FFR_{CT}: Present and Future

Bon-Kwon Koo, MD, PhD

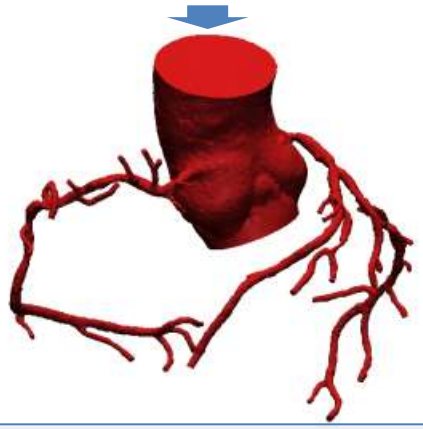
Seoul National University Hospital, Seoul, Korea

Patient-specific non-invasive FFR using CT & CFD

Computational Model based on CCTA

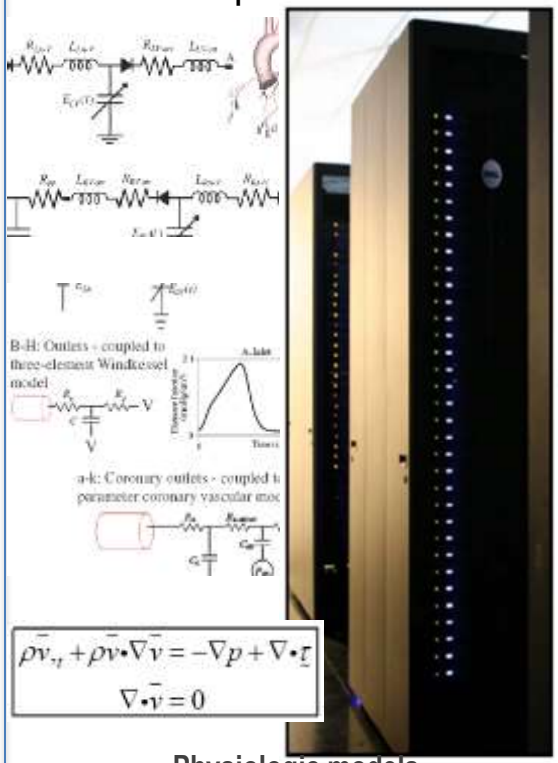
3-D anatomic model from CCTA

No additional imaging
No additional medications



Blood Flow Solution

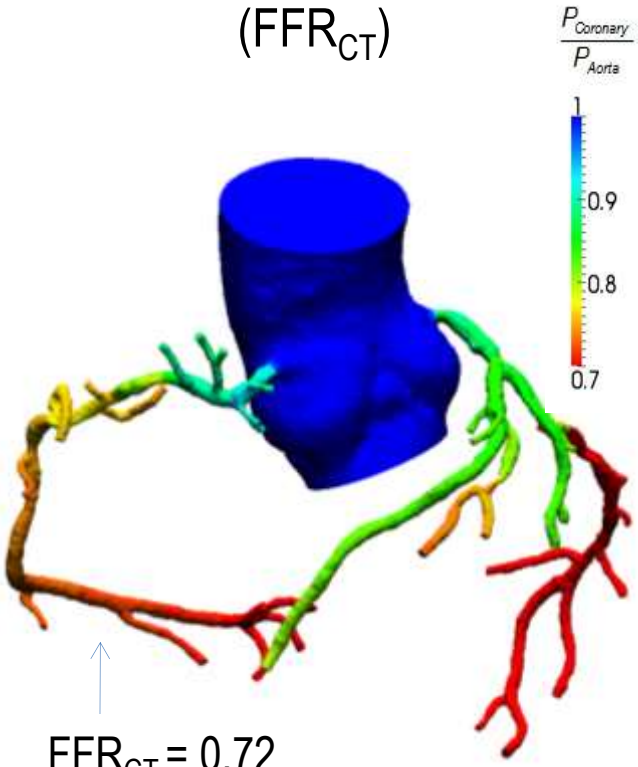
Blood flow equations solved on supercomputer



Physiologic models

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

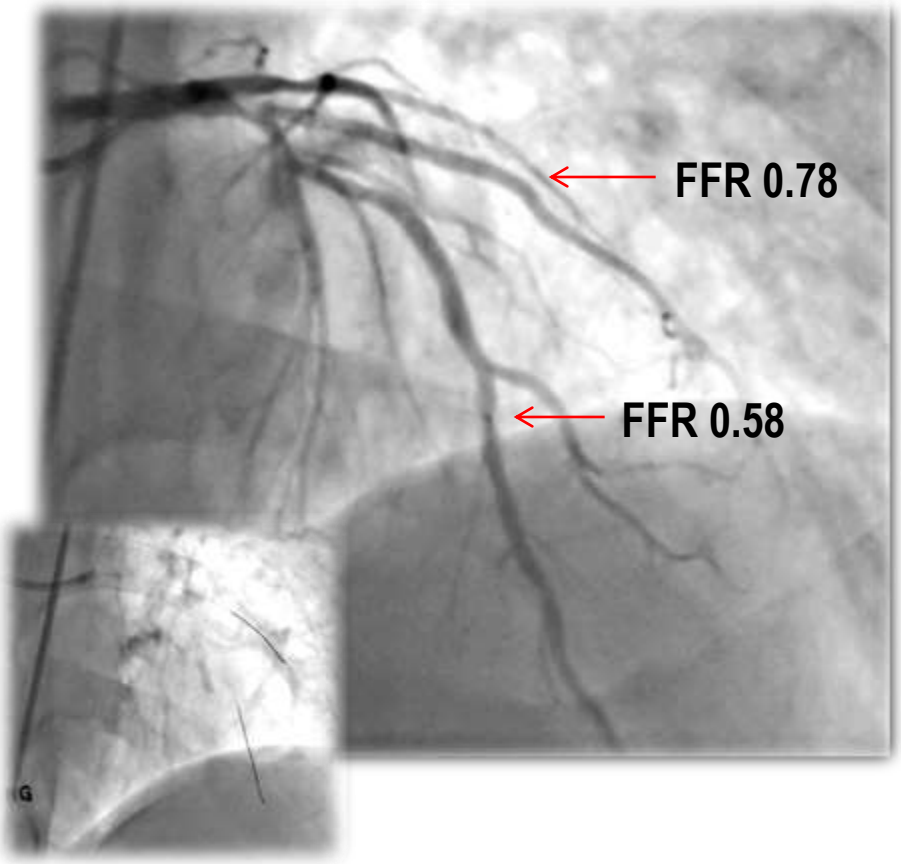
CT-derived computed FFR (FFR_{CT})

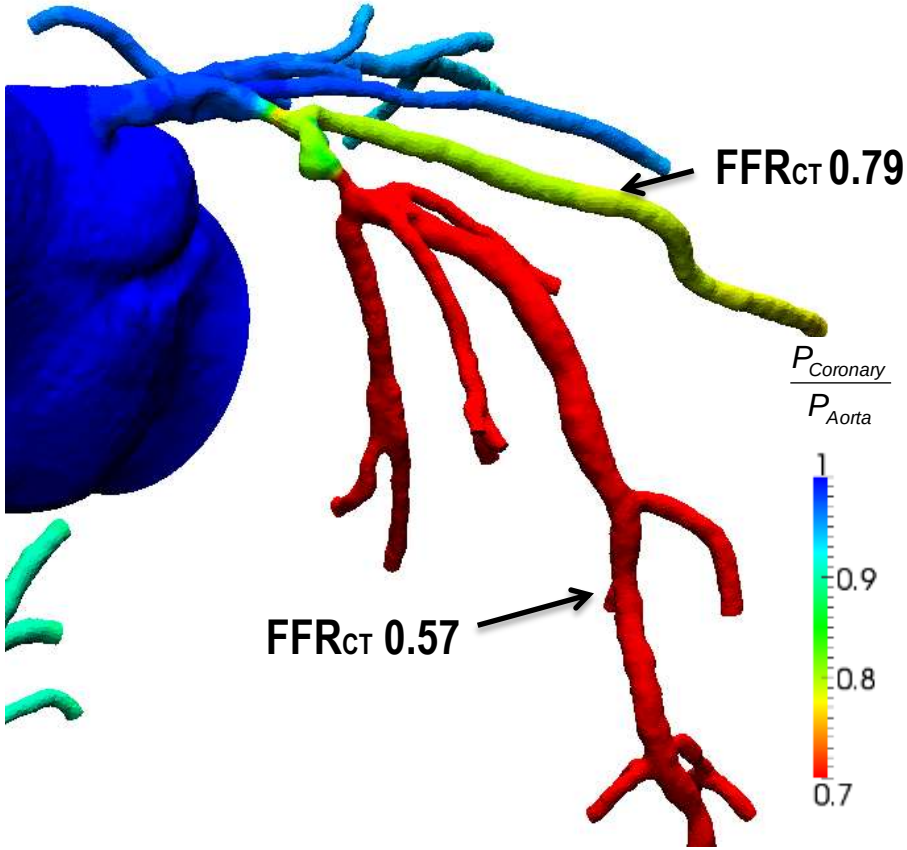


FFR_{CT} = 0.72
(can select any point on model)

LAD-Diagonal bifurcation lesions

(Case #58 from SNUH, Korea)





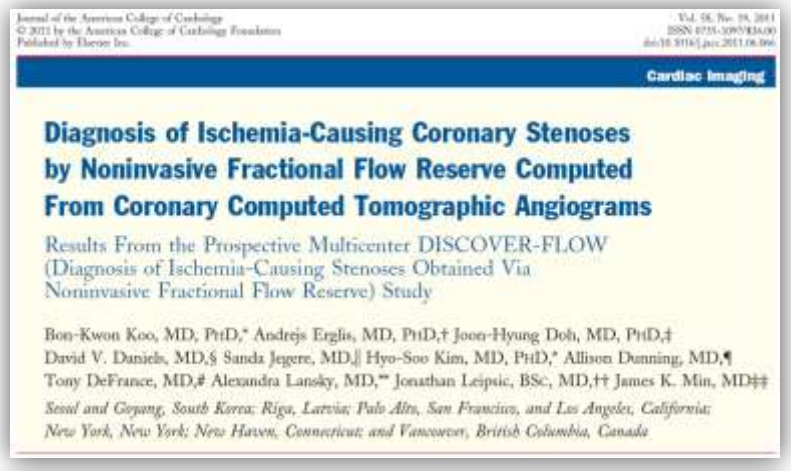
Without invasive procedure
Without pressure wire, without adenosine

FFR_{CT}: Present and Future

- **Gate keeper to invasive angiography ?**
- Replacing invasive FFR ?
- Treatment planning before angiography ?
- New researches using CT and CFD ?

Clinical Evidences on Diagnostic Performance

- **DISCOVER-FLOW**
  - 5 center FIH clinical trial
  - Completed 2011
  - N=103 patients
  - Published in JACC
- **DeFACTO**
  - 17 center clinical trial
  - Completed 2012
  - N=252 patients
  - Published in JAMA
- **NXT**
  - 10 center clinical trial
  - Completed August, 2013
  - N=251 patients
  - Published in JACC



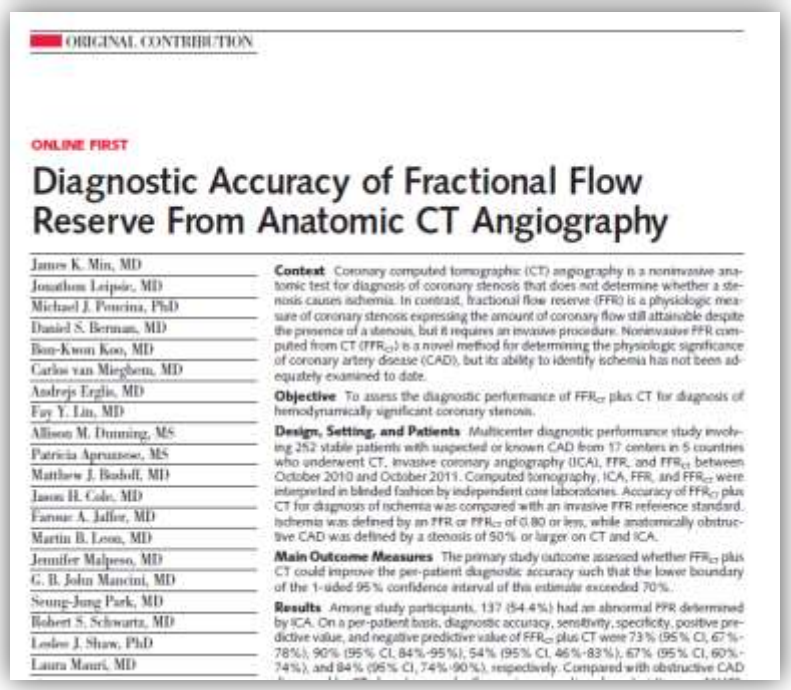
Cardiac Imaging

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



ORIGINAL CONTRIBUTION

ONLINE FIRST

Diagnostic Accuracy of Fractional Flow Reserve From Anatomic CT Angiography

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Robert S. Schwartz, MD
Leslee J. Shaw, PhD
Laura Mauri, MD

Context Coronary computed tomographic (CT) angiography is a noninvasive anatomic test for diagnosis of coronary stenosis that does not determine whether a stenosis causes ischemia. In contrast, fractional flow reserve (FFR) is a physiologic measure of coronary stenosis expressing the amount of coronary flow still attainable despite the presence of a stenosis, but it requires an invasive procedure. Noninvasive FFR computed from CT (FFR_{CT}) is a novel method for determining the physiologic significance of coronary artery disease (CAD), but its ability to identify ischemia has not been adequately examined to date.

Objective To assess the diagnostic performance of FFR_{CT} plus CT for diagnosis of hemodynamically significant coronary stenosis.

Design, Setting, and Patients Multicenter diagnostic performance study involving 252 stable patients with suspected or known CAD from 17 centers in 5 countries who underwent CT, invasive coronary angiography (ICA), FFR, and FFR_{CT} between October 2010 and October 2011. Computed tomography, ICA, FFR, and FFR_{CT} were interpreted in blinded fashion by independent core laboratories. Accuracy of FFR_{CT} plus CT for diagnosis of ischemia was compared with an invasive FFR reference standard. Ischemia was defined by an FFR or FFR_{CT} of 0.80 or less, while anatomically obstructive CAD was defined by a stenosis of 50% or larger on CT and ICA.

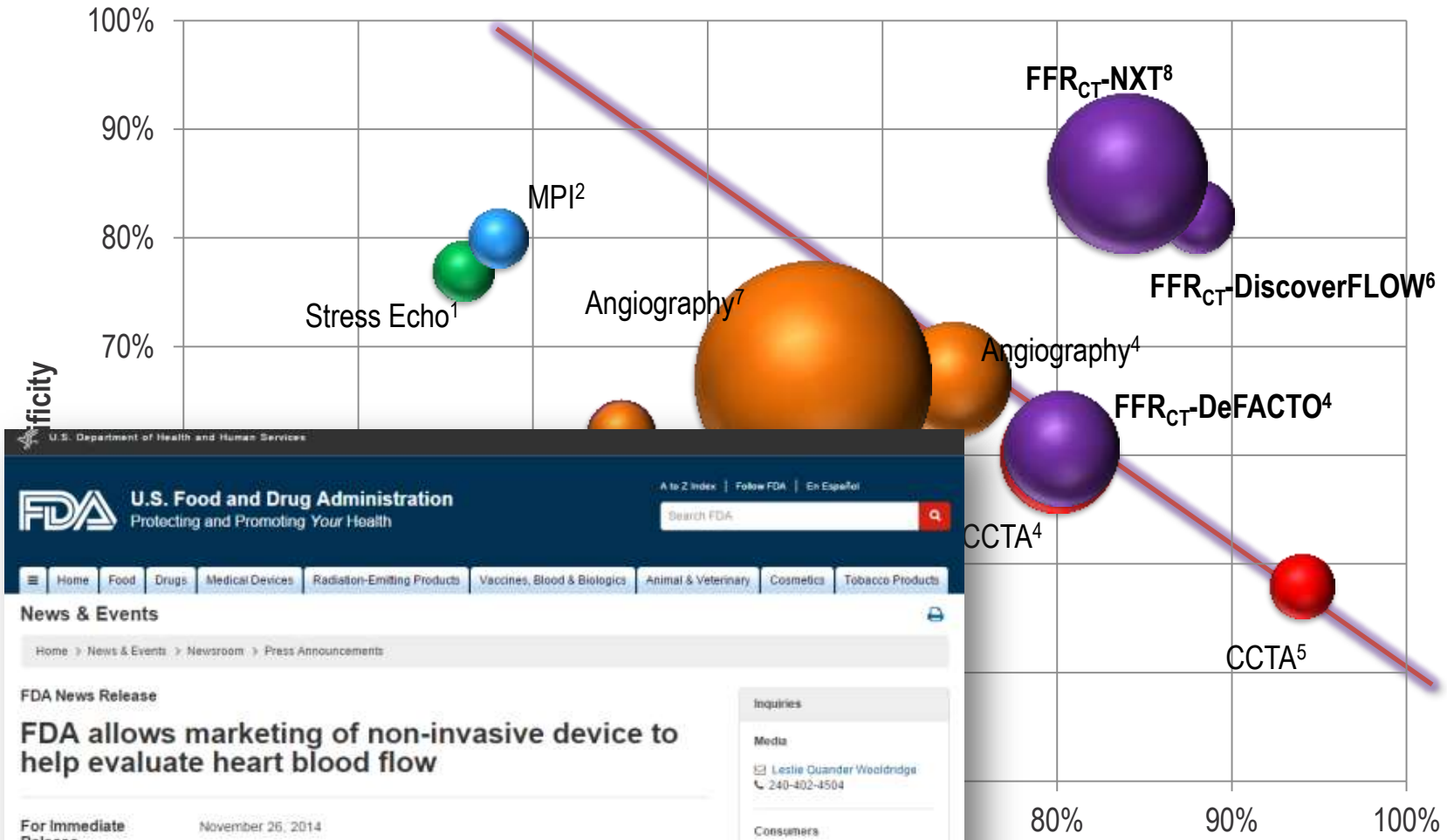
Main Outcome Measures The primary study outcome assessed whether FFR_{CT} plus CT could improve the per-patient diagnostic accuracy such that the lower boundary of the 1-sided 95% confidence interval of this estimate exceeded 70%.

Results Among study participants, 137 (54.4%) had an abnormal FFR determined by ICA. On a per-patient basis, diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of FFR_{CT} plus CT were 73% (95% CI, 67%-78%), 90% (95% CI, 84%-95%), 54% (95% CI, 46%-83%), 67% (95% CI, 60%-74%), and 84% (95% CI, 74%-90%), respectively. Compared with obstructive CAD

Diagnostic performance of FFR_{CT}

	Patient No	Sensitivity	Specificity	PPV	NPV	Accuracy
DISCOVER-FLOW	103	93%	82%	85%	91%	87%
DeFACTO	252	90%	54%	67%	84%	73%
NXT	251	86%	79%	65%	92%	81%
	Total: 606	**90%**	**72%**	**72%**	**89%**	**80%**

Non-invasive tests/FFR_{CT}/Angiography vs. FFR



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FDA News Release

FDA allows marketing of non-invasive device to help evaluate heart blood flow

For Immediate Release: November 26, 2014

Release: The U.S. Food and Drug Administration today allowed marketing of the HeartFlow FFR-CT software, which permits health care professionals to non-invasively evaluate blood flow in the coronary arteries of patients showing signs and symptoms of coronary artery disease.

Inquiries

Media

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240-402-4504

Consumers

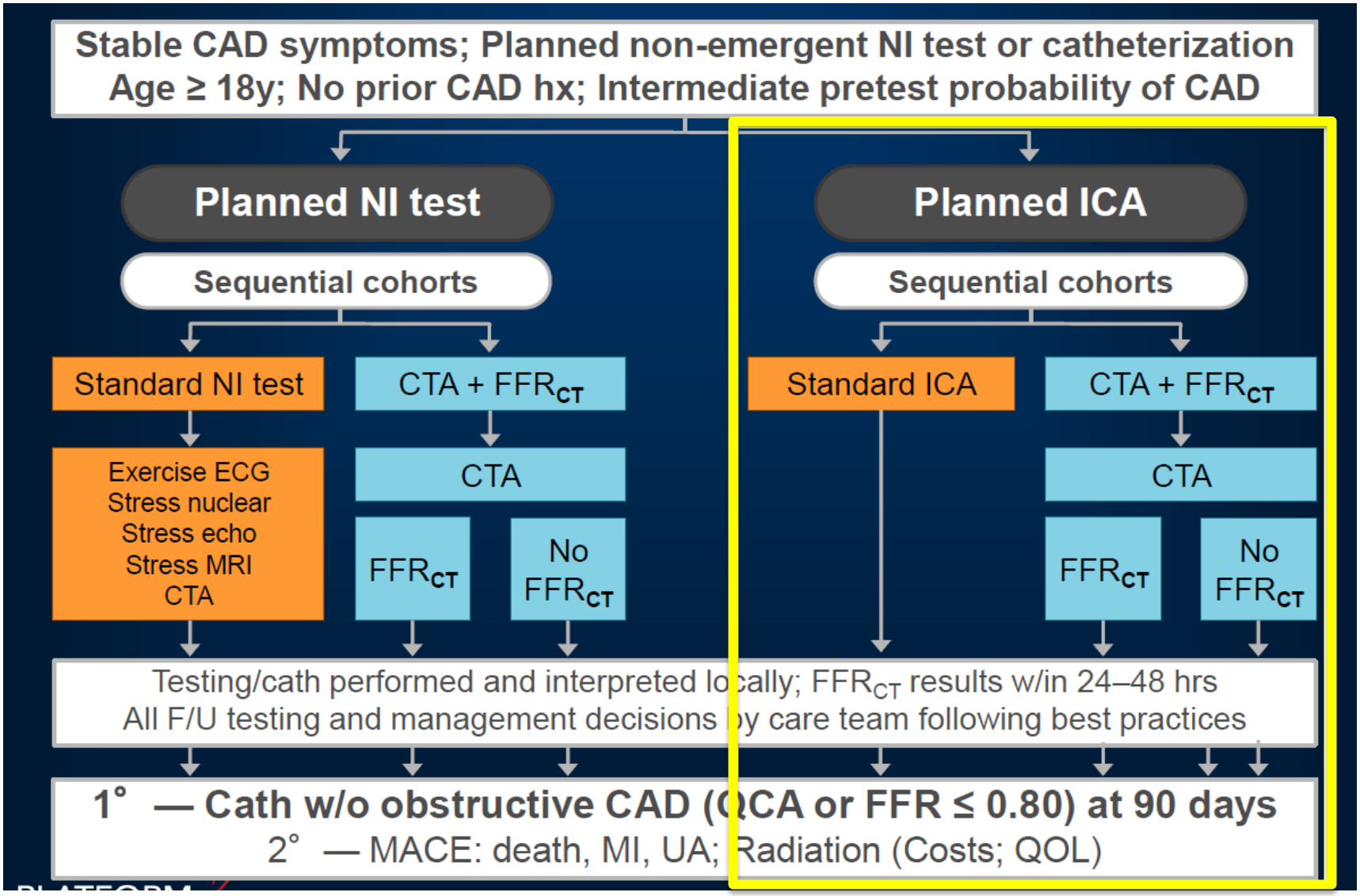
888-INFO-FDA

Share

4. Min et al. JAMA 2012;308:1237-1245
8. Norgaard et a. JACC 2014

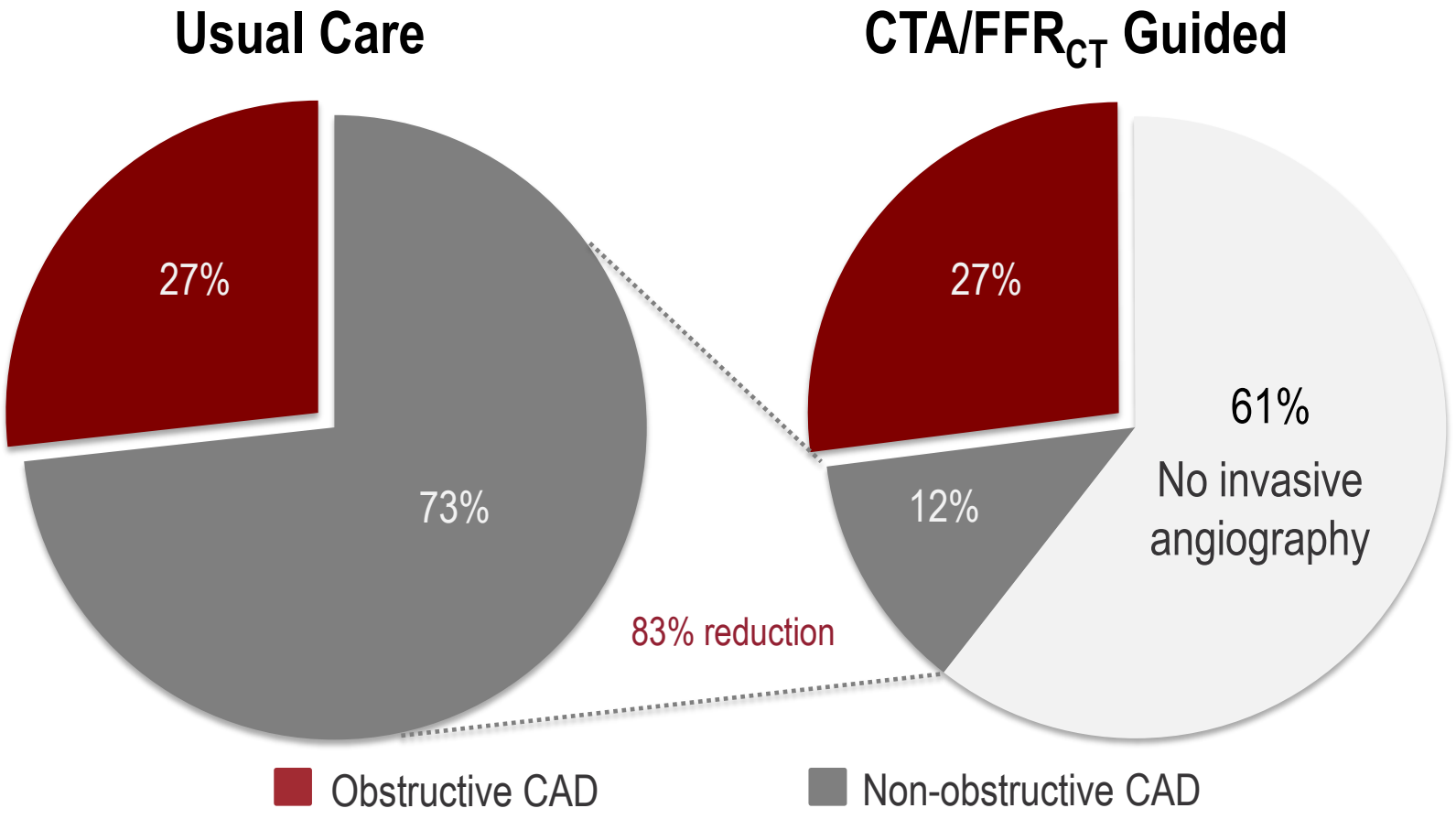
om et al. JACC 2008;52:636–43
al. JACC 2011;58:1989-97
al. JACC 2012

Clinical outcomes of FFR_{CT}-guided decision



Douglas PS, et al. EHJ 2015

Invasive catheterization with NO obstructive disease



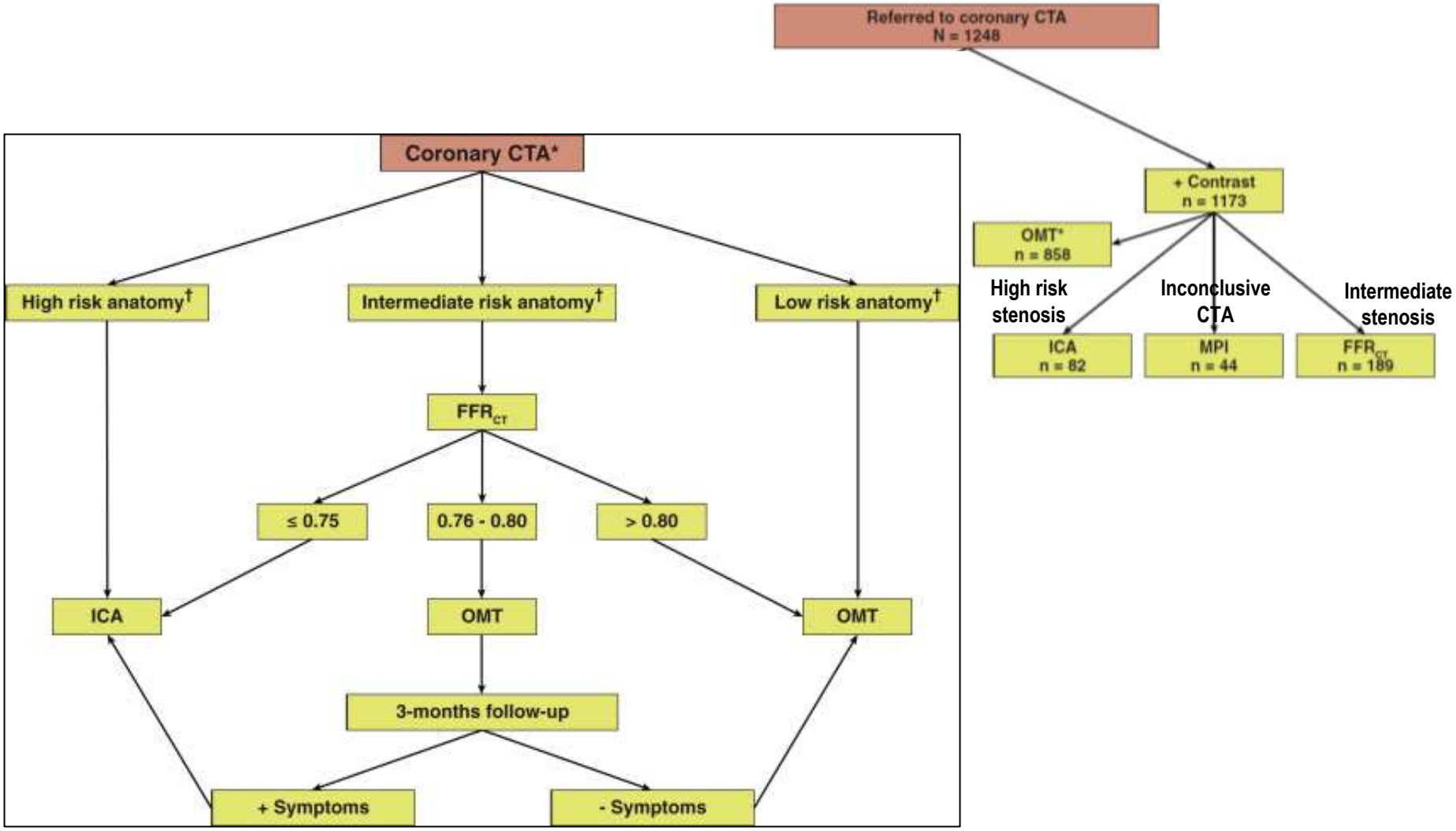
Douglas PS, et al. EHJ 2015

1-year Clinical and Safety Outcomes

	Noninvasive N=204		Invasive N=380	
	Usual care strategy N=100	FFR_{CT} strategy N=104	Usual care strategy N=187	FFR_{CT} strategy N=193
Major adverse cardiovascular events				
Number of patients	1	0	2	2
MACE components				
Death, no. (%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)
Nonfatal MI, no. (%)	1 (1.0%)	0 (0.0%)	1 (0.5%)	1 (0.5%)
Urgent revasc, no. (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)
MACE or vascular complications				
Number of patients	1	1	4	7
Cumulative radiation exposure		p<0.001		p=0.21
Mean (SD), mSv	6.42 (7.47)	9.55 (10.56)	10.36 (6.69)	10.72 (9.62)

Douglas P, et al. JACC in press

FFRCT in daily clinical practice



Norgaard BL, et al. JACC Imaging 2016

FFR_{CT}: Present and Future

- **Gate keeper to invasive angiography ? YES**
- **Replacing invasive FFR ?**
- Treatment planning before angiography ?
- New researches using CT and CFD ?

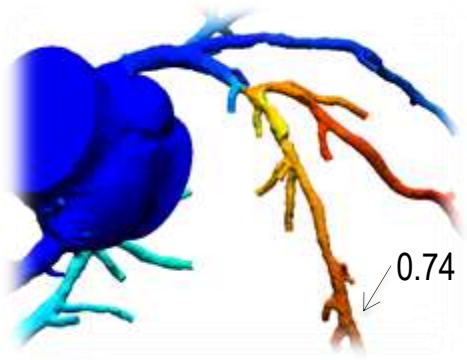
How this novel technology can change our daily practice?

Novel (fast, risk-free, non-invasive, cost-saving) **pathway**

CCTA

>50% diameter stenosis

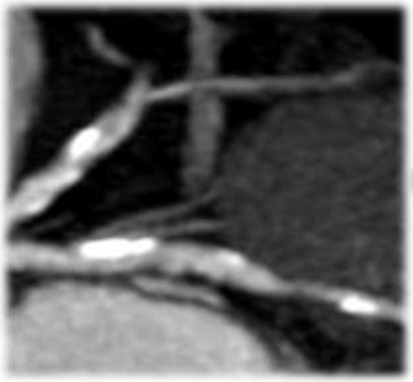
FFR_{CT}



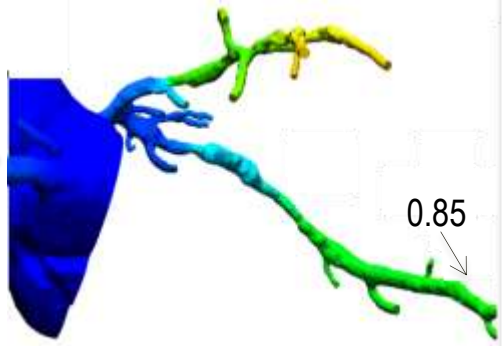
FFR_{CT} 0.74 → Invasive procedures

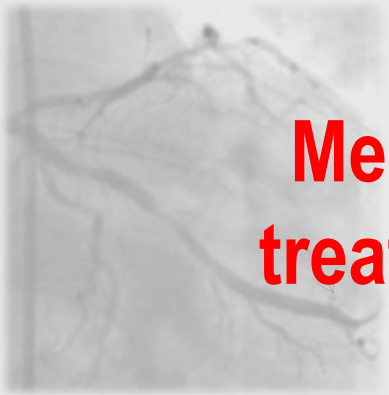
Invasive angiography

>50% diameter stenosis



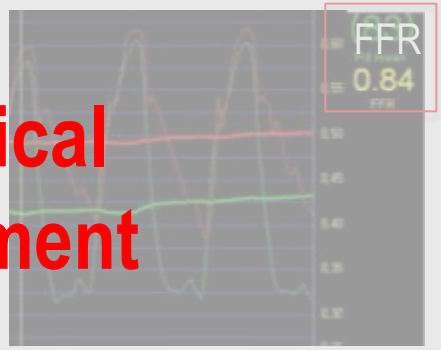
>50% diameter stenosis





>50% diameter stenosis

Medical treatment



FFR 0.84 → no ischemia

Have all conditions validated in patient-specific level?

Input data:

- **Geometry** – extracted from CCTA data
- **Boundary conditions**
  - Resting coronary blood flow (calculated from myocardial mass)
  - Hyperemic coronary blood flow (estimated from previous clinical data)

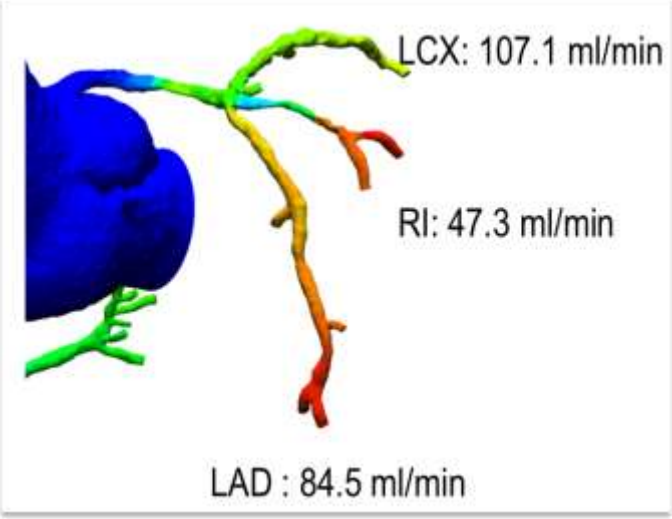
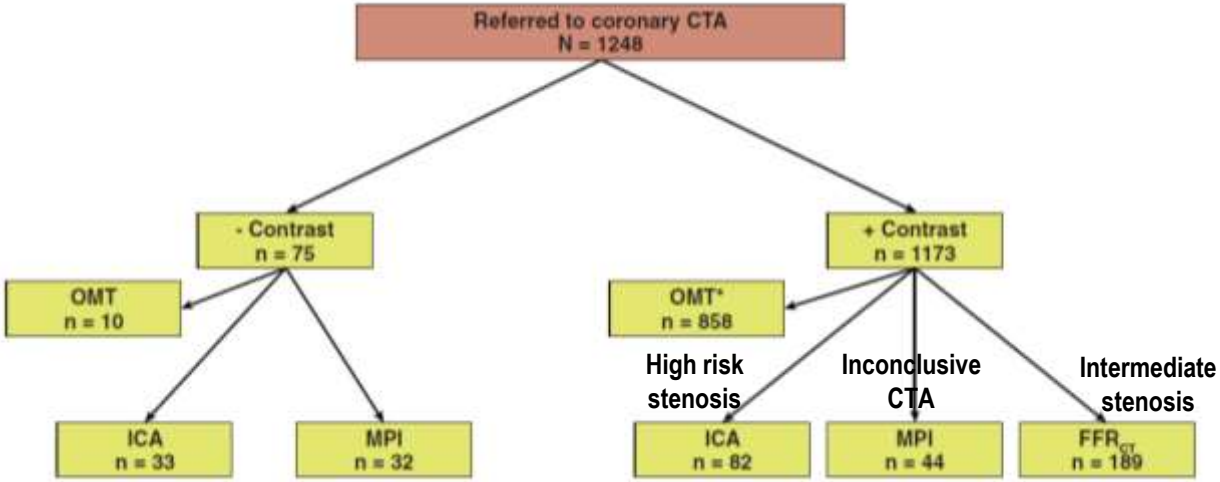
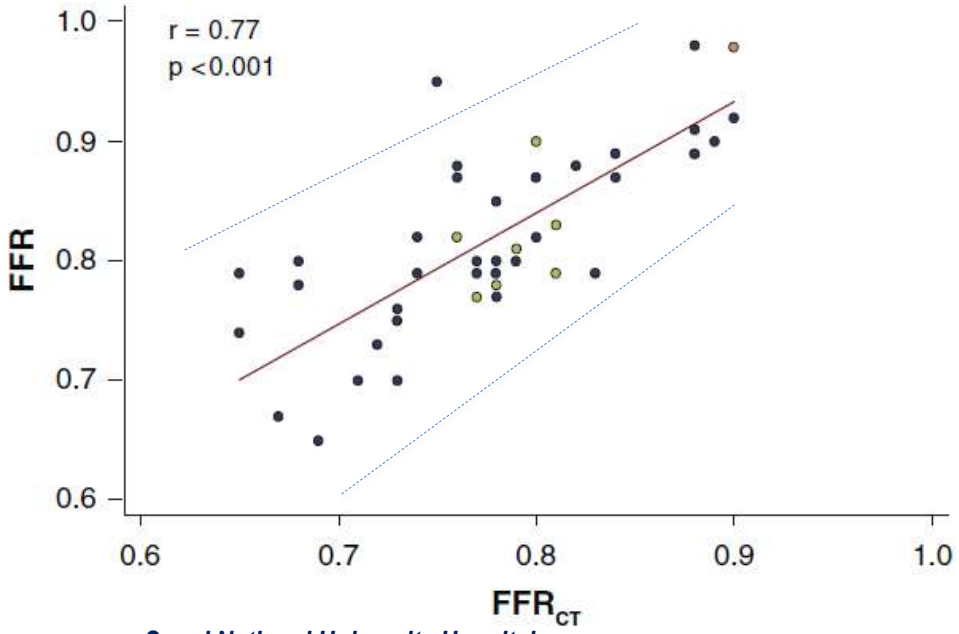


Table 2-1. Comparison of coronary flow reserve measurements using different methods in groups considered as reference (control) groups.

Number of patients	Method	CFR	Reference
17 (HTX)	D.I.	5,0±0,3	(119)
26 (HTX)	D.I.	5,2±1,3	(30)
18 (young subjects)	PET	4,1±0,9	(41)
22 (elderly subjects)	PET	3,0±0,7	(41)
28	PET	3,2±1,2	(110)
31	PET	3,8±2,1	(82)
56	PET	3,4±1,4	(181)
19	D.TTE	3,7±0,7	(69)
26 (athletes)	D.TTE	5,9±1,0	(69)
Subjects with chest pain despite angiographically normal coronary arteries (patients with hypercholesterolemia, hypertension, diabetes mellitus, smoking were included)			
85	D.I.	2,8±0,6	(93)

FFRCT in daily clinical practice





Per patient agreement 73%

Per-vessel agreement 70%

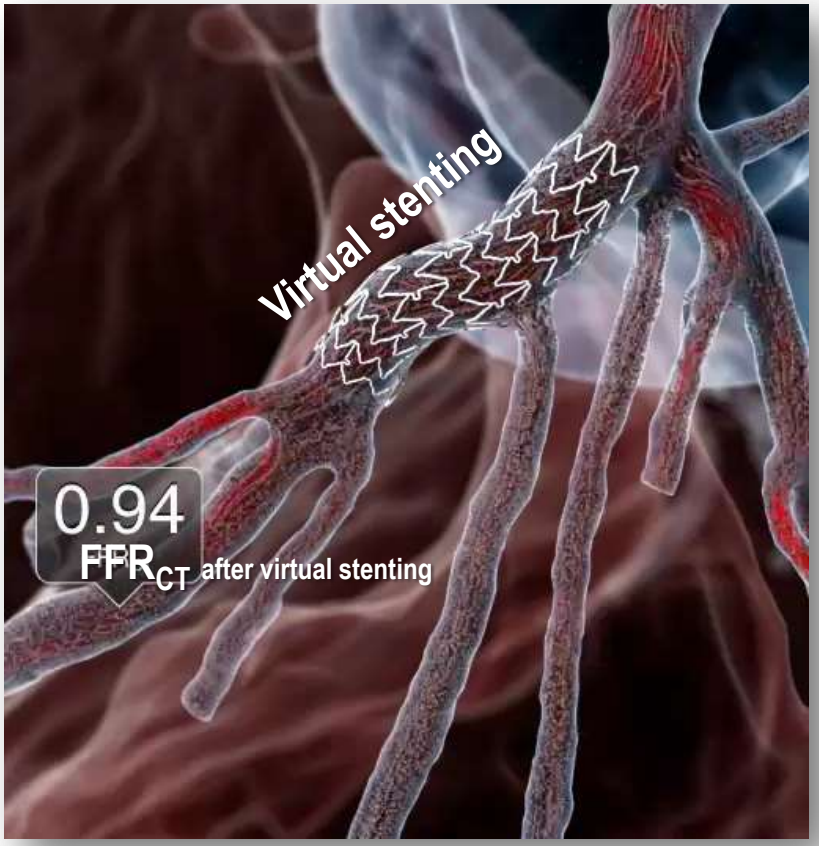
Norgaard BL, et al. JACC Imaging 2016

FFR_{CT}: Present and Future

- Gate keeper to invasive angiography ? **YES**
- Replacing invasive FFR ? **NO**
- **Treatment planning before angiography ?**
- New researches using CT and CFD ?

Image-based computerised modelling of coronary circulation: **Future direction**

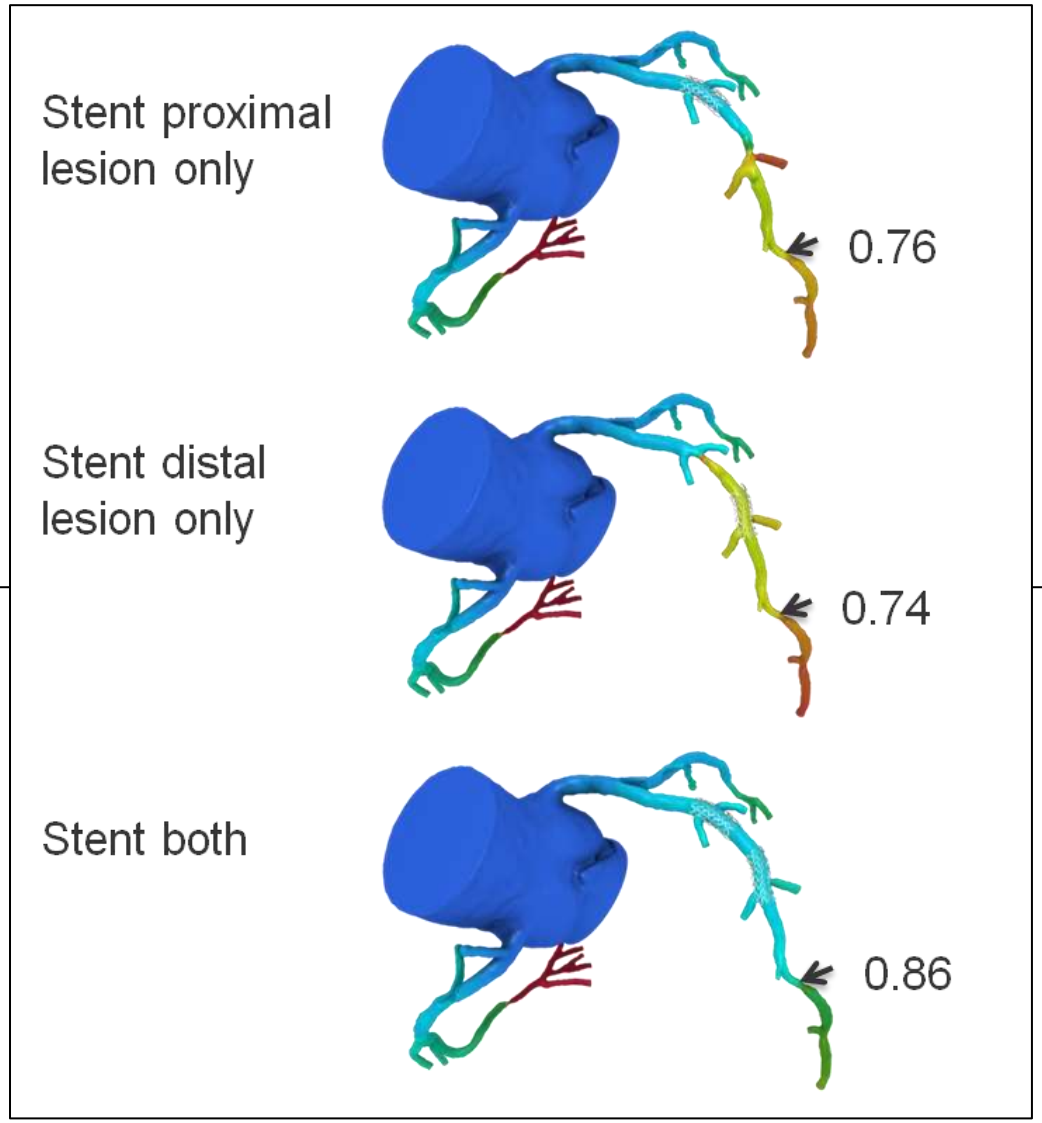
Planning the treatment strategy using **Virtual revascularization & CT-derived computed FFR**



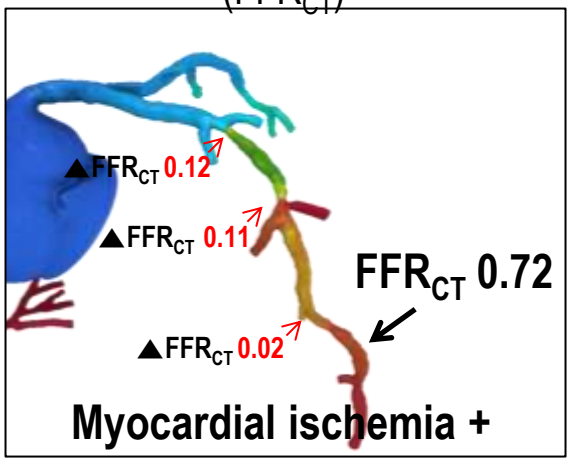
Planning the treatment strategy using
Virtual revascularization & CT-derived computed FFR

Before Stenting

After Stenting

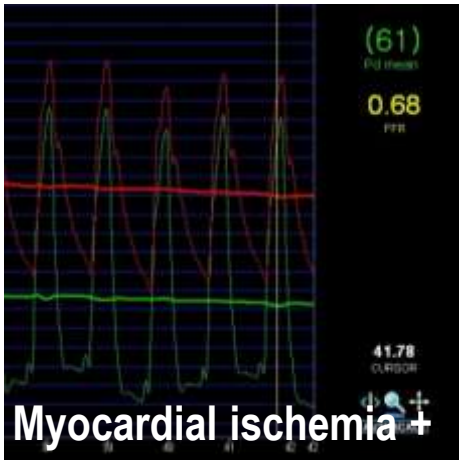
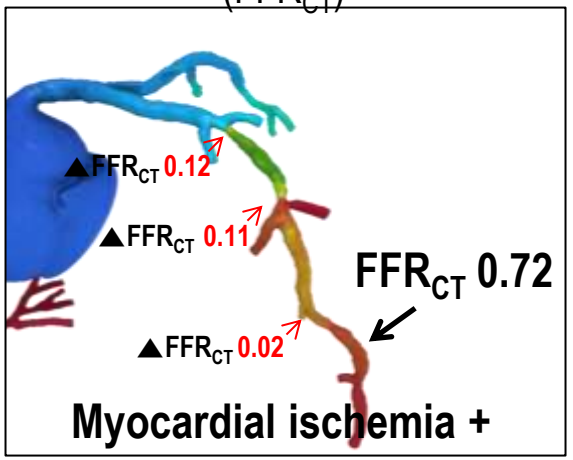
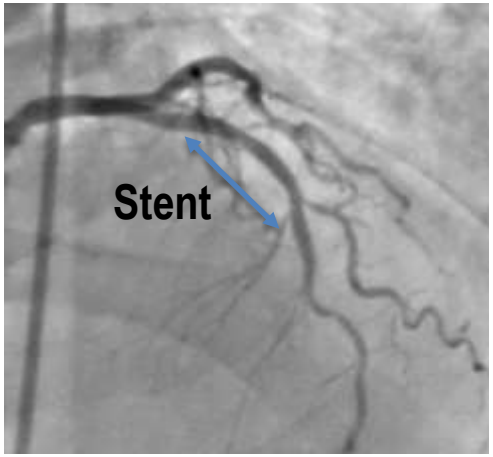
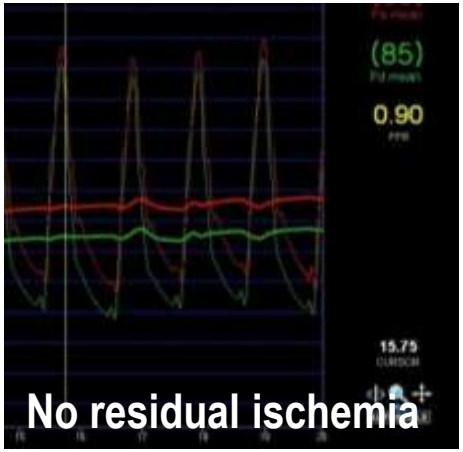
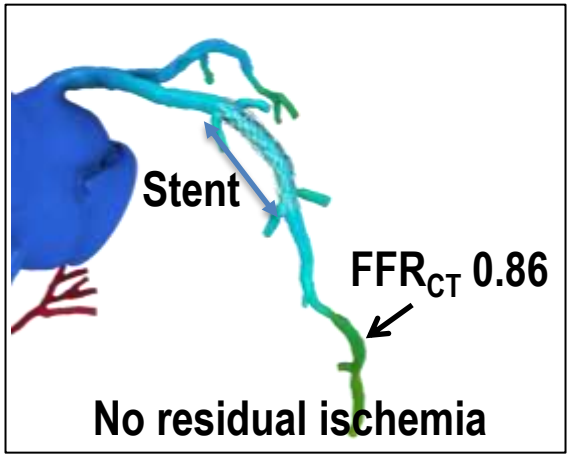


CT-derived computed FFR (FFR_{CT})



Kim KH, Koo BK, et al. JACC interv 2014

Planning the treatment strategy using
Virtual revascularization & CT-derived computed FFR

	Angiography	Invasive FFR	CT-derived computed FFR (FFR_{CT})
Before Stenting			
After Stenting			

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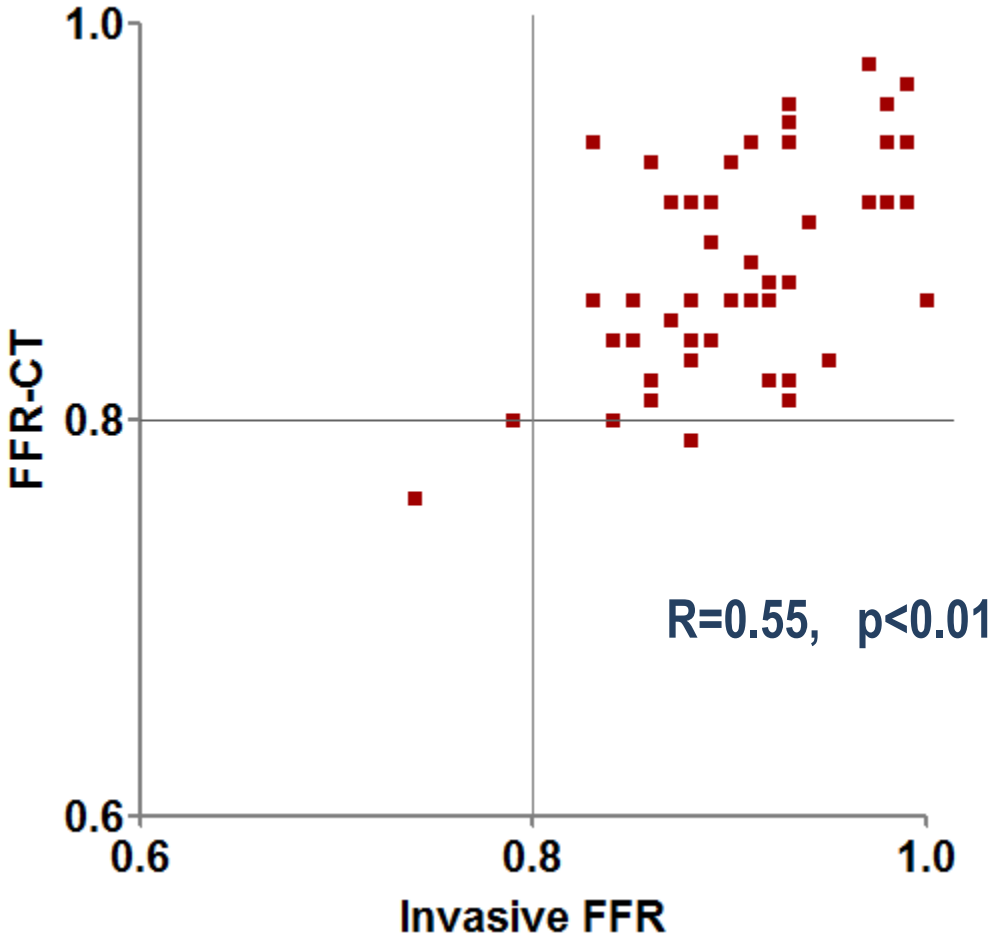
Invasive FFR vs FFR_{CT}: Post - PCI

FFR 0.90 ± 0.05

FFR_{CT} 0.88 ± 0.05

△ **0.02± 0.05**

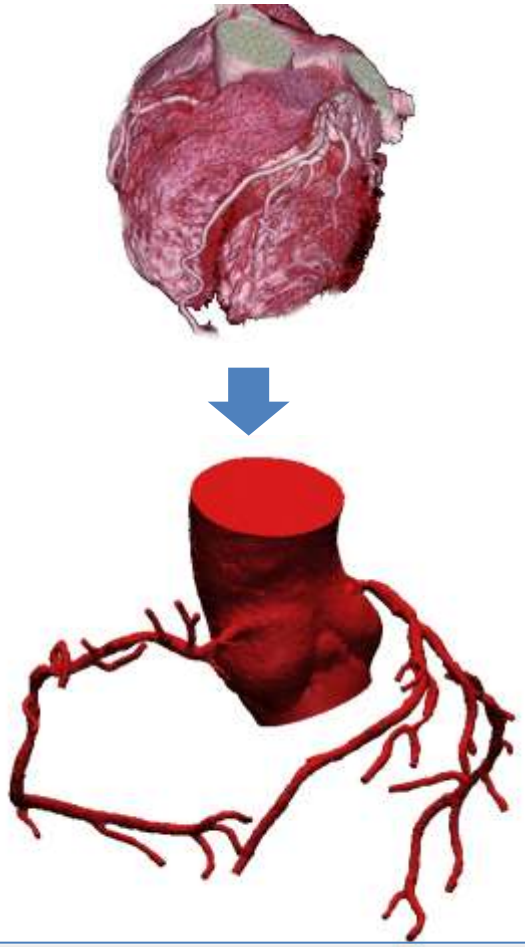


FFR_{CT}: Present and Future

- Gate keeper to invasive angiography ? **YES**
- Replacing invasive FFR ? **NO**
- Treatment planning before angiography ? **Not YET**
- **New researches using CT and CFD ?**

Patient-specific non-invasive coronary hemodynamic assessment

Non-invasive, Pt-specific



Hemodynamics

- Pressure
  - Pressure difference
  - Pressure gradient
  - Pressure recovery
  - **FFR**
- Flow velocity
- Flow rate
- Shear rate
- Shear stress – average, peak, gradient
- Traction
- Oscillatory shear index
- Particle residence time
- Turbulent kinetic energy
- ……

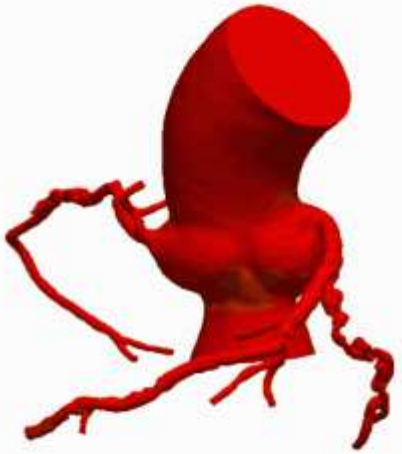
- Static
- Pulsatile
- Resting
- Hyperemic
- Exercise – mild, moderate, peak

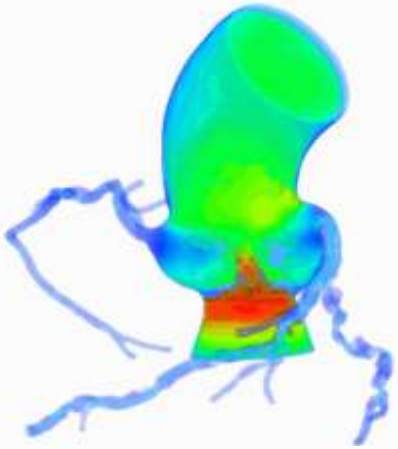
Non-invasive hemodynamic parameter measurement using CFD and cCTA

Pressure

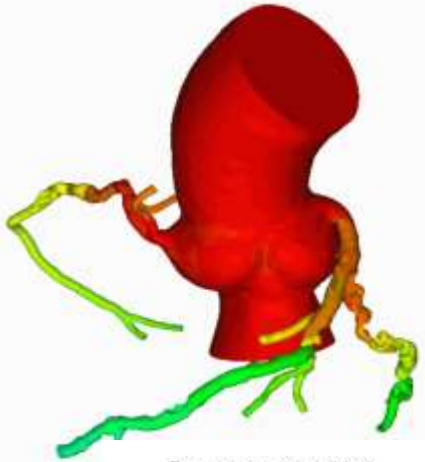
Velocity

Rest





Hyperemia



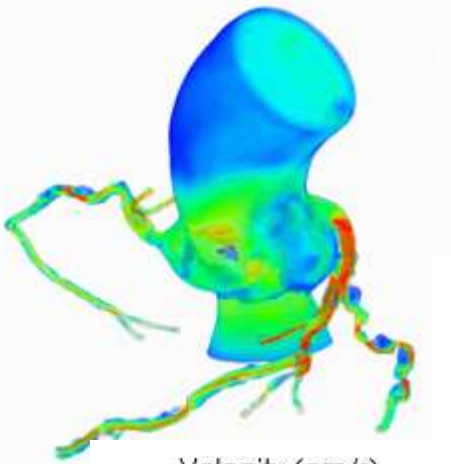
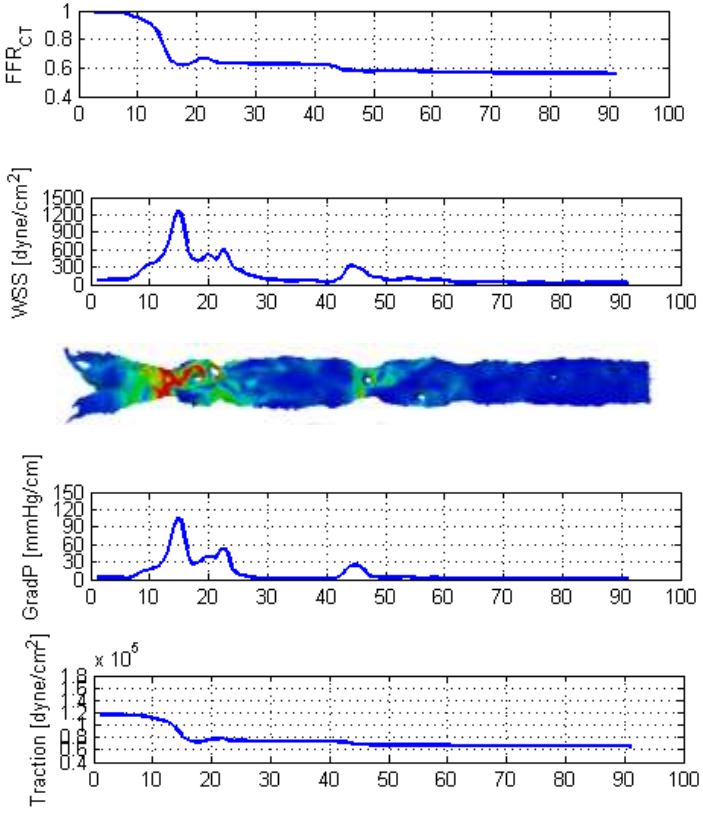


Image-based computerised modelling of coronary circulation: ***Potentials***

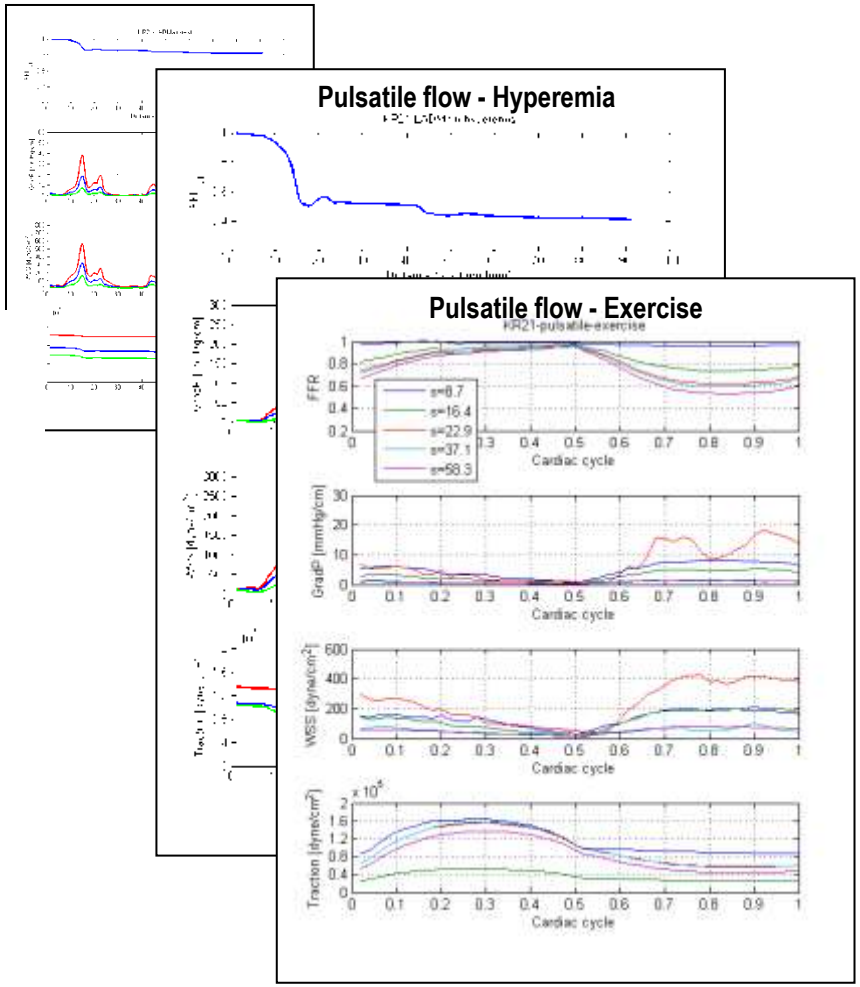
Static flow - hyperemic



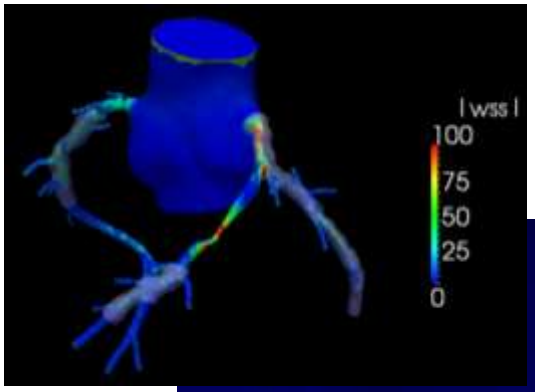
Pulsatile flow - rest

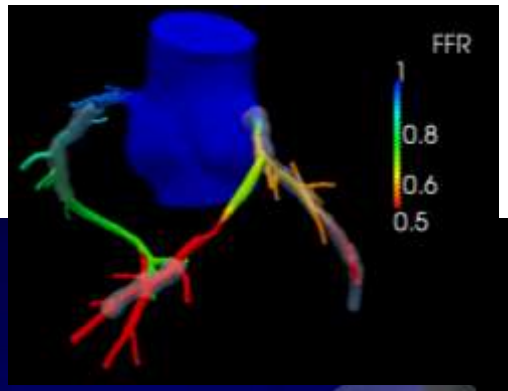
Pulsatile flow - Hyperemia

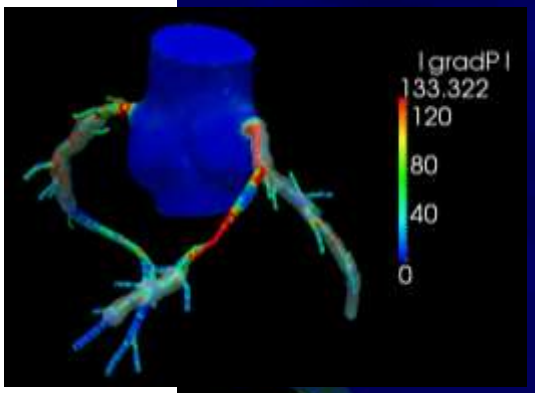
Pulsatile flow - Exercise



Total plaque force analysis







0.005|WSS

FFR

1

0.8

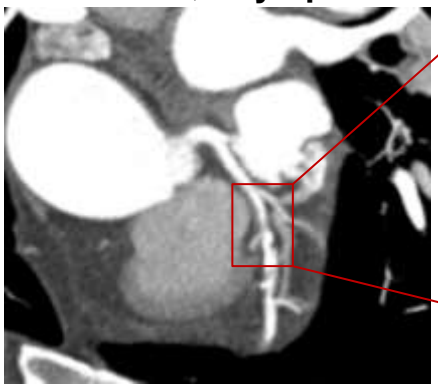
0.6

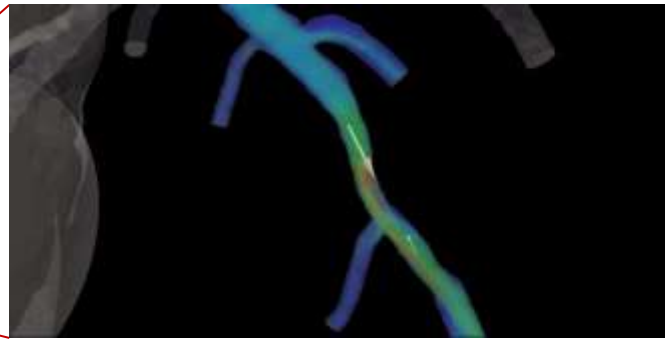
0.5

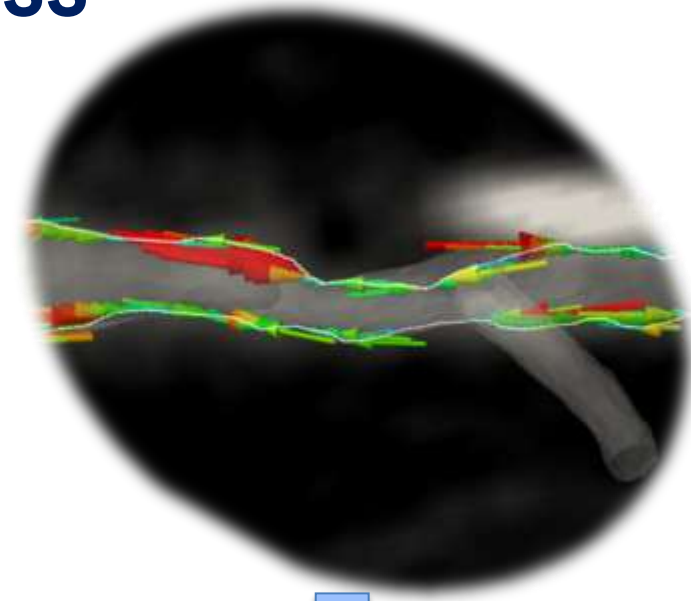
0.0005|TractionForce|

“Axial plaque stress”

2011-04 CT, Asymptomatic

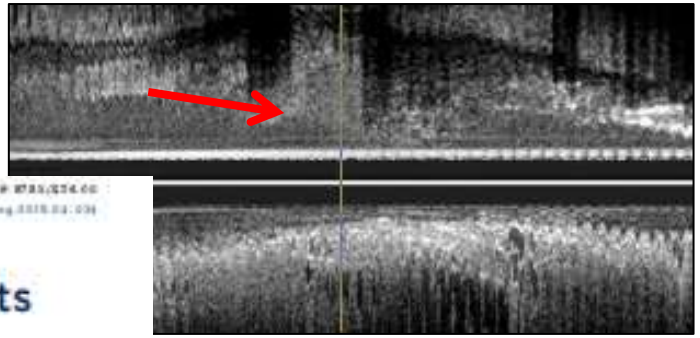






	RG	APS
Upstream	**0.14**	**9960 dyne/cm²**
Downstream	0.05	1740 dyne/cm²

2012-06 Acute MI



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Coronary Artery Axial Plaque Stress and Its Relationship With Lesion Geometry

Application of Computational Fluid Dynamics to Coronary CT Angiography

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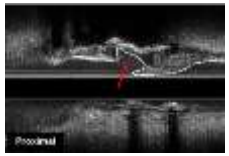
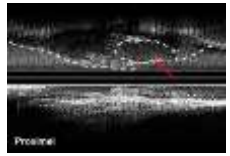
Sethuraman Sankaran, PhD,* Hiromasa Otake, MD, PhD,† Joon-Hyung Doh, MD, PhD,† Chang-Wook Nam, MD, PhD,‡
Bon-Seok Shin, MD, PhD,§ Charles A. Taylor, PhD,*‖ Bon-Kwon Koo, MD, PhD*†¶

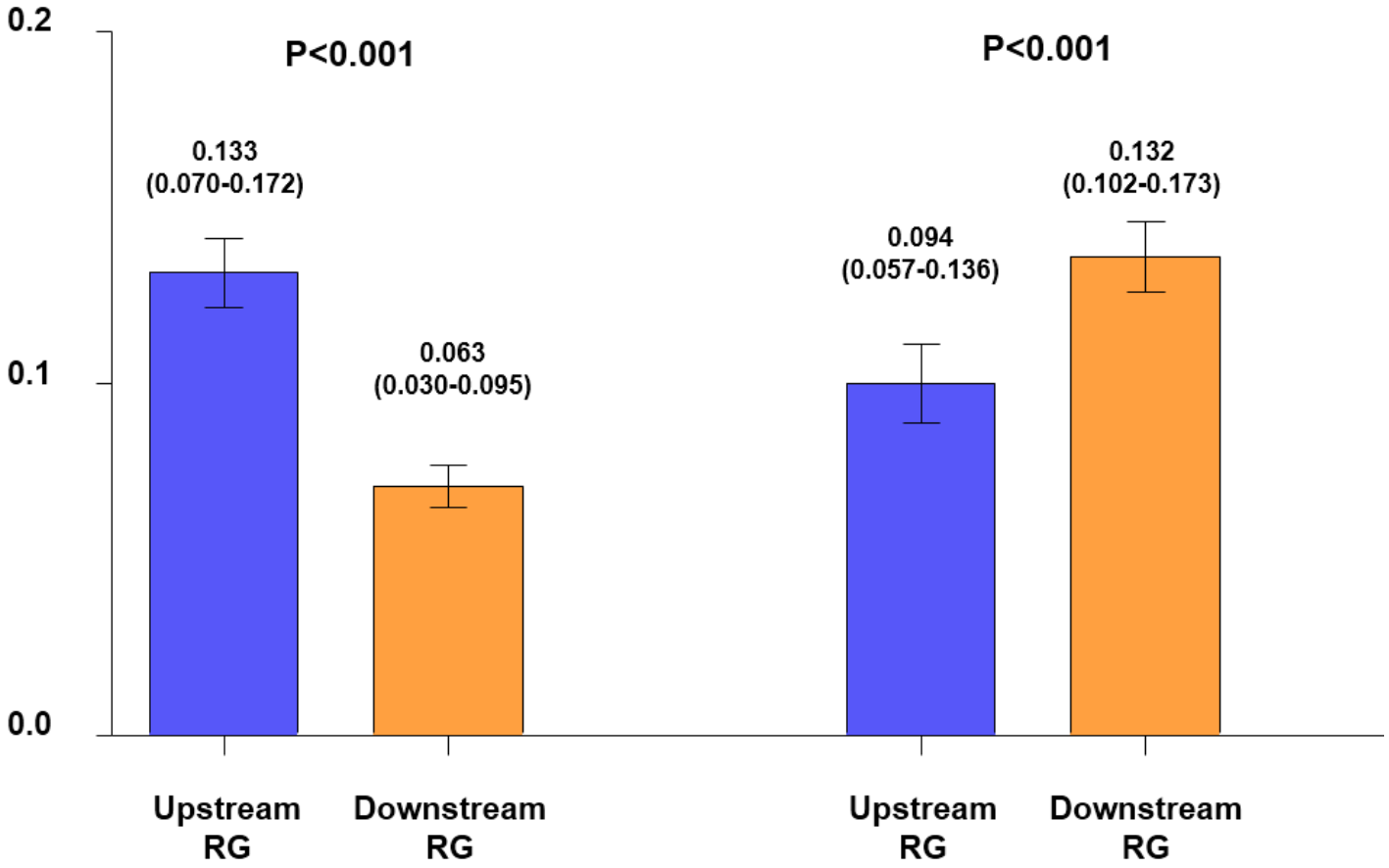
Comparison of Radius Gradient and Rupture Locations



Upstream Rupture

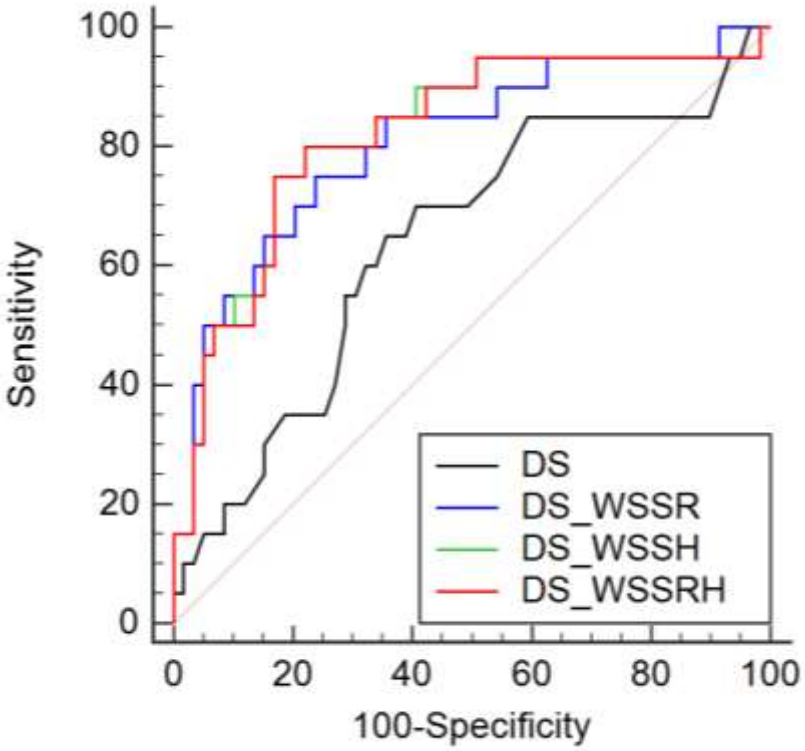
Downstream Rupture



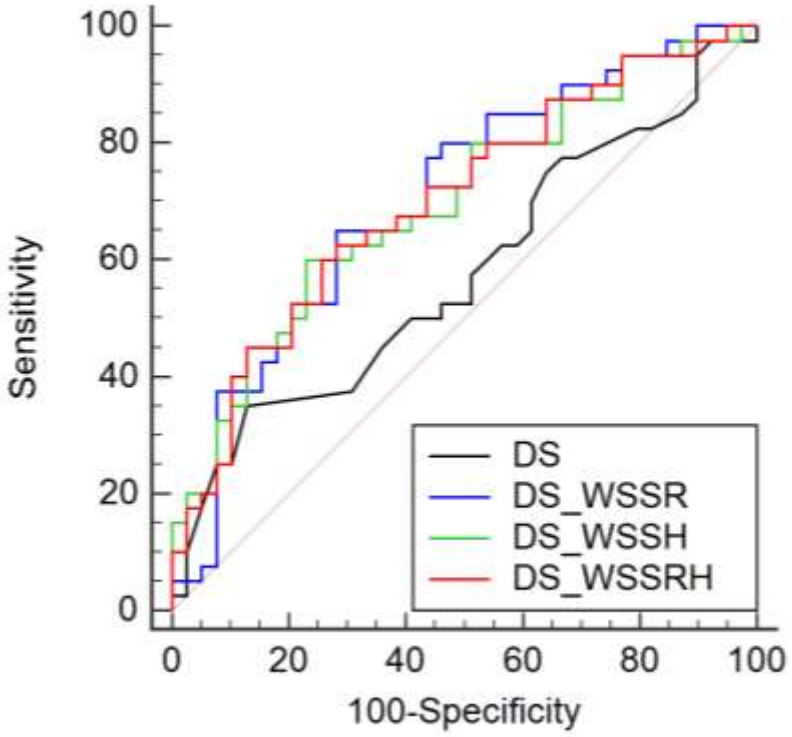


Association with Adverse plaque characteristics
: % diameter stenosis vs. WSS

Napkin ring sign



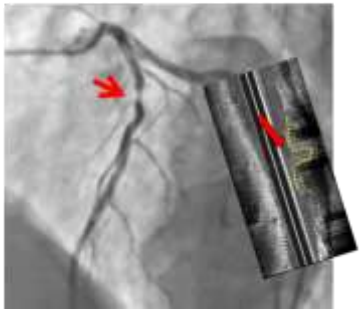
Positive remodeling



DS: % diameter stenosis, **WSSR:** resting wall shear stress, **WSSH:** hyperemic wall shear stress

Non-invasive hemodynamic assessment to predict future risk of ACS: **EMERALD study**

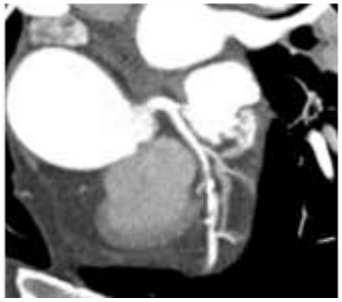
2012-06 Acute MI



Patients with Acute Coronary Syndrome
From 11 International Cardiovascular Centers
(Korea, Japan, Belgium, Denmark, the Netherlands)

Confirmed culprit lesion with coronary angiography (IVUS, OCT)

2011-04 CT, Asymptomatic



Patients who underwent Coronary CT angiography before ACS event (1 month – 2 year before the event)

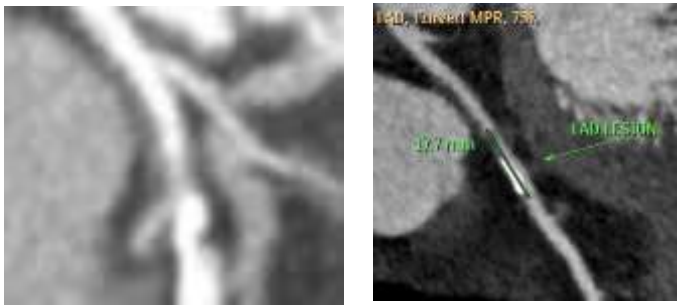
CONTROL (Group B)
Non-Culprit Lesion

CASE (Group A)
Culprit Lesion

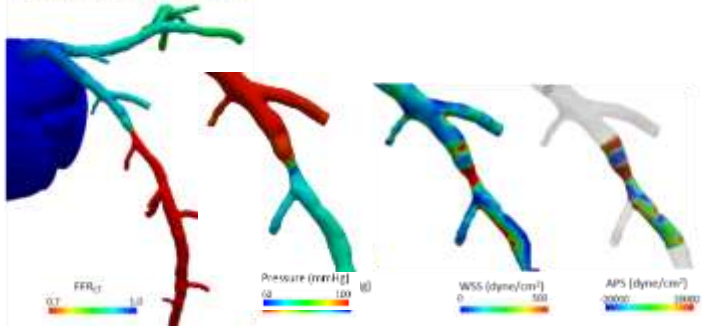
cCTA analysis
adverse plaque characteristics
(Core Lab – SNU Bundang Hospital)

CFD analysis
Non-invasive hemodynamics
(Core Lab - HeartFlow Inc.)

Adverse plaque characteristics assessment



Comprehensive non-invasive hemodynamic assessment using cCTA and CFD



EuroPCR 2016 Innovative pipeline session

FFR_{CT}: Present and Future

- Gate keeper to invasive angiography ? **YES**
- Replacing invasive FFR ? **NO**
- Treatment planning before angiography ? **Not YET**
- New researches using CT and CFD ? **YES**