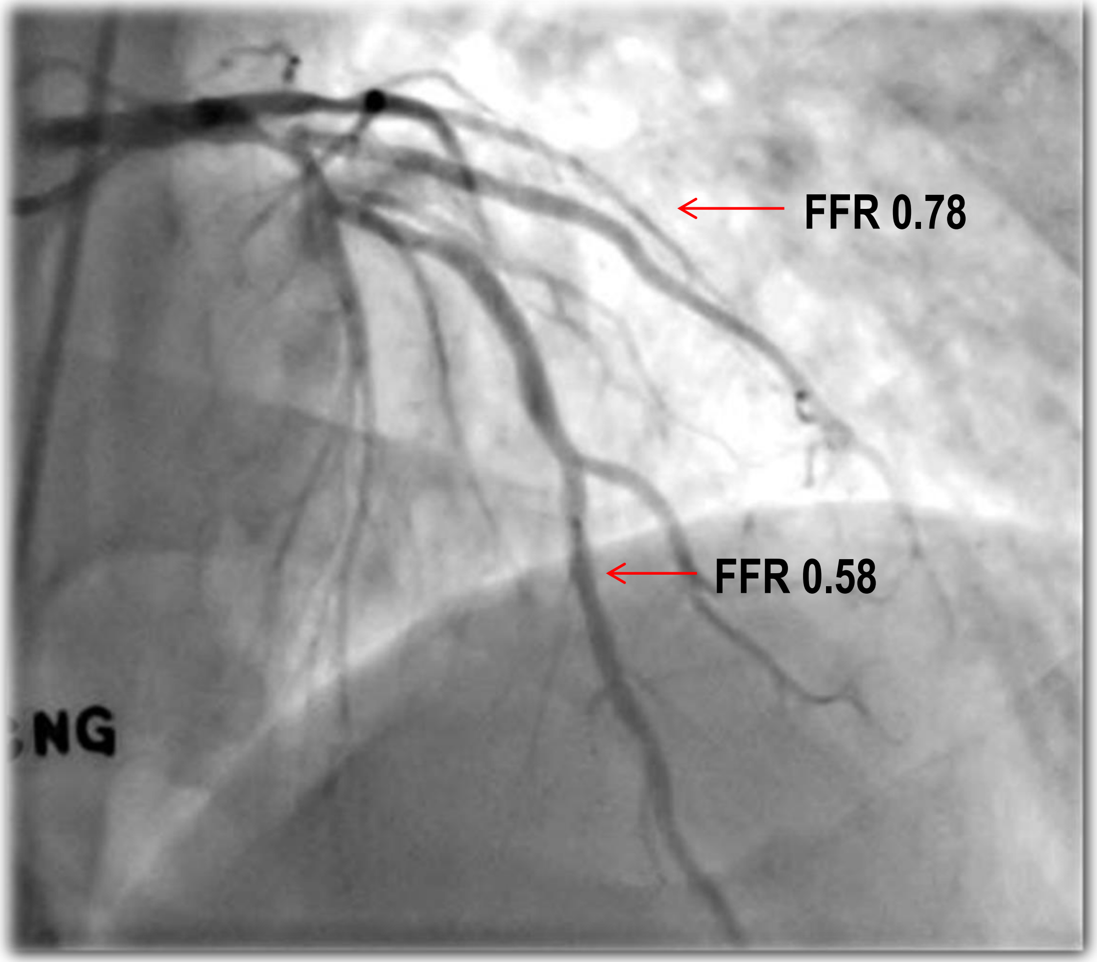
CT-FFR: We do not need invasive angiography (and FFR)

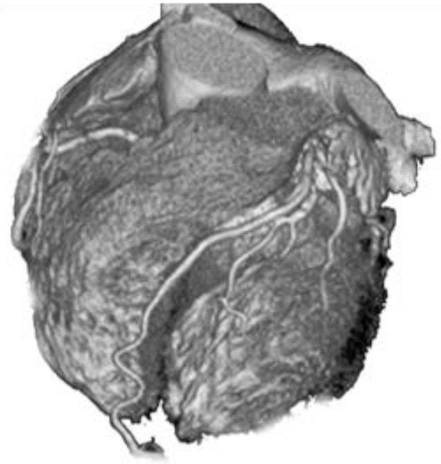
Bon-Kwon Koo, MD, PhD

Seoul National University Hospital, Seoul, Korea

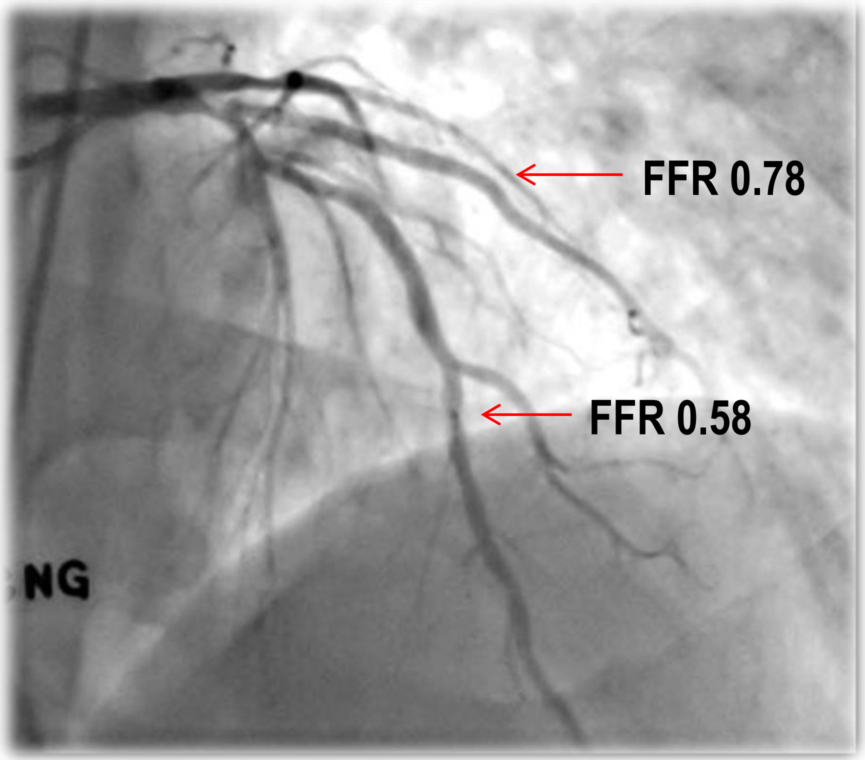
15 years ago, in the cath lab.....

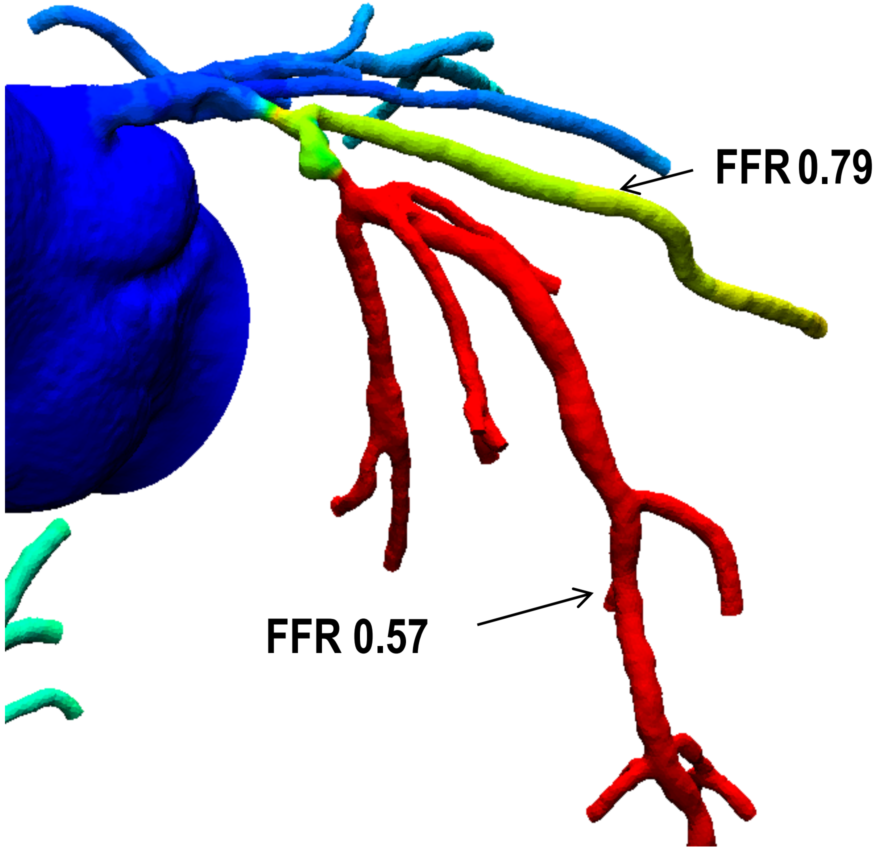


Is it possible to assess hemodynamics from images ?



Is it possible to assess hemodynamics from images?

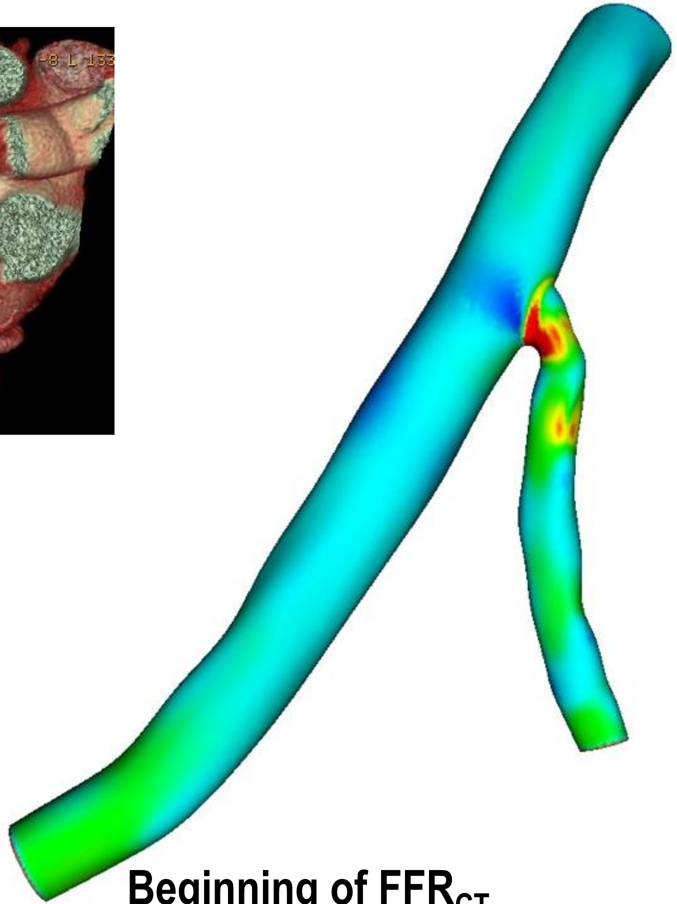




Without invasive procedure
Without pressure wire, without adenosine

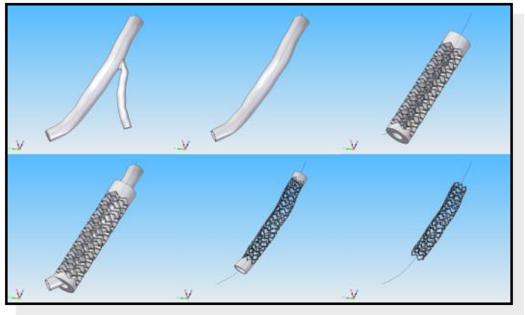
Patient-specific CFD models: the Beginnings

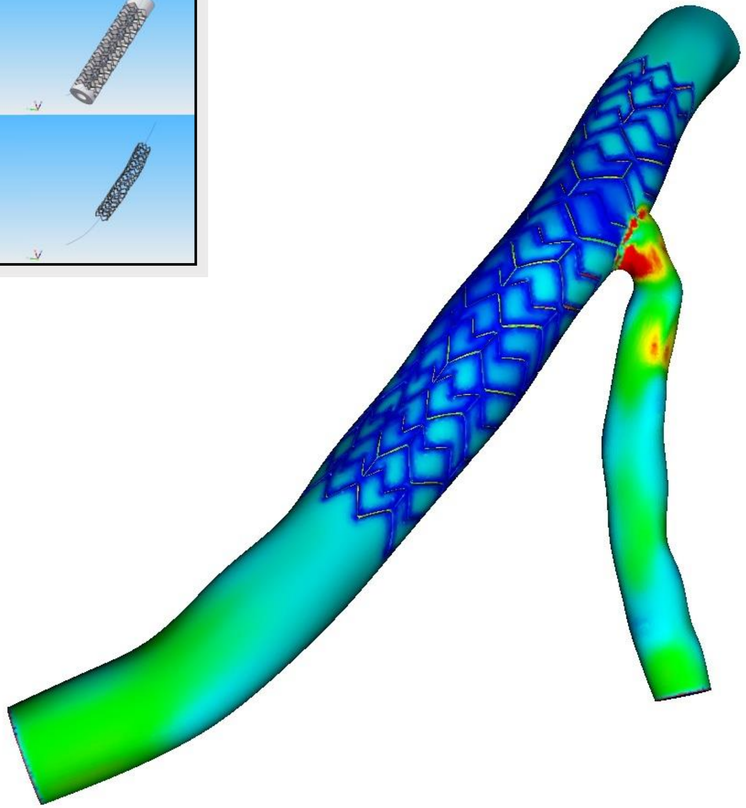
Pre-Stent



Beginning of FFR_{CT}

Post-Stent





Beginning of Treatment Planner

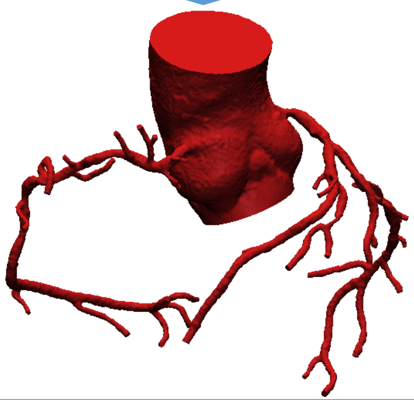
Williams, Koo, LaDisa 2008

Patient-specific non-invasive FFR using CT & CFD

Computational Model based on CCTA

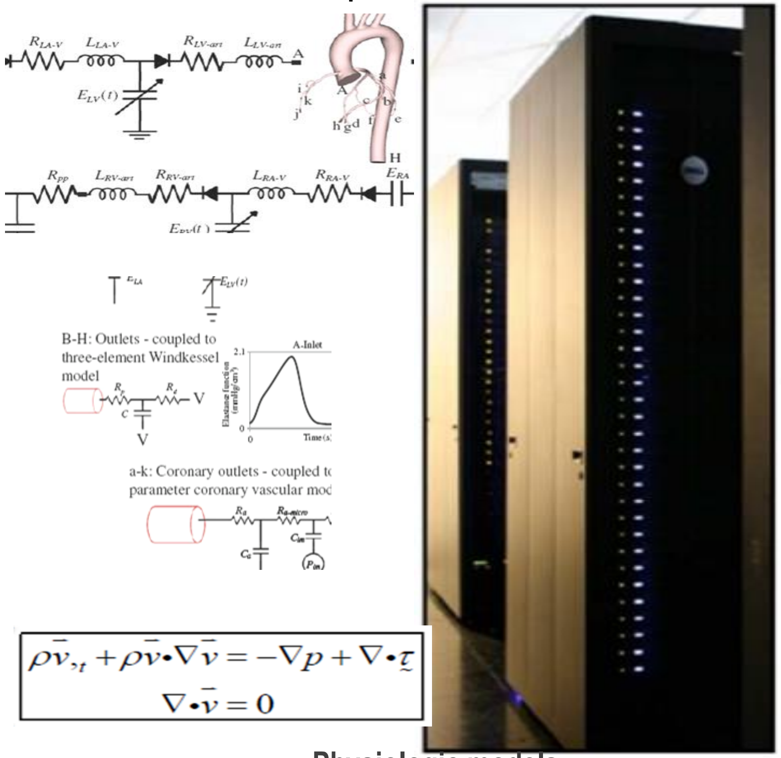
3-D anatomic model from CCTA

No additional imaging
No additional medications



Blood Flow Solution

Blood flow equations solved on supercomputer

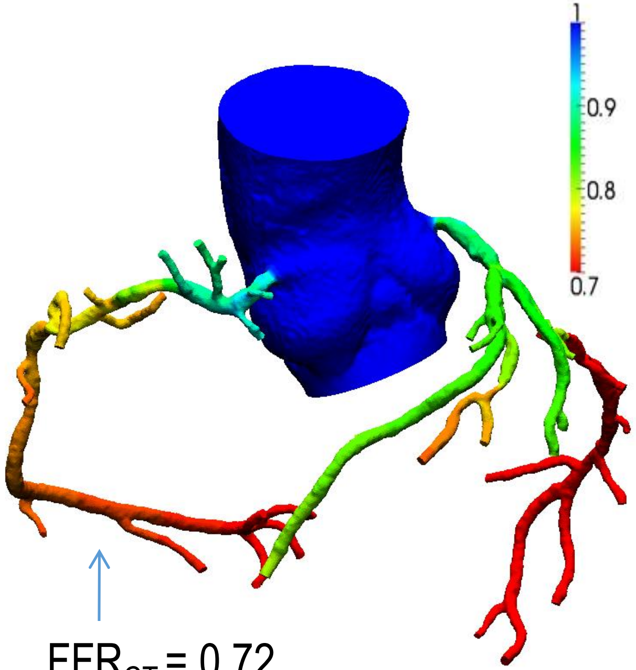


$$\rho \bar{v}_{,t} + \rho \bar{v} \cdot \nabla \bar{v} = -\nabla p + \nabla \cdot \underline{\tau}$$
$$\nabla \cdot \bar{v} = 0$$

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

CT-derived computed FFR (FFR_{CT})

$\frac{P_{Coronary}}{P_{Aorta}}$



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

Koo BK. EuroPCR 2011

Current pathway

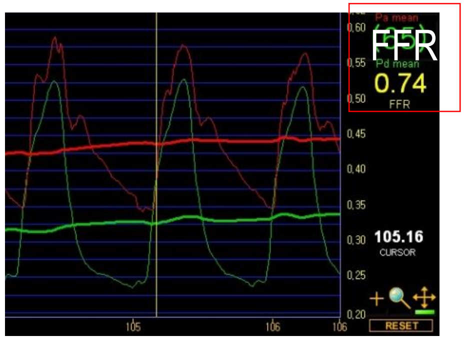
CCTA

>50% diameter stenosis

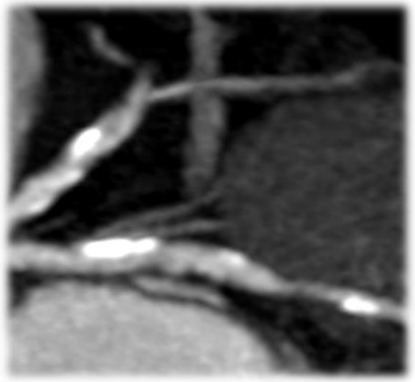
Invasive angiography

>50% diameter stenosis

FFR

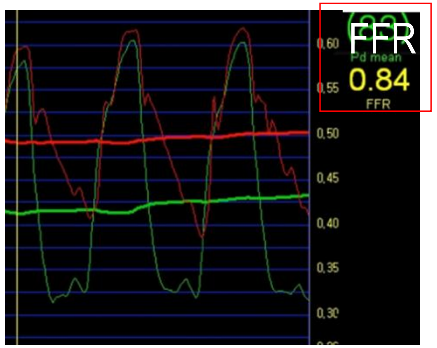


FFR 0.74 → PCI



>50% diameter stenosis

>50% diameter stenosis



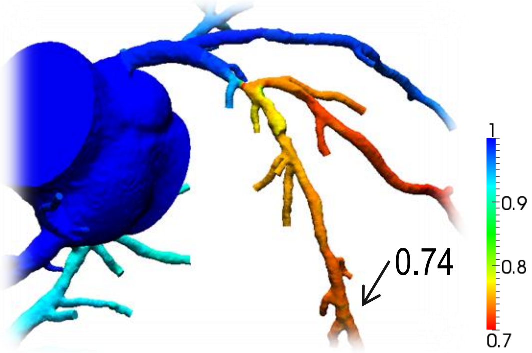
FFR 0.84
→ Medical treatment

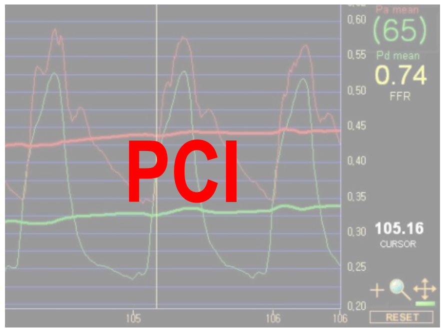
Risk-(almost) free, non-invasive, cost-saving pathway

CCTA

FFR$_{CT}$

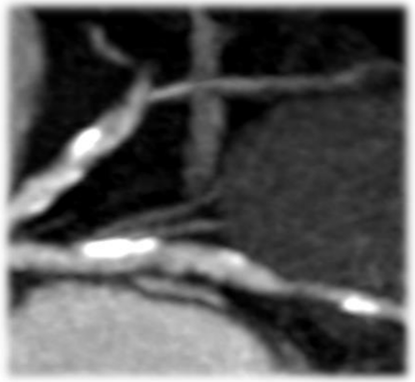
Invasive angiography and PCI

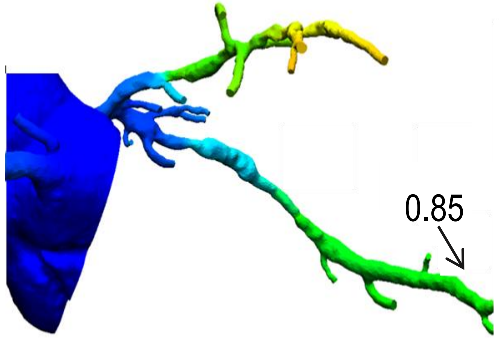


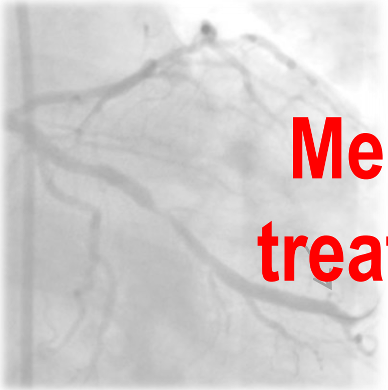


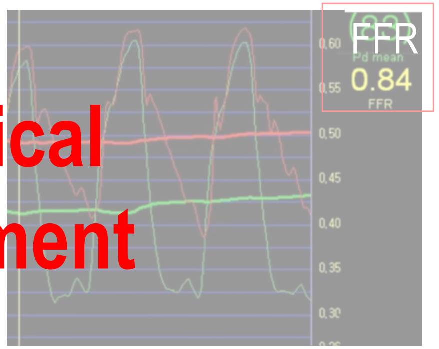
>50% diameter stenosis

FFR$_{CT}$ 0.74 → Invasive procedures









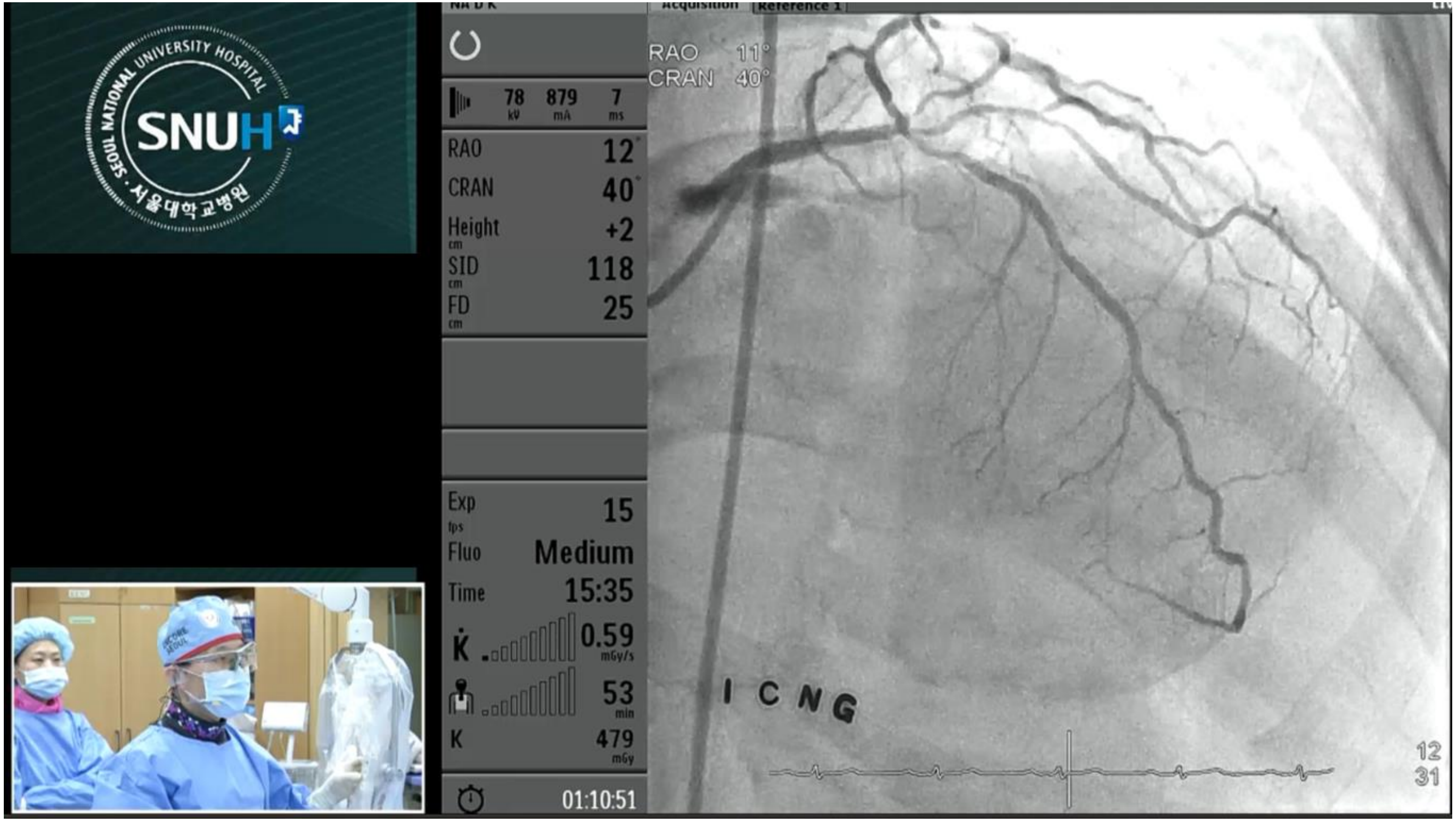
Medical treatment

>50% diameter stenosis

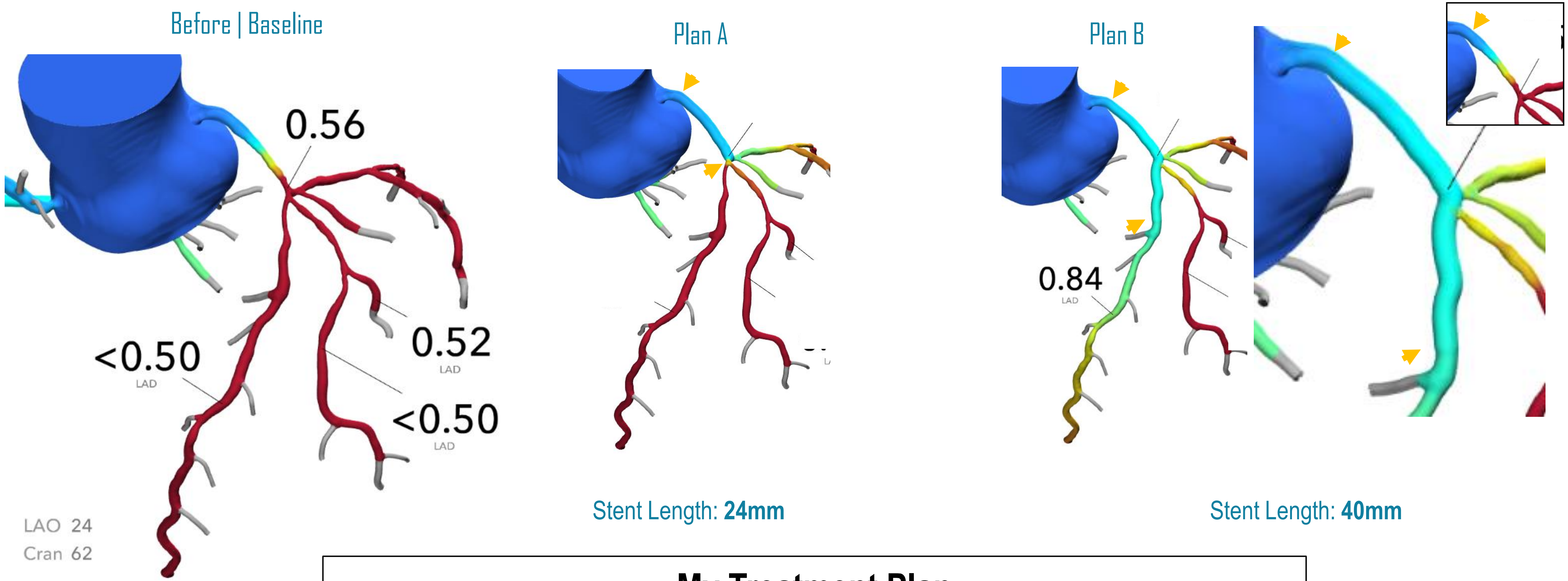
>50% diameter stenosis

FFR 0.84 → no ischemia

Treatment Planning: How to fix this lesion?



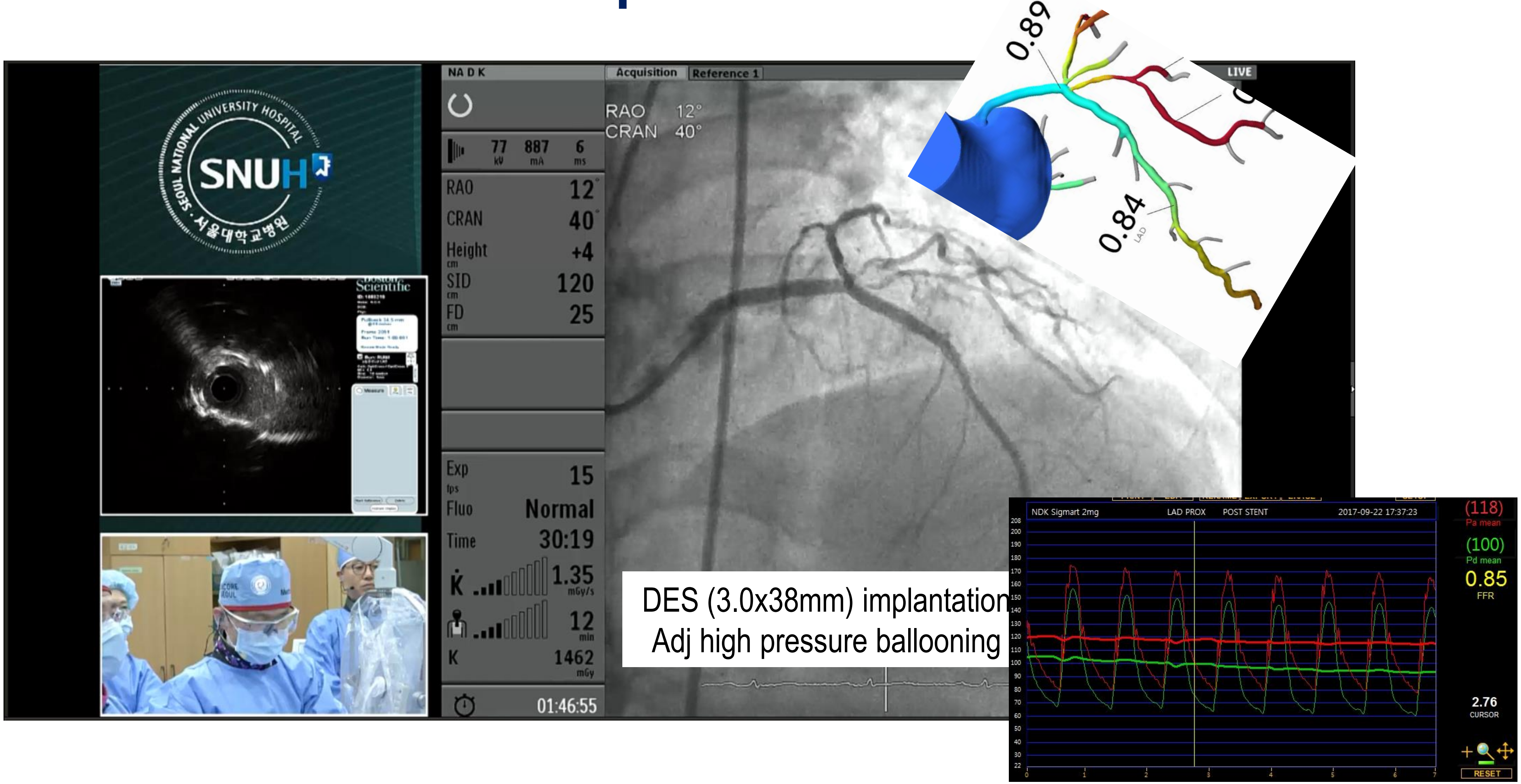
Treatment planning using CT-FFR technology



My Treatment Plan

- LM to LAD stenting, stent diameter 3.0, stent length 38-40mm
- Adjunctive balloon inflation for LM
- Leaving the diagonal ischemia alone due to long diffuse disease

PCI and post-PCI FFR



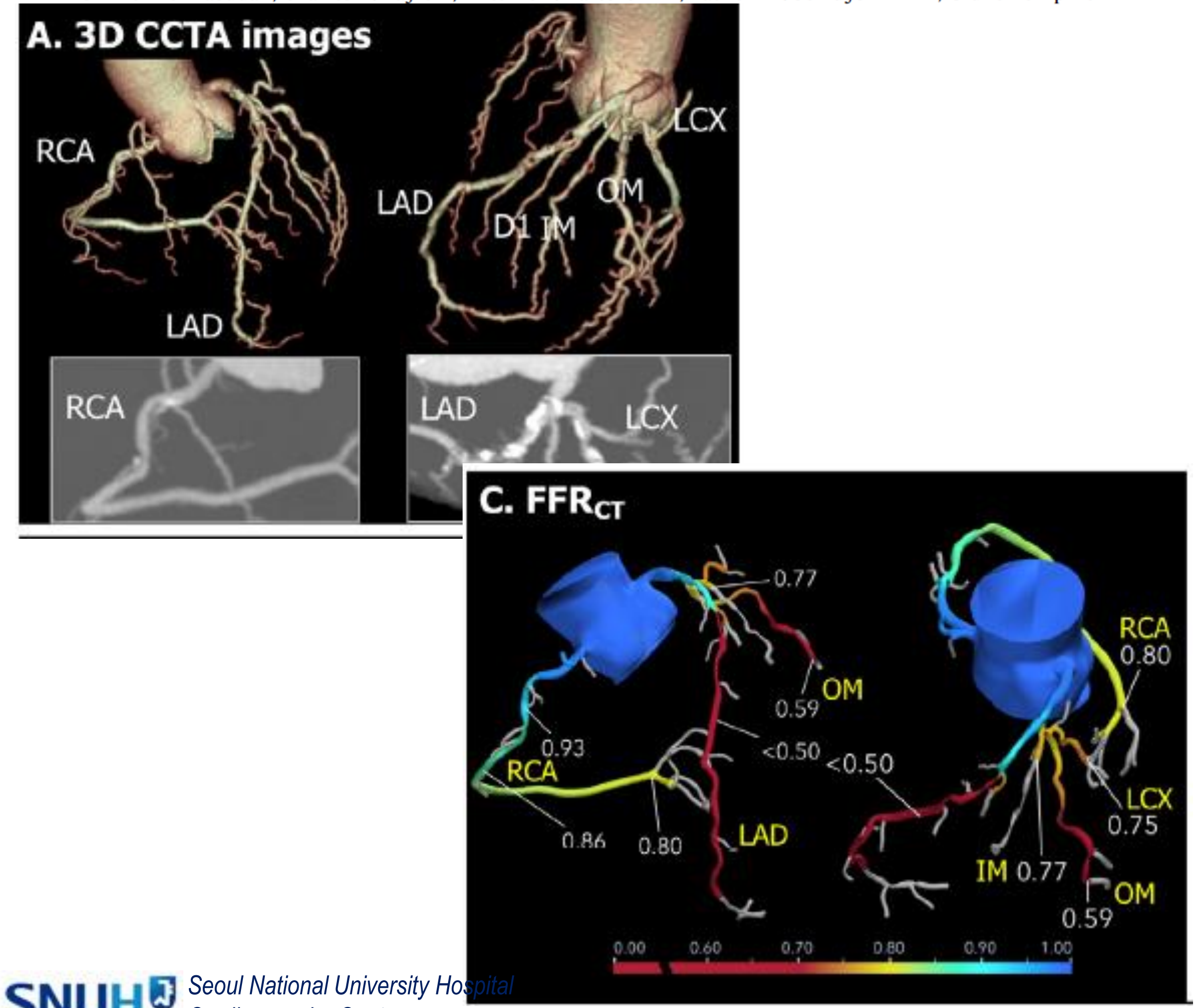
DES (3.0x38mm) implantation
Adj high pressure ballooning

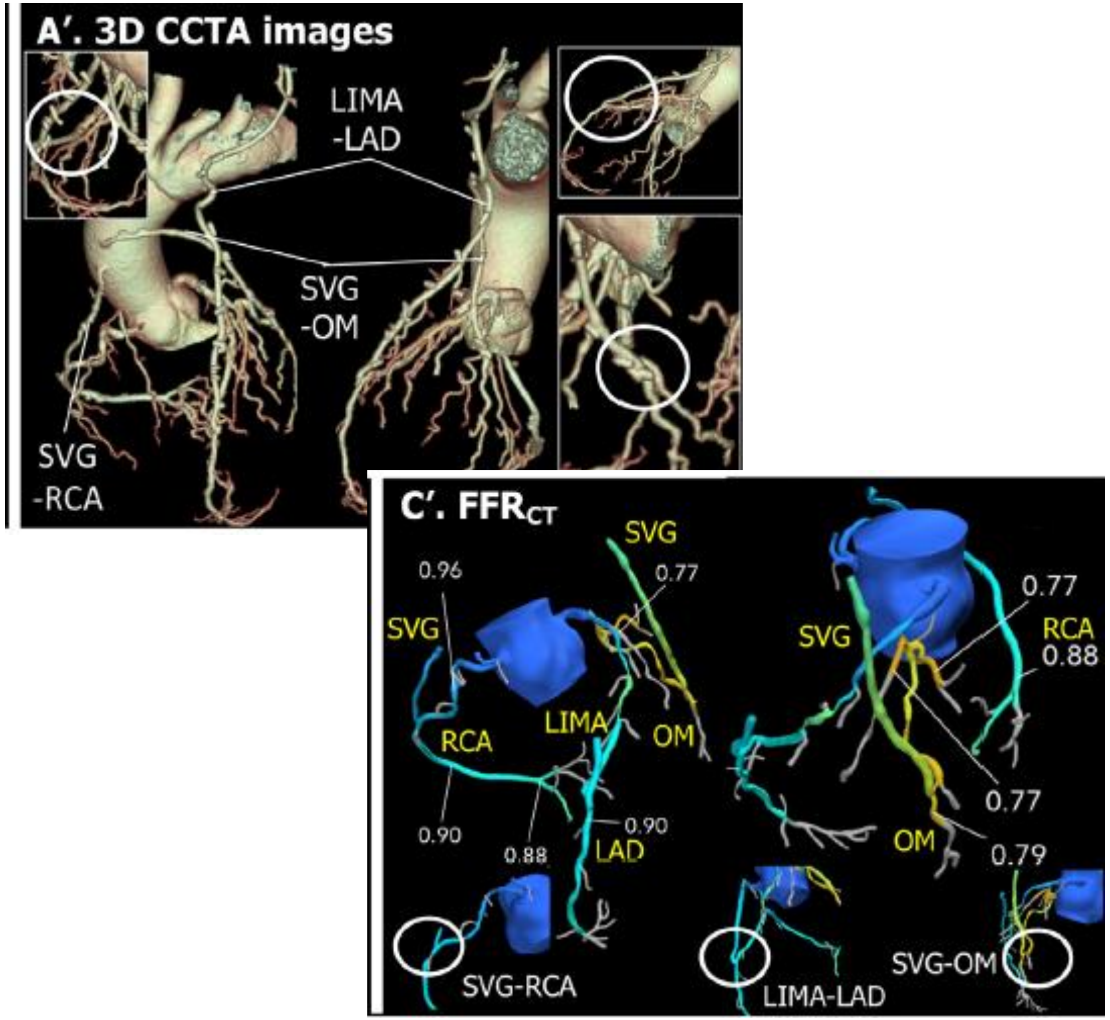
Contents lists available at ScienceDirect
Cardiovascular Revascularization Medicine

Successful coronary artery bypass grafting based solely on non-invasive coronary computed tomography angiography

Hideyuki Kawashima [a,b], Yoshinobu Onuma [a,c], Daniele Andreini [d,e], Saima Mushtaq [d], Marie-angèle Morel [a], Shinichiro Masuda [a], Charles A. Taylor [f], Antonio L. Bartorelli [d,g], Patrick W. Serruys [a,c,h,*,**], Giulio Pompilio [d,i]

This case illustrates that in a patient with 3VD, planning and execution of CABG were successfully performed based solely on CCTA combined with FFR_{CT}. Repeat imaging assessment with non-invasive CCTA and FFR_{CT} at 30-day follow-up confirmed the safety of this approach.





CT-FFR: Do we do not need invasive angiography (and FFR)?

YES?

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)

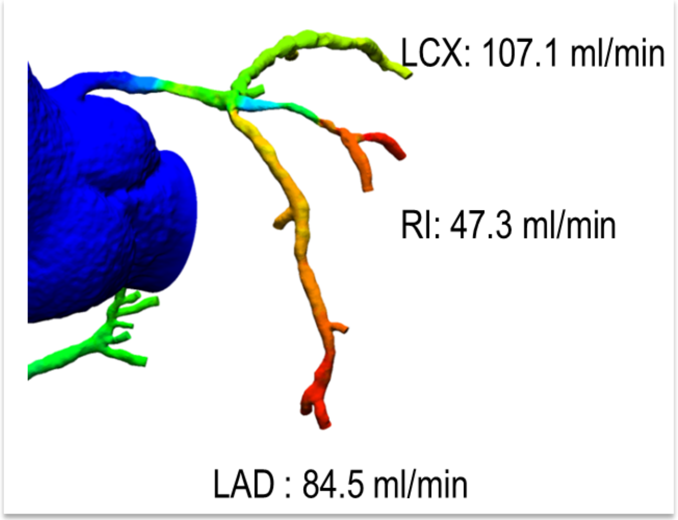


Table 2-1. Comparison of coronary flow reserve measurements using different methods in groups considered as reference (control) groups.

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)

Are these enough for replacing invasive procedure?

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ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.06.066
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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

	Sens	Specif	PPV	NPV	Accuracy
DISCOVER-FLOW	93%	82%	85%	91%	87%
DeFACTO	90%	54%	67%	84%	73%
NXT	86%	79%	65%	92%	81%
	90%	**72%**	**72%**	**89%**	**80%**

Table 1
Characteristics of studies

First author	Year	design	study population	number of evaluable patients	number of vessels	Time period between FFR and FFRCT	CFD software	threshold of ischemia FFR	threshold of ischemia FFRCT
Yang[9]	2019	retrospective, single-center	underwent CCTA for evaluation of CAD and FFR measurement	100	125	<30 days	Auto vessel	≤0.80	≤0.80
Wang[10]	2015	retrospective, single-center	suspected CAD	32	32	≤3 months	Siemens cFFR	<0.80	≤0.80
Tesche[11]	2016	retrospective, single-center	suspected or known CAD	37	37	<3 months	Siemens cFFR	≤0.80	≤0.80
Tang[12]	2019	retrospective, multicenter	suspected CAD	338	422	<3 months	United-Imaging	≤0.80	≤0.80
Tang[13]	2019	retrospective, multicenter	suspected or known CAD	136	183	<60 days	Siemens cFFR	≤0.80	≤0.80
Shi[14]	2017	retrospective, single-center	suspected CAD	29	36	4.3 days (0-14 days)	COMSOL Multiphysics	≤0.80	≤0.80
Sand[15]	2018	Prospective, single-center	patients with stable chest pain	143		ND	Heart Flow	≤0.80	≤0.80
Renker[16]	2014	retrospective, single-center	suspected or known CAD	53	67	<3 months	Siemens cFFR	<0.80	<0.80
Osawa[17]	2017	Prospective, single-center	suspected CAD	18	26	<60 days	Heart Flow	<0.80	<0.80
Nørgaard[18]	2014	Prospective, milticenter	suspected CAD	254	484	18 (1-55)days	Heart Flow	≤0.80	≤0.80
Miyajima[19]	2020	retrospective, single-center	suspected CAD	97	105	<3 months	W.I.P.	≤0.80	≤0.80
Min[20]	2012	Prospective, milticenter	suspected or known CAD	252	407	15.5 (5-33)days	Heart Flow	≤0.80	≤0.80
Kurata[21]	2017	Prospective, single-center	suspected or known CAD	21	29	55 (19-120)days	Siemens cFFR	≤0.80	≤0.80
Kruk[22]	2016	Prospective, single-center	suspected CAD	90	96	<6 months	Siemens cFFR	≤0.80	≤0.80
Koo[23]	2011	Prospective, milticenter	suspected or known CAD	103	159	2.3 (0-26)days	Heart Flow	≤0.80	≤0.80
Ko[24]	2019	Prospective, single-center	no known CAD	49	91	ND	Heart Flow	≤0.80	≤0.80
Ko[25]	2017	Prospective, single-center	Symptomatic patients with no known CAD	30	58	ND	Toshiba Medical Systems Corp	≤0.80	≤0.80
Kim[26]	2014	retrospective, multicenter	significant coronary stenoses	44	48	12 (2-40)days	Heart Flow	≤0.80	≤0.80
Kawaji[27]	2017	Prospective, single-center	suspected significant CAD	48	70	<60 days (23.6 ± 15.5)	Heart Flow	≤0.80	≤0.80
Gaur[28]	2017	Prospective, single-center	STEMI Patients	60	124	mean 1 day	Heart Flow	≤0.80	≤0.80
De Geer[29]	2015	retrospective, single-center	underwent CCTA and FFR measurement	21	23	49 (4-106 days)	Siemens cFFR	≤0.80	≤0.80
Coenen[30]	2015	retrospective, single-center	suspected or known CAD	106	189	<50 days	Siemens cFFR	≤0.80	≤0.80
Chung[31]	2017	retrospective, multicenter	suspected or known CAD	117	218	<30 days	Toshiba Medical	≤0.80	≤0.80

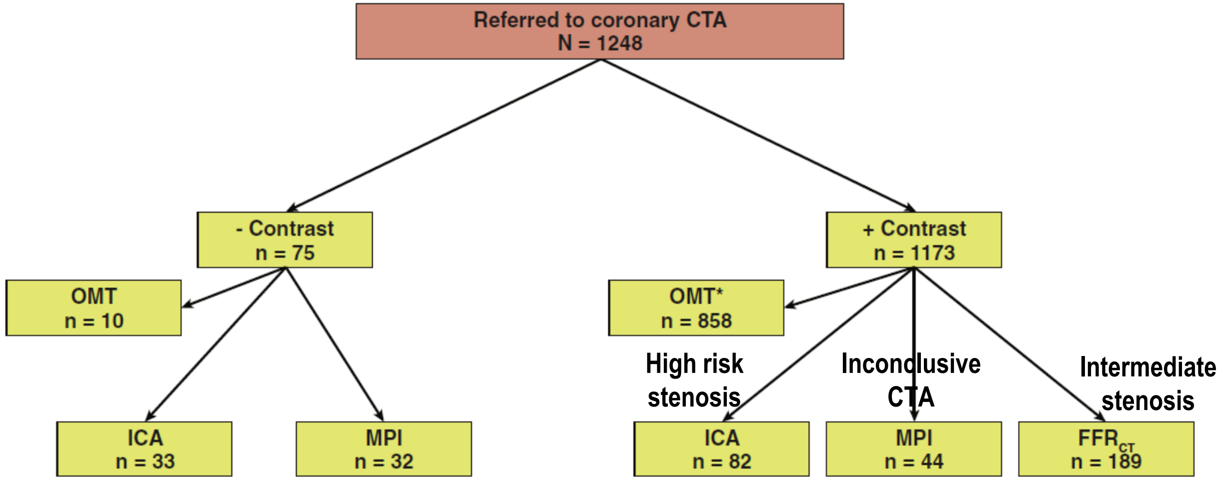
CAD= coronary artery disease; CCTA= coronary computed tomography angiography; CFD= computational fluid dynamics; FFR= fractional flow reserve; FFRCT= computed tomography-based fraction flow reserve; ND= not defined.

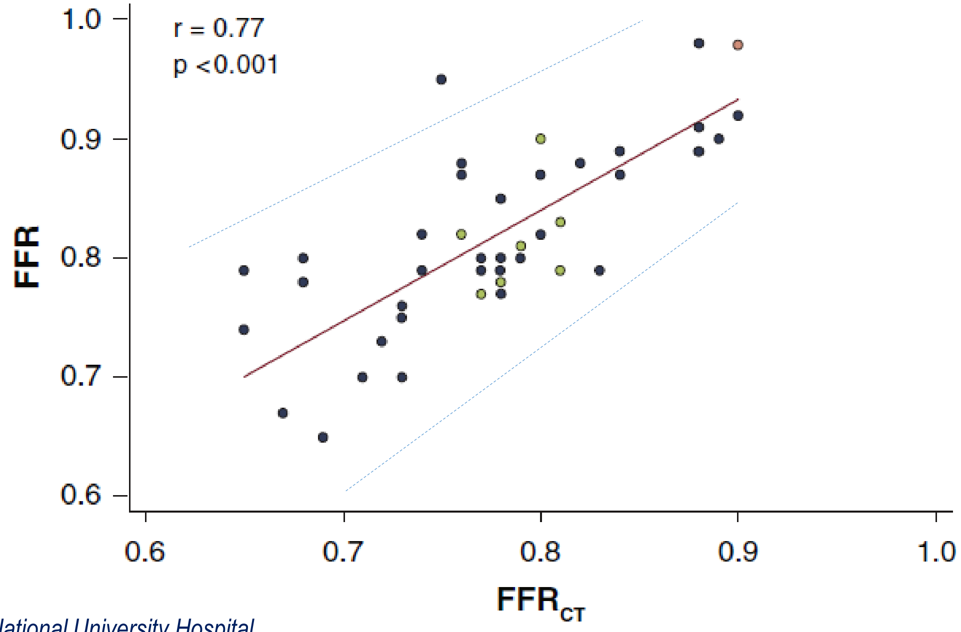
Perpatient and pervessel pooled analysis results

Level	Number of studies	Sensitivity (95%CI)	Specificity (95%CI)	AUC
Per-patient	13	0.88 (0.85-0.90)	0.79 (0.71-0.85)	0.89
Per-vessel	22	0.85 (0.82-0.87)	0.81 (0.76-0.85)	0.87

Luo Y, et al. Hellenic J Cardiol 2022

FFR_{CT} in daily clinical practice





Per patient agreement 73%

Per-vessel agreement 70%

Norgaard BL, et al. JACC Imaging 2016

CT-FFR: Do we do not need invasive angiography (and FFR)?

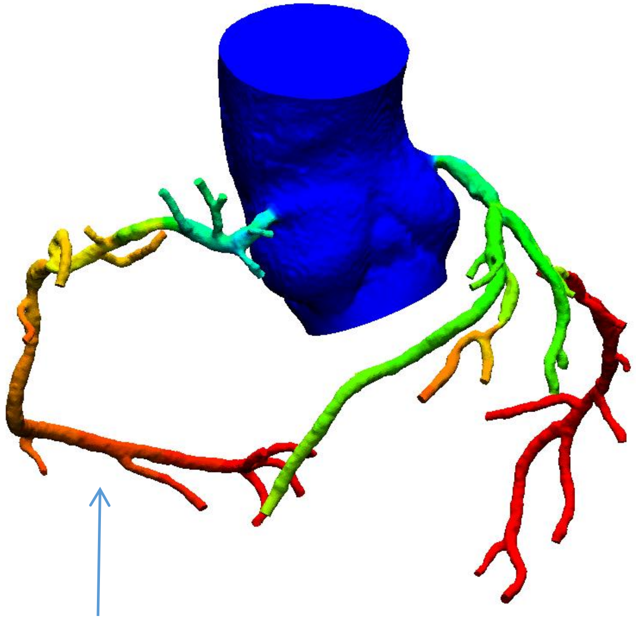
NO?

CT-FFR: Do we do not need invasive angiography (and FFR)?

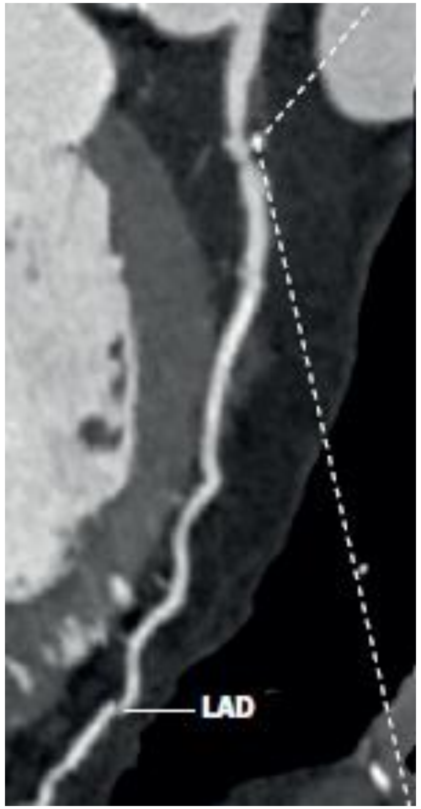
High-Risk Attributes

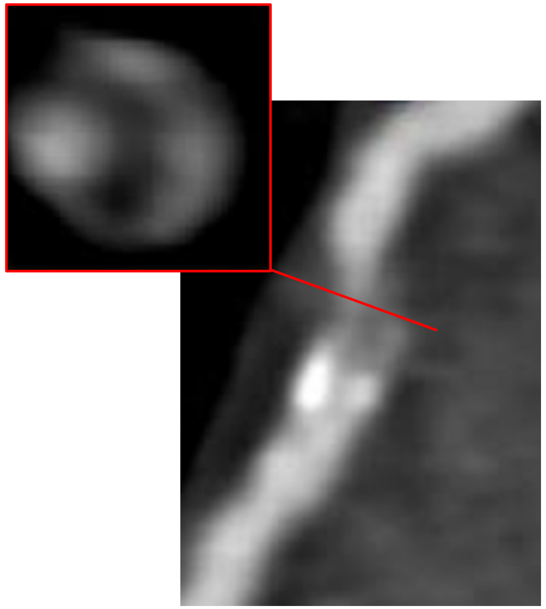
Physiologic Attributes	Plaque Attributes		
Myocardial Ischemia	+ High Global Disease Burden	+ High-Risk Plaque Characteristics	+ High Local Disease Burden

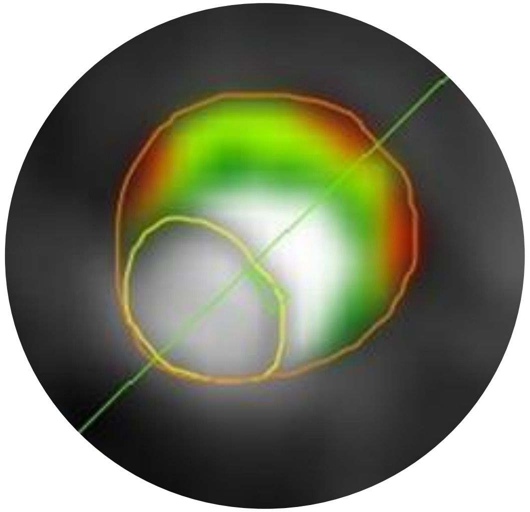
CT-derived computed FFR



$FFR_{CT} = 0.72$

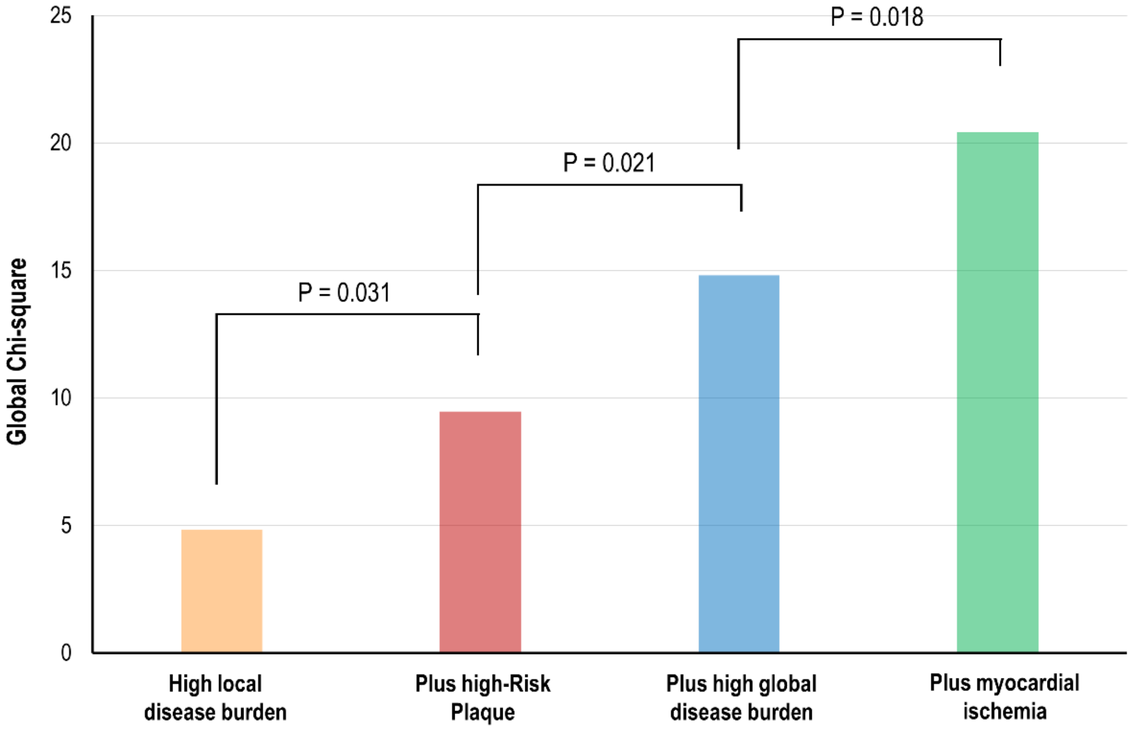


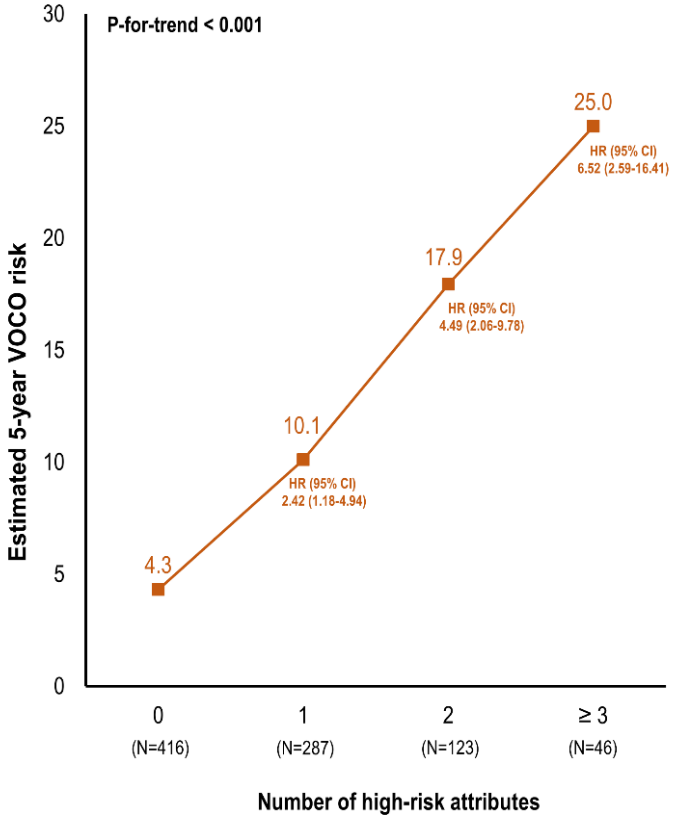




Prognostic implication of high risk attributes

Additive prognostic implications of "4 categories"



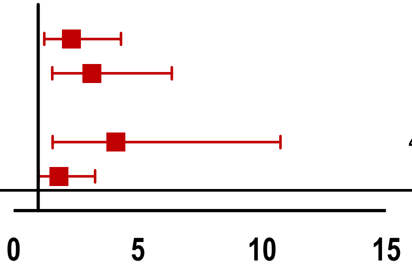


Yang SH, Koo BK, et al. JACC imaging 2021

Prognostic implications of local hemodynamics from CCTA

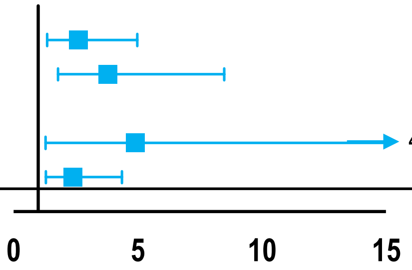
High Wall Shear Stress

Subgroup		Number of event: WSS ≥154.7 dyn/cm^2	Number of event: WSS <154.7 dyn/cm^2	Hazard ratio (95% CI)	Interaction P-value
High-risk plaque					0.661
	Yes	30/51 (58.8)	14/41 (34.1)	2.32 (1.24-4.33)	
	No	14/44 (31.8)	8/80 (10.0)	3.15 (1.56-6.37)	
FFR_{CT}					0.142
	≤0.80	27/44 (61.4)	3/22 (13.6)	4.11 (1.57-10.75)	
	>0.80	17/51 (33.3)	19/99 (19.2)	1.82 (1.01-3.29)	



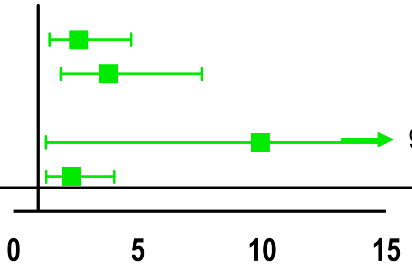
High Pressure Gradient

Subgroup		Number of event: PG ≥5.8mmHg/cm	Number of event: PG <5.8mmHg/cm	Hazard ratio (95% CI)	Interaction P-value
High-risk plaque					0.571
	Yes	33/56 (58.9)	11/36 (30.6)	2.60 (1.36-4.99)	
	No	16/49 (32.7)	6/75 (8.0)	3.80 (1.79-8.49)	
FFR_{CT}					0.323
	≤0.80	28/46 (60.9)	2/20 (10.0)	4.91 (1.29-18.73)	
	>0.80	21/59 (35.6)	15/91 (16.5)	2.39 (1.31-4.37)	



High ΔFFR

Subgroup		Number of event: ΔFFR_{CT} ≥0.06	Number of event: ΔFFR_{CT} <0.06	Hazard ratio (95% CI)	Interaction P-value
High-risk plaque					0.542
	Yes	31/46 (67.4)	13/46 (28.3)	2.63 (1.46-4.74)	
	No	13/41 (31.7)	9/83 (10.8)	3.81 (1.91-7.58)	
FFR_{CT}					0.169
	≤0.80	29/46 (63.0)	1/20 (5.0)	9.93 (1.30-75.51)	
	>0.80	15/41 (36.6)	21/109 (19.3)	2.32 (1.32-4.06)	

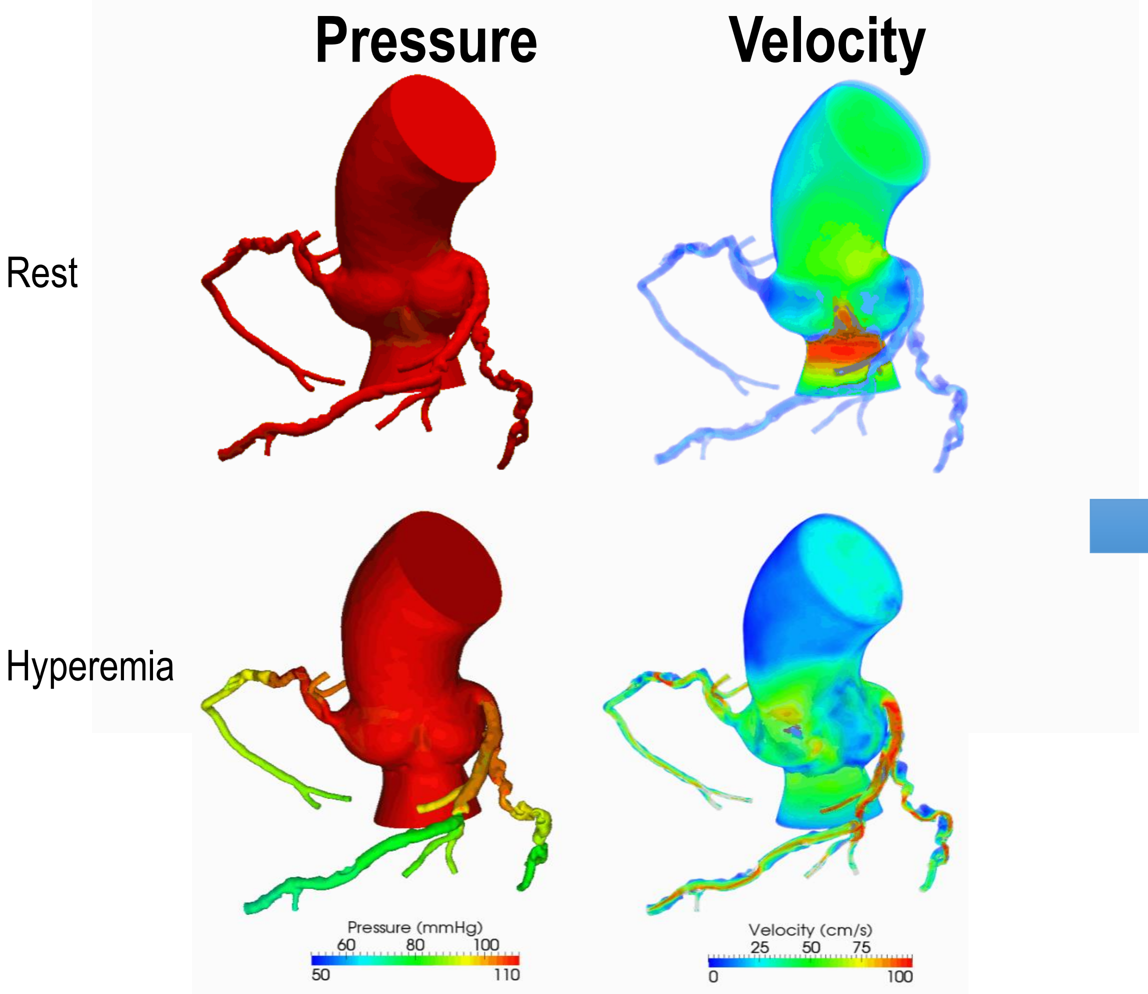


SNUH
Seoul National University Hospital
Cardiovascular Center

Yang SH, Koo BK, et al. Front CV Med 2021

Non-invasive measurement of hemodynamic parameters

Coronary CT angiography + Computational fluid dynamics



Cauchy Stress Tensor

$$\boldsymbol{T} = -p\boldsymbol{I} + \mu((\nabla \boldsymbol{v}) + (\nabla \boldsymbol{v})^T)$$

Traction vector

$$\boldsymbol{t} = \boldsymbol{T}\boldsymbol{n} = -p\boldsymbol{n} + \mu((\nabla \boldsymbol{v}) + (\nabla \boldsymbol{v})^T)\,\boldsymbol{n}$$

Wall Shear Stress (WSS)

$$\tau_{mean} = \left| \frac{1}{T} \int_0^T t_s dt \right|$$

$$t_s = t - (t \cdot n)n$$

Oscillatory Shear Index (OSI)

$$OSI = \frac{1}{2}\left(1 - \frac{\left|\frac{1}{T}\int_0^T t_s dt\right|}{\frac{1}{T}\int_0^T |t_s| dt}\right)$$

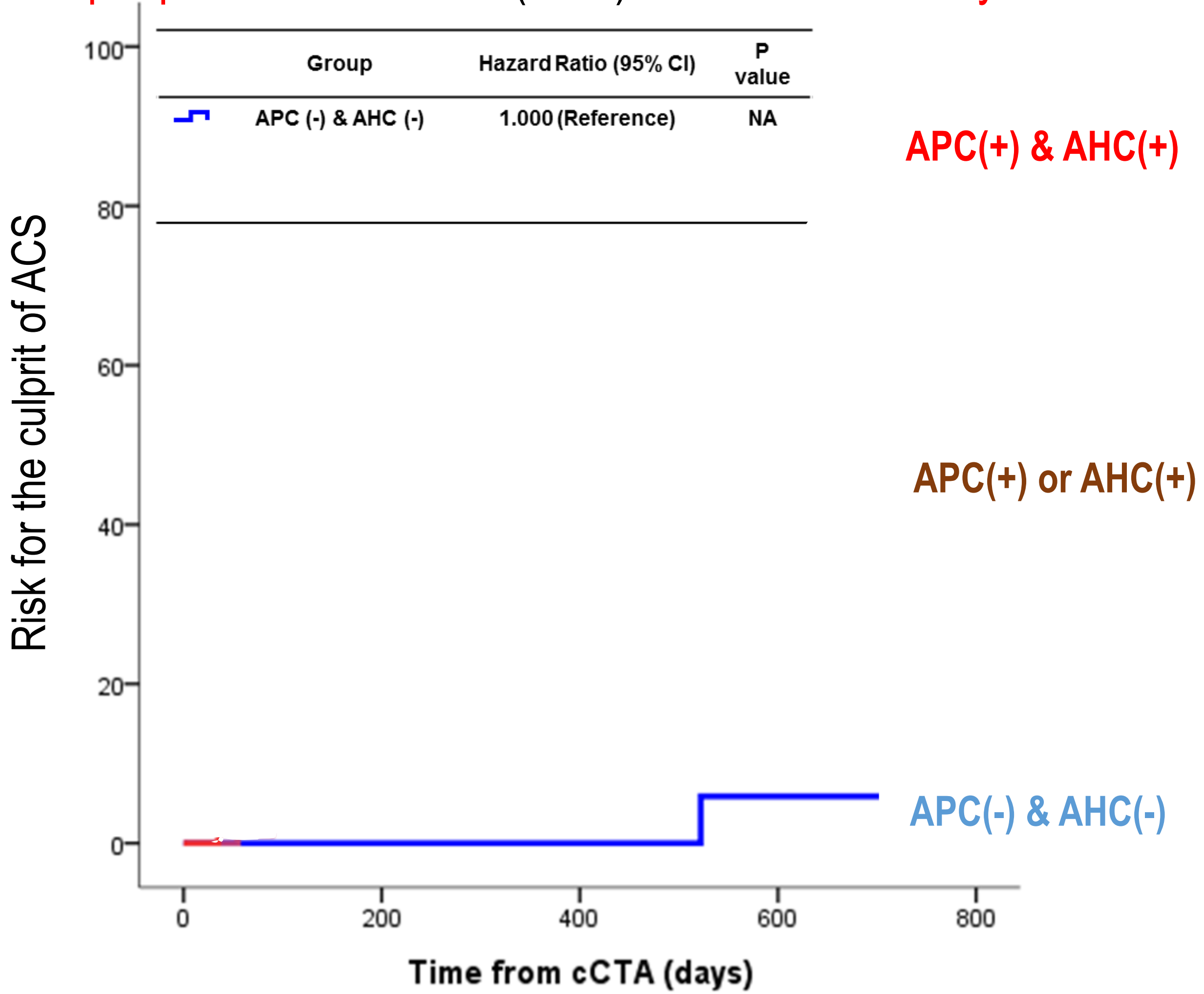
Particle Residence Time,
Turbulent Kinetic Energy,
...

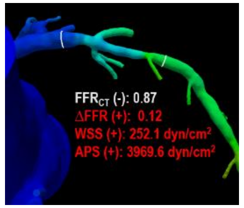
Koo BK & HeartFlow, inc

Coronary CTA + CFD

A tool to define high risk patients for acute coronary syndrome

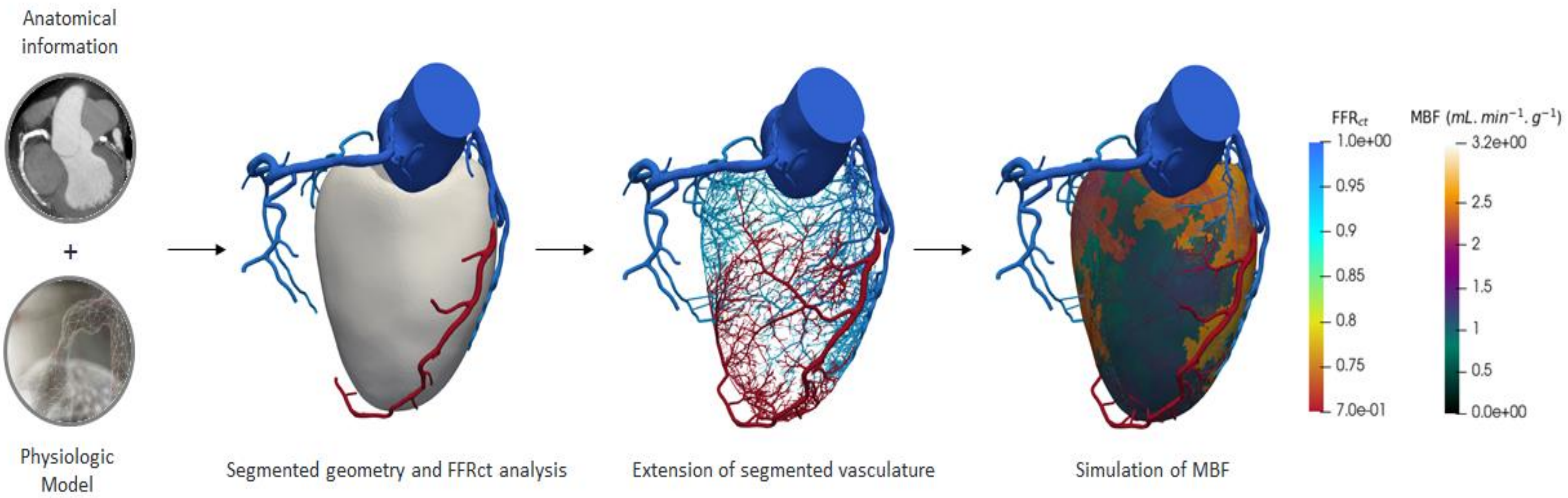
ACS risk for adverse plaque characteristics (APC) & adverse hemodynamic characteristics (AHC)





Lee JM & Choi GW, Koo BK….. JACC imaging 2018

Complete Picture of CAD from CCTA



Courtesy of Charles Taylor, PhD. HeartFlow

CT-FFR: Do we do not need invasive angiography (and FFR)?

Not yet, But already!