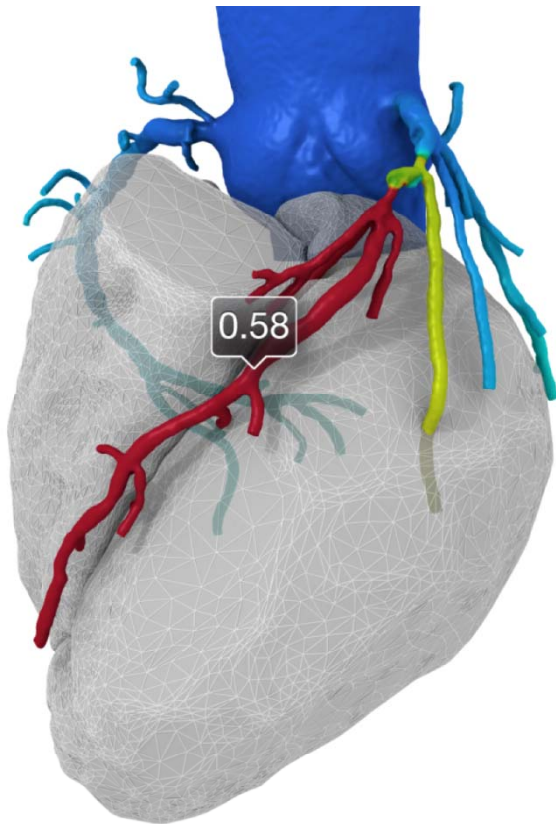

Computed FFR: *What is the Final Goal*



James K. Min, MD FACC
President, Society of Cardiovascular Computed Tomography
Associate Professor of Medicine, UCLA School of Medicine
Associate Professor of Medicine and Imaging
Co-Director, Cardiac Imaging, Cedars-Sinai Heart Institute
Director, Cardiac Imaging Research, Cedars-Sinai Medical Center

Disclosures: Research support (NHLBI; Qatar National Research Fund; GE Healthcare; Philips Medical, Vital Images, Infinitt/Xelis); Medical Advisory Board (GE Healthcare); Medical Consultant (Edwards Life Sciences); Equity Interest (TC3 Cardiovascular Core Laboratories; Cedars-Sinai Medical Center)

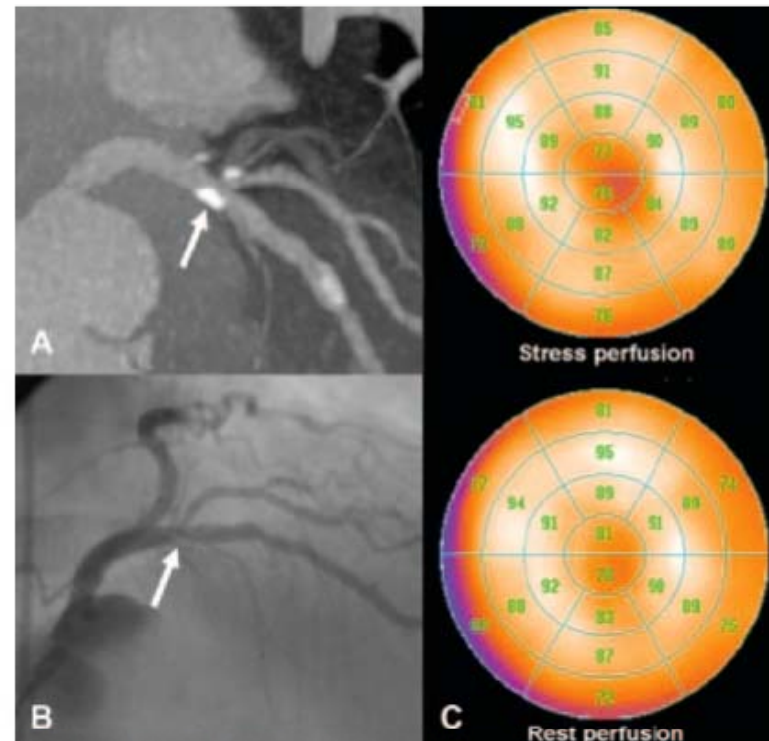
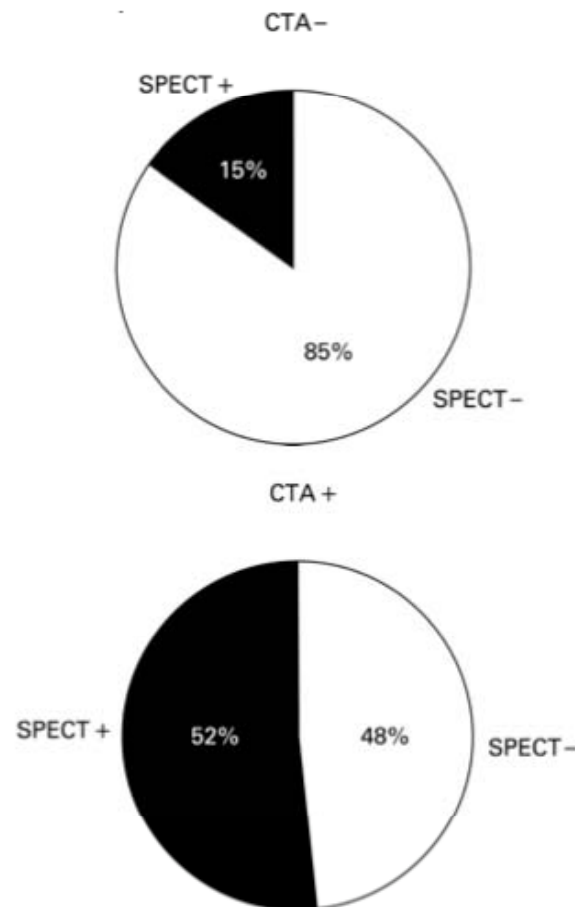
Diagnosis of Obstructive CAD

Test	Sensitivity	Specificity
Exercise ECG treadmill ¹	68%	77%
Exercise Echo treadmill ²	86%	81%
Dobutamine Echo ²	~85%	~85%
Exercise nuclear treadmill ³	87%	73%
Pharmacologic nuclear ³	89%	75%
Coronary CTA⁴	95%	83%

1. ACC/AHA 2002 Guideline Update for Exercise Testing
2. ACC/AHA/ASE 2003 Guideline Update for the Application of Echocardiography
3. ACC/AHA/ASNC Guidelines for the Clinical Use of Cardiac Radionuclide Imaging
4. ACCURACY study

Anatomic-Physiologic Disordance

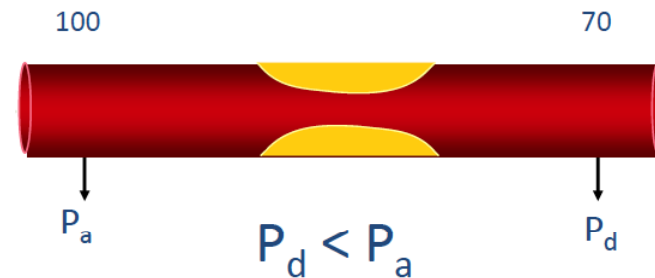
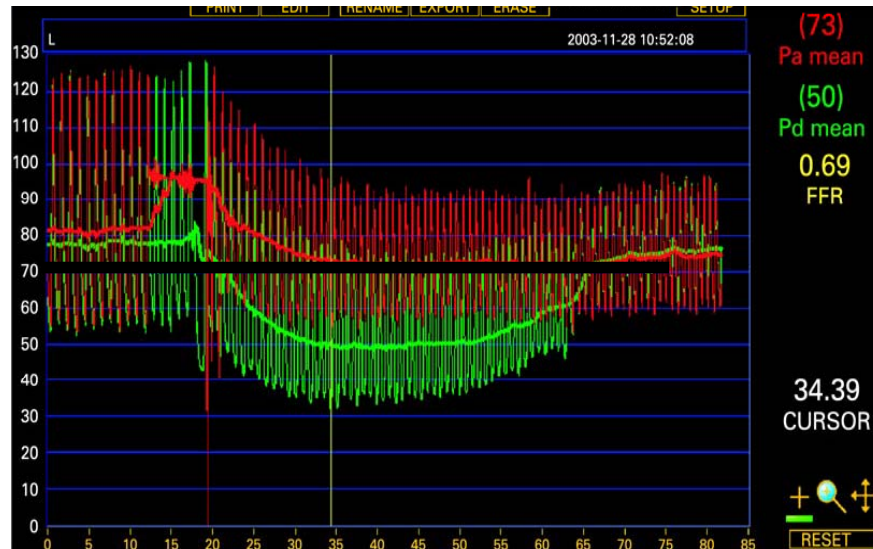
Even amongst CCTA-identified stenosis confirmed by cath, only a minority of such lesions are ischemia-causing^{1,2,3}



Source: ¹Min et al. J Am Coll Cardiol 2010; ²Schuijf et al. J Am Coll Cardiol 2006, ³Schuijf et al. Heart 2008

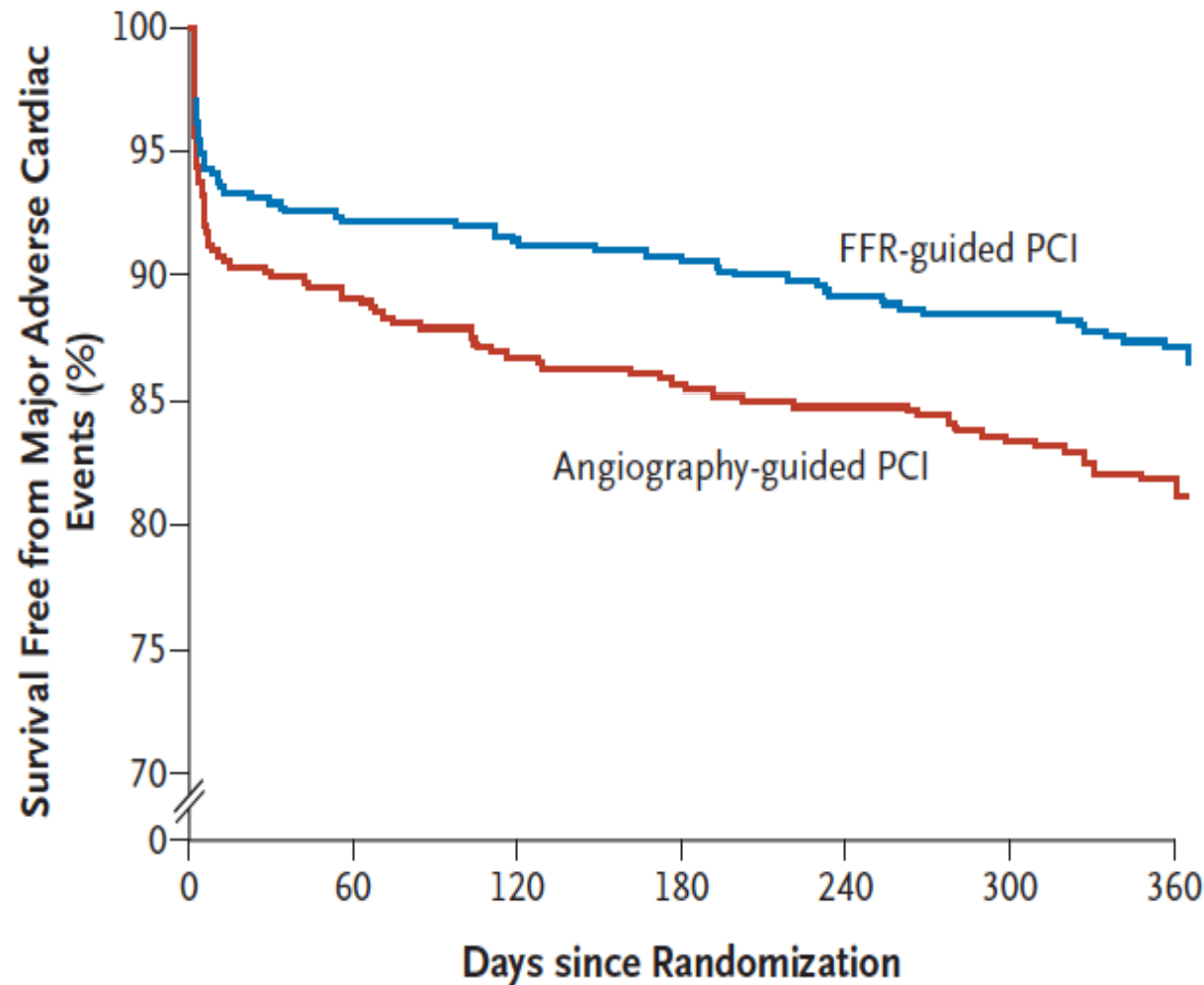
“Gold” Standard for Lesion-Specific Ischemia: Fractional Flow Reserve (FFR)

- FFR at the time of invasive coronary angiography (ICA) is the only method for specific determination of the hemodynamic significance of coronary artery lesions (*lesion-specific ischemia*)



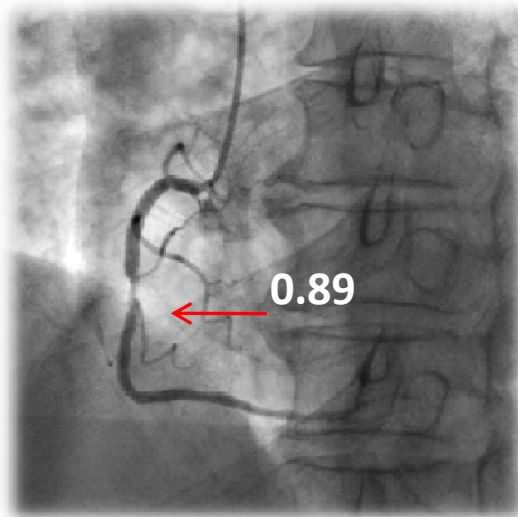
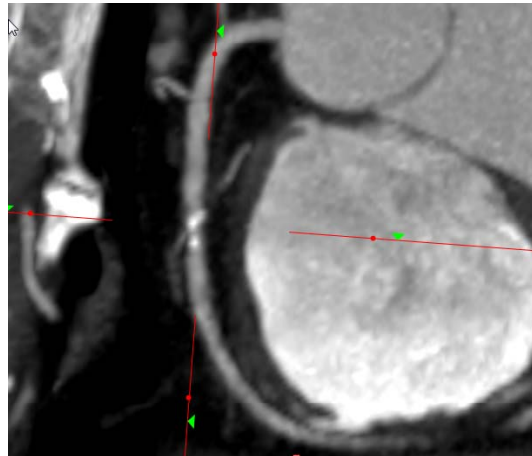
- FFR = Ratio of maximal myocardial blood flow through a diseased artery to the blood flow in the hypothetical case that this artery is normal
- Values ≤ 0.80 or ≤ 0.75 considered diagnostic of lesion-specific ischemia

Assessment of *Lesion-specific Ischemia* by FFR is the Only Method To Improve Event-free Survival

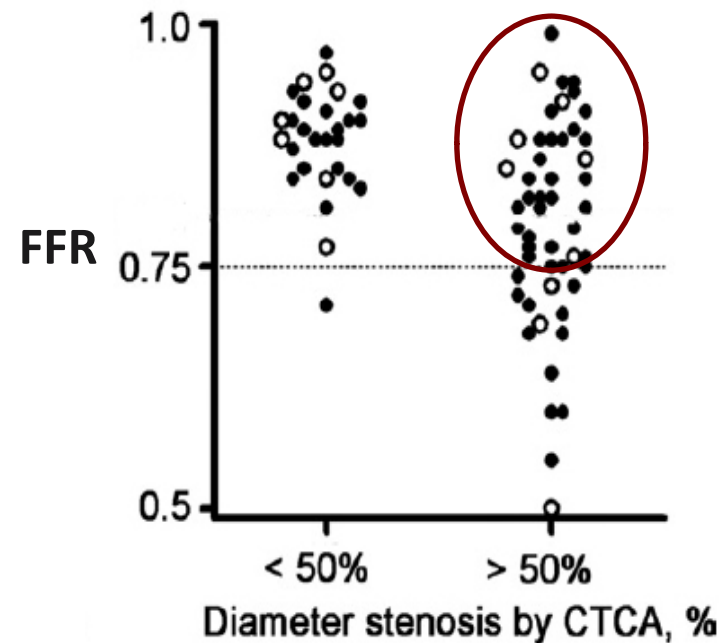


Source: Tonino et al. NEJM 2009;360:213-24; Pijls et al. J Am Coll Cardiol 2010

CCTA Stenosis Demonstrates an Unreliable Relationship to Lesion-Specific Ischemia



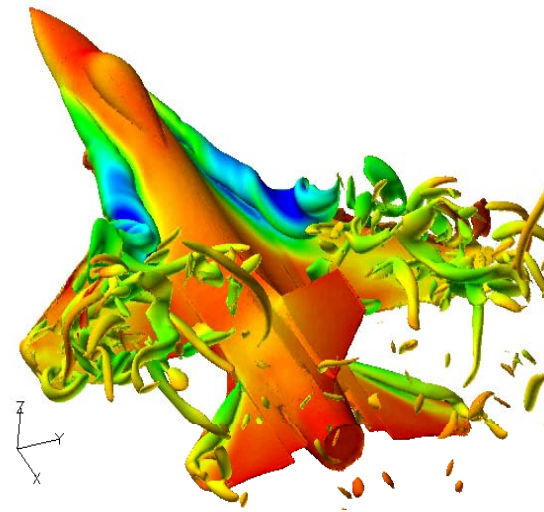
- CCTA correlates favorably with angiographic estimate of coronary stenosis but unreliably estimates hemodynamic significance of lesions as determined by FFR



75% false positives

Computational Fluid Dynamics

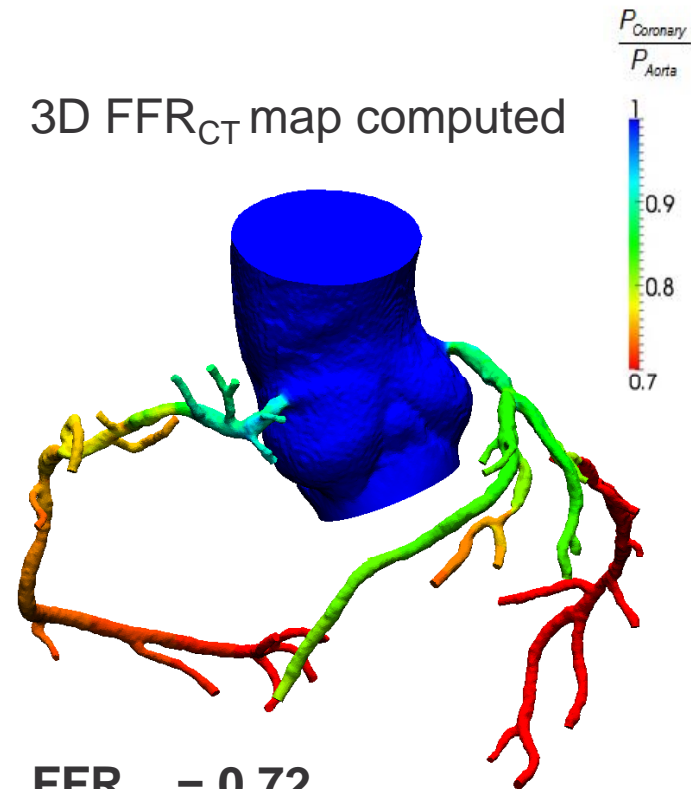
- **Computational fluid dynamics (CFD)** quantifies fluid pressure and velocity, based on physical laws of mass conservation and momentum balance
- **CFD for Patient-Specific Models of Coronary Arteries**
 1. Numerical method approximates governing equations
 2. Obtain solution for velocity / pressure at finite (but very large) number of points
 3. Simultaneously solve millions of non-linear equations and repeating process for thousands of time intervals within cardiac cycle



Images courtesy of Prof. Charbel Farhat, Dept. of Aeronautics & Astronautics, Stanford University

FFR_{CT} is determined from typically-acquired CCTA

1. **No** additional image acquisition
2. **No** excess radiation
3. **No** modification to imaging protocols (prospective or retrospective gating)
4. **No** administration of adenosine or other medications



FFR_{CT} = 0.72
(can select any point on model)

DISCOVER-FLOW: Diagnosis of ischemia-causing stenoses obtained via non-invasive fractional flow reserve

- **Objective:** To determine the diagnostic performance of non-invasive FFR_{CT} , as compared to invasively measured FFR

- **Study design**

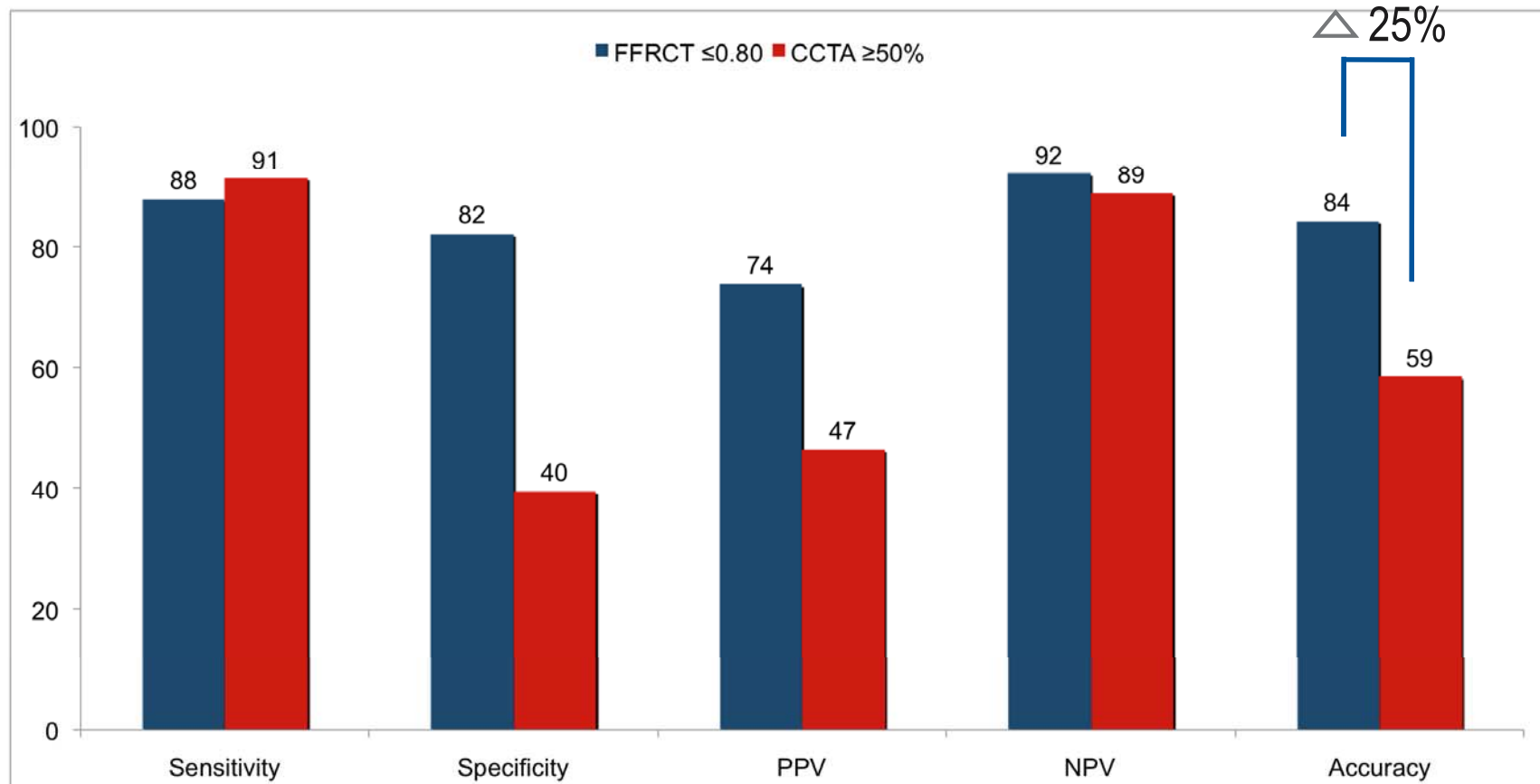
- Prospective multicenter study**

1. Seoul National University Hospital, Seoul, Korea
2. Pauls Stradins University, Riga, Latvia
3. Inje University Paik Hospital, Koyang, Korea
4. Stanford University, Stanford, CA, USA
5. New York Presbyterian Hospital, NY, USA

- Sample size calculation**

- Assumed diagnostic accuracy of CCTA stenosis for FFR-ischemia = 49%²
 - 150 vessels required to detect an improvement in diagnostic accuracy of FFR_{CT} by $\geq 25\%$
 - Type I error: 0.05, statistical power: 90%

Diagnostic Performance of FFR_{CT} and CCTA



Source: Koo et al. J Am Coll Cardiol 2011

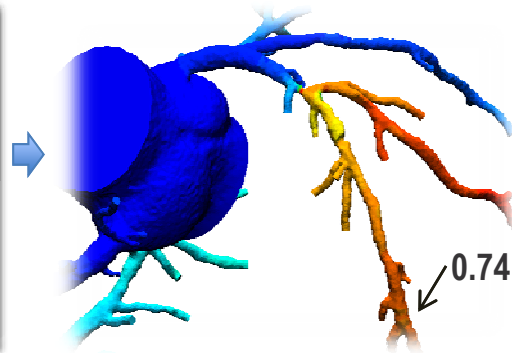
Examples – DISCOVER-FLOW

CCTA



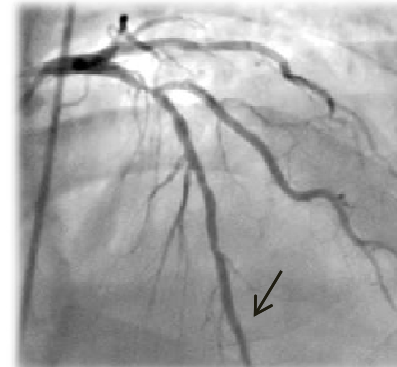
>50% diameter stenosis

FFR_{CT}



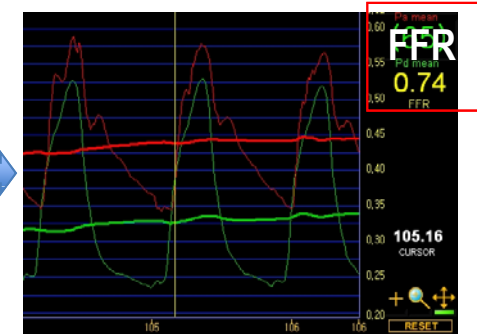
FFR_{CT} 0.74 → ischemia

Invasive angiography

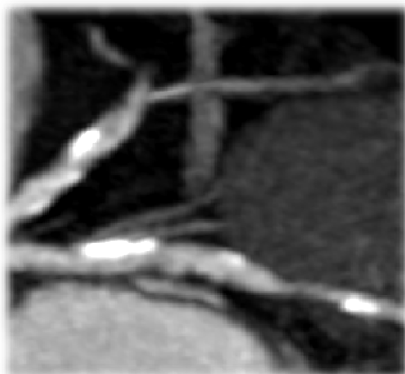


>50% diameter stenosis

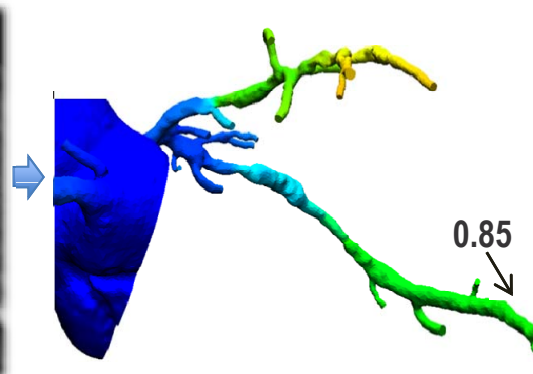
FFR



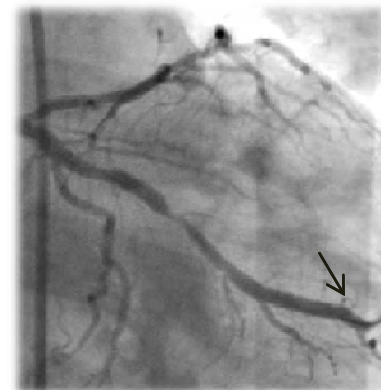
FFR 0.74 → ischemia



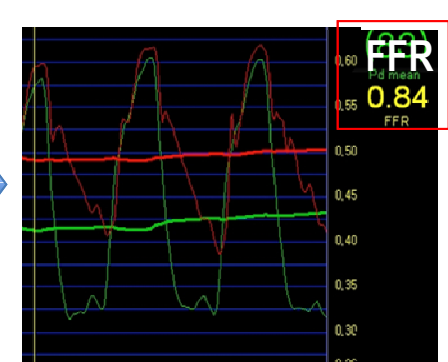
>50% diameter stenosis



FFR_{CT} 0.85 → no ischemia



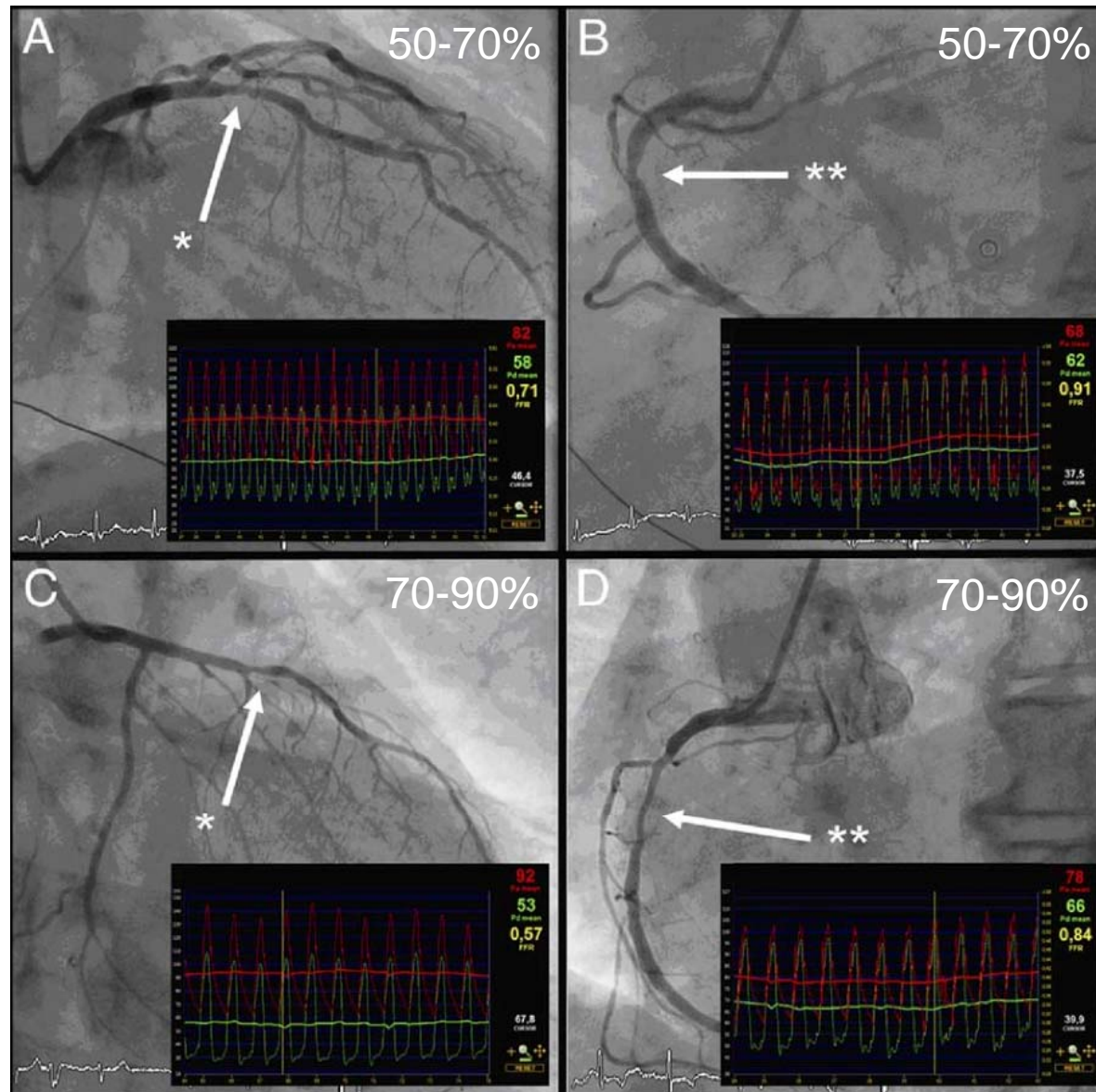
>50% diameter stenosis



FFR 0.84 → no ischemia

**Besides ischemia
assessment in severe
stenoses, in what
other scenarios will
 FFR_{CT} be useful?**

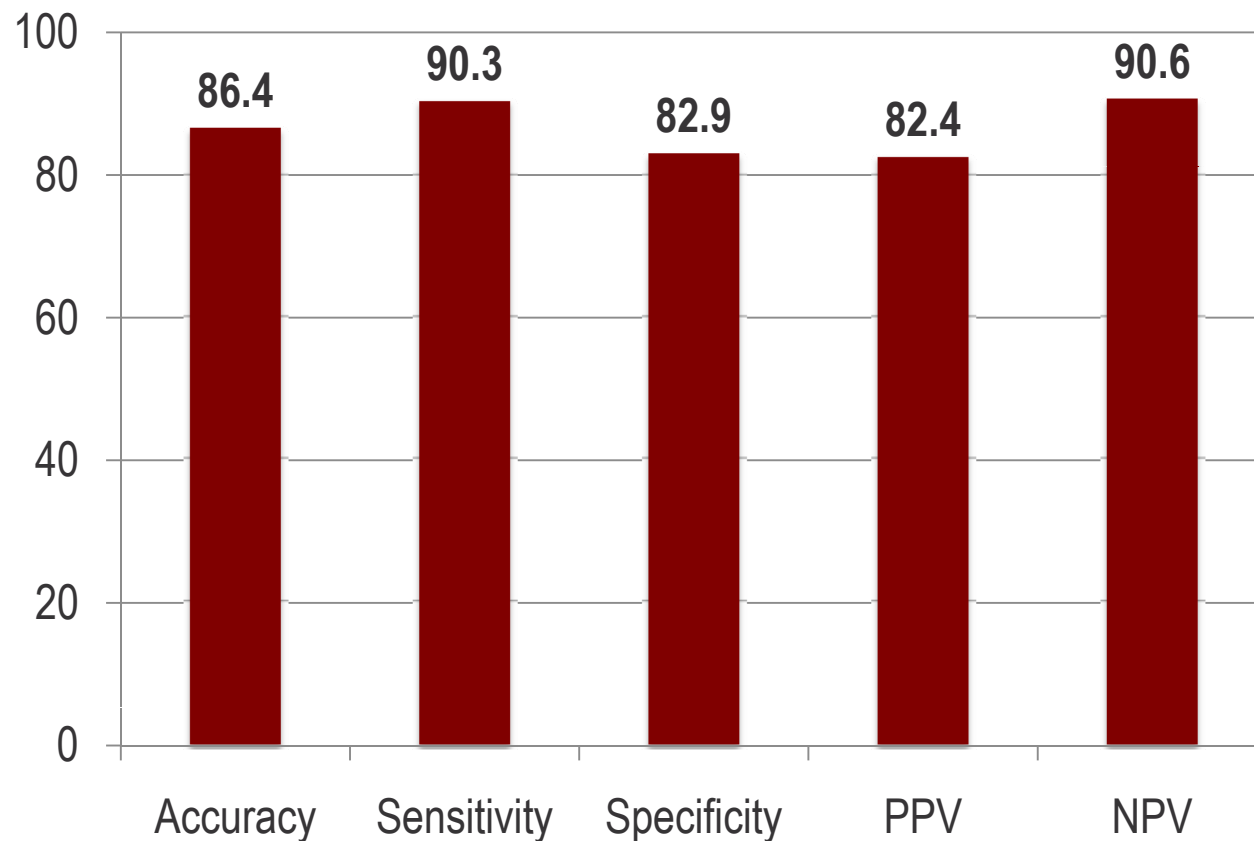
(1) Intermediate Stenoses



Source: Tonino PA et al. J Am Coll Cardiol

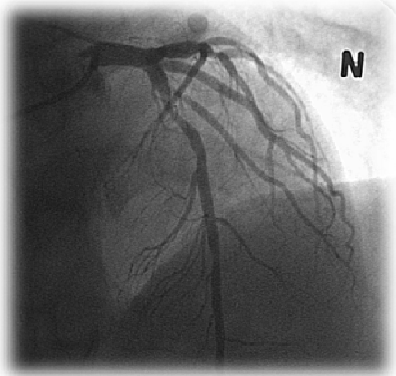
Diagnostic Performance of FFR_{CT} for 40-69% Stenoses

FFR _{CT}	Accuracy	Sensitivity	Specificity	PPV	NPV
FFR _{CT} ≤ 0.80 (95% CI)	86.4 (75.7-93.6)	90.3 (74.2-98.0)	82.9 (66.4-93.4)	82.4 (65.5-93.2)	90.6 (75.0-98.0)
FFR _{CT} ≤ 0.75 (95% CI)	83.3 (72.1-91.4)	77.3 (54.6-92.2)	86.4 (72.6-94.8)	73.9 (51.6-89.8)	88.4 (74.9-96.1)



Examples – Intermediate Stenoses

Invasive angiography



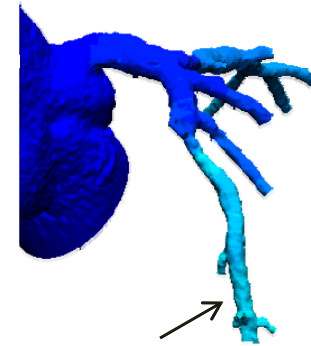
QCA %DS = 54.09%
FFR = 0.89

CCTA

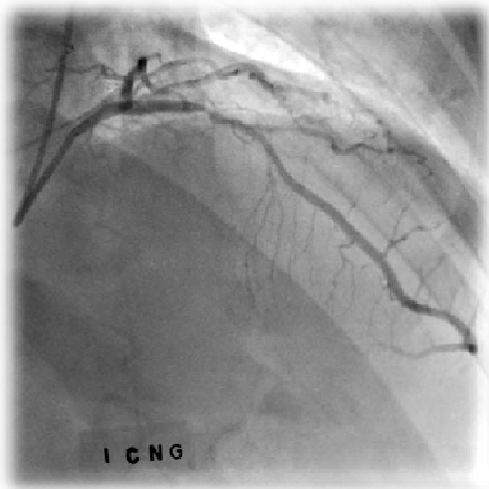


CCTA 50-69% stenosis

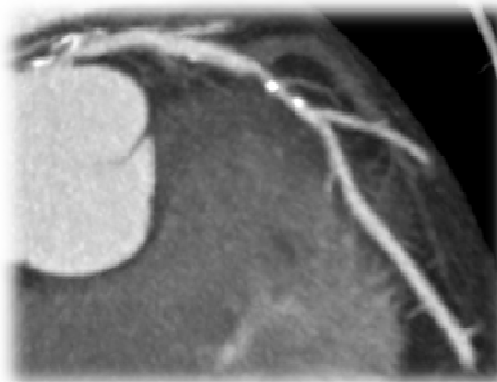
FFR_{CT}



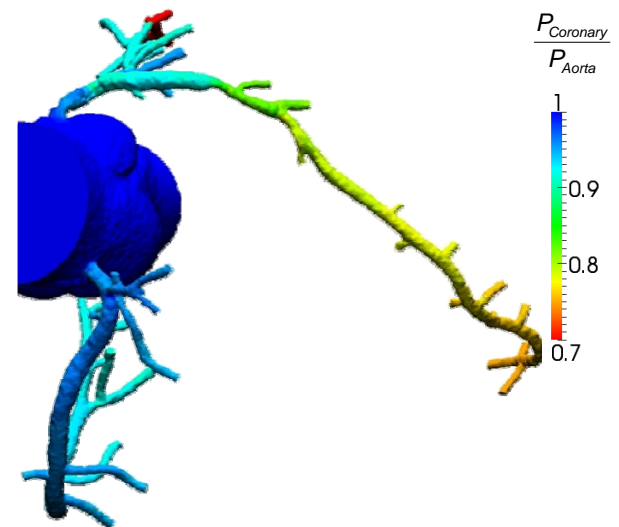
FFR_{CT} 0.93 → No ischemia



QCA %DS = 50.68%
FFR = 0.71

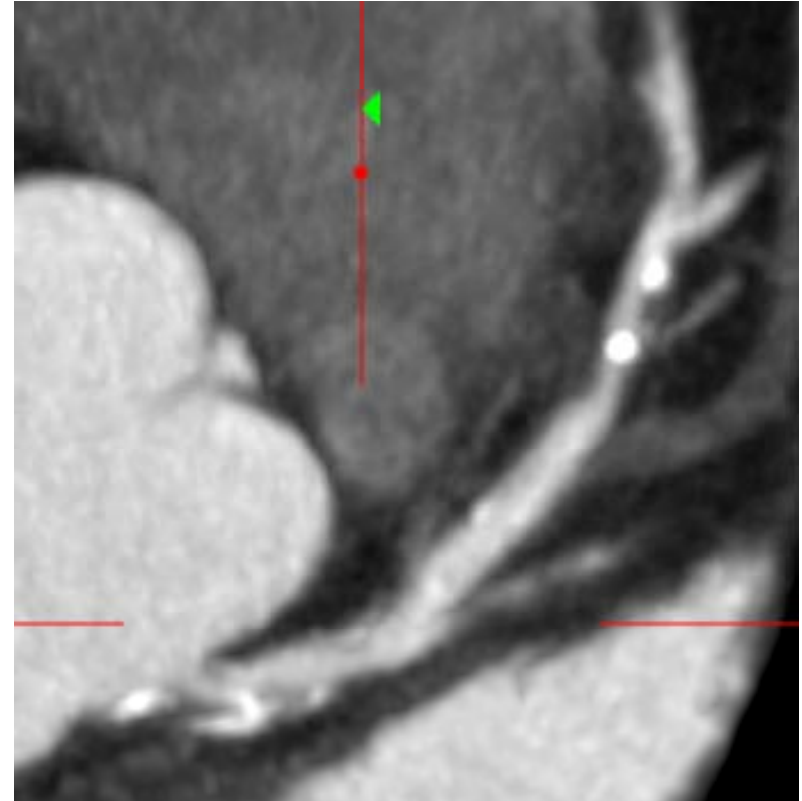
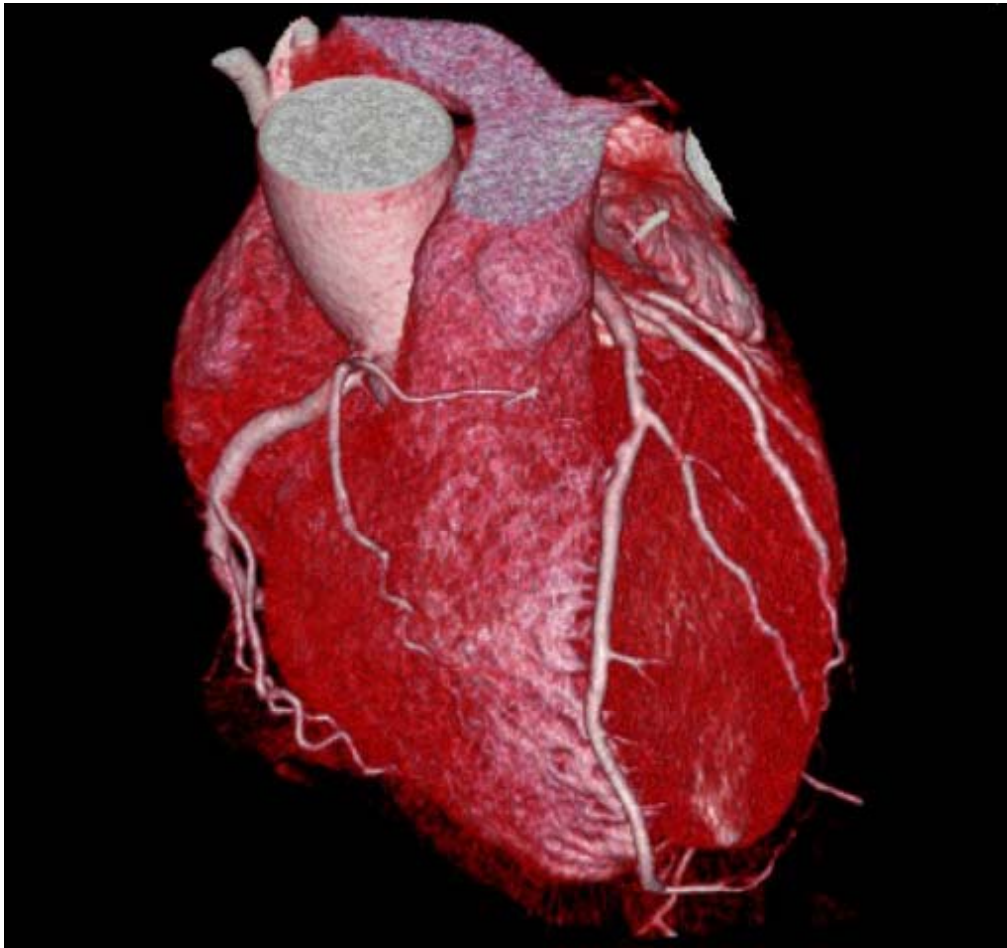


CCTA 50-69% stenosis



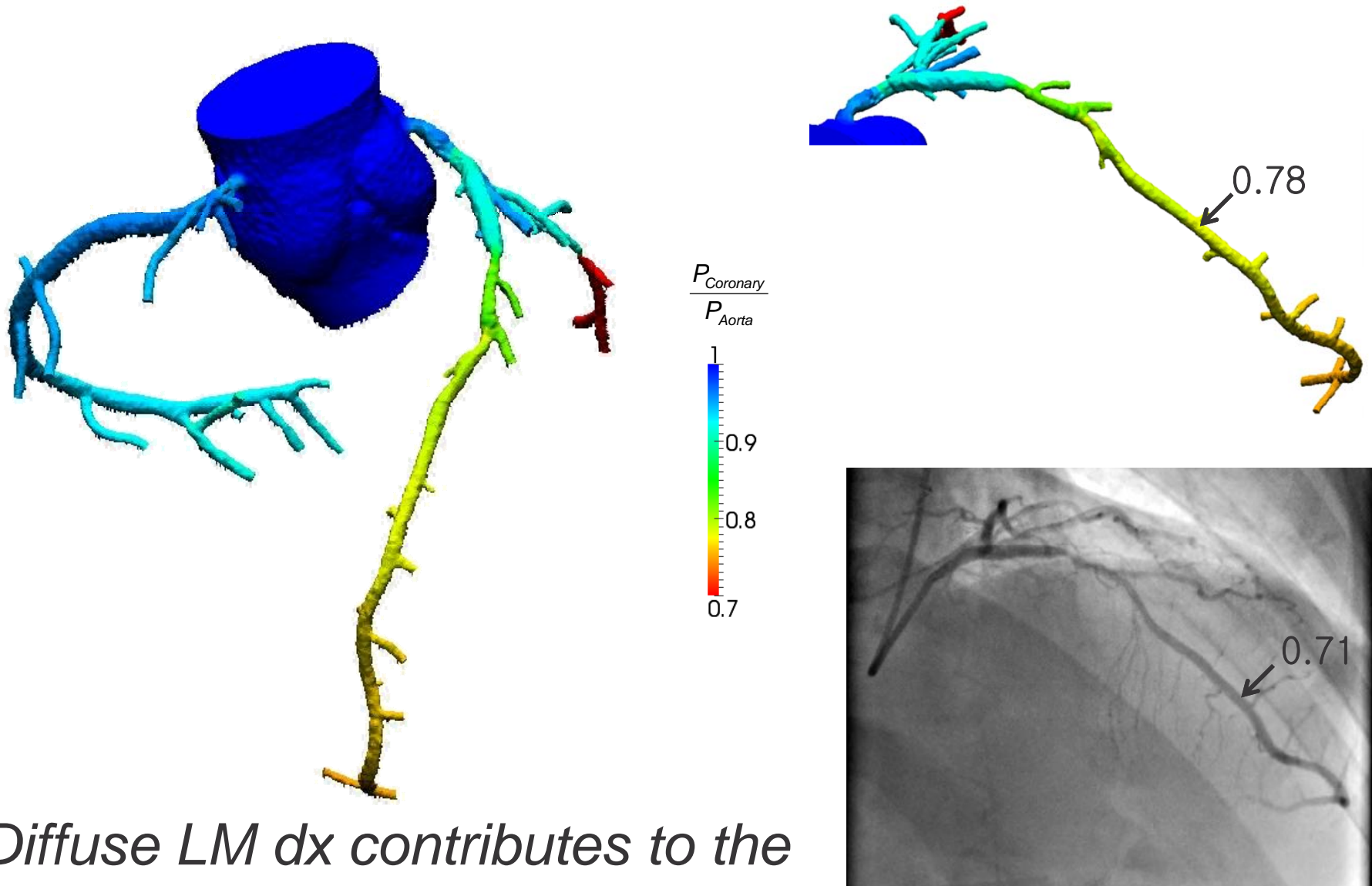
FFR_{CT} 0.78 → Ischemia

(2) Diffuse Non-Obstructive Atherosclerosis



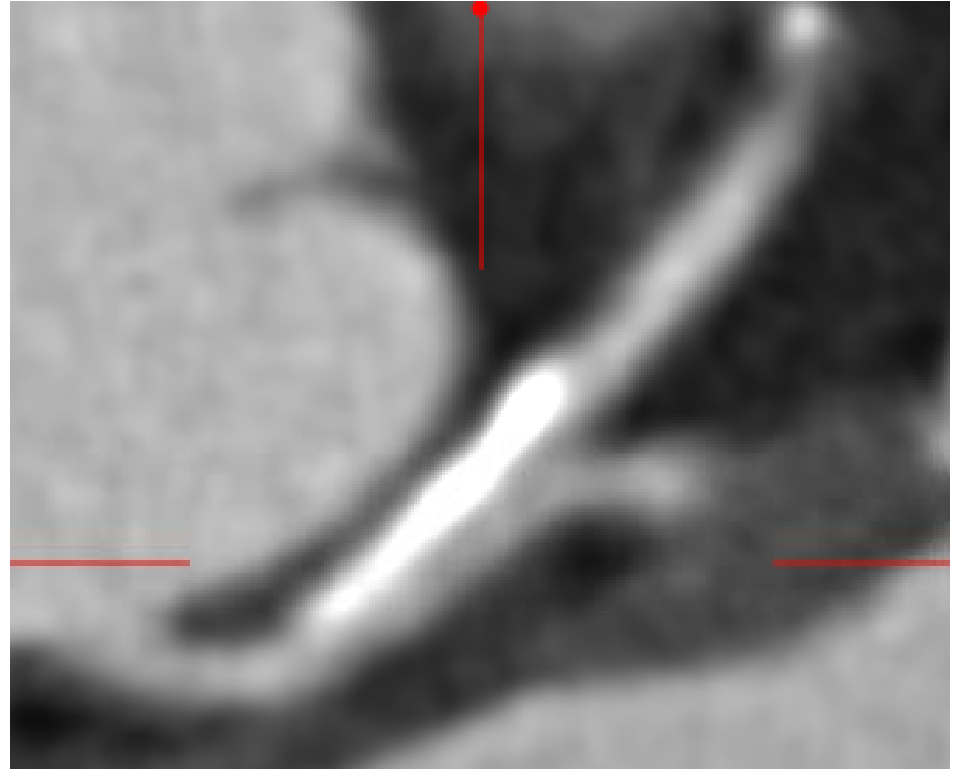
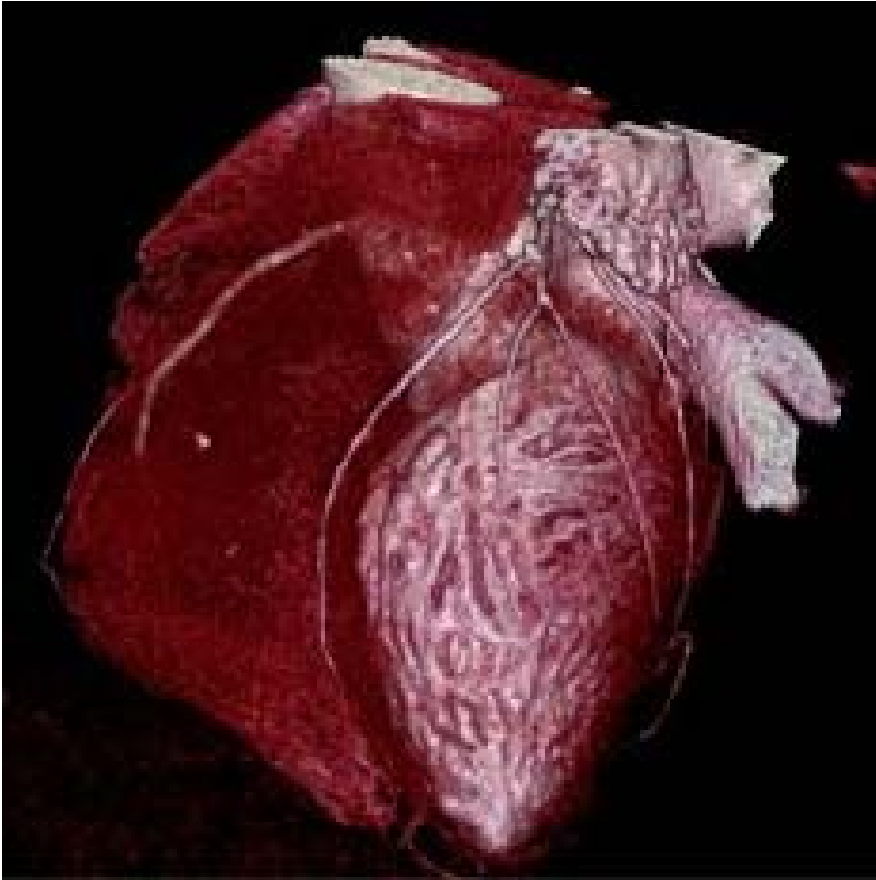
Diffuse mild left main disease with moderate LAD Dx

(2) Diffuse Non-Obstructive Atherosclerosis



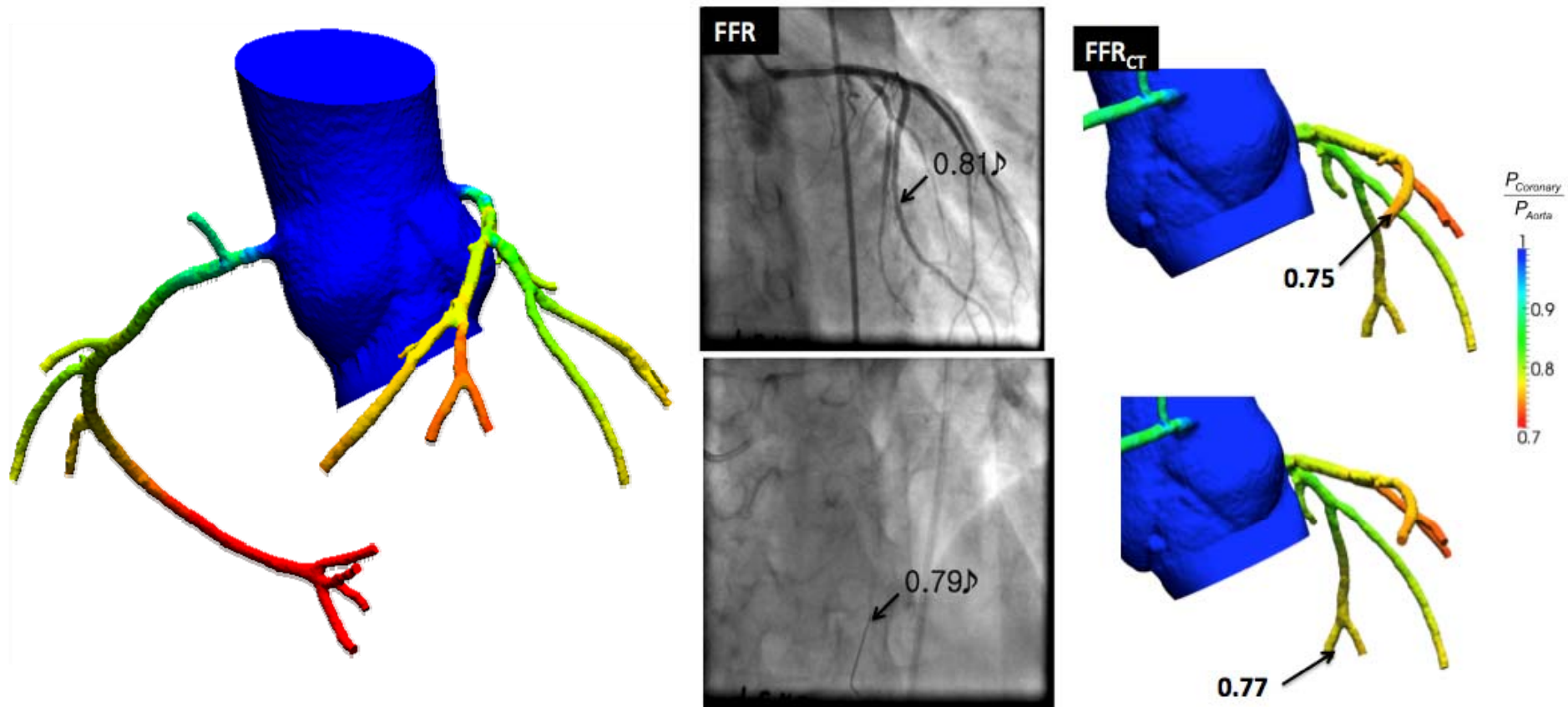
Diffuse LM dx contributes to the functional significance of the LAD

(3) Small Vessels



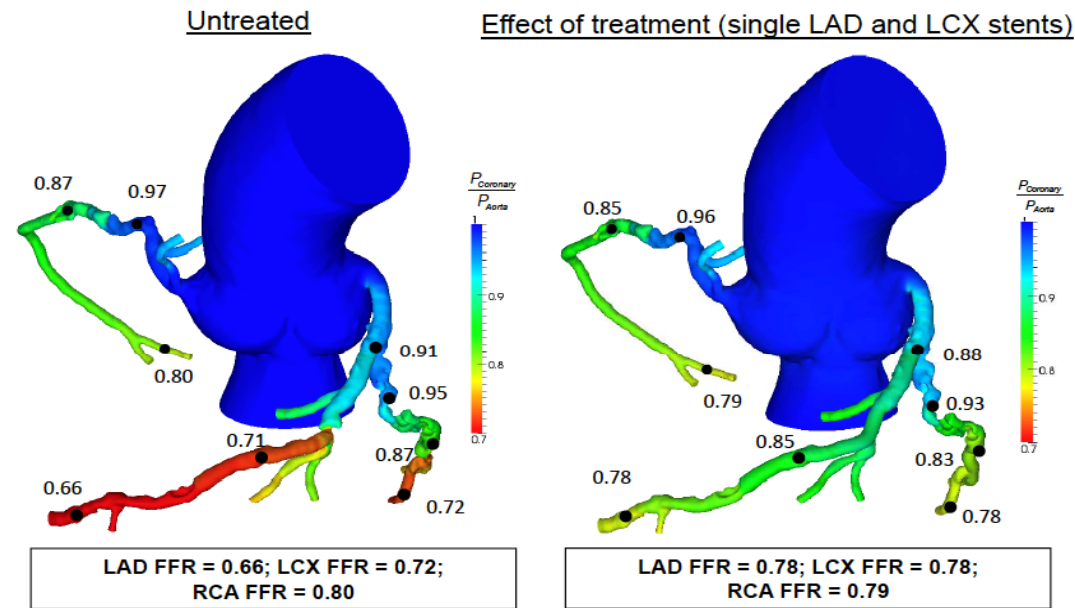
2.5 mm left main and left anterior descending artery

(3) Small Vessels

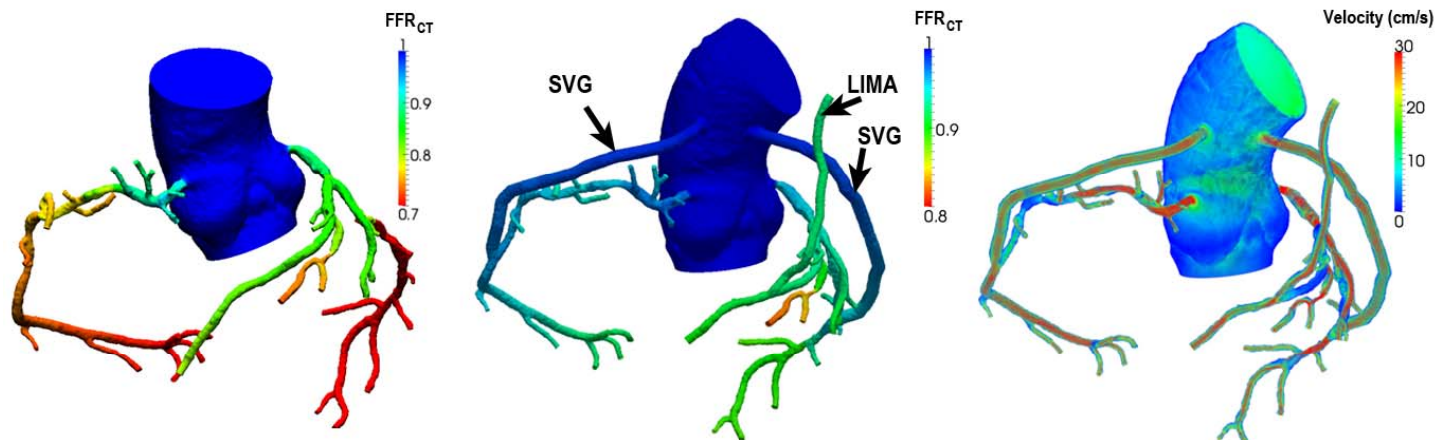


Functional 3-vessel disease

(4) Prediction of Therapeutic Benefit

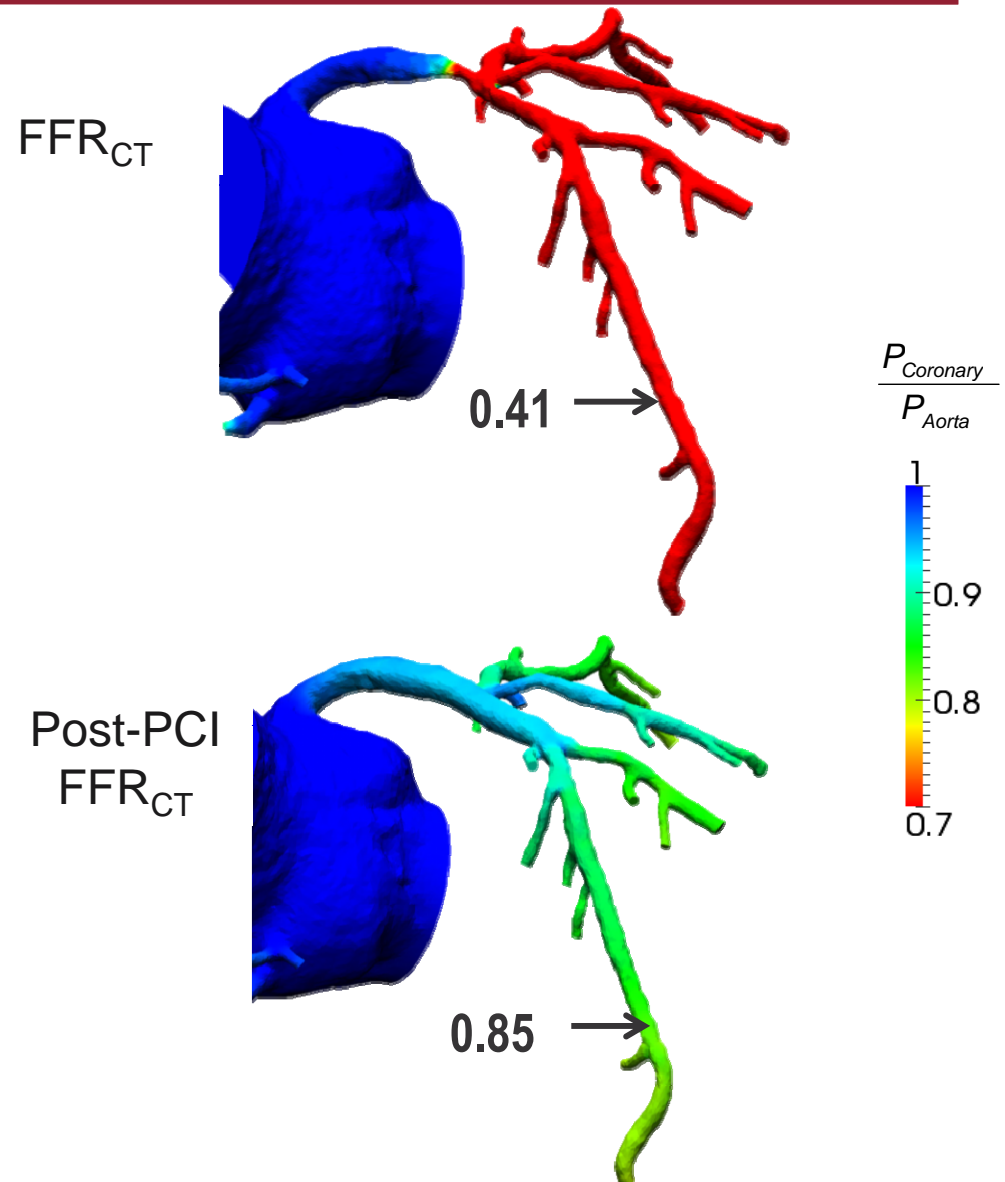
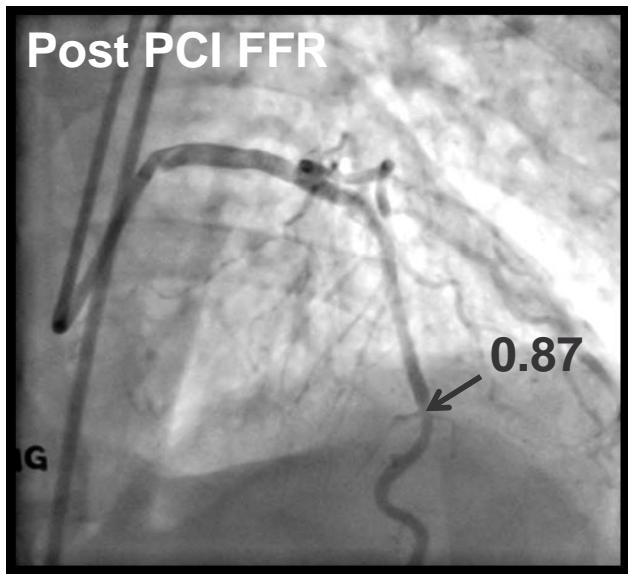
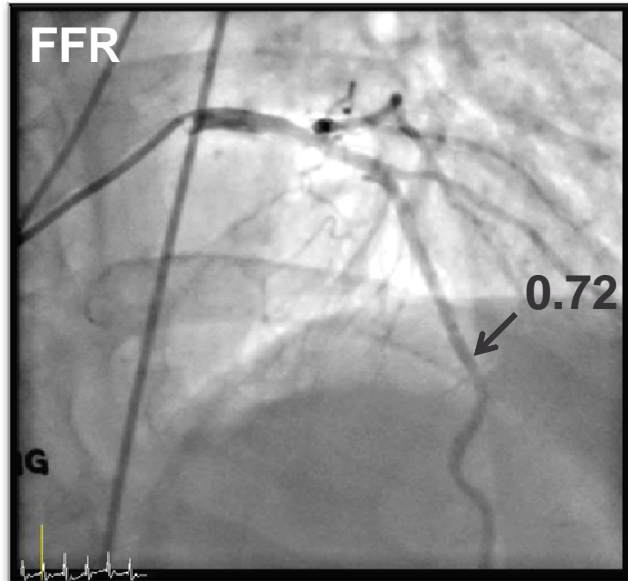


Percutaneous Revascularization by FFR_{CT}

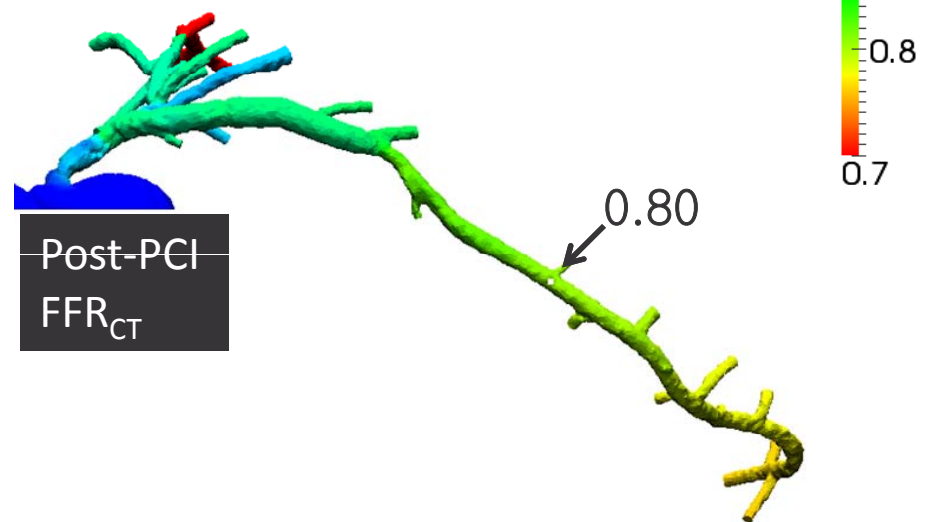
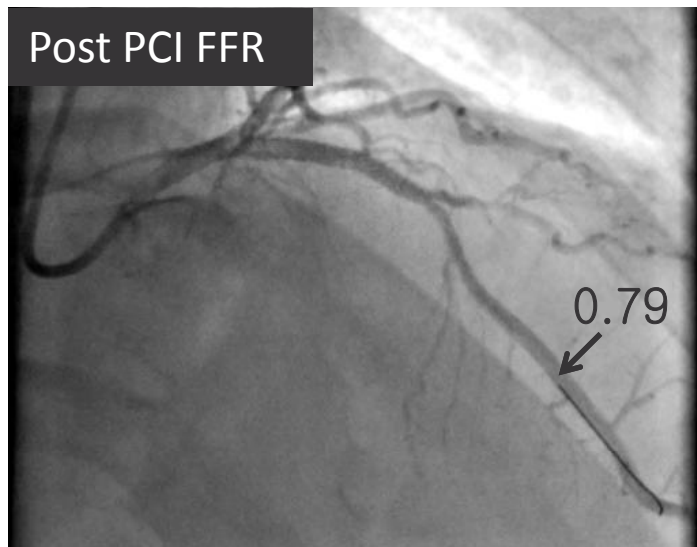
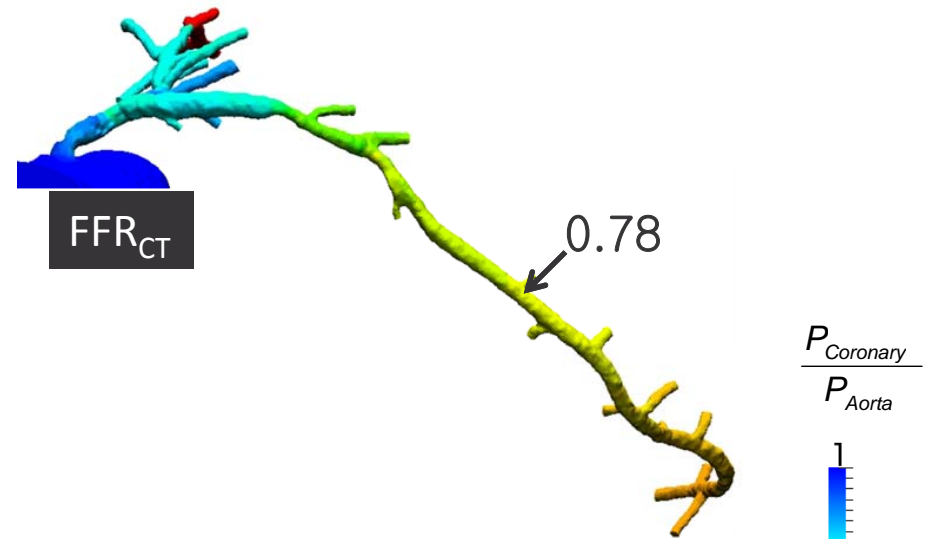
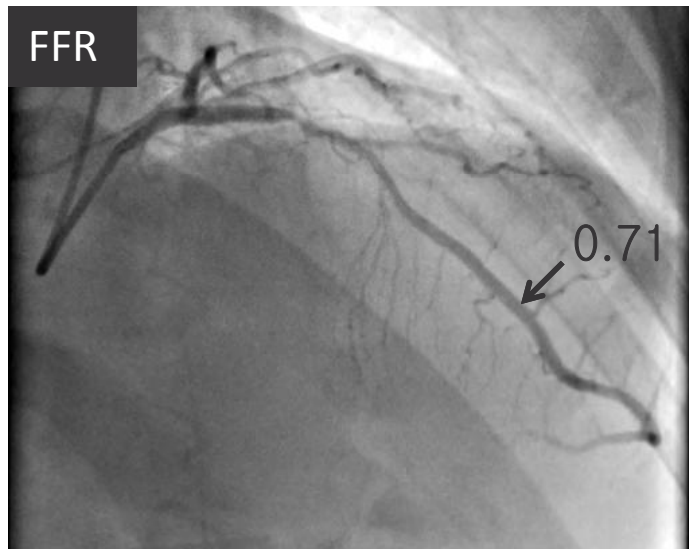


Surgical Revascularization by FFR_{CT}

Therapeutic Benefit of Revascularization



No Therapeutic Benefit of Revascularization



The DeFACTO Trial

(Determination of Fractional Flow Reserve by Anatomic Computed Tomographic AngiOgraphy)

- 17-center international study of 285 patients undergoing CCTA and invasive FFR to evaluate the *diagnostic performance of FFR_{CT}*
- Per-patient endpoint
- Enrollment completed 10/11

