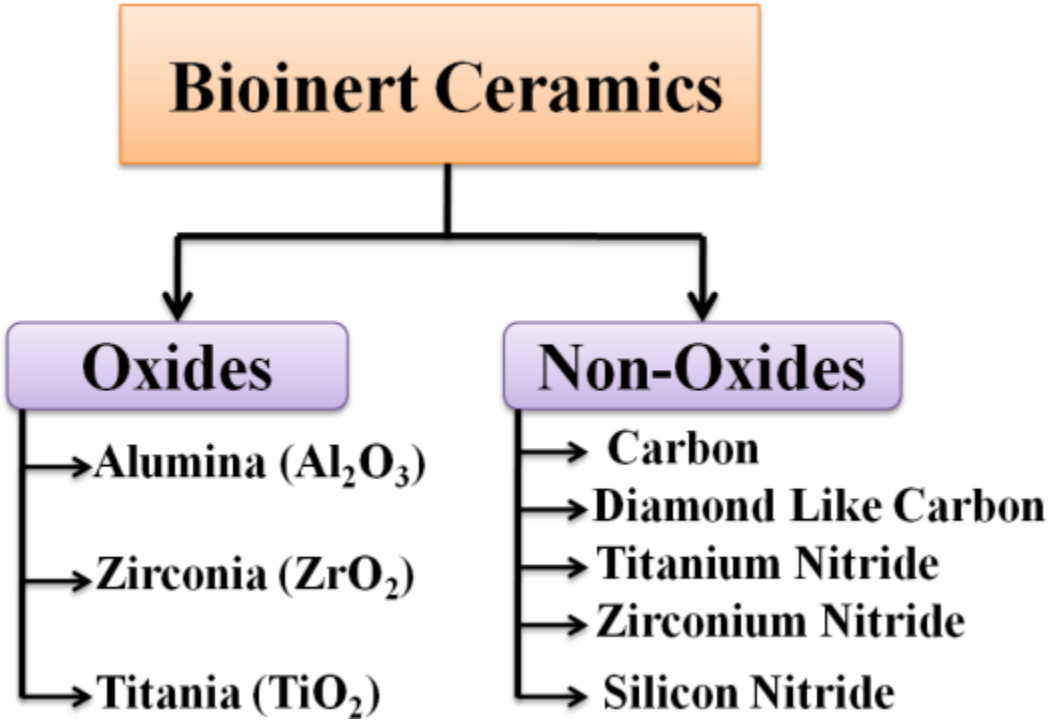
In-vitro behaviour of glass-ceramic in SBF

Piece of glass-ceramic in a simulated body fluid which contains Ca^{2+}, H^+, K^+, Mg^{2+}, Na^+, Cl^-, HCO_3^-, HPO_4^{2-}, OH^- and SO_4^{2-}



(a) Leaching (b) Dissolution (c) Precipitation

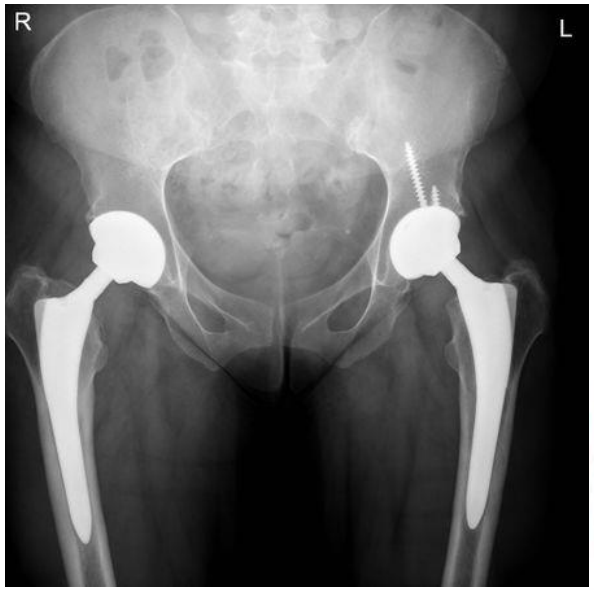
Classification of bioinert ceramics



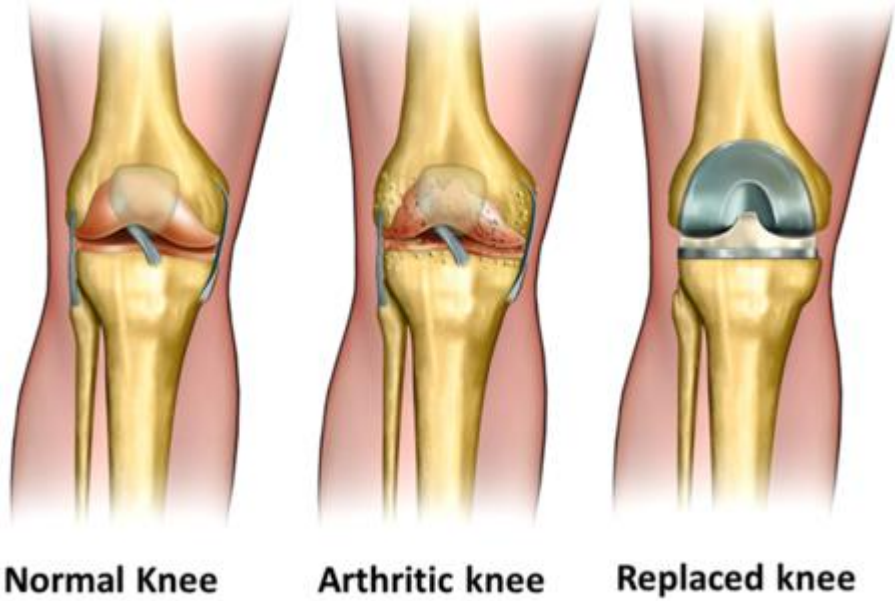
Bioinert ceramics are one type of the bioceramics and which classified based on their biological response in human body. Bioinert ceramics are usually defined as biologically inert nature or bioinert ceramics when implanted into biological system do not instigate an appropriate response or interact with the adjacent biological tissue Bioinert ceramics are corresponds to first generation of biomaterials and widely used as hip, knee replacements and dental implant, crown etc due to astonishing characteristics such as high mechanical properties like tensile, compressive, hardness, low wear, toughness and good anticorrosion in biological fluid. There are mainly three type of metal based bioinert ceramics such as alumina, zirconia and titania have been used in musculoskeletal applications [10].

Bioinert ceramics

Total Hip Replacement (Source)

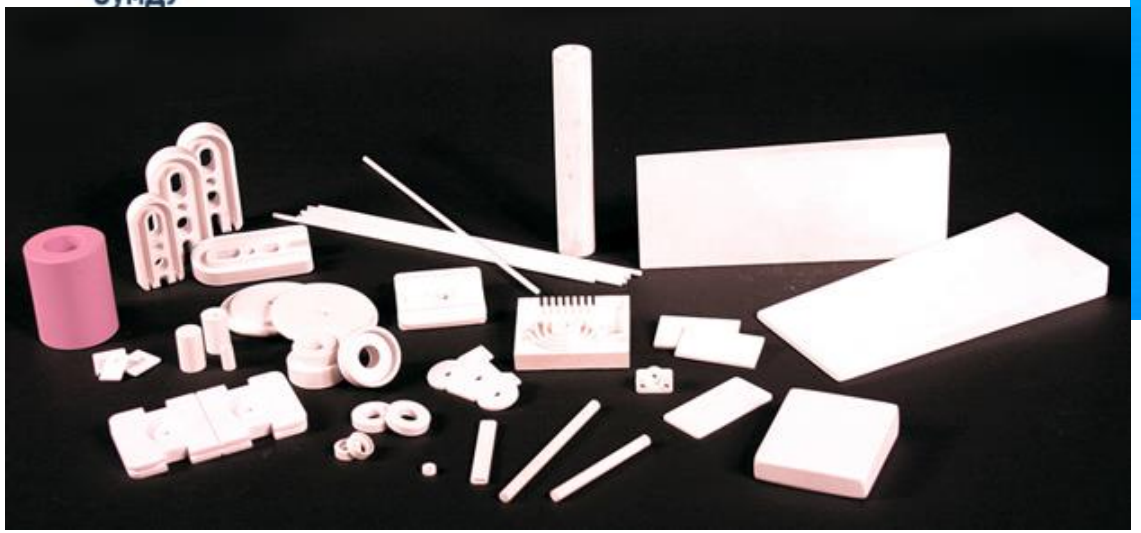


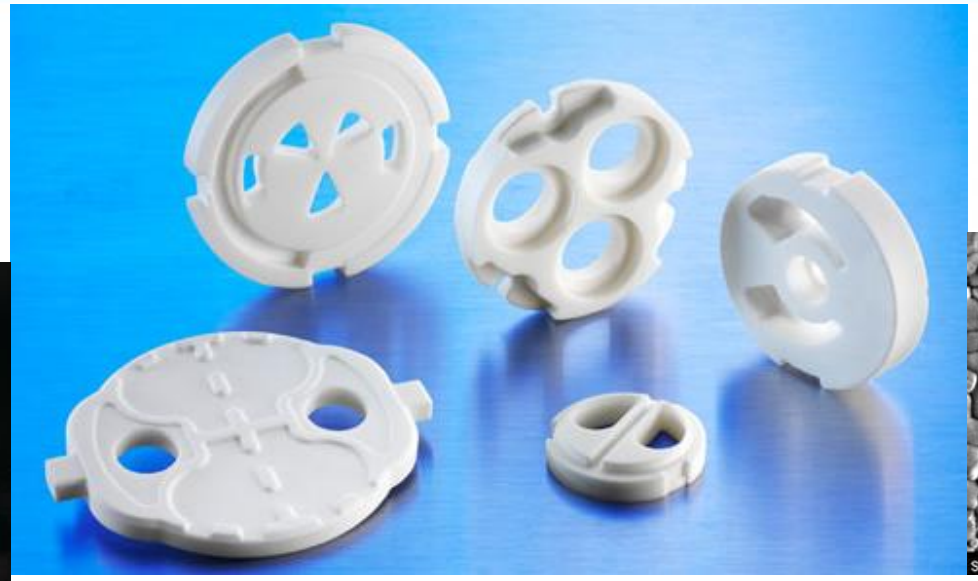
Total Knee Replacement (Source)

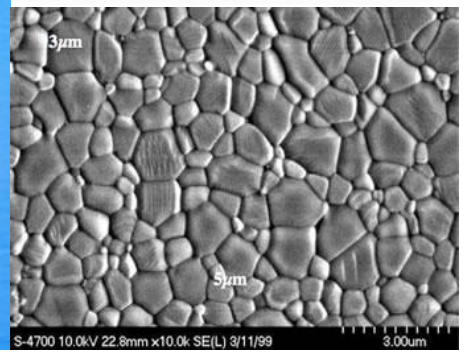


- ***Ceramics that retain structure after implantation and do not induce an immunologic response in the host***.[*10*]
- **Alumina (Al_2O_3)** Highly inert, especially under physiological conditions, and has a corrosive resistances. It also has excellent wear resistance and hardness. Has dental applications, function as vertebrae spacers and extensors.[9] The body normally reacts to alumina by forming non-adherent fibers around the implant.
- **Zirconia (ZrO_2)** Zirconia is inert under physiological conditions like Alumina. Partially stabilized Zirconia (PSZ) has a higher flexural strength, toughness, reliability, and a lower Young's modulus. Zirconia is good for long-term clinical use. It is widely used in total hip replacement (THR), and as a replacement for knees, tendons, ligaments, and teeth. Examples of Zirconia based bioceramics include Yttrium Stabilized Tetragonal Polycrystalline Zirconia (Y-TZP), and Zirconia/Alumina composites.[9]

Al_2O_3 Ceramics





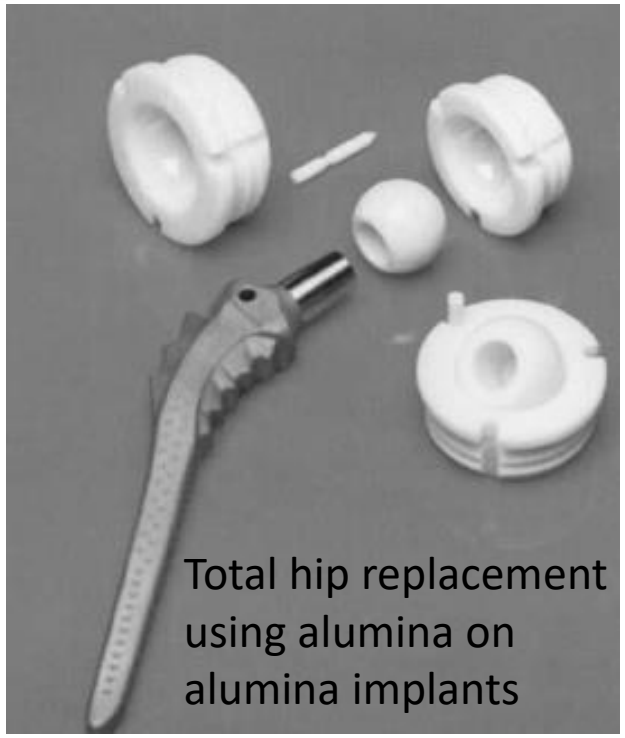


There are Properties of Alumina/Aluminum Oxide:

Good gliding properties	Low density
Bioinert and food compatible	Very good electrical insulation
Moderate to extremely high mechanical strength	
Very high compressive strength	High hardness
Moderate thermal conductivity	High corrosion and wear resistance

- The Alumina (Aluminum oxide, Al_2O_3) is one of the most clinical usage biomaterials with 45 years of clinical record in orthopeadic surgeries. The alumina can still employ successfully as pure form or with combination of other components in high performance composite form in bone tissue engineering. The key reason for the selecting alumina as bone substitute and dental implants due to its strong hardness, resistance of abrasion, low wear, corrosion resistance, excellent mechanical strength, good hydrodynamic stability and biologically compatible nature. Alumina used to develop as nanocomposites with combination of bioactive ceramics, polymers and carbon based materials for biomedical applications [10]

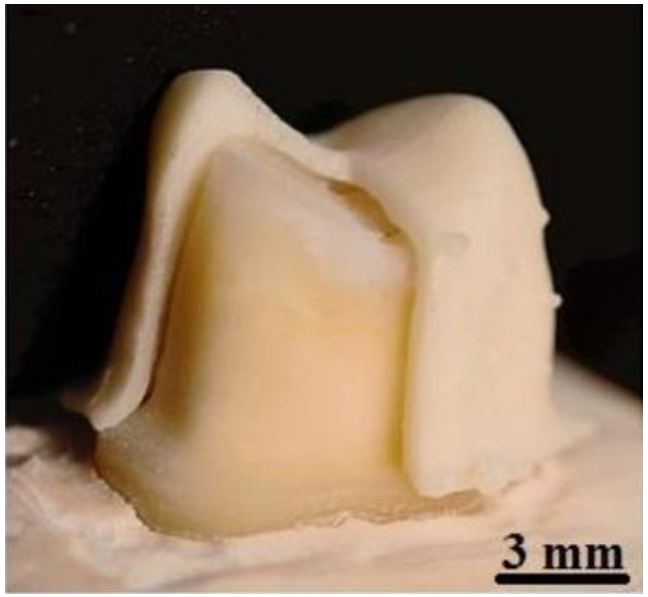
Application of Al_2O_3 Ceramics



Total hip replacement using alumina on alumina implants

Since 1989, the USA using ceramic femoral heads coupled to polyethylene in total hip replacements and non USA countries clinical surgeons were demonstrated the advantages of modern alumina-on-alumina for younger and highly active patients. In 2003 February, the FDA was successfully approved the BIOLOXR forte alumina inlays (CeramTec GmbH, Plochingen, Germany) to use in USA for orthopeadic applications.

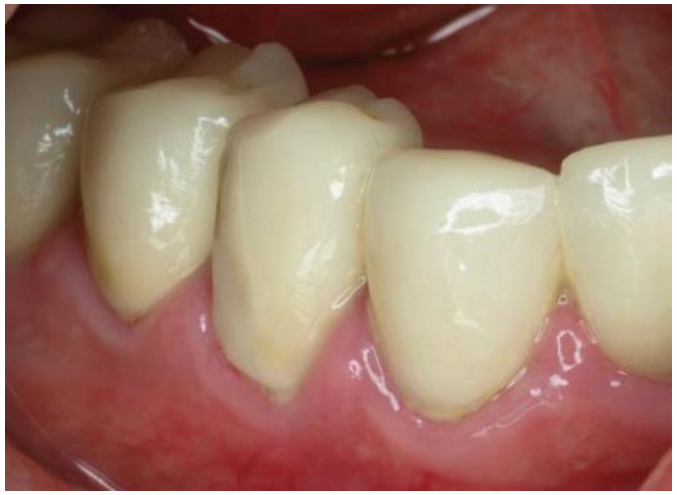
Ceram Tec AG products in the period of 2000-2013, in which 2.78 and 3.2 million of alumina matrix composite ceramic ball heads and pure alumina were used worldwide.



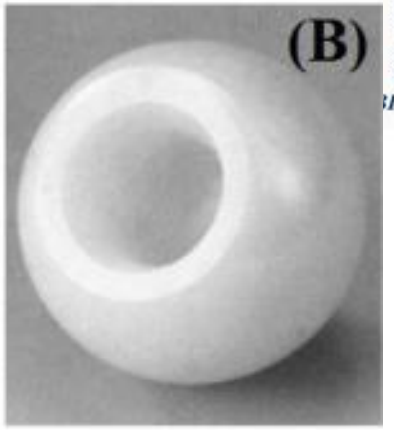
Ultraviolet-Stereolithography produced Alumina crown for dentistry

- For the last few decades, high strength alumina materials are using in all parts of mouth to develop the coping and frameworks for crowns and fixed dental implants also used to increase the mechanical strength of dental porcelains. They reported that alumina toughened zirconia substrates showed significant higher digital histology index when compared with titanium at time of 56 days. Hence, they concluded that this type of prosthetic implants can be favorable materials for dental applications.

ZrO_2 Ceramics



Zirconia full-coverage crown in dental applications

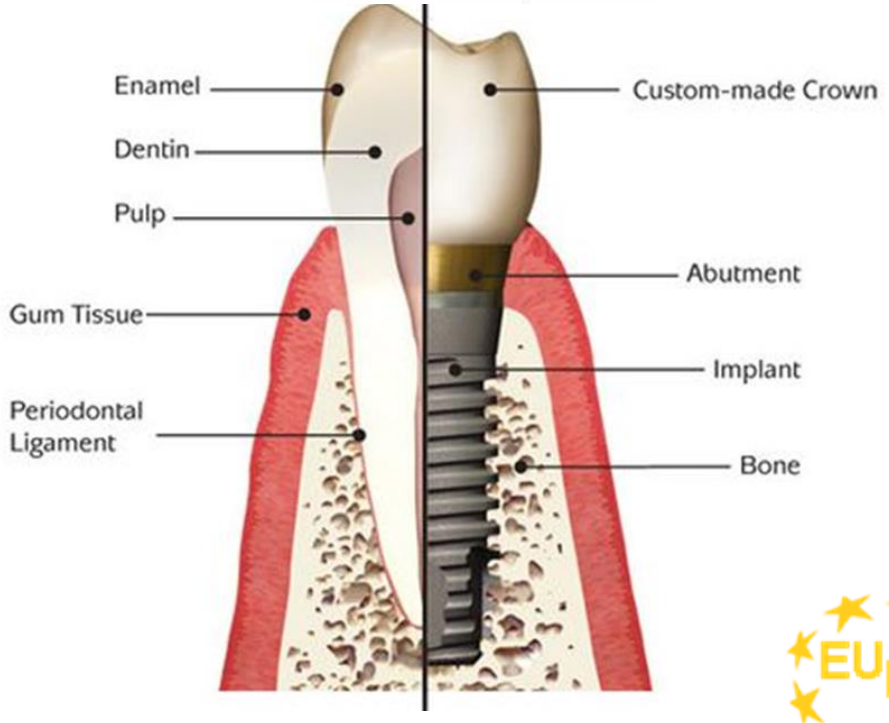


Hip prosthesis by titanium alloy with zirconia ball head and (B) zirconia femoral head

- In mid of 1980s, the zirconia ceramic was developed as a biomaterials to overcome the mechanical property limits of alumina ceramics. Zirconia was successfully employed as an alternative material to alumina with improvement of fracture toughness and used as femoral head in total hip replacements along with knee replacements. Zirconia is highly biological compatible and has excellent anticorrosion behavior in presence of human physiological conditions. As mentioned earlier that zirconia has superior mechanical properties such as fracture toughness and bending strength when compared to alumina, which made zirconia, could be highly suitable implant materials to use in large load bearing areas.

Bioinert ceramics

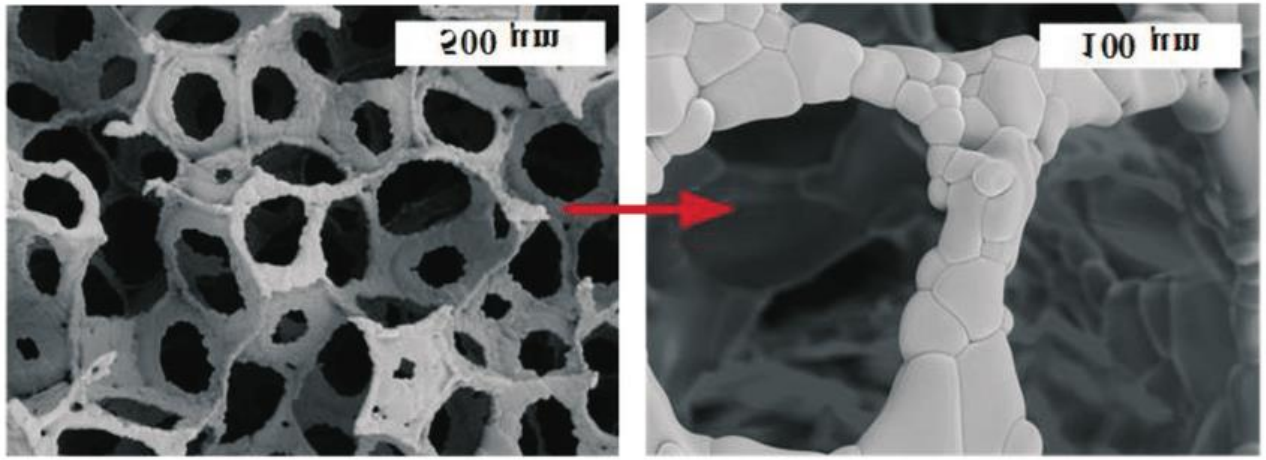
- **Issues of Y-TZP (Yttrium Stabilized Tetragonal Polycrystalline Zirconia)**
- Biomedical grade Y-TZP had the best mechanical properties of the bioinert ceramics investigated, and quickly became a standard for hip and knee replacements. In 2001, patients with Y-TZP implants reported that the implant was failing, revealing a downside to Y-TZP. It was found that due to its meta-stability, it is prone to low temperature degradation in the presence of water, which triggers a progressive aging that eventually results in surface roughening and micro-cracking. The micro-cracks eventually cause more surface defects and lead to delayed failure of the implant [11].
- For dental applications, Y-TZP was also proven to lack stability in an oral environment in long term in vivo studies. In-vitro studies performed also suggested that aging might be an issue with Y-TZP used in an oral environment [11].



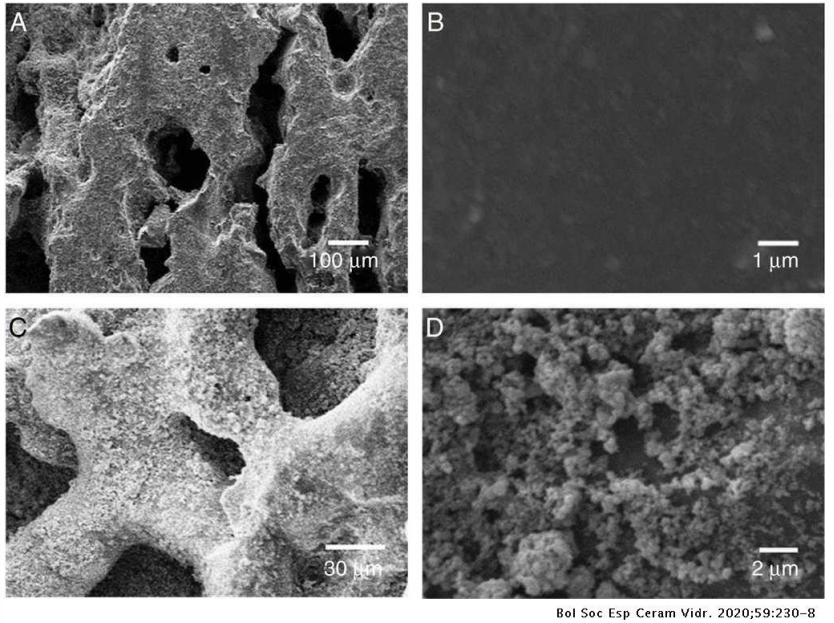
Pyrolytic Carbon

Pyrolytic Carbon are brittle and do not perform well in load bearing applications, but do not suffer from fatigue. It is commonly used in heart valves due to high strength, wear resistance, durability, and thromboresistance, or resistance to blood clotting. It can also be used for spinal inserts [11].

TiO_2 Ceramics



SEM image of TiO2 ceramics



SEM image of ceramics supported by TiO_2 nanoparticles

- Titania has been used potentially in medical applications due to their excellent low toxicity, biological compatibility, corrosion resistance behaviour, chemical resistivity and superior mechanical properties. In recent years, many researchers reported on the nanostructured TiO_2 for wide range of applications such as dental, orthopeadic, drug delivery and cell imaging. For the last few years, pure Ti and its alloys highly recommended to use in orthopedics such as fracture fixation devices, spinal fusion and artificial joints. However, Ti and its alloys have weak in bacterial restriction behaviour, osteointegration and osteoinduction property which cause failure of implants and leads to effect on their long term life span in patients. Recent reports proved that the development of nanotechnology to alter the surface property of Ti and its alloys by different techniques to create the nanoarchitectures of TiO_2

Conclusions

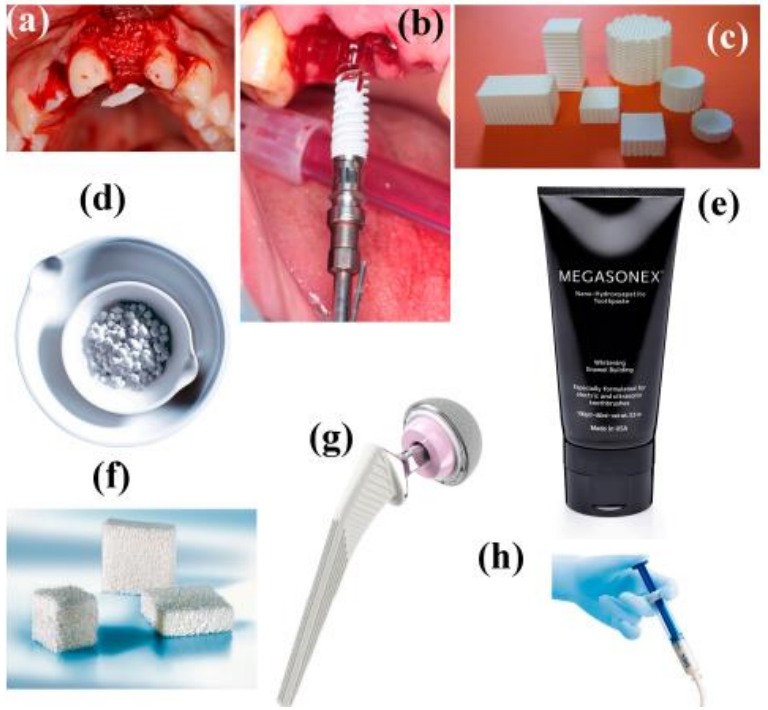
1) **WHAT ARE BIO CERAMICS?**
Bio ceramics are ceramic materials primarily used for the repair, reconstruction and replacement of diseased or damaged parts of musculo-skeletal system

2) **CHARACTERISTICS OF BIO CERAMICS** Ultra-hard, Biocompatible, Chemically inert, Physically stable, High strength, Excellent surface finish, Porous. And resistant to high temperature, Wear, corrosion and bending.

3) **MATERIALS USED AS BIO CERAMICS**
Materials that can be classified as bio ceramics include: Alumina, Zirconia, Calcium phosphates, Silica based glasses or glass ceramics, and Pyrolytic carbons

4) **TYPES OF BIOMATERIALS**
When these synthetic materials are placed within the human body, the tissues react towards the implant in a variety of ways.

5) **THE MECHANISM OF TISSUE INTERACTION** at a nanoscale level is dependant on the **RESPONSE TO THE IMPLANT SURFACE**. As such three terms for description of a biomaterial, representing the tissues responses, have been defined.These are: **BIOINERT BIOACTIVE AND BIODEGRADABLE**



Various applications and forms of commercially available CaP-related products. (a) Bone augmentation after extraction of the tooth. (b) Coated dental implant. (c) 3D Scaffold bone substitute material (3D-printed CaP cement). (d) Calcibon self-setting cement granules consisted of α-TCP, $CaHPO_4$, $CaCO_3$ and HA; (e) Megasonex® Nano-Hydroxyapatite toothpaste.

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