Disposable Miniature Pressure Sensor for Cardiologist Use

Xingwei Wang

Department of Electrical and Computer Engineering
University of Massachusetts Lowell

Xingwei_Wang@uml.edu
(978) 934-1981
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:
- Coronary: 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

<table>
<thead>
<tr>
<th></th>
<th>Angioplasty</th>
<th>Medication</th>
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<tbody>
<tr>
<td>Rate of deaths, heart attacks and strokes</td>
<td>20%</td>
<td>19.5%</td>
</tr>
<tr>
<td>Hospitalization rate for heart attacks and worsening chest pain</td>
<td>12.4%</td>
<td>11.8%</td>
</tr>
<tr>
<td>Hospitalization rate for heart attacks alone</td>
<td>13.2%</td>
<td>12.3%</td>
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<tr>
<td>Pain free after 5 years</td>
<td>74%</td>
<td>72%</td>
</tr>
<tr>
<td>Initial Cost</td>
<td>~ $8,000</td>
<td>~ $2,700</td>
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</table>

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)

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 *tomas* (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

- 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)

\[ FFR = \frac{P_d}{P_a} \]

- \( P_d \) = pressure behind (distal to) a stenosis
- \( P_a \) = pressure before the stenosis

\checkmark P_d = \text{pressure behind (distal to) a stenosis}
\checkmark P_a = \text{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
  - 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
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:

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Role</th>
<th>Responsibility</th>
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<tbody>
<tr>
<td>Xingwei Wang, PhD</td>
<td>UML</td>
<td>Principal Investigator</td>
<td>Sensor Fabrication</td>
</tr>
<tr>
<td>Kurt Barringhaus, MD</td>
<td>UMMS</td>
<td>Principal Investigator</td>
<td>Animal/Human Testing</td>
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<tr>
<td>Jill Murthi, et al</td>
<td>UML</td>
<td>CVIP Office</td>
<td>Tech Transfer, IP</td>
</tr>
<tr>
<td>Effraim Herskovic</td>
<td>UMass</td>
<td>President’s Office</td>
<td>Commercialization</td>
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# Commercialization Strategy

<table>
<thead>
<tr>
<th></th>
<th>Yr1 (09)</th>
<th>Yr2 (10)</th>
<th>Yr3 (11)</th>
<th>Yr4 (12)</th>
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<tbody>
<tr>
<td>Sensor fabrication</td>
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<tr>
<td>Sensor lab test</td>
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<tr>
<td>Animal/clinical test</td>
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<tr>
<td>Sensor packaging</td>
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<tr>
<td>FDA submission (510K)</td>
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- 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. Unstretched stainless steel coil
4. Kapton tube

Stretch distal end of guide wire to create space between each coil.

Unit: inch

OD: 0.014

SECTION A-A SCALE 20 : 1
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
OD: 356μm
ID: 254 μm

Our sensor
OD: 125μm

UML proprietary
### Advantages of UML Sensor

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

Spectrum
Transmission

- Maximum transmission occurs when the optical path difference (OPD=2nl cos θ) 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
References

