Hemodynamic force analysis improves non-invasive prediction of risk of ACS
: Results from EMERALD study

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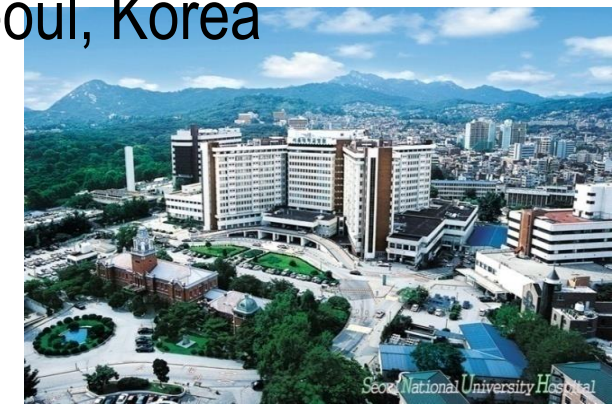
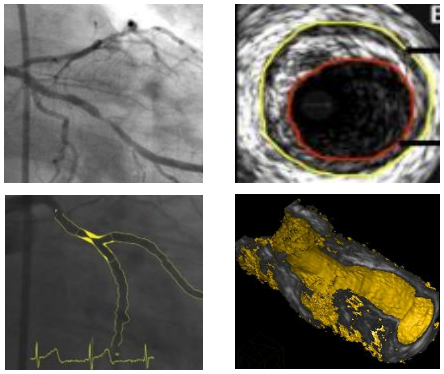
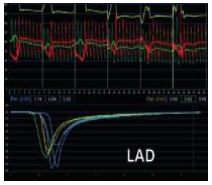


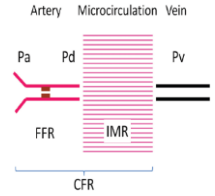
Methods for ACS risk assessment

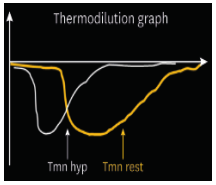
% Diameter stenosis, MLA, plaque burden…

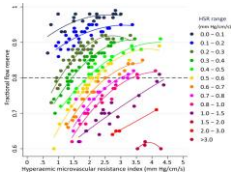


FFR, CFR, IMR, Pd/Pa…

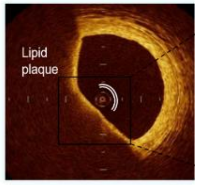


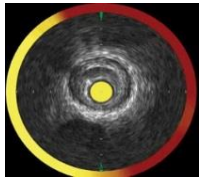






Lipid-rich plaque, positive remodeling, TFCA...





Choi G & Lee JM, et al. JACC Cardiovasc Imaging 2015;8:1156-66
Lee JM, et al. JACC Cardiovasc Imaging 2016
Lee JM, et al. Korean Circ J. 2018 Mar;48:179-190
Kaul S, Narula J, et al. J Am Coll Cardiol. 2014 Dec 16;64:2519-24

Why do we need "MORE" for ACS prediction?

TABLE 2 Prognostic Performance of Plaque Characteristics

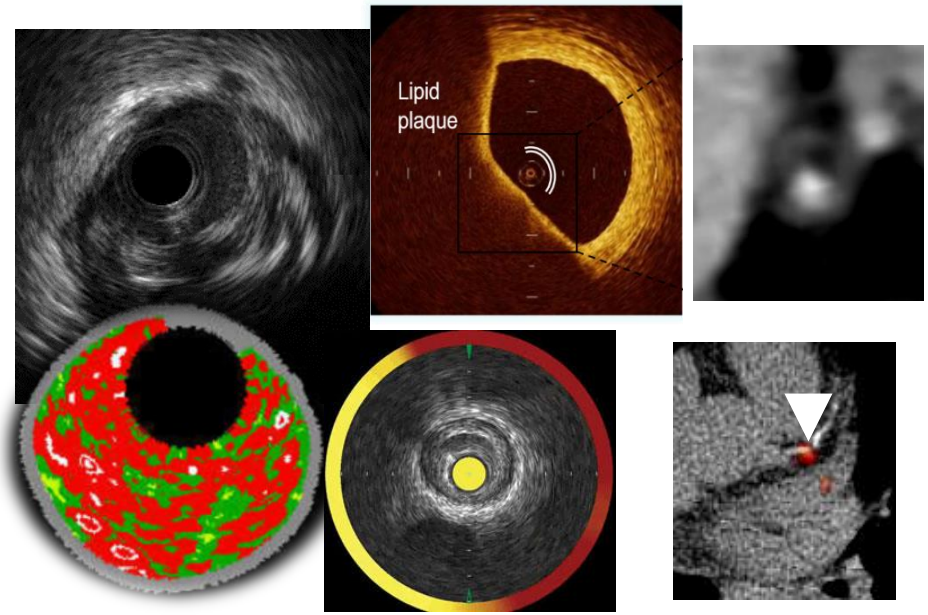
Trial (Ref. #), Follow-Up	Cohort	Endpoint	Lesion Variable	Event Rate % (n/N) + Lesion Variable	Event Rate % (n/N) − Lesion Variable	OR/HR		PPV	NPV	AUC (95% CI)
Intravascular Imaging Studies										
PROSPECT(3), 3.4 yrs (lesion-specific risk)	ACS	MACE	TCFA	4.4 (26/595)	1.2 (25/2,114)	3.8		0.04	0.99	0.71 (0.62-0.79)
			PB ≥70%	8.7 (25/288)	1.0 (30/2,941)	9.6		0.09	0.99	0.82 (0.76-0.87)
			MLA ≤4 mm^2	4.9 (30/616)	1.0 (25/2,522)	5.11		0.05	0.91	0.75 (0.67-0.82)
			All 3	18.2 (8/44)	1.6 (44/2,665)	13.6		0.18	0.98	0.86 (0.76-0.92)
PROSPECT (3), 3.4 yrs (patient-specific risk)	ACS	MACE	PB ≥70%	19.1 (42/220)	7.0 (31/440)	3.1		0.19	0.93	0.68 (0.60-0.75)
VIVA (4), 1.8 yrs (lesion-specific risk)*	ACS + SCAD	MACE	NC-VHTCFA	2.9 (5/175)	1.1 (8/756)	7.53†				NA
			PB ≥70%	NA	NA	8.13				NA
VIVA (4), 1.8 yrs (patient-specific risk)*	ACS + SCAD	MACE	NC-VHTCFA	NA	NA	1.79				NA
ATHEROREMO-IVUS (6), 1 yr (patient-specific risk)	ACS + SCAD	MACE	TCFA	10.8 (23/211)	5.6 (17/312)	1.98		NA	NA	0.62 (0.51-0.72)
			PB ≥70%	16.2 (20/124)	5.5 (21/384)	2.90				0.69 (0.55-0.80)
			MLA ≤4 mm^2	9.4 (16/182)	7.1 (23/326)	1.23‡		NA	NA	0.55 (0.38-0.72)
			All 3	23.1 (12/52)	6.8 (32/471)	3.70				0.72 (0.61-0.82)
ATHEROREMO-NIRS (2), 1 yr (patient-specific risk)	ACS + SCAD	MACE	LCP (LCBI$_{4mm}$ ≥43)	16.7 (17/102)	4.0 (4/101)	4.20		NA	NA	0.74 (0.56-0.87)
		ACM/ACS		8.8 (9/102)	1.0 (1/101)	9.36				0.82 (0.52-0.97)
		ACM/ACS/Stroke		11.8 (12/102)	1.0 (1/101)	11.9				0.85 (0.57-0.97)
PREDICTION (5), 1 yr (patient-specific risk)	ACS	PCI	PB ≥58%	22	2	17.6				0.85 (0.67-0.94)
			Low ESS	25	9	3.18				0.69 (0.56-0.79)
			Both	41	8	NA		0.11	0.94	0.80 (0.68-0.88)
Noninvasive Imaging Study										
CTA (7), 2 yrs (patient-specific risk)	SCAD	ACS	Positive remodeling + low attenuation plaque	22.2 (10/45)	0.49 (4/820)	45.6		0.16	0.95	0.95 (0.87-0.98)
Invasive Hemodynamic Assessment								0.10	0.93	
FAME-2 (8), 30 days (patient-specific risk)§	SCAD	MACE (D/MI/UR)	FFR ≤0.80	12.7 (56/441)	3.0 (5/166)	4.22		0.23	0.93	0.74 (0.59-0.85)
		D/MI		3.9 (17/441)	1.8 (3/166)	2.13‡		0.17	0.96	0.63 (0.41-0.81)
								0.09	0.99	
								0.12	0.99	

Kaul S & Narula J. JACC 2014

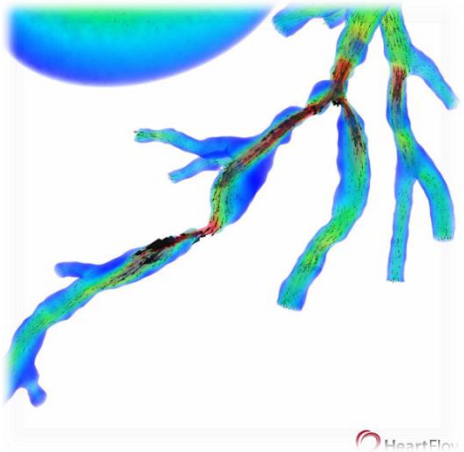
Hemodynamics for Vulnerability?

Plaque characteristics

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

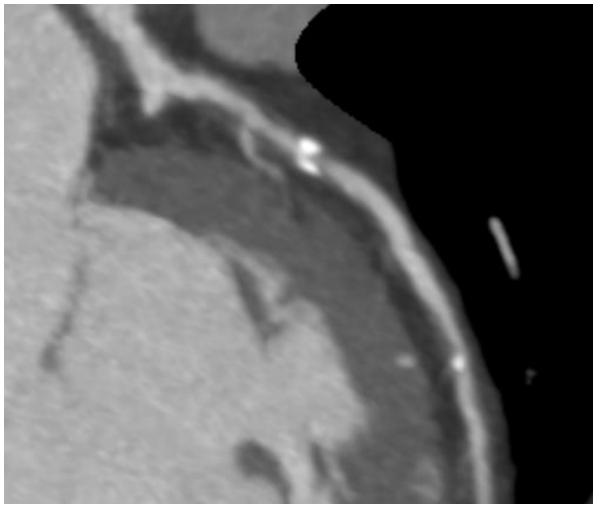


Hemodynamics

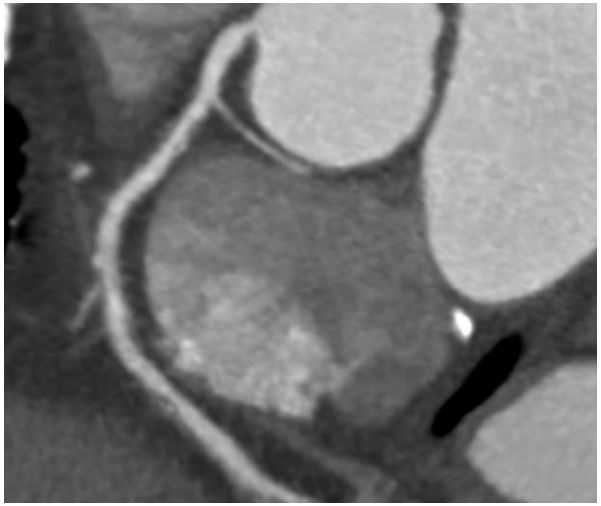


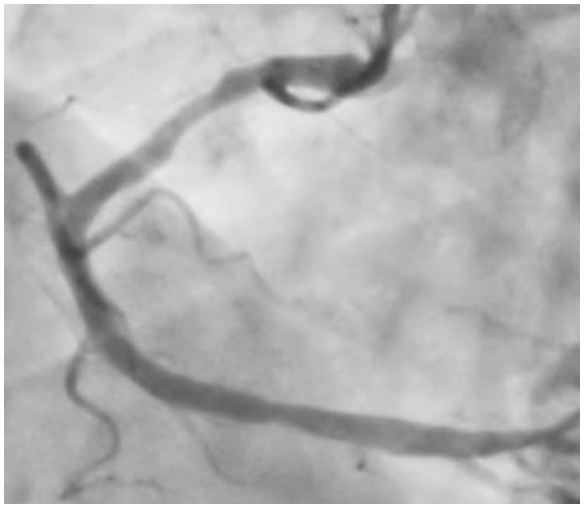
- **Pressure**
  - Pressure difference
  - Pressure gradient
  - Pressure recovery
  - FFR
- **Flow velocity**
- **Flow rate**
- **Shear rate**
- **Wall shear stress**
- **Traction**
- **Oscillatory shear index**
- **Particle residence time**
- **Turbulent kinetic energy, ...**

Any better way to identify the risk for ACS/Sudden death?

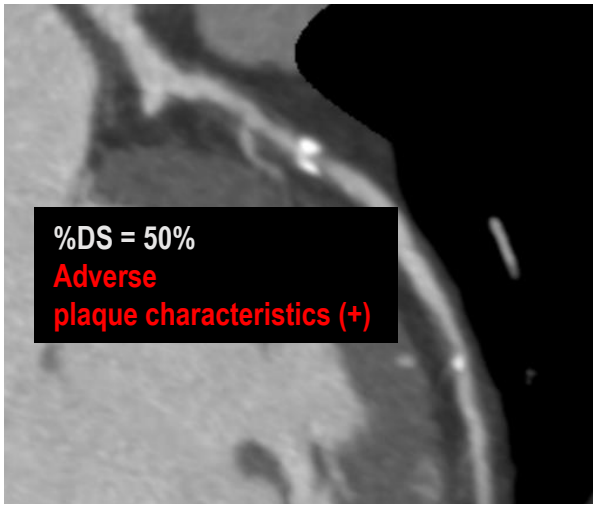


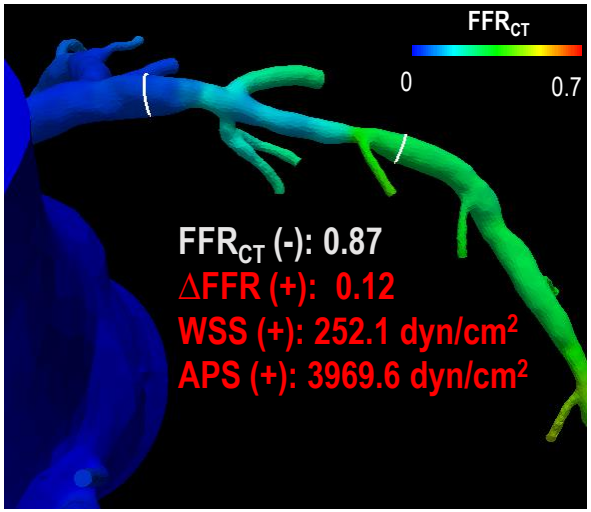
116 days later

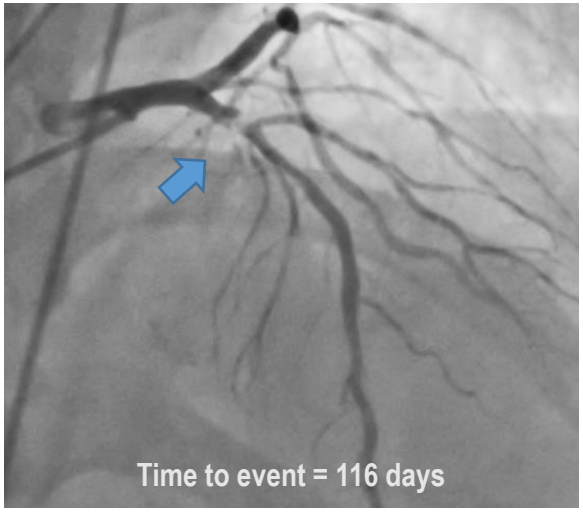


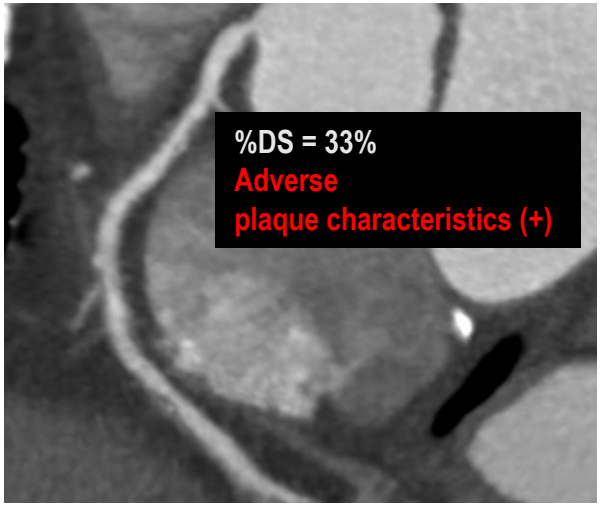


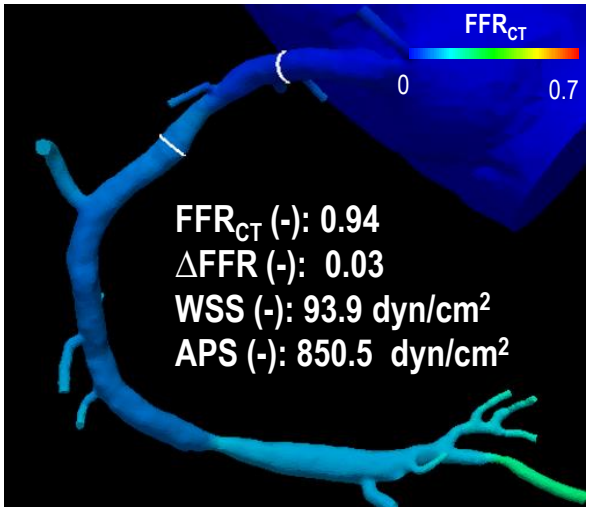
Any better way to identify the risk for ACS/Sudden death?

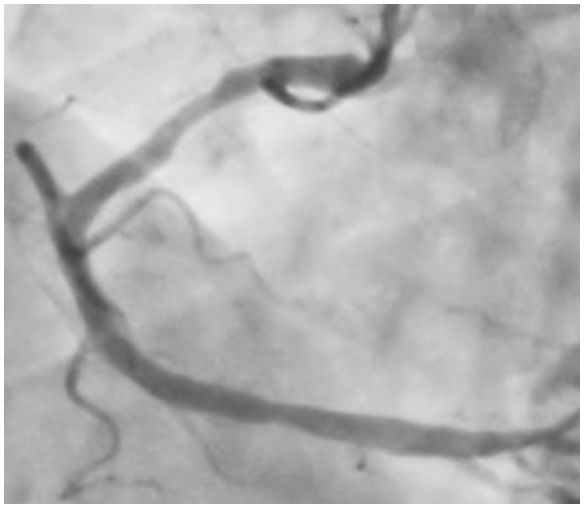






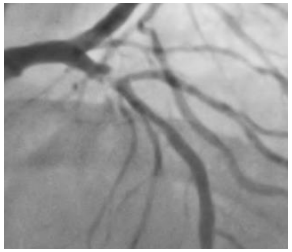






EMERALD study

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



PI: Bon-Kwon Koo, MD

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

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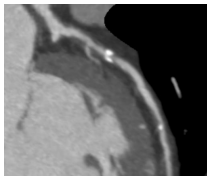
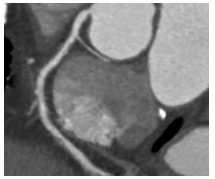
Patients who underwent Coronary CT angiography
before ACS event (1 month – 2 year before the event)
(N=120)





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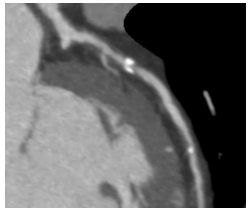
Validation with clinical data, cCTA and coronary angiography (3 independent core labs)

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 CFD core lab due to CT image quality (N=7)

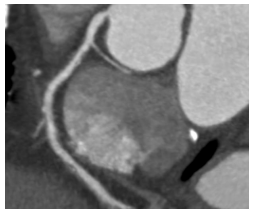
↓

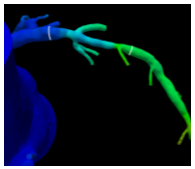
Final Enrollment for cCTA and CFD analysis
(72 patients, 216 lesions)



CASE
Culprit for subsequent ACS (N=66)

CONTROL
Non- Culprit Lesion (N=150)

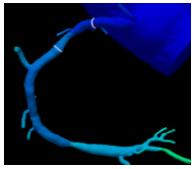




cCTA analysis
adverse plaque characteristics
(Core Lab – SNU Bundang Hospital)

+

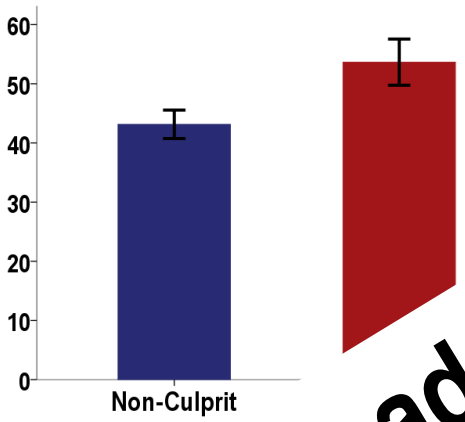
CFD analysis
Non-invasive hemodynamics
(Core Lab - HeartFlow Inc.)



EMERALD study: Culprit vs. Non-culprit

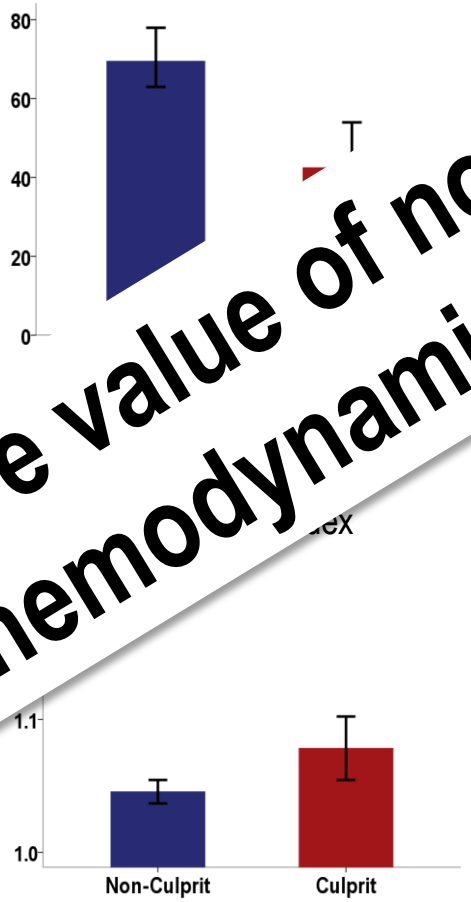
Stenosis severity

Diameter Stenosis (%)

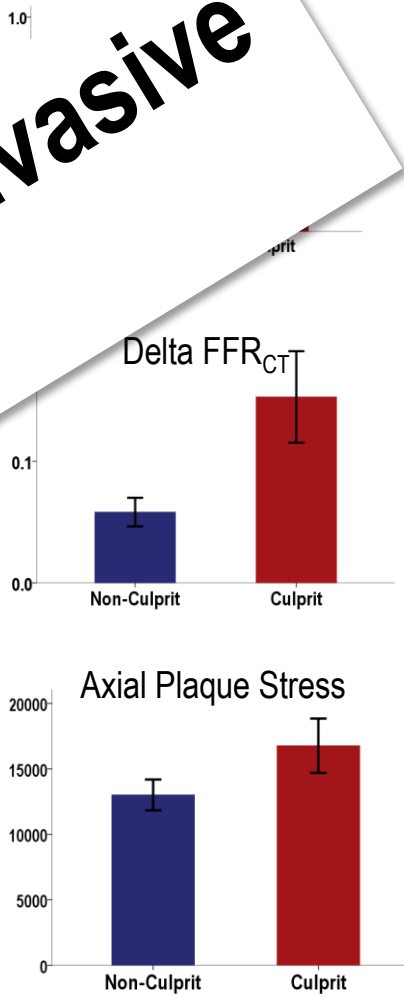


Plaque characteristics

Hounsfield Unit



Hemodynamic characteristics

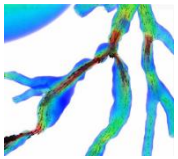


Any additive value of non-invasive hemodynamics?

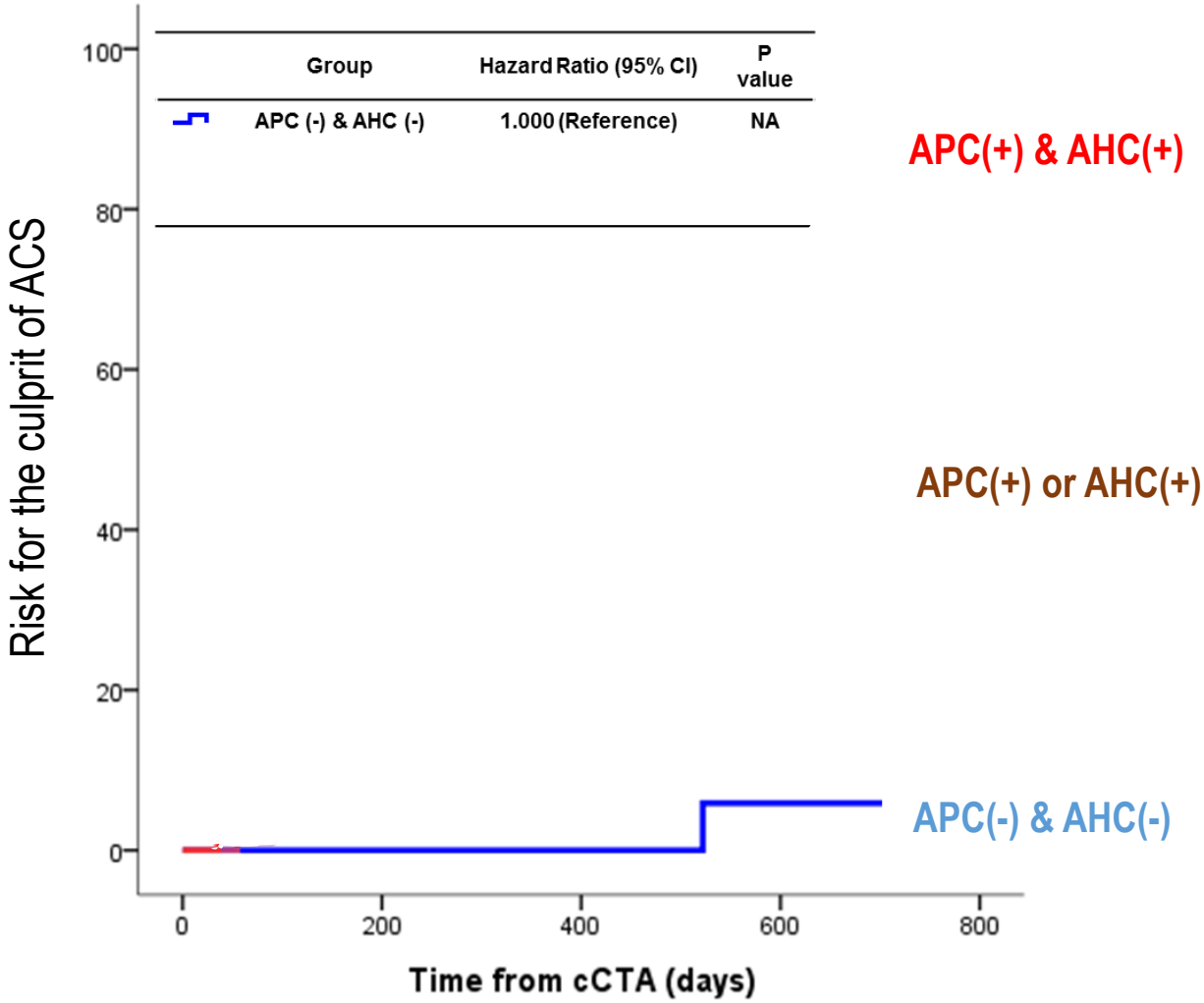
All P values: significant

Lee JM & Choi GW, Koo BK….. JACC imaging 2019

Risk for ACS according to



Adverse plaque characteristics (APC) and Adverse hemodynamic characteristics (AHC)



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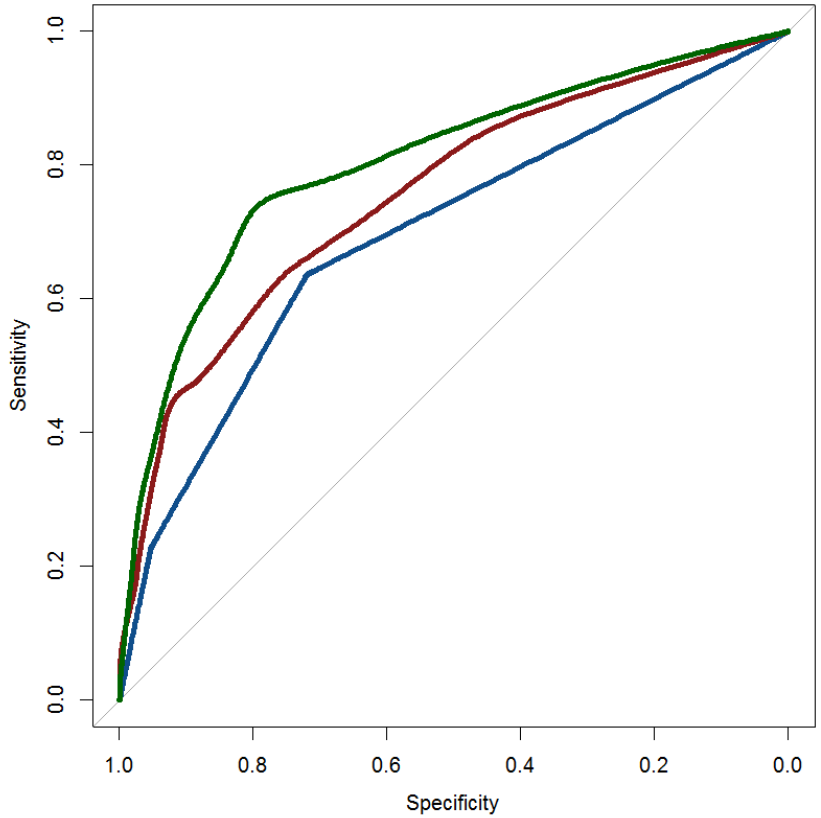
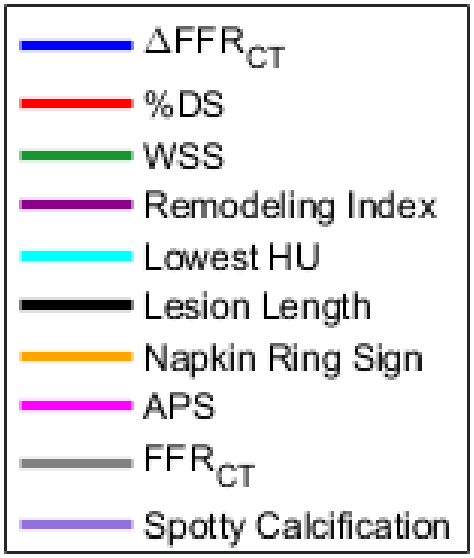
Prediction of ACS risk

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

Relative importance of lesion characteristics in ACS risk



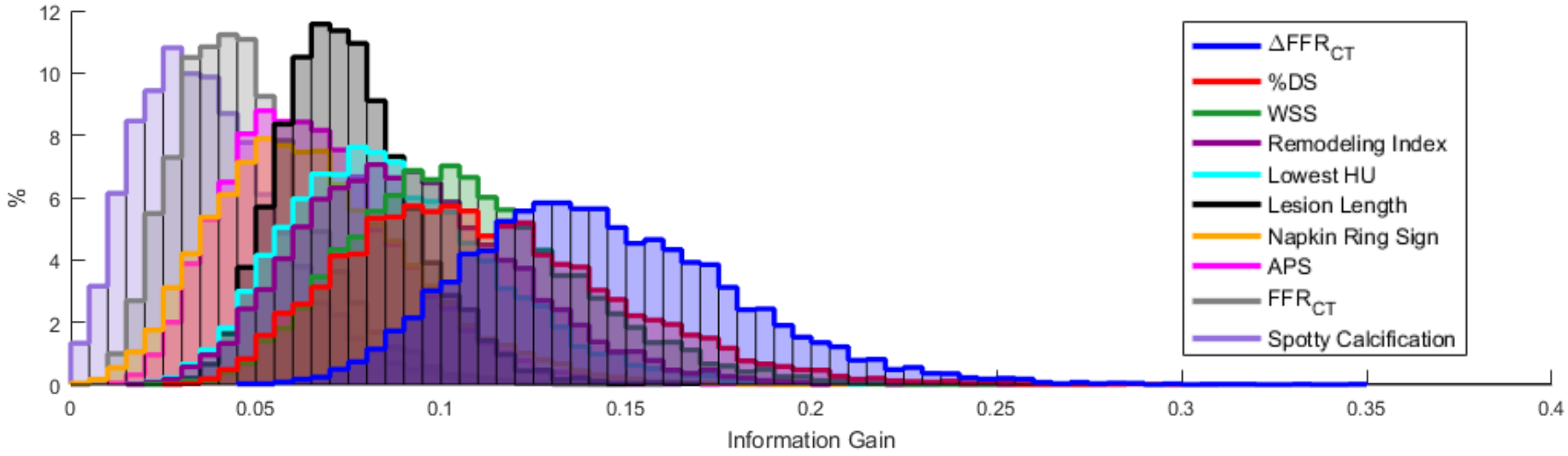
Information gain analysis

- How much “information” a feature gives us about the class = reduction in entropy
- Features that perfectly partition should give maximal information
- Unrelated features should give no information

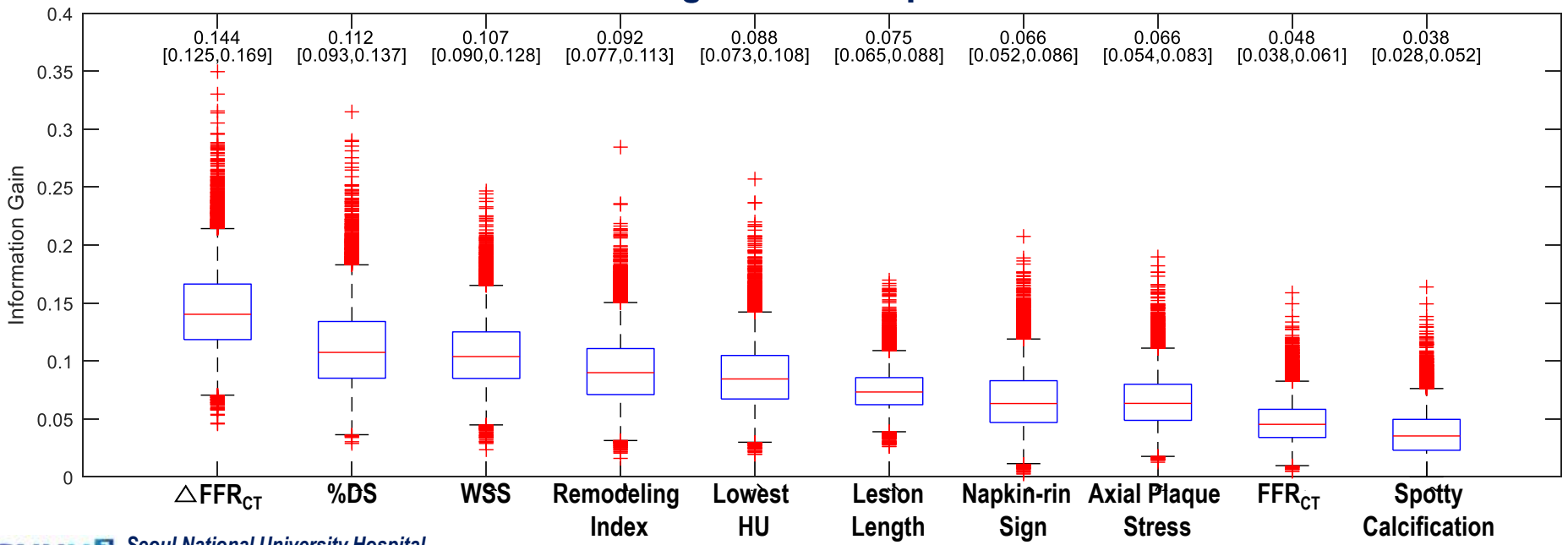
$$Gain(T, X) = Entropy(T) - Entropy(T, X)$$

Hall MA, IEEE Trans on Knowl and Data Eng 2013;15:1437-1447

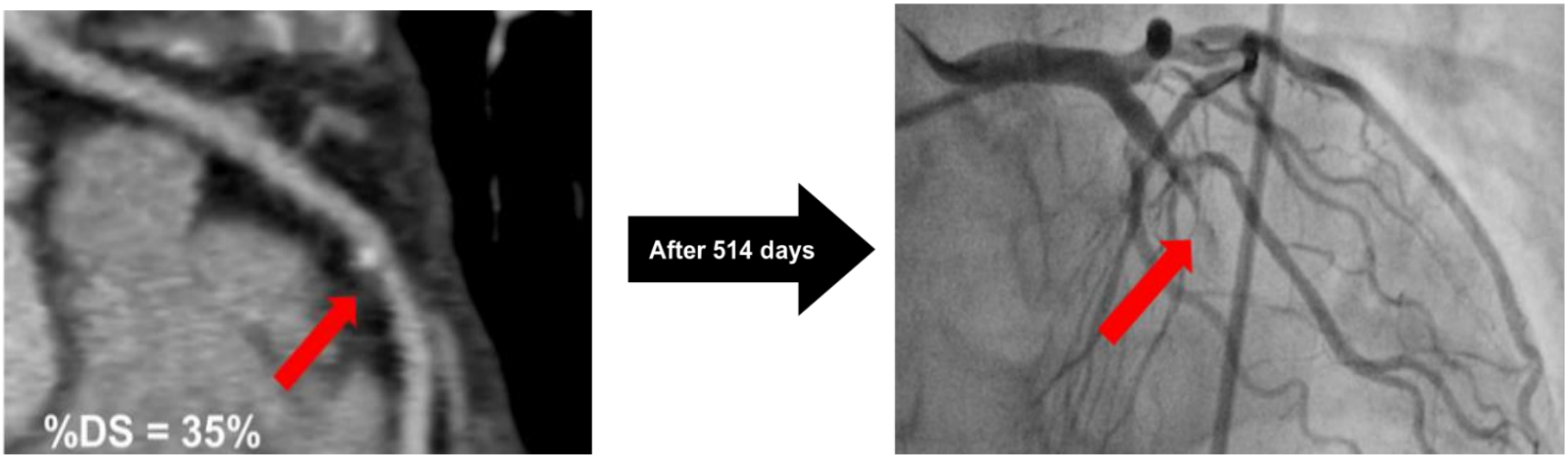
Distribution of information gain from bootstrapping analysis with 10,000 replicates



Information gain of each parameter



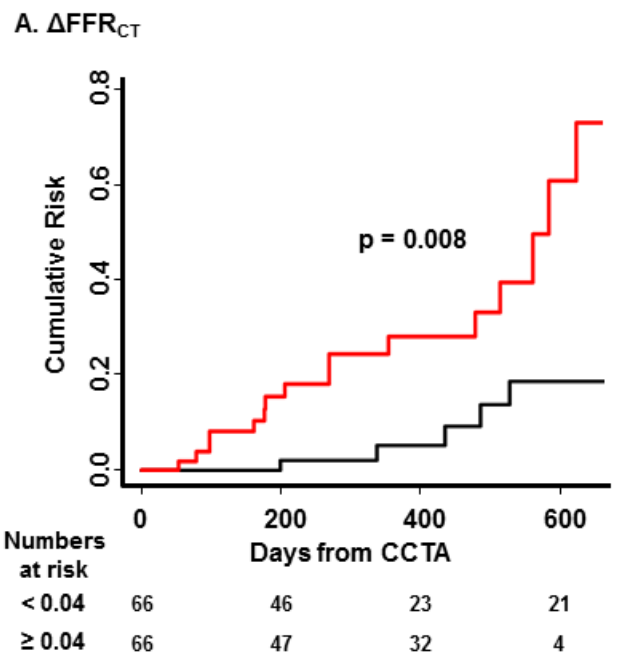
Non-obstructive lesions are not innocent!

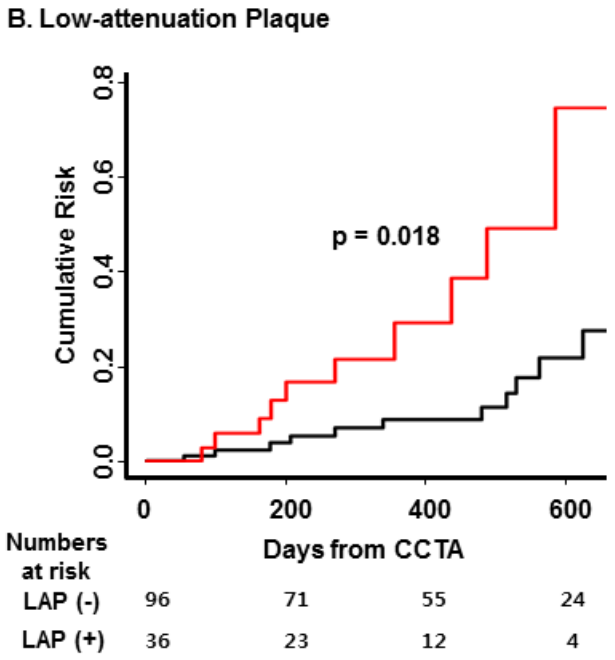


Acute fatal cardiovascular event may occur from non-obstructive lesions.

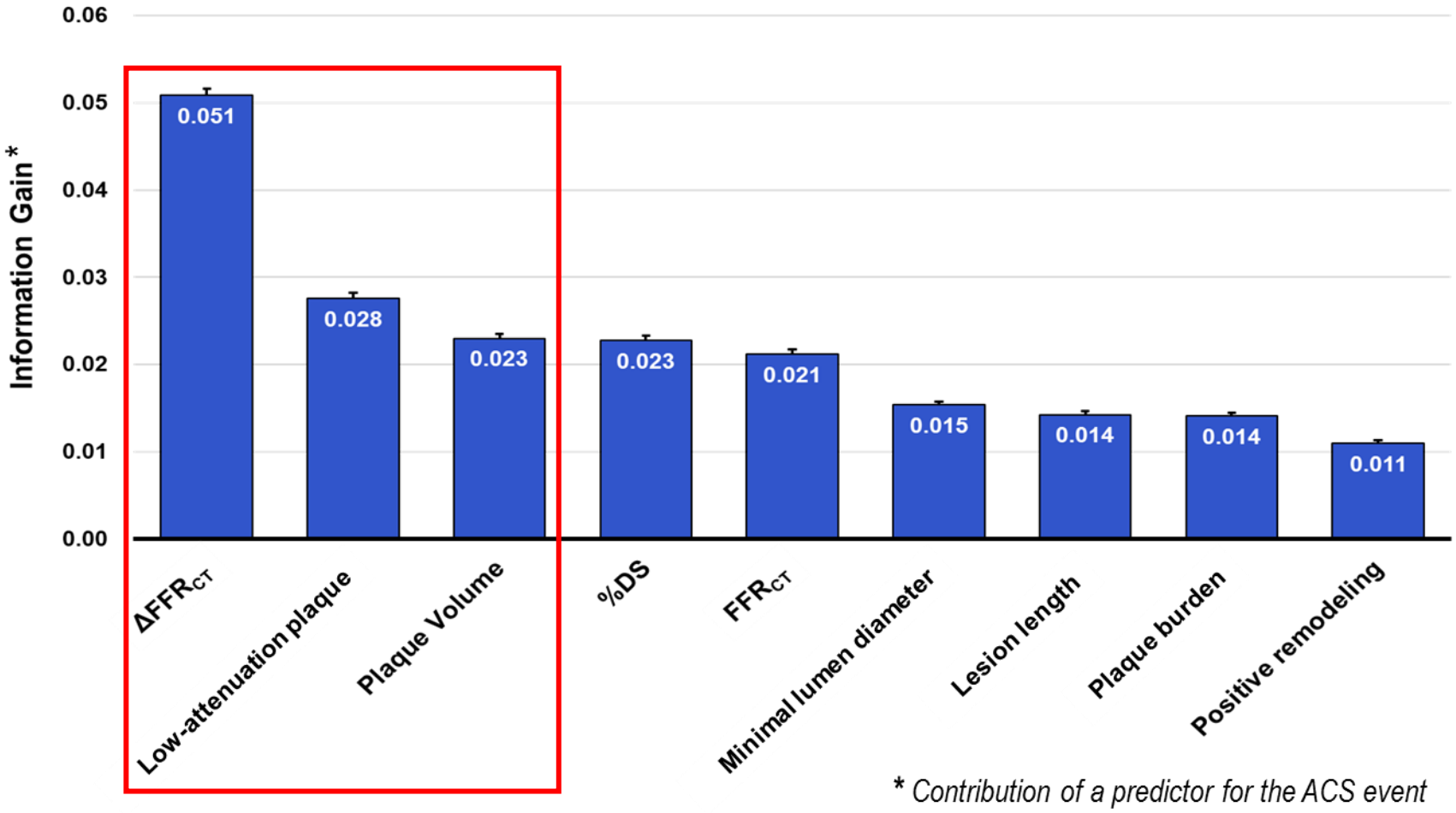
Prognostic impact of lesion characteristics

Lesion Characteristics	HR (95% CI)	95% CI	P value
Anatomical Characteristics			
% Diameter stenosis	1.54	0.78-3.02	0.214
Minimal luminal diameter	0.95	0.43-2.11	0.897
Lesion length	1.02	0.45-2.13	0.966
Plaque volume	1.25	0.50-3.12	0.639
Plaque burden	1.15	0.38-2.00	0.749
Plaque Characteristics			
Low-attenuation plaque	**2.60**	**1.36-4.95**	**0.004**
Positive remodeling	1.15	0.33-4.03	0.831
Hemodynamic Characteristics			
FFR_{CT}	0.54	0.27-1.09	0.101
ΔFFR_{CT}	**3.25**	**1.31-8.04**	**0.010**

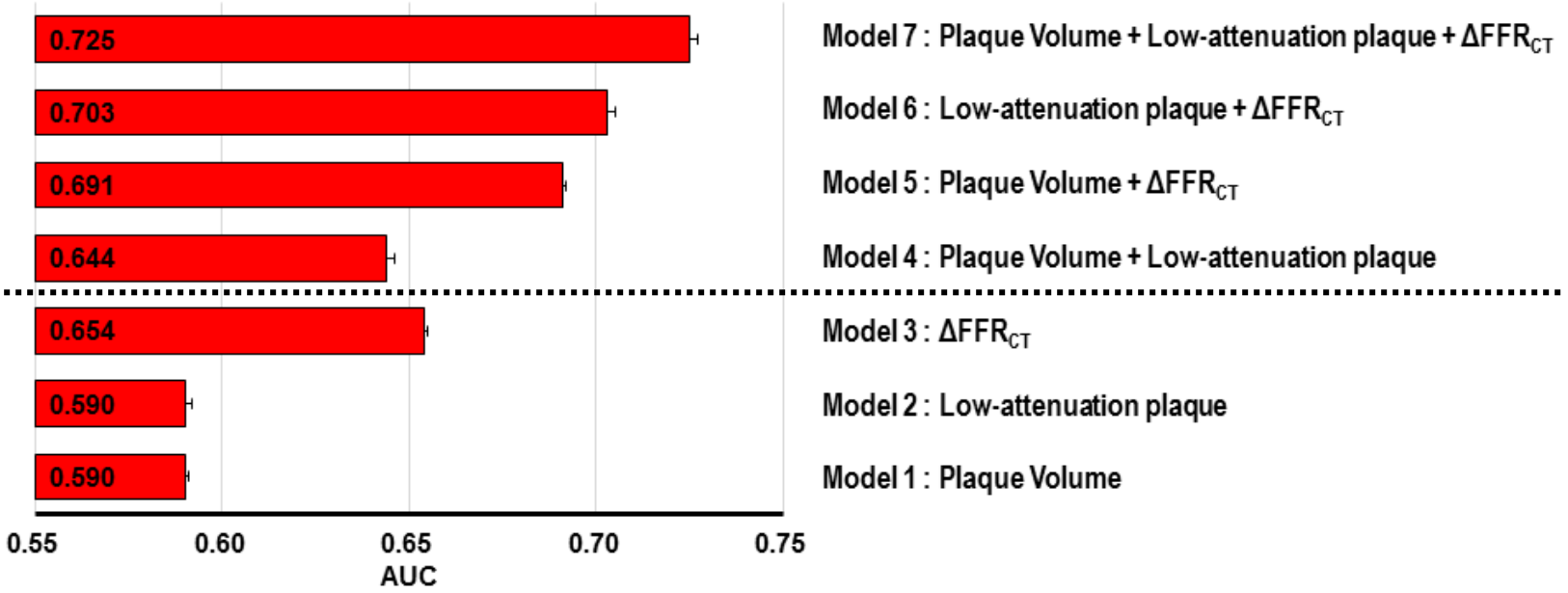




Relative importance of lesion characteristics in ACS risk



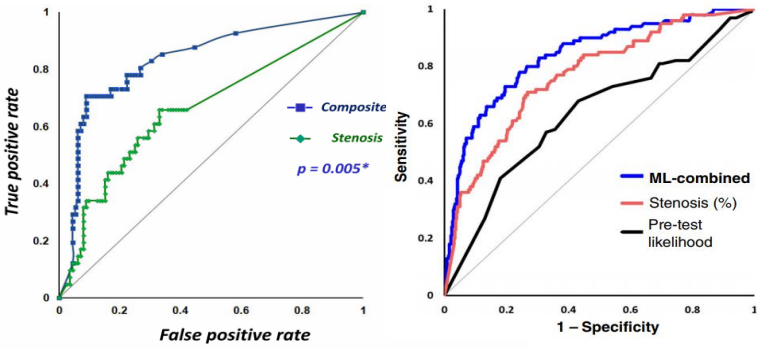
Best metric for ACS prediction in non-obstructive lesions



	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
AUC	0.590 (0.589-0.591)	0.590 (0.589-0.592)	0.654 (0.652-0.655)	0.644 (0.643-0.646)	0.691 (0.689-0.692)	0.703 (0.701-0.705)	0.725 (0.724-0.727)
P for difference	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
Model 1	-	0.923	<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

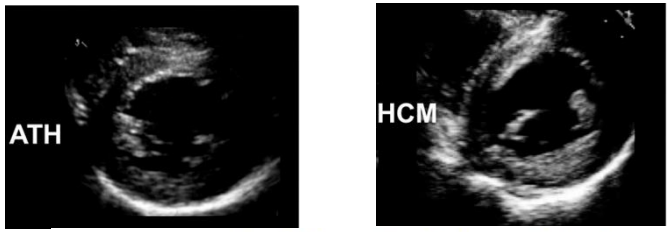
Machine Learning in Cardiovascular Disease

Functional Significance of Coronary Stenosis



Dey D, et al. Circ Cardiovasc Imaging. 2015;8:e003255
Dey D, et al. European Radiology. 2018 28:2655–2664

Discriminating Imaging Diagnosis

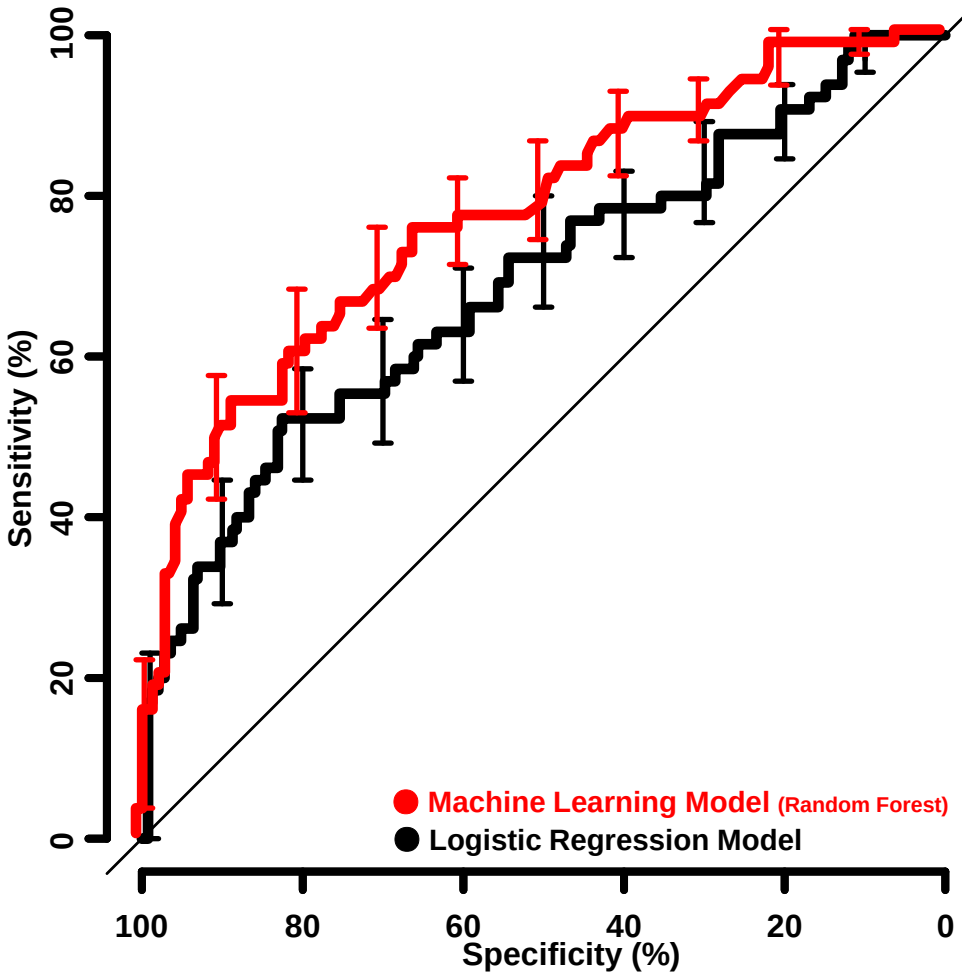


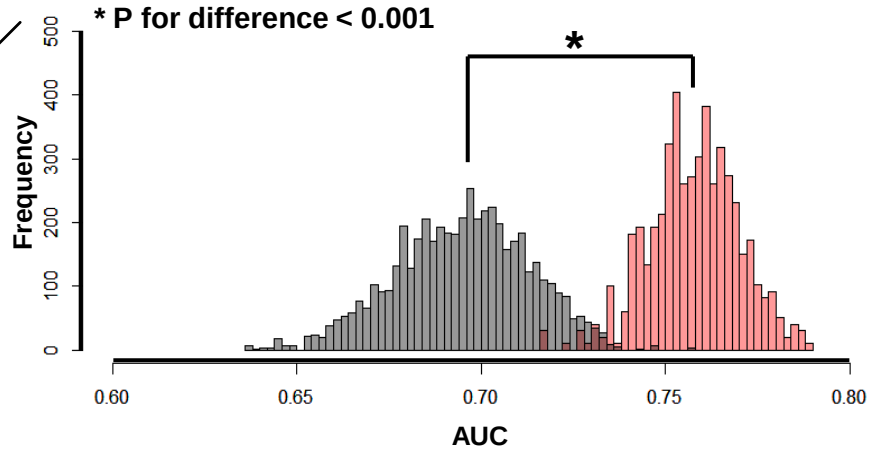
	Sensitivity	Specificity	p Value*
General model			
ML model	87	82	–
E/A	80	71	<0.001
e'†	84	74	<0.001
LS	69	77	0.04

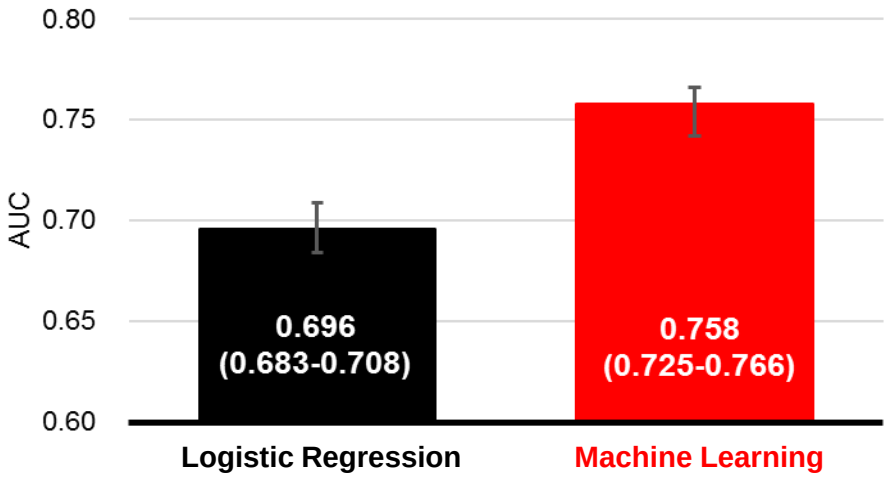
Narula S, et al. J Am Coll Cardiol. 2016 29;68(21):2287-2295

Comparison of Prediction Performance between Conventional Model and Machine Learning model

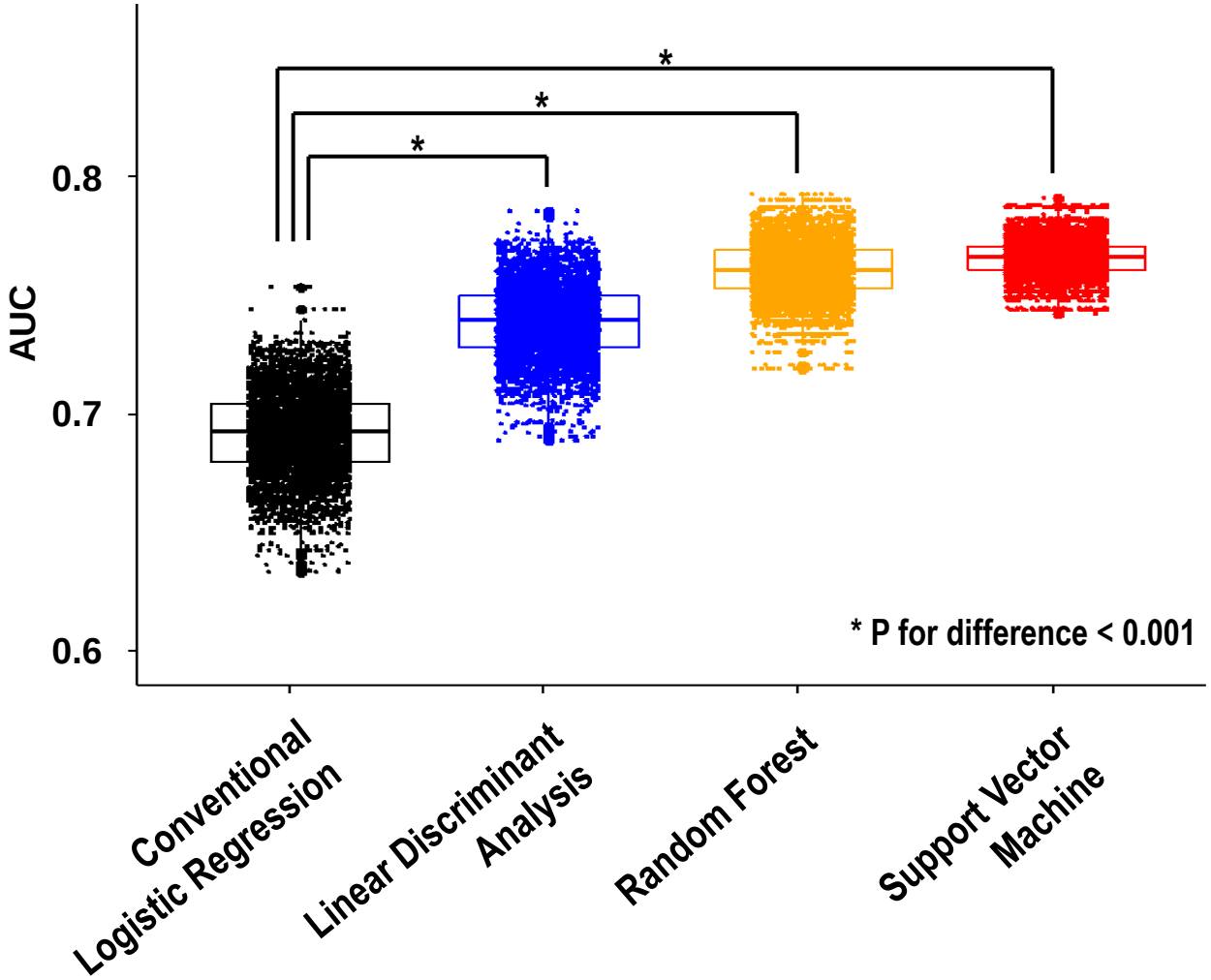
(5-fold Cross Validation with 5,000 Random Permutation)



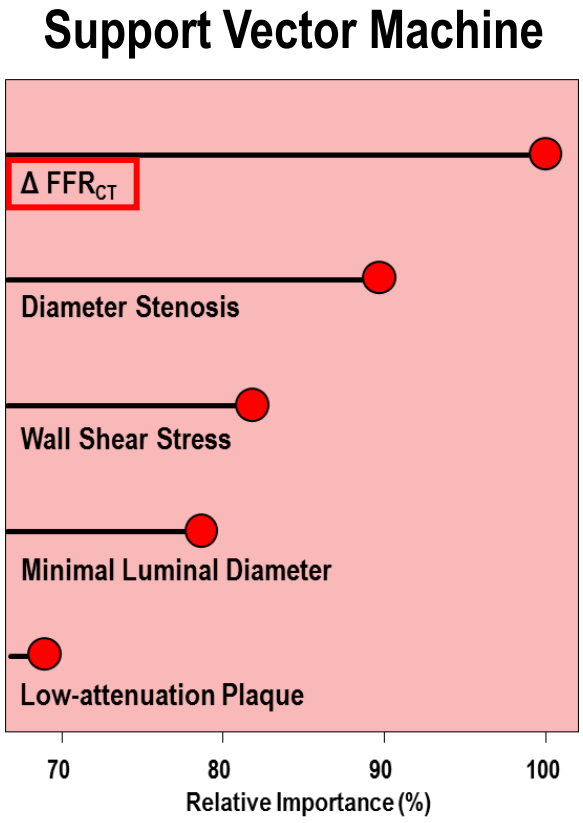


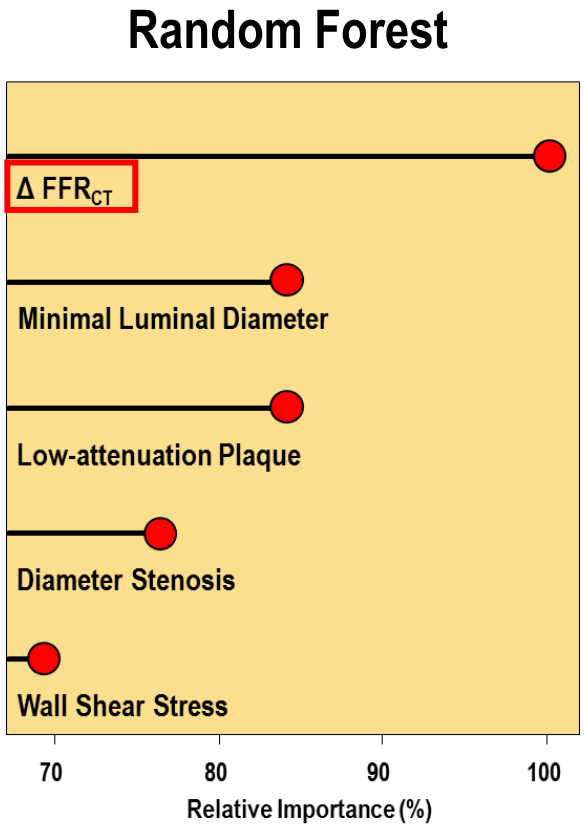


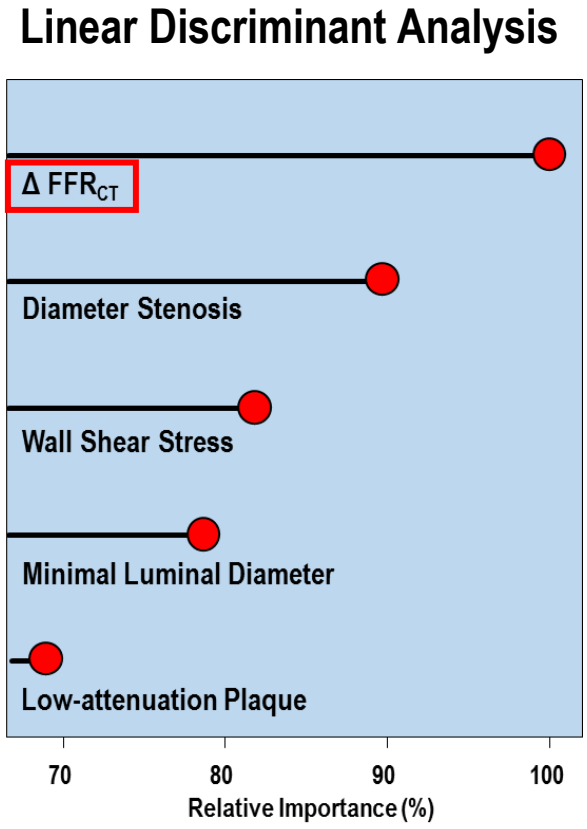
Sensitivity Analysis for Improvement in ACS risk Prediction by Various Machine Learning Algorithms



Relative Importance of Lesion Characteristics







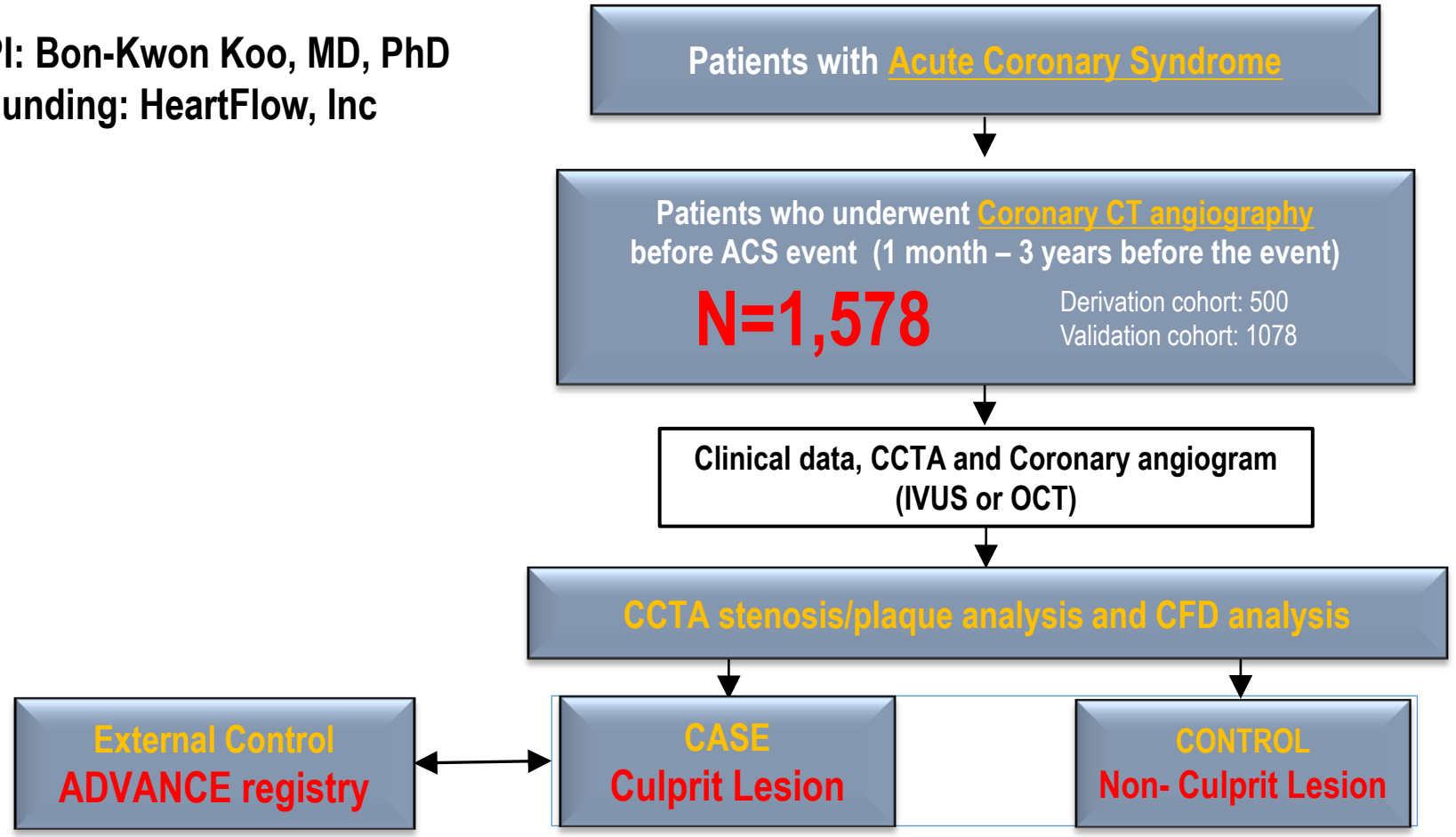
Lessons from EMERALD study

- Non-invasive hemodynamic assessment can enhance the identification of vulnerable plaques that subsequently caused ACS.
- This novel technology can improve the prediction of ACS risk and may help guide optimal treatment for high risk patients.
- Machine learning can further improve the ACS risk prediction.
- A larger study with an external control group is needed to validate this concept.

EMERALD II study

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

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



CURRENT STATUS – Participating Centers

Belgium
Aalst Hospital

Denmark
Aarhus University Hospital
Odense University Hospital
Svendborg Hospital

Germany
Charité – Universitätsmedizin Berlin

Hungary
Semmelweis University

Italy
University of Milan
Monzino Cardiology Center

United Kingdom
University of Edinburgh

South Korea
Chosun University Hospital
Chunnam National University Hospital
Inje University Ilsan Paik Hospital
Jeju University Hospital
Keimyung University Dongsan Medical Center
Samsung Medical Center
Seoul National University Hospital
Seoul National University Bundang Hospital
The Catholic University Hospital
Yeungnam University Hospital

Japan
Aichi Medical University
Ehime University Hospital
Fukuoka Sanno Hospital
Gifu Heart Center
Iwate Medical University
Kobe University Hospital
Nagoya Heart Center
National Cerebral and Cardiovascular Center
Saiseikai Kumamoto Hospital
Shin Koga Hospital
St Luke's International Hospital
Tokai University
Tokyo Medical Dental Univeristy
Tokyo Medical University Hachioji Medical Center
Toyohashi Heart Center
Tsuchiura Kyodo Hospital
Wakayama Medical University

More sites are joining for **EMERALD II**

& You All are Very Welcome to Participate!