

Η αξονική τομογραφία ως διαγνωστικό εργαλείο ΣΝ και ως εργαλείο διαστρωμάτωσης καρδιομεταβολικού κινδύνου

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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)



Appropriate Use Criteria for CCTA

1. Detection of CAD in Symptomatic Patients Without Known Heart Disease

Non-acute chest pain: Intermediate PTP for CAD

low/interm PTP for CAD w/ ECG non-interpretable or unable to exercise

Acute chest pain: Normal ECG and cardiac biomarkers
ECG uninterpretable

2. Detection of CAD/Risk Assessment in Asymptomatic Patients (no known CAD)

CCS (not CCTA!) low/interm PTP for CAD

3. Detection of CAD in Other Clinical Scenarios

Reduced left ventricular ejection fraction (low/interm PTP)

Coronary evaluation before noncoronary cardiac surgery (interm PTP)

Prior normal ECG exercise test but continued symptoms

ECG exercise testing intermediate Duke risk score

Prior stress imaging procedure equivocal

Prior CCS <400

New or worsening symptoms and normal previous imaging test

4. Prior revascularization

Evaluation of graft patency after CABG in symptomatic patients

Asymptomatic but prior LM PCI and/or stent diameter ≥ 3 mm

APPROPRIATE USE CRITERIA

ACCF/SCCT/ACR/AHA/ASE/ASNC/SCAI/SCMR 2010 Appropriate Use Criteria for Cardiac Computed Tomography

A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the Society of Cardiovascular Computed Tomography, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the American Society of Nuclear Cardiology, the Society for Cardiovascular Angiography and Interventions, and the Society for Cardiovascular Magnetic Resonance

5. Adult Congenital Heart Disease

6. Evaluation of Ventricular Morphology and Systolic Function

7. Evaluation of Intra- and Extracardiac Structures

Cardiac valves

Valvular dysfunction

aortic stenosis severity

prosthetic heart valves

8. Pericardial anatomy

9. PV anatomy

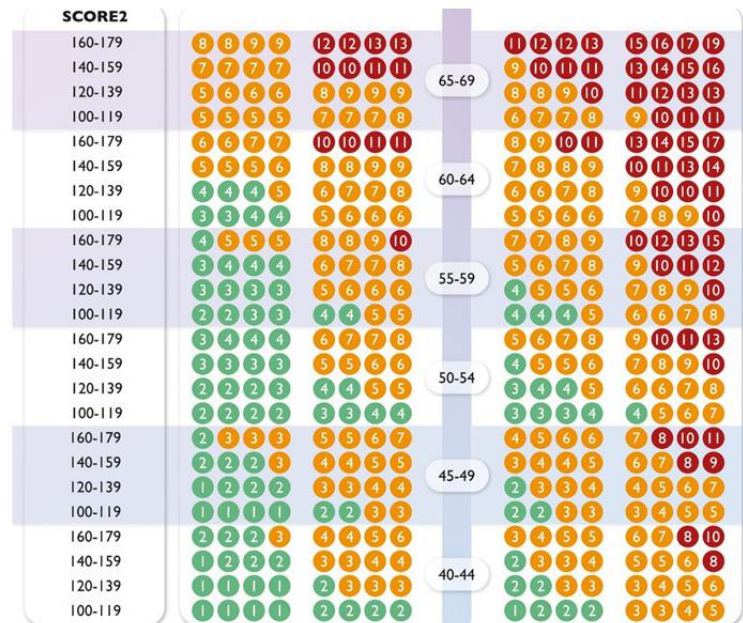
10. AF ablation

11. Noninvasive coronary vein mapping



Coronary calcium score: risk modifier

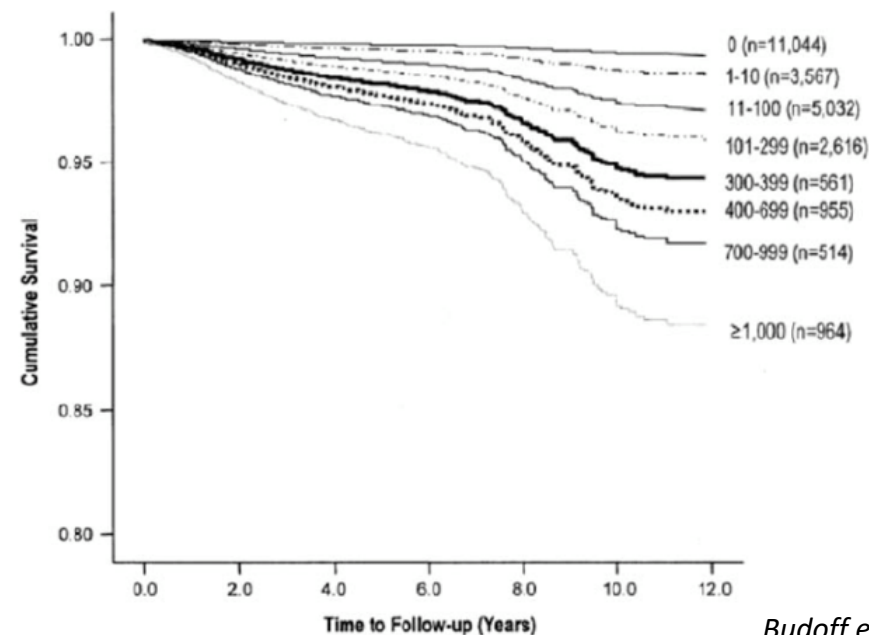
Clinical risk scores



QRISK 2-2014 International version risk calculator interface. The calculator includes fields for Age (64), Sex (Male), Ethnicity (White or not stated), and various clinical factors (smoking, diabetes, chronic kidney disease, atrial fibrillation, rheumatoid arthritis, family history of angina or heart attack, prescribed medication for high blood pressure). The results show a 10-Year ASCVD Risk of 11.3% and a Lifetime ASCVD Risk of 50%.

- SCORE2
- QRISK
- ASCVD risk

Coronary Calcium Score

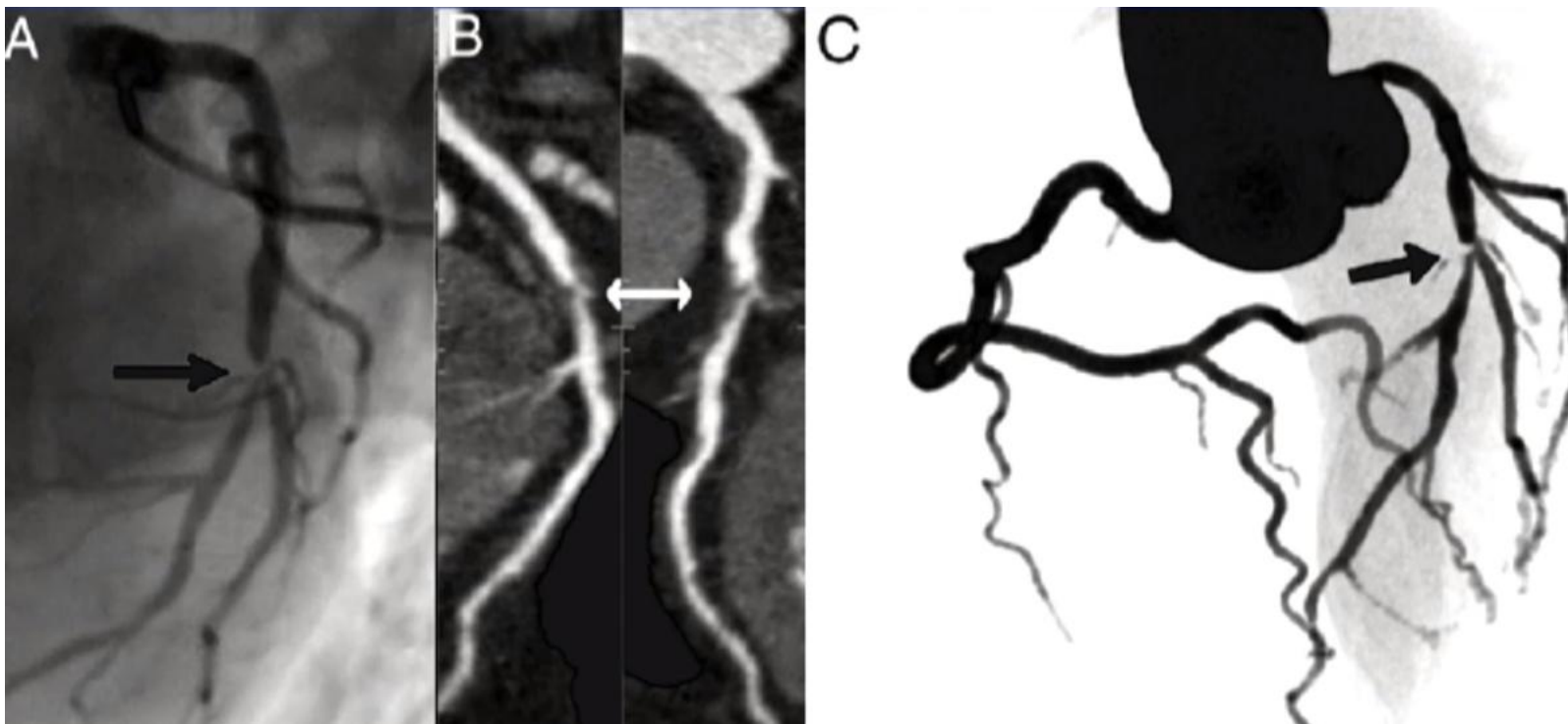


Budoff et al.

- Risk modifier
- Surrogate of coronary plaque burden
- Prognostic value – risk reclassification
- Guide initiation of treatment



Coronary calcium score: power of zero



Asymptomatic individuals: CCS=0 -> NPV for CAD >99%

Symptomatic individuals: CCS=0 -> NPV for CAD ~68%

Gottlieb et al. JACC 2010

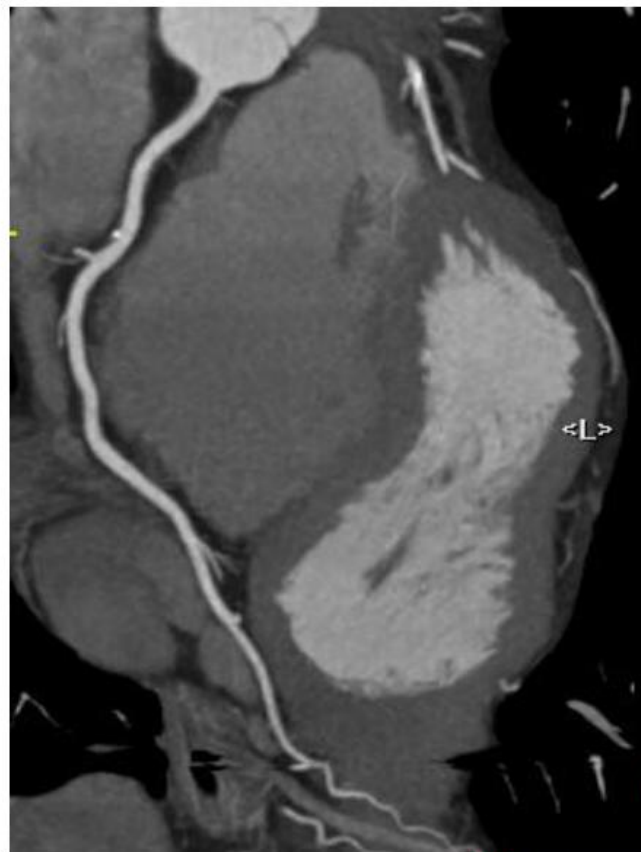
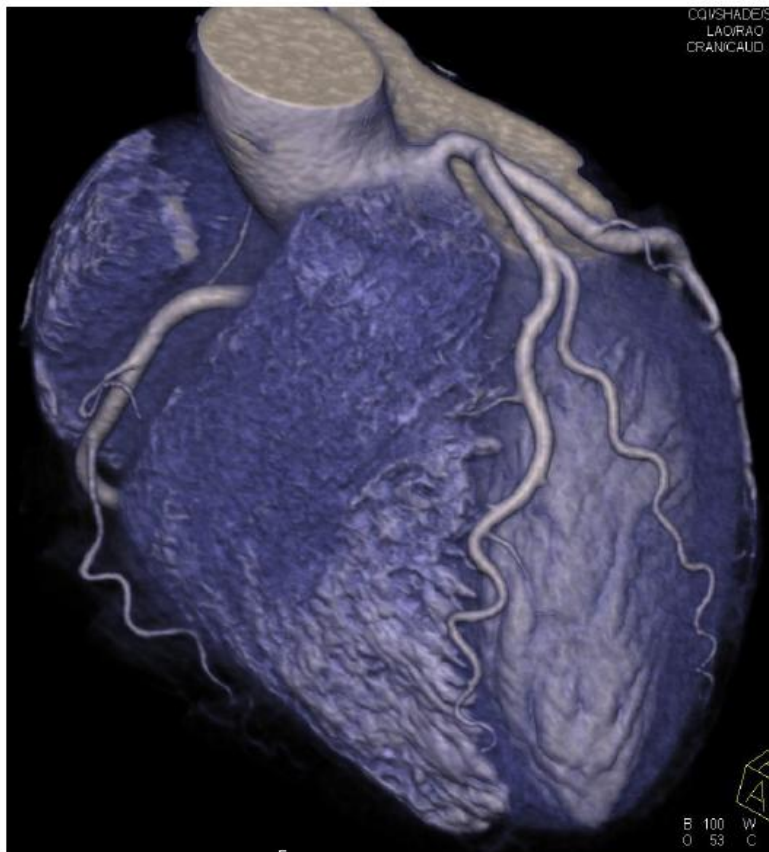
Appropriate use of CCS in asymptomatic individuals only! (Intermediate risk individuals)

If symptomatic / chest pain -> functional imaging or CCTA/ICA

(no value of CCS once CCTA is done)



CCTA for diagnosis of obstructive CAD

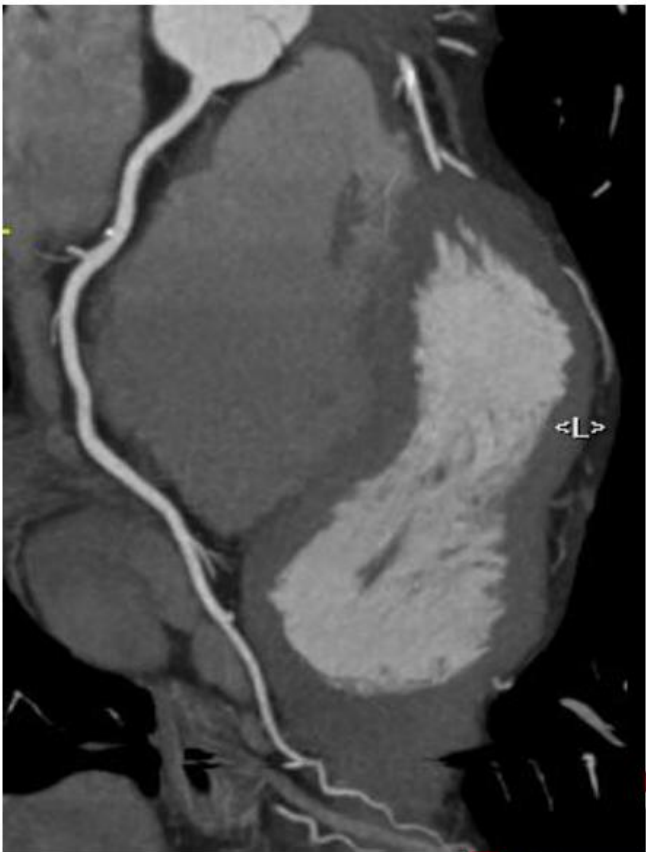


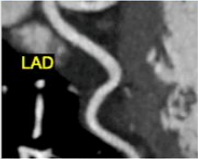
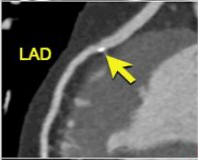
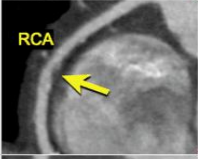
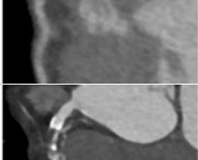
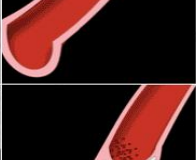
Test	Sensitivity	Specificity
Exercise ECG treadmill ¹	68%	77%
Exercise Echo treadmill ²	86%	81%
Dobutamine Echo ²	~85%	~85%
Exercise nuclear treadmill ³	87%	73%
Pharmacologic nuclear ³	89%	75%
Coronary CTA⁴	95%	83%

1. ACC/AHA 2002 Guideline Update for Exercise Testing
2. ACC/AHA/ASE 2003 Guideline Update for the Application of Echocardiography
3. ACC/AHA/ASNC Guidelines for the Clinical Use of Cardiac Radionuclide Imaging
4. ACCURACY study



CCTA for diagnosis of obstructive CAD

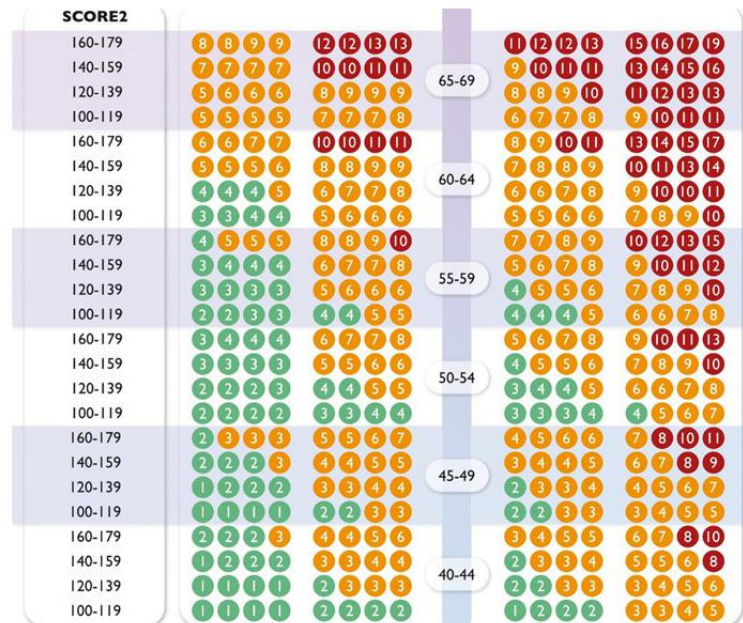


Cad-Rads	Stenosis	CT imaging	Illustration	Additional Tests
Cad-Rads 0	0% No stenosis			None
Cad-Rads 1	1-24% Minimal stenosis			None
Cad-Rads 2	25-49% Mild stenosis			None
Cad-Rads 3	50-70% Moderate stenosis			Consider functional assessment
Cad-Rads 4	A: 70-99% stenosis in 1 or 2 vessels B: >50% stenosis in the left main or >70% stenosis in 3-vessels			A: Consider functional assessment or ICA B: ICA is recommended
Cad-Rads 5	100% total occlusion			ICA and/or viability assessment



Risk stratification & treatment decisions for CAD

Clinical risk scores



ESC

- SCORE2
- QRISK
- ASCVD risk

QRISK 2-2014 International version calculator interface. The calculator shows input fields for Age (64), Sex (Male), Ethnicity (White or not stated), and various medical conditions (diabetes, chronic kidney disease, atrial fibrillation, rheumatoid arthritis, angina or a heart attack before they were 60, high blood pressure). The results show a 10-Year ASCVD Risk of 11.3% (calculated risk) and a Lifetime ASCVD Risk of 50% (calculated risk). The risk with optimal risk factors is 4.9% for 10-year and 5% for lifetime.

High-risk anatomy



- LM disease $\geq 50\%$ stenosis
- 3VD with $\geq 70\%$ stenosis, or
- 2VD with $\geq 70\%$ stenosis, including prox LAD or
- 1VD of prox LAD with $\geq 70\%$ stenosis and FFR-CT ≤ 0.8



CCTA as first line modality for assessment of obstructive CAD

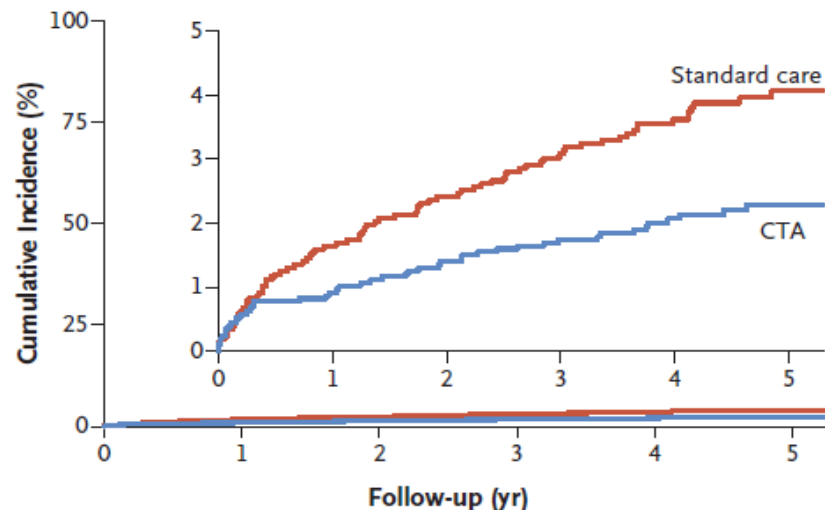


The Scottish Computed Tomography of the HEART (SCOT-HEART) Trial



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

A Death from Coronary Heart Disease or Nonfatal Myocardial Infarction



No. at Risk

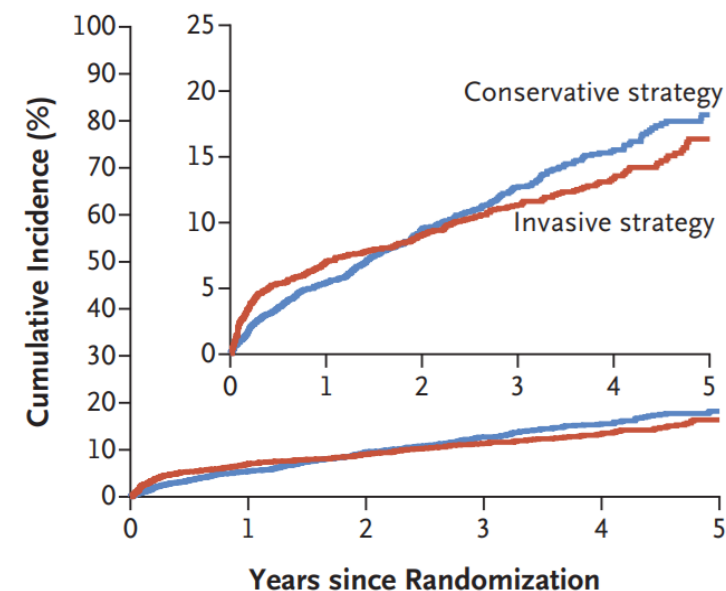
Standard care	2073	2033	2008	1994	1572	856
CTA	2073	2051	2029	2015	1588	872

Newby et al. NEJM 2018



The NEW ENGLAND
JOURNAL of MEDICINE

All-cause death or non-fatal myocardial infarction



No. at Risk

Conservative strategy	2591	2431	1907	1300	733	293
Invasive strategy	2588	2364	1908	1291	730	271

Maron et al. NEJM 2020



1st line imaging modality in low/moderate PTP for obstructive CAD

Non-invasive anatomical imaging tests in the initial diagnostic management of individuals with suspected obstructive coronary artery disease—coronary computed tomography angiography, if available and supported by local expertise—Section 3

In individuals with suspected CCS and low or moderate (>5%–50%) pre-test likelihood of obstructive CAD, CCTA is recommended to diagnose obstructive CAD and to estimate the risk of MACE.

I

A

Non-invasive tests in the initial diagnostic management of individuals with suspected chronic coronary syndrome—stress echocardiography, if available and supported by local expertise—Section 3

In individuals with suspected CCS and moderate or high (>15%–85%) pre-test likelihood of obstructive CAD, stress echocardiography is recommended to diagnose myocardial ischaemia and to estimate the risk of MACE.

I

B

During stress echocardiography, when two or more contiguous myocardial segments are not visualized, it is recommended to use commercially available intravenous ultrasound contrast agents (microbubbles) to improve diagnostic accuracy.

I

B

During stress echocardiography, myocardial perfusion using commercially available intravenous ultrasound contrast agents (microbubbles) is recommended to improve diagnostic accuracy and to refine risk stratification beyond wall motion.

I

B

During stress echocardiography, Doppler left anterior descending coronary artery flow reserve may be considered to improve risk stratification beyond wall motion and to assess microvascular function.

IIb

B

Systematic and routine increased coronary pressure assessment of all coronary vessels is not recommended.

Selection of individual diagnostic tests in individuals with suspected chronic coronary syndrome—Section 3

To rule out obstructive CAD in individuals with low or moderate (>5%–50%) pre-test likelihood, CCTA is recommended as the preferred diagnostic modality.

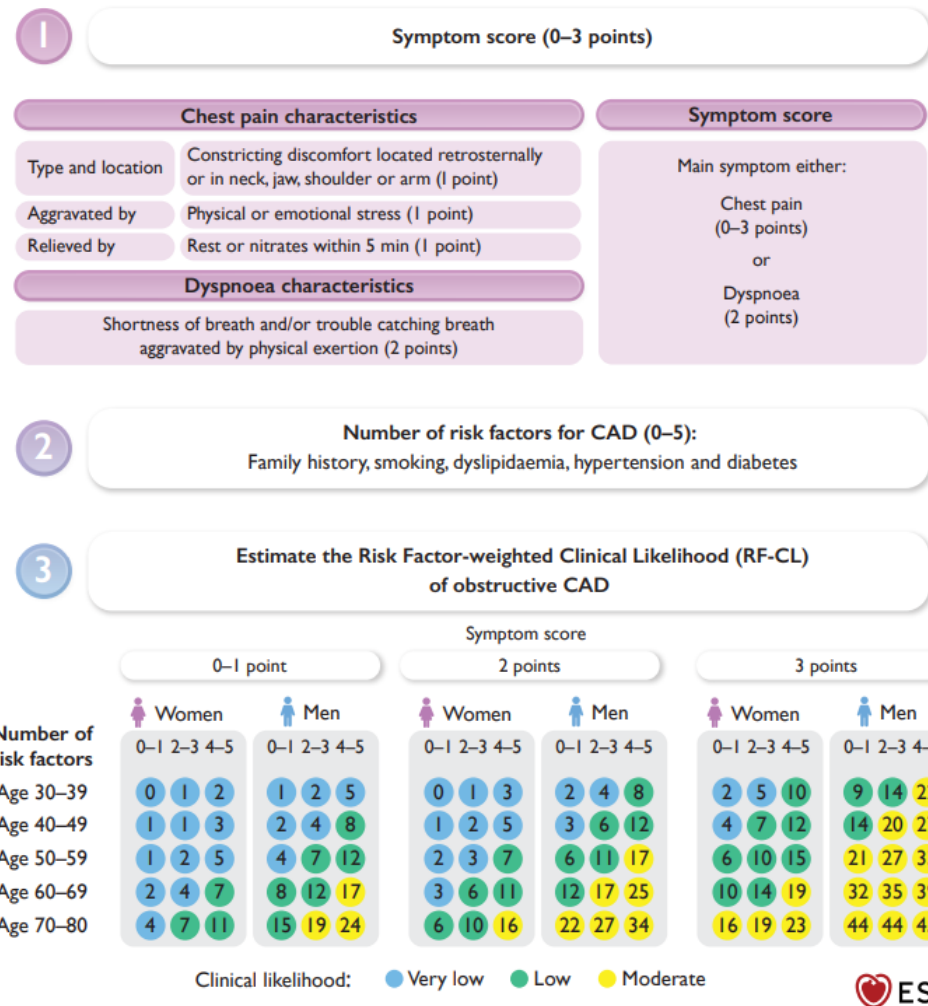
I

B

CCTA is recommended in individuals with low or moderate (>5%–50%) pre-test likelihood of obstructive CAD if functional imaging for myocardial ischaemia is not diagnostic.

I

B

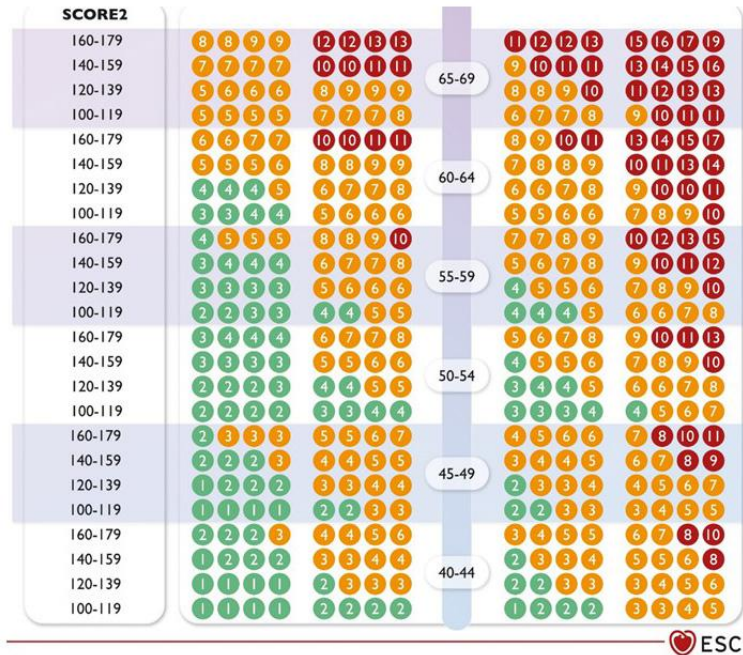


CCTA for risk stratification



Risk stratification & treatment decisions for CAD

Clinical risk scores



- SCORE2
- QRISK
- ASCVD risk

QRISK 2-2014 International version calculator interface. Input fields include Age (64), Sex (Male), Ethnicity (White or not stated), and various medical conditions (diabetes, chronic kidney disease, atrial fibrillation, rheumatoid arthritis, angina or a heart attack before they were 60, Are you prescribed medication for..., high blood pressure). Calculated risk percentages are shown for 10-Year ASCVD Risk (11.3% calculated risk, 4.9% risk with optimal risk factors**) and Lifetime ASCVD Risk (50% calculated risk, 5% risk with optimal risk factors). Recommendation Based On Calcul... is displayed at the bottom.

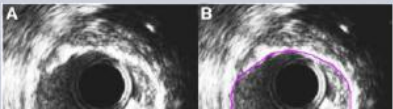
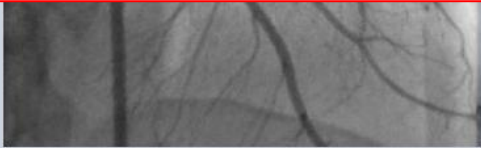
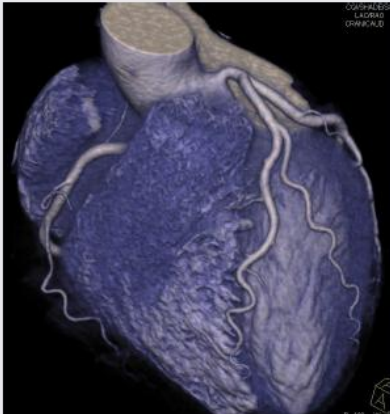
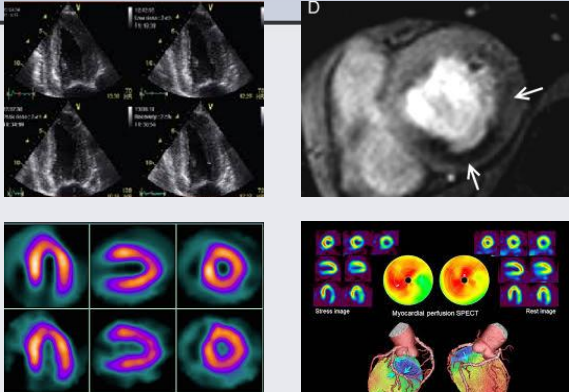
Symptoms / Luminal stenosis



- >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

	<u>ANATOMY</u> <i>Identify obstructive CAD</i>	<u>FUNCTION</u> <i>Identify lesion-specific ischemia that may benefit from PCI</i>
	 	
	 	 <i>Stanford</i>
Non-invasive		

CCTA BONUS: Detection of non-obstructive coronary plaques!



No plaque on CCTA = clinical reassurance

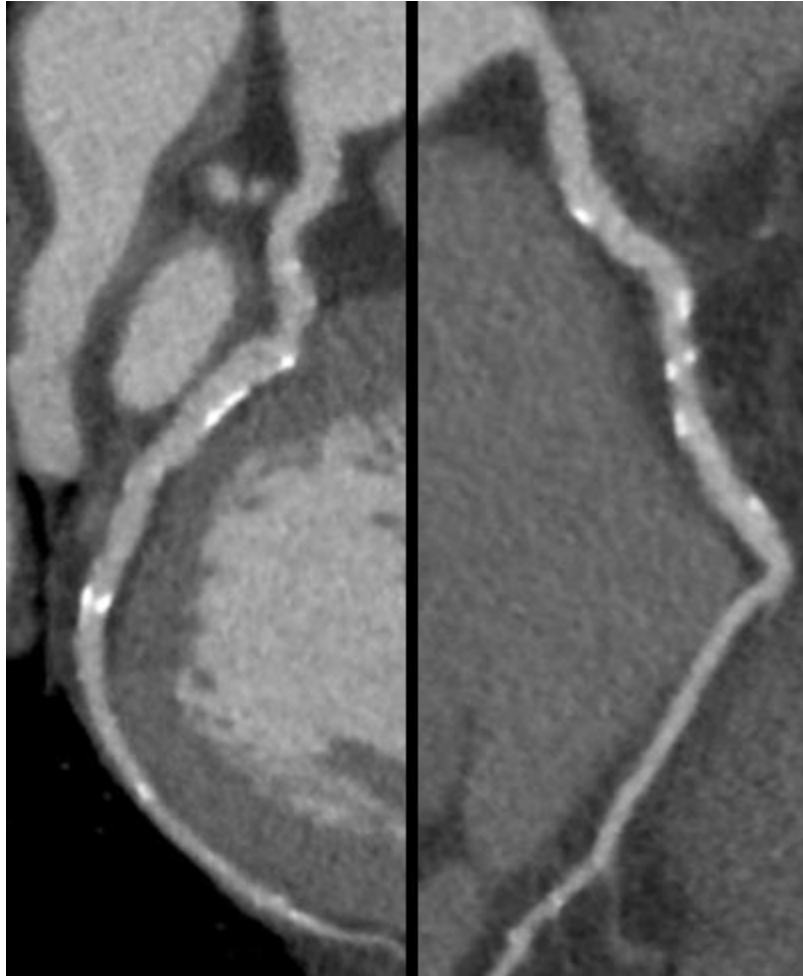


- Atypical symptoms
- No major risk factors
- Low-intermediate PTP
- >85% of patients referred for a CCTA
- No plaque
- Clinical reassurance





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



Revisiting the definition of CAD in the era of CCTA

CAD

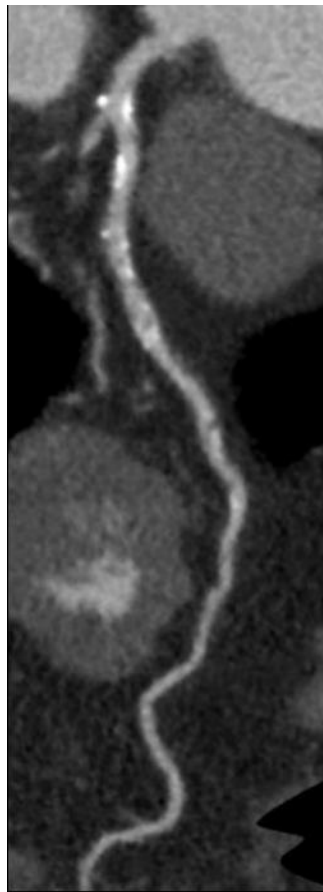
No



Non-obstructive



Obstructive

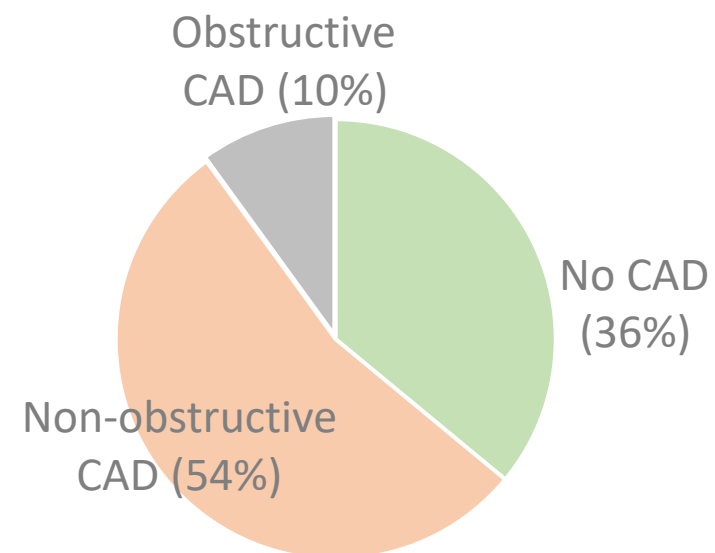


CCTA as the preferred 1st modality to screen for suspected CAD (Class IB)

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

Copenhagen General Population Study, Denmark

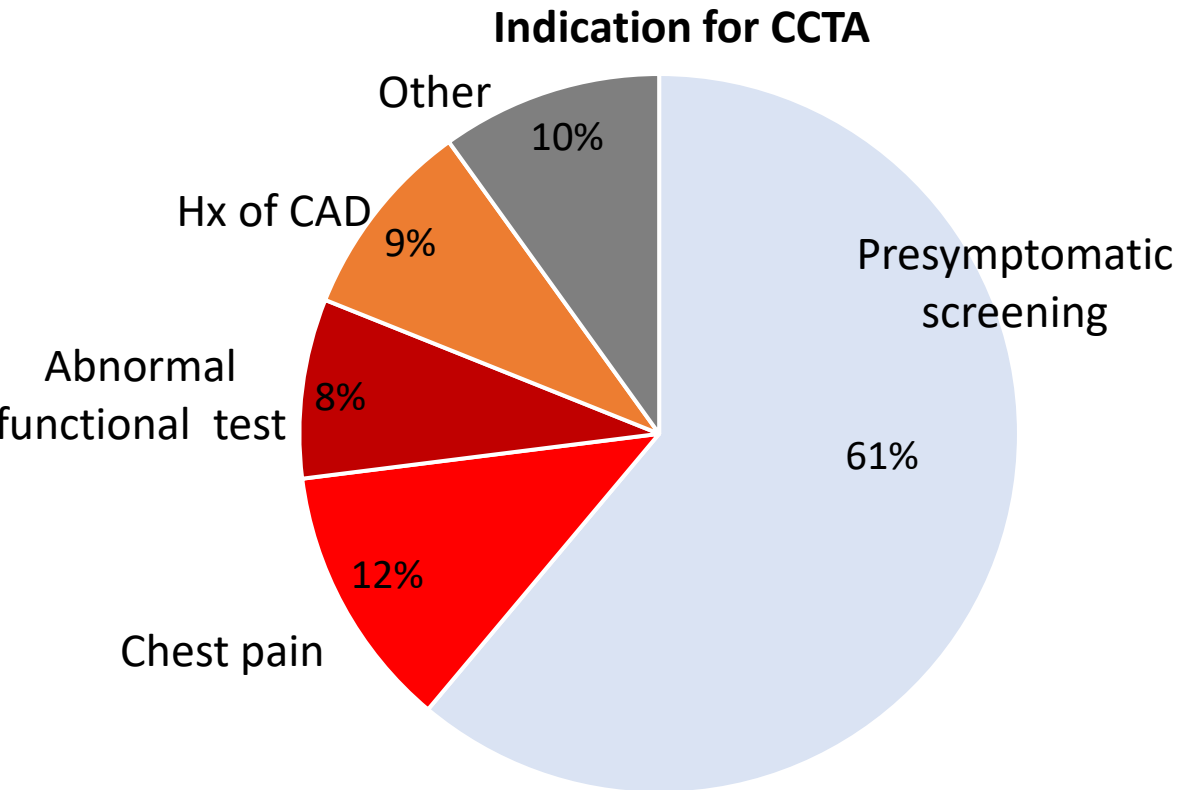
9533 asymptomatic persons >40y w/o known IHD





Contemporary use of CCTA in Greece

COronary **CO**puted Tomography **A**ngiography – **G**reek **R**egistry (**COCOA-GR**)





Revisiting the definition of CAD in the era of CCTA

CAD

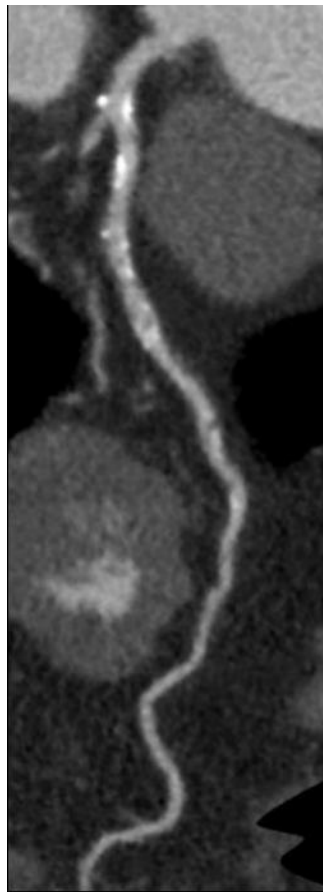
No



Non-obstructive



Obstructive



Obstructive-extensive CAD
Obstructive-non-extensive CAD
Nonobstructive-**extensive** CAD
Non-obstructive-non-extensive

~12x RR

~8x RR

~3x RR

ref

- **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

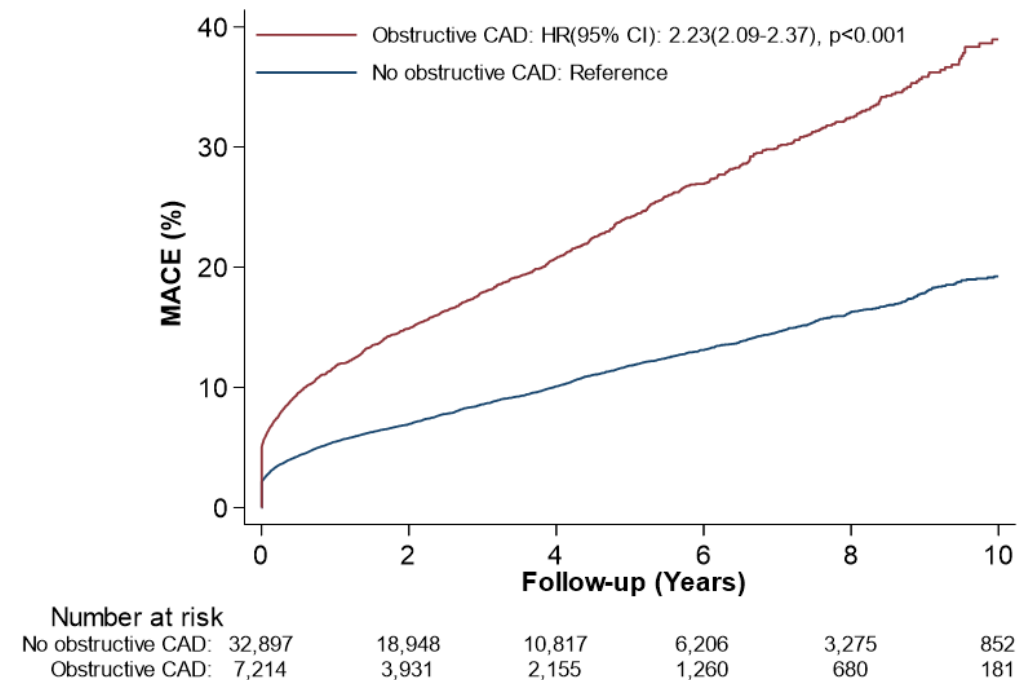
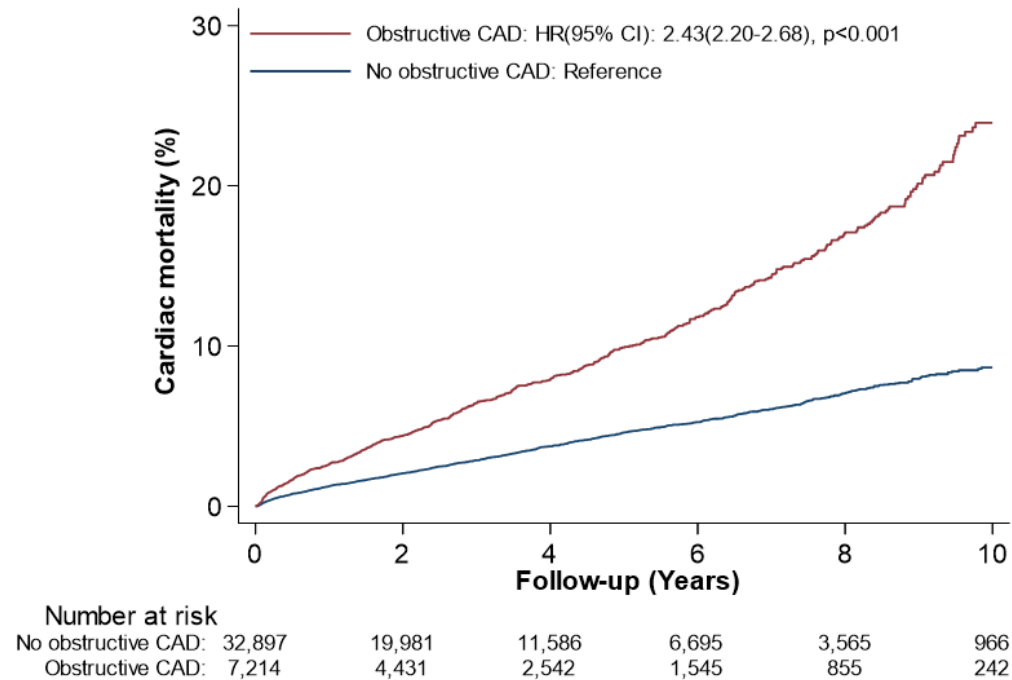


Inflammatory risk and cardiovascular events in patients without obstructive coronary artery disease: the ORFAN multicentre, longitudinal cohort study



Kenneth Chan*, Elizabeth Wahome*, Apostolos Tsiachristas, Alexios S Antonopoulos, Parijat Patel, Maria Lyasheva, Lucy Kingham, Henry West, Evangelos K Oikonomou, Lucrezia Volpe, Michail C Mavragiannis, Edward Nicol, Tarun K Mittal, Thomas Halborg, Rafail A Kotronias, David Adlam, Bhavik Modi, Jonathan Rodrigues, Nicholas Srean, Attila Kardos, John P Greenwood, Nikant Sabharwal, Giovanni Luigi De Maria, Shahzad Munir, Elisa McAlindon, Yogesh Sohan, Pete Tomlins, Muhammad Siddique, Andrew Kellon, Cheerag Shirodaria, Francesca Pugliese, Steffen E Petersen, Ron Blankstein, Milind Desai, Bernard J Gersh, Stephan Achenbach, Peter Libby, Stefan Neubauer, Keith M Channon, John Deanfield, Charalambos Antoniades, on behalf of the ORFAN Consortium

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



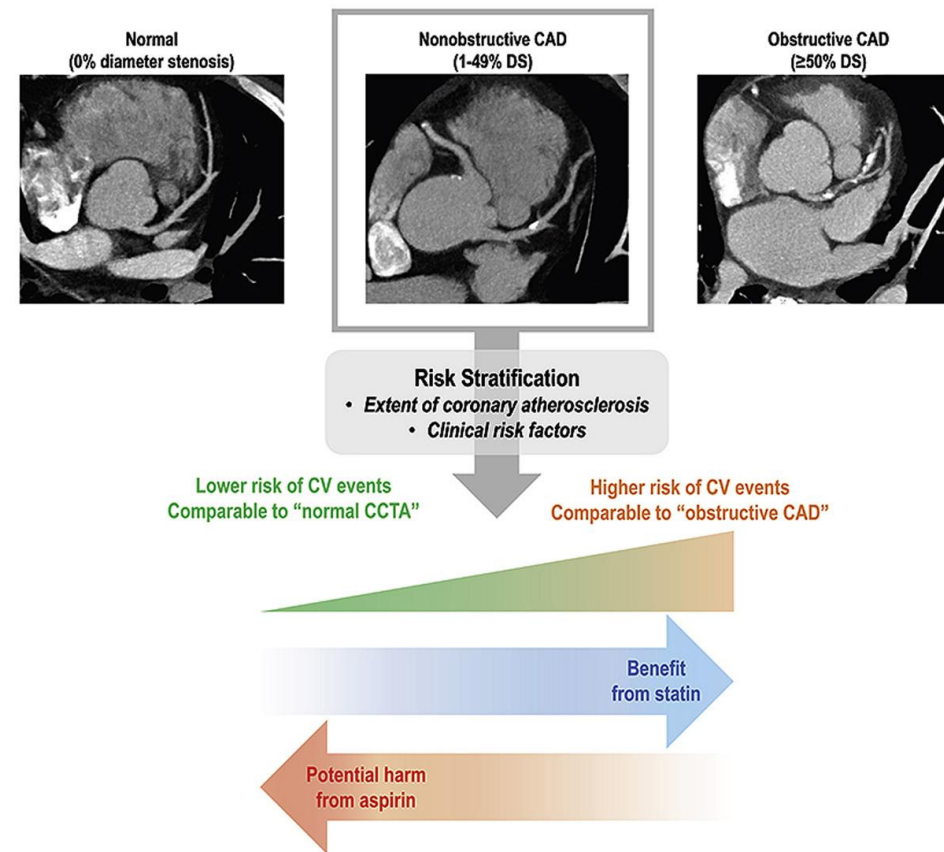


Assessing coronary plaque burden on CCTA reports

Coronary Plaque Burden

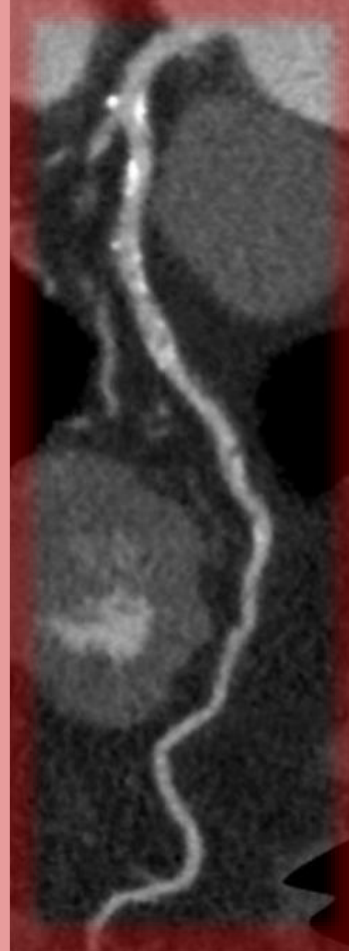
	Amount of plaque	Calcium score	SIS*	Visual
P1	Mild	1-100	≤2	1-2 vessels with mild amount of plaque
P2	Moderate	101-300	3-4	1-2 vessels with moderate amount; 3 vessels with mild amount of plaque
P3	Severe	301-999	5-7	3 vessels with moderate amount; 1 vessel with severe amount of plaque
P4	Extensive	>1000	≥8	2-3 vessels with severe amount of plaque

Reducing risk by **facilitating evidenced therapy**
or those with coronary artery disease independent of
symptom characteristics.



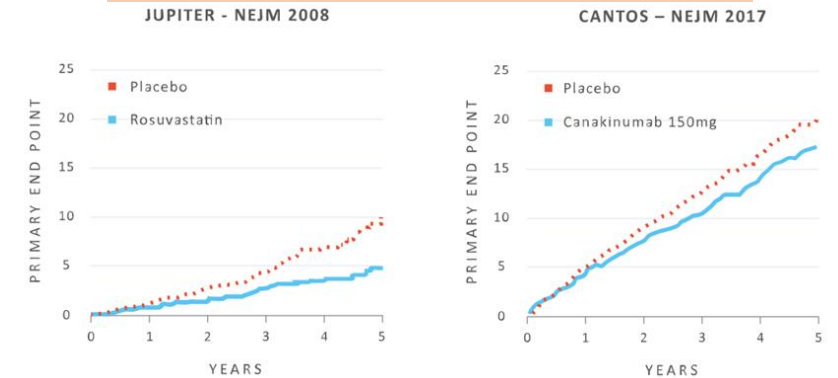


Remaining challenges: detecting vascular inflammation



- 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

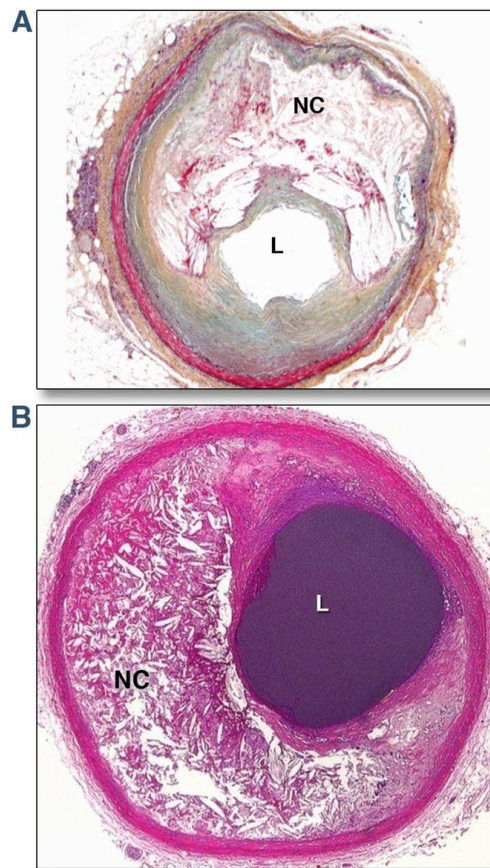


CRP non-specific (>50% have high residual inflammation in 2ndary prevention based on CRP)



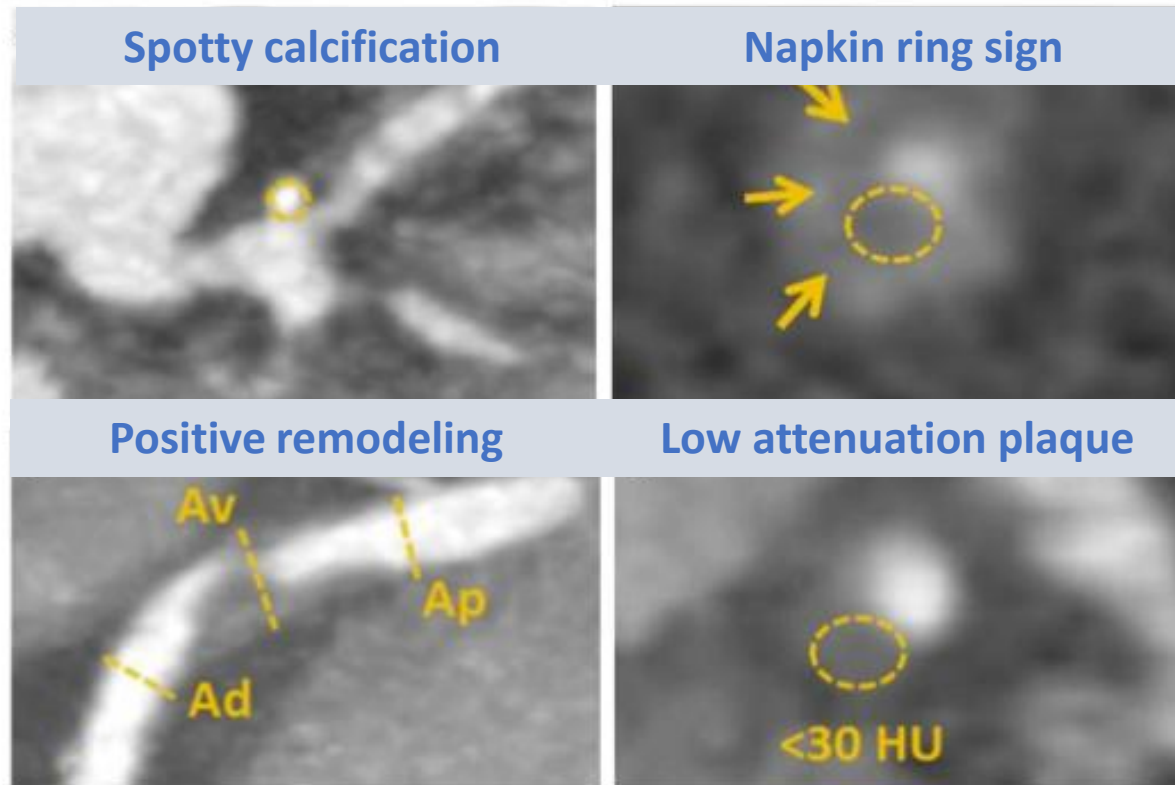
High risk plaque on CCTA

The *vulnerable* plaque



High-risk plaque (HRP) on CCTA

2 or more features



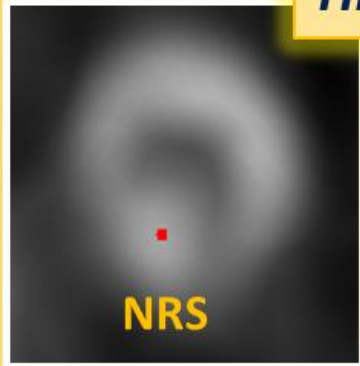
CAD-RADS 2.0–2022

Coronary Artery Disease-Reporting and Data System

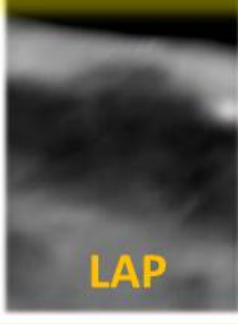


High-risk plaque on CCTA and risk stratification

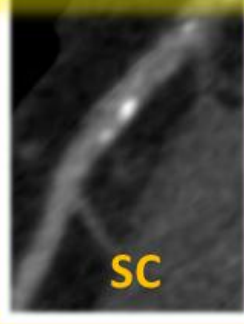
High-risk plaque features



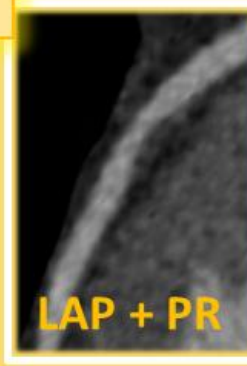
NRS



LAP



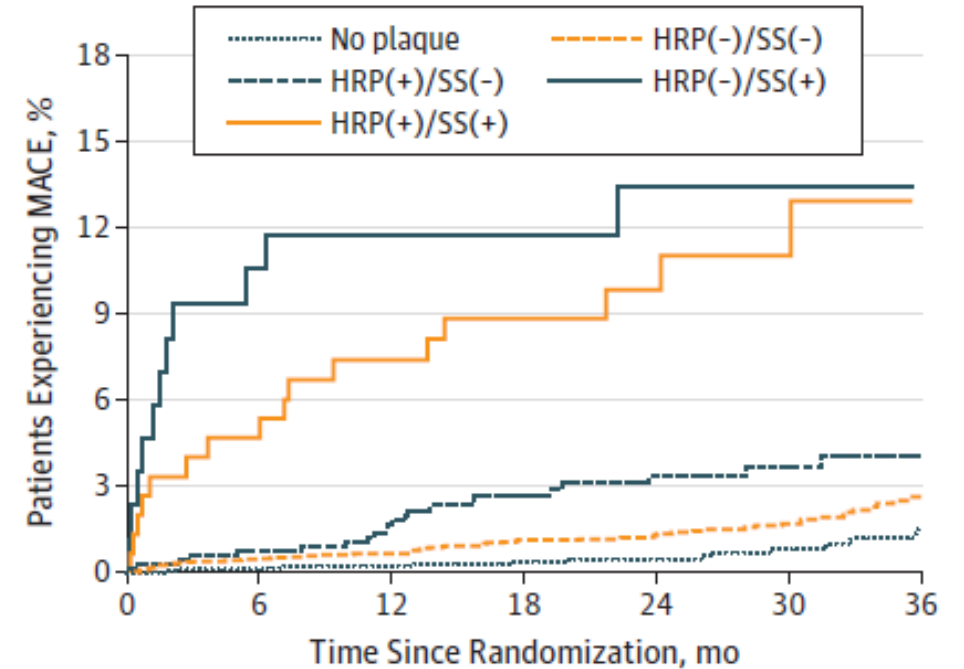
SC



LAP + PR

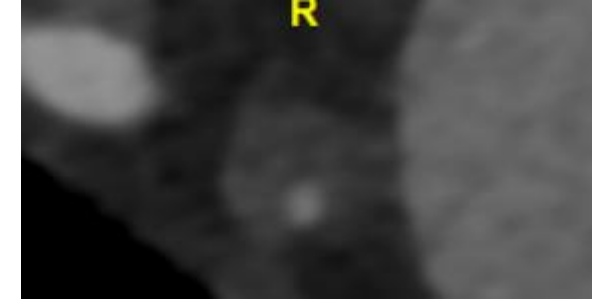
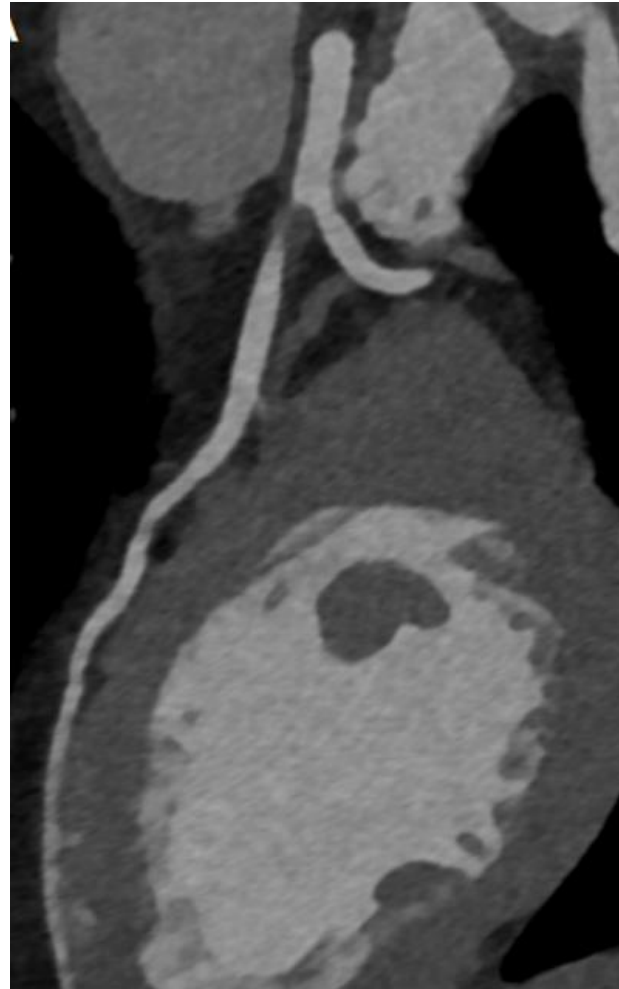
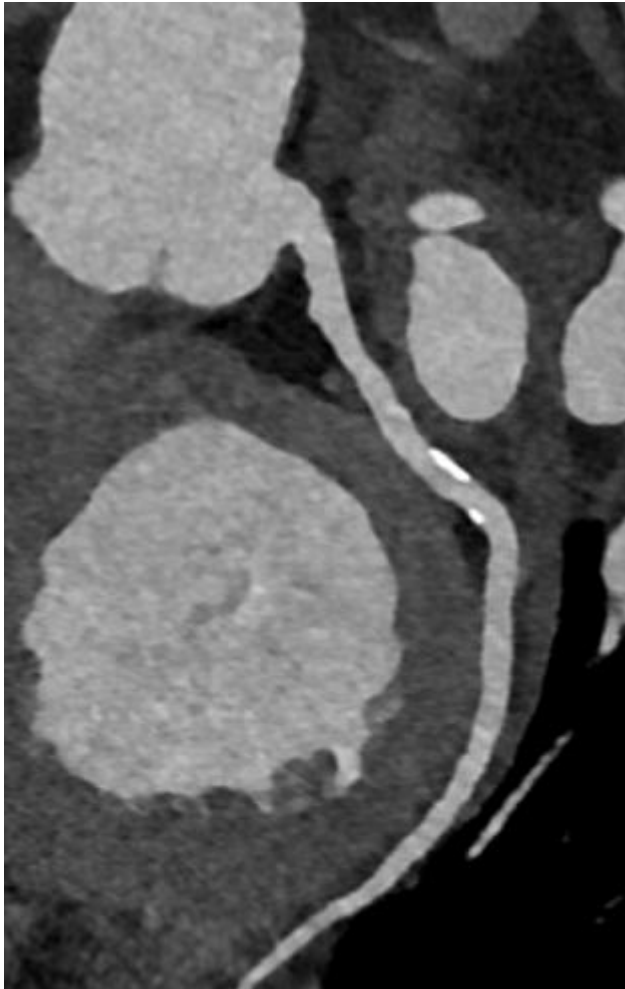
Frequent > 30%
Low positive predictive value

PROMISE study 4,415 pts
CCTA + plaque phenotyping





Unprecedented image CCTA quality with Photon Counting CT



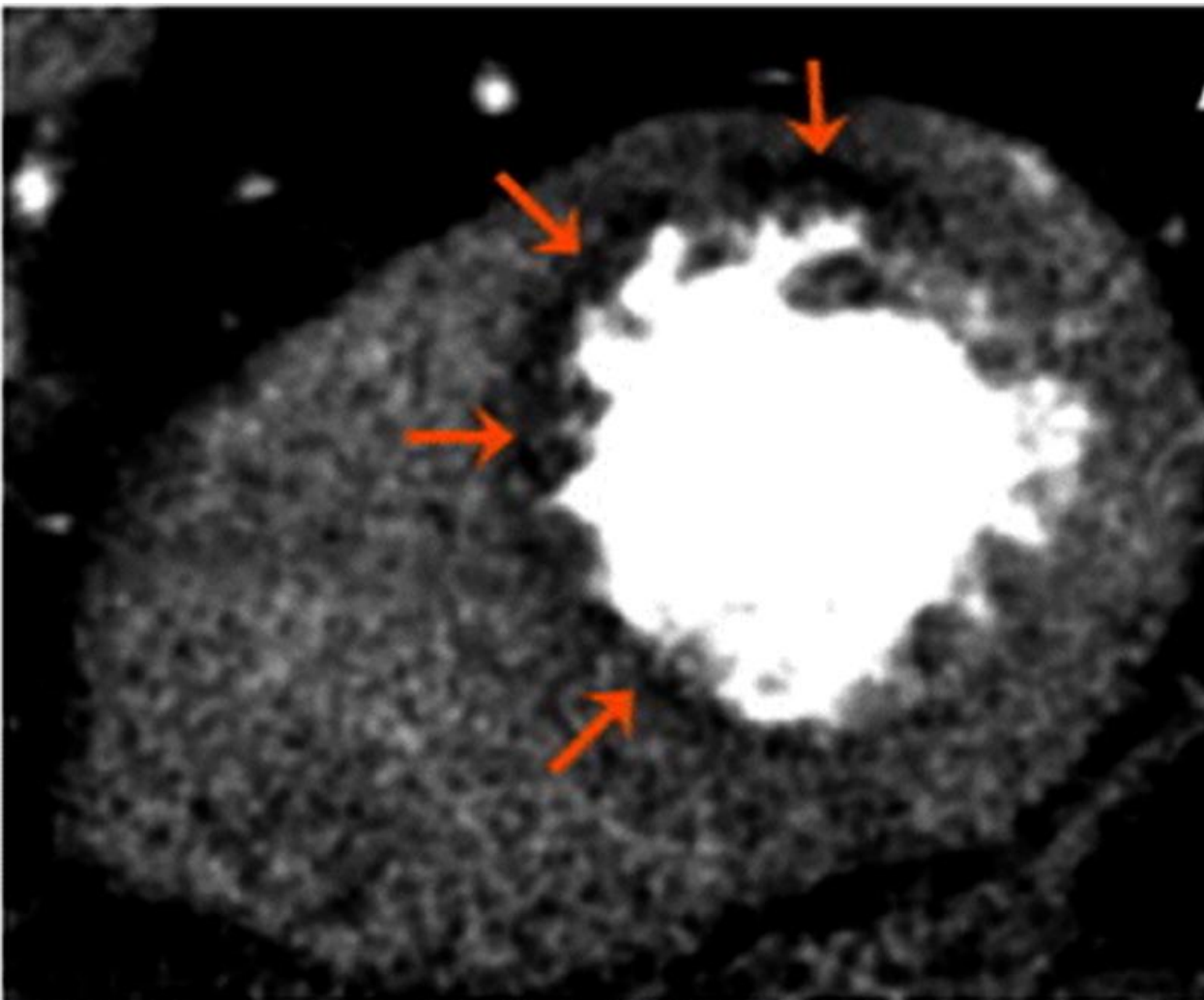
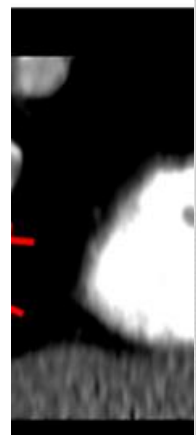
- Ultra high-quality images
- No limitations from calcium / stents
- Capacity for tissue characterization
- <0.5 sec



Functional assessment of plaques by CT



CT-perfusion imaging for ischaemia detection



Strengths

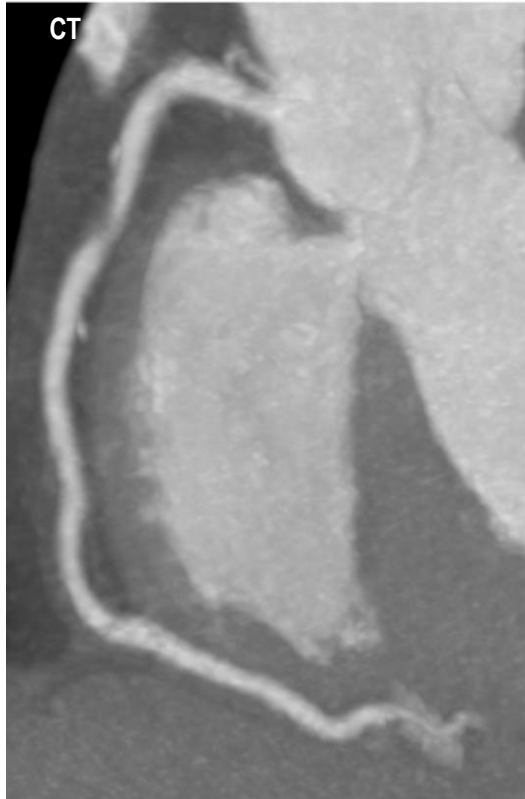
- Good diagnostic accuracy for ischaemia

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

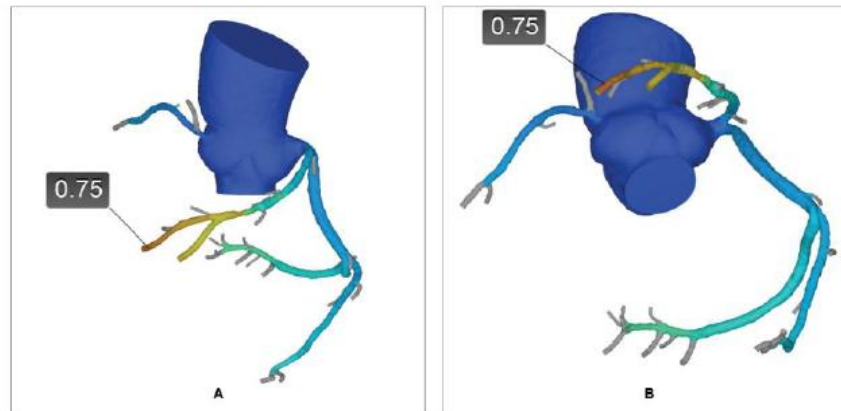


Patient ID 29-0070-G-C
Birth Date Not provided
CT Study Date 1/14/2014

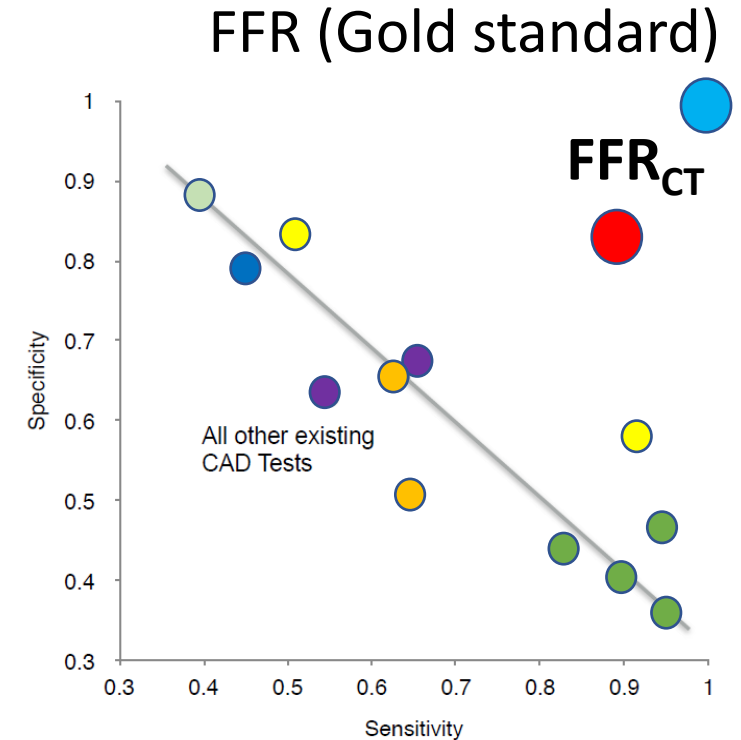
Summary

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

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



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



Danad et al. EHJ 2016

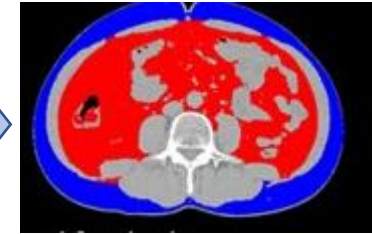
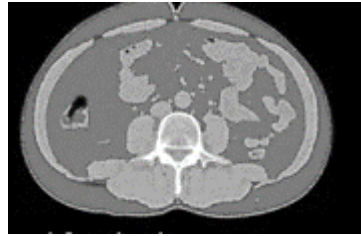
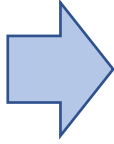
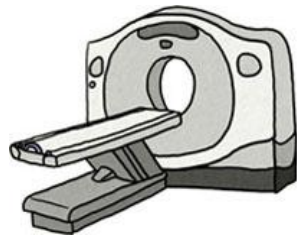
Assessing cardiometabolic risk by CT imaging



Visceral vs. abdominal fat and cardiovascular disease risk

CT imaging of
abdominal fat

Fat: -190 to -30 HU

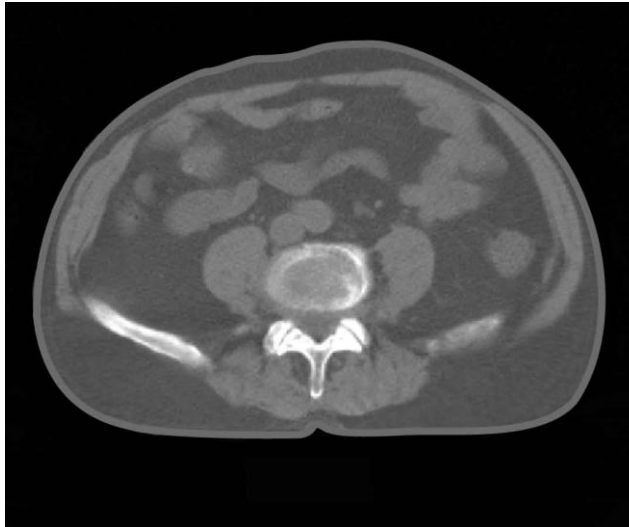


Visceral fat

subcutaneous fat

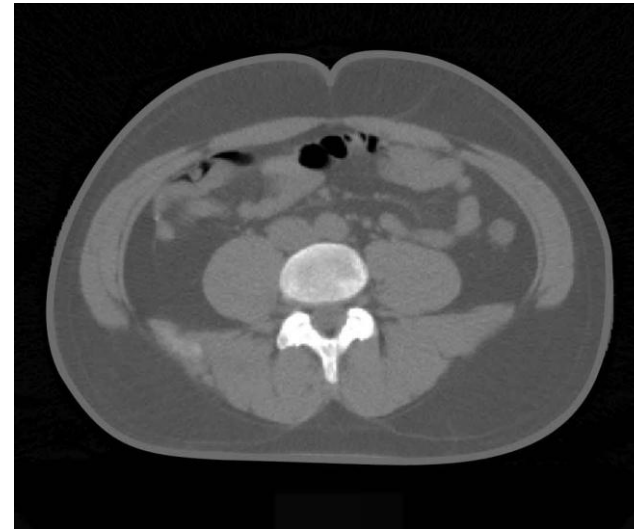
Same WC but different fat distribution

Case 1



- Waist Circumference: 91 cm
- Intra-abdominal Fat: 190 cm²
- Subcutaneous Fat: 162 cm²

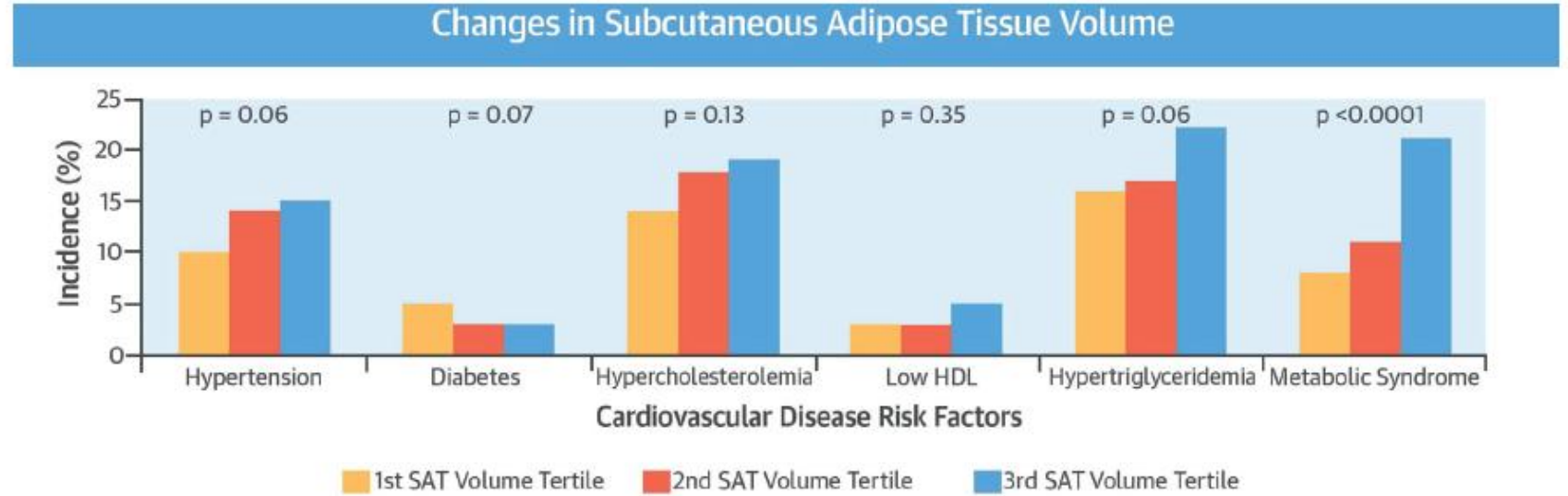
Case 2



- Waist Circumference: 93 cm
- Intra-abdominal Fat: 98 cm²
- Subcutaneous Fat: 274 cm²



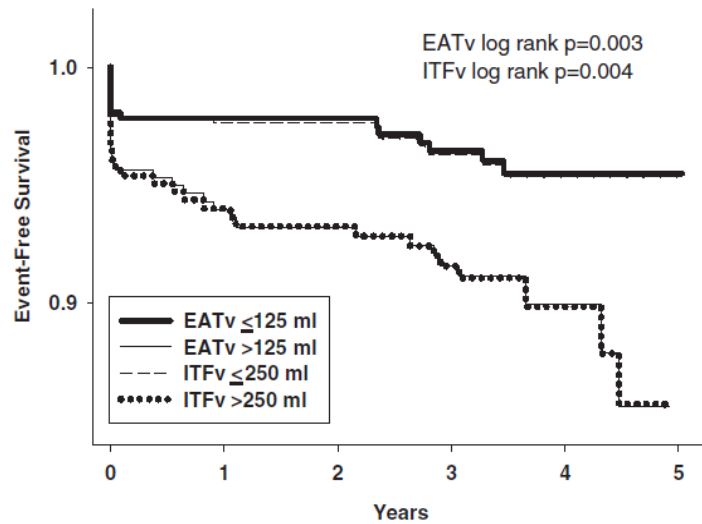
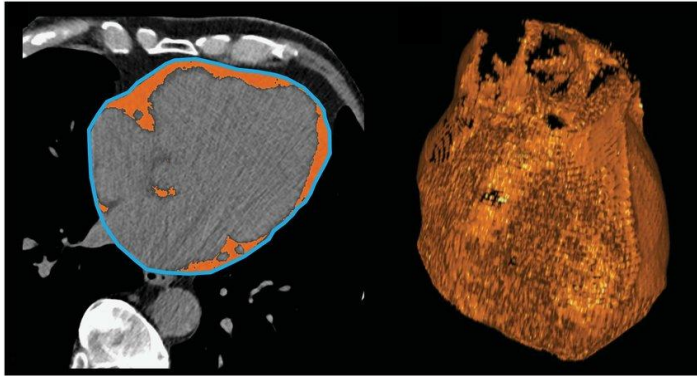
Visceral vs. abdominal fat and cardiovascular disease risk





Ectopic adiposity and cardiovascular disease risk

Epicardial adiposity

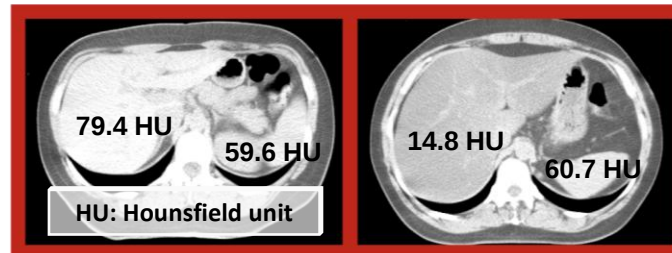


Forouzandeh Circ Cardiovasc Imaging. 2013;6:58-66.

Fatty liver



$$\frac{\text{Mean Liver Attenuation Value}}{\text{Mean Spleen Attenuation Value}} \rightarrow \text{CTL/CTS ("Fatty Liver" Index)}$$

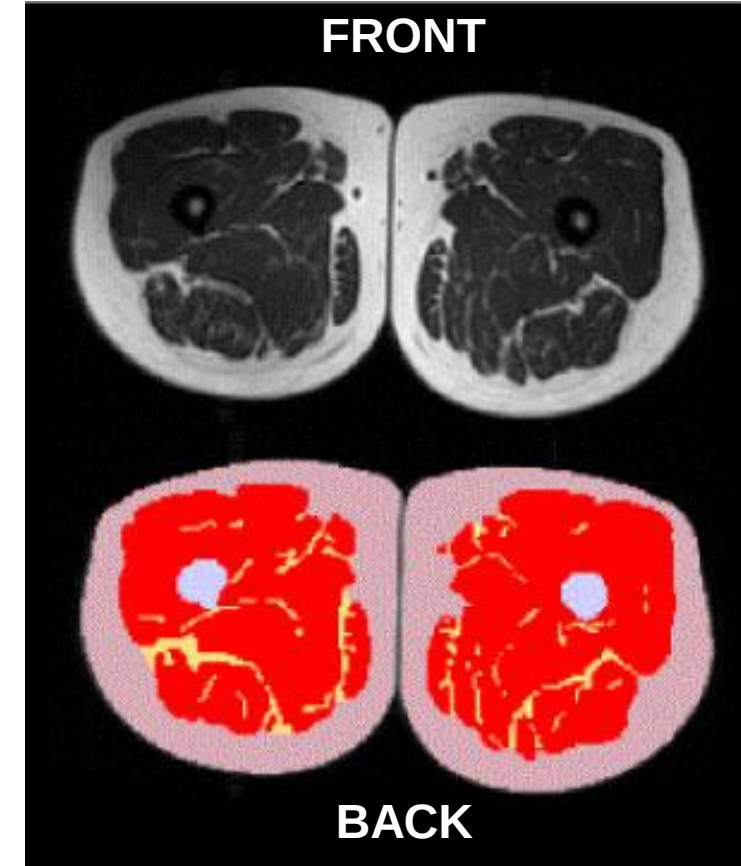


Normal Liver
CTL/CTS = 1.33

"Fatty Liver"
CTL/CTS = 0.24

Intramuscular fat

FRONT



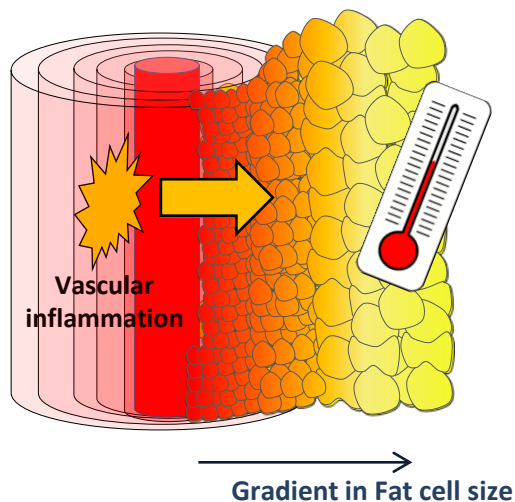
BACK

Han et al. Cardiovasc Diabetol (2017) 16:54

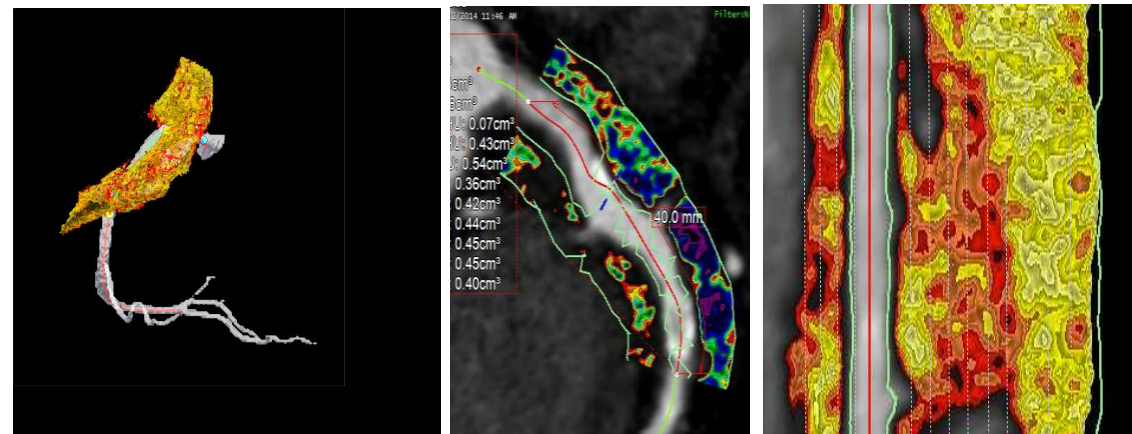
Detecting vascular inflammation by perivascular fat imaging



Perivascular fat as a sensor of coronary inflammation



Perivascular Fat Attenuation Index (FAI_{PVAT})



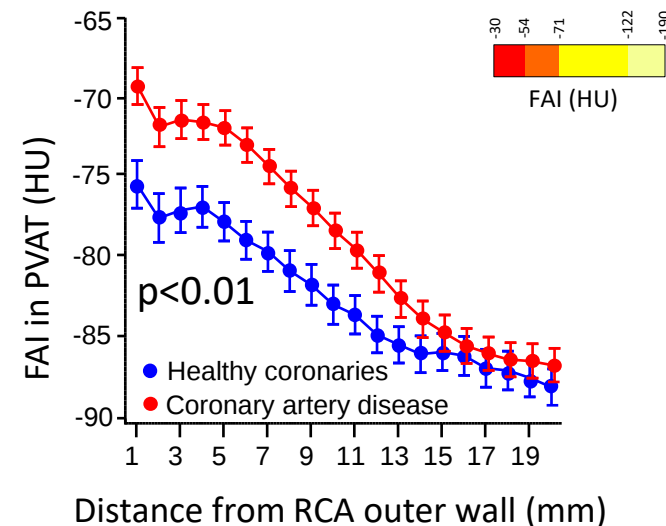
UK Intellectual Property Office, ref. 1414496.8, August 2014

Low FAI

High FAI

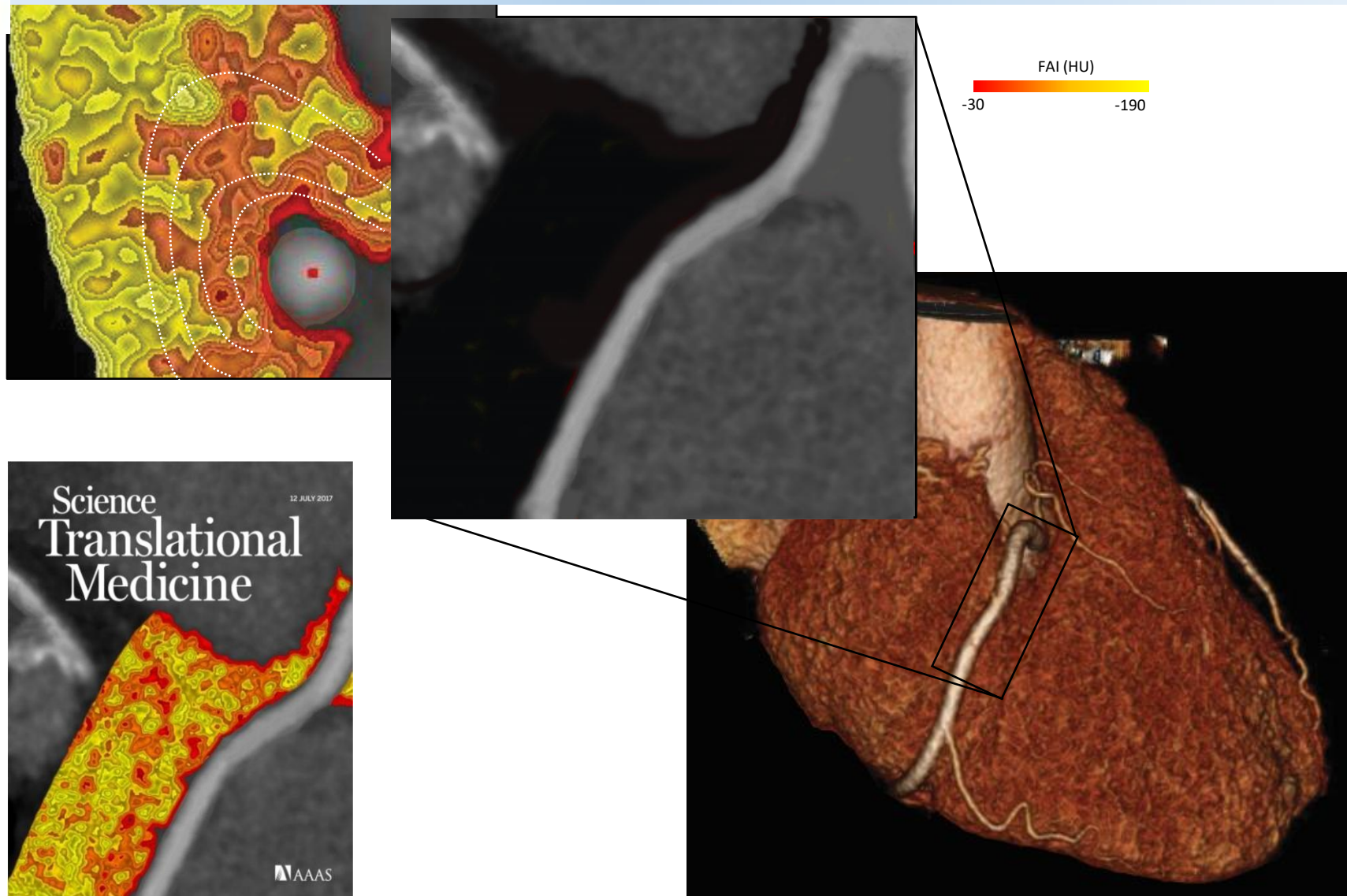
- 3D mapping of human coronary arteries using mathematical models. Images from 1400 a
- ✓ 1400 a
 - ✓ 902 CABG patients
 - ✓ 4273 CTAs (CAD, ACS, “healthy” coronaries)

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



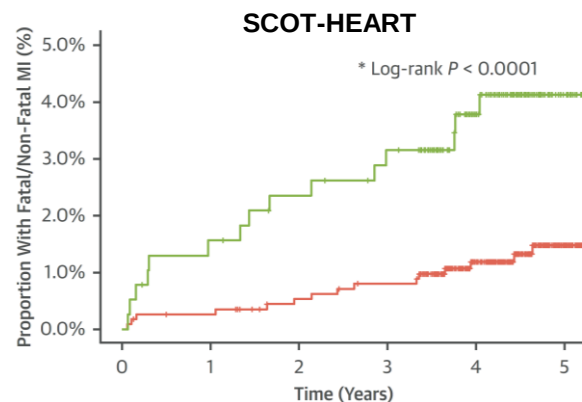
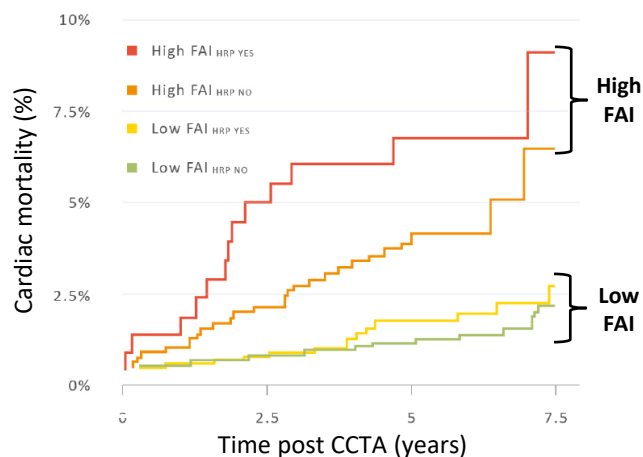
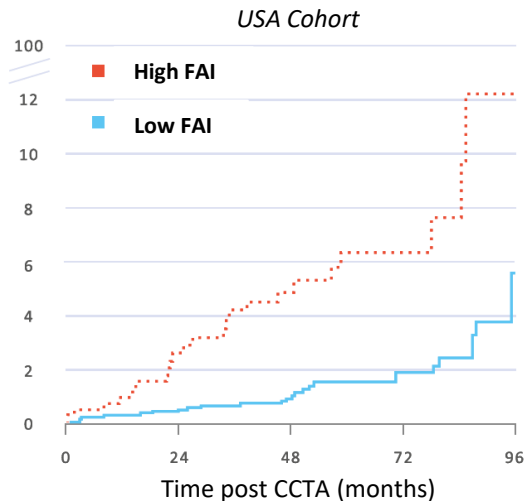
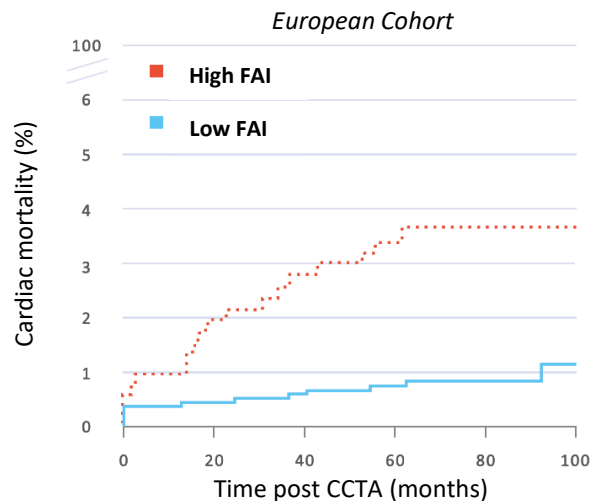


Perivascular fat as a sensor of coronary inflammation





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

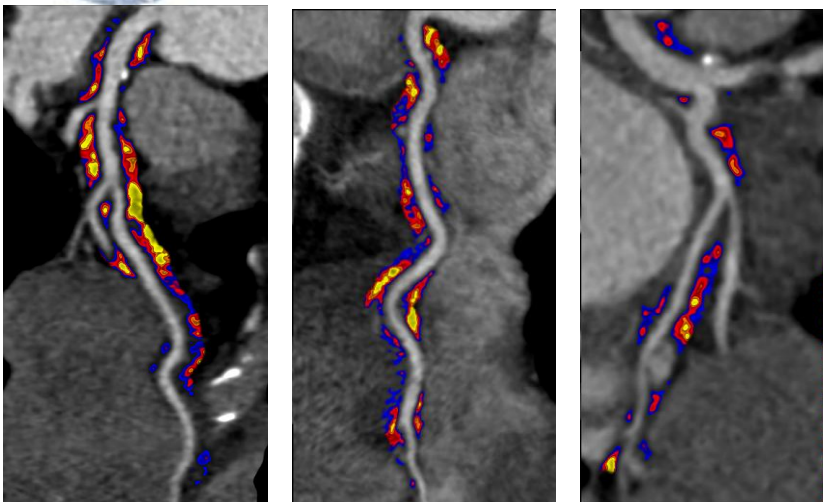
2. *J Am Coll Cardiol* 2020; 76 (6) 755–757

3. *J Am Coll Cardiol Img.* 2022, 15 (6) 1078–1088

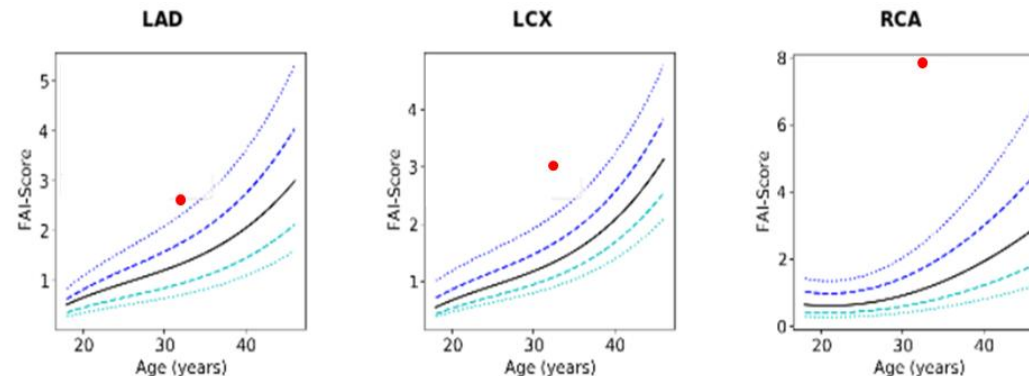


Measuring FAI-Score Identifies High Risk Patients

CASE A

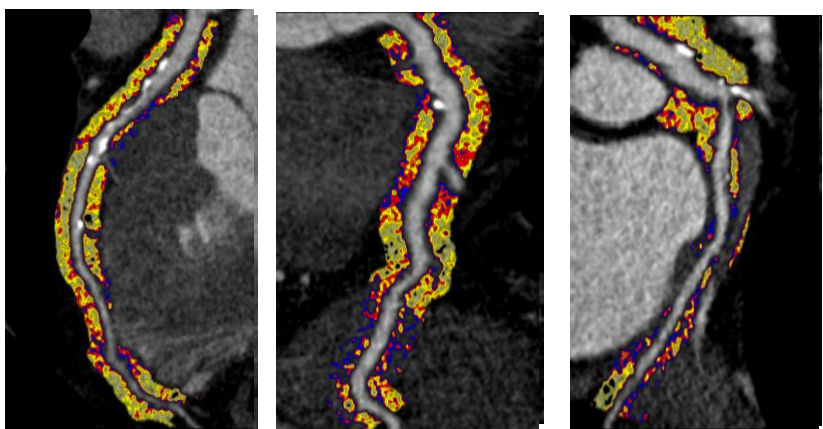


CaRi-Heart® Risk (8y risk for cardiac death: 31.2%)

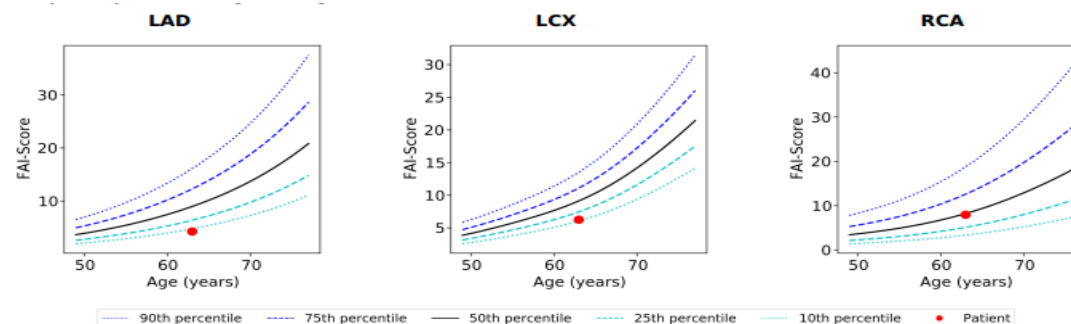


Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	2.7	93rd percentile
Left Circumflex Artery	3.0	99th percentile
Right Coronary Artery	7.7	99th percentile

CASE B



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

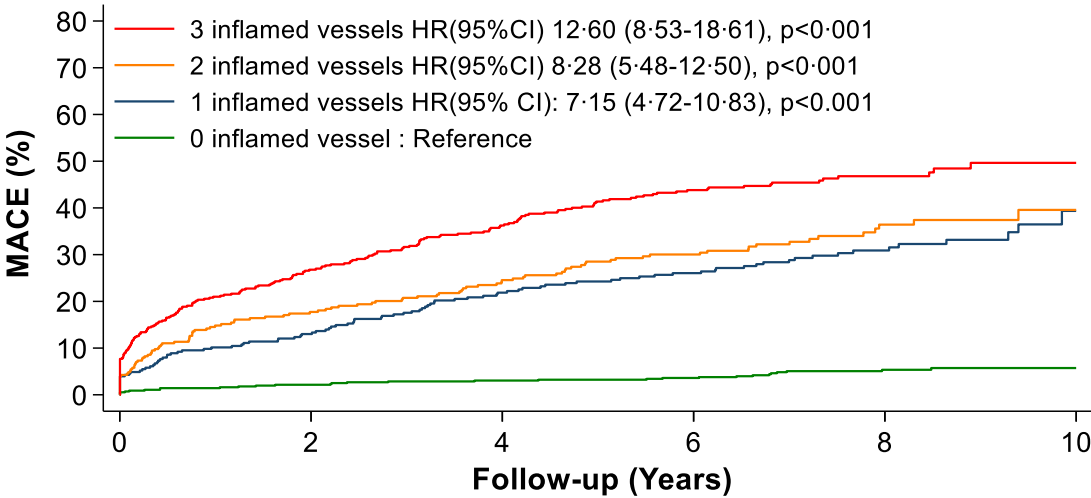


Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	4.2	6th percentile
Left Circumflex Artery	6.3	12th percentile
Right Coronary Artery	7.9	48th percentile



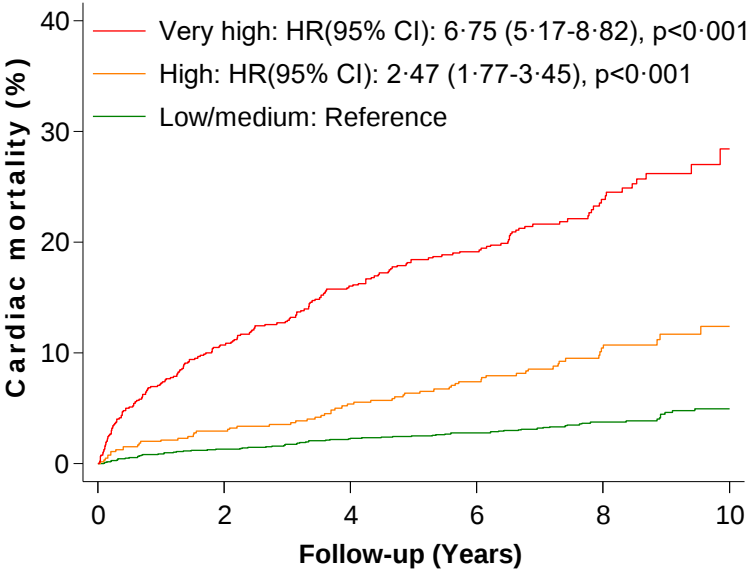
Vascular inflammation for cardiovascular risk prediction (ORFAN)

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

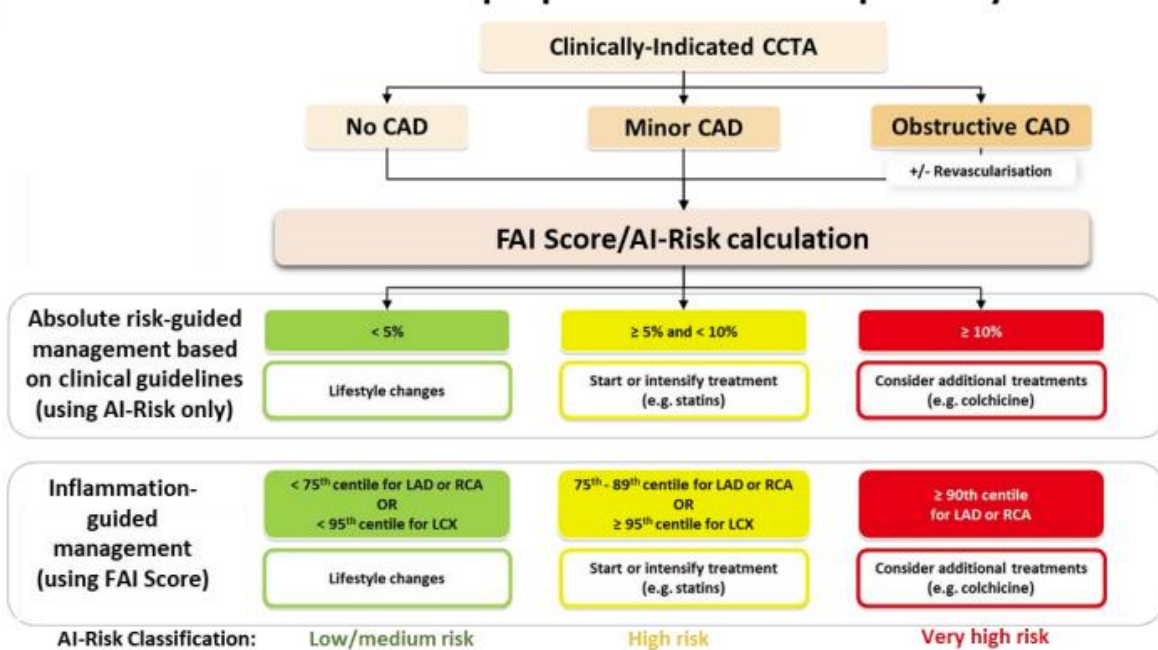
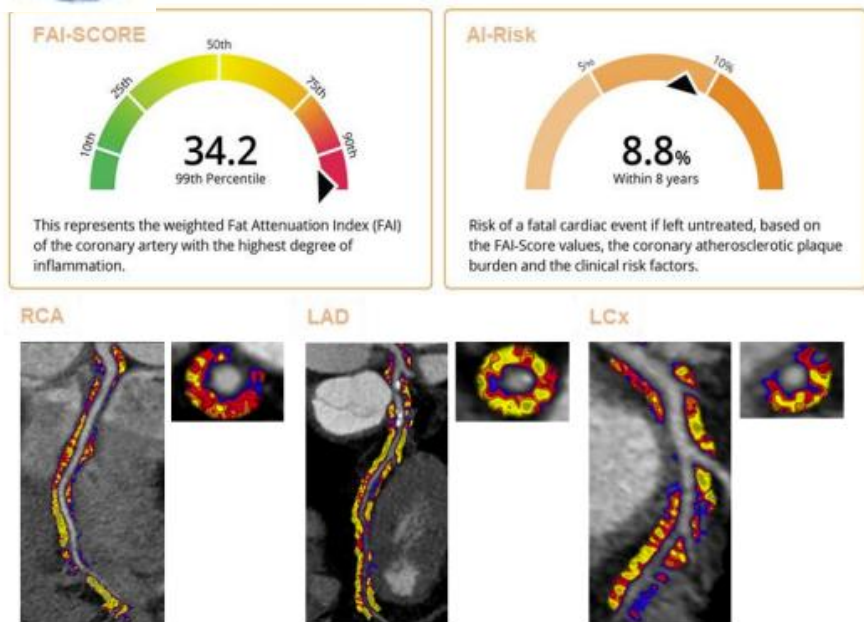
AI-Risk Classification



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	

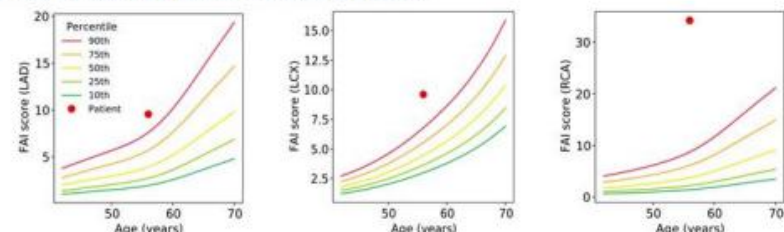


Imaging of coronary inflammation by pericoronary fat (AI-Risk)



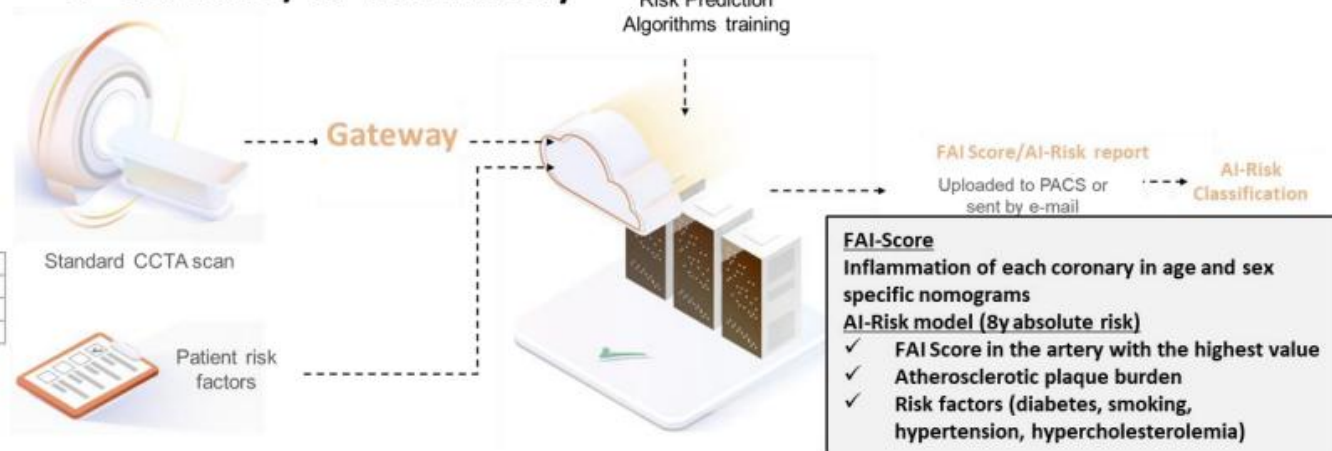
B

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

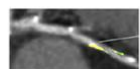
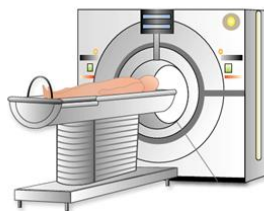
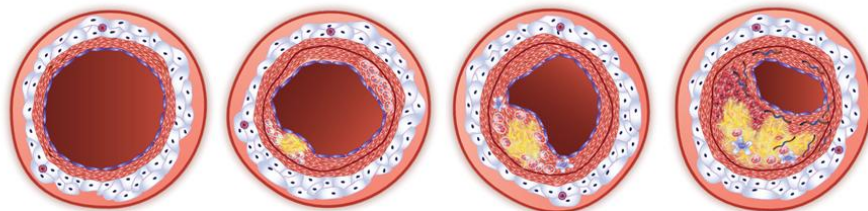




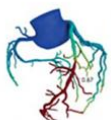
CTCA: One-Stop-Shop for Coronary Diagnostics

Enhanced Diagnostics

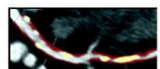
40% No plaque
40% Minor plaque
5% Equivocal plaque
15% Anatomically significant stenoses



Anatomical assessment of stenoses



FFR_{CT}: haemodynamic significance of equivocal or minor plaques to guide revascularization



Plaque composition

AI-based evaluation of coronary artery/plaque inflammatory burden (FAI and FRP)

CTCA

- ✓ Guiding revascularization procedures
 - ✓ Risk stratification
 - ✓ Guiding prevention treatments
 - ✓ Saving costs
 - ✓ Reducing procedural risks
- Ultimately better quality, patient-friendly, healthcare

Improved Risk Stratification



Patient's risk factors and demographics

Personalised cardiovascular risk prediction using Artificial Intelligence

Features extraction from computed tomography images

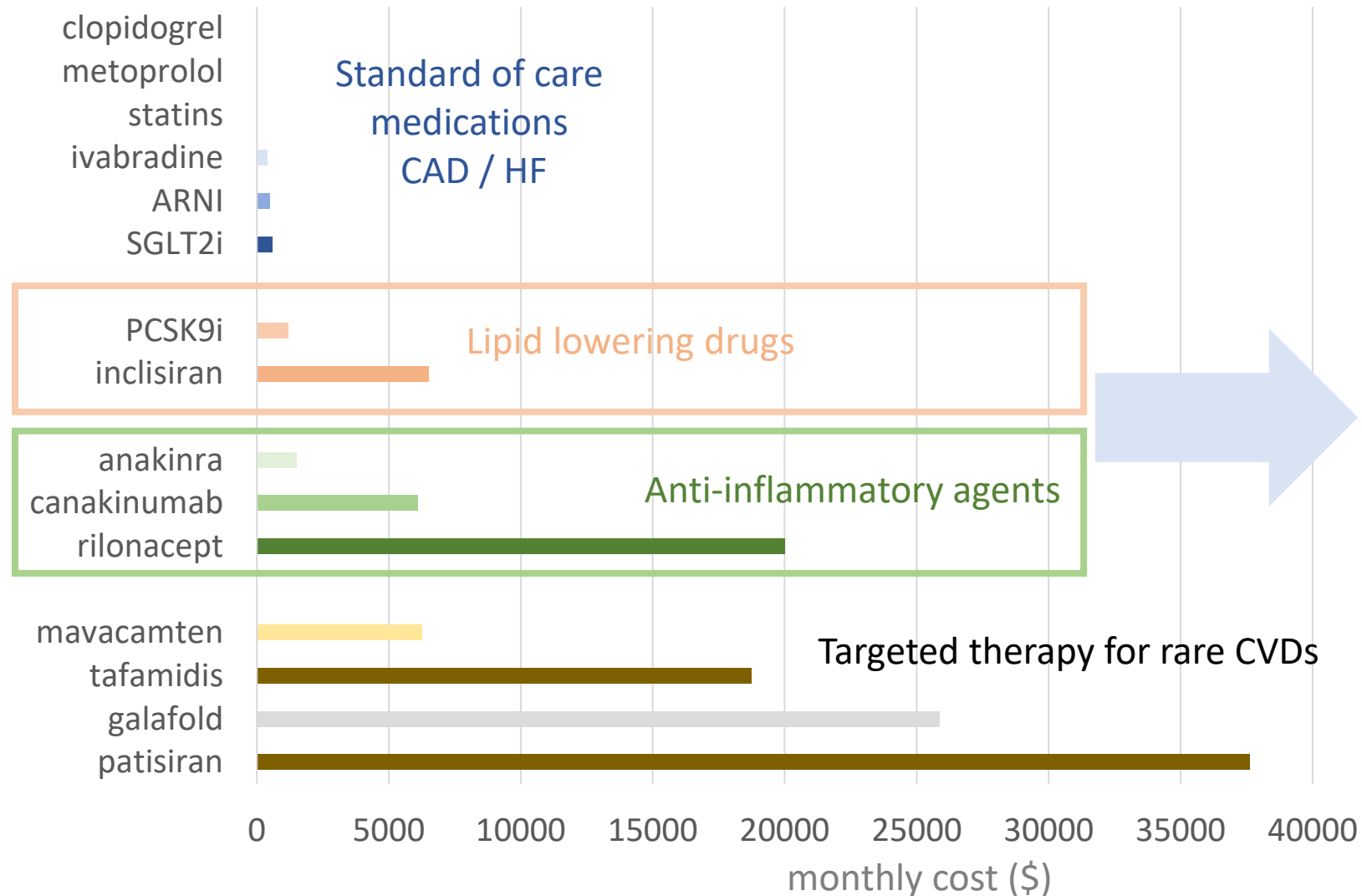


Continuous upgrade and algorithm re-training





CCTA-guided treatment of coronary atherosclerosis



Prevalence
of disease

many pts eligible for
but high cost tx!

Cost of tx



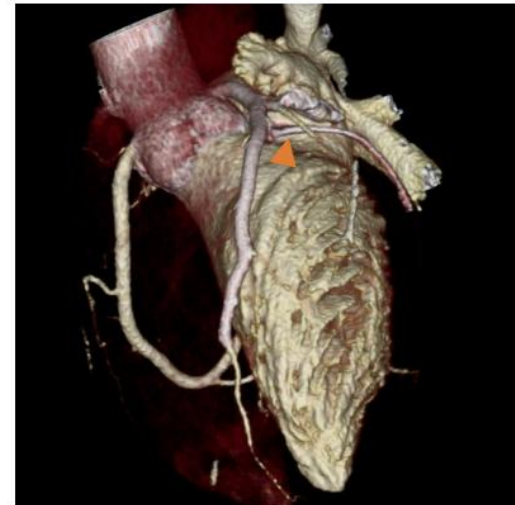
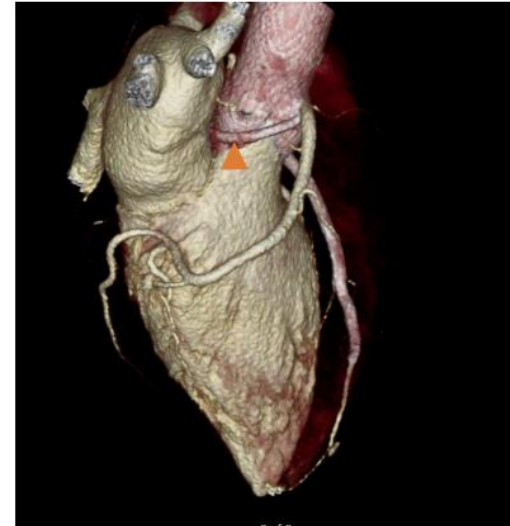
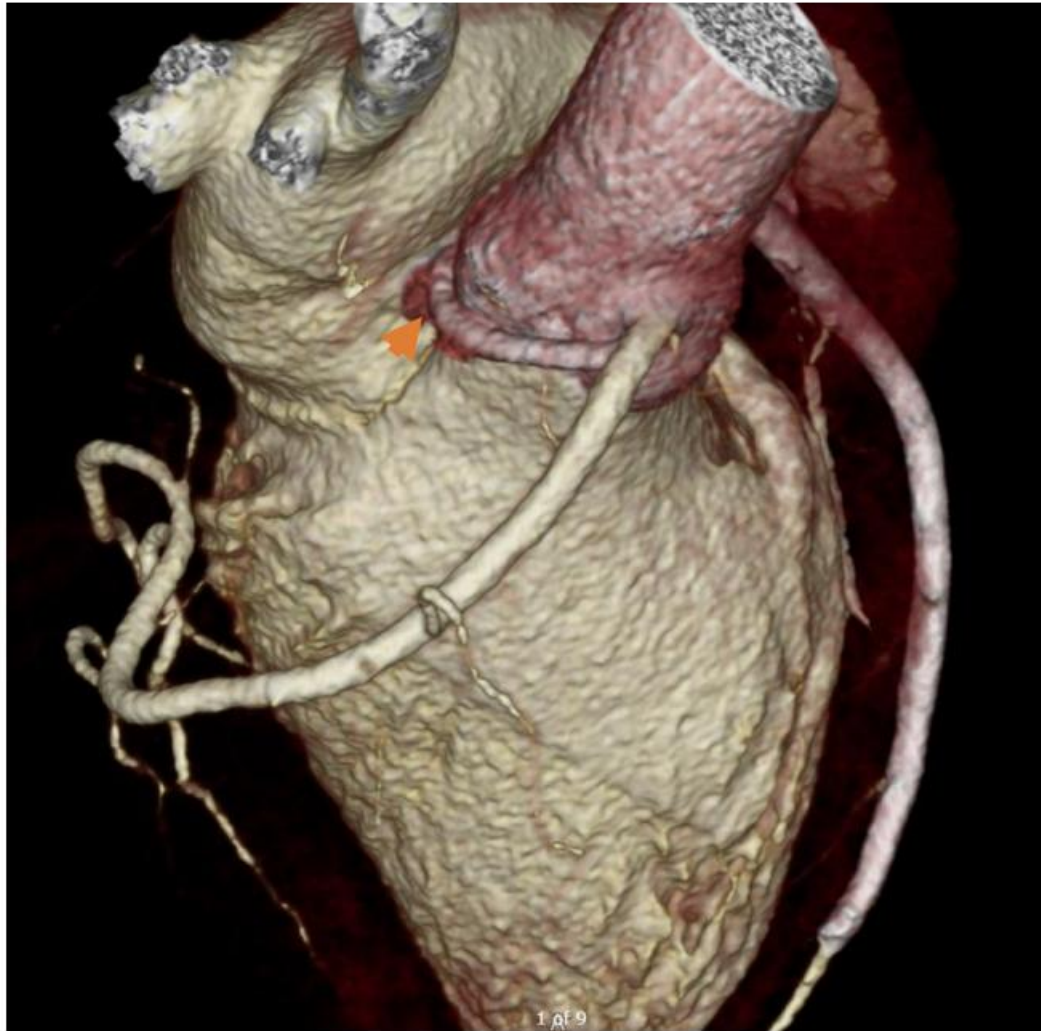
Αλέξιος Αντωνόπουλος
e-mail: antonopoulosal@yahoo.gr



Other uses of CCTA



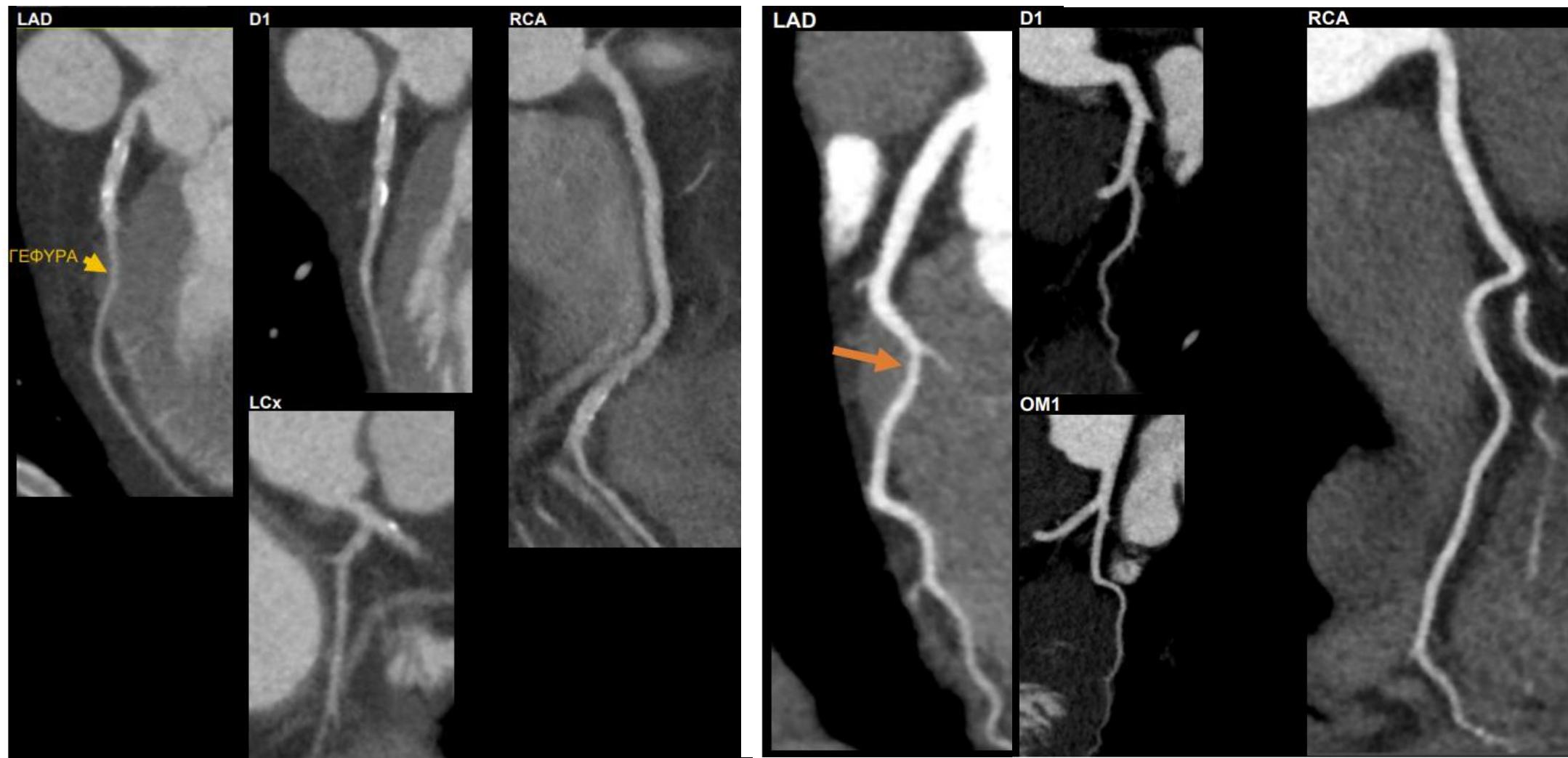
Anomalous coronary arteries



- 19M
- Footballer
- Deepening of inferior TWI on ETT
- Assessment for CAA
- 80keV
- 85DLP
- ~1mSV

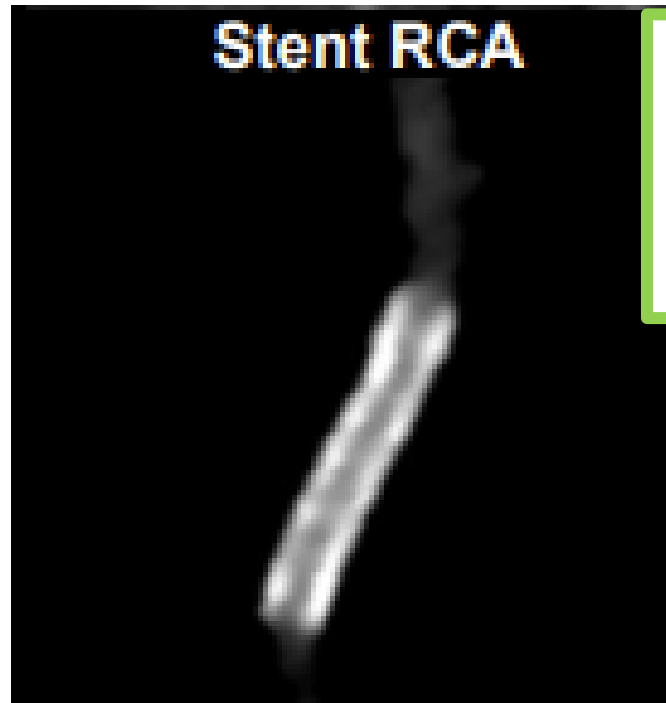


Myocardial bridges





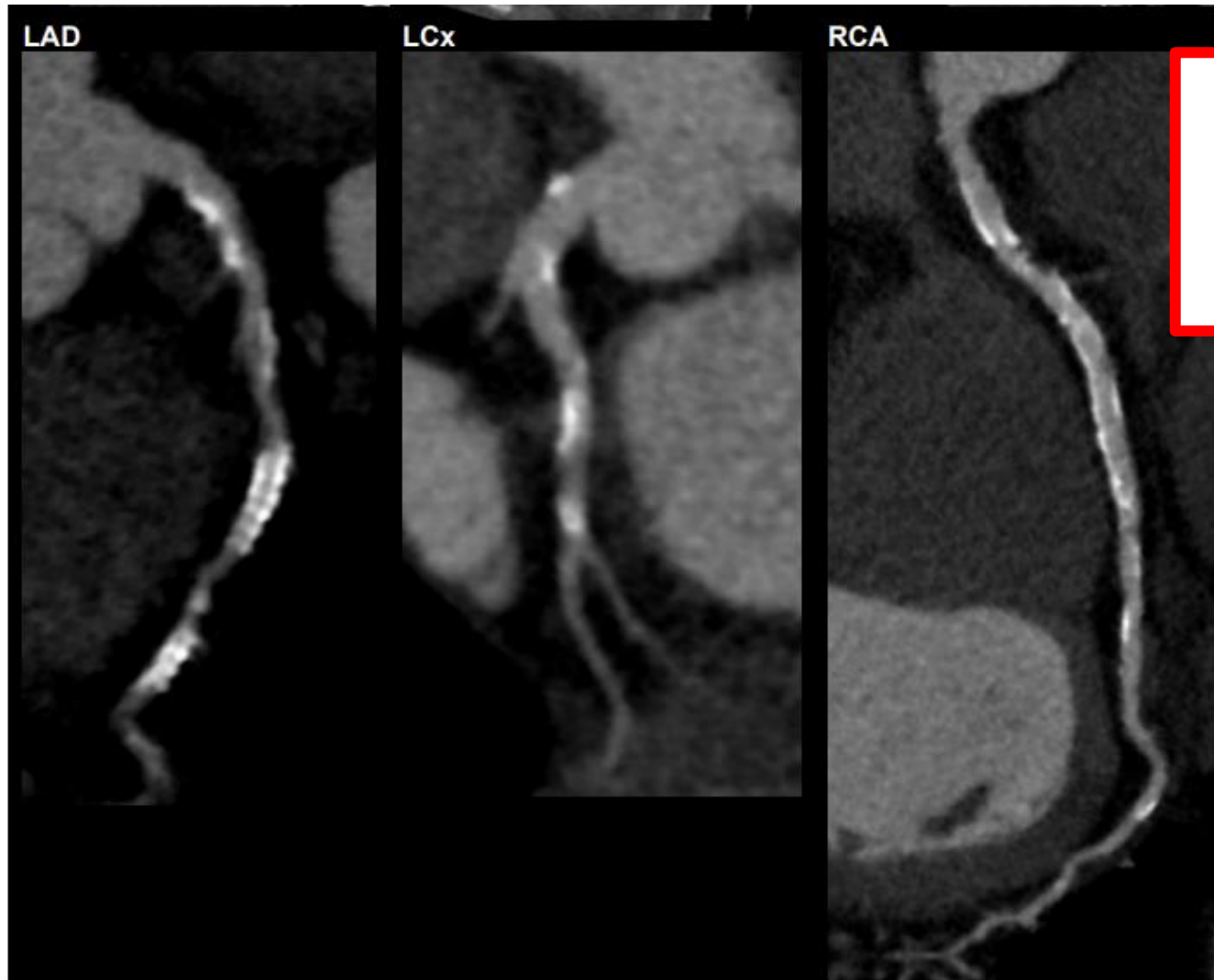
Coronary stents



- Not the best modality
- OK if proximal, large stents (>3mm)
- Not good for distal, smaller stents



Coronary stents



Not the best modality
OK if proximal, large stents (>3mm)
Not good for distal, smaller stents



For intervention planning (prior to CABG or PCI)

