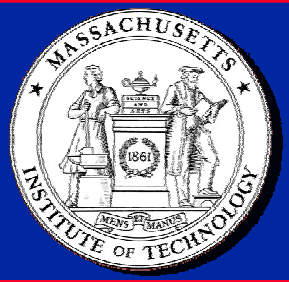
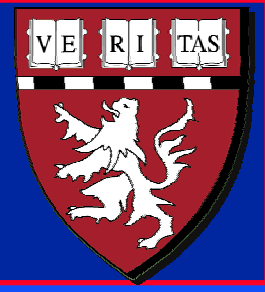


Massachusetts Institute of Technology
Harvard Medical School
Brigham and Women's Hospital
VA Boston Healthcare System



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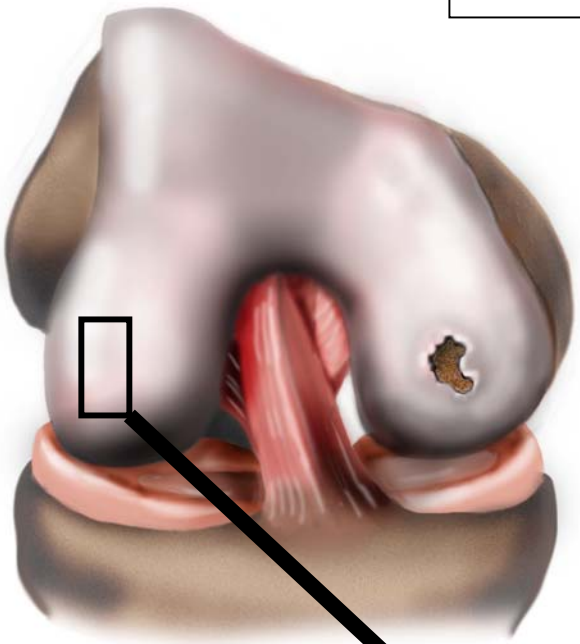
BIOMATERIALS-TISSUE INTERACTIONS: INTRODUCTION

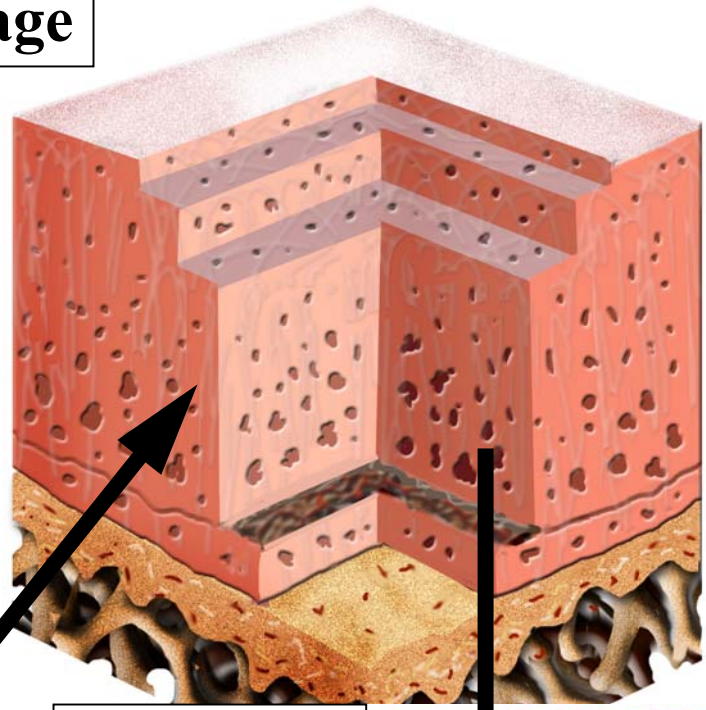
M. Spector, Ph.D. and I.V. Yannas, Ph.D.

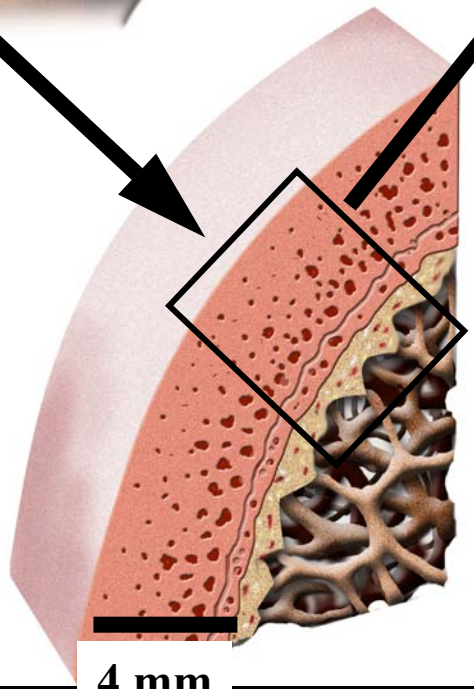
TISSUE

- **Tissue** is a biological structure made up of cells of the same type.
  - Cells of the same phenotype (*i.e.*, same genes expressed).
  - An aggregation of morphologically similar cells and associated extracellular matrix acting together to perform one or more specific functions in the body.
  - There are four basic types of tissue: muscle, nerve, epithelia, and connective.
  - An **organ** is a structure made up of 2 or more tissues.

Articular Cartilage

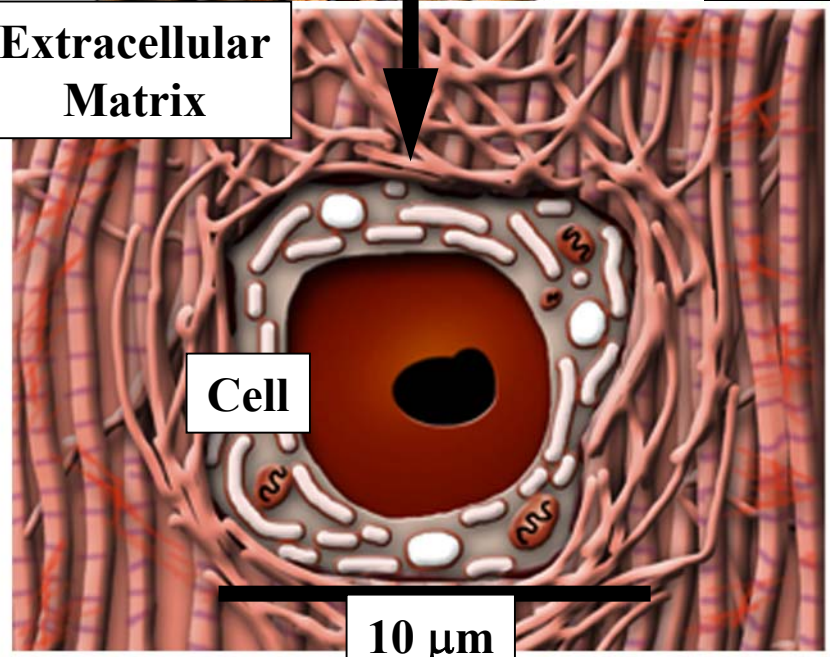






4 mm

Extracellular Matrix



Cell

10 μm

ENGINEERING

- Production of a product for human good using existing knowledge.
  - Science is the process of acquisition of new knowledge.
  - Technology is the means by which products are produced.

BIOMATERIALS-TISSUE INTERACTIONS

Permanent versus Absorbable Biomaterials

- Roles of permanent biomaterials for the production of permanent implants versus the roles as absorbable scaffolds for tissue engineering

BIOMATERIALS-TISSUE INTERACTIONS

Effects of Biomaterials on Tissue

- In Bulk Form
  - Tissue formation
  - Attachment
  - Remodeling
- In Particle (Molecular) Form
  - Tissue degradation

BIOMATERIALS-TISSUE INTERACTIONS

Effects of Biomaterials on Cells

- In Bulk Form
  - Cell attachment
  - Cell proliferation (mitosis)
  - Production of matrix molecules and enzymes (synthesis)
  - Migration
  - Contraction
  - Release of pre-packaged reactive molecules (exocytosis)
- In Particle (Molecular) Form
  - Ingestion of particles (endocytosis)

BIOMATERIALS-TISSUE INTERACTIONS

Permanent Biomaterials

- Positive Response
  - Tissue attachment
- Adverse Responses
  - Contraction
  - Reaction to particles; tissue destruction
- Passive Response

Total Hip and Knee Replacement Prostheses

Images removed due to copyright considerations

BIOMATERIALS-TISSUE INTERACTIONS

Permanent Biomaterials

- Positive Response
  - Tissue attachment
- Adverse Responses
  - Contraction
  - Reaction to particles; tissue destruction
- Passive Response

Food and Drug Administration
Breast Implant Complications

Photographs of
Breast Implant Complications

http://www.fda.gov/cdrh/breastimplants/breast_implants_photos.html

FDA has developed this website for displaying photographs and/or illustrations of breast implant complications.

This website is not intended to be photographic representation of all breast implant complications. FDA will continue to add photographs and/or illustrations of complications associated with saline-filled and silicone gel-filled implants as they become available.

You should refer to the breast implant consumer handbook, which is available on the FDA breast implant website at

http://www.fda.gov/cdrh/breastimplants/

for a description of potential breast implant complications.

http://www.fda.gov/cdrh/breastimplants/breast_implants_photos.html

BREAST IMPLANTS
Capsular Contracture

Capsular contracture occurs when the scar tissue or capsule that normally forms around the implant tightens and squeezes the implant. It may be more common following infection, hematoma (collection of blood), and seroma (collection of watery portion of blood). There are four grades of capsular contracture.

The Baker grading is as follows

Grade I	the breast is normally soft and looks natural
Grade II	the breast is a little firm but looks normal
Grade III	the breast is firm and looks abnormal (visible distortion
Grade IV	the breast is hard, painful, and looks abnormal (greater distortion)

Additional surgery may be needed to correct the capsular contracture. This surgery ranges from removal of the implant capsule tissue to removal (and possibly replacement) of the implant itself. Capsular contracture may happen again after this additional surgery.

Breast Implant Position and “Capsular Contraction”

Contracted Fibrous Tissue Capsule

Boston Globe, July 22, 1991

BREAST IMPLANTS
Capsular Contracture

Capsular contraction

Photograph shows Grade IV capsular contracture in the right breast of a 29-year-old woman seven years after subglandular (on top of the muscle and under the breast glands) placement of 560cc silicone gel-filled breast implants.

BREAST IMPLANTS Capsular Contracture

Removed implant: viewing the outside of the fibrous capsule

Implant

Capsule

Inside of the fibrous capsule

Implant

Images removed due to copyright considerations

http://www.implantforum.com/capsular-contracture/

BREAST IMPLANTS
Capsular Contracture

What is Capsular Contracture?

Scar tissue that forms around the implant which causes the breasts to harden (similar to what a contracted muscle feels like) as the naturally forming scar tissue around the implant tightens and squeezes it. While capsular contracture is an unpredictable complication, it is also the most common complication of breast augmentation.

How can Capsular Contracture be prevented?

Textured implants help deter contracture because of their rough surface which is intended to discourage a hard capsule from forming.

Under the muscle (sub-pectoral or 'partial sub-muscular') placement of the implant reduces risk of capsular contracture by an average of 8 - 10%. Whereas over the muscle (in front of the muscle or 'sub-mammary') has 10 - 25% or more chance of capsule contracture.

BREAST IMPLANTS
Capsular Contracture

How can Capsular Contracture be prevented?

Massage and or compression. This is usually only done with smooth implants and may be suggested for a period between a few weeks to as long as you have your implants. Do not massage bruises!

The "no-touch" technique. This method includes meticulously rewashing surgical gloves before handling any instrument and implants. Only the head surgeon touches the implant, using a unique Teflon cutting board and immediately inserting the implant underneath the muscle. All of these measures help ensure that no foreign substance attach themselves to the implant, which could inflame the surrounding tissue and cause complications such as capsular contracture.

BIOMATERIALS-TISSUE INTERACTIONS

Permanent Biomaterials

- Positive Response
  - Tissue attachment
- Adverse Responses
  - Contraction
  - Reaction to particles; tissue destruction
- Passive Response

“Small Particle Disease”
Particles Released From Implants

Newsweek, April 29, 1991

Images removed due to copyright considerations

Sci. 295:1994 (2002)

BIOMATERIALS-TISSUE INTERACTIONS

Permanent versus Absorbable Biomaterials

- Roles of permanent biomaterials for the production of permanent implants versus the roles as absorbable scaffolds for tissue engineering

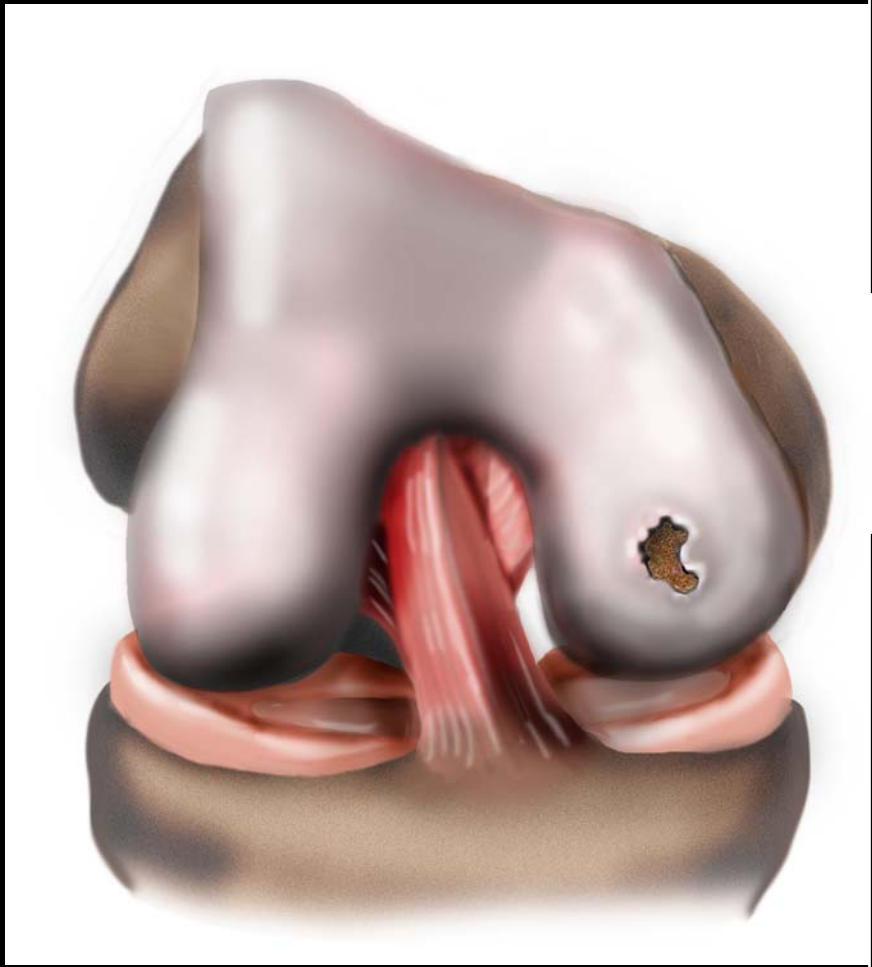
BIOMATERIALS-TISSUE INTERACTIONS

Absorbable Biomaterials

- Materials as scaffolds for tissue engineering

Image of newspaper clipping – removed due to copyright considerations.
Laura Meckler, "Transplant waiting list climbs over 75,000."
Pittsburgh Post-Gazette, March 10, 2001.

The Clinical Problem

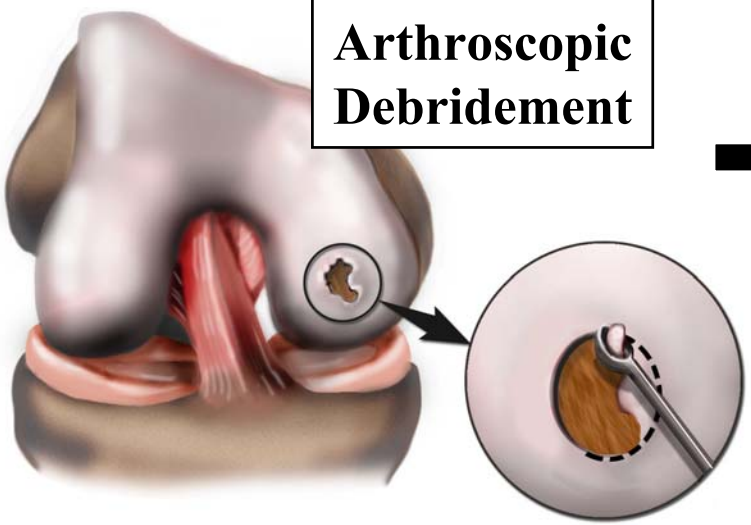


Articular Cartilage Defects

- Incidence is high and increasing due to increasing activity levels
- Causes pain and disability
- Profoundly impacts the quality of life

Articular Cartilage Defects Do Not Heal

- Avascular
- Aneural
- Low cell density
- Cells of low mitotic activity
- Cells cannot freely migrate through the extracellular matrix



Arthroscopic Debridement

"Microfracture"

Image removed due to copyright considerations

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Osteochondral Autograft

Current Clinical Practice

Image removed due to copyright considerations

Image removed due to copyright considerations

Total Knee Replacement

Cells injected under a tissue or collagen cover

Autologous Chondrocyte Implantation

This process has been commercialized by Genzyme (for USD$11,500).

M Brittberg, *et al*., NEJM 33:889 (1994)

Debridement of the Degenerative Tissue in the Lesion

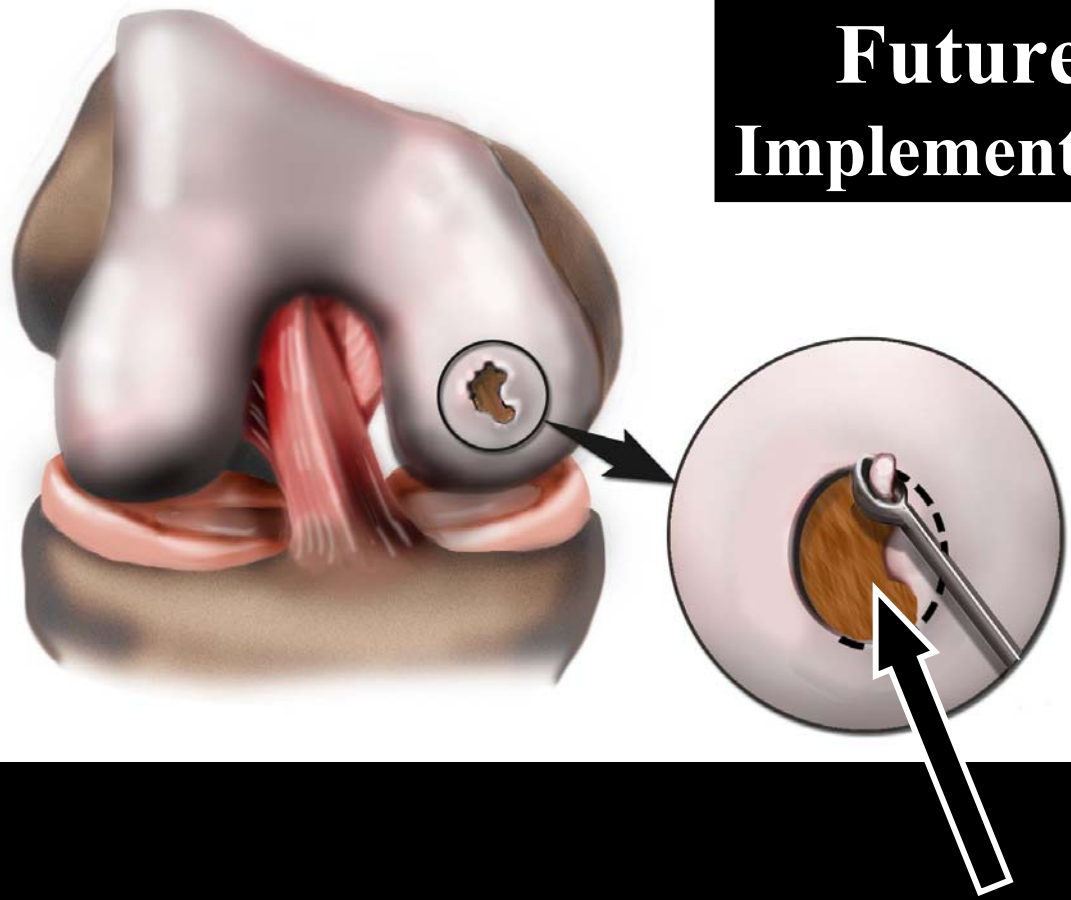
Collagen Membrane Used as Covering Material to Contain the Cells

Applying and Suturing the Collagen Membrane

Injecting the Autologous Chondrocytes grown in Vitro Cells

Video clips removed due to copyright considerations

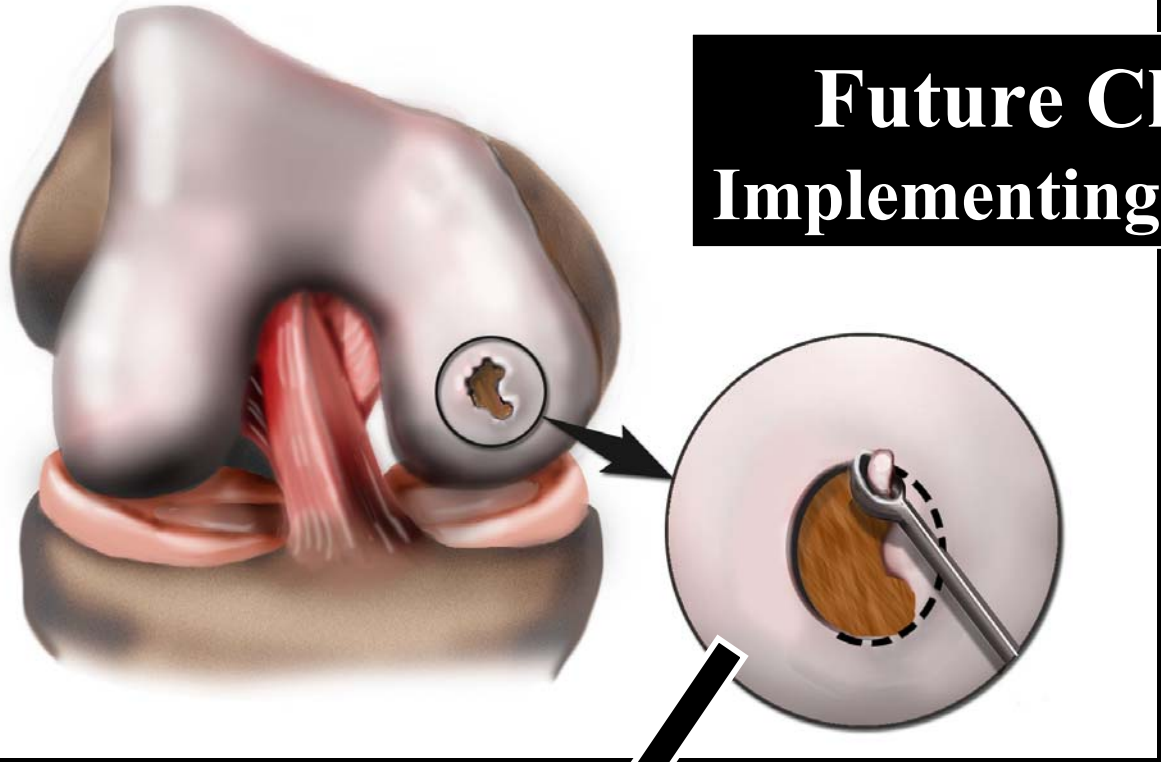
Future Clinical Practice
Implementing Tissue Engineering



Implantation of a cell-seeded matrix

"Tissue engineered" cartilage implanted in a rabbit model did not remodel (Advanced Tissue Sciences, Inc.).

Future Clinical Practice
Implementing Tissue Engineering



Implantation of the matrix alone

Image removed due to copyright considerations.

Image removed due to copyright considerations.

"Microfracture":
Stem cells from bone marrow infiltrate the defect

-FGF-2

TISSUE FORMATION AND REMODELING *IN VITRO*

Images removed due to copyright considerations.
See Veilleux NH, Yannas IV, Spector M. "Effect of passage number and collagen type on the proliferative, biosynthetic, and contractile activity of adult canine articular chondrocytes in type I and II collagen-glycosaminoglycan matrices in vitro." Tissue Eng. 2004 Jan-Feb;10(1-2):119-27.

+FGF-2

Canine chondrocytes grown in a type II collagen-GAG scaffold for 2 weeks. (Safranin O stain for GAGs)

BIOMATERIALS-TISSUE INTERACTIONS