Define Vulnerable Plaque

Coronary Physiology Perspective

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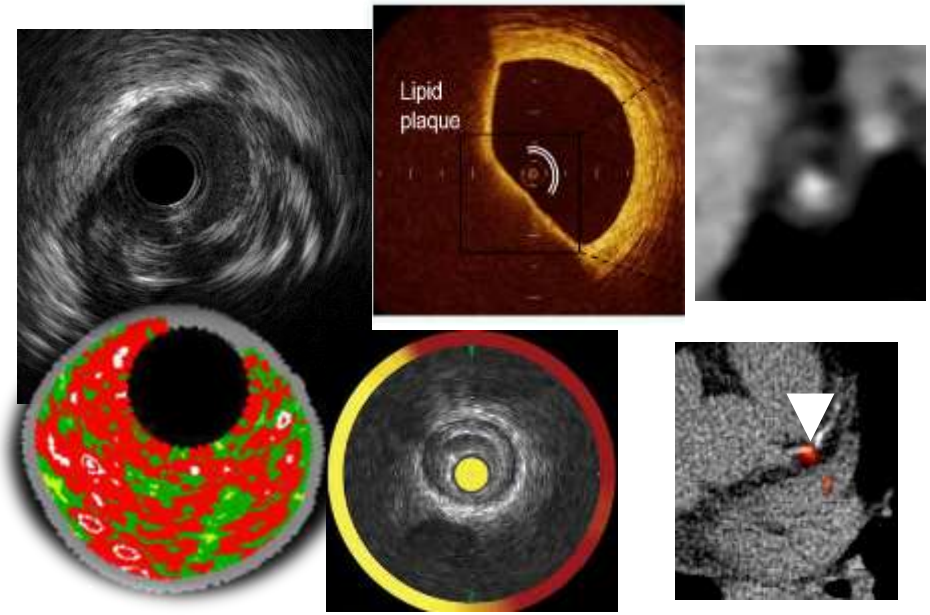
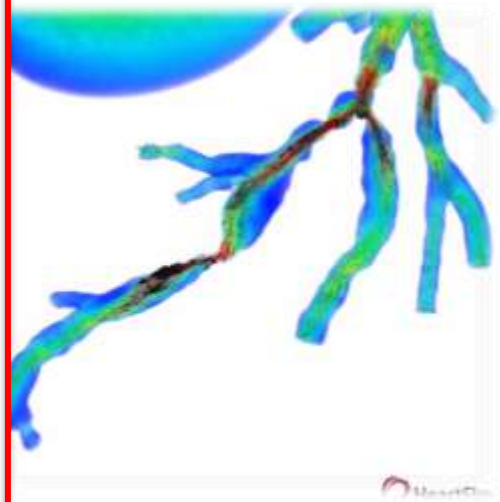
Vulnerability?

Plaque characteristics

Positive remodeling, posterior attenuation, lipid, cap thickness, TcFA, calcium, napkin ring, low density,…….



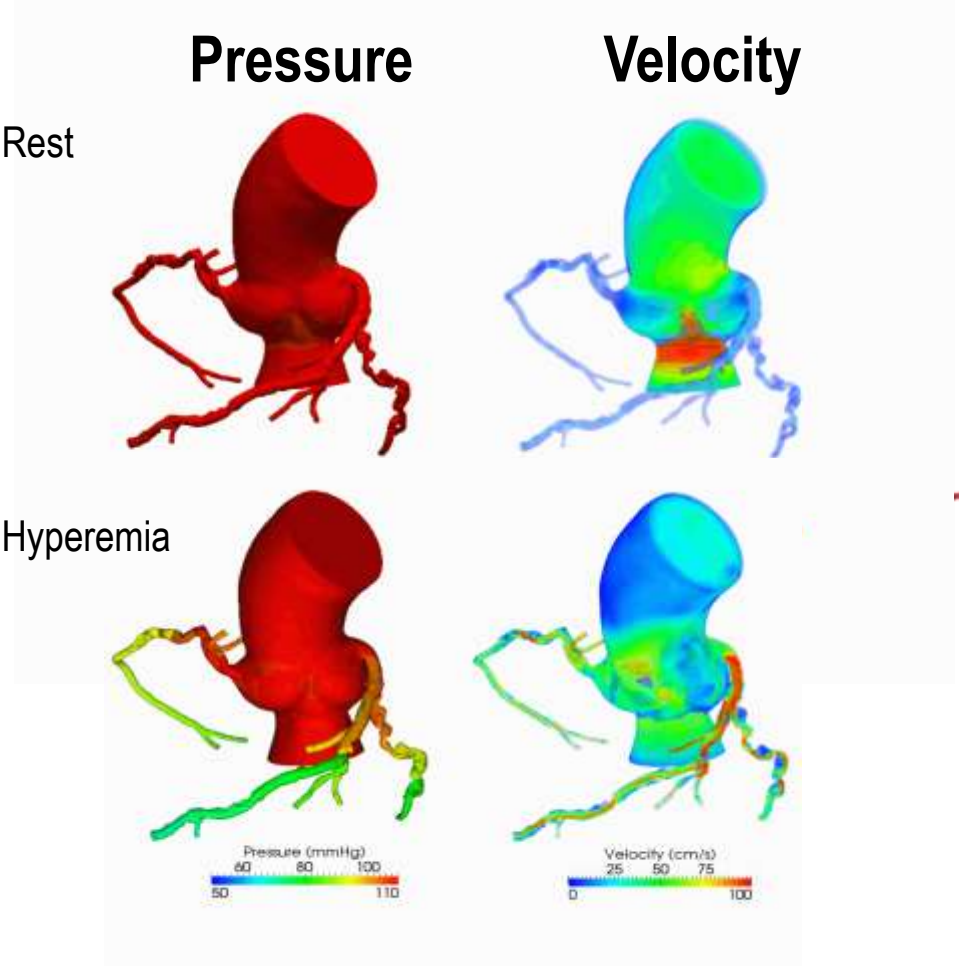
Hemodynamics



- Pressure
  - Pressure difference
  - Pressure gradient
  - Pressure recovery
  - FFR
- Flow velocity
- Flow rate
- Shear rate
- Wall shear stress
- Traction
- Oscillatory shear index
- Particle residence time
- Turbulent kinetic energy, ...

Non-invasive measurement of hemodynamics

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)

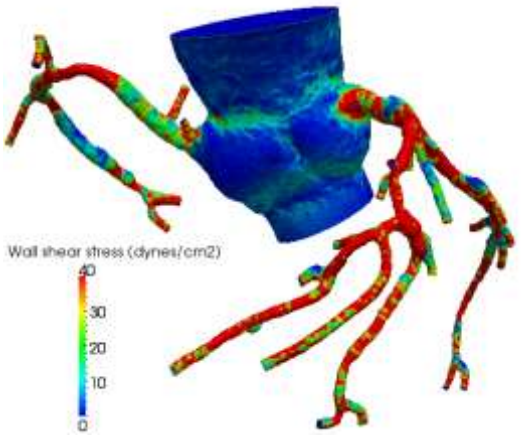
$$OSI = \frac{1}{2}\left(1 - \frac{\left|\frac{1}{T}\int_0^T t_s dt\right|}{\frac{1}{T}\int_0^T |t_s| dt}\right)$$

Particle Residence Time,
Turbulent Kinetic Energy,
…

Koo BK & HeartFlow, inc
Total plaque force project since 2013

Total Plaque Force Project

- To investigate the clinical relevance of hemodynamic force acting on the plaque
- **Project launching: Mar 12, 2013**



1st WSS model
: Mar 10, 2013

- **Projects**

  # 1: Validation of concept/methodology, role of WSS: *Heart 2016*

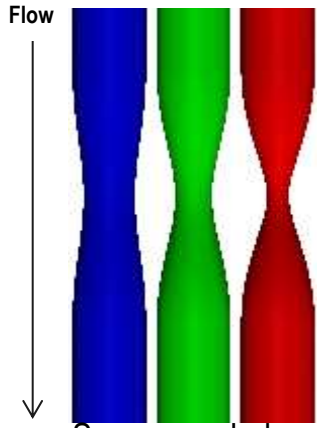
  # 2: Establishment of novel indices: APS and RG: *JACC imaging 2015*

  # 3: Validation of APS and RG using IVUS data: *JACC imaging 2017*

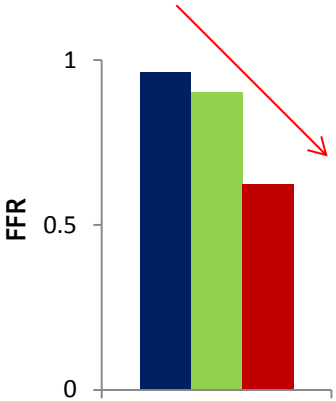
  # 4: Clinical validation of total plaque stress analysis: *JACC imaging 2018*

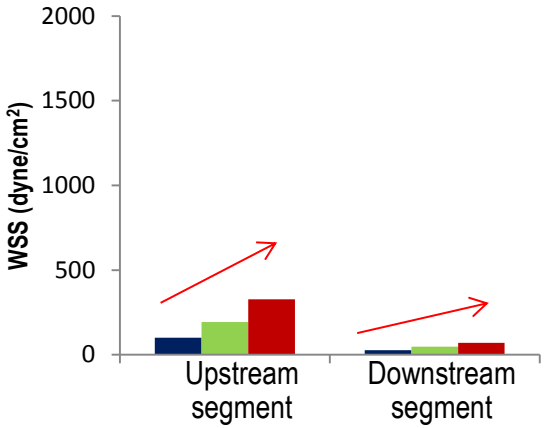
  # 5, 6, 7……..

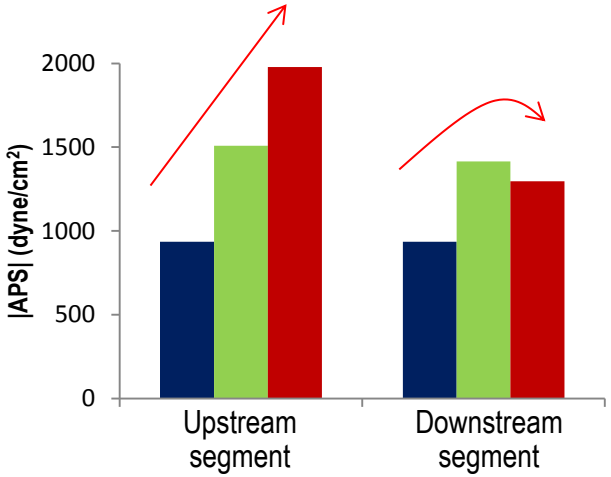
From Simple Idealized Models

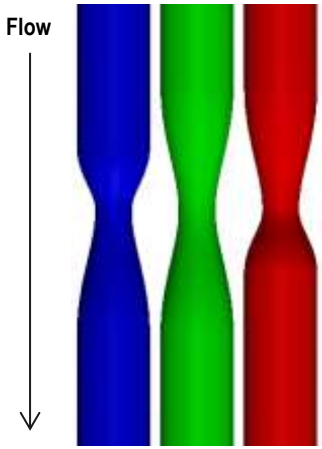


Same morphology
Different severity









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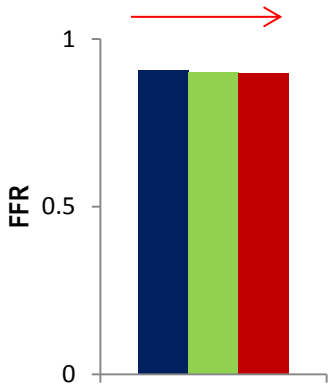
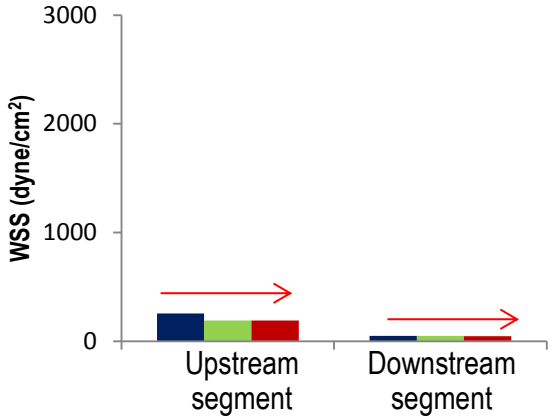
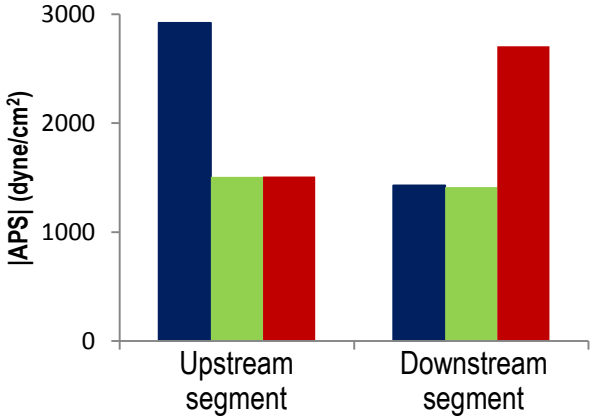
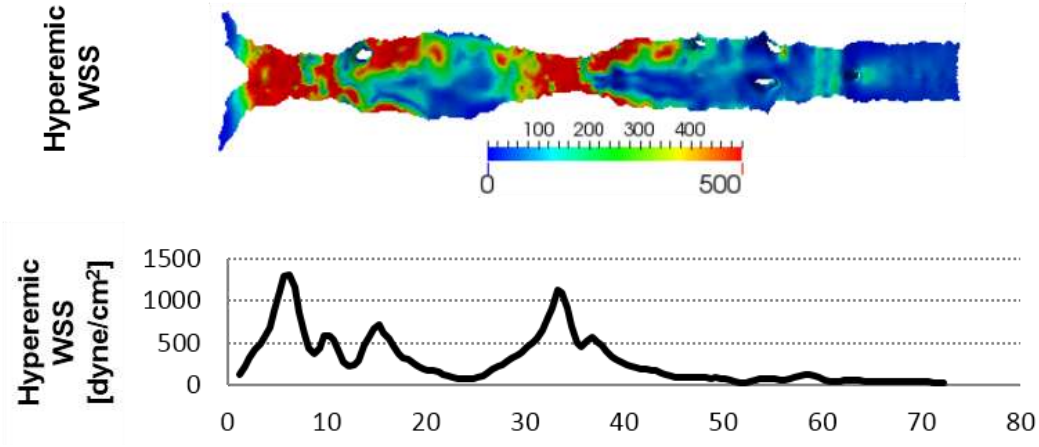


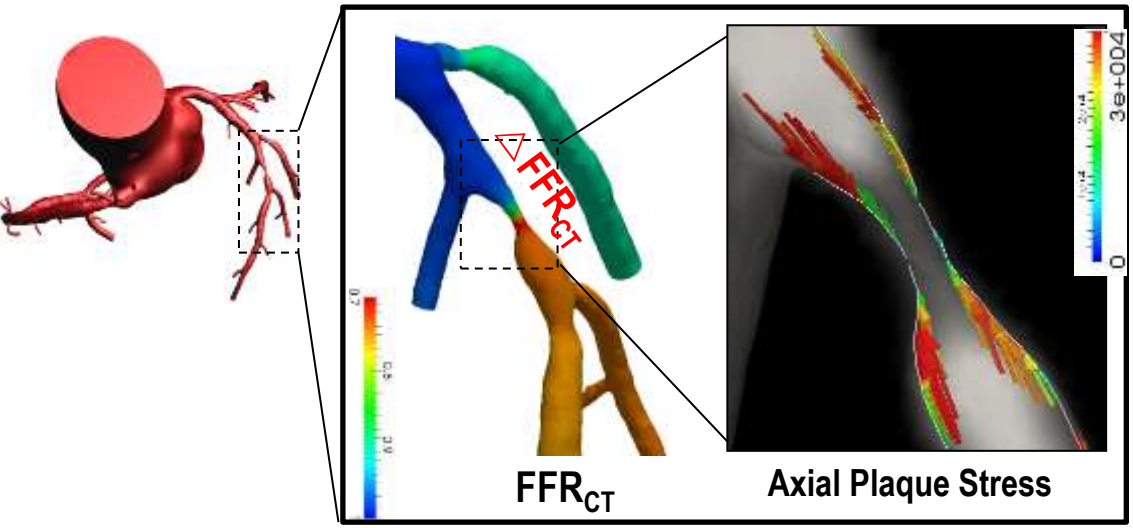


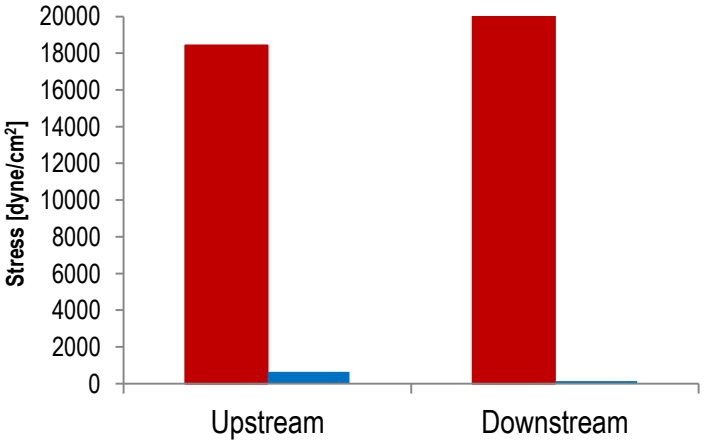


Choi G & Lee JM, Koo BK, et al. JACC imaging 2015

To Patient-specific Models







Choi G & Lee JM, Koo BK, et al. JACC imaging 2015
Park JB, Koo BK, et al. Heart 2016
Lee JM, Koo BK, et al. JACC imaging 2016

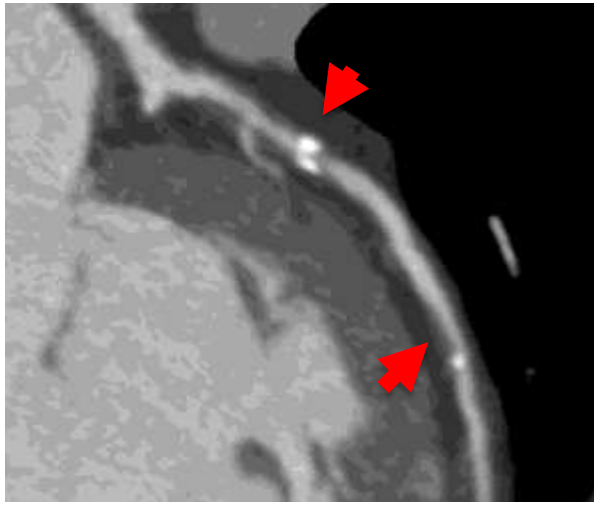
Non-invasive hemodynamic metrics

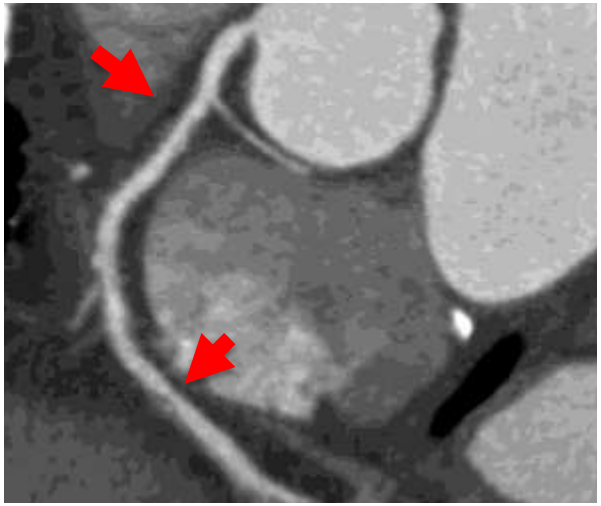
: FFR_{CT}, ΔFFR_{CT}, WSS, APS…..

: Just another toy or Clinically relevant index?

How can we identify the culprit (vulnerable) lesion for future ACS?

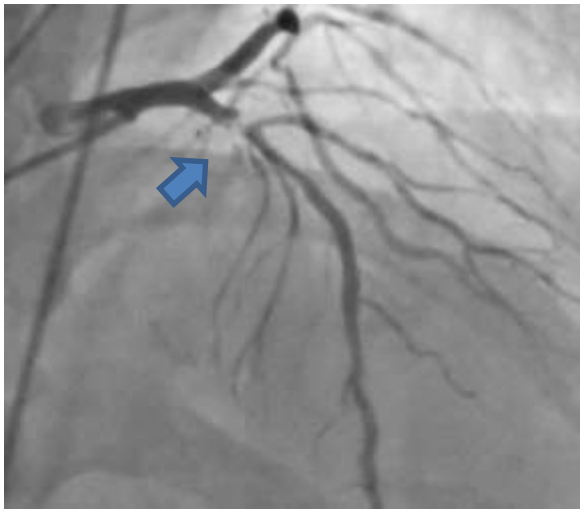
M/69, Asymptomatic

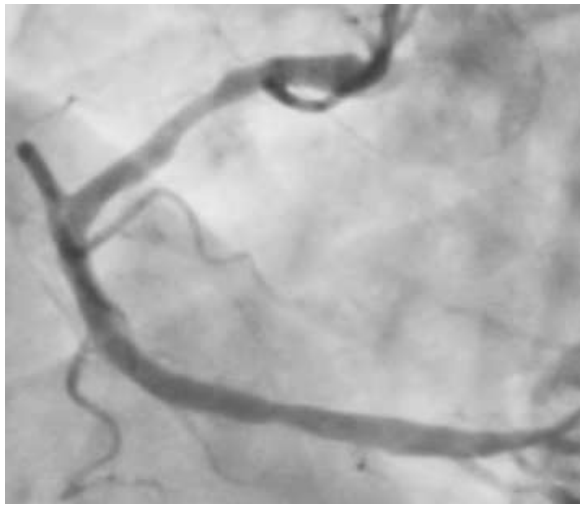




116 days later, the patient visited ER.

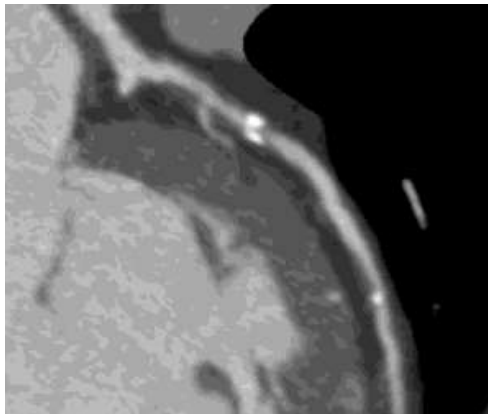
M/70, Non-ST elevation MI



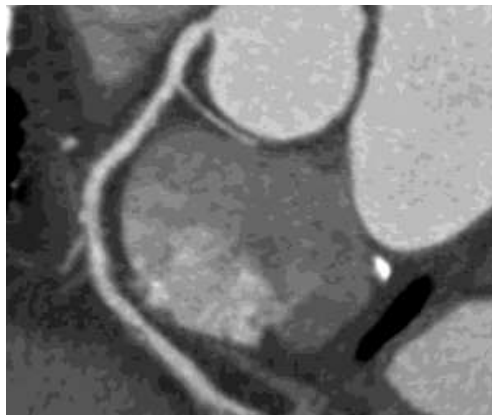


How can we identify the culprit lesion for future ACS?

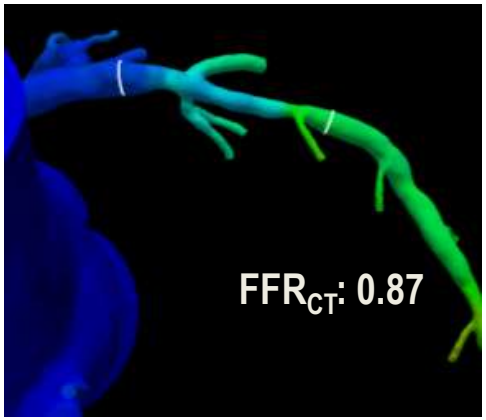
Current Paradigm



Stenosis severity
Adverse plaque characteristics



Non-invasive hemodynamic assessment

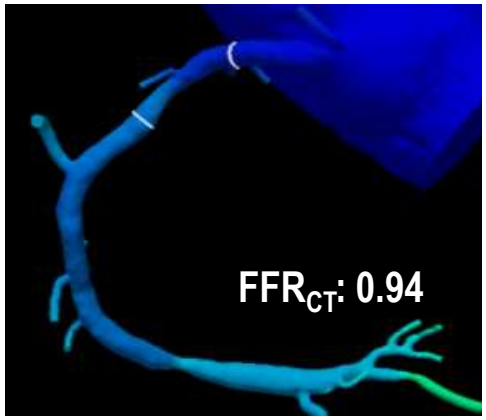


$$\triangle FFR_{CT} = \text{proximal } FFR_{CT} - \text{distal } FFR_{CT} = \frac{P_X}{P_{Aorta}} - \frac{P_Y}{P_{Aorta}} = \frac{\Delta P}{P_{Aorta}}$$

where X and Y represent the lesion start and ending points, respectively, and P represents pressure.

$$WSS_{lesion} = \frac{1}{A}\int_X^Y \left\|\overrightarrow{WSS}\right\| dA$$

where A represents the surface area of defined lesion from X and Y



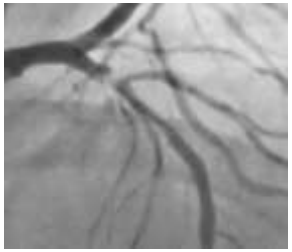
$$\left|\text{Axial Plaque Stress}_{lesion}\right| = \left|\frac{1}{A}\int_X^Y (\vec{t}\cdot\vec{c})\,dA\right|$$

where $\vec{t}\cdot\vec{c}$ represents the dot product of the traction vector ($\vec{t}$) and tangential vector of vessel centerline ($\vec{c}$).

De Bruyne B, et al. N Engl J Med 2014:371:1208-17
Samady H, et al. Circulation 2011;124:779
Park JB, et al. Heart 2016;102:1655-61
Choi G & Lee JM, et al. JACC Cardiovasc Imaging 2015;8:1156-66
Lee JM, et al. JACC Cardiovasc Imaging 2016

EMERALD study

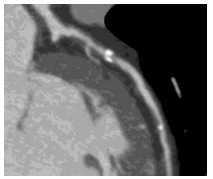
Exploring the **ME**chanism of the Plaque **R**upture in **A**cute Coronary Syndrome using Coronary CT Angiography and Computational **L** Fluid **D**ynamics

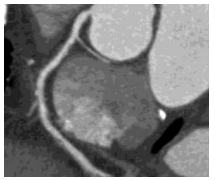


Patients with Acute Coronary Syndrome
From 11 International Cardiovascular Centers
(Korea, Japan, Belgium, Denmark, the Netherlands)

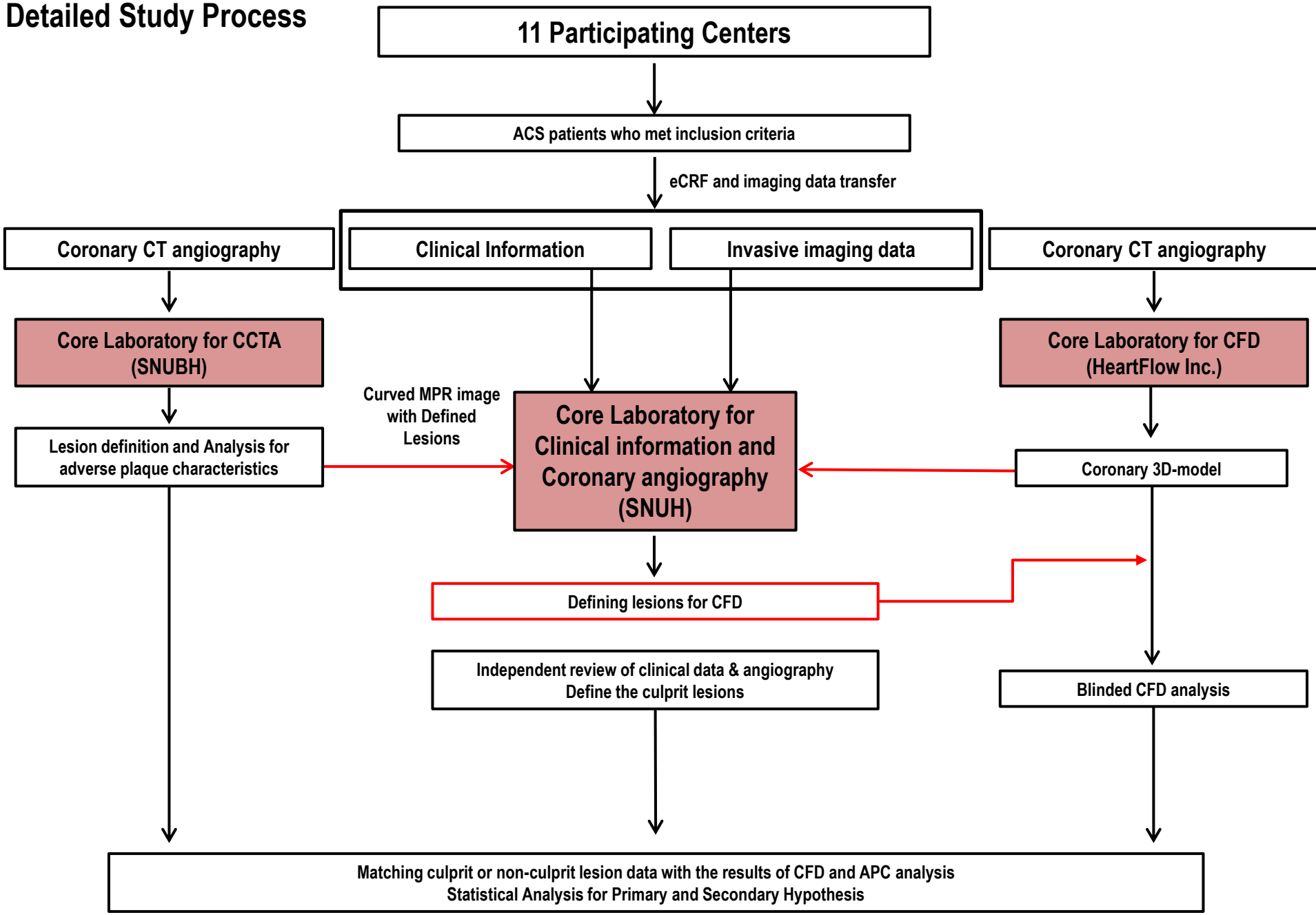
↓

Patients who underwent Coronary CT angiography
before ACS event (1 month – 2 year before the event)
(N=120)





Detailed Study Process



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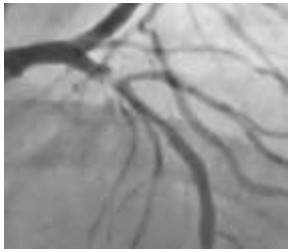

Patients with Acute Coronary Syndrome
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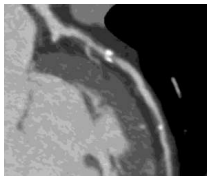
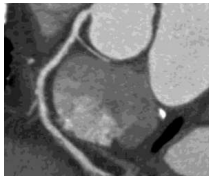




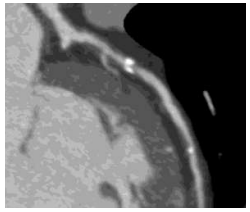
Patients who underwent Coronary CT angiography
before ACS event (1 month – 2 year before the event)
(N=120)

Validation with clinical data, cCTA and coronary angiography (3 independent core labs)

Exclusion (N=41)
- No adequate CT image: 27
- Unclear diagnosis or No definite culprit lesion on Angiography: 10
- No definite lesion on cCTA: 4

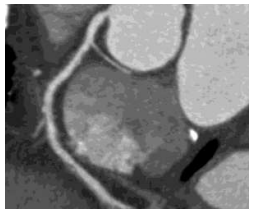
Exclusion by core laboratory due to CT image quality (N=7)

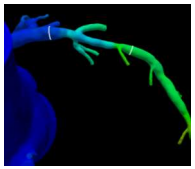
Final Enrollment for cCTA and CFD analysis
(72 patients, 216 lesions)



CASE
Culprit for subsequent ACS (N=66)

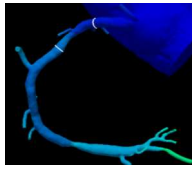
CONTROL
Non- Culprit Lesion (N=150)





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

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



Characteristics of the Patients and Lesions

Patients (n = 72)	
Age, years	69·9 ± 12·7
Male	54 (75·0%)
Median interval between cCTA and ACS, days	**338·0 (161·5-535·0)**
Cardiovascular Risk Factors	
Hypertension	46 (63·9%)
Diabetes mellitus	37 (51·4%)
Hypercholesterolemia	35 (48·6%)
Clinical Presentation	
Myocardial infarction	**67 (93·0%)**
NSTEMI	41 (56·9%)
STEMI	26 (36·1%)
Unstable angina	5 (6·9%)

Lesion characteristics (n = 216)	
Lesion location	
Left main to LAD	**87 (40·3%)**
LCX / RCA	48 (22·2%) / 81 (37·5%)
Culprit vessel (n=66)	
Left main to LAD	39 (59·1%)
LCX / RCA	9 (13·6%) / 18 (27·3%)
Lesion profile	
Minimal lumen area, mm^2	2·75 ± 1·59
Diameter stenosis, %	**46·9 ± 16·1**
Distance from ostium to MLA, mm	47·1 ± 22·6
Lesion length, mm	17·6 ± 7·4
FFR_{CT}	0·77 ± 0·15

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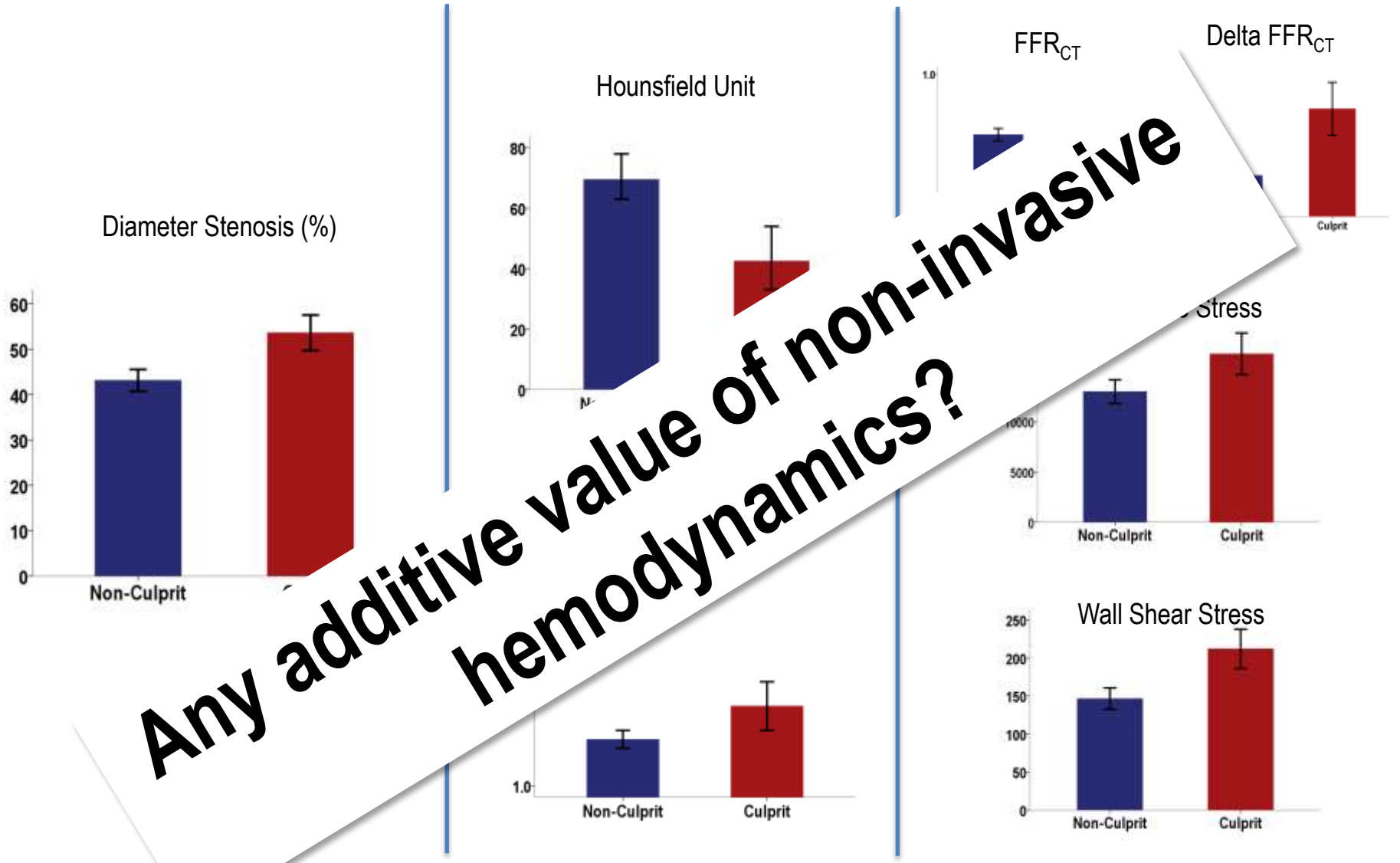
EMERALD study: Culprit vs. Non-culprit



Any additive value of non-invasive hemodynamics?

All P values: significant

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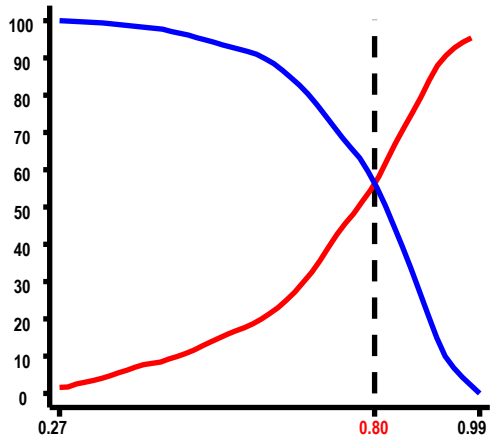
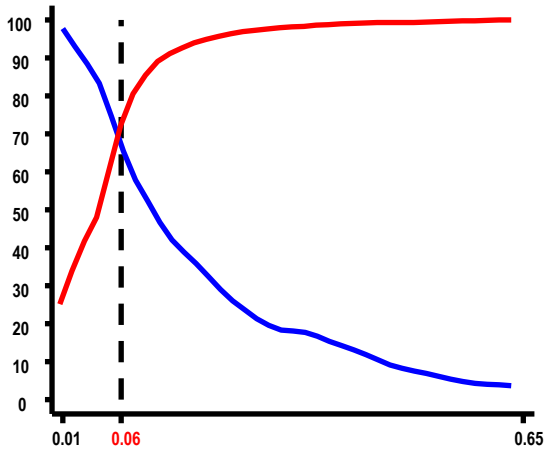
Cut-off Value for Adverse Hemodynamic Characteristics (AHC)

FFR_{CT}: 0.80



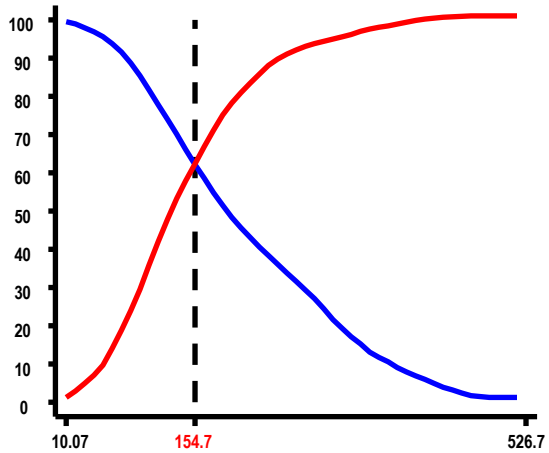
FFR_{CT}	
BCV	0.80
Sensitivity	54.6%
Specificity	58.0%
PPV	40.0%
NPV	71.3%
Accuracy	56.8%

△FFR_{CT}: 0.06



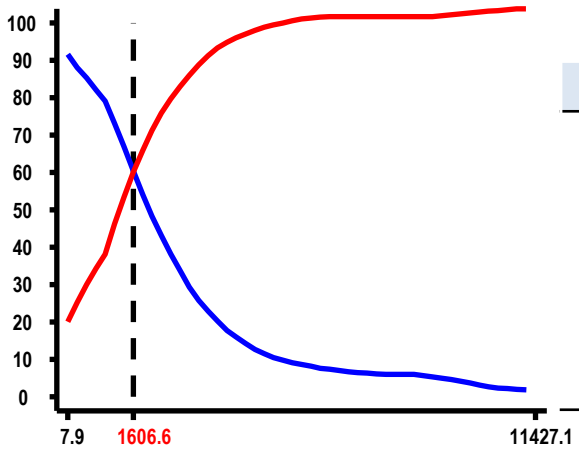
Delta FFR_{CT}	
BCV	0.06
Sensitivity	62.3%
Specificity	71.3%
PPV	52.8%
NPV	78.7%
Accuracy	68.2%

Wall Shear Stress (dyn/cm^2): 154.7



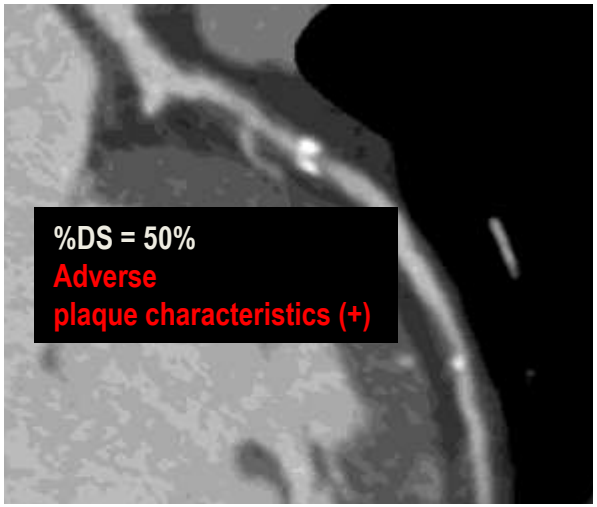
Wall Shear Stress	
BCV	154.7
Sensitivity	64.9%
Specificity	61.3%
PPV	46.3%
NPV	77.3%
Accuracy	62.6%

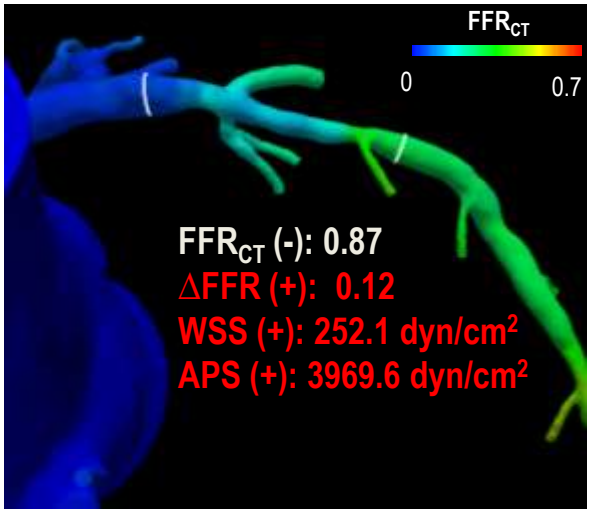
Axial Plaque Stress (dyn/cm^2): 1606.6

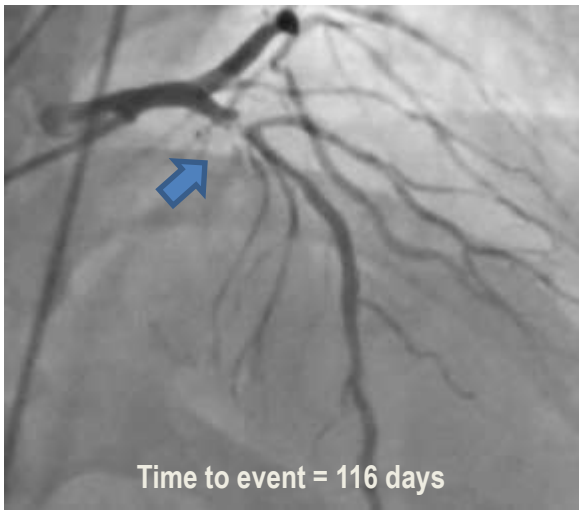


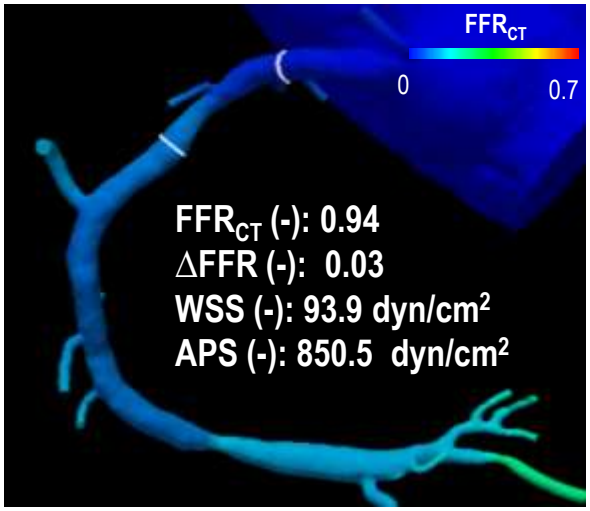
Raw APS	
BCV	1606.6
Sensitivity	59.7%
Specificity	62.0%
PPV	41.2%
NPV	77.5%
Accuracy	61.3%

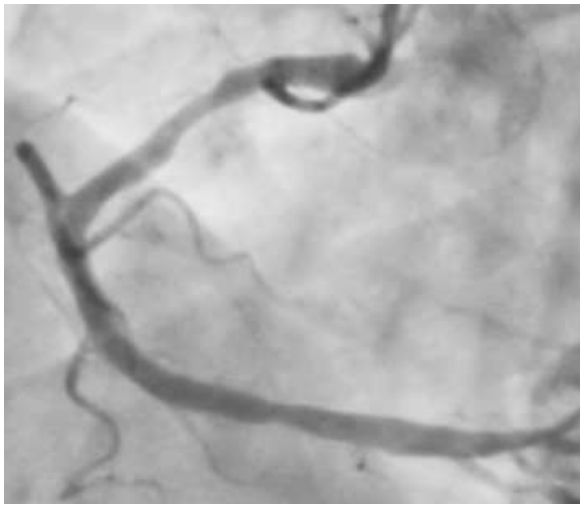
How can we identify the culprit lesion for future ACS?











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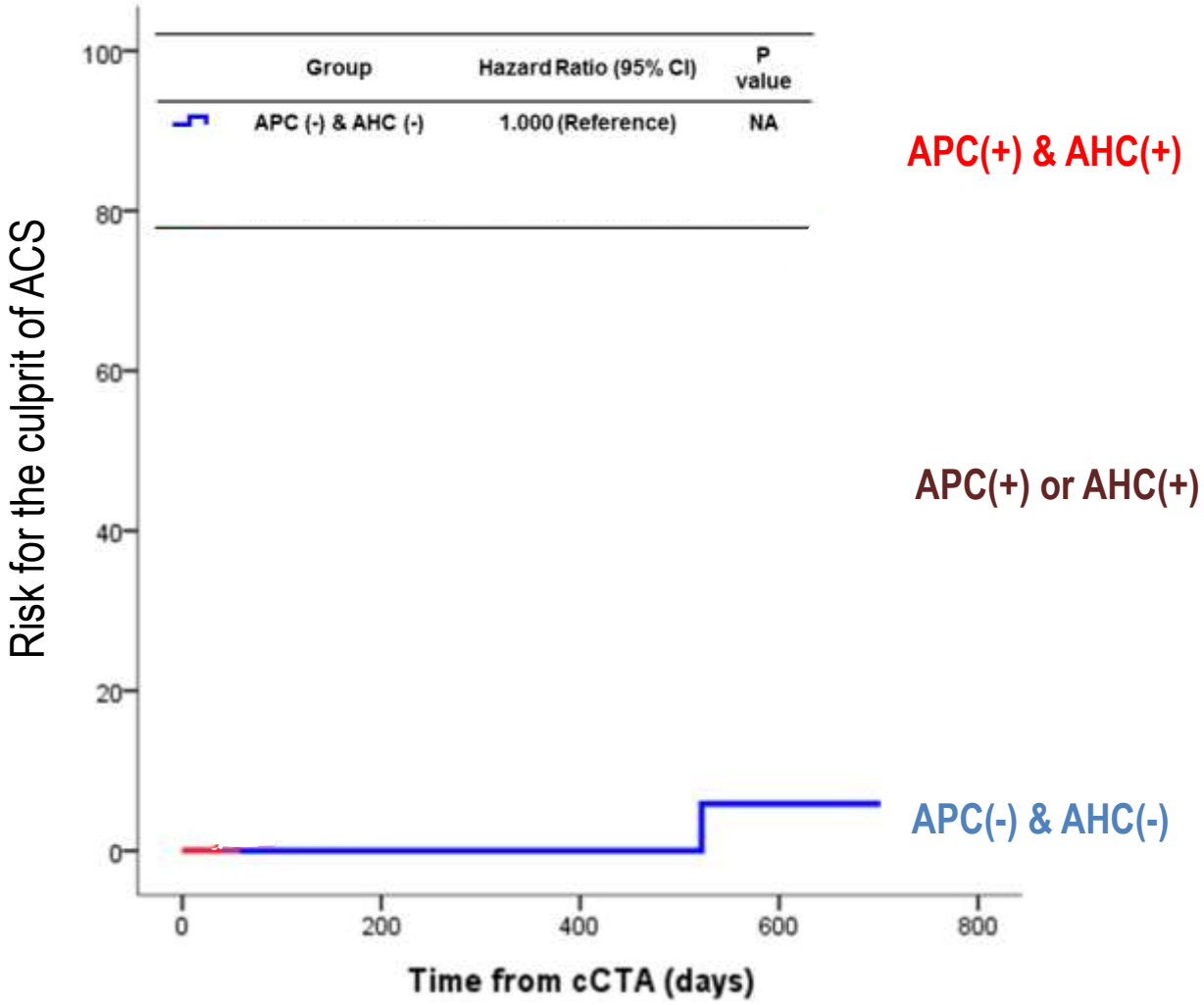
Plaque characteristics (APC), Hemodynamic characteristics (AHC) and Risk for the culprit of future ACS



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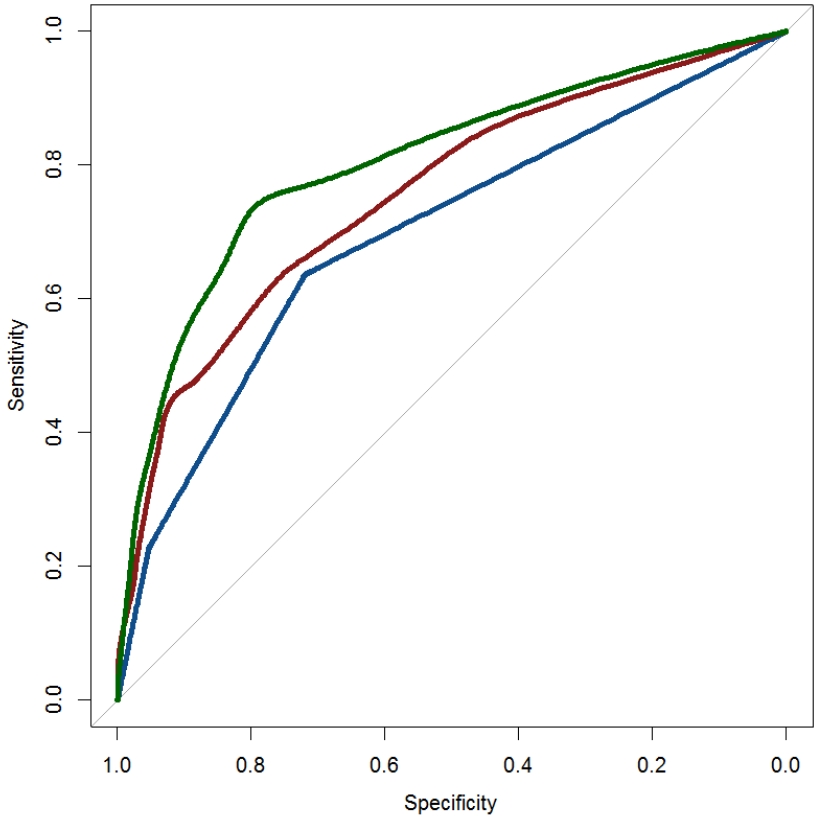
Prediction of ACS risk

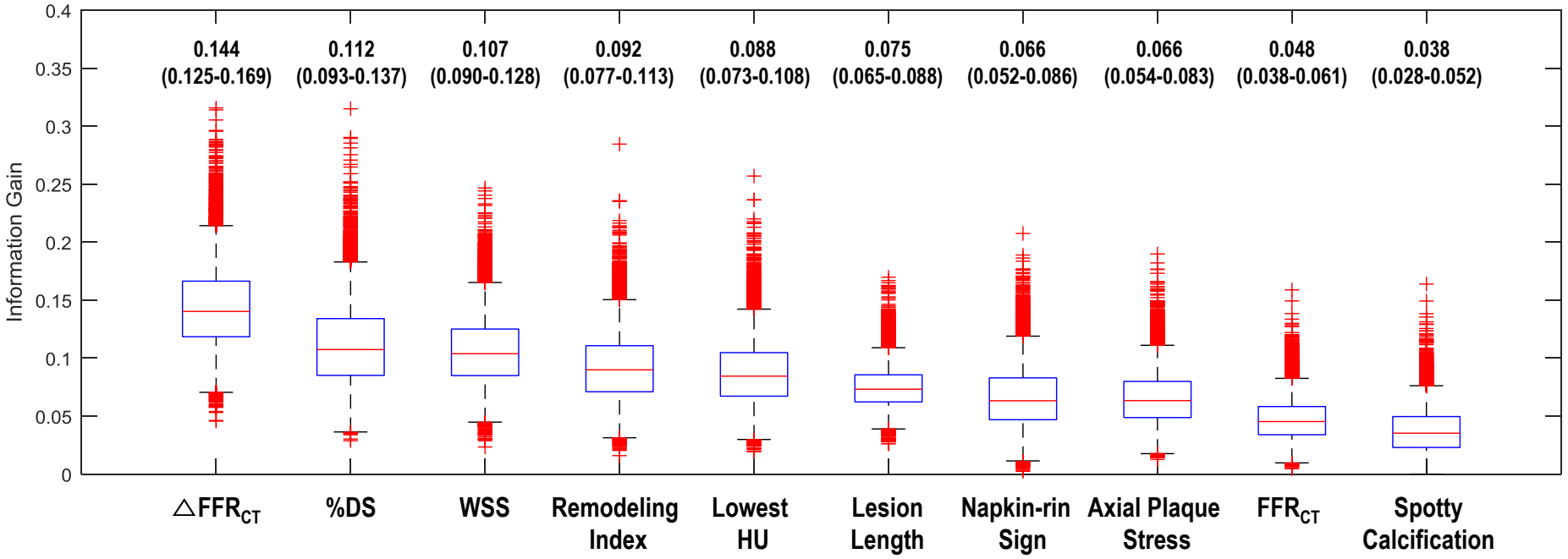
Model 1: % diameter stenosis (%DS)+Lesion length(LL)
Model 2: %DS/LL + adverse plaque characteristics (APC)
Model 3: %DS/LL + APC + adverse hemodynamic characteristics (AHC)



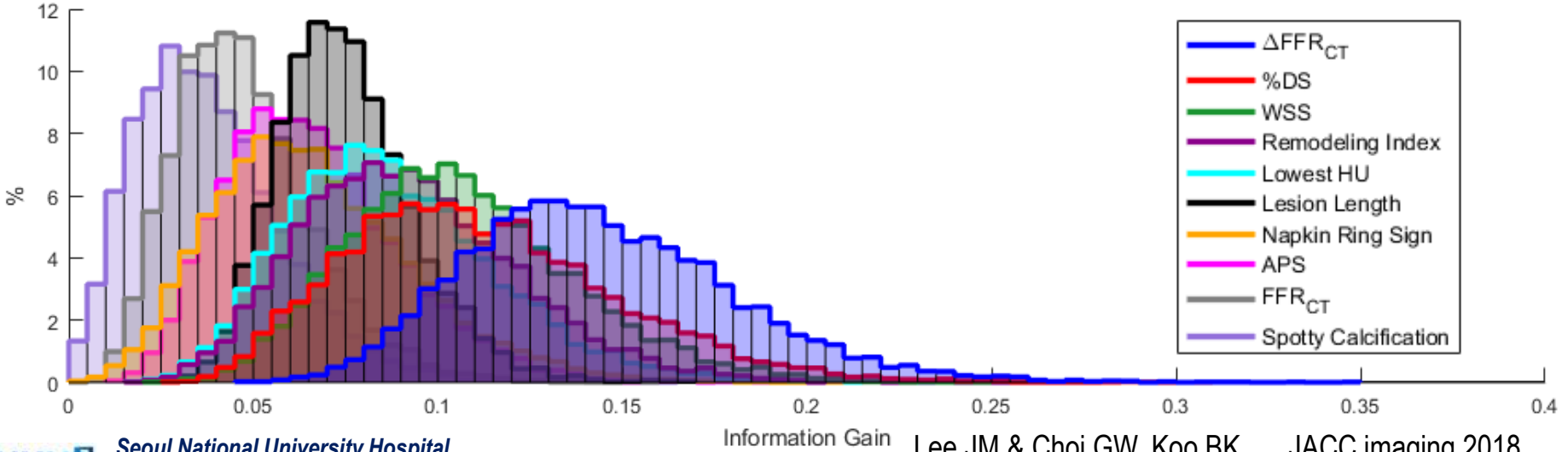
Prediction Model	C-index	Difference with Prev. Model	P value	NRI	P value	IDI	P value
Model 1	0.709						
Model 2	0.747	0.038	0.006	0.355	0.001	0.671	<0.001
Model 3	0.789	0.025	0.014	0.287	0.047	0.368	<0.001

SNUH

Information gain of each parameter



Distribution of information gain from bootstrapping analysis with 10,000 replicates



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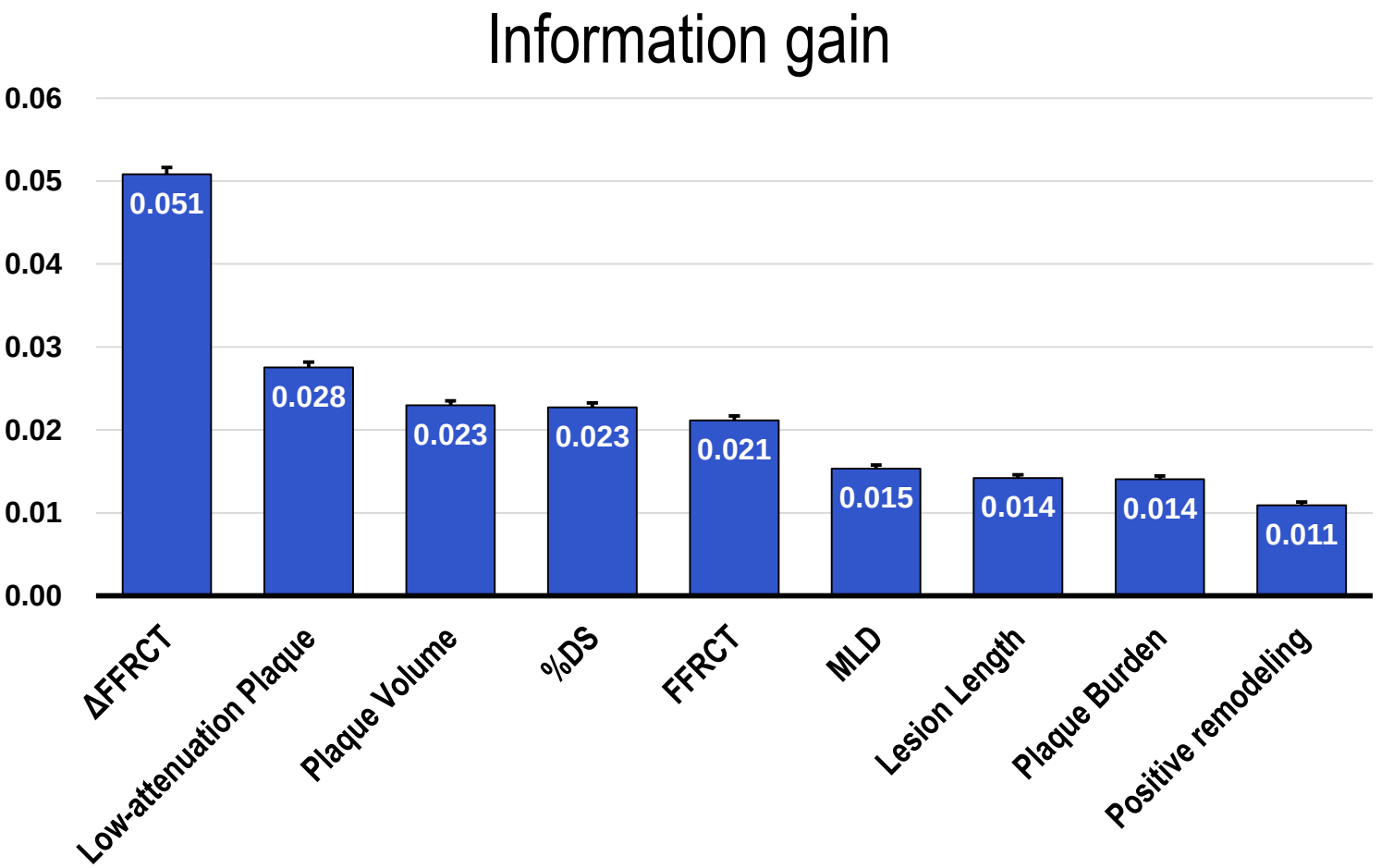
Contribution in Non-Obstructive lesions



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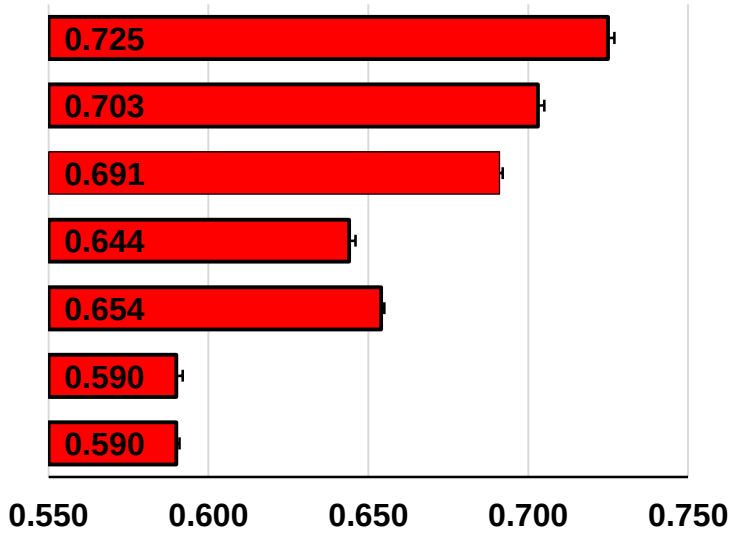
Contribution of different index in Non-Obstructive lesions



Model 7 : Plaque Volume + Low-attenuation plaque + ΔFFR_{CT}

Model 6 : Low-attenuation plaque + ΔFFR_{CT}

Model 5 : Plaque Volume + ΔFFR_{CT}

Model 4 : Plaque Volume + Low-attenuation plaque

Model 3 : ΔFFR_{CT}

Model 2 : Low-attenuation plaque

Model 1 : Plaque Volume

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
AUC	**0.59**	**0.59**	**0.65**	**0.64**	**0.69**	**0.70**	**0.73**

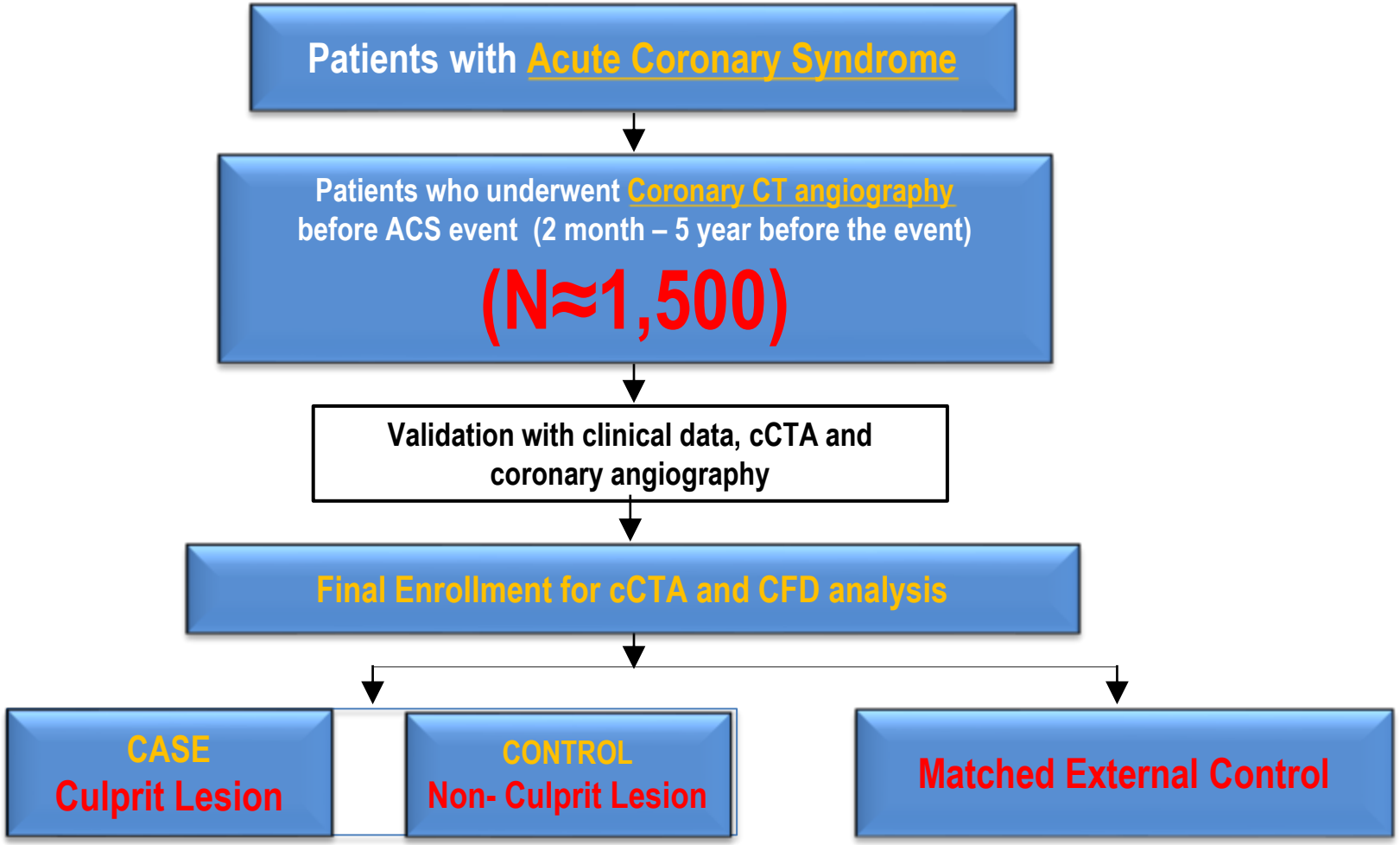
P for difference	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
Model 1	.	0.92	<0.001	<0.001	<0.001	<0.001	<0.001
Model 2		.	<0.001	<0.001	<0.001	<0.001	<0.001
Model 3			.	<0.001	<0.001	<0.001	<0.001
Model 4				.	<0.001	<0.001	<0.001
Model 5						<0.001	<0.001
Model 6						.	<0.001

Park JS, Lee JM, Koo BK (Unpublished data)

EMERALD II study

Exploring the MEchanism of Plaque Rupture in Acute Coronary Syndrome using Coronary CT Angiography and ComputationaL Fluid Dynamics II

- **PI: Bon-Kwon Koo, MD, PhD**
- **Funding: HeartFlow, Inc**



Conclusion

- Non-invasive hemodynamic assessment enhanced the identification of vulnerable plaques that subsequently caused ACS.
- Application of this novel technology in daily practice can improve the prediction of ACS risk and may help guide optimal treatment for high risk patients.
- The EMERALD II study will confirm the value of non-invasive hemodynamics in ACS risk assessment.