순환기 춘계통합학술대회
2012. 4. 20. 14:50-15:15

Coronary hemodynamics by Cardiac CT

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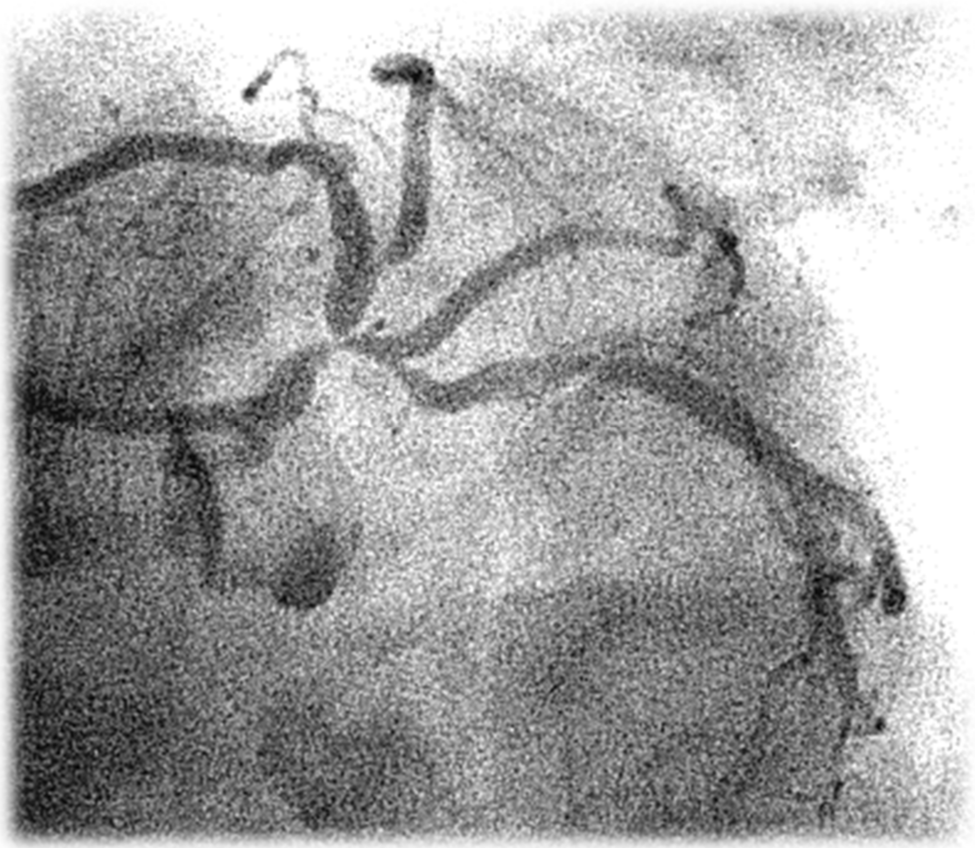
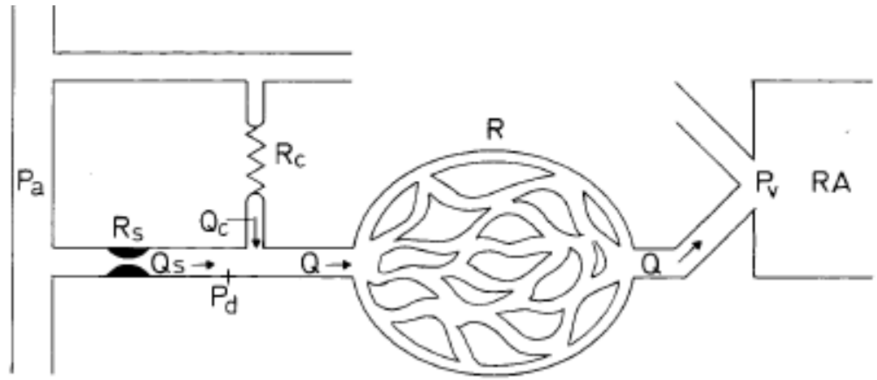
구 본 권

I love "Images", But, I hate "Hemodynamics" !





$$= \left(1 - \frac{\Delta^{(2)}P}{P_a^{(2)} - P_w^{(2)}}\right) : \left(1 - \frac{\Delta^{(1)}P}{P_a^{(1)} - P_w^{(1)}}\right) \quad (5b)$$

The expression $FFR_{cor}^{(2)}/FFR_{cor}^{(1)}$ represents the improvement of FFR_{cor} of the dilated artery and is identical to what we called pressure-corrected maximum flow ratio (MFR_c) in a previous study[9].

Equation 5a can also be derived directly from figure 4.7 by the following:

$$\frac{Q_s^{(2)}}{Q_s^{(1)}} = \frac{Q^{(2)} - Q_c^{(2)}}{Q^{(1)} - Q_c^{(1)}} = \frac{(P_d^{(2)} - P_v^{(2)})/R - (P_a^{(2)} - P_d^{(2)})/R_c}{(P_d^{(1)} - P_v^{(1)})/R - (P_a^{(1)} - P_d^{(1)})/R_c}$$

and by substituting Equation 1b.

Theoretically, maximum blood flow through the myocardium can be compared before and after the intervention by:

$$\frac{Q^{(2)}}{Q^{(1)}} = \frac{(P_d^{(2)} - P_v^{(2)})/R}{(P_d^{(1)} - P_v^{(1)})/R} = \frac{P_d^{(2)} - P_v^{(2)}}{P_d^{(1)} - P_v^{(1)}} \quad (6a)$$

or, if correction for pressure changes is made, by:

$$\frac{FFR_{myo}^{(2)}}{FFR_{myo}^{(1)}} = \frac{P_d^{(2)} - P_v^{(2)}}{P_a^{(2)} - P_v^{(2)}} : \frac{P_d^{(1)} - P_v^{(1)}}{P_a^{(1)} - P_v^{(1)}}$$

$$= \left(1 - \frac{\Delta^{(2)}P}{P_a^{(2)} - P_v^{(2)}}\right) : \left(1 - \frac{\Delta^{(1)}P}{P_a^{(1)} - P_v^{(1)}}\right) \quad (6b)$$

In the case of coronary interventions, it should be realized that flow at maximum vasodilation is directly proportional to the driving pressure (P_a - P_v). Therefore, the ratio between maximum flow through the coronary artery before (situation 1) and after the intervention (situation 2) can be written as follows:

$$\frac{Q_s^{(2)}}{Q_s^{(1)}} = \frac{Q_s^{(2)}}{Q_s^{(2)N}} \cdot \frac{Q_s^{(2)N}}{Q_s^{(1)N}} \cdot \frac{Q_s^{(1)N}}{Q_s^{(1)}}$$

$$= FFR_{cor}^{(2)} \cdot \frac{P_a^{(2)} - P_v^{(2)}}{P_a^{(1)} - P_v^{(1)}} \cdot \frac{1}{FFR_{cor}^{(1)}}$$

$$= \frac{FFR_{cor}^{(2)}}{FFR_{cor}^{(1)}} \cdot \frac{P_a^{(2)} - P_v^{(2)}}{P_a^{(1)} - P_v^{(1)}}$$

By substitution of Equations 1b and 2:

$$\frac{Q_s^{(2)}}{Q_s^{(1)}} = \frac{P_d^{(2)} - P_w^{(2)}}{P_d^{(1)} - P_w^{(1)}} \quad (5a)$$

Note that for evaluation of the functional improvement of a stenotic artery after PTCA, $FFR_{cor}^{(2)}/FFR_{cor}^{(1)}$ theoretically is a better measure than $Q_s^{(2)}/Q_s^{(1)}$ because the first expression is independent of arterial pressure. From Equation 2 it is clear that

$$\frac{FFR_{cor}^{(2)}}{FFR_{cor}^{(1)}} = \frac{P_d^{(2)} - P_w^{(2)}}{P_a^{(2)} - P_w^{(2)}} : \frac{P_d^{(1)} - P_w^{(1)}}{P_a^{(1)} - P_w^{(1)}}$$

Evaluation of coronary artery disease

Is there a room for more?

- Clinical information: Symptom, risk factors, …..
- Functional study: SPECT, TMT, …..
- Coronary CT angiography
- Invasive coronary angiography
- Intravascular ultrasound
- Virtual histology
- Optical Coherance Tomography …..

Cardiology Is Flow

Yoram Richter, PhD; Elazer R. Edelman, MD, PhD

Panta rhei. *(Everything flows)*.[1]

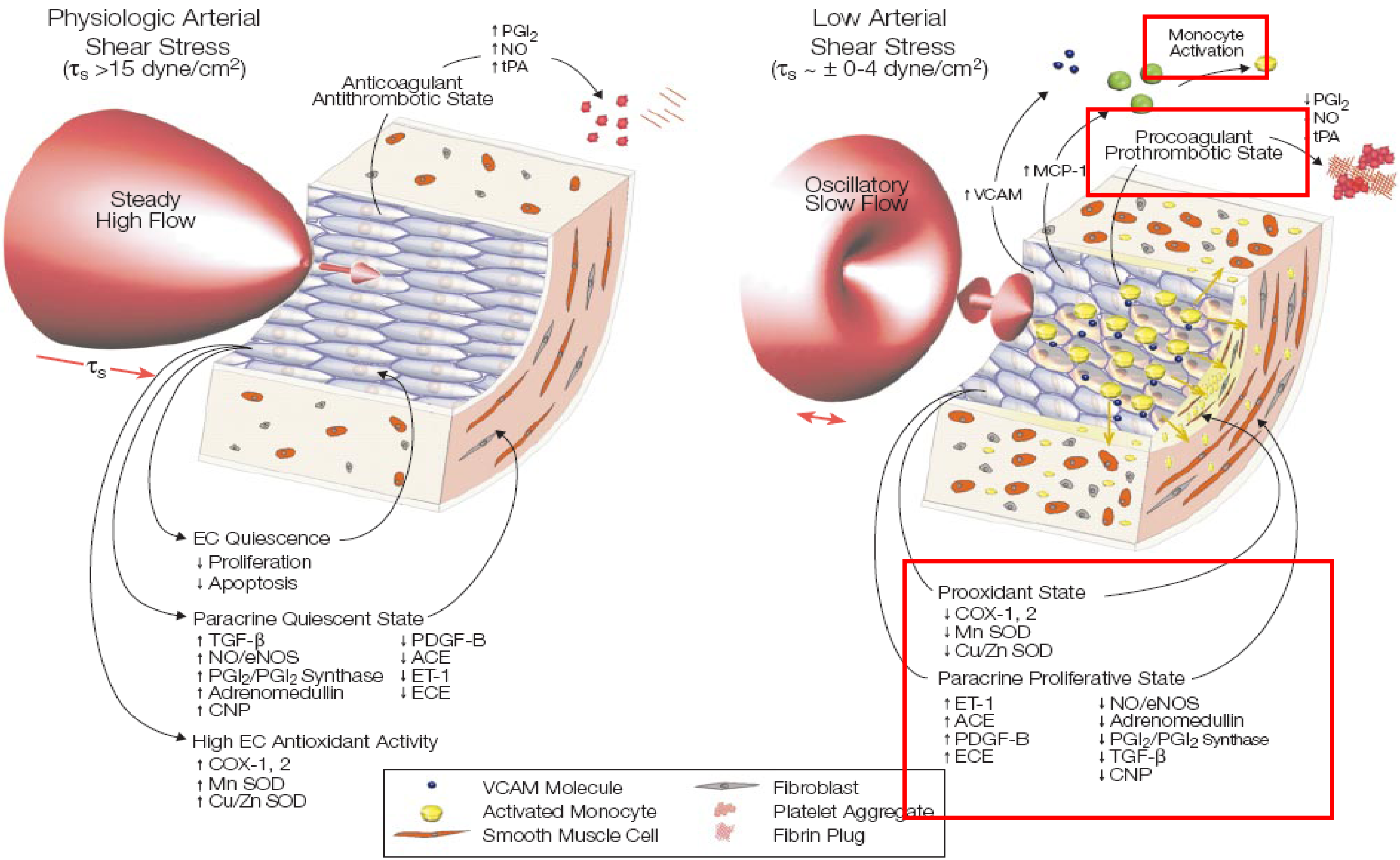
Cardiology is about flow. The primary purpose of the

rosis. Flow disturbances are therefore ubiquitous; they are a fundamental feature of the vascular system. An entire field of study arose correlating disease with its overlying flow pat-

- **Quality of FLOW: wall shear stress, OSI…..**
- **Quantity of FLOW: flow velocity, pressure…..**

Low or abnormal wall shear stress

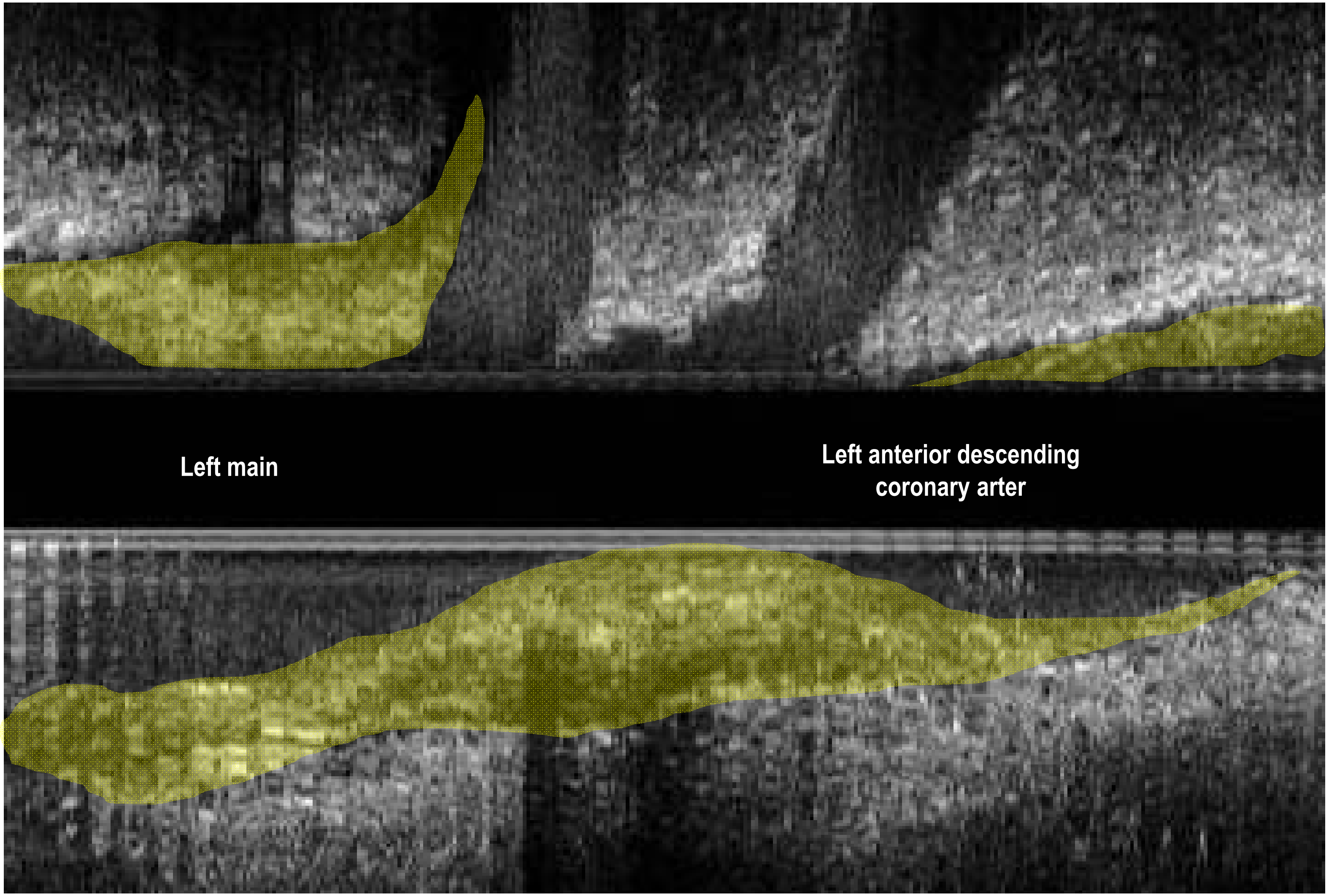
→ Proliferative, pro-inflammatory, pro-thrombotic stimulus



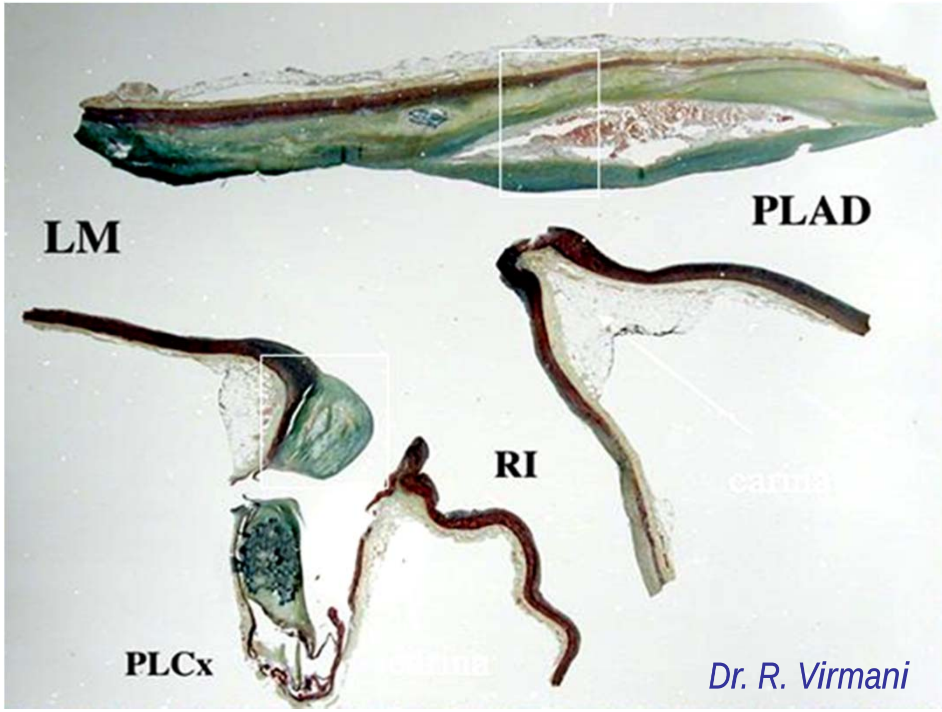
Malek AM, JAMA 1999

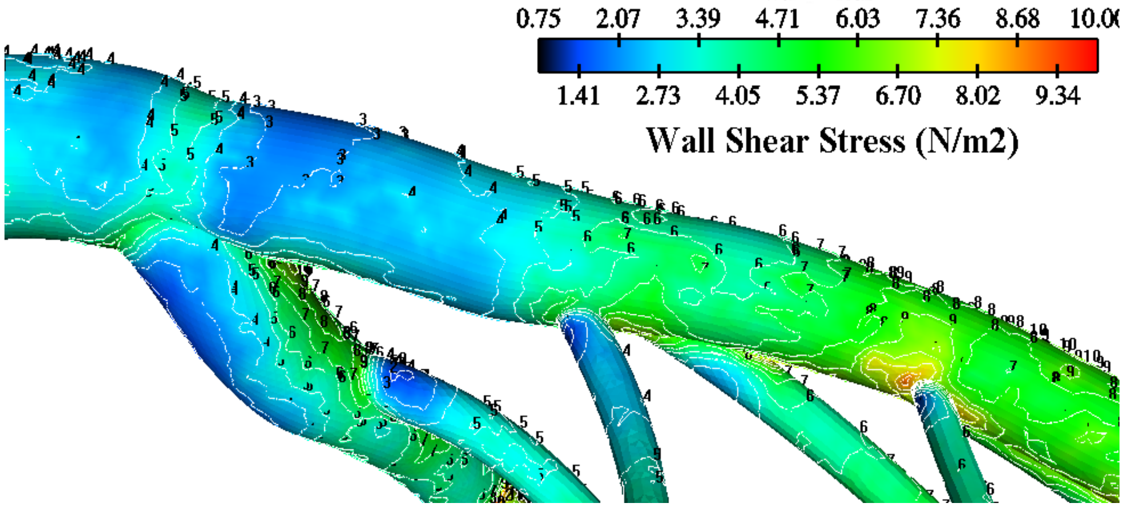
Anatomy & Hemodynamics

Why “the plaque” is there?

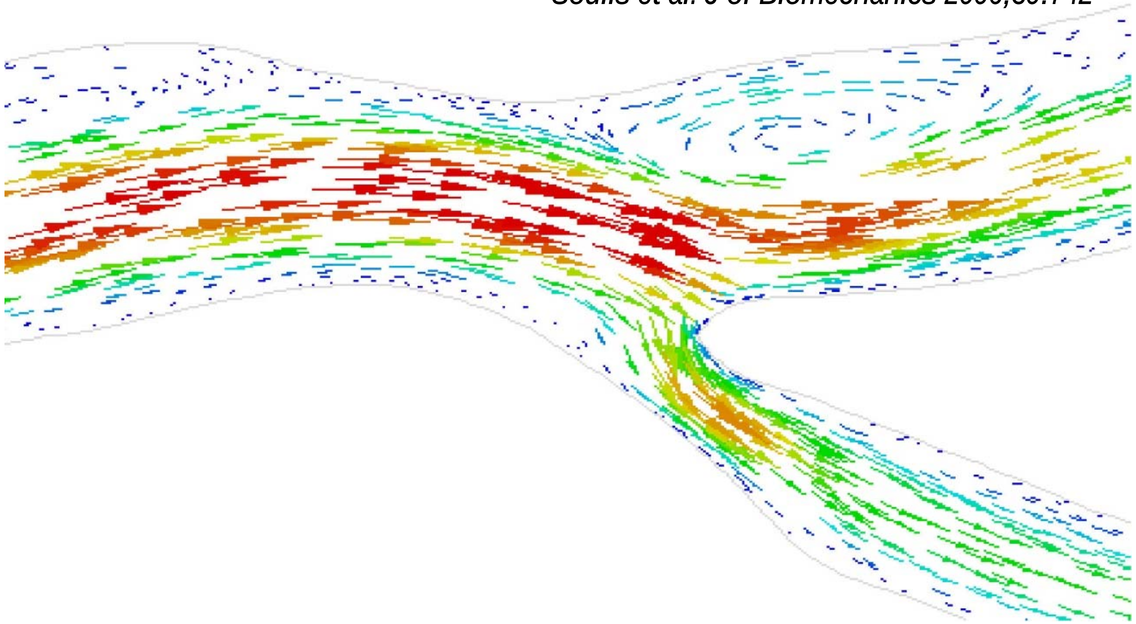


Plaque location: accordant to abnormal flow



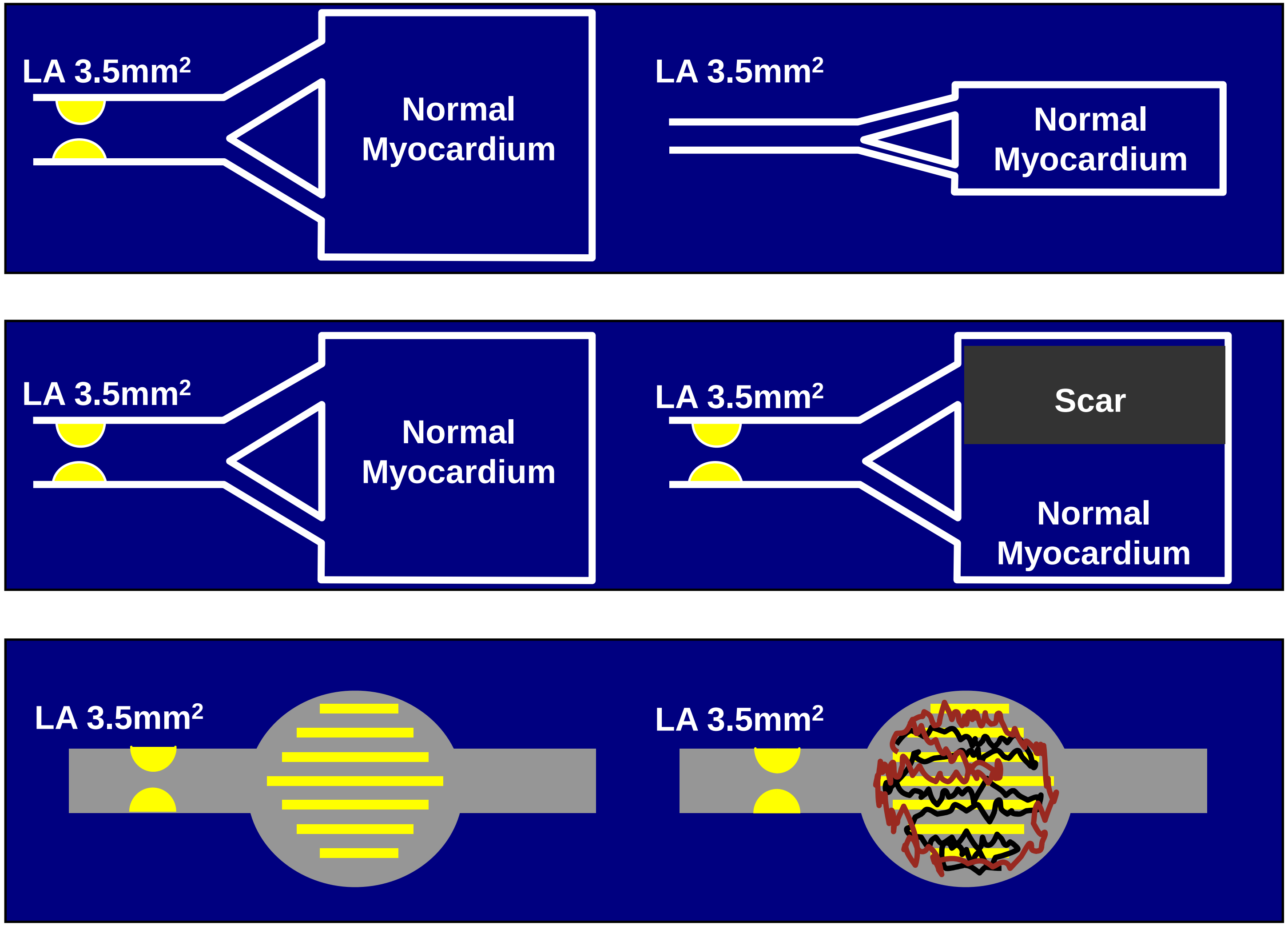


Soulis et al. J of Biomechanics 2006;39:742



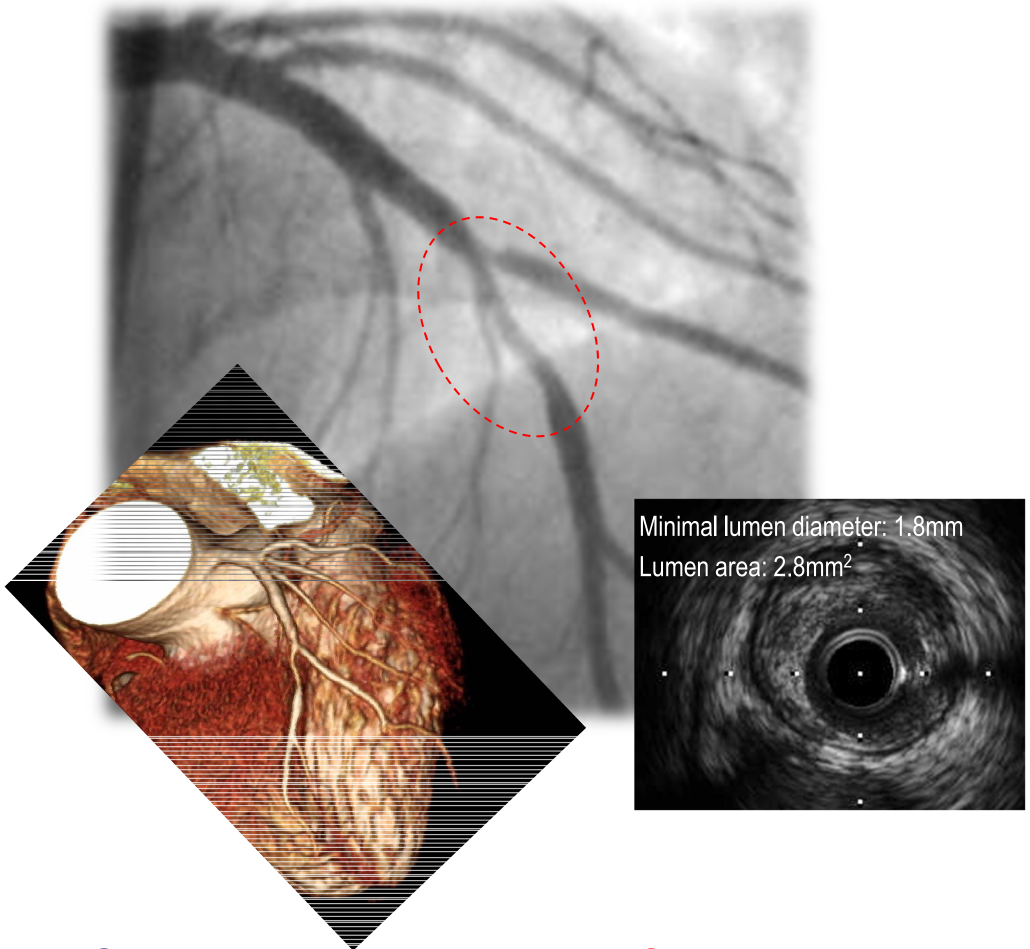
G. Giannakoulas, 2007

Can anatomy predict the functional significance?



LA: Lumen cross sectional area

Anatomy vs. Hemodynamics

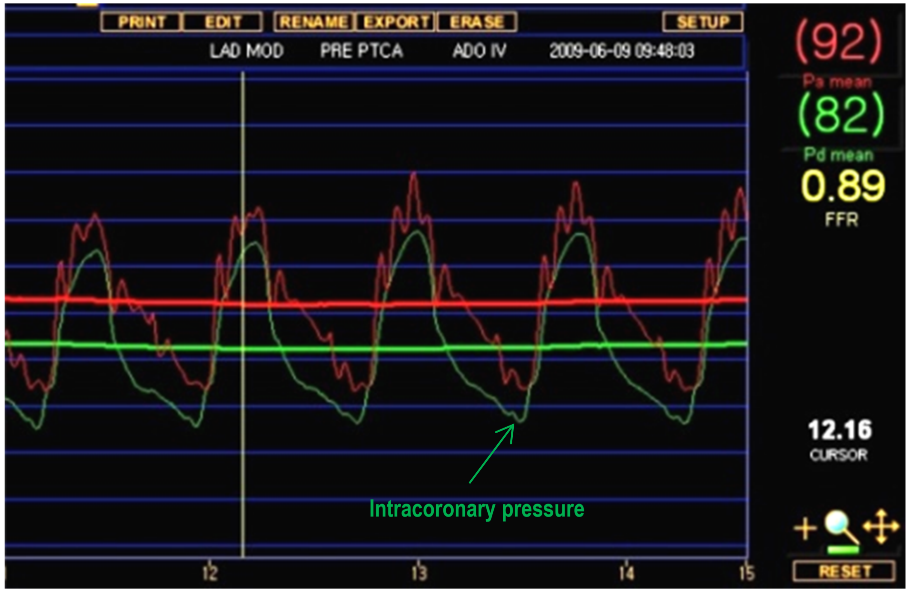


CT angiography: significant

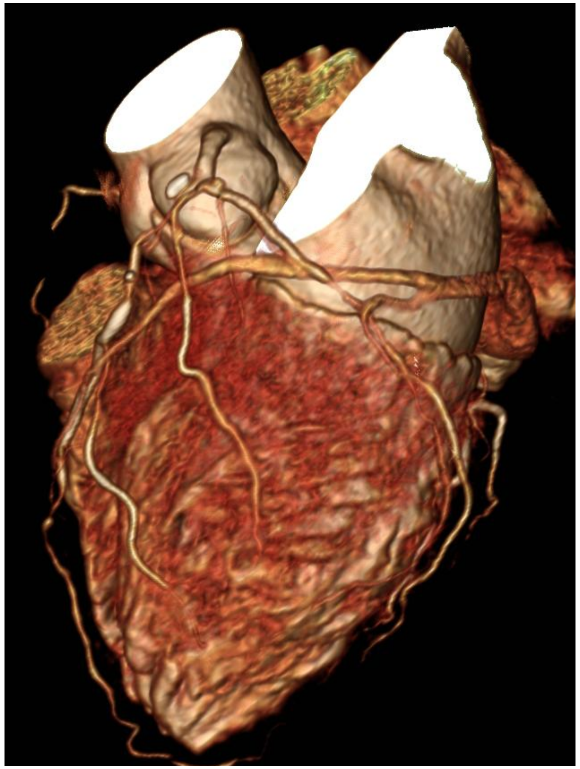
Angiography: significant

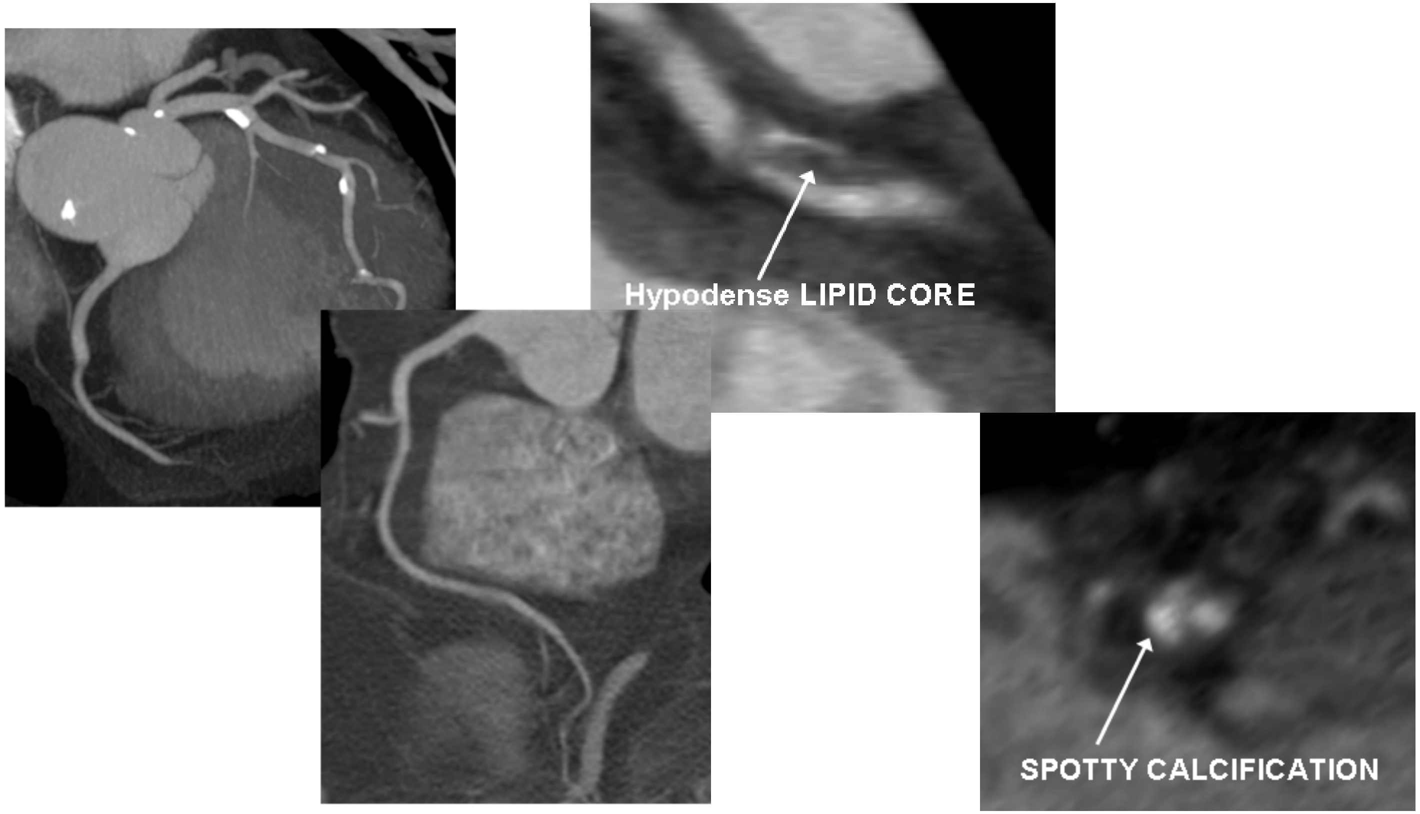
Intravascular ultrasound: significant

Pressure drop by LAD stenosis: 11%



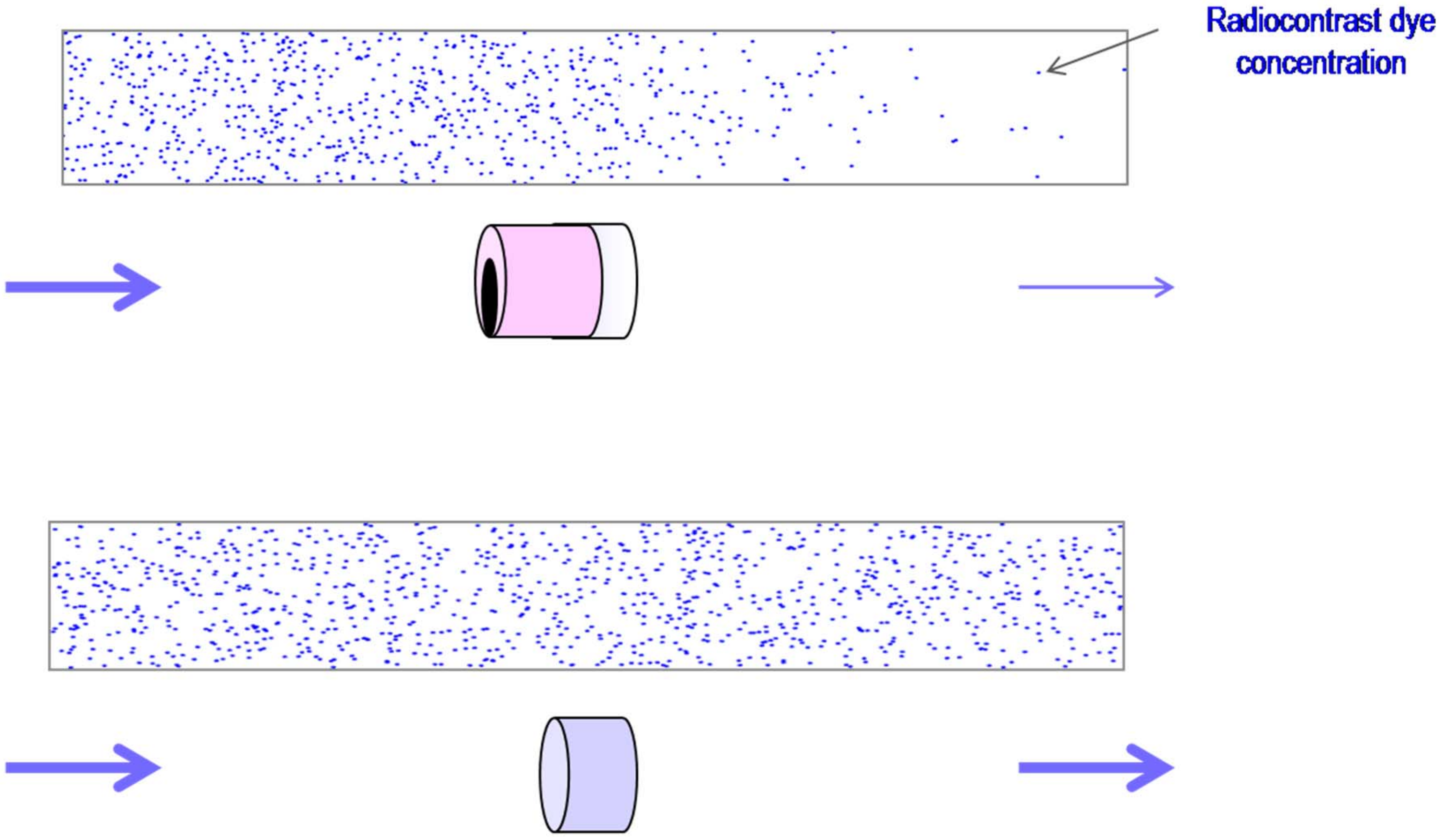
Can CCTA provide hemodynamic information?





- Quality of FLOW: wall shear stress, OSI…..
- Quantity of FLOW: **flow velocity**, pressure…..

Relation between Stenosis, Flow speed, and Density



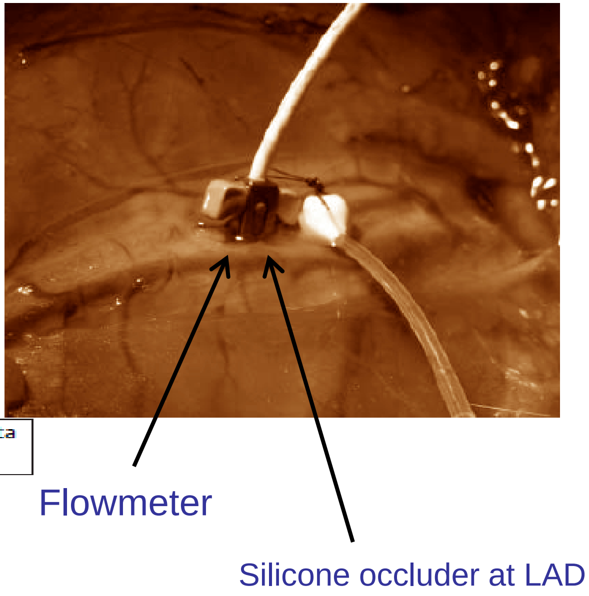
Poiseuille's law:

$$\text{Blood flow} = \pi \times \text{radius}^4 \times \text{difference in pressure}/8 \times \text{viscosity} \times \text{length}$$

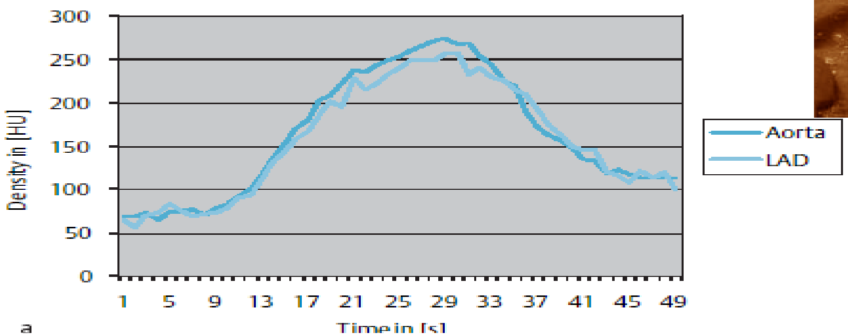
Courtesy of Jin-Ho Choi, MD, Samsung Medical Center

CT time-density curve vs. Flow

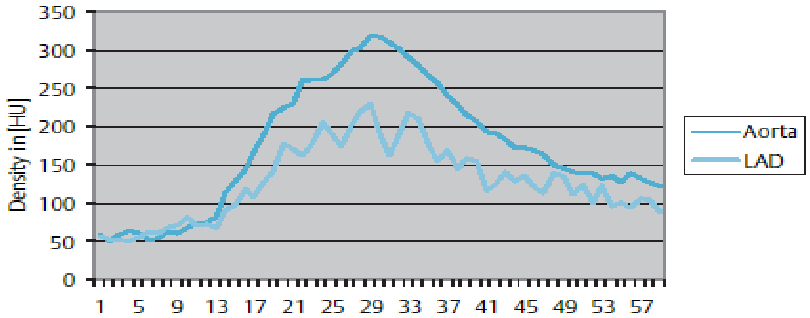
Animal study



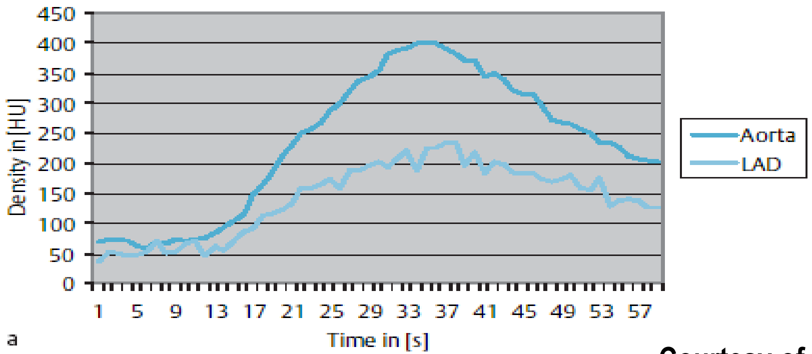
Flow = 100%



Flow = 43%



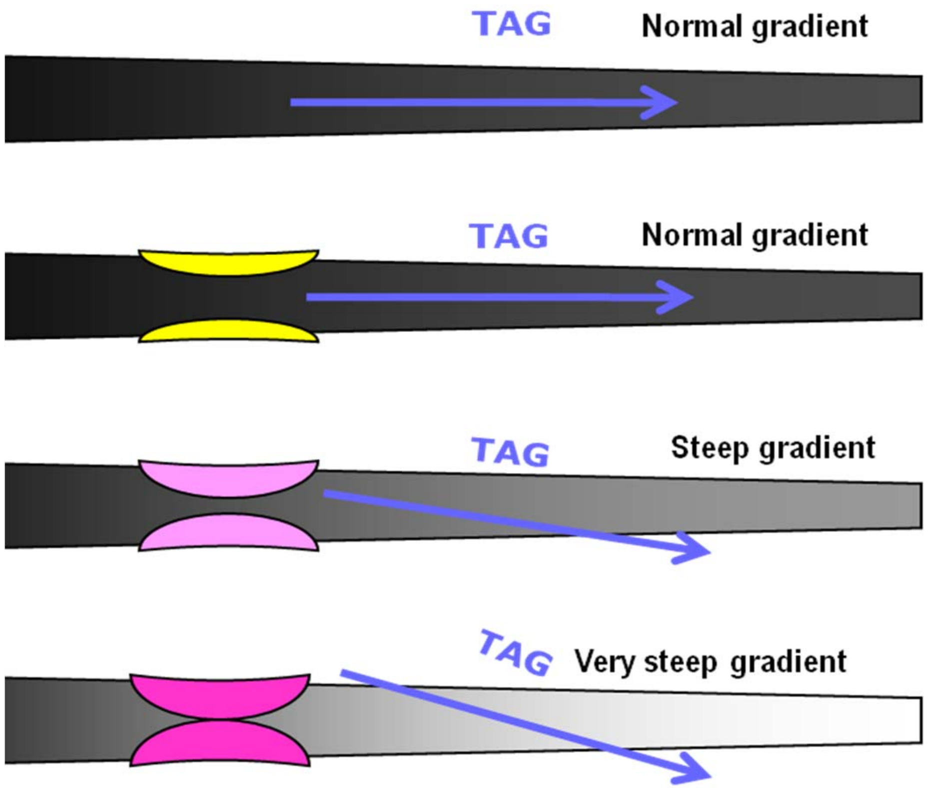
Flow = 10%

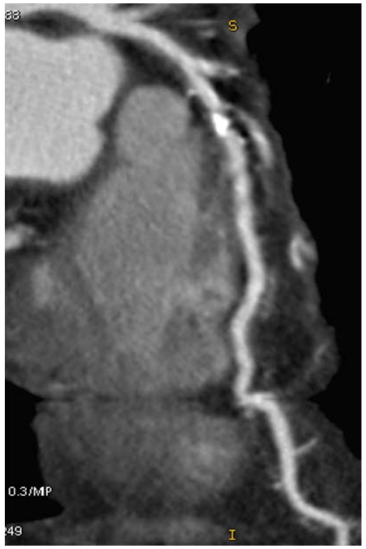


Courtesy of Jin-Ho Choi, MD, Samsung Medical Center

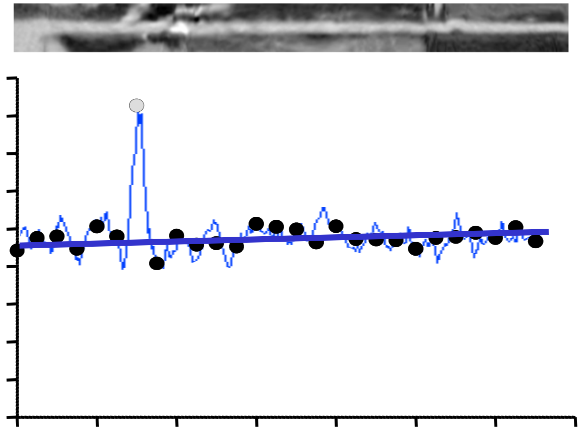
Transluminal Attenuation Gradient (TAG)

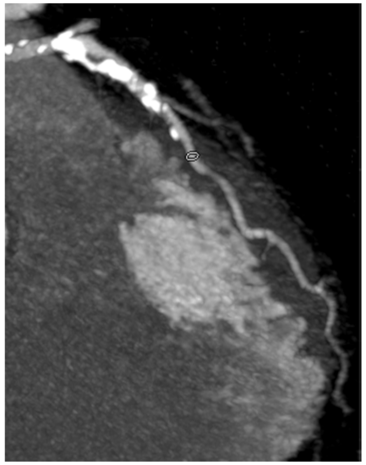
TAG = ΔHU / vessel axial length (mm)



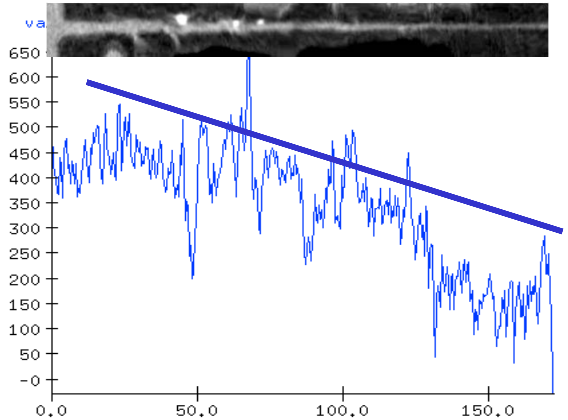


TAG = 1.42 (HU/10mm)





TAG = -15.42 (HU/10mm)



Courtesy of Jin-Ho Choi, MD, Samsung Medical Center

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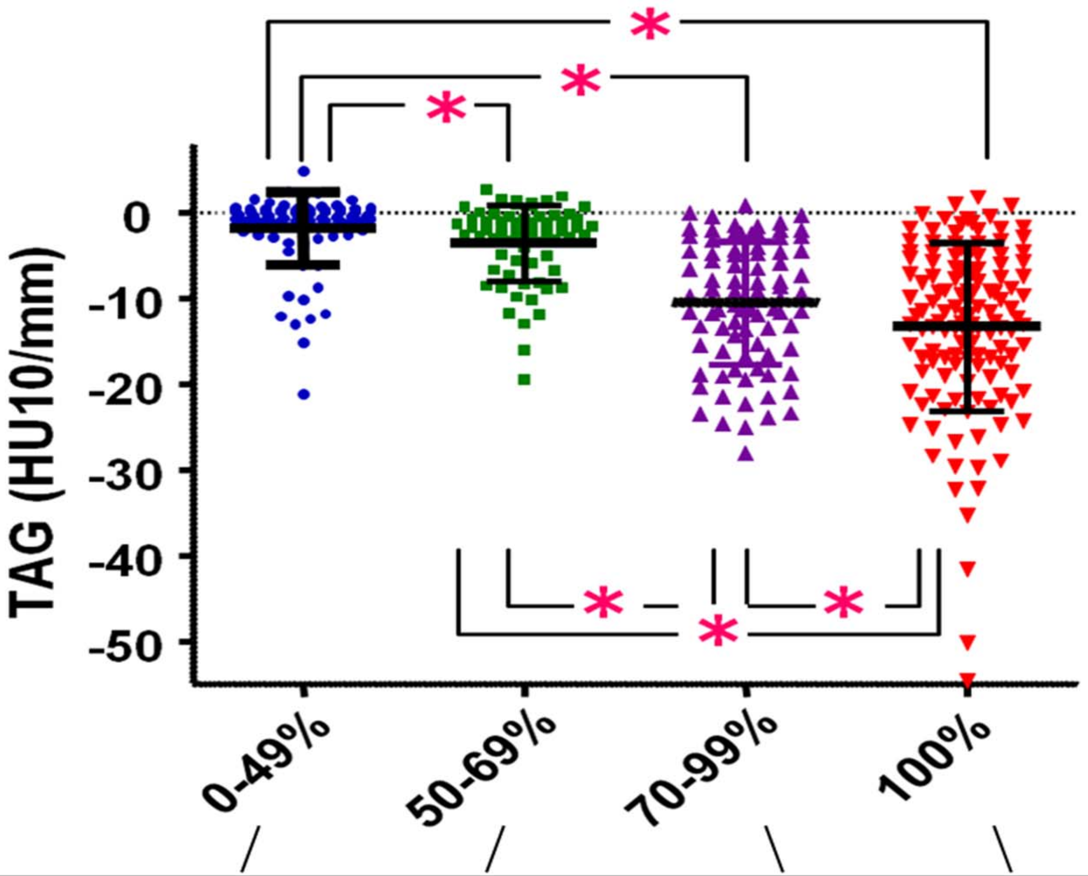
Transluminal Attenuation Gradient (TAG)

TAG = ΔHU / vessel axial length (mm)

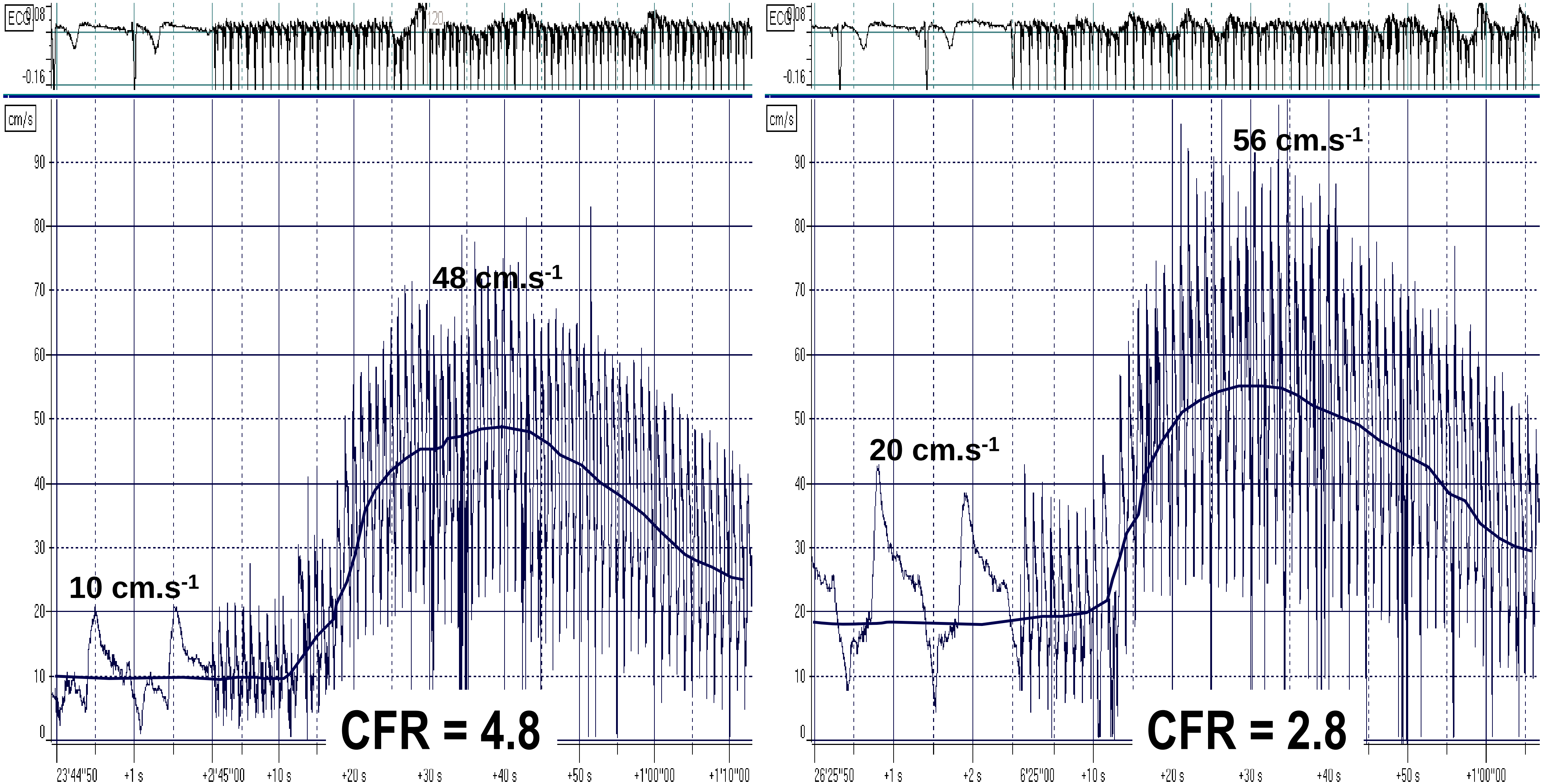


N	84	68	87	131
TAG (HU/10mm)	-1.91±4.25	-3.54±4.43	-10.55±7.20	-13.37±9.81

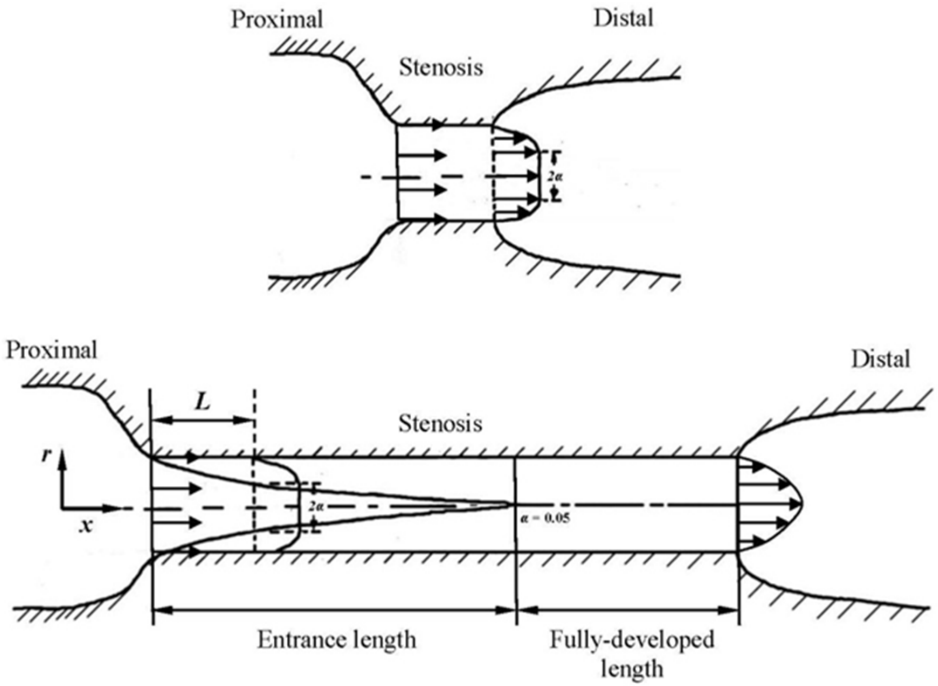
Courtesy of Jin-Ho Choi, MD, Samsung Medical Center

Pitfalls of Coronary Flow Velocity

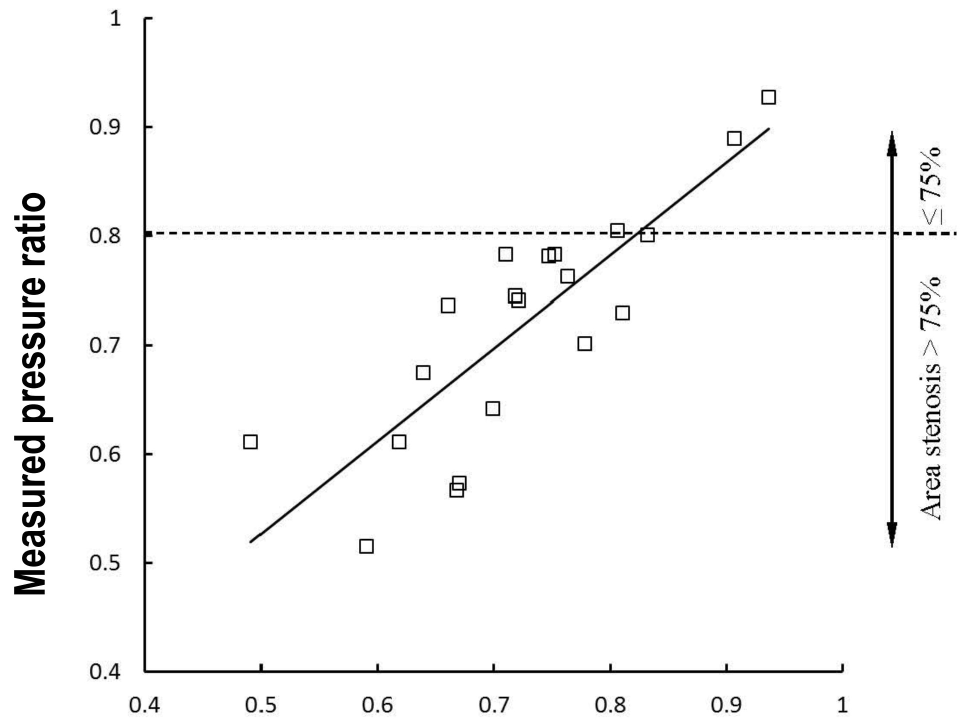
Variation of “Resting Flow (Velocity)”



Estimation of pressure changes from geometry

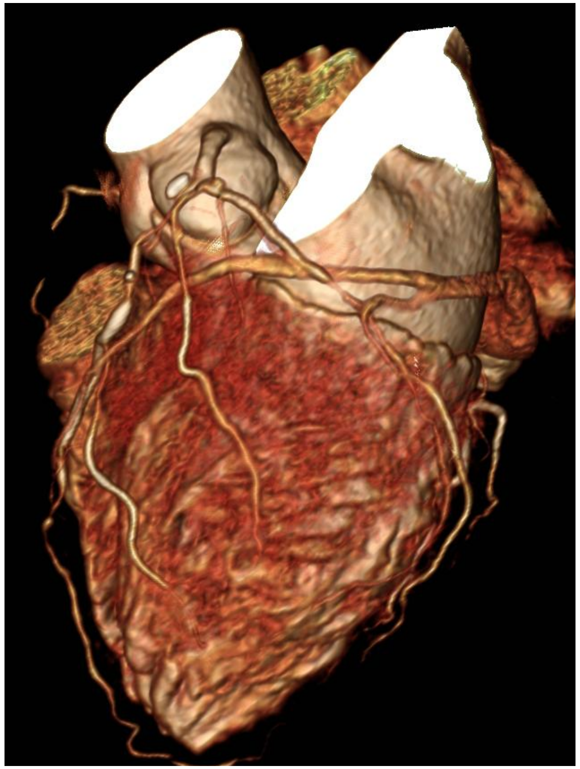


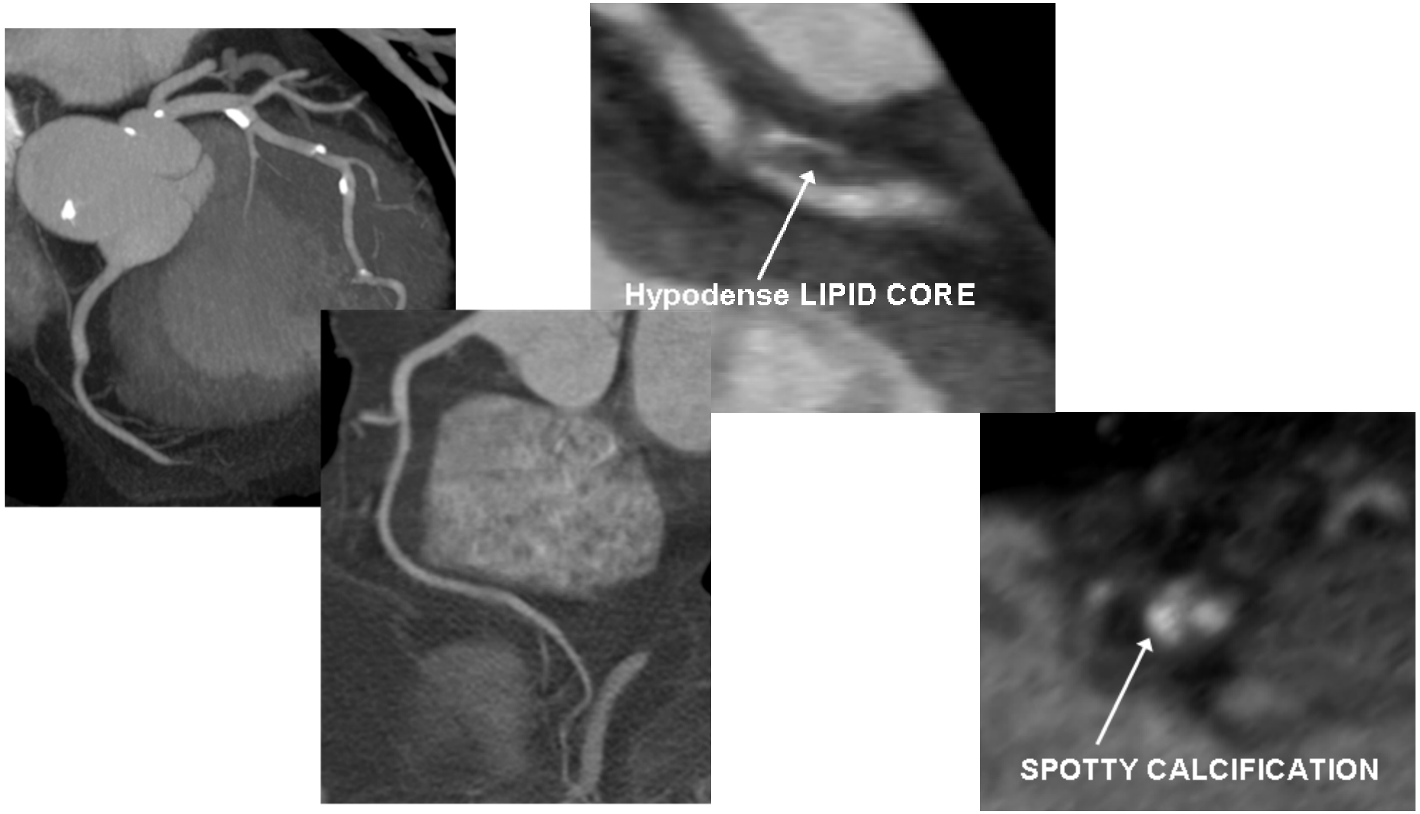
$$\Delta P = \Delta P_{convective} + \Delta P_{diffusive} + \Delta P_{expansion}$$



Courtesy of Professor Kassab, Purdue University

Can CCTA provide hemodynamic information?

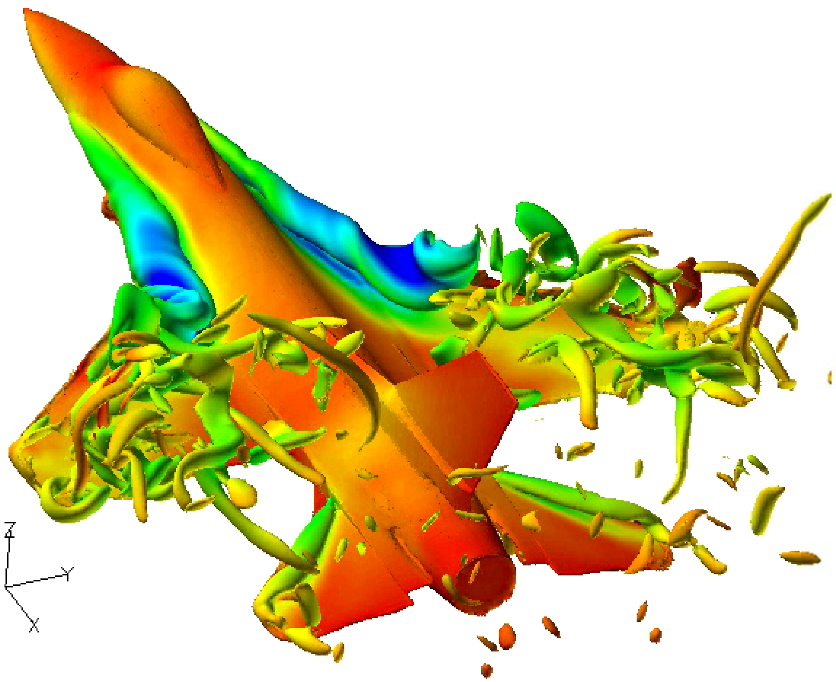




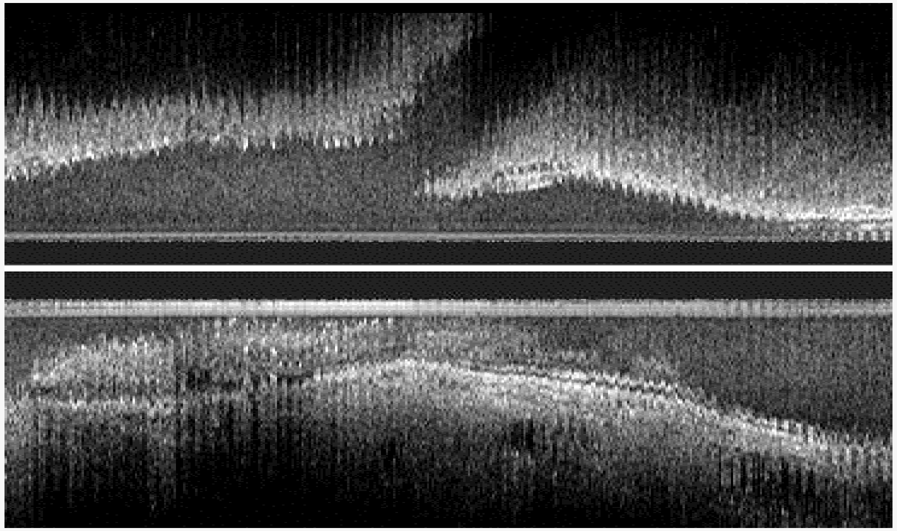
- Quality of FLOW: **wall shear stress, OSI…..**
- Quantity of FLOW: **flow velocity, pressure…..**

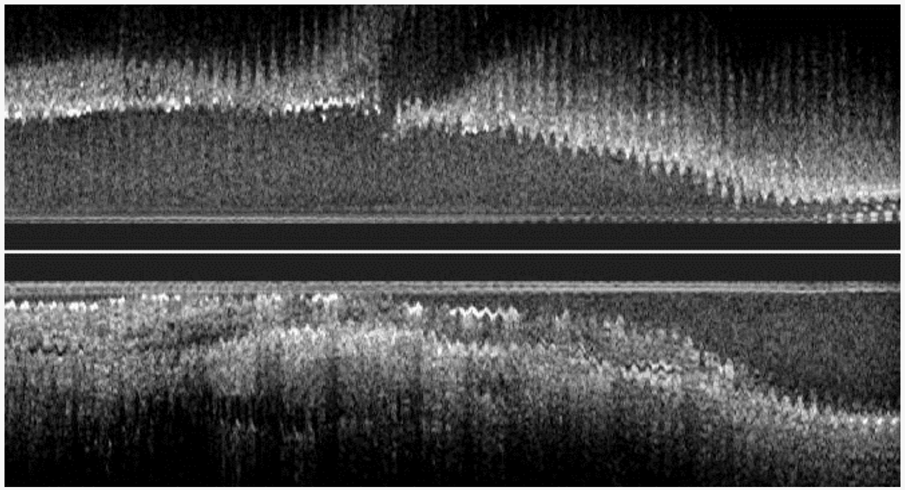
Computational Fluid Dynamics (CFD)

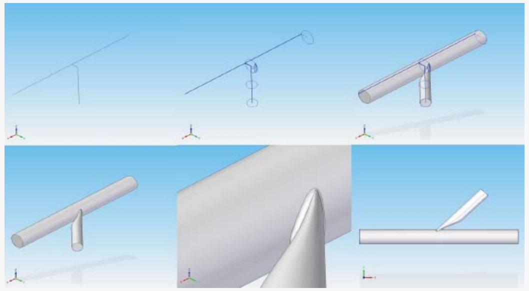
- Computational fluid dynamics (CFD) quantifies fluid pressure and velocity, based on physical laws of mass conservation and momentum balance
- CFD is widely used in the aerospace and automotive industries for design and testing

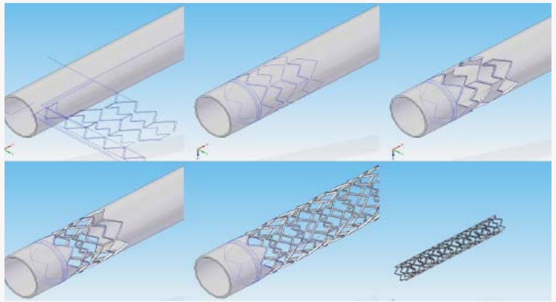


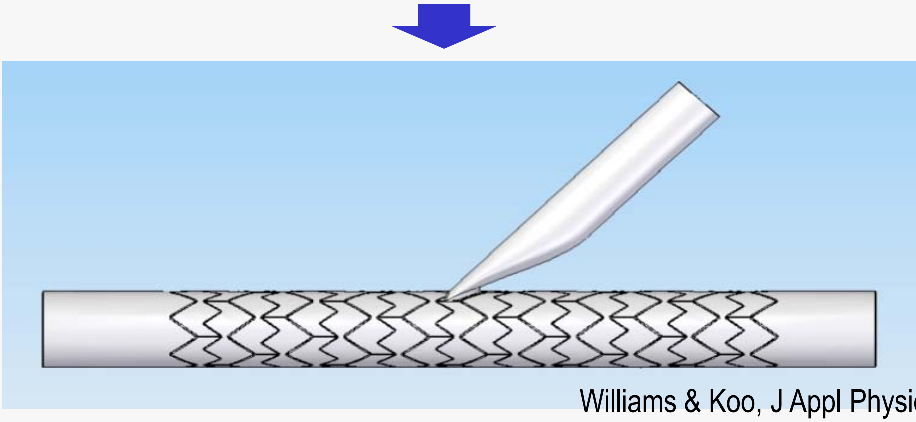
Application of CFD to coronary artery disease: Modeling







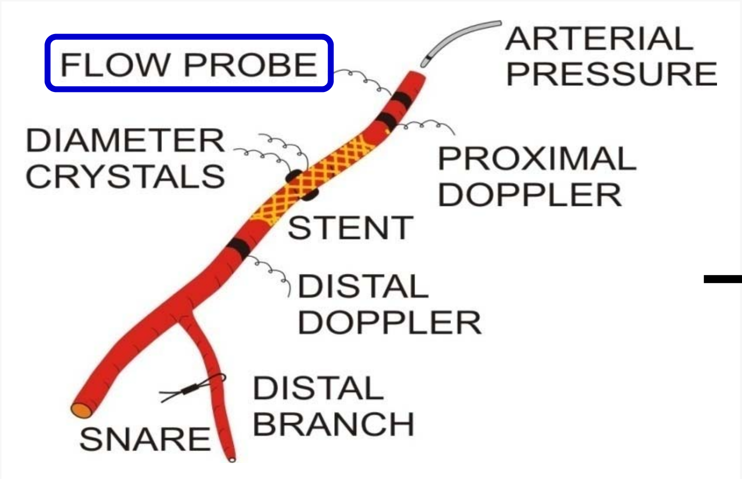




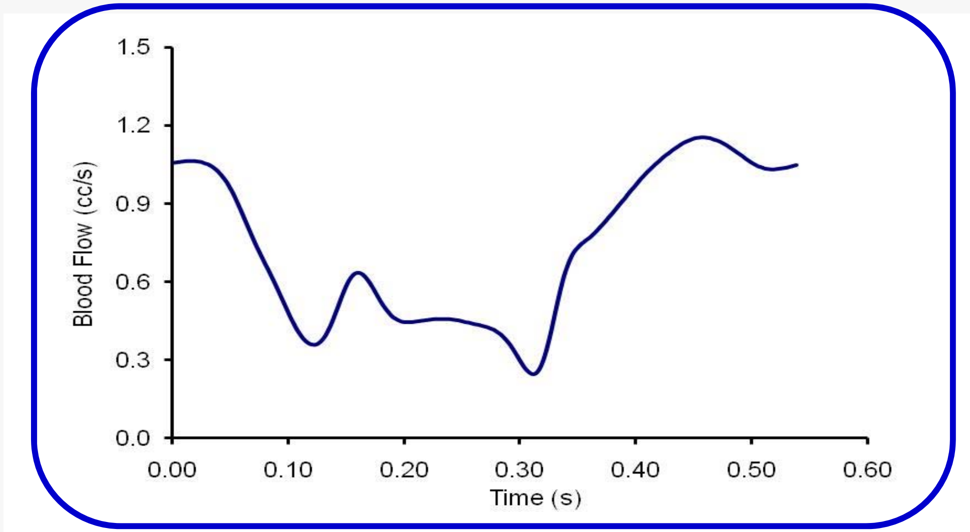
Williams & Koo, J Appl Physiol 2010

Inflow waveforms and estimates of downstream coronary vascular resistance obtained from previous investigations

Inlet

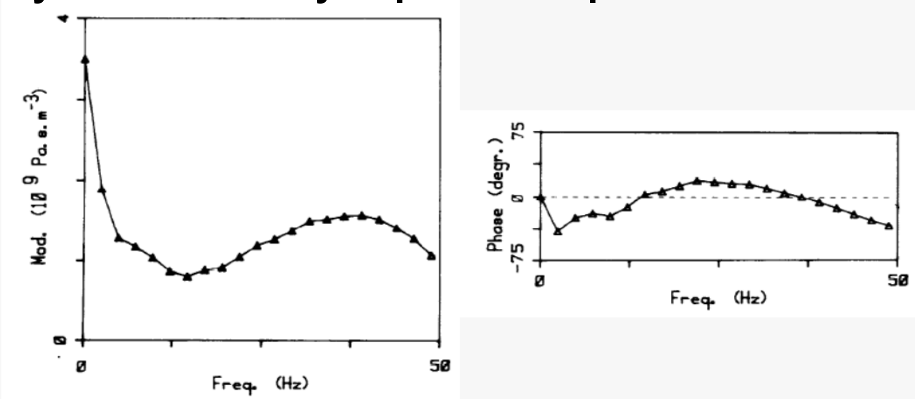


LaDisa et al. J Appl Physiol 93: 1939–46, 2002.

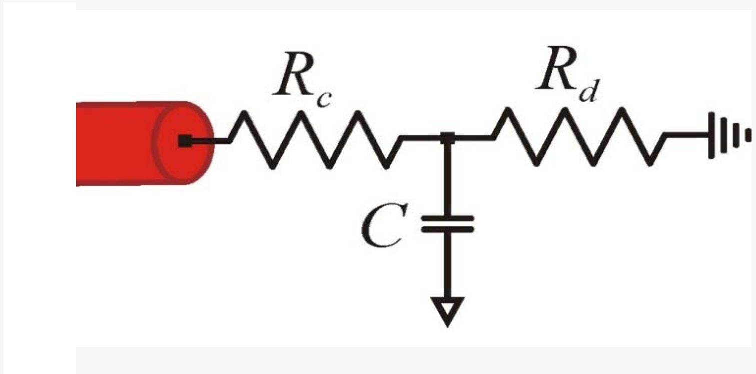


Outlets

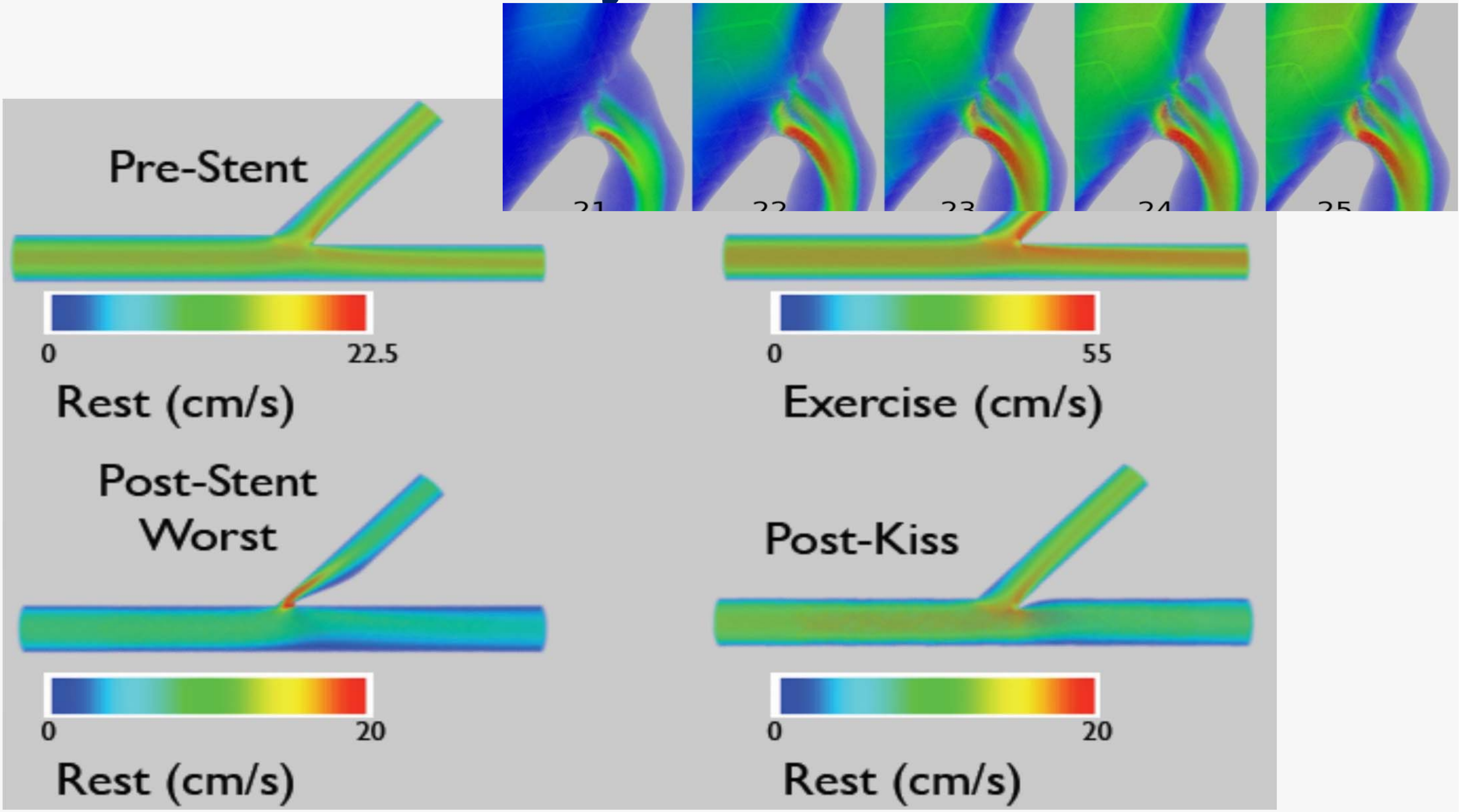
Systolic coronary impedance spectra



Van Huis et al. AJP - Heart. 253 (22): H317-H324, 1987.



Velocity Profiles



Williams & Koo, J Appl Physiol 2010

Stent cross over & Distal MB over-expansion

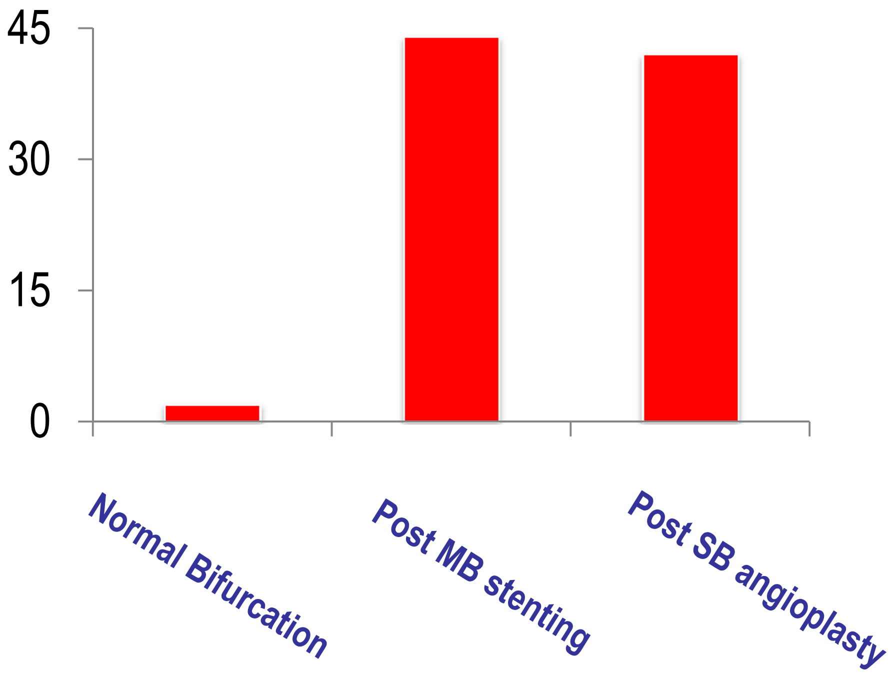
Time Averaged Wall Shear Stress

Shear stress distribution

Post MB stenting

Post SB angioplasty

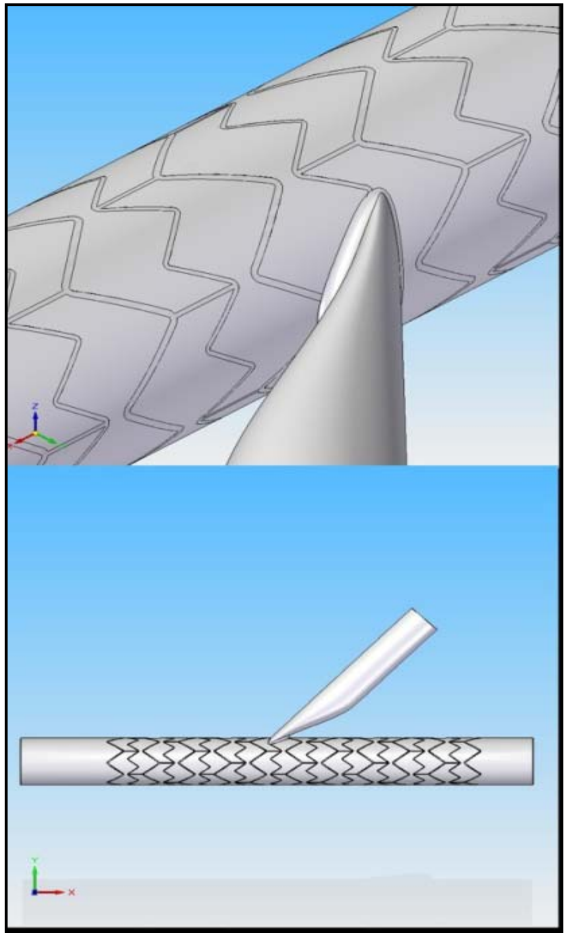
% area of low WSS (< 4dyne/cm^2)



Williams & Koo, J Appl Physiol 2010

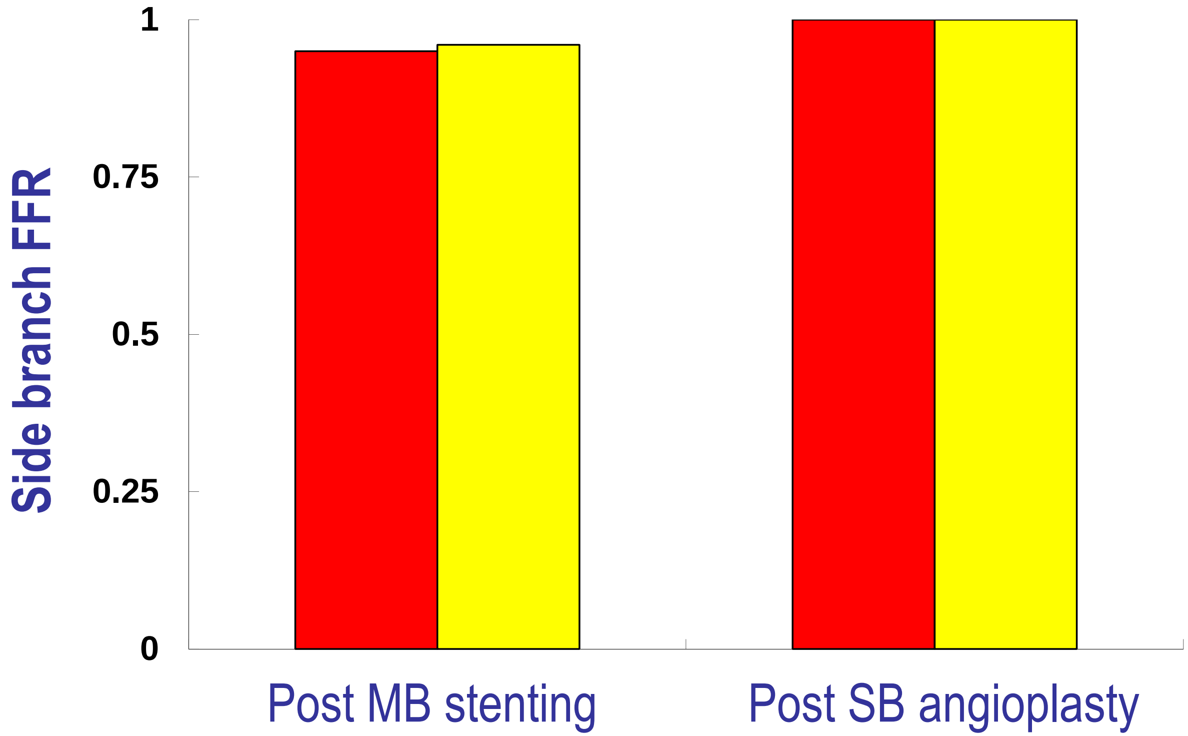
Stent cross over & Distal MB over-expansion

Fractional flow reserve of Side branch



Post MB stenting

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



Williams & Koo, J Appl Physiol 2010

Clinical relevance of “abnormal flow”?

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ISSN 0735-1097/10/$36.00
doi:10.1016/j.jacc.2010.01.021
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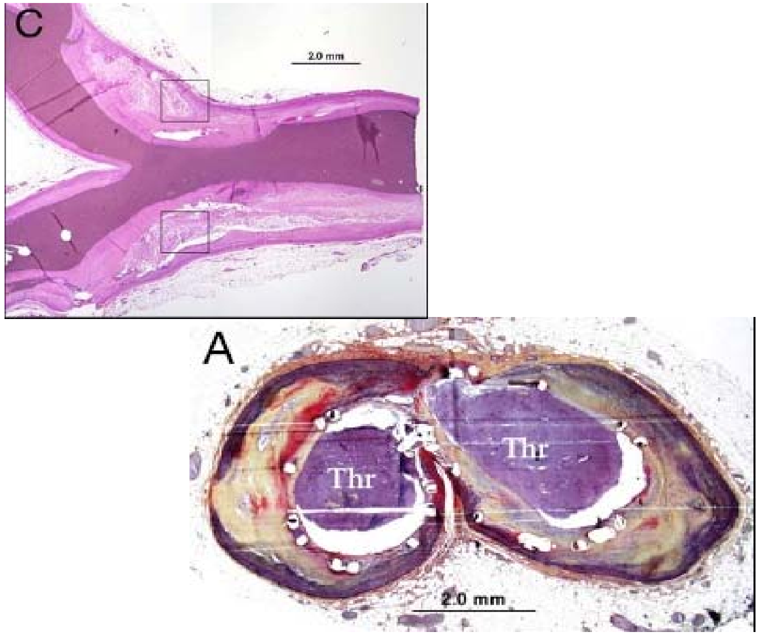
Pathological Findings at Bifurcation Lesions

The Impact of Flow Distribution on Atherosclerosis and Arterial Healing After Stent Implantation

Gaku Nakazawa, MD,* Saami K. Yazdani, PHD,* Aloke V. Finn, MD,† Marc Vorpahl, MD,* Frank D. Kolodgie, PHD,* Renu Virmani, MD*
Gaithersburg, Maryland; and Atlanta, Georgia



Limitations of current CFD analyses

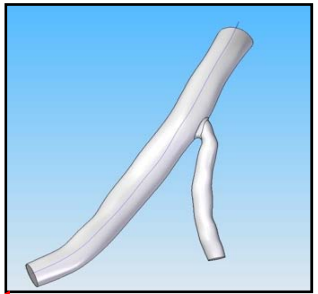
- Simple models, not patient-specific
- Not completely reflects human coronary circulation
- No established clinical relevance

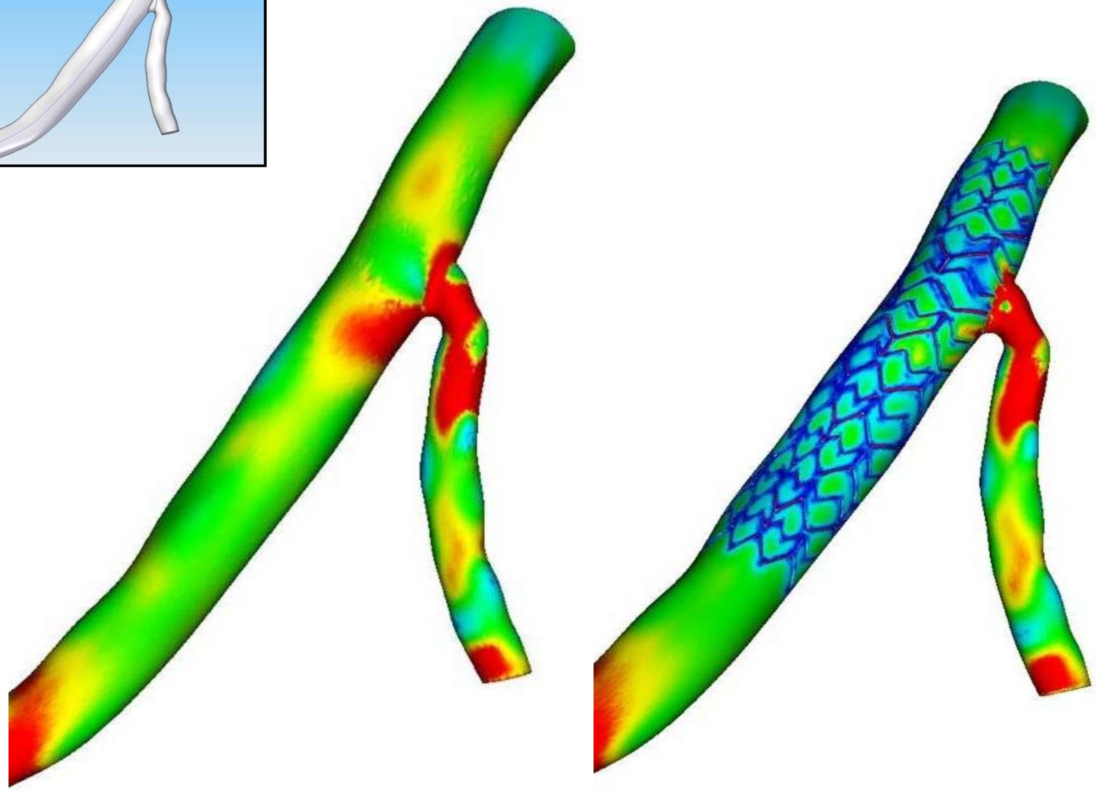
Patient-specific modeling using CCTA

Computational Model based on CCTA

3-D anatomic model from CCTA

No additional imaging
No additional medications



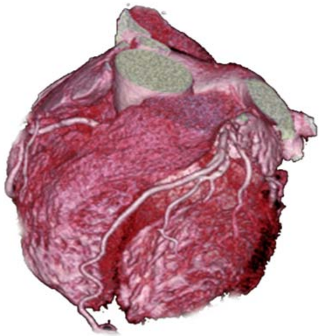


Koo & LaDisa, 2010

Patient-specific non-invasive coronary hemodynamic assessment

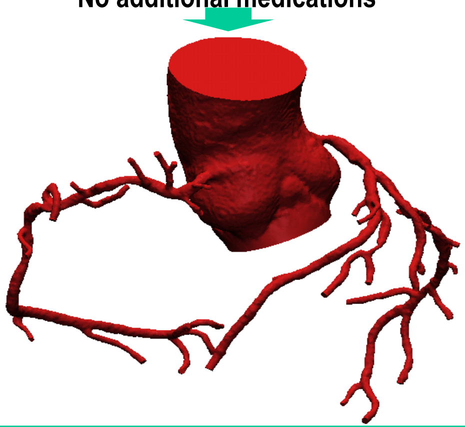
Computational Model based on CCTA

3-D anatomic model from CCTA



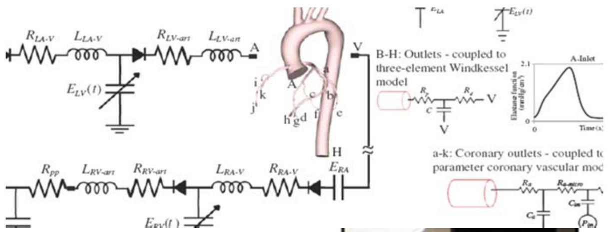
No additional imaging

No additional medications

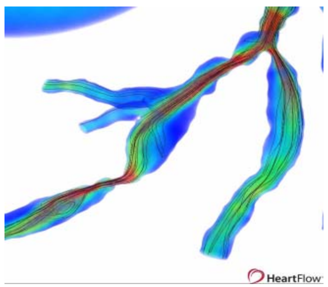


Blood Flow Solution

Blood flow equations solved on supercomputer

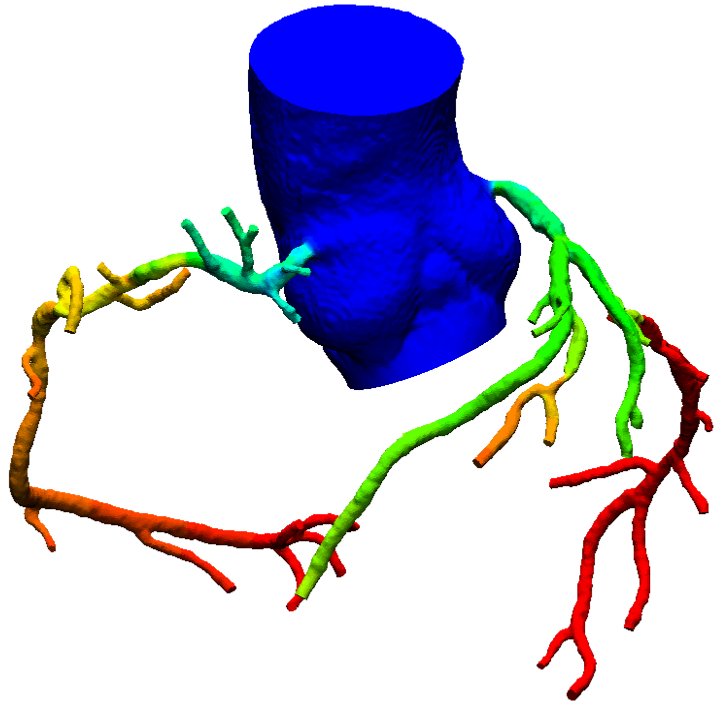


$$\rho \bar{v}_{,t} + \rho \bar{v} \cdot \nabla \bar{v} = -\nabla p + \nabla \cdot \underline{\tau}$$
$$\nabla \cdot \bar{v} = 0$$



Physiologic models

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



How is FFR computed from static coronary CT?

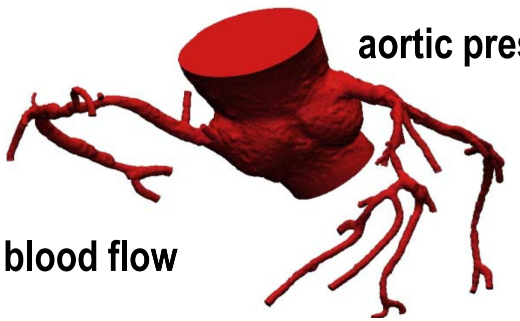
A novel example: Flow through the coronary arteries

Input data:

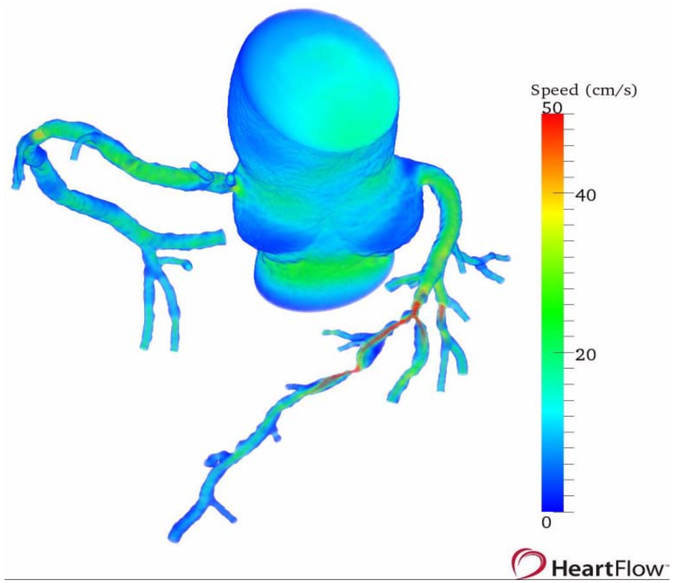
- Geometry – extracted from CCTA anatomic data
- Boundary conditions
  - Resting coronary blood flow (calculated from myocardial mass)
  - Mean blood pressure (estimated from brachial artery pressure)
  - Coronary microcirculatory resistance (derived from morphometry data)
- Fluid properties – viscosity and density of blood

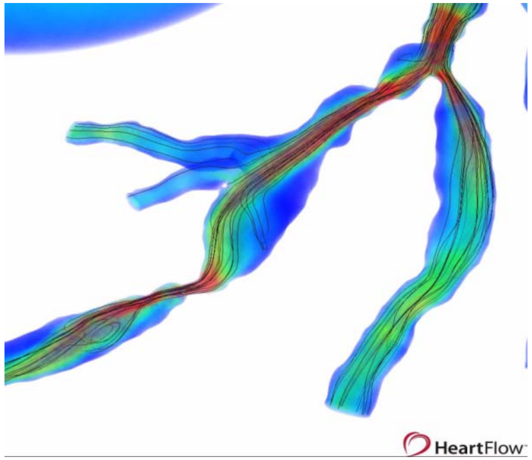
Calculated data:

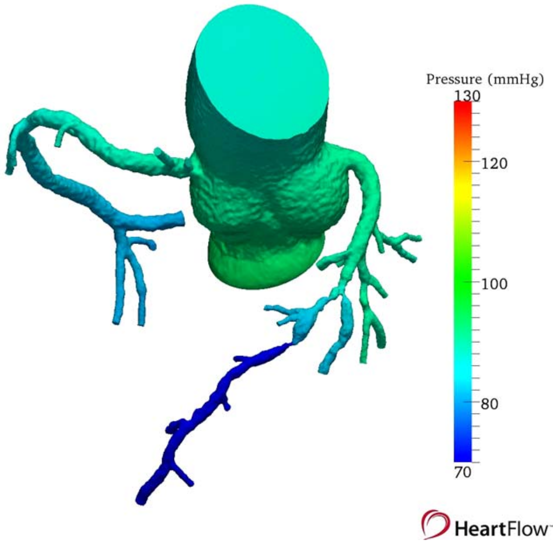
- Velocity and pressure of blood in coronary arteries
- FFR, CFR, etc…



Patient-specific CFD analysis



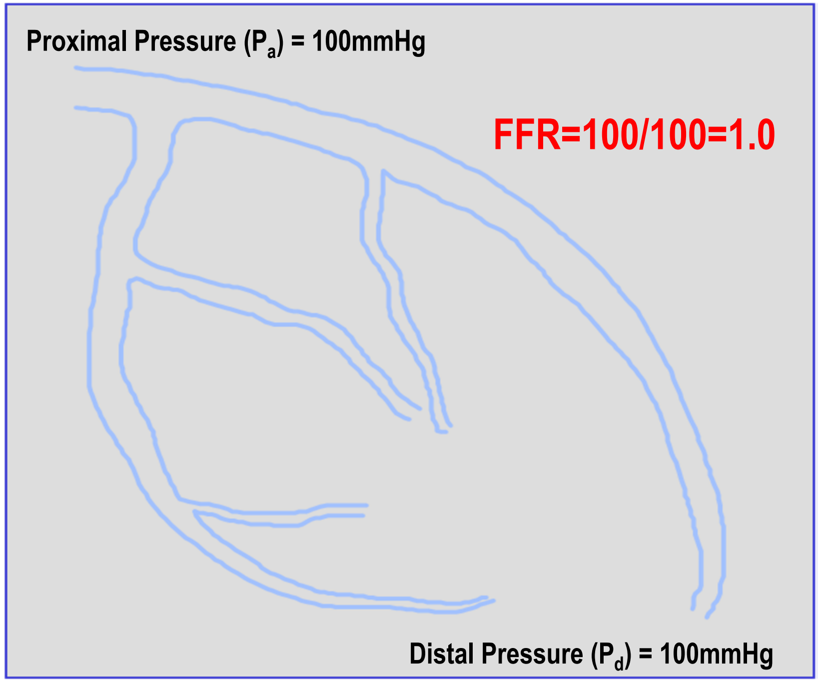


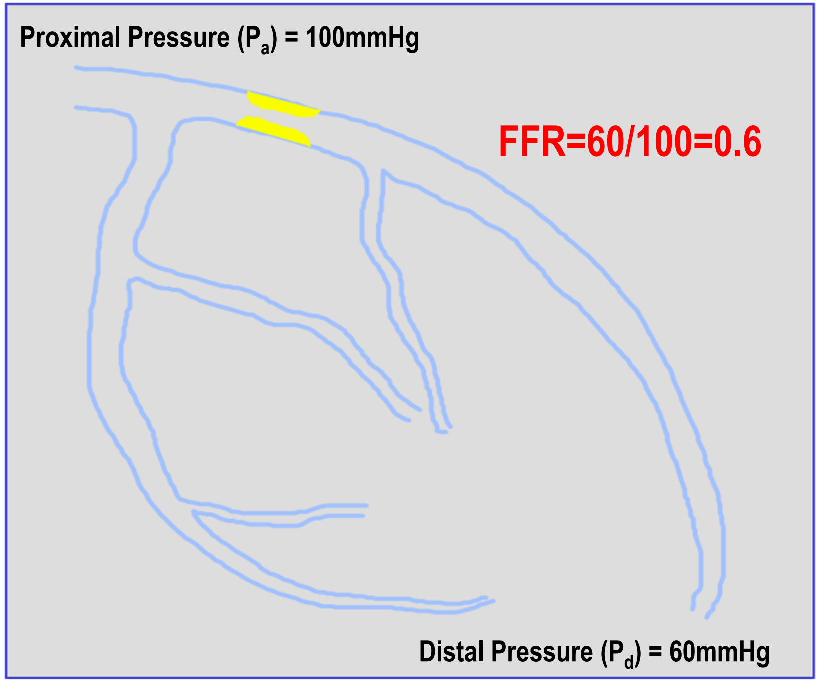


Koo BK, European Bifurcation Club 2010

Estimation of flow by pressure: Fractional flow reserve (FFR)

$$FFR = \frac{\text{Maximum flow in presence of stenosis}}{\text{Normal maximum flow}} = \frac{Q^{S}_{max}}{Q^{N}_{max}} = \frac{(Pd\text{-}Pv)/R}{(Pa\text{-}Pv)/R} = \frac{\text{Distal Pr } (P_d)}{\text{Proximal Pr } (P_a)}$$



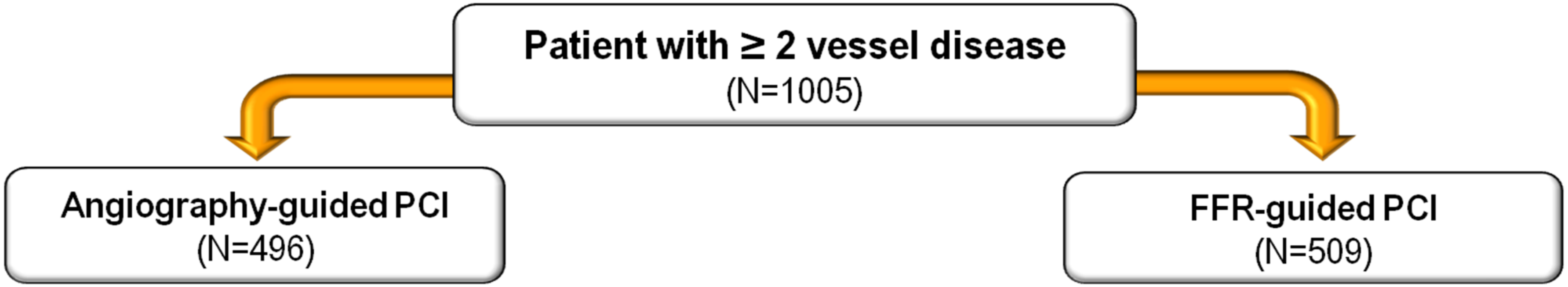


Not significant		Significant stenosis

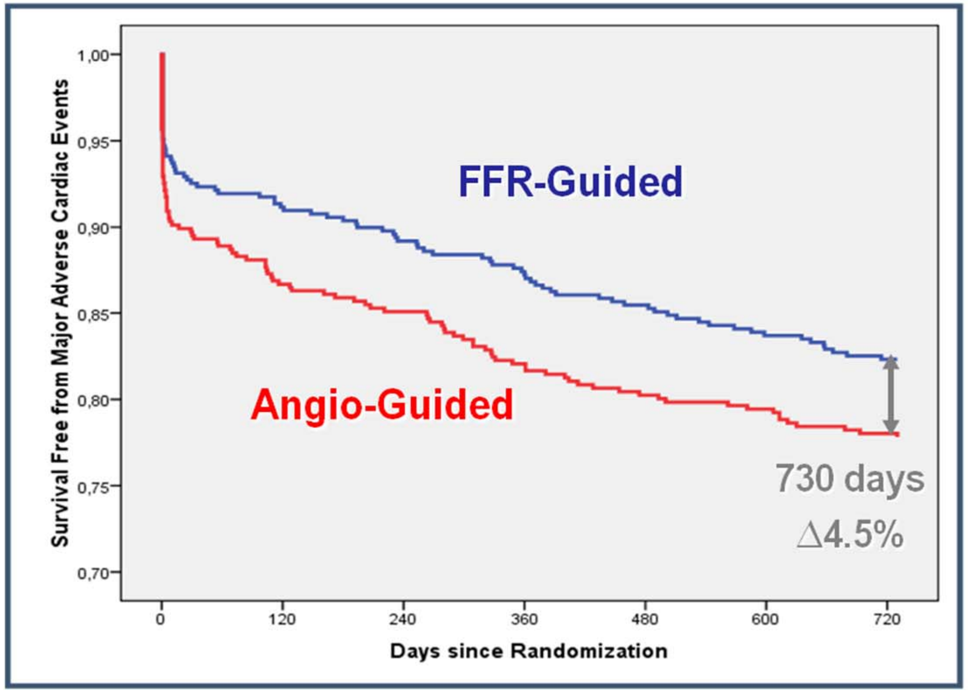
FFR 1.0 0.80 0.75 0

PCI: percutaneous coronary intervention

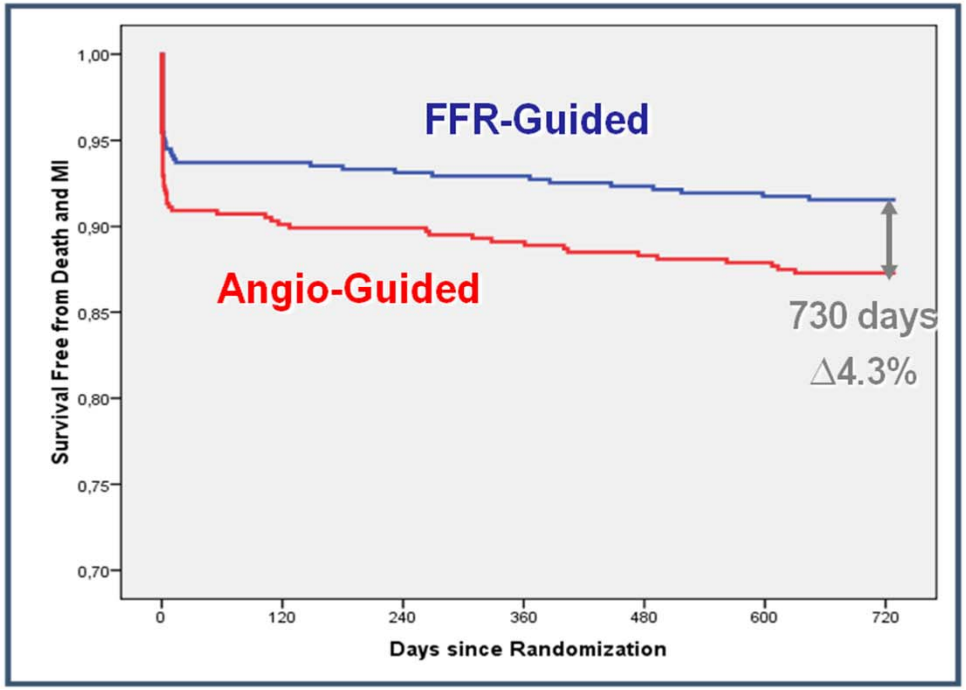
FAME study



2 Year MACE-free Survival



2 Year Death/MI-free Survival



Tonino, et al. NEJM 2009; Pijls, et al. JACC 2010

FFR is good for the patients and (relatively) simple……….

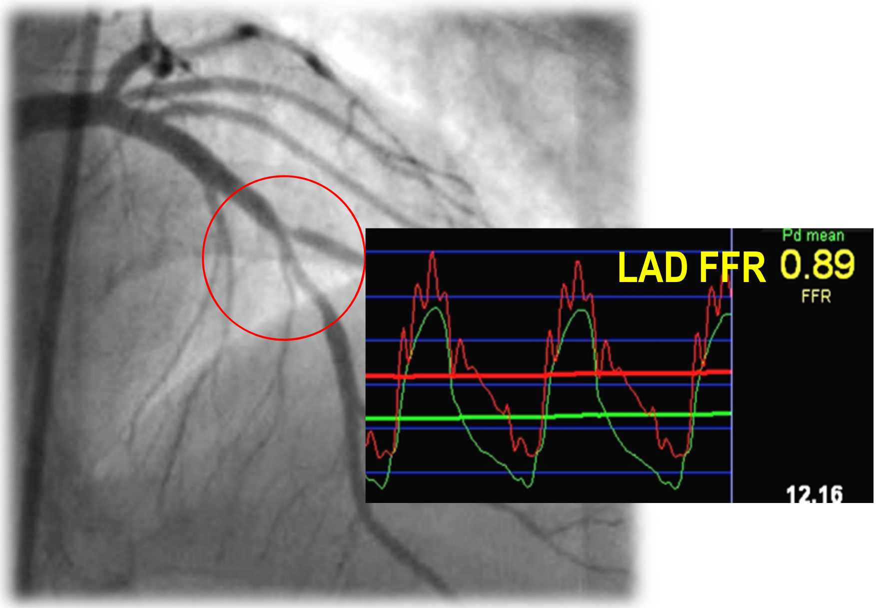
European Heart Journal (2010) 31, 2501–2555
doi:10.1093/eurheartj/ehq277
ESC/EACTS GUIDELINES

Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

	Class[a]	Level[b]
FFR-guided PCI is recommended for detection of ischaemia-related lesion(s) when objective evidence of vessel-related ischaemia is not available.	I	A
DES[d] are recommended for reduction of restenosis/re-occlusion, if no contraindication to extended DAPT.	I	A
Distal embolic protection is recommended during PCI of SVG disease to avoid distal embolization of debris and prevent MI	I	B

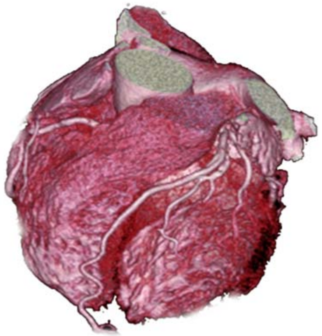
But, requires invasive procedure and expensive…… cannot provide 3D anatomical information….



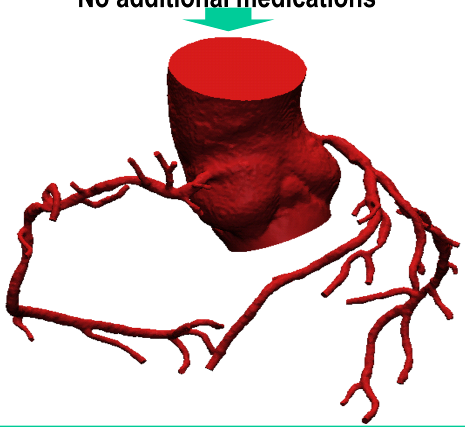
Patient-specific non-invasive FFR using CT & CFD

Computational Model based on CCTA

3-D anatomic model from CCTA

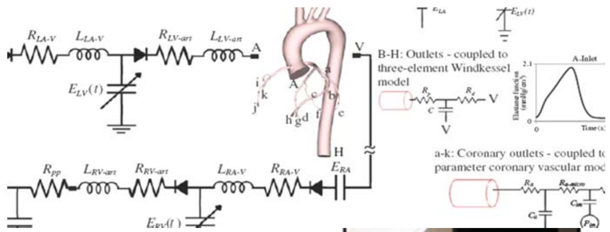


No additional imaging
No additional medications

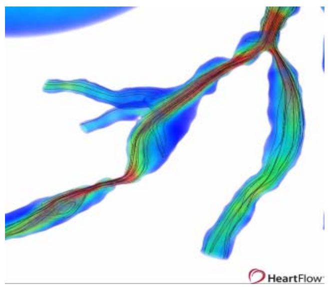


Blood Flow Solution

Blood flow equations solved on supercomputer

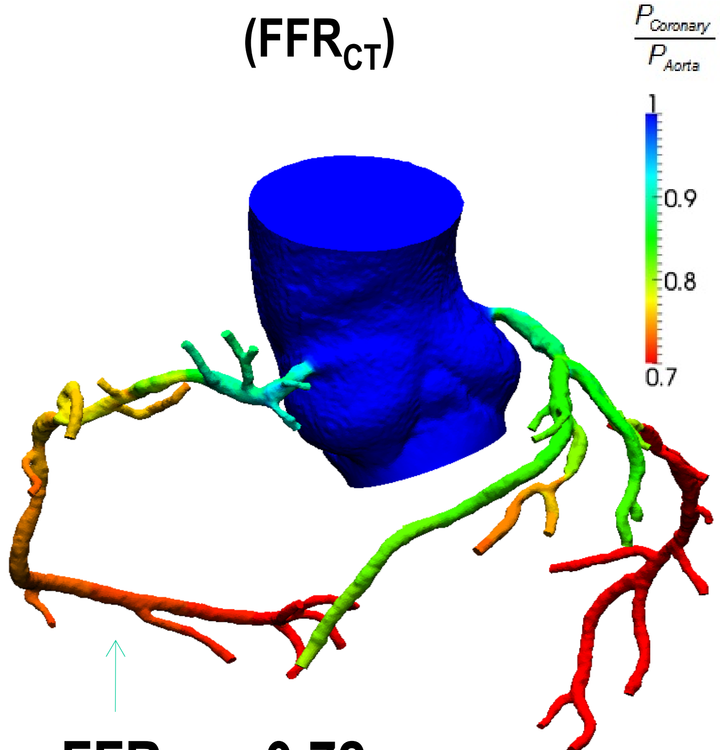


$$\rho \bar{v}_{,t} + \rho \bar{v} \cdot \nabla \bar{v} = -\nabla p + \nabla \cdot \underline{\tau}$$
$$\nabla \cdot \bar{v} = 0$$



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

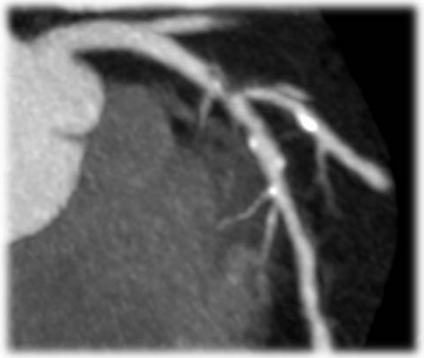
CT-derived computed FFR (FFR_{CT})



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

Case Examples

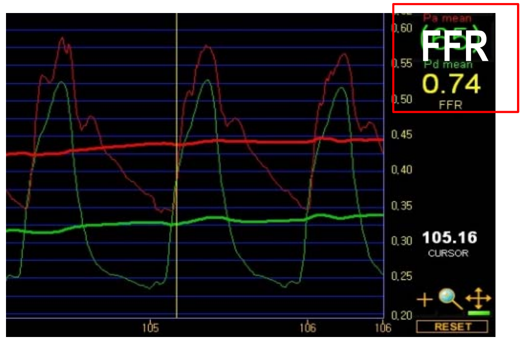
CCTA	FFR_{CT}	Invasive angiography	FFR



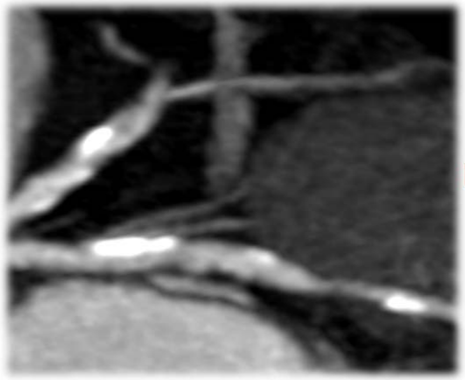
>50% diameter stenosis

FFR_{CT} 0.74 → ischemia

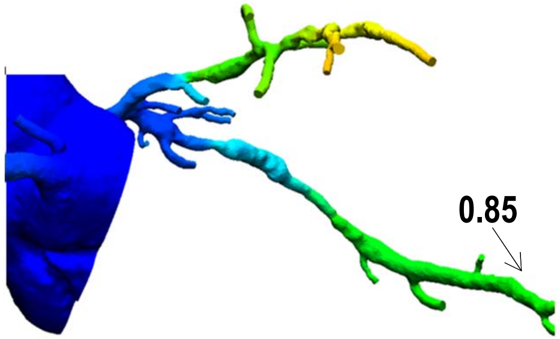
>50% diameter stenosis



FFR 0.74 → ischemia

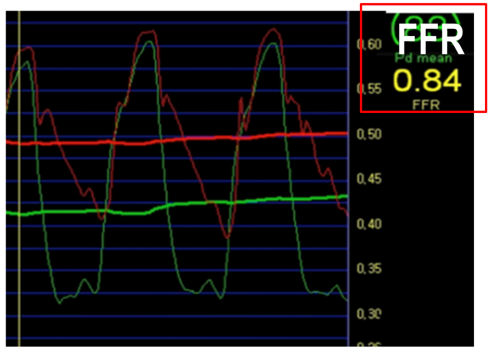


>50% diameter stenosis



FFR_{CT} 0.85 → no ischemia

>50% diameter stenosis



FFR 0.84 → no ischemia

First-in-Human study: DISCOVER-FLOW

Cardiac Imaging

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.

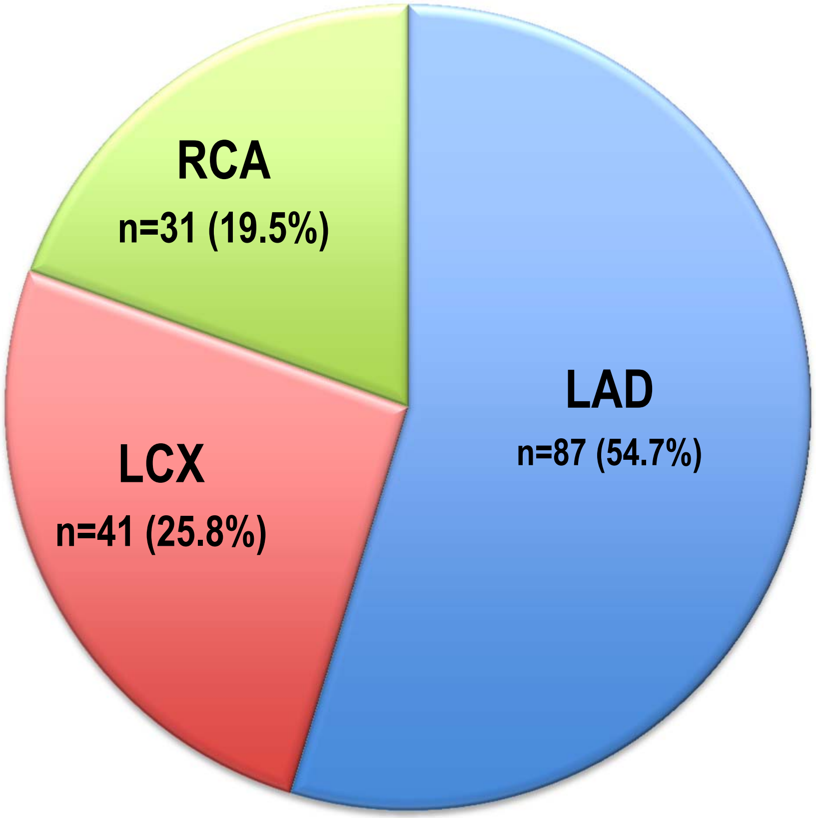
Results Fifty-six percent of patients had ≥1 vessel with FFR ≤0.80. On a per-vessel basis, the accuracy, sensitivity, specificity, positive predictive value, and negative predictive value were 84.3%, 87.9%, 82.2%, 73.9%, 92.2%, respectively, for FFR_{CT} and were 58.5%, 91.4%, 39.6%, 46.5%, 88.9%, respectively, 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; NCT01189331) (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

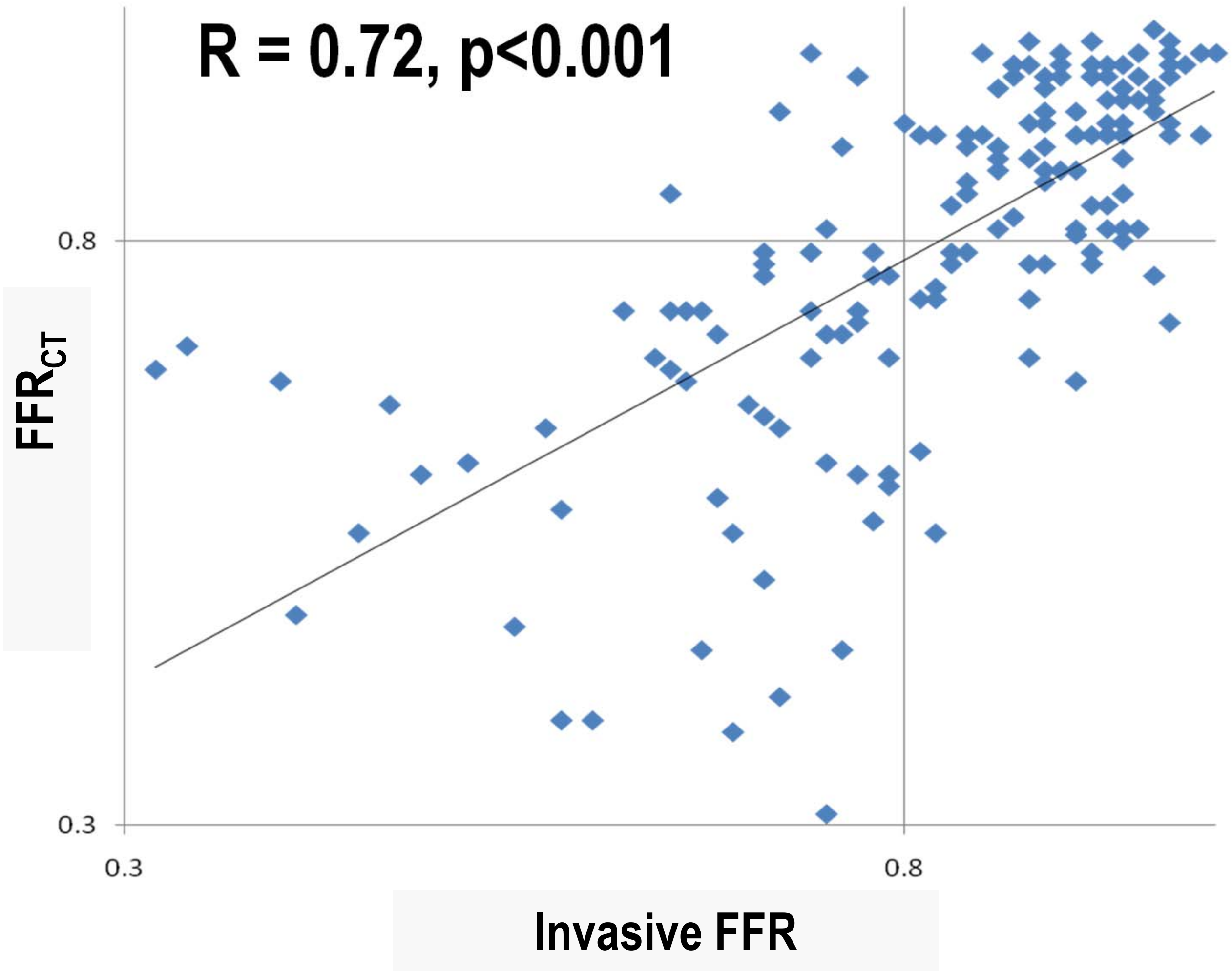
Variable	
Age	63 ± 9 yrs
Male	72 %
Hypertension	65 %
Diabetes	26 %
Current smoker	36 %
BMI	26 ± 4
Prior MI	17 %
Prior PCI	16 %
LV ejection fraction	62 ± 6 %



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

Invasive FFR vs. Non-invasive FFR_{CT}

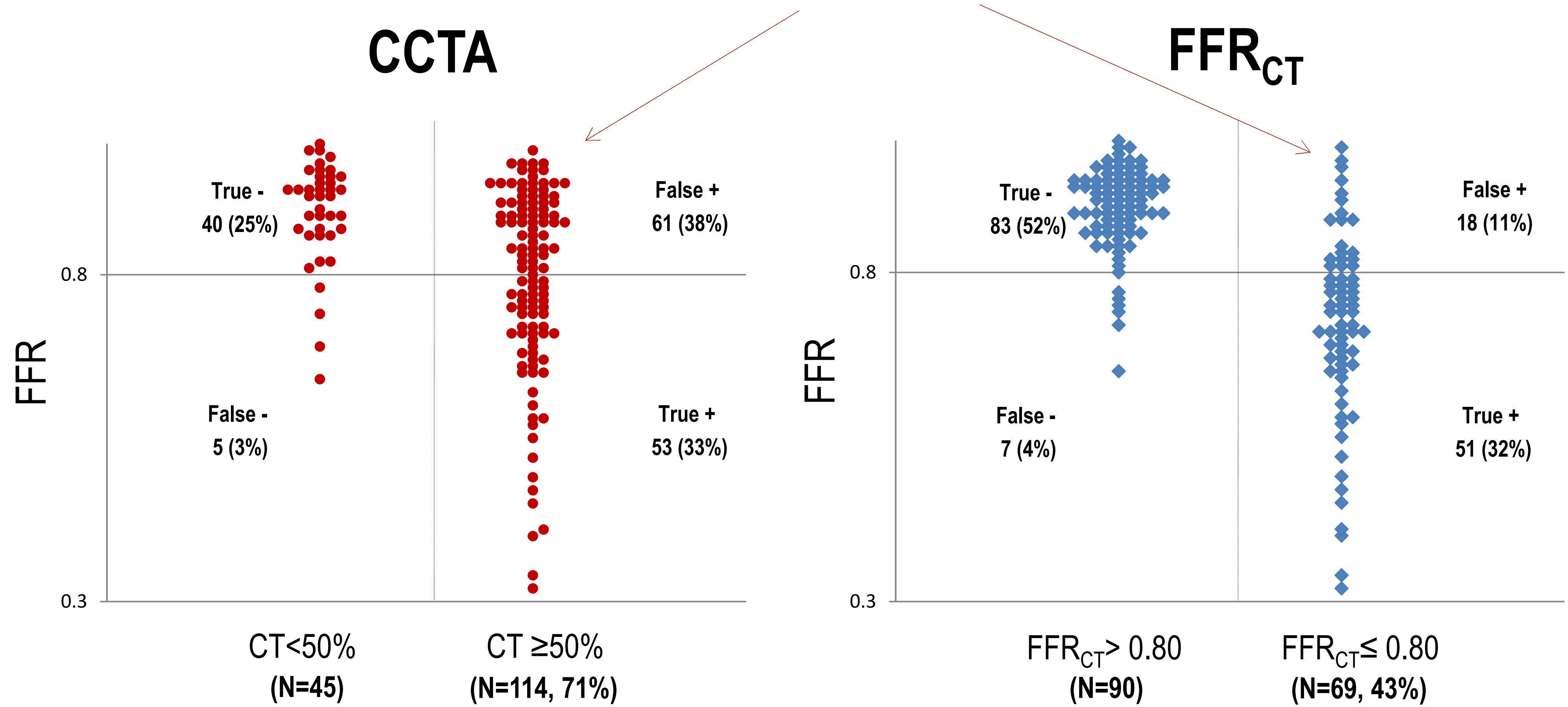
FFR	0.82 ± 0.13
FFR_{CT}	0.80 ± 0.14
△	0.02 ± 0.12



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

FFR vs. CT and FFR_{CT}

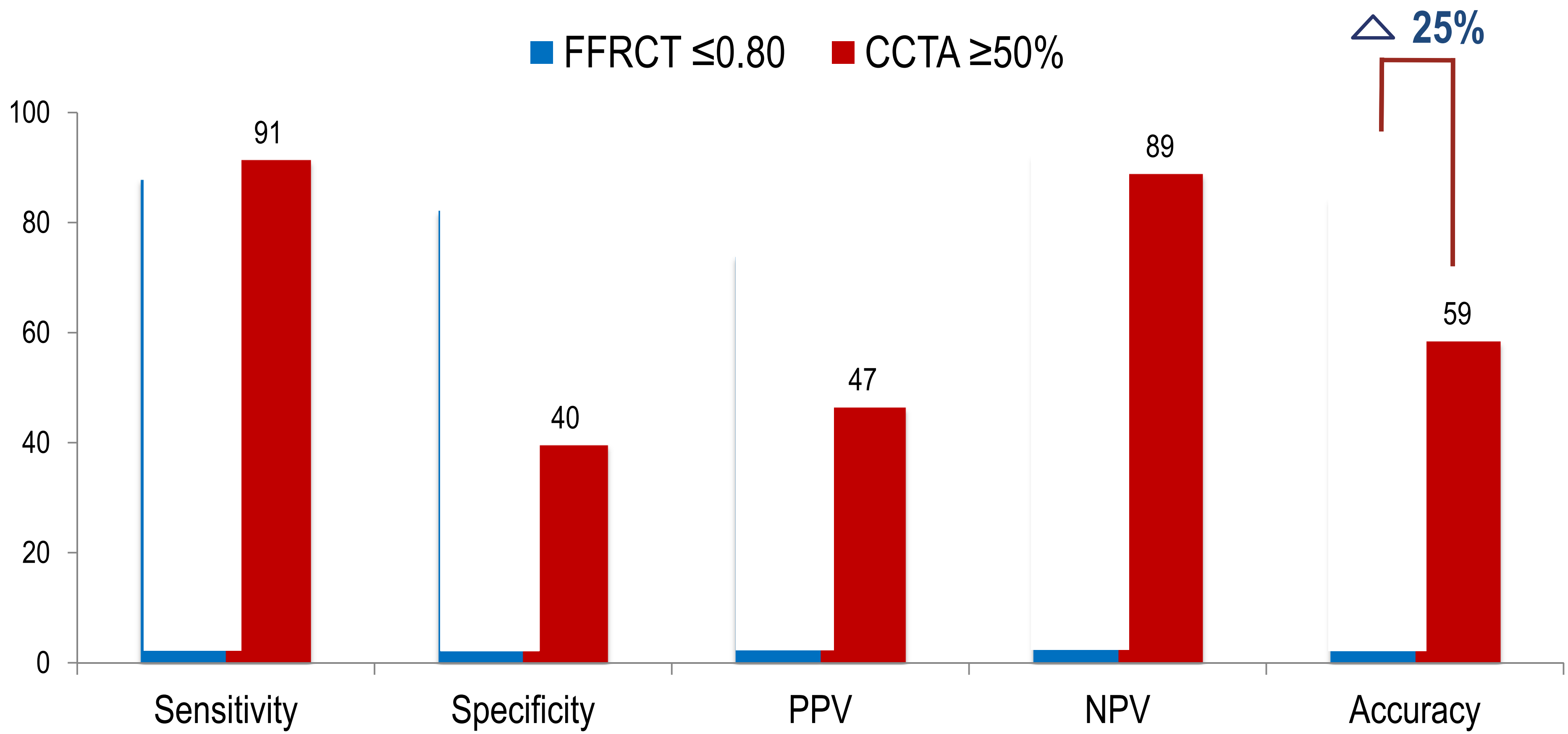
Reduction of false positives: 70%



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

Diagnostic performance of FFR_{CT} and CCTA

Per-vessel analysis (n=159)

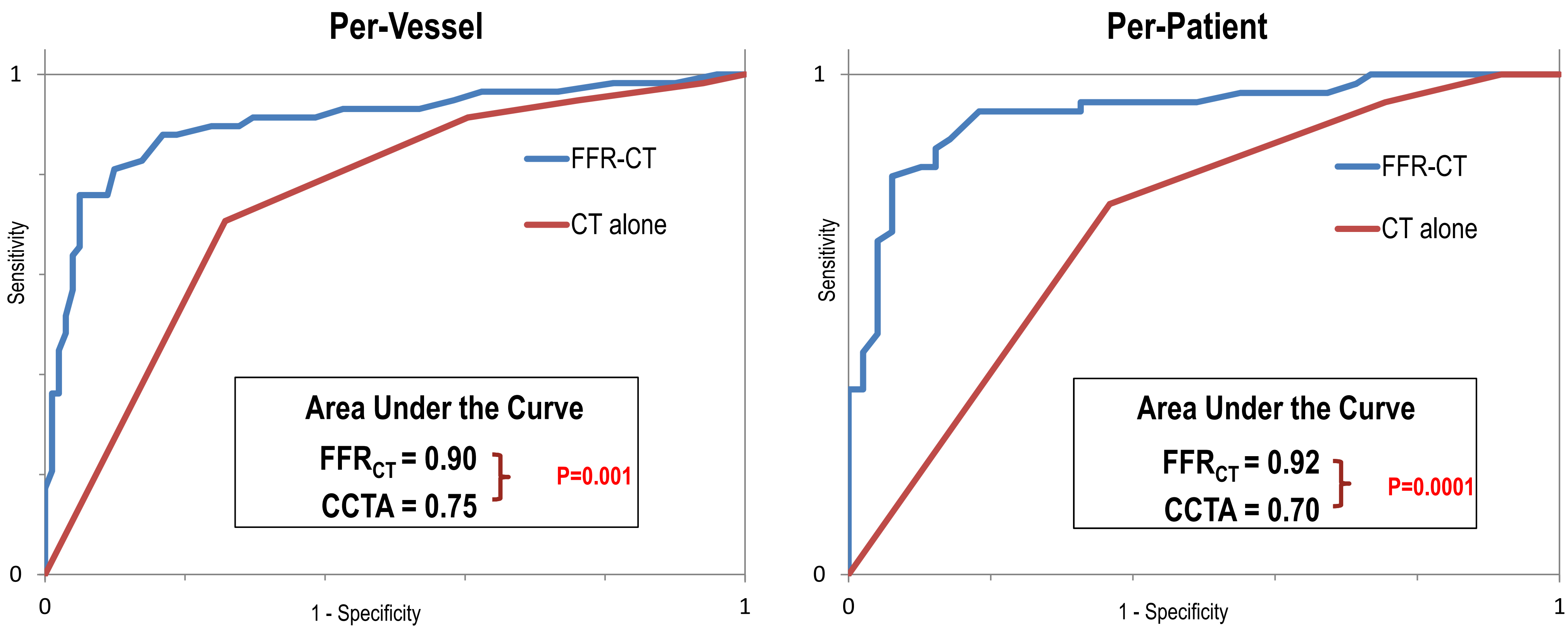


PPV: positive predictive value, NPV: negative predictive value

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

Diagnostic performance of CCTA and FFR_{CT}

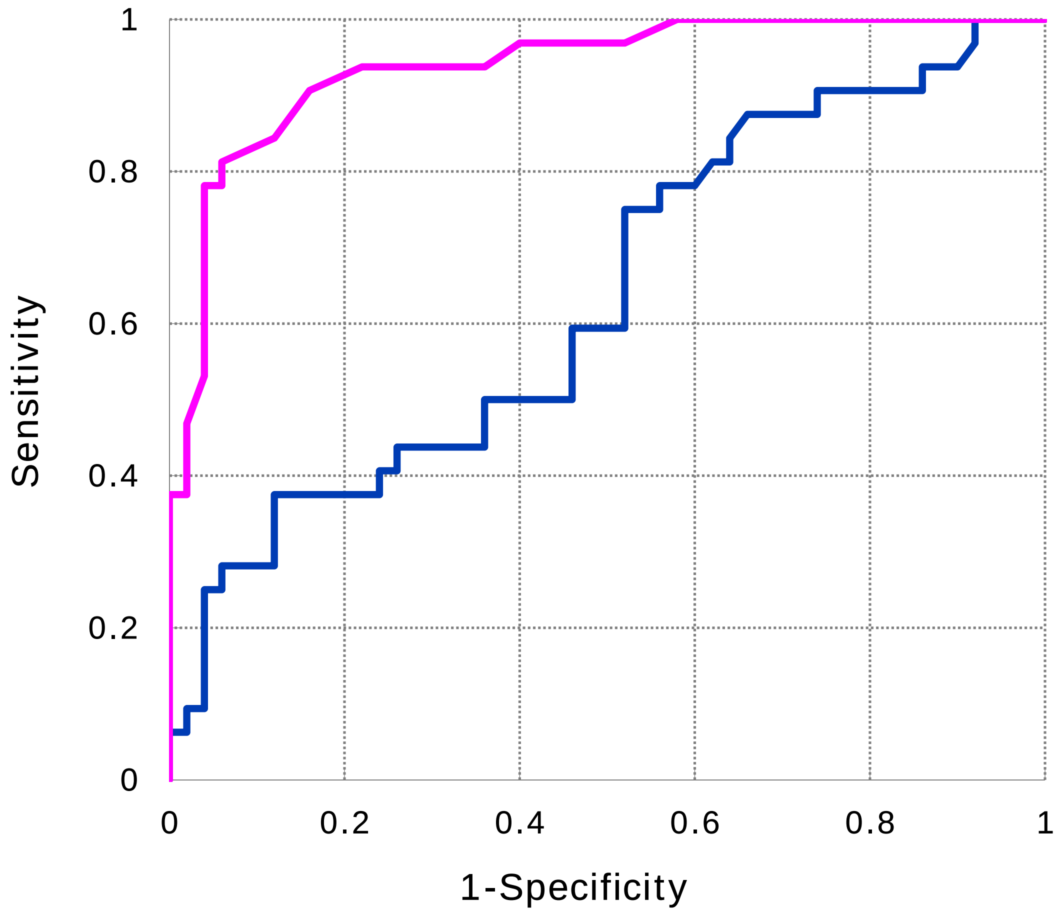
ROC curve analysis



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

FFR vs. TAG and FFR_{CT}

Overall vessels (N = 82)

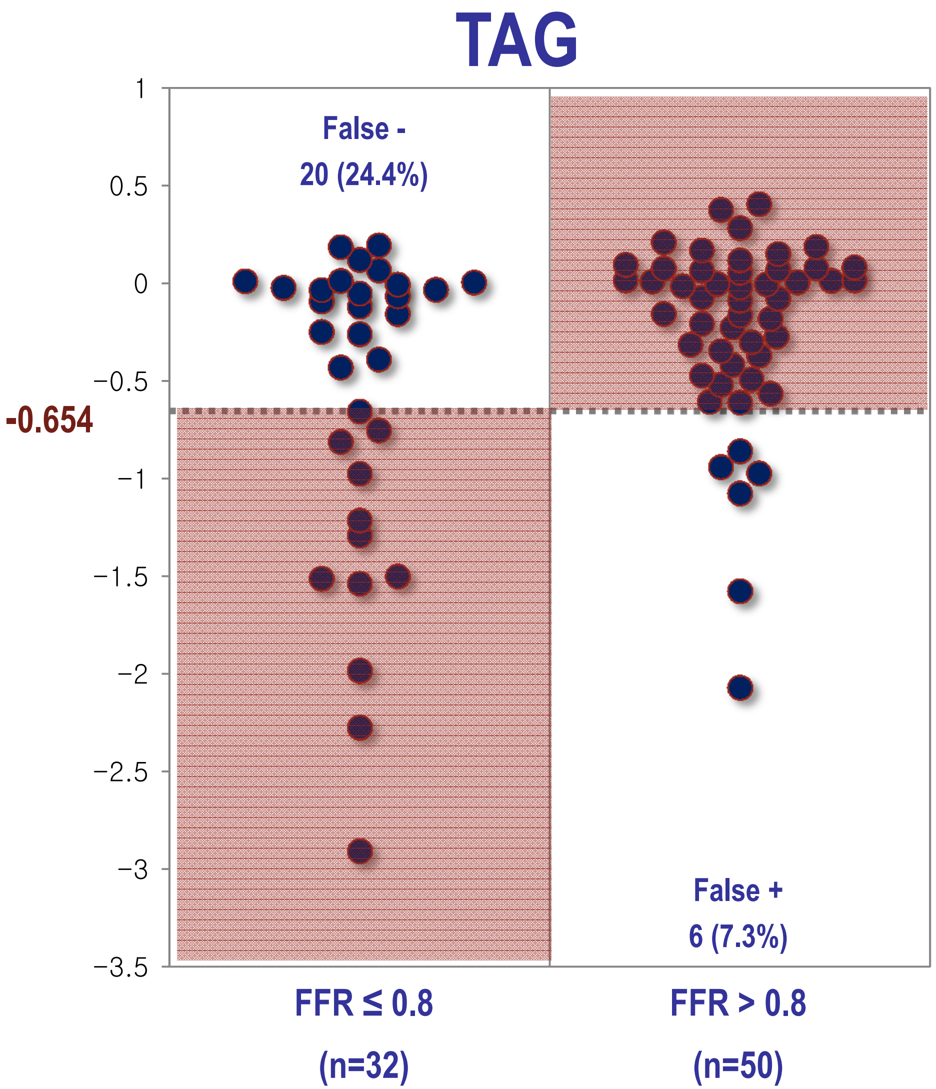


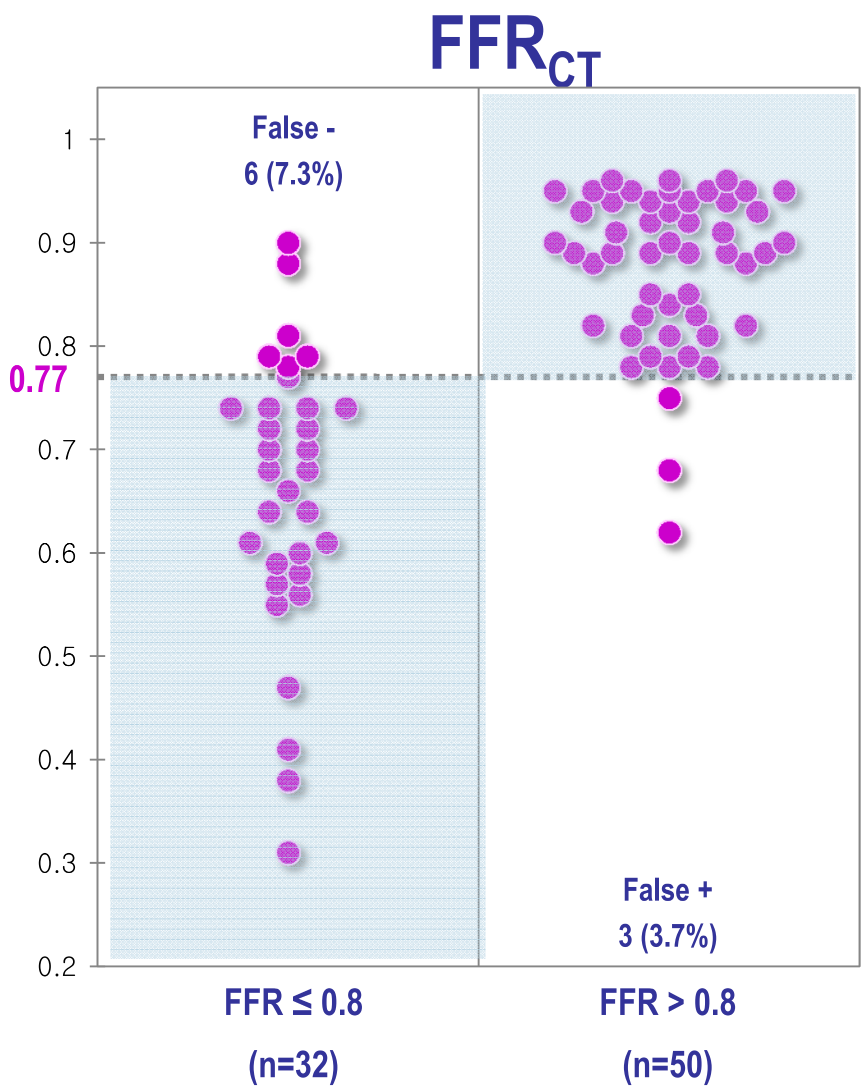
Area under the curve

FFR_{CT}	**0.94** (95% CI: 0.86-0.98)	P<0.001
TAG	**0.63** (95% CI: 0.52-0.74)	

Yoon YY, Choi JH, Koo BK, ACC 2012

FFR vs. TAG and FFR_{CT}

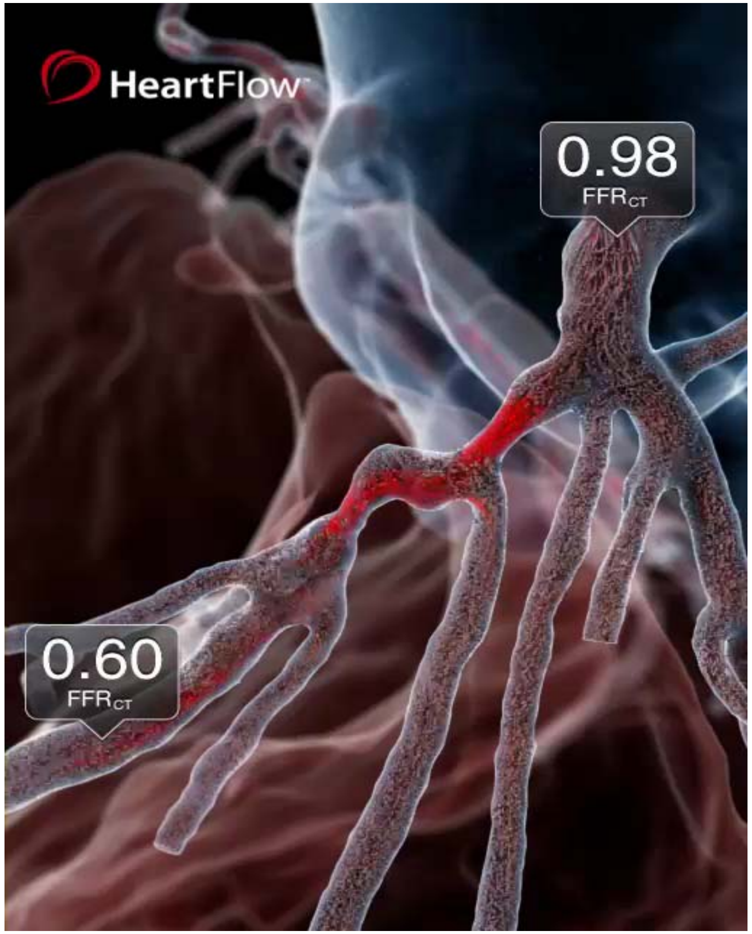


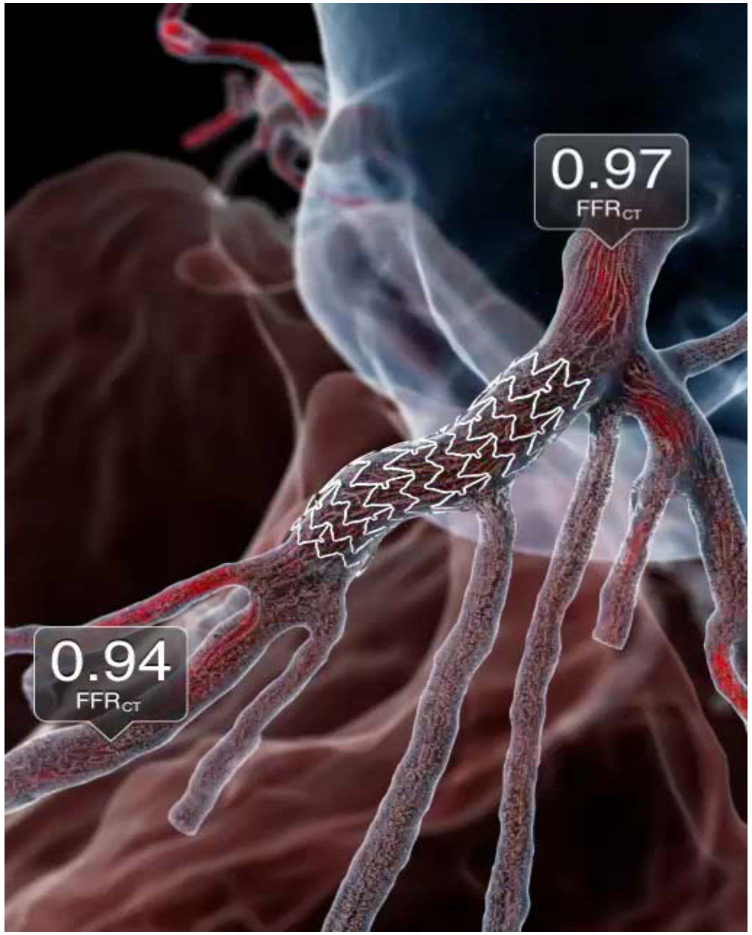


Yoon YY, Choi JH, Koo BK, ACC 2012

Treatment planning prior to invasive procedures

Virtual PCI and post-PCI FFR_{CT}



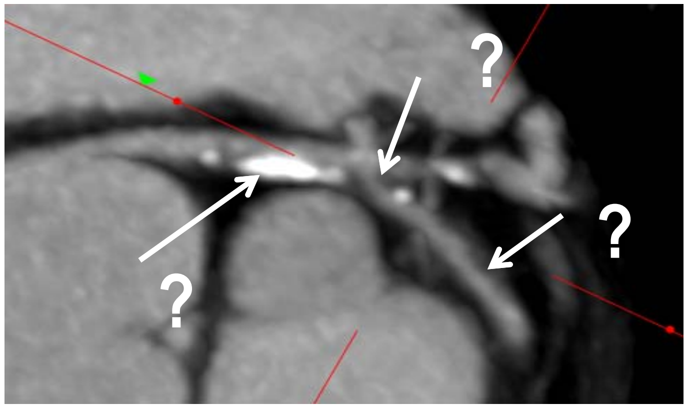


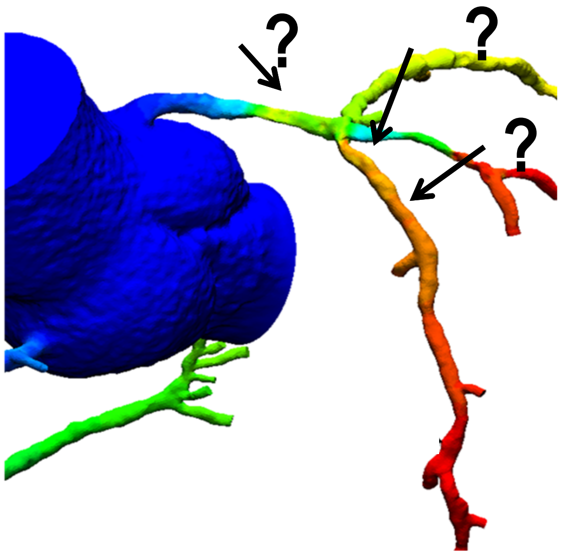
What is the best treatment option for the patient?

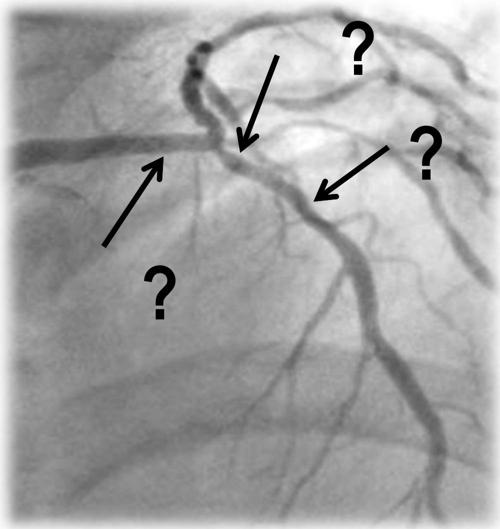
Which lesions are flow limiting?

How many stents are needed?

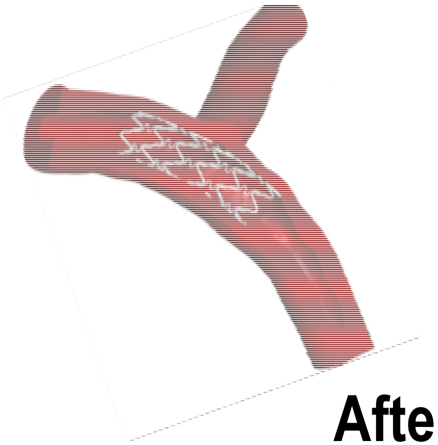
What will be the effect of a stent on the flow to other lesions?





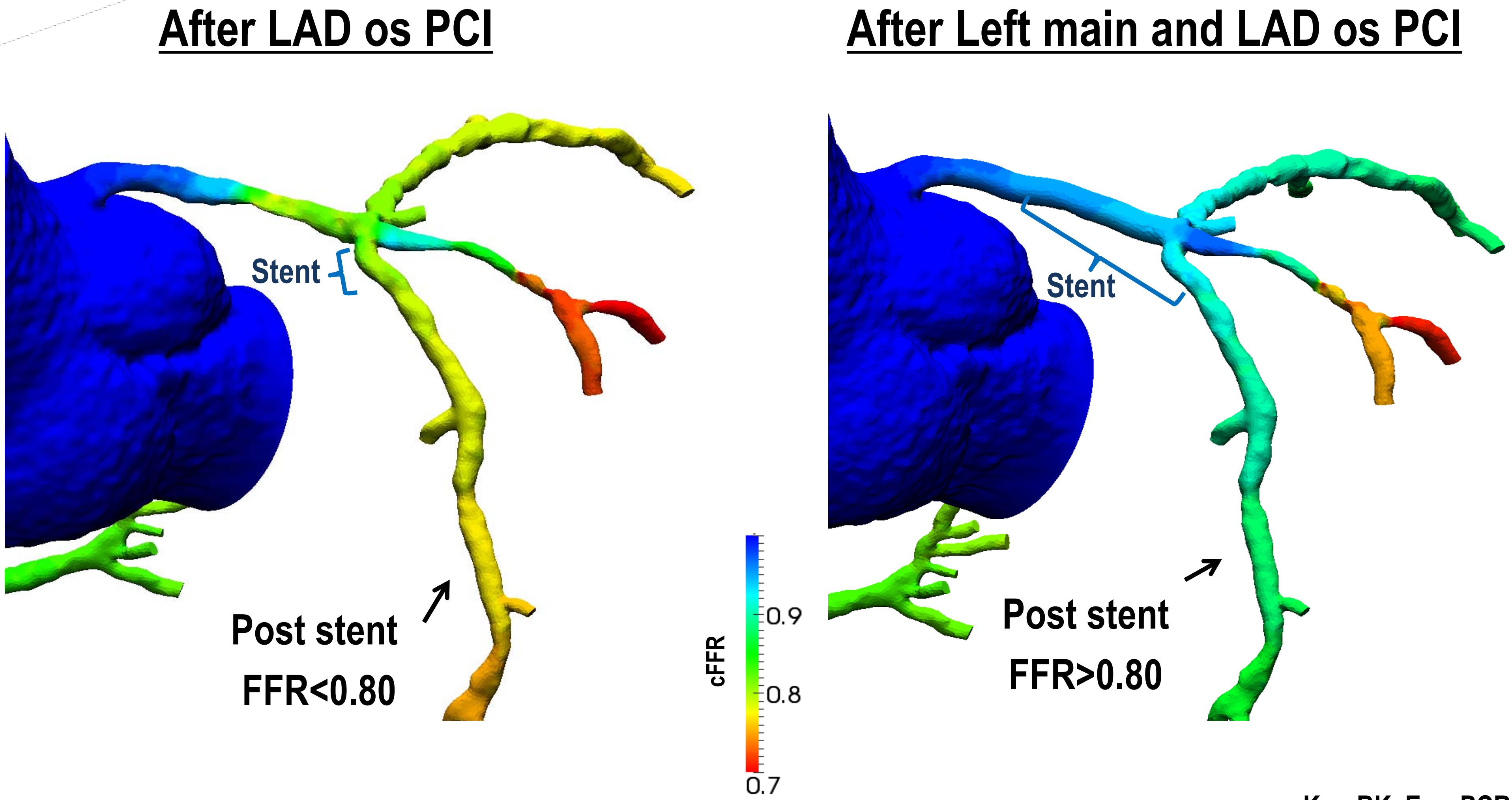


Koo BK, EuroPCR 2011



Treatment planning prior to invasive procedures

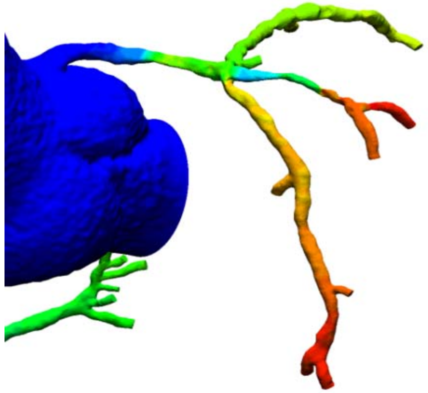
Virtual PCI and post-PCI FFR_{CT}



Koo BK, EuroPCR 2011

Treatment planning prior to invasive procedures

- Virtual PCI and post-PCI flow rates-

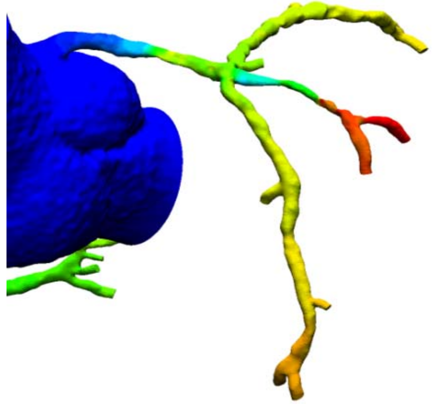


LCX: 107.1 ml/min

RI: 47.3 ml/min

LAD : 84.5 ml/min

Original

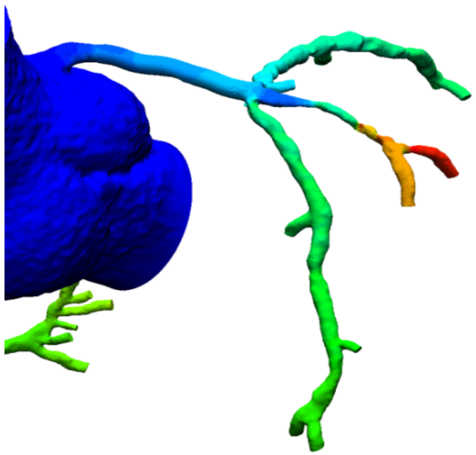


LCX: 107.2 ml/min

RI: 48.0 ml/min

LAD: 87.5 ml/min

After LAD os PCI



LCX: 116.7 ml/min

RI: 48.0 ml/min

LAD: 92.1 ml/min

After Left main PCI

LCX: 121.6 ml/min

RI: 49.4 ml/min

LAD: 99.5 ml/min

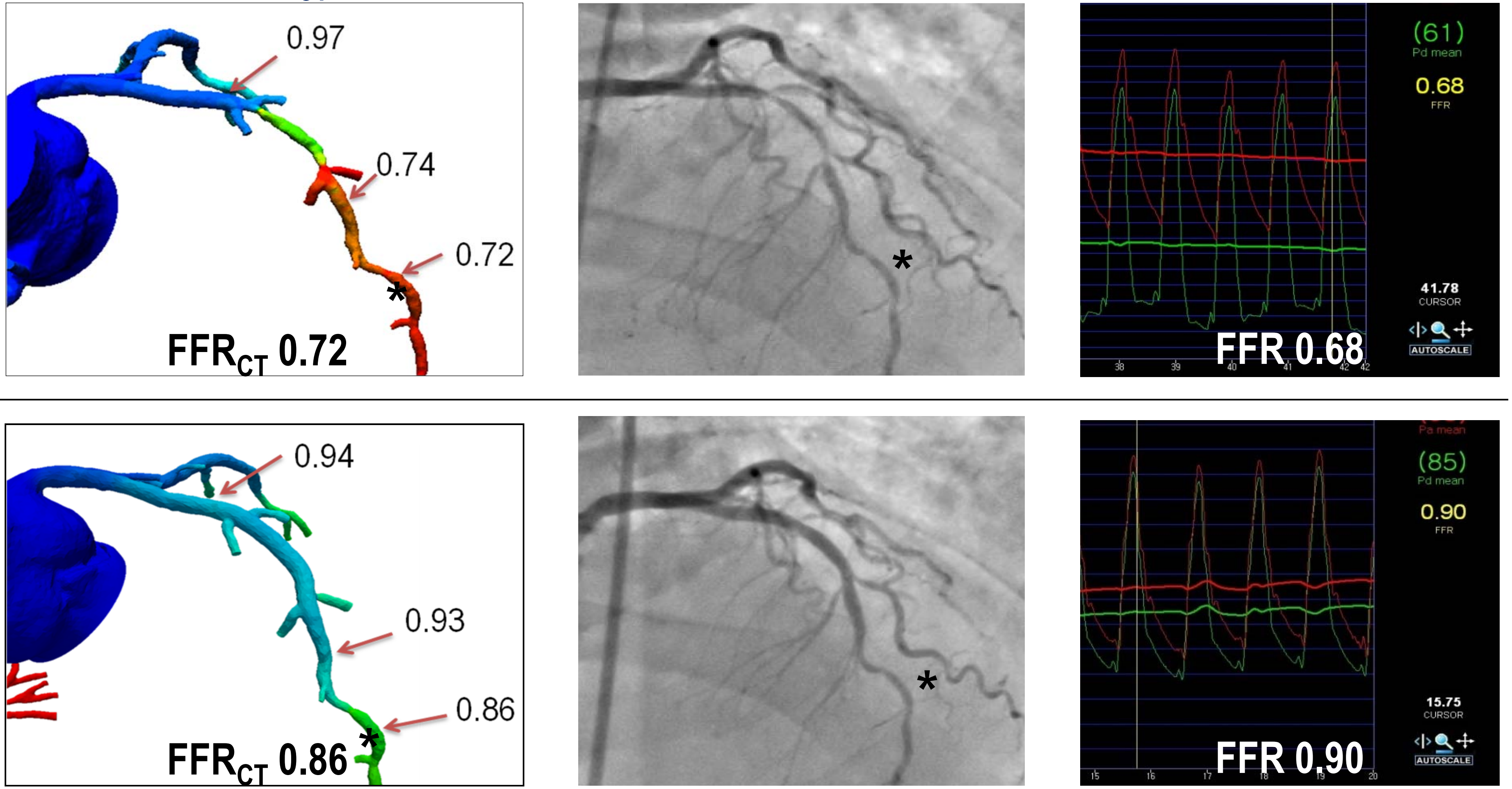
After all PCI

FFR vs. FFR_{CT} after Stenting

CT-derived computed FFR (FFR_{CT}) | Angiography | Invasive FFR

Before Stenting

After Stenting



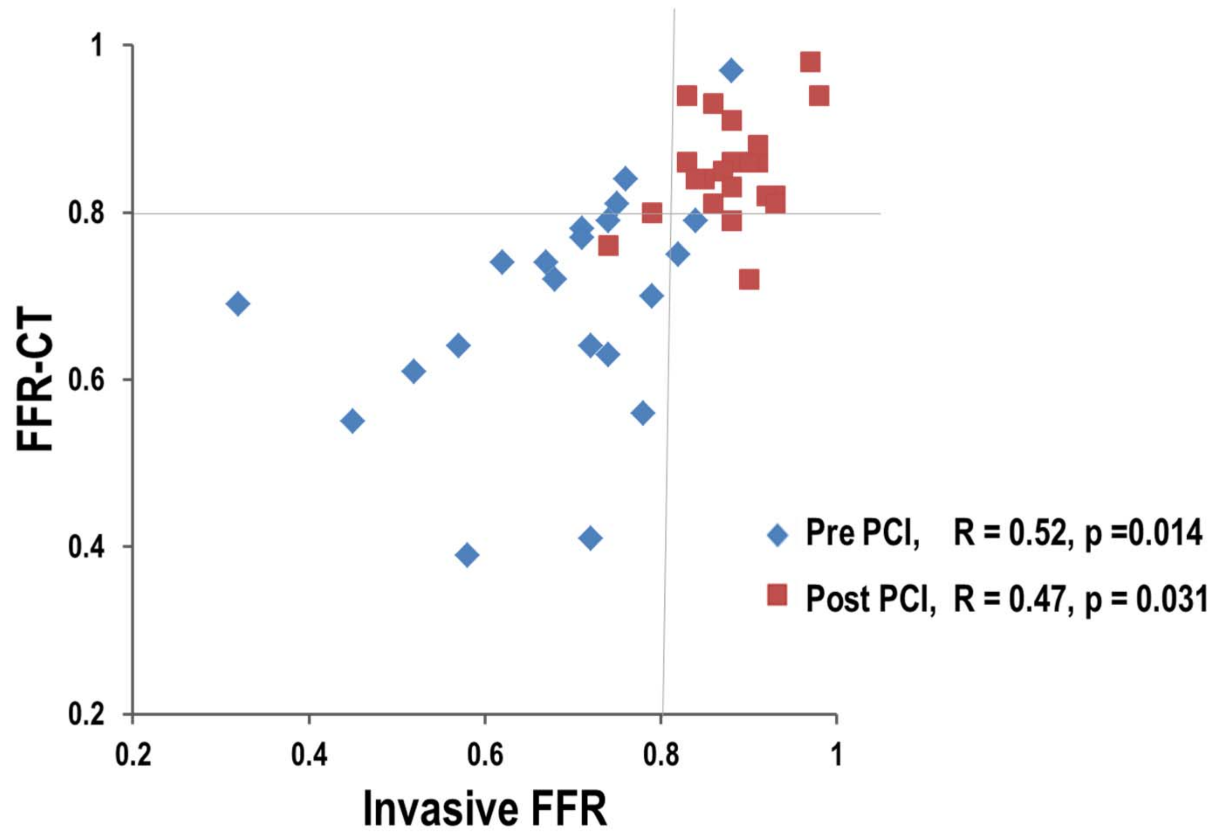
Invasive FFR vs FFR_{CT}

Pre-PCI

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

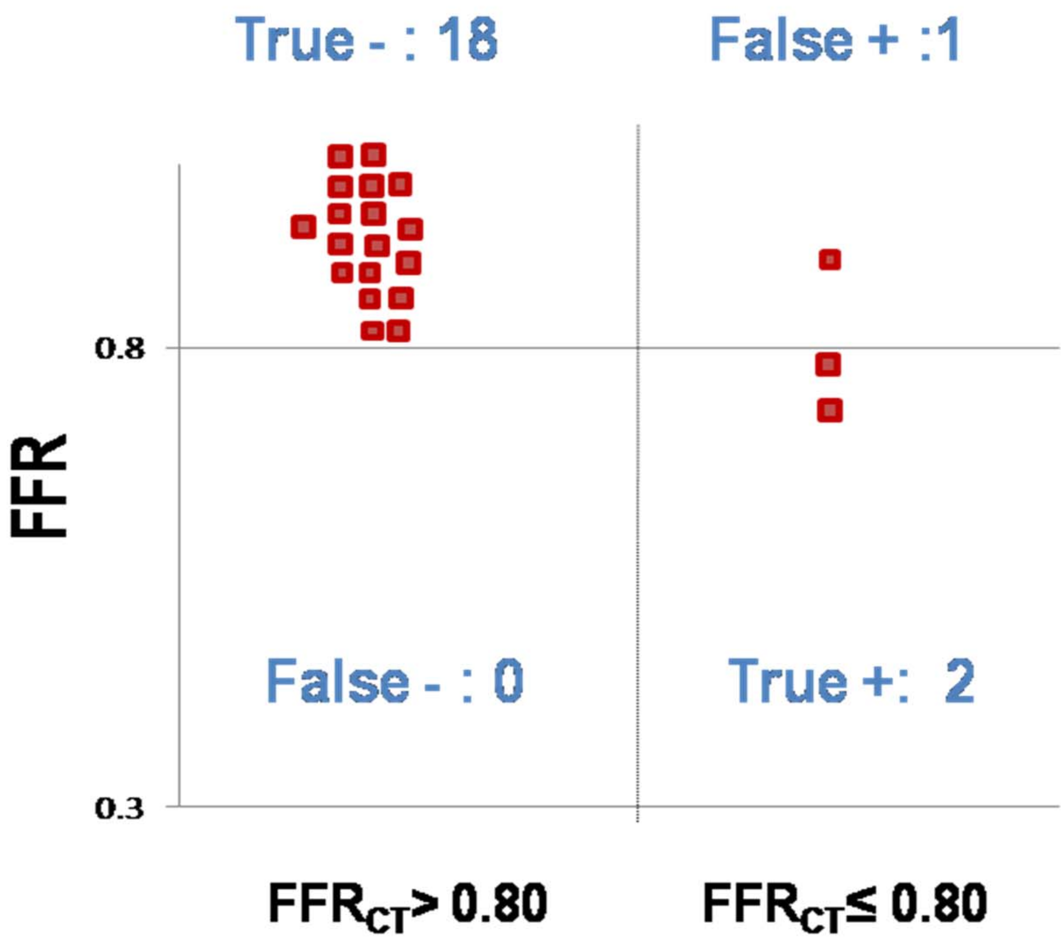
Post-PCI

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



Koo BK, Kim KH, et al. EuroPCR 2012

Invasive FFR vs FFR_{CT} after stenting



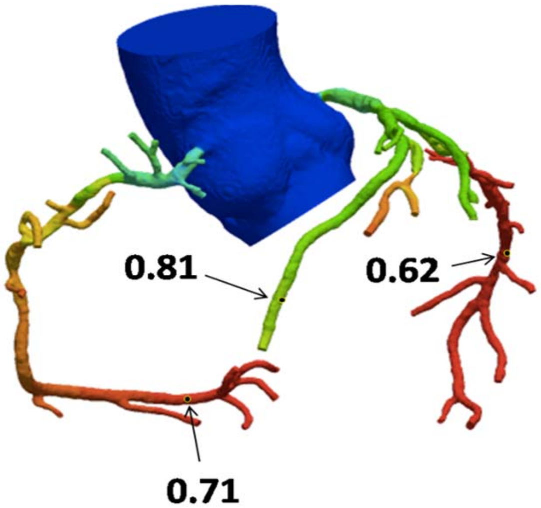
Diagnostic performance of FFR_{CT}

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

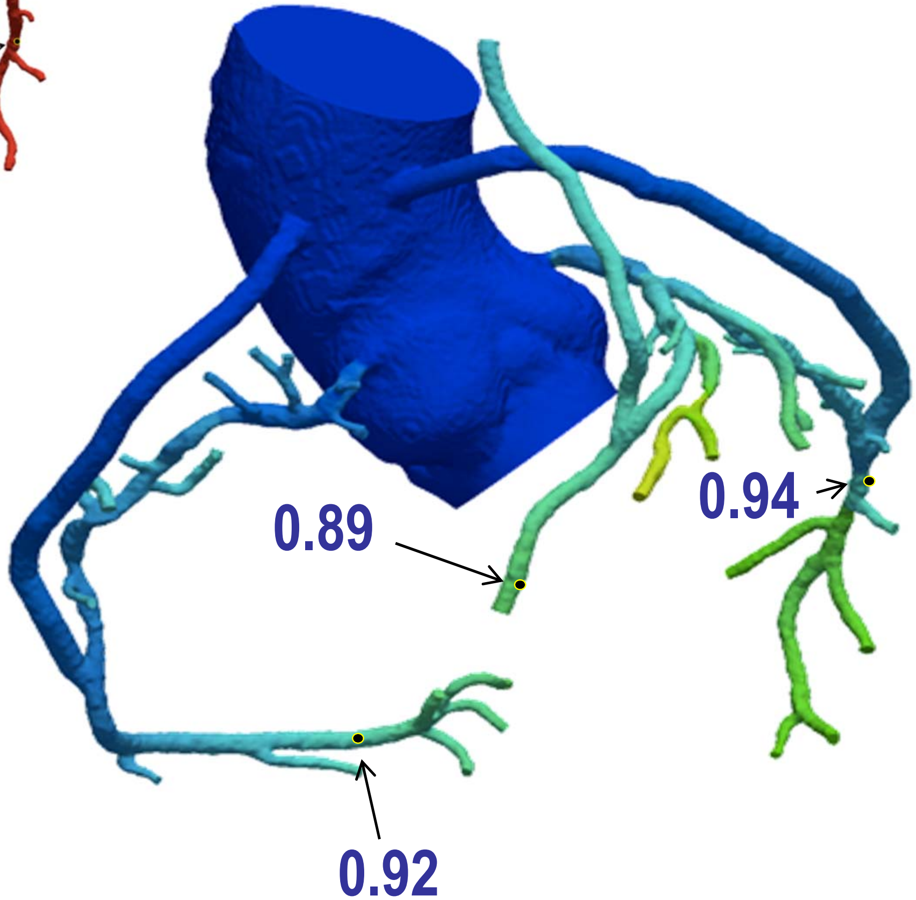
Koo BK, Kim KH, et al. EuroPCR 2012

CABG Planner

CABG before the surgery, with your computer



FFRCT after LIMA + 2SVGs



Conclusion

- Assessment of coronary hemodynamic parameters using CCTA is feasible with various novel technologies.
- Application of computational fluid dynamics to static CT images can provide quantitative and qualitative flow information.
- FFR_{CT} can predict the functional significance of stenoses and can 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.

Acknowledgement

HeartFlow, USA: Charles Taylor, PhD, Tim Fonte, PhD, Gilwoo Choi, PhD

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Paul Strandins university, Latvia: Andrejs Erglis, MD, PhD

Purdue university, USA: Ghassan Kassab, PhD, Yunlong Huo, MD, PhD

Cedars Sinai Hospital, USA: James K. Min, MD

Marquette university, USA: John LaDisa Jr., PhD