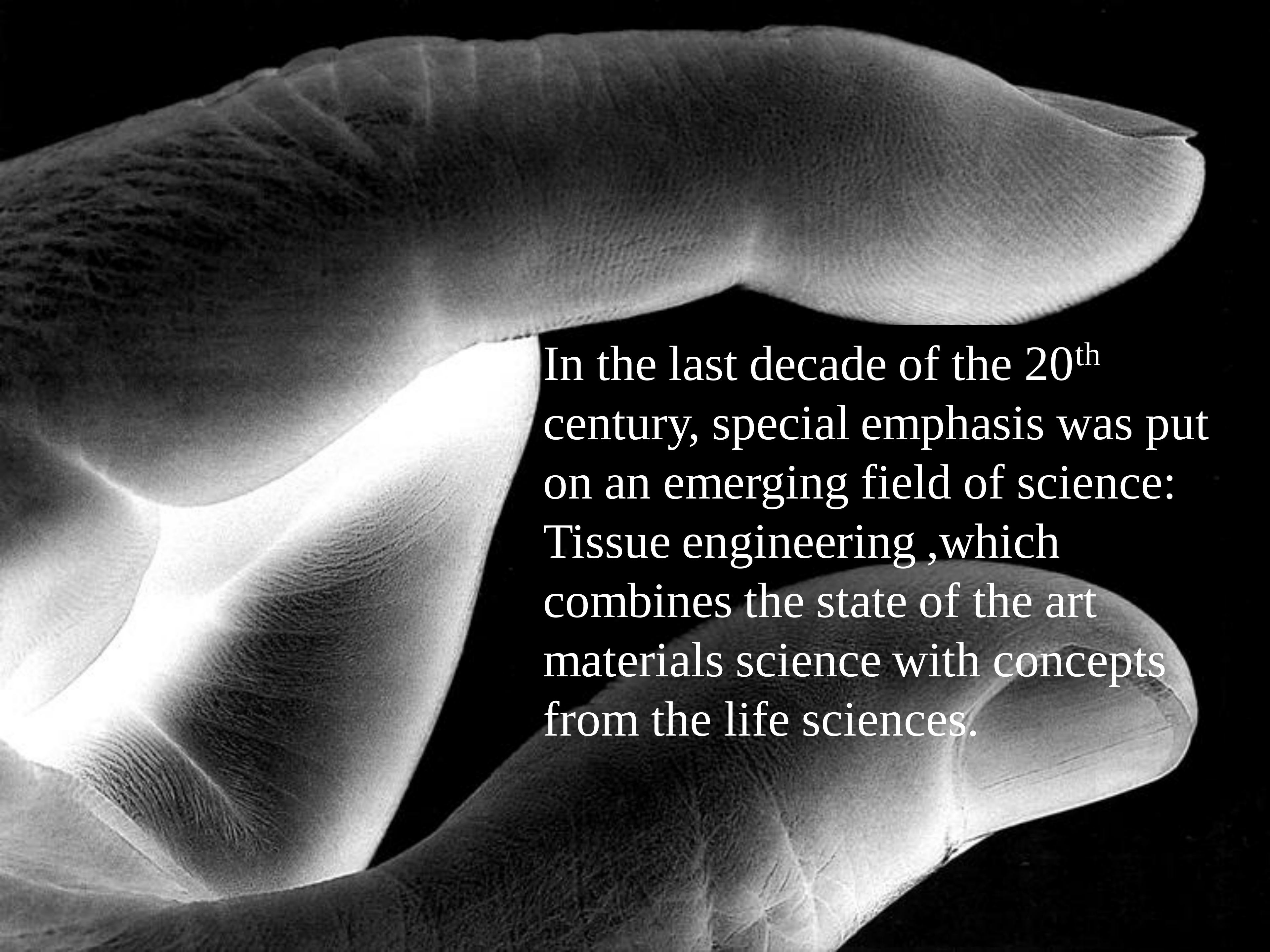
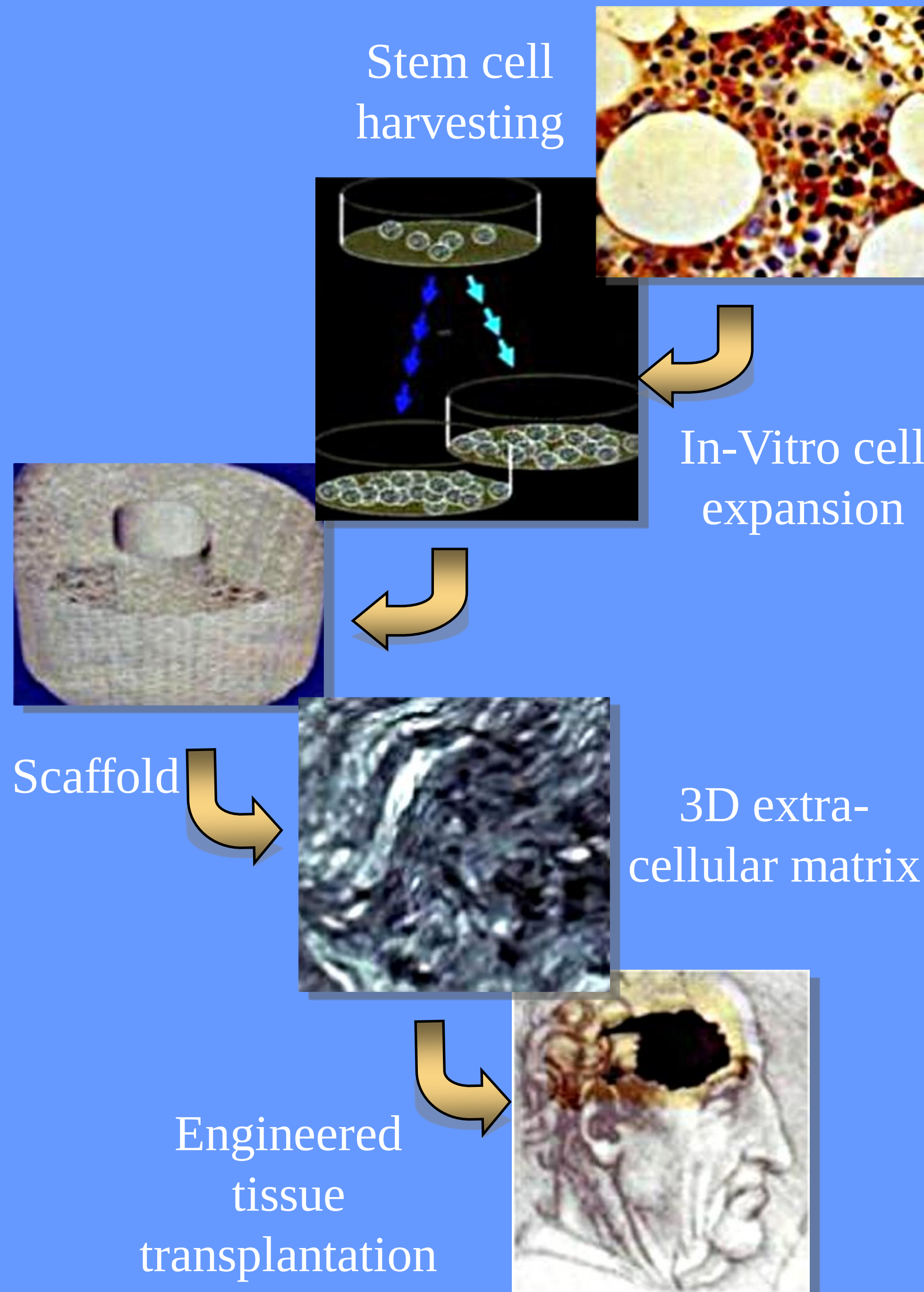
Recent Advances
In
Tissue Engineering



In the last decade of the 20th century, special emphasis was put on an emerging field of science: Tissue engineering ,which combines the state of the art materials science with concepts from the life sciences.

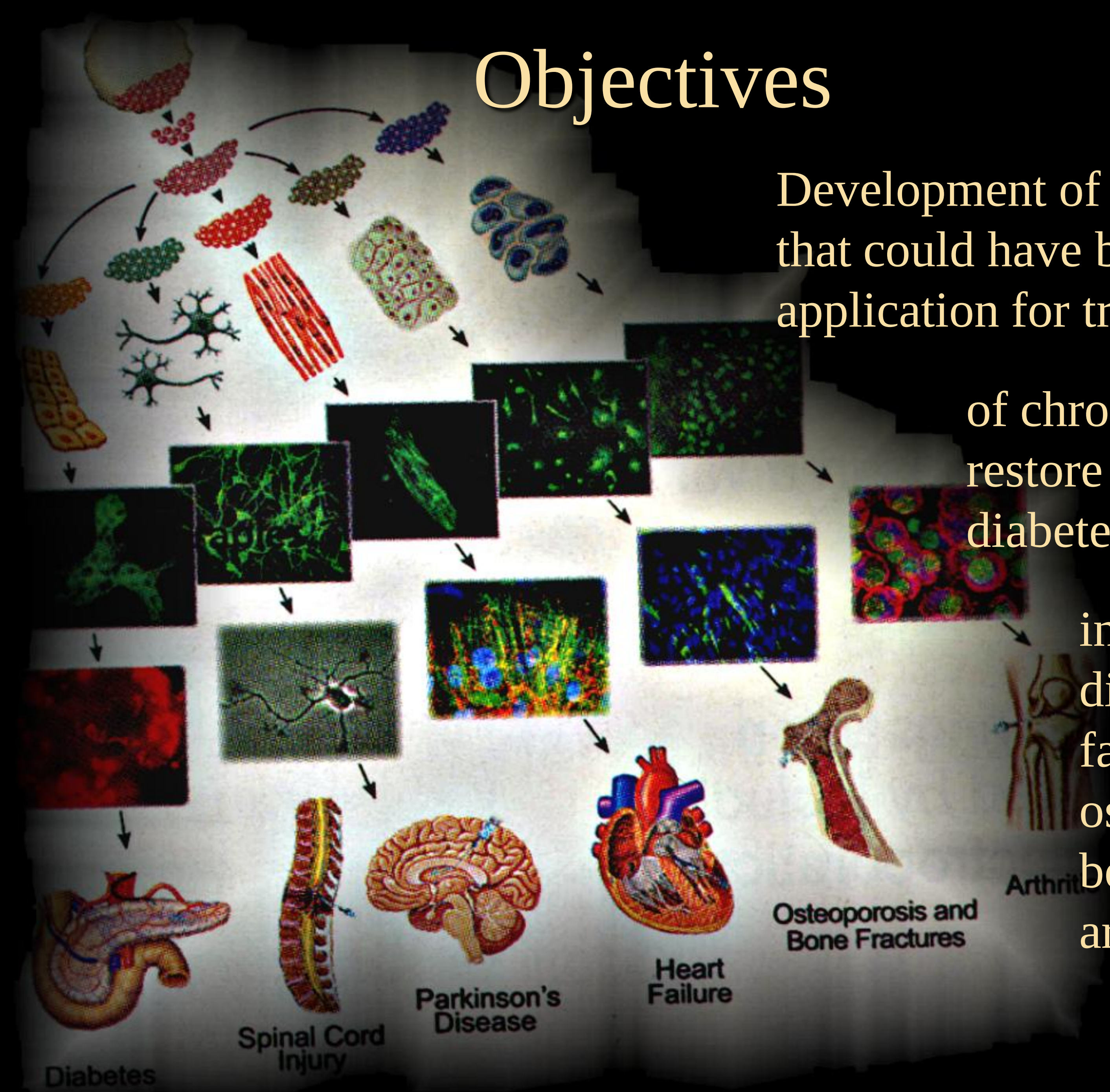
Objectives

Production of tissues and organ substitutes/ equivalents that can replace or restore the natural features and physiological functions of normal tissues in-vivo.

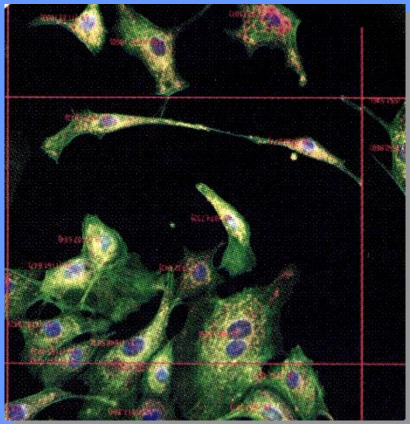


Objectives

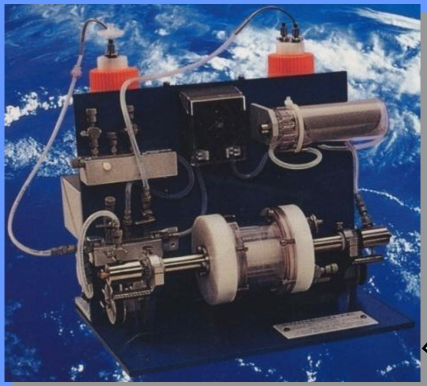
Development of therapies that could have broad application for treatment of chronic diseases: to restore organ function e.g. diabetes, spinal cord injury, Parkinson's disease, heart failure, osteoporosis, and bone fracture, and arthritis.



Engineered Tissue



Cells

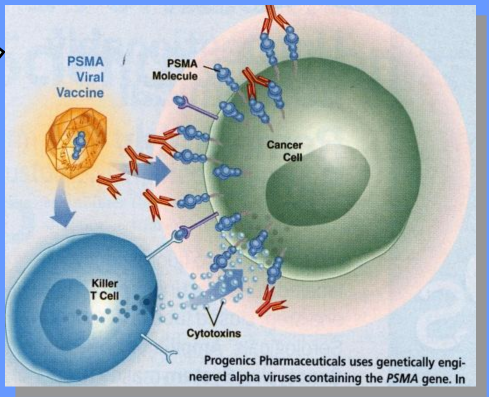


Bioreactor Design

Scaffolds

Upscaling

Preservation



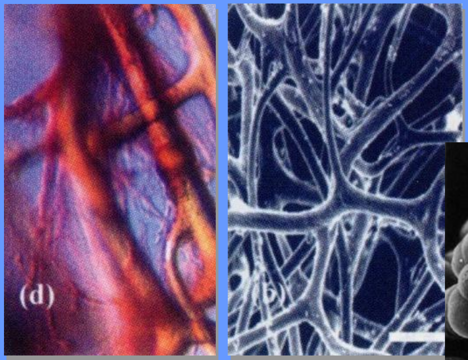
Immunoisolation/
Compatibility

Scaffolds in Tissue Engineering
They play the role of the extracellular matrix "ECM"

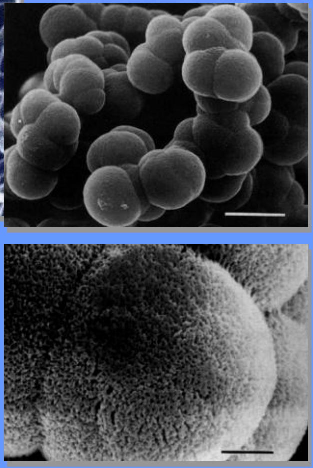
Biopolymers "Natural & Synthetic"

Natural: collagen, glycosaminoglycans, starch, chitosan,……..etc.

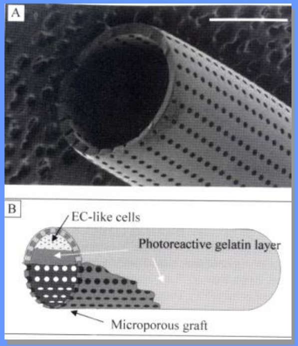
Synthetic: Poly(α-hydroxyesters) & copolymers (FDA-20 years ago)

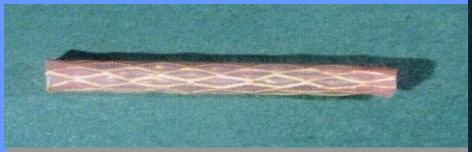


Skeleton of marine sponge collagen fiber

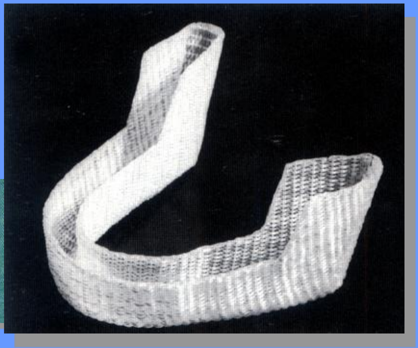


Hydrogel and microspheres





Vascular scaffolds

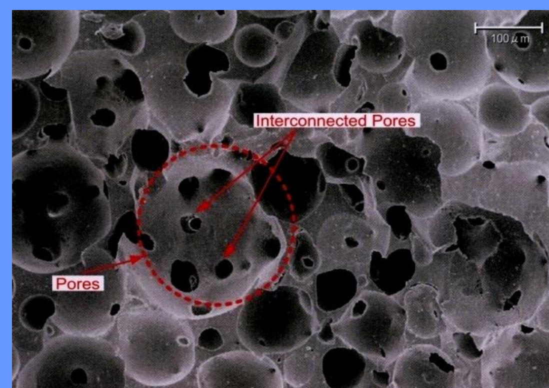


Hard tissue scaffolds

Scaffolds in Tissue Engineering
"Natural sources"

Permanent
bovine teeth

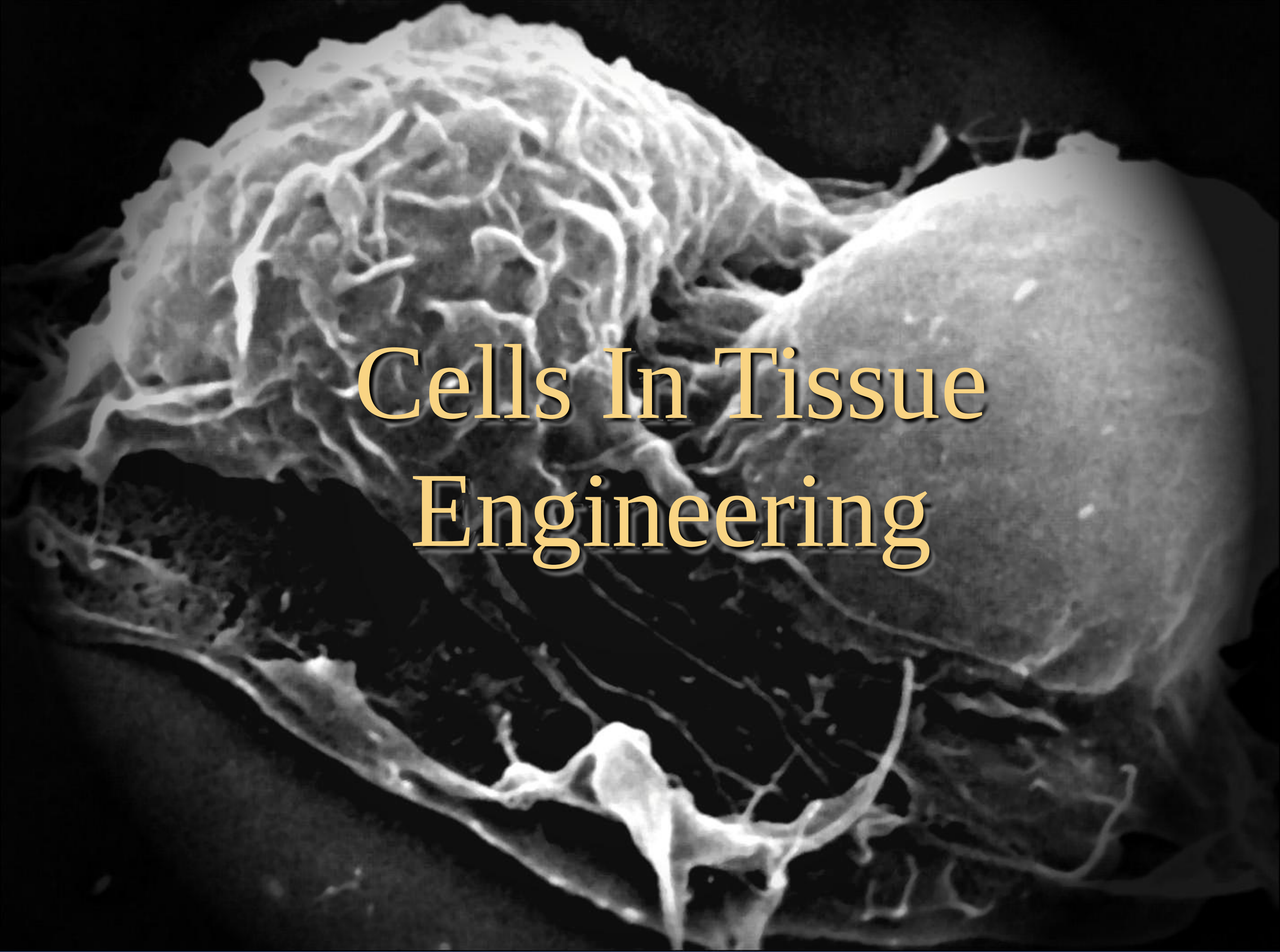
Alkali treated
teeth
calcinated



Bovine bone

Demineralized
bone powder

Cells In Tissue Engineering



Sources Of Cells

Autologous cells from patient

Allogeneic cells from donor

Undifferentiated stem cells (1998)

*Adult stem cells from

-bone marrow

-Circulating blood

-Tissues

*Embryonic stem cells from

-Early human embryos (4-5 days blastocyst)

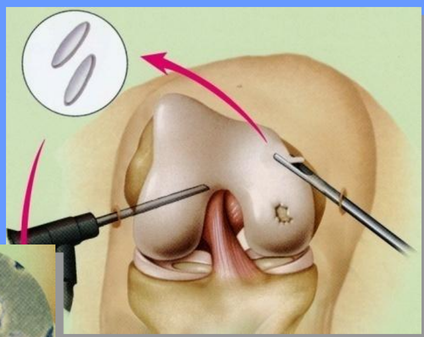
*Fetal stem cells from

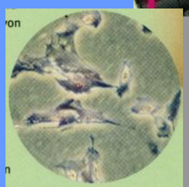
-Fetal tissue that was destined to be part of the gonads e.g. cord blood.

Fully Differentiated cells (1960)

- Chondrocytes → To produce cartilage
- Osteoblasts → To produce bone
- Glial cells → To produce nerve tissue
- Myocytes → To produce muscle

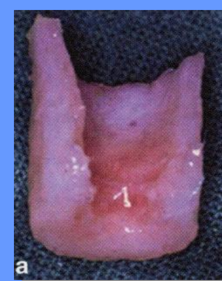
Engineering Cartilage



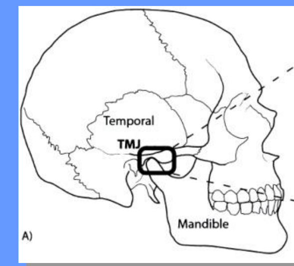


2000

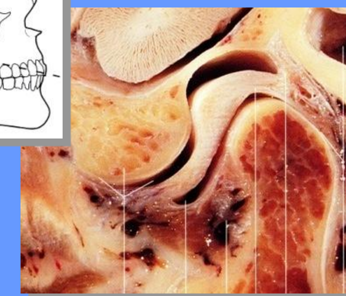
Knee cartilage engineering



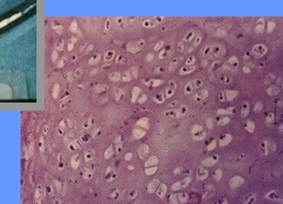
Trachea engineering



TMJ



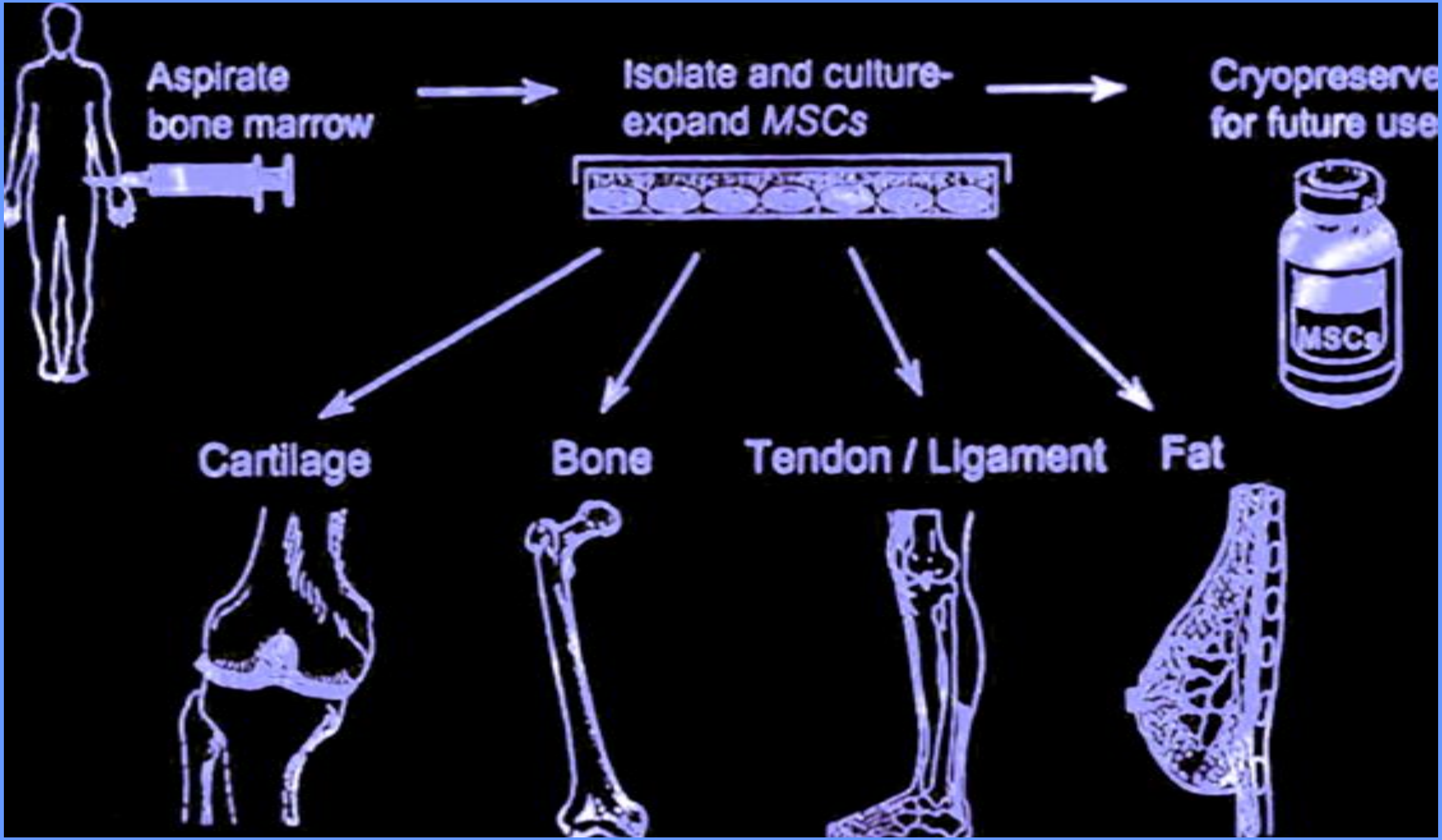
2004



Ear engineering

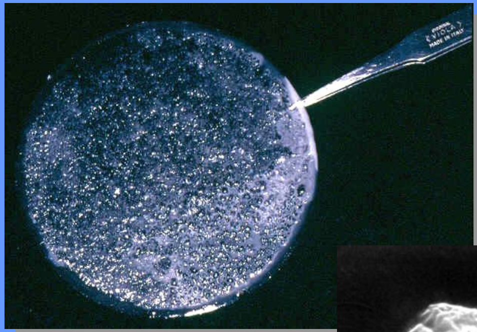
Adult Stem Cells

From Bone Marrow- “Mesenchymal stem cells”



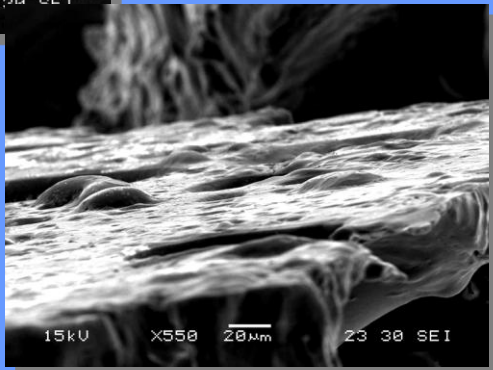
Seeding Bone Marrow Mesenchymal Stem Cells Onto Porous Scaffolds Of Poly (Lactide-co-glycolide)

Rabbit Model

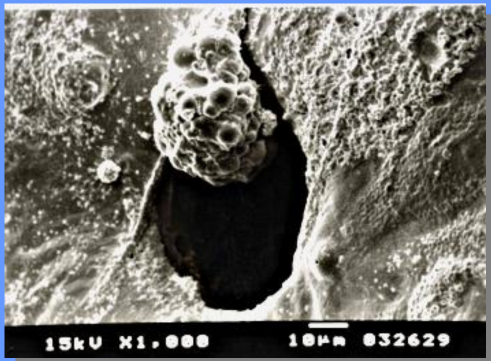


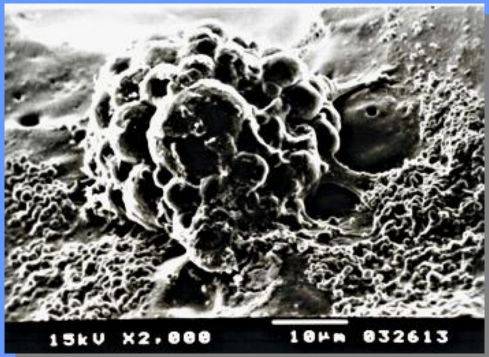
Porous PLG scaffolds

One hour BMScs



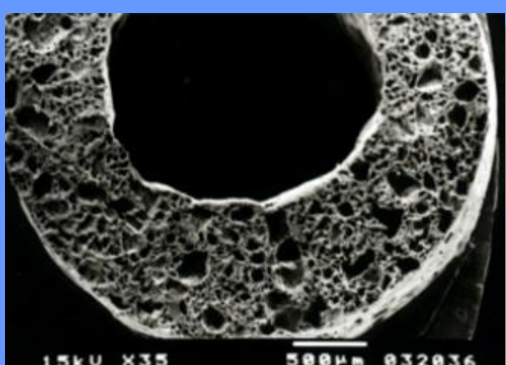
One hour BMScs

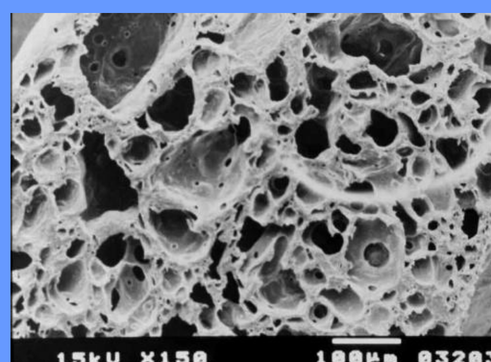


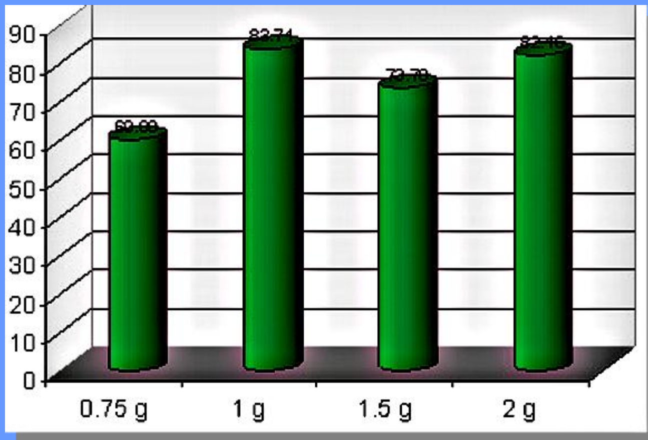


6 days

Engineering 3D Porous Scaffolds For Alveolar Bone Regeneration







Marei MK., Nouh SR., Fata MM., et al: Tissue Engineering 2003;9:713-731

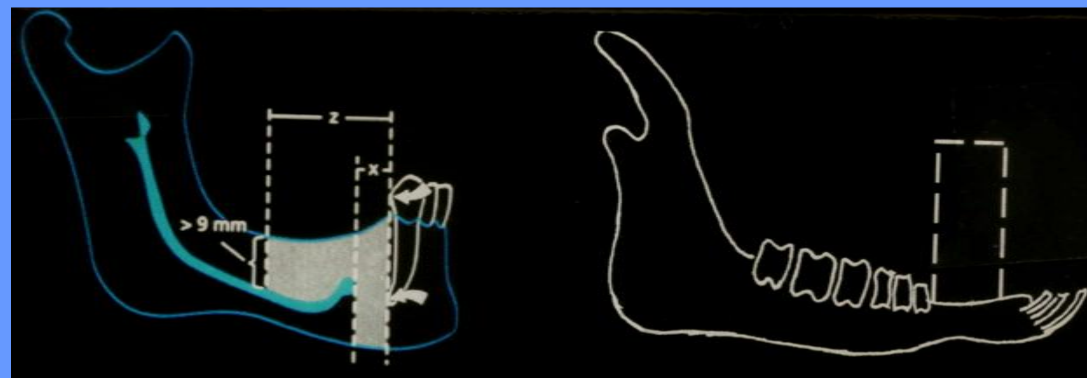
Biomechanical Model For The Regenerated Alveolar Bone Under Masticatory Force

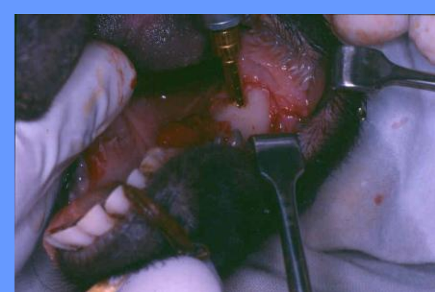
3/ point bending

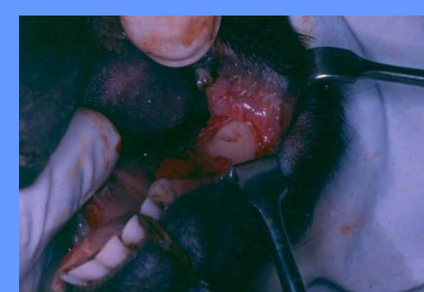
Parallel Plates

Tissue Engineering Around Endosseous Dental Implants

Goat Model

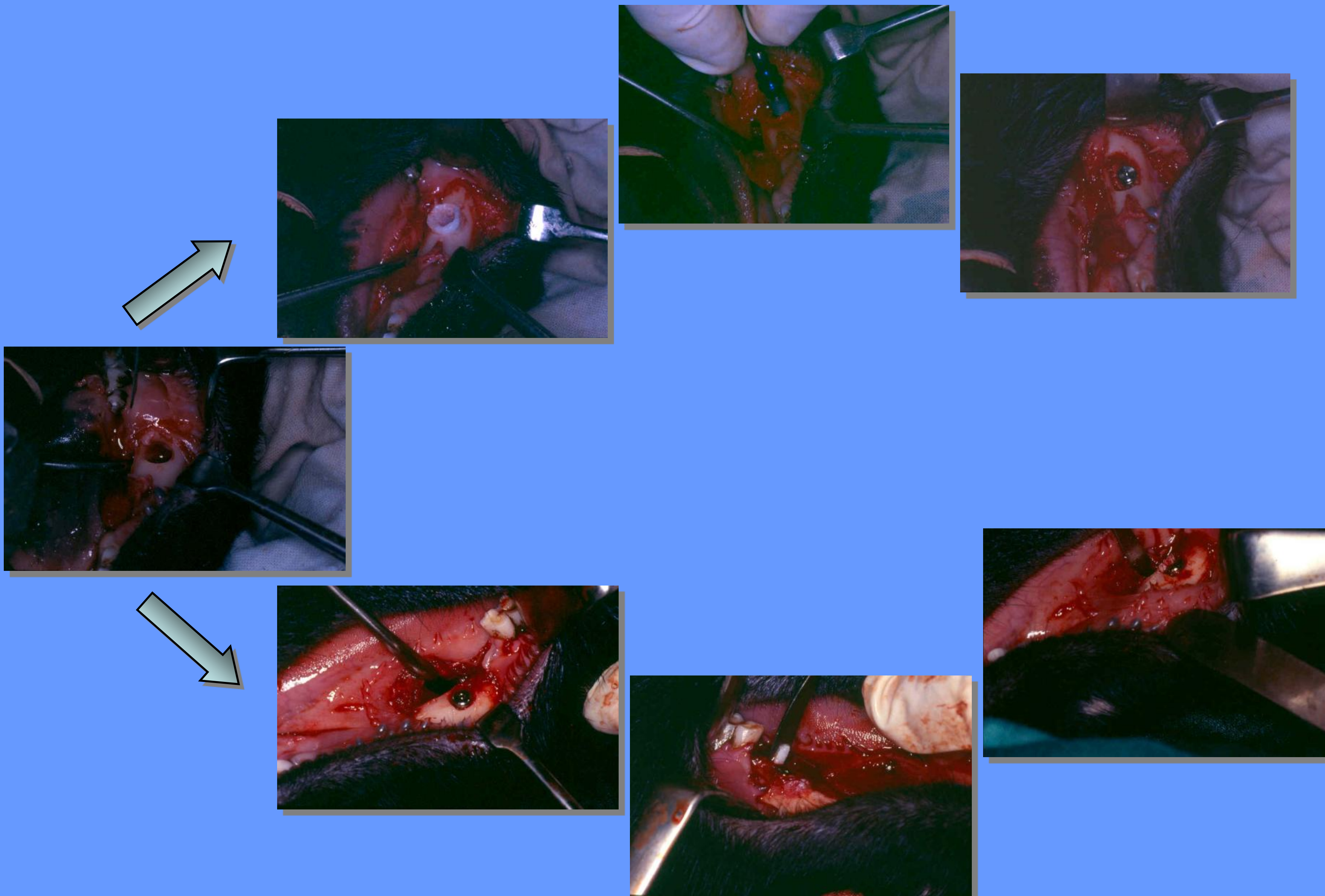




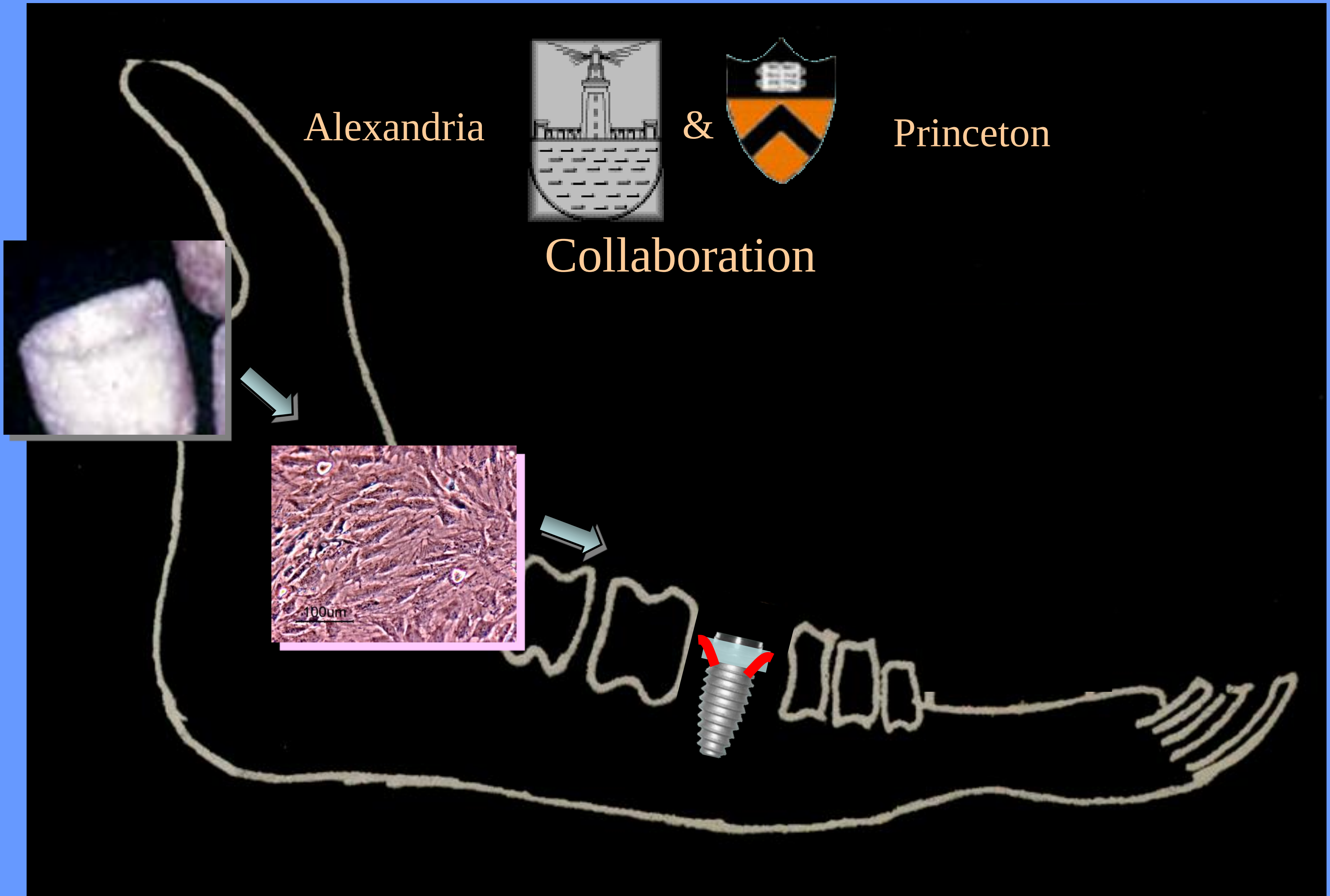


Tissue Engineering Around Endosseous Dental Implants

Goat Model



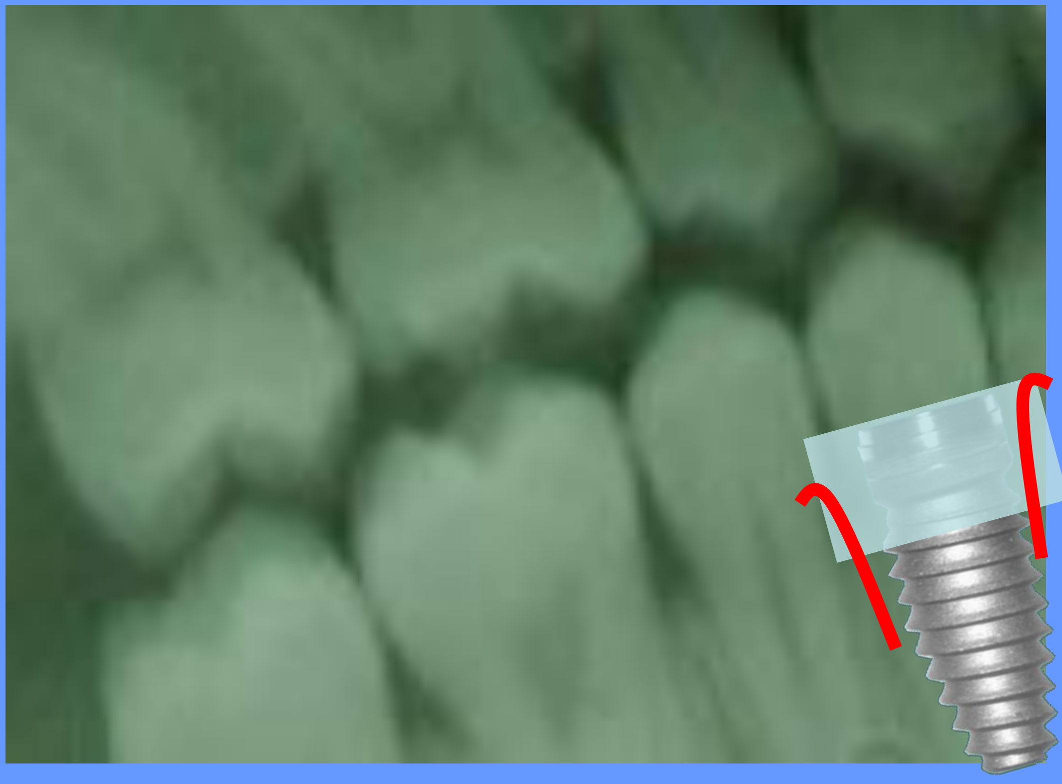
Tissue Engineering Around Endosseous Dental Implants



Orthopedic Implants: Dental Implants

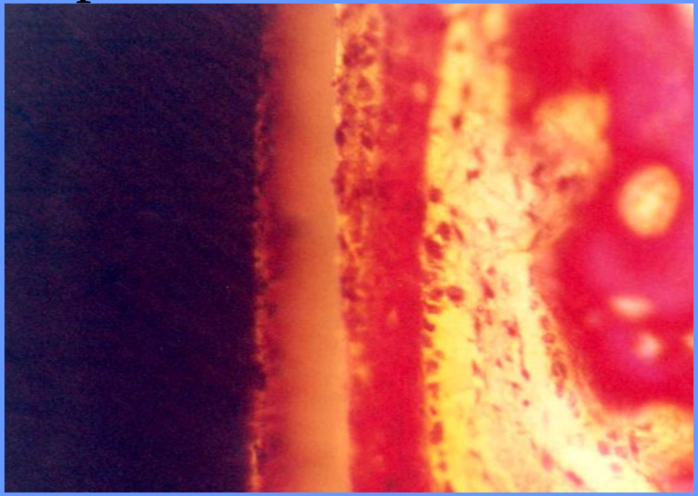
Research → Clinical use   Ti-6Al-4V

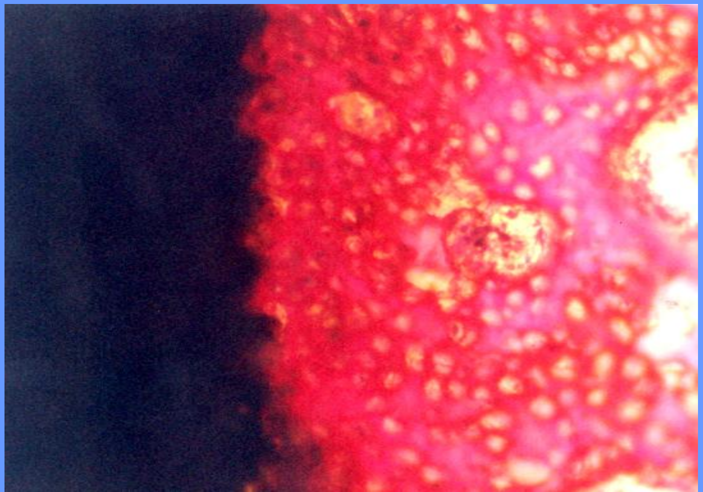
- **Wound Healing (short term)**
  - Micromotion
  - Accelerate Cellular Adhesion
- **Implant Working Life (long term)**
  - Stress Shielding
  - Increase cellular adhesion



Osteogenic Titanium Biomedical Systems

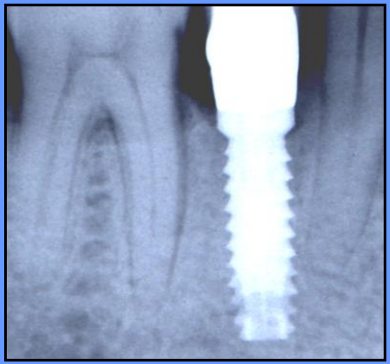
- An estimated 8-10 % of Americans have orthopedic implants - have a limited lifespan





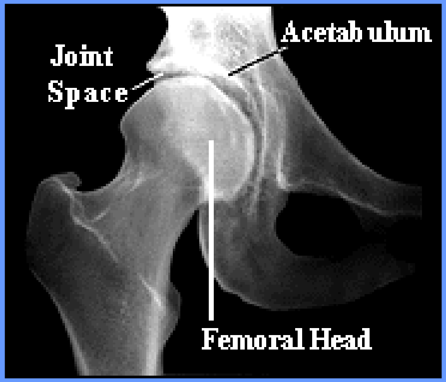
Implant Innovations, Inc.

Dental Implants



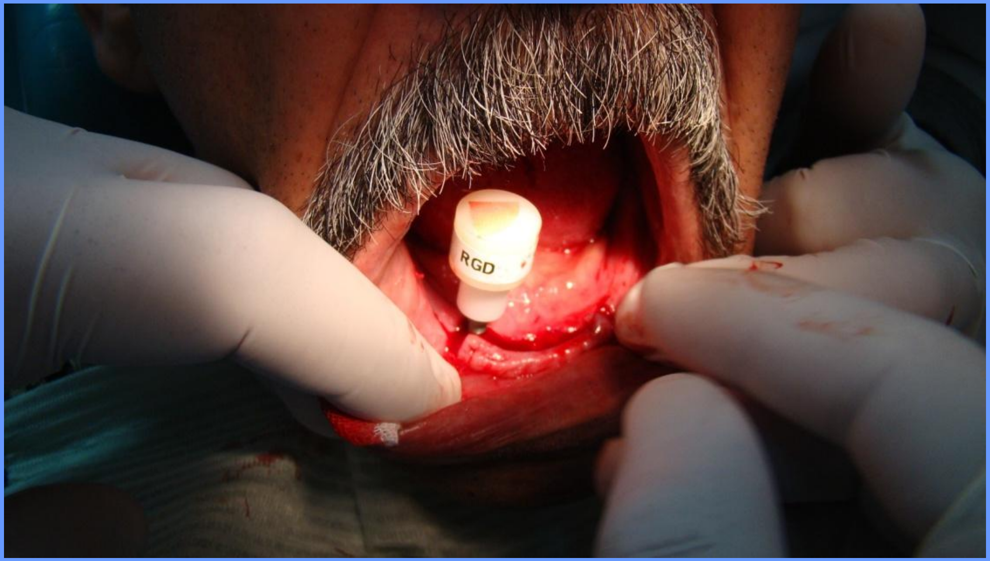
Stryker Howmedica Osteonics

Hip Implants



Human Trial of RGD-Coated Screw in Alexandria - Egypt

- 1st Human Trial on the 24th of March



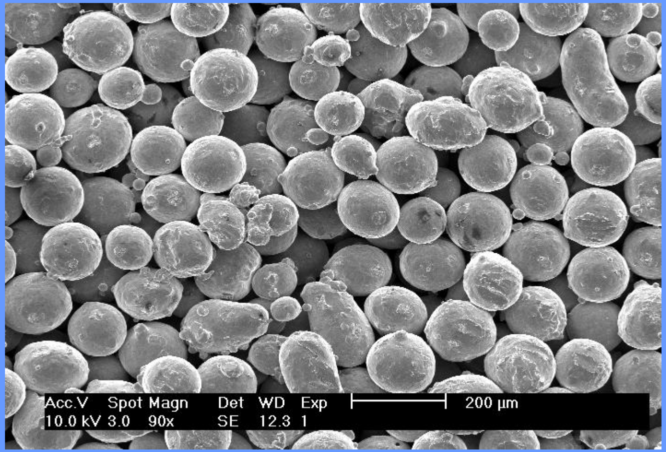
Introduction to Porous Metallic Biomaterials

- **Porous metallic biomaterials are used extensively in medicine and orthopedics – why**
- **Only a few metallic materials are biocompatible, *e.g.* Ti and Zr alloys.**
- **However, others are somewhat cytotoxic. But this is managed by the body's physiological processes, *e. g.* stainless steels and Co-Cr alloys**
- **Cell/pore interactions are explored next in porous Ti and Co-alloys**

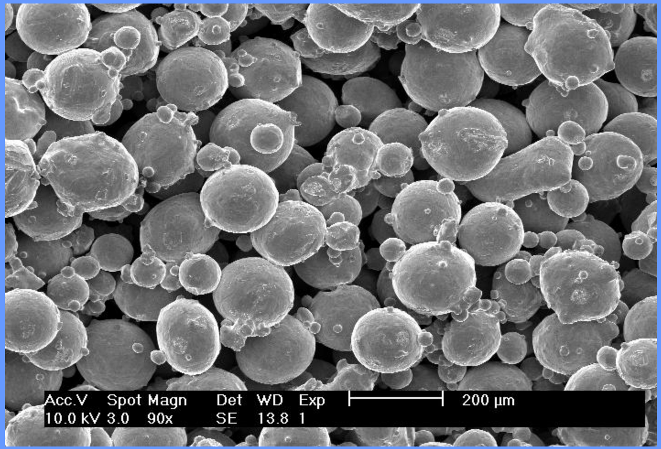
Porous Titanium Alloy

Ti-6Al-4V

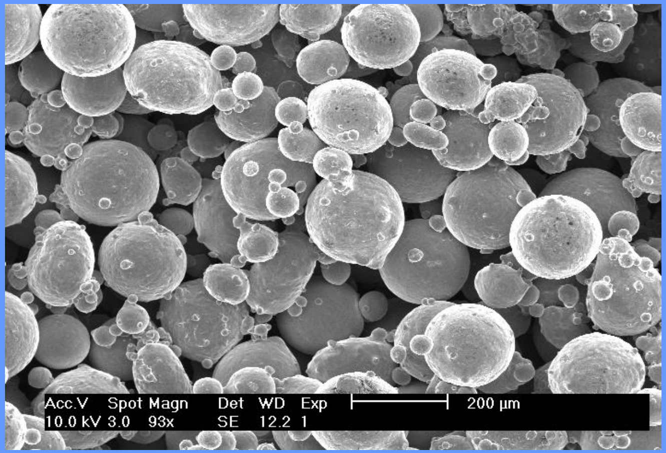
Sample A: 135um



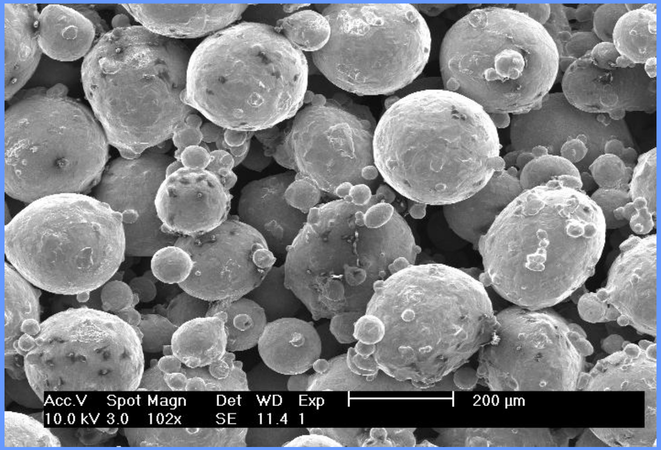
Sample B: 175um



Sample C: 185um

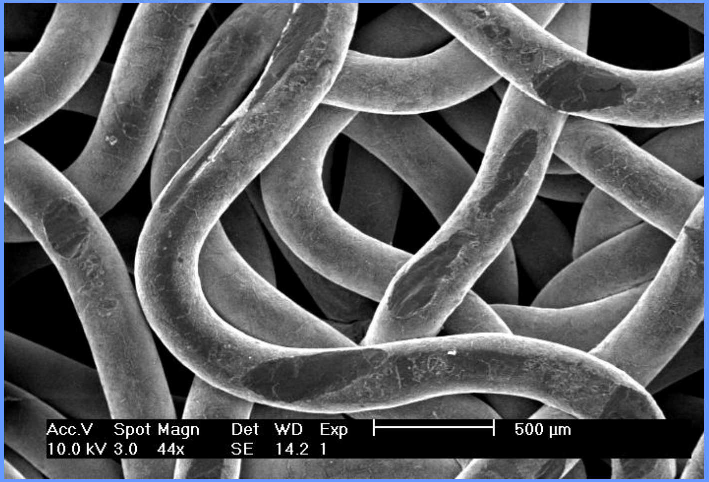


Sample D: 250um

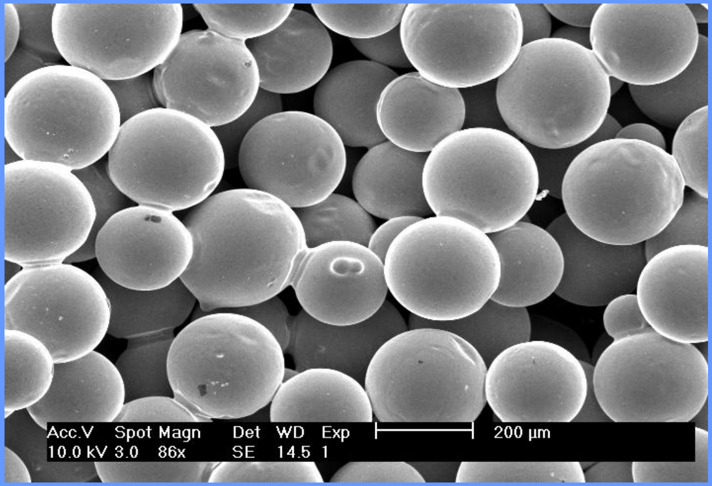


Zimmer Control Samples

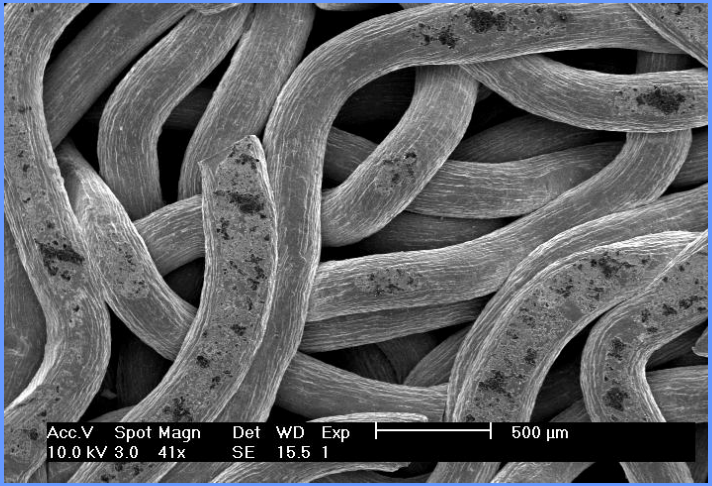
Cobalt Chromium Fiber



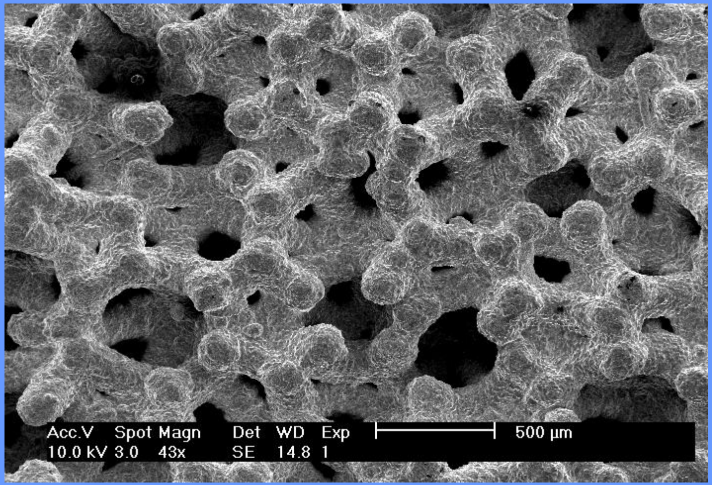
Cobalt Chromium Particle



Titanium Fiber

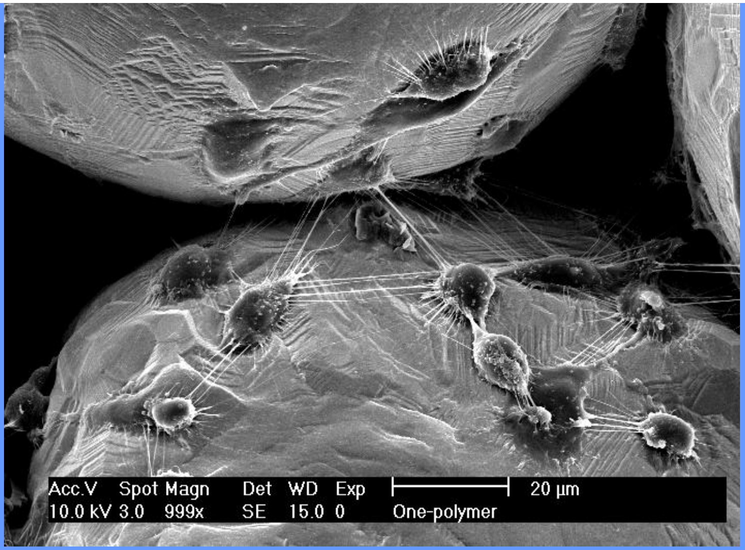


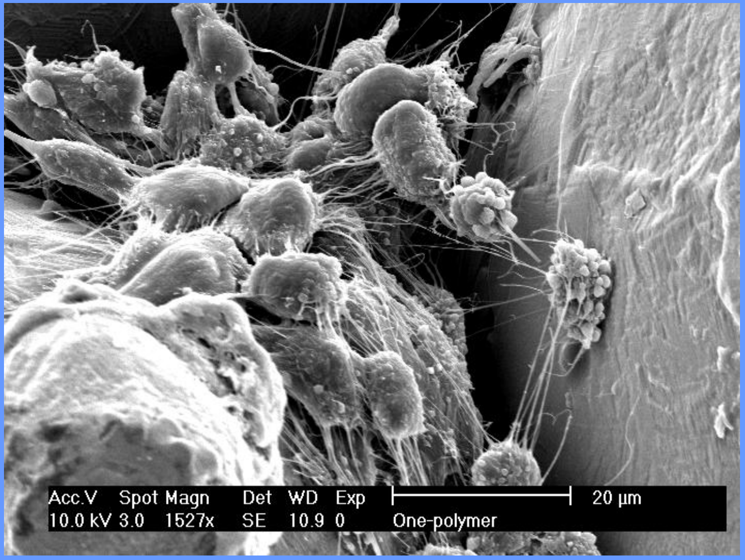
Titanium Mesh



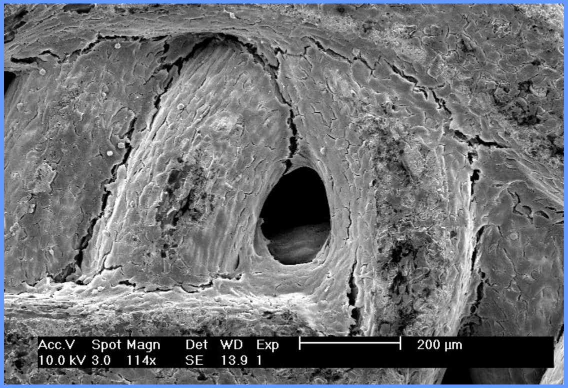
2 Day Ti-6Al-4V Powder

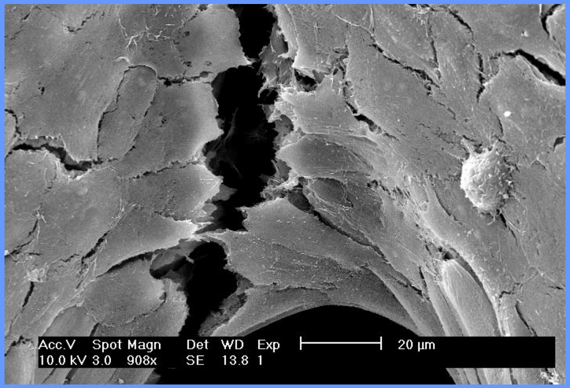
- Higher cell concentration
- Enhanced projections spanning across and between particle surfaces
- Increased cellular interaction and cluster formations

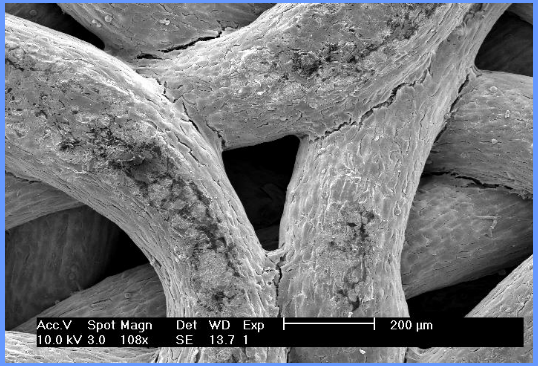


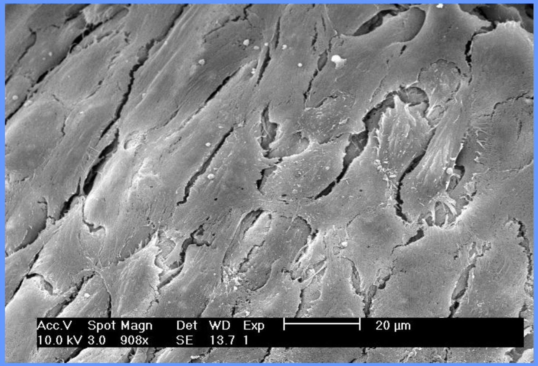


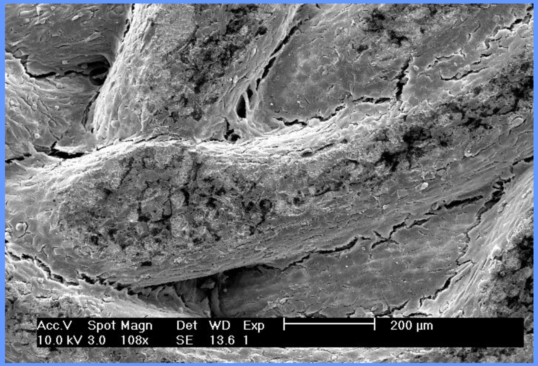
Titanium Fiber
9 Day



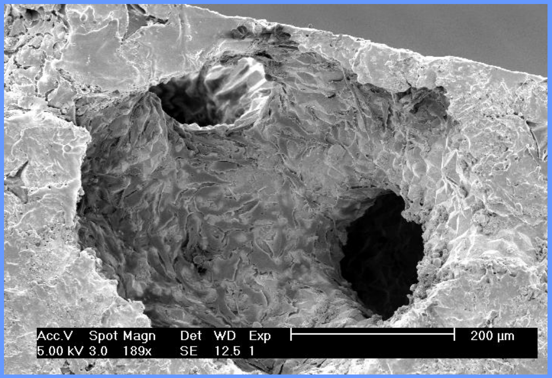


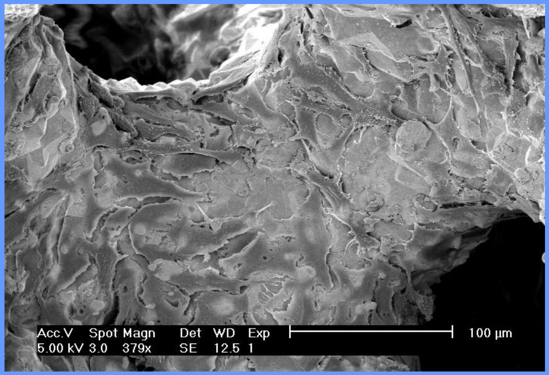


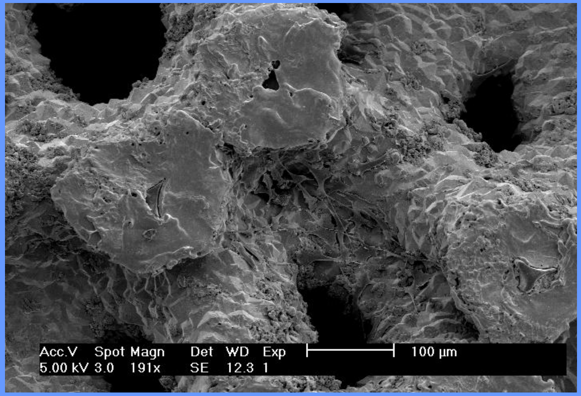


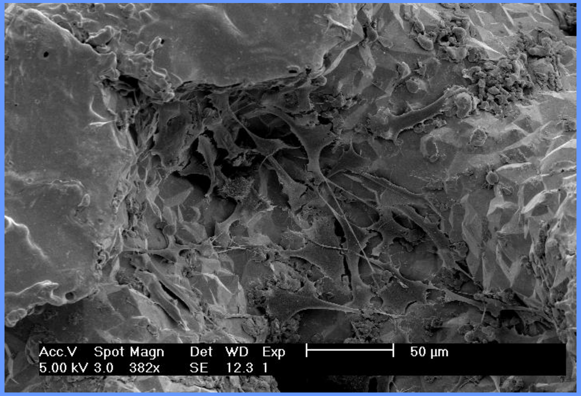


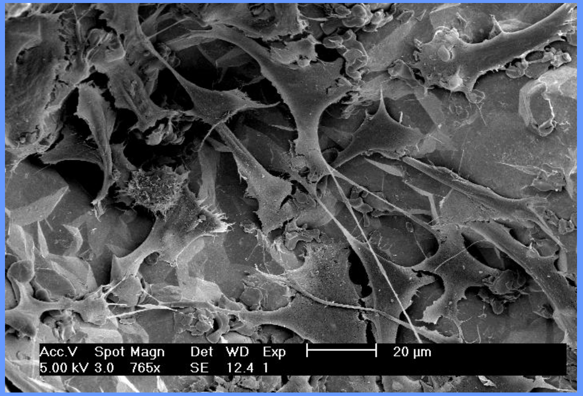
Titanium Mesh
9 Day





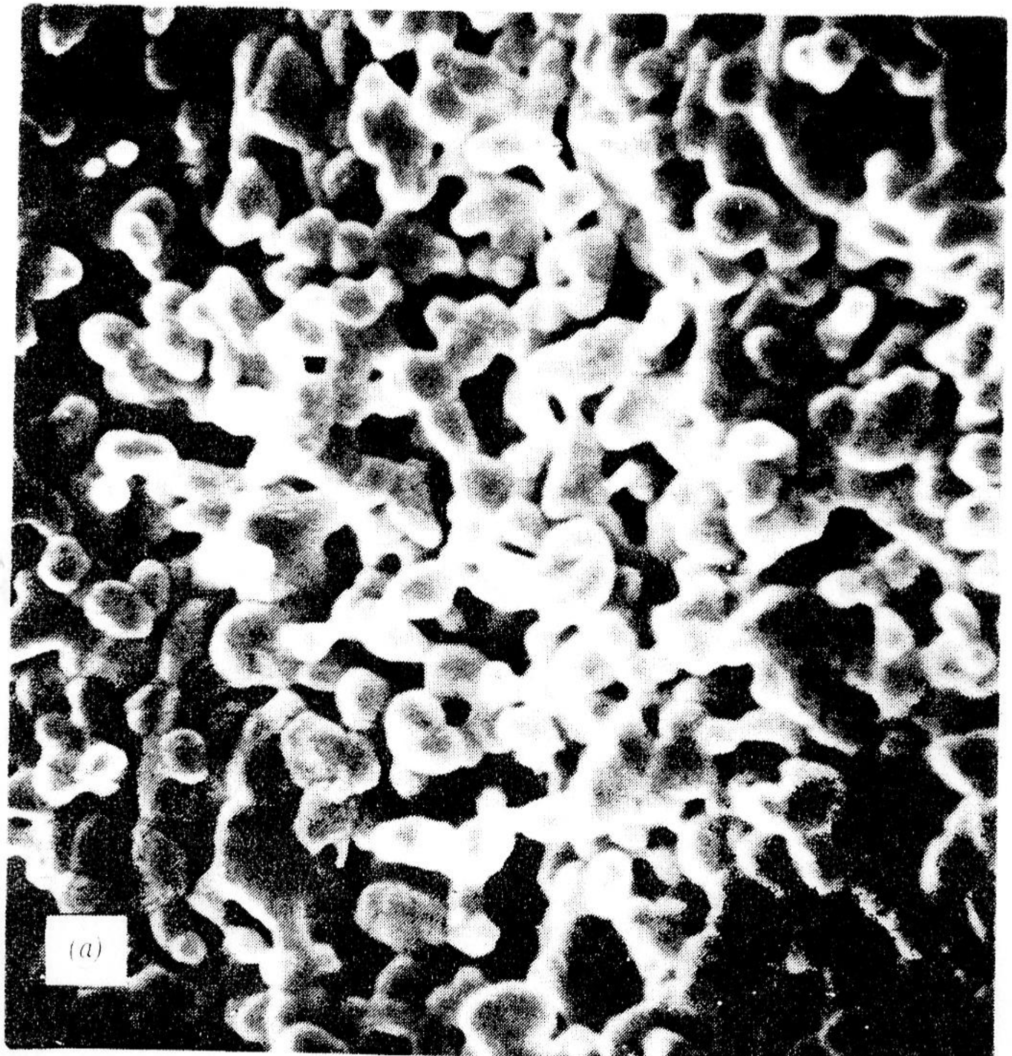






Introduction to Porous Ceramics – Properties and Processing

- Porous ceramic implants offer the combined advantage of inertness combined with mechanical instability of the convoluted interface that develops during bone ingrowth
- Mechanical requirements restrict the uses of porous ceramics to non-load bearing applications
- In such cases – porous ceramics may provide functional implant when pores exceed ~ 100μm
- Implant can serve as a structural bridge or scaffold for bone formation
- Porous materials have been made via investment casting with corals with appropriate pore sizes e.g. porous Al_2O_3, T_1O_2, calcium phosphates


(a)

Types of Bioceramics – Tissue Attachment

- No one material is suitable for all biomedical applications
- Bioceramics are generally used to repair or replace hard connective tissues
- Their success depends on the stable attachment to connective tissue

<u>Types of Implant – Tissue Response</u>

TABLE 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.

The Mechanism of Tissue Attachment to Bioceramics

- The mechanism of tissue attachment is directly related to the type of tissue response at the implant-tissue interface
- No implanted material is inert because all materials elicit a response from living tissues
- There are 4 types of tissue response and 4 ways of attaching tissue to the skeletal system

Biocermic-Tissue Attachment and Their Classification

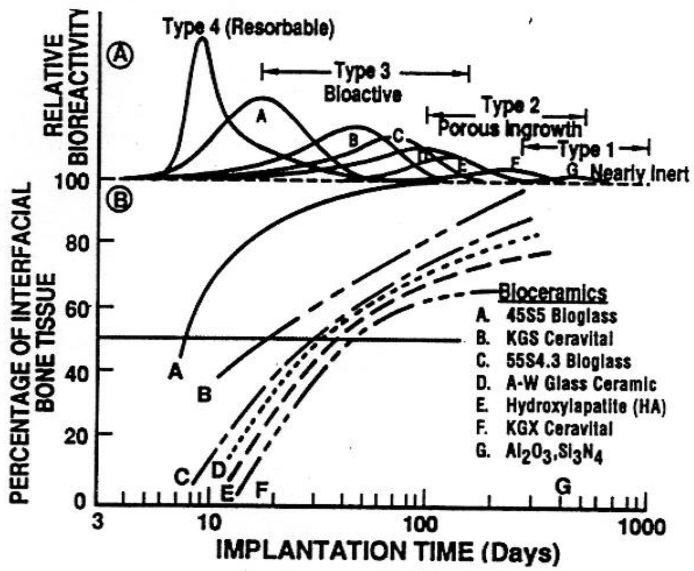
Type of attachment	Example
1. Dense, nonporous, nearly inert ceramics attach by bone growth into surface irregularities by cementing the device into the tissues or by press-fitting into a defect (termed "morphological fixation").	Al_2O_3 (single crystal and polycrystalline)
2. For porous inert implants, 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

Chemical Activity and Bond/Bone Formation Rate at Interference

- The relative chemical activity of the different types of bioceramics and glasses depend strongly on the rate of formation of an interfacial bond of ceramic with bone
- The interfacial reaction influences the thickness of the interfacial zone
- Interfaces are not chemically or biologically bounded when the rate of reaction is slow – relative motion occurs and fibrous capsule forms in soft and hard tissues

<u>Bioactivity Spectra of Various Bioceramic Implants</u>

<u>A(relative rate of bioactivity), B (time dependence of bone formation rate at interface)</u>



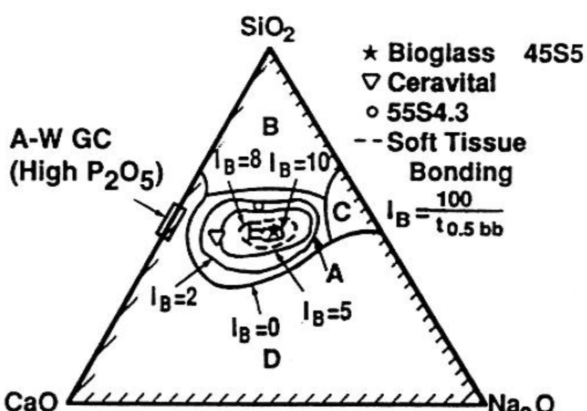
Bioactive Glasses, Ceramics, and Glass Ceramics

- Bioactive ceramics consist of SiO_2, Na_2O, CaO, and P_2O_5 in specific proportions
- Certain compositions of glasses, ceramics, and glass ceramics and composites have been used to bond to bone
- These materials are known as bioactive ceramics
- A common characteristic is the time dependent kinetic modifications of the interface that occurs upon implantation
- The surface forms a biologically active carbonated HA layer that promotes bonding of interface with tissues
- Materials that are bioactive develop adherent interfaces that resist mechanical forces
- The interfacial strength of adhesion is greater than the cohesive strength of the implant material of tissue

Compositional Depnedence of Bone/Tissue Bonding

- **The compositional – dependence of bone and soft tissue bonding on Na_2-CaO-P_2S_2-SiO_2 glasses is shown below**
- **All the glasses in the figure contain a constant wt.% of P_2O_5**
- **Compositions in the middle form a bond with bone**
- **Compositions in A form good bongs with bone while those in region B behave as inert materials and form fibrous capsules at the implant interface**
- **Glasses in region C are resorbable and disappear within 10-30 days**
- **Glasses in region D are not technically practical and have not been tested in implants**

<u>Compositional Dependence of Bone Bonding with Bioactive Silicate Glasses</u>



Emerging Applications and Ethical Issues

- Artificial skin for burns or wound healing
- Facial reconstruction and bone growth
- Organ factories
  - Ethical considerations need to be considered
  - Can organs be harvested from fetuses?
  - Under what conditions should this be allowed?
- Cloning – even more serious issues need to be resolved…

Summary and Concluding Remarks

- This class presents an introduction to tissue engineering – from cells to tissue and organs
- Examples of tissue & organs engineered from resorbable and non-resorbable scaffolds were presented
- Initial results suggest the potential to grow bone and a number of organs – much work to be done
- The effects of surface texture were also explored e.g. laser vs rough vs porous structures
- The class compared the design of polymer, metal and ceramic porous structures and interfaces
- Tissue engineered systems have the potential to replace conventional implants in medicine ….