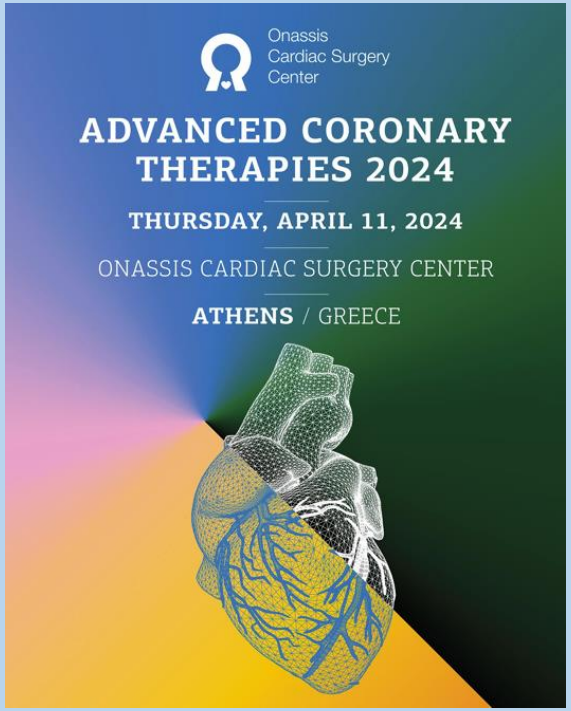

Evolving Imaging Approaches for a Full Evaluation of Coronary Disease: CTA Anatomy, Plaque Structure and Functional Characteristics

10/4/2024

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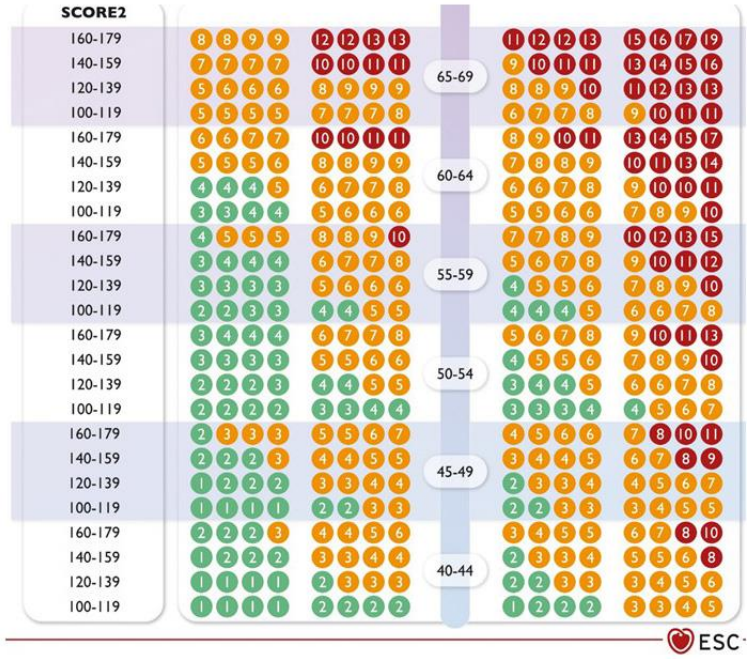
Disclosures

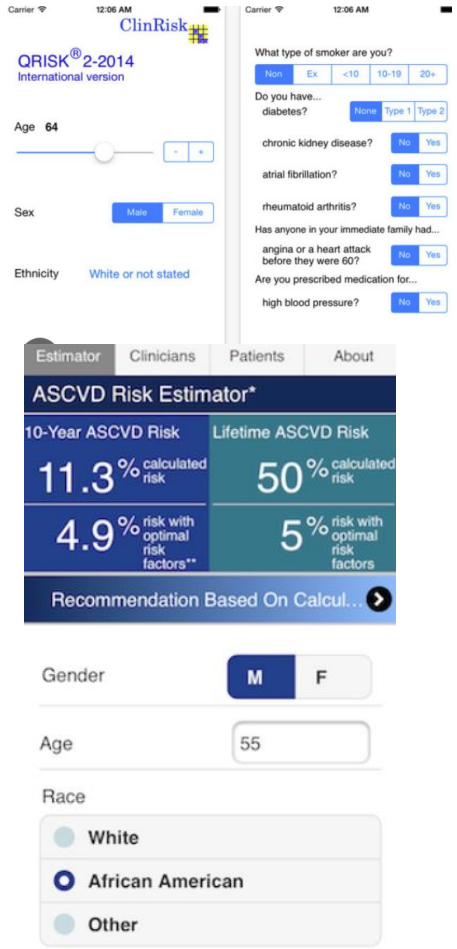
Patent holder of GB2015/052359, GR2018/0100490 and GR2018/0100510 with royalties paid to Caristo Diagnostics Ltd

Shareholder of Caristo Diagnostics Ltd, a medical imaging company (family member)

Risk stratification & treatment decisions for CAD

Clinical risk scores



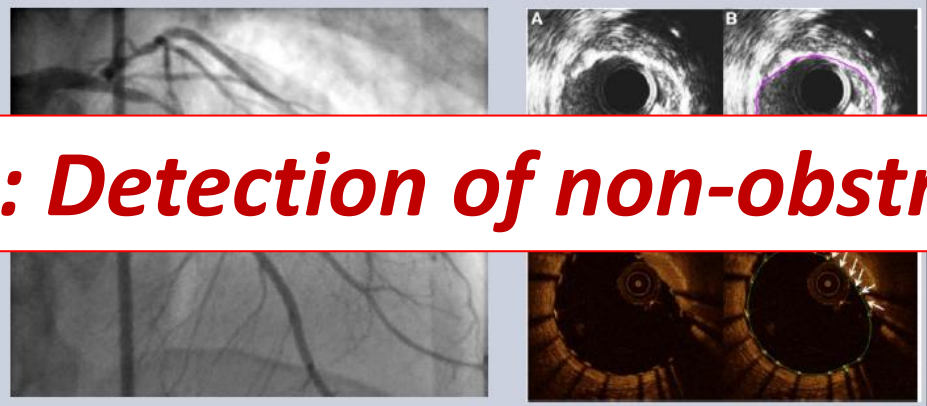
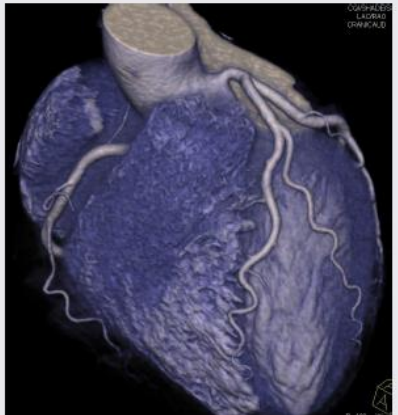
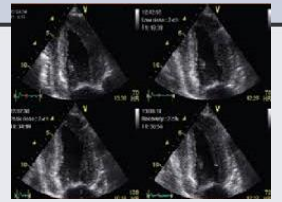
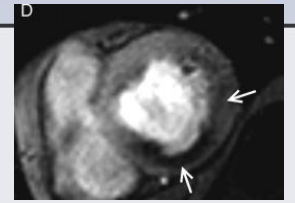
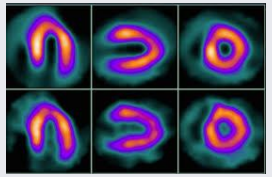
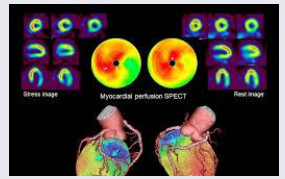


- SCORE2
- QRISK
- ASCVD risk

Symptoms / Luminal stenosis

- >50% of heart attacks occur in people with minor coronary artery stenoses (*Fishbein et al. Circulation. 1996;94:2662-2666)*
- Many patients at risk missed by current tests that rely on detecting luminal stenosis
- First presentation is often MI or death

CCTA for diagnosis of obstructive CAD

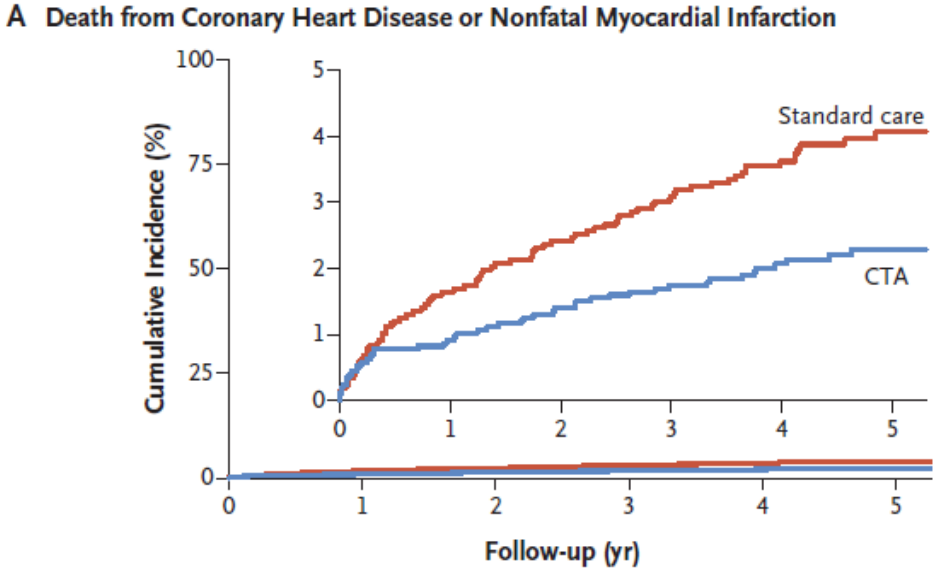
	ANATOMY ***Identify obstructive CAD***	***FUNCTION*** ***Identify lesion-specific ischemia that may benefit from PCI***
		
Non-invasive		   

CCTA BONUS: Detection of non-obstructive coronary plaques!

The use of CCTA for diagnostic assessment of CAD

The Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial

CHD death or non-fatal myocardial infarction
HR 0.59 (95%CI 0.41–0.84), p=0.004



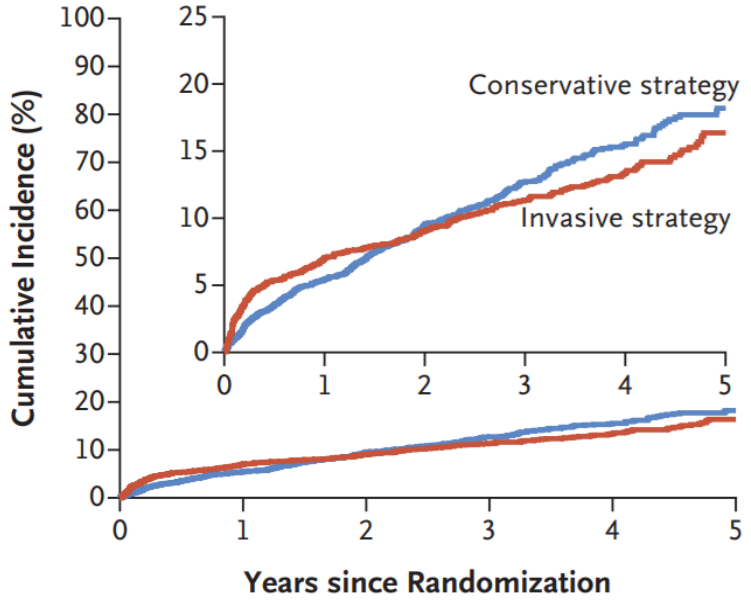
No. at Risk						
Standard care	2073	2033	2008	1994	1572	856
CTA	2073	2051	2029	2015	1588	872

Newby et al. NEJM 2018

ISCHEMIA TRIAL

The NEW ENGLAND JOURNAL of MEDICINE

All-cause death or non-fatal myocardial



No. at Risk						
Conservative strategy	2591	2431	1907	1300	733	293
Invasive strategy	2588	2364	1908	1291	730	271

Maron et al. NEJM 2020

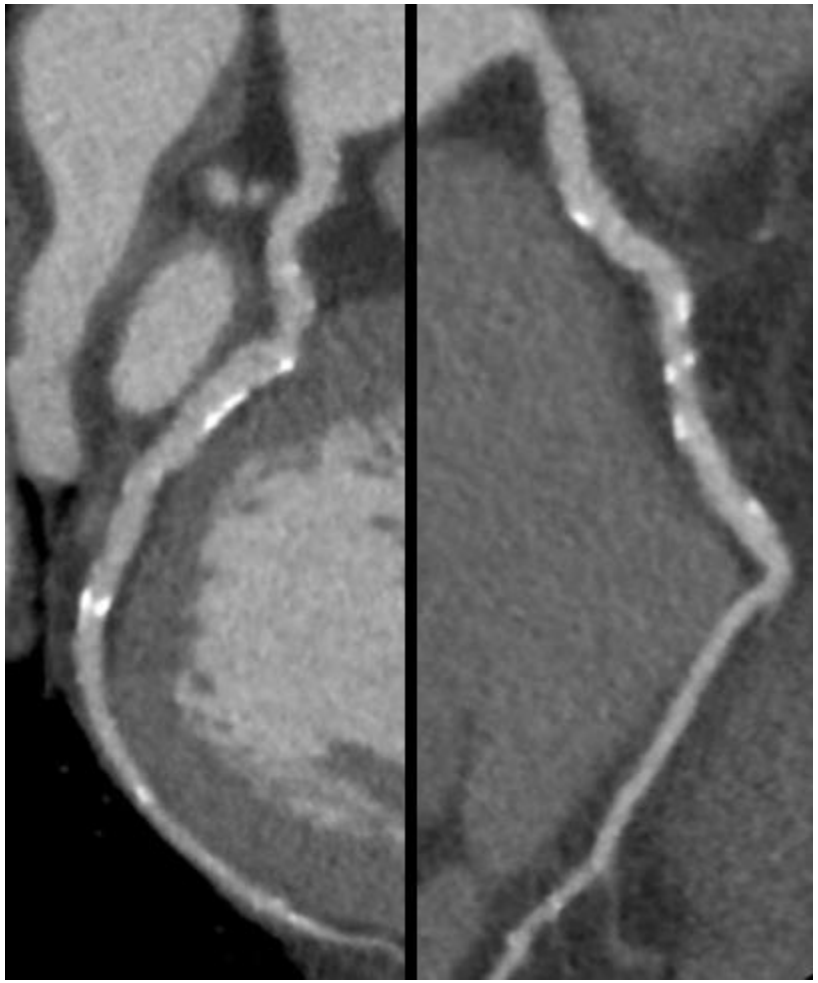
No plaque on CCTA = clinical reassurance

- Atypical symptoms
- No major risk factors
- Low-intermediate PTP
- >85% of patients referred for a CCTA

- No plaque
- Clinical reassurance

Personal archive

No significant luminal stenosis but extensive disease



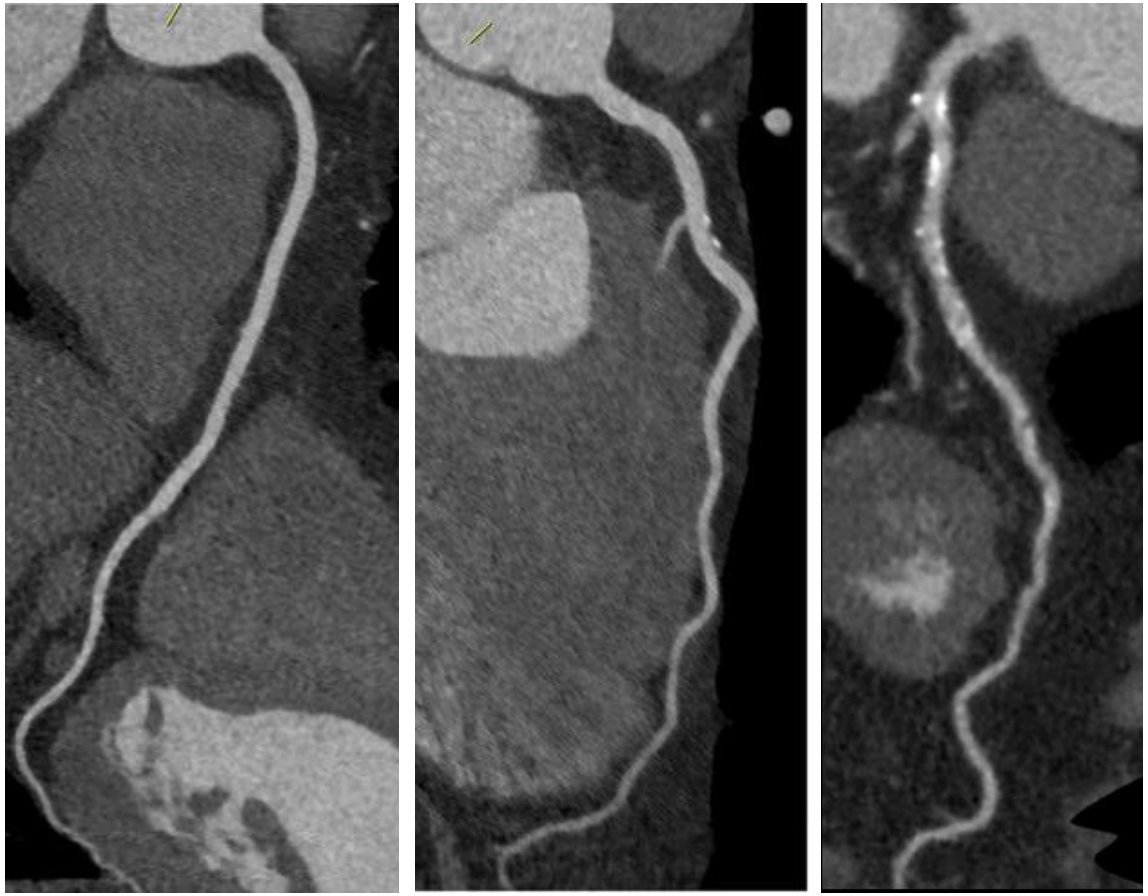
- No significant luminal stenosis
- No obstructive CAD (>50%)
- Moderate-high atheroma burden
- At risk for events
- Better control of RF
- Guiding treatment

Personal archive

Revisiting the definition of CAD in the era of CCTA

CAD

No | Non-obstructive | Obstructive

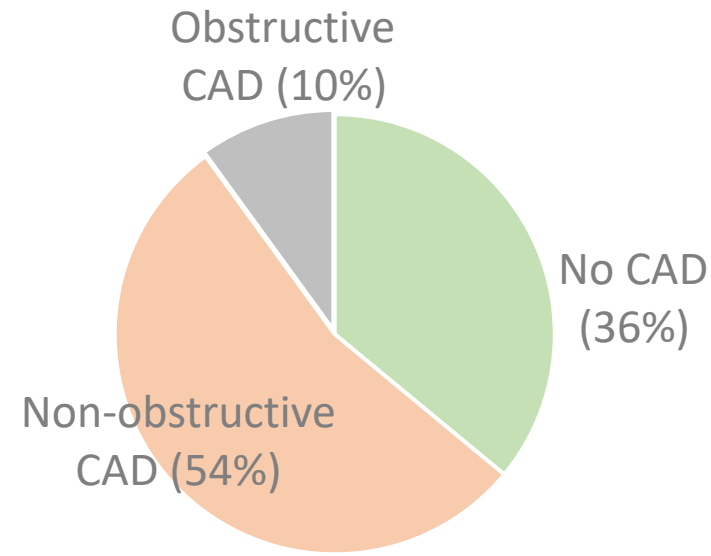


CCTA as the preferred 1st modality to screen for suspected CAD (Class IB)

*in the absence of relative contraindications that may compromise diagnostic quality (arrhythmia, obesity etc.)

Copenhagen General Population Study, Denmark

9533 asymptomatic persons >40y w/o known IHD

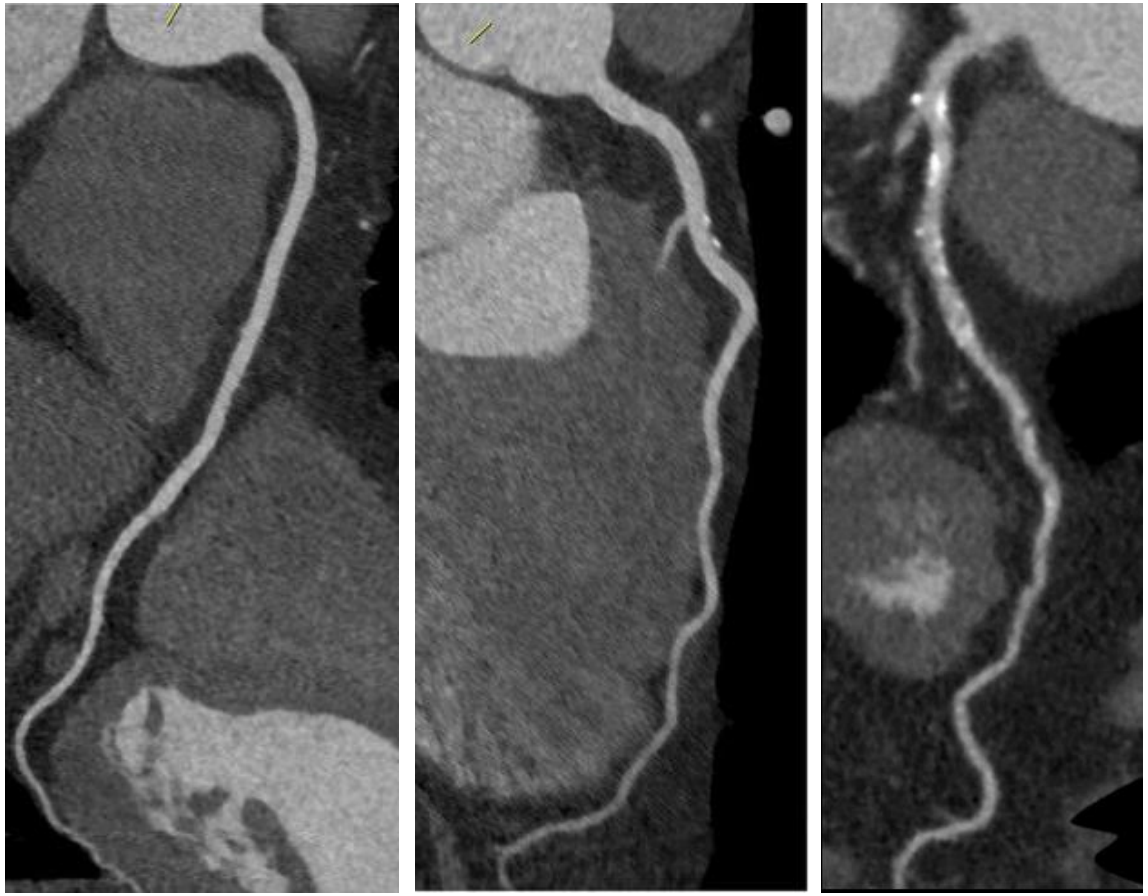


Fuchs et al. Ann Intern Med. doi.org/10.7326/M22-3027

Revisiting the definition of CAD in the era of CCTA

CAD

No | Non-obstructive | Obstructive



CCTA as the preferred 1st modality to screen for suspected CAD (Class IB)

*in the absence of relative contraindications that may compromise diagnostic quality
(arrhythmia, obesity etc.)

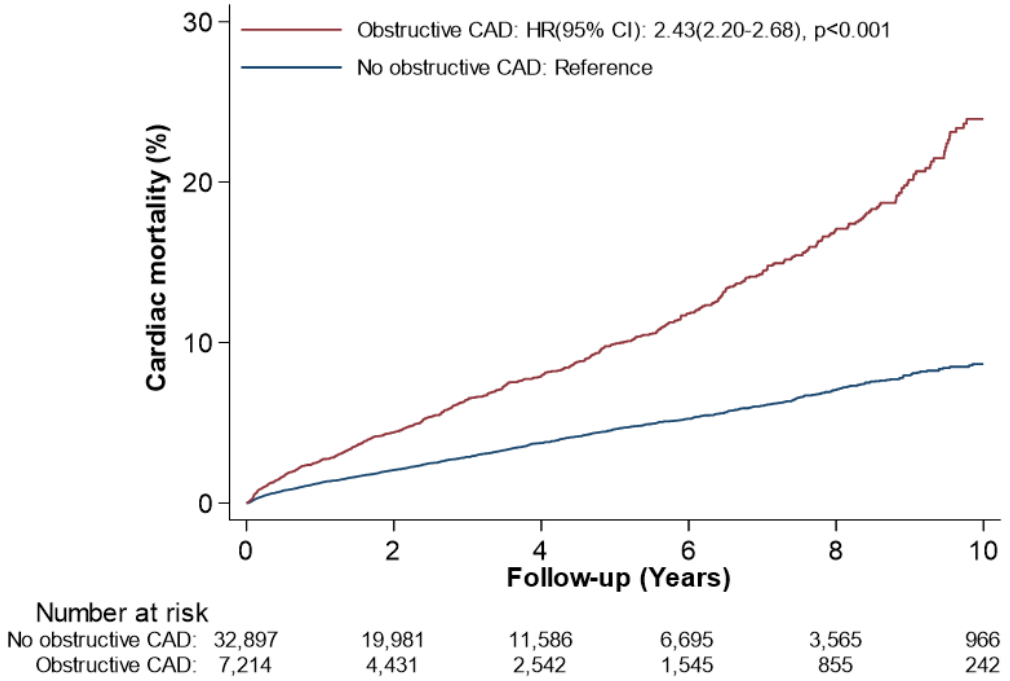
Obstructive-extensive CAD	**~12x RR**
Obstructive-non-extensive CAD	**~8x RR**
Nonobstructive-extensive CAD	**~3x RR**

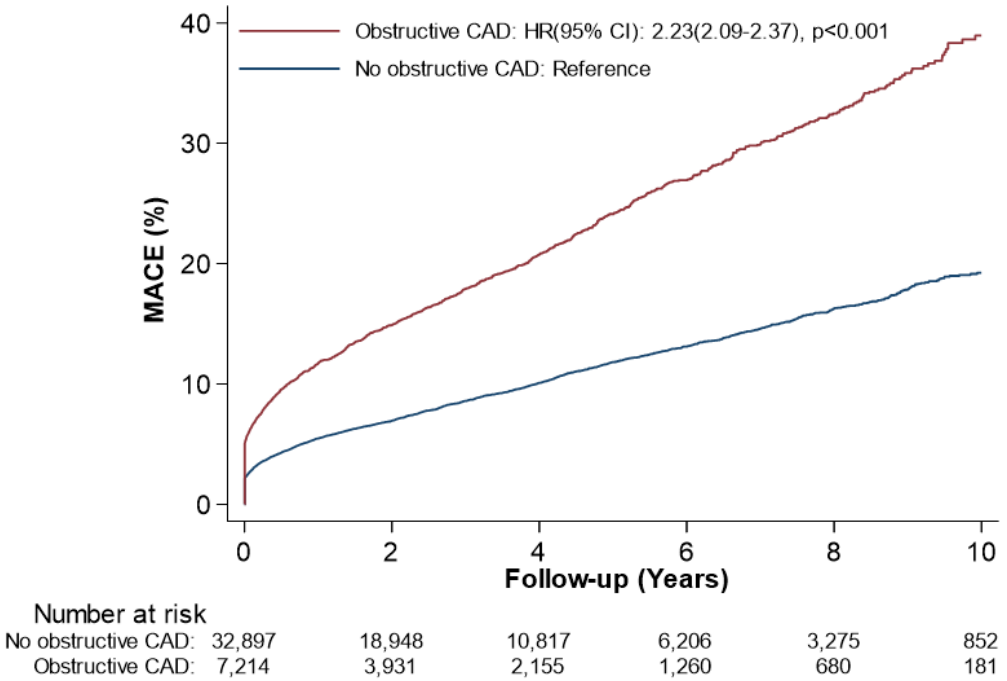
- **Plaque burden**, not stenosis per se, is the main predictor of risk for CVD events and death

Fuchs et al. Ann Intern Med. doi.org/10.7326/M22-3027
Mortensen et al. J Am Coll Cardiol 2020;76:2803–13

ORFAN study: No-obstructive CAD on CCTA

ORFAN study ~40,000 patients undergoing CCTA in the UK

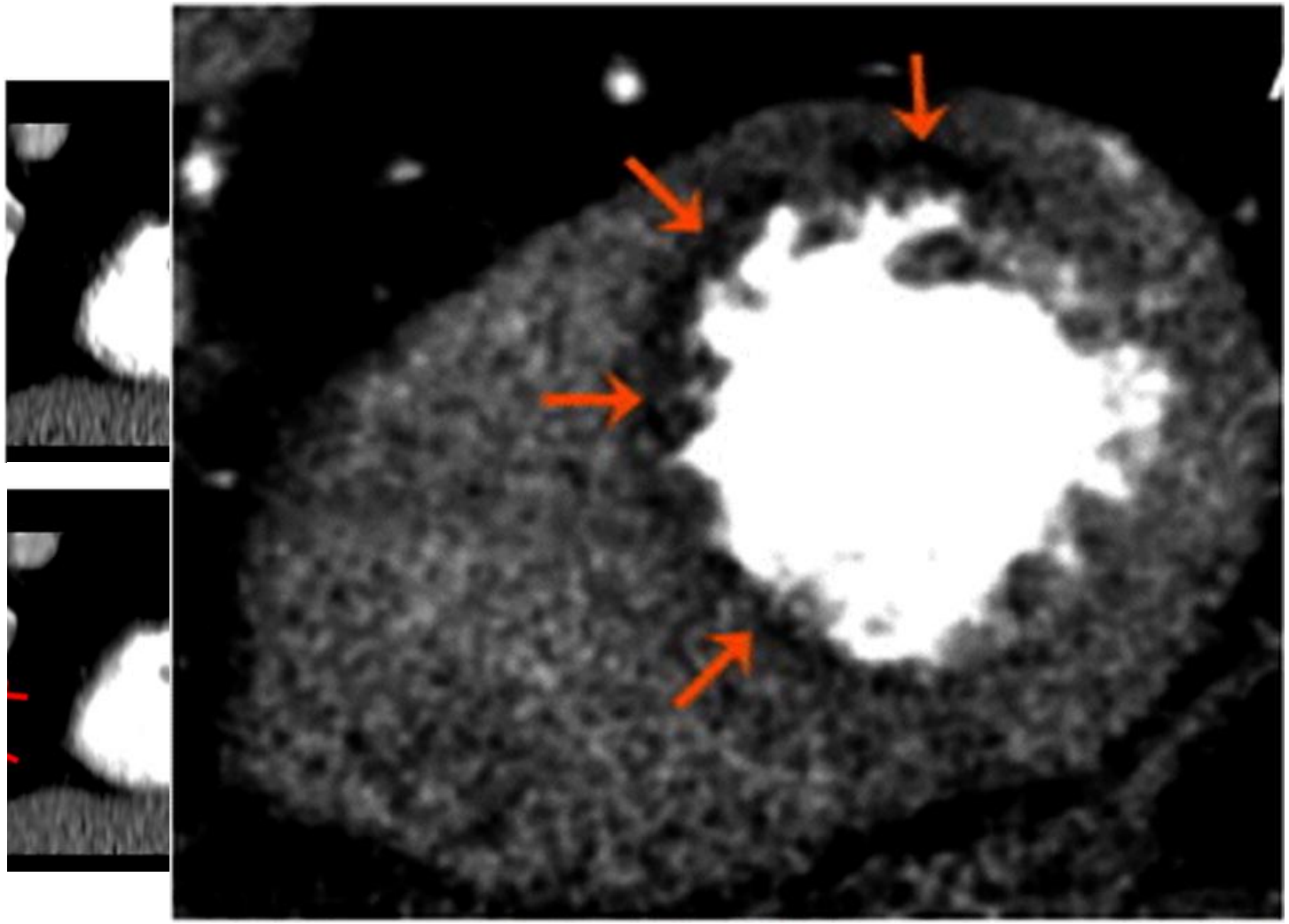




Ken C et al. The Lancet 2024 (accepted)

Functional assessment of plaques by CT

CT-perfusion imaging for ischaemia detection



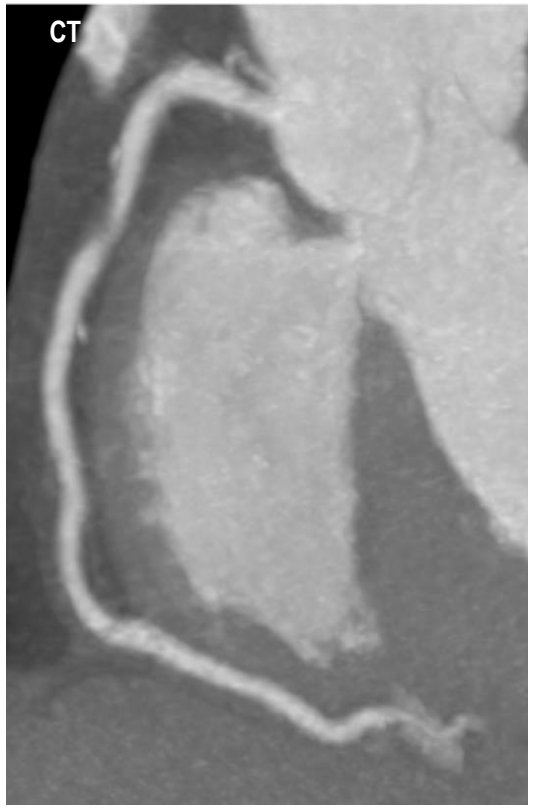
Strengths

- Good diagnostic accuracy for ischaemia

Limitations

- Repeated scanning
- High radiation dose
- Scan logistics
- Limited clinical adoption
- Consensus on scanning acquisition details

FFR-CT for functional assessment of stenoses on CCTA



[redacted]

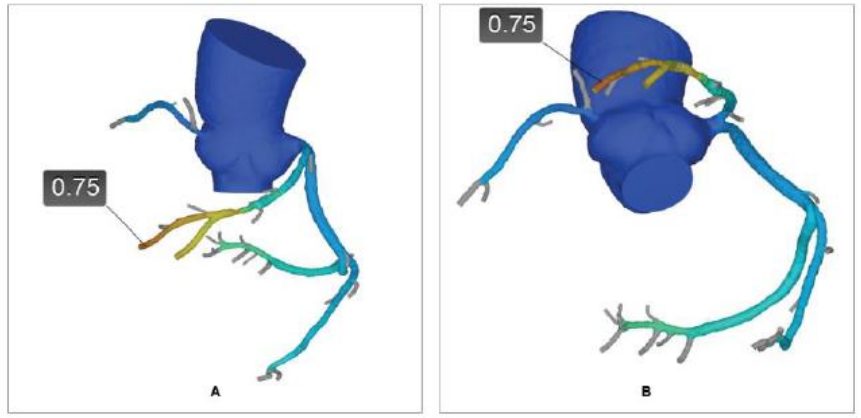
Patient ID 29-0070-G-C
Birth Date *Not provided*
CT Study Date 1/14/2014

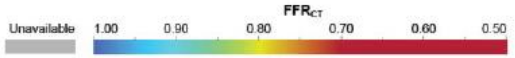
Summary

CORONARY ARTERY		FFR_{CT}
Left Main	LM	0.98
Left Anterior Descending System	LAD	0.75
Left Circumflex System	LCx	0.86
Right Coronary Artery System	RCA	0.94

FFR_{CT} 1.00 0.90 0.80 0.70 0.60 0.50

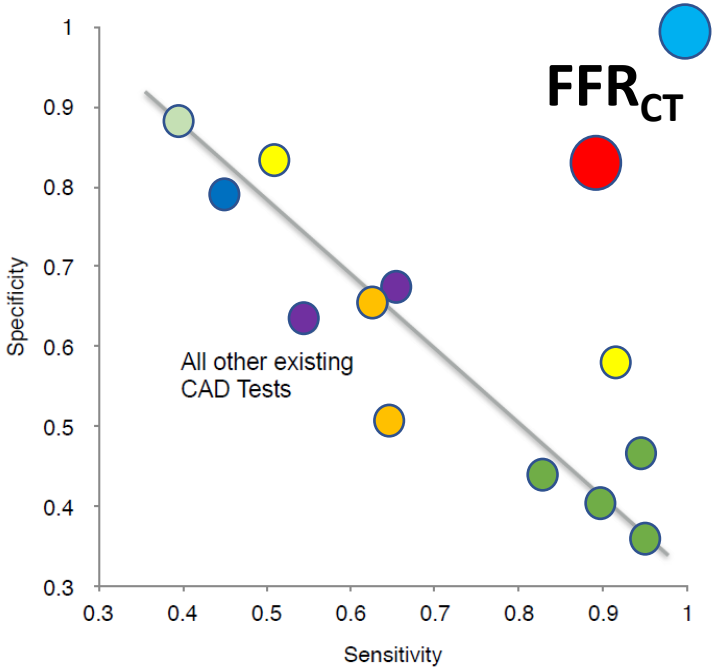
Measured Fractional Flow Reserve (FFR) values ≤ 0.80 suggest hemodynamic (functional) significance (1,2,3).





- CCTA
- CCTA+TAG
- CMR
- Stress echo
- ICA - QCA
- IVUS

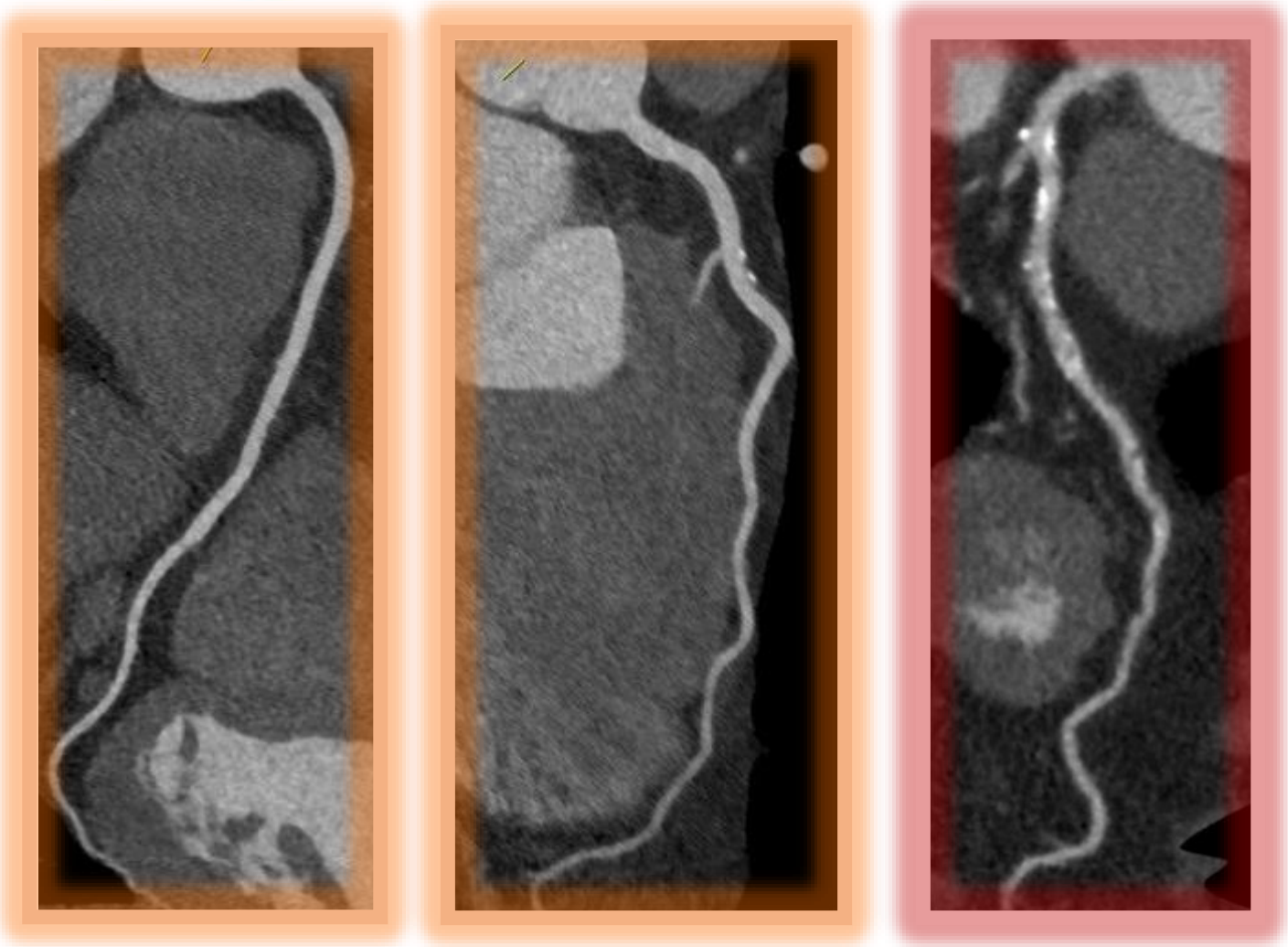
FFR (Gold standard)



Danad et al. EHJ 2016

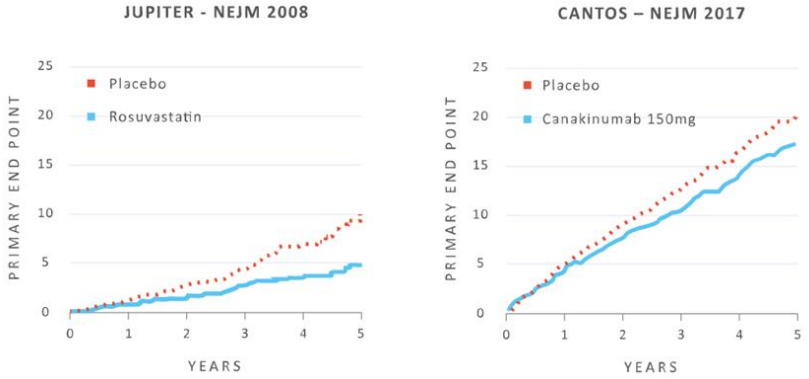
Remaining challenges: detecting vascular inflammation

Remaining challenges: detecting vascular inflammation



- The vulnerable “healthy” individual who will develop atheroma
- The vulnerable “healthy” individual who has minor atheroma at risk for ACS
- The vulnerable patient with advanced disease, who despite OMT remains at risk for ACS (due to rupture of either significant or “minor” plaques)

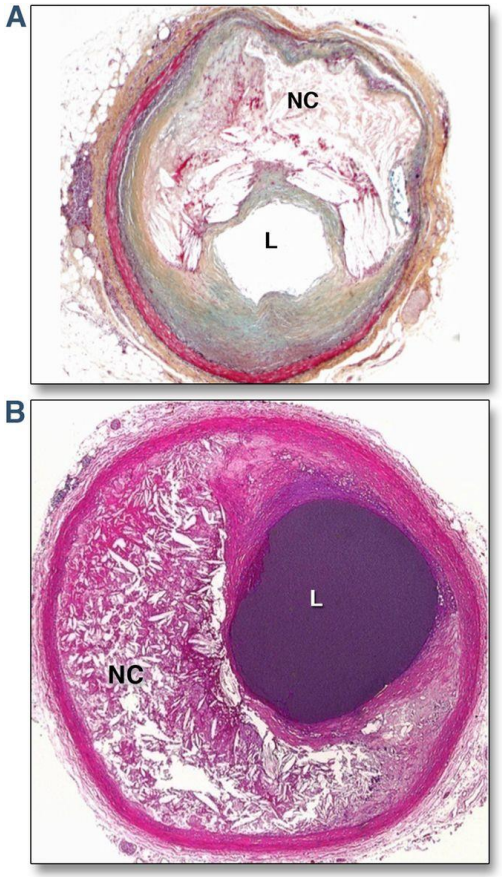
Treating vascular inflammation



CRP non-specific (>50% have high residual inflammation in 2ndary prevention based on CRP)

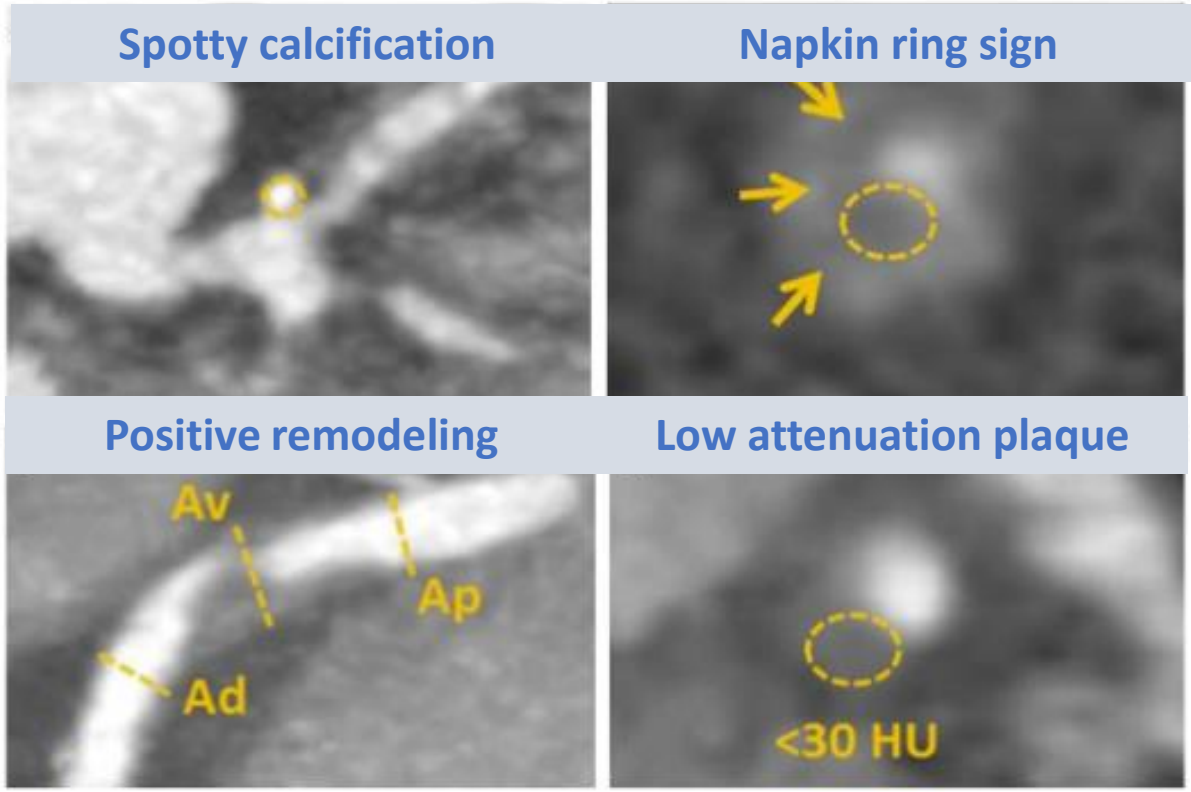
High risk plaque on CCTA

The *vulnerable* plaque



High-risk plaque (HRP) on CCTA

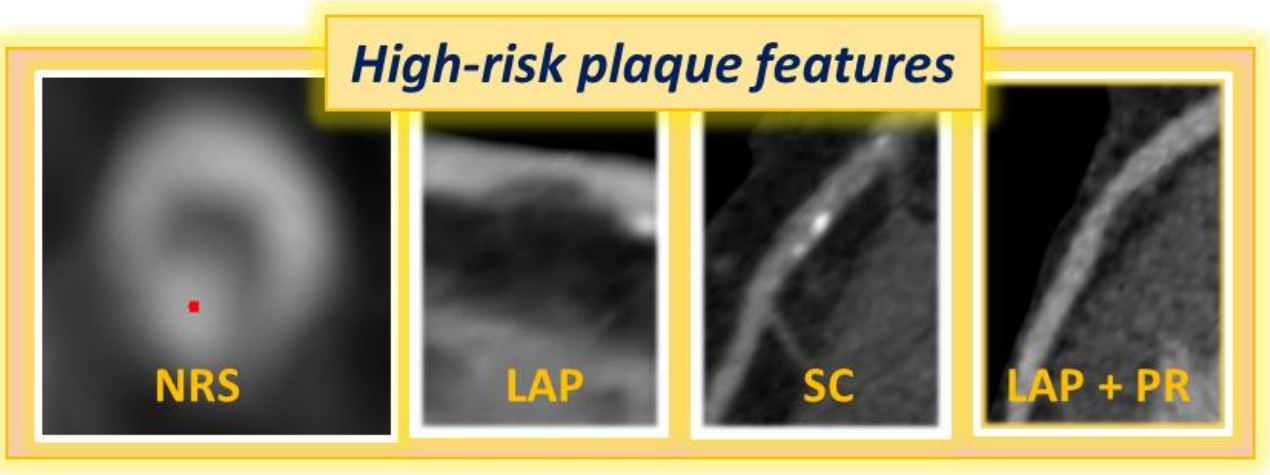
2 or more features



CAD-RADS 2.0–2022

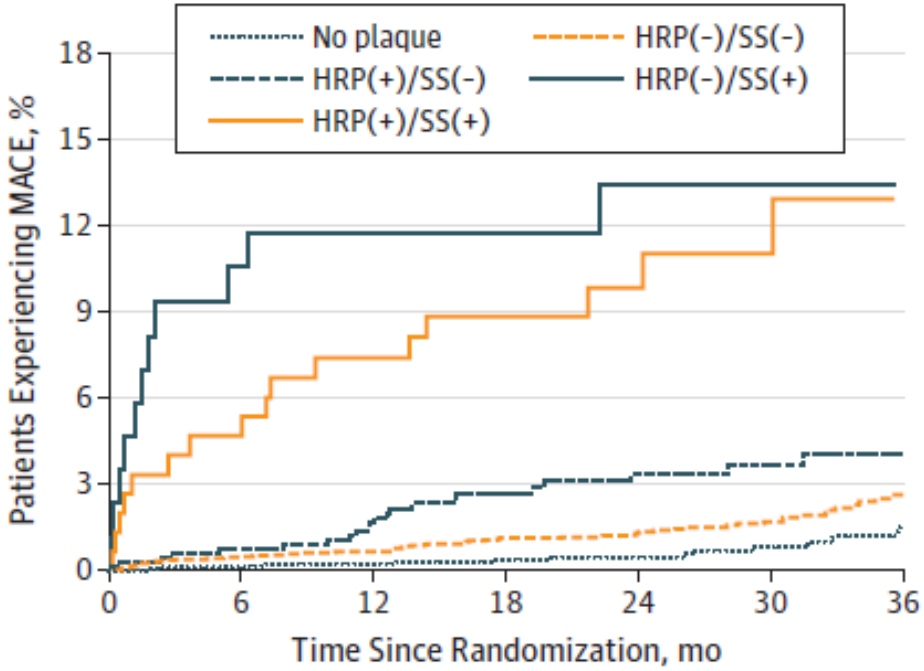
Coronary Artery Disease-Reporting and Data System

High-risk plaque on CCTA and risk stratification



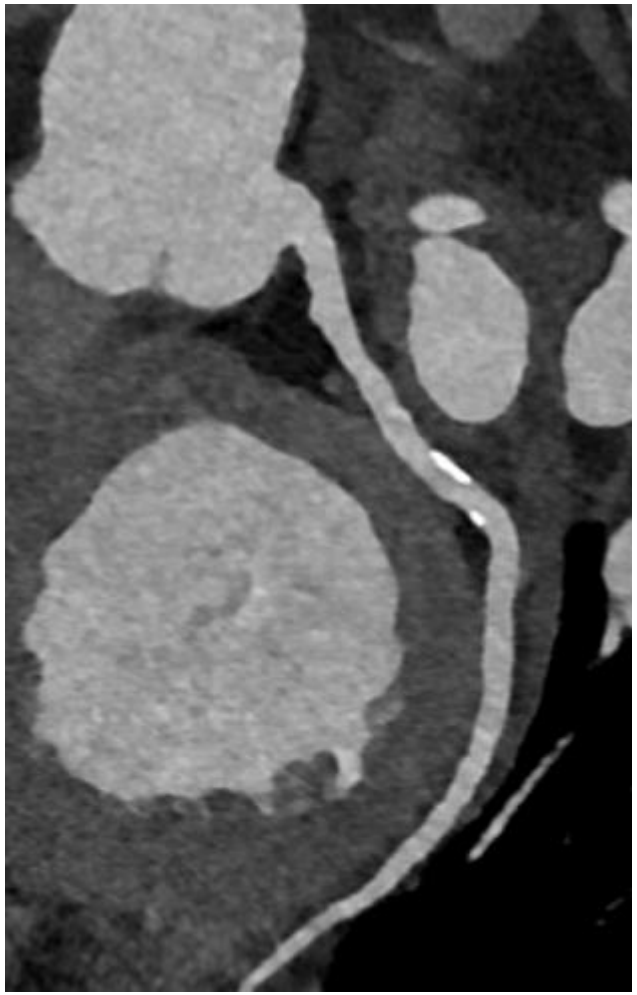
Frequent > 30%
Low positive predictive value

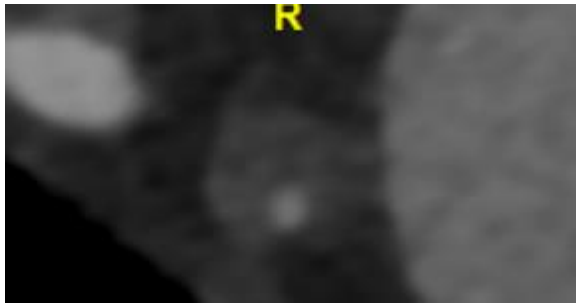
PROMISE study 4,415 pts
CCTA + plaque phenotyping



Ferencik et al JAMA Cardiology 2018

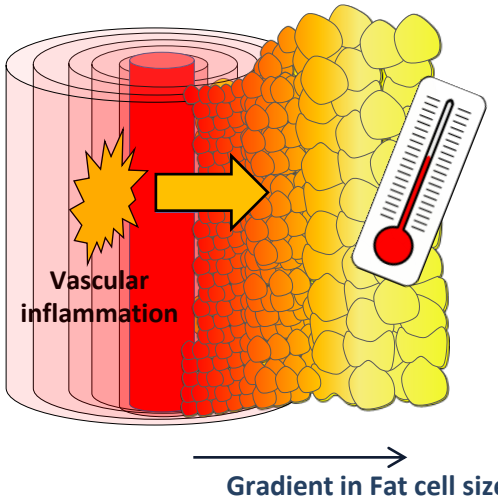
Unprecedented image CCTA quality with Photon Counting CT



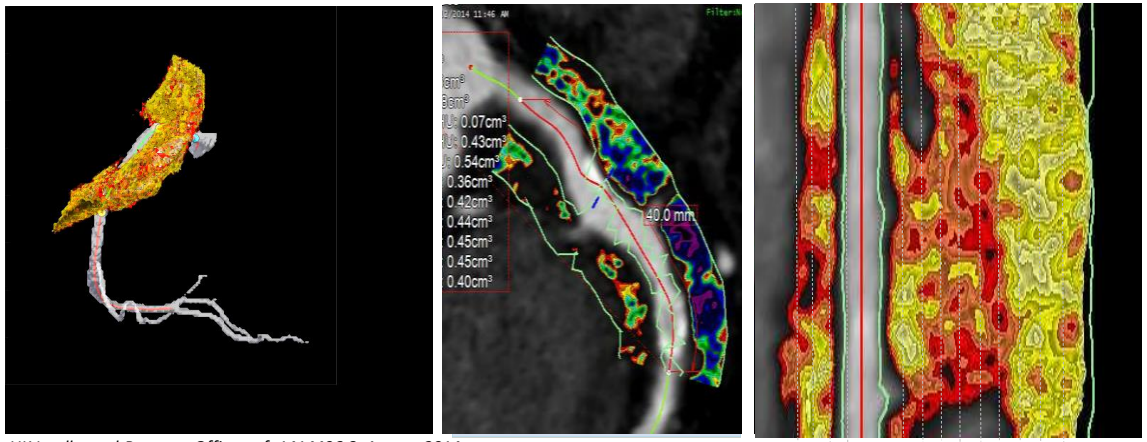


courtesy of Prof. Antoniades (UOXF)

Perivascular fat as a sensor of coronary inflammation



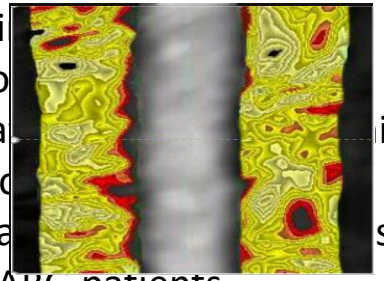
Perivascular Fat Attenuation Index (FAI$_{PVAT}$)

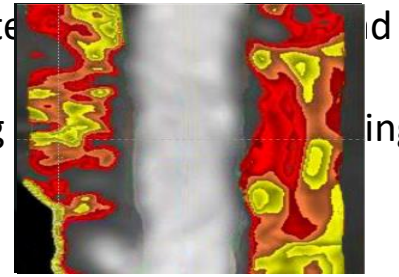


UK Intellectual Property Office, ref. 1414496.8, August 2014

Low FAI **High FAI**

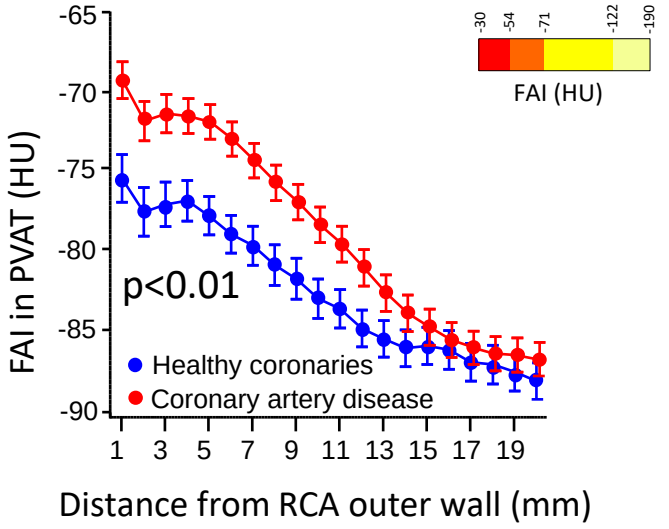
3D mappi- inte d the human co Mathema- ing ing with Images fr



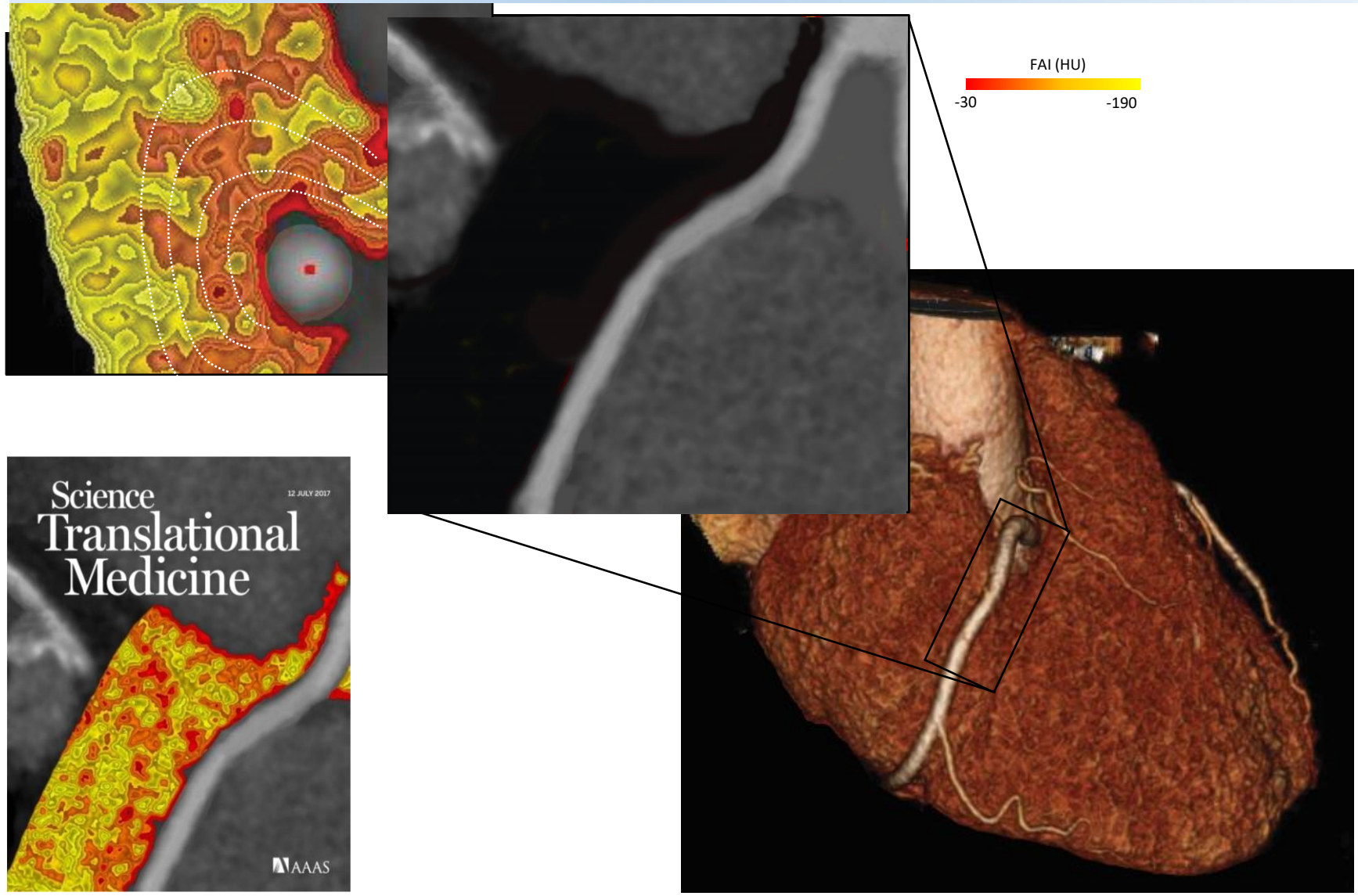


- ✓ 1400 a s
- ✓ 902 CABG patients
- ✓ 4273 CTAs (CAD, ACS, "healthy" coronaries)

Antonopoulos A, Sanna F et al. *Science Translational Medicine 2017*

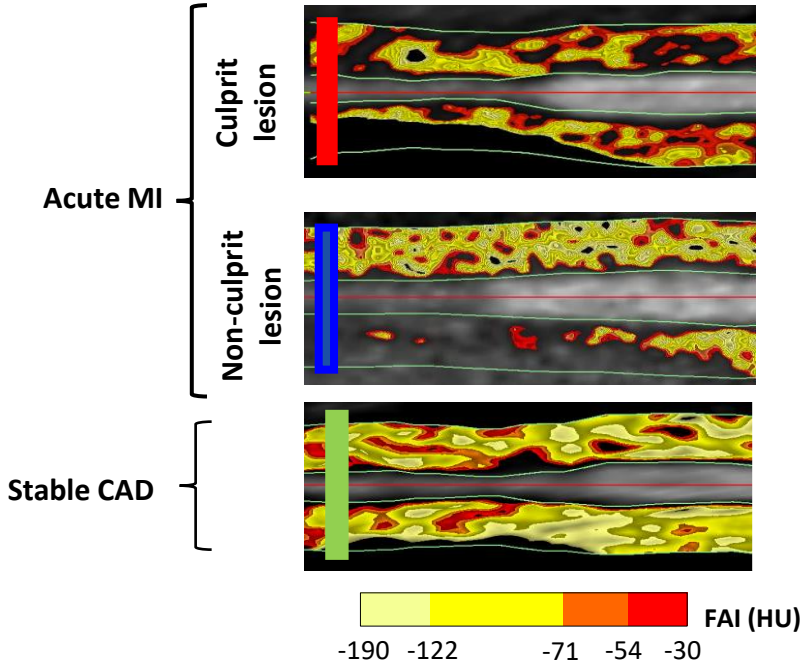


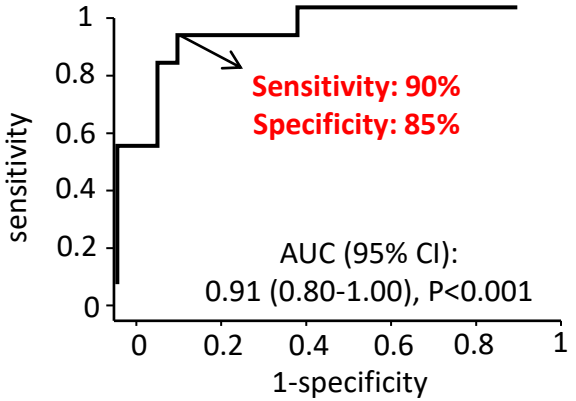
Perivascular fat as a sensor of coronary inflammation

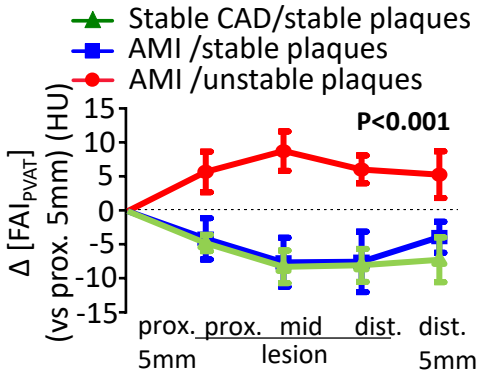


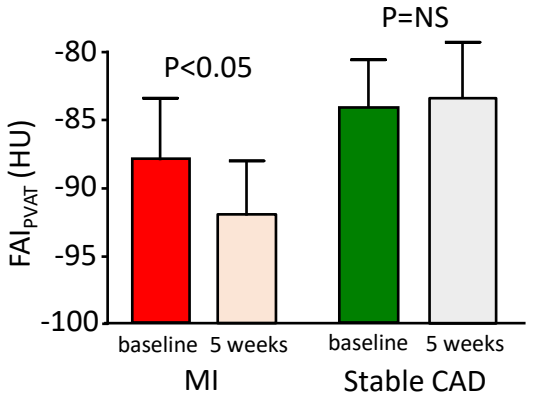
Antonopoulos A, Sanna F et al. *Science Translational Medicine 2017*

Tracking coronary inflammation and its resolution post AMI





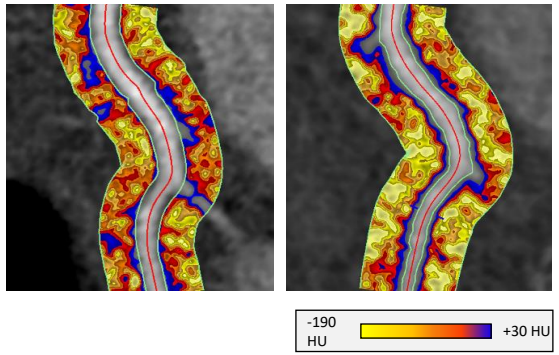


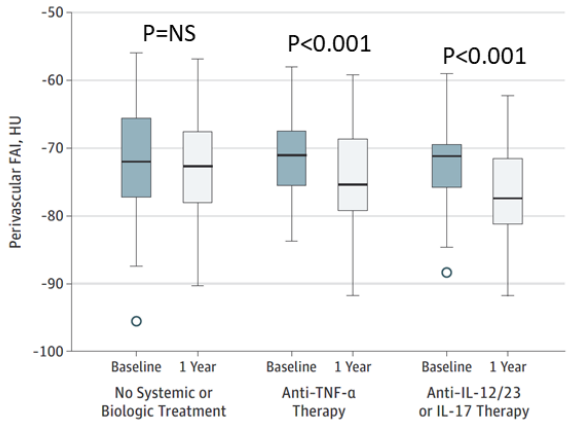


Antonopoulos A, Sanna F et al. *Science Tansl Med 2017*

FAI tracks Dynamic Changes in Response to Treatment

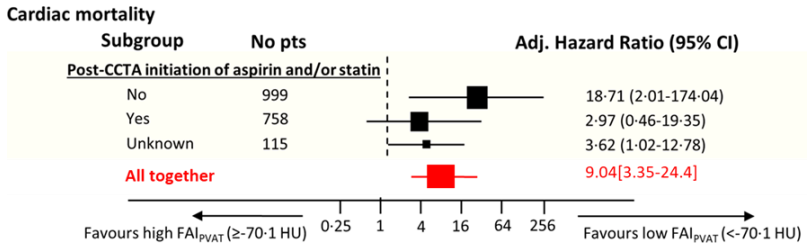
Changes of FAI in psoriasis patients after treatment with biologics





Elnabawi Y ….Mehta N; JAMA Cardiol 2019

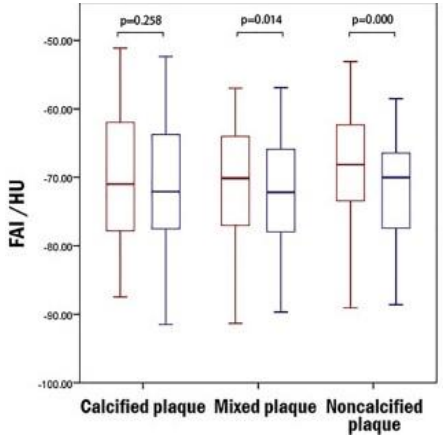
Changes of FAI with Statin Treatment



Oikonomou et al. *Lancet* 2018

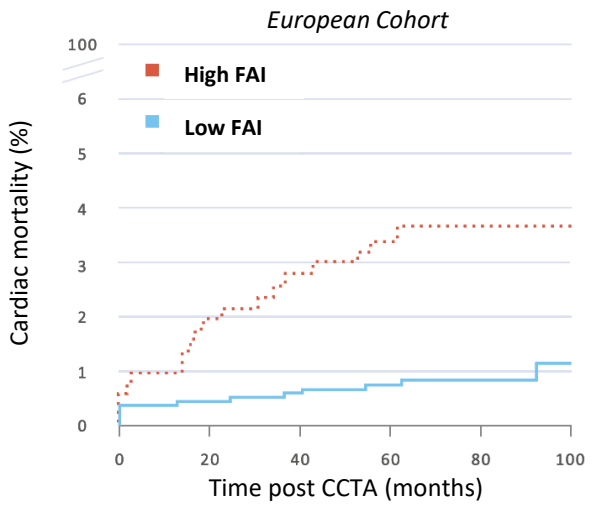
With treatment decision based on CCTA alone:

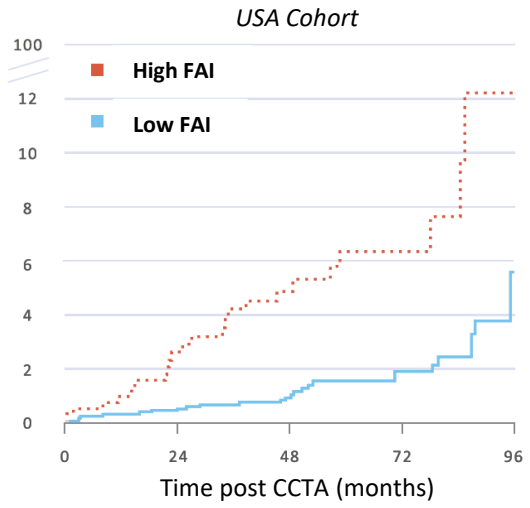
18x greater risk for patients with high FAI left untreated

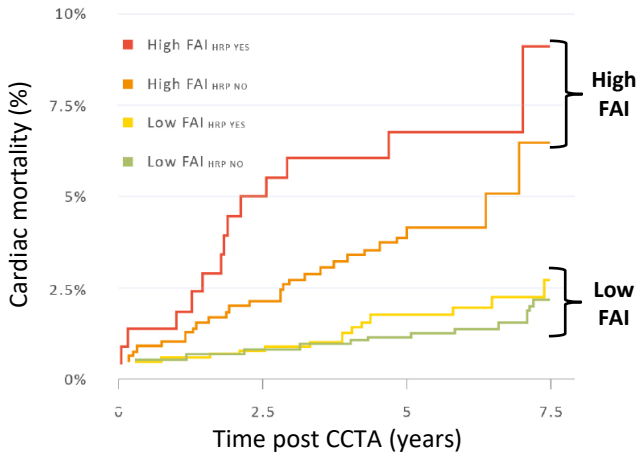


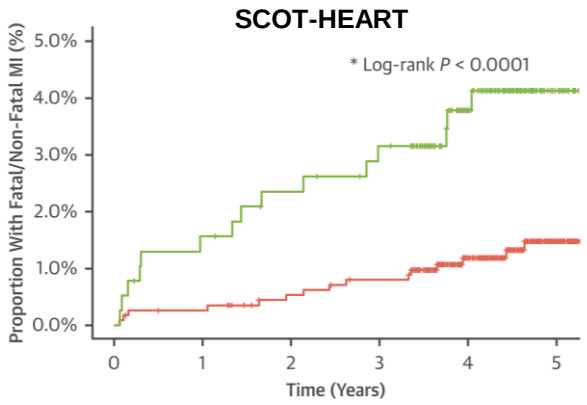
Dai et al et al. *Int J Cardiol* 2020

FAI Predicts Future Heart Attack Risk









CRISP-CT Study Design [1]

- 4000 participants from Europe and US
- Up to 10 years follow up

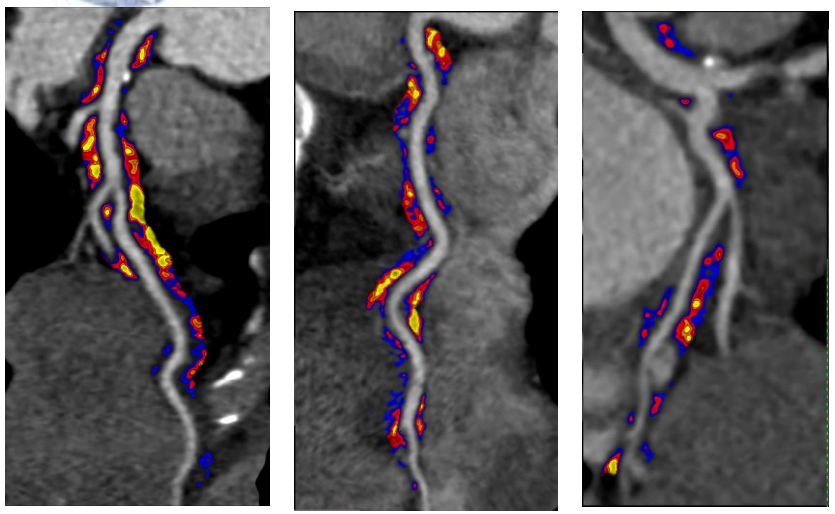
CRISP-CT Findings

- Abnormal FAI associated with a
  - **6-9x** higher risk for **fatal heart attacks**
  - **5x** higher risk for **non-fatal heart attacks**
- After adjusting for all conventional risk factors (e.g., smoking, age, diabetes, high cholesterol)
- FAI is more predictive of future heart attacks than high-risk plaque (HRP) features [2]
- Findings confirmed in SCOT-HEART using uncorrected perivascular attenuation (PCAT) [3]

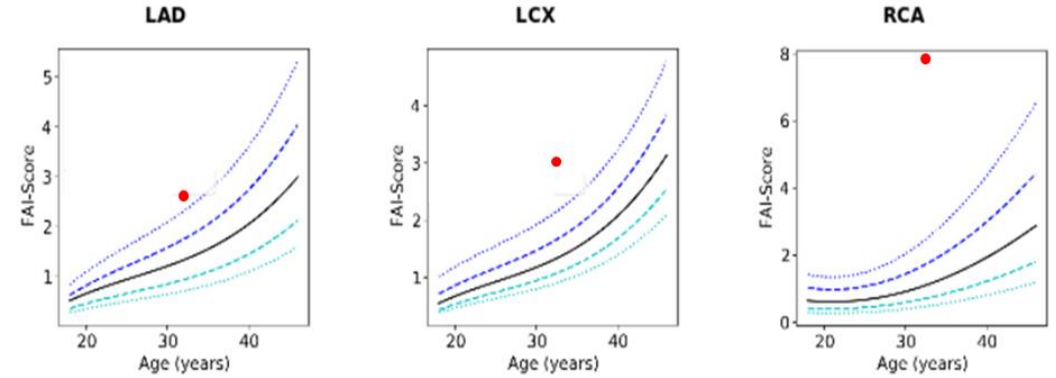
1. *Lancet* 2018; 392: 929–39
2. *J Am Coll Cardiol* 2020; 76 (6) 755–757
3. *J Am Coll Cardiol Img*. 2022, 15 (6) 1078–1088

Measuring FAI-Score Identifies High Risk Patients

CASE A

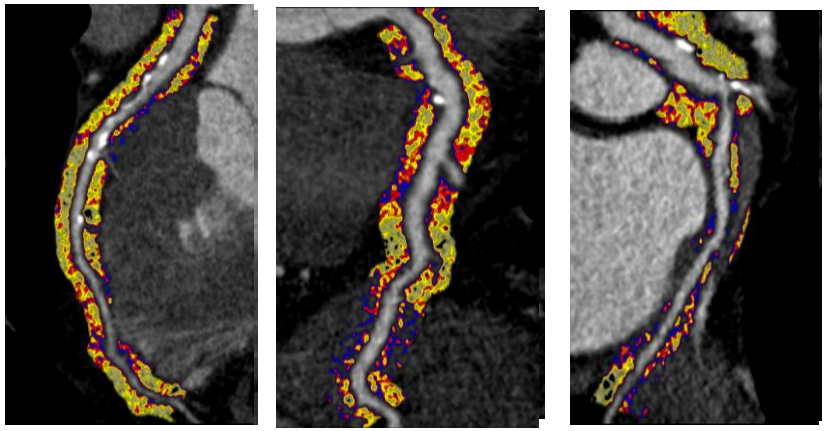


CaRi-Heart® Risk (8y risk for cardiac death: 31.2%

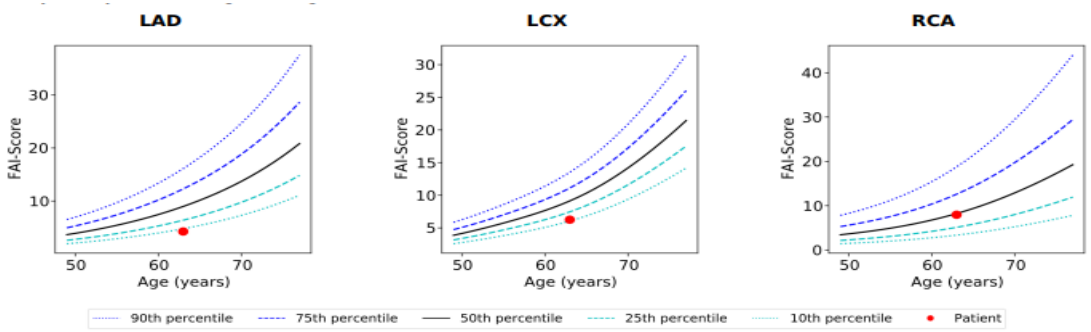


Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	**2.7**	93rd percentile
Left Circumflex Artery	**3.0**	99th percentile
Right Coronary Artery	**7.7**	99th percentile

CASE B



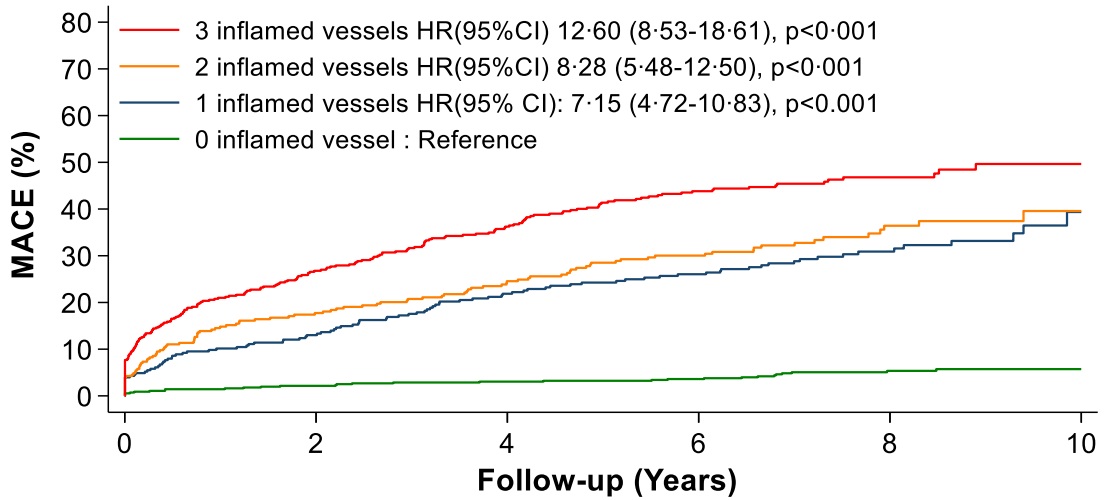
CaRi-Heart® Risk (8y risk for cardiac death: 9.8%



Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	**4.2**	6th percentile
Left Circumflex Artery	**6.3**	12th percentile
Right Coronary Artery	**7.9**	48th percentile

Vascular inflammation for cardiovascular risk prediction (ORFAN)

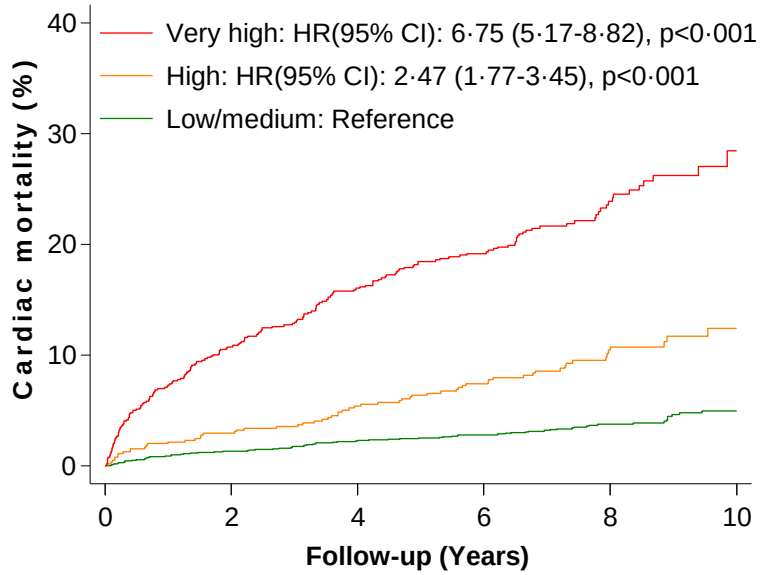
Number of inflamed vessels in predicting MACE



Number at risk

0 inflamed vessel	558	543	534	520	315	85
1 inflamed vessel	328	272	231	203	104	18
2 inflamed vessels	329	249	215	178	76	14
3 inflamed vessels	494	321	254	198	88	14

AI-Risk Classification

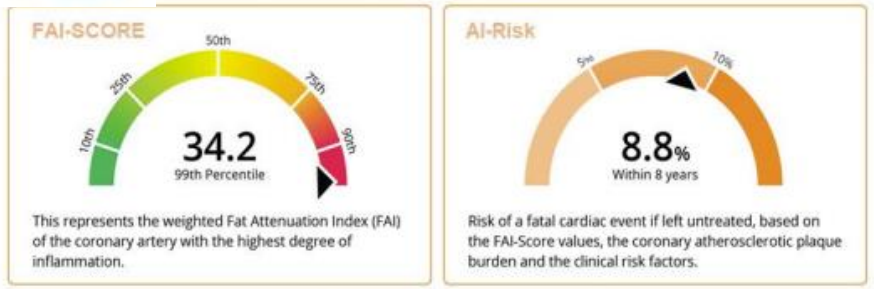


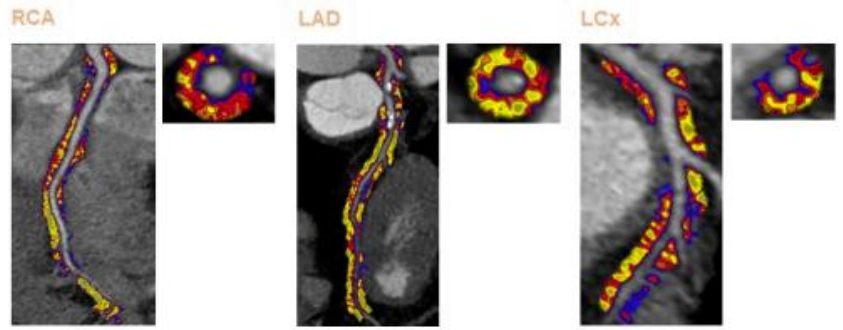
Number at risk

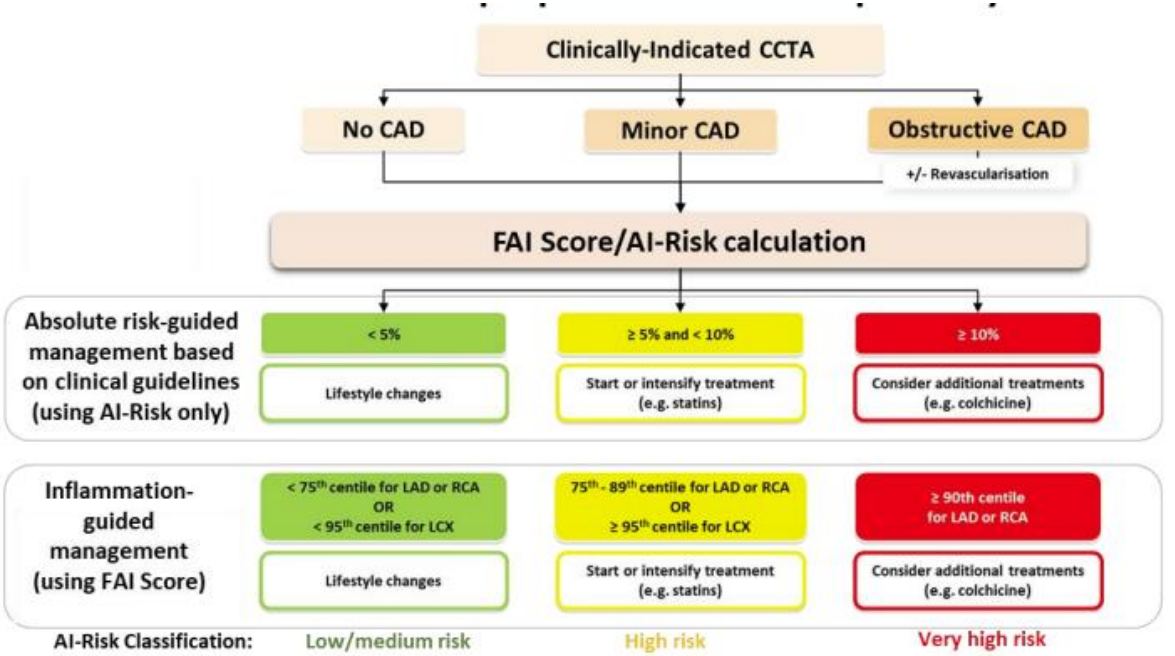
Low/medium:	1,804	1,747	1,693	1,633	956	269
High:	662	617	569	523	295	74
Very high:	913	736	639	544	240	47

Ken C et al. The Lancet 2024 (accepted)

Imaging of coronary inflammation by pericoronary fat (AI-Risk)

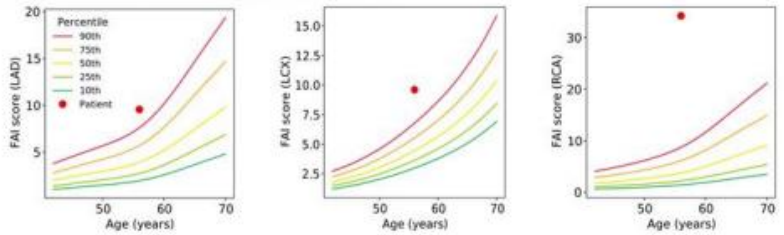






B

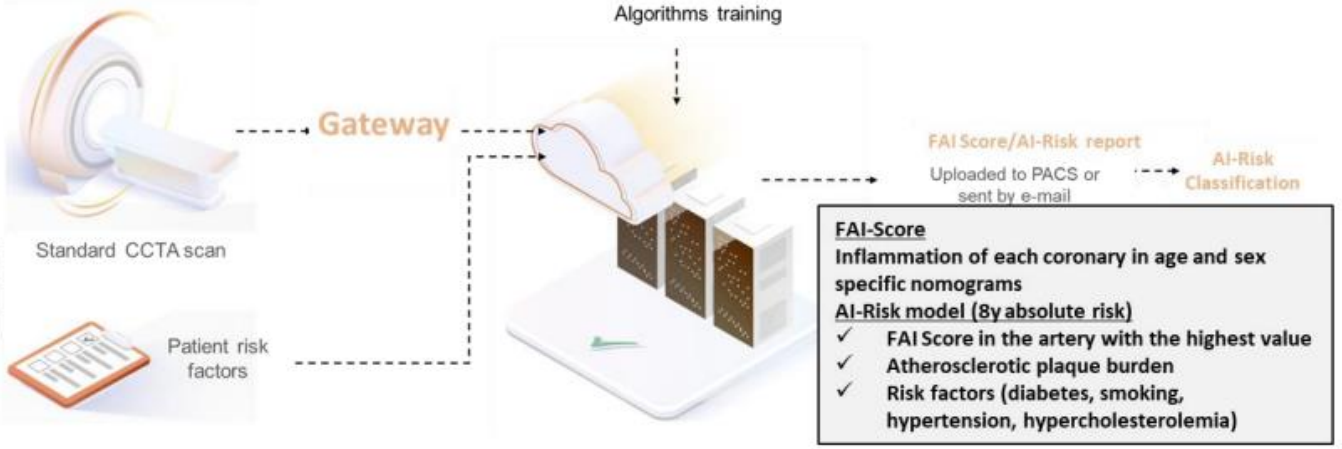
FAI-SCORE - RELATIVE RISK, ADJUSTED FOR AGE AND GENDER



Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	9.5	95th percentile
Left Circumflex Artery	9.6	99th percentile
Right Coronary Artery	34.2	99th percentile

D FAI Score / AI-Risk delivery

Large, international clinical datasets for Risk Prediction Algorithms training

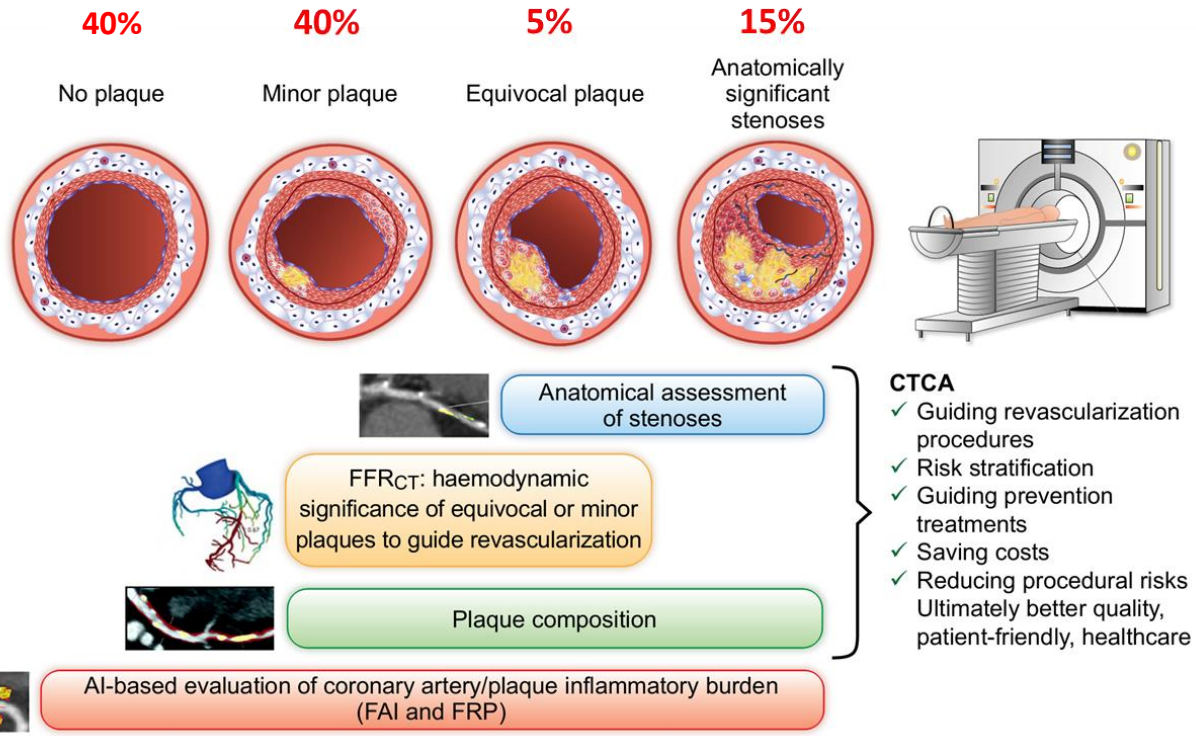


FAI-Score
Inflammation of each coronary in age and sex specific nomograms
AI-Risk model (8y absolute risk)
- ✓ **FAI Score in the artery with the highest value**
- ✓ **Atherosclerotic plaque burden**
- ✓ **Risk factors (diabetes, smoking, hypertension, hypercholesterolemia)**

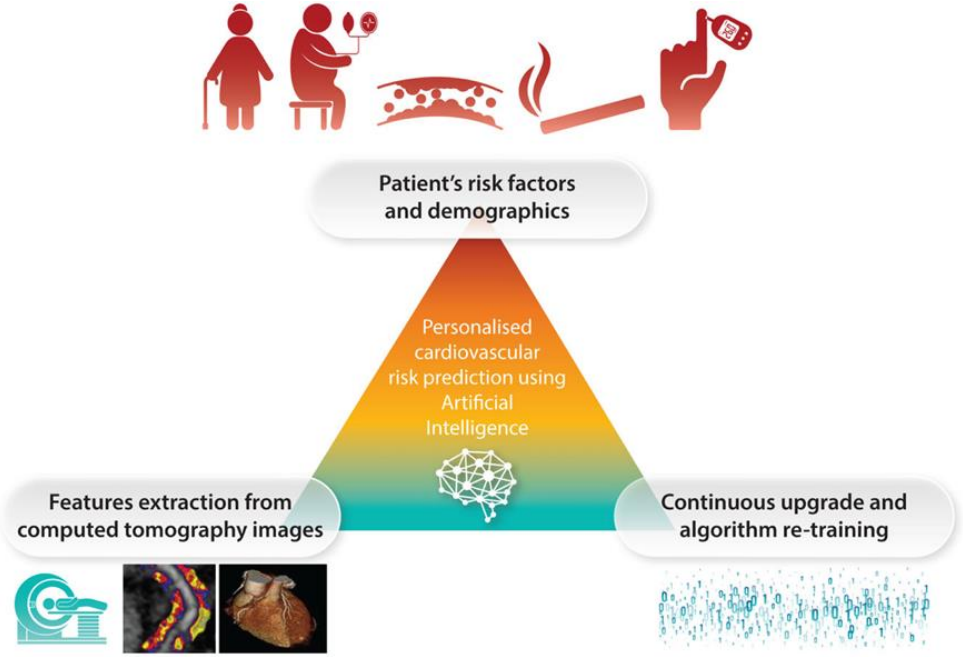
Antoniades C et al. AHA Scientific Sessions 2023

CTCA: an One-Stop-Shop for Coronary Diagnostics

Enhanced Diagnostics



Improved Risk Stratification



Antonopoulos AS et al. Eur J Prev Cardiology 2021
Antoniades & West; Eur Heart J 2021

Imaging-guided treatment decisions for high-cost therapeutics