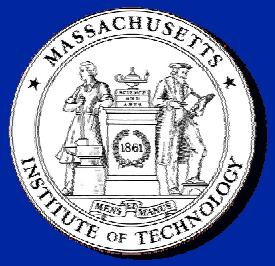
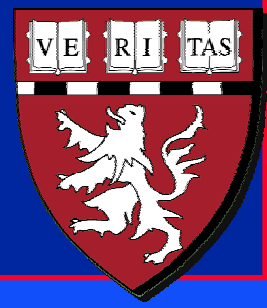


Massachusetts Institute of Technology
Harvard Medical School
Brigham and Women's/Massachusetts General Hosp.
VA Boston Healthcare System



2.79J/3.96J/BE.441/HST522J

BIOMATERIALS FOR JOINT REGENERATION-I

M. Spector, Ph.D. and I.V. Yannas, Ph.D.

TISSUES COMPRISING JOINTS

	Permanent Prosthesis	Regeneration Scaffold
Bone	Yes	Yes
Articular cartilage	No	Yes*
Meniscus	No	Yes*
Ligaments	No	Yes*
Synovium	No	No

* In the process of being developed

WOUND HEALING
Roots of Tissue Engineering

Injury

↓

Inflammation
(Vascularized tissue)

↓

Reparative
Process

4 Tissue Categories
Connective Tissue
Epithelium
Nerve
Muscle

Regeneration*
CT: bone
Ep: epidermis
Muscle: smooth
*spontaneous

Repair (Scar)
CT: cartilage
Nerve
Muscle: cardiac, skel.

TISSUE ENGINEERING

What is tissue engineering?

- Production of tissue *in vitro* by growing cells in porous, absorbable scaffolds (matrices).

Why is tissue engineering necessary?

- Most tissues cannot regenerate when injured or diseased.
- Even tissues that can regenerate spontaneously may not completely do so in large defects (*e.g.*, bone).
- Replacement of tissue with permanent implants is greatly limited.

TISSUE ENGINEERING

Problems with Tissue Engineering

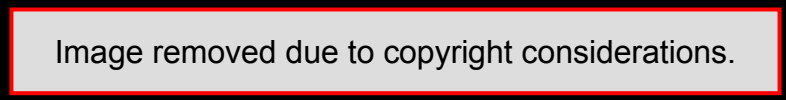
- Most tissues cannot yet be produced by tissue engineering (*i.e.*, *in vitro*).
- Implantation of tissues produced *in vitro* may not remodel *in vivo* and may not become integrated with (bonded to) host tissue in the body.

Solution

- Use of implants to facilitate formation (regeneration) of tissue *in vivo*.
  - "Regenerative Medicine"
  - Scaffold-based regenerative medicine

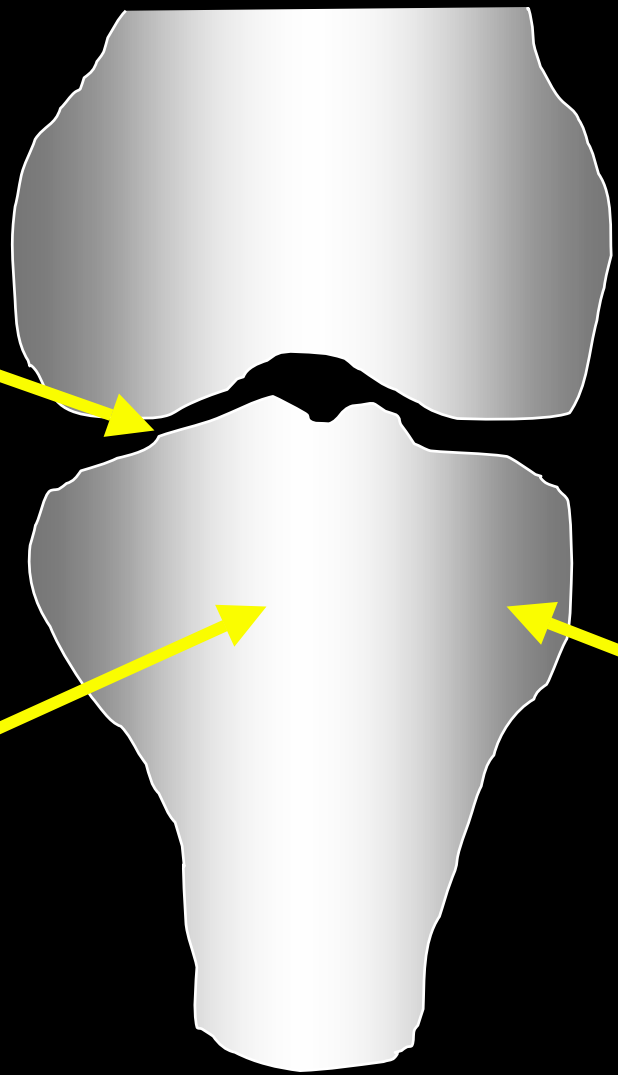
ISSUES RELATED TO PERFORMANCE OF BONE GRAFT SUBSTITUTE MATERIALS

- Incorporation of the graft into host bone (to stabilize the graft material) by bone formation on the surface of the graft material (osteoconduction).
- Modulus matching of the graft material to host bone to prevent stress shielding.
- Osteoclastic resorption of the graft (versus dissolution) may be important because osteoclasts release regulators of osteoblast function.



Migration of synthetic hydroxyapatite particles from the periodontal defect in which they were implanted.

Defect in the Proximal Tibia Filled with Particles of Synthetic Hydroxyapatite, 1yr f-u



Potential for breakdown of the overlying art. cart. due to high stiffness of the subchondral bone?

Region of high density and stiffness (cannot be drilled or sawn)

Bone loss due to stress-shielding?

BONE GRAFTS AND GRAFT SUBSTITUTES

Bone	Components of Bone	Calcium Phosphate Ceramics
Autograft	Mineral Alone (Anorganic Bone, Bio-Oss)	Hydroxyapatite (Including Sintered Bone)
Allograft*	Organic Matrix (Demineralized Bone)	Tricalcium Phosphate
Xenograft		Other
		Calcium Sulfate
		Calcium Carbonate

* Works well; potential problems of transmission of disease and low grade immune reaction

BONE MINERAL VERSUS SYNTHETIC HYDROXYAPATITE

	Bone Mineral	Synthetic Calcium Phosphates
Chemical	Calcium-deficient carbonate apatite and other calcium phosphate phases	Hydroxyapatite Whitlockite (TCP)
Crystalline	Small crystalline size; noncrystalline phase	Large crystallites; high crystallinity
Mechanical	Lower strength; lower modulus	Dense; higher strength; higher modulus

DESIREABLE PROPERTIES OF A BONE GRAFT MATERIAL

	Strength mod./high	[1]Modulus near bone	[2]Osteo-conduct.	[3]Osteoclast resorption
Allograft	Yes	Yes	Yes	Yes
Anorganic Bone	No[4]	Yes	Yes	Yes
Synthetic HA	Yes	No	Yes	?
Calcium Sulfate	No	Yes	?	?
Polymers	No	Yes	No	No

[1] Important to prevent stress shielding

[2] Bone forms on the surface of the material; important for the initial incorporation of the graft.

[3] Important as osteoclasts release regulators of osteoblast function.

[4] Material cannot be used for immediate load bearing support.

COMPRESSIVE PROPERTIES

	Ultimate Comp. Str. (MPa)	Modulus of Elasticity (GPa)
Cortical Bone	140 - 200	14 - 20
Cancellous Bone	5 - 60	0.7 - 1.5
Synthetic HA	200 - 900	34 - 100
Bone Mineral	25 (anorganic bone)	6

Bone Mineral; organic matter removed bone - Bio-Oss

Image removed due to copyright considerations

Image removed due to copyright considerations

OsteoGraf

Synthetic Hydroxyapatites

OsteoGen

Image removed due to copyright considerations

Image removed due to copyright considerations

V. Benezra Rosen, *et al.*
Biomat. 2001;23:921-928

Bio-Oss; anorganic bovine bone

IR Spectroscopy

Syn. HA

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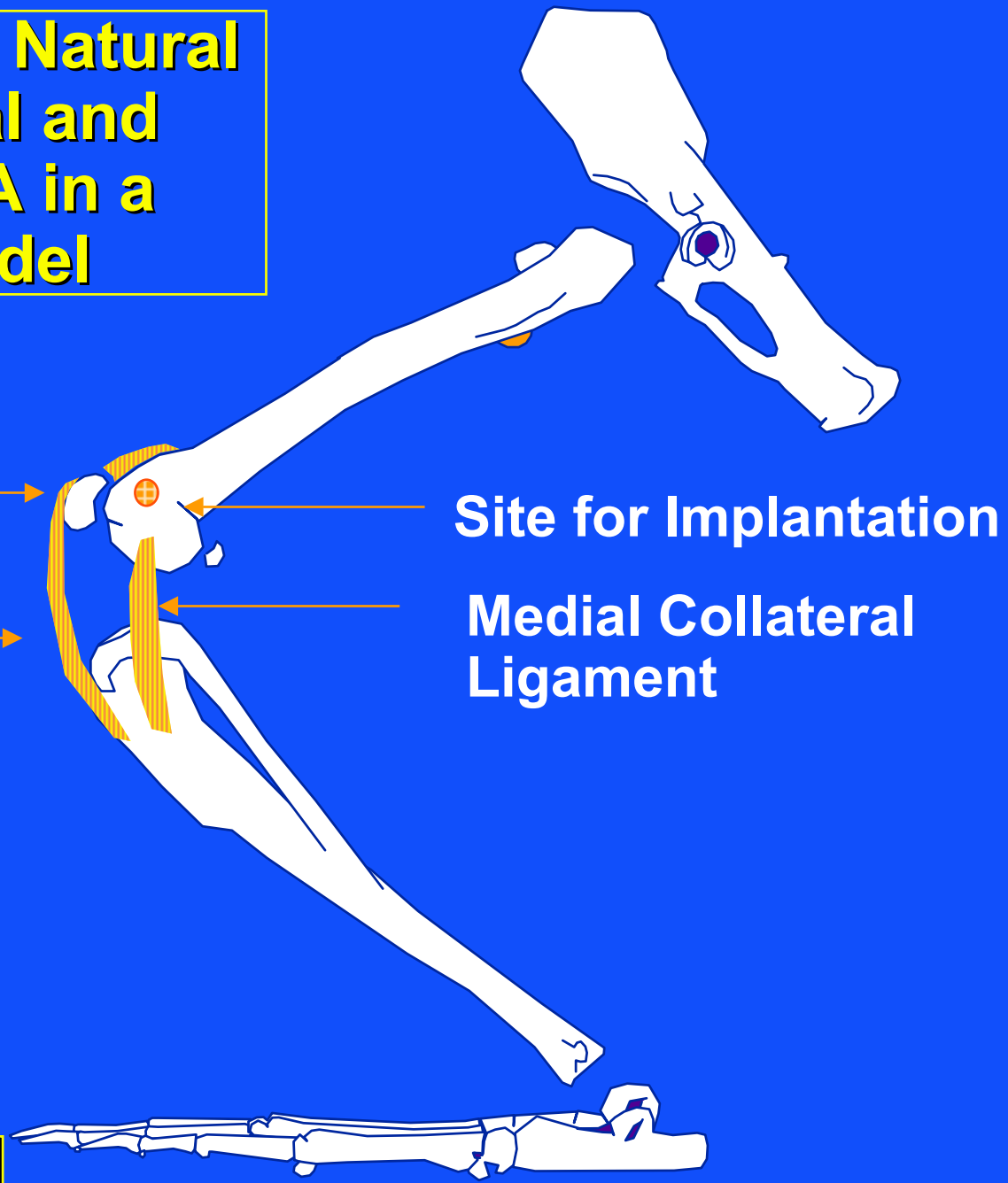
Image removed due to copyright considerations

Bio-Oss

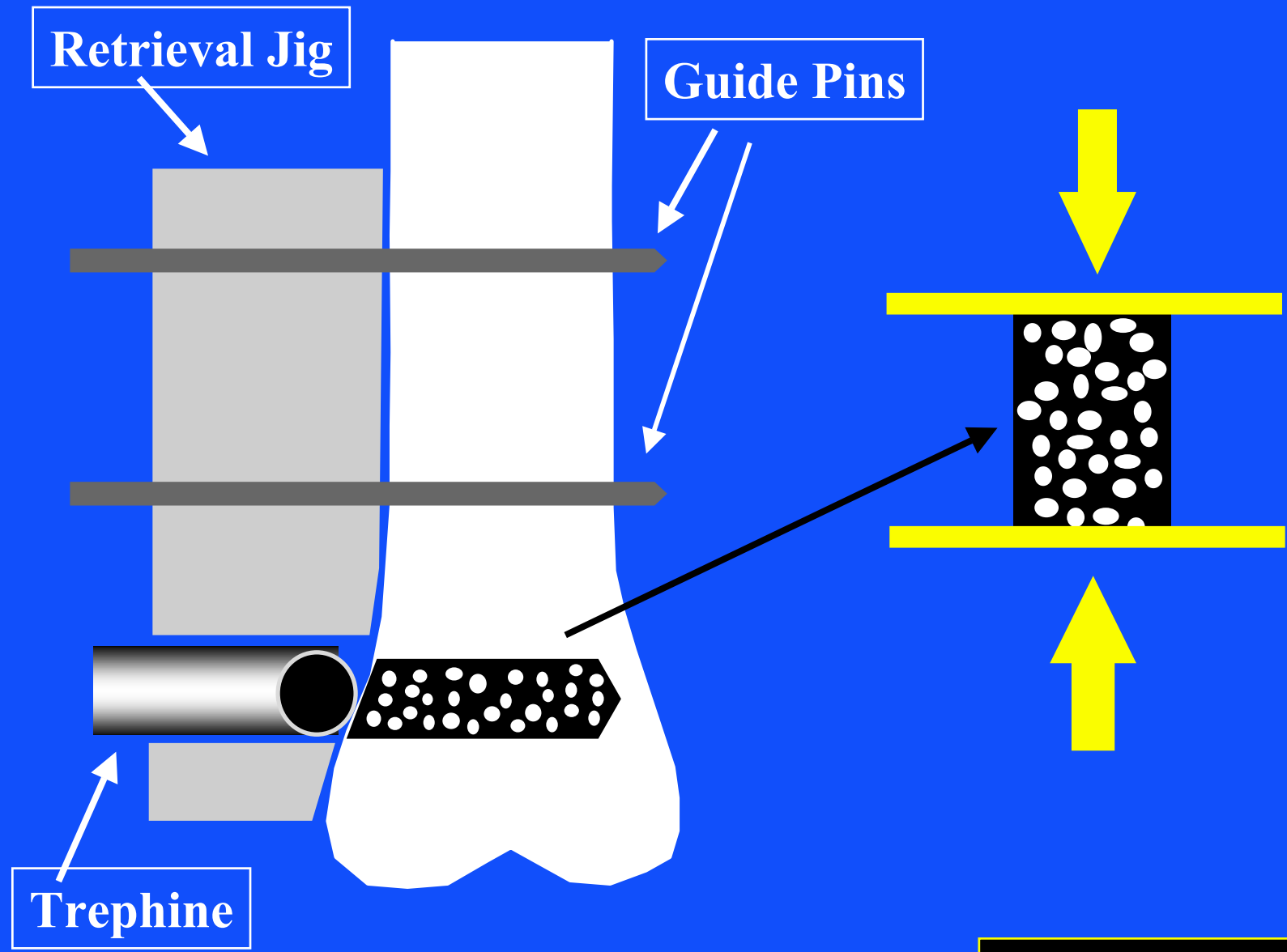
Image removed due to copyright considerations

X-ray Diffraction showing crystallinity

Comparison of Natural Bone Mineral and Synthetic HA in a Rabbit Model



T. Orr, *et al.*
Biomat. 2001;22:1953-1959



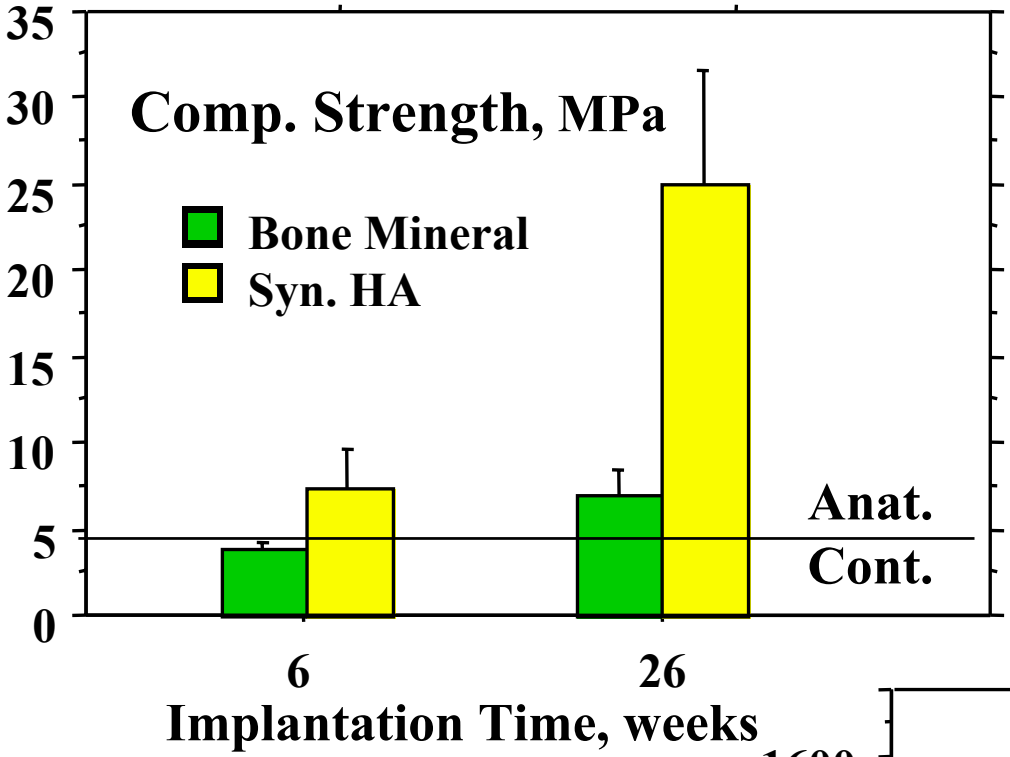
T. Orr, *et al.*
Biomat. 2001;22:1953-1959

Synthetic Hydroxyapatite

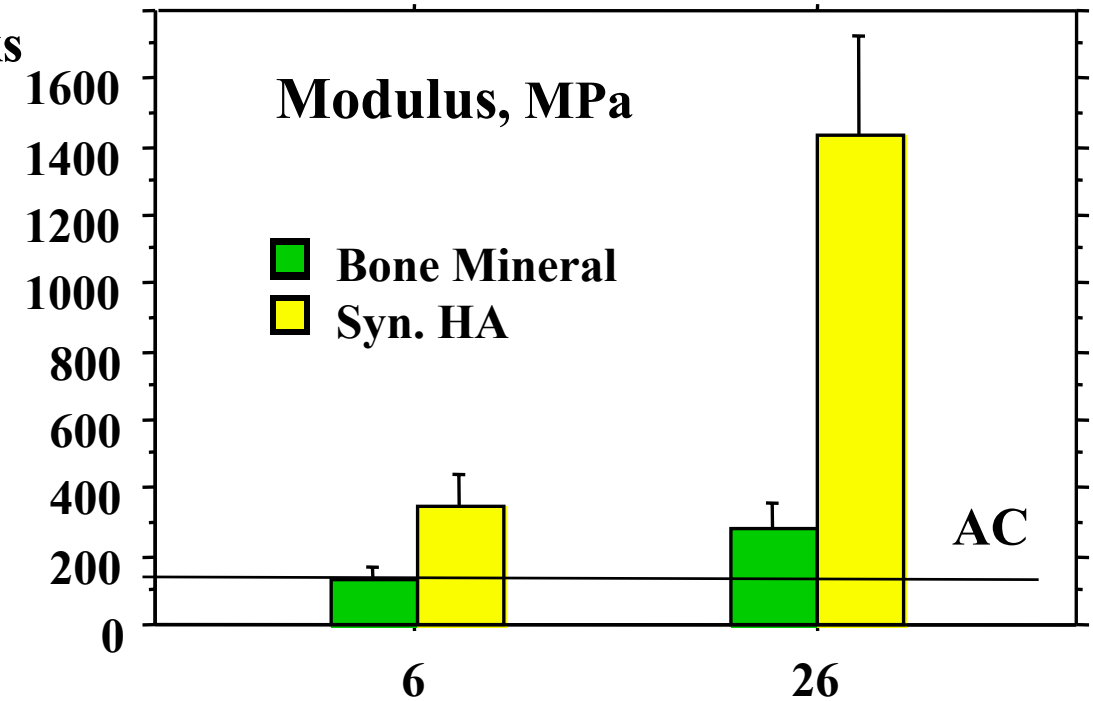
Photos removed due to copyright considerations.

Natural Bone Mineral
Bio-Oss, 40 days

Photos removed due to copyright considerations.



The strength of the site implanted with syn. HA is high but so to is the modulus (stiffness); bone mineral may provide adequate strength while having a near-normal modulus.



T. Orr, *et al.*
Biomat. 2001;22:1953-1959

Bio-Oss
Biopsy from ankle fusion patient
6 mo.

Photos removed due to copyright considerations.

BONE GRAFT MATERIALS

- Allograft bone remains a valuable substance for grafting; care must be taken with respect to the transmission of disease.
- Many off-the-shelf bone graft substitute materials are now available and should be of value for many applications.
- Need to be aware of how the increase in stiffness caused by certain materials will affect the surrounding tissues so that we do not cause greater problems than we are trying to solve.