Massachusetts Institute of Technology
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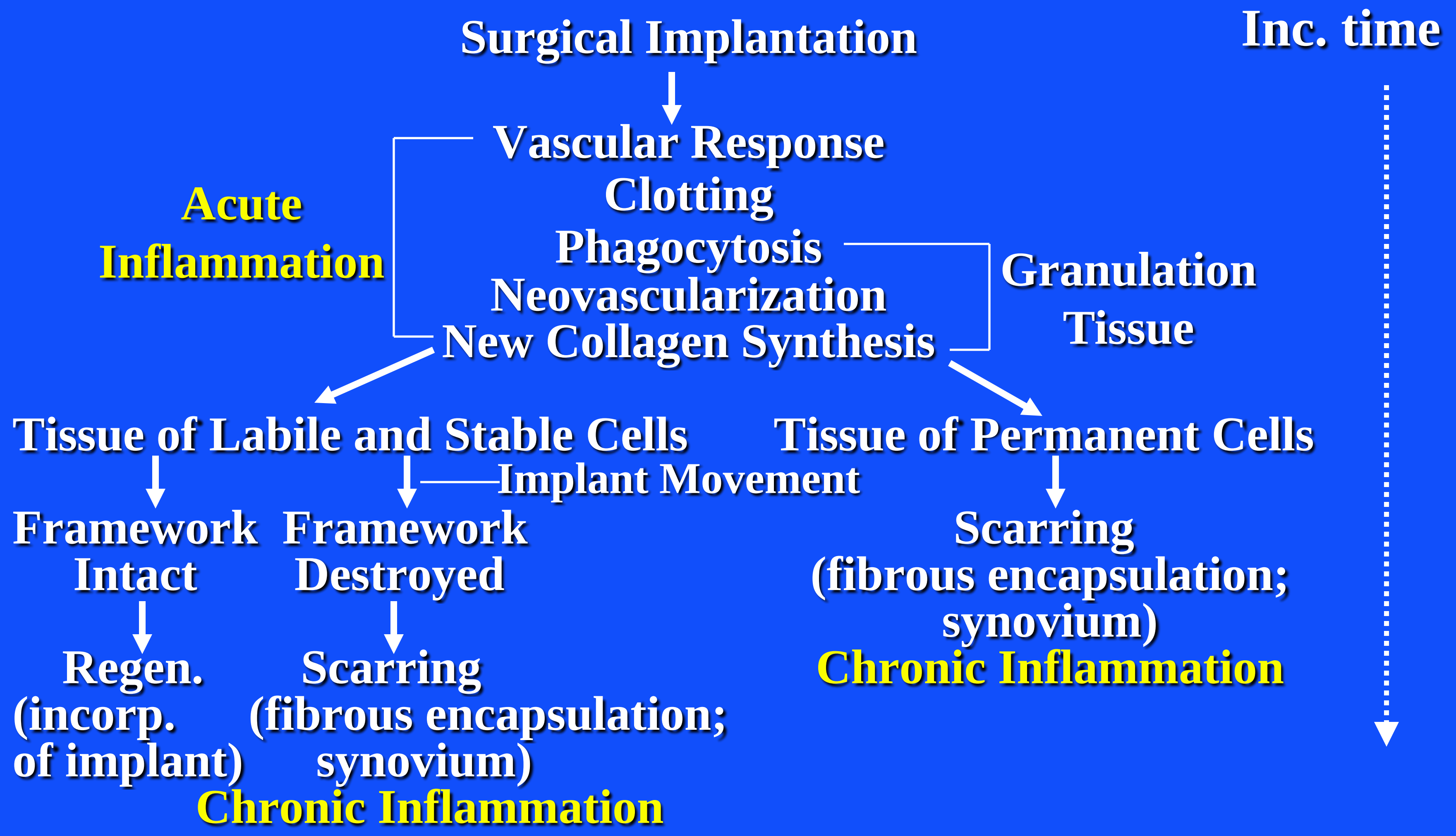
FORMATION OF SOFT TISSUE AND BONE AROUND IMPLANTS:
The Chronic Response to Implants

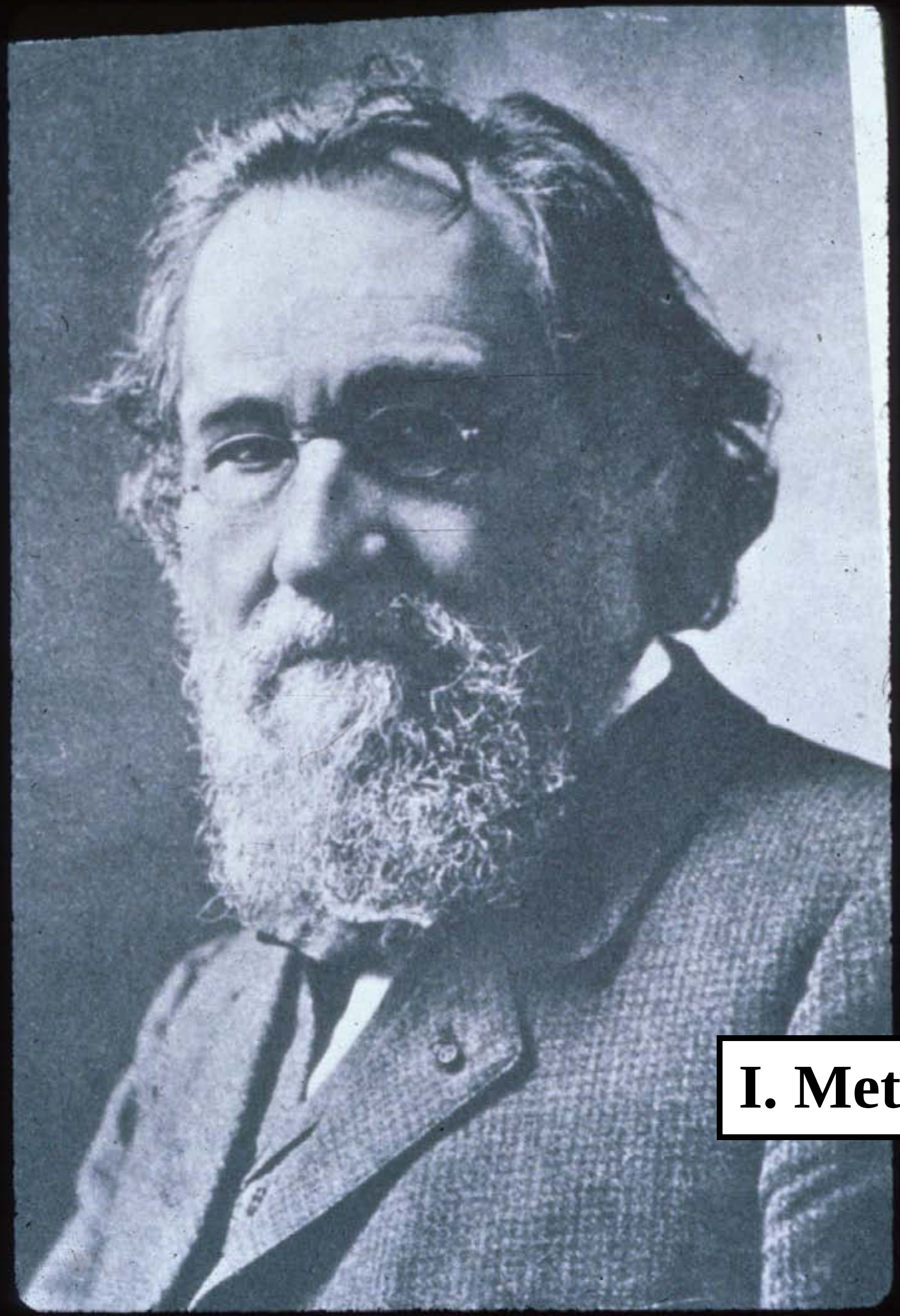
M. Spector, Ph.D.

MAST CELLS
Wikipedia

- Mast cells were first described by Paul Ehrlich in his 1878 doctoral thesis on the basis of their unique staining characteristics and large granules.
- These granules also led him to the mistaken belief that they existed to nourish the surrounding tissue, and he named them "mastzellen," a German term, meaning "feeding-cells."

RESPONSE TO IMPLANTS: WOUND HEALING





I. Metchnikoff

Smith-Peterson

In 1923 a piece of glass was removed from a patient's back; it had been there for a year. It was surrounded by a minimal amount of fibrous tissue, lined by a glistening synovial sac, containing a few drops of clear yellow fluid.

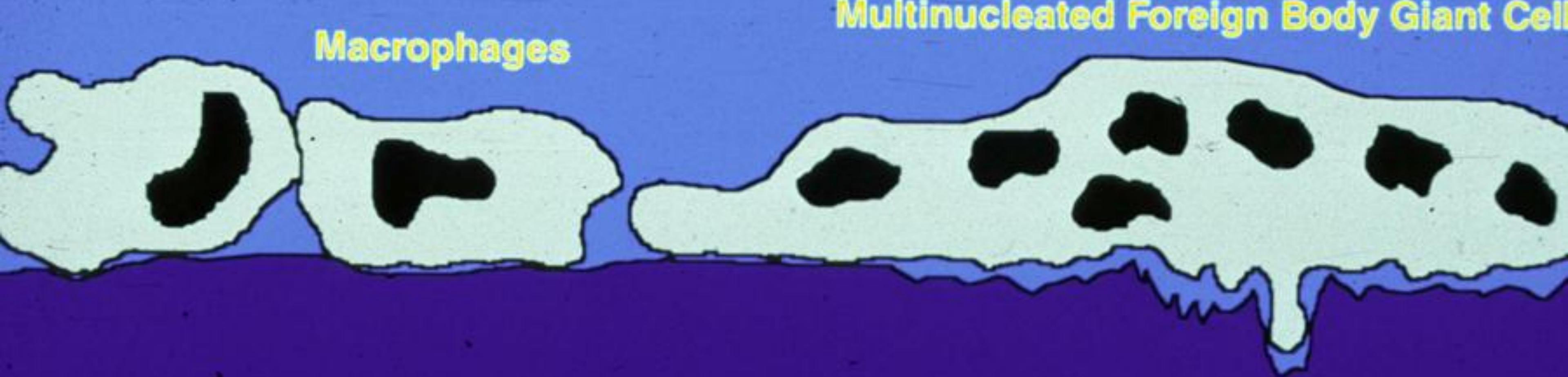
See J. Bone Jt. Surg., 30-B:59 (1948)

Slides of histology photos removed due to copyright restrictions.

- Synovium: Macrophage-like (Type A) and Fibroblast-like (Type B) Cells
- Tissue response to a cylindrical implant of polysulfone in lapine skeletal muscle, 2 yrs. post-op
- Polyethylene implant, 6 mos. post-op
- Porous Coated Co-Cr Tibial Component (retrieved 1 yr. post-op)

MACROPHAGES ON SURFACES

- Macrophages are attracted to surfaces (dead space)
- Fuse to form MFBGC
- More MFBGCs on irregular surface



CHRONIC RESPONSE TO IMPLANTS

- Persistence of macrophages* at the implant surface
- Presence of fibroblasts*
- Proliferation and increased matrix synthesis of fibroblasts can result from mechanical perturbation by the implant or by agents released by the implant, leading to an increase in the thickness and density of the scar tissue.
- Fibroblast contraction can result in scar contracture.

* Constituents of synovium

MACROPHAGE AND FIBROBLAST INTERACTIONS IN SYNOVIUM

Ions → Mechanical force →

Macrophage + Part. —Endocytosis→ Sol. Part + Reg.

Fibroblast + ECM —Mitosis→ + Reg.

Fibroblast + ECM —Migration→ + Reg.

Fibroblast + ECM —Synthesis→ + Reg.

Fibroblast + ECM —Contraction→ + Reg.

RESPONSE TO IMPLANTS: WOUND HEALING

Surgical Implantation

↓

Vascular Response
Clotting
Phagocytosis
Neovascularization
New Collagen Synthesis

Acute Inflammation (Vascular Response through New Collagen Synthesis)

Granulation Tissue (Phagocytosis through New Collagen Synthesis)

Inc. time

Tissue of Labile and Stable Cells
- ↓ Framework Intact ↓ Regen. (incorp. of implant)
- ↓ (Implant Movement) Framework Destroyed ↓ Scarring (fibrous encapsulation; synovium)
  Chronic Inflammation

Tissue of Permanent Cells
- ↓ Scarring (fibrous encapsulation; synovium)
  Chronic Inflammation

IMPLANT MATERIALS/BIOMATERIALS TISSUE RESPONSE

Soft Tissue (that does not regenerate)

- Fibrous capsule (scar)
  - Synovium: fibrous tissue interspersed with macrophages
  - Wound healing response of repair (scar formation) coupled with macrophage accretion at the "dead space" - chronic inflammation

Bone

- Tissue integration and tissue bonding
- Why don't macrophages remain at the biomaterial surface?

TISSUE INTEGRATION
TISSUE BONDING

- **Tissue Integration (Osseointegration)**
  - **Apposition of tissue (bone) to the implant (contact of bone with the surface but not necessarily bonding); no macrophage layer?**
  - **Regeneration of tissue up to the surface of the implant**
- **Tissue Bonding (Bone Bonding)**
  - **Chemical bonding of tissue (*viz.*, bone) to the surface**
  - **Protein adsorption and cell adhesion**
  - **Biomaterials: calcium phosphates and titanium (?)**

Dental Implant Designs and Materials

Carbon

Titanium

Photos of various dental implants
removed due to copyright restrictions.

Alumina

Blade Implant

Photos of three installed dental implants removed due to copyright restrictions.

“Commercially pure” Titanium

Branemark Dental Implant

Photo of “Original Branemark implant fixture” removed due to copyright restrictions. See http://www.oral-implants.com/home1.htm

Dr. Per-Ingvar Branemark

http://www.oral-implants.com/home1.htm

Photo sequence showing installation of dental implants removed due to copyright restrictions. See http://www.oral-implants.com/home1.htm

http://www.oral-implants.com/home1.htm

Osseointegration:
Control of Surgical Trauma

Image removed due to copyright restrictions.

Guidelines for drilling into bone

- Remove as little of the host periosteum as possible
- Drill speed less than 1500 rpm
- Cool (with water) during drilling and tapping
- Drill using smaller diameter than tap
- Drill tool rake angle 25°-35°
- Always tap for stabilizing screws
- Tap same diameter and same metal as screw

T. Albrektsson, CRC Crit. Rev. Biocompat., 1:53 (1984)

Osseointegration

Images removed due to copyright restrictions.
See Figure 5a (tissue-titanium interrelationship at the interface zone) and Fig. 6c in Albrektsson, T. et al. *Ann. Biomed. Engr*. 11 no. 1 (1983): 1-27.
http://dx.doi.org/10.1007/BF02363944

T. Albrektsson, *et al*., Ann. Biomed. Engr., 11:1 (1983)
T. Albrektsson, CRC Crit. Rev. Biocompat., 1:53 (1984)

b. Gingiva:
Epithelium regenerates

Osseointegration

d. Bone

Diagram removed due to copyright restrictions.
See Figures 5b, c and d in Albrektsson, T. et al.
Ann. Biomed. Engr. 11 no. 1 (1983): 1-27.
http://dx.doi.org/10.1007/BF02363944

c. Sub-gingival CT

T. Albrektsson, *et al*., Ann. Biomed. Engr., 11:1 (1983)

Osseointegration

Images removed due to copyright restrictions.
See Figure 7 (schematic of interface zone between connective tissue and titanium) in Albrektsson, T. et al. *Ann. Biomed. Engr*. 11 no. 1 (1983): 1-27.
http://dx.doi.org/10.1007/BF02363944

T. Albrektsson, *et al*., Ann. Biomed. Engr., 11:1 (1983)

Implants with Porous Coatings in Bone

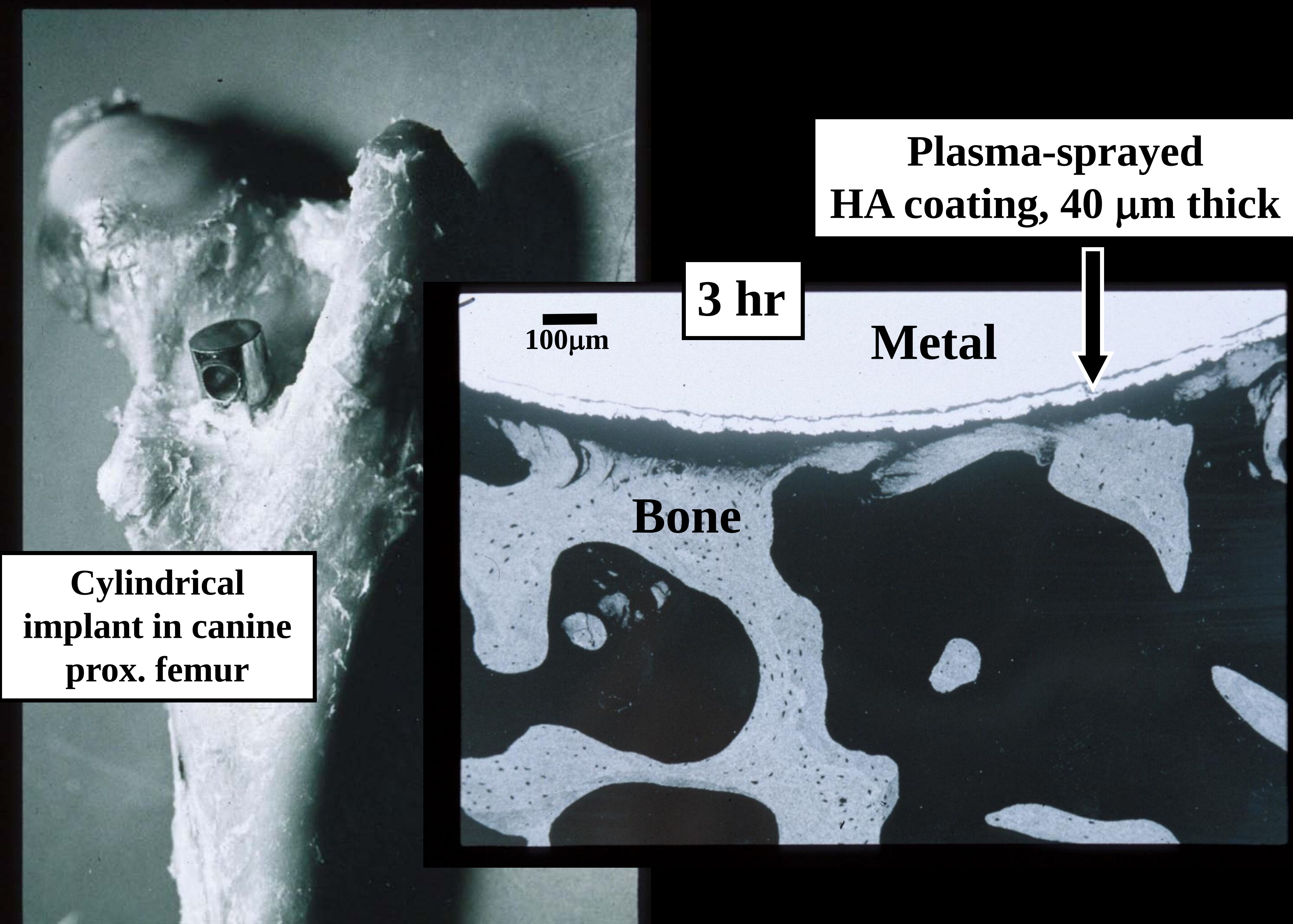
Metal stem

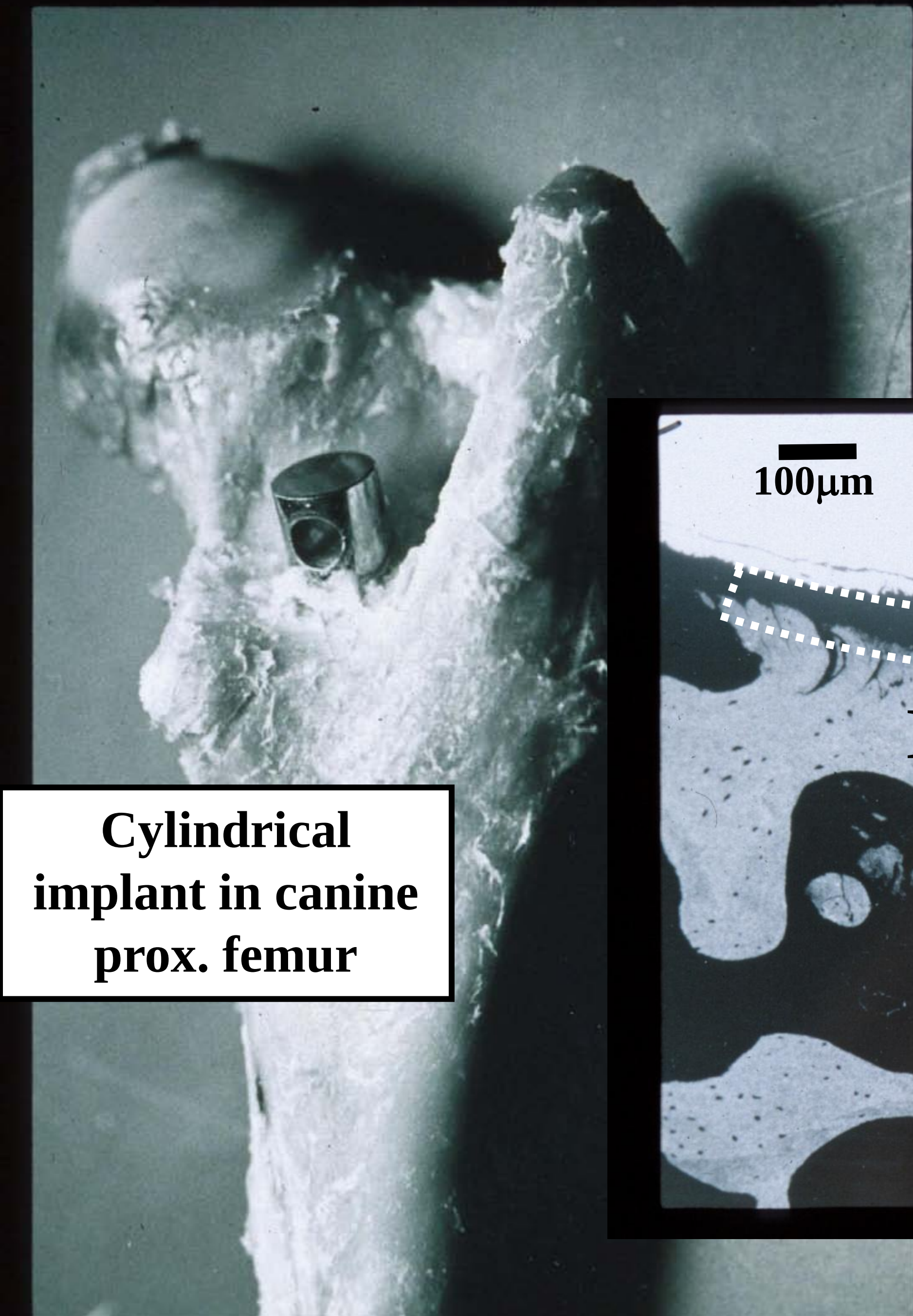
Beaded porous coating

Images removed due to copyright restrictions.

Hydroxyapatite-Coated Implants

Several photos of implants removed
due to copyright restrictions.


Plasma-sprayed
HA coating, 40 μm thick
3 hr
100μm
Metal
Bone
Cylindrical
implant in canine
prox. femur


Cylindrical
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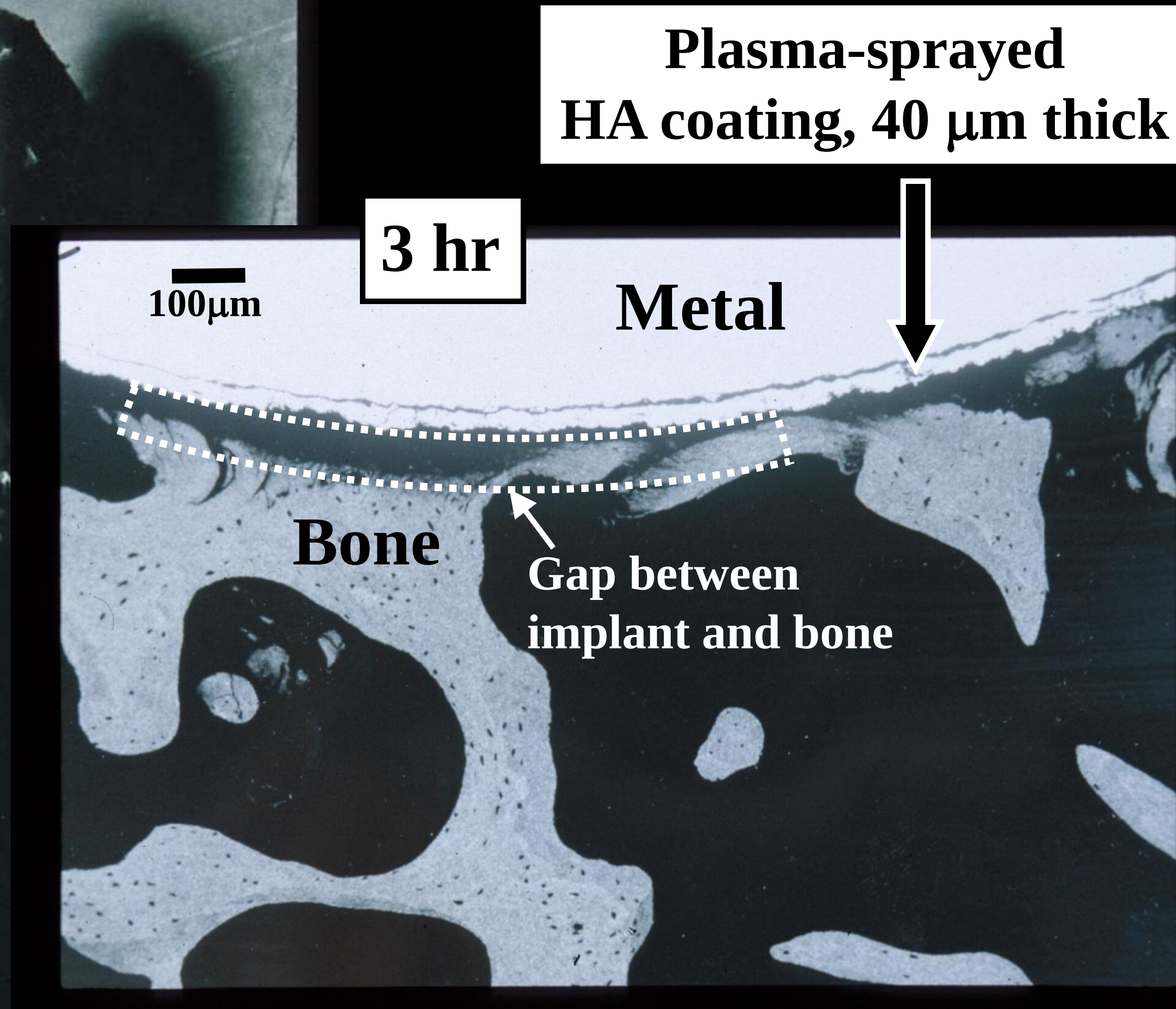
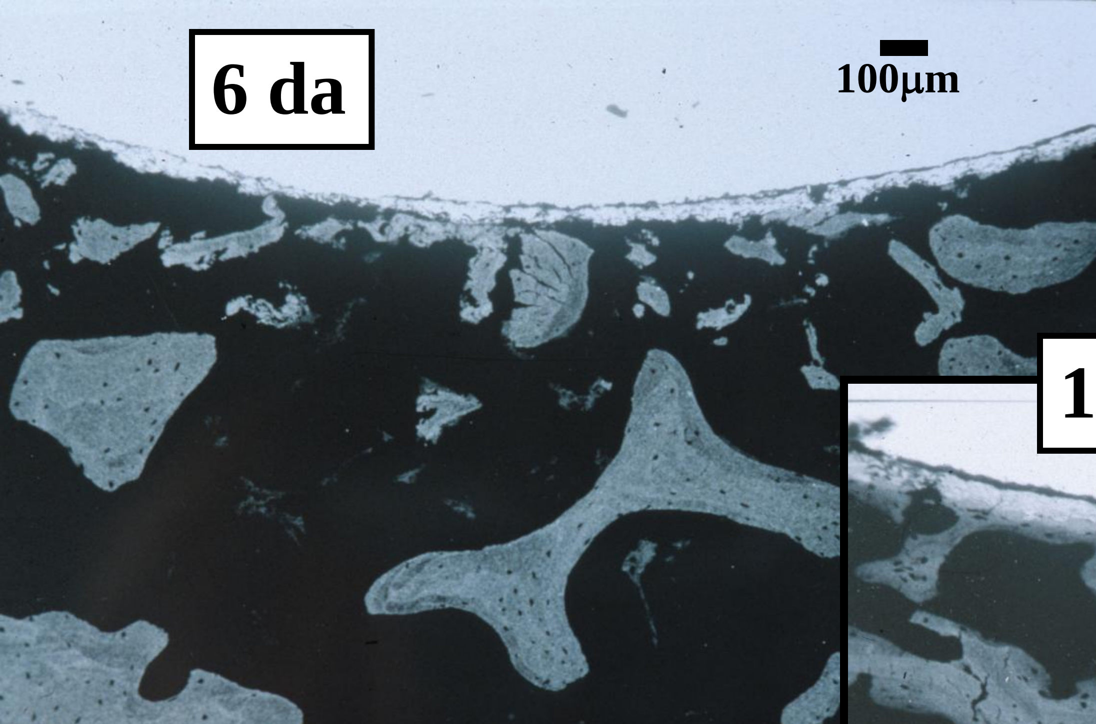
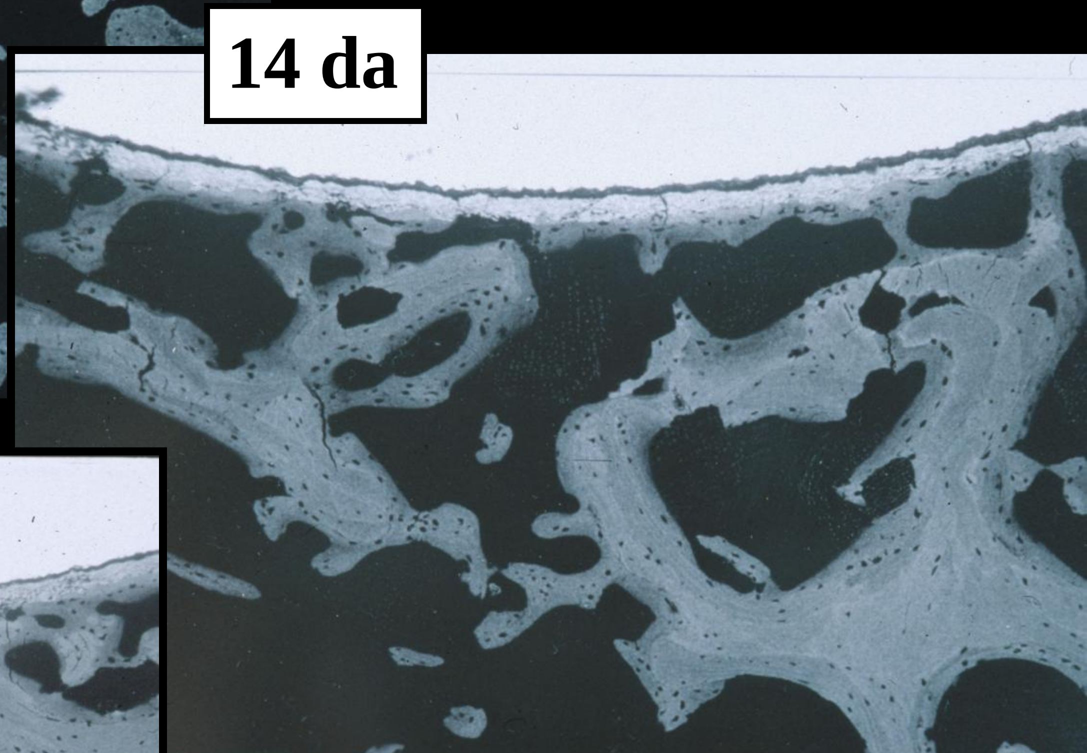
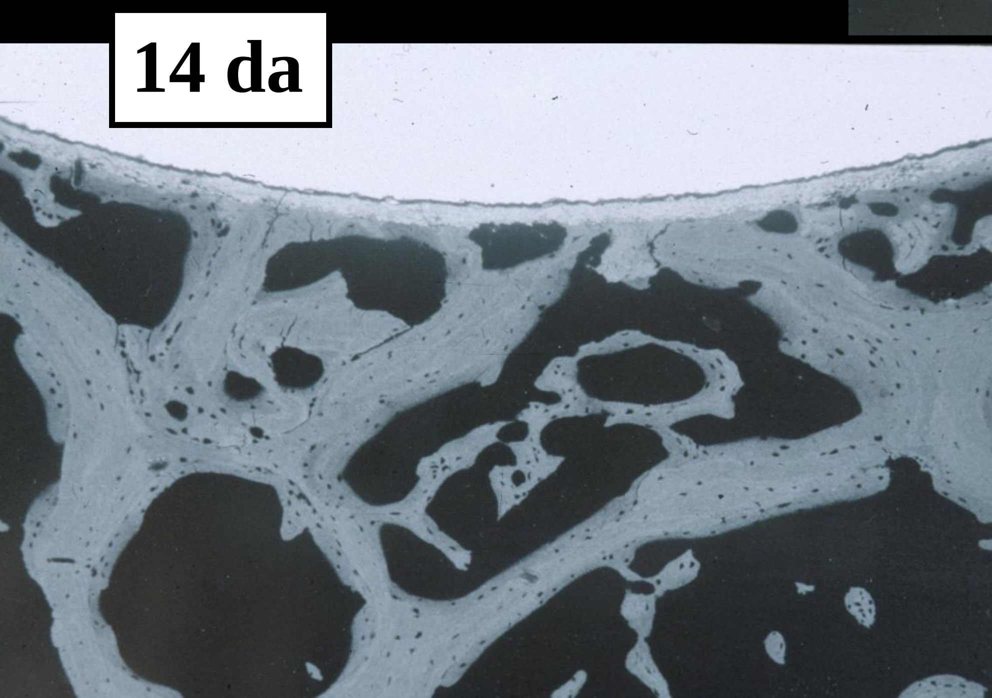

Plasma-sprayed
HA coating, 40 μm thick
3 hr
100μm
Metal
Bone
Gap between
implant and bone

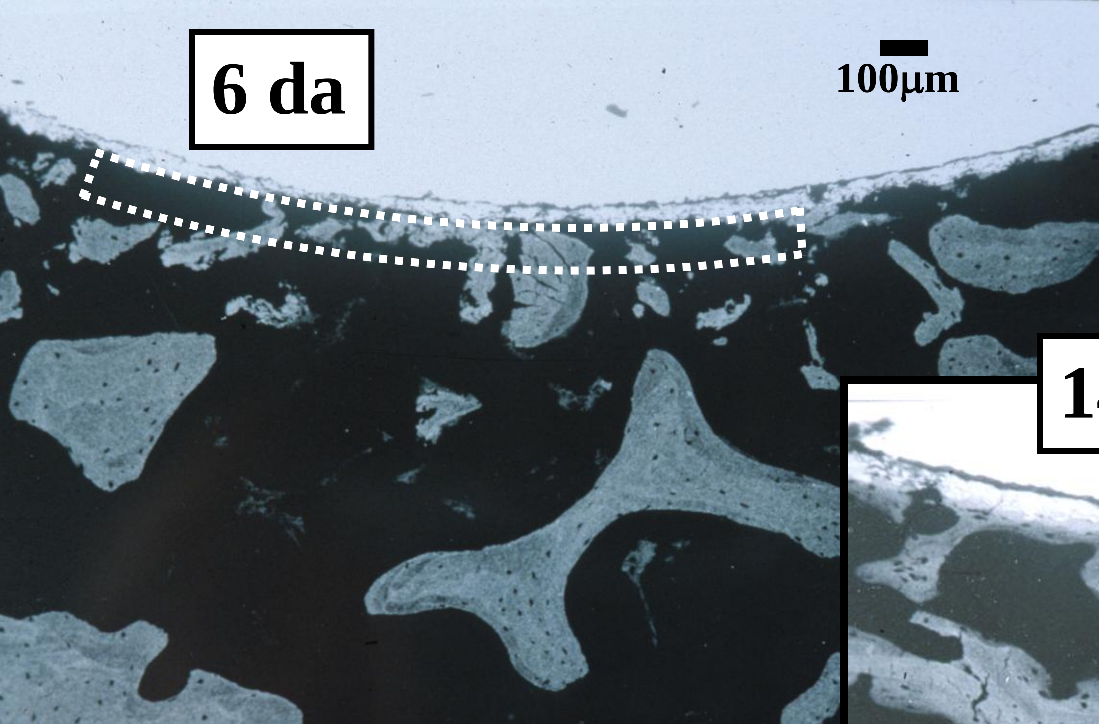
Plasma-Sprayed Hydroxyapatite Coating

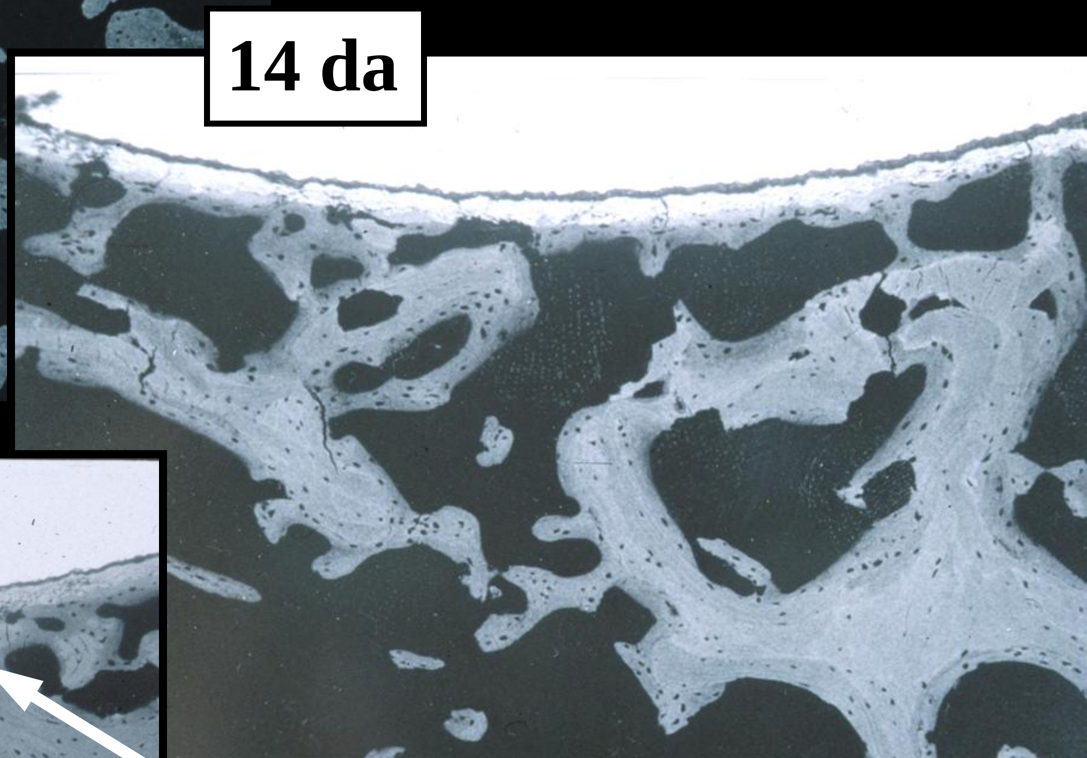


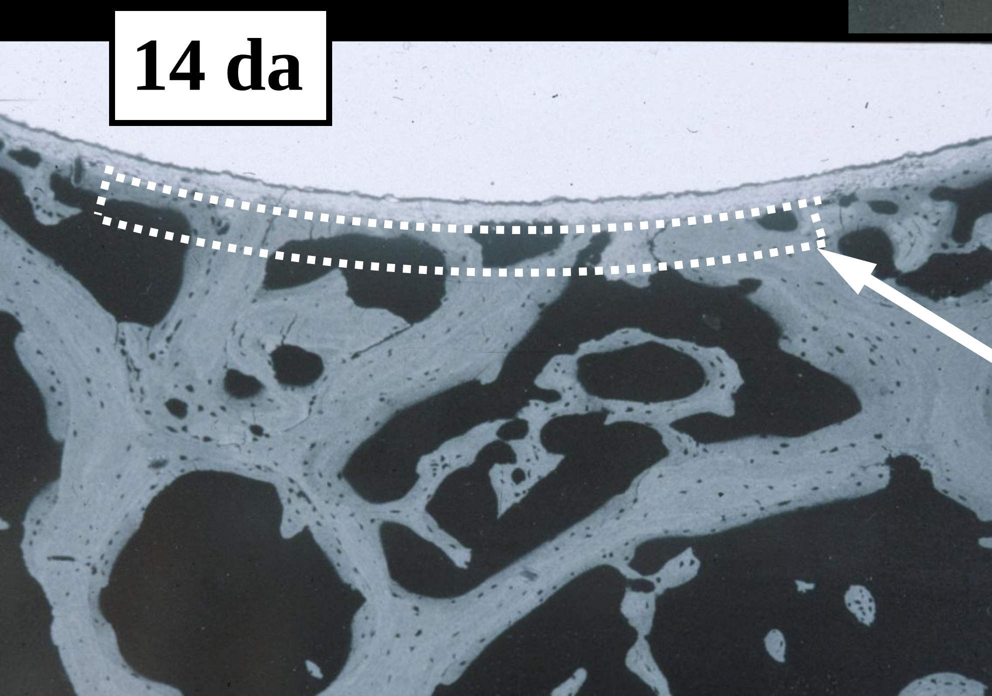




Plasma-Sprayed Hydroxyapatite Coating

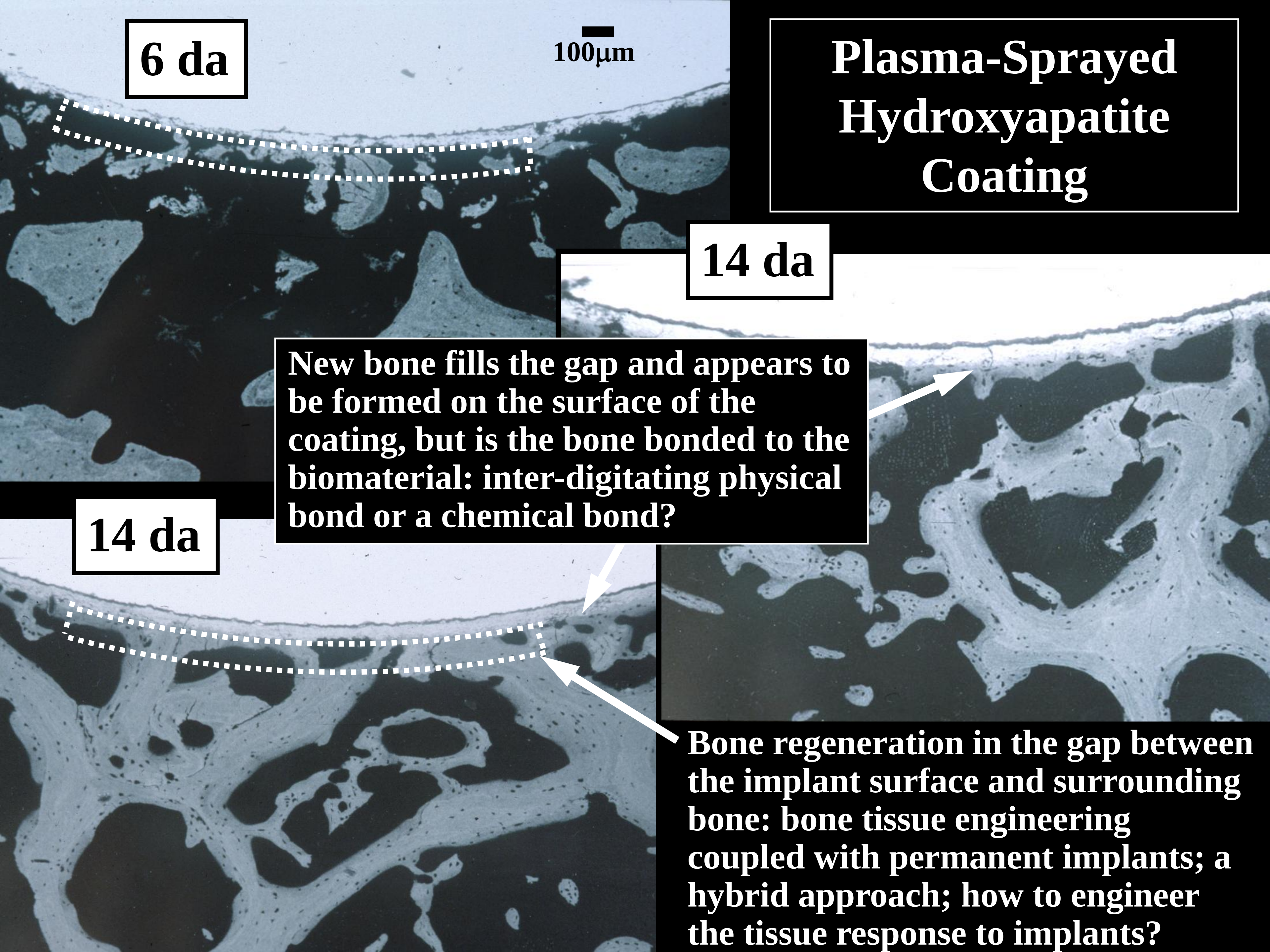






Bone regeneration in the gap between the implant surface and surrounding bone: bone tissue engineering coupled with permanent implants; a hybrid approach; how to engineer the tissue response to implants?

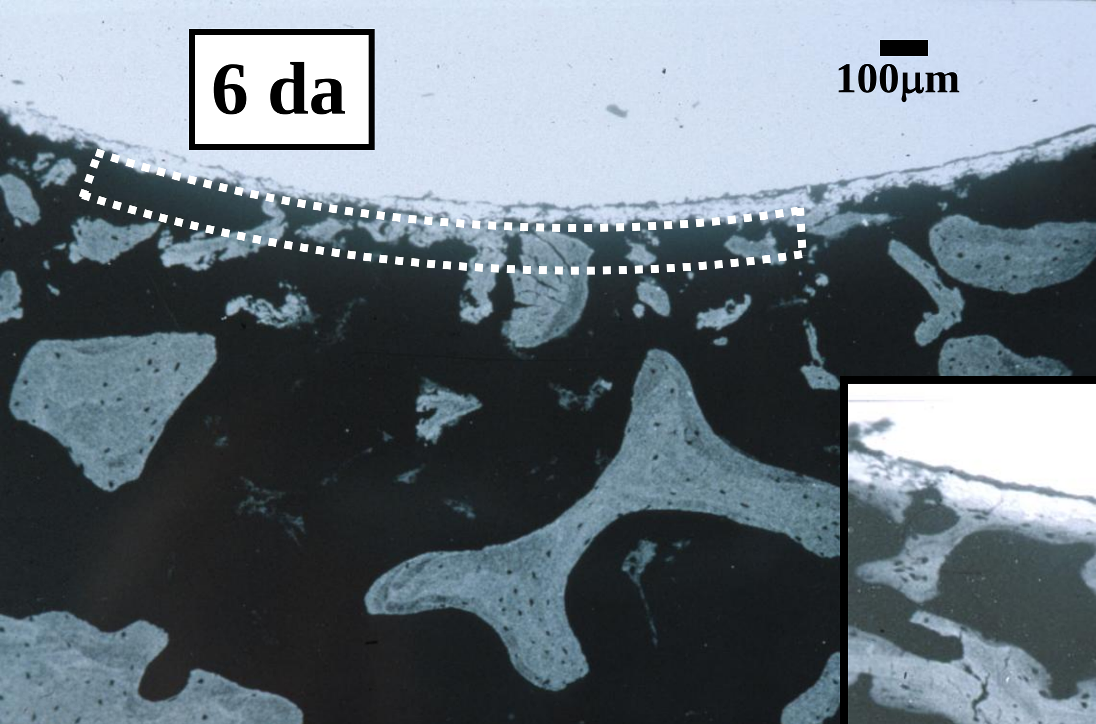
Plasma-Sprayed Hydroxyapatite Coating

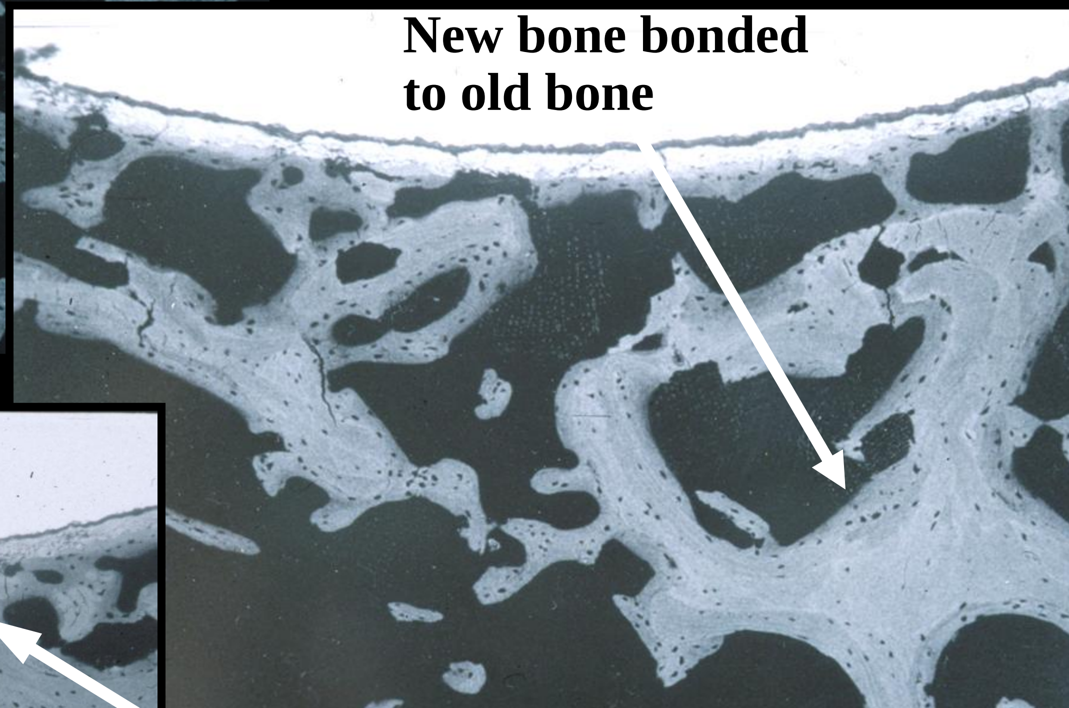


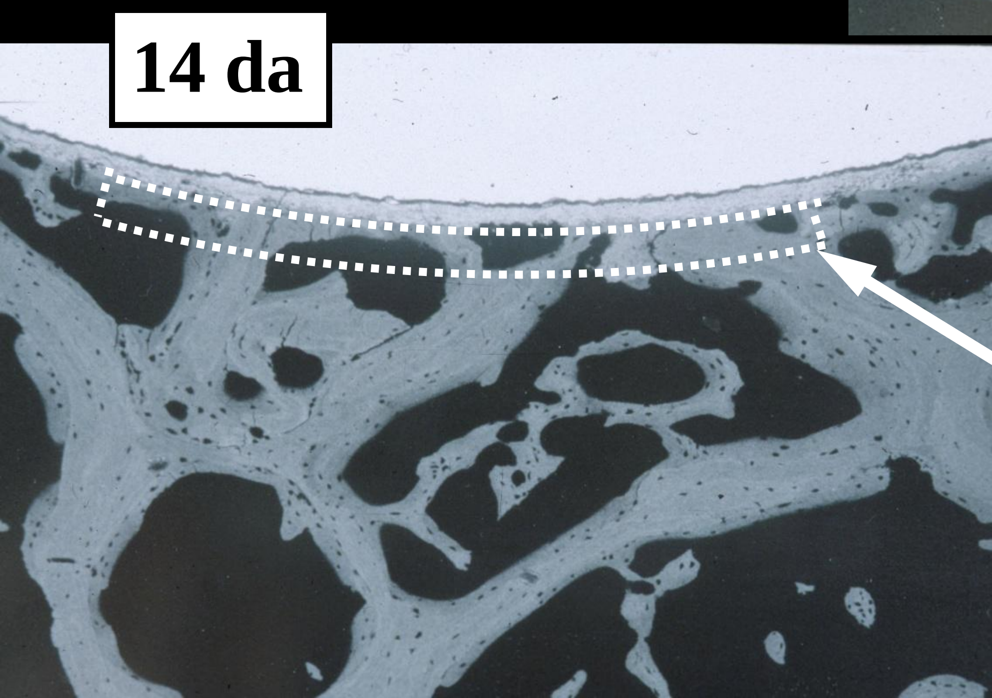
New bone fills the gap and appears to be formed on the surface of the coating, but is the bone bonded to the biomaterial: inter-digitating physical bond or a chemical bond?

Bone regeneration in the gap between the implant surface and surrounding bone: bone tissue engineering coupled with permanent implants; a hybrid approach; how to engineer the tissue response to implants?

Plasma-Sprayed Hydroxyapatite Coating

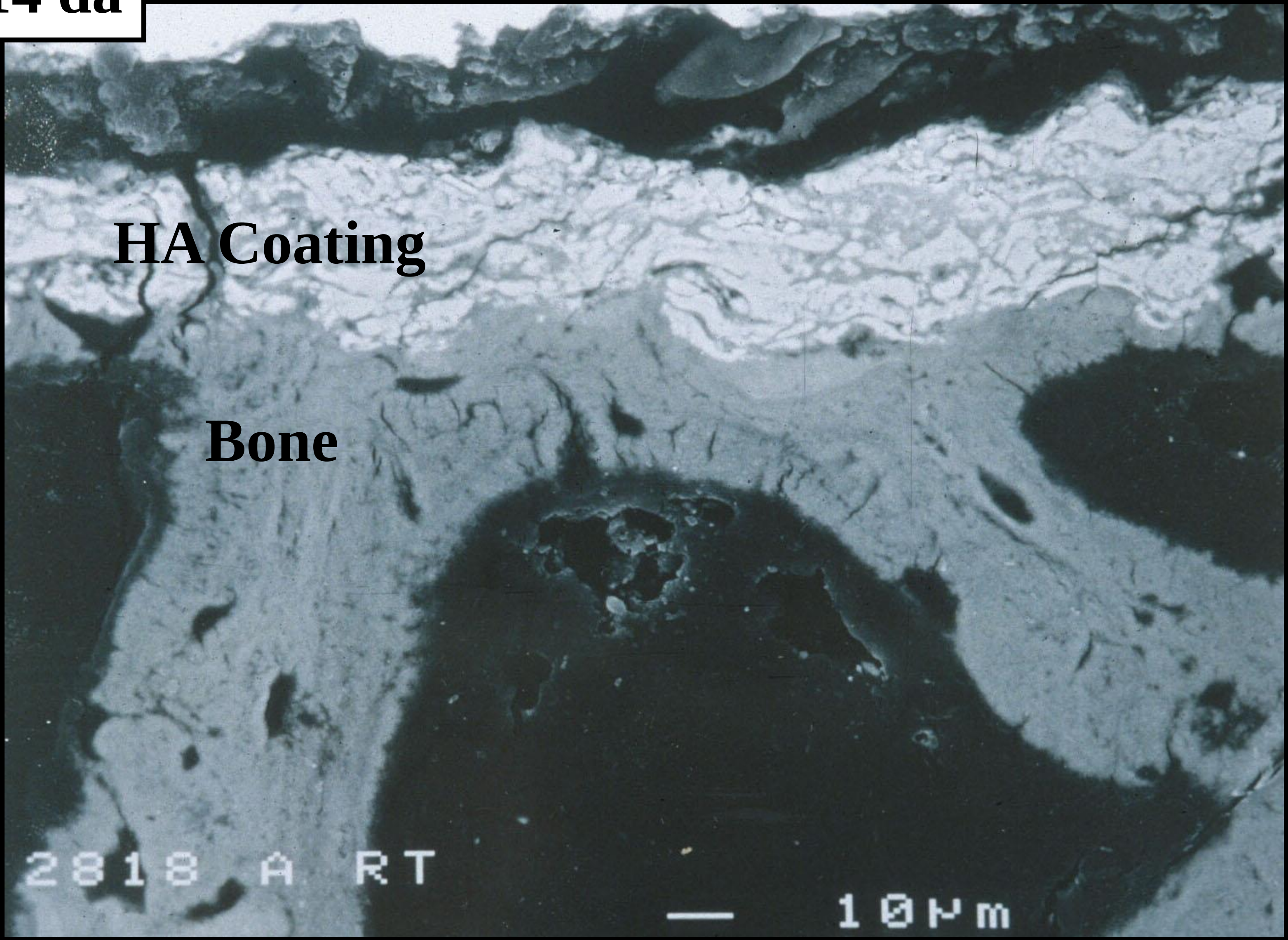






Bone regeneration in the gap between the implant surface and surrounding bone: bone tissue engineering coupled with permanent implants; a hybrid approach; how to engineer the tissue response to implants?

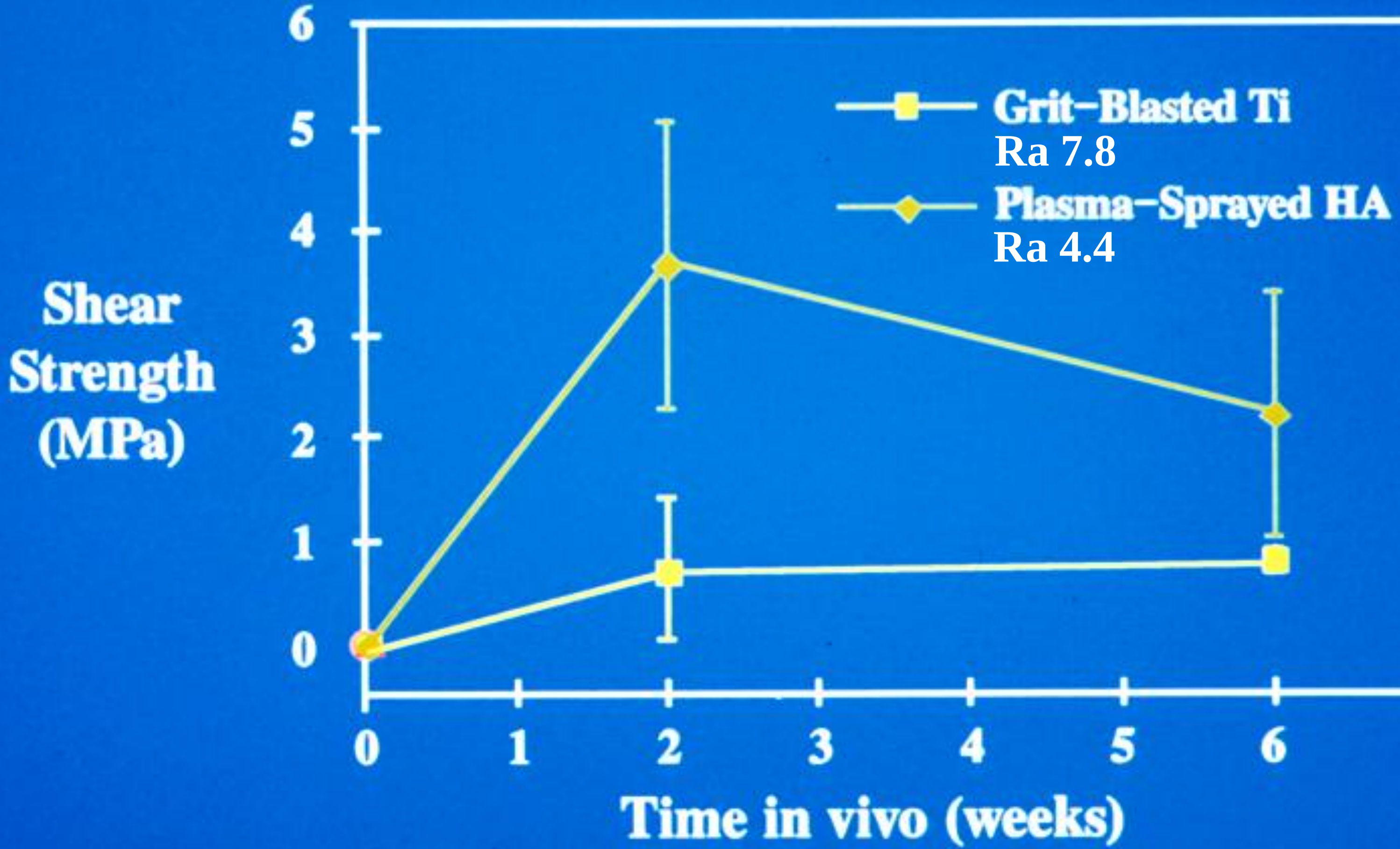
14 da

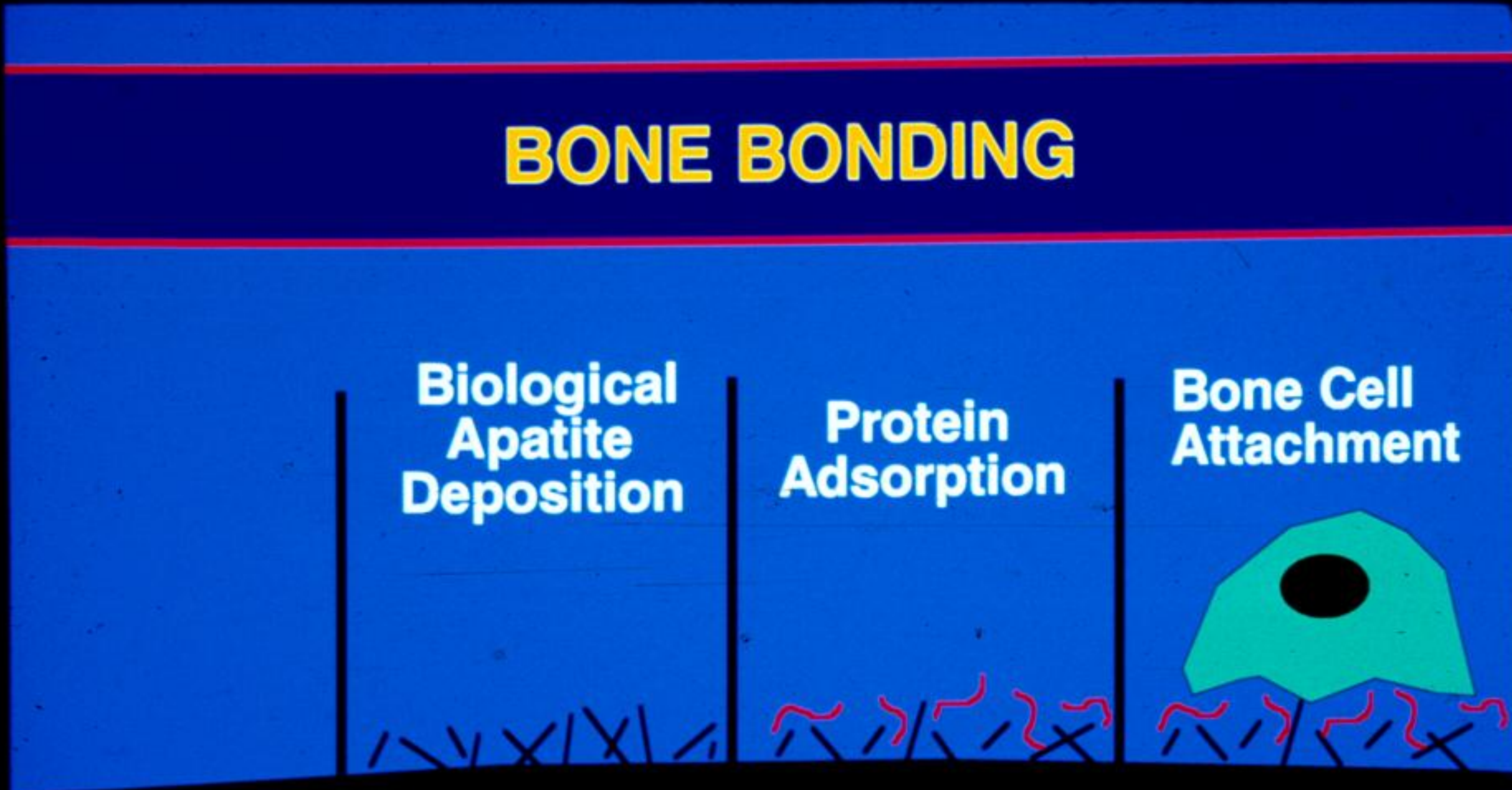


TISSUE INTEGRATION
TISSUE BONDING

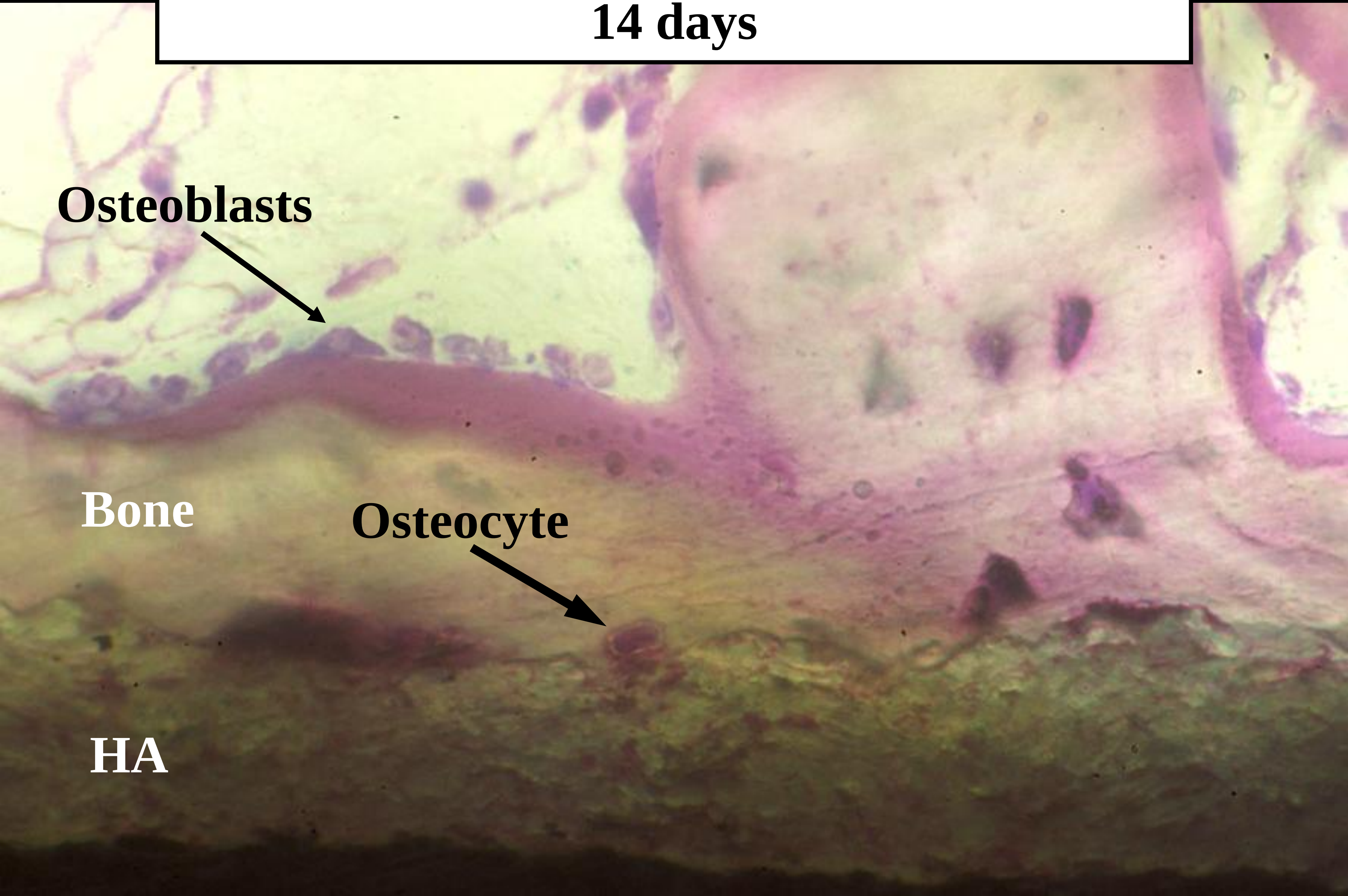
- **Osseointegration (*i.e.*, bone apposition to the implant; not necessarily bonding) is demonstrated by light microscopy**
- **How to determine if bone bonding to the implant has occurred?**
  - **Mechanical testing**
  - **Transmission electron microscopy to demonstrate the continuity of mineral from the implant to bone, at the ultrastructural level (*i.e.*, nanometer scale)**

BONE BONDING




BONE BONDING
Biological Apatite Deposition
Protein Adsorption
Bone Cell Attachment

Plasma-Sprayed Hydroxyapatite Coating
14 days



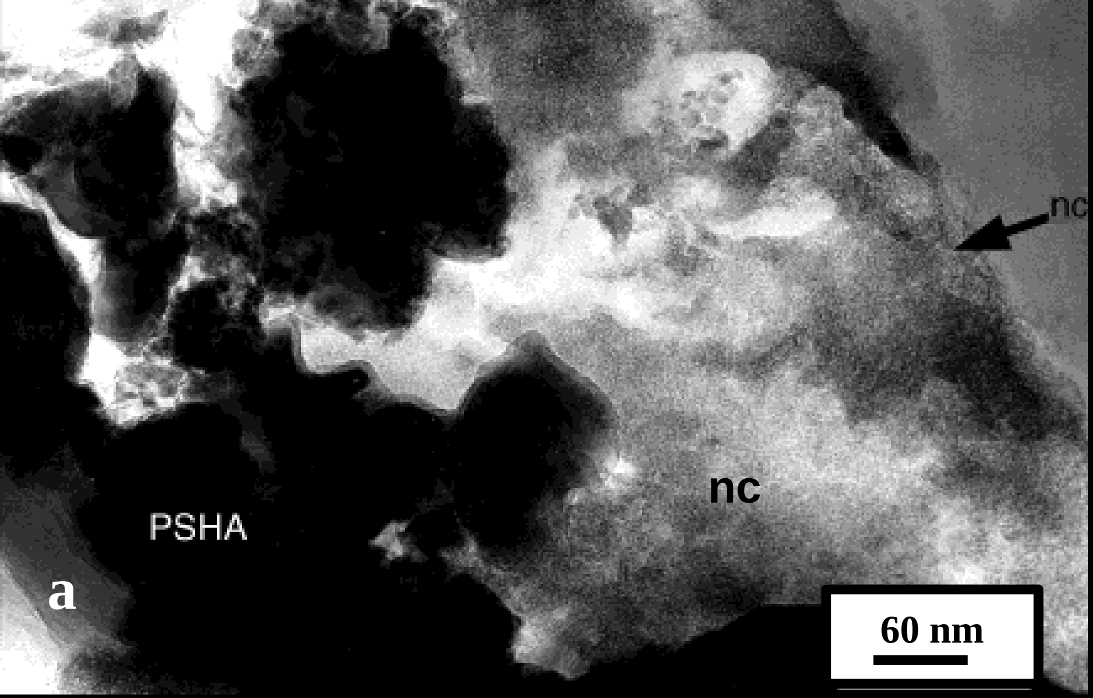
BONE BONDING

Images removed due to copyright restrictions.
See Table 1; a photo of implants; and graph of % bone apposition.
In Hacking, S. A., et al. "Relative contributions of chemistry and topography to the osseointegration of hydroxyapatite coatings." *Clin Orthop Relat Res* 405 (2002): 24-38.

TEM of PSHA coating 3 hrs. post-implantation in a canine model showing plate-like apatite crystallites viewed *en face* and on edge.

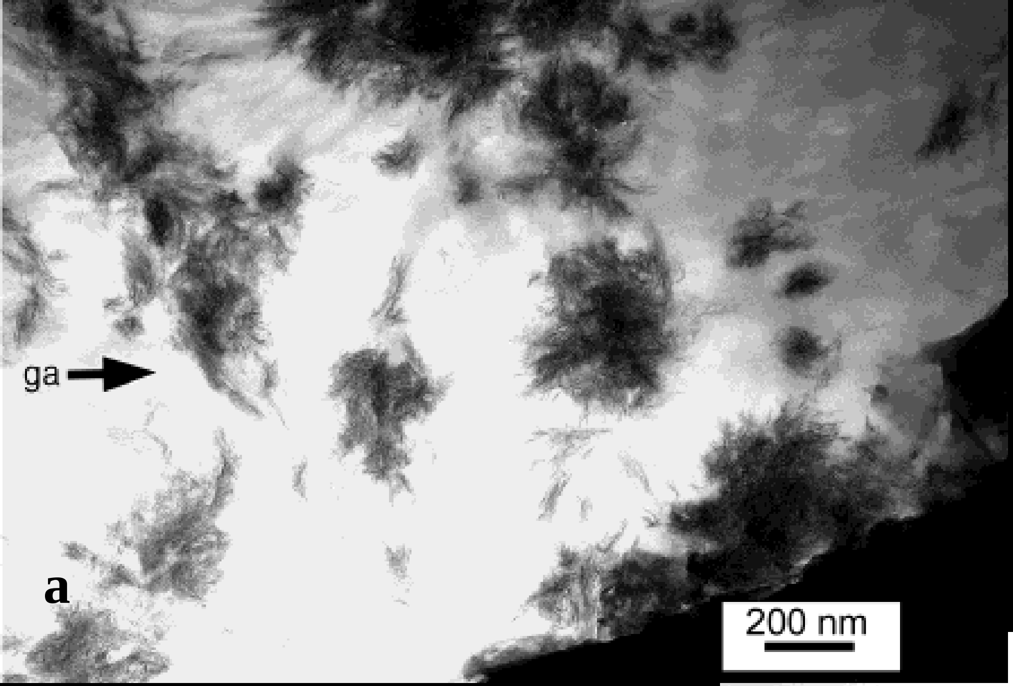
AE Porter, *et al*., Biomat. 2002;23:725

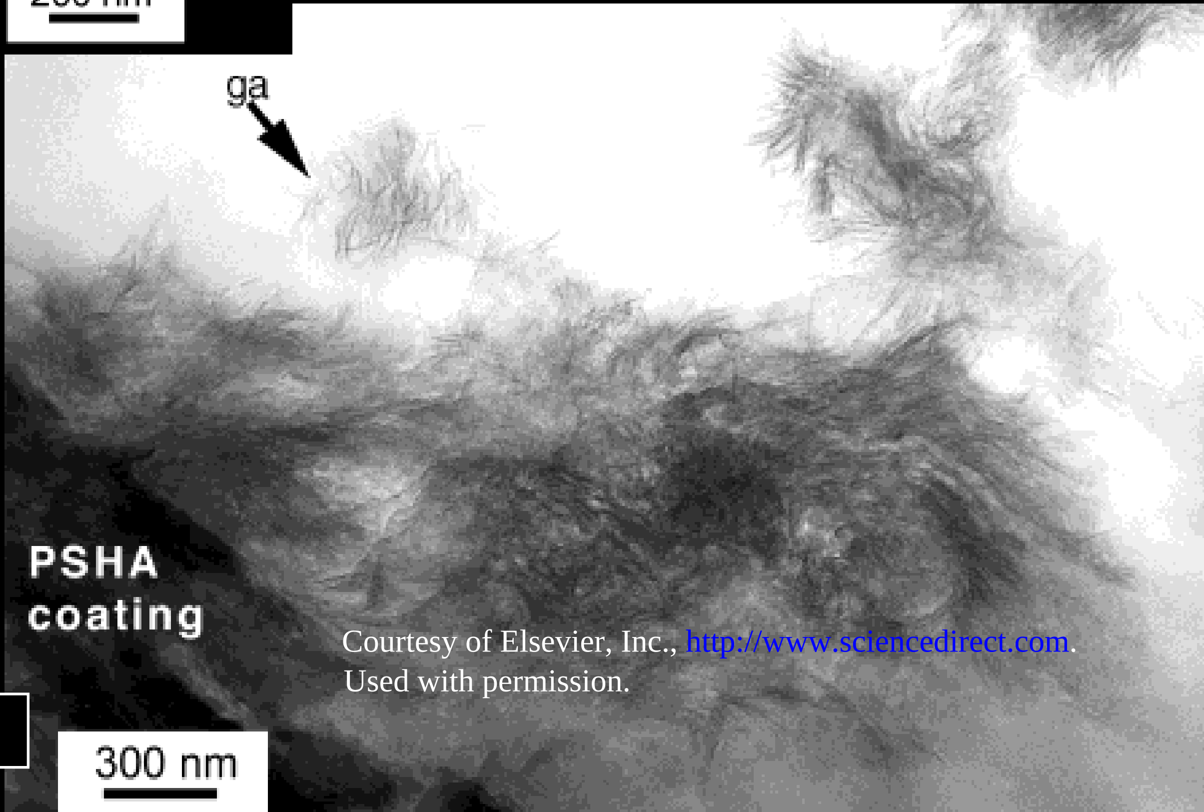
TEM of PSHA coating 3 days post-implantation in a canine model



AE Porter, *et al*., Biomat. 2002;23:725

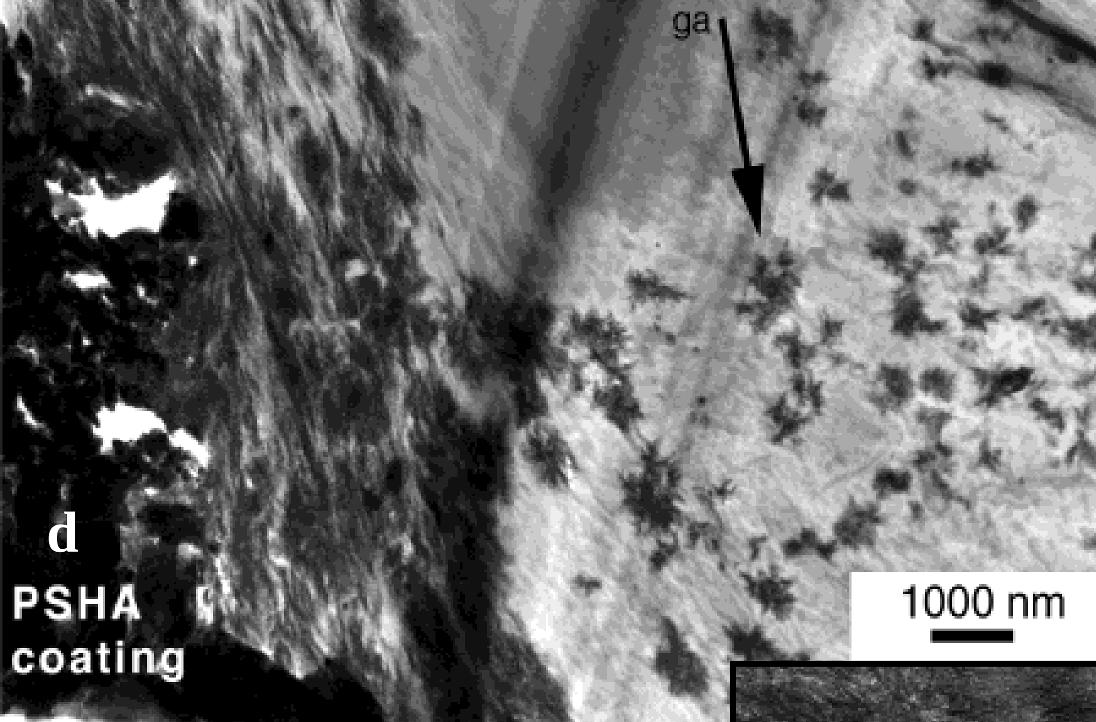
TEM of PSHA coating 10 days post-implantation in a canine model

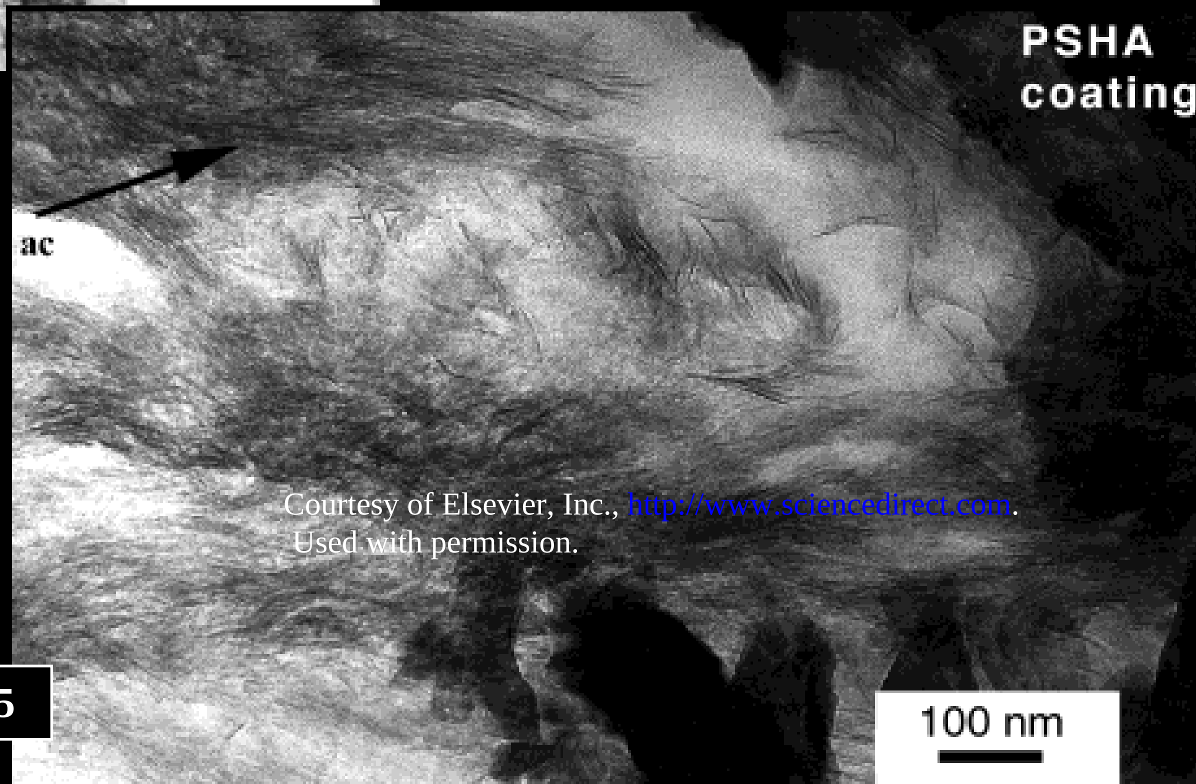




AE Porter, *et al*., Biomat. 2002;23:725

TEM of an annealed PSHA coating 10 days post-implantation in a canine model





AE Porter, *et al*., Biomat. 2002;23:725

TEM of PSHA coating 10 days post-implantation in a canine model

Non-annealed

Image removed due to copyright restrictions.
See Figure 6a in Porter, AE et al.
Biomat 23 (2002): 725-733.
http://dx.doi.org/10.1016/S0142-9612(01)00177-6

Annealed

Image removed due to copyright restrictions.
See Figure 6c in Porter, AE et al.
Biomat 23 (2002): 725-733.
http://dx.doi.org/10.1016/S0142-9612(01)00177-6

AE Porter, *et al*., Biomat. 2002;23:725

RESPONSE TO IMPLANTS: WOUND HEALING

Surgical Implantation

Inc. time

Acute Inflammation
- Vascular Response
- Clotting
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Granulation Tissue
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- New Collagen Synthesis

Tissue of Labile and Stable Cells
- Framework Intact → Regen. (incorp. of implant)
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Chronic Inflammation

Tissue of Permanent Cells
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