JCR 2011 12.9 13:15-13:30

Non-invasive Assessment of Fractional Flow Reserve

: *A Dream Come True?*

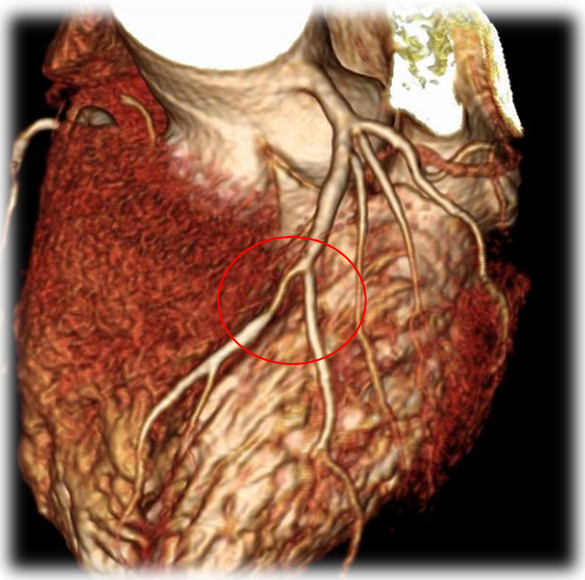
Bon-Kwon Koo, MD, PhD

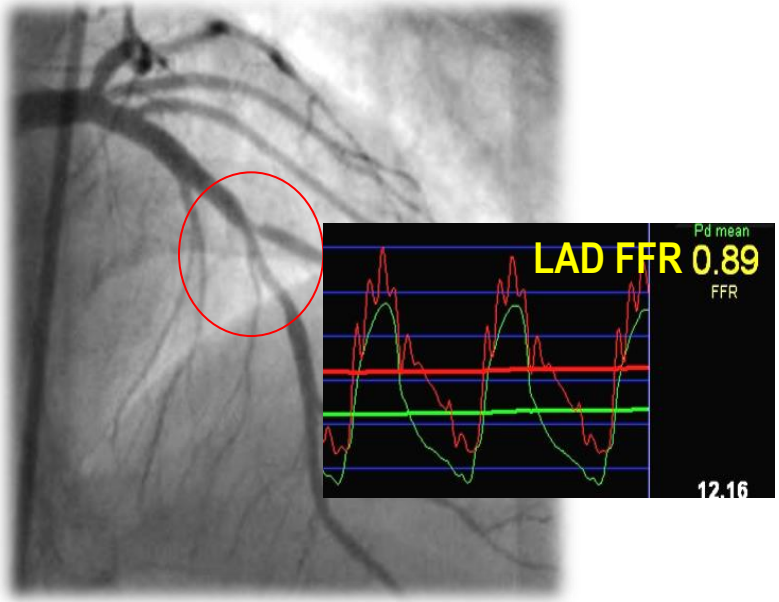
Seoul National University Hospital, Seoul, Korea

Evaluation of CAD: *Anatomy vs. Function*

- Coronary CT angiography (CCTA) provides accurate 3D anatomical information. However, CCTA does not reliably predict functional significance of a lesion.

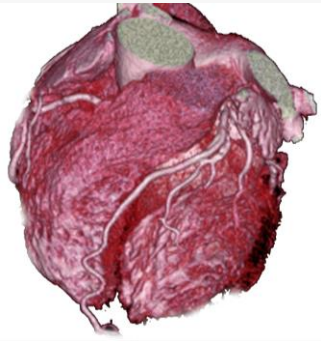
- Fractional flow reserve (FFR) is the gold standard for diagnosis of a lesion that causes myocardial ischemia. However, FFR requires invasive procedures.

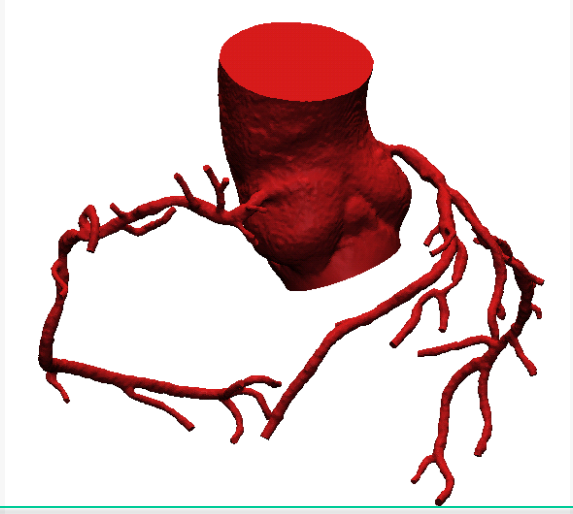




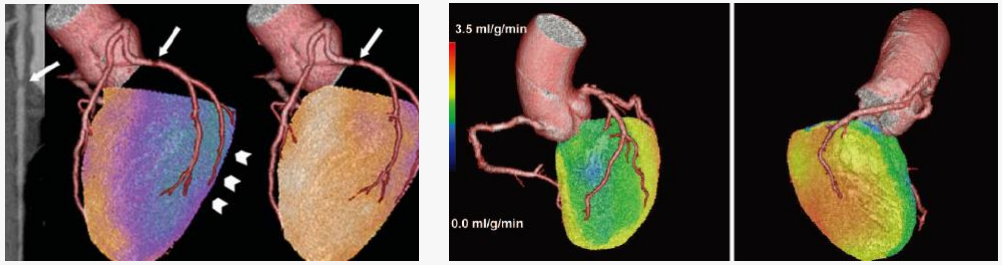
Non-invasive FFR (functional assessment of CAD)

3-D Model based on CCTA

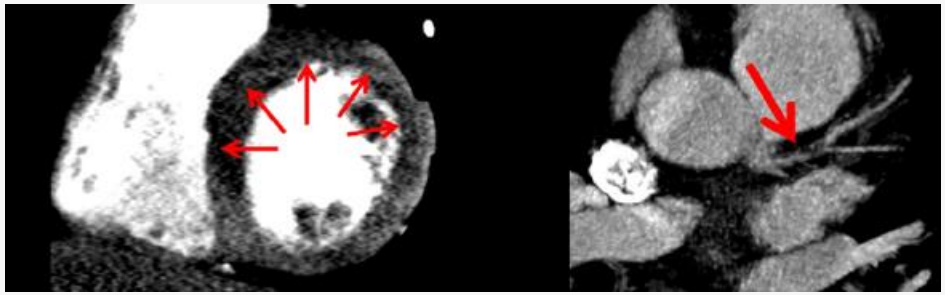




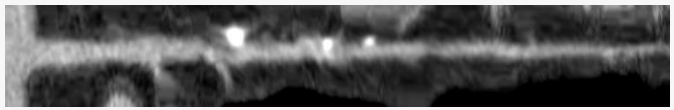
Hybrid imaging: CCTA + SPECT/PET



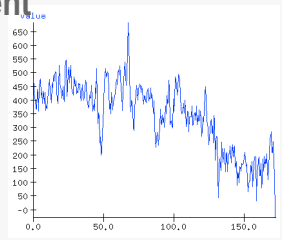
Stress CT perfusion imaging



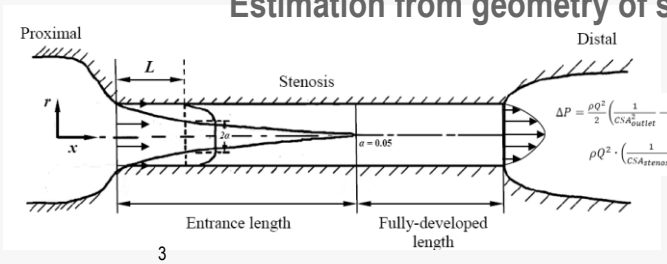
Transluminal attenuation gradient



TAG = -15.42 (HU/10mm)



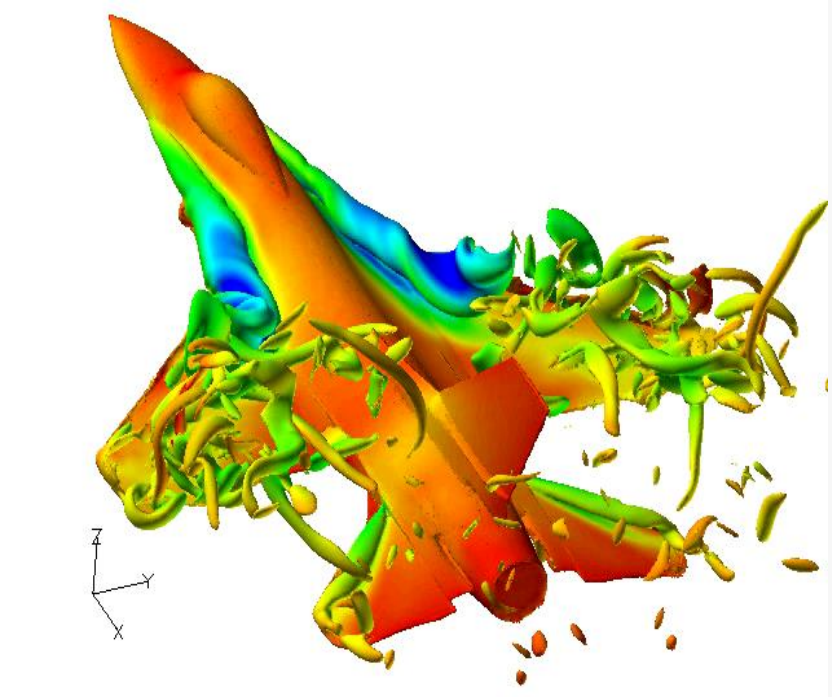
Estimation from geometry of stenosis



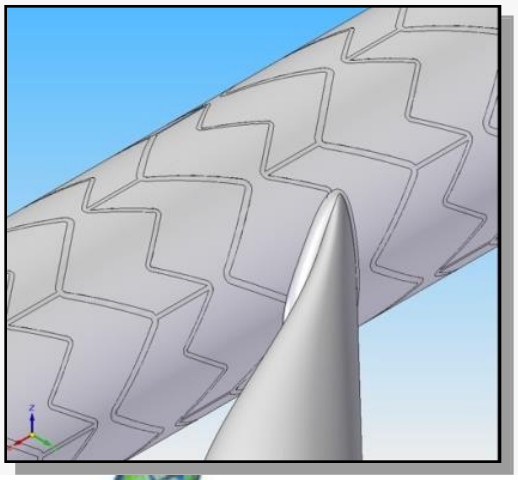
$$\Delta P = \frac{\rho Q^2}{2}\left(\frac{1}{CSA_{outlet}^2} - \frac{1}{CSA_{inlet}^2}\right) + \frac{\rho Q^2}{2 \cdot CSA_{stenosis}^2}\frac{96}{5}\int_{0.05}^{1}\frac{(1+4\alpha+9\alpha^2+4\alpha^3)}{\alpha(3+2\alpha)(3+2\alpha+\alpha^2)^2}d\alpha + \int_0^{L_{vessel}-L_{entrance}}\frac{8\pi\mu}{CSA^2}Q dx + \rho Q^2 \cdot \left(\frac{1}{CSA_{stenosis}} - \frac{1}{CSA_{distal}}\right)\cdot\left(\frac{1}{CSA_{stenosis}} - \frac{1}{3}\cdot\frac{1}{CSA_{distal}}\right) \quad [A12]$$

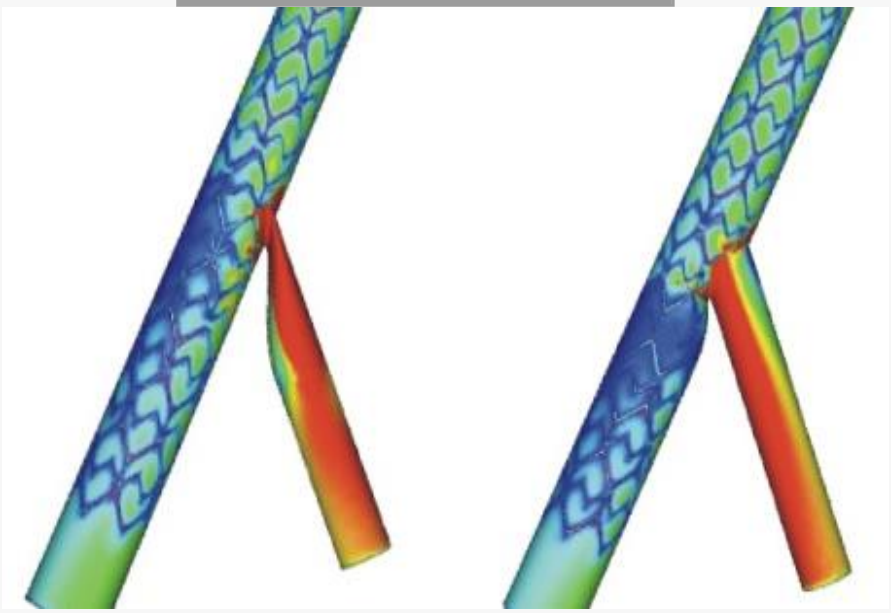
Computational Fluid Dynamics (CFD)

- Computational fluid dynamics (CFD) quantifies fluid pressure and velocity, based on physical laws of mass conservation and momentum balance
- CFD is widely used in the aerospace and automotive industries for design and testing

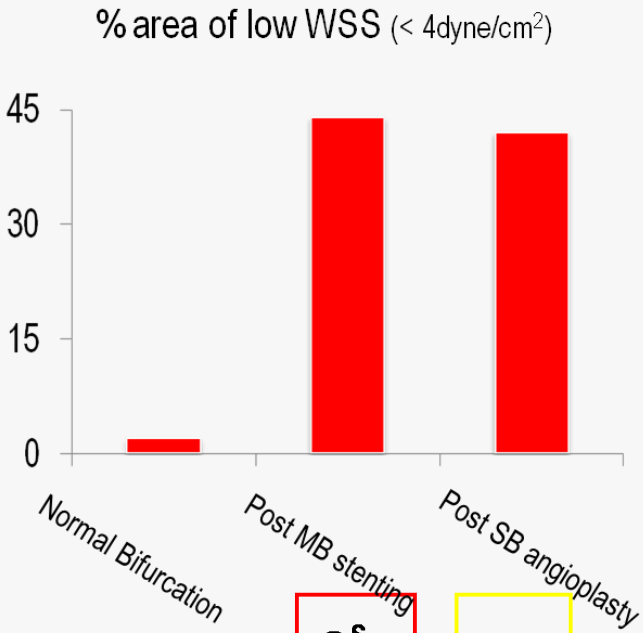


CFD in simple and idealized coronary models

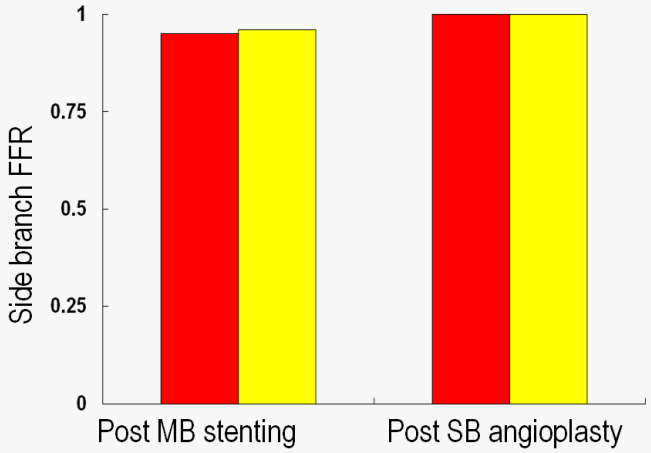




Post MB stenting Post SB angioplasty



$$FFR = \frac{Q^S_{max}}{Q^N_{max}} = \frac{P_d}{P_a}$$

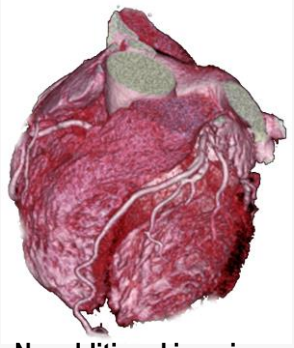


Williams & Koo, et al. J Appl Physiol 2010

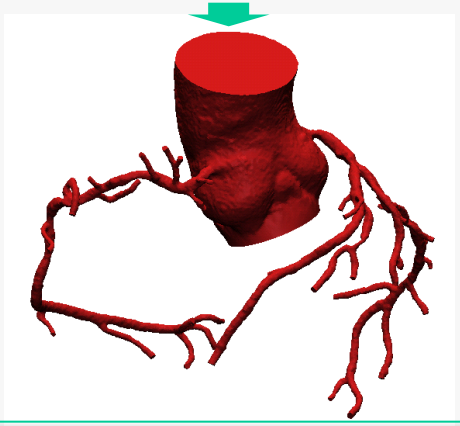
Patient-specific non-invasive FFR using CT & CFD

Computational Model based on CCTA

3-D anatomic model from CCTA

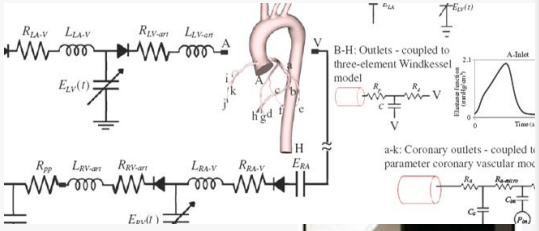


No additional imaging
No additional medications

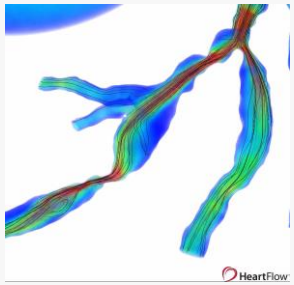


Blood Flow Solution

Blood flow equations solved on supercomputer



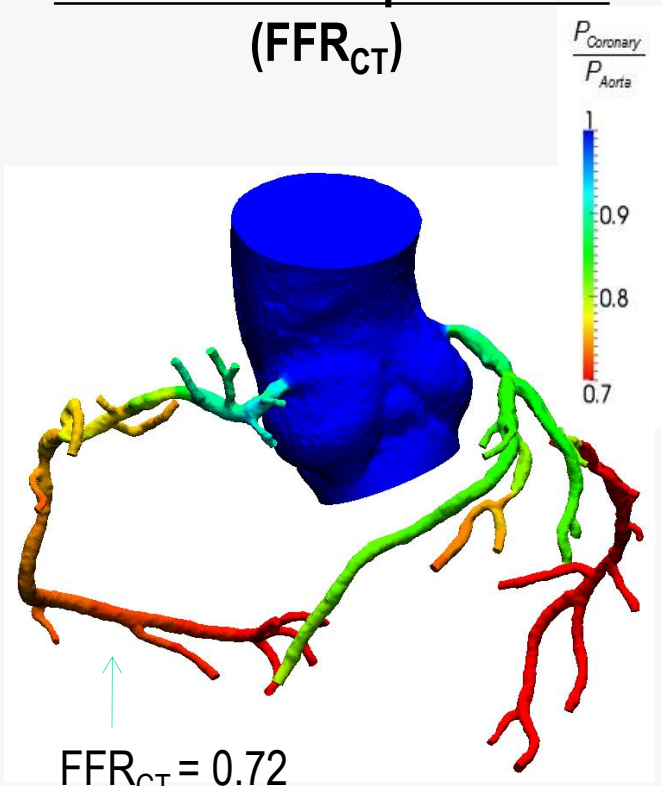
$$\rho \bar{v}_{,t} + \rho \bar{v} \cdot \nabla \bar{v} = -\nabla p + \nabla \cdot \tilde{\tau}$$
$$\nabla \cdot \bar{v} = 0$$



Physiologic models

- Myocardial demand
- Morphometry-based boundary condition
- Effect of adenosine on microcirculation

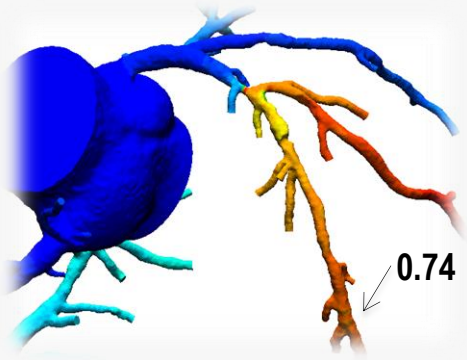
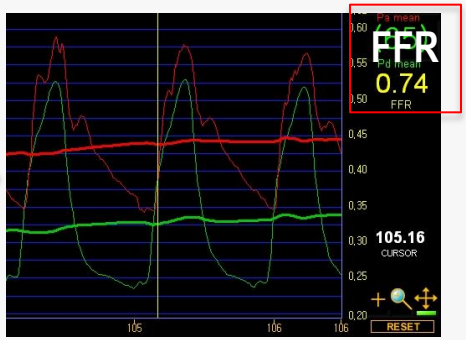
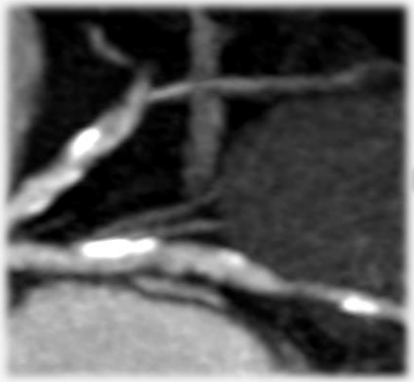
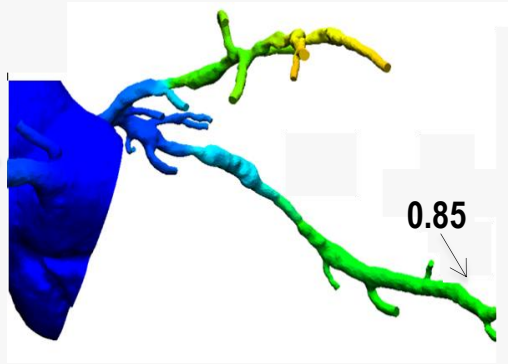
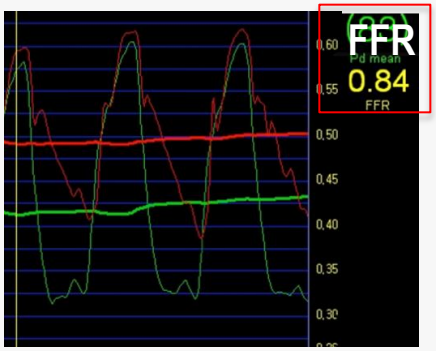
CT-derived computed FFR (FFR_{CT})



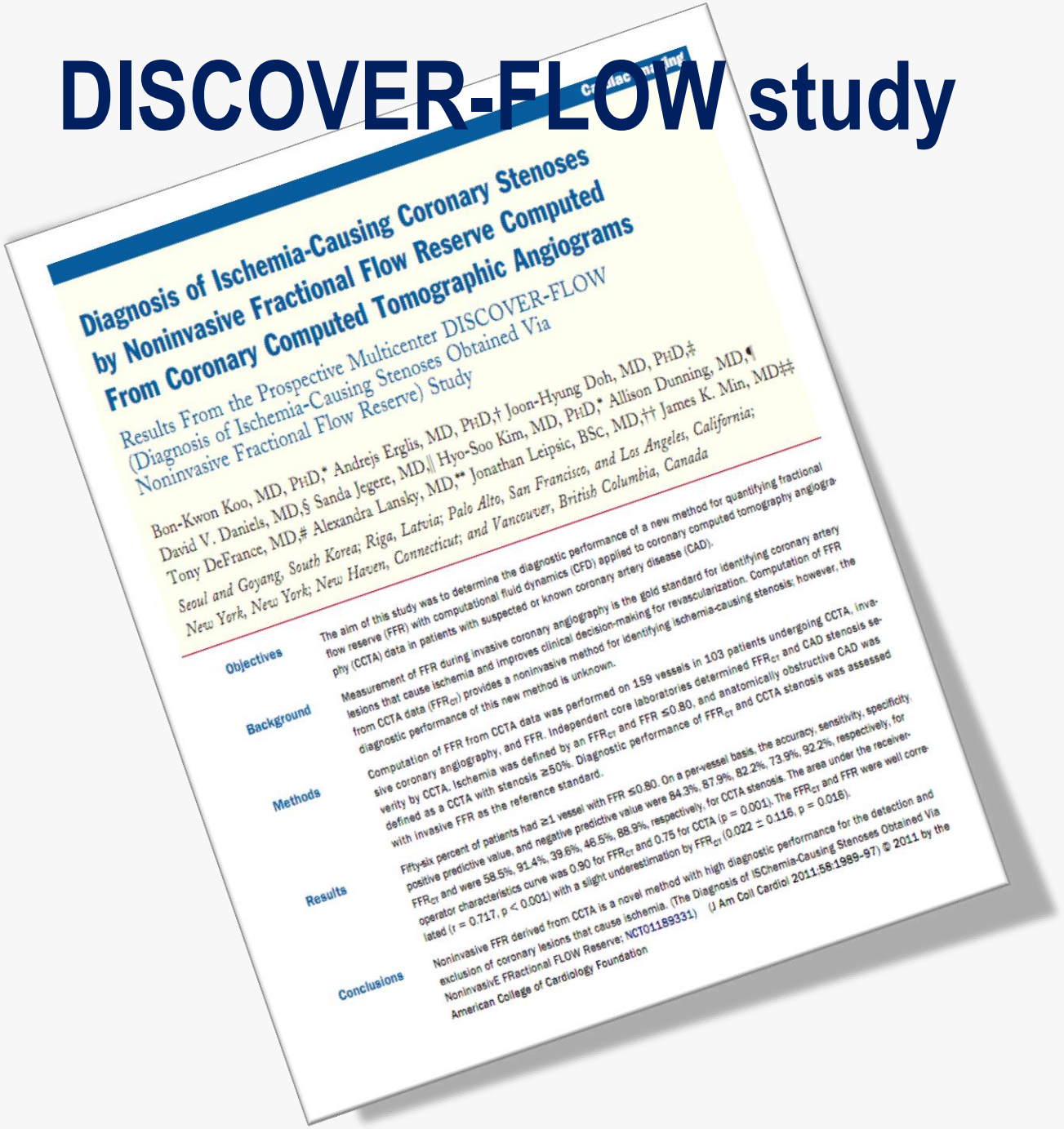
FFR_{CT} = 0.72
(can select any point on model)

6

Case Examples

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

DISCOVER-FLOW study



Diagnosis of Ischemia-Causing Coronary Stenoses by Noninvasive Fractional Flow Reserve Computed From Coronary Computed Tomographic Angiograms

Results From the Prospective Multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) Study

Bon-Kwon Koo, MD, PhD,* Andrejs Erglis, MD, PhD,† Joon-Hyung Doh, MD, PhD,‡ David V. Daniels, MD,§ Sanda Jegere, MD,‖ Hyo-Soo Kim, MD, PhD,* Allison Dunning, MD,¶ Tony DeFrance, MD,# Alexandra Lansky, MD,** Jonathan Leipsic, BSc, MD,†† James K. Min, MD‡‡

Seoul and Goyang, South Korea; Riga, Latvia; Palo Alto, San Francisco, and Los Angeles, California; New York, New York; New Haven, Connecticut; and Vancouver, British Columbia, Canada

Objectives The aim of this study was to determine the diagnostic performance of a new method for quantifying fractional flow reserve (FFR) with computational fluid dynamics (CFD) applied to coronary computed tomography angiography (CCTA) data in patients with suspected or known coronary artery disease (CAD).

Background Measurement of FFR during invasive coronary angiography is the gold standard for identifying coronary artery lesions that cause ischemia and improves clinical decision-making for revascularization. Computation of FFR from CCTA data (FFR_{CT}) provides a noninvasive method for identifying ischemia-causing stenosis; however, the diagnostic performance of this new method is unknown.

Methods Computation of FFR from CCTA data was performed on 159 vessels in 103 patients undergoing CCTA, invasive coronary angiography, and FFR. Independent core laboratories determined FFR_{CT} and CAD stenosis severity by CCTA. Ischemia was defined by an FFR_{CT} and FFR ≤0.80, and anatomically obstructive CAD was defined as a CCTA with stenosis ≥50%. Diagnostic performance of FFR_{CT} and CCTA stenosis was assessed with invasive FFR as the reference standard.

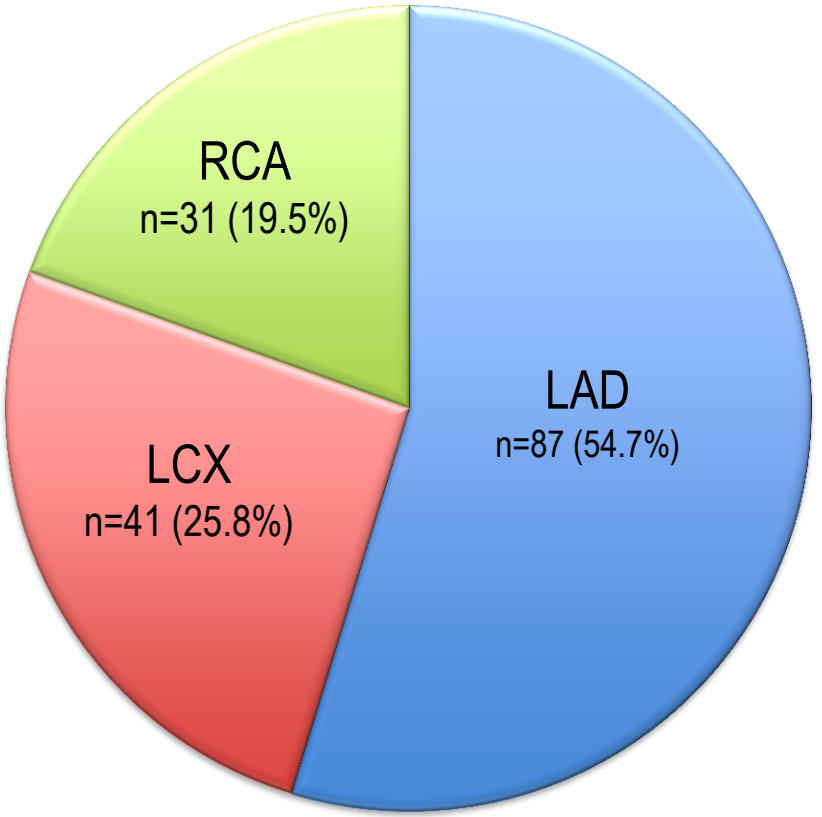
Results Fifty-six percent of patients had ≥1 vessel with FFR ≤0.80. On a per-vessel basis, the accuracy, sensitivity, specificity, positive predictive value, and negative predictive value were 84.3%, 87.9%, 82.2%, 73.9%, 92.2%, respectively, for FFR_{CT} and were 58.5%, 91.4%, 39.6%, 46.5%, 88.9%, respectively, for CCTA stenosis. The area under the receiver-operator characteristics curve was 0.90 for FFR_{CT} and 0.75 for CCTA ($p = 0.001$). The FFR_{CT} and FFR were well correlated ($r = 0.717$, $p < 0.001$) with a slight underestimation by FFR_{CT} (0.022 ± 0.116, $p = 0.016$).

Conclusions Noninvasive FFR derived from CCTA is a novel method with high diagnostic performance for the detection and exclusion of coronary lesions that cause ischemia. (The Diagnosis of iSChemia-Causing Stenoses Obtained Via NoninvasivE FRactional FLOW Reserve; NCT01199331) (J Am Coll Cardiol 2011;58:1989–97) © 2011 by the American College of Cardiology Foundation

Patients and lesions

- Oct 2009 – Jan 2011
- 159 vessels in 103 patients

Variable	
Age	63 ± 9 yrs
Male	72 %
Hypertension	65 %
Diabetes	26 %
Current smoker	36 %
BMI	26 ± 4
Prior MI	17 %
Prior PCI	16 %
LV ejection fraction	62 ± 6 %

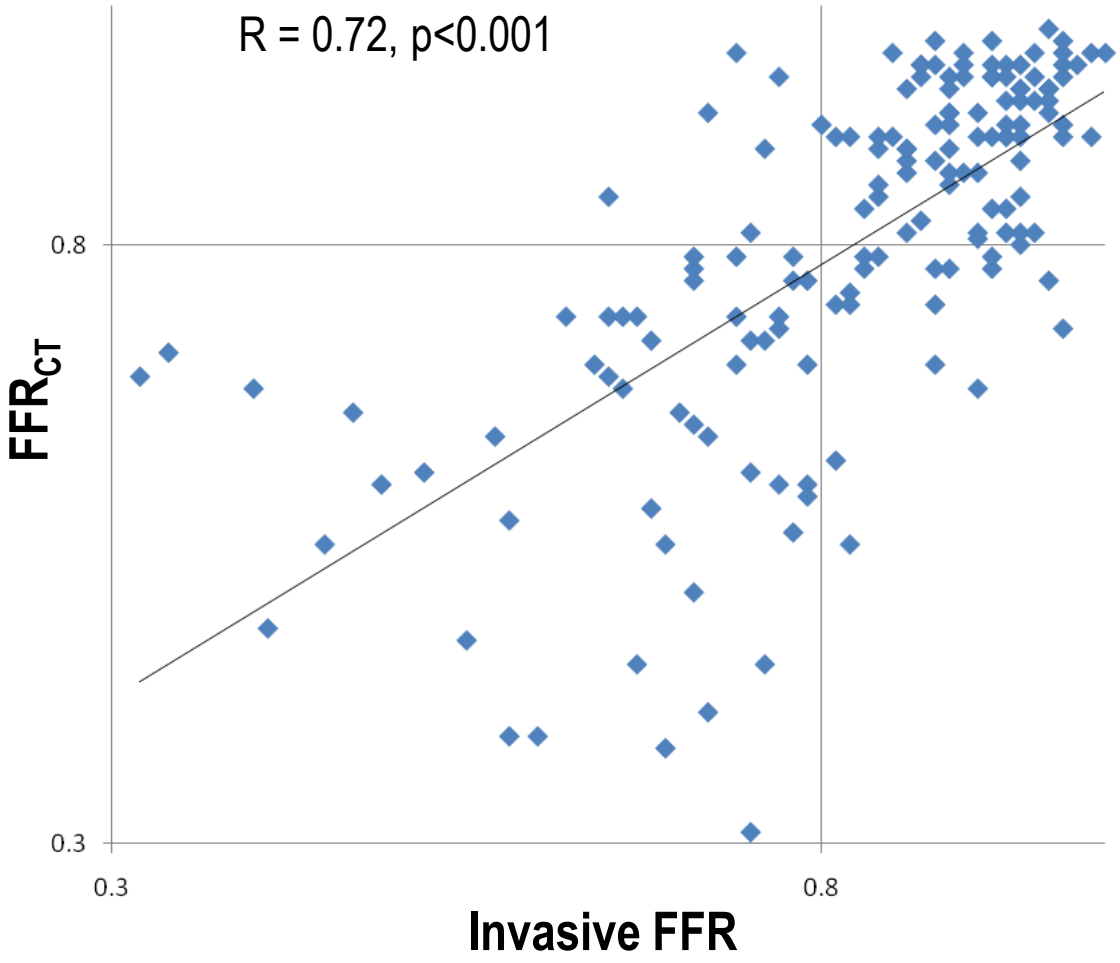


DISCOVER-FLOW: Koo BK, et al, J Am Coll Cardiol, 2011

9

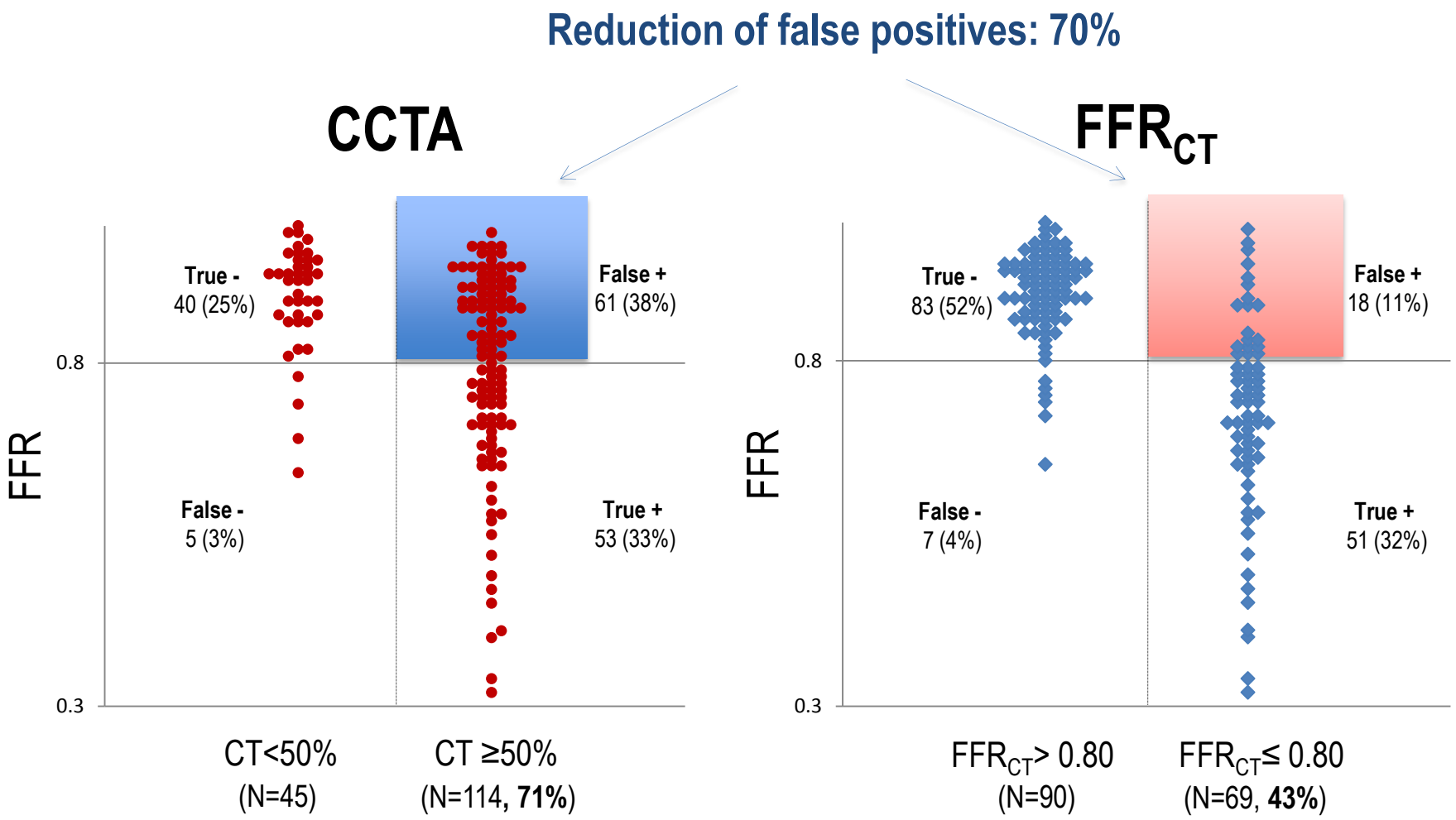
Invasive FFR vs. Non-invasive FFR_{CT}

FFR	0.82 ± 0.13
FFR_{CT}	0.80 ± 0.14
△	**0.02 ± 0.12**



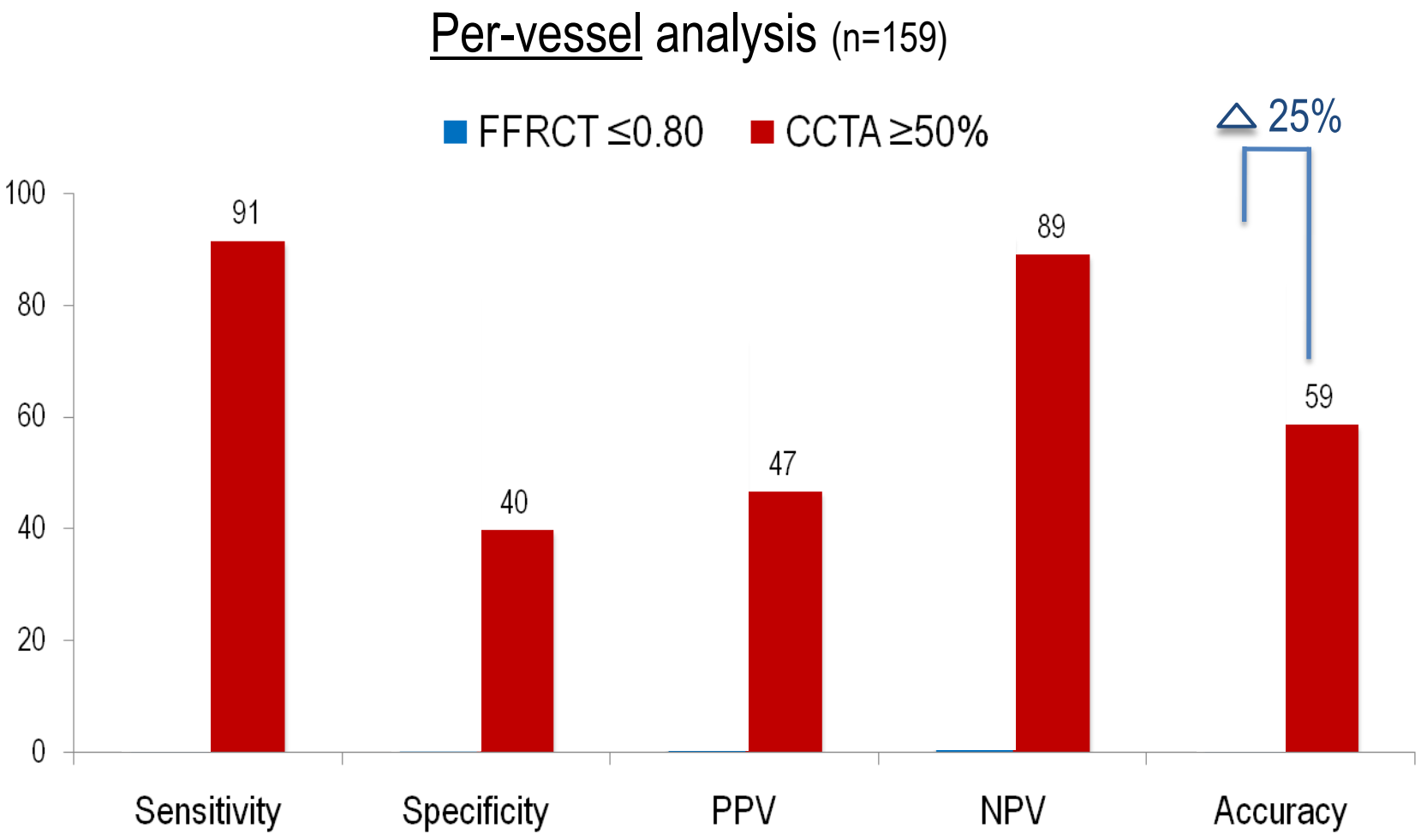
DISCOVER-FLOW: Koo BK, et al, J Am Coll Cardiol, 2011

FFR vs. CT and FFR_{CT}



DISCOVER-FLOW: Koo BK, et al, J Am Coll Cardiol, 2011

Diagnostic performance of FFR_{CT} and CCTA

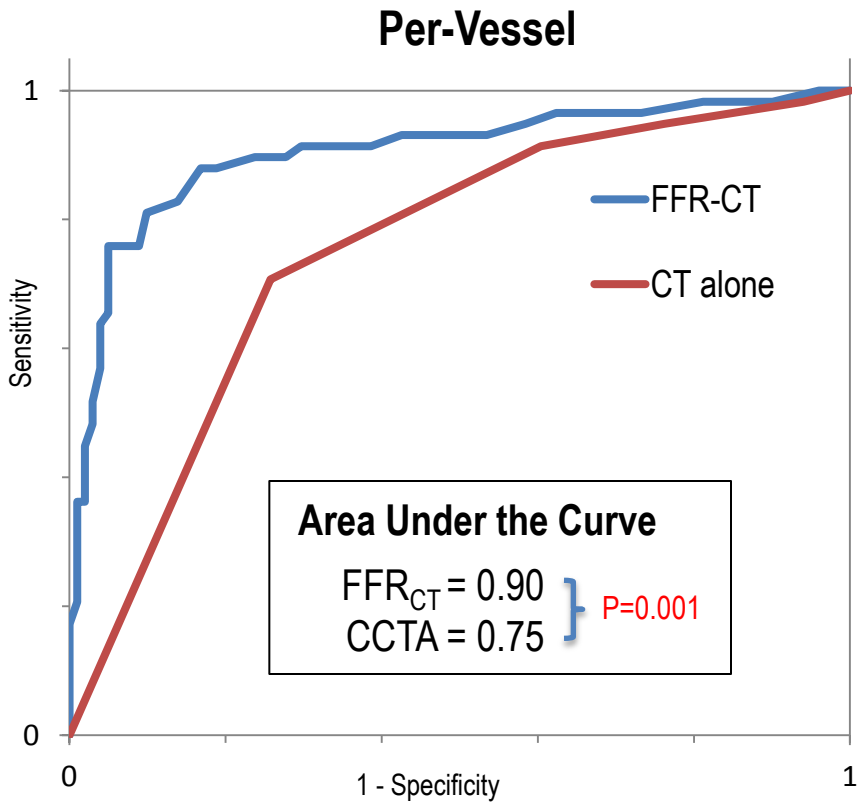


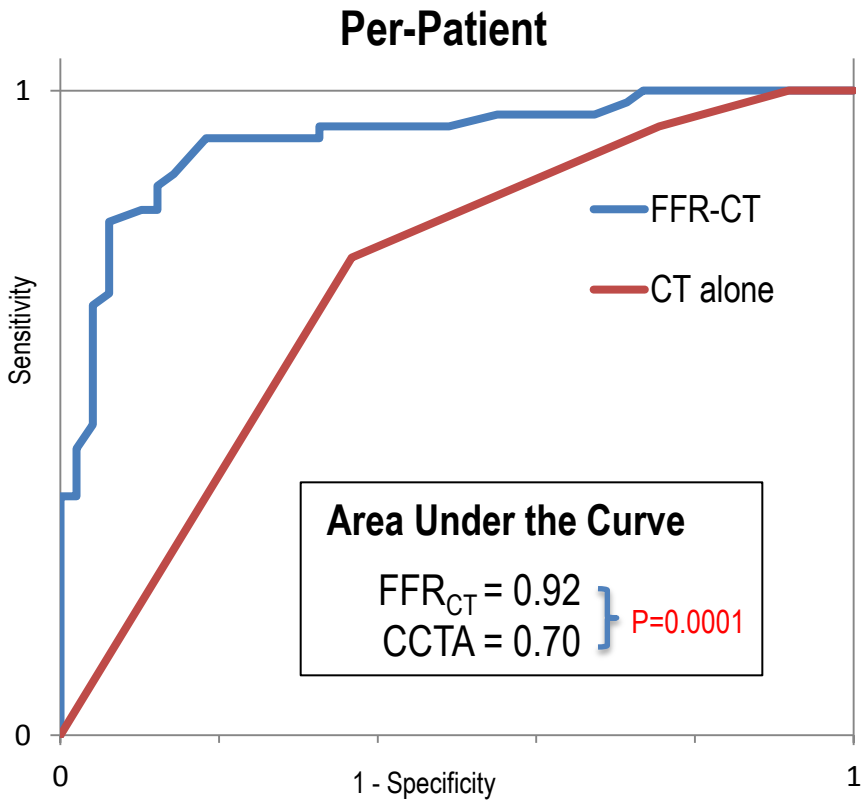
PPV: positive predictive value, NPV: negative predictive value

DISCOVER-FLOW: Koo BK, et al, J Am Coll Cardiol, 2011

Diagnostic performance of CCTA and FFR_{CT}

ROC curve analysis



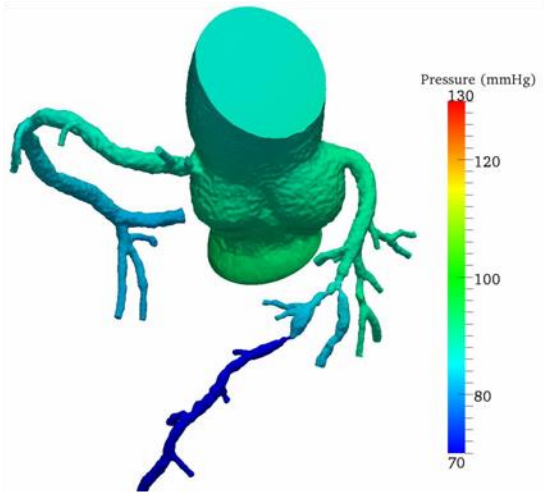


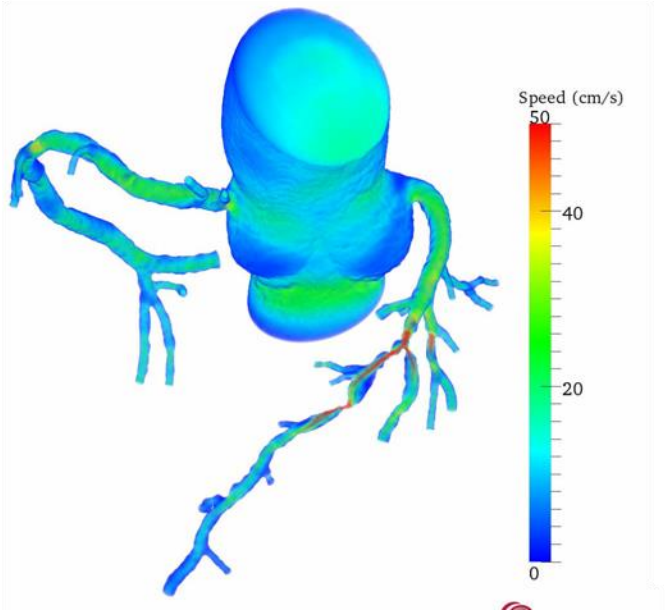
DISCOVER-FLOW: Koo BK, et al, J Am Coll Cardiol, 2011

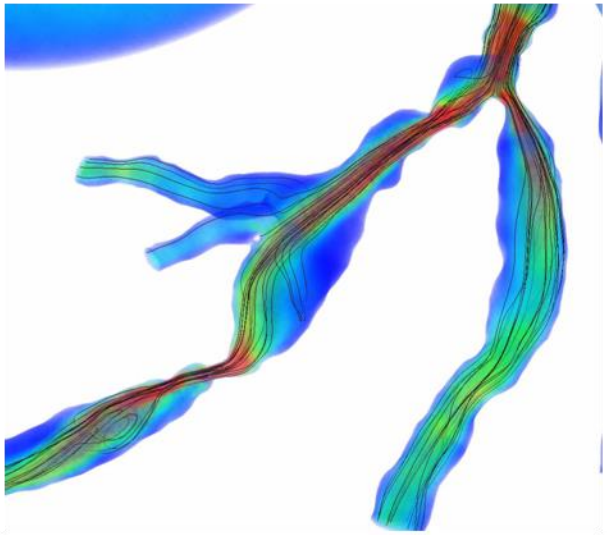
DISCOVER-FLOW study showed …..

- Non-invasive FFR from CT images is feasible without any additional imaging or medications.
- This prospective multicenter study demonstrated
  - **FFR_{CT}** had excellent correlation with invasively measured FFR.
  - **FFR_{CT}** was superior to CCTA for diagnosis of lesion-specific ischemia.
    - Three-fold reduction in false positives
    - Two-fold increase in true negatives
- This technology may reduce unnecessary invasive coronary angiography and revascularization procedures.

Potential of patient-specific CFD analysis

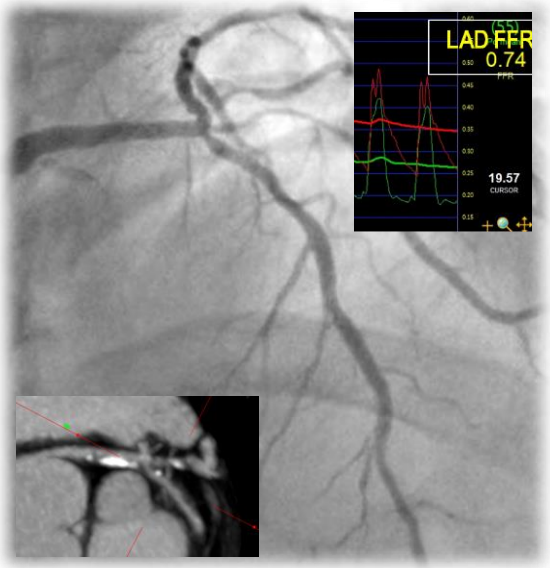


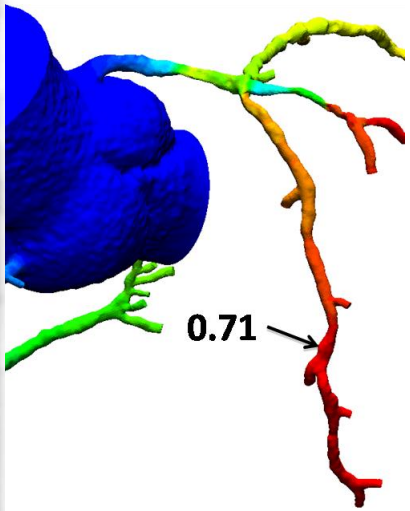


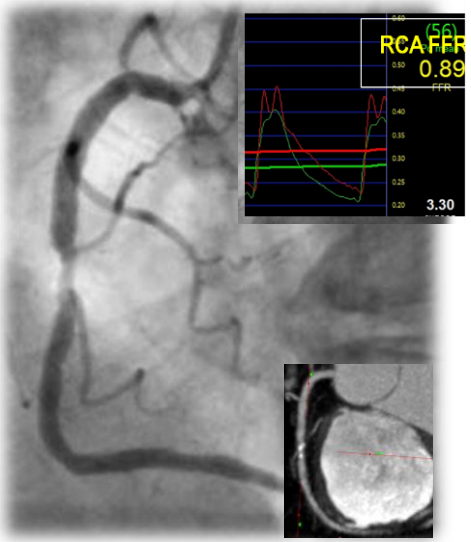


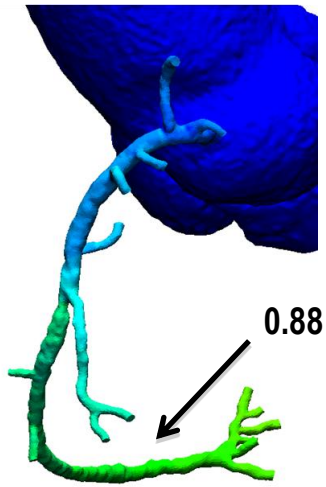
Koo BK, European Bifurcation Club,2010

Treatment planning prior to invasive procedures









CCTA: 2 vessel disease

Non-invasive FFR_{CT}: 1 vessel disease

} **Non-invasive assessment prior to the cath lab**

Angiography: 2 vessel disease

Invasive FFR: 1 vessel disease

} **Invasive assessment in the cath lab**

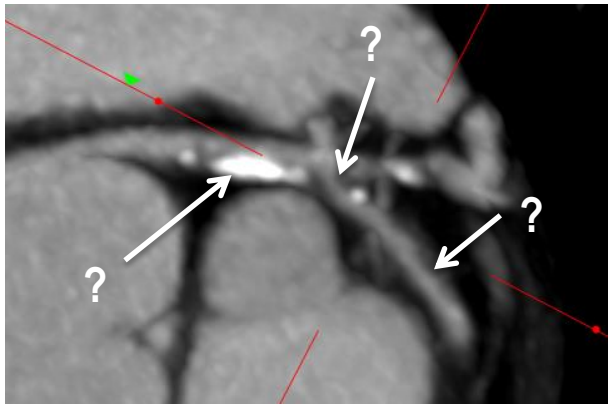
Koo BK, EuroPCR 2011

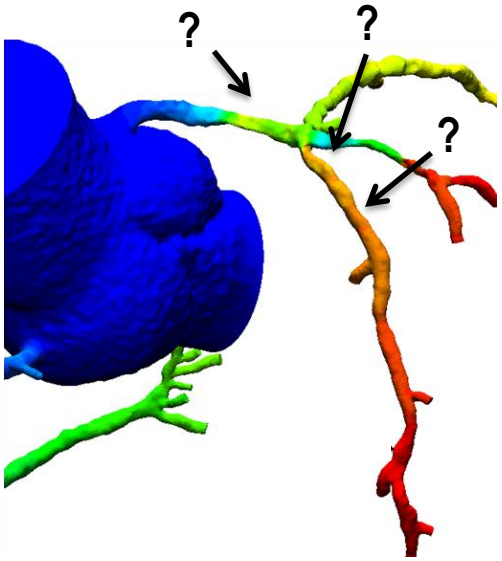
What is the best treatment option for the patient?

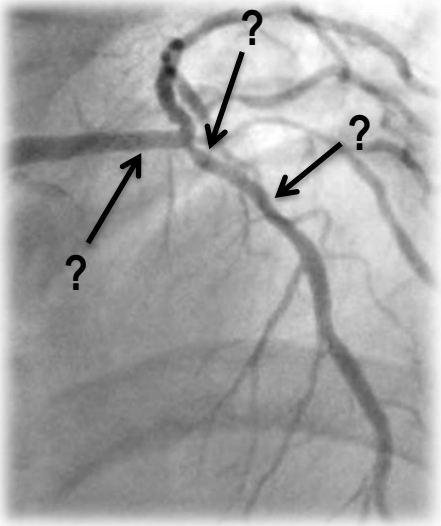
Which lesions are flow limiting?

How many stents are needed?

What will be the effect of a stent on the flow to other lesions?

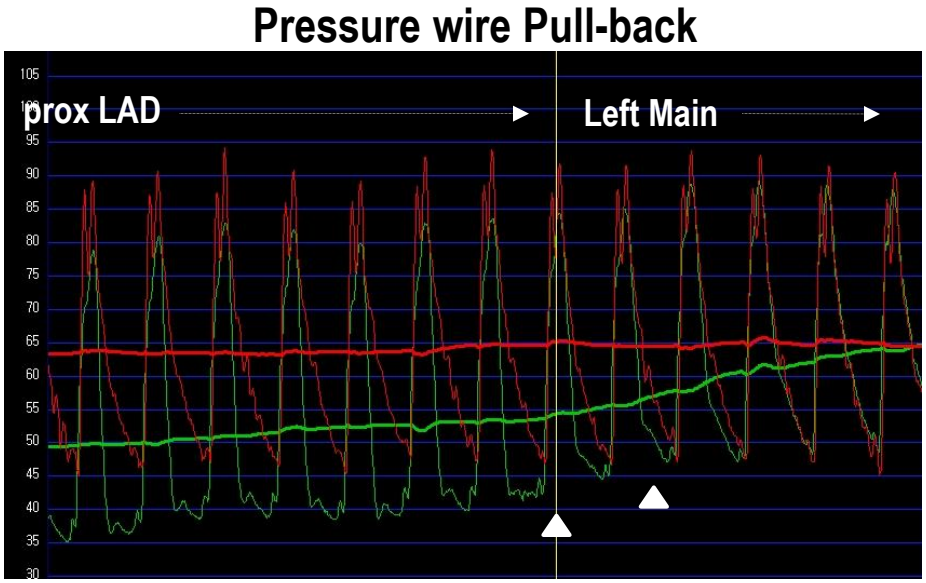


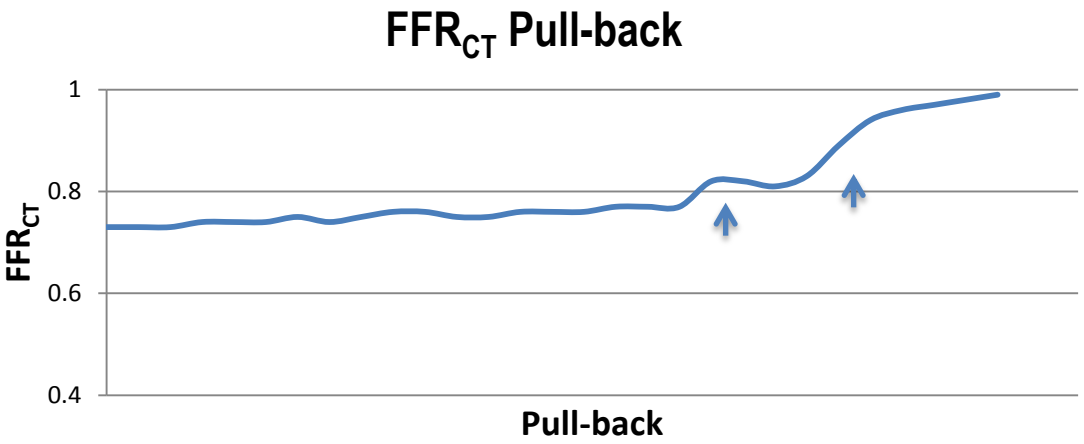


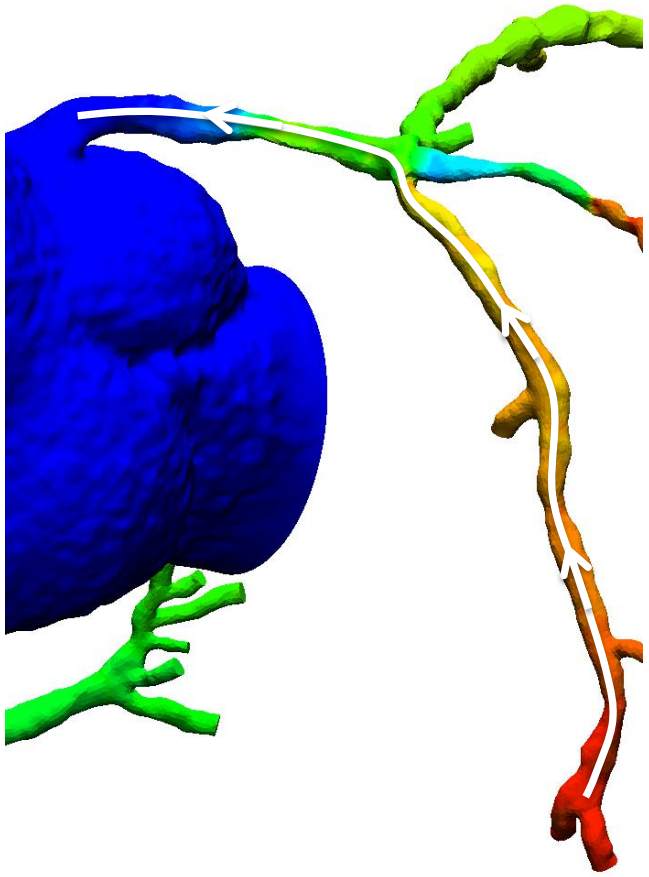


Koo BK, EuroPCR 2011

Pressure wire pull-back vs. FFR_{CT} pull-back





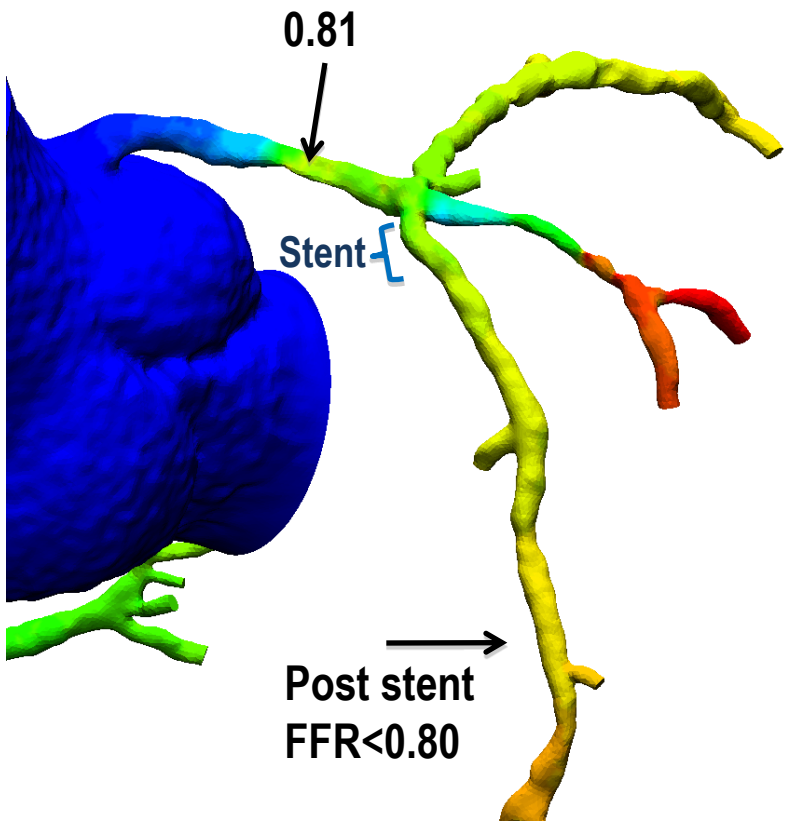


Koo BK, EuroPCR 2011

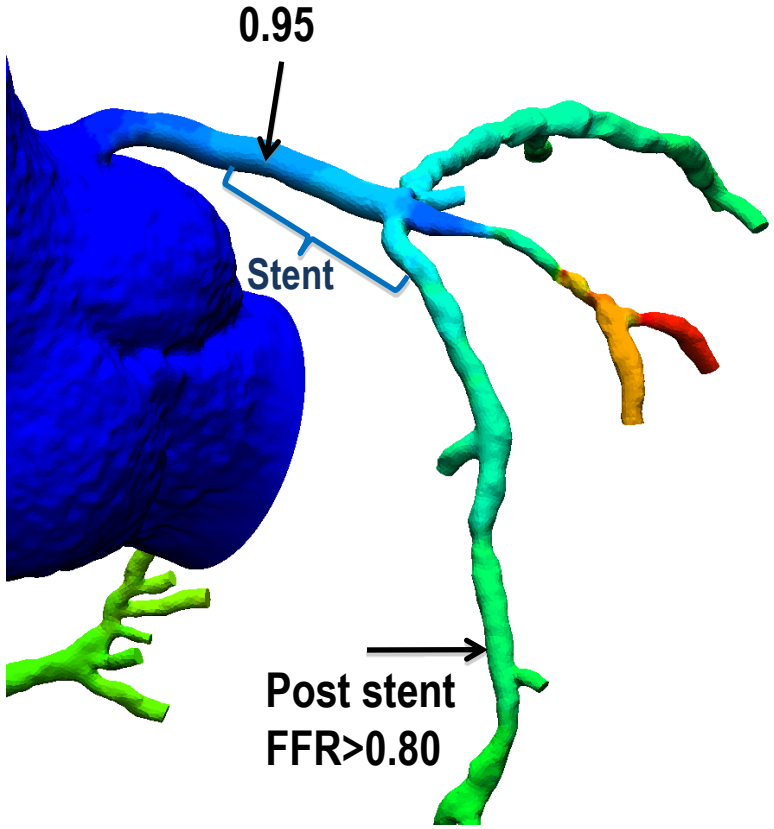
Treatment planning prior to invasive procedures

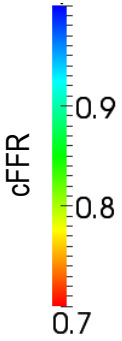
Virtual PCI and post-PCI FFR_{CT}

After LAD os PCI



After Left main and LAD os PCI





Koo BK, EuroPCR 2011

Treatment planning using virtual coronary intervention

and

CT-derived computed fractional flow reserve

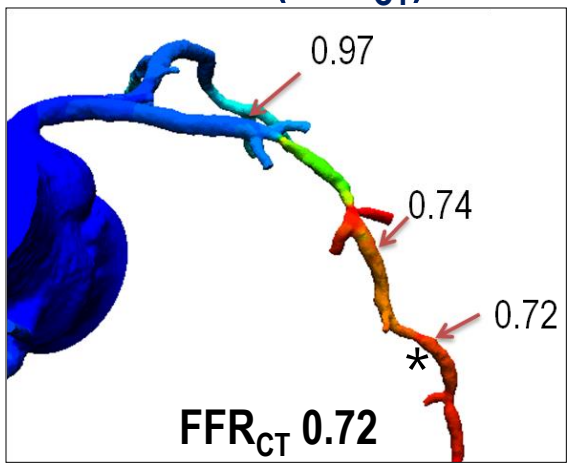
FFR vs. FFR_{CT} after Stenting

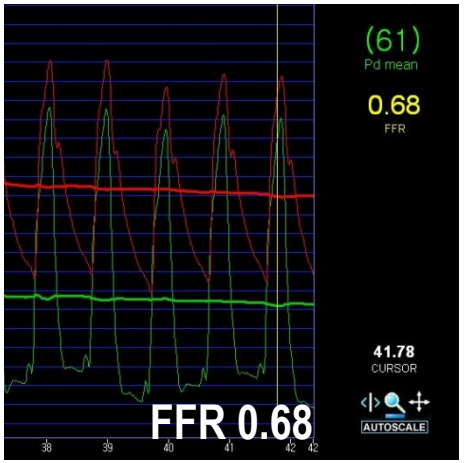
CT-derived computed FFR (FFR_{CT})

Angiography

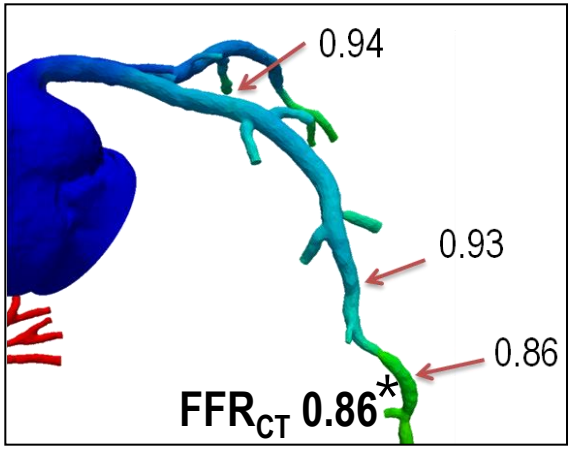
Invasive FFR

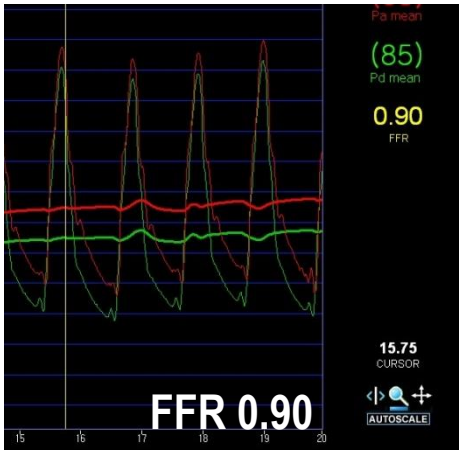
Before Stenting





After Stenting





Baseline Characteristics (n=21)

Quantitative coronary angiography

Before stenting	
Reference diameter, mm	2.86 ± 0.37
Minimal lumen diameter, mm	0.94 ± 0.39
% Diameter stenosis	67.1 ± 13
Lesion length, mm	18.3 ± 10.2
After stenting	
Reference diameter, mm	2.82 ± 0.31
Minimal lumen diameter, mm	2.54 ± 0.36
% Diameter stenosis	10.1 ± 8.5
Stent length, mm	25.6 ± 10.1
Stent diameter, mm	3.0 ± 0.25

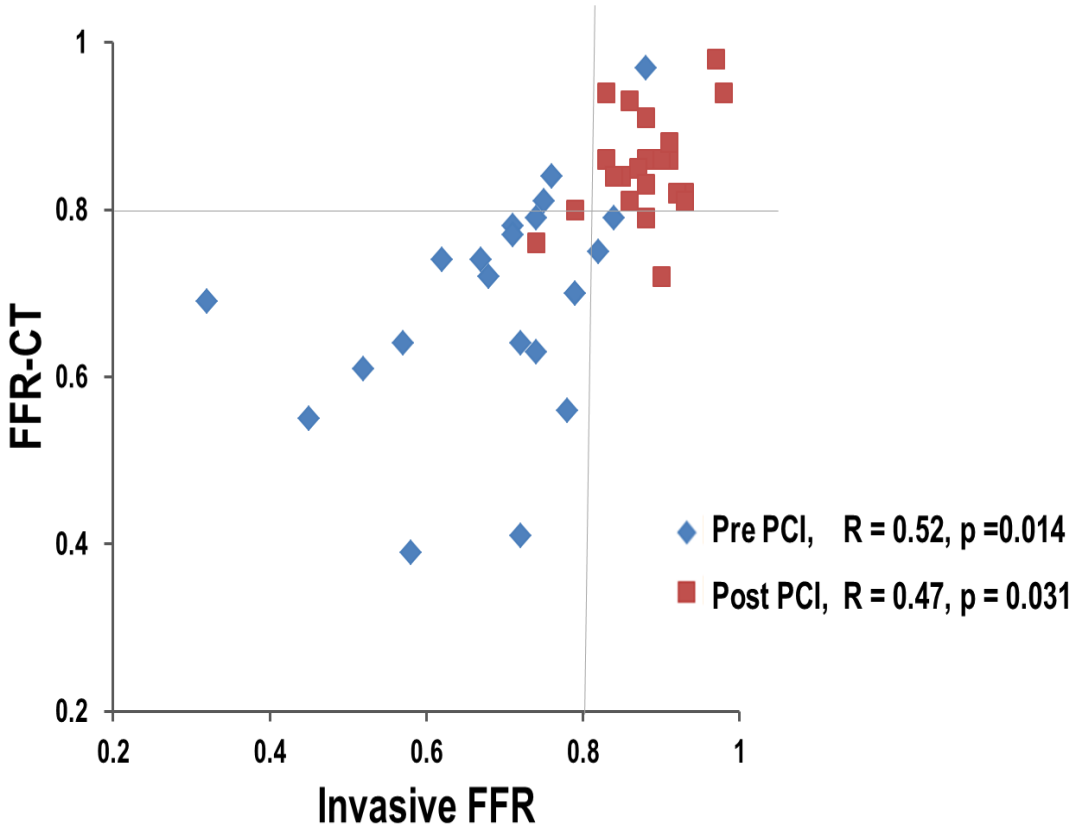
Invasive FFR vs FFR_{CT}

Pre-PCI

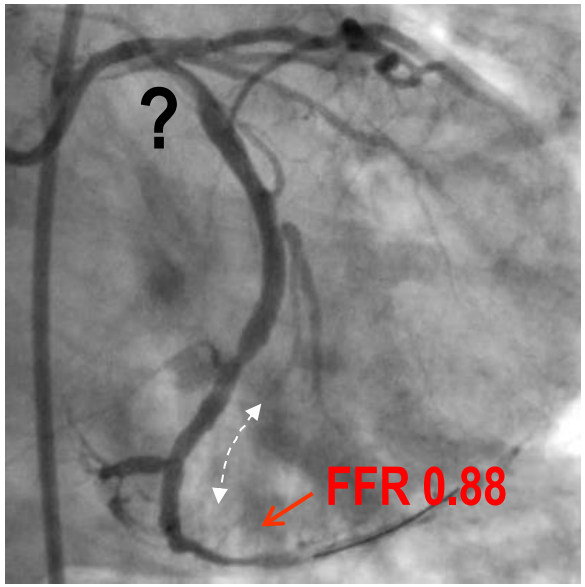
FFR	0.68 ± 0.13
FFR_{CT}	0.69 ± 0.13
△	0.01 ± 0.12

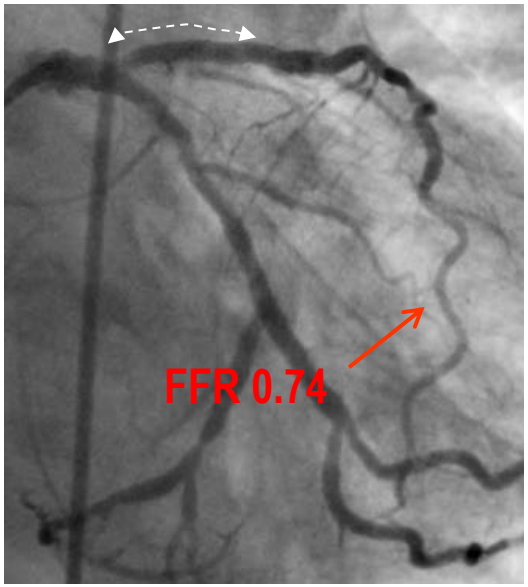
Post-PCI

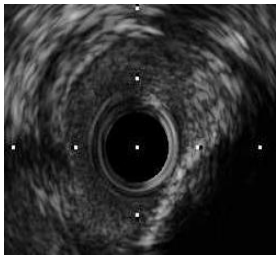
FFR	0.88 ± 0.05
FFR_{CT}	0.86 ± 0.05
△	0.02 ± 0.12

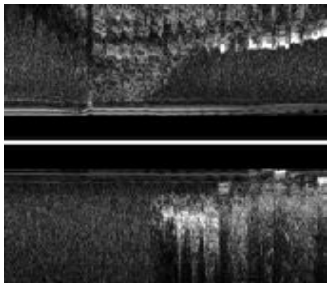


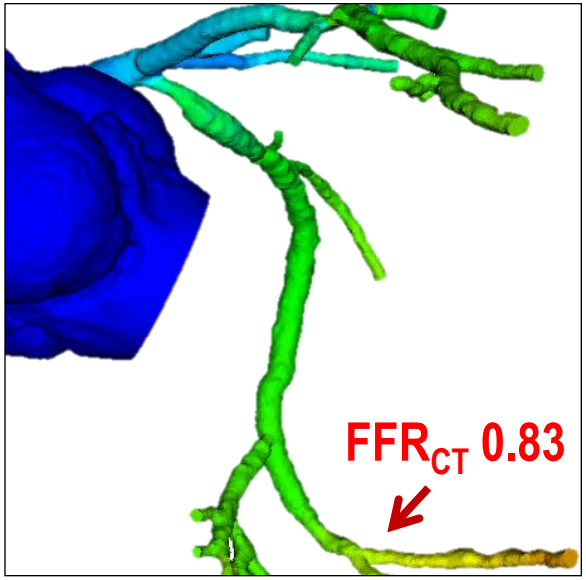
Planning your strategy…..

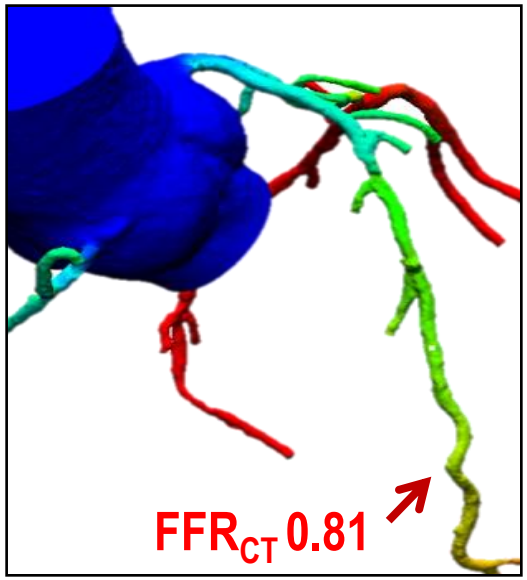




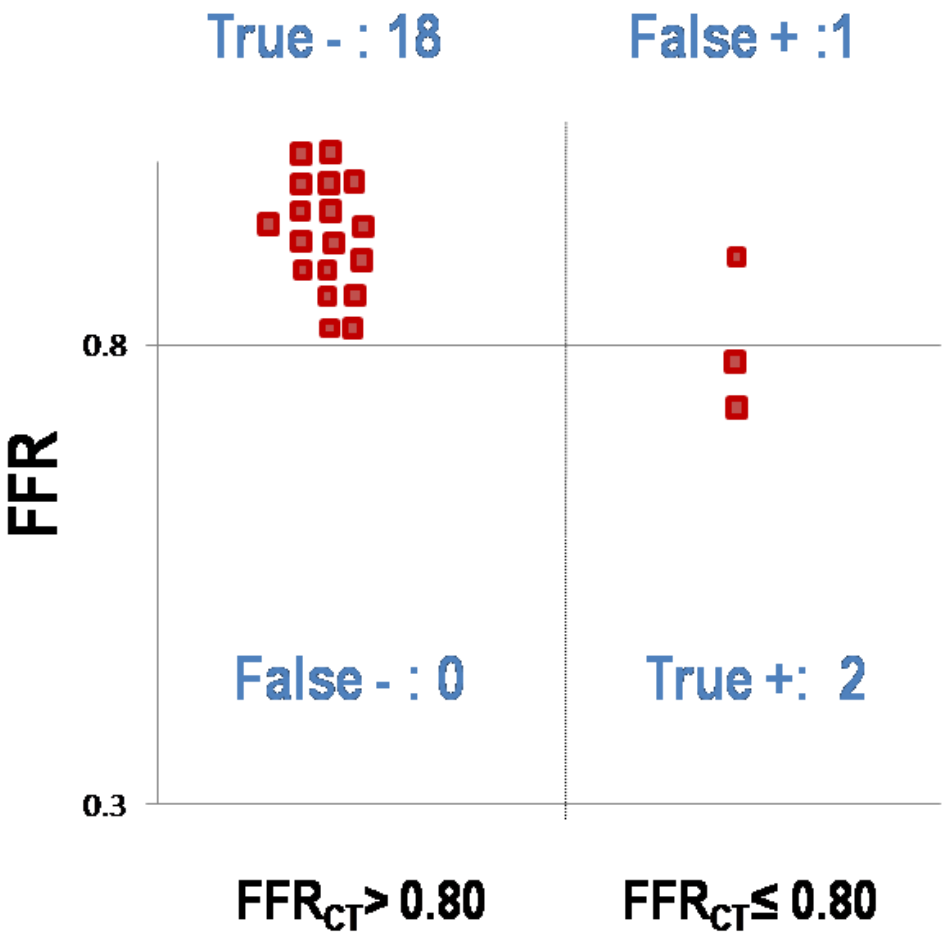








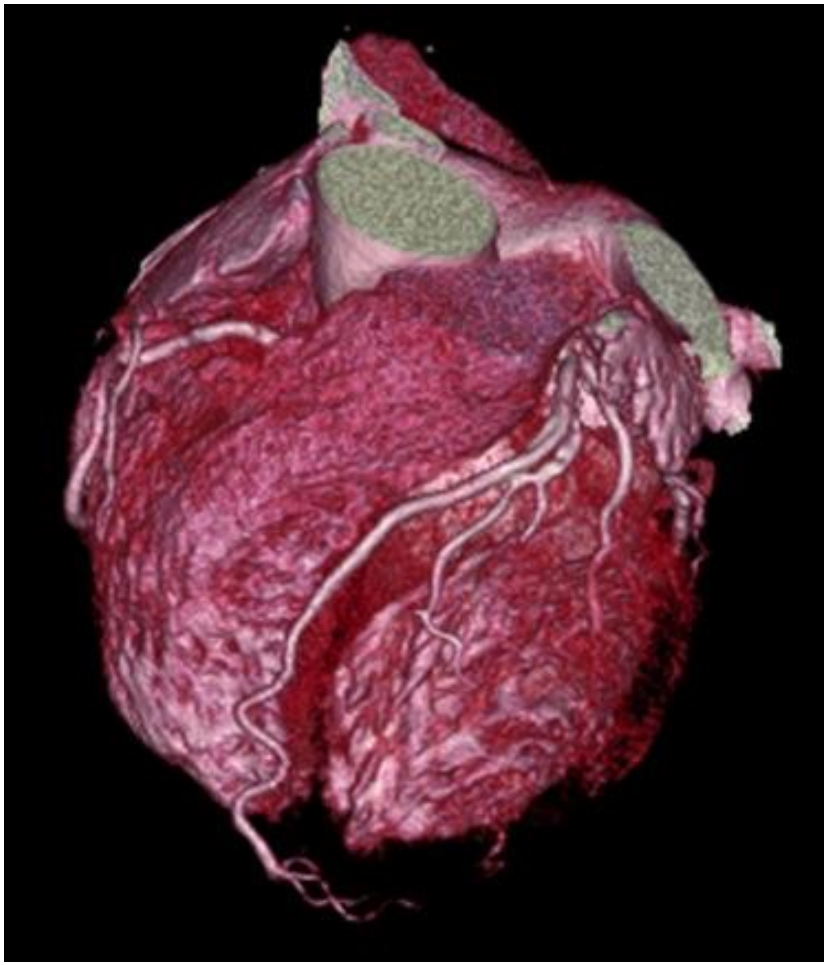
Invasive FFR vs FFR_{CT} after stenting

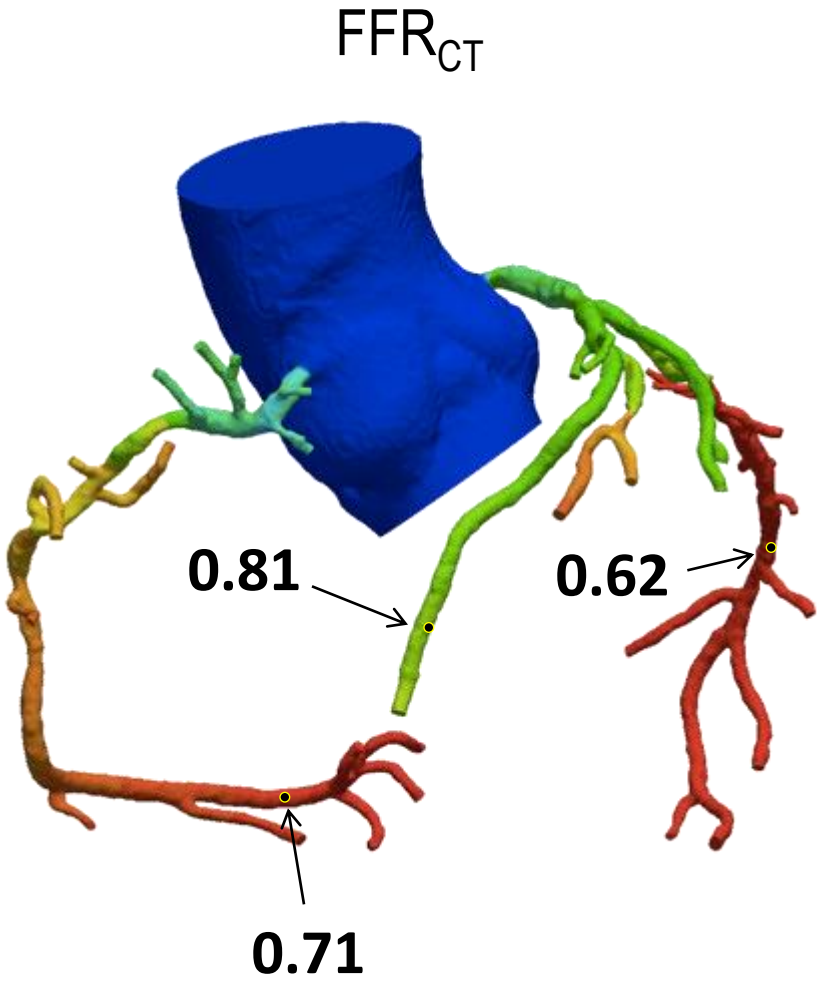


Diagnostic performance of FFR_{CT}

- Diagnostic accuracy **95%**
- Sensitivity **100%**
- Specificity **94%**

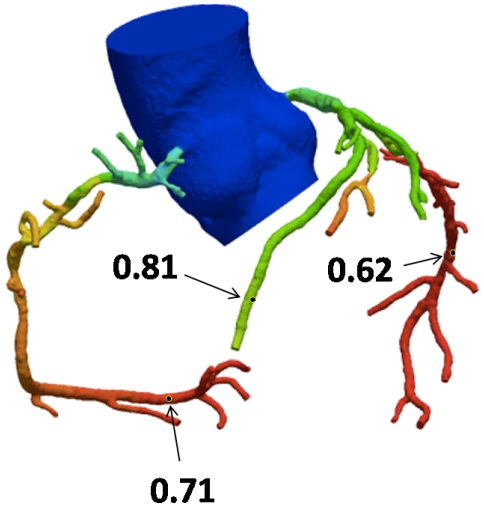
Planning the bypass surgery



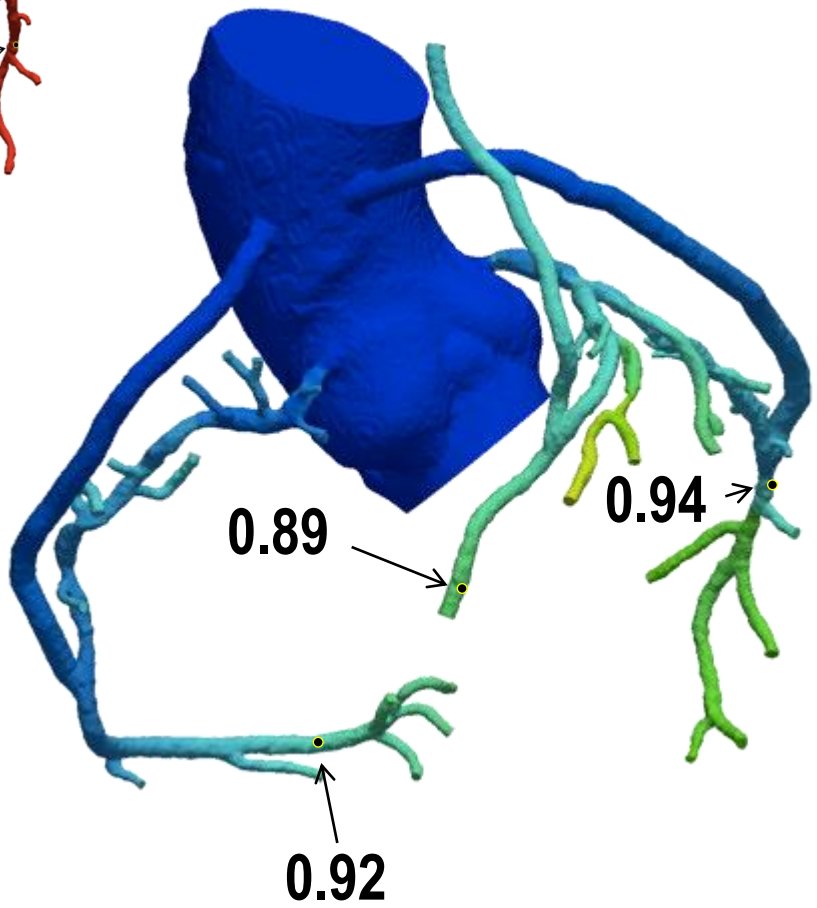


CABG Planner

CABG before the surgery, with your computer



FFRCT after LIMA + 2SVGs



Conclusion

- FFR can be estimated prior to invasive procedures using various novel technologies based on coronary CT angiography.
- CT-derived computed FFR can predict the functional significance of coronary stenoses and may also be helpful in planning the treatment strategy before the invasive procedures.
- Further studies are needed to evaluate the efficacy and to overcome the pitfalls of novel technologies.

28

Non-invasive Assessment of Fractional Flow Reserve

: *A Dream Come True?*

Already, but not yet!