Molecular Imaging for Atherosclerosis

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Why is Molecular Imaging Necessary?

- Biomarkers
  - LDL is not the whole story
- Imaging
  - Normal stress test does not mean no risk
  - CT angiogram
  - Angiogram = luminogram
- Genetics
  - How much did the human genome project cost?

Cardiovascular Experimental Imaging and Therapeutics (CVEIT)

Molecular Imaging of Atherosclerosis

- See it
  - Early detection of disease state
- Measure it
  - Measuring burden of disease
  - Imaging biopsy
  - Alternative to MACE
- Treat it
  - And measure it again
  - Response to therapy

Molecular Imaging

- State of the art of invasive molecular imaging of atherosclerosis

- Technical challenges for existing technologies

- Role of nanotechnologies and software to extend our vision to a cellular level

- Directions for technology development.

Development of Molecular Imaging Technologies

Imaging technologies
– Conventional and novel
– Limited to extending existing imaging sources and combining with other modalities
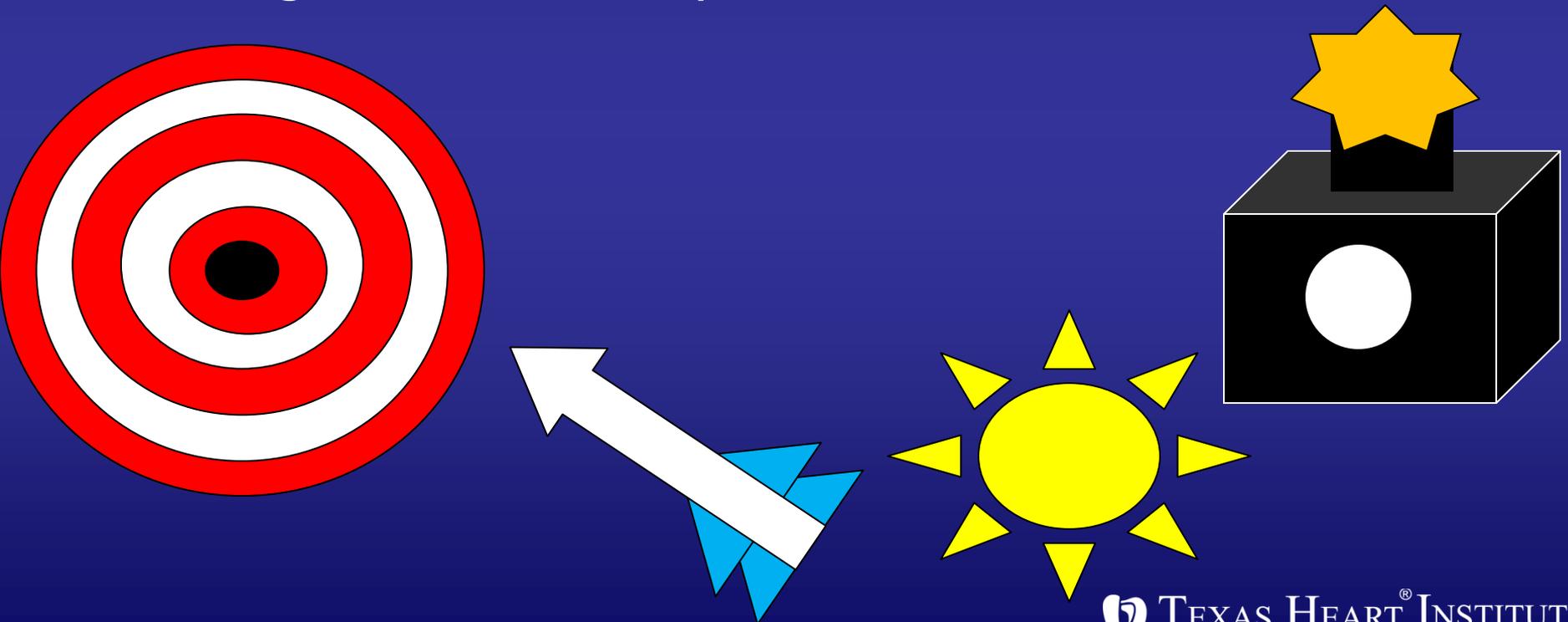
Nanotechnologies
– Extend the vision of conventional imaging
– Dependent on tissue of interest and technically challenging

Software development
– Processing and image acquisition
– Post processing for reconstruction and interfacing for interpretation

4 Components of Molecular Imaging

- Imaging modality- visualization tool/camera
- Imaging energy source- attached to targeting vehicle
- Targeting vehicle- antibodies, ligands, nanoparticles
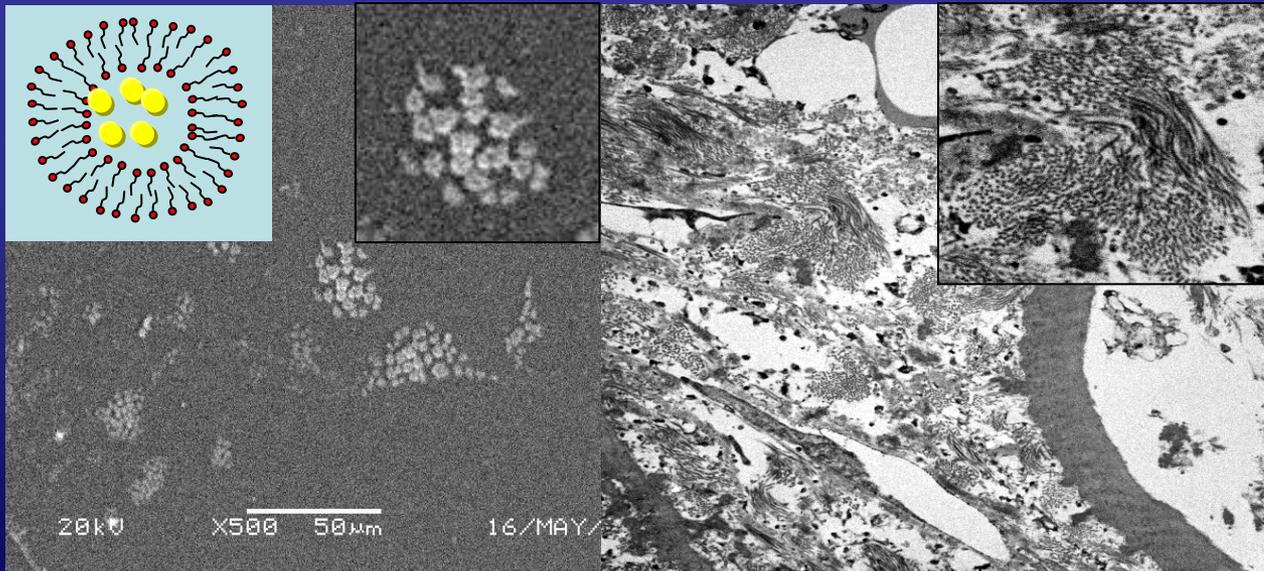- Target of interest- myocardium, lumen

Targets for Atherosclerosis

Sanz J, Fayad ZA. Imaging of atherosclerotic cardiovascular disease. Nature 2008;451:953–957.
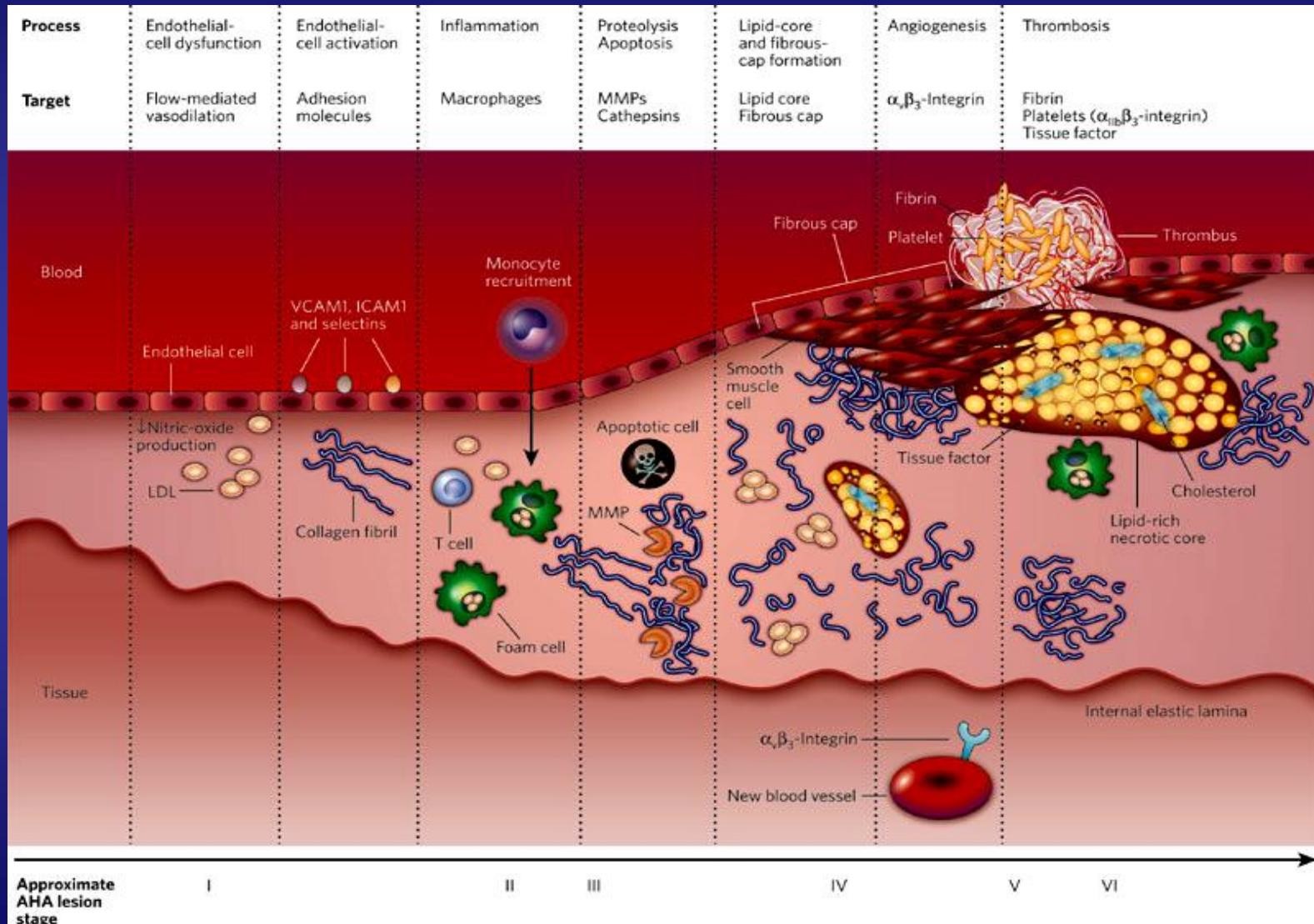
Molecular Targeting Vehicles

<u>Limitations</u>
- Exposure to blood pool
- Metabolism and pharmacokinetics
- Shear stress of blood flow
- Volume of agent- intravenous vs arterial

Walton et al. Vasc Med 2010 Aug;15(4):307-13

TEXAS HEART® INSTITUTE
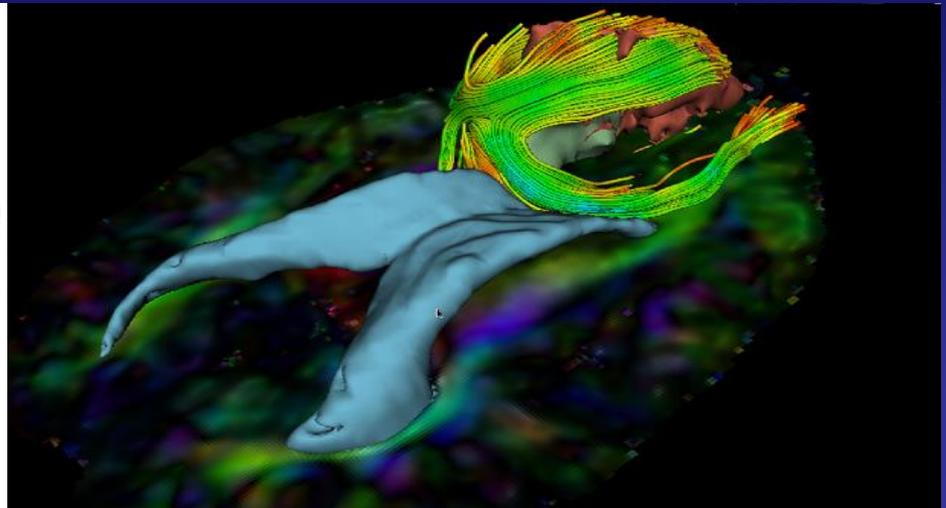*at St. Luke's Episcopal Hospital*

Liposomes for Molecular Imaging
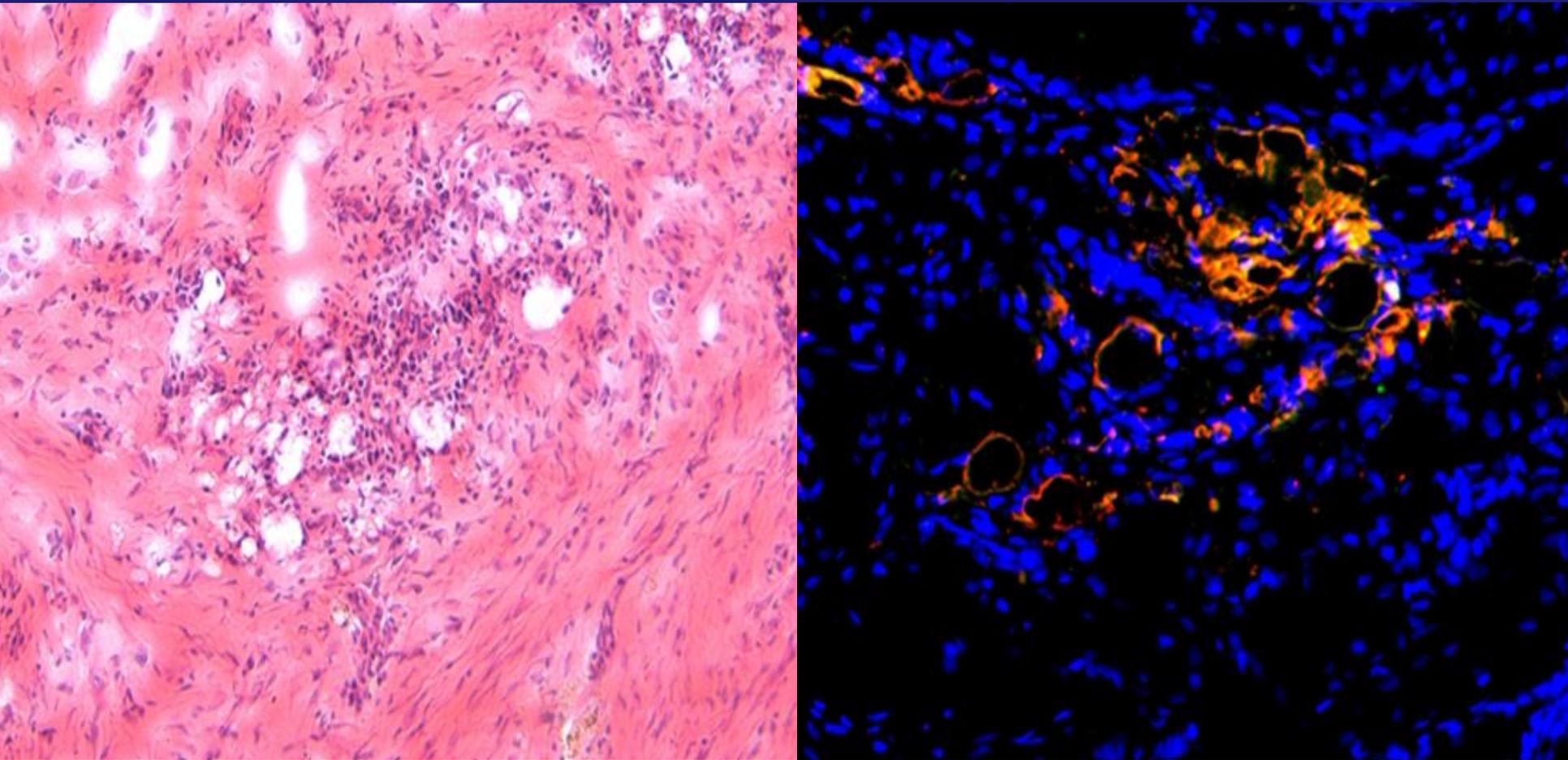
In vivo delivery of Alexa555 siRNA labeled nanoparticles. X200 magnification Blue: Hoescht Red: Alexa555
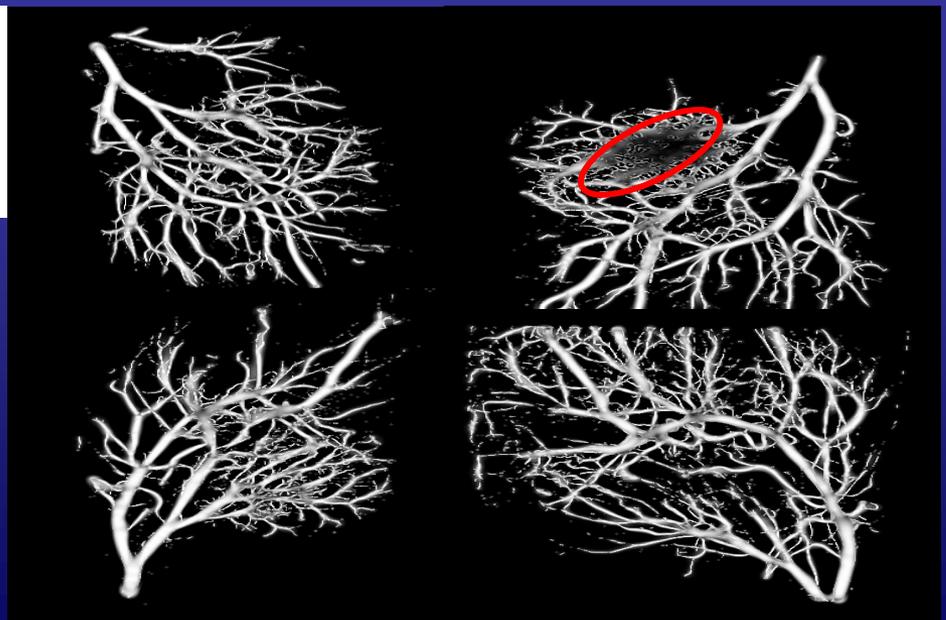
TEXAS HEART® INSTITUTE
at St. Luke's Episcopal Hospital

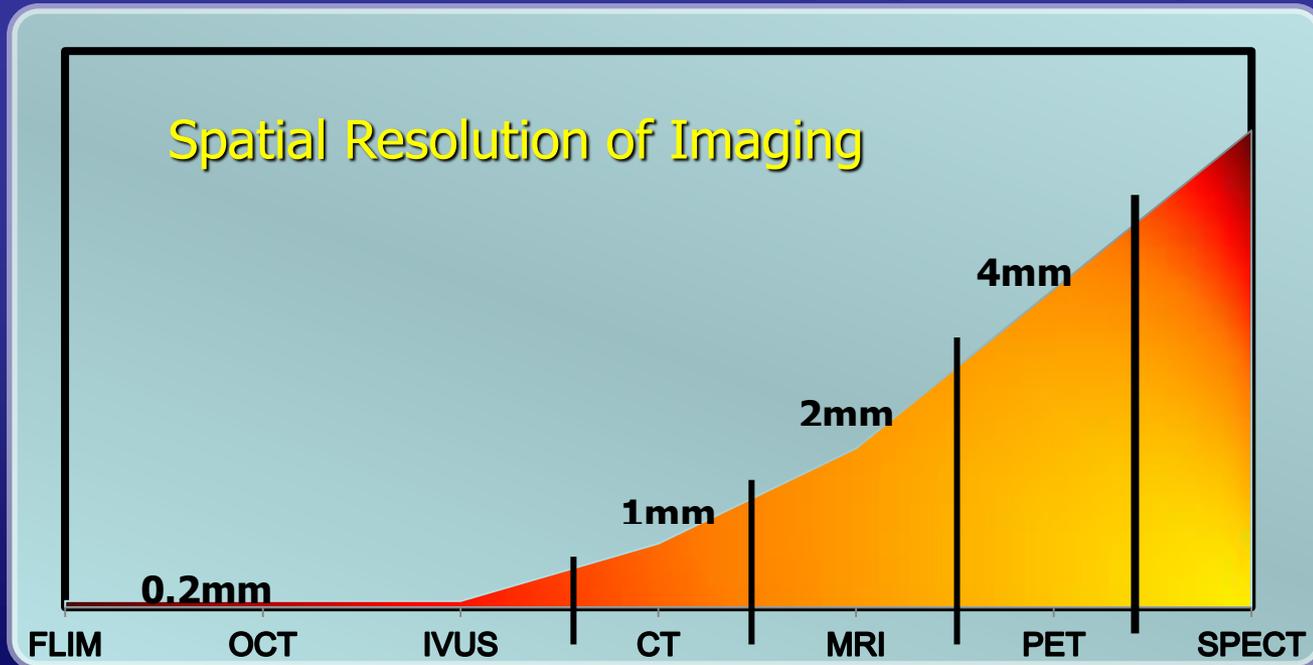# Software Technologies

MATLAB
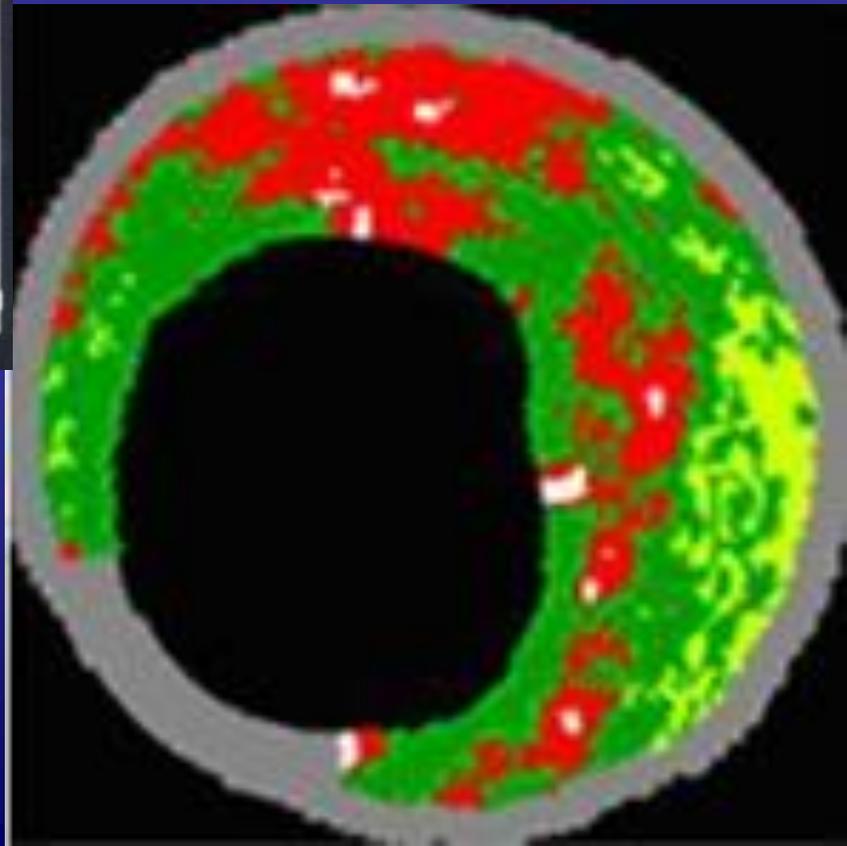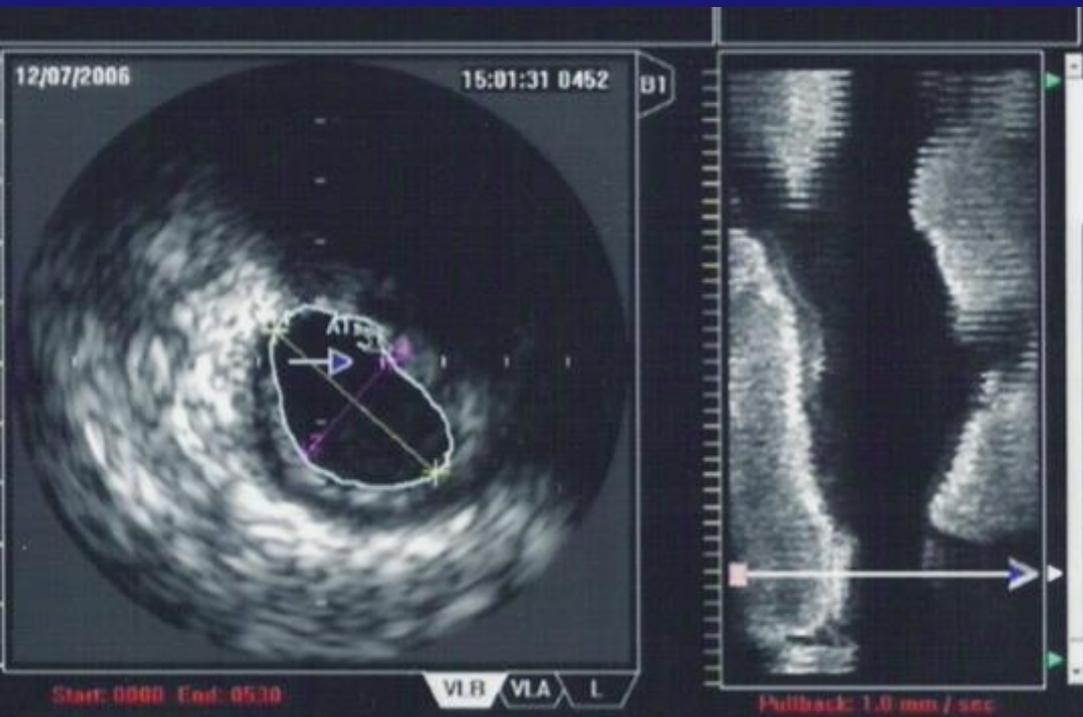
Yuan et al presented at ACC 2011

Imaging Modalities

- <u>Invasive</u>
  - Intravascular ultrasound (IVUS)
  - Optical coherence tomography (OCT)
  - Near-infrared (NIR)
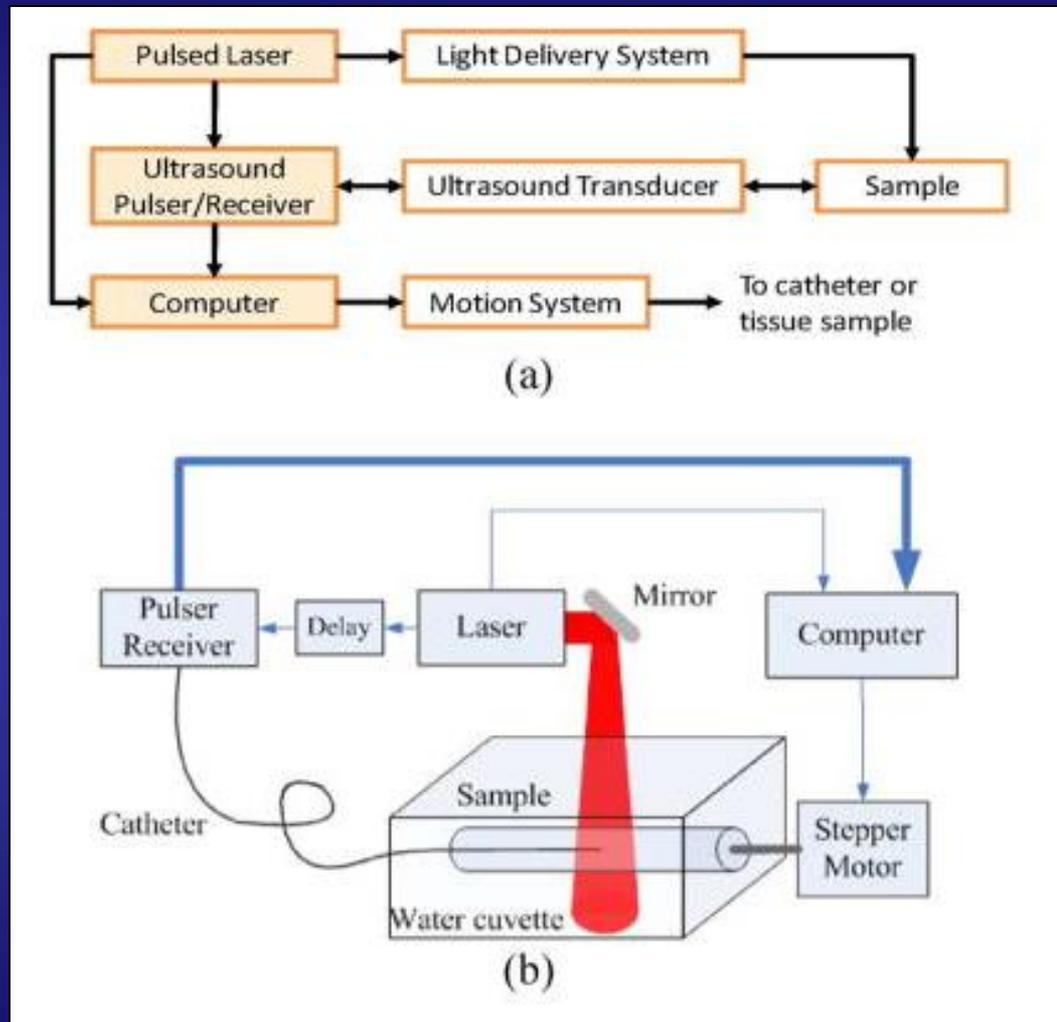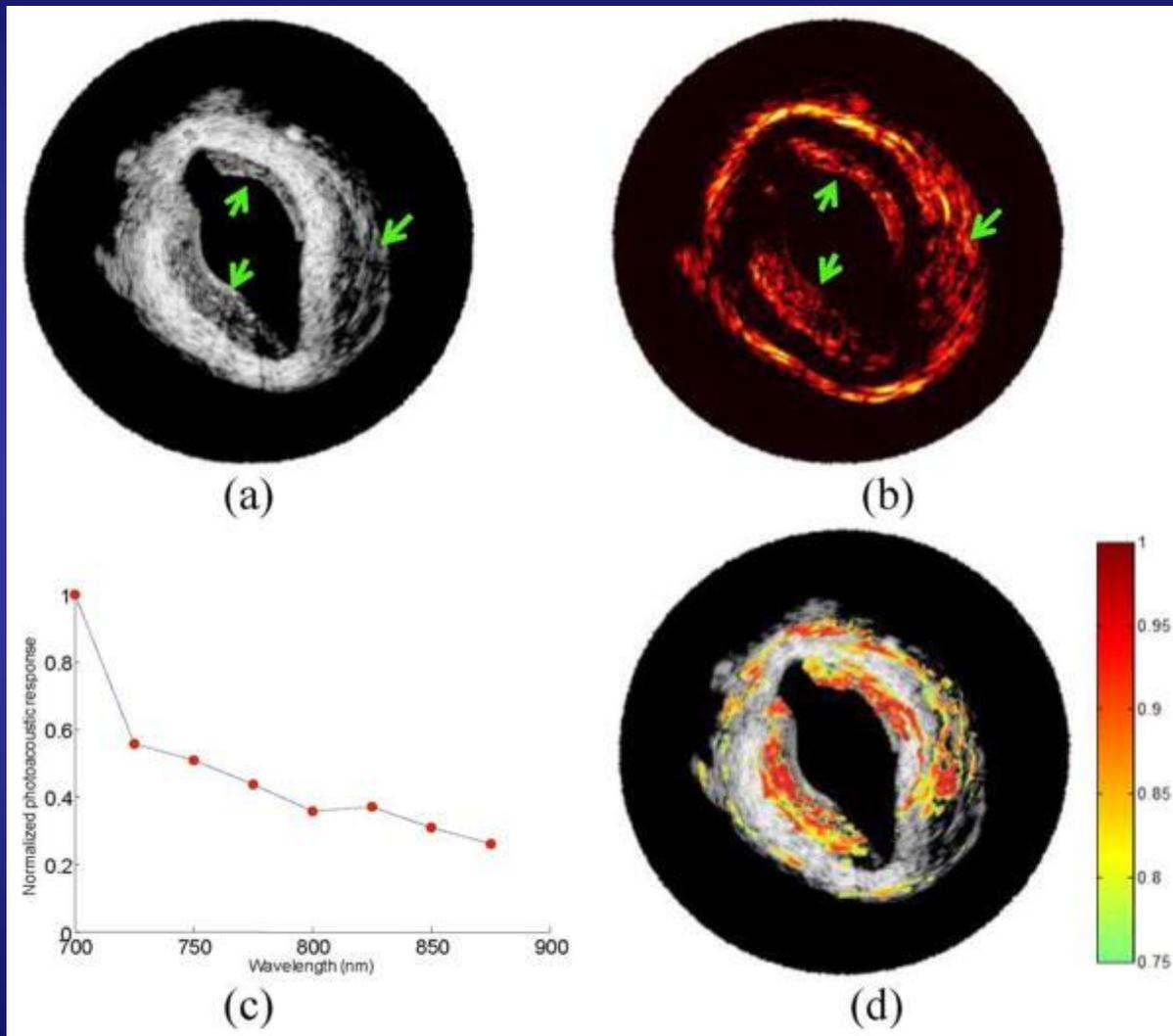 - Flourescence lifetime imaging module (FLIM)

Spatial Resolution of Imaging

FLIM	OCT	IVUS	CT	MRI	PET	SPECT

0.2mm   1mm   2mm   4mm

Invasive Molecular Imaging - IVUS

IVUS with Virtual Histology

IVUS/IVPA

Invasive Molecular Imaging

Near Infrared Lipid Imaging
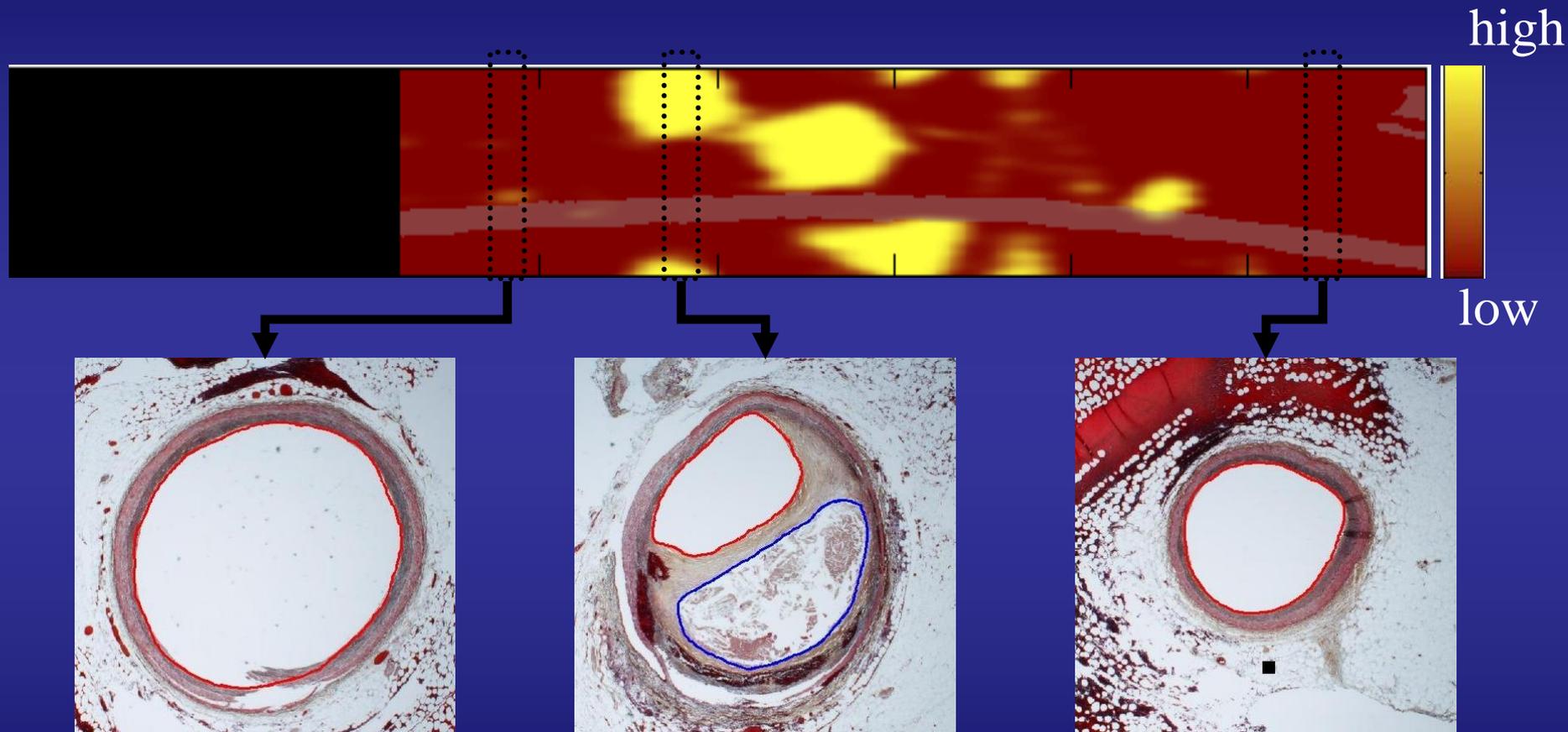

- LipiScan by InfraReDx
- FDA approved
- NIR imaging coupled with IVUS (40 MHz rotational catheter)
- Spectra processed by algorithm and displayed as image of lipid core plaque.
- 3.2 F monorail catheter with scanning laser
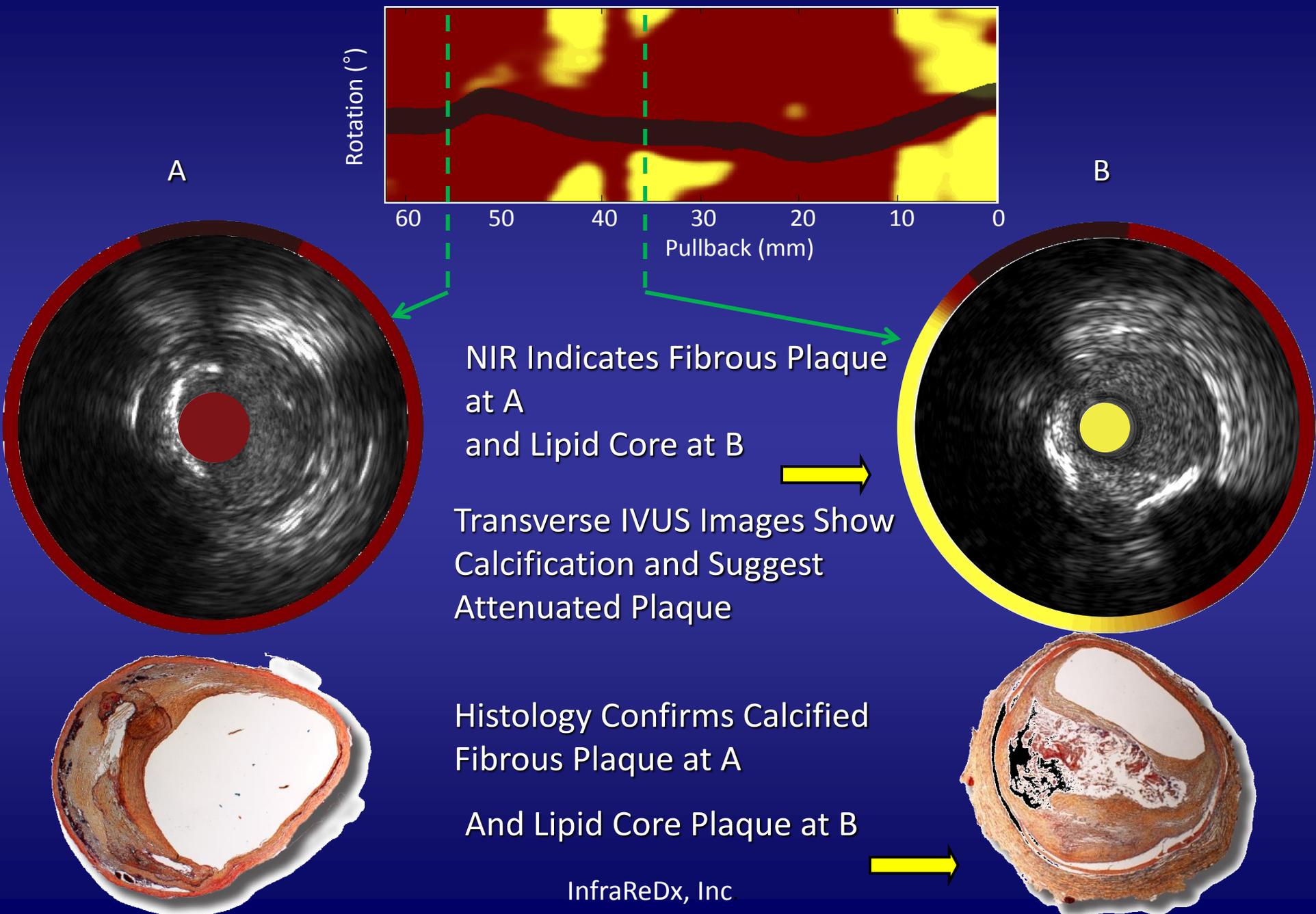
Near Infrared Lipid Imaging
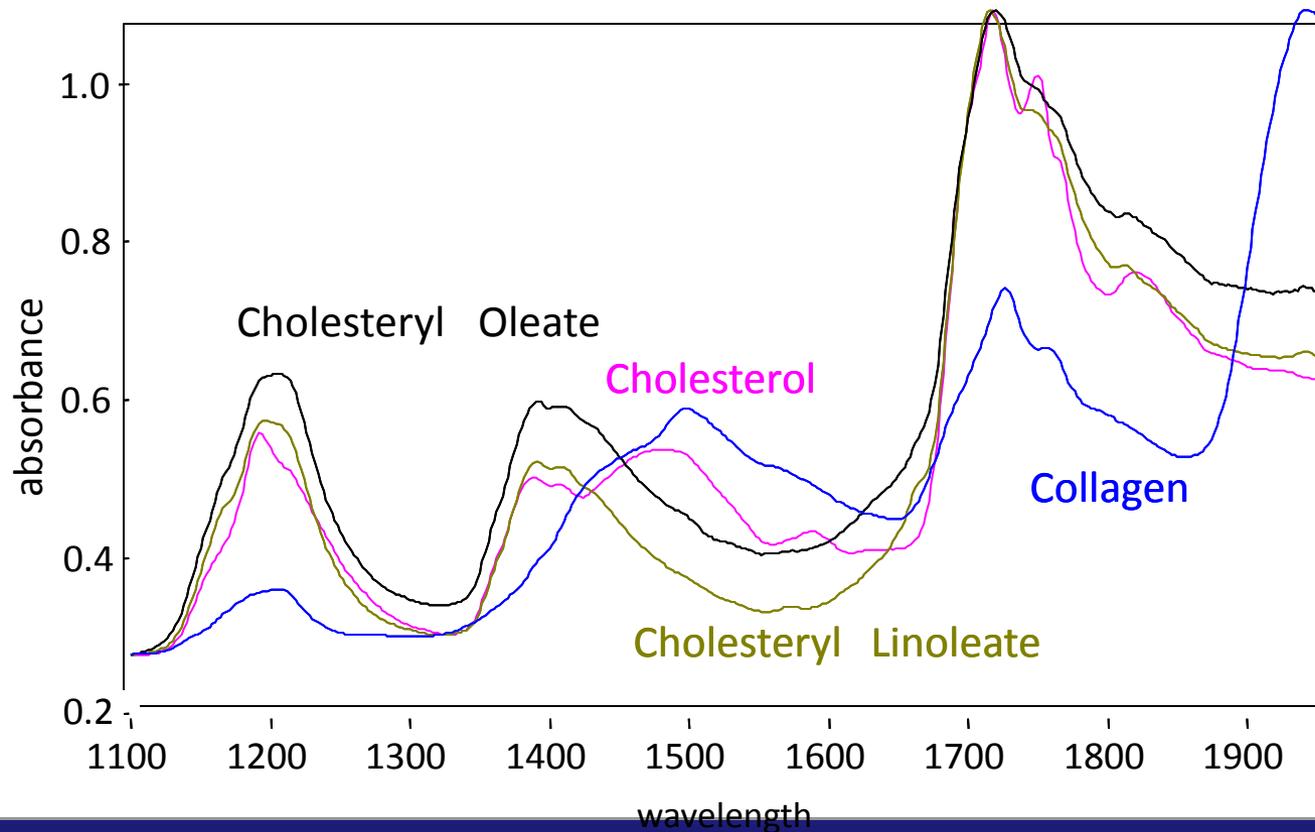
Diffuse Reflectance NIR Spectroscopy can Identify Chemical Composition

InfraReDx, Inc.

Near Infrared Lipid Imaging


high

low

InfraReDx, Inc.

Simultaneous IVUS and NIR Imaging of a Coronary Autopsy Specimen

A

B

Rotation (°)

60 50 40 30 20 10 0

Pullback (mm)

NIR Indicates Fibrous Plaque at A
and Lipid Core at B

Transverse IVUS Images Show Calcification and Suggest Attenuated Plaque

Histology Confirms Calcified Fibrous Plaque at A

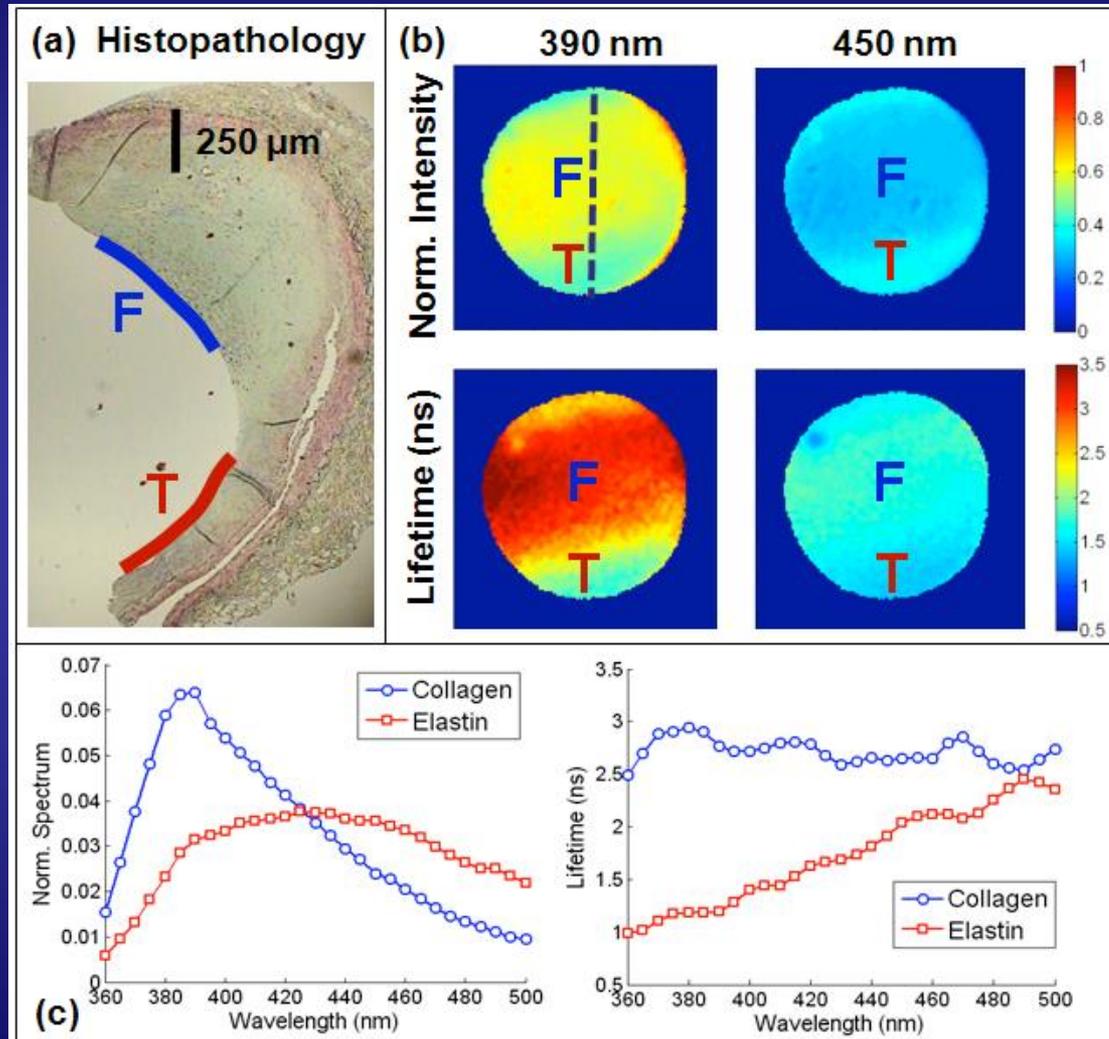And Lipid Core Plaque at B

InfraReDx, Inc.

Invasive Molecular Imaging

Texas A&M University, Department of Bioengineering
Javier Jo, PhD and Brian Applegate, PhD
- Intravascular catheter
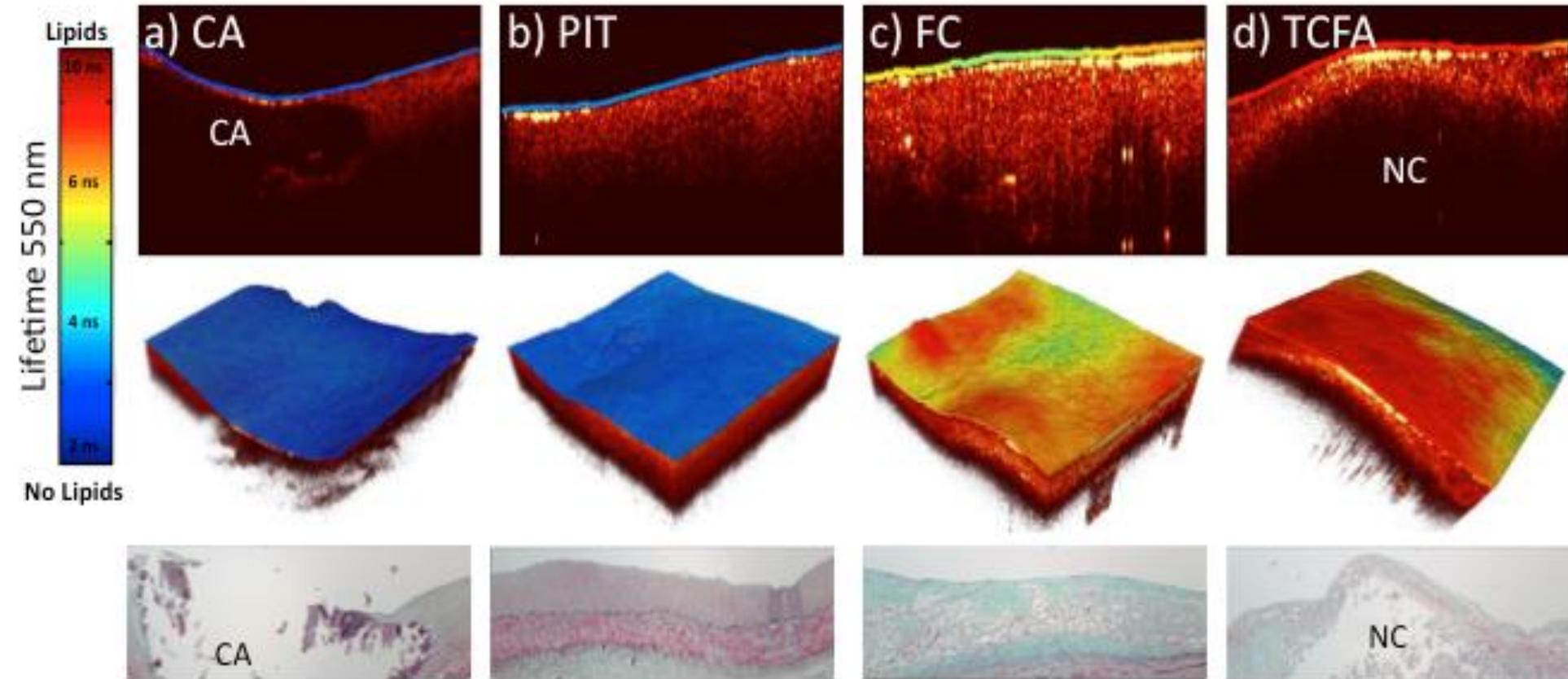- Dual-modality imaging system combining OCT and FLIM
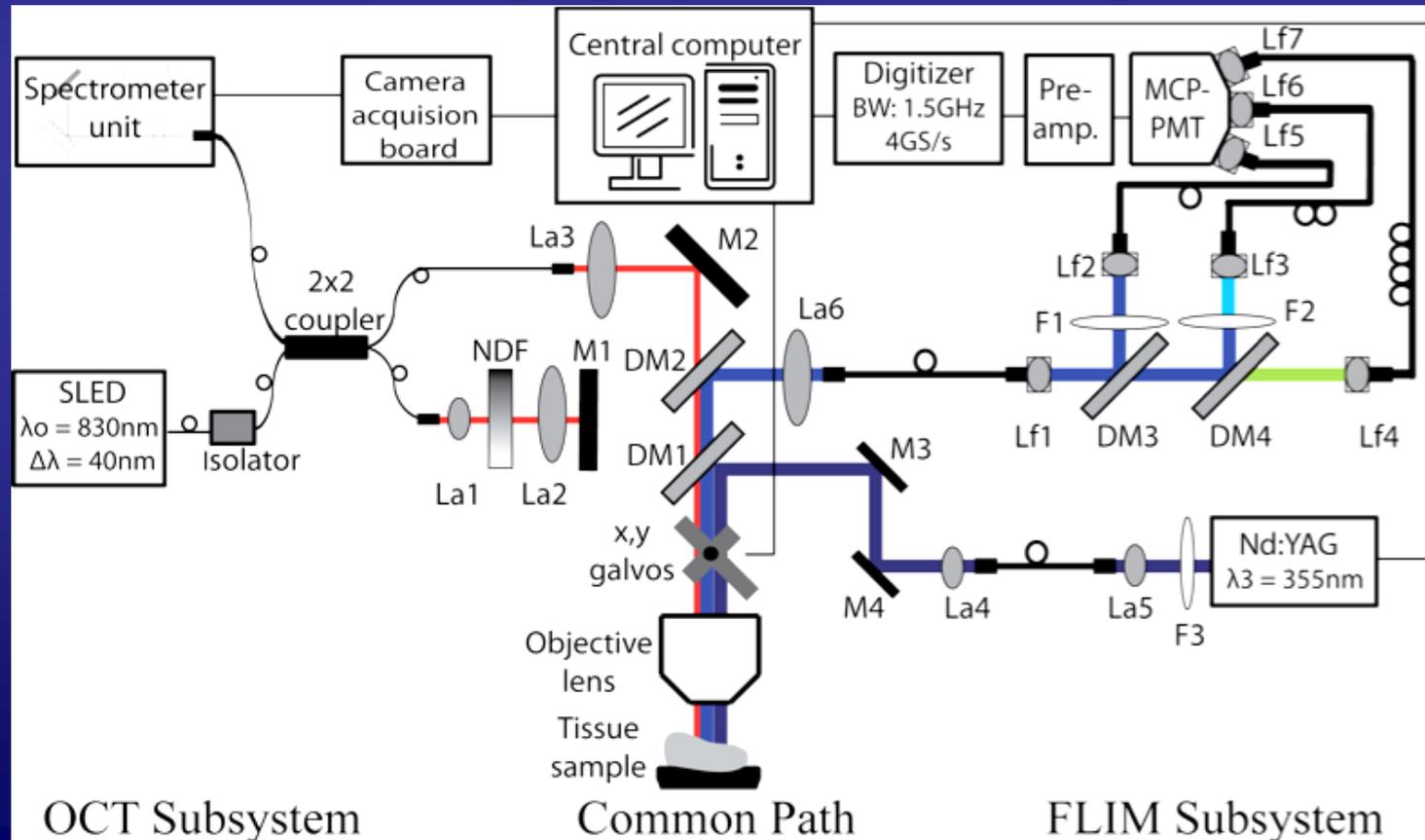
Invasive Molecular Imaging

Used With permission from Jo, TAMU

OCT/FLIM

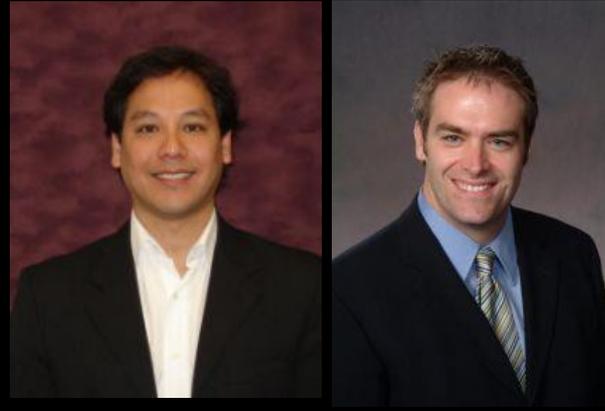# Molecular Imaging of Atherosclerosis

Summary

- Identification of metabolically active plaque
- Expansion of angioplasty indications for "vulnerable plaque"
- Invasive evaluation of high risk patients
- Monitoring conventional drug therapy
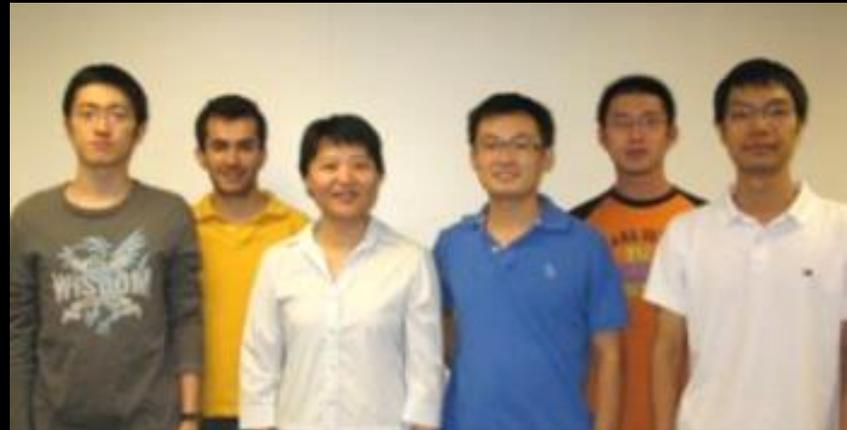- New metric for drug development
  - Beyond MACE

Texas A&M Univ.
– Javier Jo, PhD
– Brian Applegate, PhD

Univ. of Houston
– Xiaojing Yuan, PhD
– Ning Situ, PhD

MDACC
– Gabe Lopez-Berestein, MD