# Disposable Miniature Pressure Sensor for Cardiologist Use

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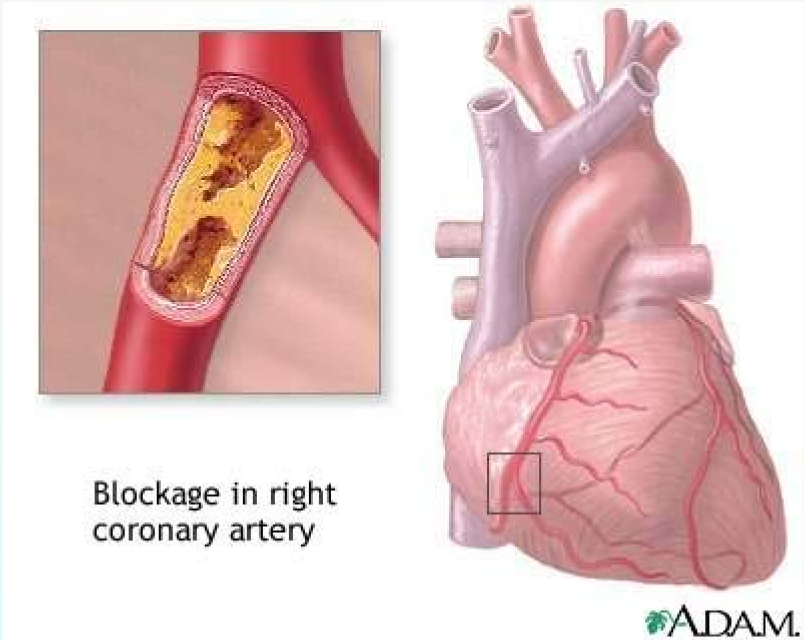
# Coronary Artery Disease

- Build up of plaque (fat and cholesterol)
- Arteries become narrowed and hardened
- Less blood flow to the heart muscle
- Heart muscle tissue can be damaged
- Atherosclerosis - hardening of the arteries



# Symptoms?

**Angina (chest pain)**

- Exercise or stress
- Arteries are too narrow
- Not enough blood and oxygen to meet the increased demand

**Heart attack**

- Artery becomes completely blocked
- Cutting off blood and oxygen to part of the heart
- Causing that tissue to die

# Background

- Coronary artery disease (CAD)
  - Kills ~ 871,000 people/year
  - Leading cause of death in US
  - 14 million US patients /year [1]
- Coronary angioplasty
  - ~650,000 U.S. patients /year
  - More than 2 million /year worldwide
  - Nearly 3 million /year by 2010
  - Annual medical cost > 112 Billion

# The 1st Balloon Angioplasty

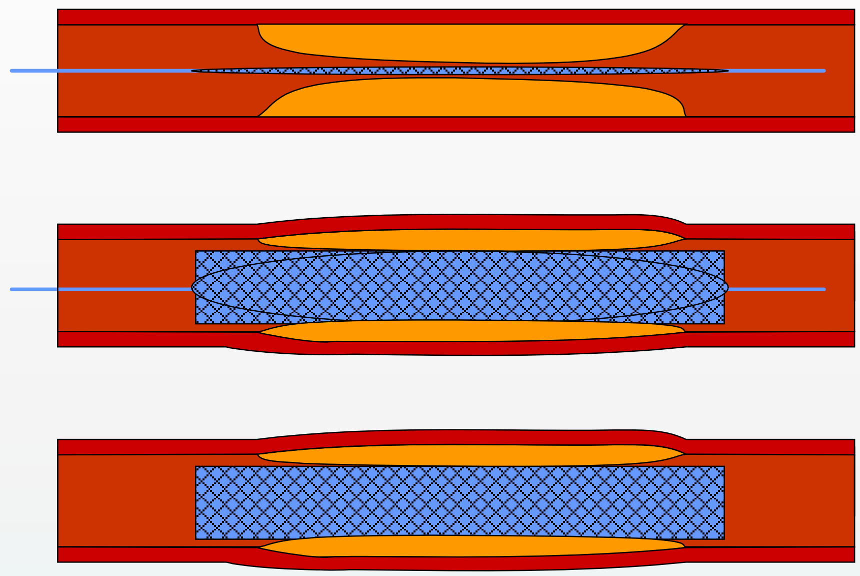
- Dr. Andreas Gruentzig
- The first successful balloon angioplasty in the heart
- in (which year?)
  1977
- in (which country?)
  Switzerland
- Launched a new medical subspecialty - interventional cardiology
- Using catheters with a variety of devices on the tip, to treat heart problems without surgery.

# What is Angioplasty?

- Surgery?

  Non-surgical procedure

- Open blocked heart arteries
- Coronary: The arteries that supply the heart muscle with blood.



Interesting Latin Words:

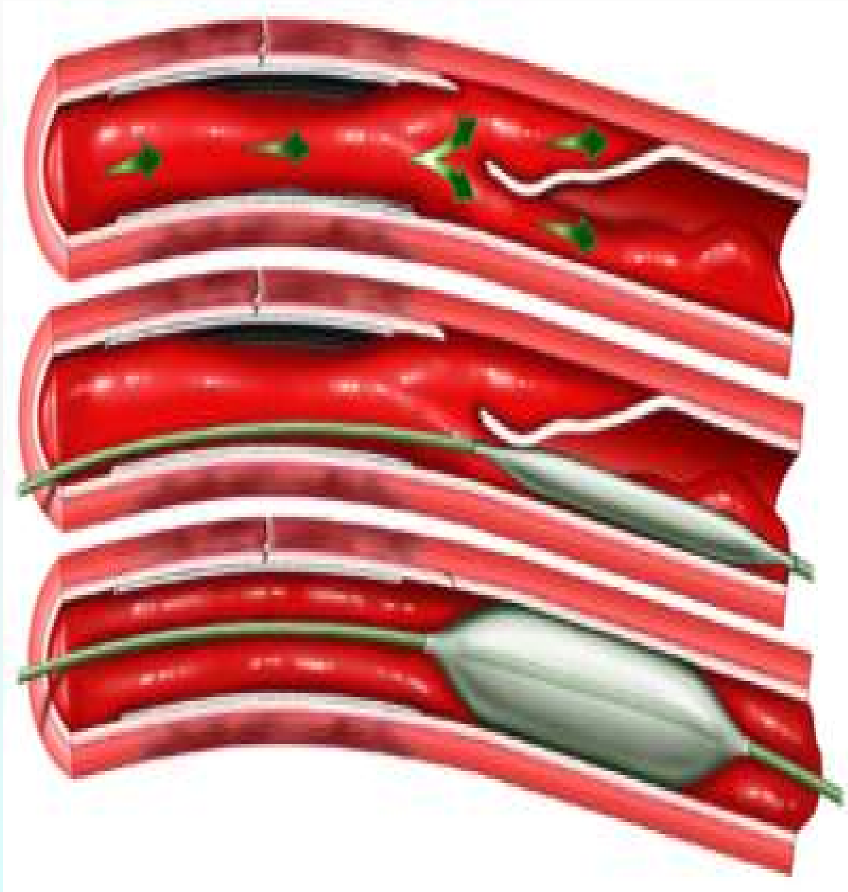
Coronory: crown

Angio: vessel

Plasty: repair

# Balloon Angioplasty

- Guide a catheter with a small balloon tip to the narrowing
- Inflate the balloon
  - Compress the fatty matter into the artery wall
  - Stretch the artery open to increase blood flow to the heart

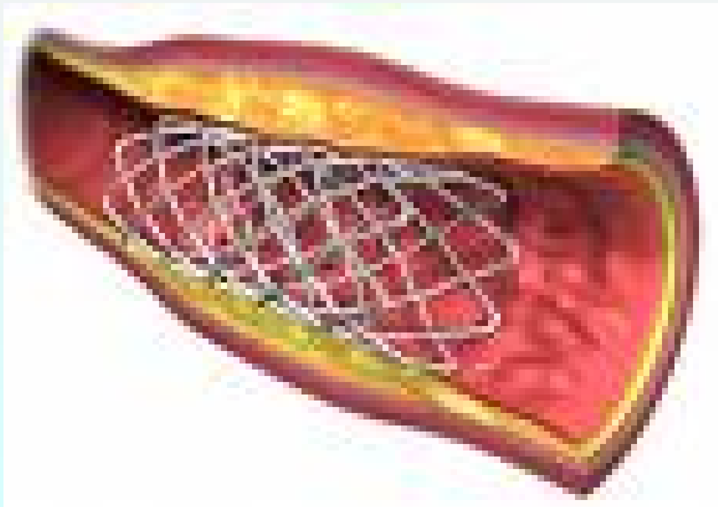


http://www.ehealthmd.com/library/angioplasty/AGO_types.html

# Stent-a Small Metal Mesh Tube

- Inflate the balloon tip
- Expand the stent to the size of the artery to hold it open
- Relate and remove the balloon
- First coronary **stent** was approved in (which year?)

  1993



# Rotoblation

- Guide a special catheter with an acorn-shaped, diamond-coated tip
- The tip spins around at a high speed and grinds away the plaque
- The microscopic particles are washed safely away in your blood stream and filtered out by your liver and spleen
- Hard, calcified plaque

# Atherectomy

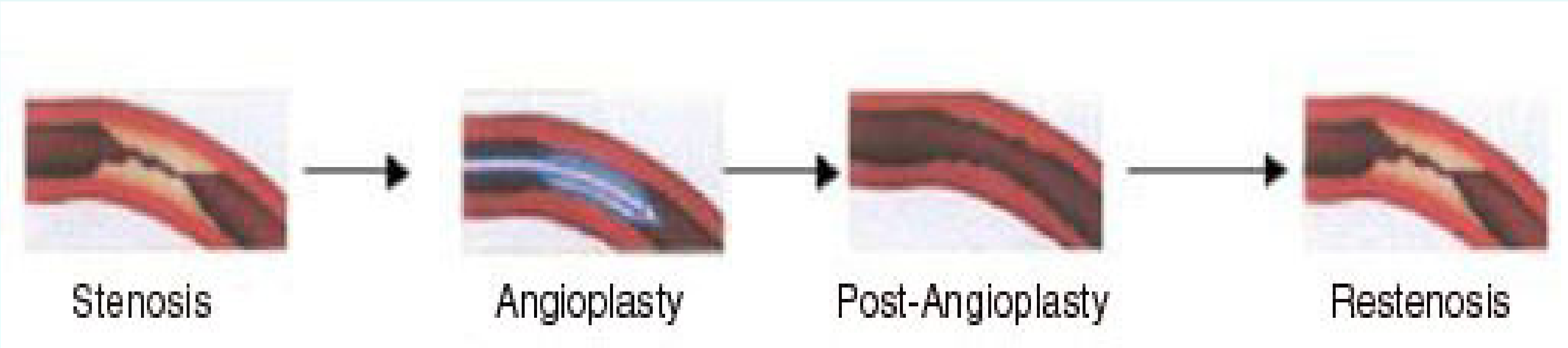
- Catheter has a hollow cylinder on the tip with an open window on one side and a balloon on the other
- Inflate the balloon
- Pushing the window against the fatty matter
- A blade (cutter) within the cylinder rotates and shaves off any fat that protruded into the window. (up to 1,200 revolutions per minute)
- The shavings are caught in a chamber within the catheter and removed.

# Cutting Balloon

- Catheter has a special balloon tip with small blades
- Inflate the balloon
- Small blades score the plaque
- Balloon compresses the fatty matter into the artery wall.
- Laser angioplasty uses laser energy to destroy plaque

# Restenosis

- Gradual re-narrowing of the artery
- Blood clots at or near the site of the treatment.
- Anti-clotting drugs
- Coronary stents coated with anti-clotting drugs



# Why restenosis?

- Walls of the artery may recoil to their original position (hours after angioplasty)

- Angioplasty create tiny cracks in the plaque -> Causes injury to the artery wall
- Body attempts to heal itself
  - Platelets accumulate causes blood clots
  - Thrombin causes cells of artery to multiply and form new tissues

# Angioplasty VS. Bypass Surgery

- Open up the narrowed vessel
- 1-2 days hospital stay
- Local anesthesia
- Chest not opened
- No heart-lung machine
- Death rate ~0.1%
- Successful in 98% patients
- Major complications: 1.5%
- Emergency bypass surgery: 0.1%
- Restenosis – redo the angioplasty next few months

- Create a different blood vessel
- 1-2 weeks
- General anesthesia
- Open chest
- Needs; risk of stroke
- 1% to 2%
- Severe plaques
- Many narrowings in arteries -> higher risk
- Weakly pumping heart

# Angioplasty V.S. Medication

| | **Angioplasty** | **Medication** |
|---|---|---|
| **Rate of deaths, heart attacks and strokes** | **20%** | **19.5%** |
| **Hospitalization rate for heart attacks and worsening chest pain** | **12.4%** | **11.8%** |
| **Hospitalization rate for heart attacks alone** | **13.2%** | **12.3%** |
| Pain free after 5 years | 74% | 72% |
| Initial Cost | ~ $8,000 | ~ $2,700 |

Riskier and no more beneficial than medication

- Drug therapy could account for as much as $1 billion a year in medical savings ($5,000 * 200,000 patients ~ $1,000,000,000)

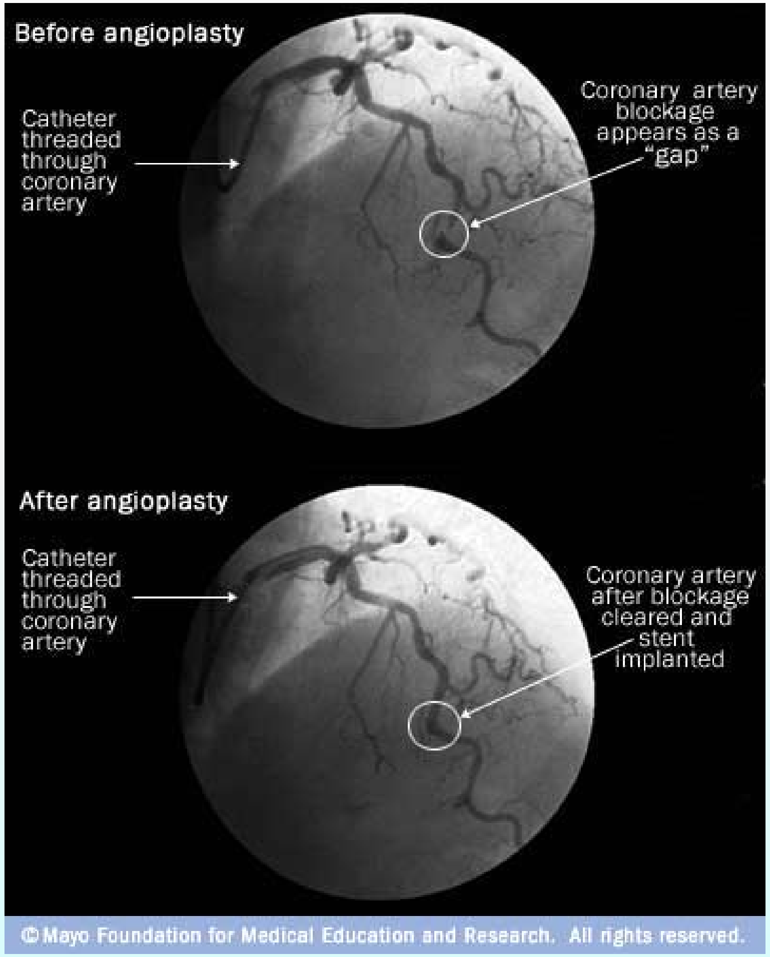
Source: *The New England Journal of Medicine,* March 2007 (2,287 patients)

# Comments from Doctors

- "In low-risk patients with stable coronary artery disease, aggressive lipid-lowering therapy is at least as effective as angioplasty and usual care in reducing the incidence of ischemic events." [4]
- "In this small pilot study, intensive medical therapy and PTCA were comparable at suppressing ischemia in stable patients after AMI. ..Corroboration of these preliminary findings in a larger cardiac-event trial is warranted." [5]

# Who Needs Angioplasty?

- How many blockage
- Where is the blockage
- Extent of the blockage
- Evaluate the last angioplasty
- Assess blood flow

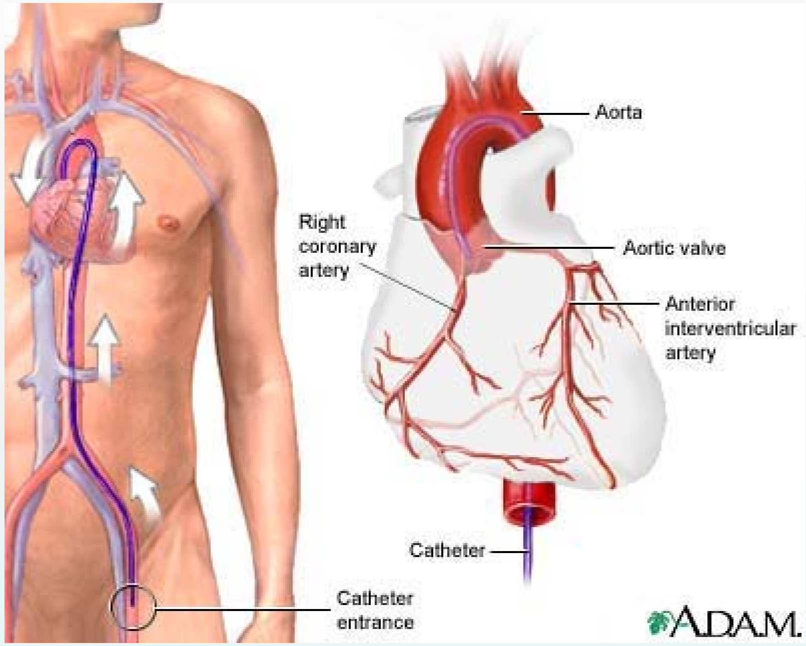


# **Coronary angiogram** (cardiac catheterization)

- Thread a **catheter** through the blood vessels to the heart
- Inject a special contrast **dye** that shows up on x-rays into the arteries
- Take X-ray images
- Look for narrowed areas in the arteries
- Determine how severe the narrowings are

# How to do Angiogram?

- Numb: local anesthesia
- Insert a sheath (a thin plastic tube) into an artery from groin or arm
- Pass a catheter through the sheath and guide up the blood vessel to the arteries surrounding the heart.




http://www.mayoclinic.com/health/coronary-angiography/HB00048

# How to do Angiogram (2)?

- Inject a small amount of contrast material through the catheter
- Photograph as it moves through the heart's chambers, valves, and major vessels
- Tell whether the coronary arteries are narrowed and/or whether the heart valves are working correctly

# Problems of Angiogram

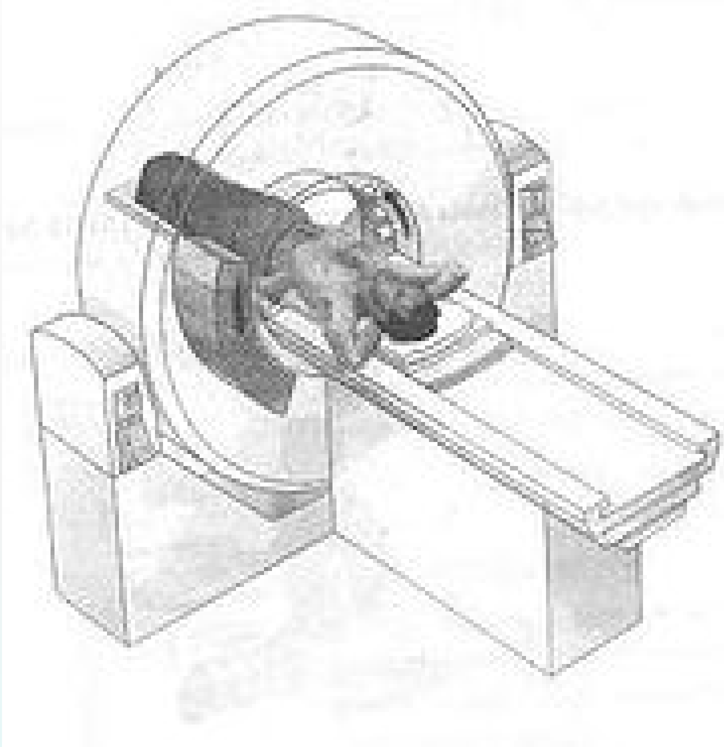
- Potential risks -> stroke; heart attacks
- Allergic to the iodine dyes
- Kidney damage
- Infection
- Trauma to the catheterized arteries
- Radiation exposure from the X-rays

# X-Ray

- Body is made up of various substances with differing densities
- Denser substances (e.g. calcium rich bones) absorb X-ray photons -> film unexposed ->translucent blue
- Lower-density tissues (e.g. fat, skin, organs) -> black part of the film
- Reveal the internal structure of the body on film

# Computerized Tomography (CT)

- An X-ray source rotates around the object
- X-ray sensors are positioned on the opposite side of the circle from the X-ray source
- large series of 2D X-ray images
- 3D image inside of an object



Greek words: Tomography *tomos* (slice) and *graphein* (to write).

# Problems of Cardiac CT Angiography

- Heart is effectively imaged more than once ->a relatively high radiation exposure around 12 mSv
- A chest X-ray: ~0.02 to 0.2 mSv
- Natural background radiation exposure: ~0.01 mSv/day
- 100-600 chest X-rays or over 3 years worth of natural background radiation

# Angiogram -> ??

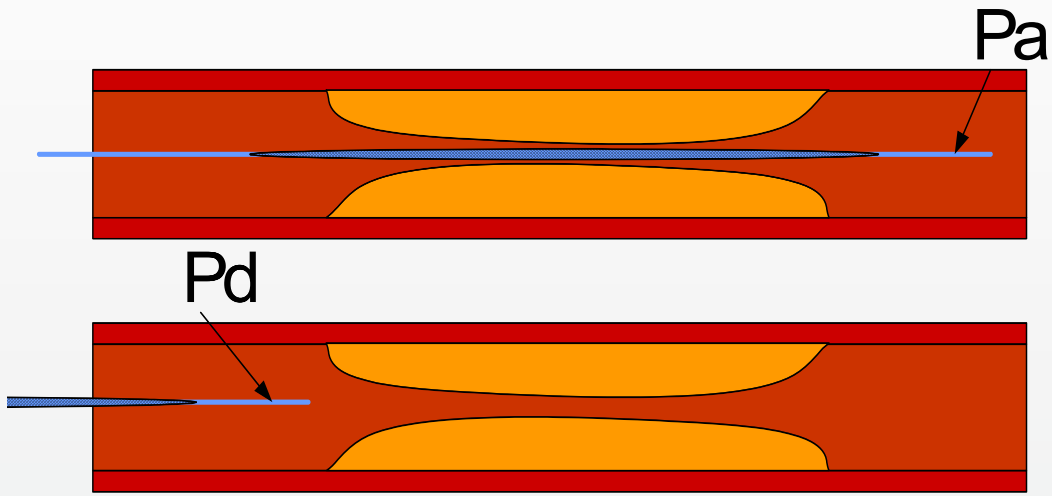
**Angiogram**

- Not always clear to decide which narrowing is the culprit lesion
- May underestimate or overestimate narrowing

**??**

- Account collateral flow
- Functional evaluation

# Fractional Flow Reserve (FFR)




FFR= Pd/Pa

✓ *Pd* = pressure behind (distal to) a stenosis

✓ Pa = pressure before the stenosis

# FFR

- http://www.youtube.com/watch?v=xTaz-OkJPoo

# Abnormal?

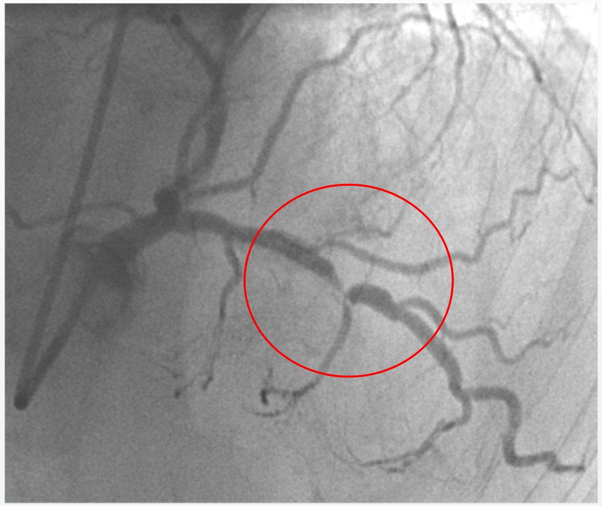
- Maximal flow down a vessel in the presence of a stenosis compared to the maximal flow in the hypothetical absence of the stenosis
- No absolute cut-off point
- Cut-off point: 0.75-0.80

# St. Jude’s hydrophilic PressureWire® Certus

- http://www.youtube.com/watch?v=DM-L5m9d_20 (sensor)
- http://www.youtube.com/watch?v=fi37C9rq0nw (pressurewire 8)
- http://www.youtube.com/watch?v=SgCkKJpVSd8 (insertion of the sensor)
- http://www.youtube.com/watch?v=OaTOj8Ct3Pk (pullback)
- http://www.youtube.com/watch?v=Luq62Mt8rH8 (the stent placement)

# Coronary Artery Disease (CAD)

- 14 million patients
- $100 Billion annually



- Percutaneous Coronary Intervention (PCI)
  - Angioplasty with or without stent (90%)
  - Over 1 million/year
  - $8 billion/year

# CAD: PCI vs Medical Therapy

- PCI Limitations
  - Not helpful if stenosis is <40%
  - Expense
  - Renarrowing or occlusion

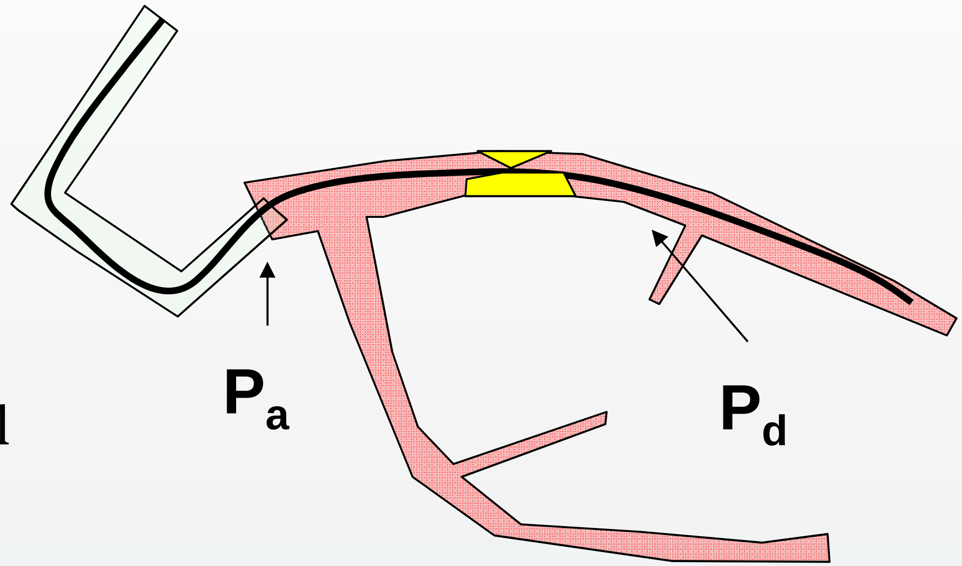
- Medicines often effective
  - Many PCIs may not be needed
  - Medical savings: $2.1 Billion

- Intermediate Lesions may not be responsible for symptoms
  - Proceed with PCI

    vs
  - Determine coronary blood flow (FFR)

# Fractional Flow Reserve (FFR)

- Means of determining coronary blood flow
- Defined as the pressure before a stenosis divided by the pressure beyond a stenosis during maximal dilation of the artery
- Current Market: $600 million/year
  - St. Jude; Volcano
  - Clinical adoption ~10%
    - Wire expense
    - Device delivery




- Fractional flow reserve (FFR) = $P_d/P_a$
  - $P_d$ = blood pressure beyond stenosis
  - $P_a$ = blood pressure before stenosis
- Abnormal FFR < 0.75

The NEW ENGLAND JOURNAL of MEDICINE

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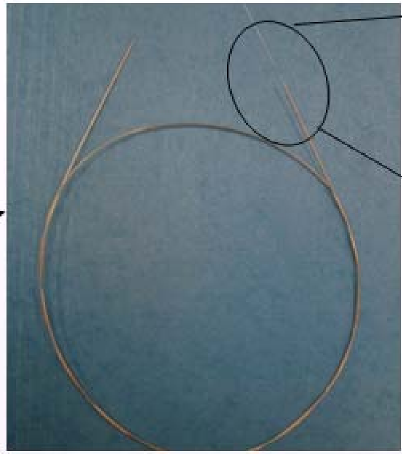
# Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention

- FFR-guided approach reduces
  - Number of stents deployed
  - Procedural expense
  - Death/myocardial infarction (MI)
- Optical sensor guidewire
  - Decreased expense
  - Improved steerability

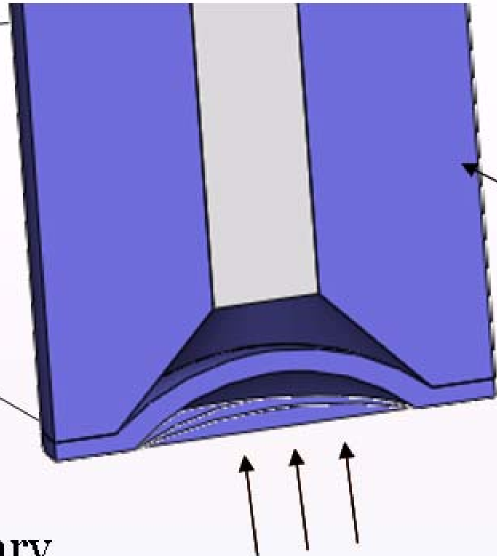
# FAME Trials

- http://www.youtube.com/watch?v=yLfW5k7v2yk

# UML Optical Pressure Sensor



Standard guidewire
OD: 356µm
ID: 254 µm



Our sensor
OD: 125µm

UML proprietary

**Cross-Campus Development and Commercialization Team:**

| | | | |
|---|---|---|---|
| Xingwei Wang, PhD | UML | Principal Investigator | Sensor Fabrication |
| Kurt Barringhaus, MD | UMMS | Principal Investigator | Animal/Human Testing |
| Jill Murthi, et al | UML | CVIP Office | Tech Transfer, IP |
| Effraim Herskovic | UMass | President's Office | Commercialization |

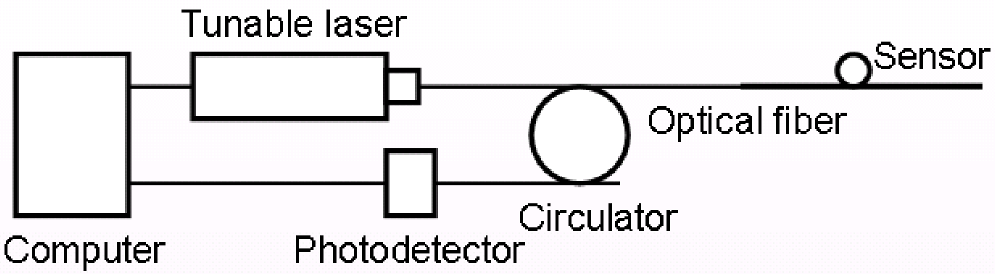
# Commercialization Strategy

| | Yr1 (09) | Yr2 (10) | Yr3 (11) | Yr4 (12) |
|---|---|---|---|---|
| Sensor fabrication | | | | |
| Sensor lab test | | | | |
| Animal/clinical test | | | | |
| Sensor packaging | | | | |
| FDA submission (510K) | | | | |

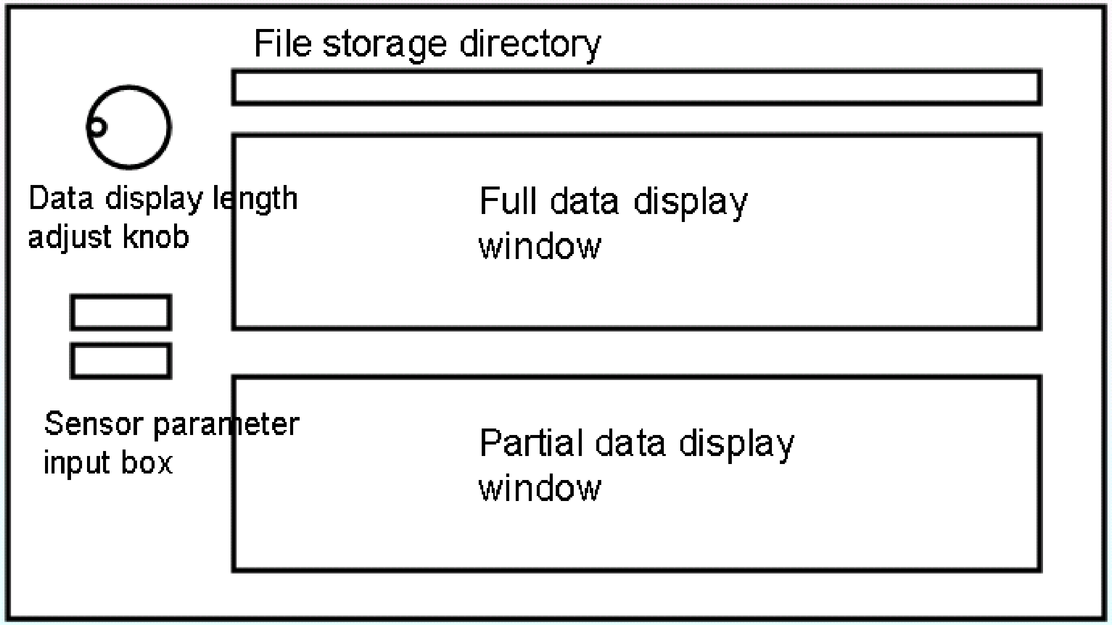
- Proposed CVIP work – Phase I (accomplished) Proposed CVIP work – Phase II (2011)
- Future work

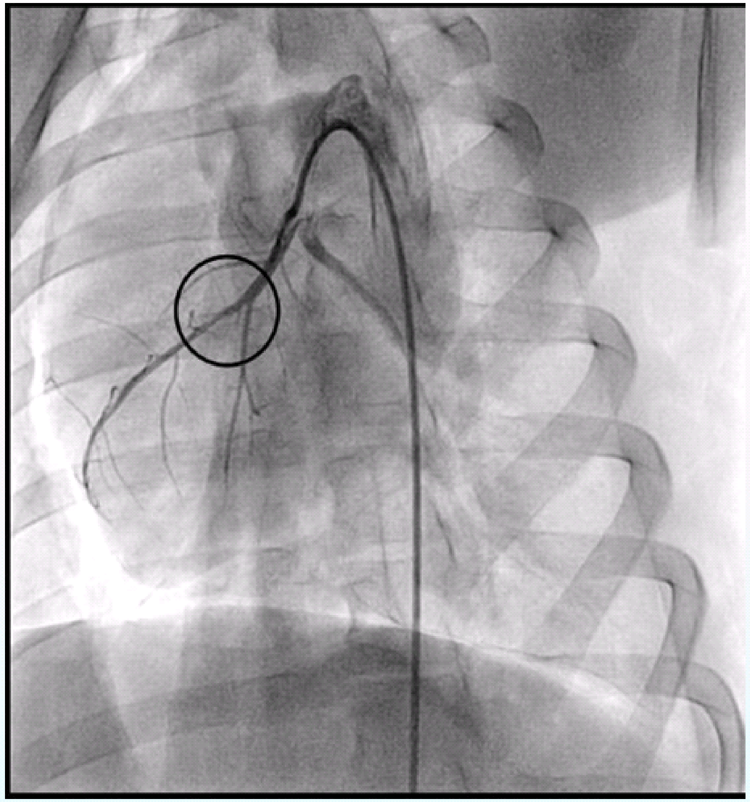
- Initial estimated market penetration: 10%
- Annual Sales: $60 million/year for the first 2 years
- IP: PCT International Application, PCT/US10/40460 (29 June 2010)
- No other affordable optical sensors available

# Optical Fiber: Proof of Concept



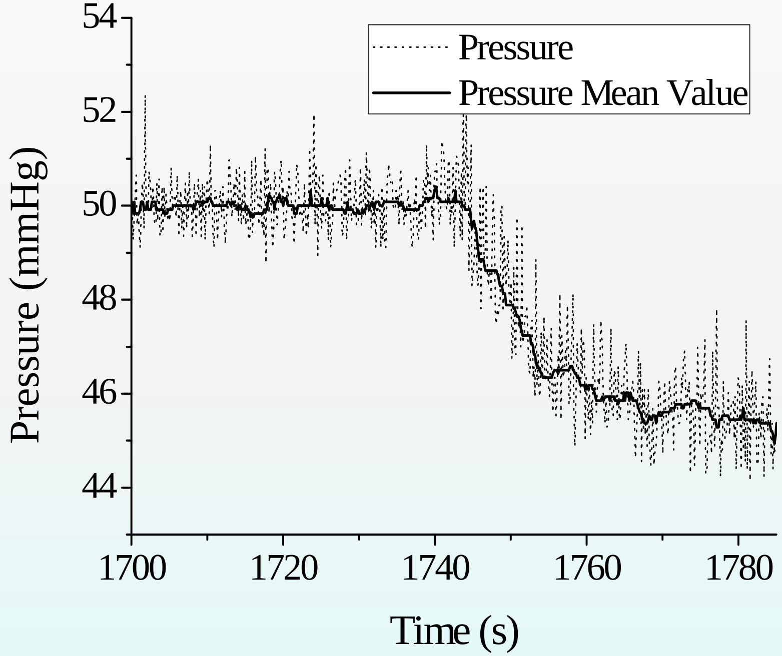

Schematic diagram of experiment setup.

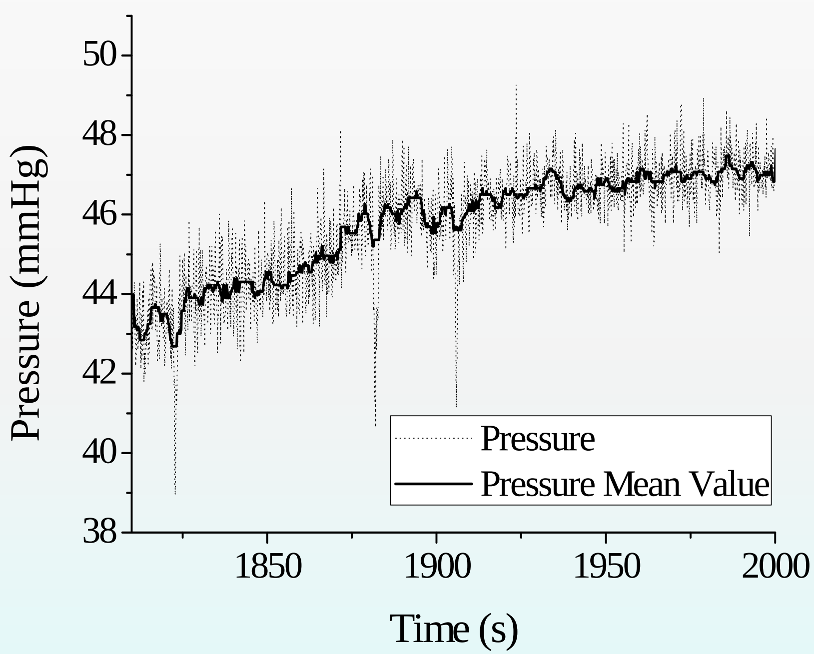


Coronary angiography following introduction of the UML fiber pressure sensor into the LAD.

# UML Optical Sensor Identifies Coronary Stenosis-Induced Arterial Pressure Gradient

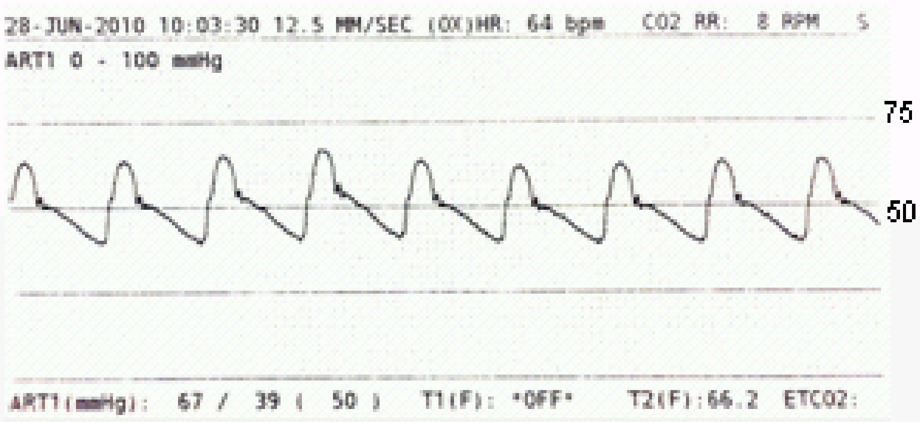


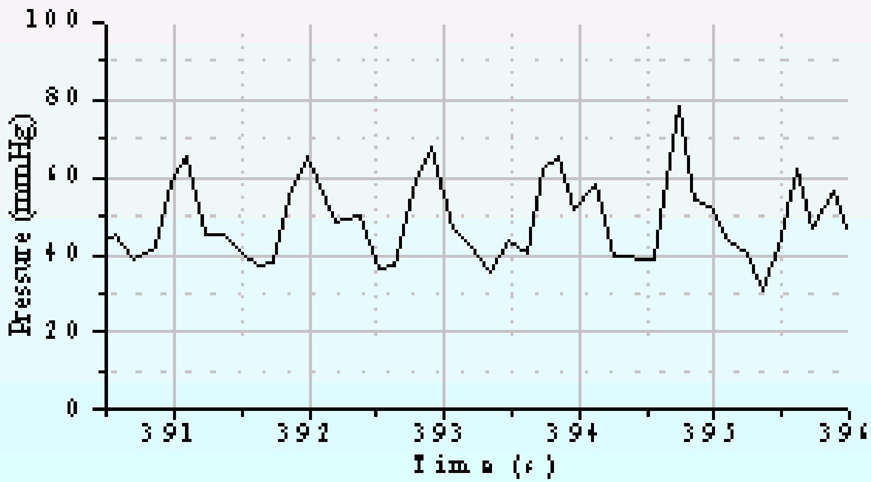

Pressure measured by UML pressure sensor decreased from 50 mmHg to 45 mmHg, caused by complete occlusion of coronary vessel.

Blood pressure measured by UML sensor increased gradually following partial deflation with resolution of the occlusion.

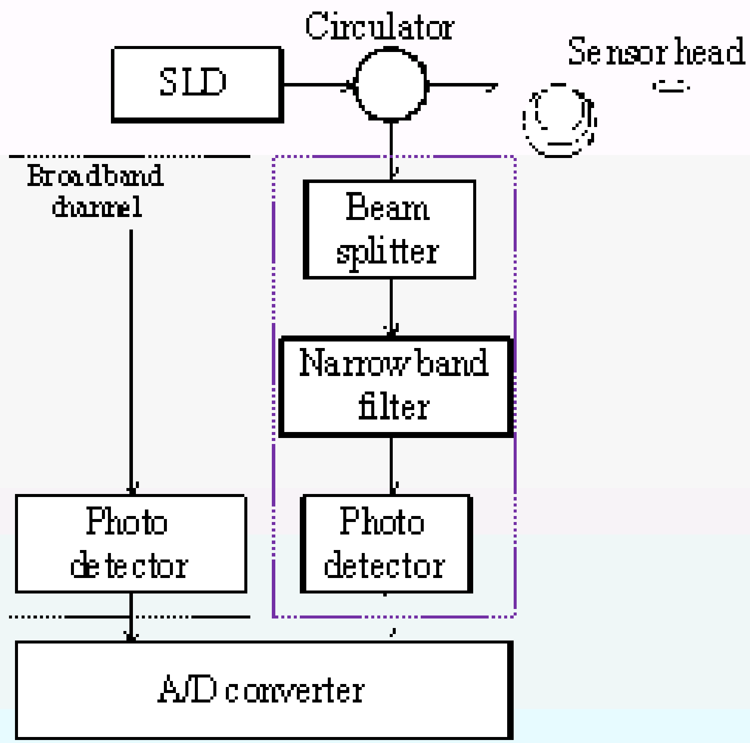
# UML Optical Sensor Accurately Reflects Systolic and Diastolic Blood Pressure




Catheter transducer: 67/39

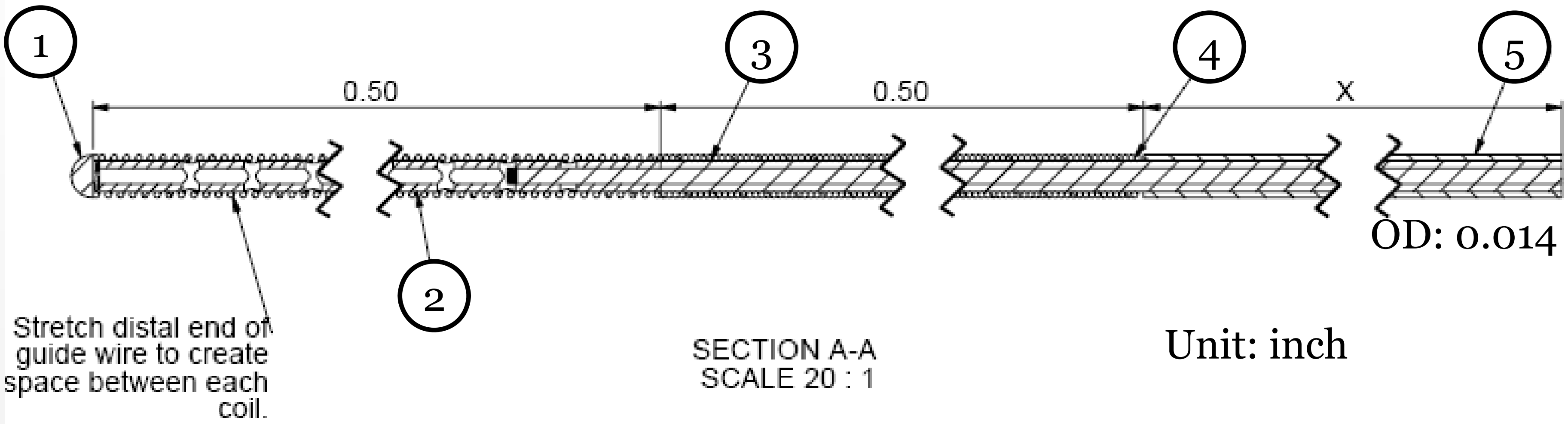


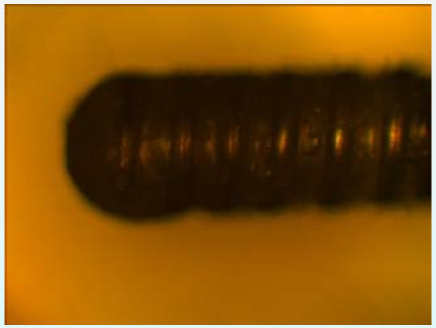

Optical sensor: 65/38




SCIIB system schematic

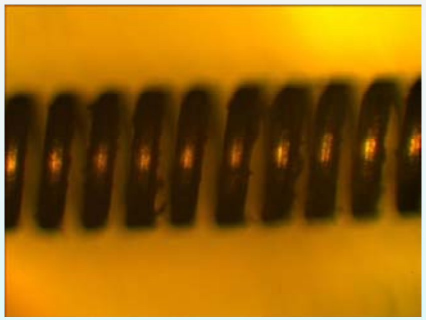
# Sensor Packaging Design



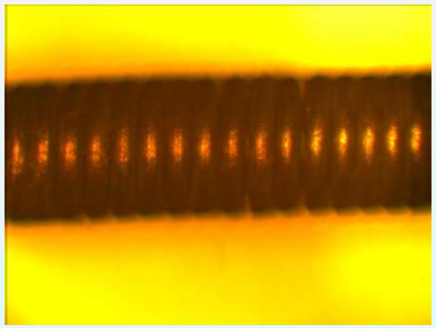
1

Biocompatible epoxy bead



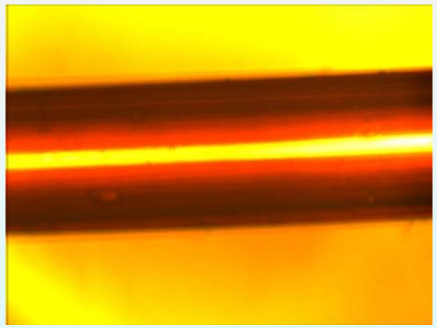
2

Stretched stainless steel coil



3 4

Unstretched stainless steel coil



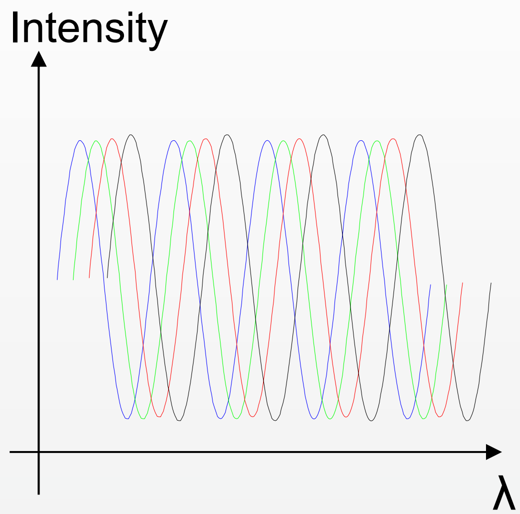
5

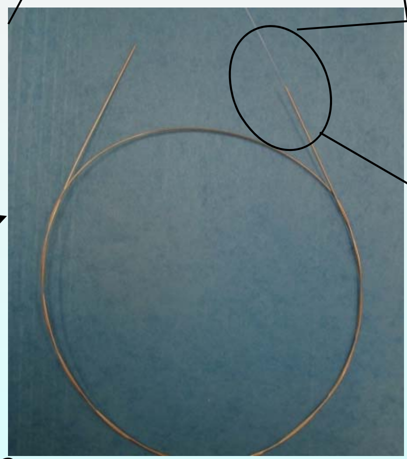
Kapton tube

# Summary

- UML optical sensor will advance care of patients with coronary artery disease in a cost-conscious manner
- Wire and system refinements are planned but preclinical studies require additional support
- Results from preclinical studies will set the stage for clinical studies and FDA approval
- Expansion into other clinical environments and take advantage of the optical sensor's superior accuracy and resistance to electromagnetic interference

# UML Optical Pressure Sensor



Standard guidewire
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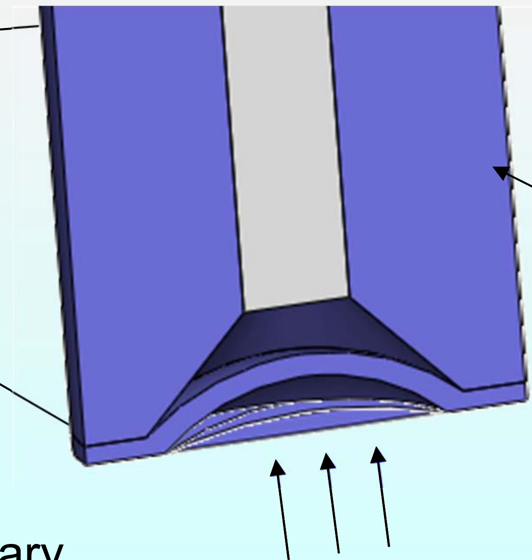


Our sensor
OD: 125µm

UML proprietary

# Advantages of UML Sensor

| **UML Sensor** | **PressureWire® (RADI Medical Systems, Sweden)** |
|---|---|
| Optical | Electrical |
| Immune to EMI | Susceptible to EMI |
| Biocompatible material | Electrical wires inside the patient body |
| ~ $50 | ~ $600 |
| 0.1 mmHg resolution | 1-2 mmHg resolution |
| Drift TBD<br>Hysteresis: 0.53%; Repeatability: 1.04% | 1.5-3.0% drift |

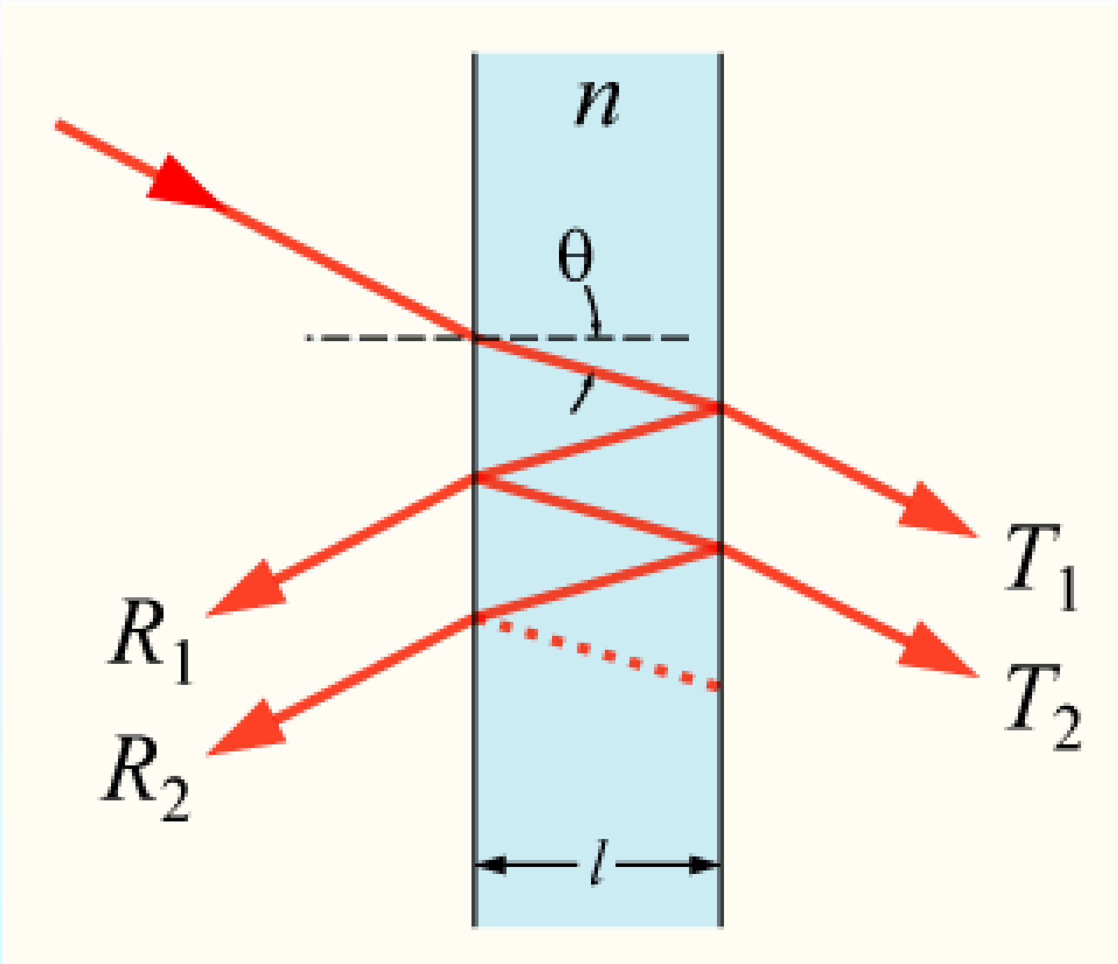
# Market Estimation

- Initial market thrust: angioplasty
  - **$8 billion/year**
- MicroMedical Group Inc. expects
  - Pressure sensor: **$60 million market**
    - $50/sensor*1.2 million patients
  - First 2 yrs: market penetration of 10%
  - Sales: ~ **$6 million** annually
- Cardiologists acceptance
- No affordable optical sensor available

# Can These Procedures Cure Coronary Artery Disease?

- Operation: 1.5-2.5 hours
- Preparation and recovery: several hours
- Several weeks for arteries heal (stent)
- Rarely used: Rotoblation; atherectomy; cutting ballon.
- Cure coronary artery disease?
  - ✓Will not cure.
  - ✓Lifestyle factors: smoking and diet
  - ✓An exercise program

# Fabry-Perot interferometer

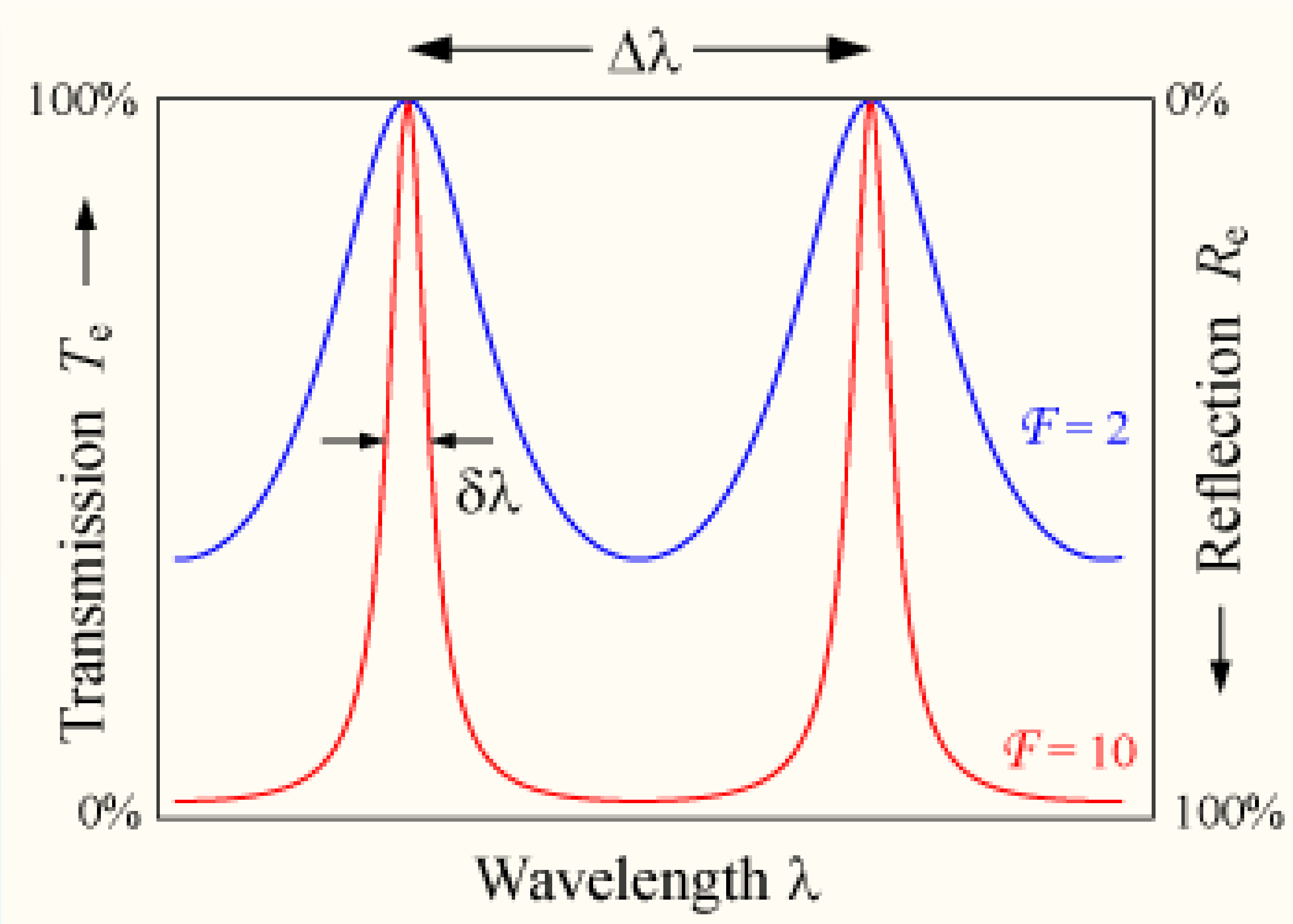


# EFPI

- The required sensing length may be reduced by having the light double back through multiple reflections along its propagation path.
- The use of a single-cavity extrinsic Fabry–Pérot interferometer (EFPI) as a guided-wave/bulk-biomaterial interaction biosensor.

J. L. Elster, M. E. Jones, M. K. Evans, S. M. Lenahan, C. A. Boyce, W. Velander, and R. VanTassell, “Optical fiber extrinsic Fabry–Pérot interferometric (EFPI)-based biosensors,” *SPIE*, vol. 3911, pp. 105–112,2000.

# Spectrum



Δλ
100%
0%
0%
100%
Transmission $T_e$
Reflection $R_e$
δλ
$\mathcal{F} = 2$
$\mathcal{F} = 10$
Wavelength λ

# Transmission

- Maximum transmission occurs when the optical path difference (OPD=2$nl$ cos $\theta$) between each transmitted beam is an integer multiple of the wavelength

$$\delta = \left(\frac{2\pi}{\lambda}\right) 2nl\cos\theta$$

$$Te = \frac{(1-R)^2}{1+R^2-2R\cos(\delta)}$$

# FP biosensor

- Biomolecule attachment
- OPD change
- Spectrum demodulation

# Reference

- **X. Wang**, K. Cooper, A. Wang, J. Xu, Z. Wang, Y. Zhang, and Z. Tu, "Label-free DNA detection on the surface of silica optical fiber tip". *Appl. Phys. Lett*. Vol. **89**, 163901 (October 2006).

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- [1] http://www.redwoodeditor.com/content/SCAI/scai/
- [2] Tonino PA, De Bruyne B, Pijls NH, *et al* (January 2009). "Fractional flow reserve versus angiography for guiding percutaneous coronary intervention". *N. Engl. J. Med.* 360 (3): 213–24. doi:10.1056/NEJMoa0807611. PMID 19144937.
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- [4] Habib A. Dakik, MD; Neal S. Kleiman, MD; John A. Farmer, MD; Zuo-Xiang He, MD; Juliet A. Wendt, MD; Craig M. Pratt, MD; Mario S. Verani, MD; John J. Mahmarian, MD, (*Circulation*. 1998;98:2017-2023.) © 1998 American Heart Association, Inc. "Intensive Medical Therapy Versus Coronary Angioplasty for Suppression of Myocardial Ischemia in Survivors of Acute Myocardial Infarction - A Prospective, Randomized Pilot Study", Presented in part at the 46th Scientific Sessions of the American College of Cardiology, Anaheim, Calif, March 17, 1997 and published in abstract form (*J Am Coll Cardiol*. 1997;29(suppl A):53A.