Biomaterials for Medical Devices and Drug Delivery: Advances and Opportunities

Workshop

New Frontiers in Chemical Engineering:
Impact on Undergraduate Curriculum

Worcester Polytechnic Institute

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Genzyme Corporation
Cambridge, Massachusetts
May 7, 2004

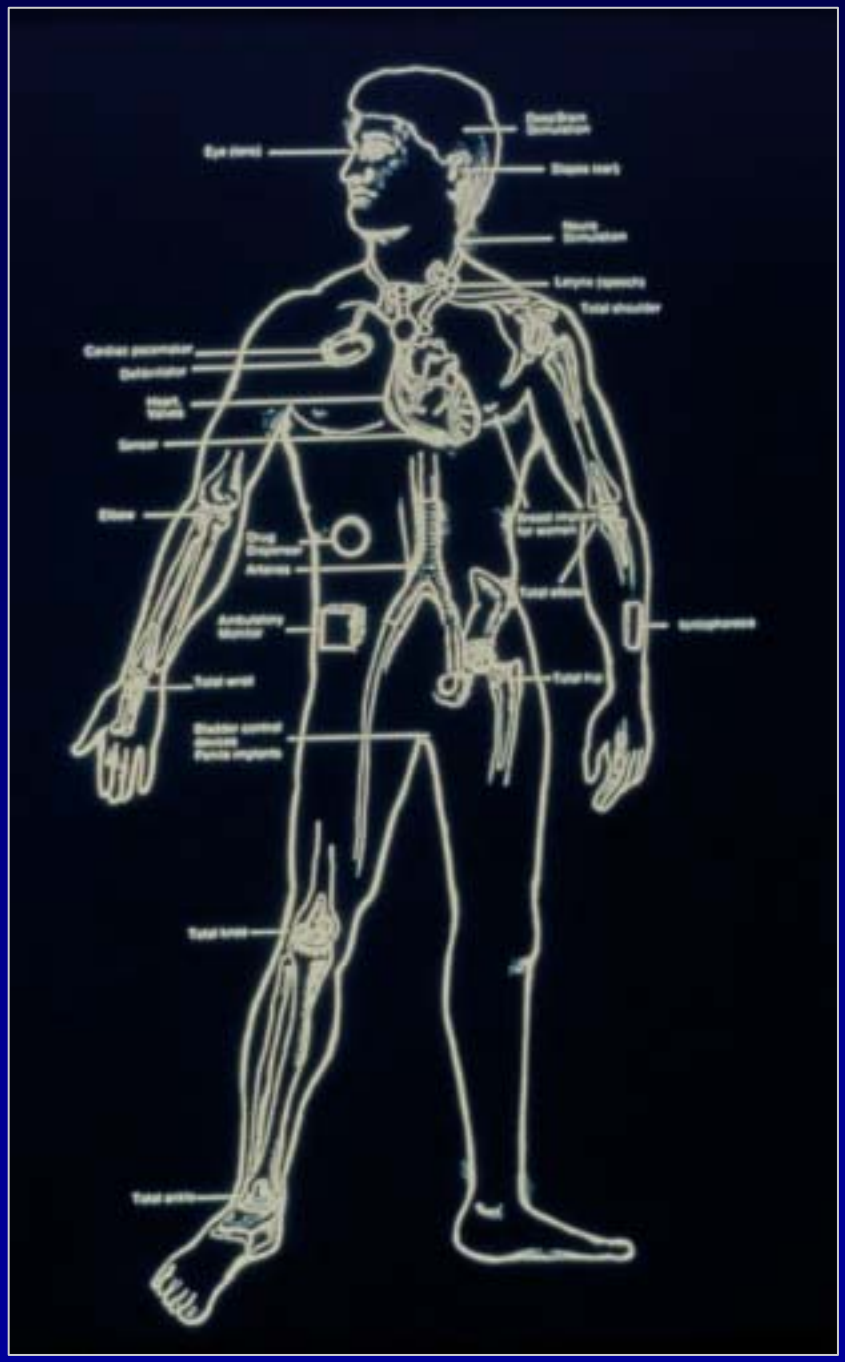
Biomaterial

A non-viable material used in a medical device intended to interact with biological systems

Williams, D.F., ed. Definitions in Biomaterials, Elsevier, N.Y. (1987)

Cardiac Pacemaker Components

Structural Biomaterials


Eye (lens)
Cardiac pacemaker
Defibrillator
Spinal
Elbow
Arteries
Total wrist
Total knee
Total ankle
Total hip
Total shoulder
Larynx (speech)

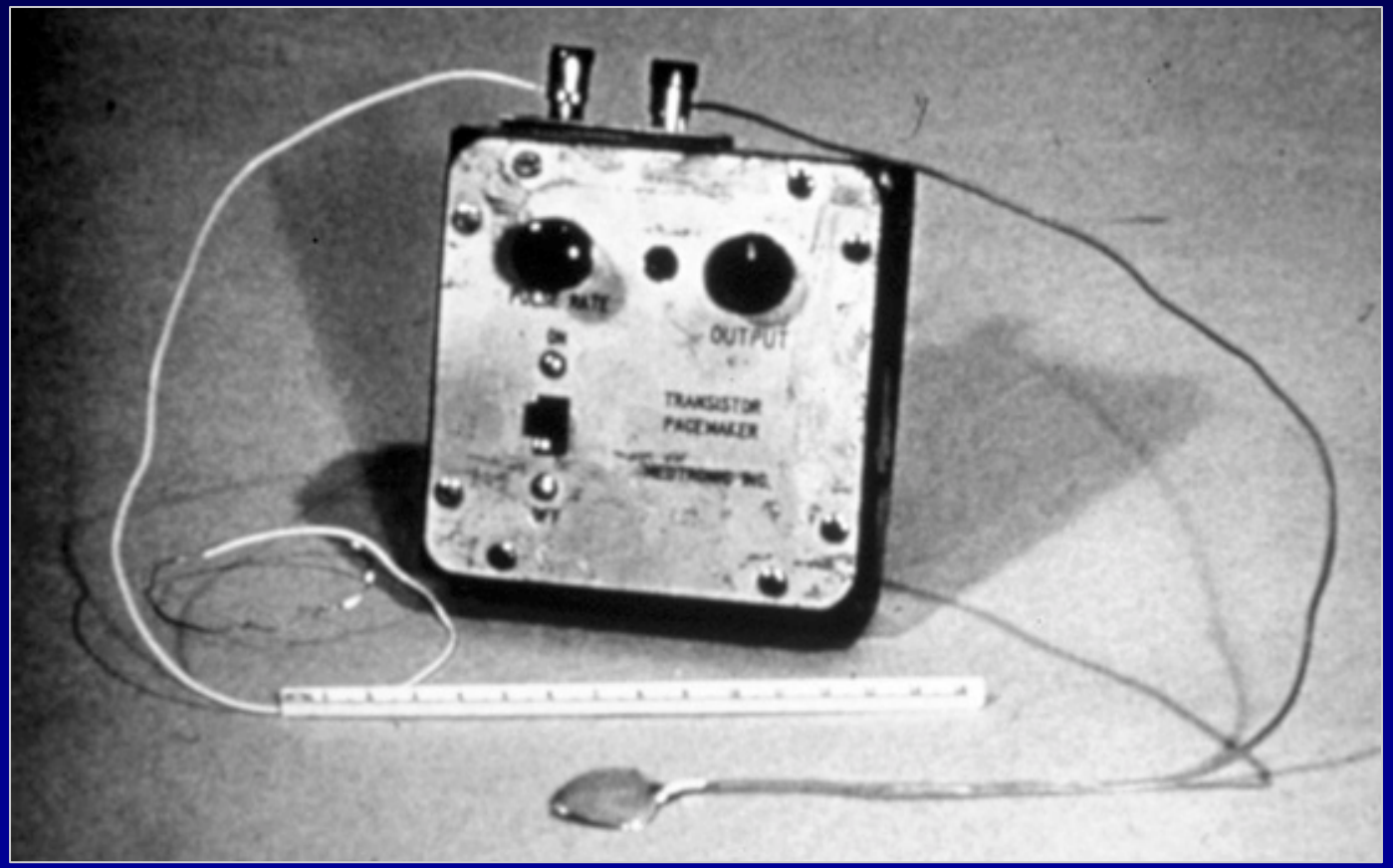
Kolff Artificial Kidney, 1943

Console Cardiac Pacemaker

Pre-1957

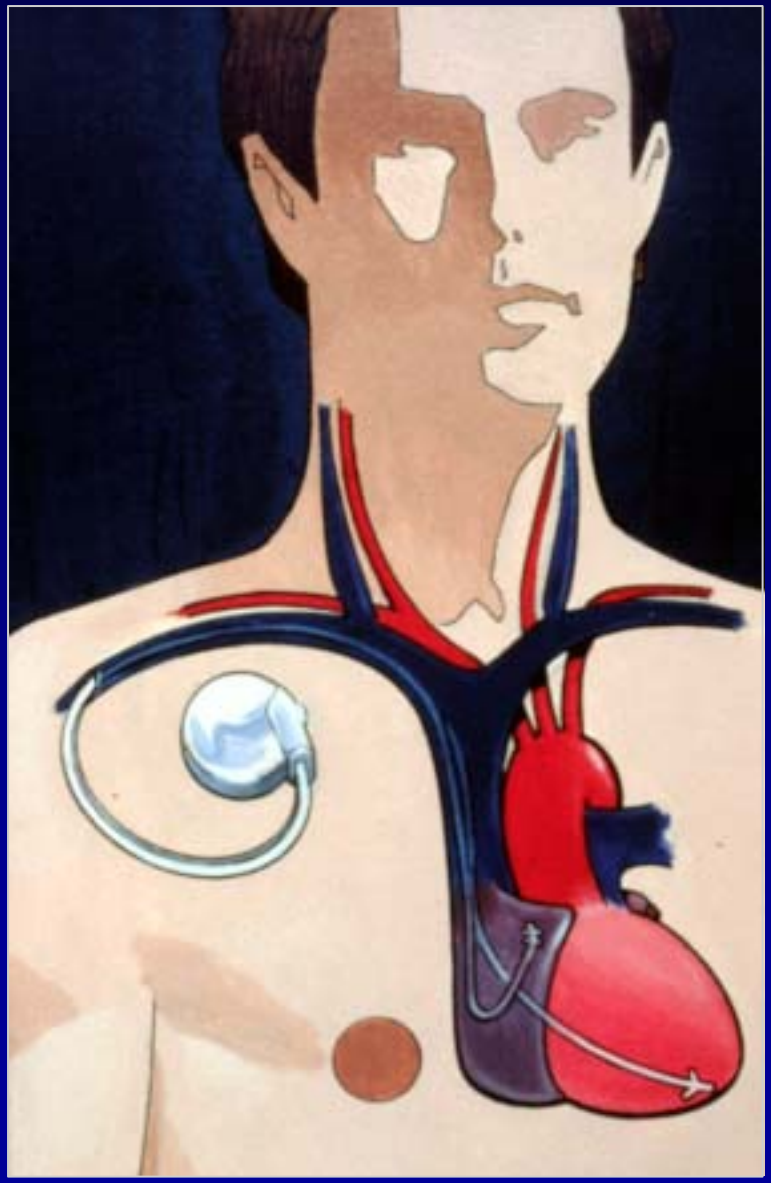
First Transistorized Pacemaker

1957



Earl E. Bakken, co-founder of Medtronic, Inc., built the company's first heart pacemaker (shown here) in 1957 for use by Dr. C. Walton Lillehei of University of Minnesota Hospitals. This device brought reliable, wearable, battery-powered pacing to persons whose hearts beat to slowly to support their circulatory systems.

Cardiac Pacemaker Implant

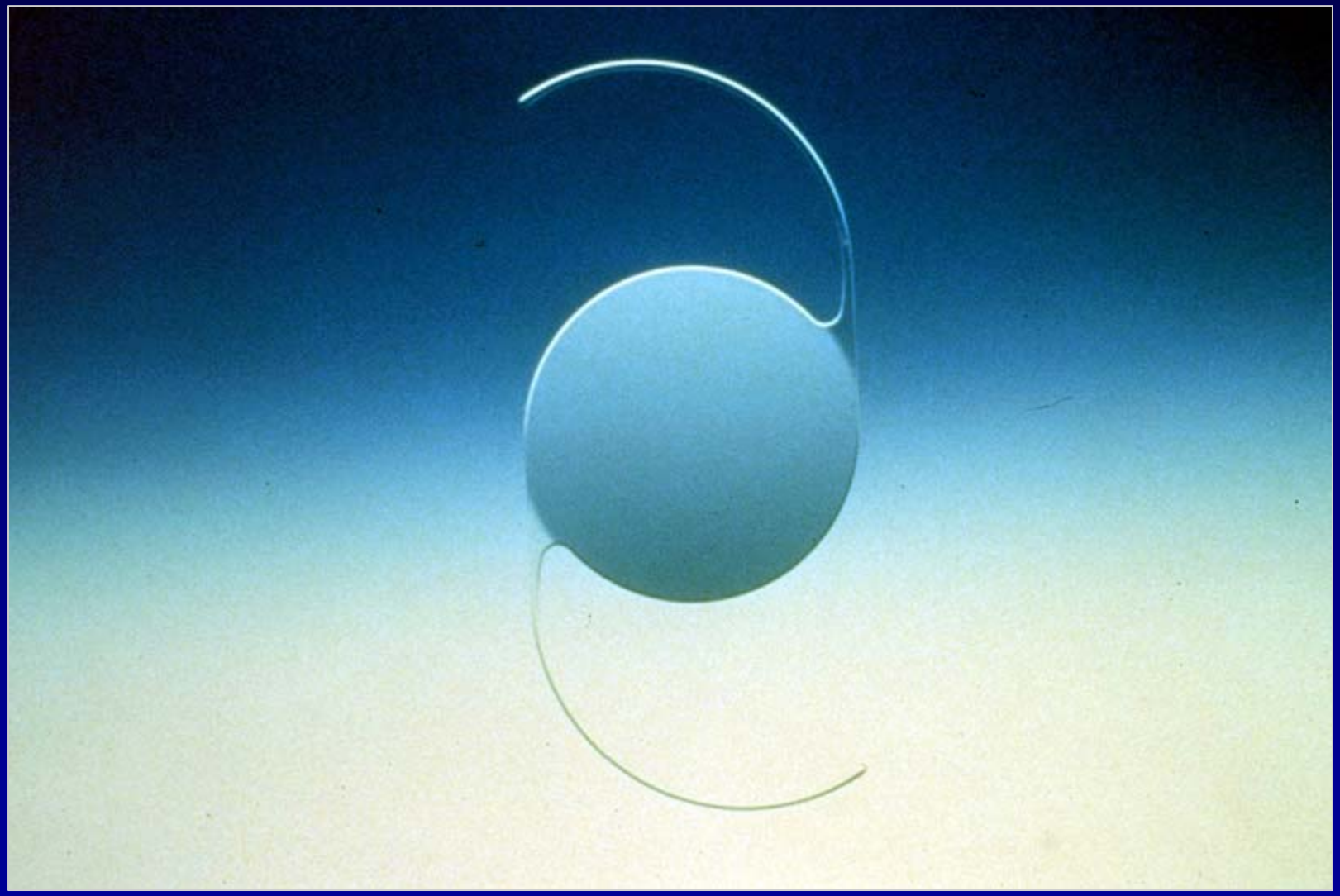


Implantable Cardiac Pacemakers

Medtronic/Hall Mechanical Heart Valve

Total Artificial Hip

PMMA Intraocular Lens

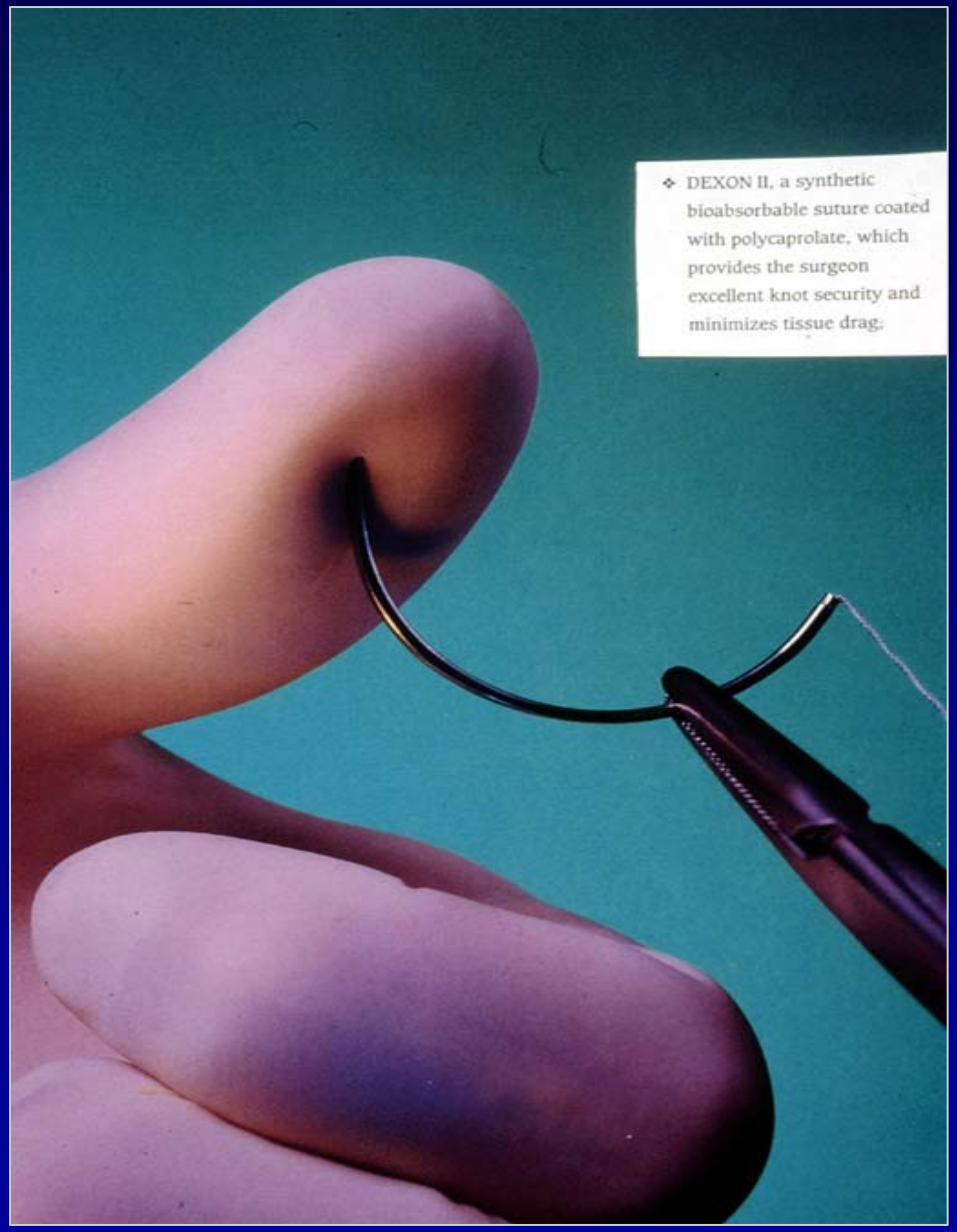


Implantable Artificial Heart

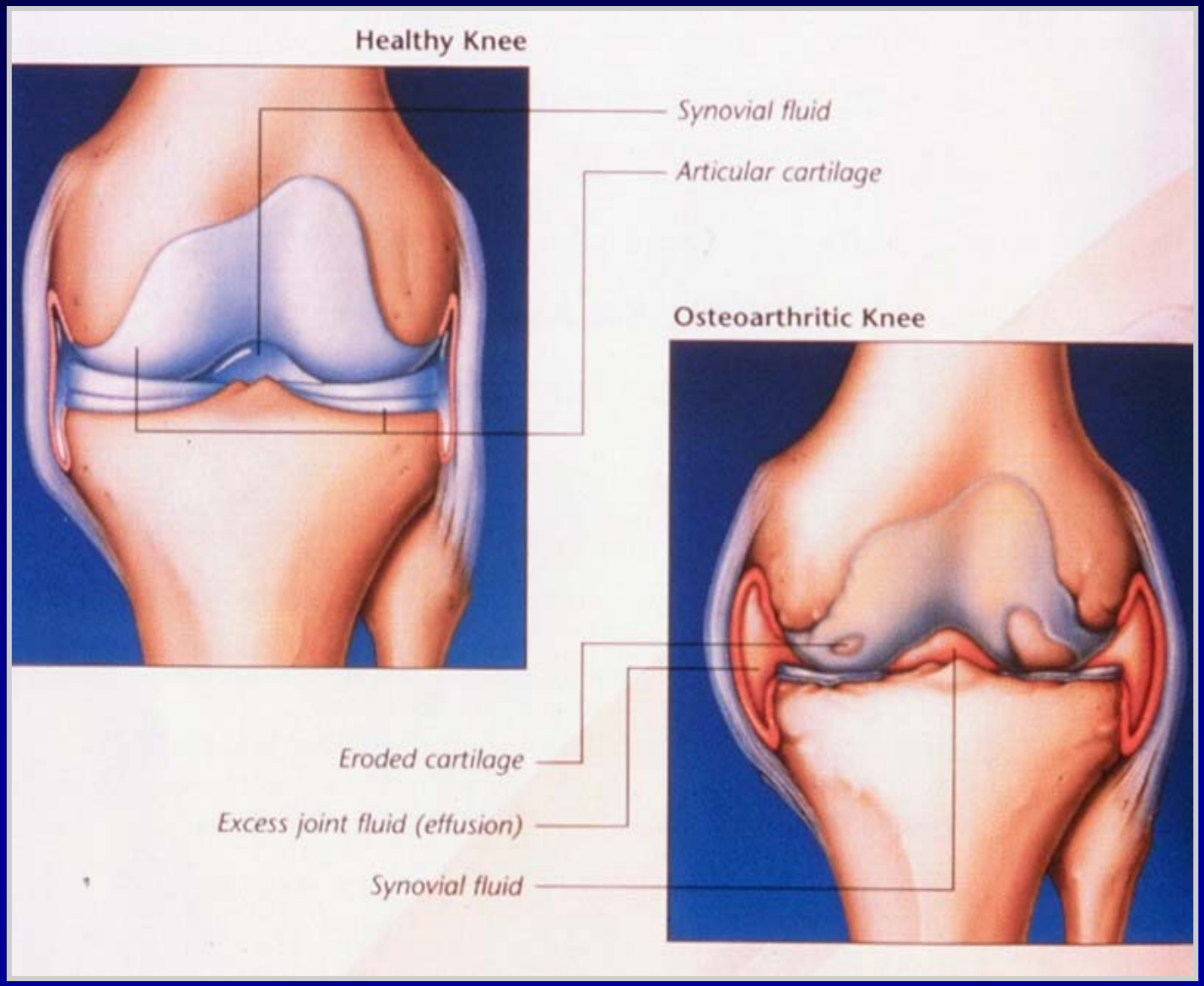
Jarvik-7 Device

Bioresorbables
Hydrogels

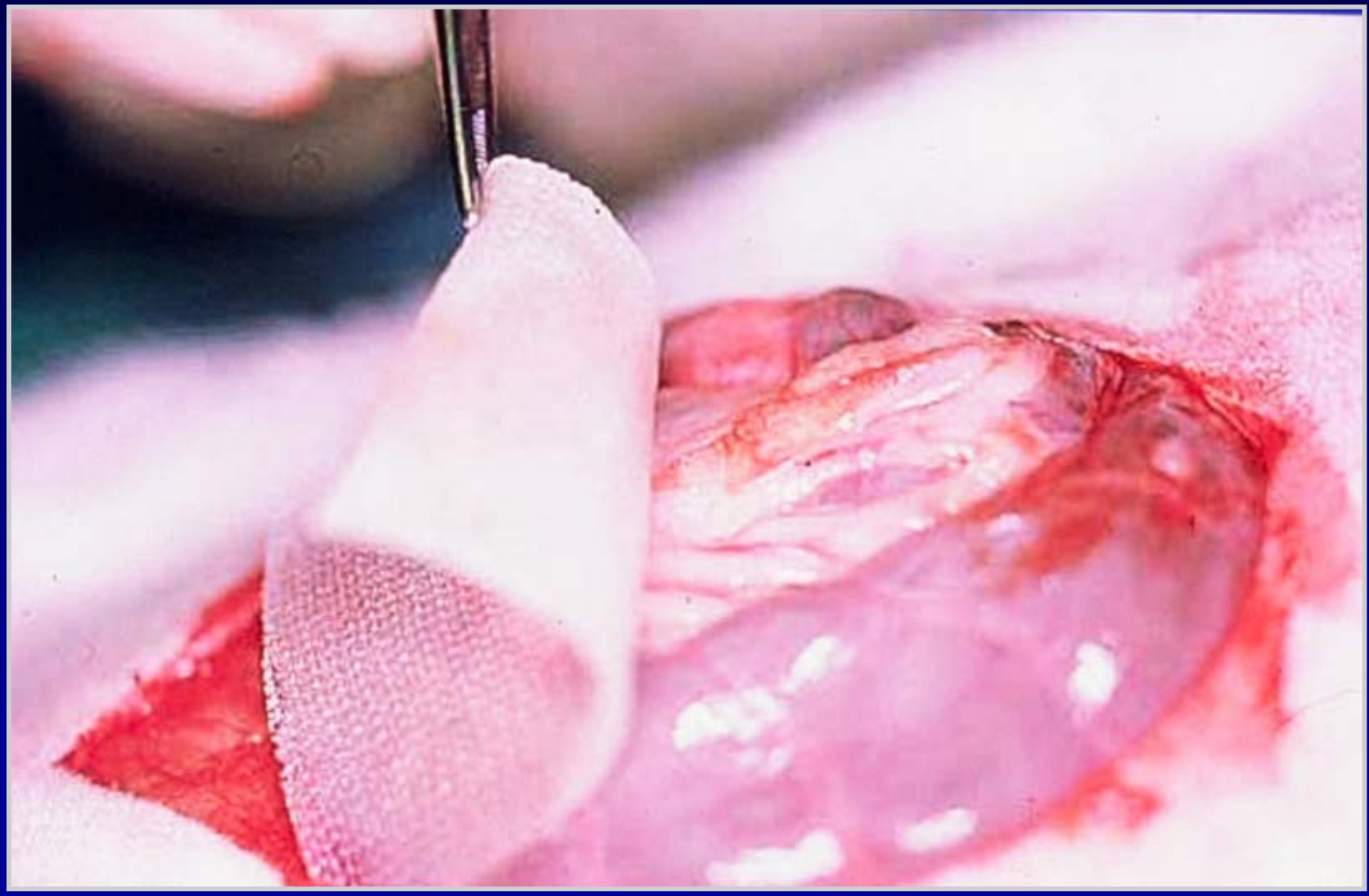
Bioresorbable Suture



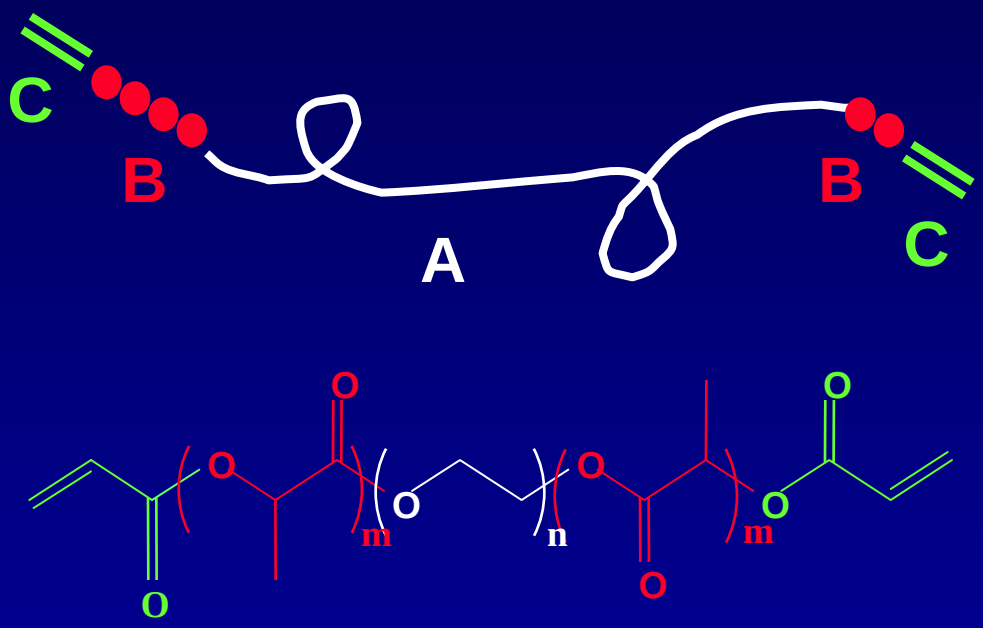
Healthy/Osteoarthritic Knee



SepraMesh™ Hernia Repair Product



Focal Macromer Structure



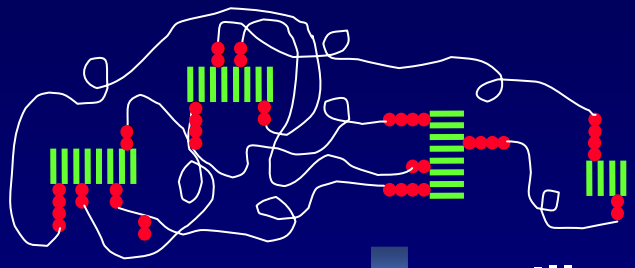
A: PEG Water Soluble/Biocompatible Polymer

B: Ester-containing Biodegradable Moieties

C: Acrylate Photopolymerizable End Caps

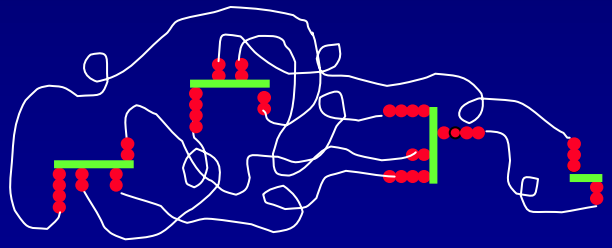
Formation and Degradation of FocalGel™

Micelles of Macromer in Solution



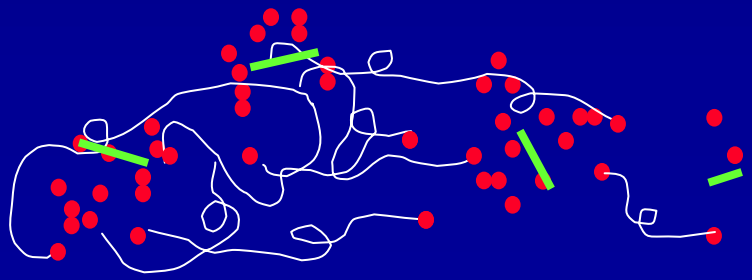
Illumination

Crosslinked Hydrogel



Hydrolysis

Hydrolytic Dissolution of Hydrogel



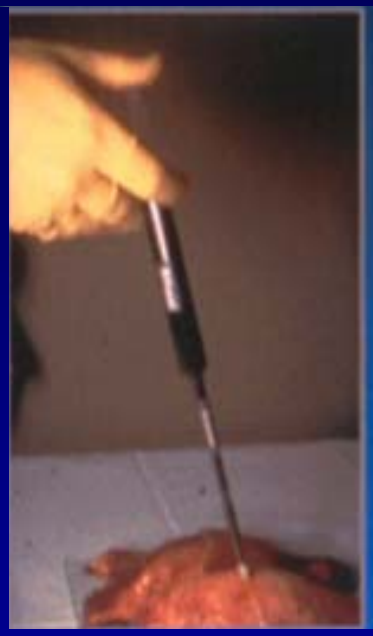
Acrylate

Lactate

PEG

Hydrogel Sealant Application

Brush on Primer



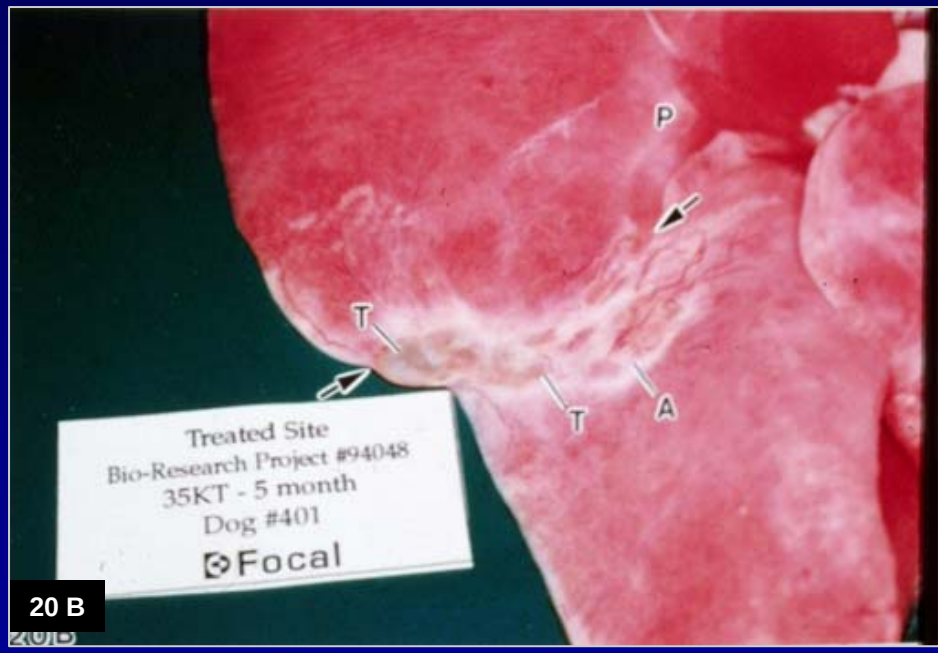
Brush in Sealant

Drip

Illuminate

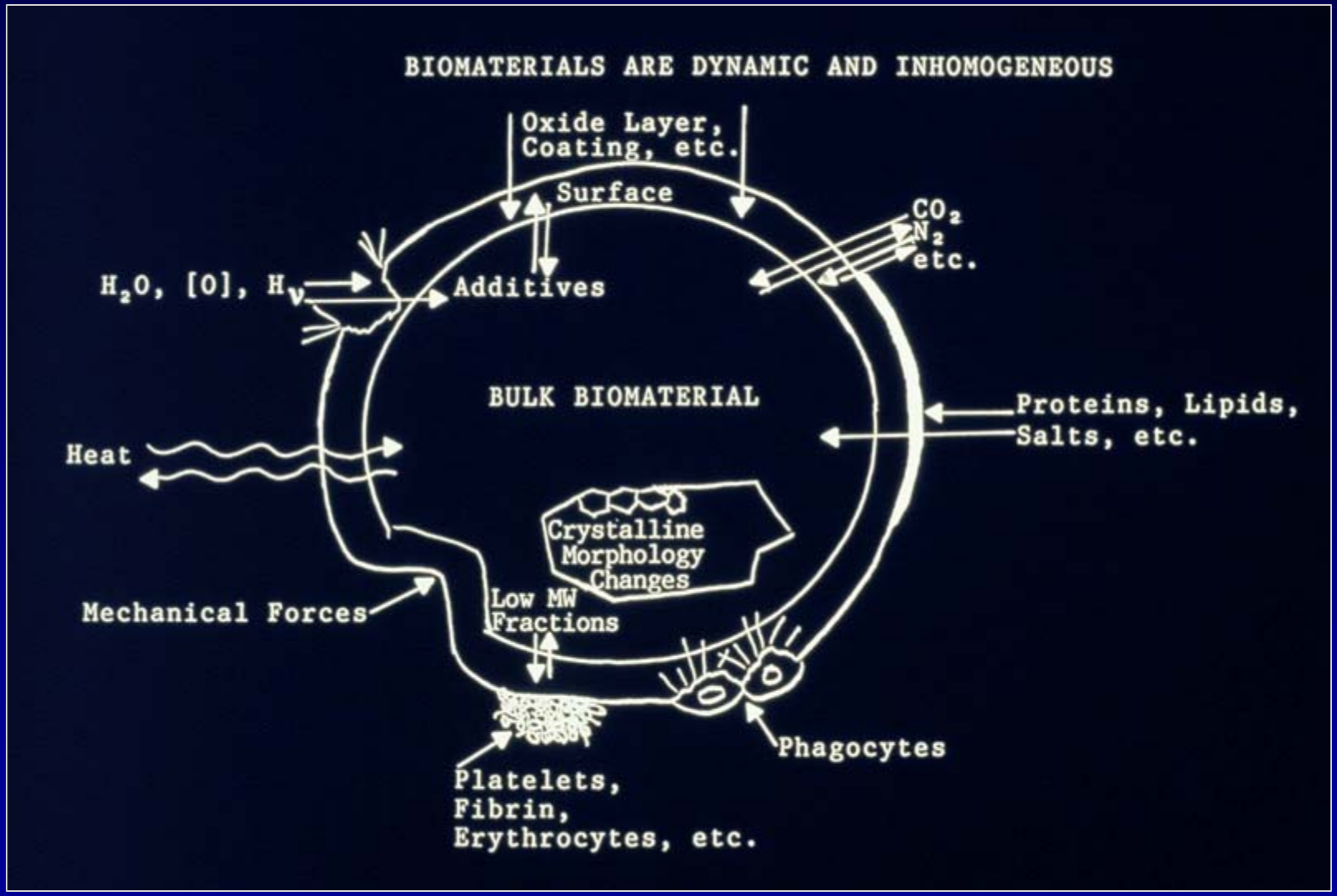
Five Month Lung Sealant Study

20 A

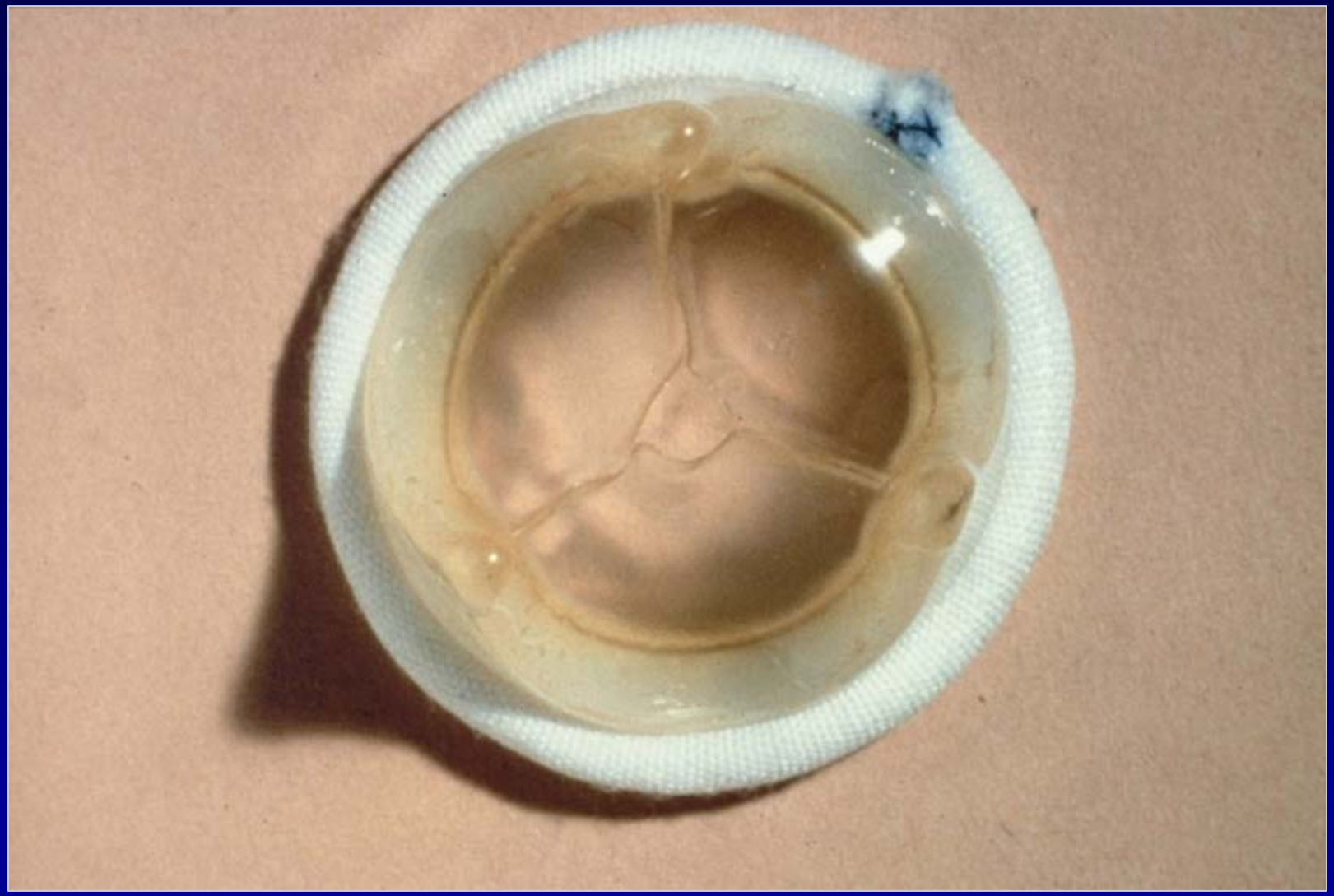


20 B

Biofouling
Biodegradation

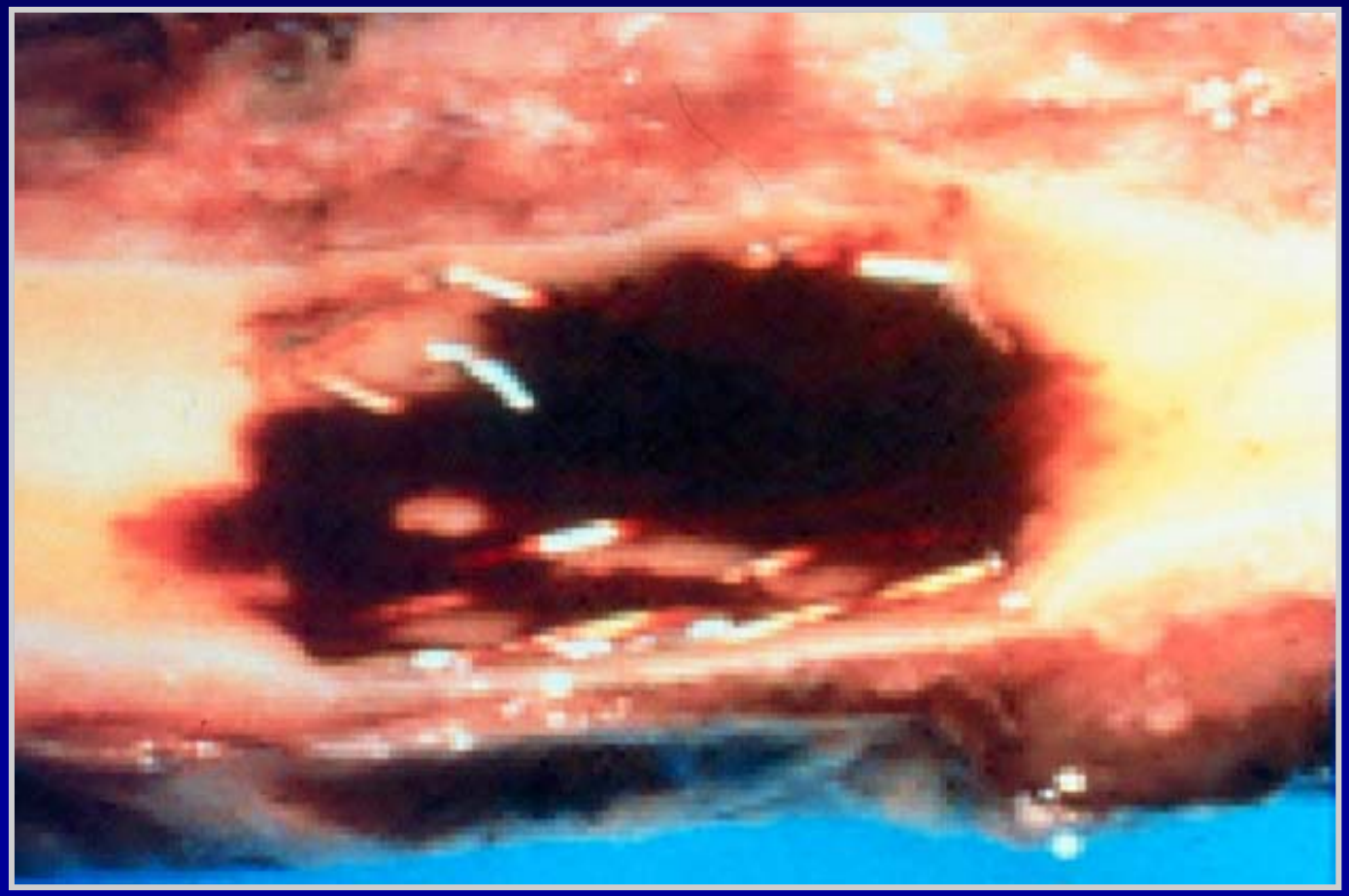

BIOMATERIALS ARE DYNAMIC AND INHOMOGENEOUS
Oxide Layer, Coating, etc.
Surface
CO_2
N_2
etc.
H_2O, [O], H_ν
Additives
BULK BIOMATERIAL
Proteins, Lipids, Salts, etc.
Heat
Crystalline Morphology Changes
Low MW Fractions
Mechanical Forces
Phagocytes
Platelets, Fibrin, Erythrocytes, etc.

Polyurethane Trileaflet Heart Valve

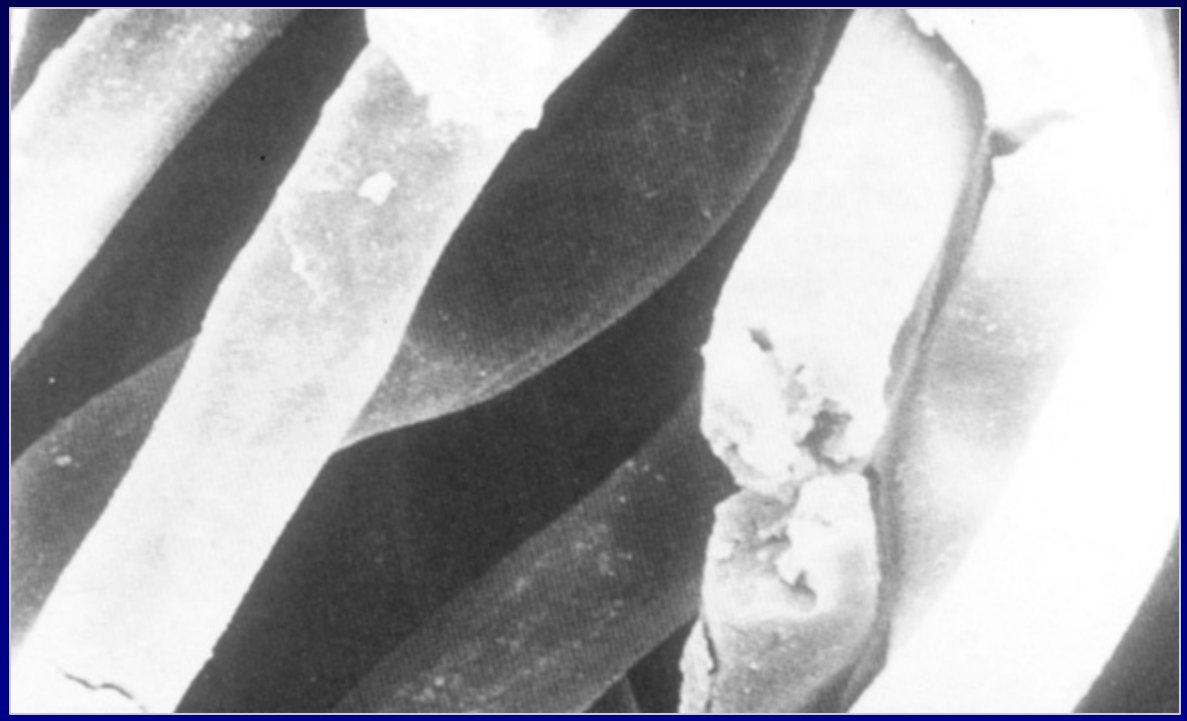


Calcification of Polyurethane Heart Valve In Vivo

Stented Artery Showing Mural Thrombus



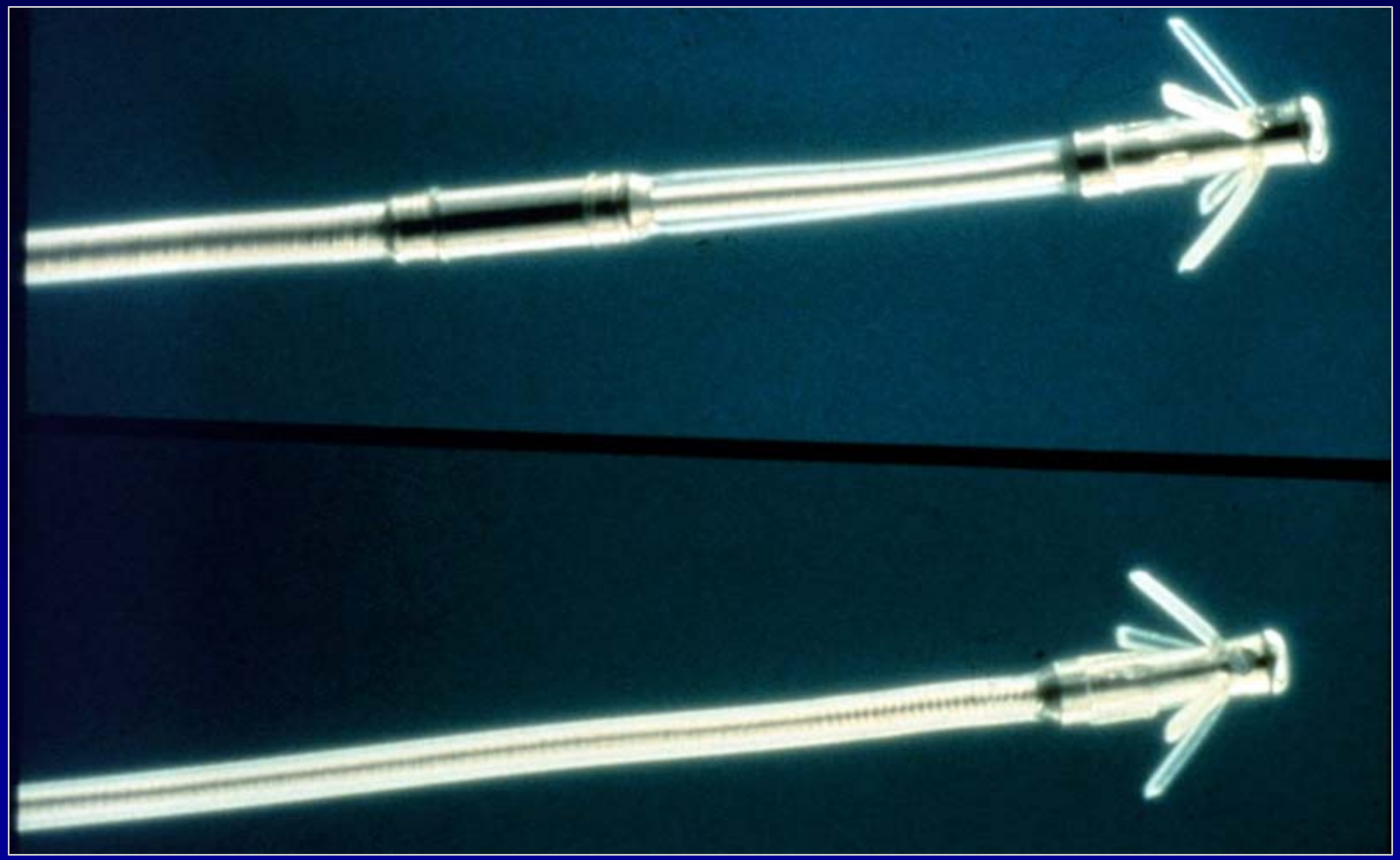
Hydrolytic Degradation of Polyester Vascular Prosthesis



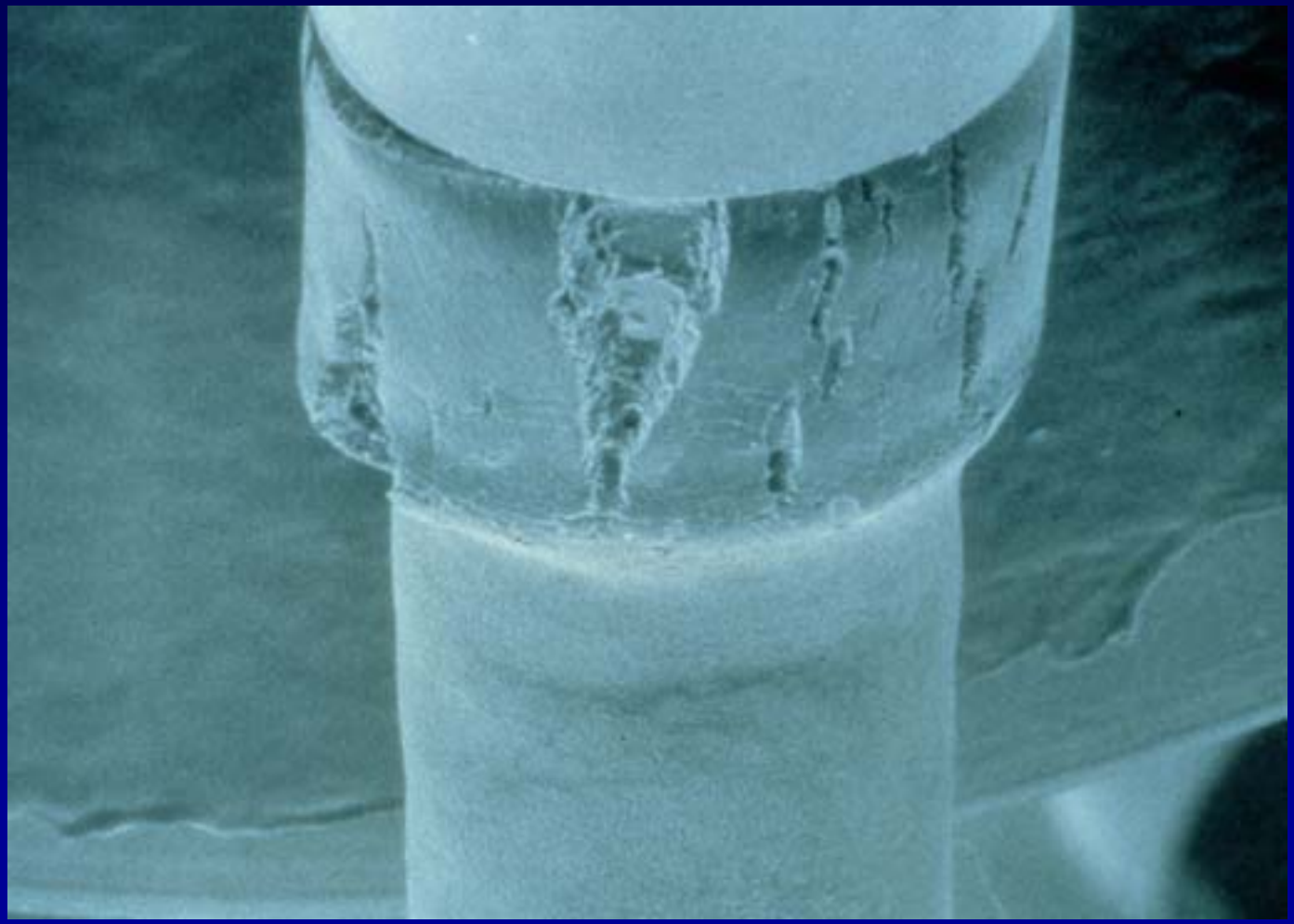
SEM photomicrograph of fractured fibers removed from retrieved and cleaned vascular prosthesis after 84 months implantation showing embrittled appearance possibly due to chemical degradation (original magnification x 1250)

King. M.W. (1985, ASTM STP 85)

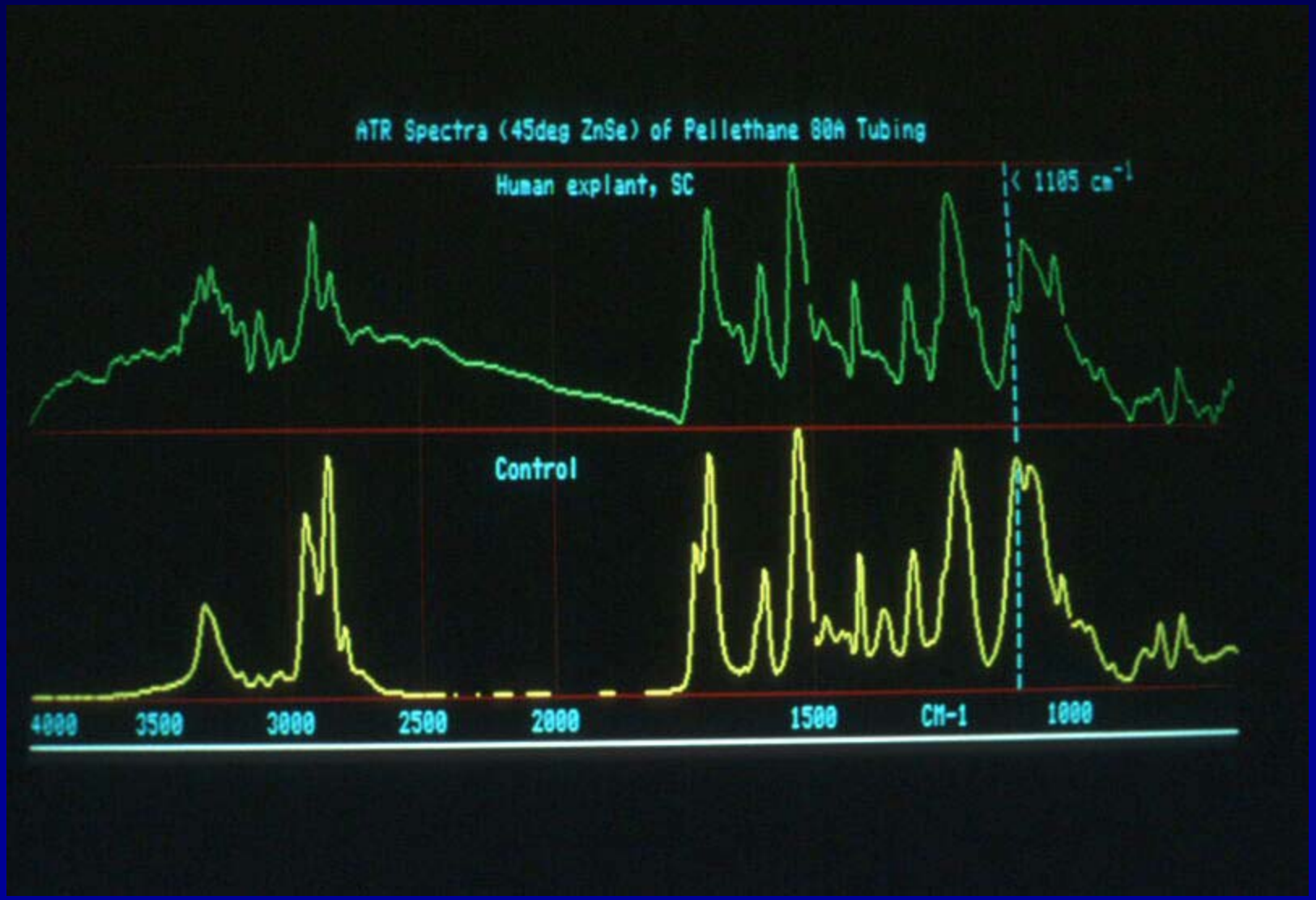
Bipolar and Unipolar Polyurethane Insulated Pacemaker Leads



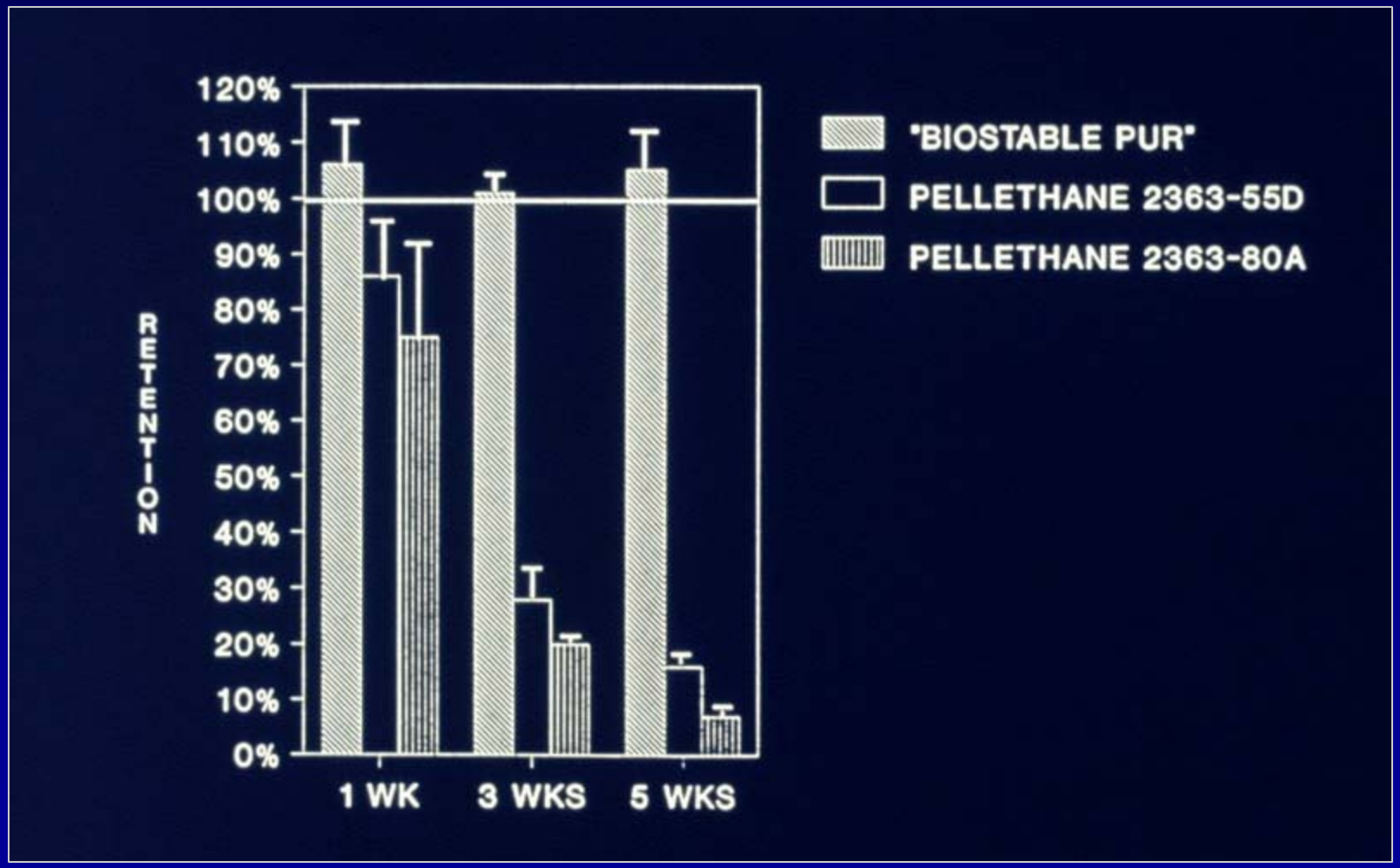
Stress Cracked Cardiac Pacing Lead Insulation



Surface Chemical Changes of Stress Cracked Polyurethane

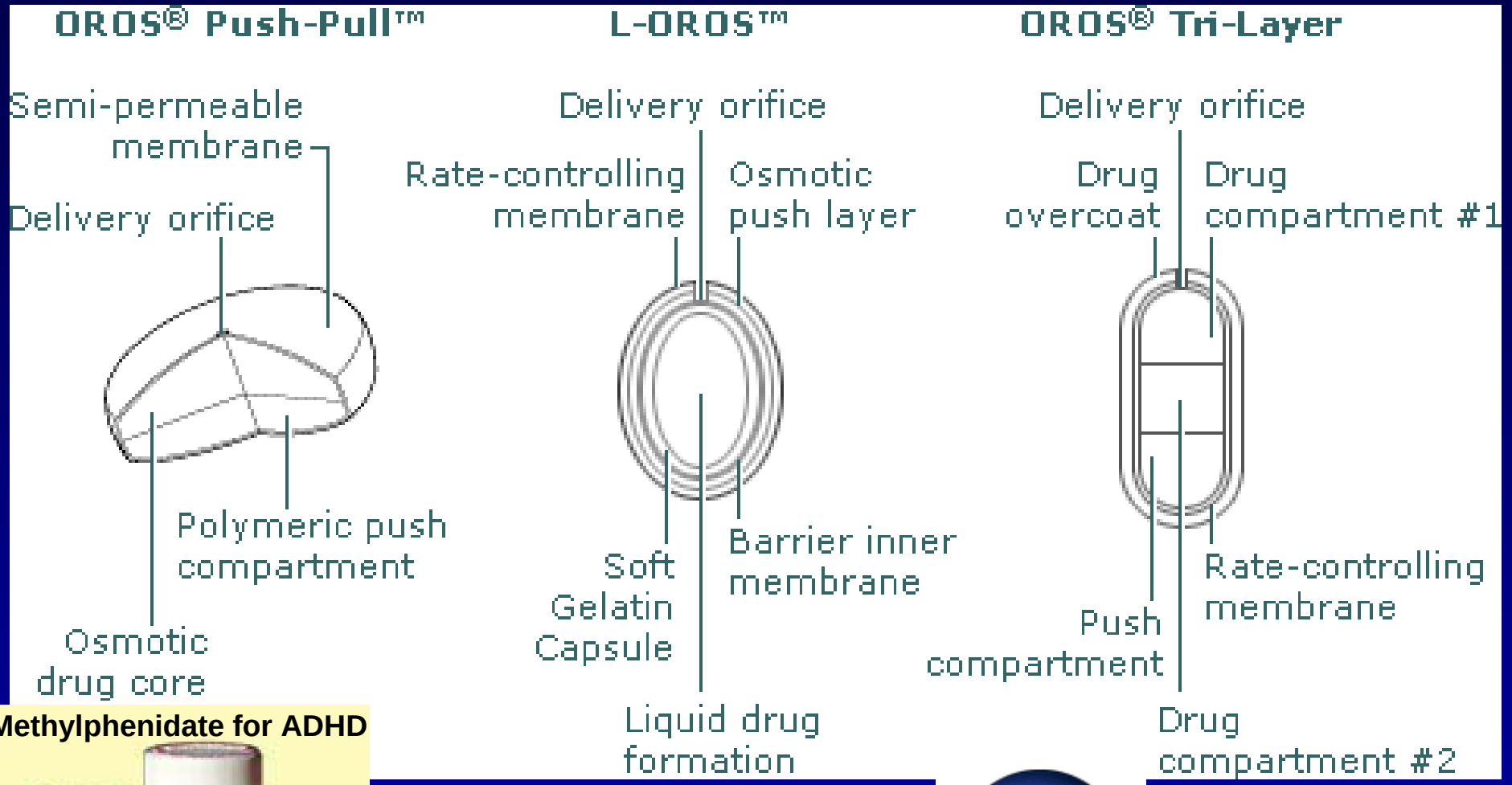


Polyurethane Tensile Strength Retention In Oxidant (vs Ringer's = 100%)



Sustained Drug Delivery

ALZA Sustained Oral Drug Delivery



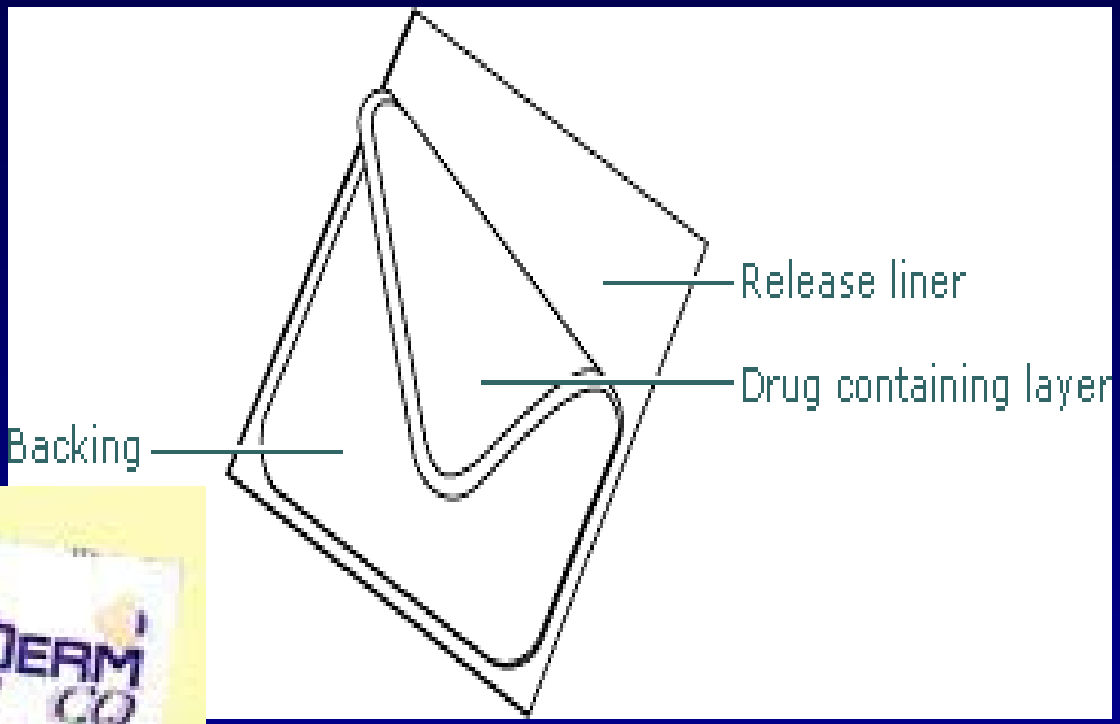
Methylphenidate for ADHD

(2002)

Procardia^{R} XL Nifedipine (1989)

Sudafed® Products

ALZA Transdermal Patch



(1991)

Other Products:
OCUSERT^{R} Pilocarpine (1974)
Transderm-Nitro^{R} (1981)
Transderm-Scop^{R} (1981)
Estraderm^{R} (1986)
Duragesic^{R} Fentanyl (1990)

Iontophoretic Drug Delivery

FIG. 1

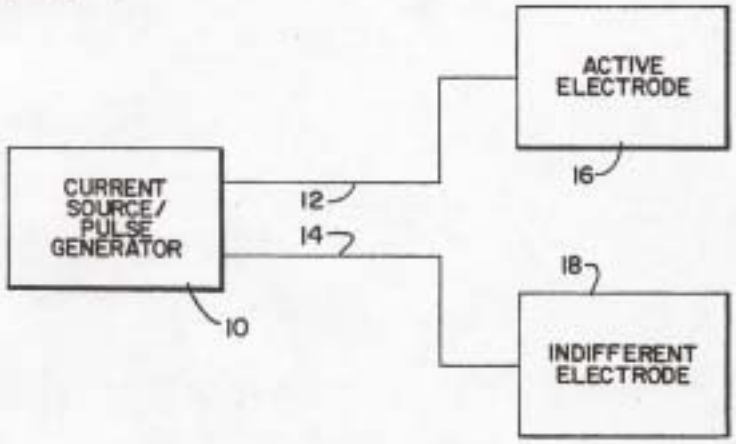
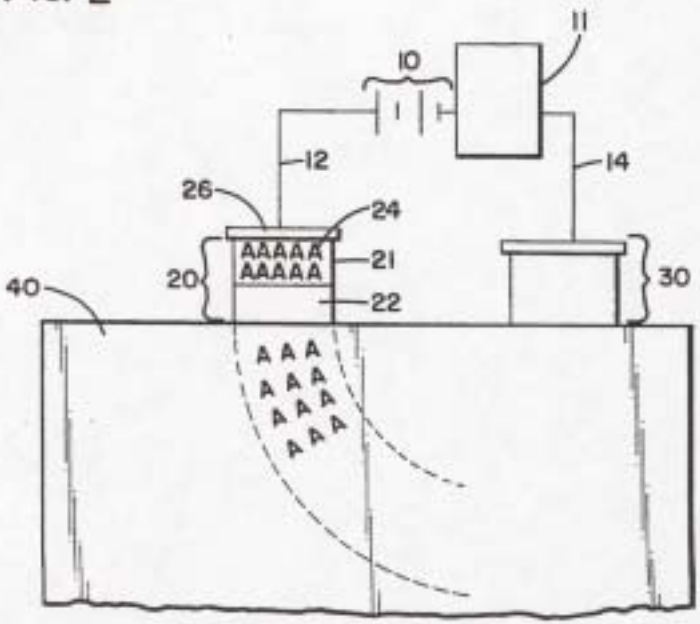
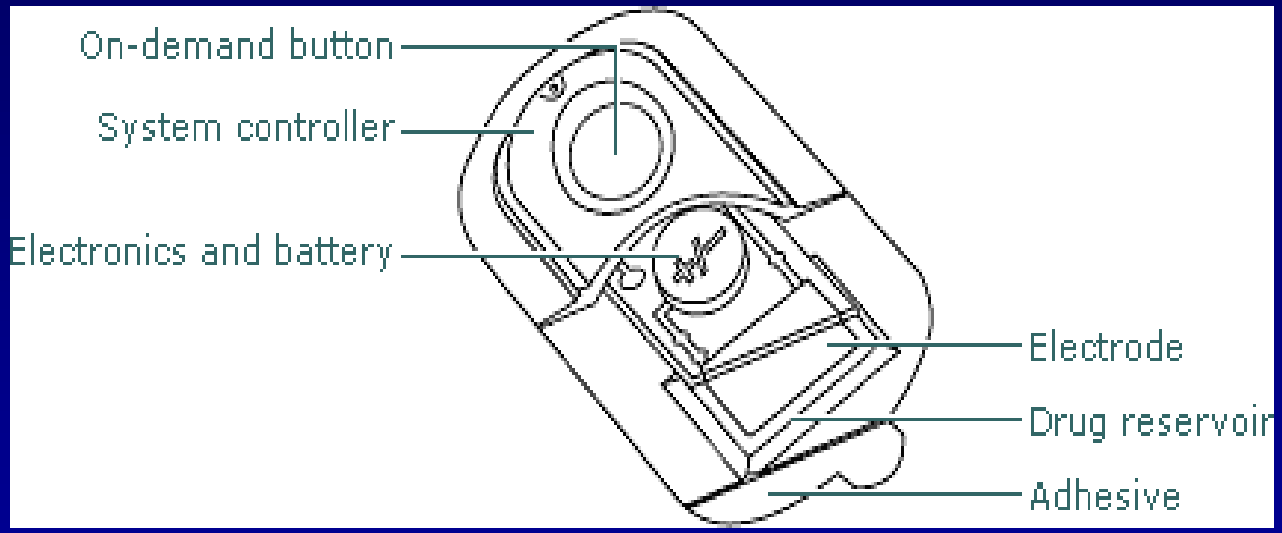
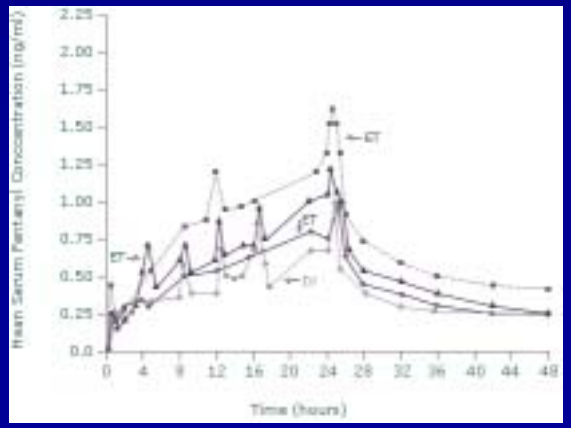


FIG. 2



ALZA E-TRANS® Iontophoresis System

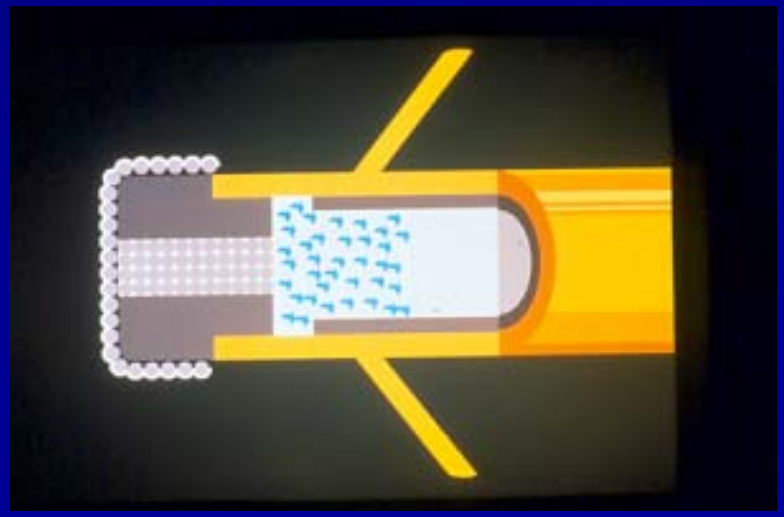




Bipolar Pacemaker System

Endocardial Pacing Lead

Steroid Eluting Pacing Lead (porous tip, steroid plug, tine)

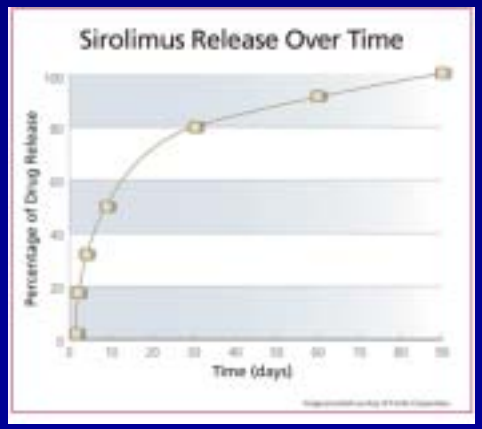


Cordis Cypher™ Sirolimus Eluting Stent

SIRIUS Trial Results

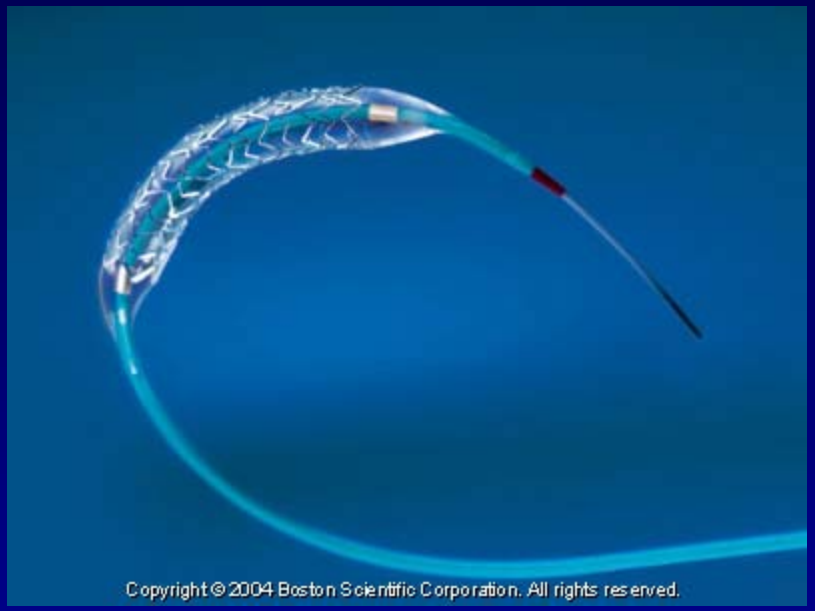
	Sirolimus Treated	Control
Restenosis (8 mo)	3%	35%
MACE (9 mo)	7.1%	18.9%

Approved in U.S., 2003



Cordis website

Taxus™ Express™ Paclitaxel Eluting Coronary Stent

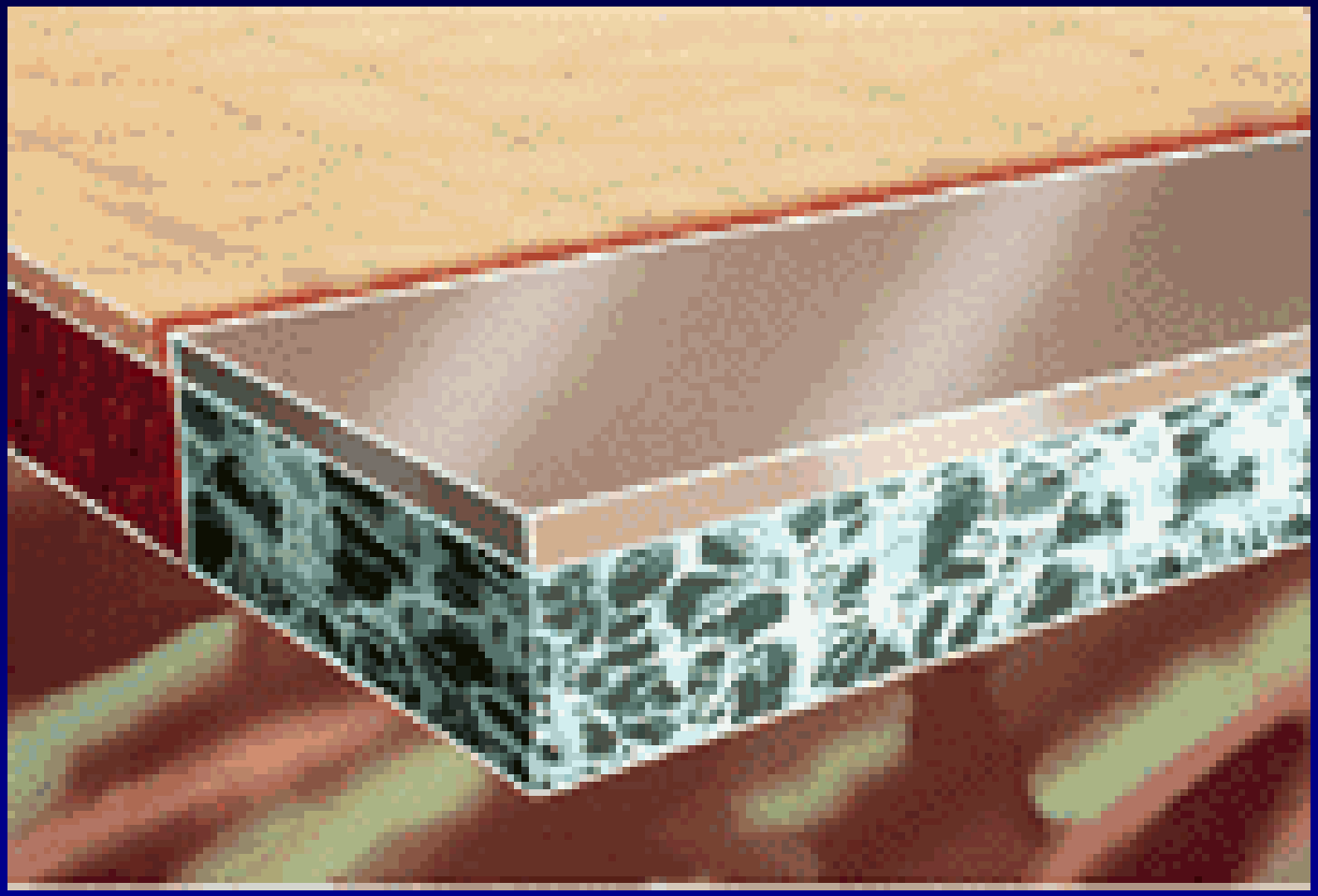


9 Month Results	**Paclitaxel Coated**	**Control**
Restenosis	**5.5%**	**24.4%**
MACE	**8.5%**	**15.0%**

FDA approval in U.S.: March 4, 2004
Sales in first 2 weeks on U.S. market: $42 Million*

*Source, Boston Globe, March 23, 2004, p.D2

Tissue Engineering
Cell Therapy
Gene Therapy



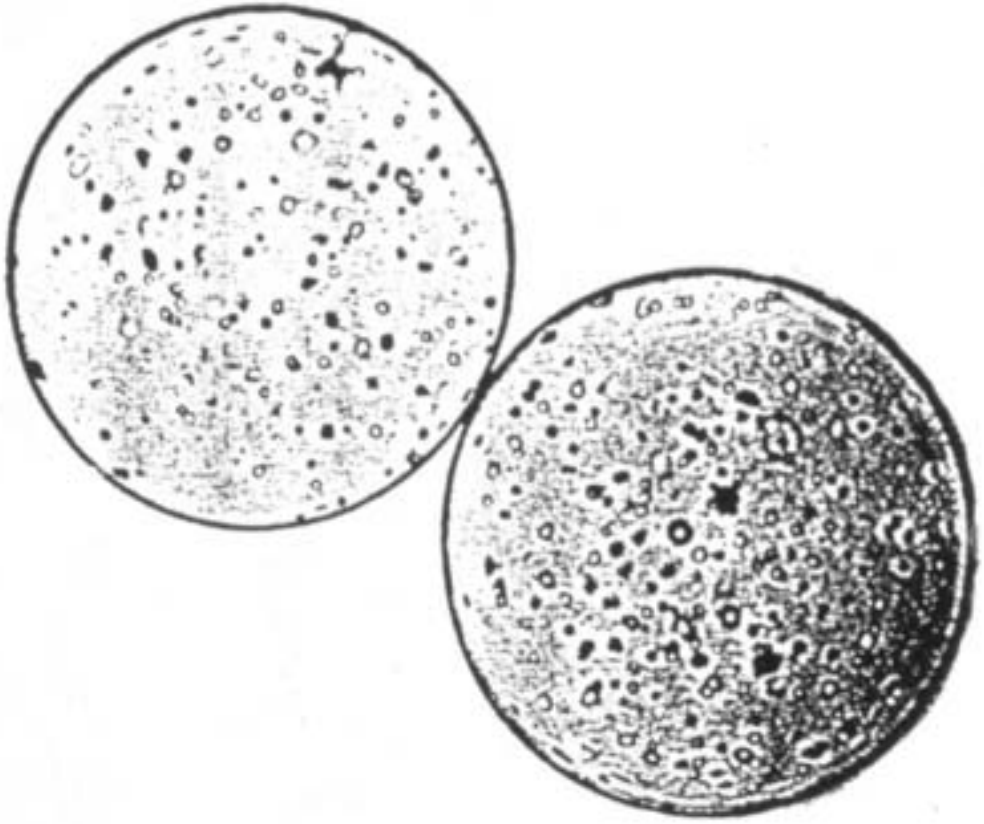
INTEGRA® Dermal Regeneration Template Function

INTEGRA® Dermal Regeneration Template is a skin replacement system for the treatment of deep partial-thickness or full-thickness thermal injury to the skin. INTEGRA® Dermal Regeneration Template is applied following excision of the burn wound to viable tissue.

www.integra-ls.com/bus-lifesci_main.htm

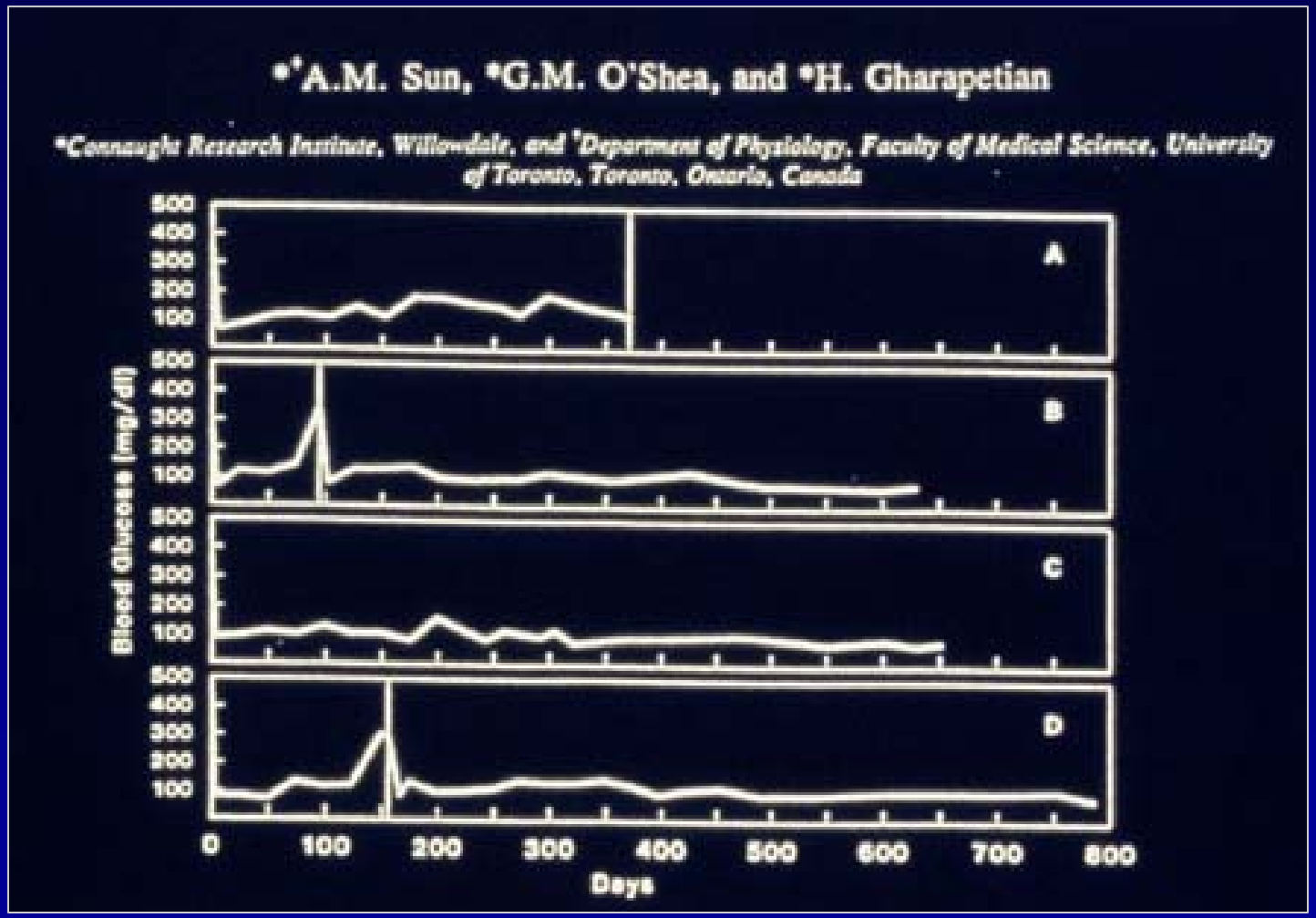
Hybrid Bio-Artificial Pancreas

S. Darquy et al.: B-cell immunoisolation by microencapsulation
Diabetologia 28, pp. 776-780 (1985)



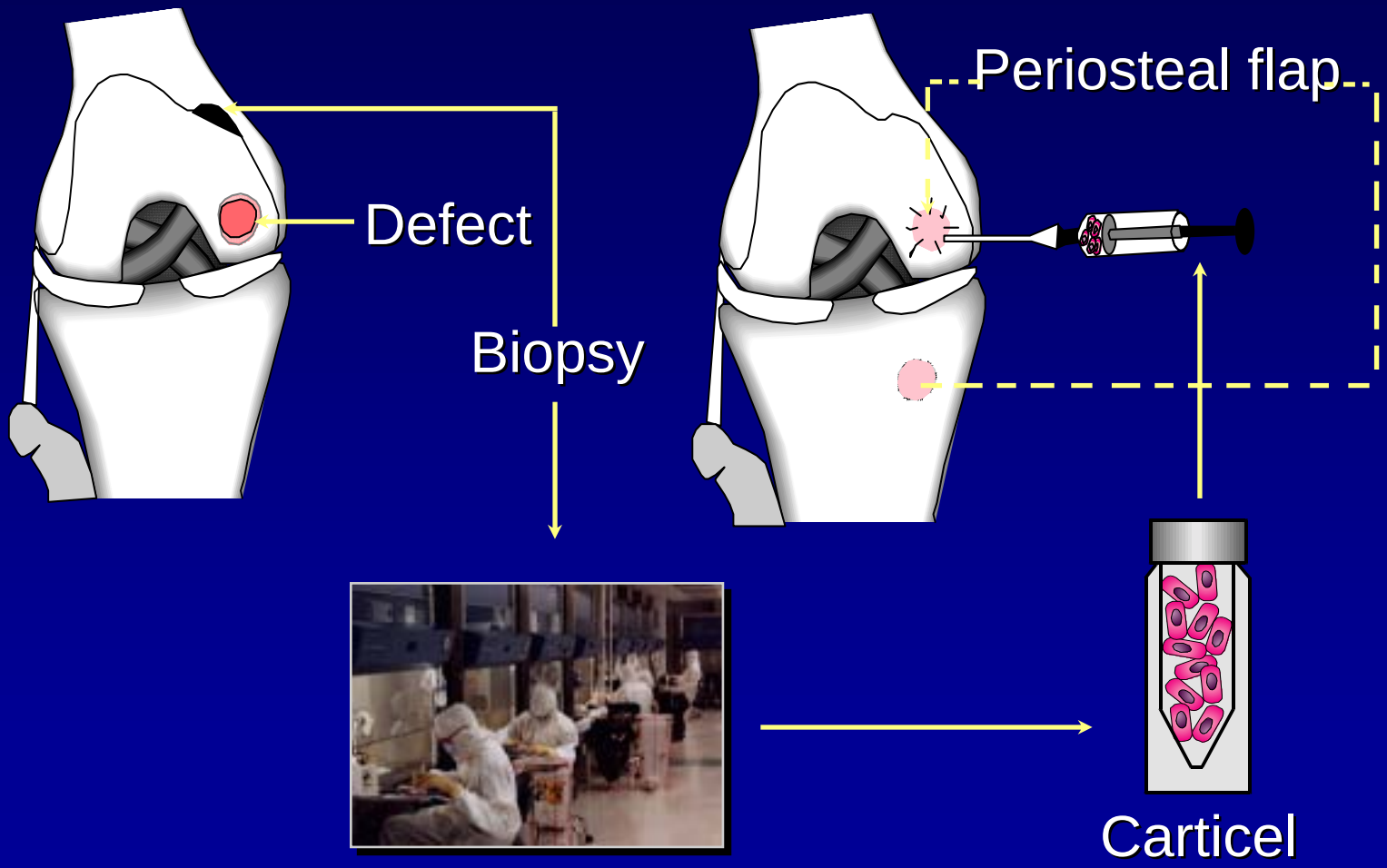
Microencapsulated RINm5F cells 24 h after preparation. Note the absence of any cell grown outside the capsule

Gel Encapsulated Islets as Bio-artificial Pancreas

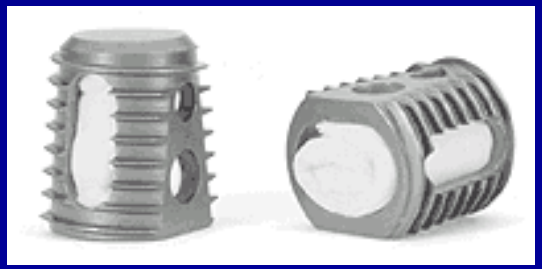


Fasting blood glucose levels in rats transplanted with Islets that were encapsulated in alginate-polylysine-alginate membranes

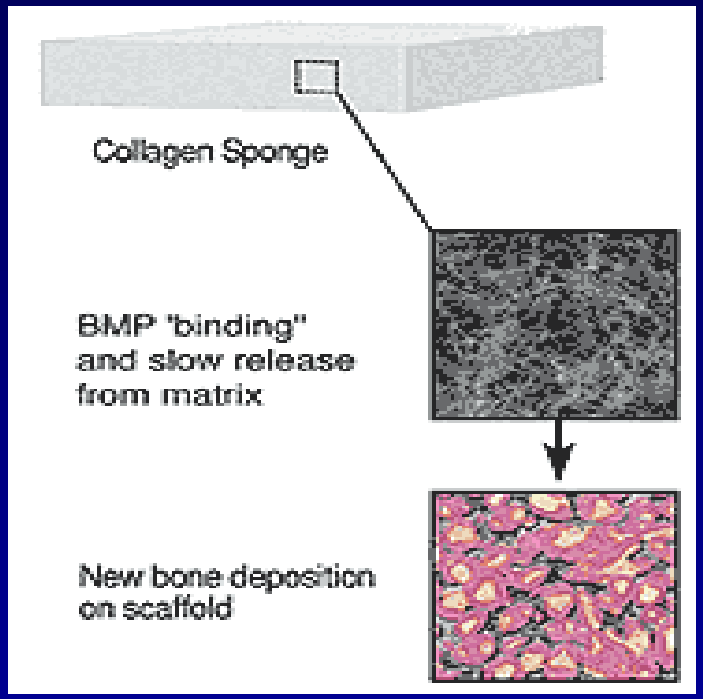
Implantation of Carticel®
Autologous Cultured Chondrocytes



Medtronic Sofamor Danek INFUSE^{R} Bone Graft and Cage Lumbar Fusion Device



FDA Approved July 2, 2002



First Approved Device Using Genetically Engineered Protein (BMP-2)

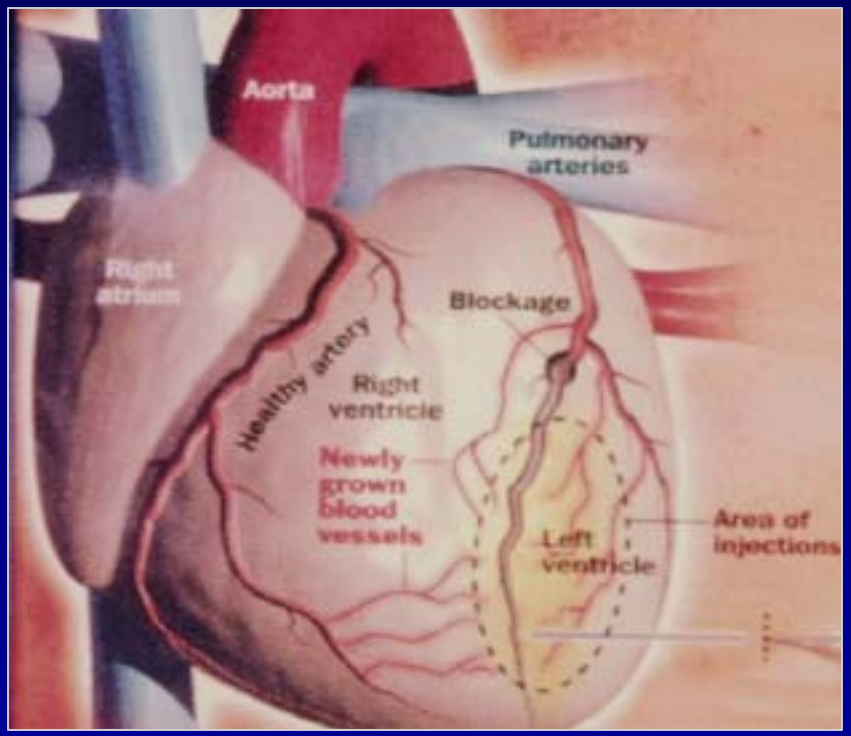
Cardiac Cell Therapy: Working Hypothesis

Cells delivered to infarcted regions of the heart may inhibit ventricular dilatation and progression to heart failure

Gene Therapy
Clinical Trials Initiated by Genzyme

- Cystic Fibrosis (Single Gene)
- Cancer (Fusion Vaccines for Melanoma)
- Coronary Artery Disease (Angiogenesis)
- Peripheral Artery Disease (Angiogenesis)

Therapeutic Angiogenesis for Ischemic Diseases



A significant proportion of CAD and PVD patients cannot benefit from standard therapies.

Therapeutic angiogenesis could be a useful adjunct to existing procedures and promote improved perfusion of areas not amenable to bypass or angioplasty

Ad2/HIF-1α PAD Study 2A: Patient 27 Screening

Placebo, Day 1

Placebo, Day 60

Placebo, 6 mo.

Study 1 Patient 27: 6 months (Placebo)
Study 2A Roll Over: Day 1 (1 x 10e10 vp)

Placebo, 6 mo.
Rollover, Day 1

Rollover, 6 mo.

Rollover, 12 mo.

Emerging Medical Technologies

- Drug-Loaded Stent
- Resorbable Stent
- Robotic Surgery
- Implantable Mini Blood Pump
- Ventricle-Coronary Artery Shunt
- Functional Electrical Stimulation (Artificial Sight, Hearing, Movement)
- Nanotechnology
- Tissue Augmentation
- Drug Discovery and Therapy
- Sustained, Local Drug Delivery
- Biohybrid Organs
- Guided Tissue Regeneration
- Transgenic Organ Generation
- Genomics/Proteomics
- Protein Engineering
- Gene Therapy
- Gene Expression Analysis (µ-arrays)
- Immunotherapy (Alzheimers, Cancer, Etc)
- Cell Multiplication & Transplantation
- Cell Function Regulation
- Extracellular Matrix ProductionCytokine, Growth Factor Therapy
- Stem Cell Expression and Therapy

Chemical Engineering Opportunities in Medical Industries

- Medical Devices
- Biomaterials
- Drug Delivery
- Drug Development
- Biomedical Engineering
- Biological Engineering
- Tissue Engineering
- Biomolecular Engineering

- Research
- Development
- Manufacturing
- Business Development
- Project Management
- General Management
- Information Technology
- Intellectual Property

Chemical Engineers in Biomaterials and Drug Delivery

- Kristi Anseth
- Dawn Applegate
- Rena Bizios
- Stuart Cooper
- Elazer Edelman
- Jennifer Elisseeff
- Morton Friedman
- Linda Griffiths
- Jennifer Hill-West
- Allan Hoffman
- Jeff Hubbell
- Joachim Kohn
- Kenneth Keller
- Bob Langer
- Cato Laurencin
- Michael Lysaght
- Edith Mathiowitz
- Edward Merrill
- Larry McIntire
- David Mooney
- Laura Niklason
- Nicholas Peppas
- Buddy Ratner
- Molly Shoichet
- David Tirrell
- George Truskey
- Gordana Vunjak-Novakovic
- Joyce Wong