

Use of FFR_{CT} to Diagnose Lesion-Specific Ischemia

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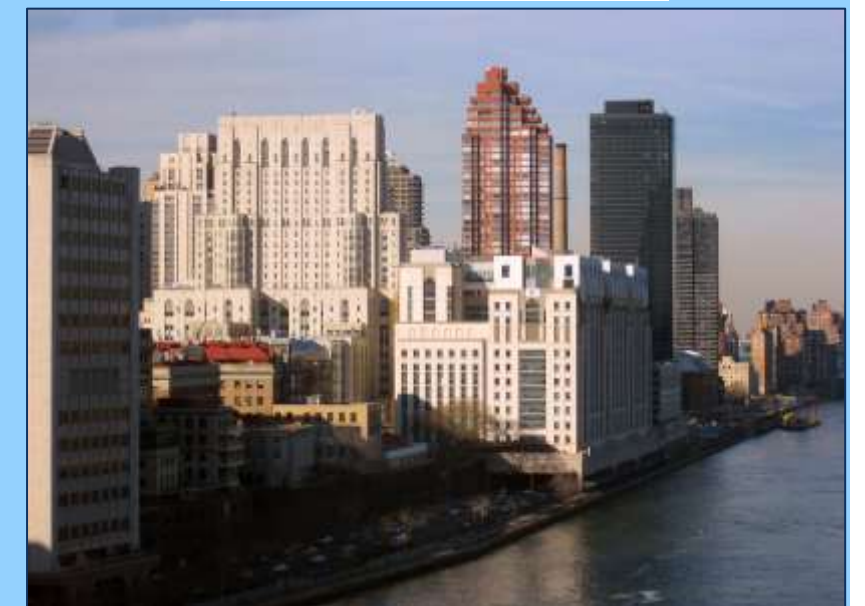
New York, New York



Weill Cornell Medical College



NewYork-Presbyterian



Disclosures

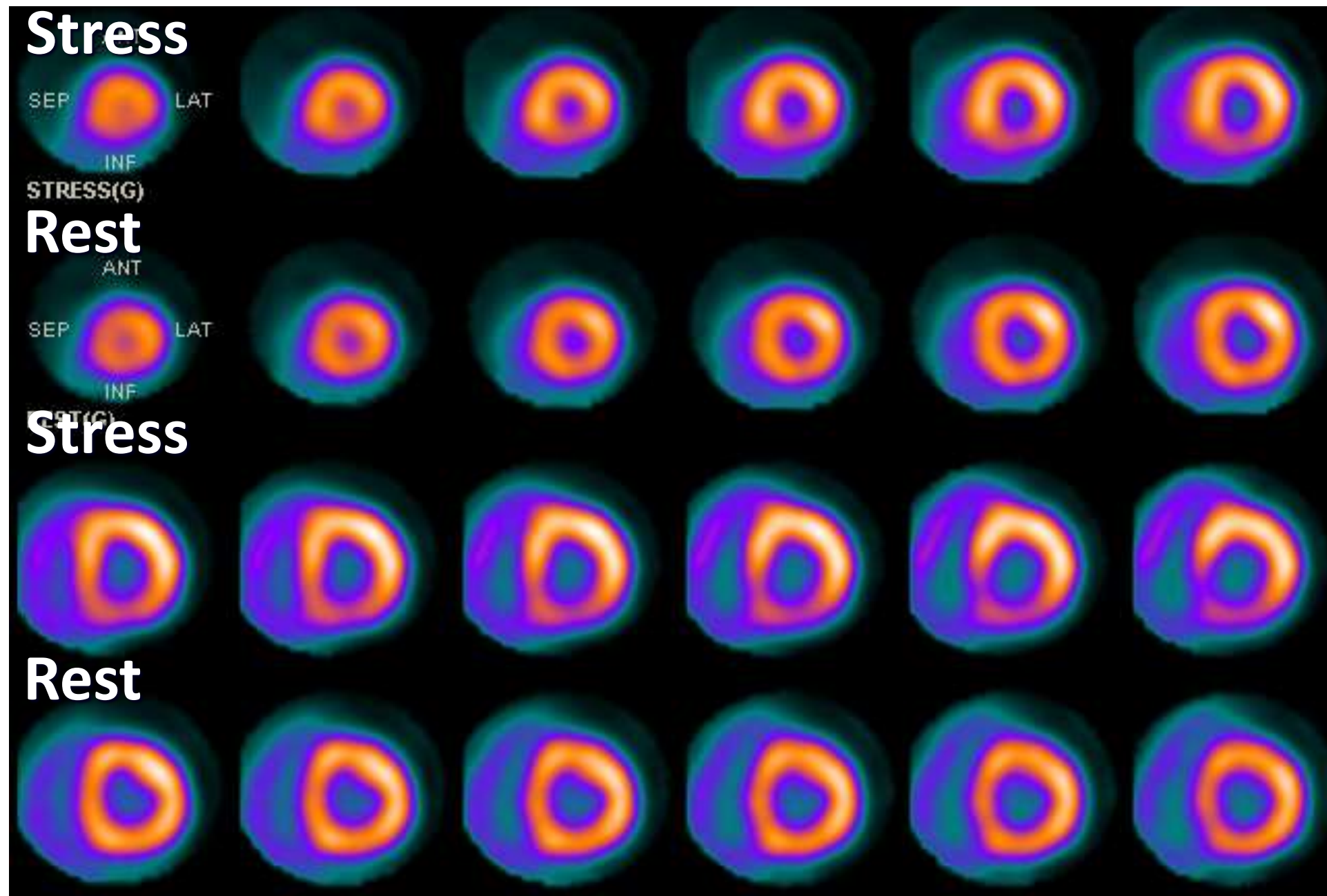
- **Extramural Research Support:**
 - Dalio Institute of Cardiovascular Imaging @ NYPH / WCMC (Dalio Foundation)
 - NIH R01 HL115150
 - NIH R01 HL111141
 - NIH R01 HL118019-01
 - NIH U01 HL105907
 - NPRP 09-370-3-089
- **Equity Interest:** MDDX, Autoplaq
- **Consultant / Medical Advisory Board:** Abbott Vascular, Arineta, Astra Zeneca, Cardiovascular Research Foundation, GE Healthcare, HeartFlow, Myokardia

Case: 62 y/o Caucasian man

(Performed @ Cornell / NewYork-Presbyterian 4/15/15)

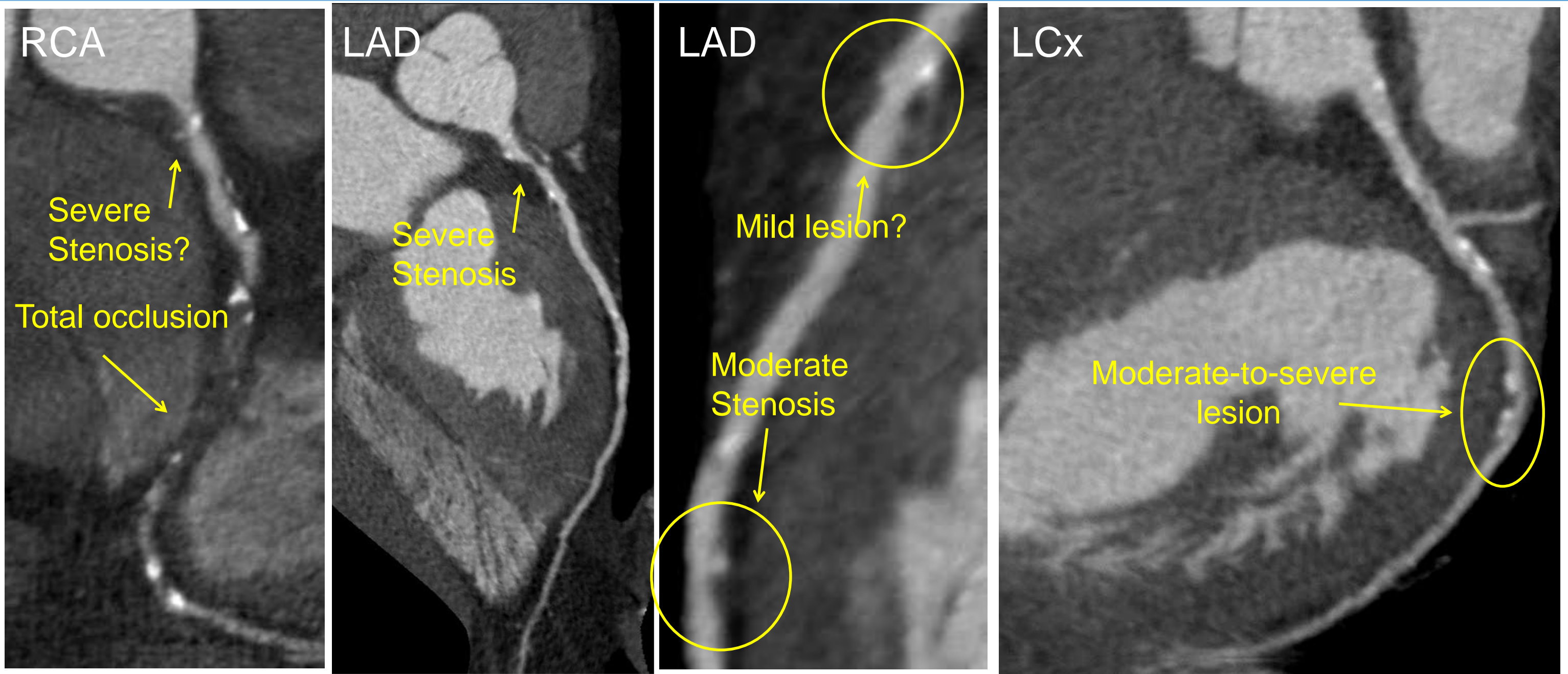
- **Symptoms:** Exertional chest pain with slow walking; no dyspnea; no syncope; symptoms despite medical therapy
- **Past Medical History:** HTN, CAD, dyslipidemia
- **Medications:** metoprolol; nitroglycerin; statin; aspirin
- **Prior testing:** Abnormal SPECT

Case: 62 y/o Caucasian man

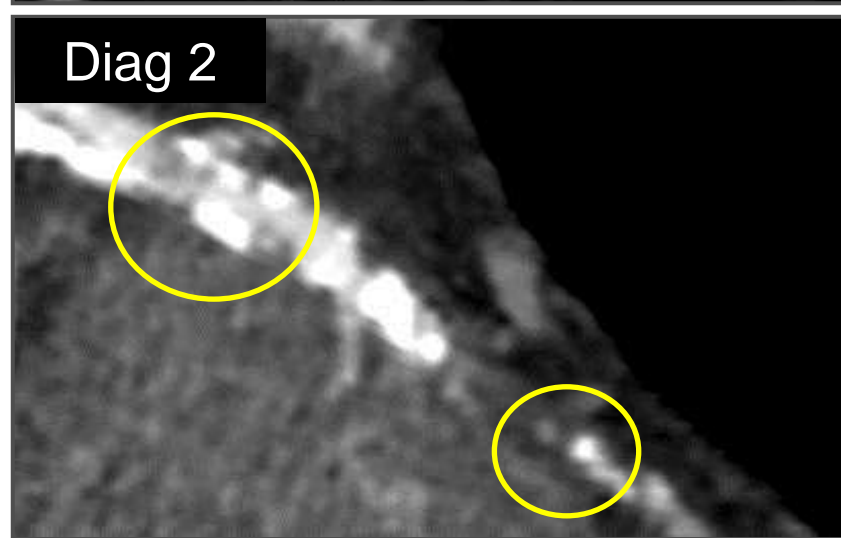
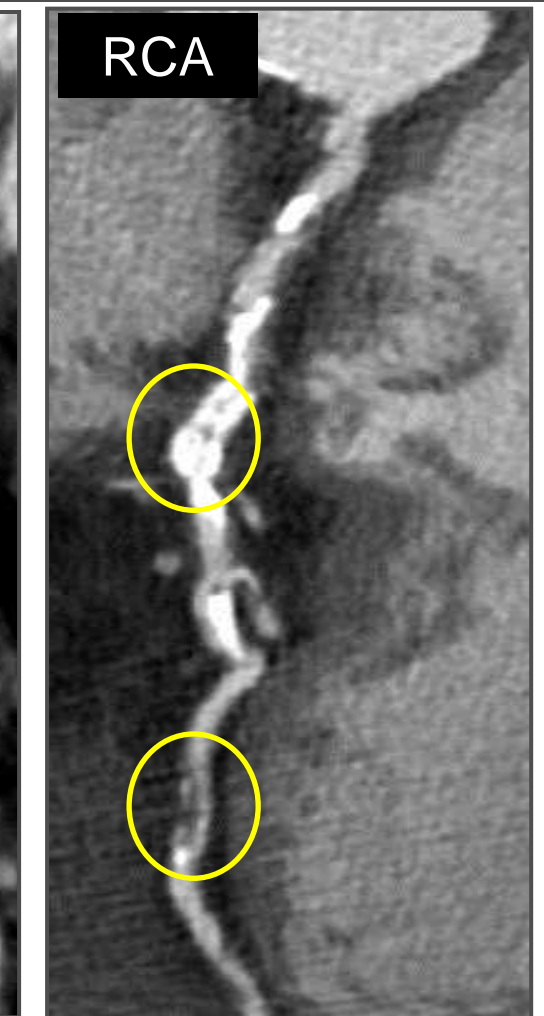
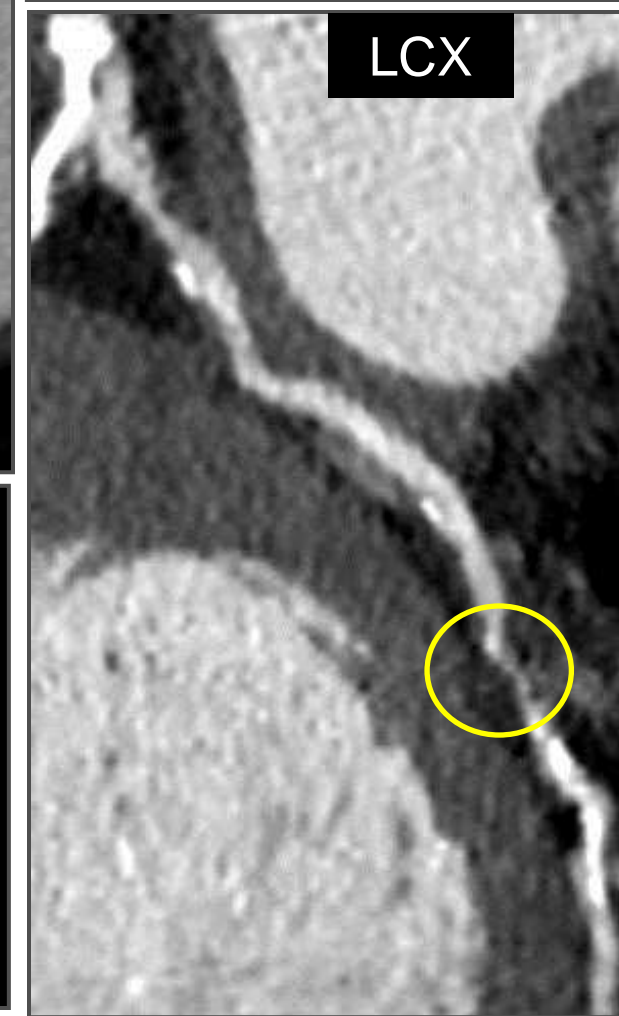
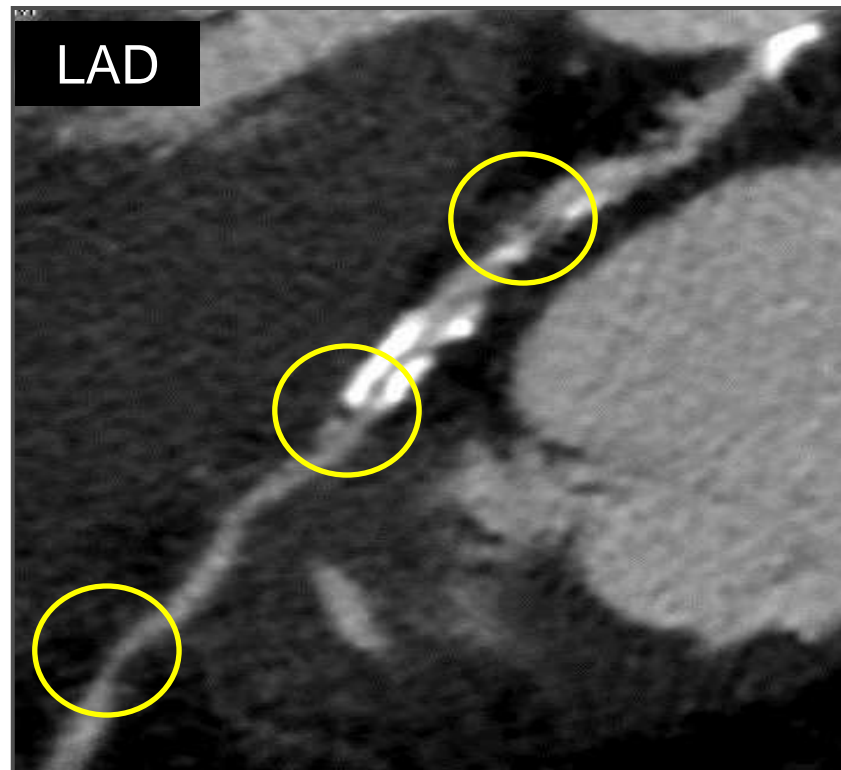


Case: 62 y/o Caucasian man

(Performed @ Cornell / NewYork-Presbyterian 4/15/15)



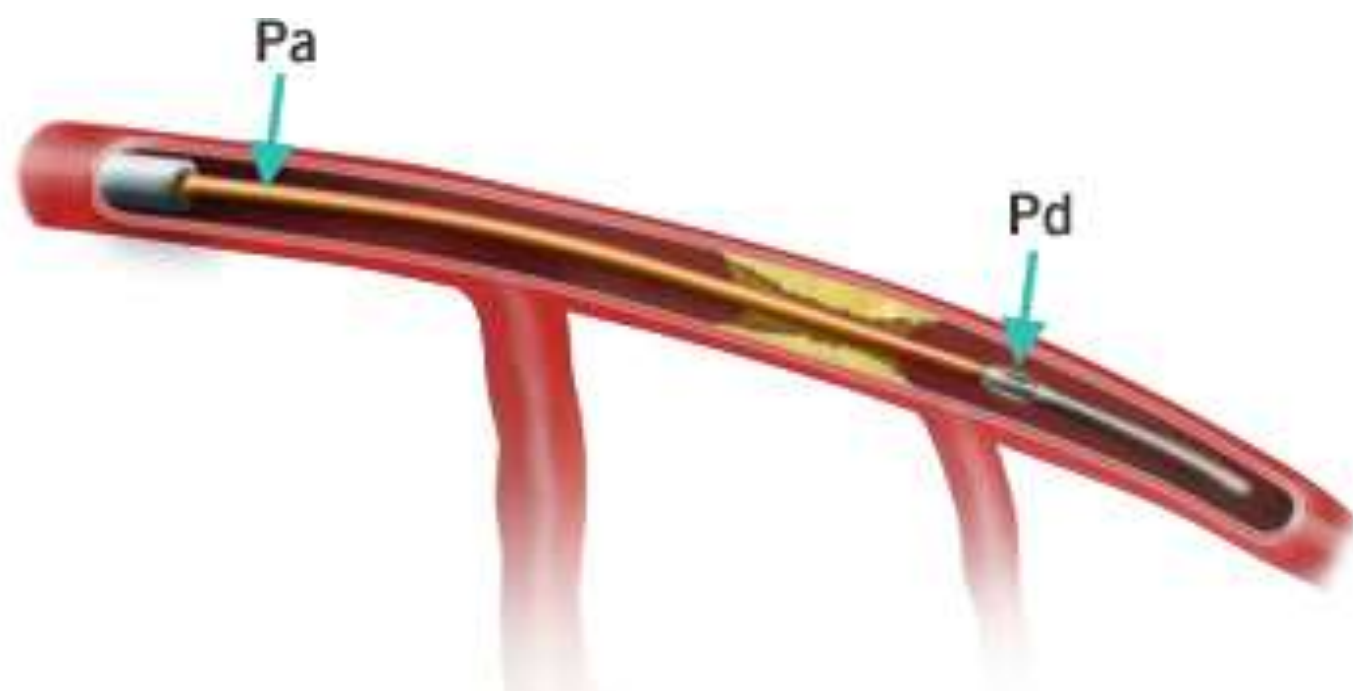
Lesion-Specific Ischemia



“Gold” standard for lesion-specific ischemia Invasive Fractional Flow Reserve (FFR)

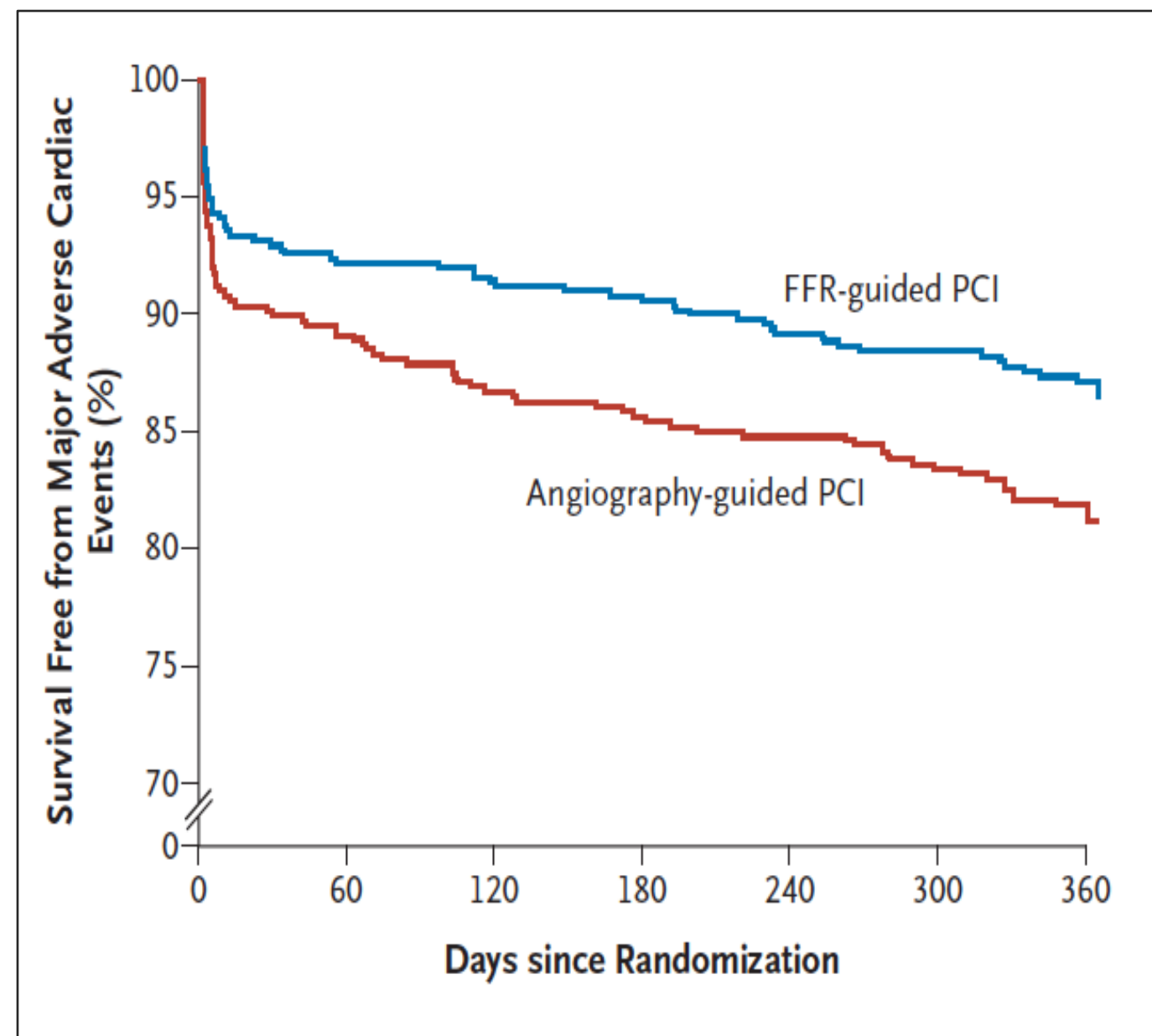
FAME RCT, N=1,005
Multivessel CAD
“Anatomy vs. Physiology”

Maximal MBF through a diseased artery
MBF in the hypothetical case the artery is normal



Lesion-specific ischemia: $FFR \leq 0.80$

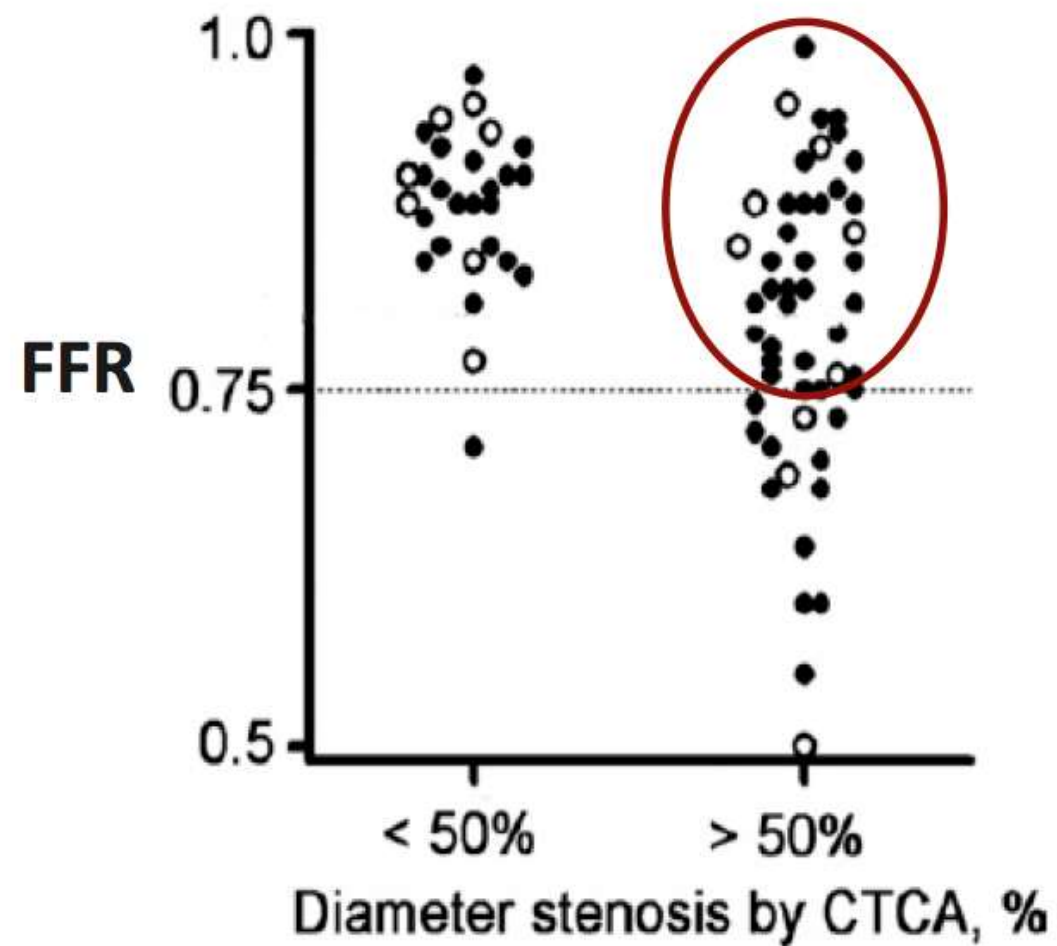
- Only method to **pinpoint ischemia-causing lesions**
- Only method to guide revascularization to **improve event-free survival**



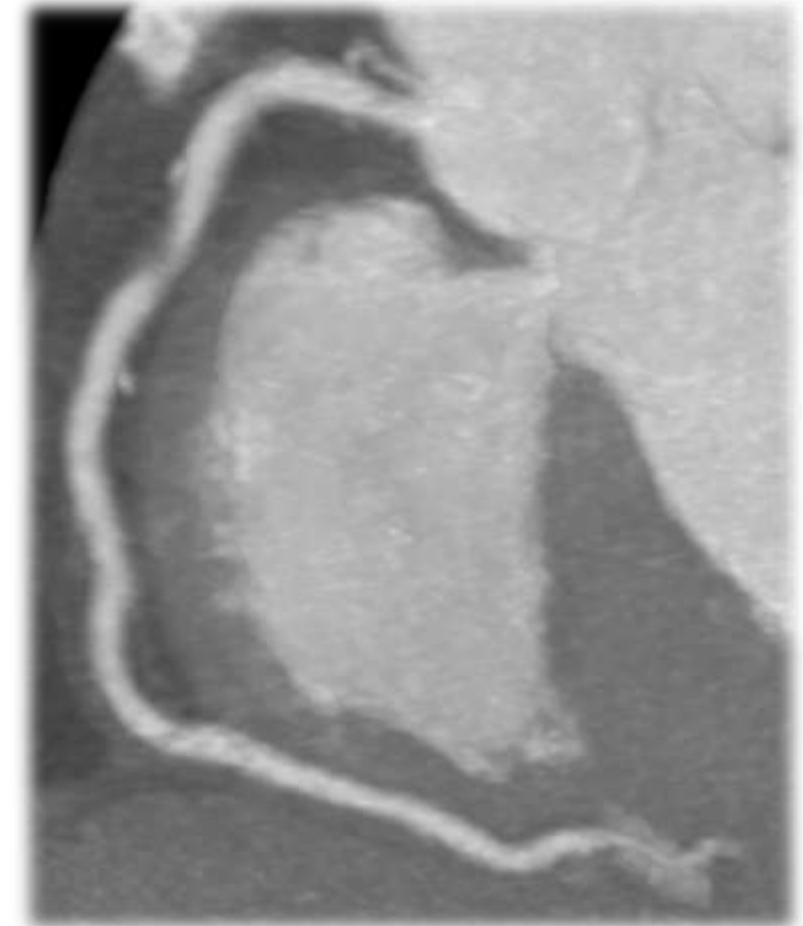
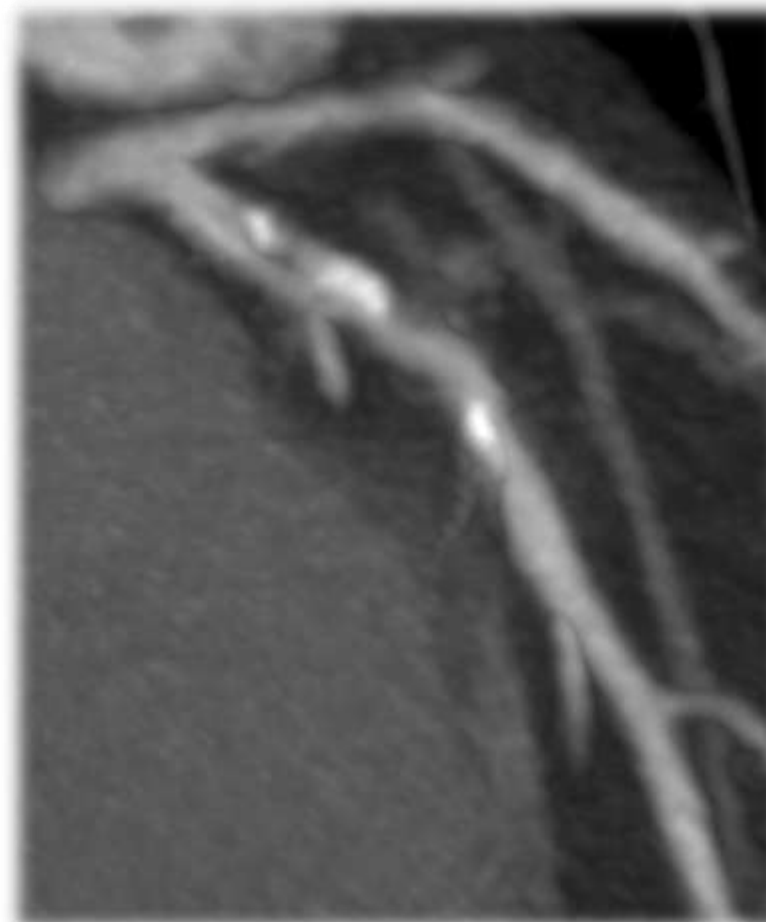
CT to Diagnosis and Exclude Lesion Ischemia

Only one of these patients has hemodynamically significant CAD.

Who has ischemia?

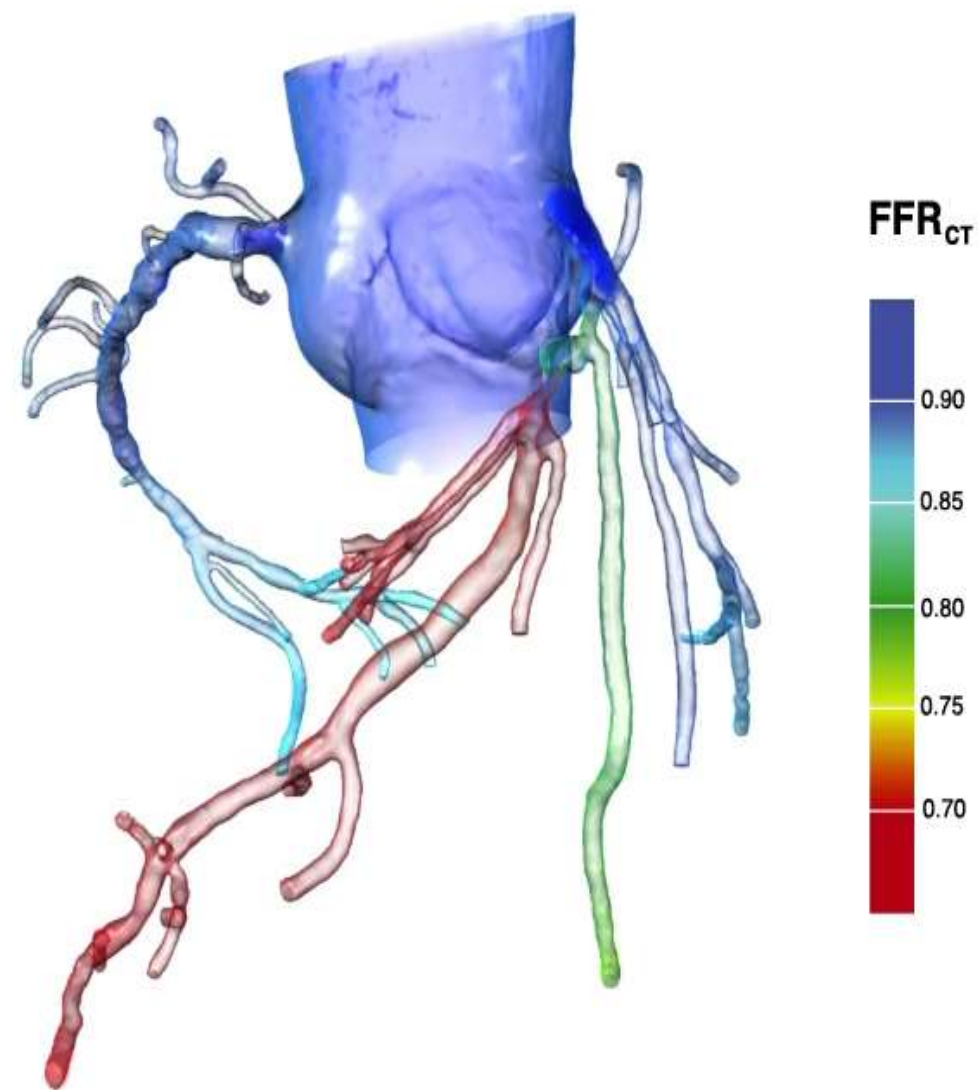


75% false positives



Non-invasive FFR_{CT}

FDA Approval 11/14

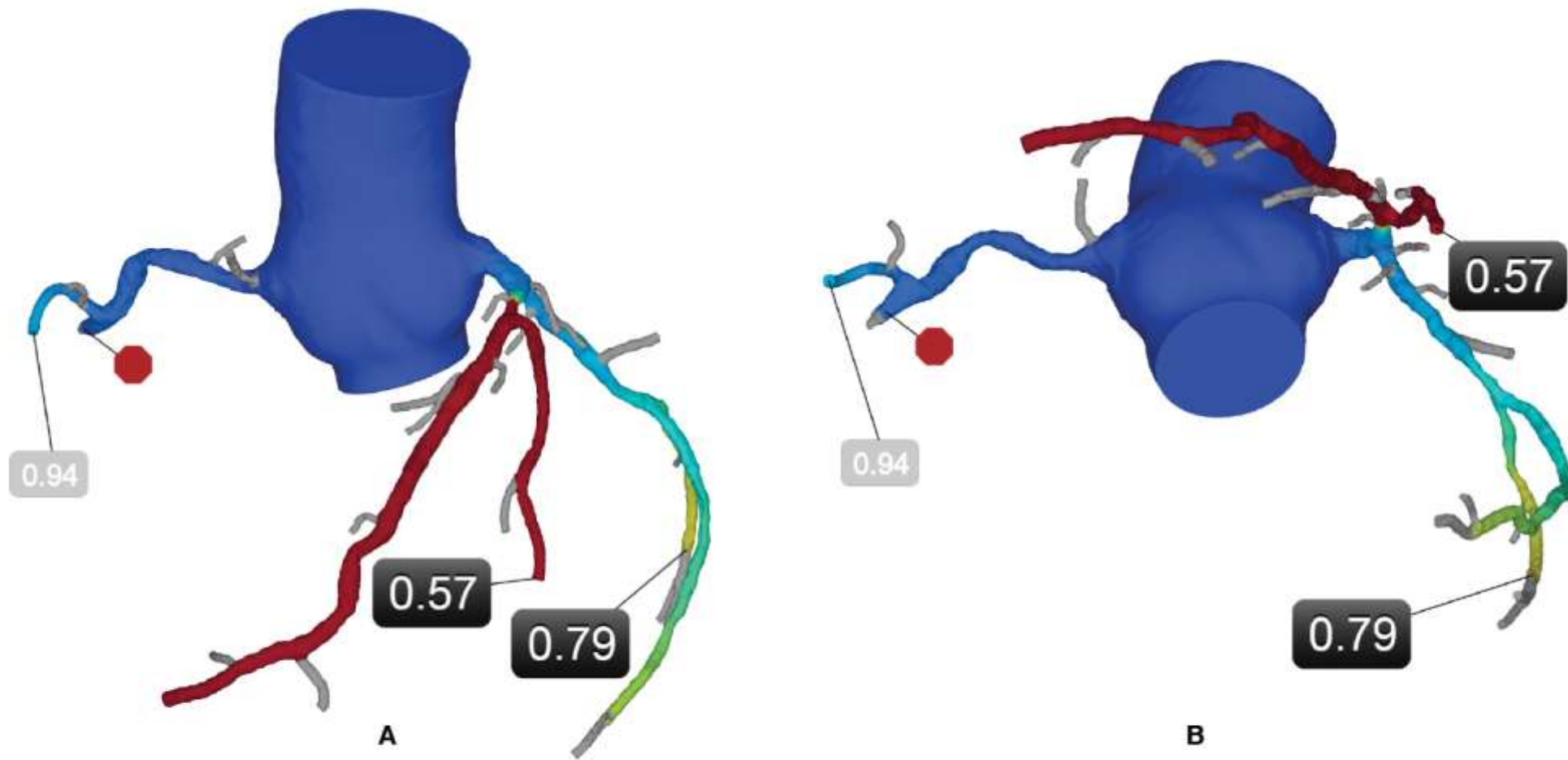


- From typically acquired CCTA
- No additional radiation
- No modification to imaging protocols
- No administration of medications

Case: 62 y/o Caucasian man

(Performed @ Cornell / NewYork-Presbyterian 4/15/15)

FDA Approval 11/14



Summary: The Right Coronary Artery System has an occlusion. The Left Anterior Descending System and Left Circumflex System each have an $FFR_{CT} \leq 0.80$.

CORONARY ARTERIES & SYSTEMS	FFR_{CT}	FFR_{CT}
Left Main Artery	—	0.00 0.20 0.40 0.60 0.80 1.00
Left Anterior Descending System	0.57	
Left Circumflex System	0.79	
Right Coronary Artery System	●	

MAY BE FUNCTIONALLY SIGNIFICANT^{1,2,3}



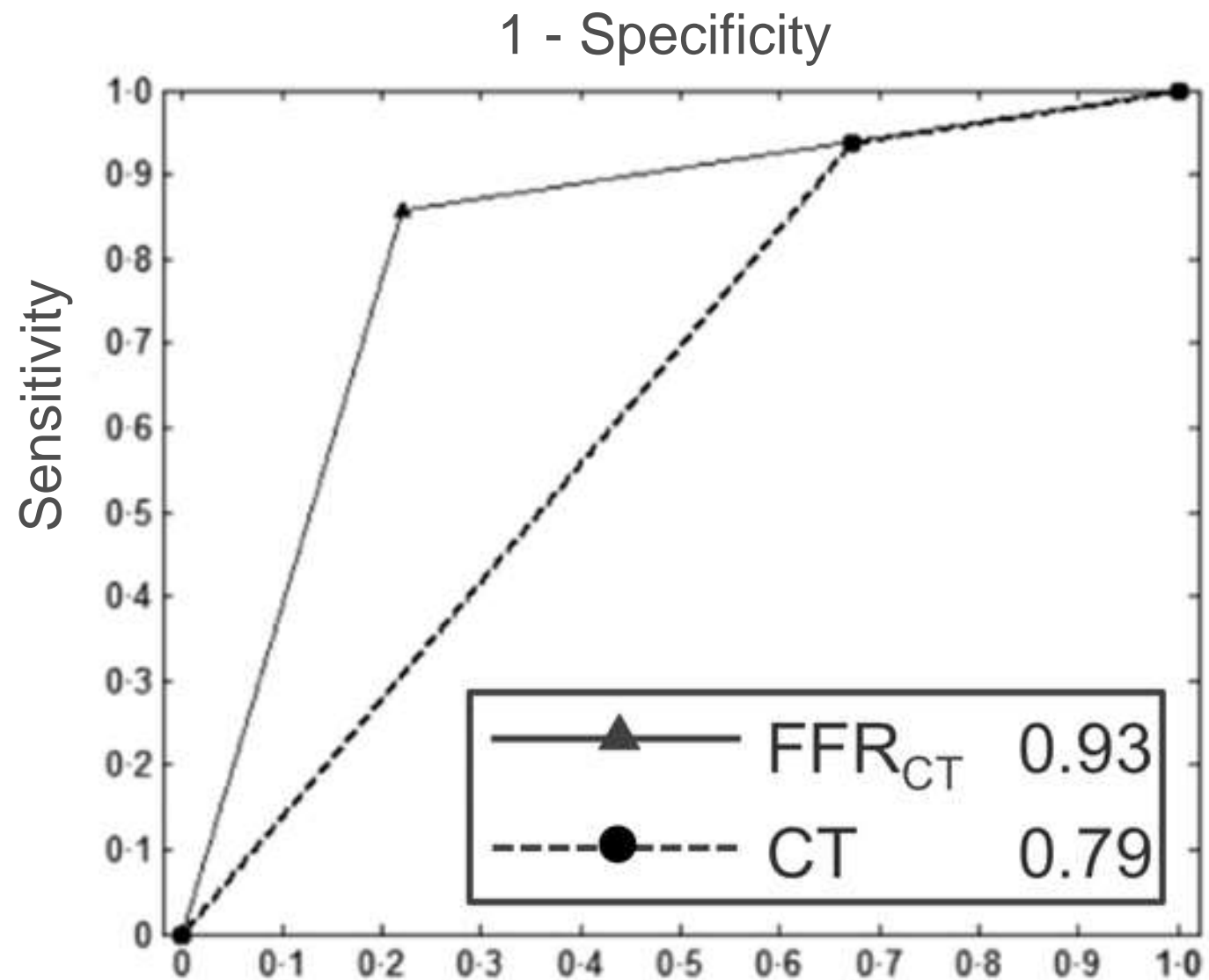
FFR_{CT}: Three (3) Prospective Multicenter Trials

	DISCOVER-FLOW	DeFACTO	NXT
Principal Investigator	Min (JACC)	Min (JAMA)	Norgaard (JACC)
Primary end point	Per pt. diag accuracy	Per pt. diag accuracy; lower limit 95% CI 0.7	Per pt. AUC
Study sites/ countries	4 / 3	17 / 5	10 / 8
Site expertise qualification	FFR	CT or FFR	CT plus FFR
CT training of site	Yes	No	Yes
FFR training of site	No	No	Yes
CT quality check	No	No	Yes
CT results reading	Core lab	Core lab	Site
FFR results report	Site	Site	Site with core lab overview
Vessel size for inclusion	≥ 2.0 mm	≥ 1.5 mm	≥ 2.0 mm
Software version*	V 1.0 manual	V 1.2 partial automation ~6 hrs	V 1.4 automation; <4 hours

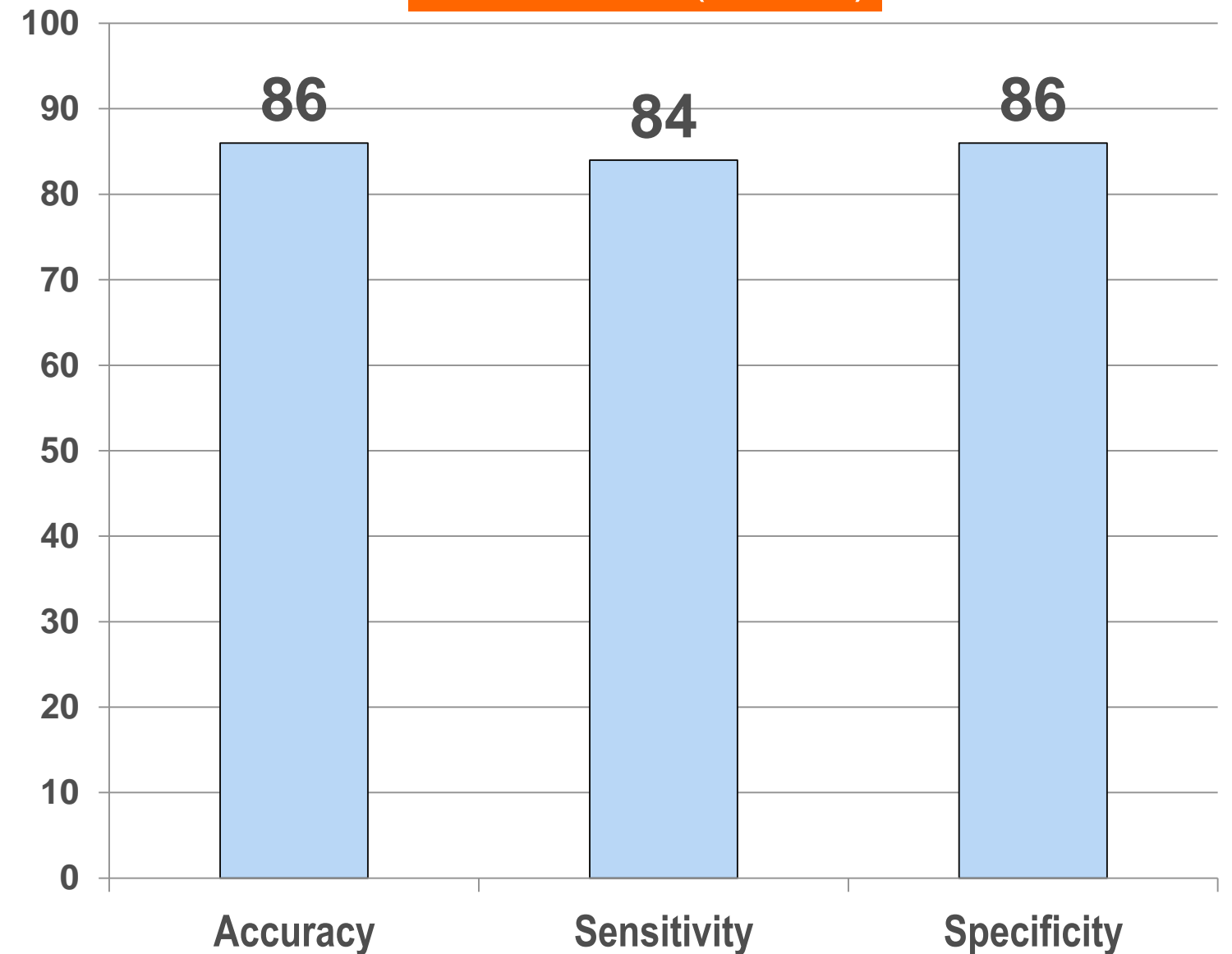
NXT: Discrimination of ischemia

Prospective multicenter
N=251 (n=484 vessels)
Comparator: Invasive FFR

Per-Patient (n=251)



Per-Vessel (n=484)



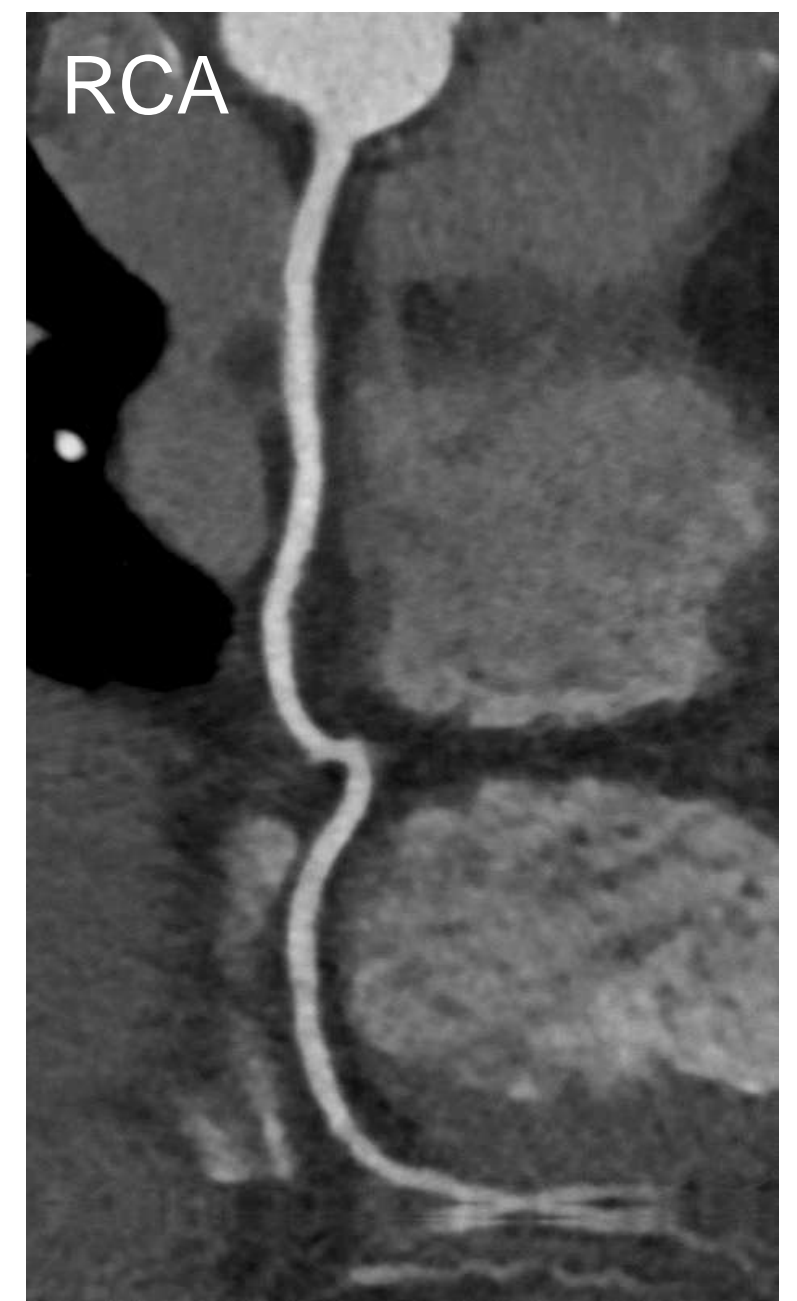
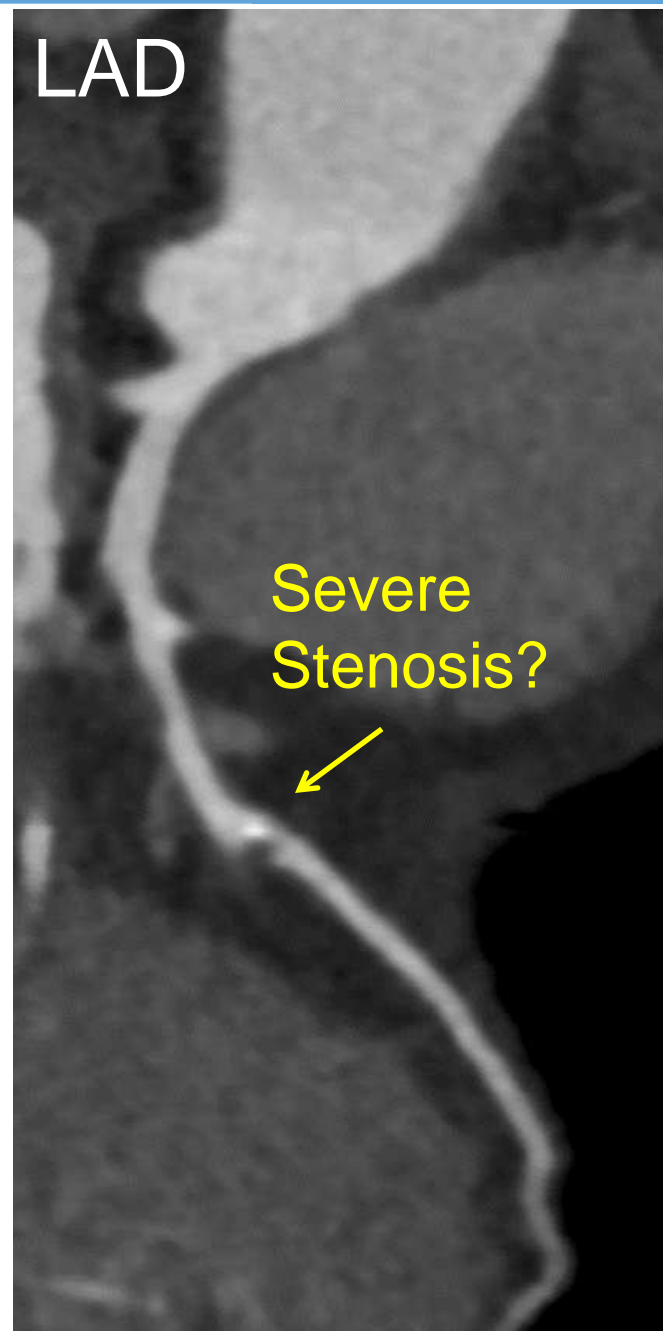
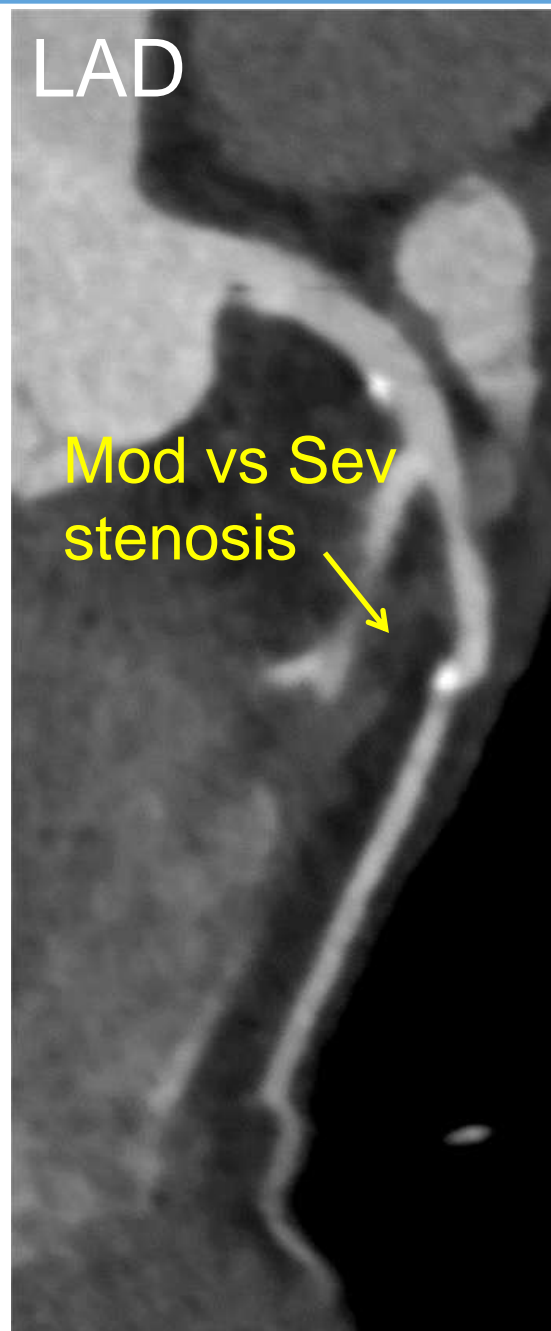
Case: 80 y/o Caucasian man

(Performed @ Cornell / NewYork-Presbyterian 4/23/15)

- **Symptoms:** Atypical chest pain with exertion
- **Past Medical History:** HTN, dyslipidemia
- **Medications:** metoprolol; statin; aspirin
- **Prior testing:** None

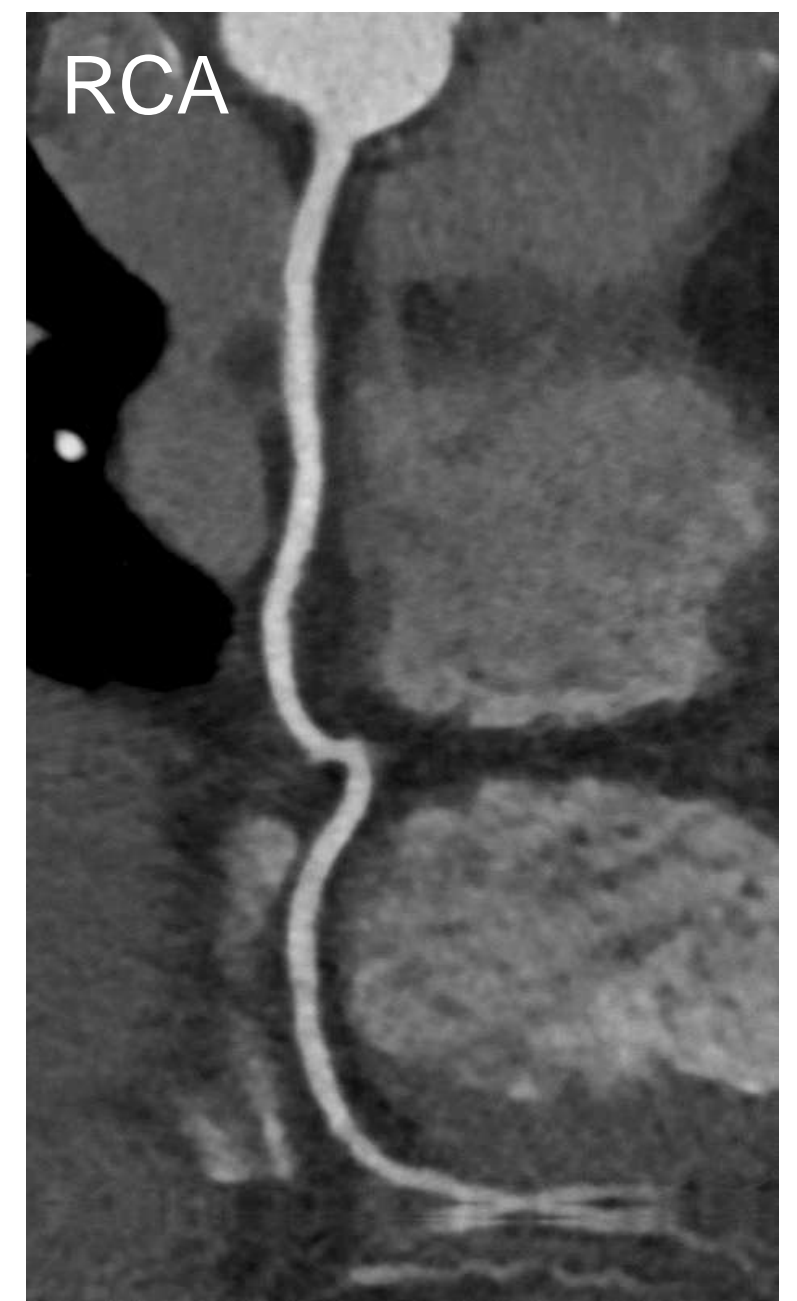
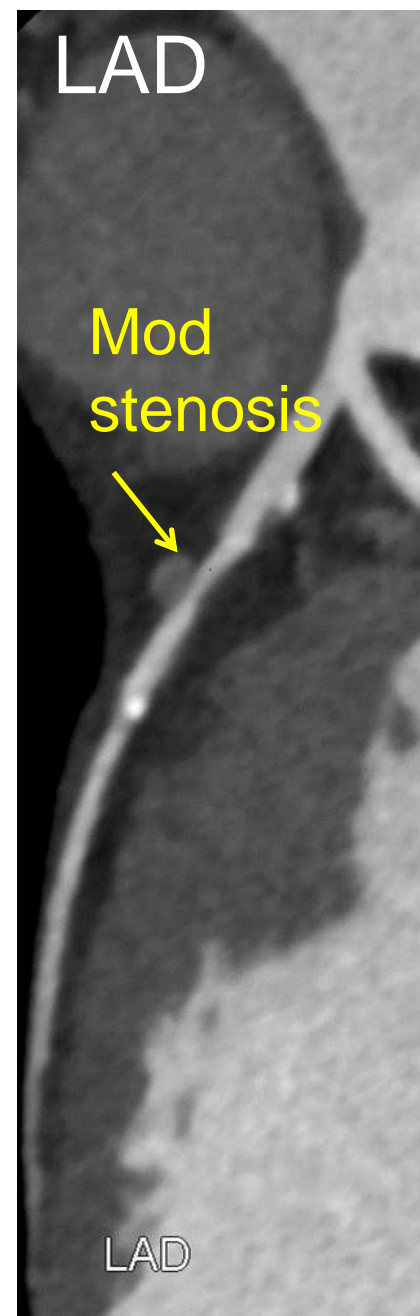
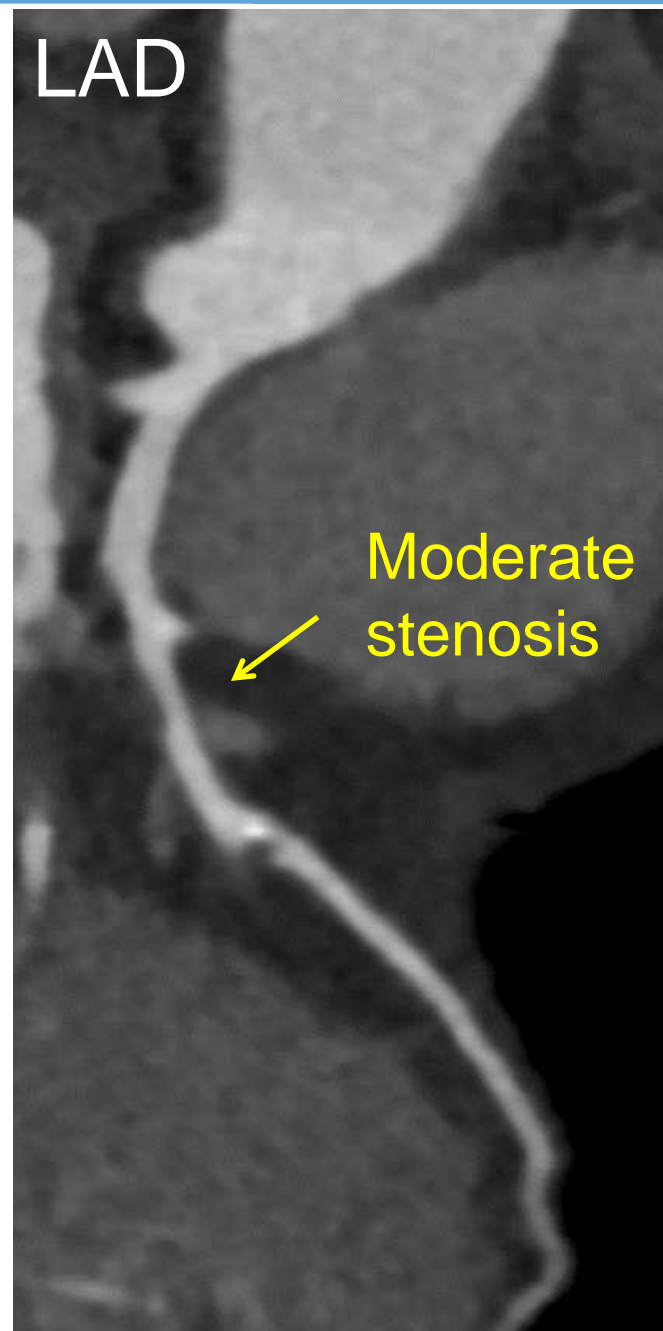
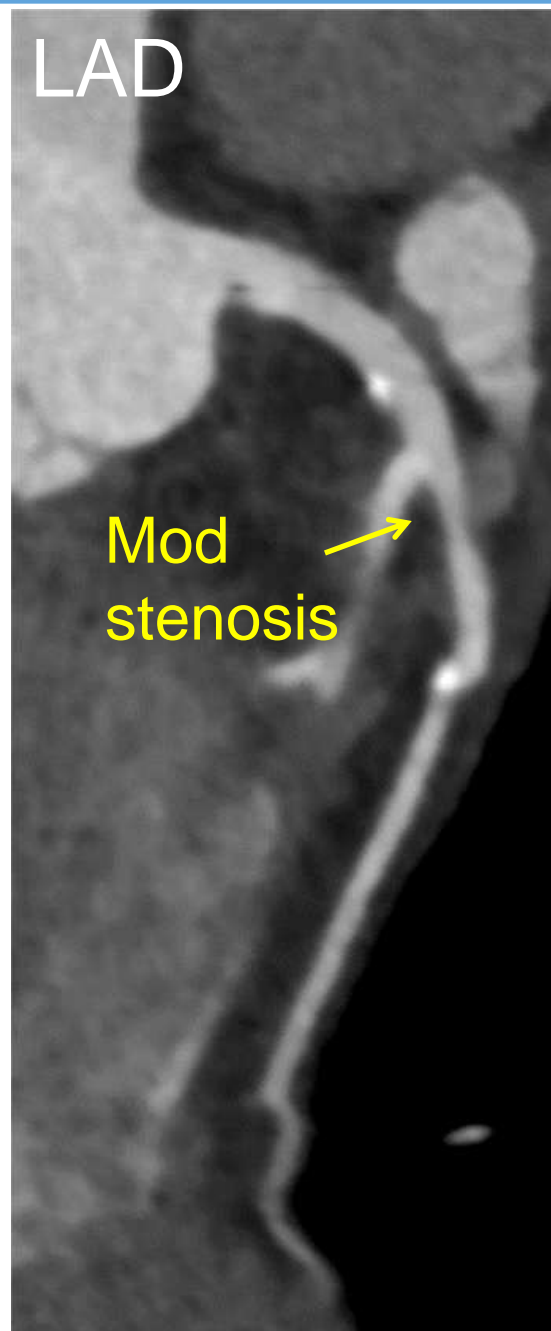
Case: 80 y/o Caucasian man

(Performed @ Cornell / NewYork-Presbterian 4/23/15)



Case: 80 y/o Caucasian man

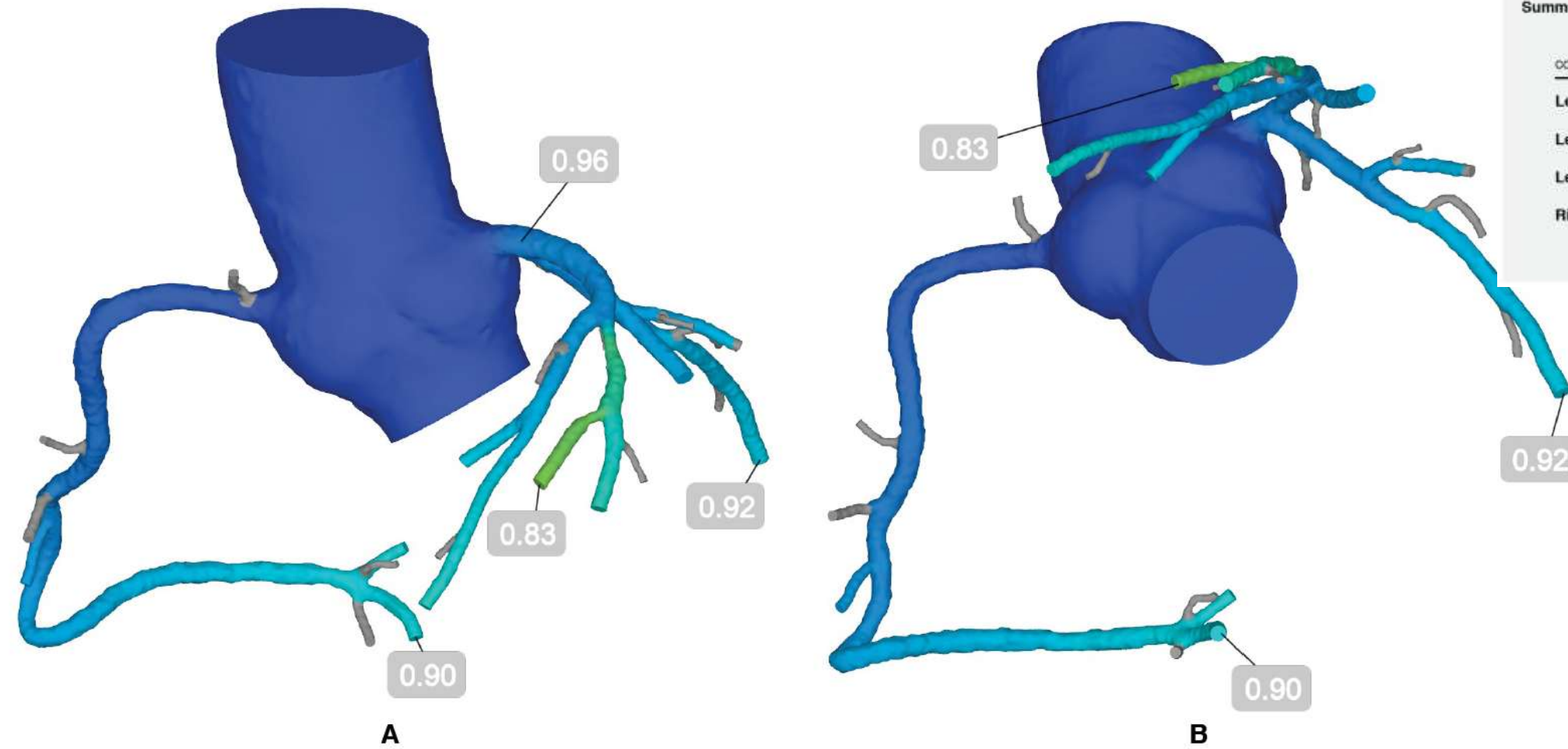
(Performed @ Cornell / NewYork-Presbterian 4/23/15)



Case: 80 y/o Caucasian man

(Performed @ Cornell / NewYork-Presbyterian 4/23/15)

- **Non-severe stenoses**
- **Continuum of FFR**



Summary: FFR_{CT} is > 0.80 in all coronary vessels.

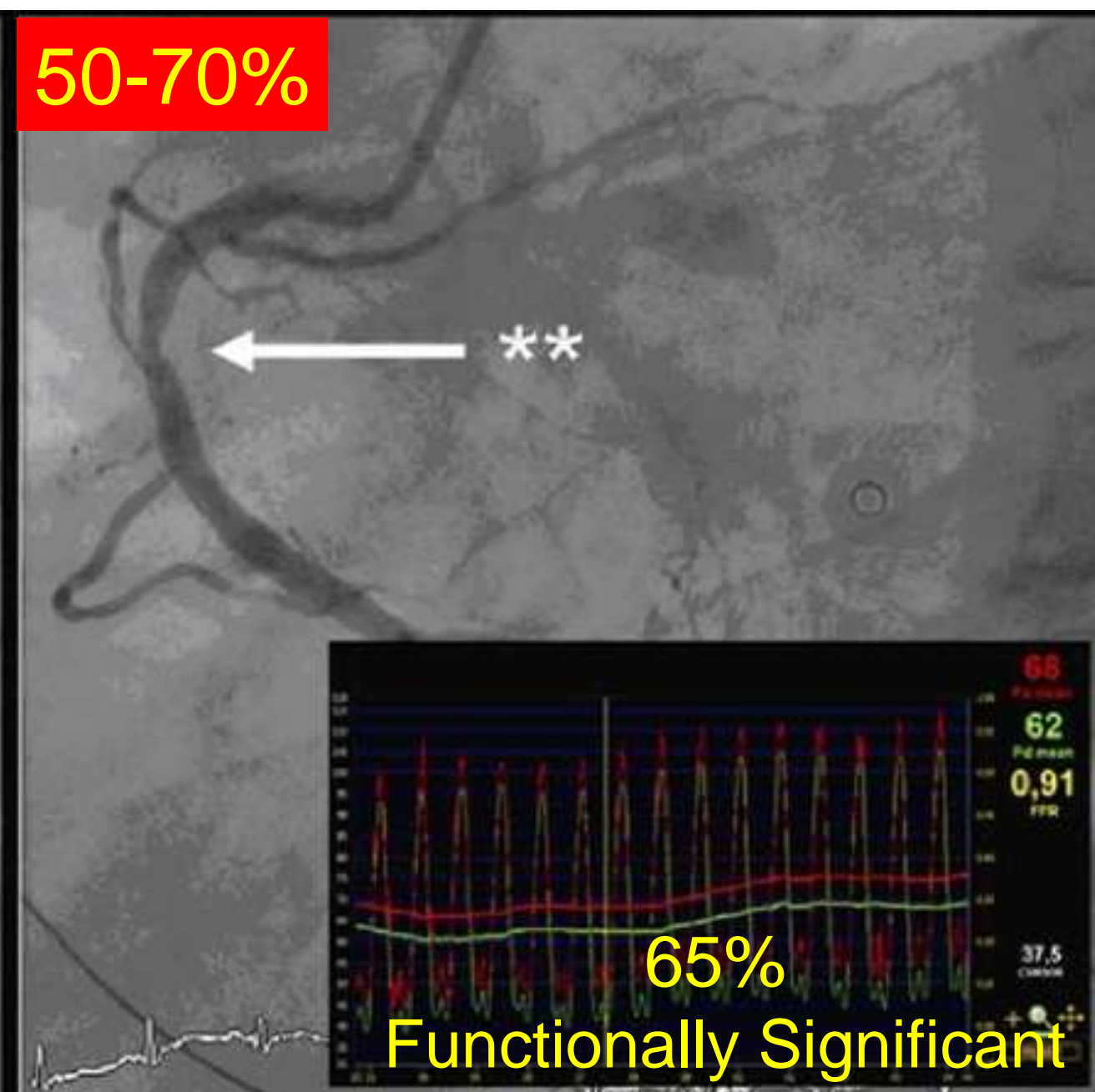
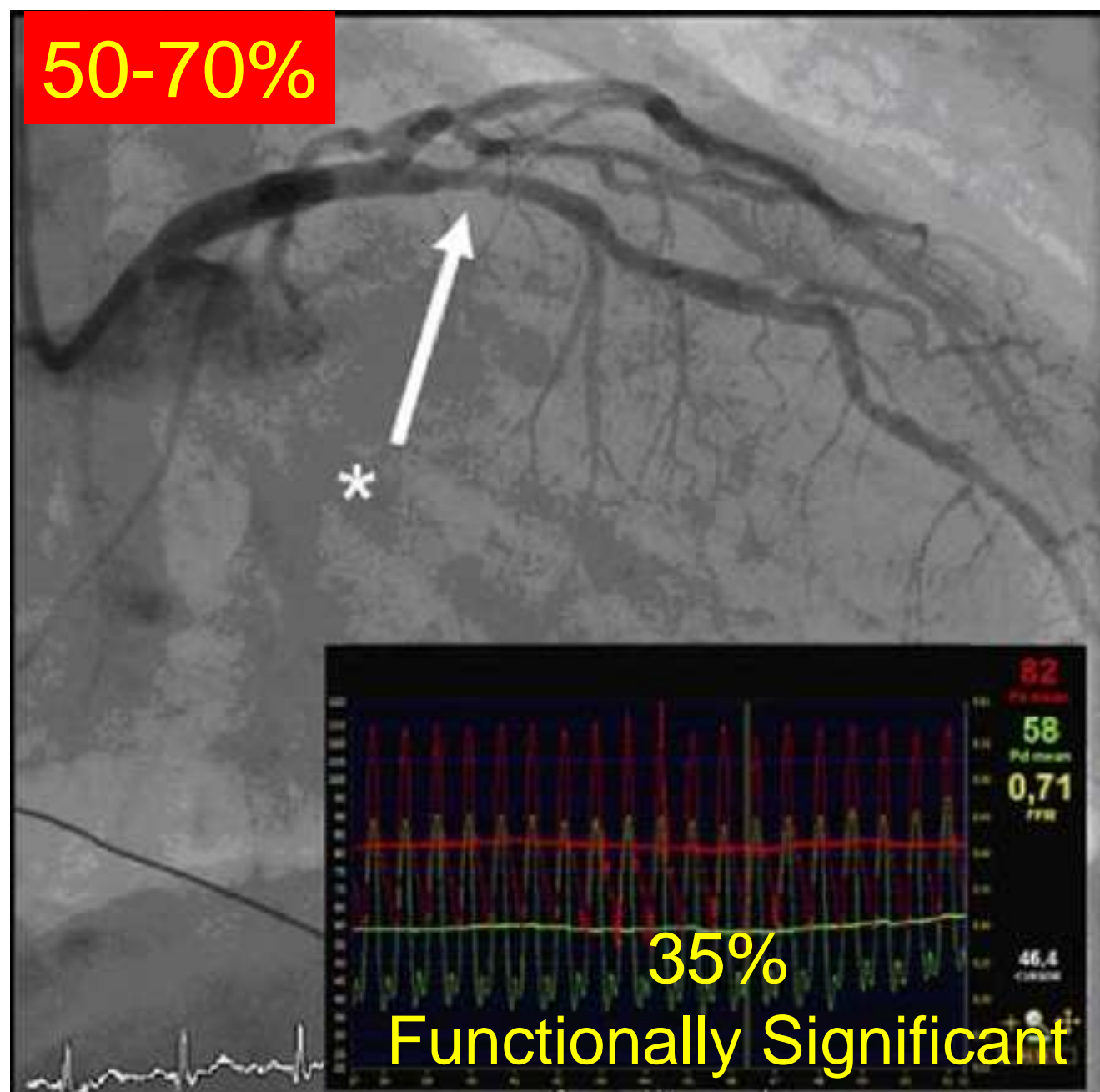
CORONARY ARTERIES & SYSTEMS	FFR_{CT}
Left Main Artery	0.96
Left Anterior Descending System	0.83
Left Circumflex System	0.92
Right Coronary Artery System	0.90

MAY BE FUNCTIONALLY SIGNIFICANT ^{1,2,3}



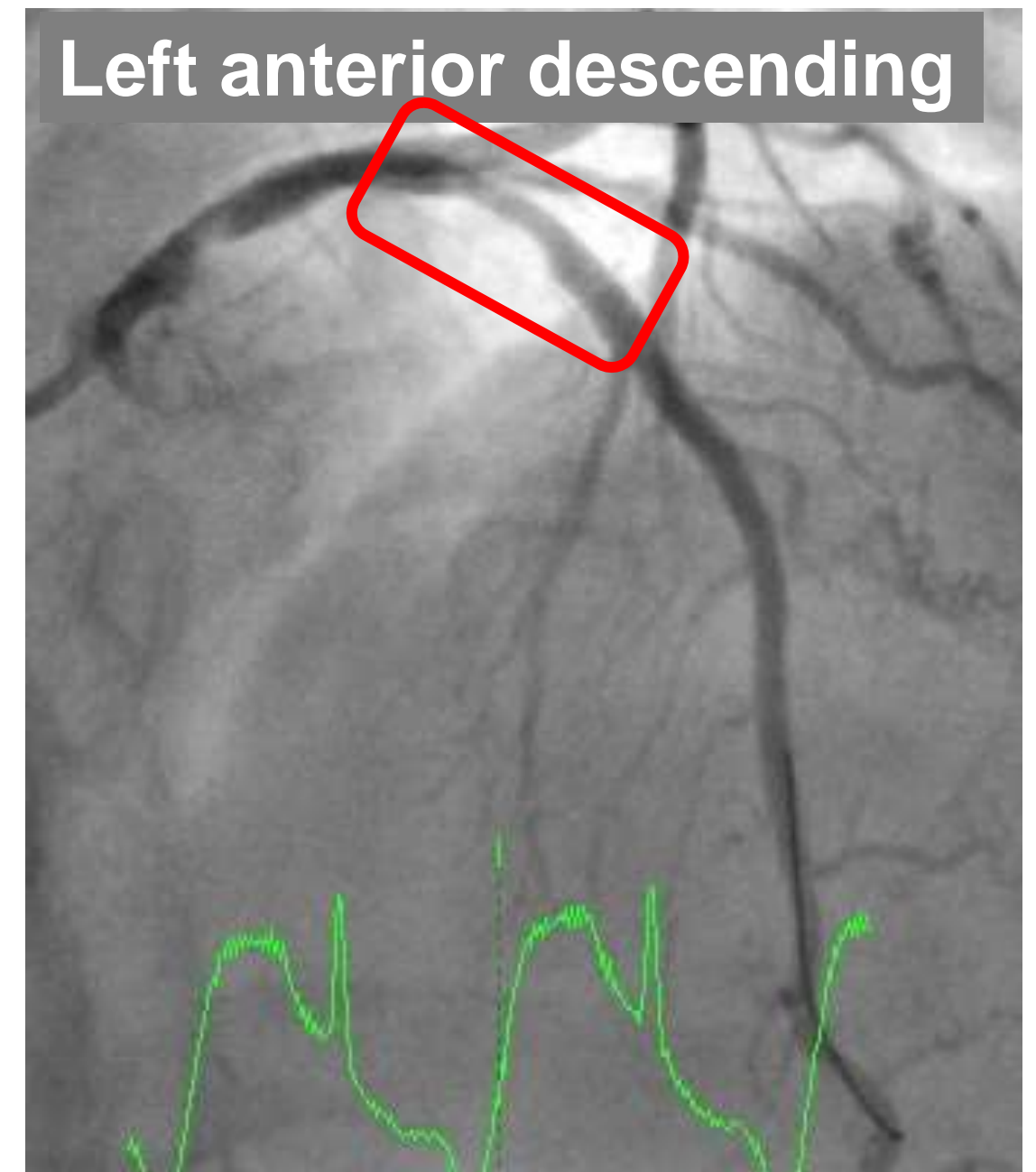
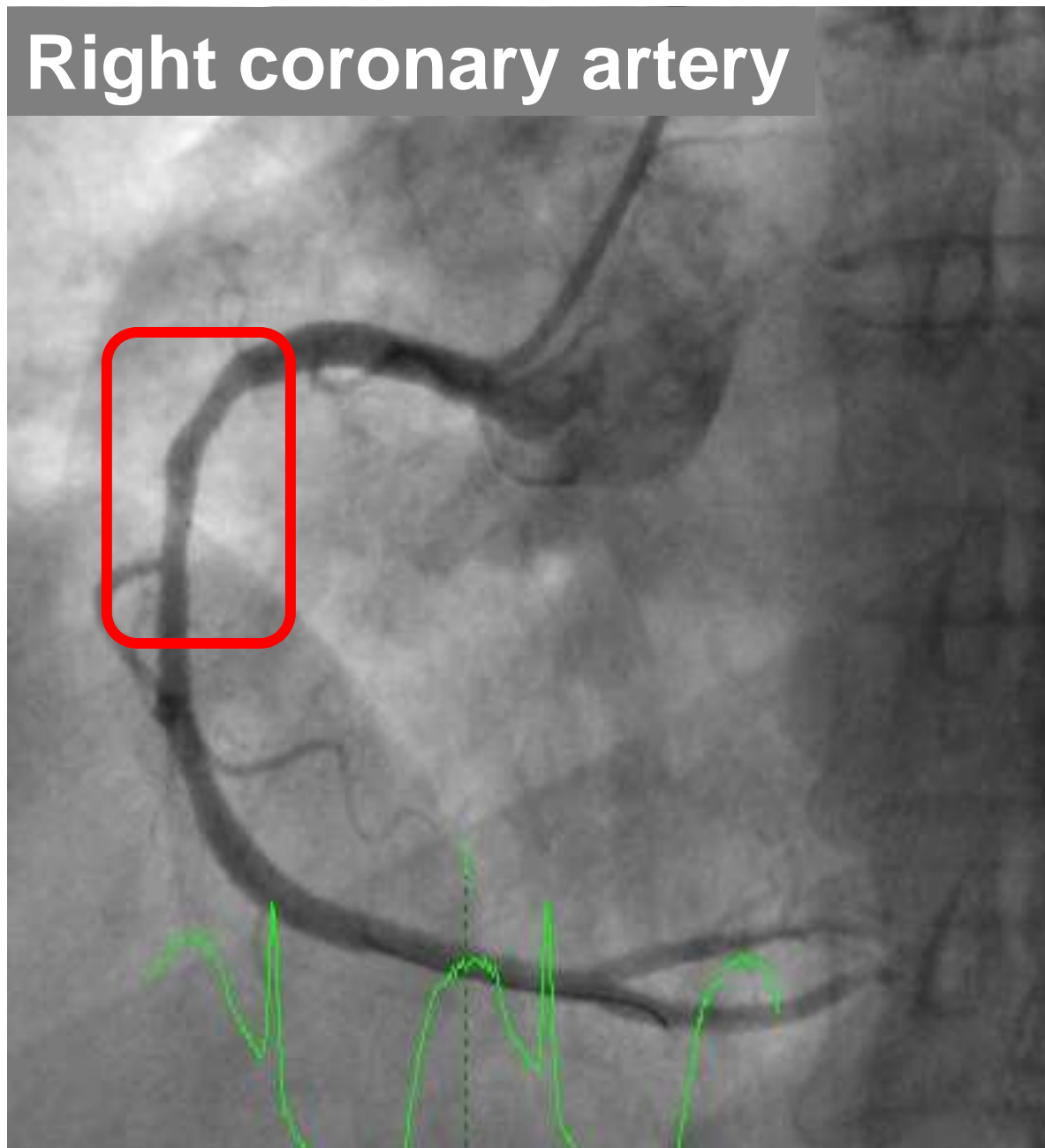
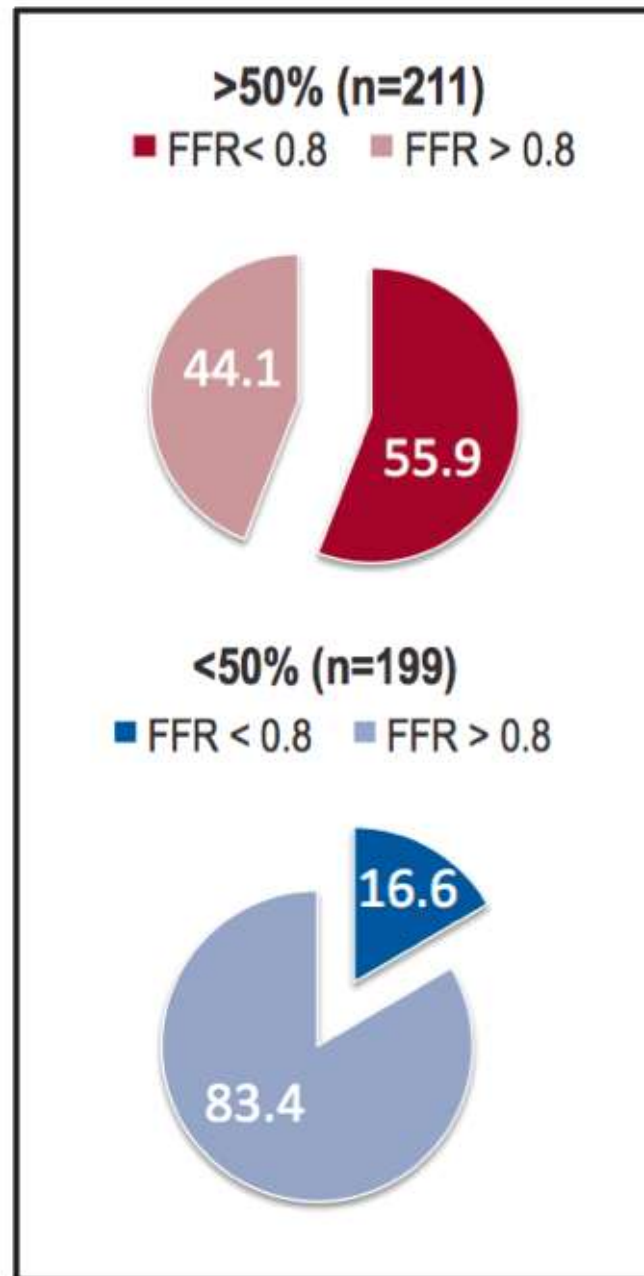
FFR: Beyond High-Grade Stenoses

FAME Trial
47% of all lesions



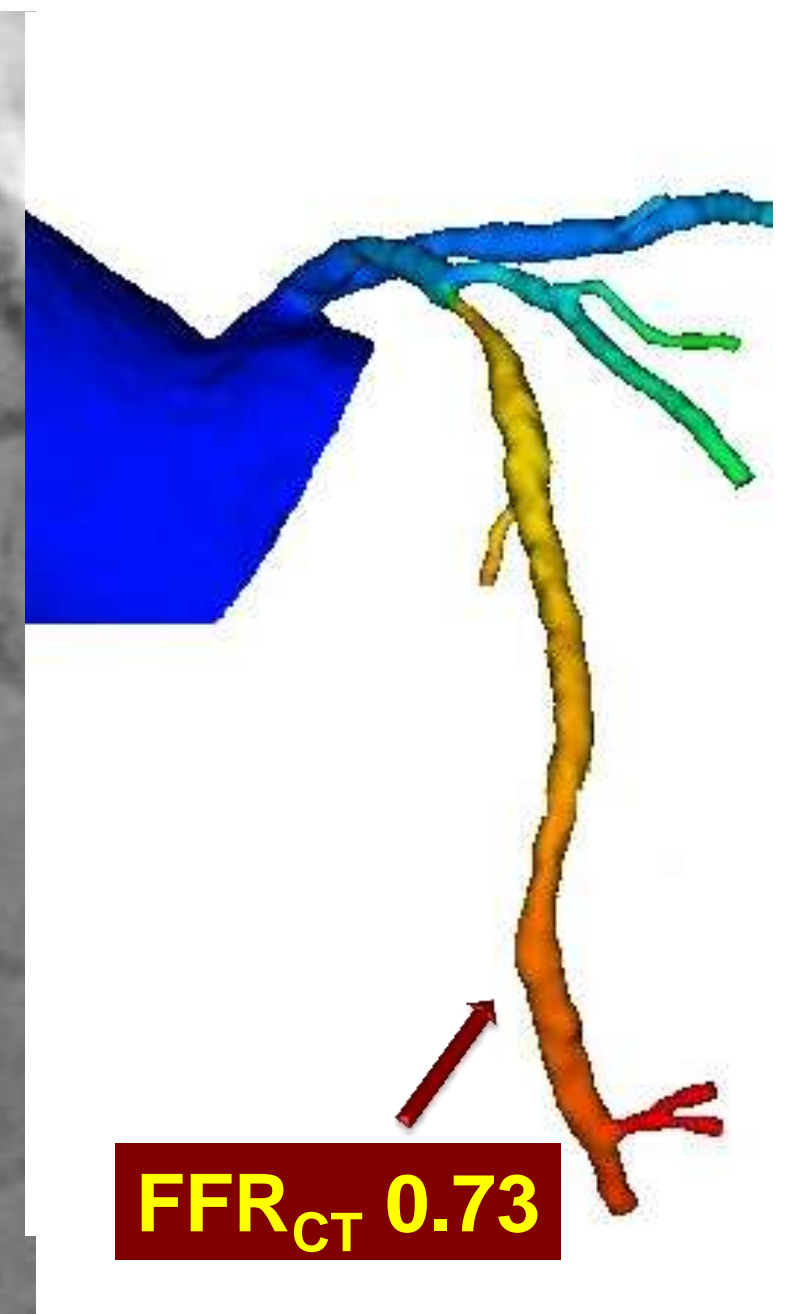
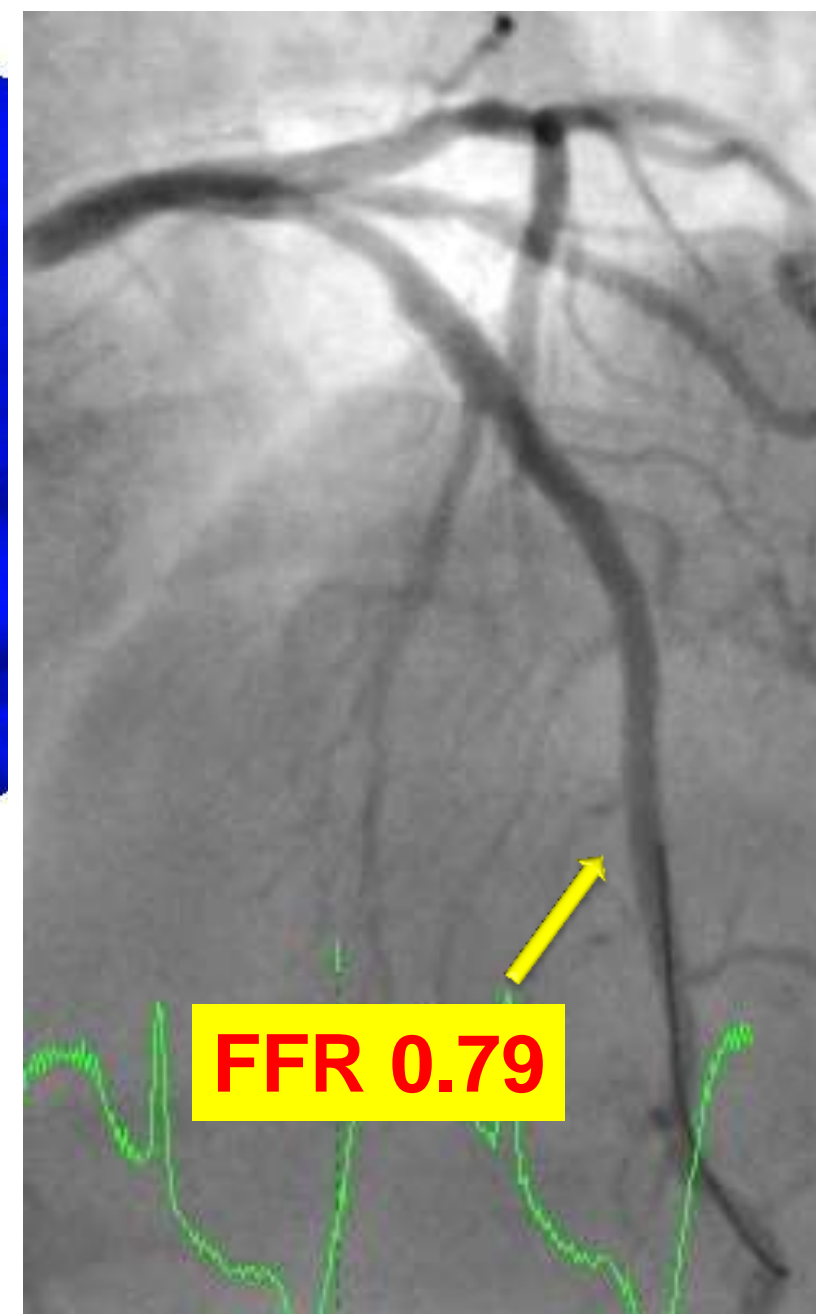
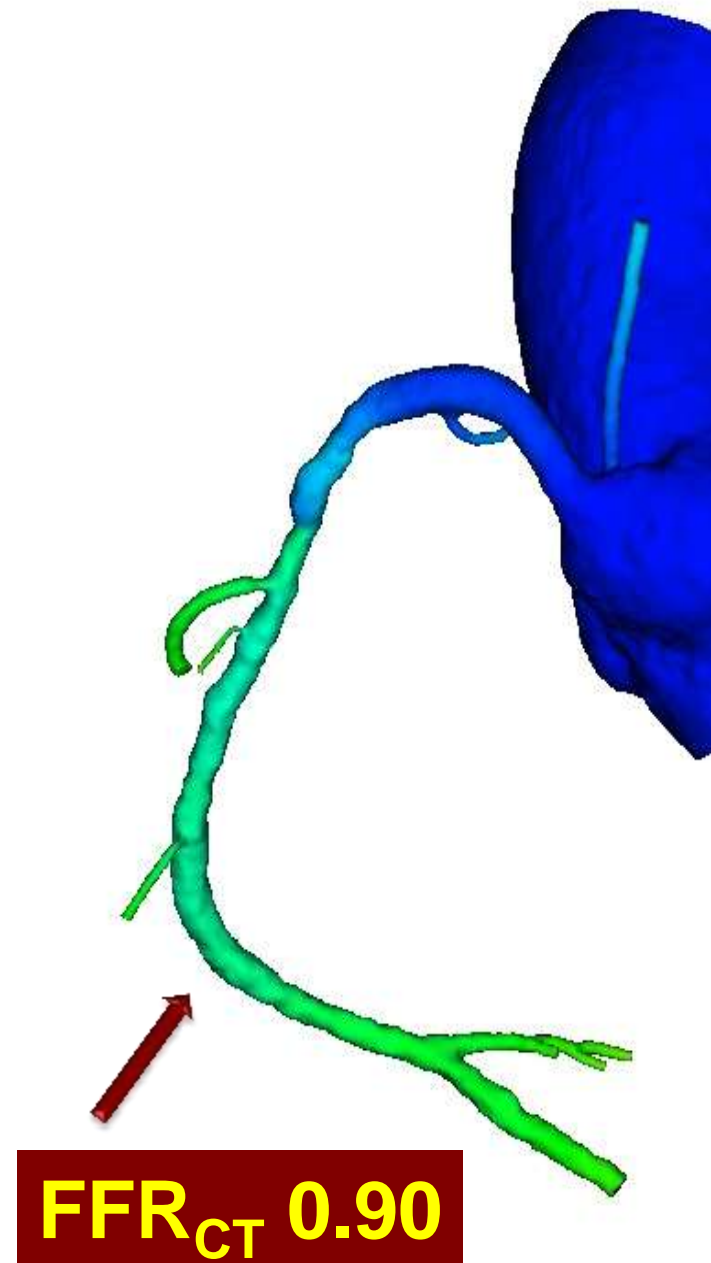
FFR_{CT}: “Non-obstructive” Stenoses

Prospective multicenter
N=252
Comparator: Invasive FFR

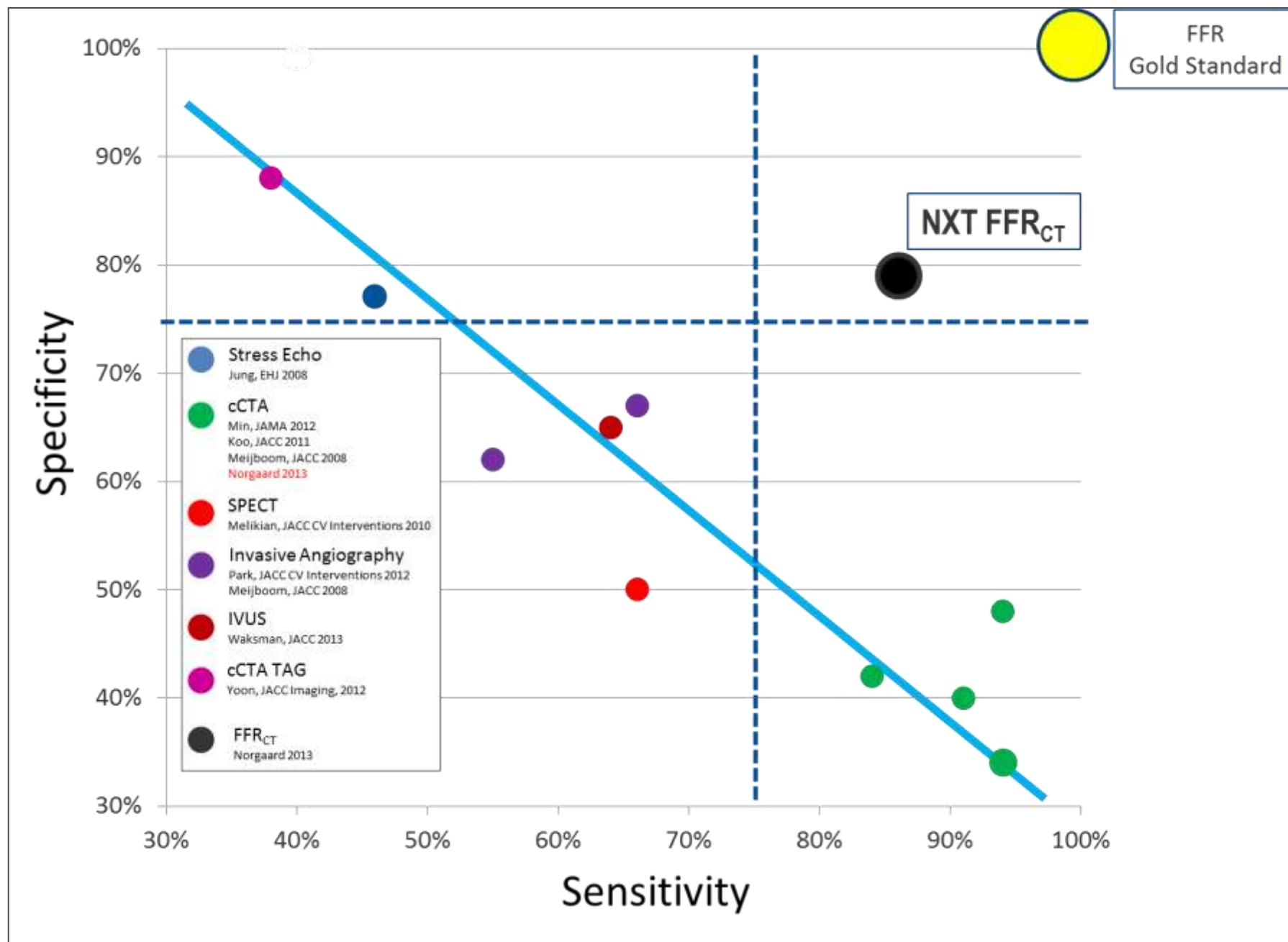


FFR_{CT}: Intermediate Stenoses

- 95% NPV
- 45% NRI



FFR_{CT} Superior to All Methods to Date



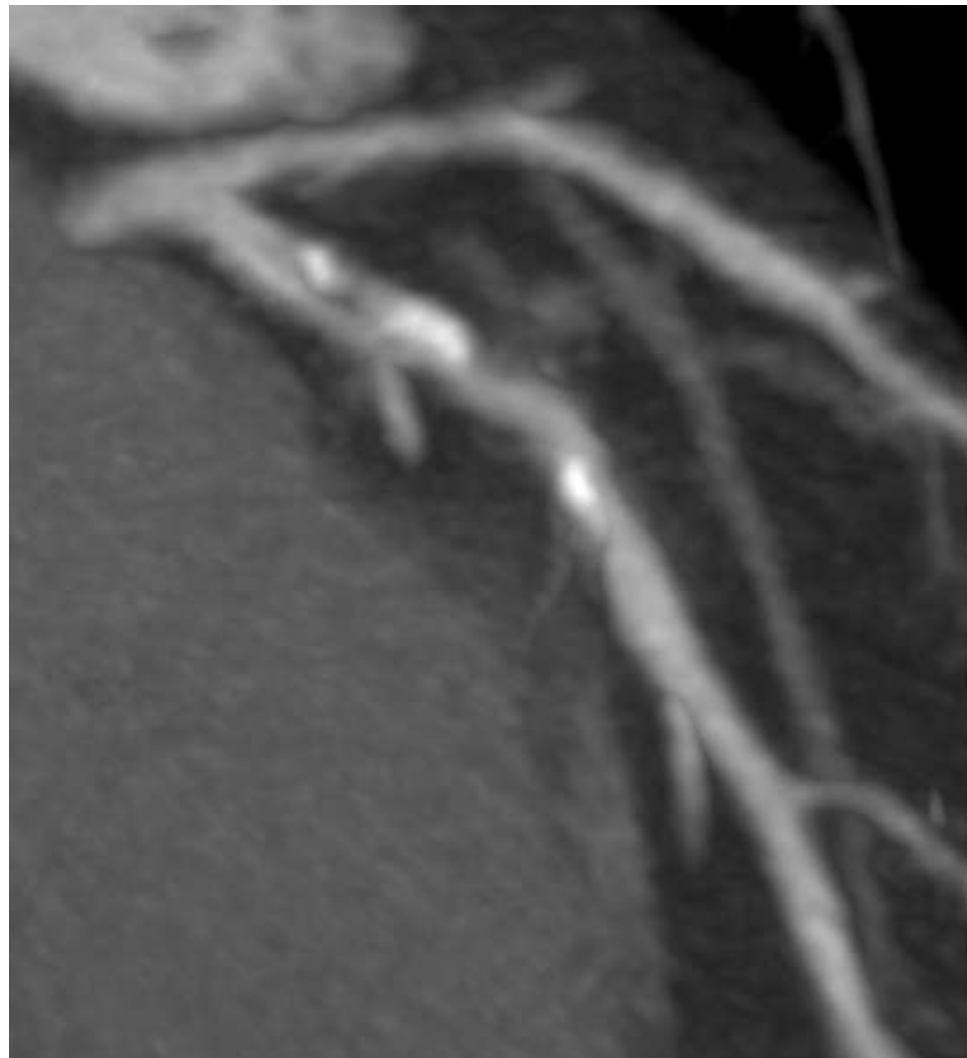
Conclusions: FFR_{CT}

FDA approval 11/15

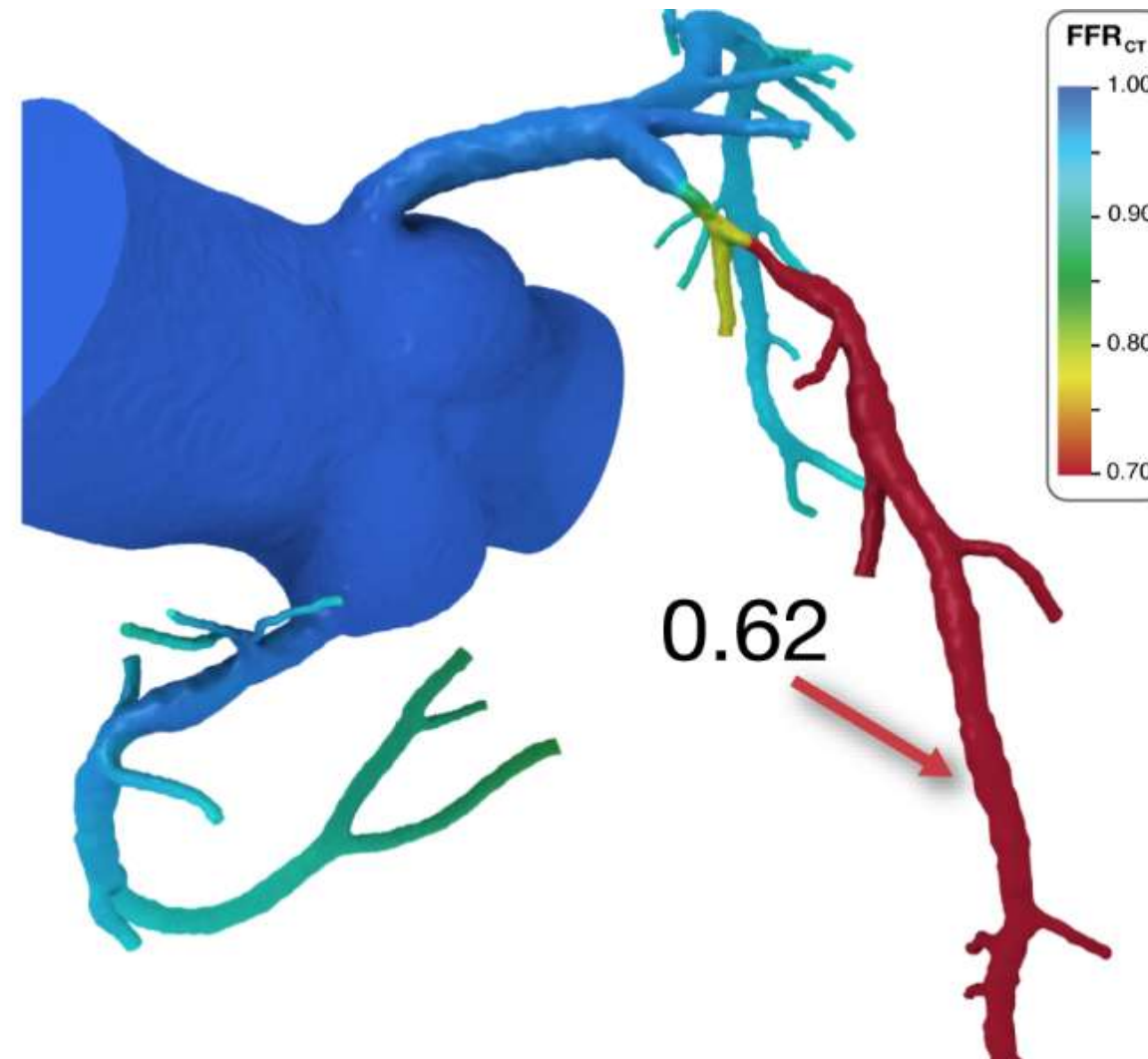
- Superior to all modalities for lesion-specific ischemia: 86% accuracy
- FFR_{CT} useful across all ranges of stenosis severity:
 1. Severe: 75% false positives
 2. Intermediate: ~50% prevalence, FFR_{CT} 95% NPV
 3. Non-obstructive (<50% stenosis): 17% ischemic
 4. Tandem lesions
- FFR_{CT} enables assessment of lesion-specific ischemia across a continuum, rather than simply as a binary measure

Thank you.

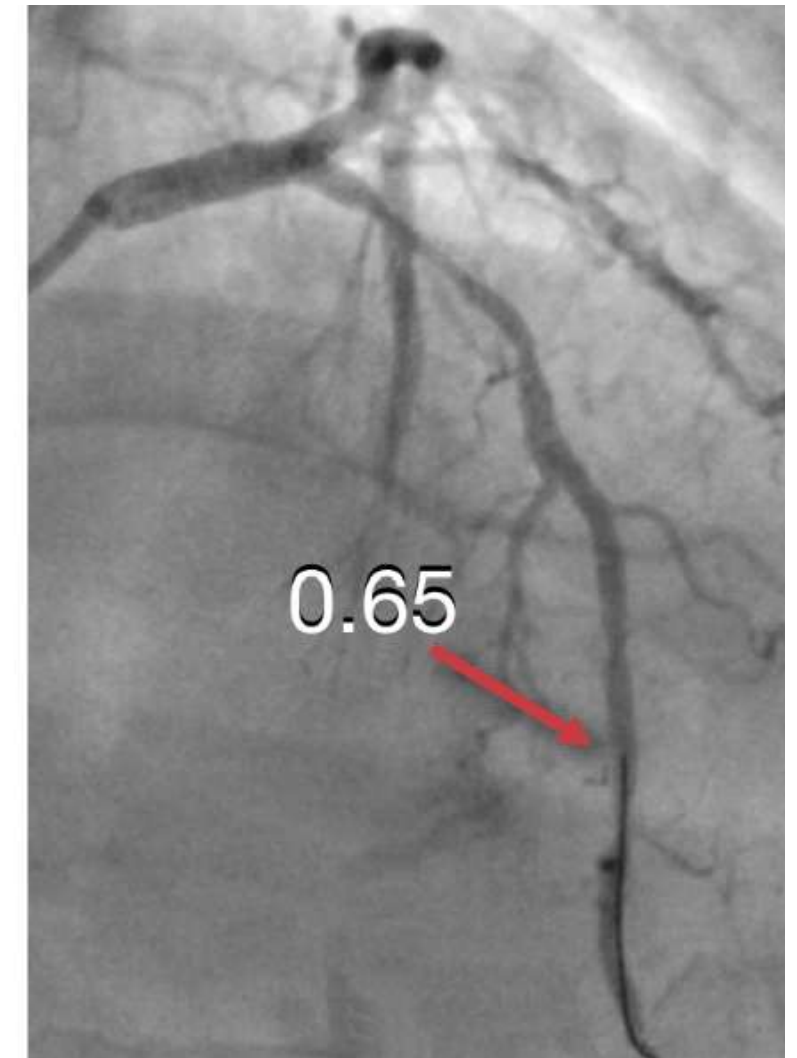
FFR_{CT}: Severe LAD Stenosis



CT: Severe Stenosis

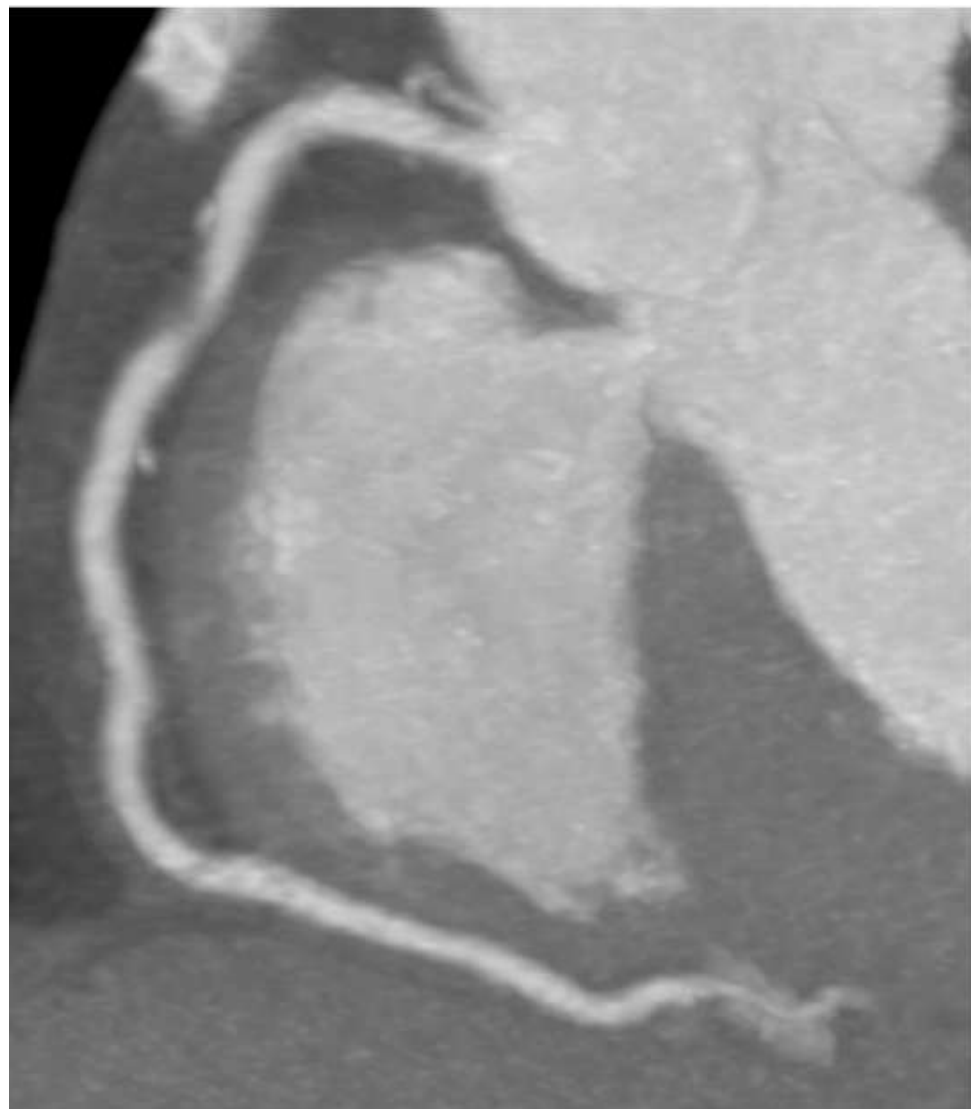


FFR_{CT}: Lesion-specific Ischemia

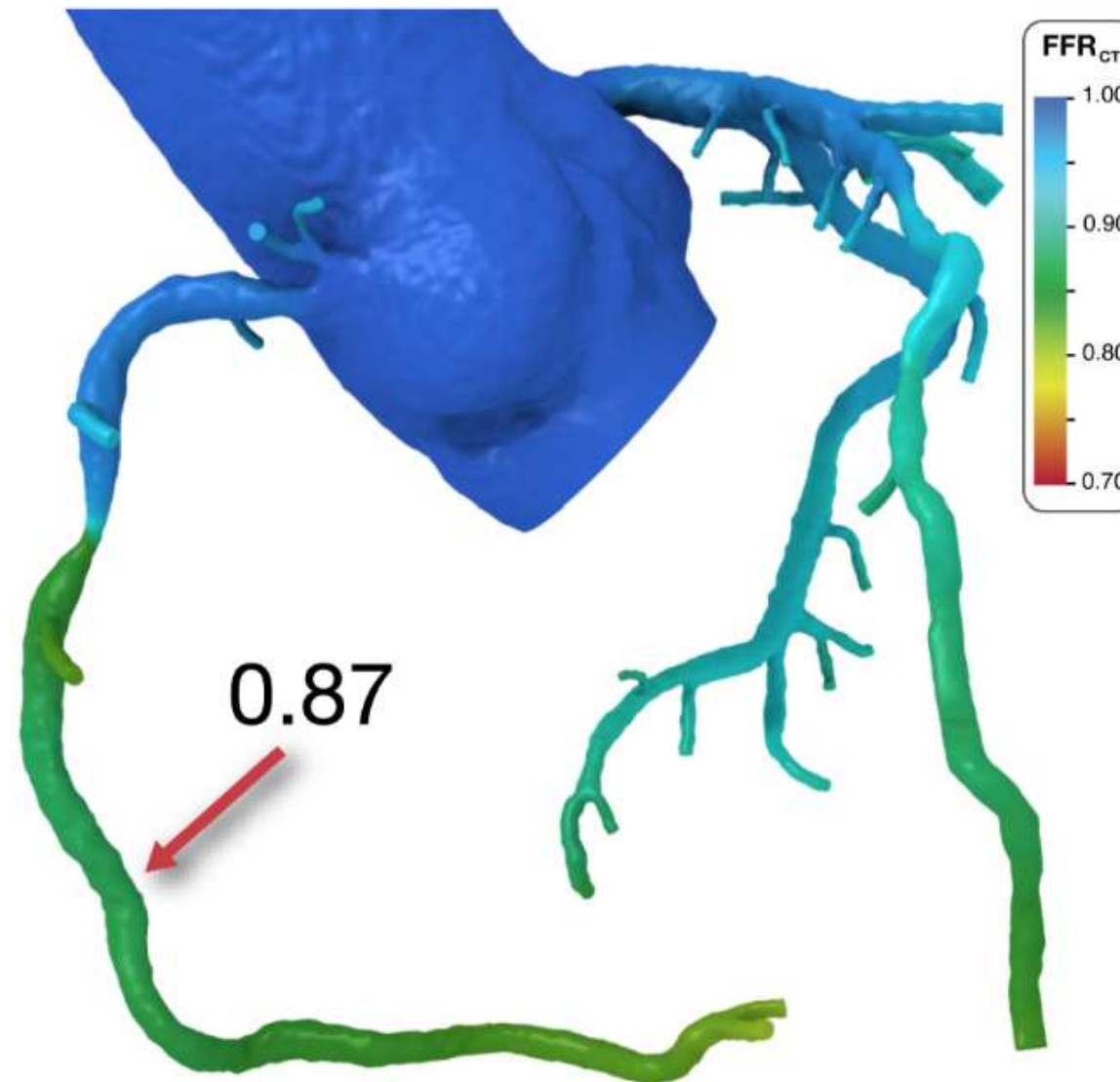


FFR: Ischemia

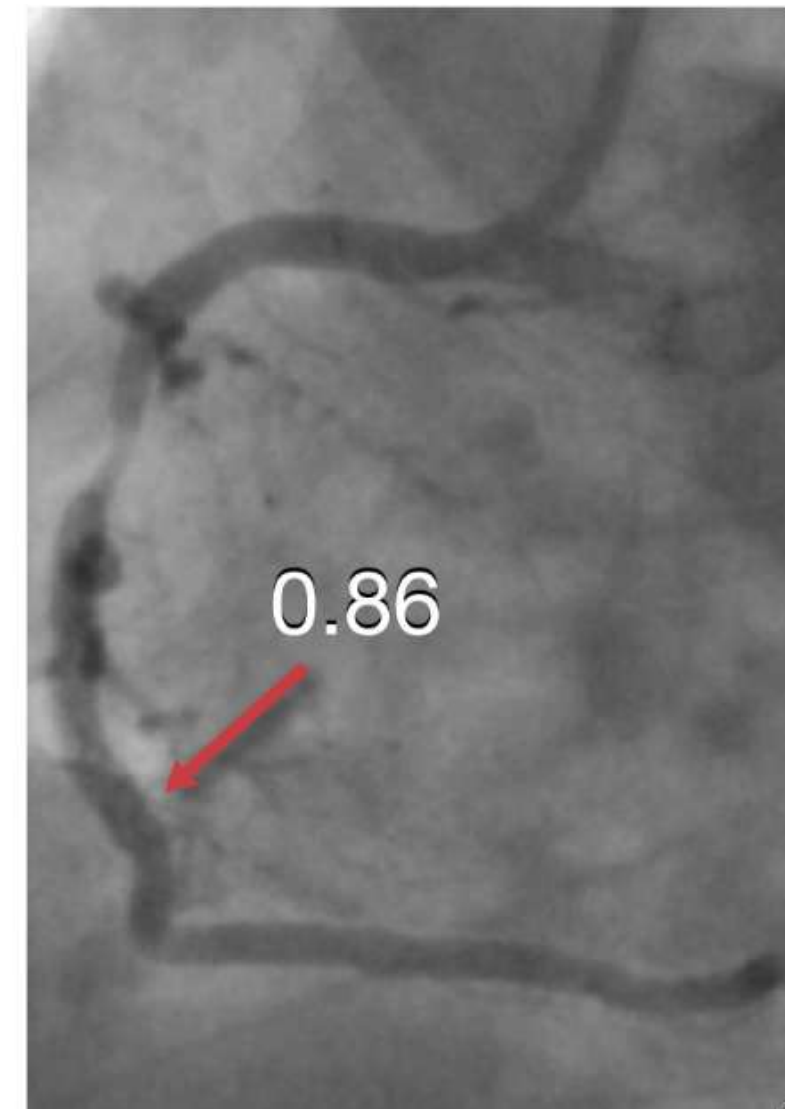
FFR_{CT}: Severe RCA Stenosis



CT: Severe Stenosis



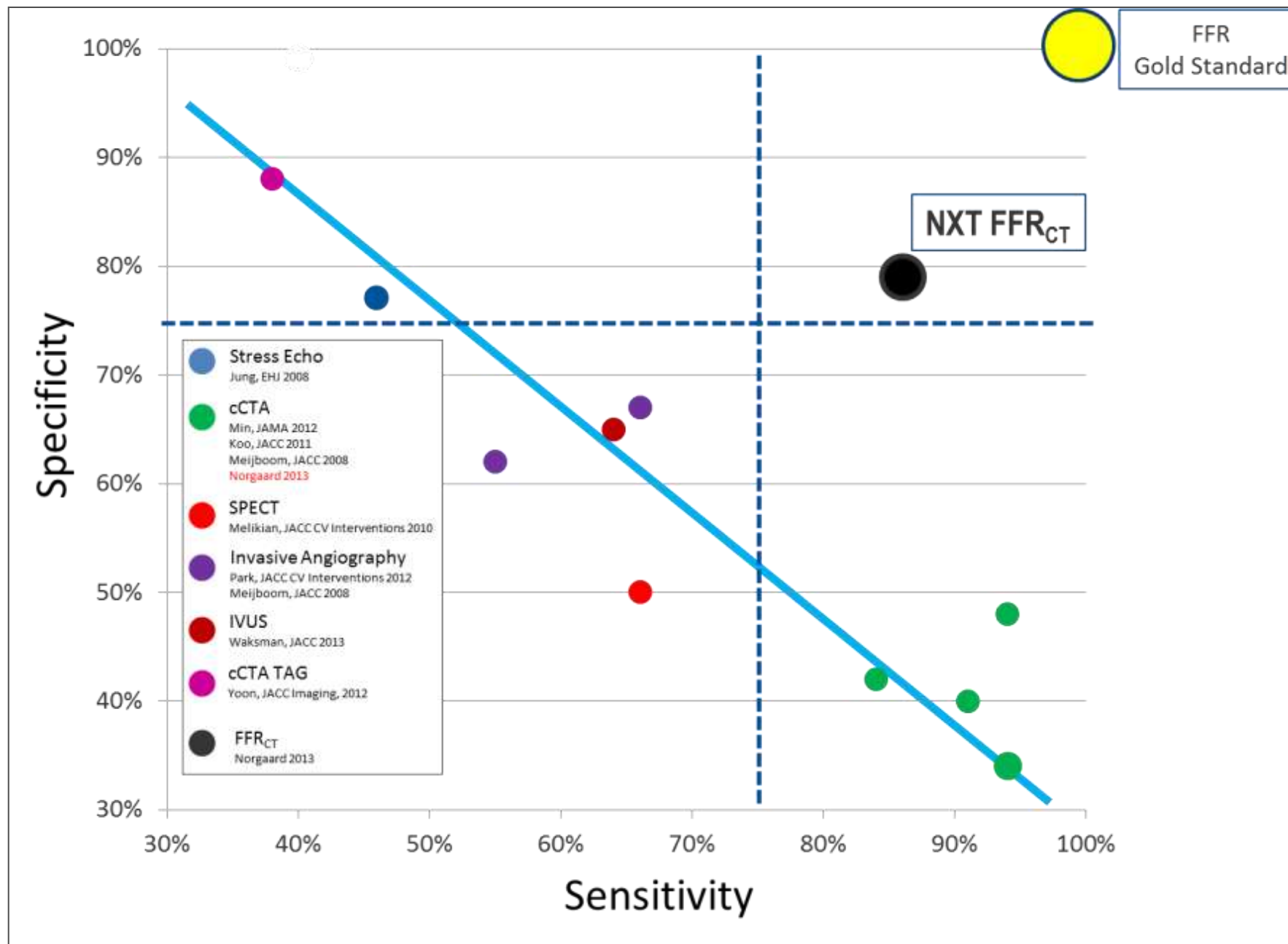
FFR_{CT}: No Ischemia



FFR: No Ischemia

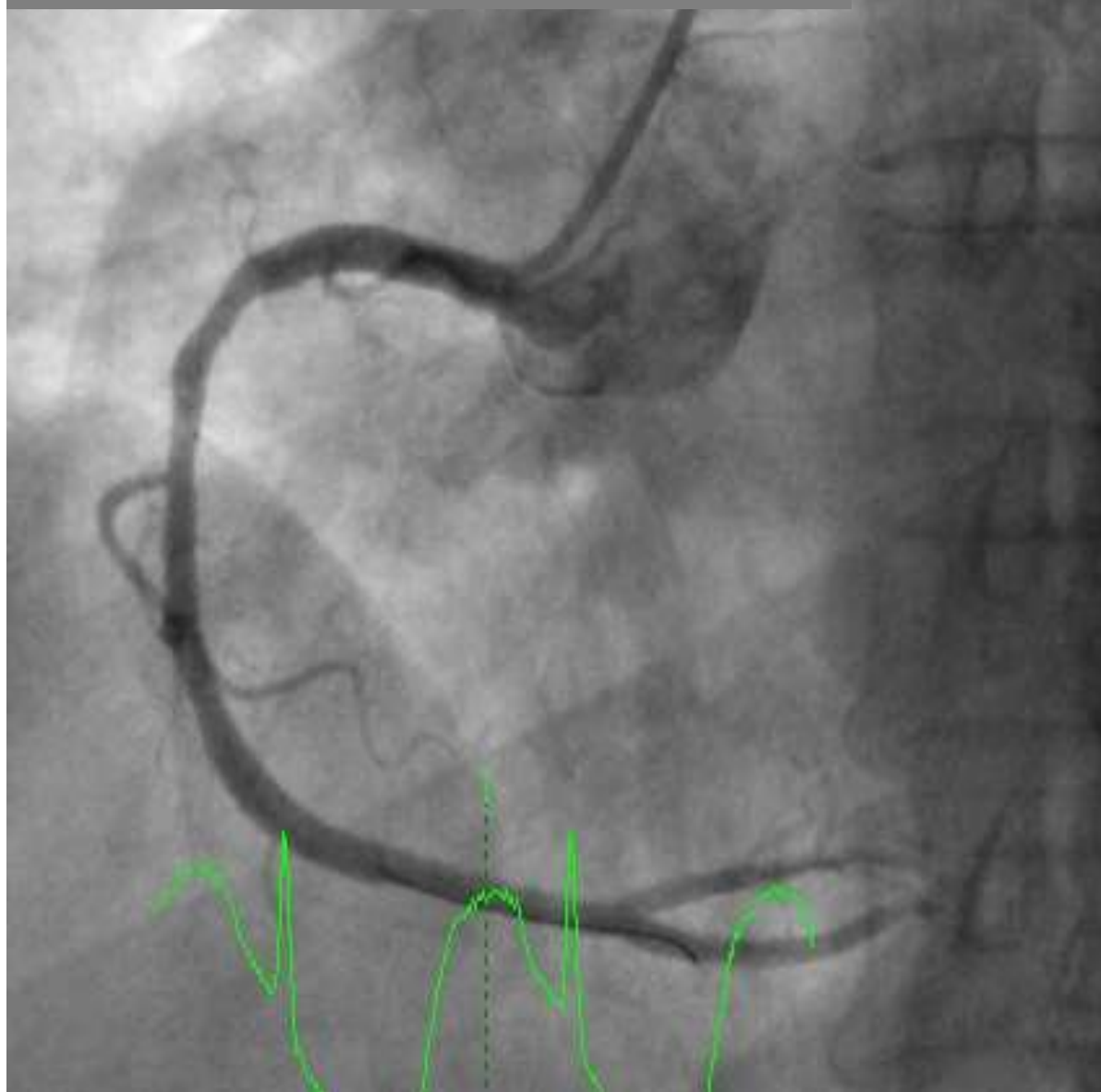
FFR_{CT}: Lesion-specific ischemia

FFR_{CT} superior to all methods to date

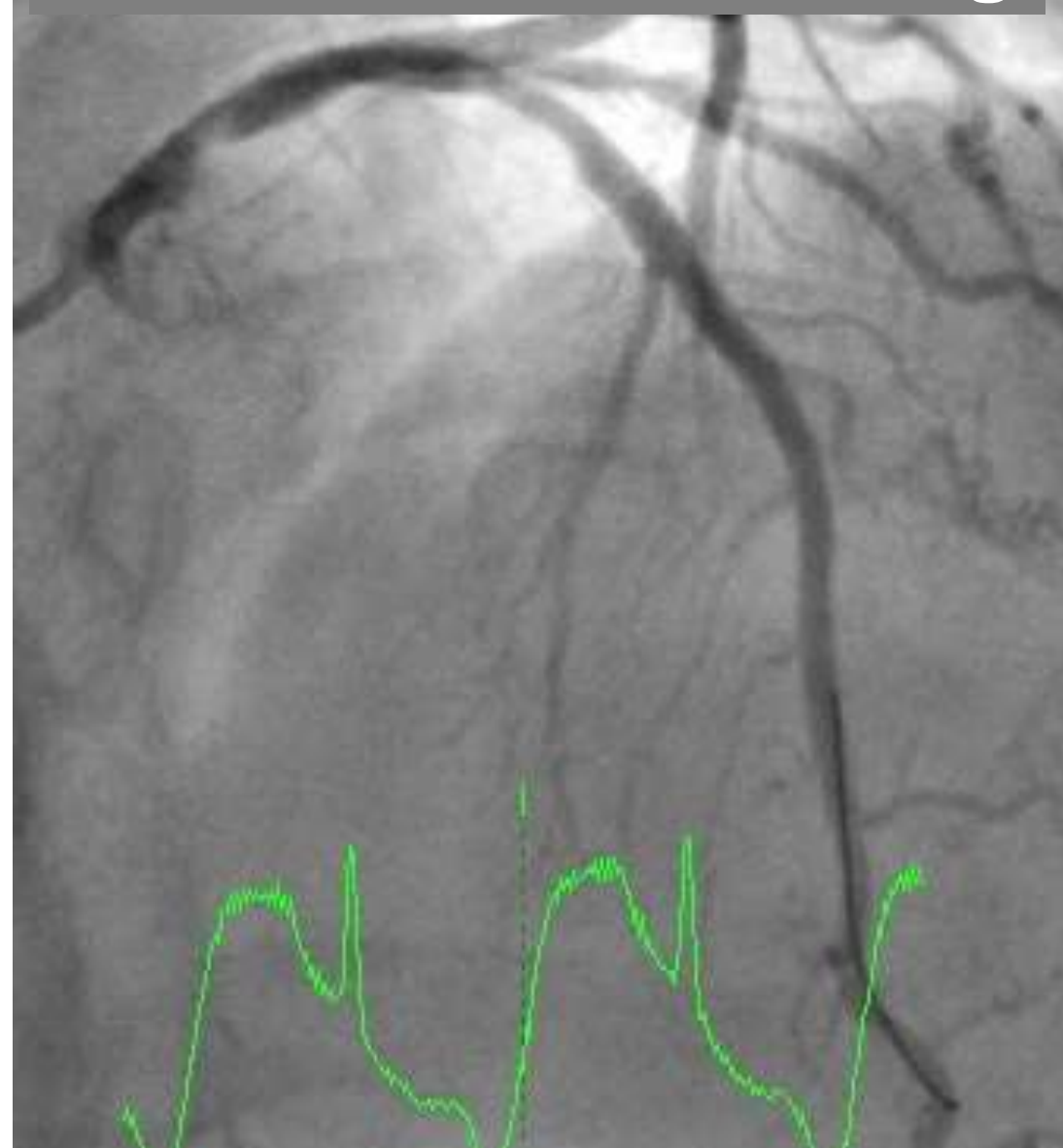


FFR_{CT}: Intermediate Stenoses

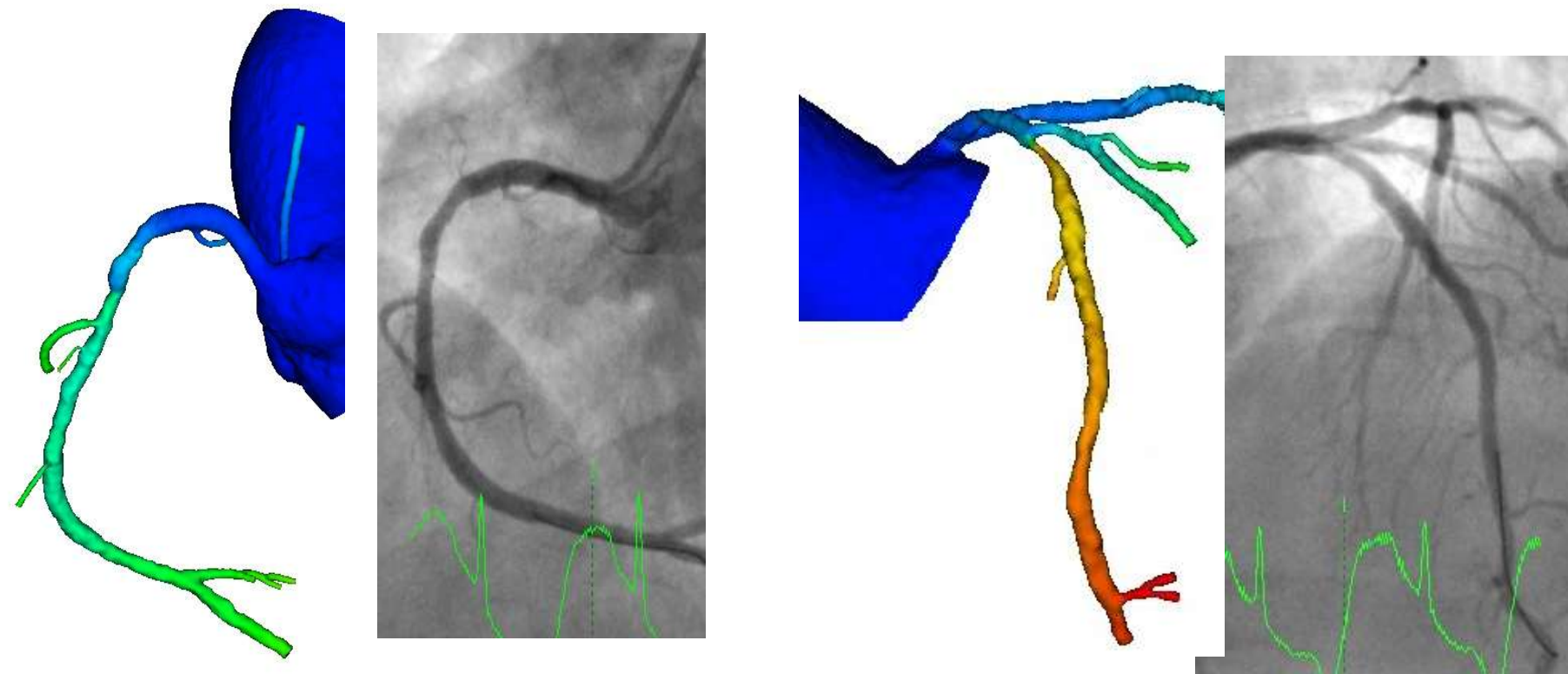
Right coronary artery



Left anterior descending

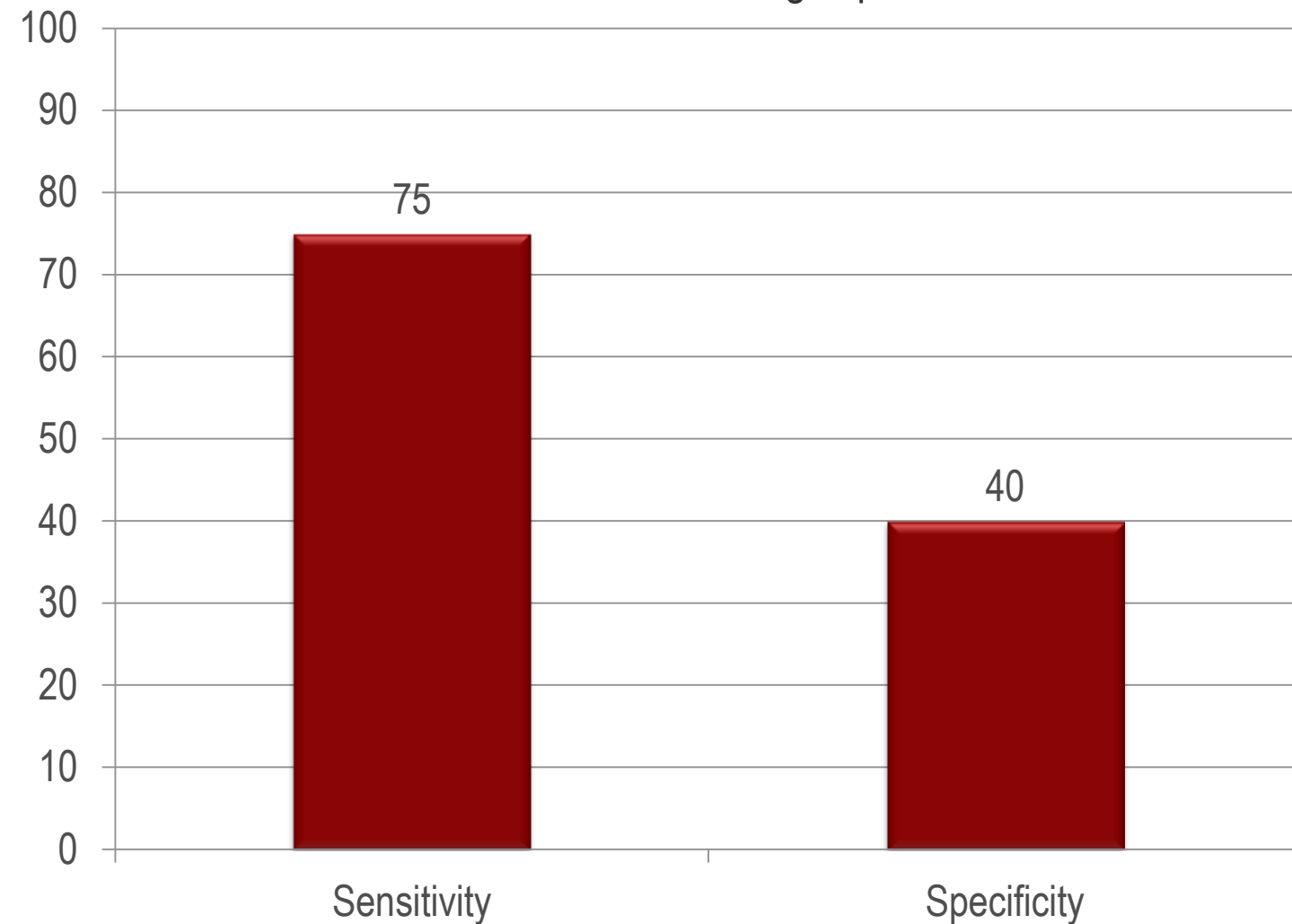


FFR_{CT}: Intermediate Stenoses



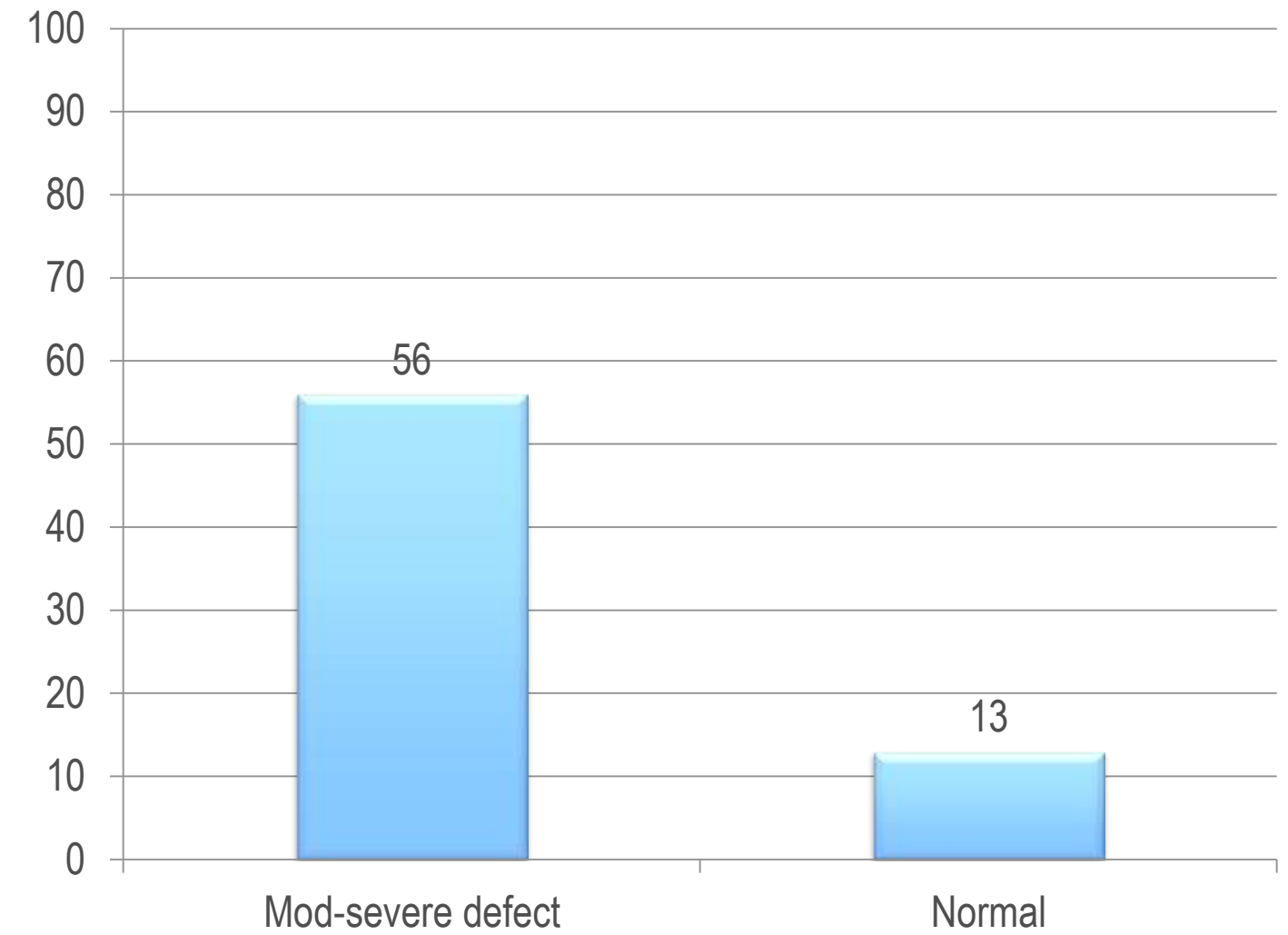
Ischemia testing fails to identify high-risk CAD: LM or 3VD

Diagnostic accuracy of nuclear stress testing is poor



MPI: LM / 3VD (n=2310)

Half of stress tests normal or mildly abnormal



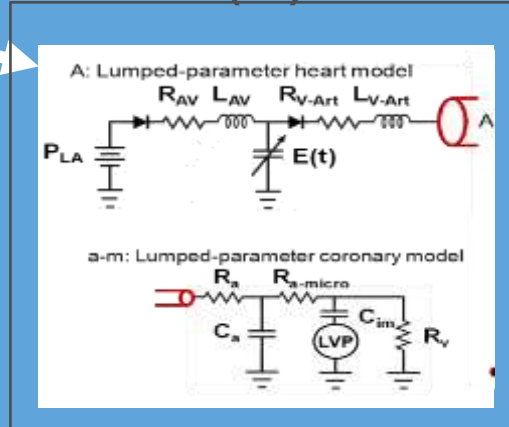
MPI: LM>50% stenosis (n=101)

Blinded FFR_{CT} Analyses

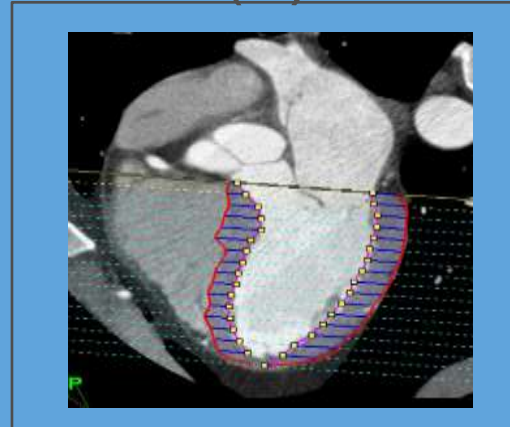
(1)



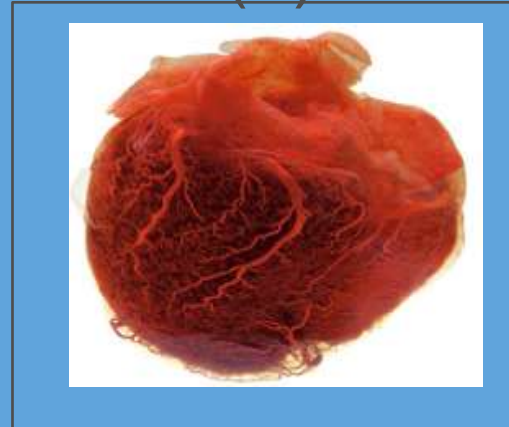
(2)



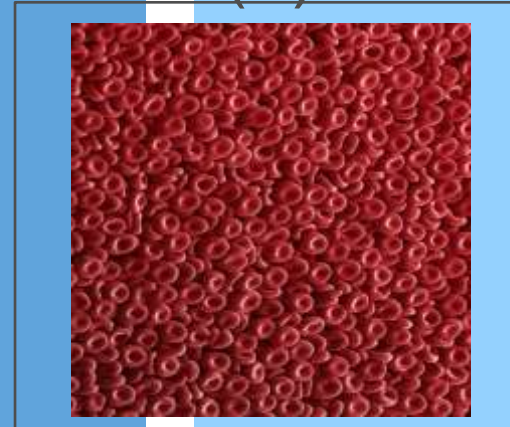
(3)



(4)



(5)



(6)



Image-based Modeling -- Comprehensive segmentation of coronary arteries and aorta to determine patient-specific coronary geometry

Heart-Vessel Interactions – lumped parameter

Segmentation of Left Ventricular Myocardial Mass – relating time-varying coronary resistance to transmural pressure

Calculation of microcirculatory resistance – Use of allometric scaling laws to relate patient-specific “form” to function relationships of (e.g. mass / size of object related to physiology)

Patient-specific Physiologic Conditions - fluid viscosity (hematocrit), blood pressure, heart rate

Induction of Hyperemia – Standard prediction model to “virtually” force complete smooth muscle cell relaxation

Blinded FFR_{CT} Analyses

Patient-Specific Determination of Hyperemic Flow and Pressure

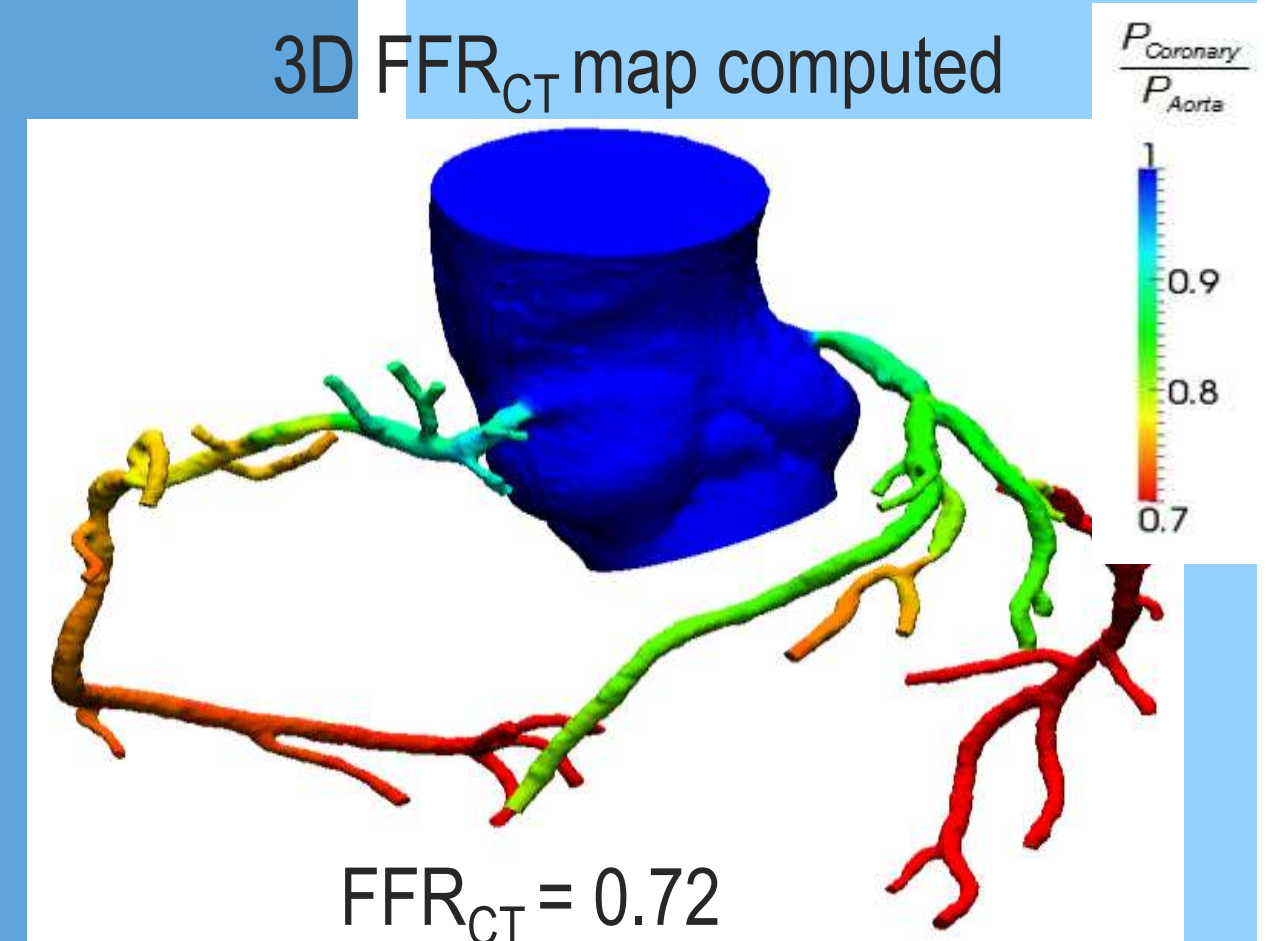
Numerical method approximates governing equations

Obtain solution for velocity and pressure at finite (but very large) number of points

Simultaneous solving of millions of partial linear equations

Repeating process for thousands of time intervals within cardiac cycle

3D FFR_{CT} map computed

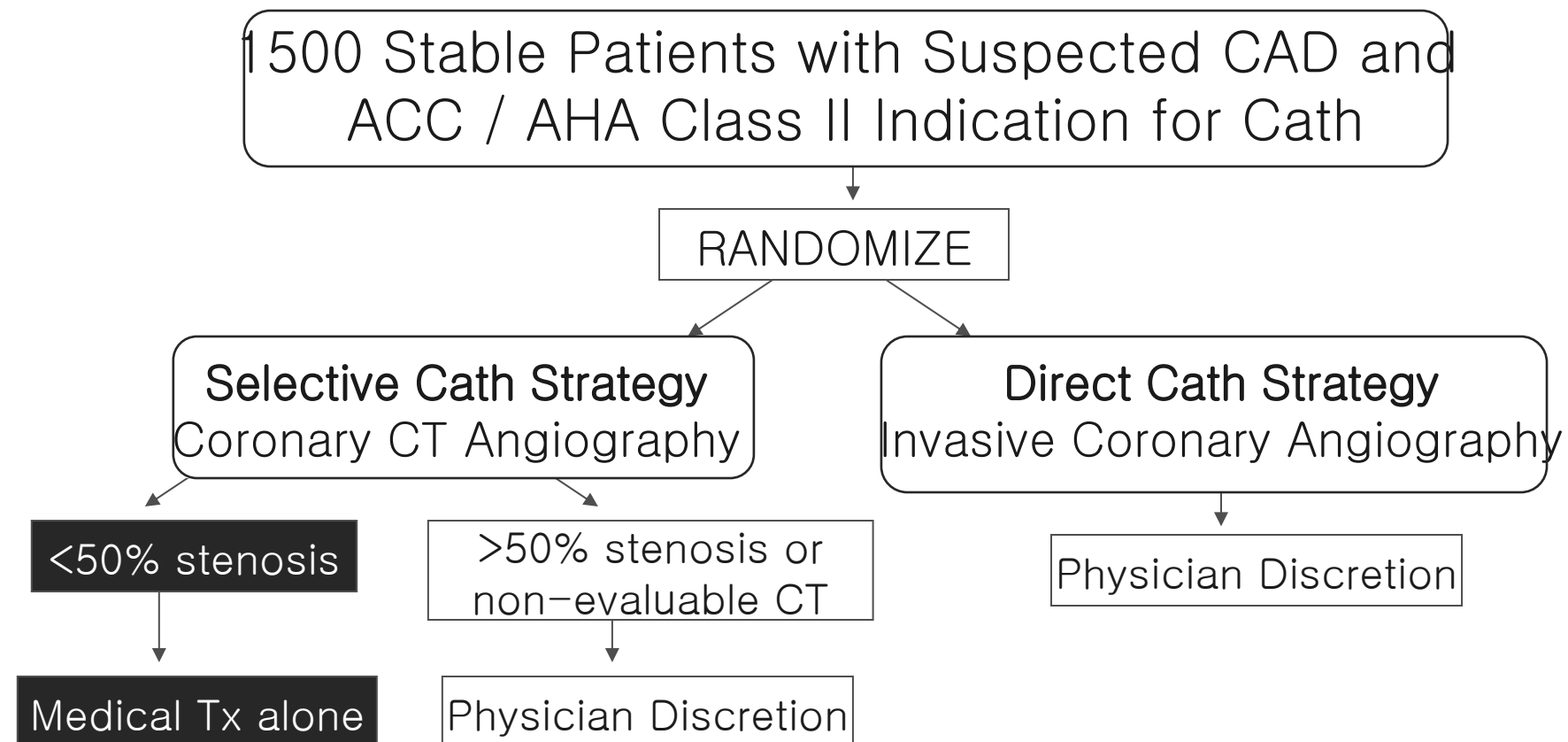


(can select any point on model)

- From typically acquired CCTA
- No additional image acquisition
 - No excess radiation
- No modification to imaging protocols
 - Prospective or retrospective ECG gating
- No administration of adenosine or other

CONSERVE: CT as a “gatekeeper” to the cath lab

RCT open label
N=1500
Duration: 1 year f/u



- Co-Primary endpoint: Non-inferiority for major adverse cardiovascular events
- Co-Primary endpoint: Cardiovascular and overall healthcare costs
- Secondary analysis: CT + FFR_{CT}

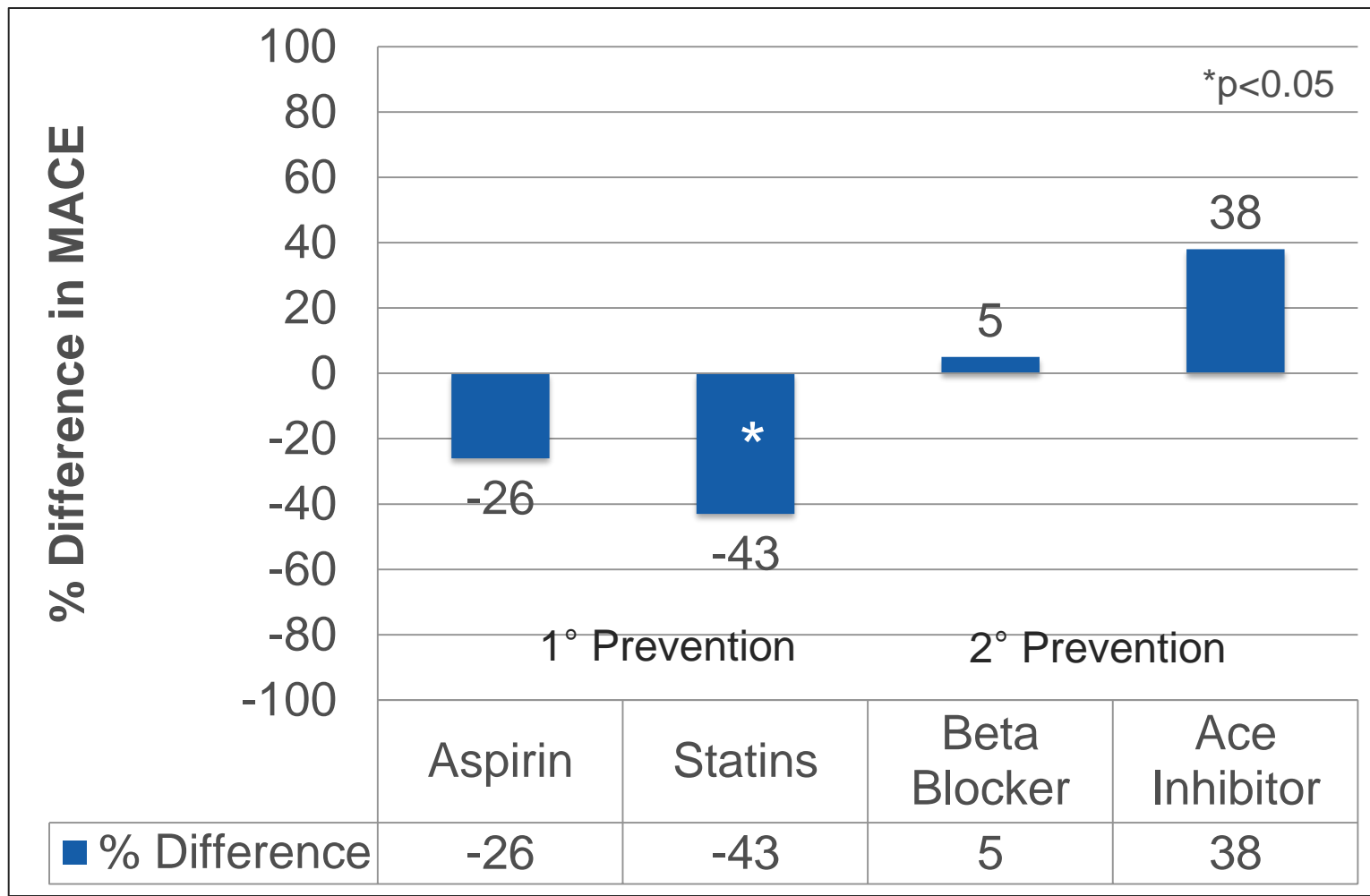


Effective Therapy That Improves Event-Free Survival

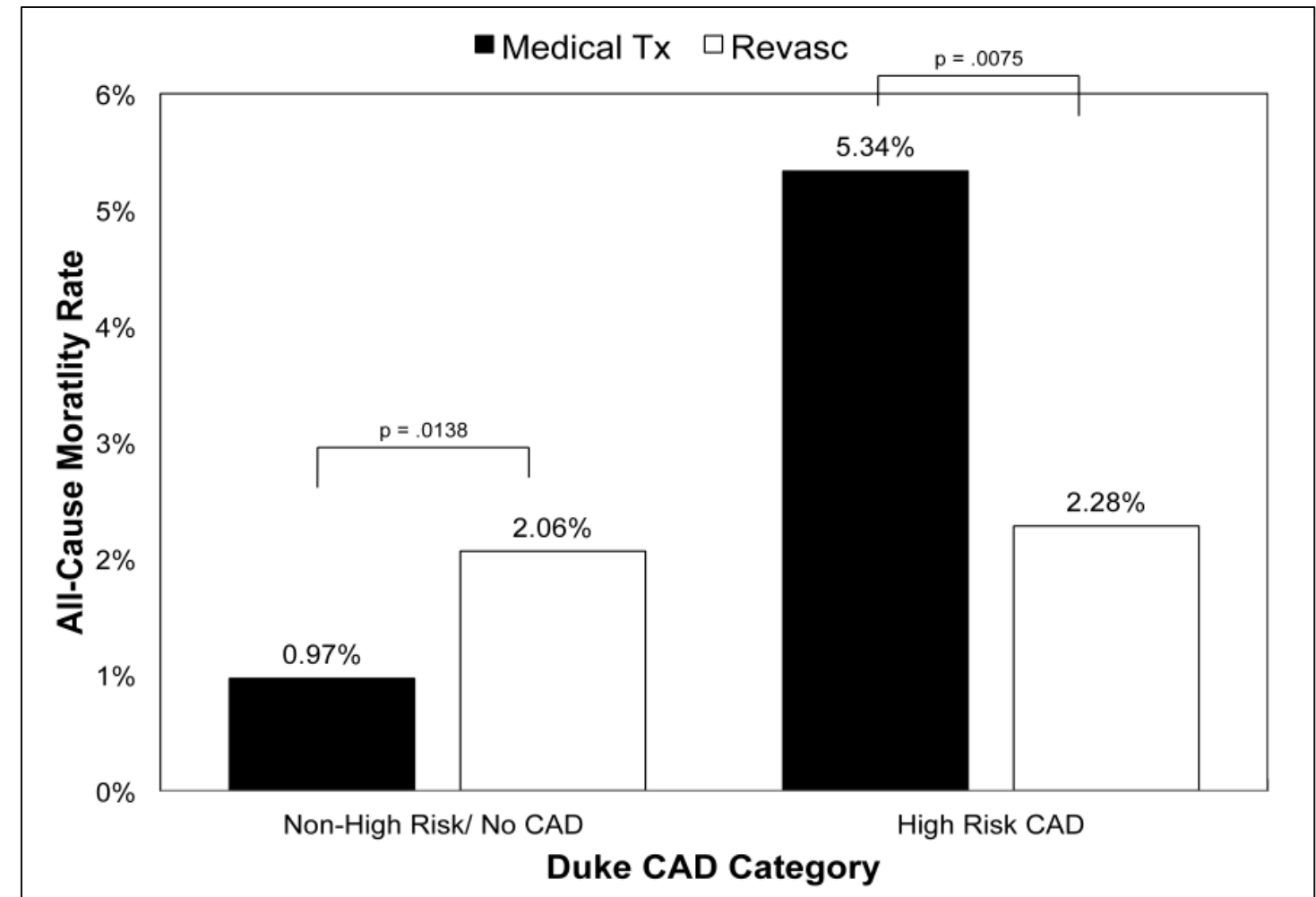
1° vs. 2° Prevention
Med Tx vs Revasc

- N=1,637 patients with >50% stenosis
- Outcome: MACE @ 3 years

- N=15,223 (high risk vs. non-high risk dx)
- Outcome: Mortality @ 2.1 years



Medical Therapy



Coronary Revascularization

NON-INVASIVE FFR FROM CT (FFR_{CT})

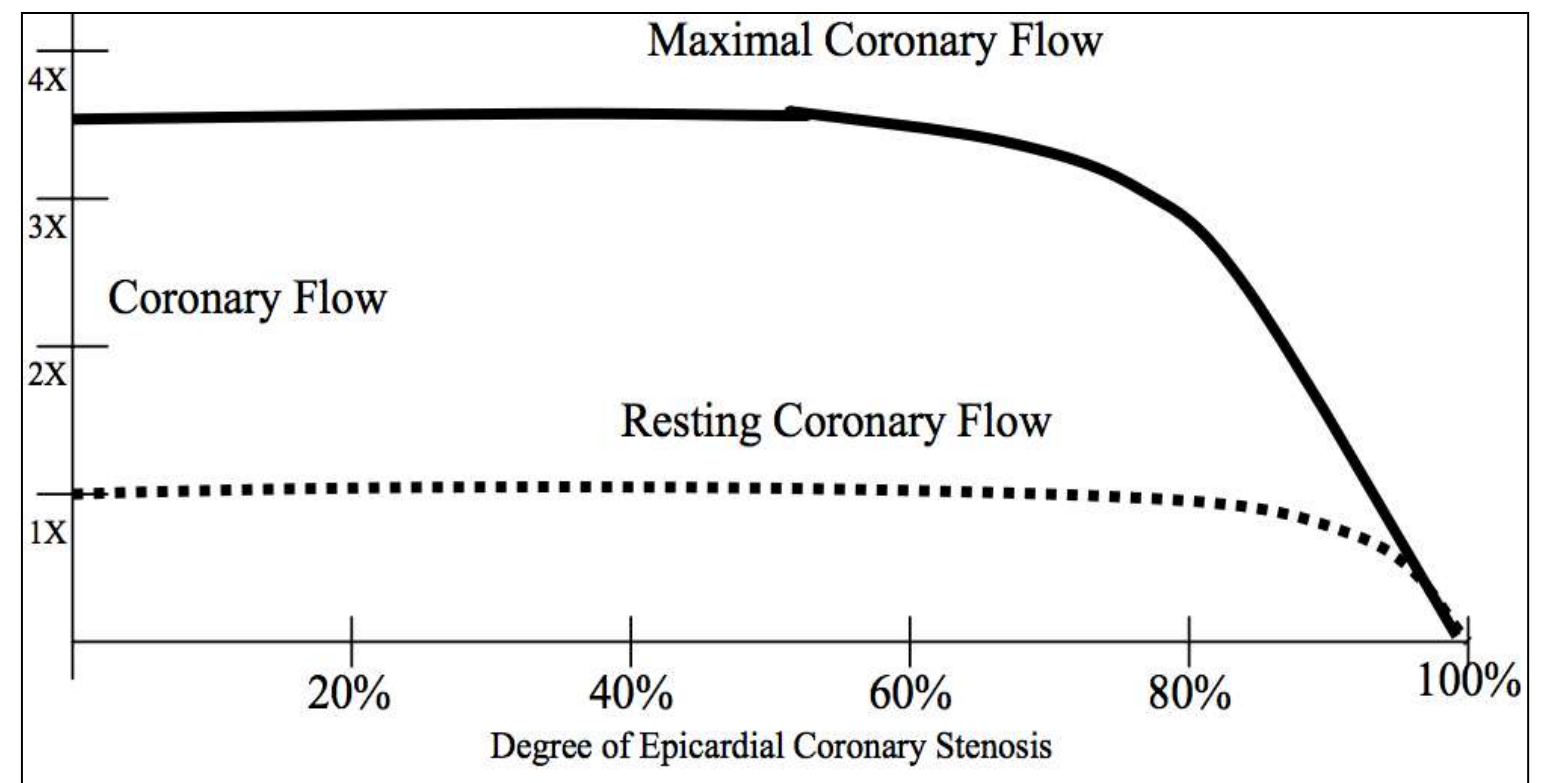
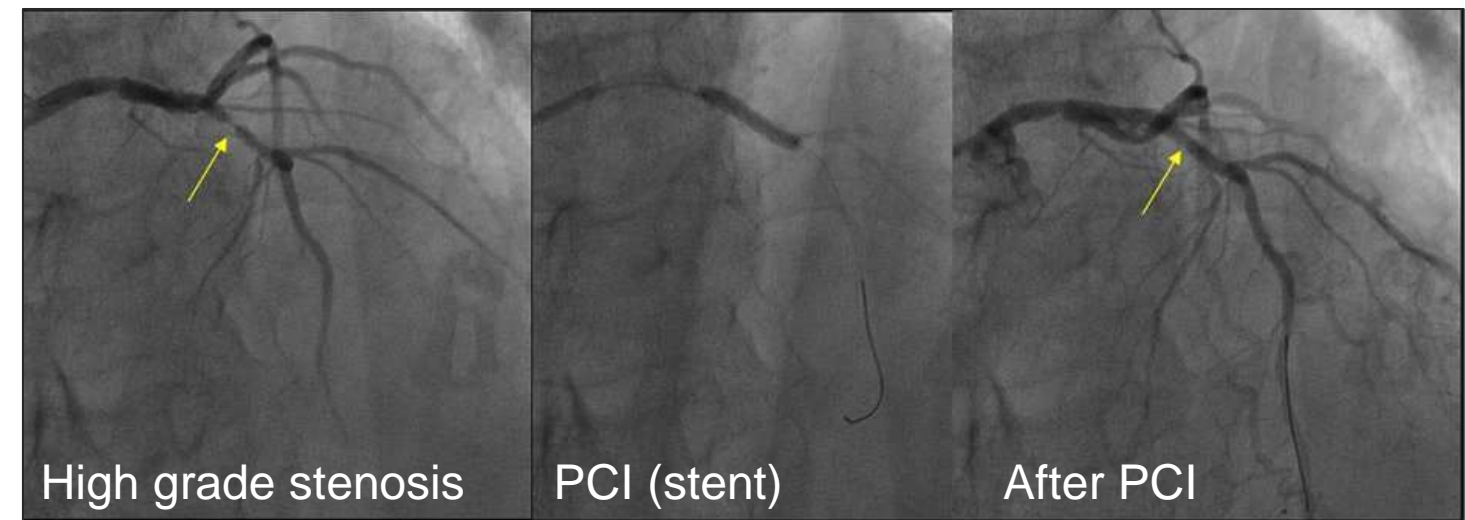
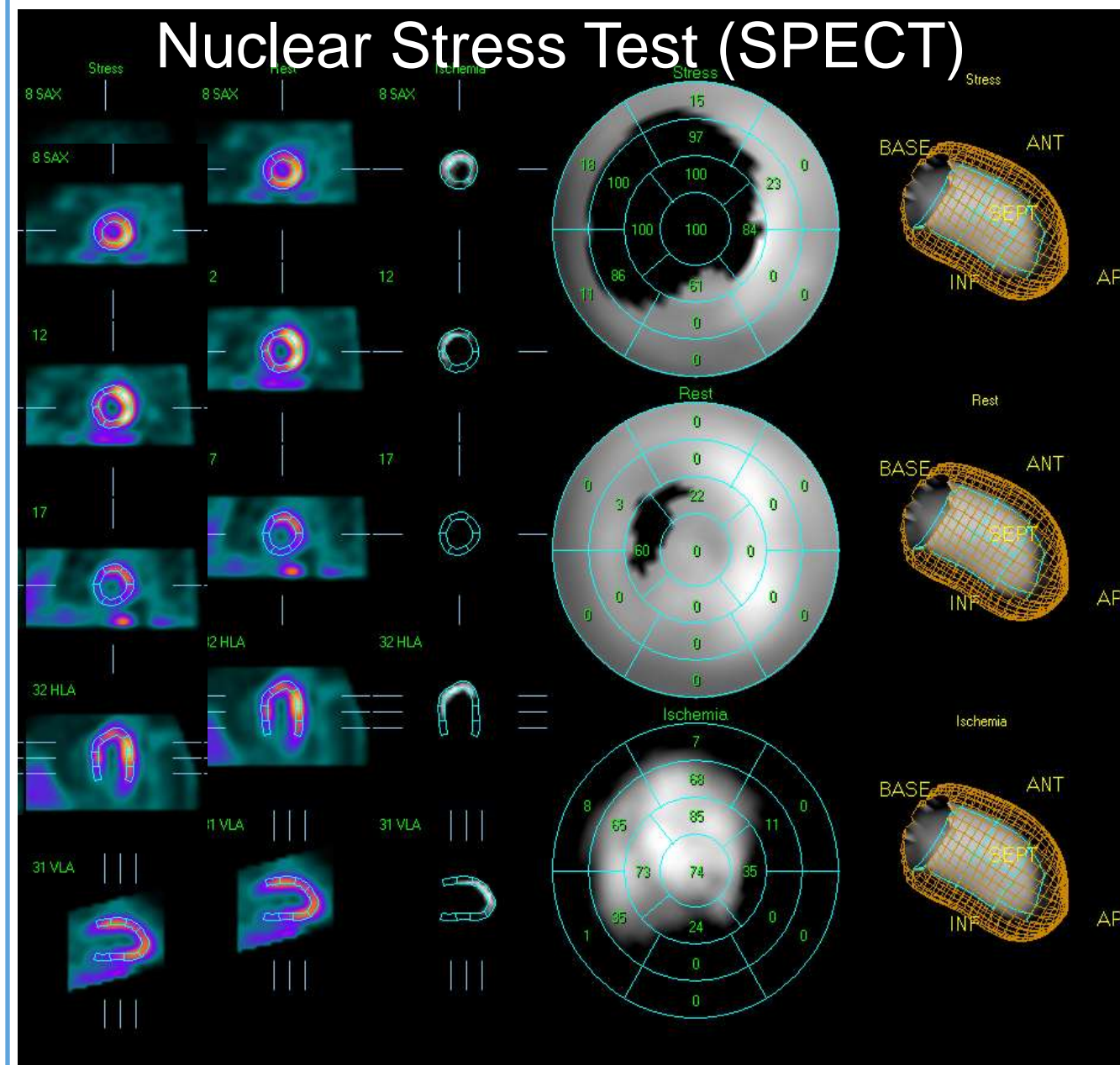
CFD applied to CT:
Solve equations of human
blood flow



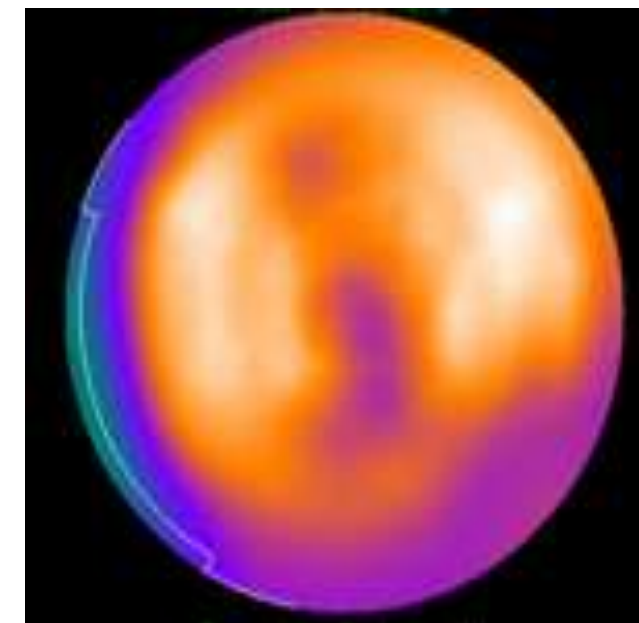
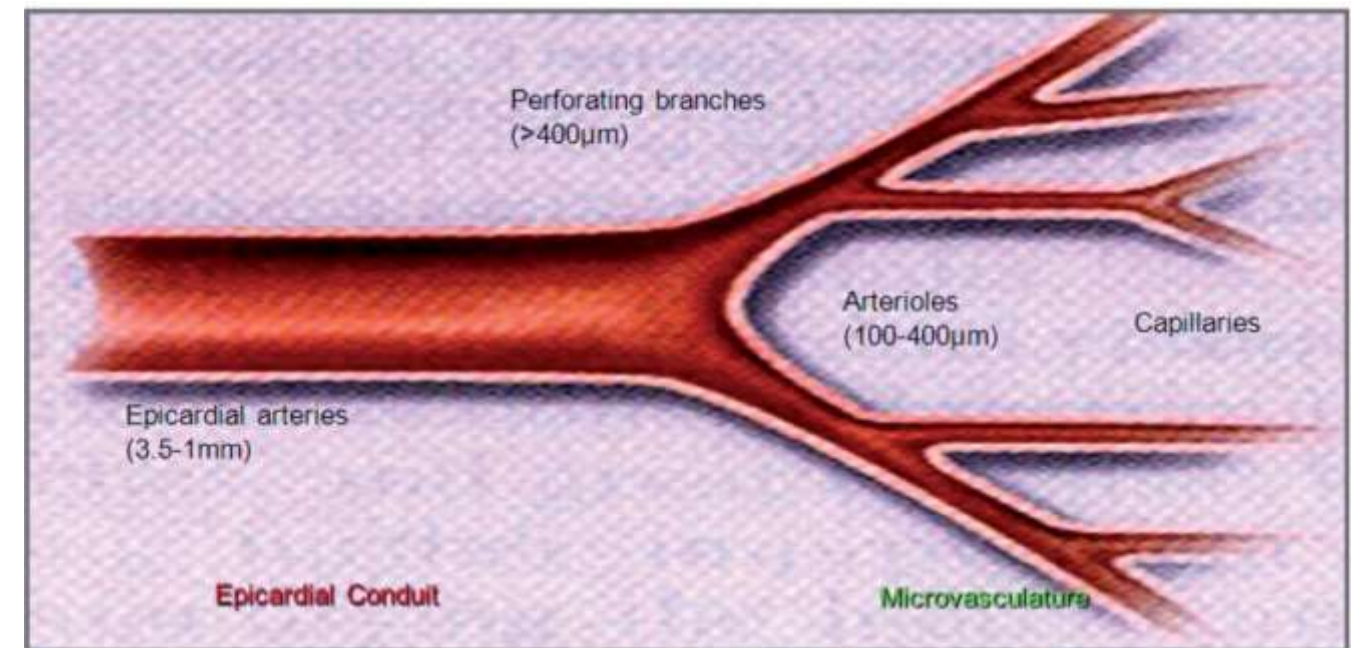
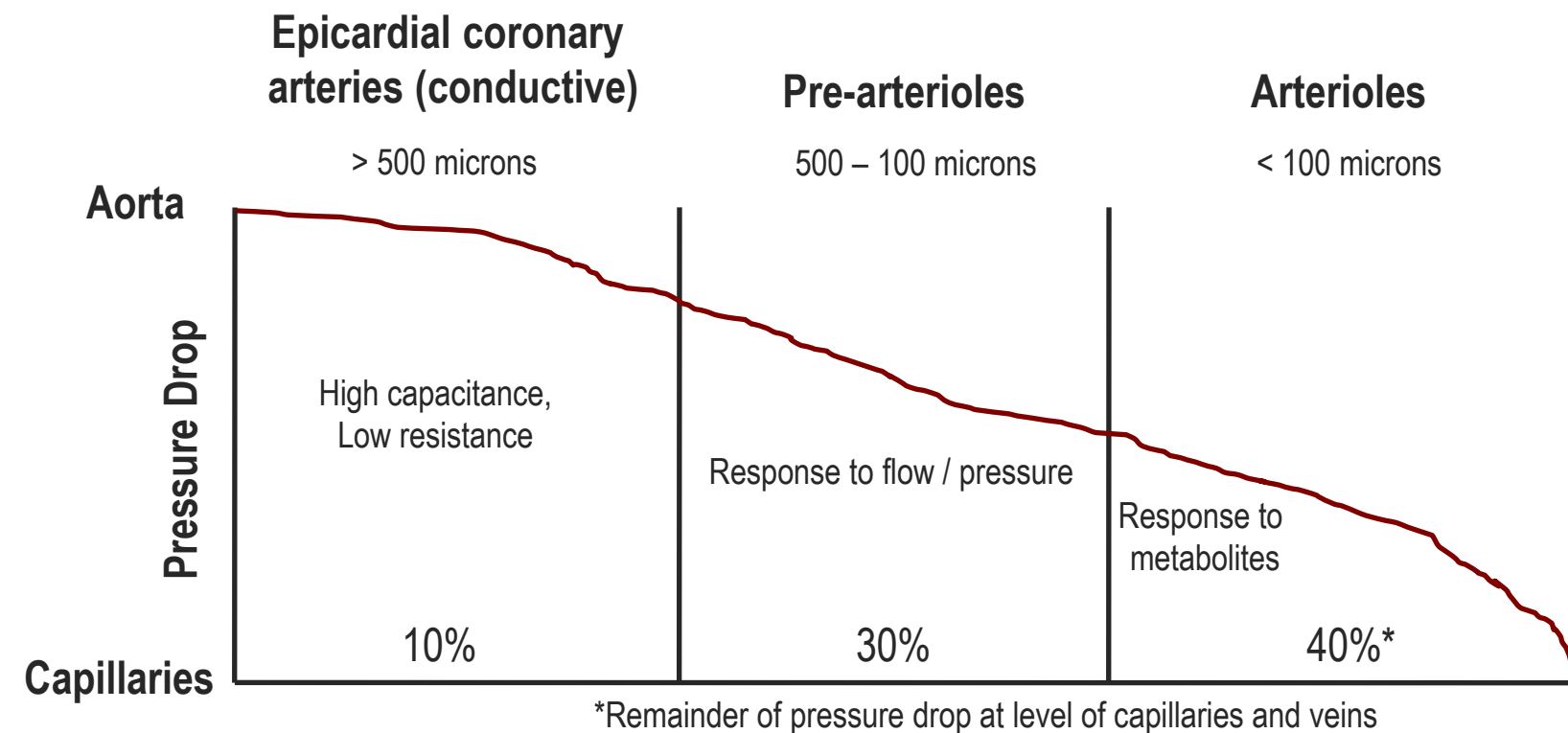
Diagnostic performance of coronary CT angiography

	Sensitivity	Specificity	PPV	NPV
ACCURACY	94	83	48	99
N=230, Stable Chest Pain; No known CAD; No exclusion (CACs, HR, BMI); CAD prevalence 13%				
Europe	99	64	85	97
N=360, Acute and Stable Chest Pain; No known CAD; CAD prevalence 68%				
MEDIC	95	91	71	99
N=415 (83), 20-80% pretest LK of CAD				
CorE64	85	90	91	83
N=291, Stable Chest Pain; No known / Known CAD; Exclusion CACs>600; CAD prevalence 56%				

The problem with the way we do things: ischemia testing

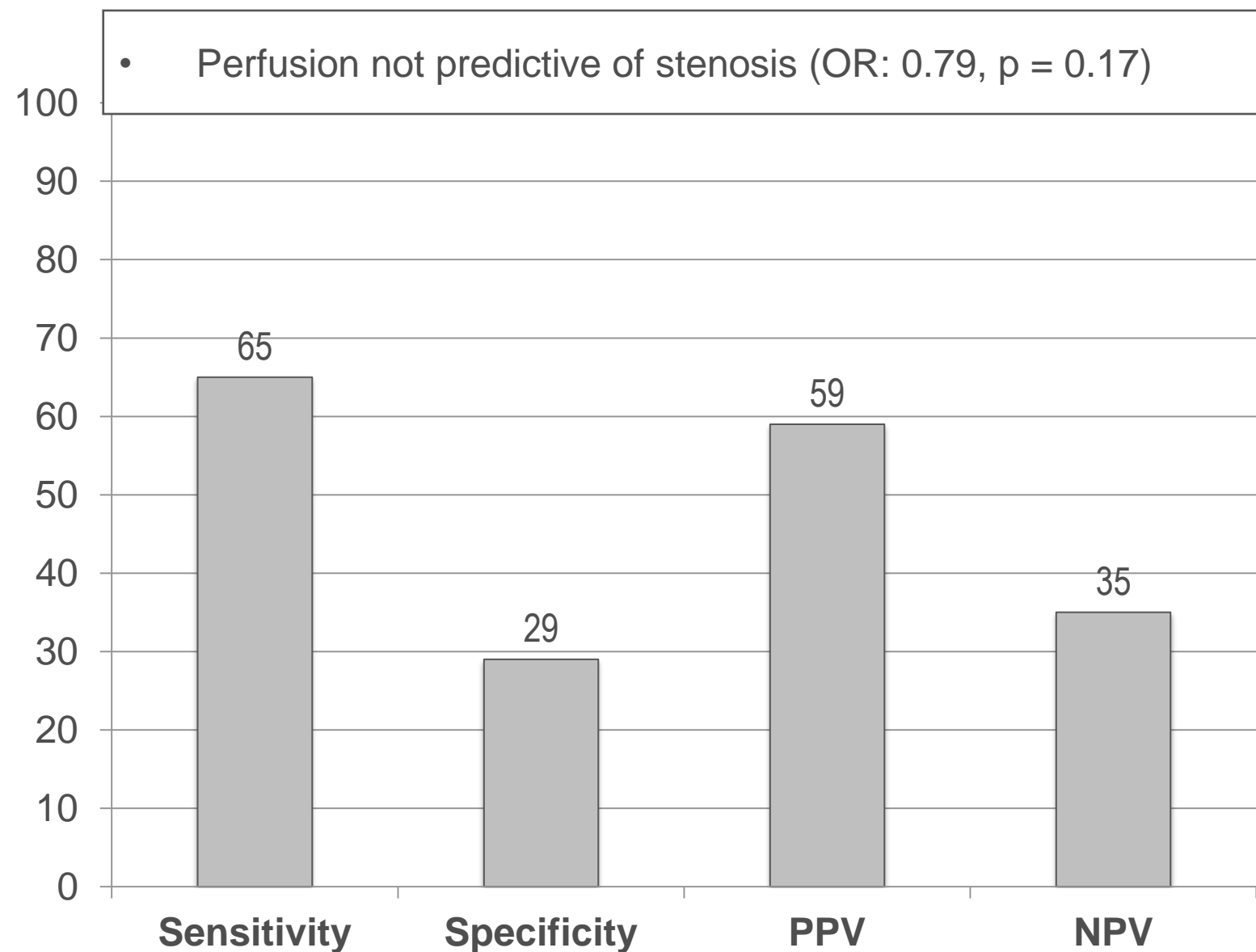


Ischemia evaluation is based upon a physiologically-flawed concept

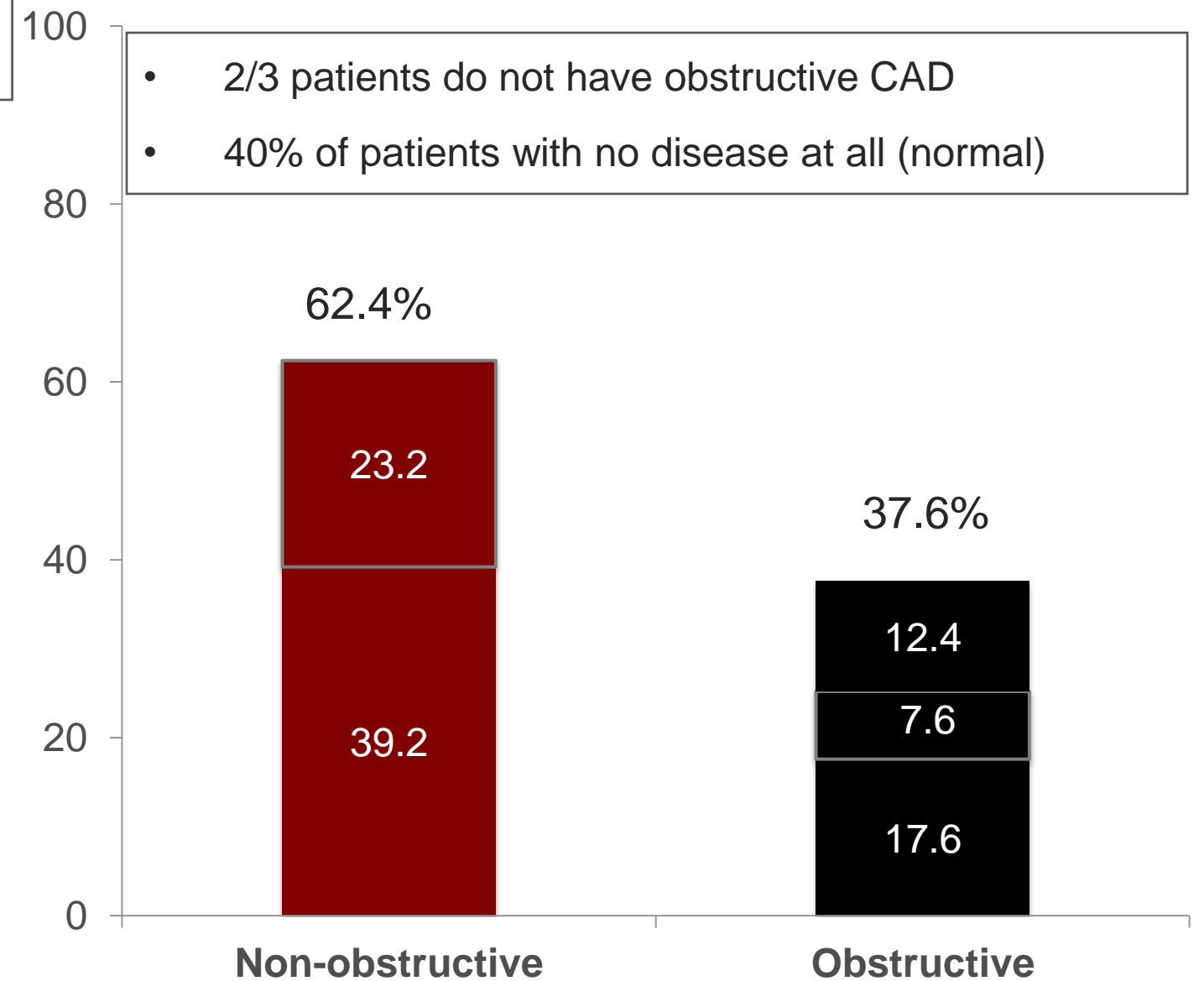


- Perfusion is simply a **surrogate for CAD**
- Epicardial coronary arteries **do not significantly contribute to match myocardial blood supply / demand**

Ischemia testing fails to diagnose CAD

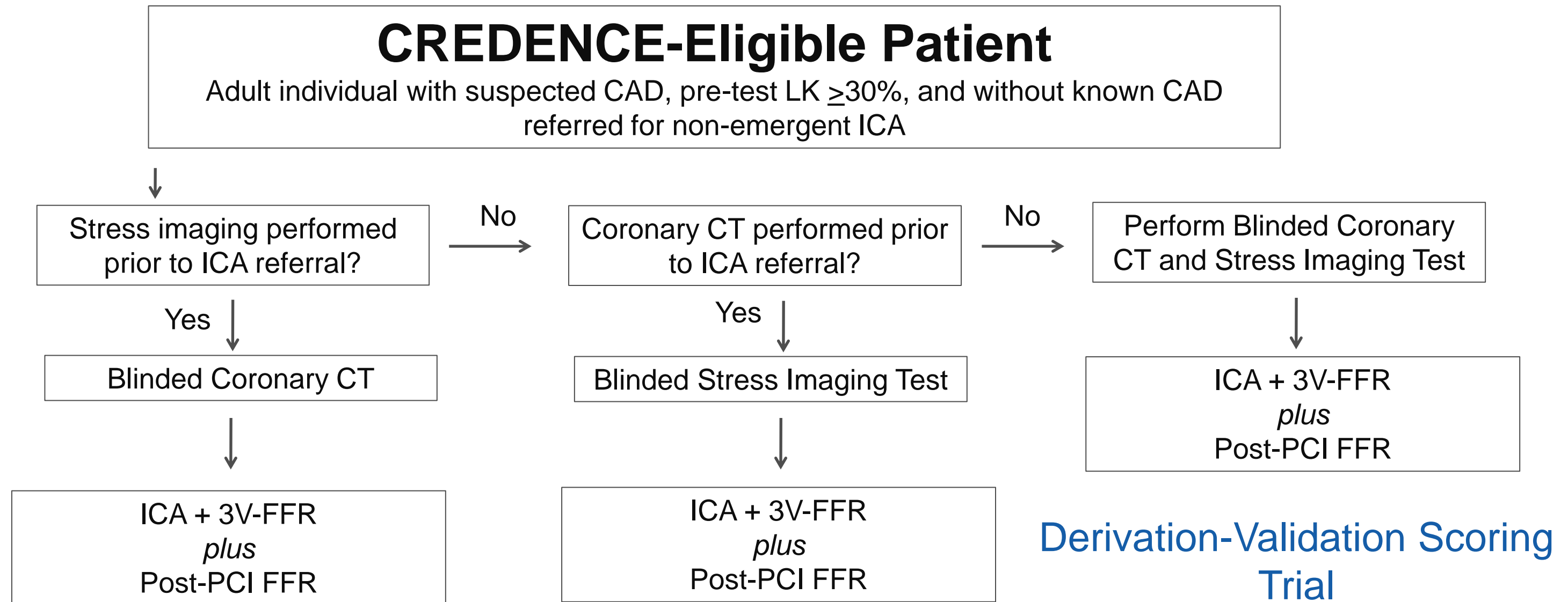


n=6,198 @ 47 centers



n=398,978

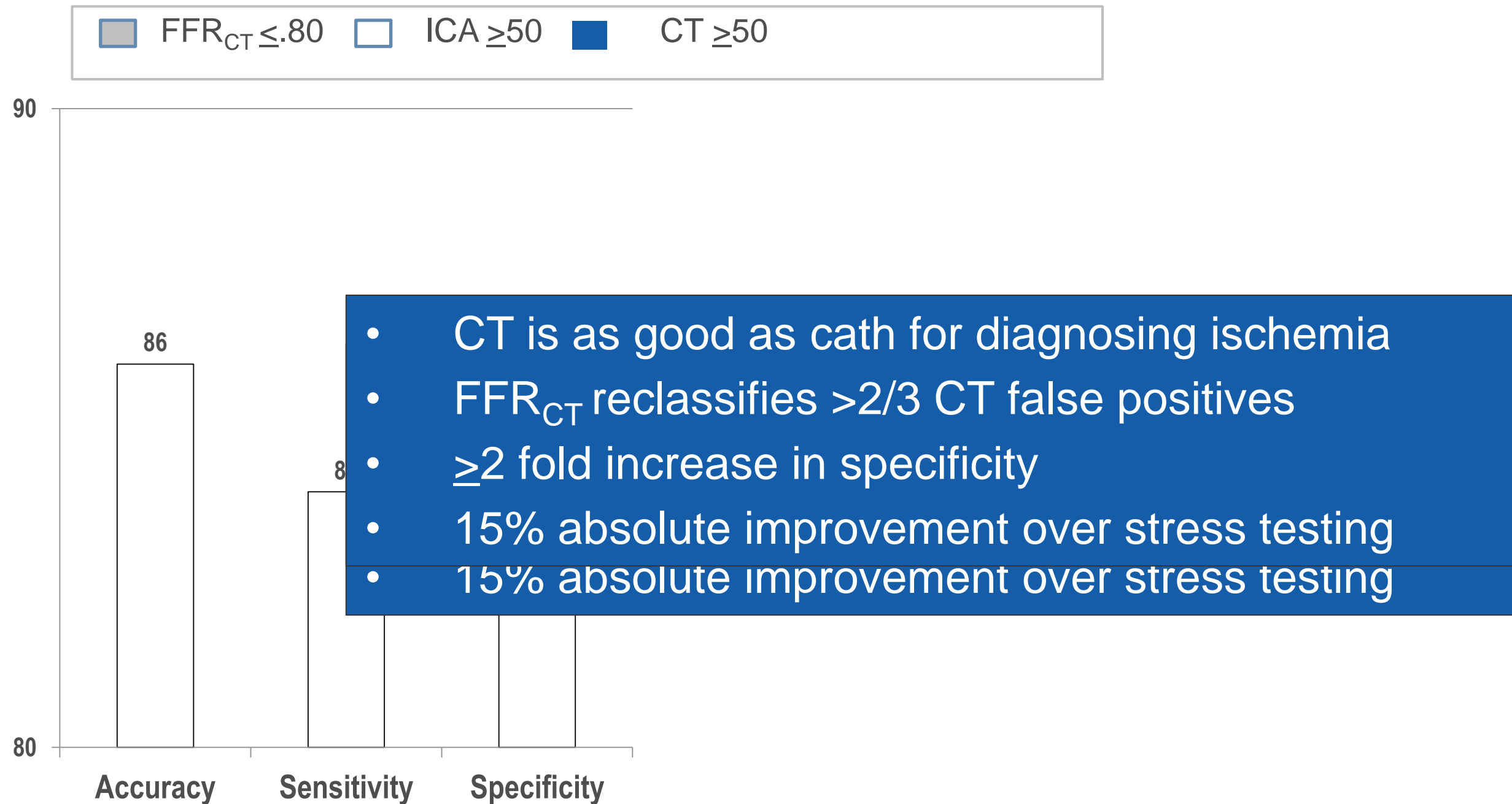
CREDENCE, A Head-to-Head Comparison of CT/FFR_{CT} vs. Myocardial Perfusion Imaging



Primary Endpoint: Diagnostic Accuracy of Stenosis-FFR_{CT} vs. Myocardial Perfusion Imaging

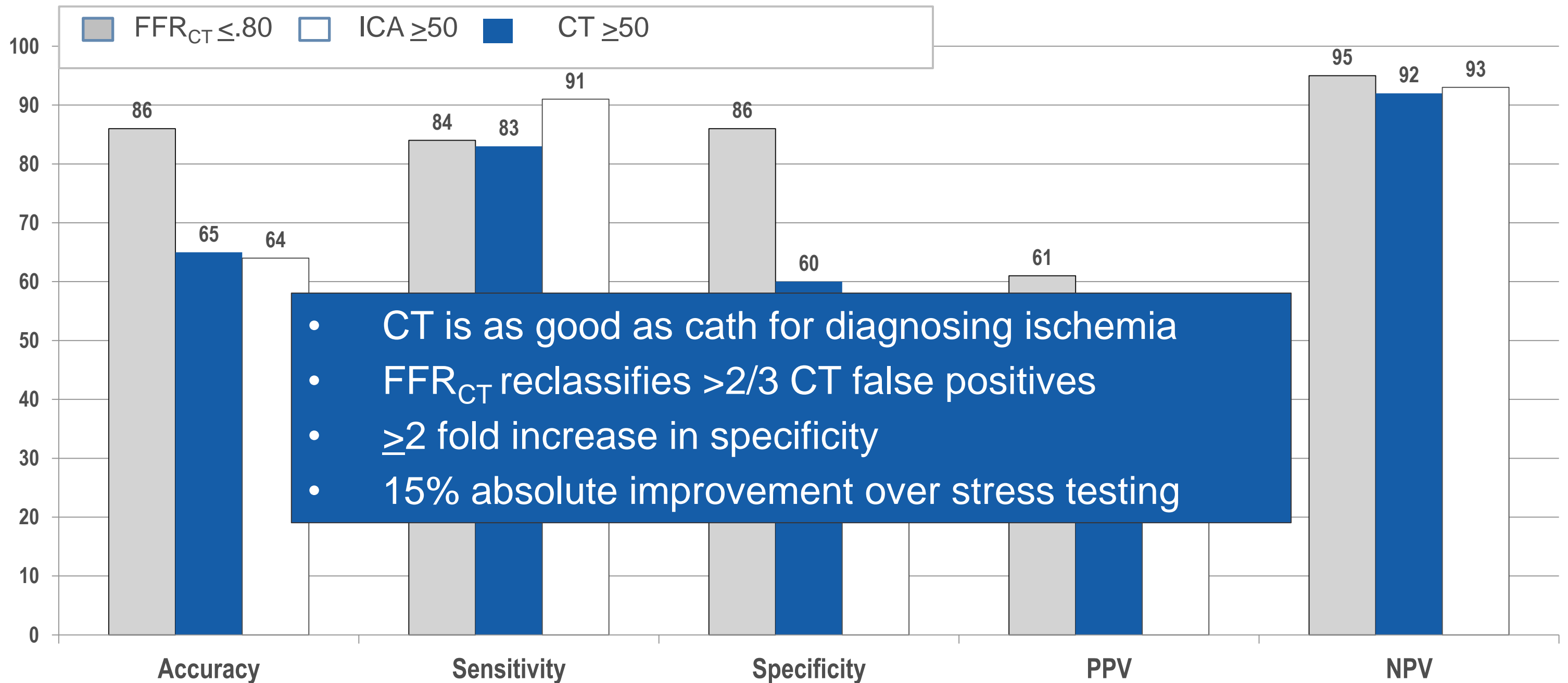
NXT: FFR_{CT} accuracy (per-vessel)

FFR_{CT} superior to both CT and cath



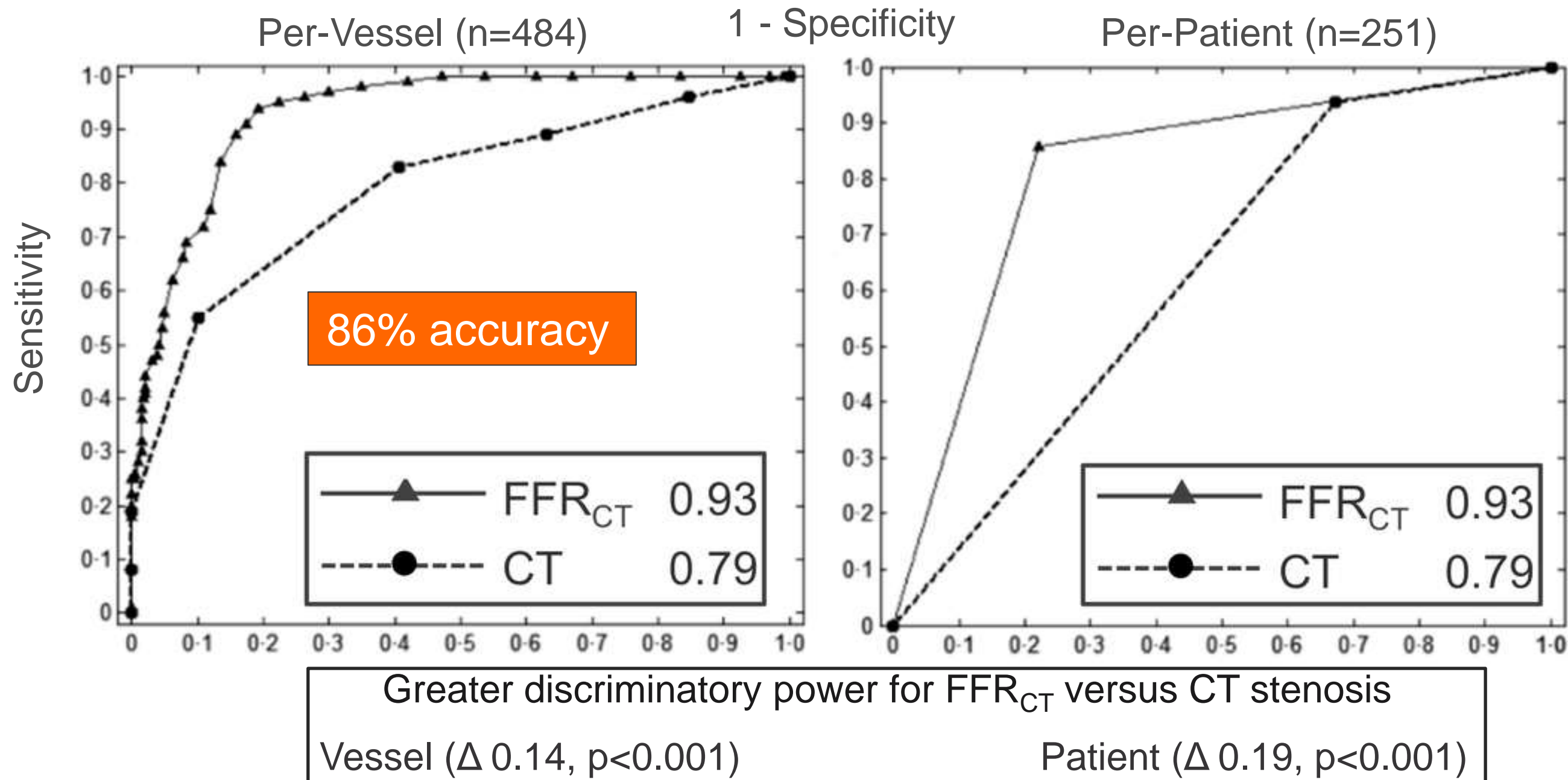
NXT: FFR_{CT} accuracy (per-vessel)

FFR_{CT} superior to both CT and cath



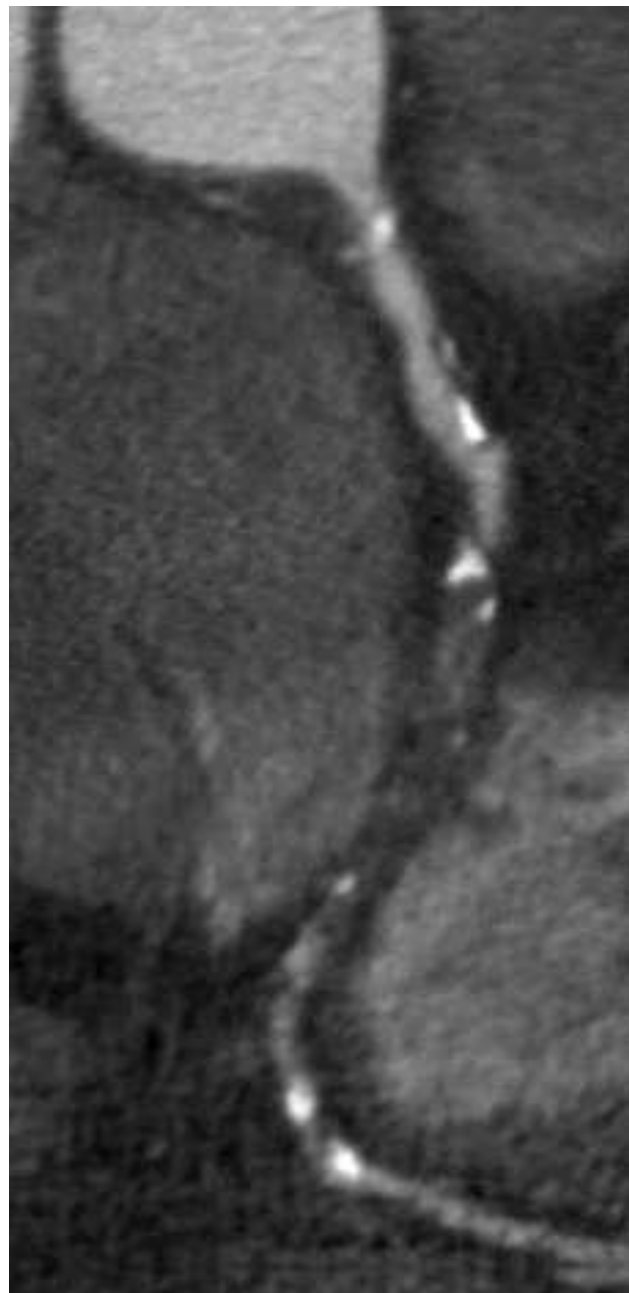
NXT: Discrimination of ischemia

Prospective multicenter
N=251 (n=484 vessels)
Comparator: Invasive FFR



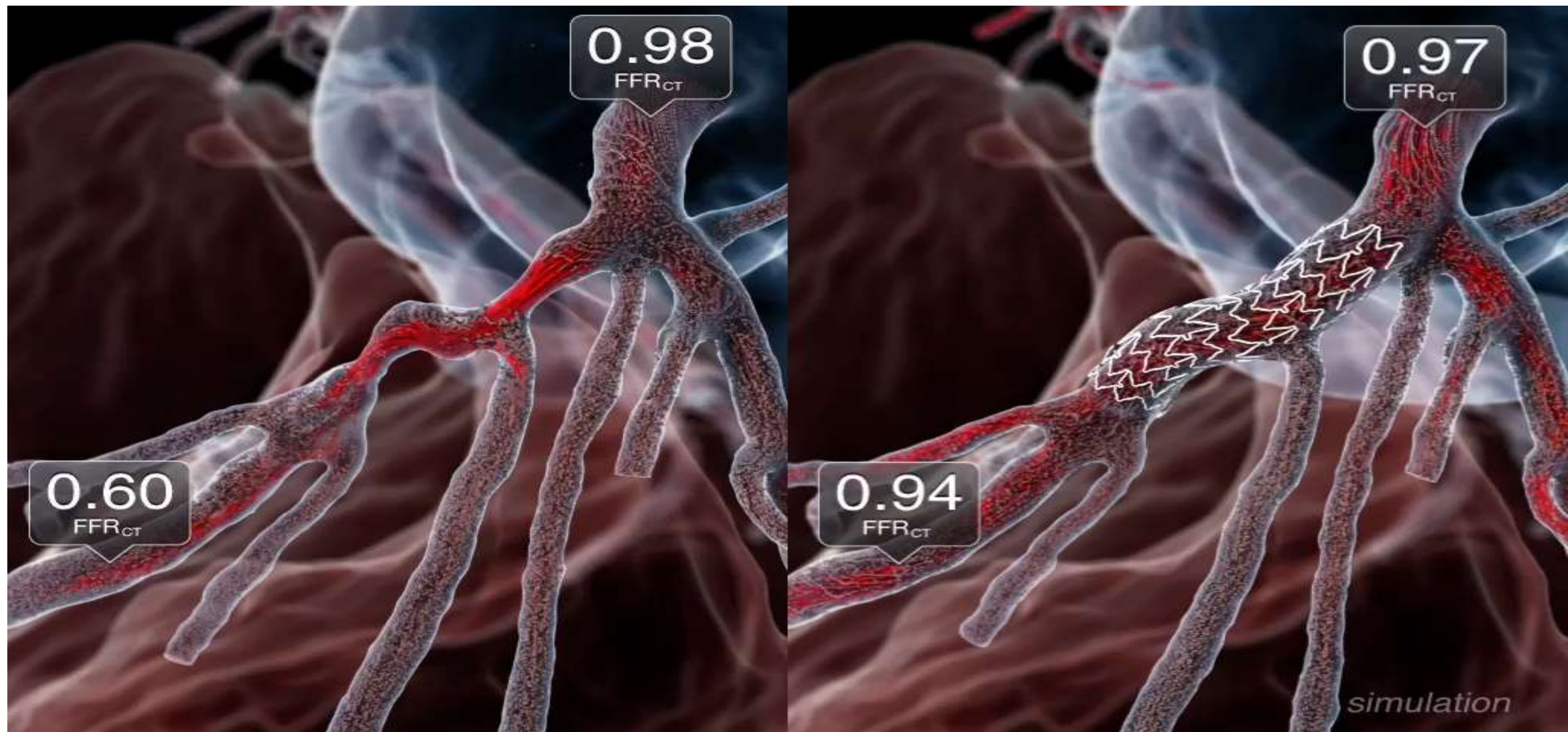
Case: 62 y/o Caucasian man

(Performed @ Cornell / NewYork-Presbyterian 4/15/15)



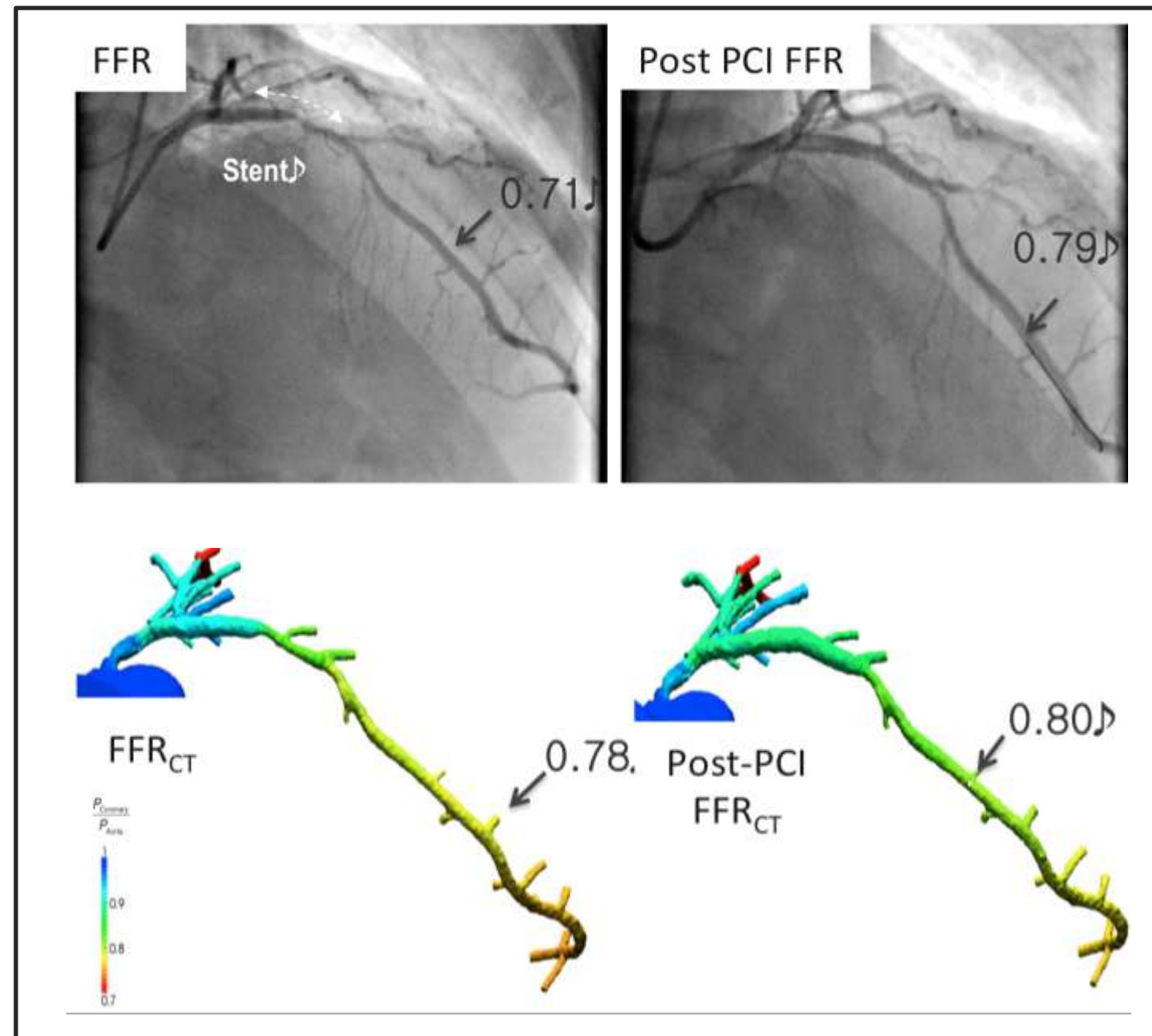
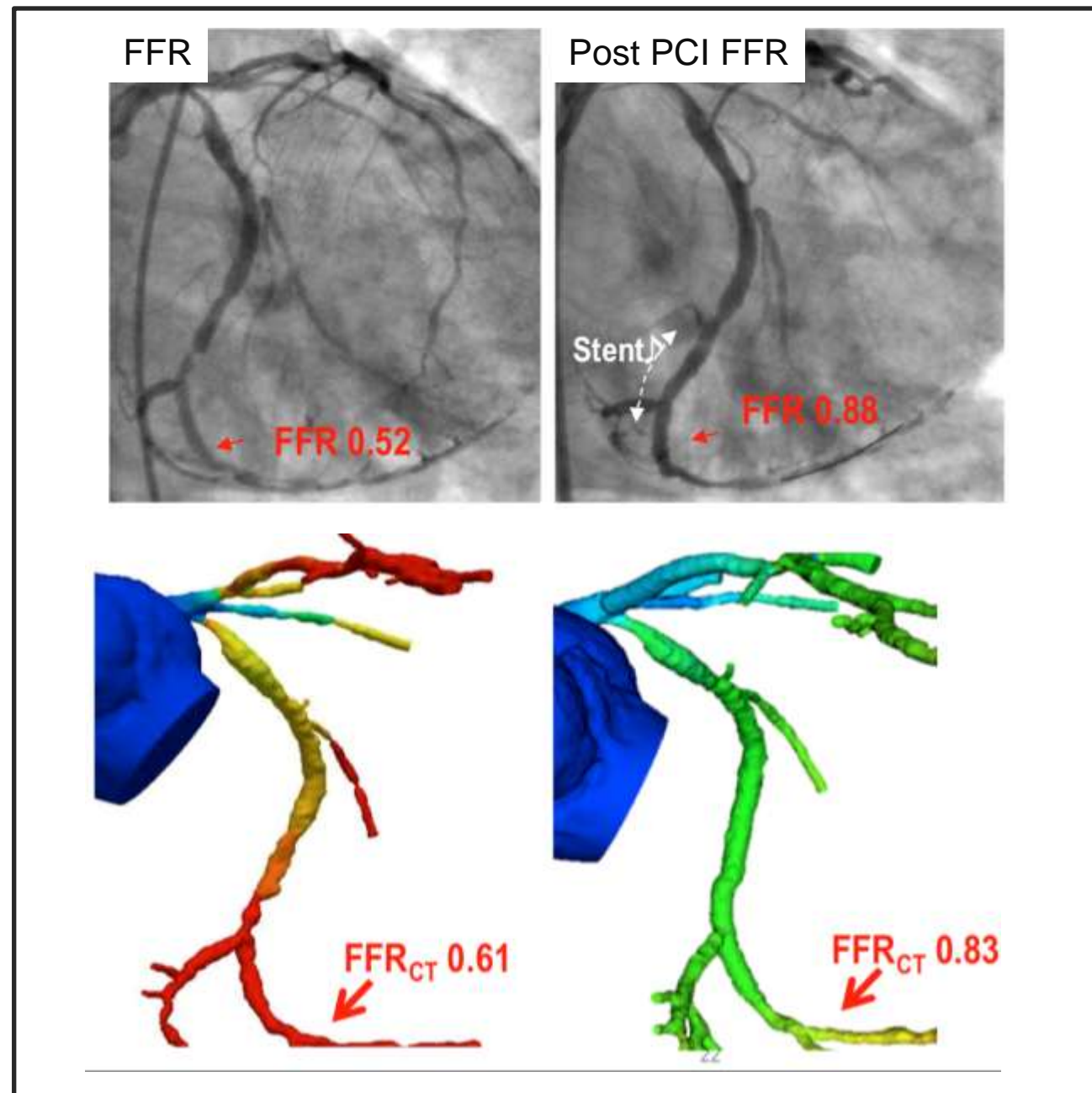
- Unfavorable anatomic plaque features
- Long occlusion (>20 mm)
- Calcified entry
- High-grade stenoses distal to CTO

Future of FFR_{CT} : Virtual Stenting

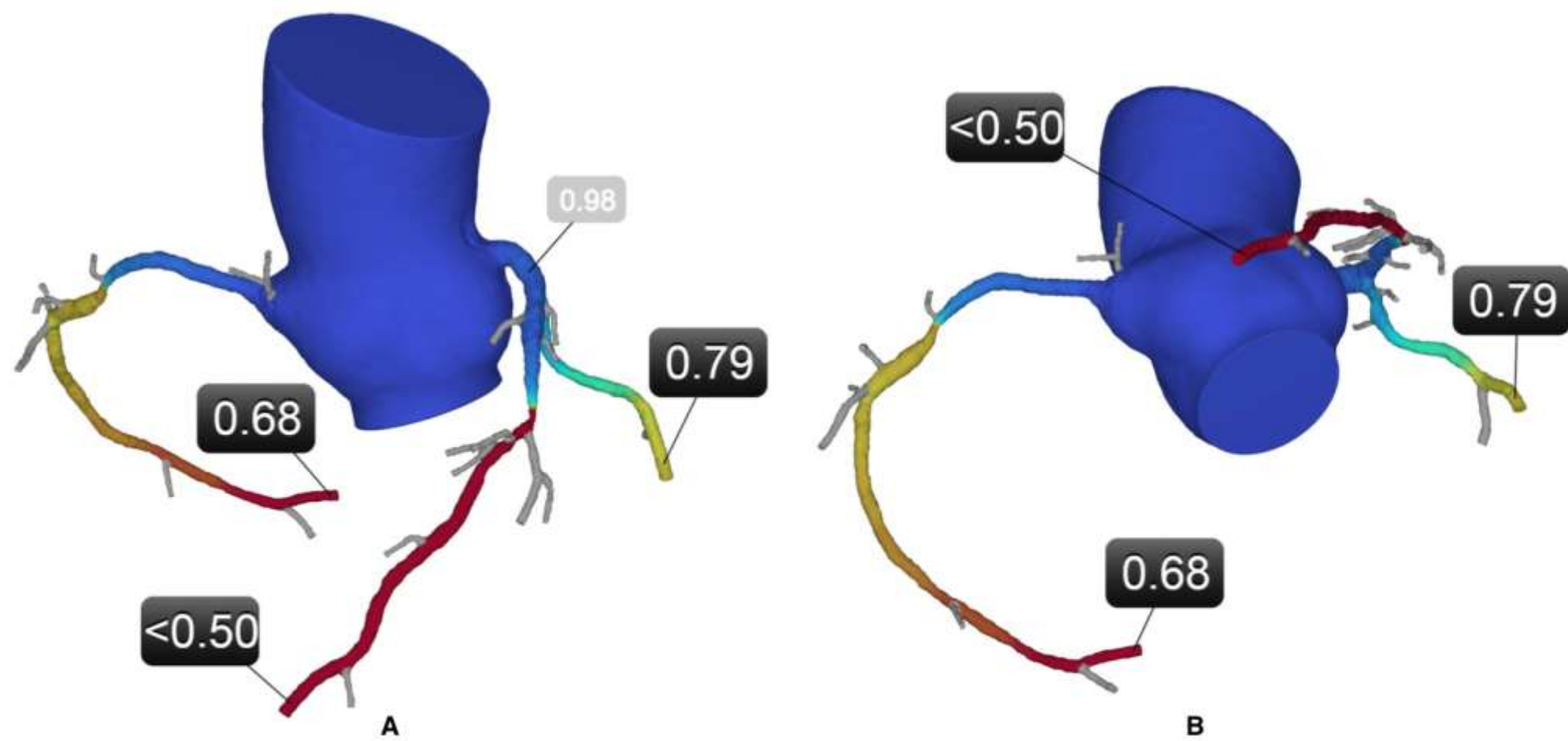


Future of FFR_{CT} : Virtual Stenting

44 patients
Accuracy 96%
Sens / Spec 100% / 96%



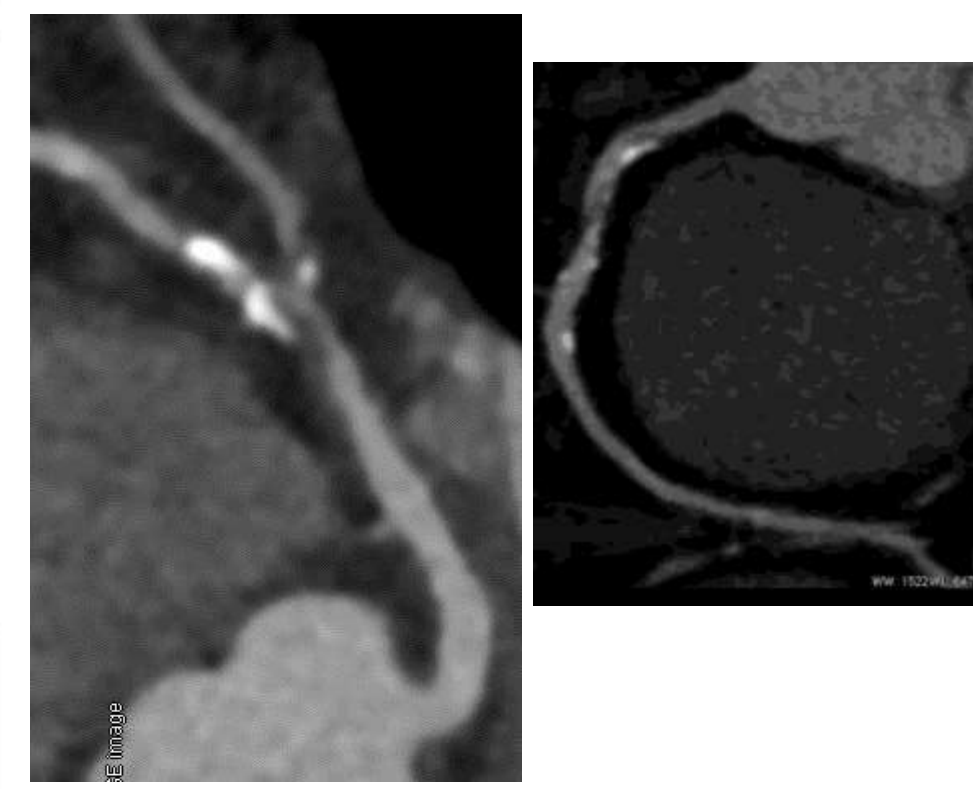
Case: 63 y/o Asian man (HeartFlow FFR_{CT} Analysis)



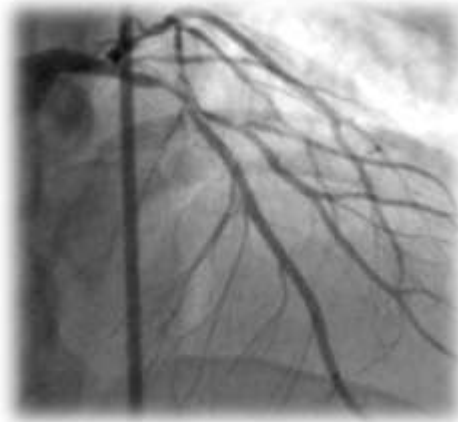
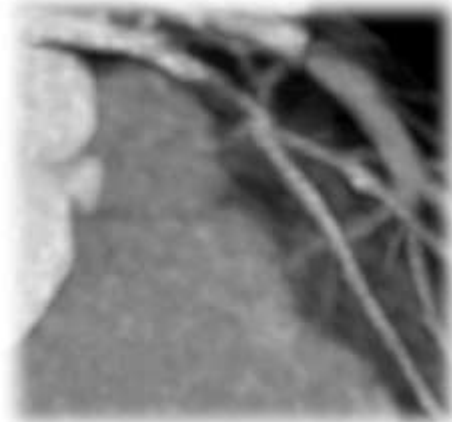
Summary: The Left Anterior Descending System, Left Circumflex System, and Right Coronary Artery System each have an FFR_{CT} ≤ 0.80.

CORONARY ARTERIES & SYSTEMS	FFR _{CT}	FFR _{CT} (0.00 to 1.00)
Left Main Artery	0.98	[Blue bar]
Left Anterior Descending System	< 0.50	[Red bar]
Left Circumflex System	0.79	[Yellow bar]
Right Coronary Artery System	0.68	[Red bar]

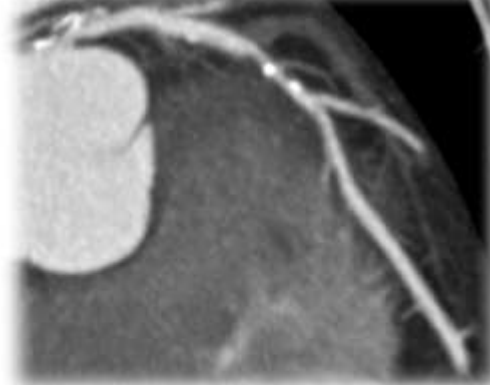
MAY BE FUNCTIONALLY SIGNIFICANT ^{1,2,3}



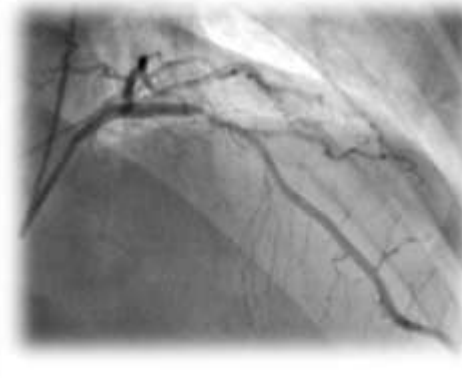
Optimal Diagnostic Approach to Symptomatic CAD



(1) Anatomic CAD Concordant with ICA

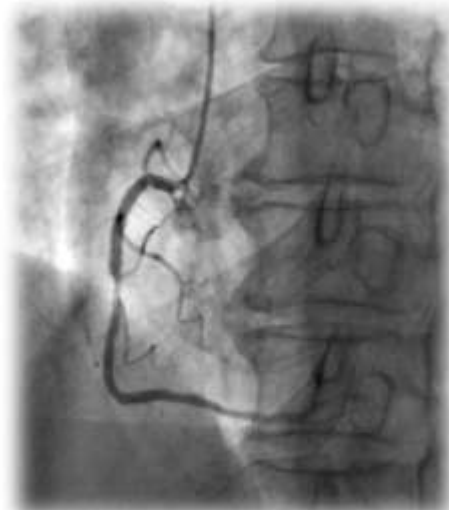
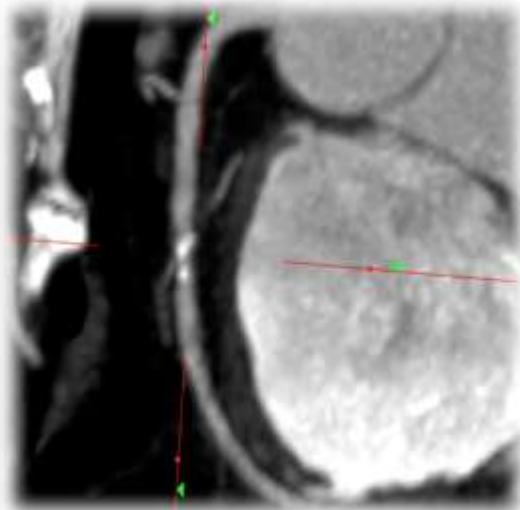


CCTA 50-69% stenosis

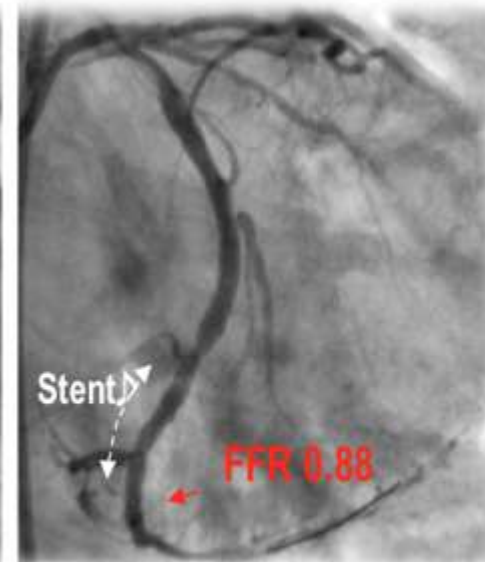
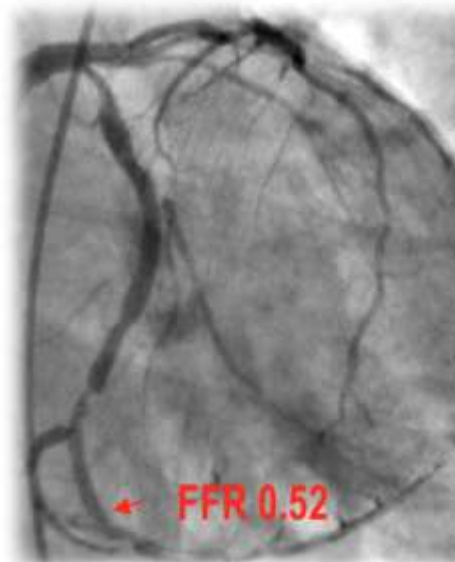


QCA %DS = 50.68%

(2) Effectively Prognosticate Outcomes



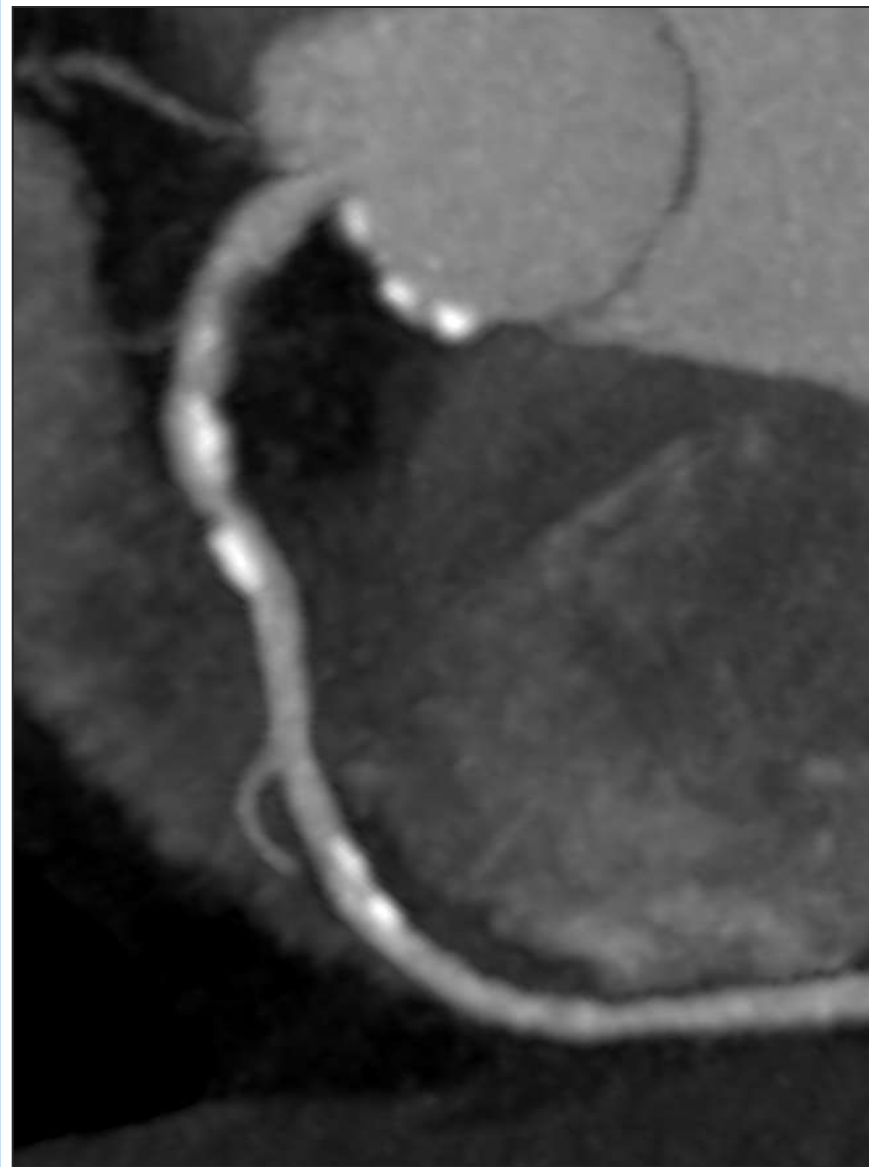
(3) Identify Lesion-Specific Ischemia



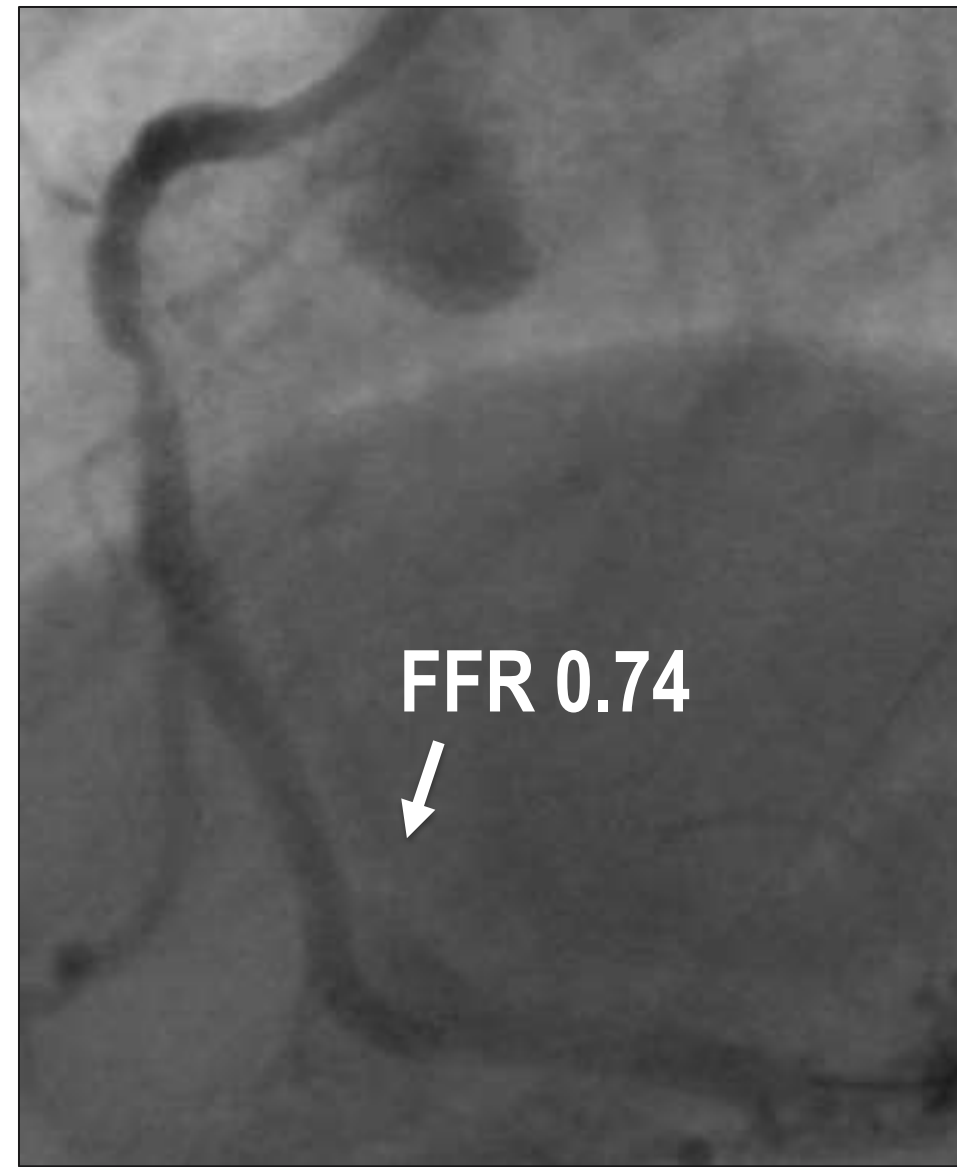
(4) Plan Revascularization Strategy

- From typically acquired CCTA
- No additional radiation
- No modification to imaging protocols
- No administration of medications

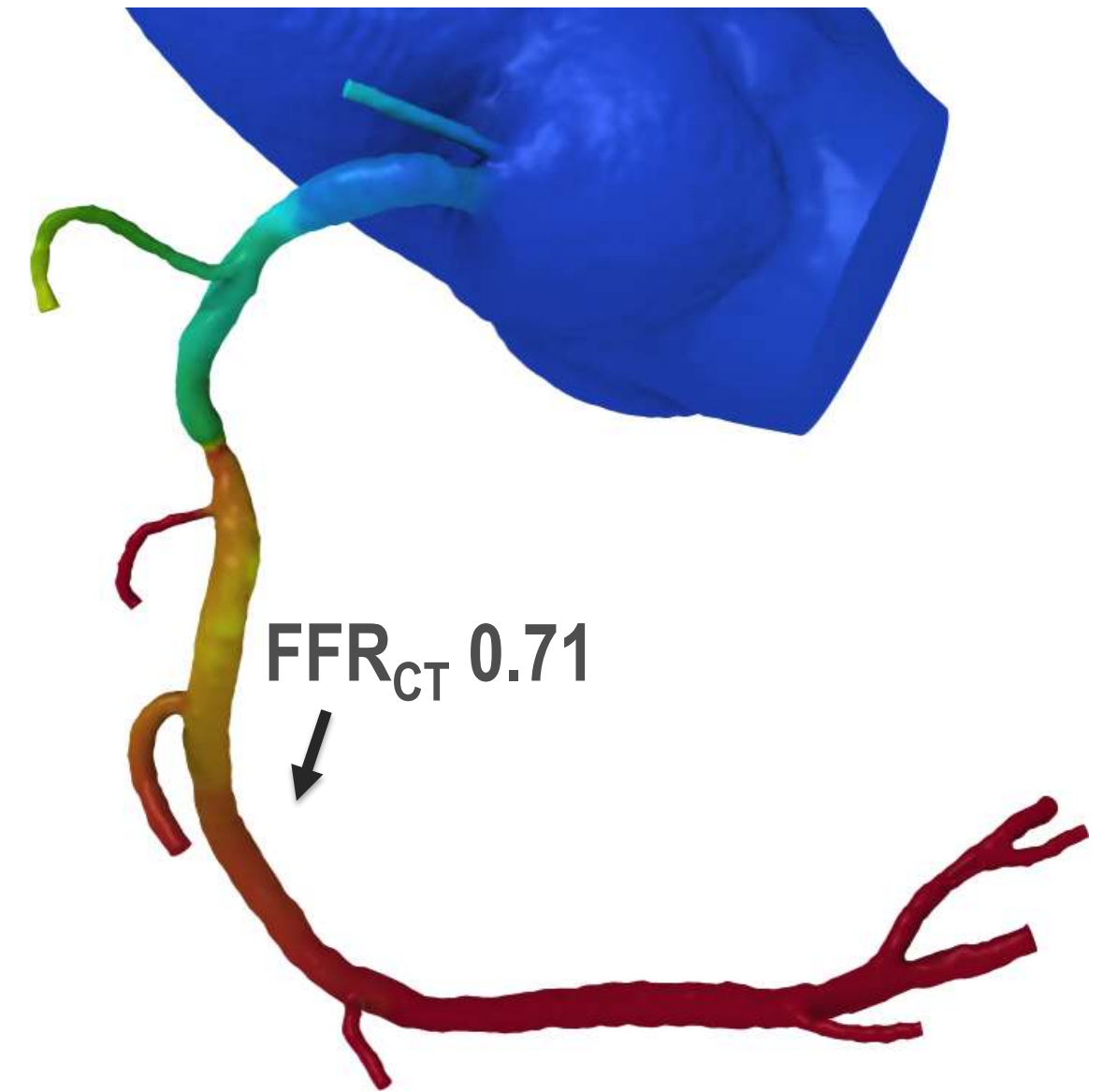
FFR_{CT}: Intermediate Stenoses



CT: Mild-Moderate Stenosis



FFR_{CT}: No Ischemia



FFR: No Ischemia