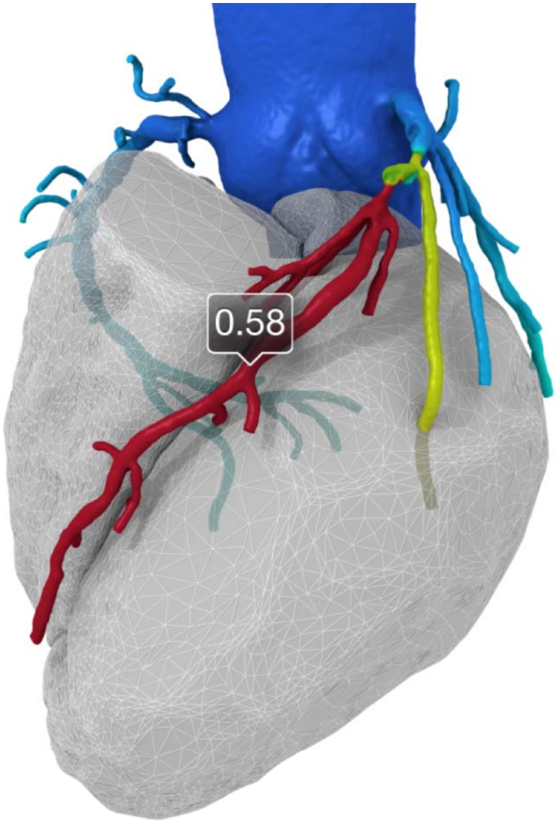
Computed FFR:
Where are we and where do we go?



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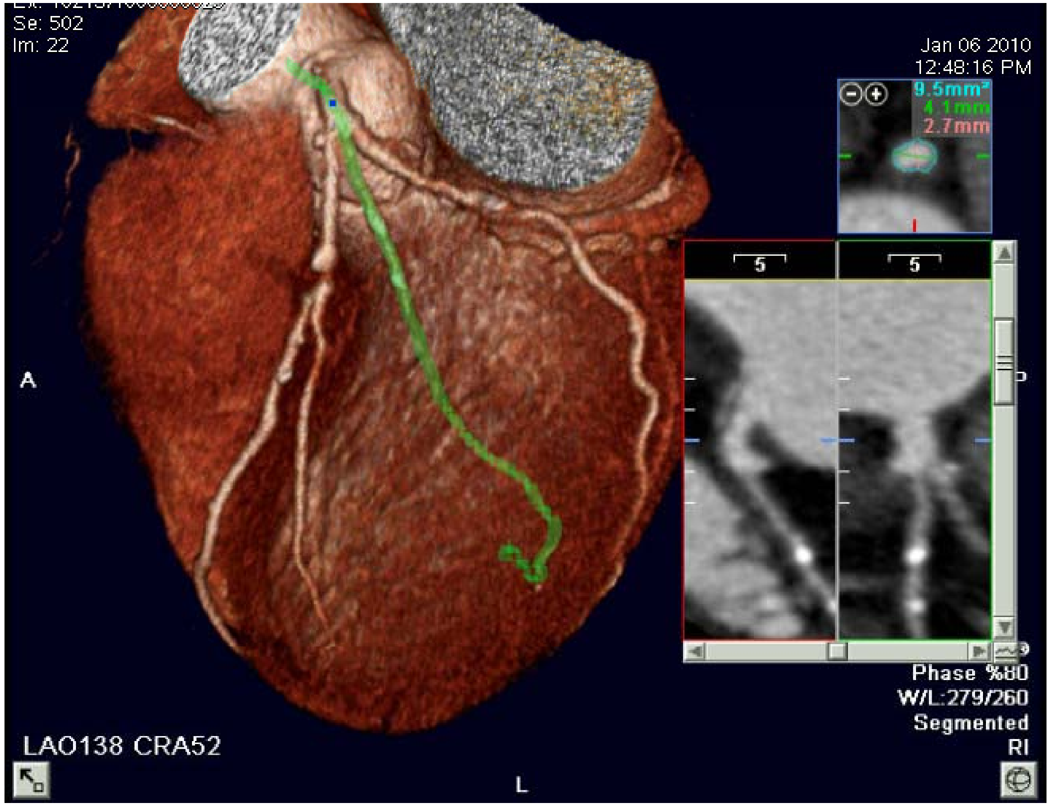
Coronary CT Angiogram, circa 2005



- ✓ Non-invasive
- ✓ High spatial resolution (0.5-0.7mm)
- ✓ High temporal resolution (165-200 ms)
- ✓ Robust volume coverage (2-4cm)
- ✓Quick (5-12 sec)

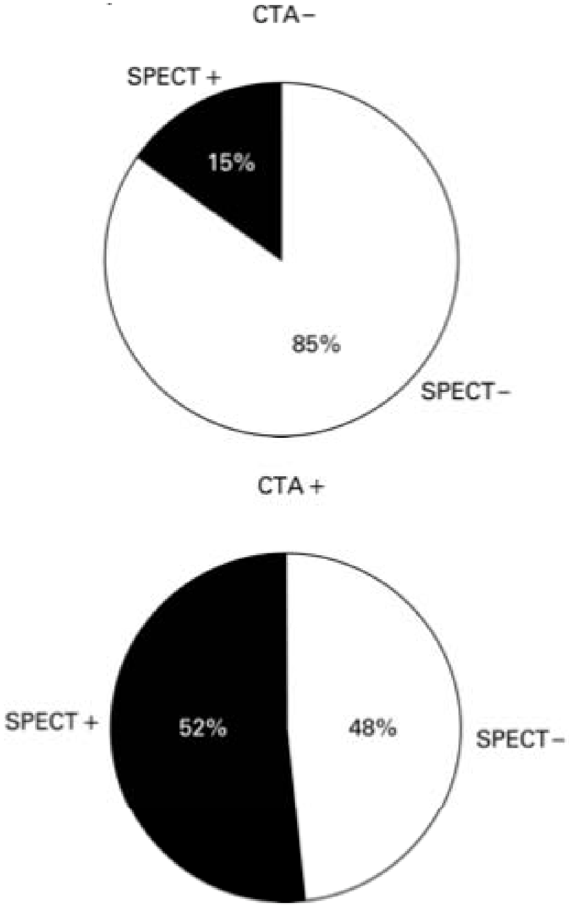
Diagnosis of Obstructive CAD

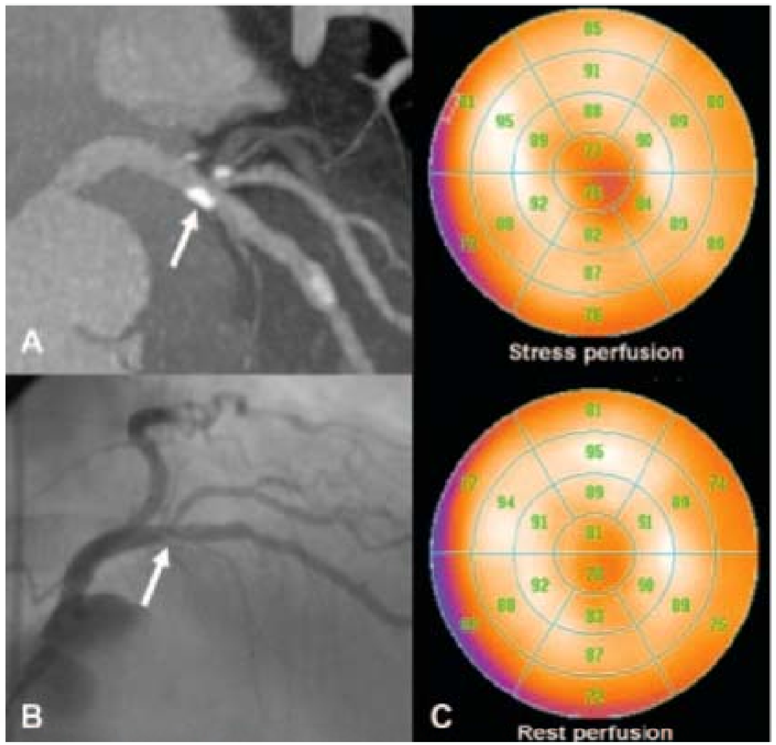
Test	Sensitivity	Specificity
Exercise ECG treadmill[1]	68%	77%
Exercise Echo treadmill[2]	86%	81%
Dobutamine Echo[2]	~85%	~85%
Exercise nuclear treadmill[3]	87%	73%
Pharmacologic nuclear[3]	89%	75%
Coronary CTA[4]	**95%**	**83%**

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]

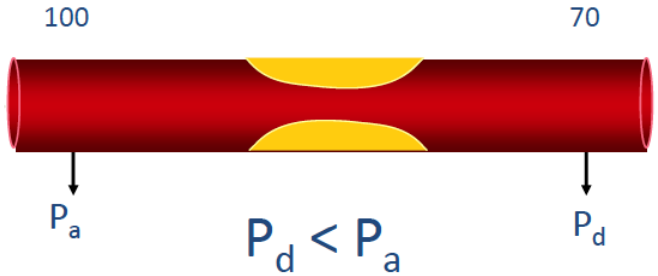




Source: [1]Min et al. J Am Coll Cardiol 2010; [2]Schuijf et al. J Am Coll Cardiol 2006, [3]Schuijf et al. Heart 2008

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

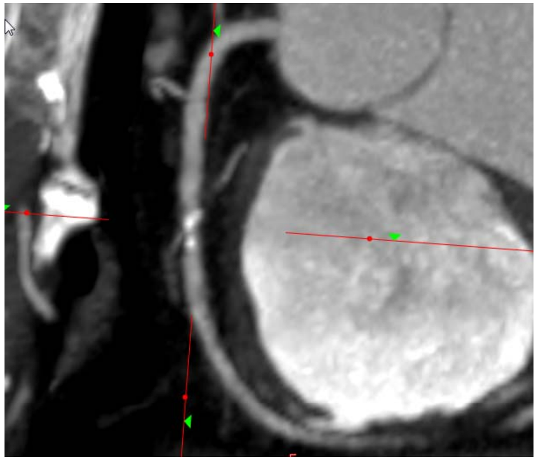
- FFR at the time of invasive coronary angiography (ICA) is the only method for specific determination of the hemodynamic significance of coronary artery lesions *(lesion-specific ischemia)*

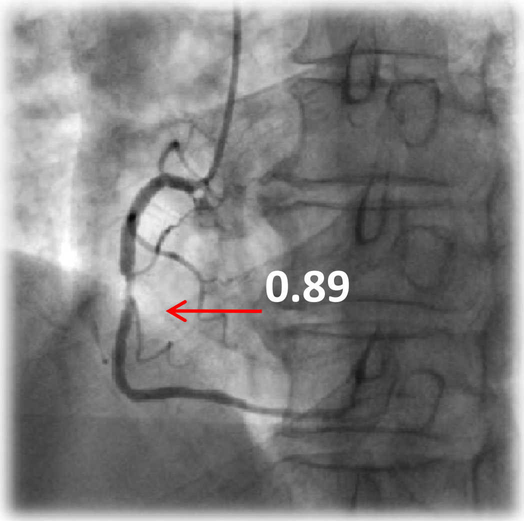


- FFR = Ratio of maximal myocardial blood flow through a diseased artery to the blood flow in the hypothetical case that this artery is normal
- Values $\leq$0.80 or $\leq$0.75 considered diagnostic of lesion-specific ischemia

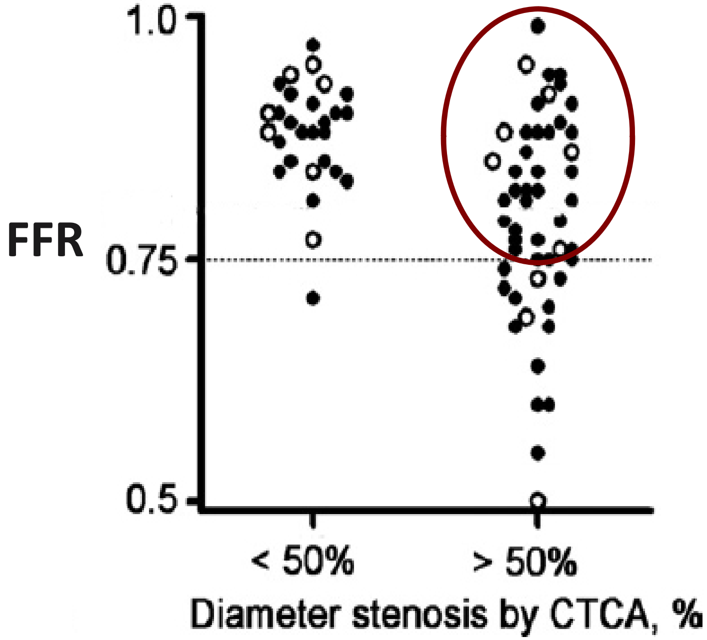
Source: Pijls NH et al. J Am Coll Cardiol. 2007; Pijls NH et al. J. Am. Coll. Cardiol. 2010

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

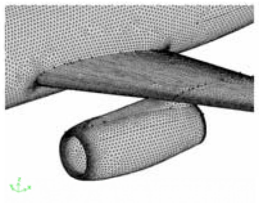


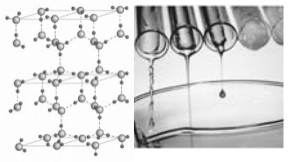
75% false positives

Source: Meijboom et al. J Am Coll Cardiol 2008

Can we determine FFR from CCTA?

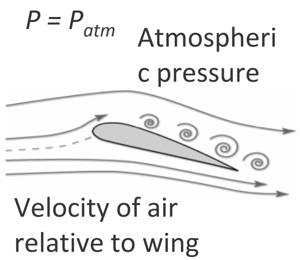
Detailed maps of pressure and velocity can be obtained computationally





Input Data

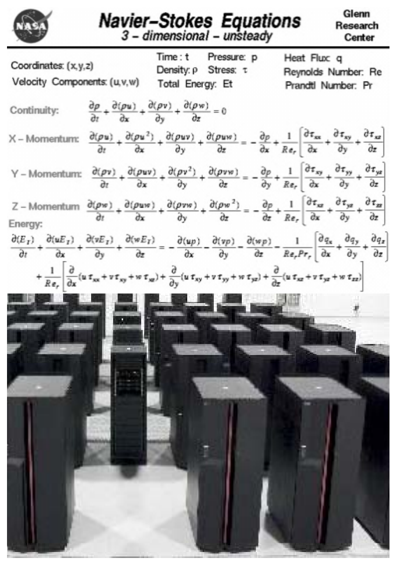
- Geometry - obtained from design specifications
- Fluid properties – viscosity and density of air



Boundary Conditions

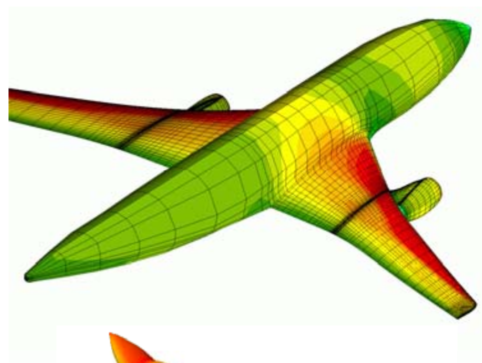
- Velocity of incoming air relative to wing
- Atmospheric pressure

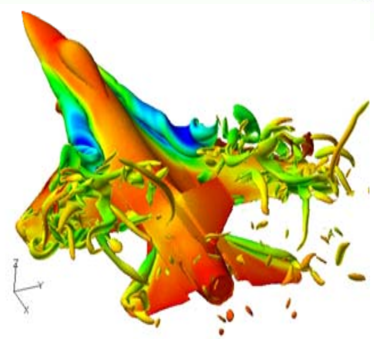
Equations of fluid flow solved on supercomputers



Computed velocity, pressure, lift and drag

- Geometry represented as a mesh
- Equations of fluid flow solved for each point on this mesh



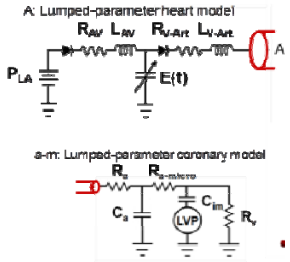


Source: Courtesy of Charley Taylor, Stanford University

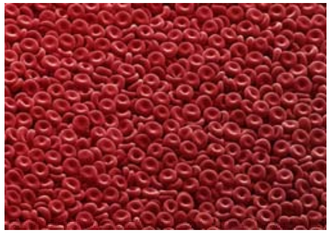
Simulating coronary blood flow uses similar principles but is even more complicated

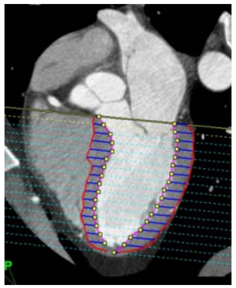
Patient-specific geometry

Heart-Vessel Interactions



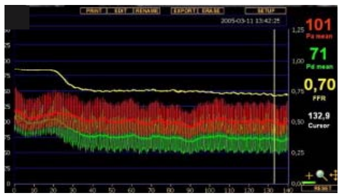
Complex fluid Properties





Flow demand related to myocardial mass, cardiac work, etc…

Microcirculatory resistance depends on complex vessel structure



Physiology changes due to administration of drugs to induce hyperemia

Inputs

- Accurate coronary geometric models including branching structure and pathology
- Physiologic models personalized using minimal measured data

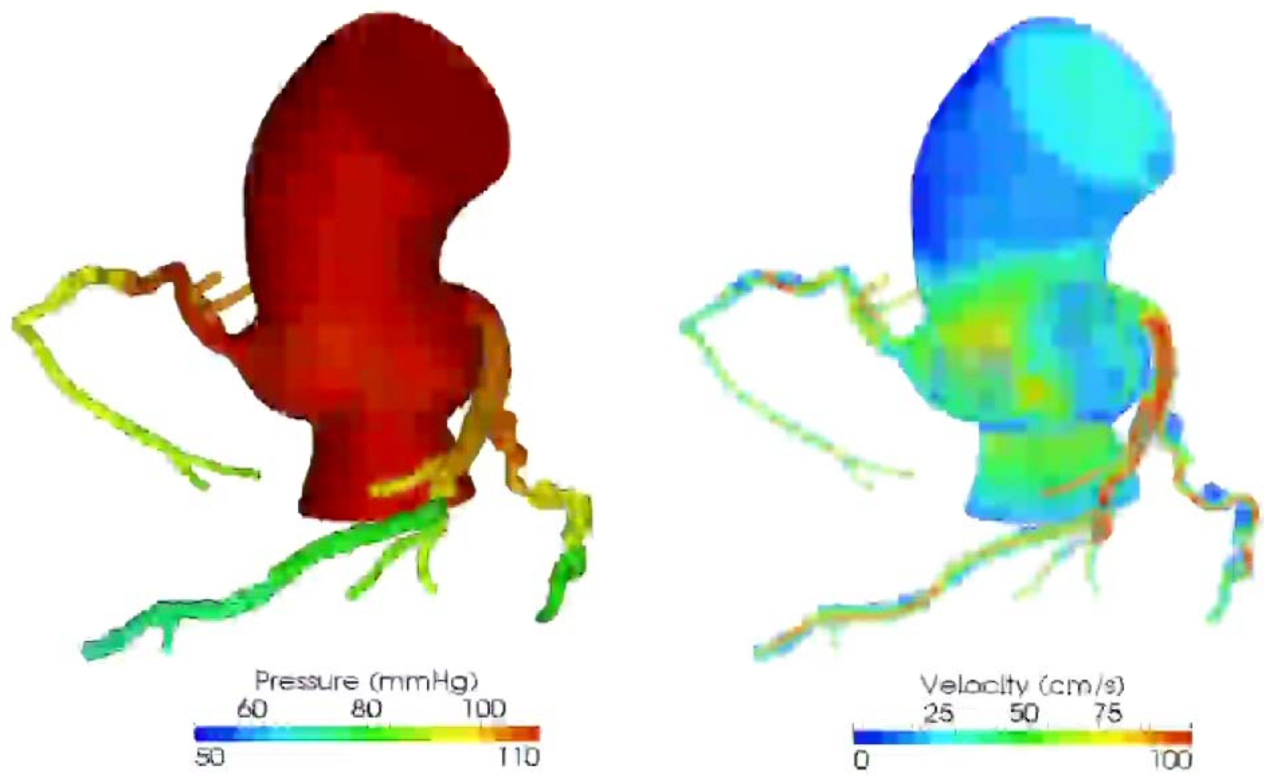
Boundary Conditions

- Heart/vascular interaction
- Aortic impedance
- Time-varying coronary resistance related to intramyocardial pressure
- Models to simulate hyperemia

Numerical Methods

- Anisotropic, adaptive, boundary layer mesh generation to reduce computation time
- Tight coupling between heart model and aorta/coronary model
- High performance parallel incompressible flow solver

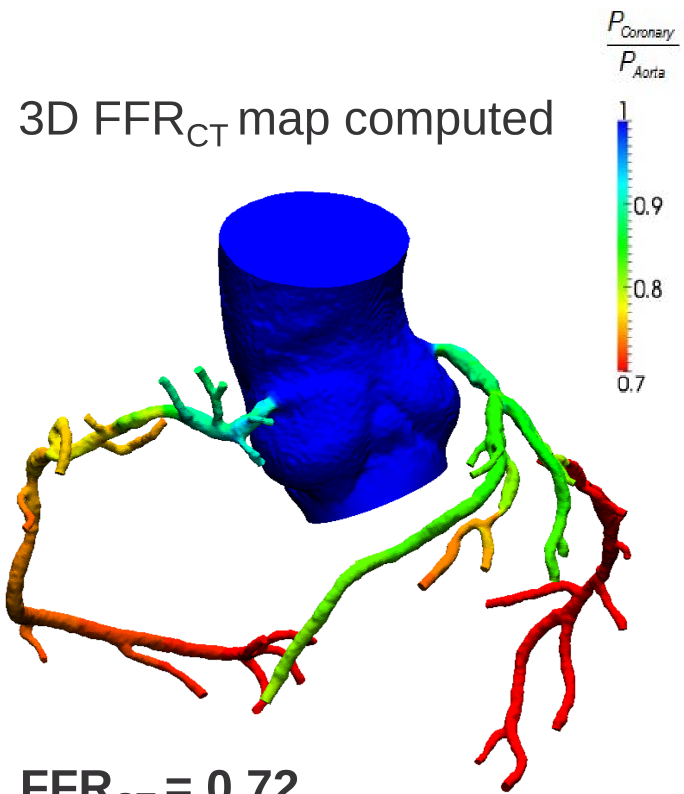
FFR_{CT} is determined from typically-acquired CCTA



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

3D FFR_{CT} map computed



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

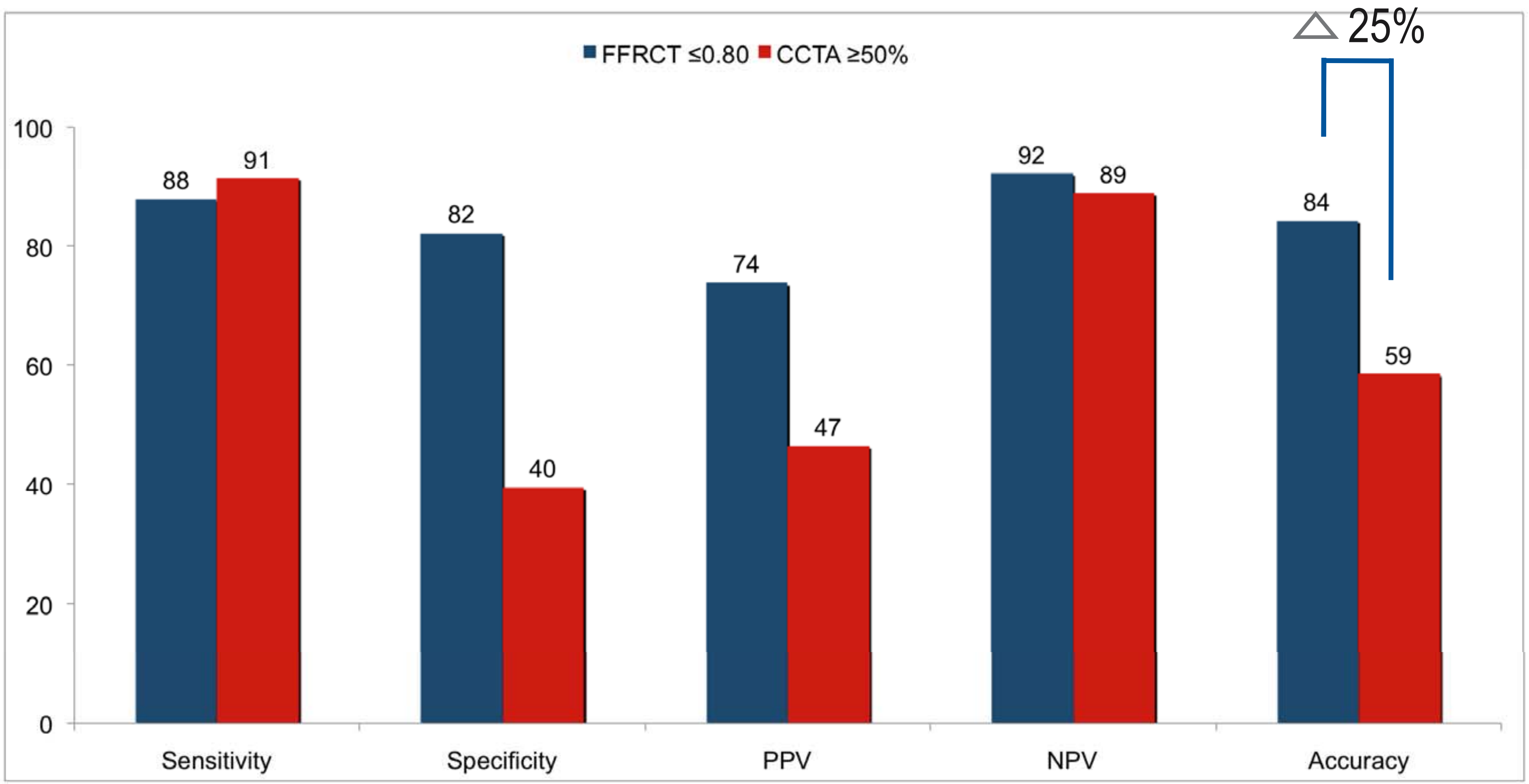
  1. Seoul National University Hospital, Seoul, Korea
  2. Pauls Stradins University, Riga, Latvia
  3. Inje University Paik Hospital, Koyang, Korea
  4. Stanford University, Stanford, CA, USA
  5. New York Presbyterian Hospital, NY, USA

  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 ≥ 25%
  - Type I error: 0.05, statistical power: 90%

Source: Koo et al. J Am Coll Cardiol 2011; [2]Meijboom et al. J Am Coll Cardiol 2008

Diagnostic Performance of FFR_{CT} and CCTA

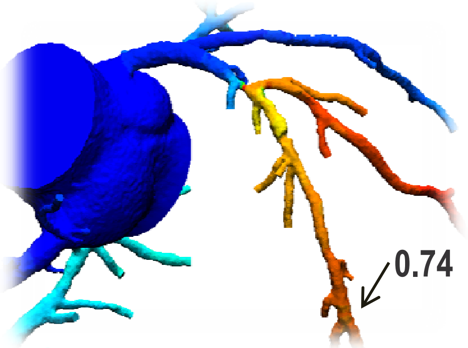


Source: Koo et al. J Am Coll Cardiol 2011

Examples – DISCOVER-FLOW

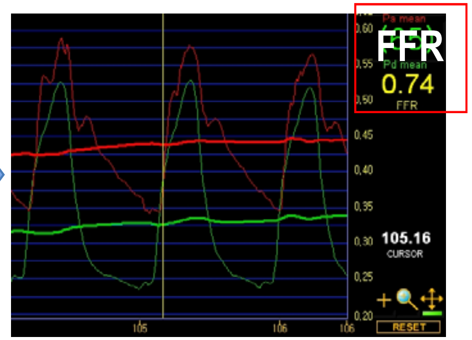
CCTA	FFR_{CT}	Invasive angiography	FFR

>50% diameter stenosis

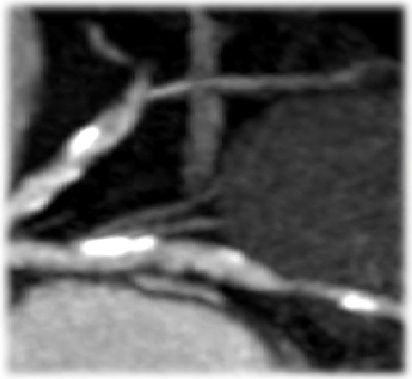


FFR_{CT} 0.74 → ischemia

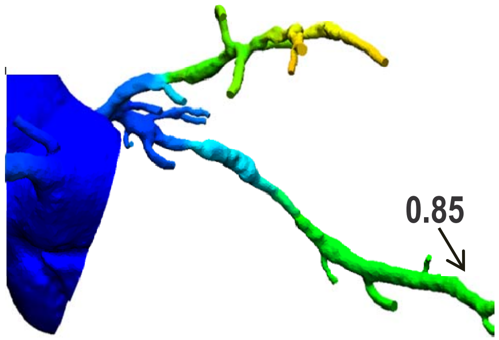
>50% diameter stenosis



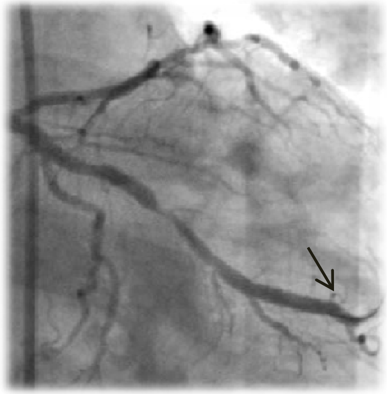
FFR 0.74 → ischemia



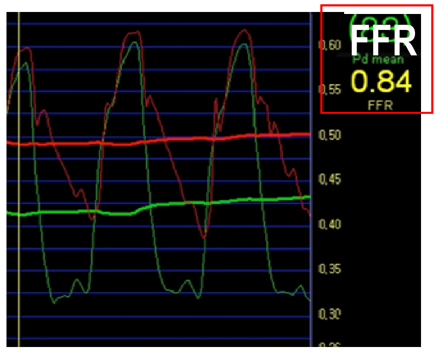
>50% diameter stenosis



FFR_{CT} 0.85 → no ischemia



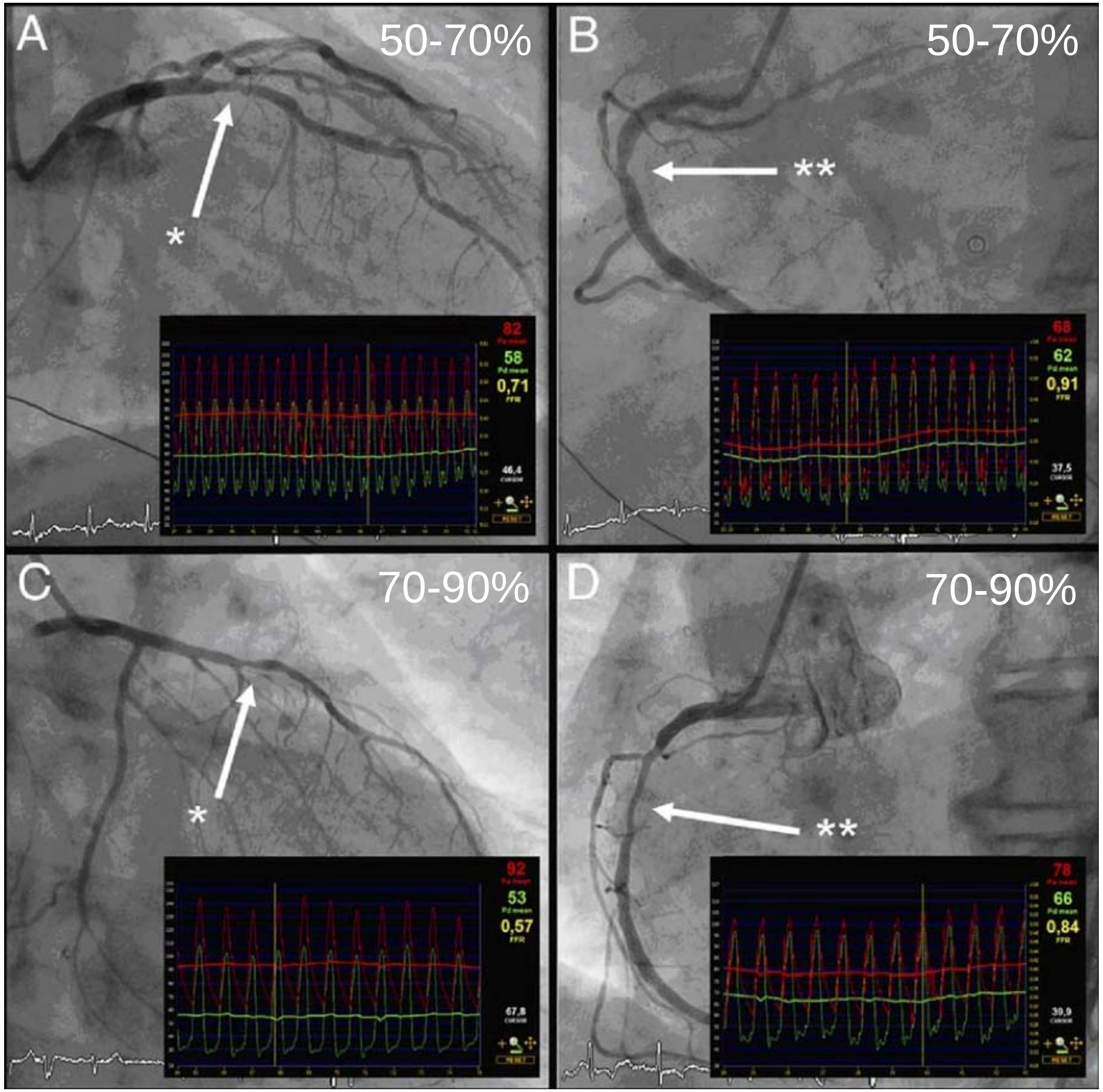
>50% diameter stenosis



FFR 0.84 → no ischemia

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

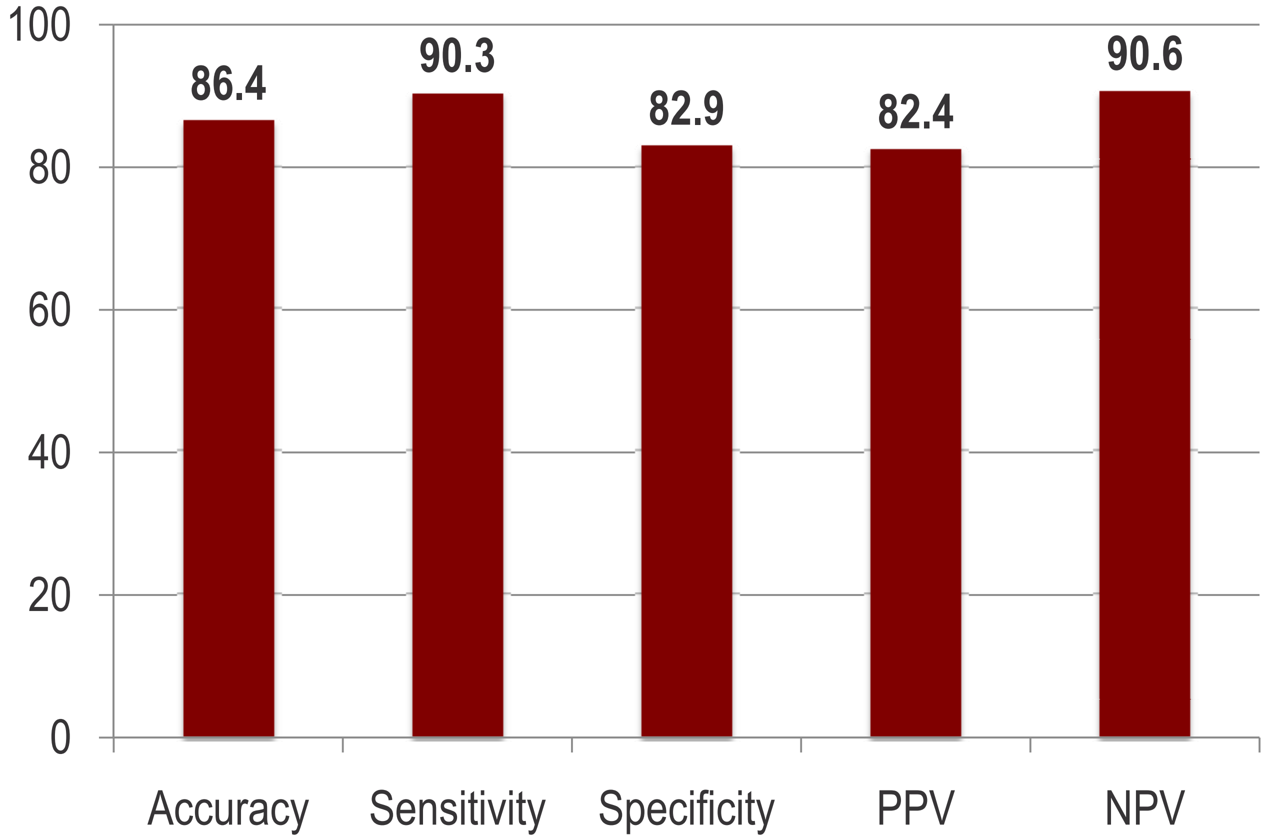
(1) Intermediate Stenoses



Source: Tonino PA et al. J Am Coll Cardiol

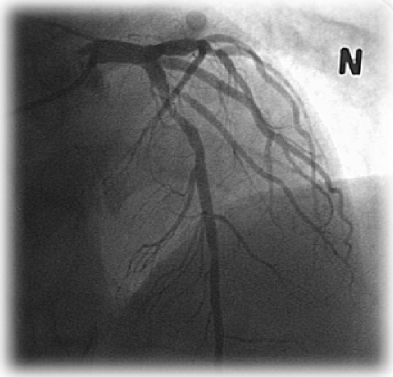
Diagnostic Performance of FFR_{CT} for 40-69% Stenoses

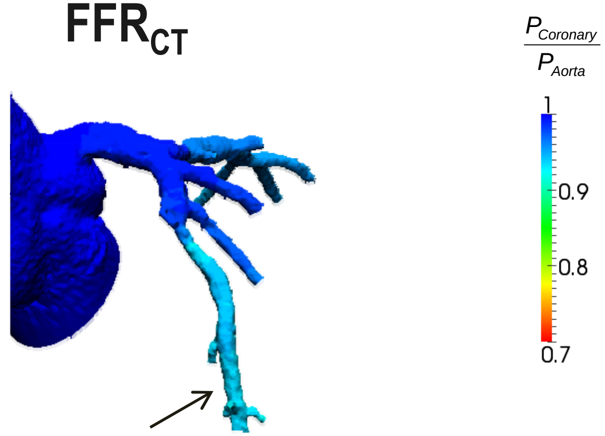
FFR_{CT}	Accuracy	Sensitivity	Specificity	PPV	NPV
$FFR_{CT} \leq 0.80$ (95% CI)	86.4 (75.7-93.6)	90.3 (74.2-98.0)	82.9 (66.4-93.4)	82.4 (65.5-93.2)	90.6 (75.0-98.0)
$FFR_{CT} \leq 0.75$ (95% CI)	83.3 (72.1-91.4)	77.3 (54.6-92.2)	86.4 (72.6-94.8)	73.9 (51.6-89.8)	88.4 (74.9-96.1)



Examples – Intermediate Stenoses

Invasive angiography | CCTA | FFR_{CT}

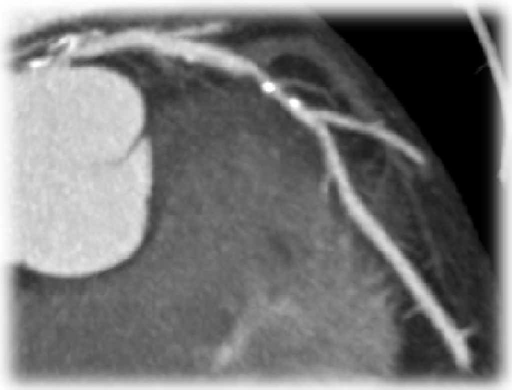


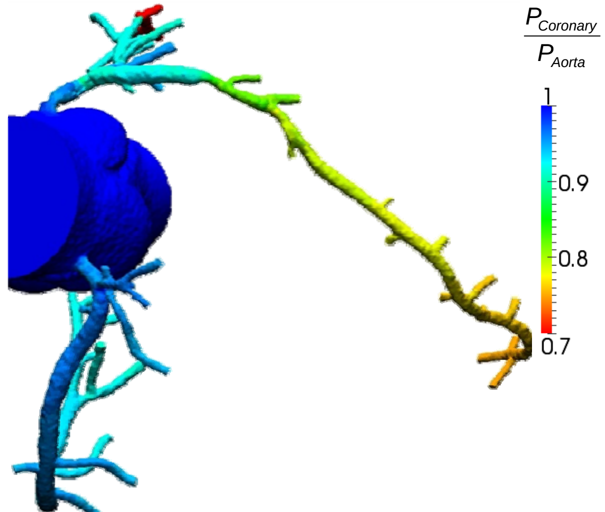


QCA %DS = 54.09%
FFR = 0.89

CCTA 50-69% stenosis

FFR_{CT} 0.93 → No ischemia



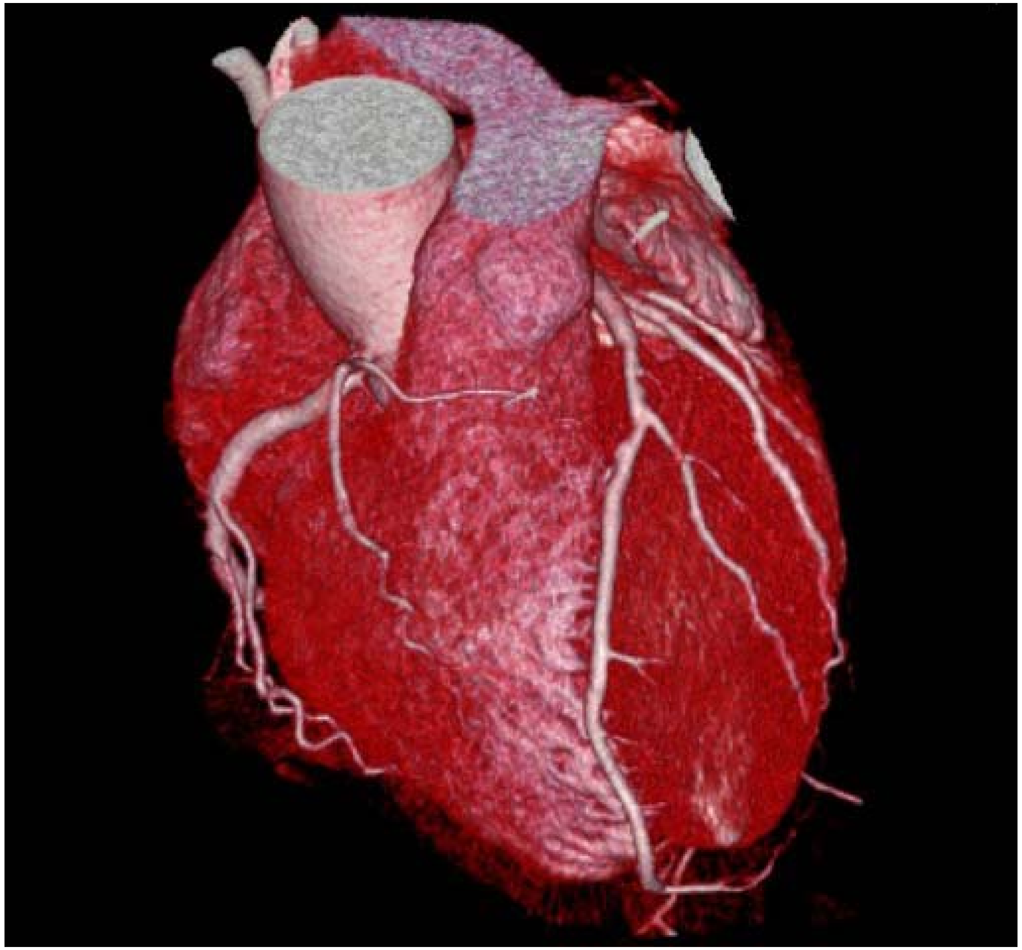


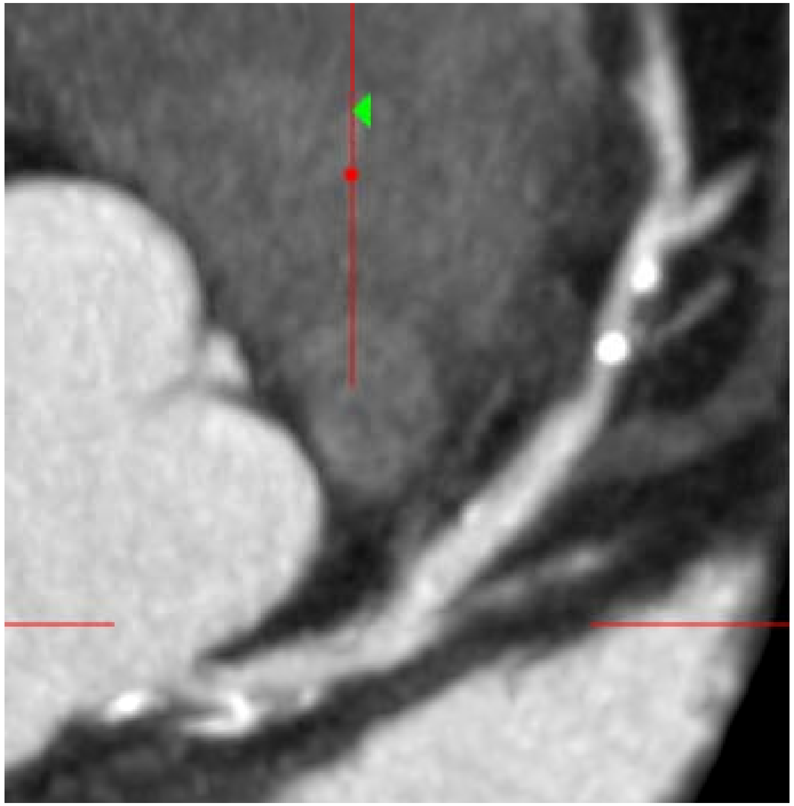
QCA %DS = 50.68%
FFR = 0.71

CCTA 50-69% stenosis

FFR_{CT} 0.78 → Ischemia

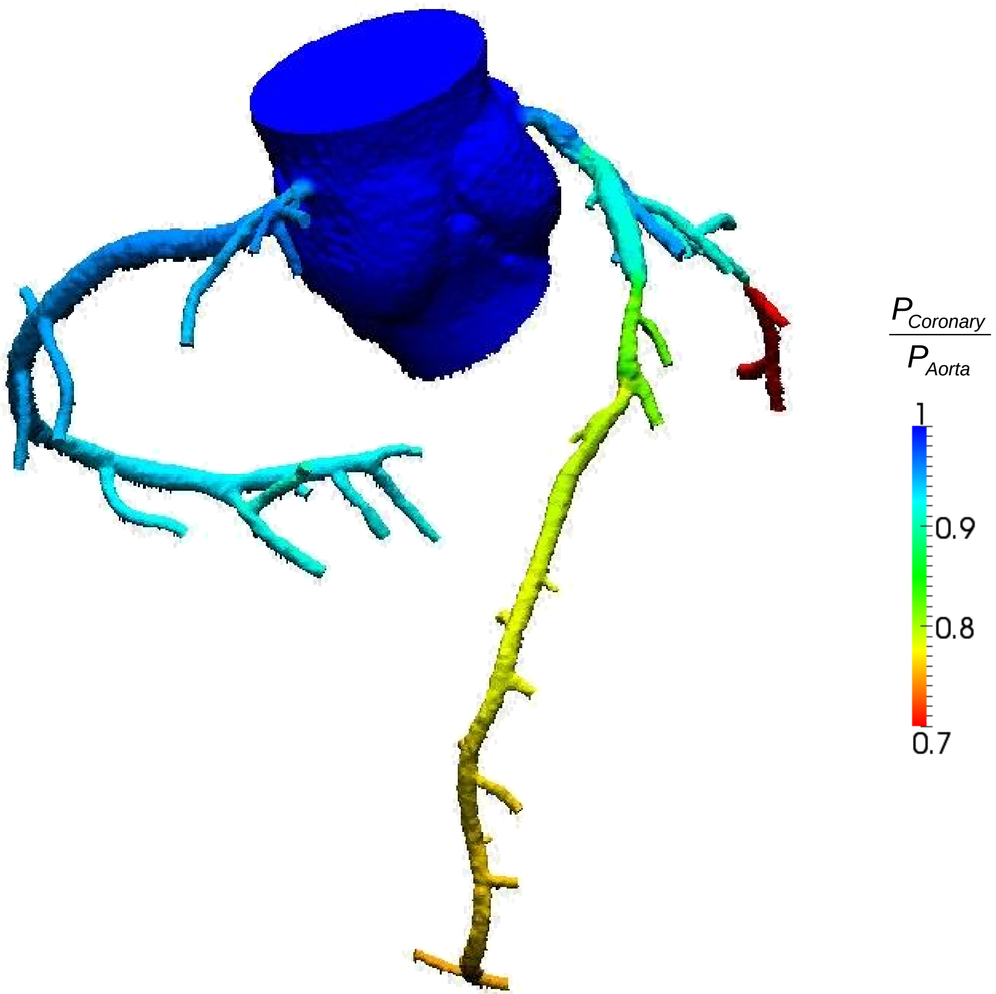
(2) Diffuse Non-Obstructive Atherosclerosis

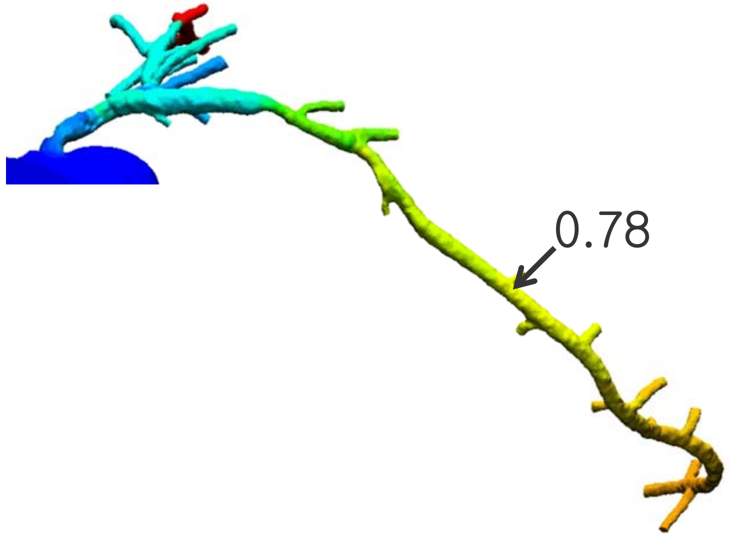


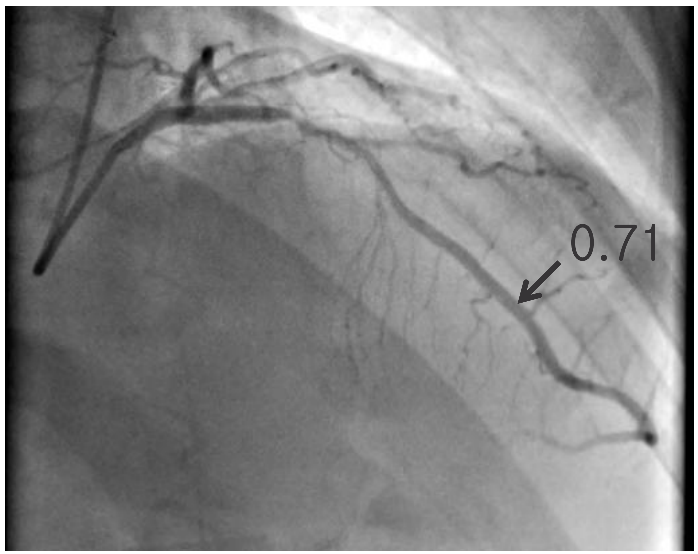


Diffuse mild left main disease with moderate LAD Dx

(2) Diffuse Non-Obstructive Atherosclerosis

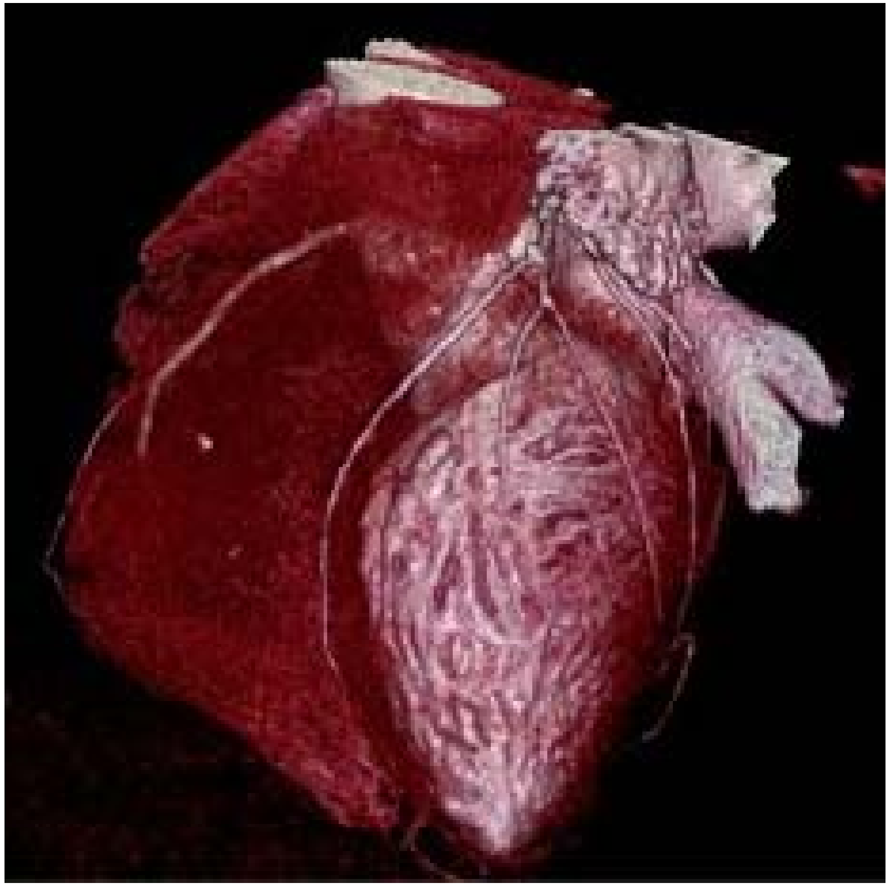


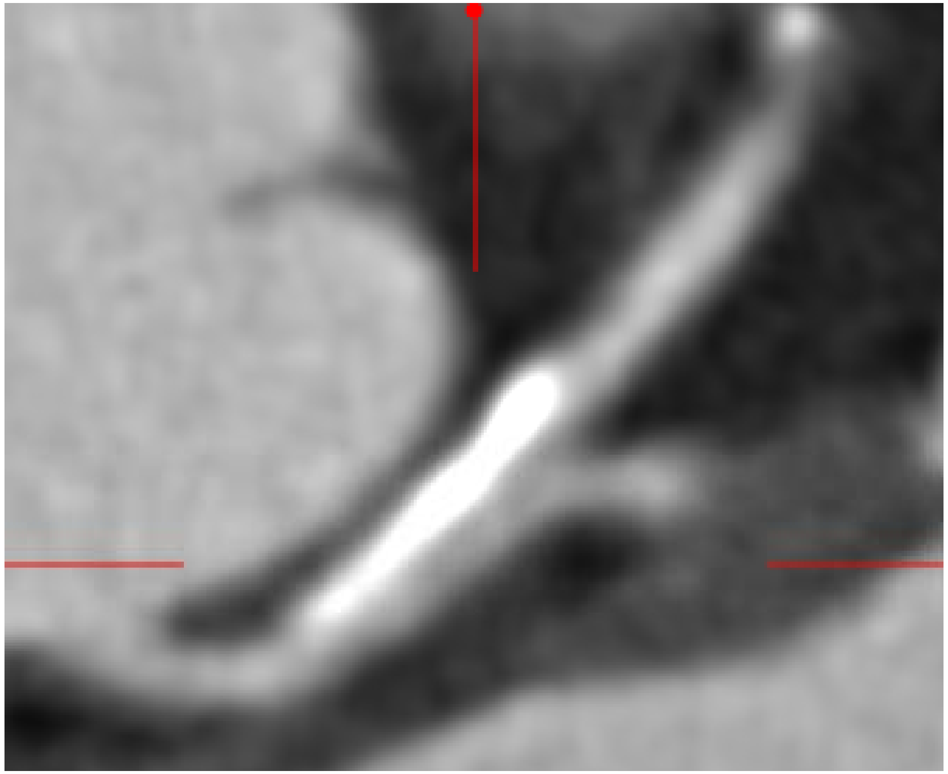




Diffuse LM dx contributes to the functional significance of the LAD

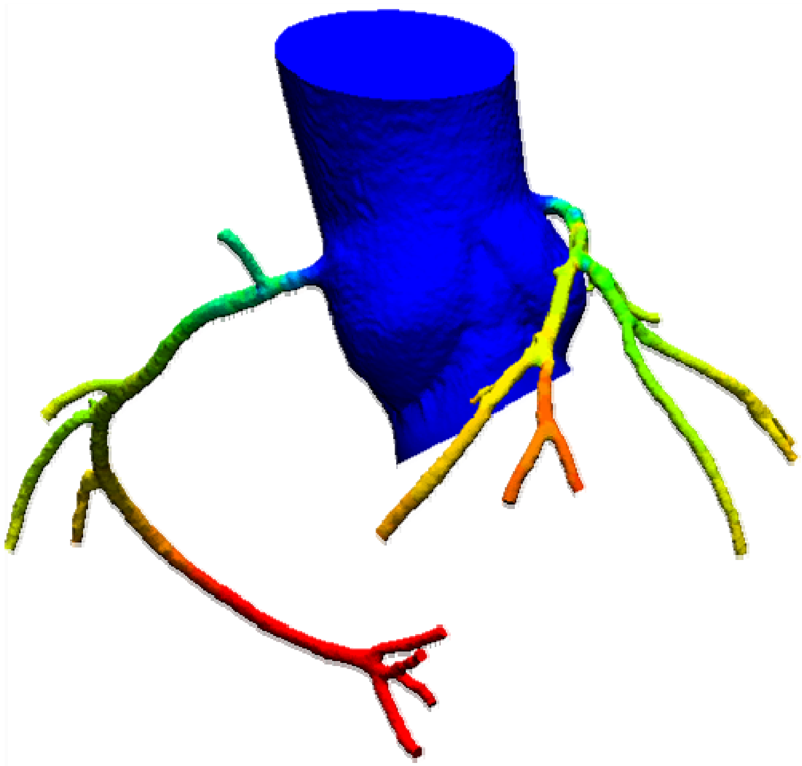
(3) Small Vessels

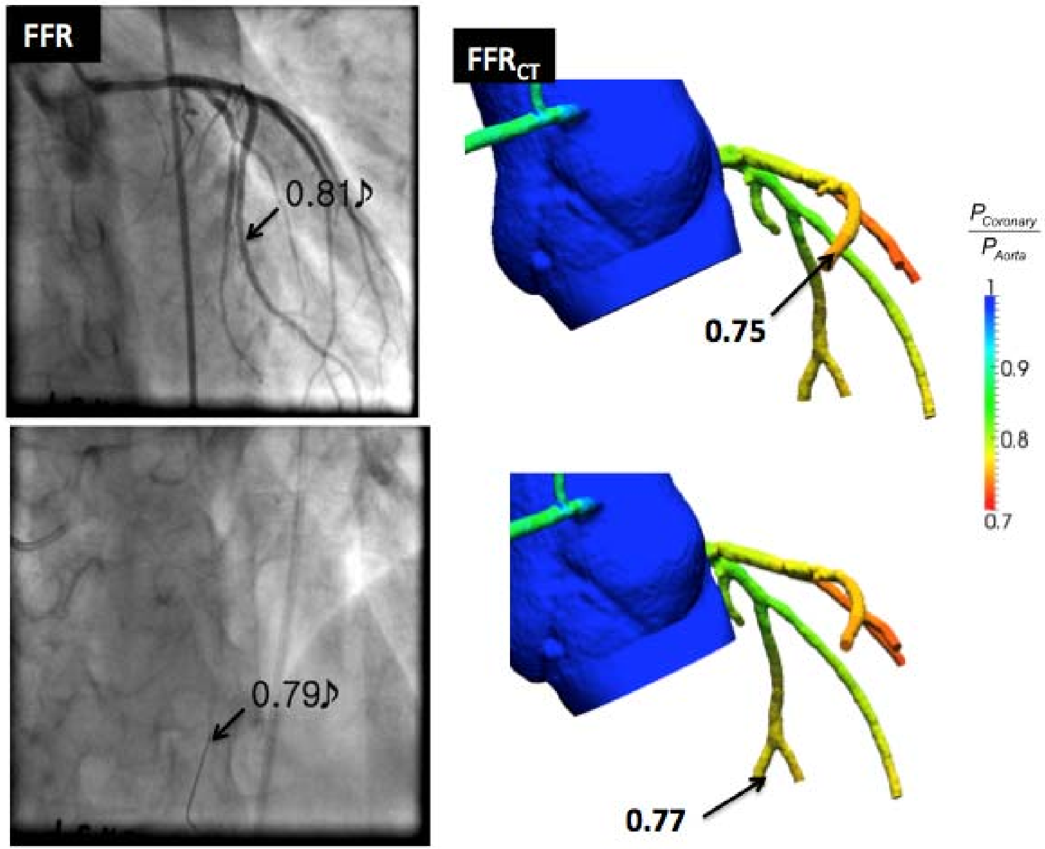




2.5 mm left main and left anterior descending artery

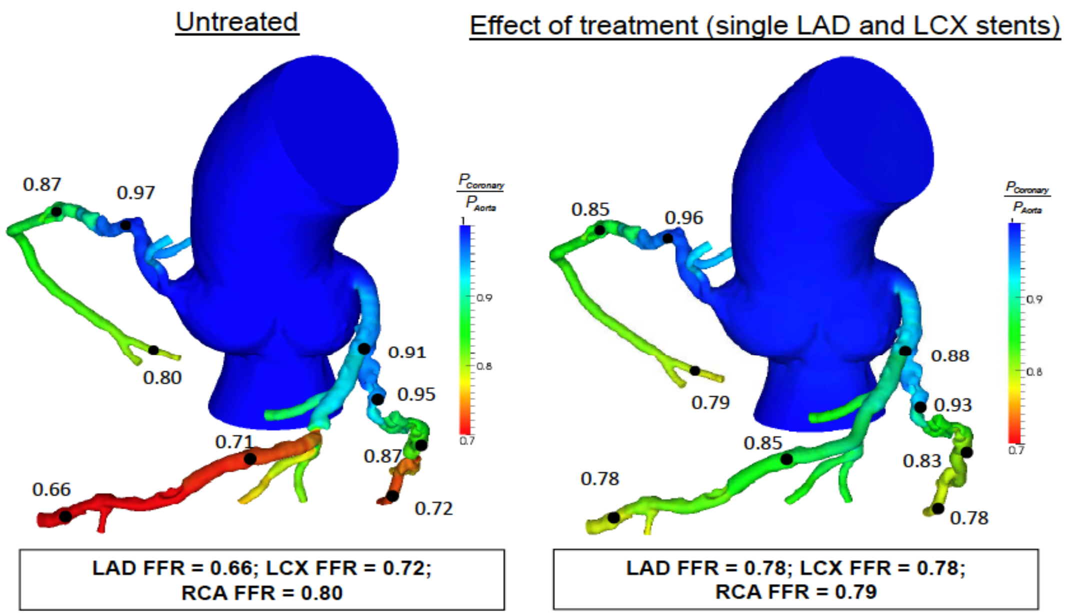
(3) Small Vessels



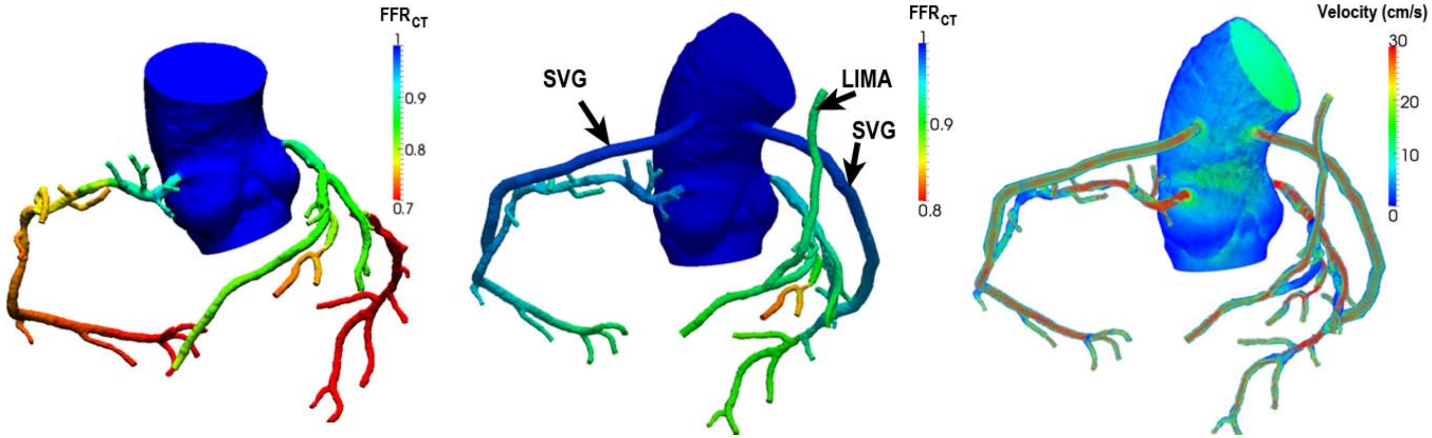


Functional 3-vessel disease

(4) Prediction of Therapeutic Benefit

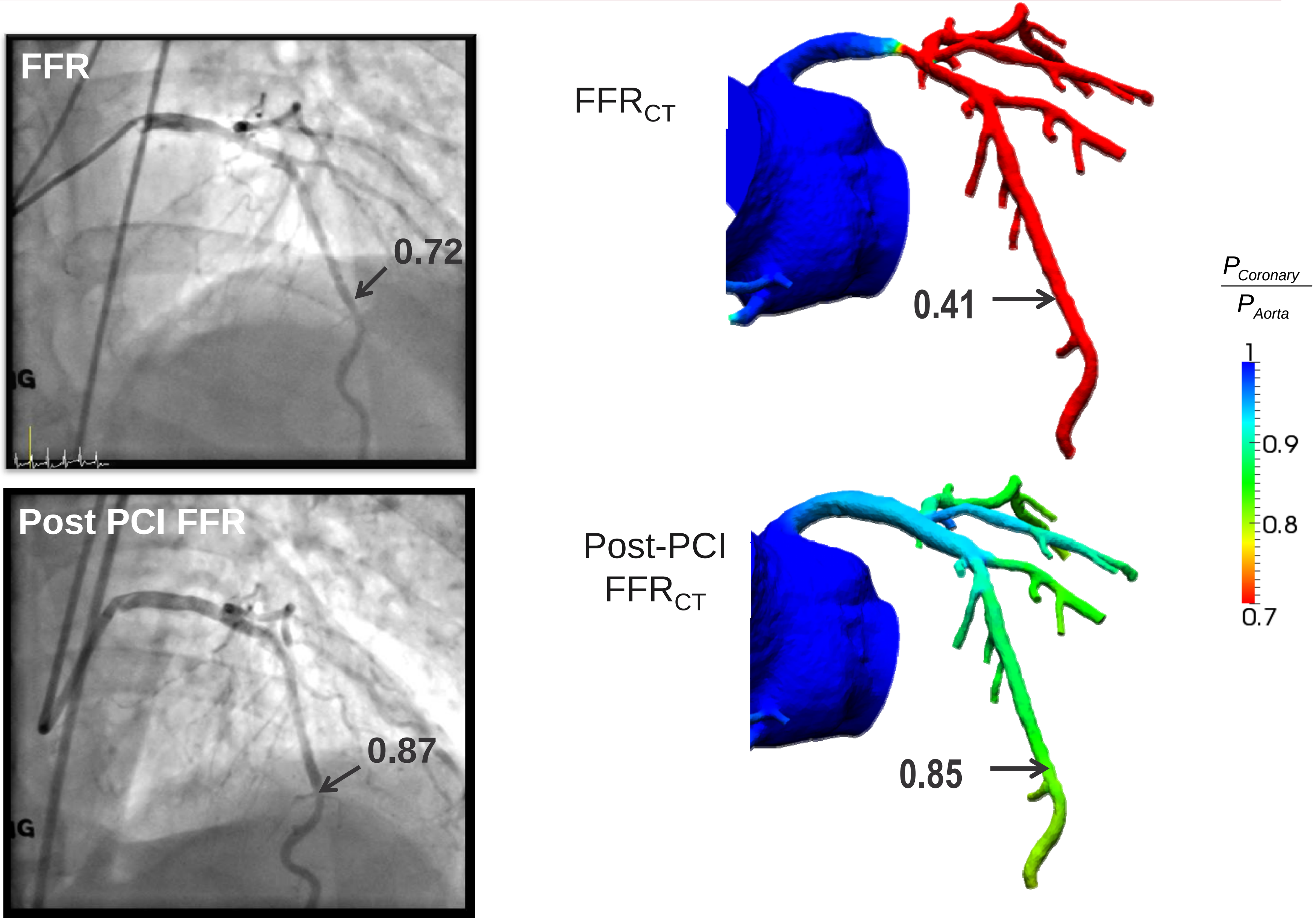


Percutaneous Revascularization by FFR_{CT}

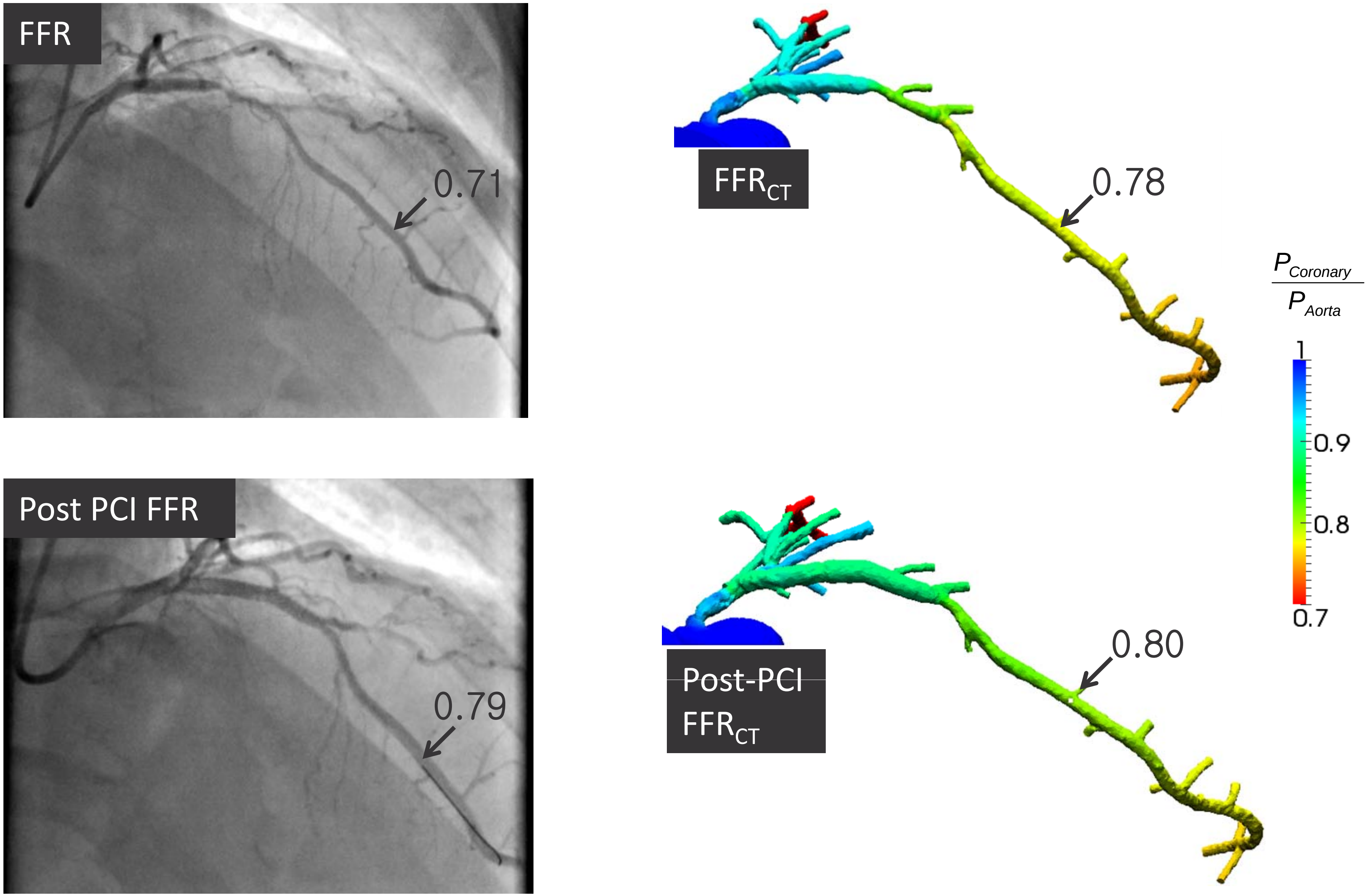


Surgical Revascularization by FFR_{CT}

Therapeutic Benefit of Revascularization



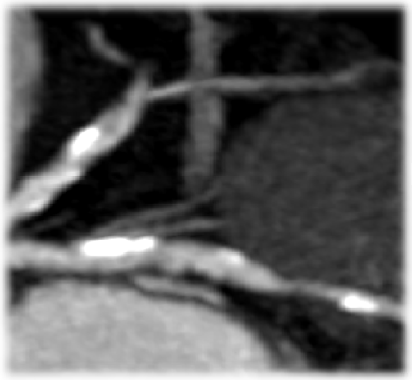
No Therapeutic Benefit of Revascularization



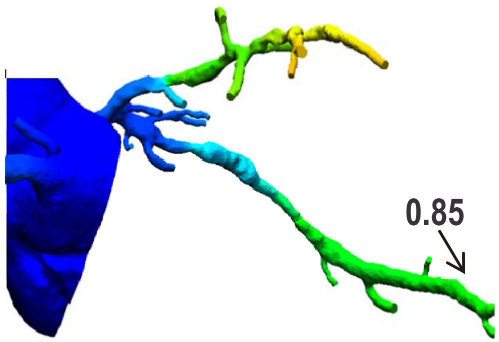
The DeFACTO Trial

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

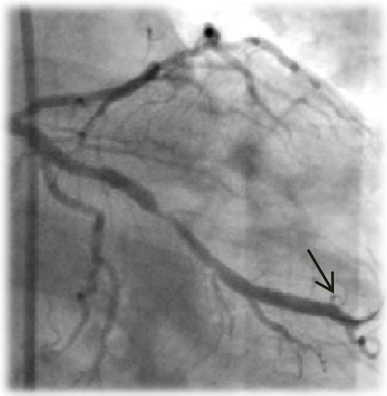
- 17-center international study of 285 patients undergoing CCTA and invasive FFR to evaluate the *diagnostic performance of* FFR_{CT}
- Per-patient endpoint
- Enrollment completed 10/11



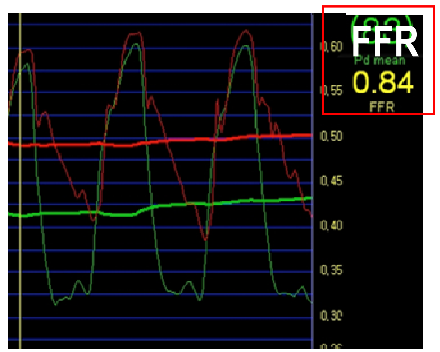
>50% diameter stenosis



FFR_{CT} 0.85 → no ischemia



>50% diameter stenosis



FFR 0.84 → no ischemia

Source: http://clinicaltrials.gov/ct2/show/NCT01233518?term=defacto&rank=1