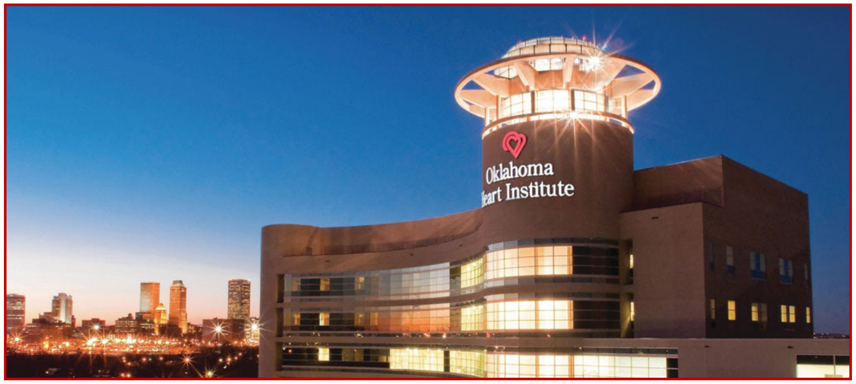
Fractional Flow Reserve from Coronary CT Angiography

0.9 0.8 0.7 0.6

(and some neat CT images)

Victor Cheng, M.D.
Director, Cardiovascular CT
Oklahoma Heart Institute



Oklahoma Heart Institute

Disclosures

- Tornadoes scare me

Treating CAD

- “Fixing” obstructive coronary artery disease (CAD) is beneficial when…

  Patient has acute coronary syndrome

  Patient is compromised by CAD
  - Symptomatic (angina, heart failure)
  - Reduced ejection fraction
  - Ventricular arrhythmia
  - Myocardial ischemia / Reduction in blood flow

The Problem…

- Noninvasive testing for CAD generates anatomy
    - Coronary CT angiogram (CTA); highly sensitive, but we guess about hemodynamic significance

… or measures hemodynamic significance of coronary artery disease (“ischemia”)

- Exercise treadmill
- stress echo
- Radionuclide myocardial perfusion imaging
- Vasodilator cardiac MRI
- Less sensitive for CAD

But not both…

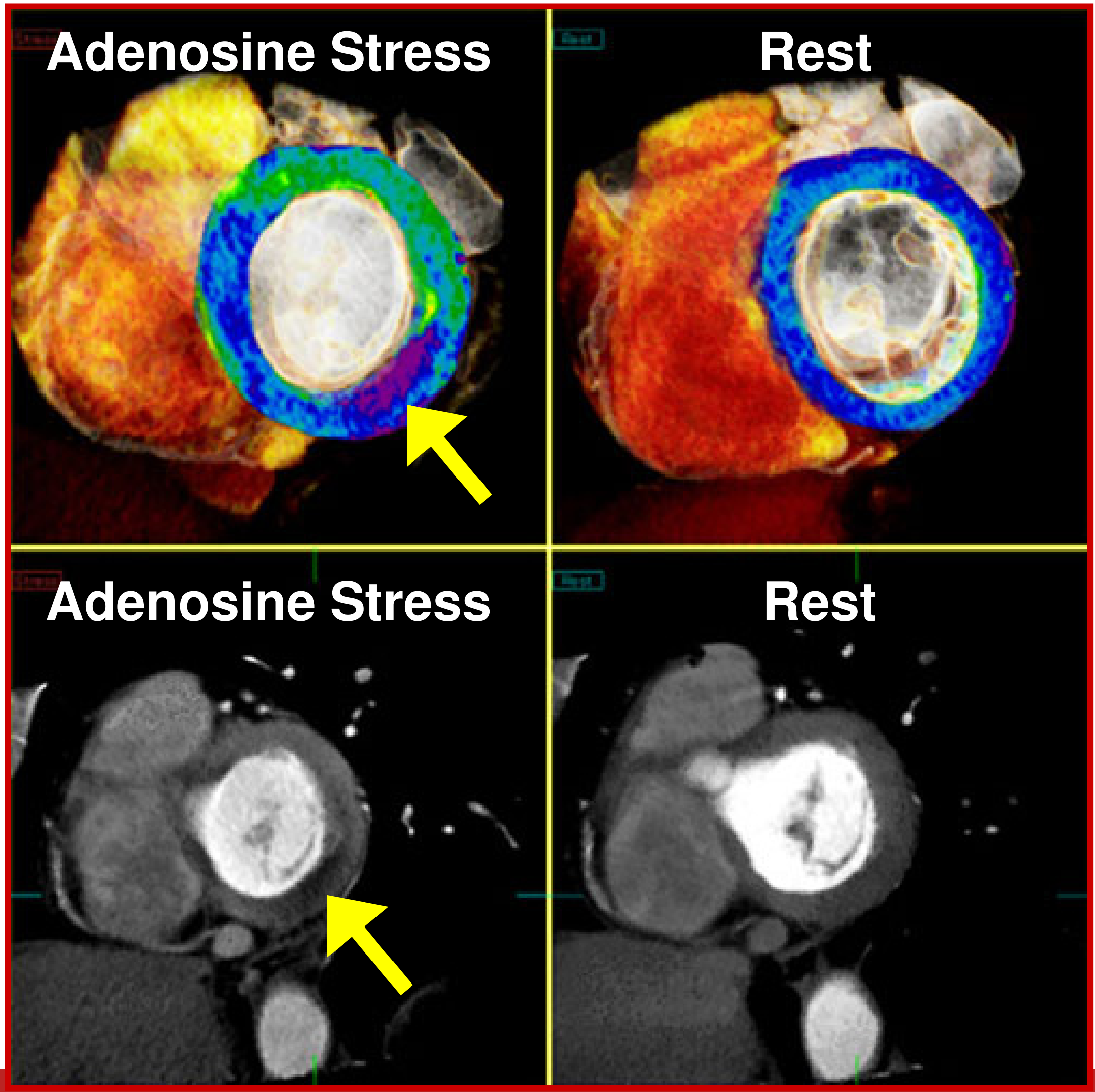
Simultaneous Anatomy and Flow?

- Can CTA generate blood flow information?

Option 1: Produce rest/stress perfusion image

Iodine flows into the myocardial in proportion to blood flow, and reduced coronary blood flow can be visually detected as lower iodine signal (not as brightly "enhanced")

CT Myocardial Perfusion



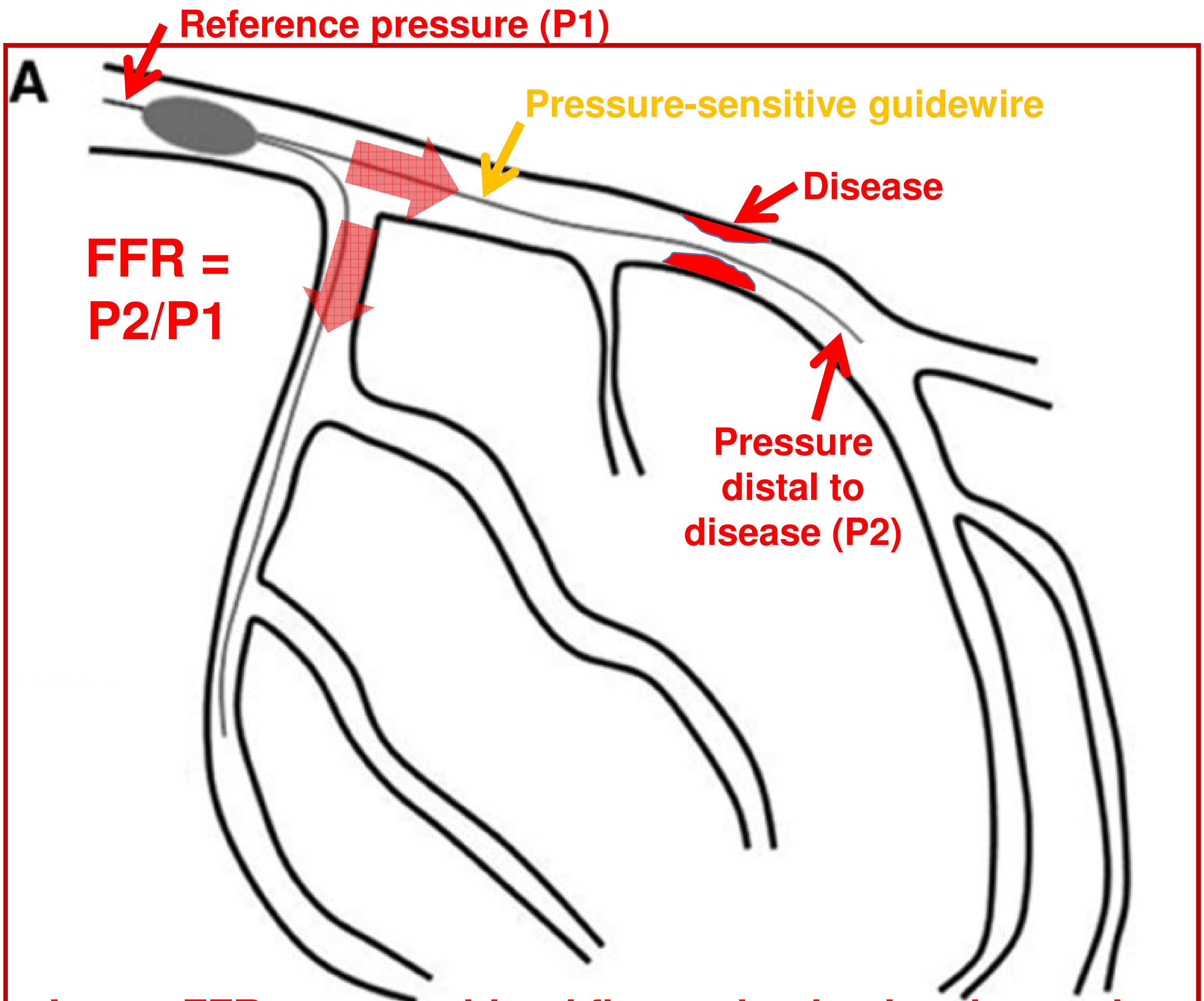
Simultaneous Anatomy and Flow?

- Can CTA generate blood flow information?

  Option 2: Generate fractional flow reserve (FFR)

FFR: Brief Overview

- Coronary artery obstructions that look similar on cath often times do not cause the same degree of flow reduction
- As blood flow drops, fluid pressure drops
- Under maximum blood flow state (induced by adenosine or nitroglycerin), pressure is proportional blood flow
- If we measure pressure just distal to an obstruction under maximum blood flow state, that should tell us by how much blood flow is reduced



Lower FFR = greater blood flow reduction by obstruction

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 15, 2009 VOL. 360 NO. 3

Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention

The NEW ENGLAND JOURNAL of MEDICINE

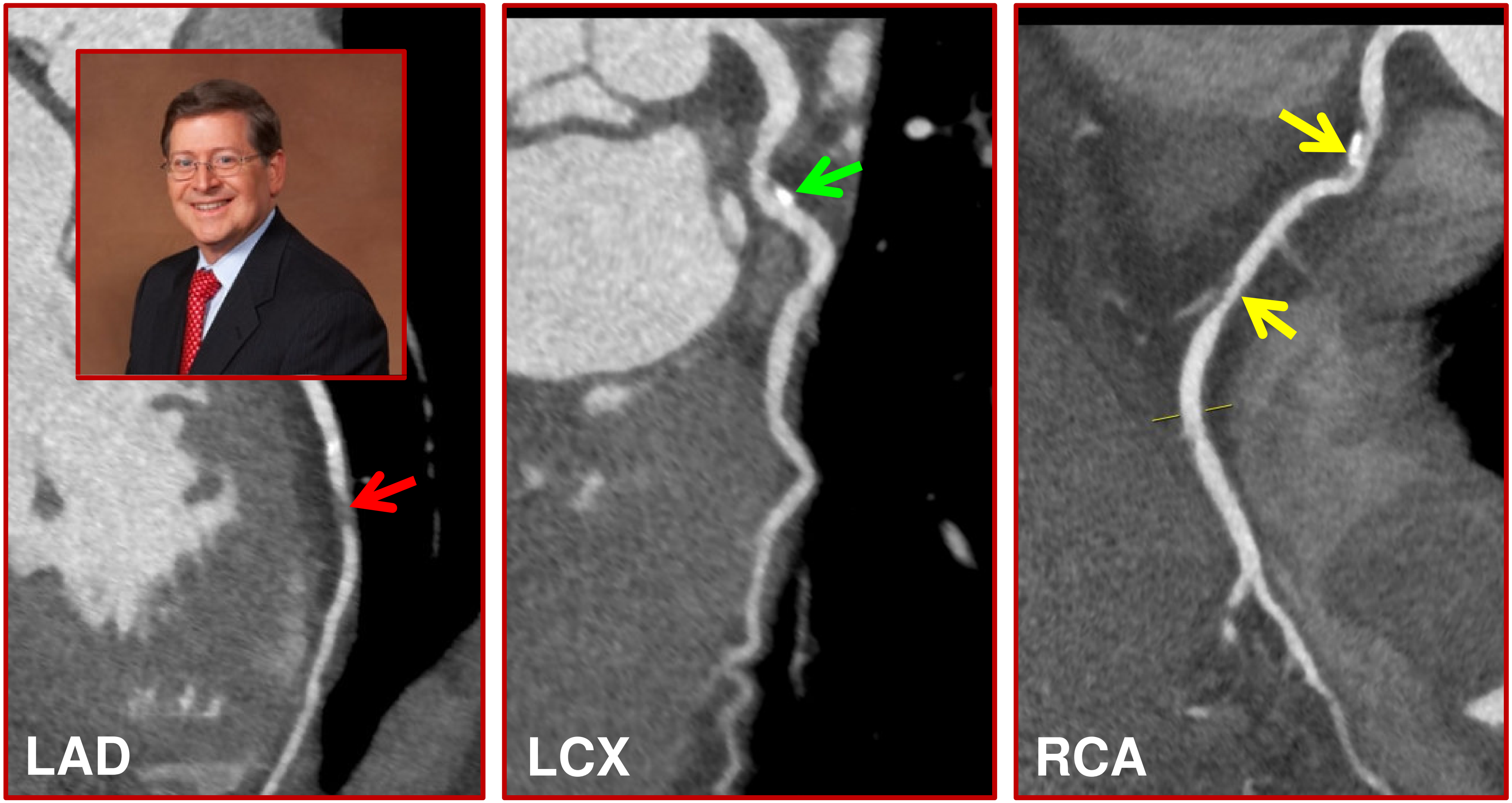
ESTABLISHED IN 1812 SEPTEMBER 13, 2012 VOL. 367 NO. 11

Fractional Flow Reserve–Guided PCI versus Medical Therapy in Stable Coronary Disease

- **FAME**: 1005 patients with stable multivessel stenotic CAD on cath
- Randomized to PCI only if FFR < 0.80 or PCI based on standard angiographic guidance
- FFR-directed PCI had lower subsequent death or myocardial infarction (7.3% vs 11.1%)

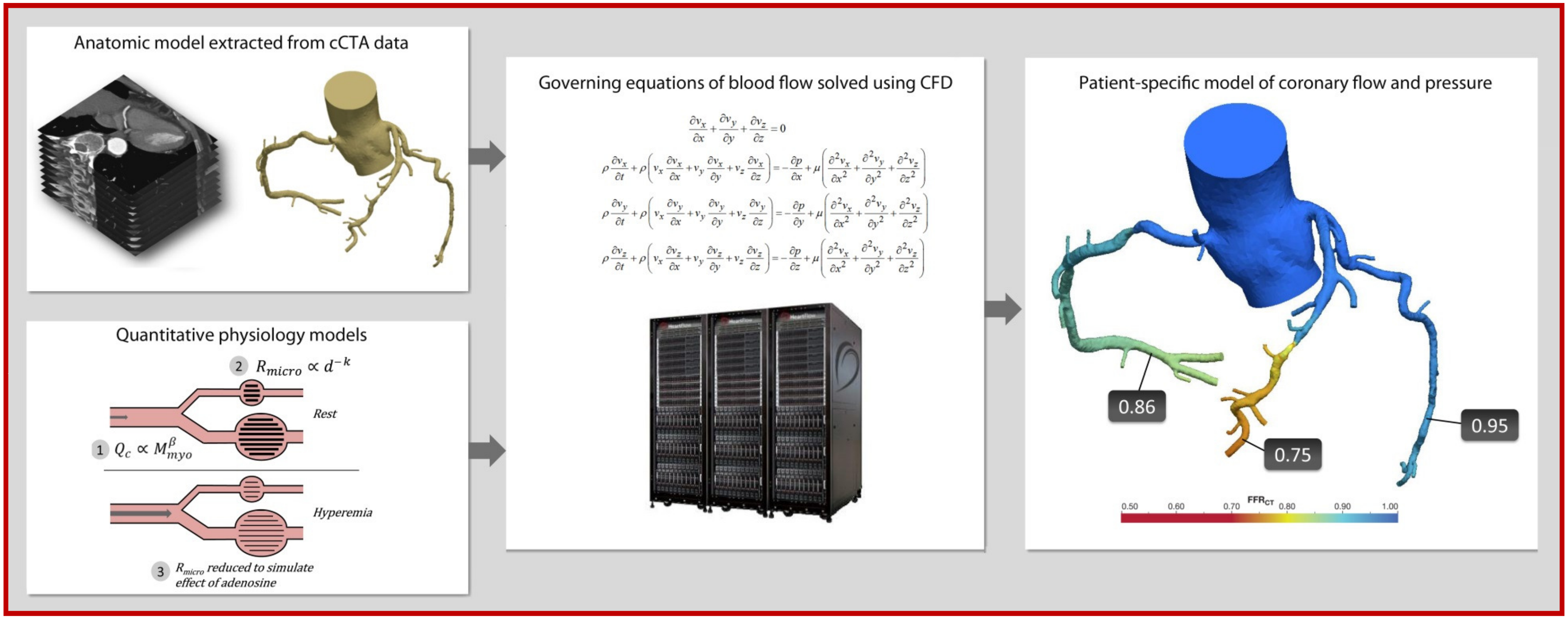
- **FAME 2**: 888 patients with stable stenotic CAD on cath
- Randomized to PCI if FFR < 0.80 or optimal medical therapy
- FFR-directed PCI had dramatically reduced rate of subsequent urgent revascularization (1.6% vs 11%)

Neat #1



Neat #2

FFR from CTA

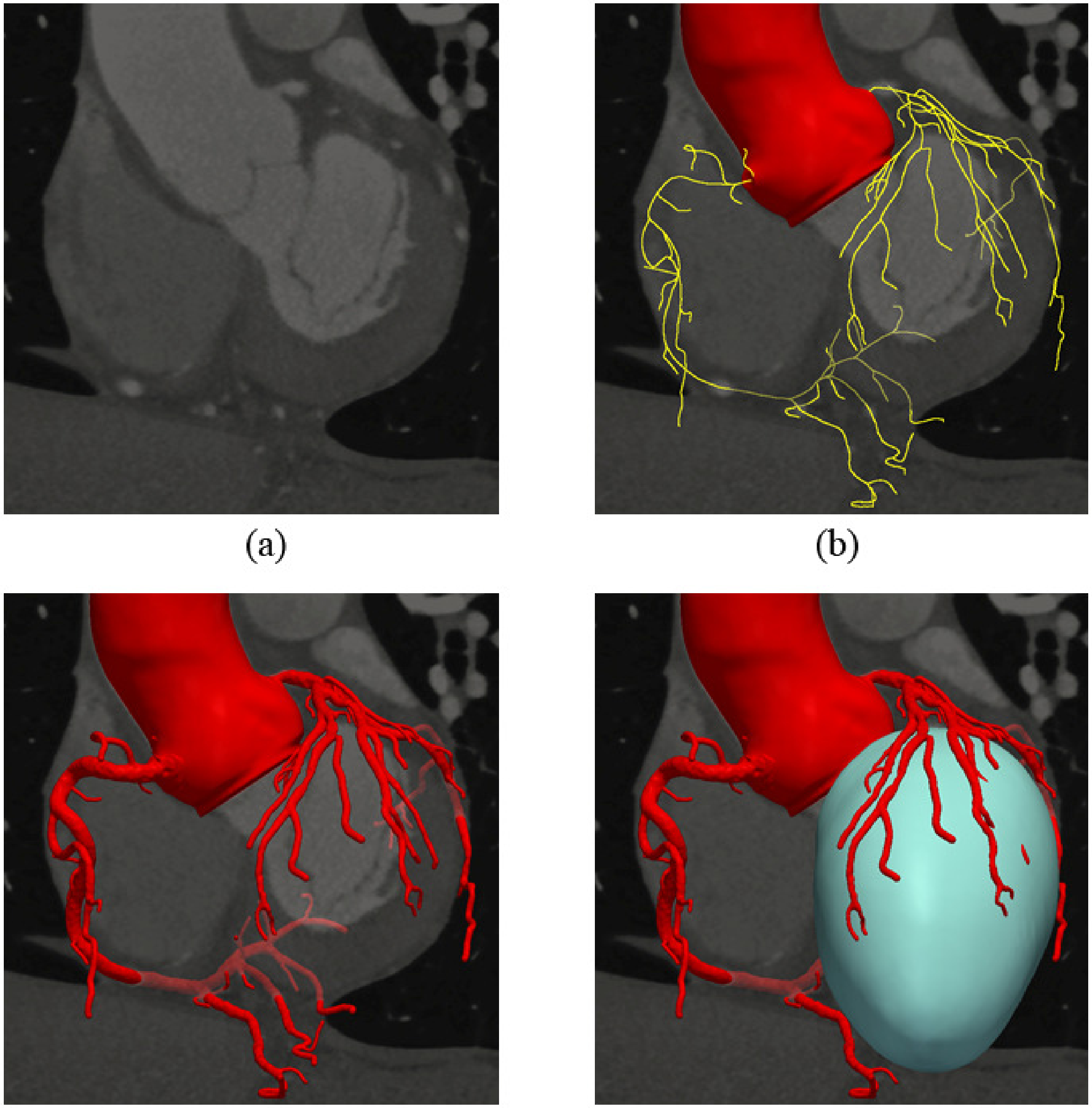


C.A. Taylor, T.A. Fonte, J.K. Min, et al. (2013) Computational Fluid Dynamics Applied to Cardiac Computed Tomography for Noninvasive Quantification of Fractional Flow Reserve: Scientific Basis. *Journal of the American College of Cardiology*. Vol. 61, Issue 22, pp. 2233-2241.

Courtesy Paul Temple from HeartFlow.

May 5, 2017

Oklahoma Heart Institute



Build anatomic heart model from CTA

Assign myocardial territory to individual arteries

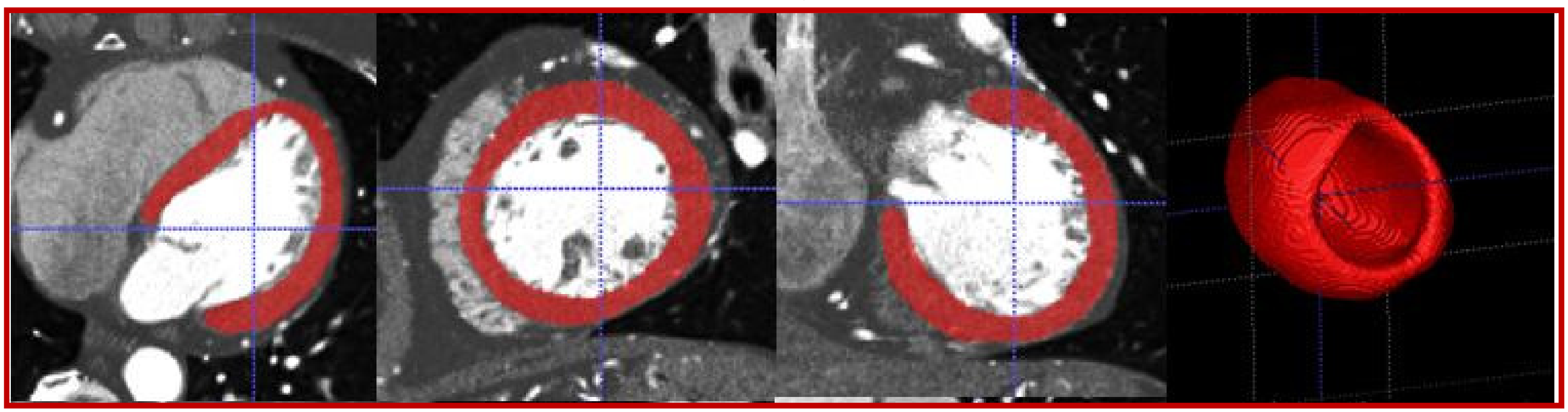
Requires good quality CTA image data

FFR from CTA

1: Model REST coronary blood flow given left ventricular myocardial mass and assignment of myocardium to each coronary artery

Allometric scaling laws can be applied to estimate physiologic parameters, e.g. coronary flow, under baseline conditions given organ mass

$$Q_c^{rest} \mu \, M_{myo}^{\beta}$$



Courtesy Paul Temple from HeartFlow.

FFR from CTA

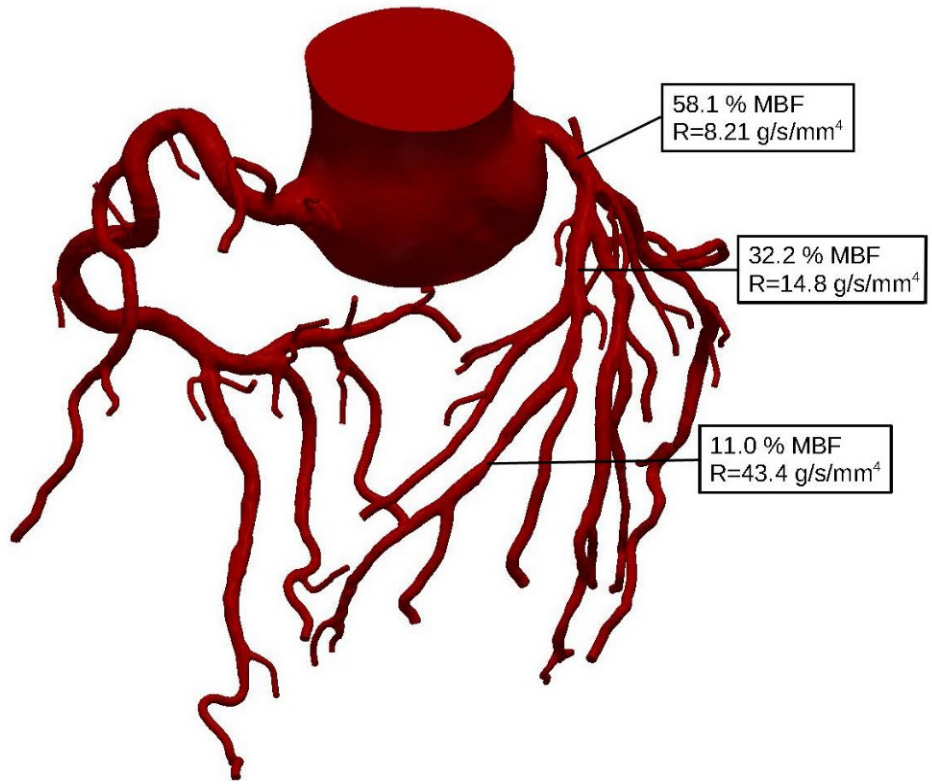
2: Model microcirculatory vascular bed flow resistance at REST, inversely proportional to size of feeding vessel.

1. Healthy and diseased vessels adapt to amount of flow they carry
2. Power law relationships of form $Q \propto d^k$ apply to different vascular beds – including coronary arteries
3. Since mean pressure (P) is essentially constant down the length of the coronary arteries at rest

AND **$P = QR$**

AND **$Q \propto d^k$**

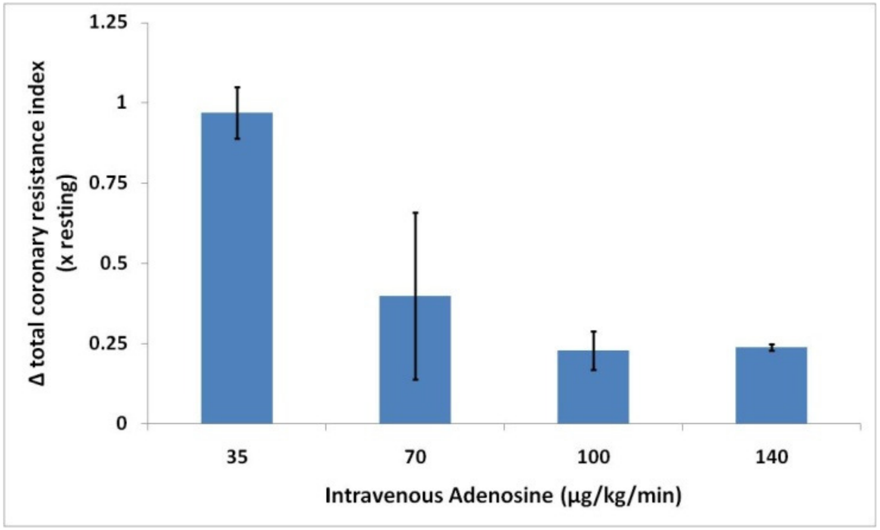
THUS **$R \propto d^{-k}$**



FFR from CTA

3: Model predictable change in microcirculatory resistance in response to ADENOSINE

1. When the heart lacks O_2, breakdown of ATP results in release of adenosine → vasodilation
2. Exogenous administration of adenosine elicits maximum hyperemic response by forcing complete smooth muscle cell relaxation
3. Standard of care for induction of hyperemia in non-invasive tests and the cath lab



Intravenous administration of adenosine elicits remarkably consistent vasodilatory response in normal subjects at sufficient doses

FFR from CTA

- Now we have:
  - Resting coronary blood flow
  - Resting coronary vascular resistance
  - Adenosine-induced coronary vascular resistance
- And adenosine-induced coronary blood flow can be determined!

And… Watson is needed

4: Solve equations of mass and momentum conservation to calculate coronary flow with ADENOSINE

$$\frac{\partial v_x}{\partial x} + \frac{\partial v_y}{\partial y} + \frac{\partial v_z}{\partial z} = 0$$

MASS conservation: This law states that blood is an incompressible fluid

$$\rho \frac{\partial v_x}{\partial t} + \rho \left(v_x \frac{\partial v_x}{\partial x} + v_y \frac{\partial v_x}{\partial y} + v_z \frac{\partial v_x}{\partial z} \right) = -\frac{\partial p}{\partial x} + \mu \left(\frac{\partial^2 v_x}{\partial x^2} + \frac{\partial^2 v_y}{\partial y^2} + \frac{\partial^2 v_z}{\partial z^2} \right)$$

$$\rho \frac{\partial v_y}{\partial t} + \rho \left(v_x \frac{\partial v_y}{\partial x} + v_y \frac{\partial v_y}{\partial y} + v_z \frac{\partial v_y}{\partial z} \right) = -\frac{\partial p}{\partial y} + \mu \left(\frac{\partial^2 v_x}{\partial x^2} + \frac{\partial^2 v_y}{\partial y^2} + \frac{\partial^2 v_z}{\partial z^2} \right)$$

$$\rho \frac{\partial v_z}{\partial t} + \rho \left(v_x \frac{\partial v_z}{\partial x} + v_y \frac{\partial v_z}{\partial y} + v_z \frac{\partial v_z}{\partial z} \right) = -\frac{\partial p}{\partial z} + \mu \left(\frac{\partial^2 v_x}{\partial x^2} + \frac{\partial^2 v_y}{\partial y^2} + \frac{\partial^2 v_z}{\partial z^2} \right)$$

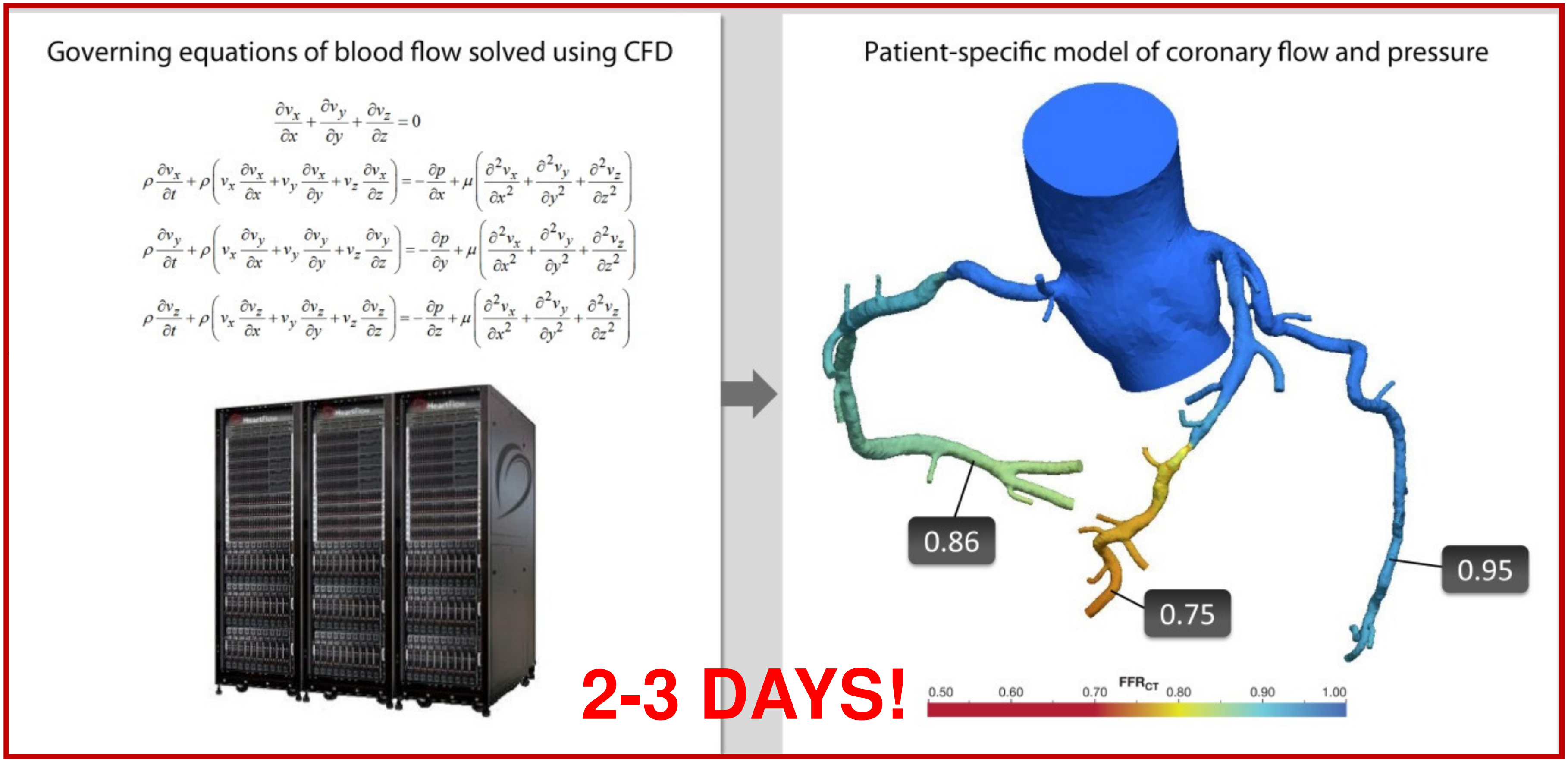
MOMENTUM conservation: These equations come from the application of Newton's 2nd law, F=ma to a fluid

where ρ is the fluid density, and μ is the fluid viscosity (both assumed known).

We solve these for $v_x(x, y, z, t), v_y(x, y, z, t), v_z(x, y, z, t), p(x, y, z, t)$

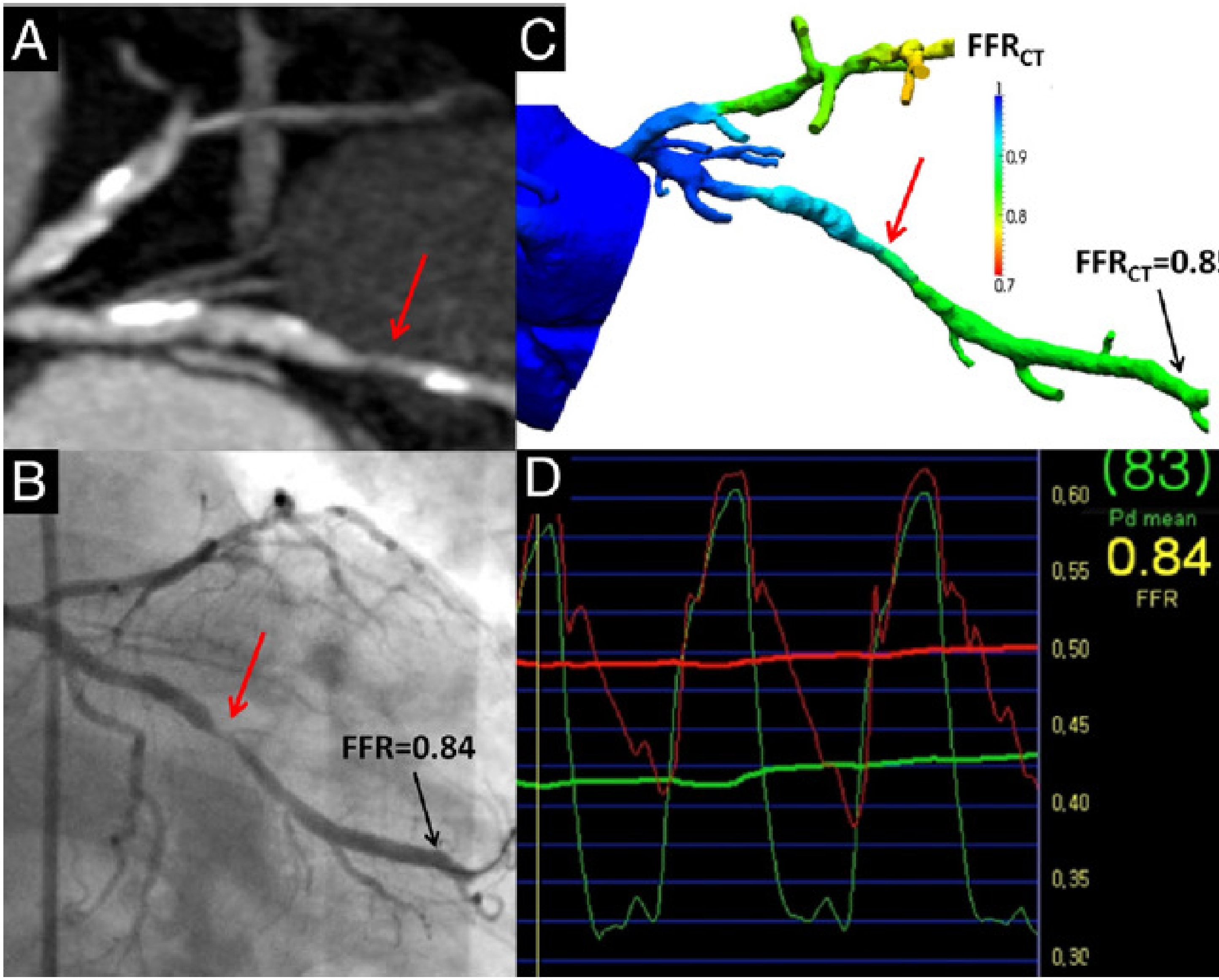
for every point in the 3D model and over whatever time interval we are interested in.

Make a supercomputer do it



May 5, 2017

Oklahoma Heart Institute

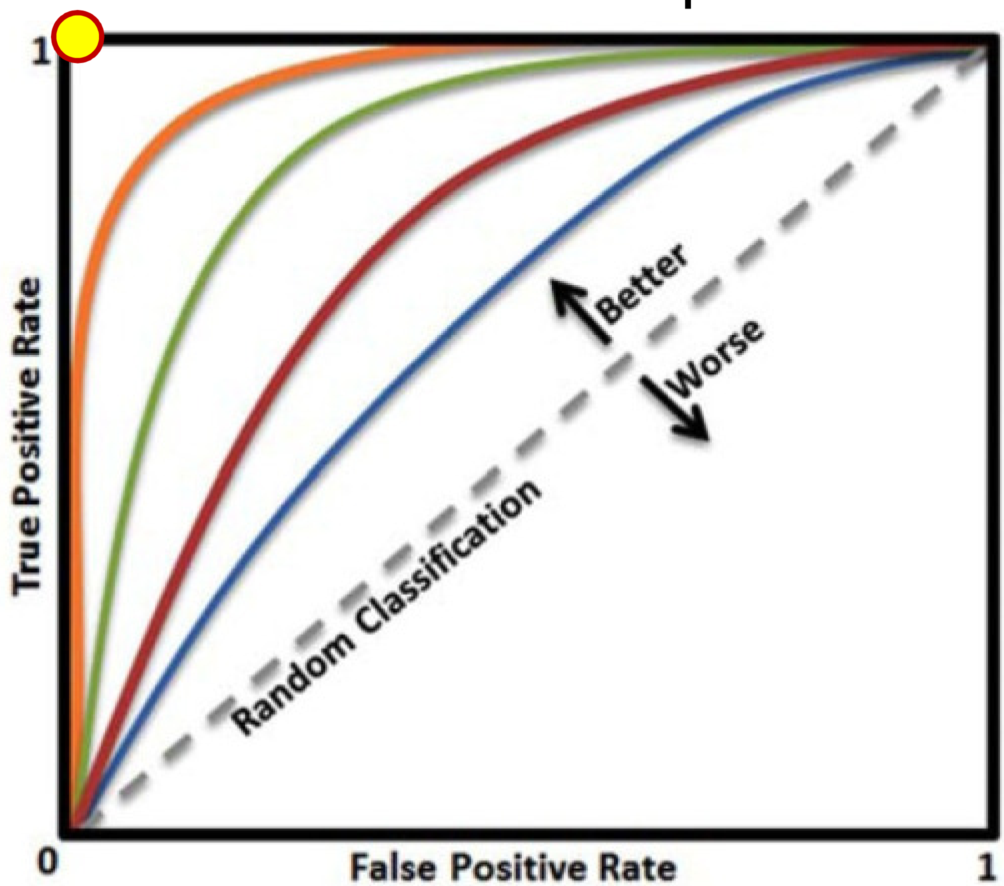


Koo, et al. *JACC* 2011.

May 5, 2017

ROC Curve

- ROC = Receiver-Operator Characteristic

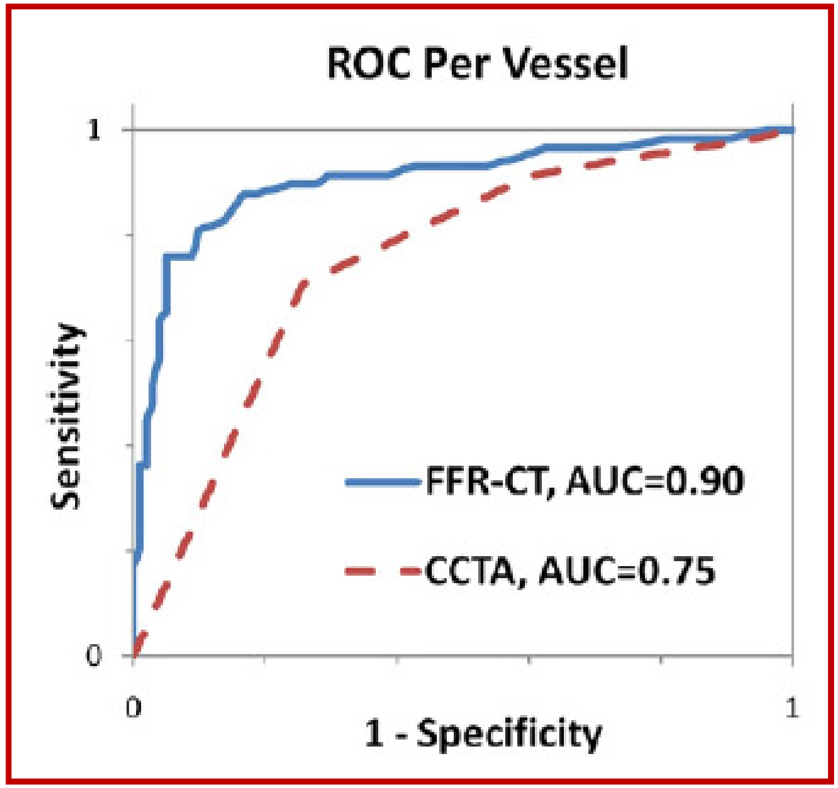


- For most tests, an alteration to increase sensitivity (true positive) rate also increases false positive rate.
- The most accurate test achieves nearly 100% true positive with nearly 0% false positive rate
- ROC curve describes overall accuracy as Area Under the Curve (AUC)

Testing FFR-CT

- DISCOVER-FLOW
- 103 patients underwent CTA, cath with FFR, blinded FFR-CT
- Cath-FFR<0.8 = reference

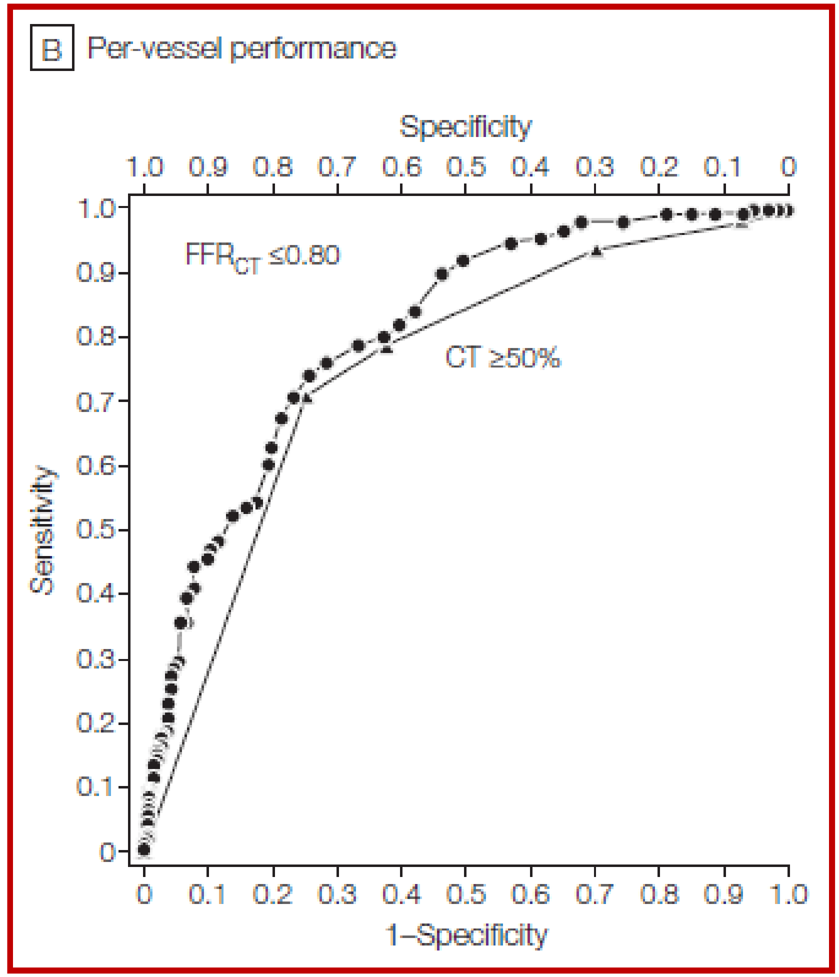
- Specificity improved: 40% to 82% (reduced false positives!)
- Sensitivity similar: 88% vs 91%



Testing FFR-CT

- DE FACTO
- 252 patients underwent CTA, cath with FFR, blinded FFR-CT
- Cath-FFR<0.8 = reference

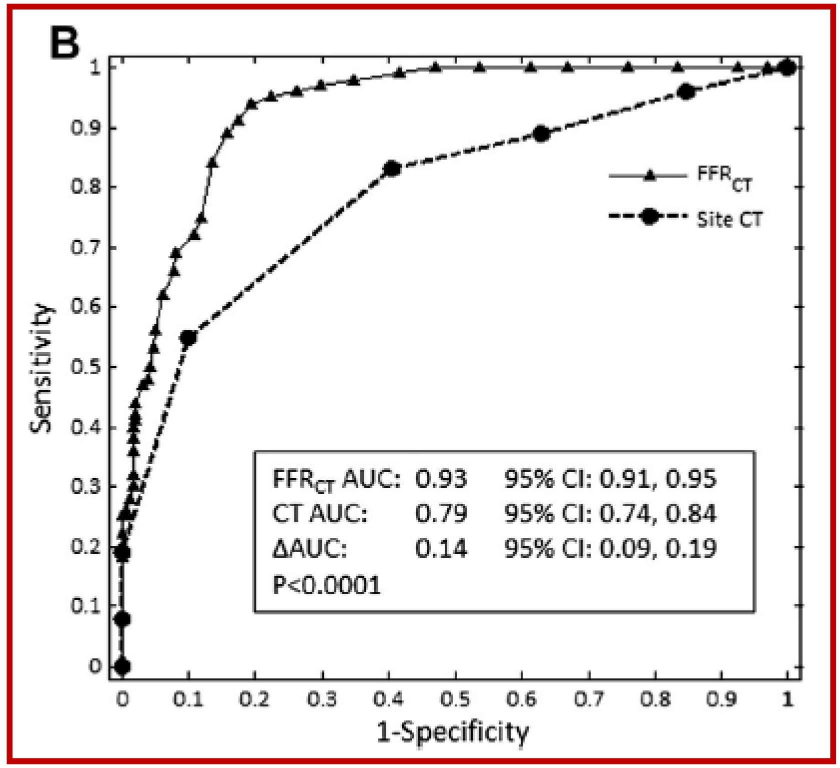
- Specificity improvement not as good: 40% to 52%
- Sensitivity similar: 84% vs 90%



Testing FFR-CT

- NXT
- 254 patients underwent CTA , cath with FFR, blinded FFR-CT
- Cath-FFR<0.8 = reference

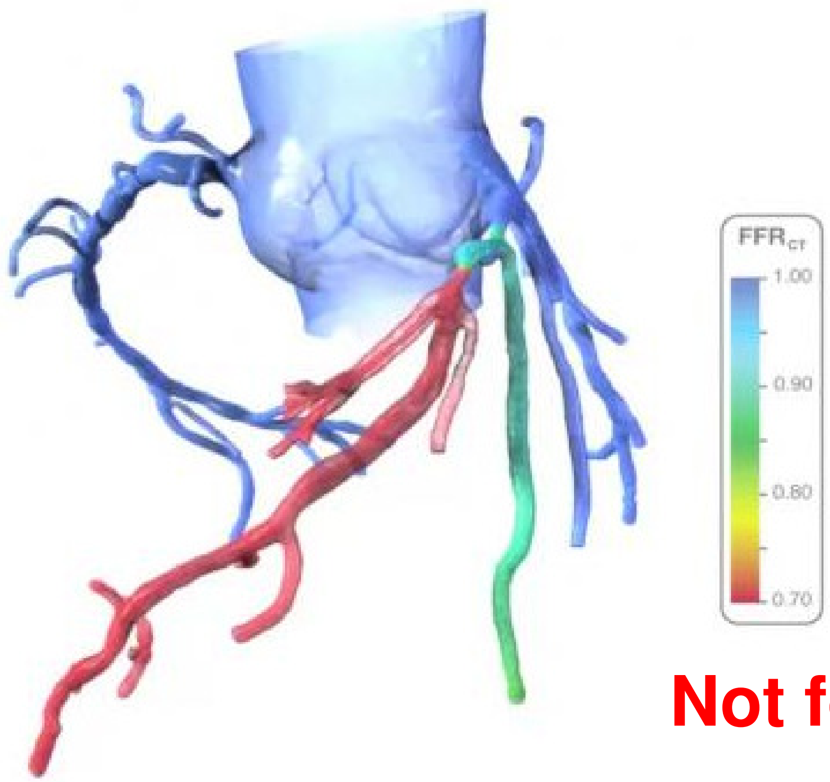
- Specificity improved: 60% to 86%
- Sensitivity similar: 83% vs 84%



TECHNOLOGY | NOVEMBER 26, 2014

FDA Clears FFR-CT

Non-invasive computed tomography imaging exam can evaluate coronary blood flow without a diagnostic catheterization



Not for stents or grafts

Confirmation

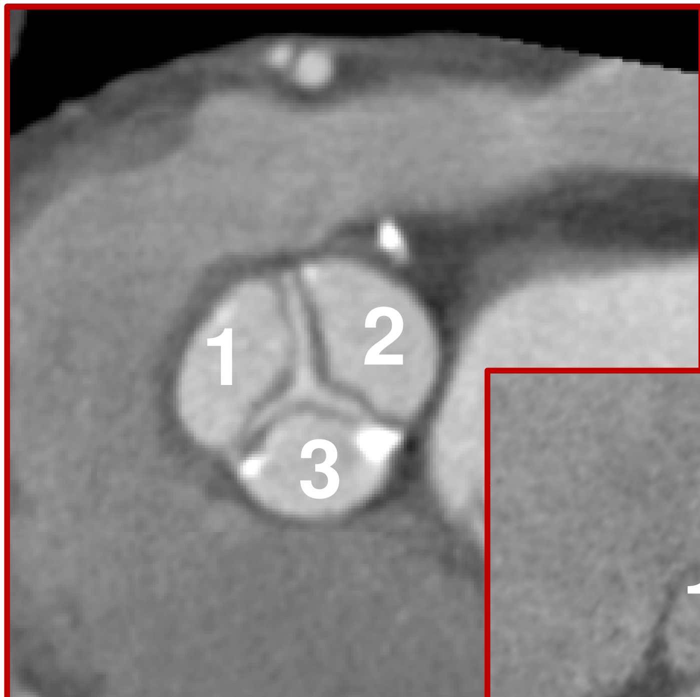
- 2 meta-analyses since FDA approval both found
  - FFR-CT improved specificity and overall accuracy for ischemic disease compared to CTA only
  - Adding FFR-CT did not change sensitivity
- **FFR-CT effectively cuts the rate of incorrectly assuming disease on CTA causes ischemia**

(Baumann S, et al. *Acad Radiol* 2016)

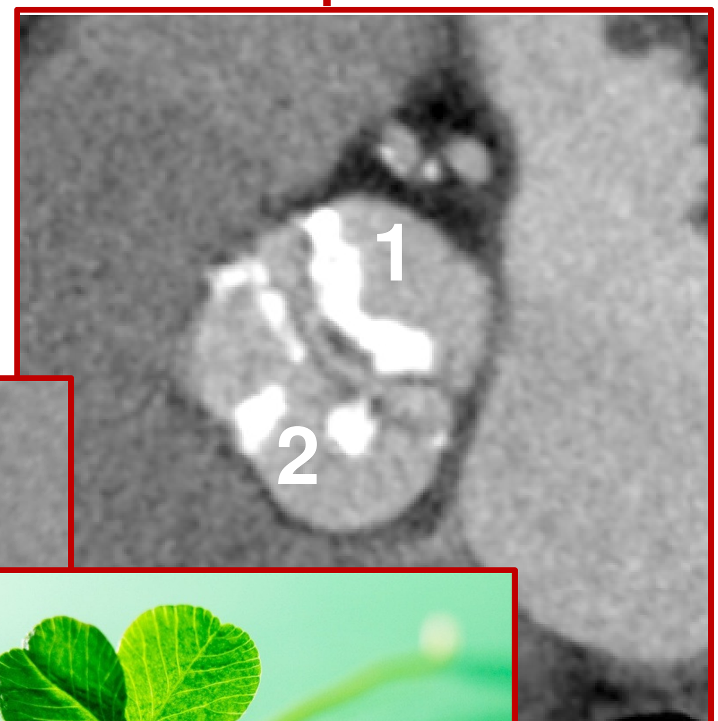
(Tan XW, et al. *Int J Cardiol* 2017)

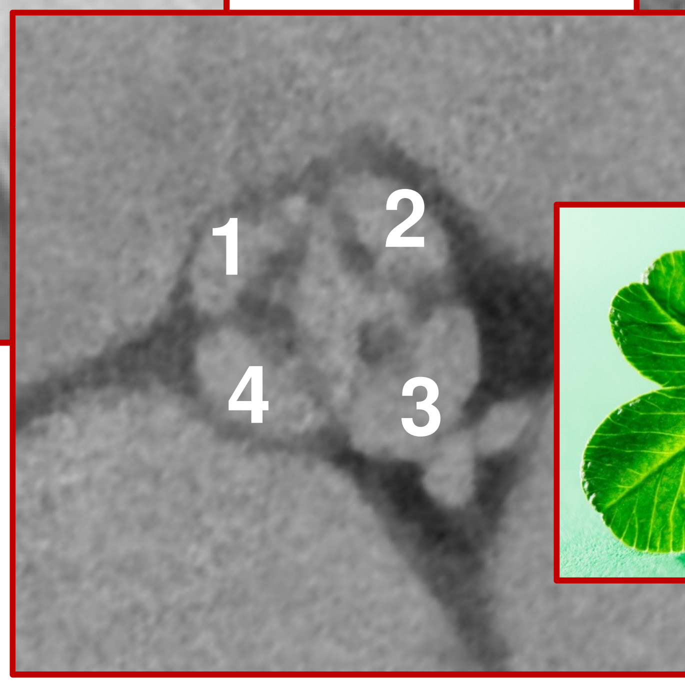
Neat #3

Tricuspid: 95%



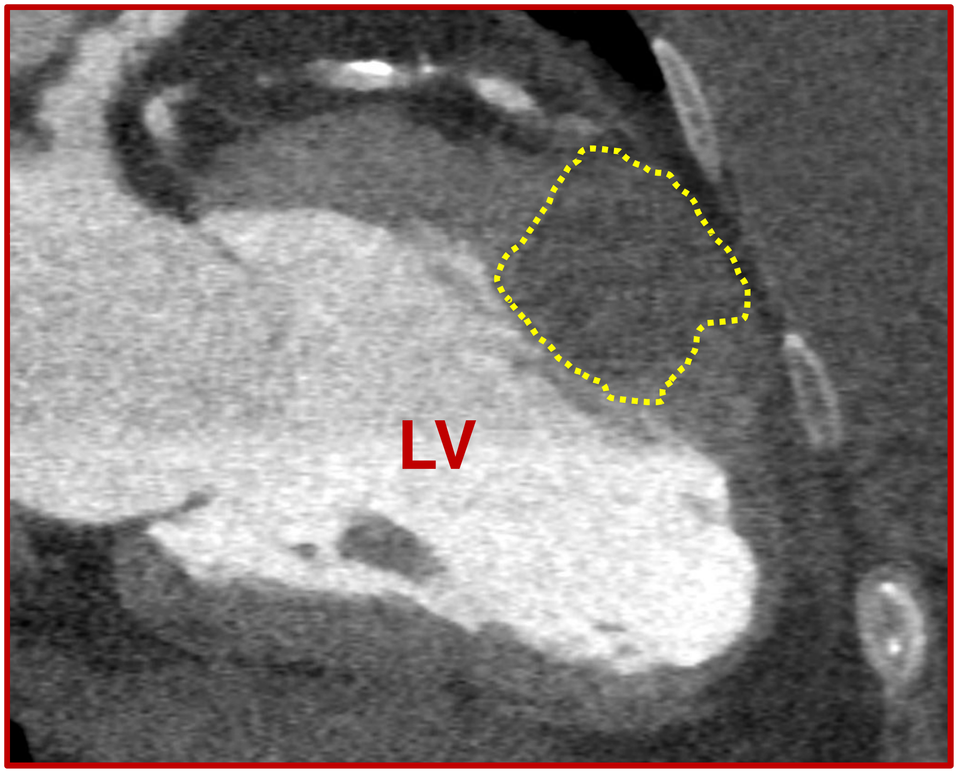
Bicuspid: 5%

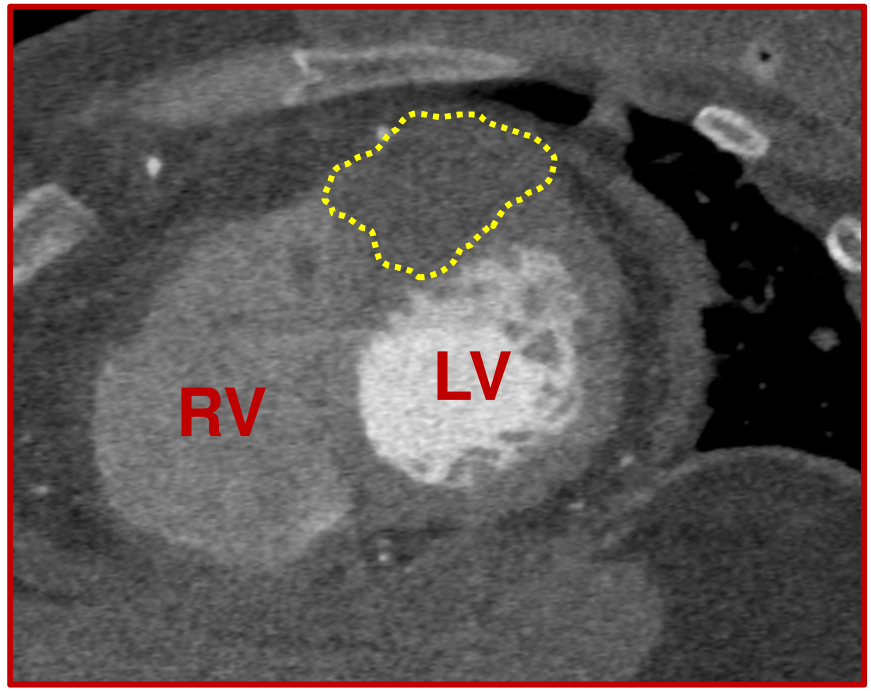




Quadricuspid: 0.01-0.04%

Neat #4





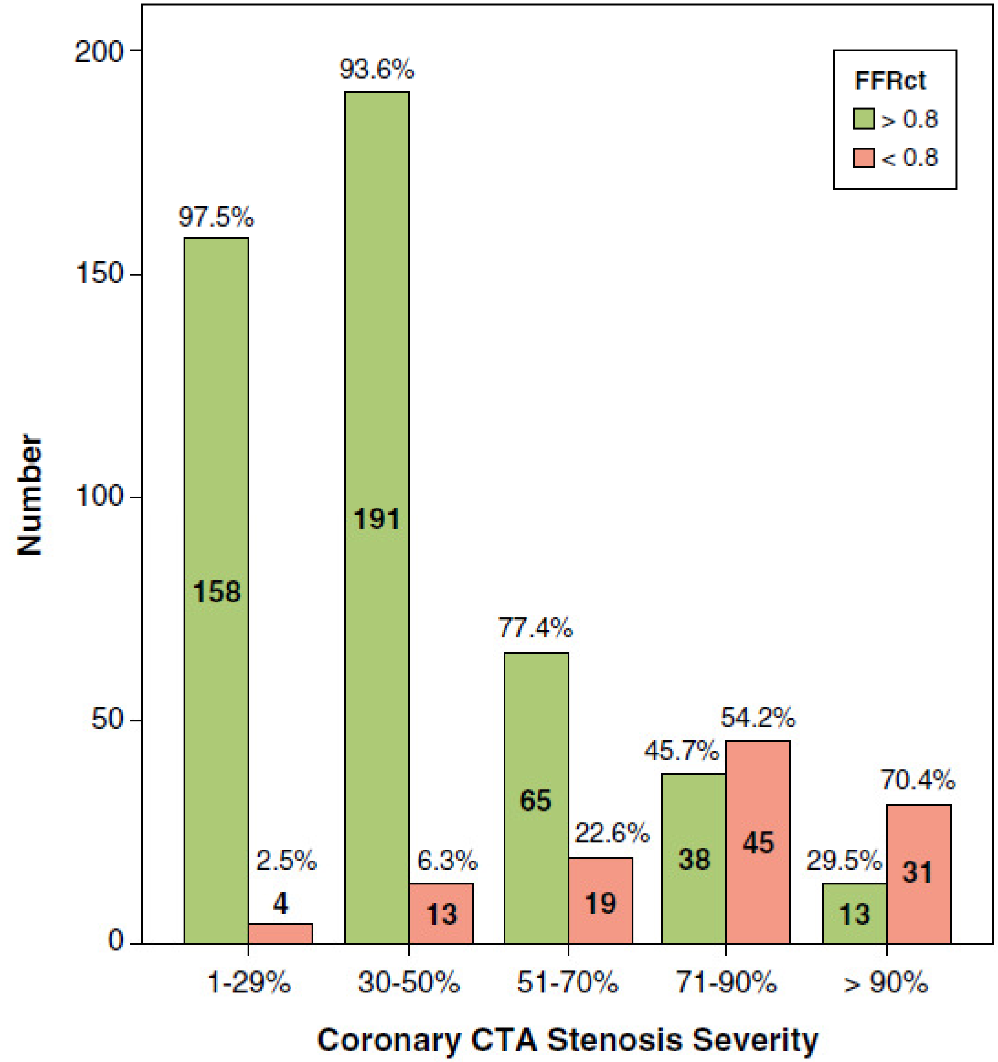
FFR-CT impact on decision making

- RIPCORD
- 200 patients with CTA + FFR-CT
- 3 blinded interventionalists made consensus initial plan of management based on CTA alone
- Then FFR-CT results are provided, and the interventionalists decide whether to modify plan

- In 72 patients (36%), FFR-CT changed management approach

FFR-CT impact on decision making

- RIPCORD
- **36% of management plans changed after FFR-CT**
- FFR-CT eliminated need for more information after CTA
- FFR-CT positive (<0.8)
  - 23% of 51-70% stenoses
  - 54% of 71-90% stenoses
  - 70% of >90% stenoses

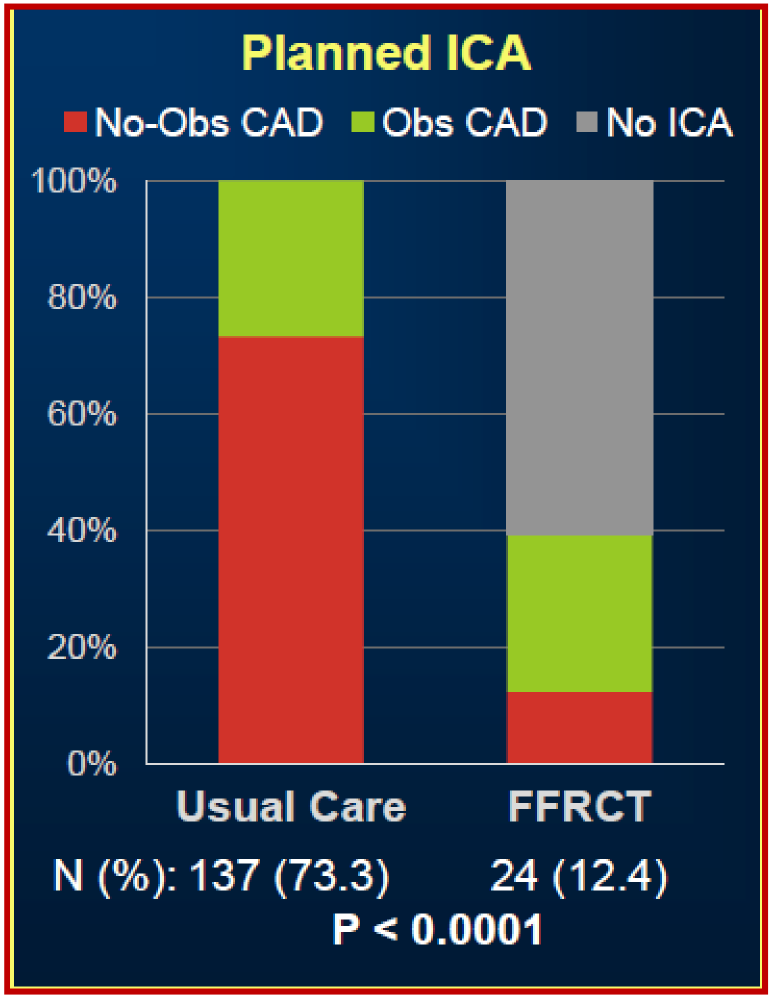


FFR-CT impact on cath

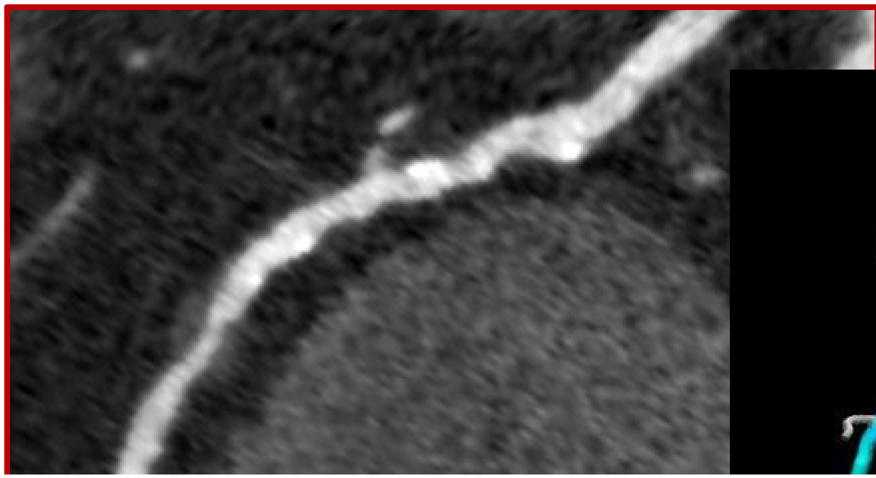
- PLATFORM
- 584 patients intermediate probability for stenotic CAD
  – 204 planned for noninvasive testing
  – 380 planned for cath
- Both groups randomized to original plan or CT with FFR-CT
- Outcomes
  – Rate of coronary catheterization
  – Cardiac events at 90 days

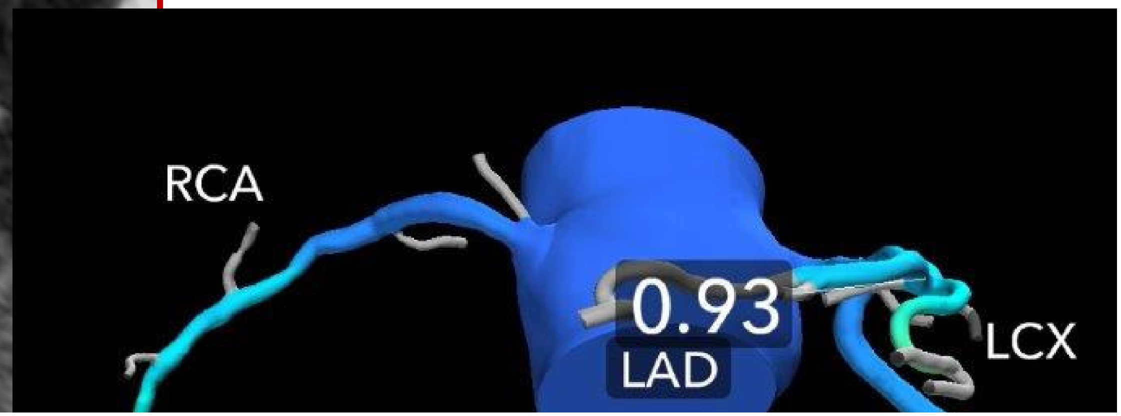
FFR-CT impact on cath

- PLATFORM
- In the group originally headed for cath, use of FFR-CT
  - Cancelled 60% of caths, none of these patients had a cardiac event at 90 days
  - Resulted in 60% less cath showing nonobstructive disease (73% vs 12%)
- No difference in overall rate of revascularization



OHI Case





ERROR: stackunderflow
OFFENDING COMMAND: ~

STACK: