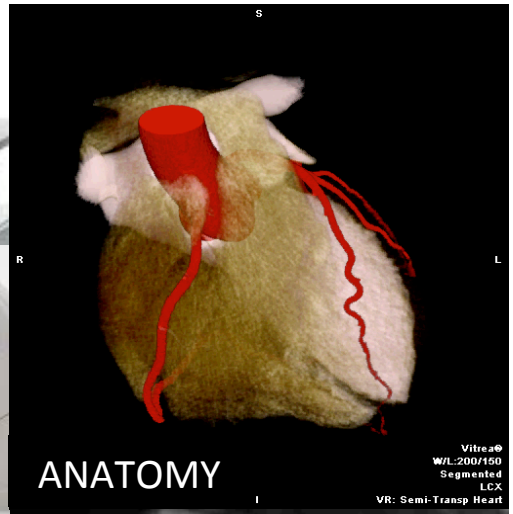
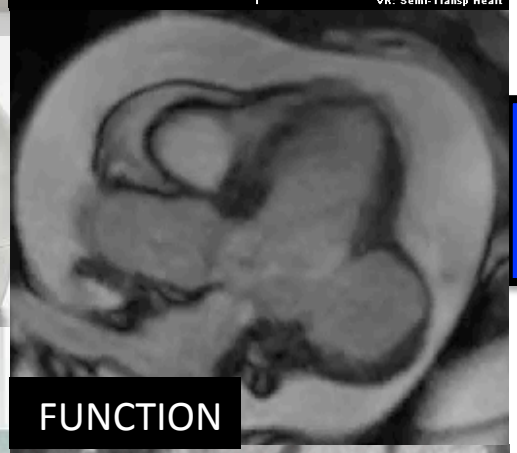
Picturing the Heart in 2020

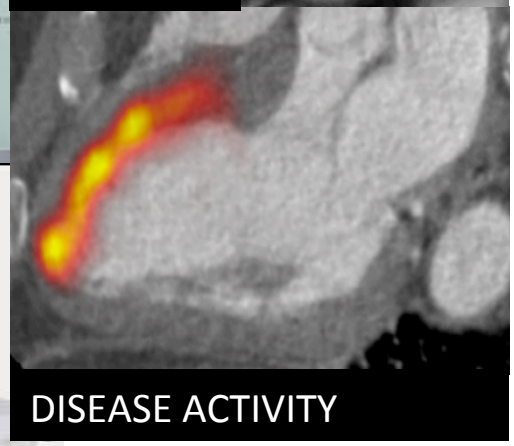
Dr Marc Dweck

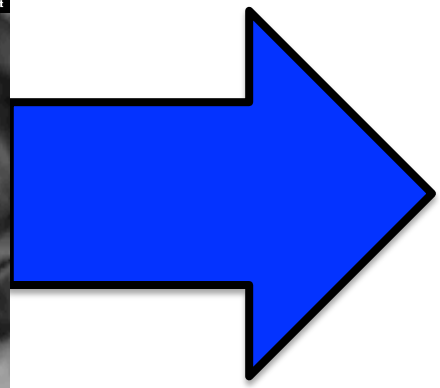
BHF Intermediate Clinical Research Fellow

& Consultant Cardiologist









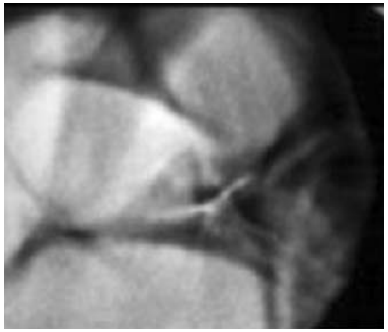
IMPROVED PATIENT CARE & OUTCOMES

Outline

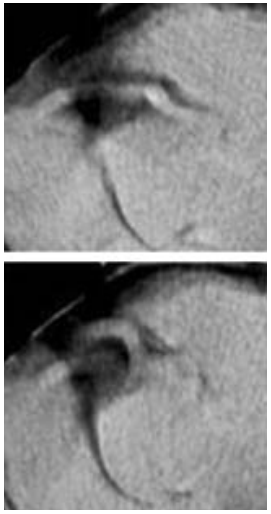
- Novel imaging approaches in coronary artery disease
- CT coronary angiography
- Magnetic resonance imaging
- PET imaging

Advances in CT imaging

1990 → 1996 → 2002 → 2003 → 2005

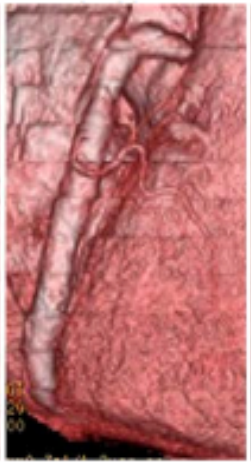


1 slice



1 slice
Overlapping
algorithm

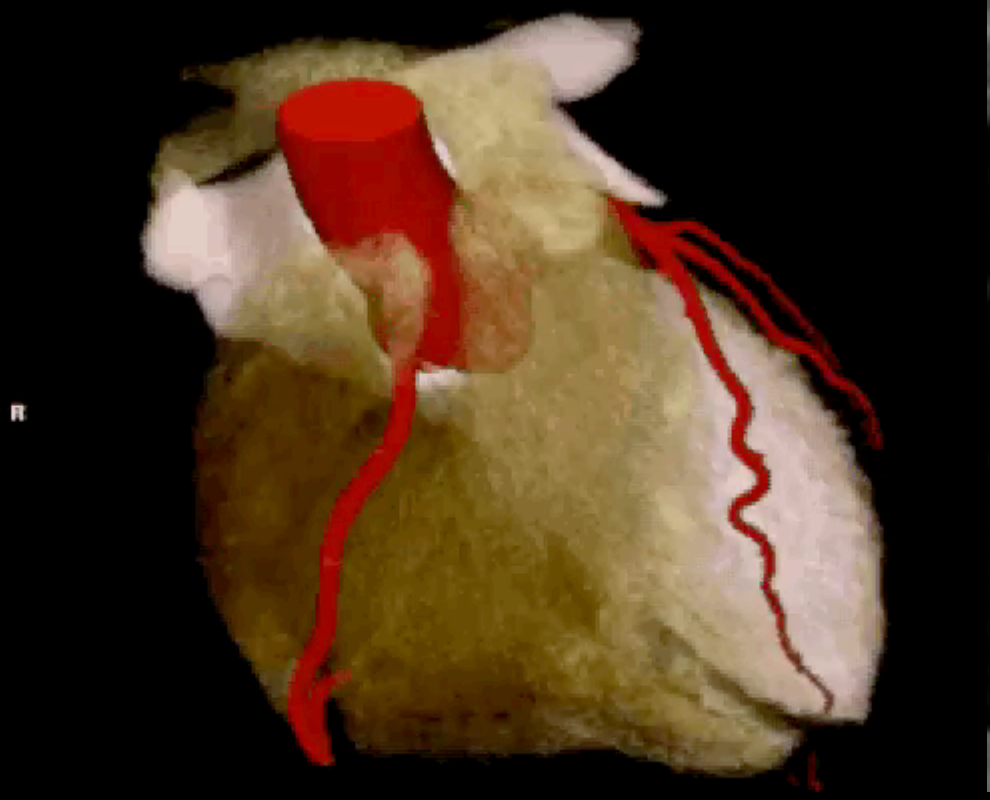
4 slice



16 slice

64 slice

Int J Cardiovasc Imaging 2009, 25: 31-42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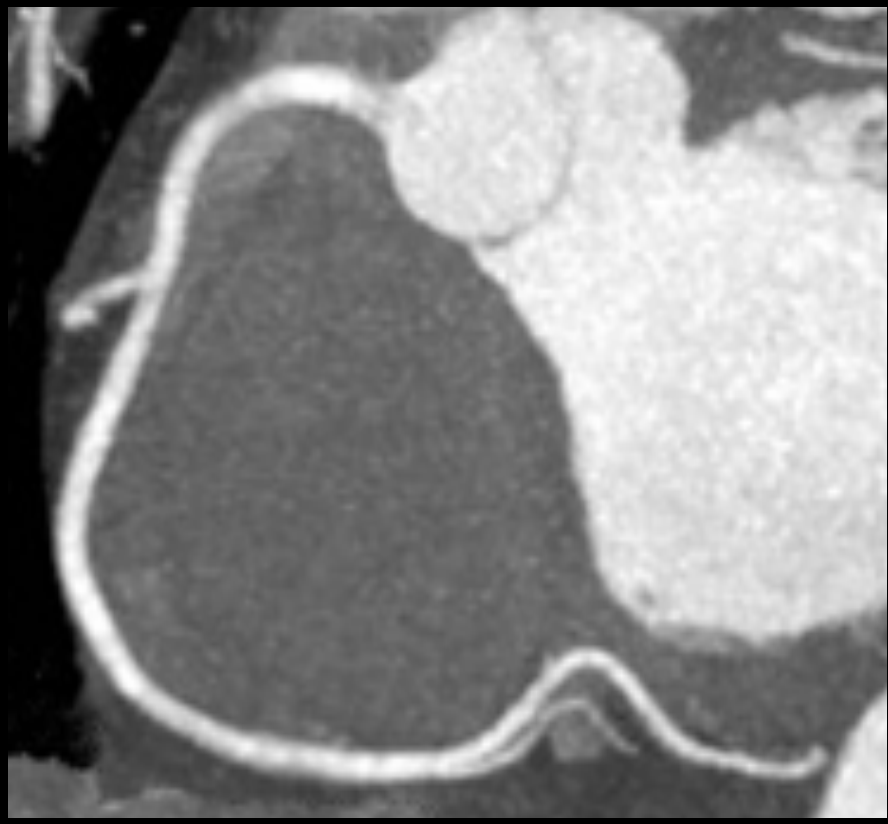
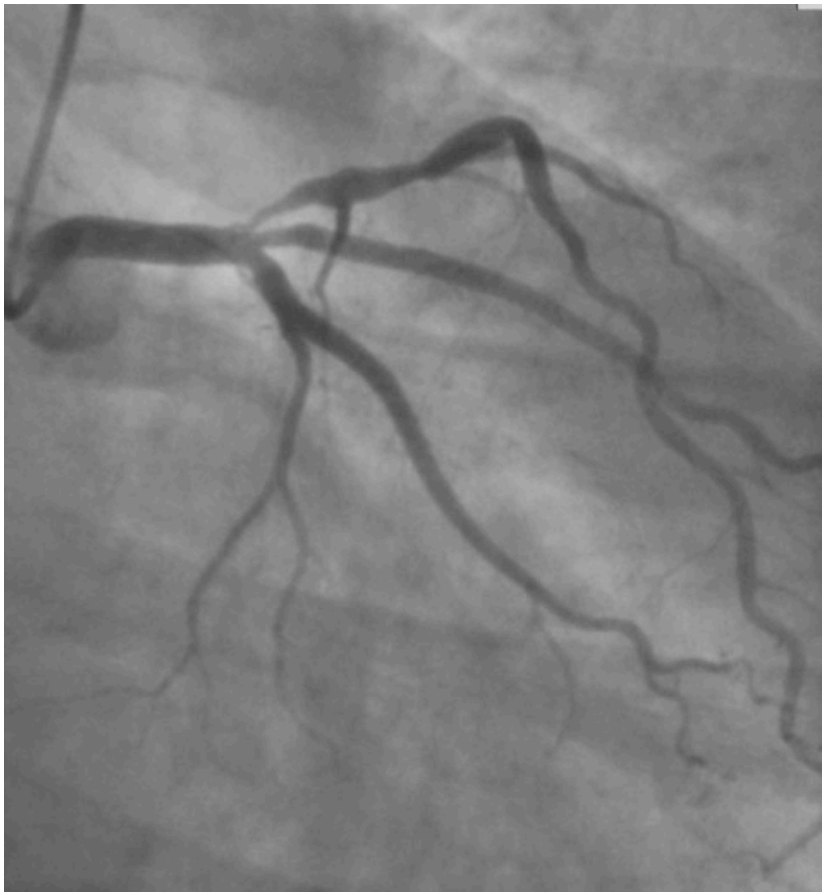
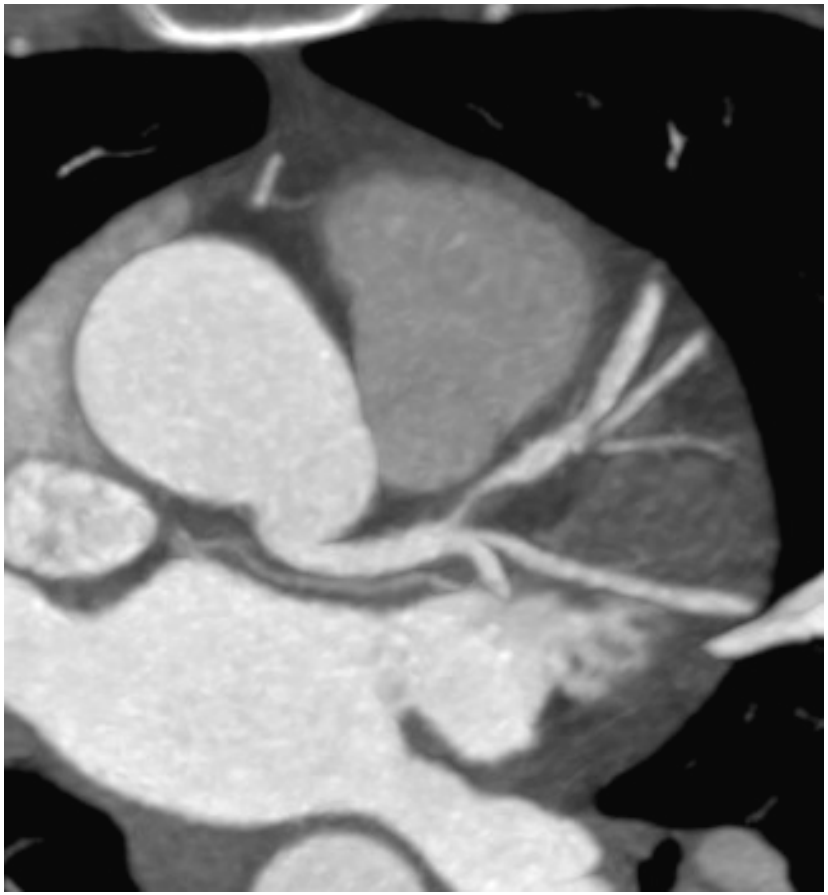


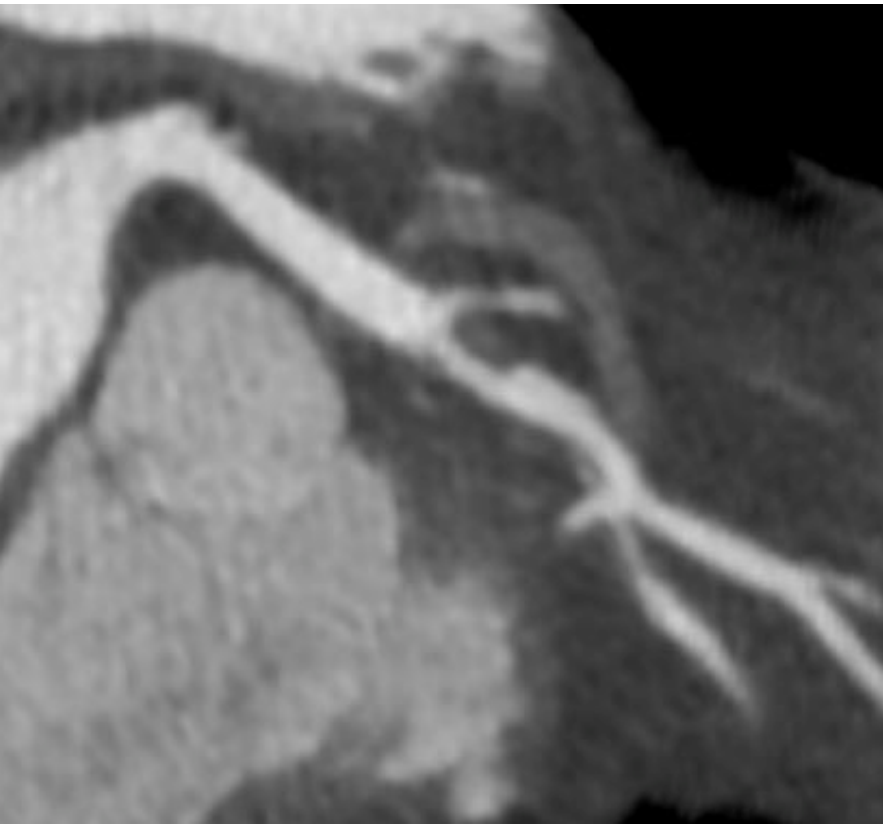
Directly Identifies Plaque

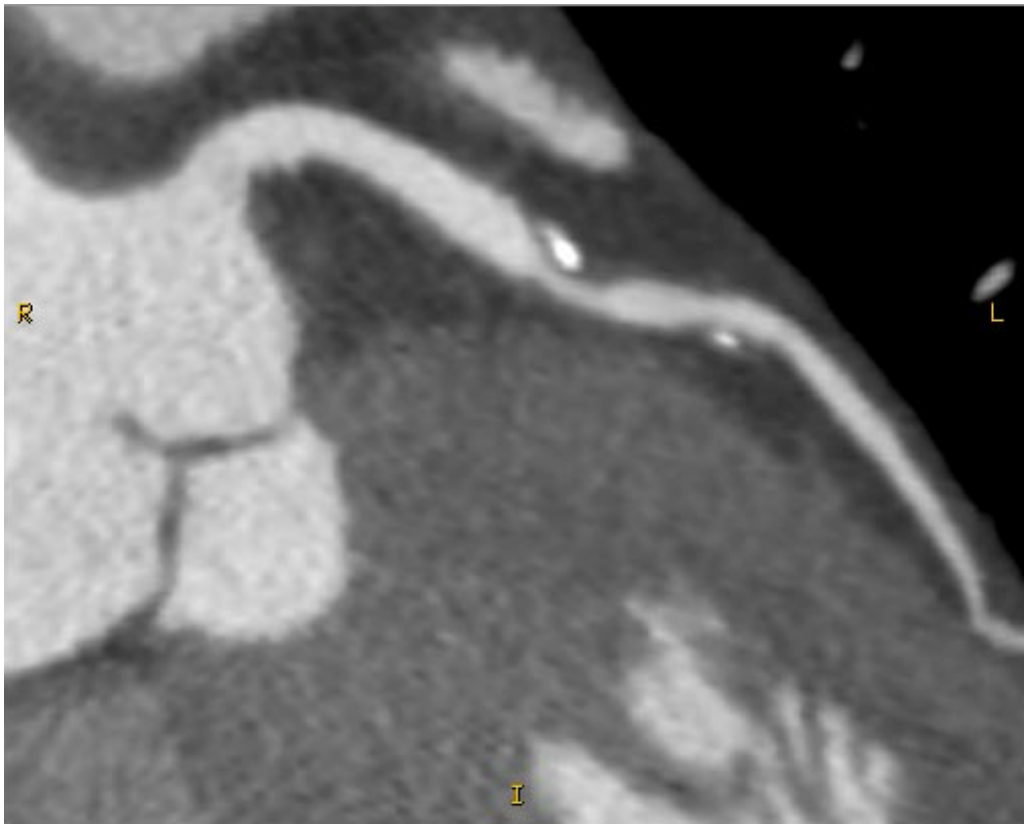




Obstructive Coronary Atherosclerosis

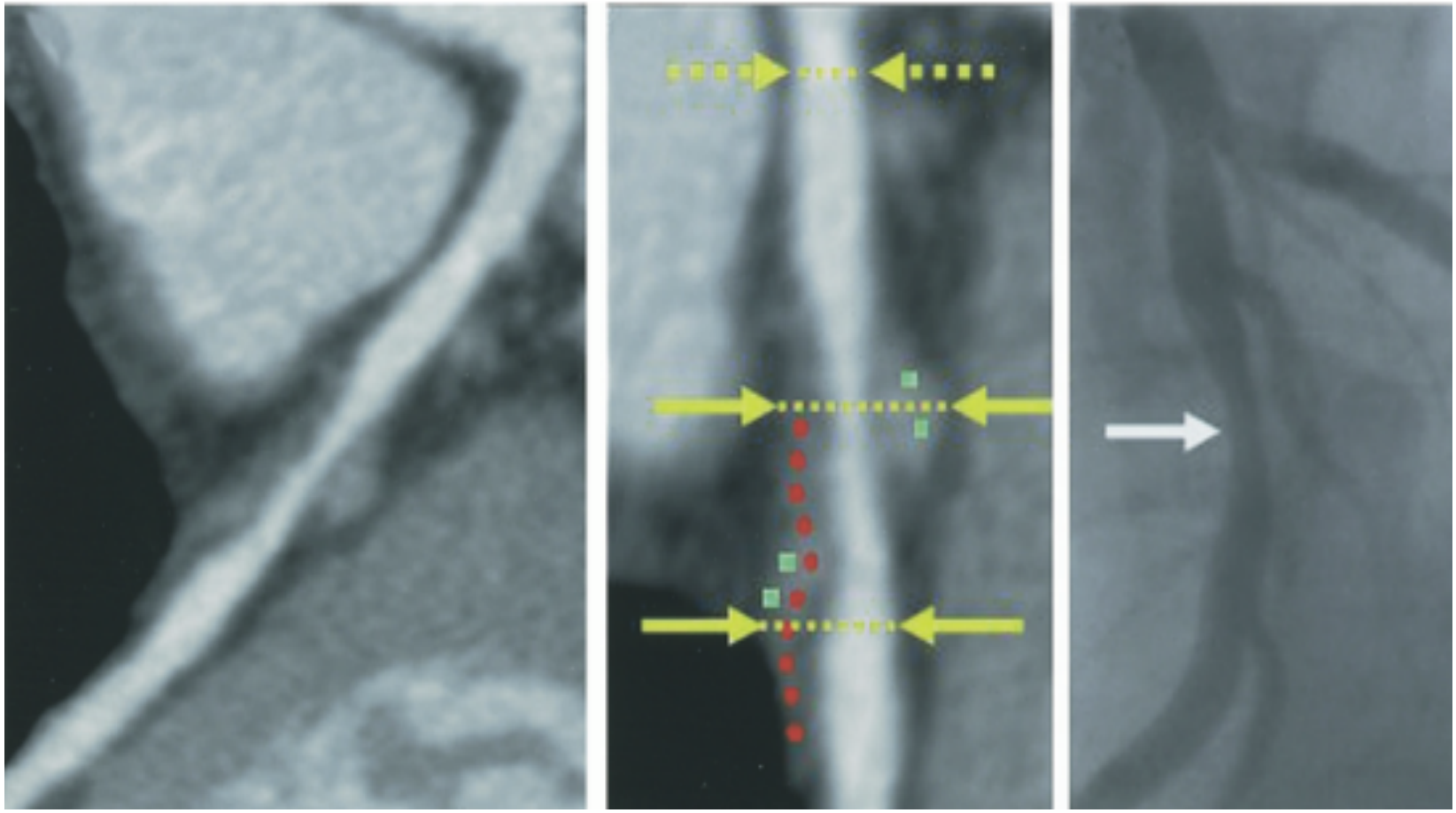
~90% Specificity and Sensitive for Obstructive Coronary Heart Disease



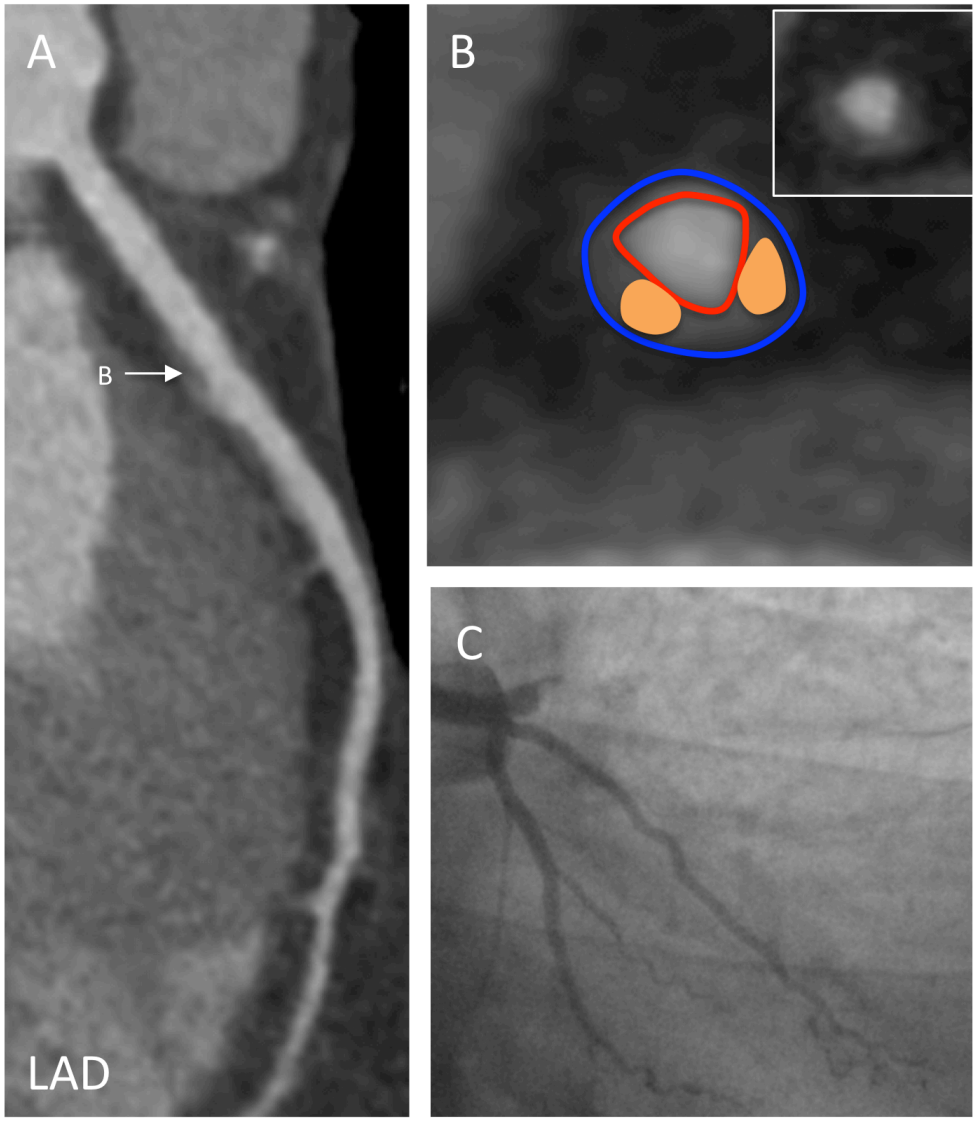


Buddoff JACC 2008 Miller NEJM 2008

Non- Obstructive Coronary Atherosclerosis

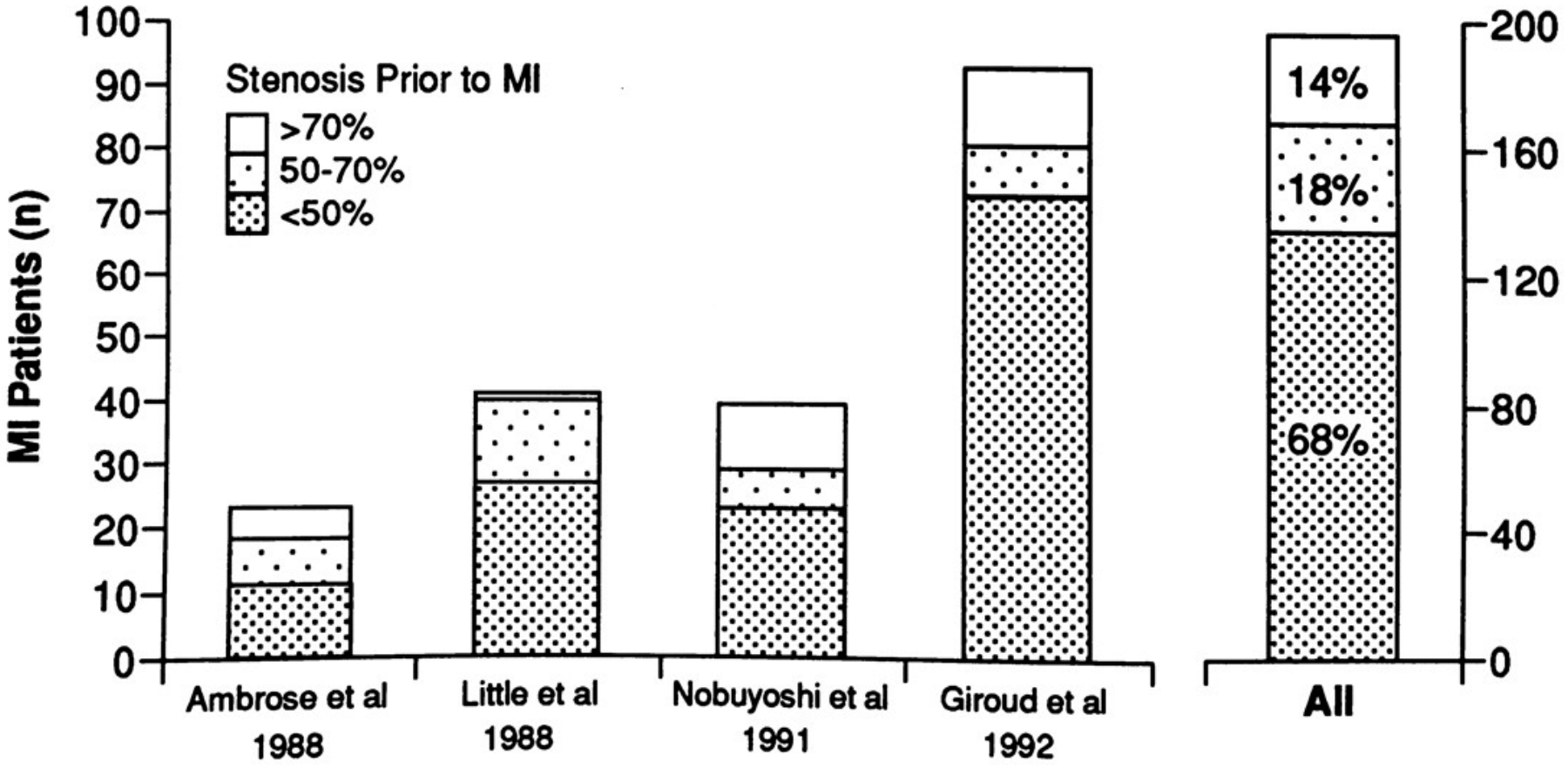


MI arising from a non-obstructive plaque



Dweck JACC 2016

Importance of Non-Obstructive Disease



Falk Circulation 1995

Plaque Burden is the Only Independent Predictor of Clinical Events

	Univariable analysis	Multivariable analysis #
Adverse plaque *	3.00 (1.60, 5.63) p=0.001	1.15 (0.54, 2.47) p =0.714
Coronary Artery Calcium Score **	1.99 (1.49, 2.68) p <0.001	1.72 (1.16, 2.56) p=0.007
Obstructive coronary artery disease	3.35 (1.81, 6.19) p <0.001	1.36 (0.63, 2.95) p=0.431
Male Gender	2.12 (1.06, 4.24) p=0.033	1.21 (0.58, 2.53) p=0.610
Cardiovascular Risk score $	1.00 (0.98, 1.03) p=0.861	-

Williams *et al*. *JACC in press*

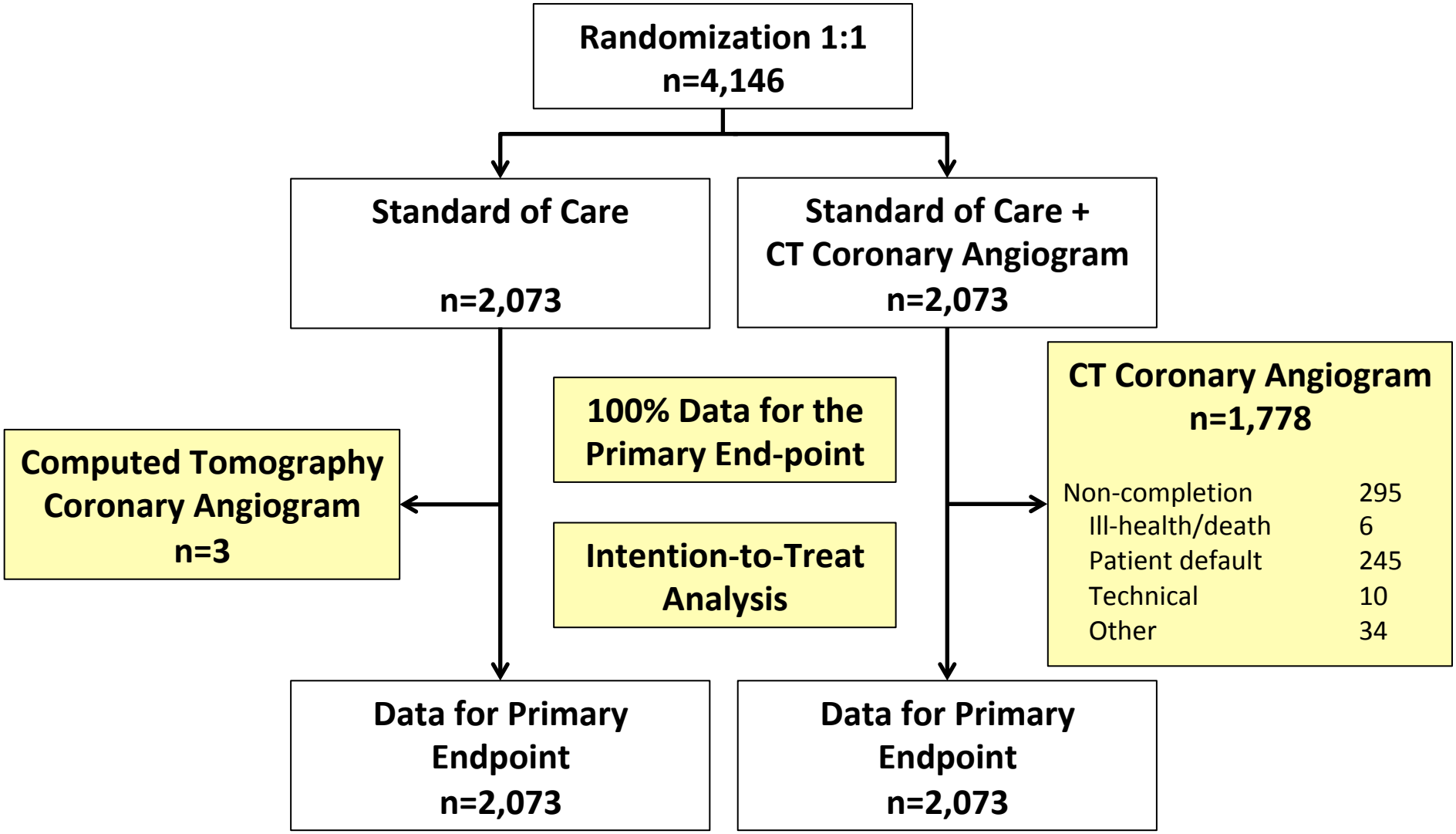
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Coronary CT Angiography and 5-Year Risk of Myocardial Infarction

The SCOT-HEART Investigators*

SCOT-HEART
Trial Population



SCOT-HEART Trial

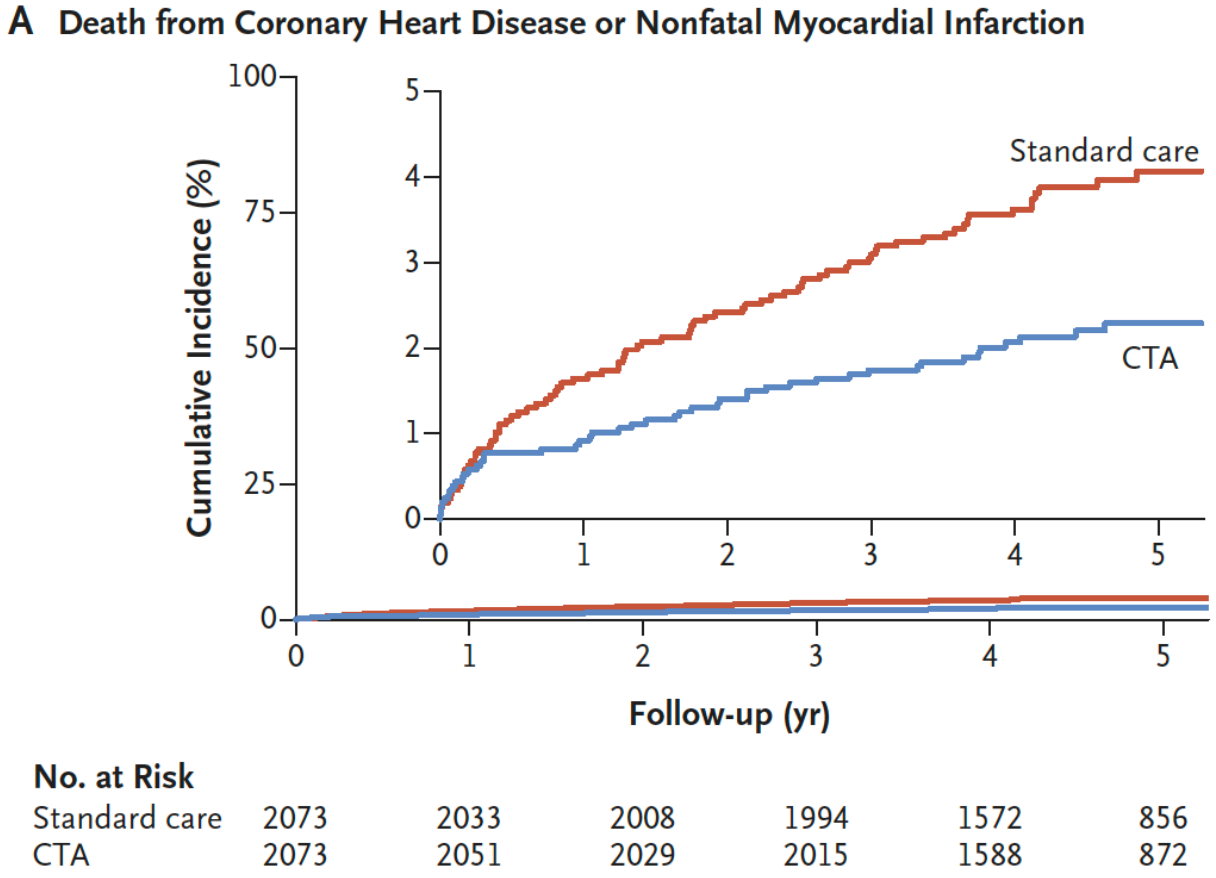
The 5-Year Data

Pre-specified 5-year assessment of Coronary CT Angiography on:

- Coronary heart disease death or non-fatal myocardial infarction
- Invasive coronary angiography and coronary revascularisation
- Prescription of preventative therapies

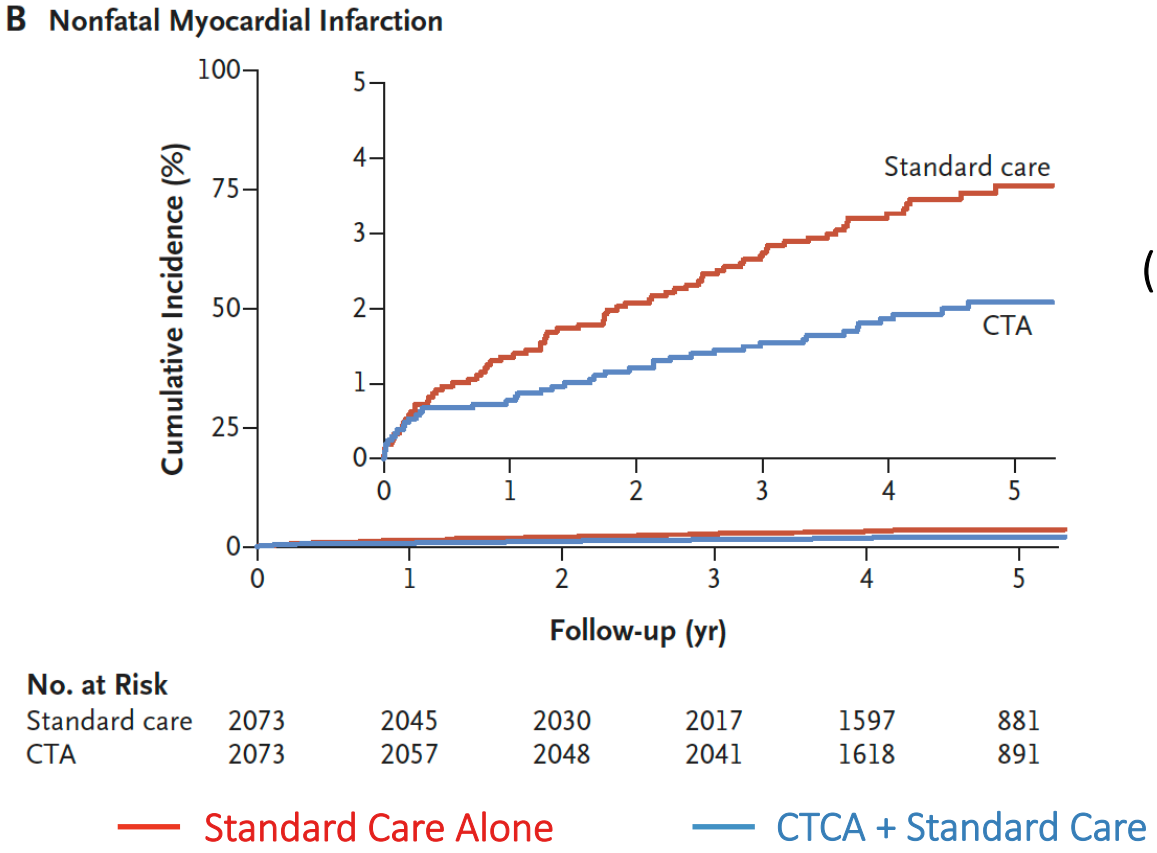
Trials. 2012;13:184

Fatal or Non-fatal MI



Hazard Ratio 0.59
(95% CI, 0.41 to 0.84)
P=0.004

Non-fatal Myocardial Infarction

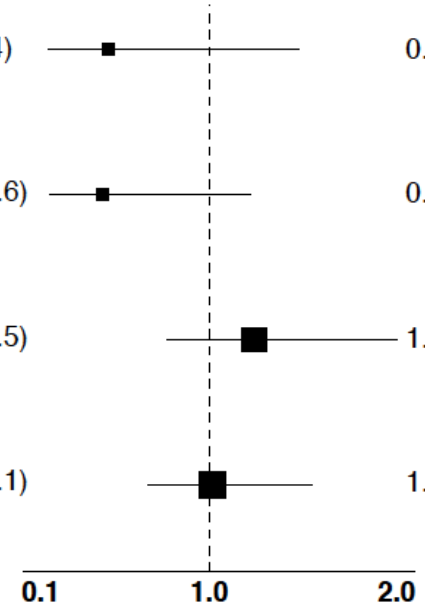


Hazard Ratio 0.60
(95% CI, 0.41 to 0.87)
P=0.007

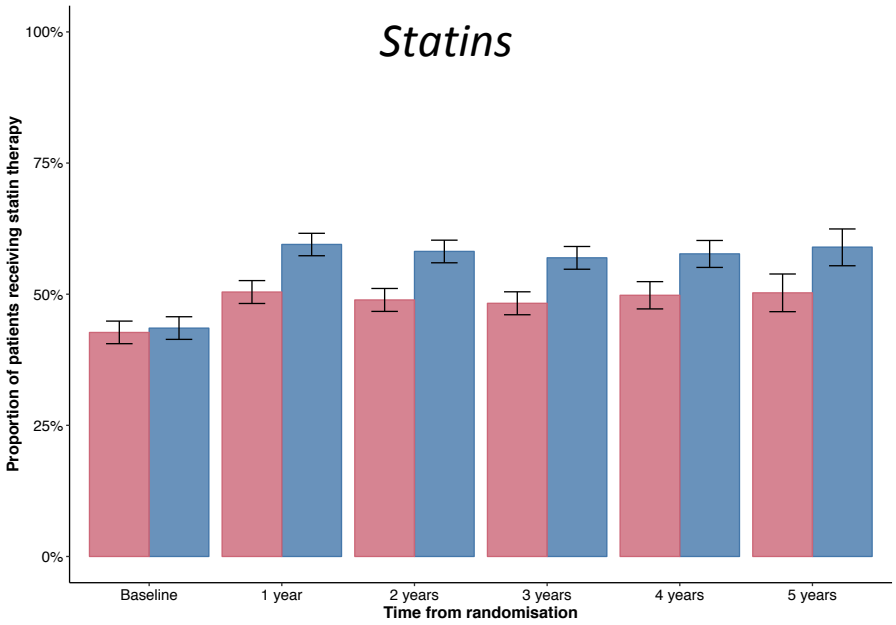
Mortality

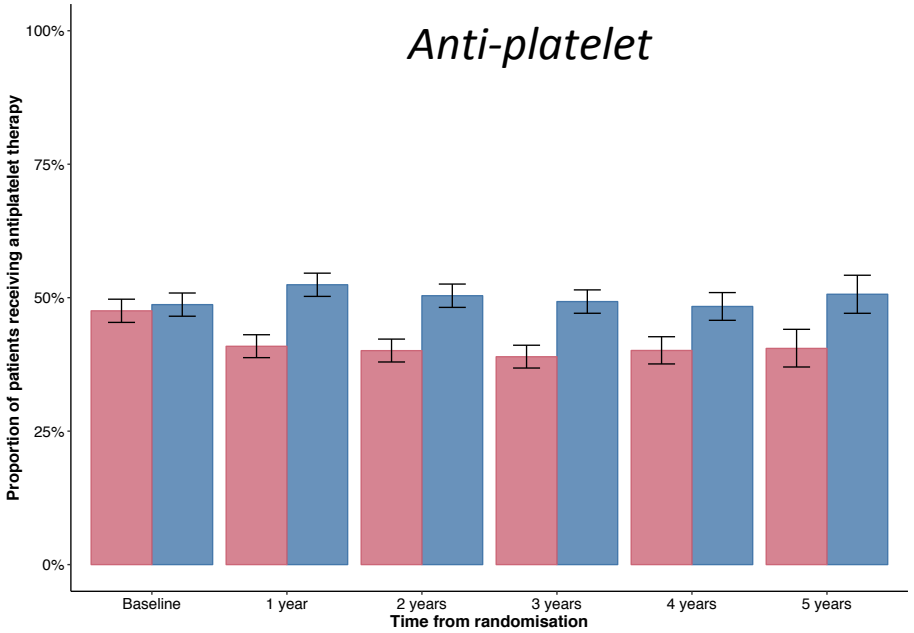
Cardiovascular and Non-cardiovascular Death

Cause of Death	All Participants	CCTA	Standard Care	Hazard Ratio (95% CI)		P Value
Coronary Heart Disease	13 (0.3)	4 (0.2)	9 (0.4)	0.46	(0.14, 1.48)	0.193
Cardiovascular	17 (0.4)	5 (0.2)	12 (0.6)	0.43	(0.15, 1.22)	0.111
Non-cardiovascular	69 (1.7)	38 (1.8)	31 (1.5)	1.24	(0.77, 2.00)	0.368
All-cause	86 (2.1)	43 (2.1)	43 (2.1)	1.02	(0.67, 1.55)	0.936



Statin & Anti-Platelet Therapy Use over 5 Years



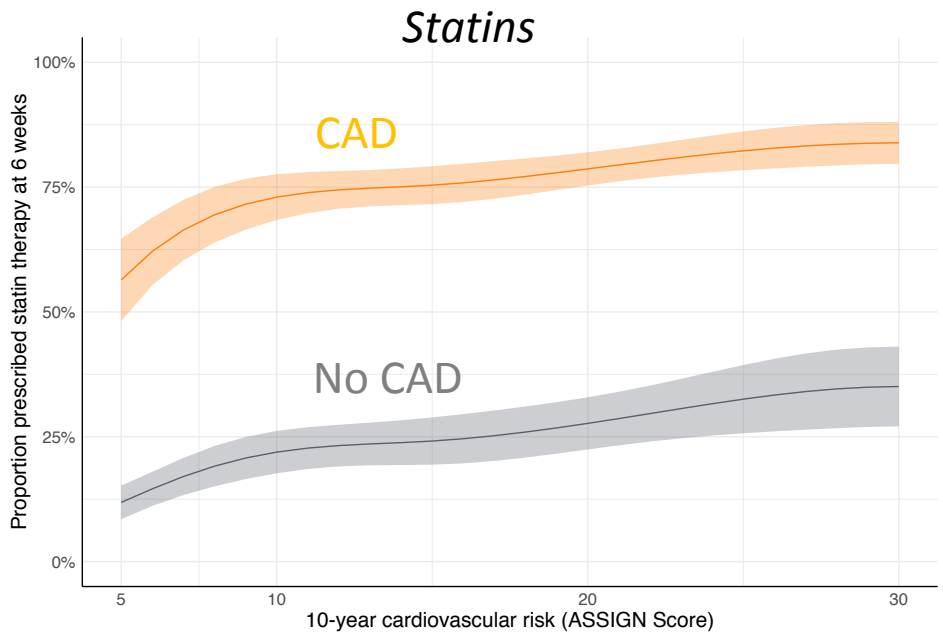


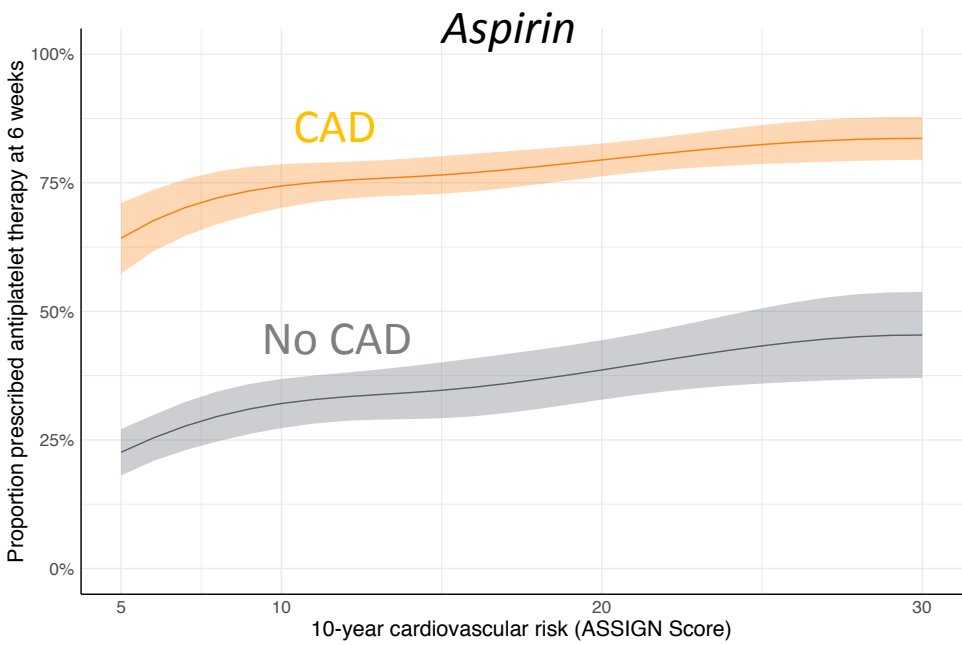
CT: blue
Standard care: red

The Right Patient Gets the Right Treatment

Adamson EHJ Under review

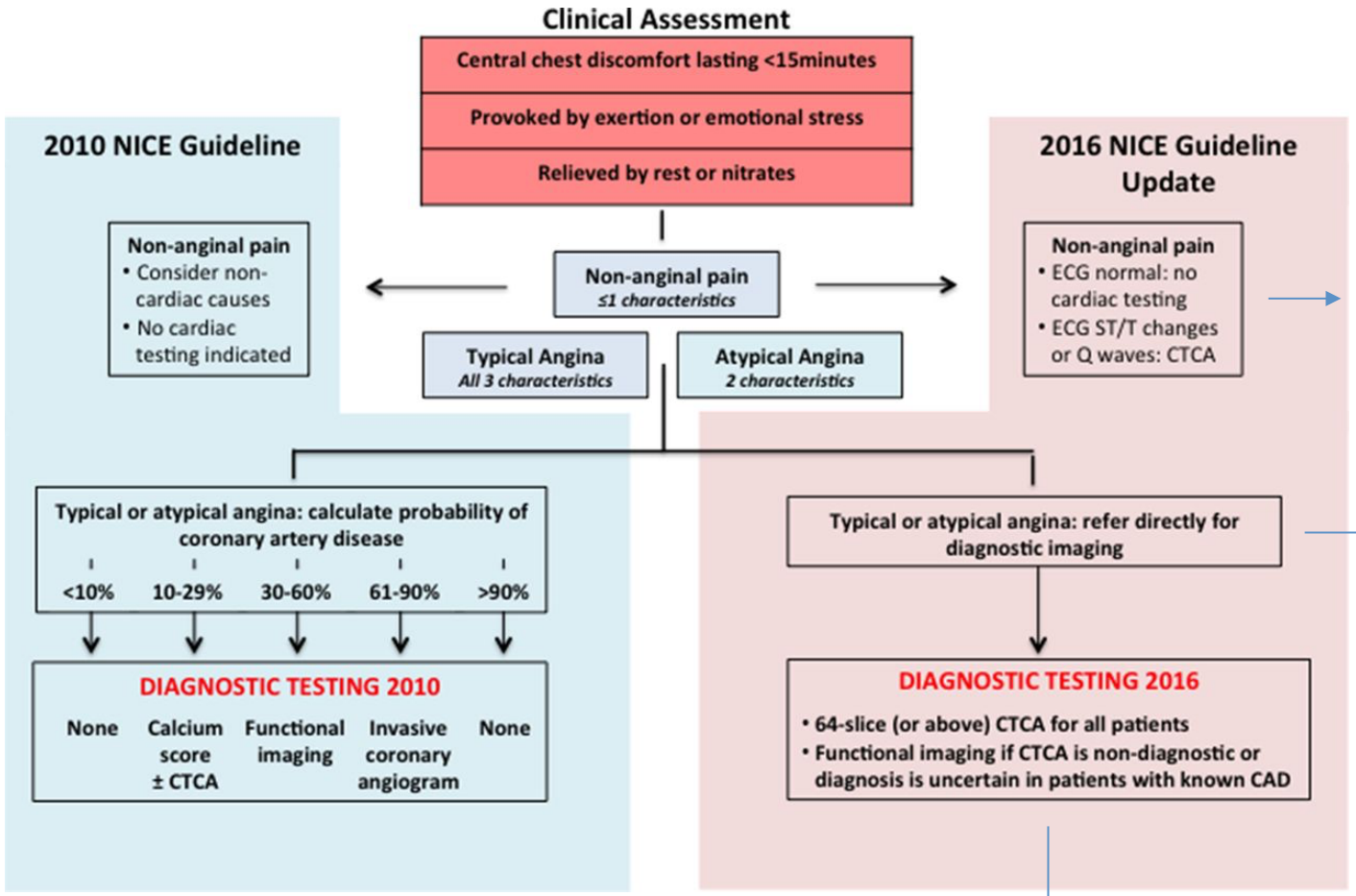
Aspirin & Statin Use in Patient with and without CAD on CT imaging





The Right Patient Gets the Right Treatment

Adamson EHJ Under review



BACK TO CLINIC TO REASSESS SYMPTOMS

Angio if 3VD/LMS or recalcitrant symptoms

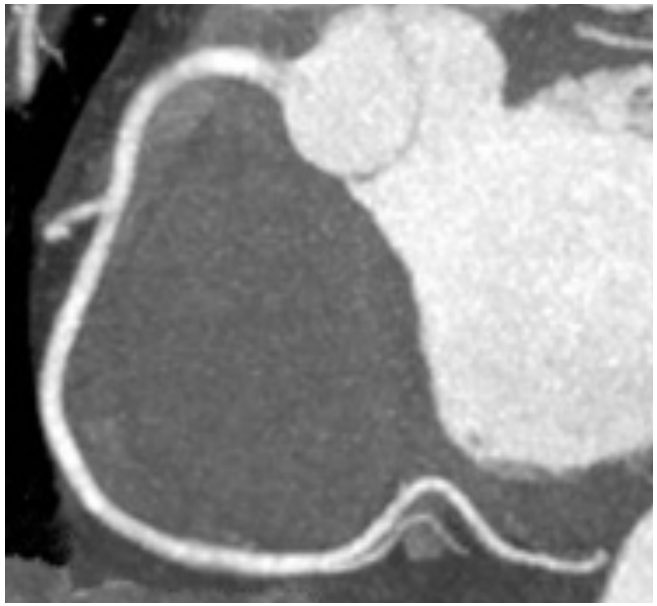
Stop meds if normal coronary arteries

What about CT imaging in the ED?

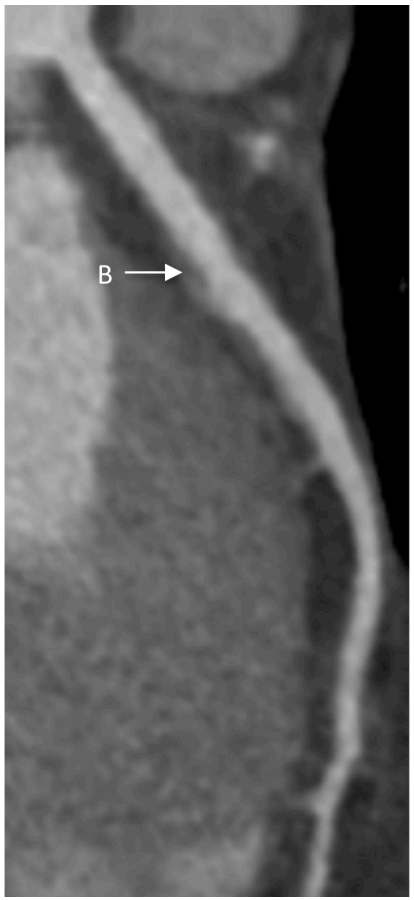
- Have they had a heart attack?
- Do they have plaque?
- Do they have prognostic disease?

Have they had a heart attack?

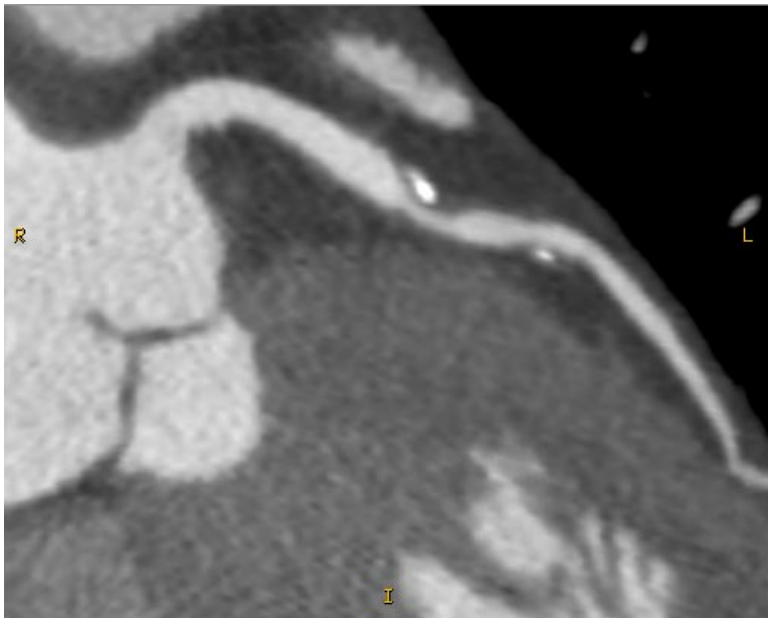
Normal



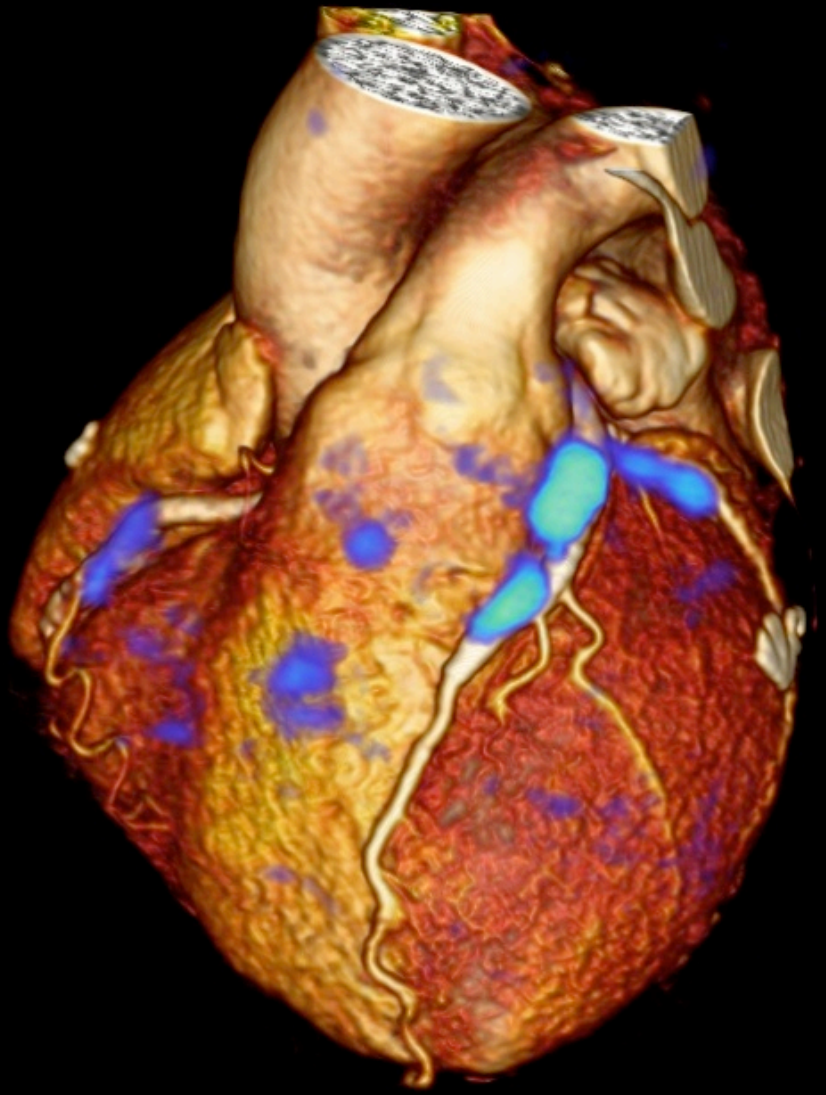
Non-obstructive



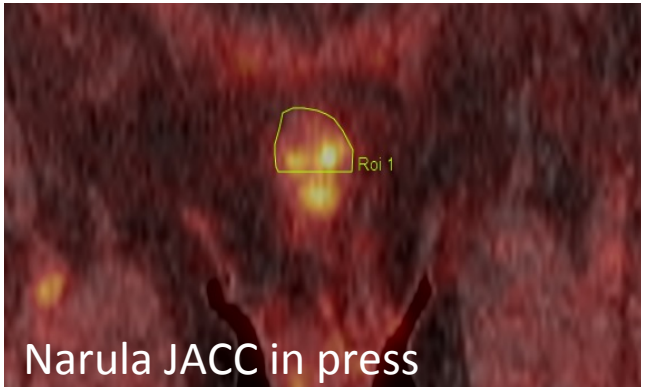
Obstructive



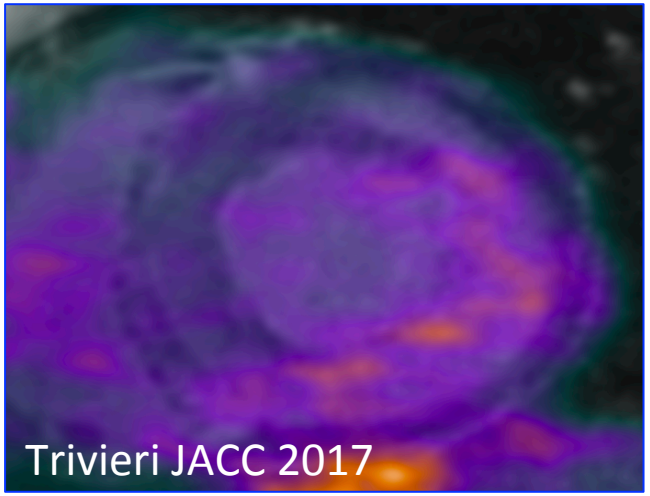
CAN WE BETTER IDENTIFY CULPRIT PLAQUE IN THE CORONARY ARTERIES?

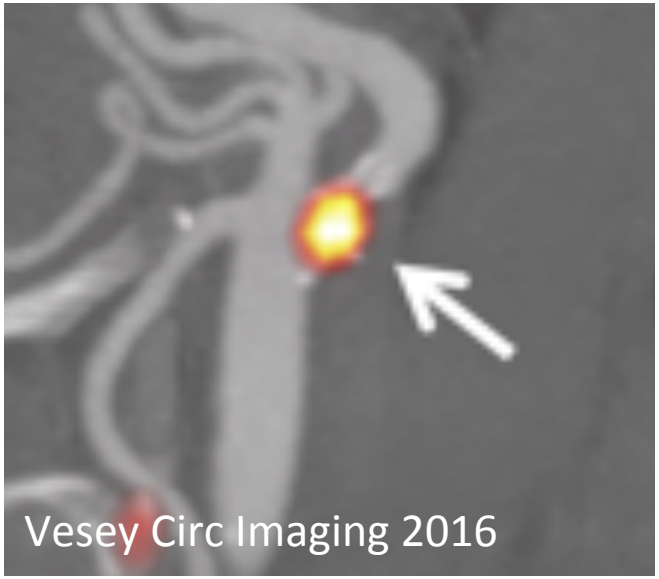


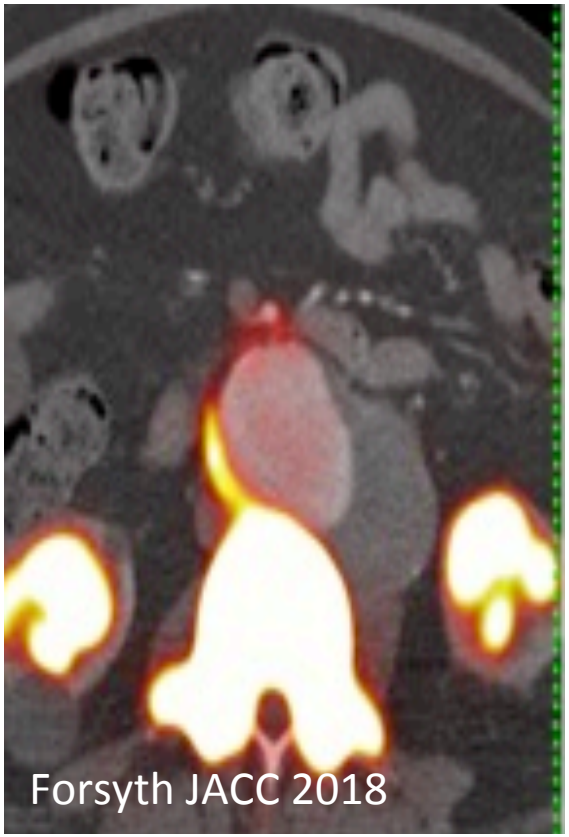
18F-Fluoride PET

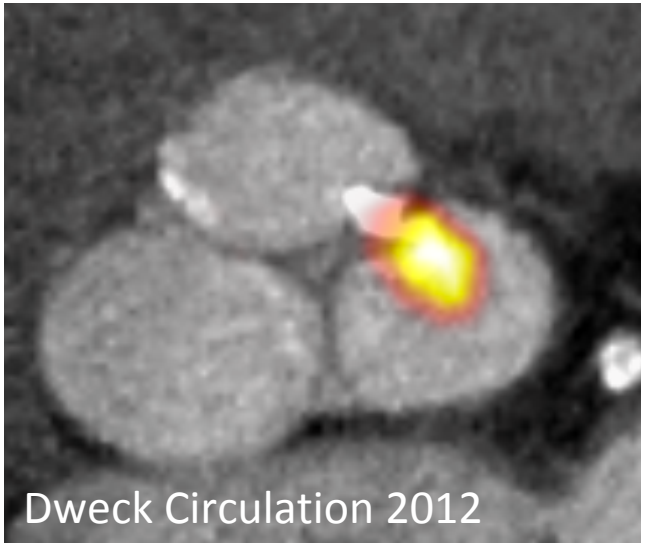


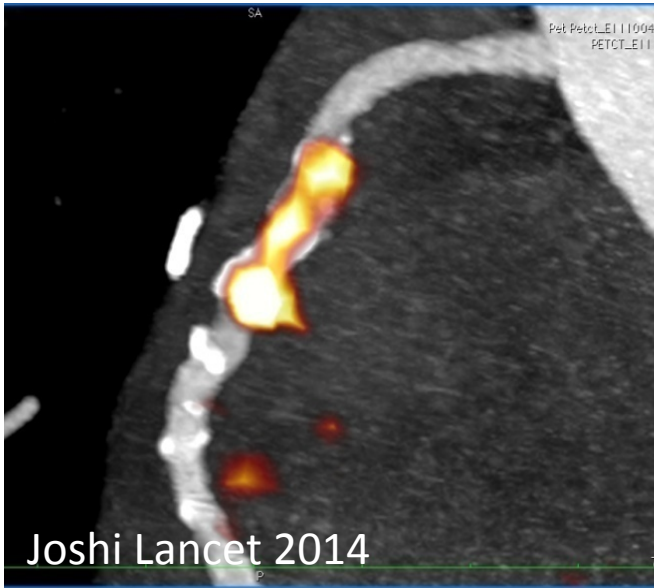
Narula JACC in press

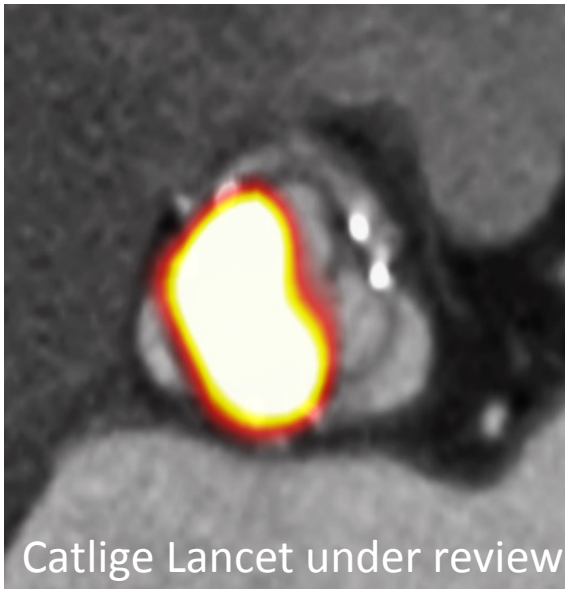

Trivieri JACC 2017

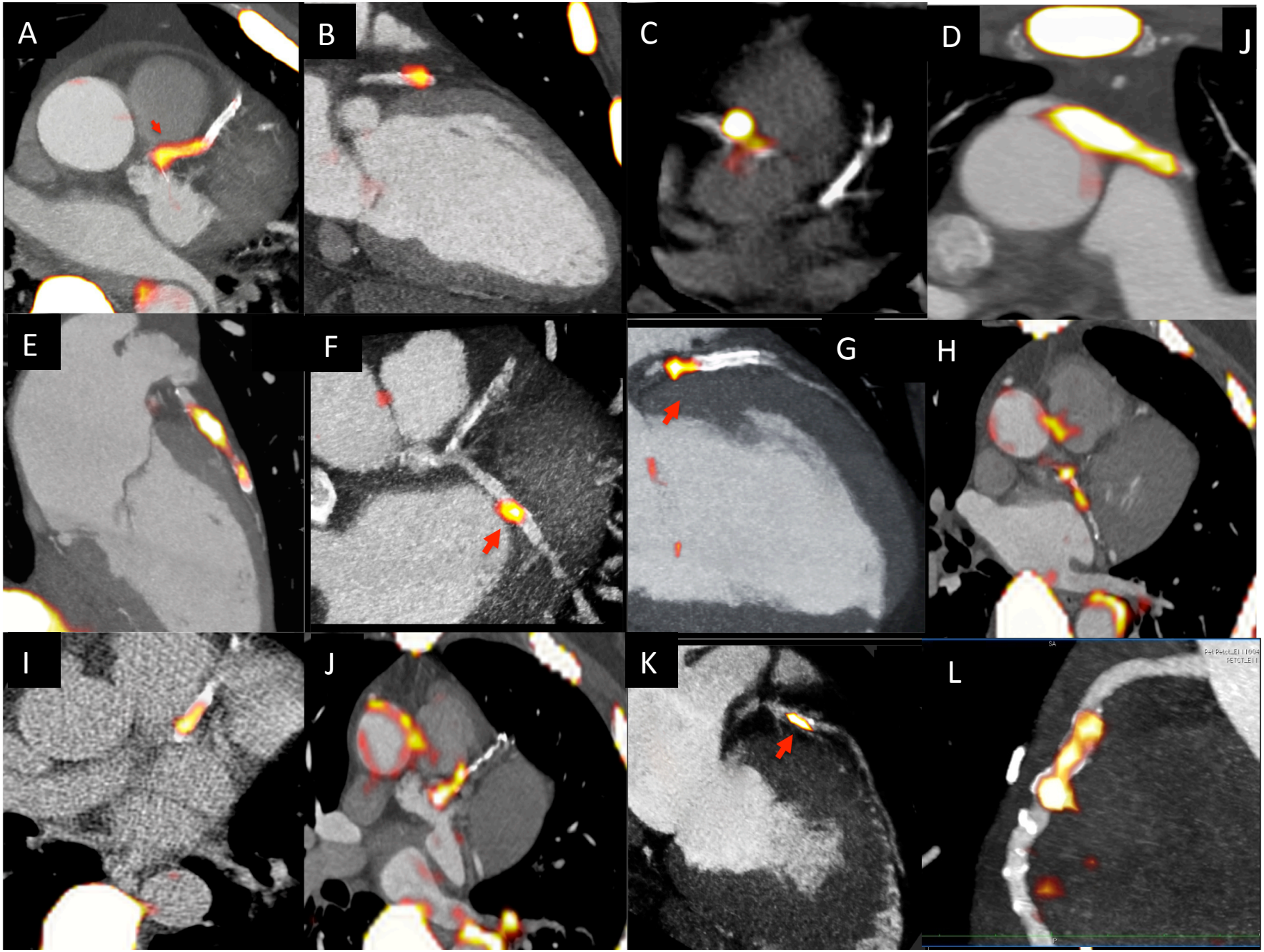

Vesey Circ Imaging 2016


Forsyth JACC 2018


Dweck Circulation 2012


Joshi Lancet 2014


Catlige Lancet under review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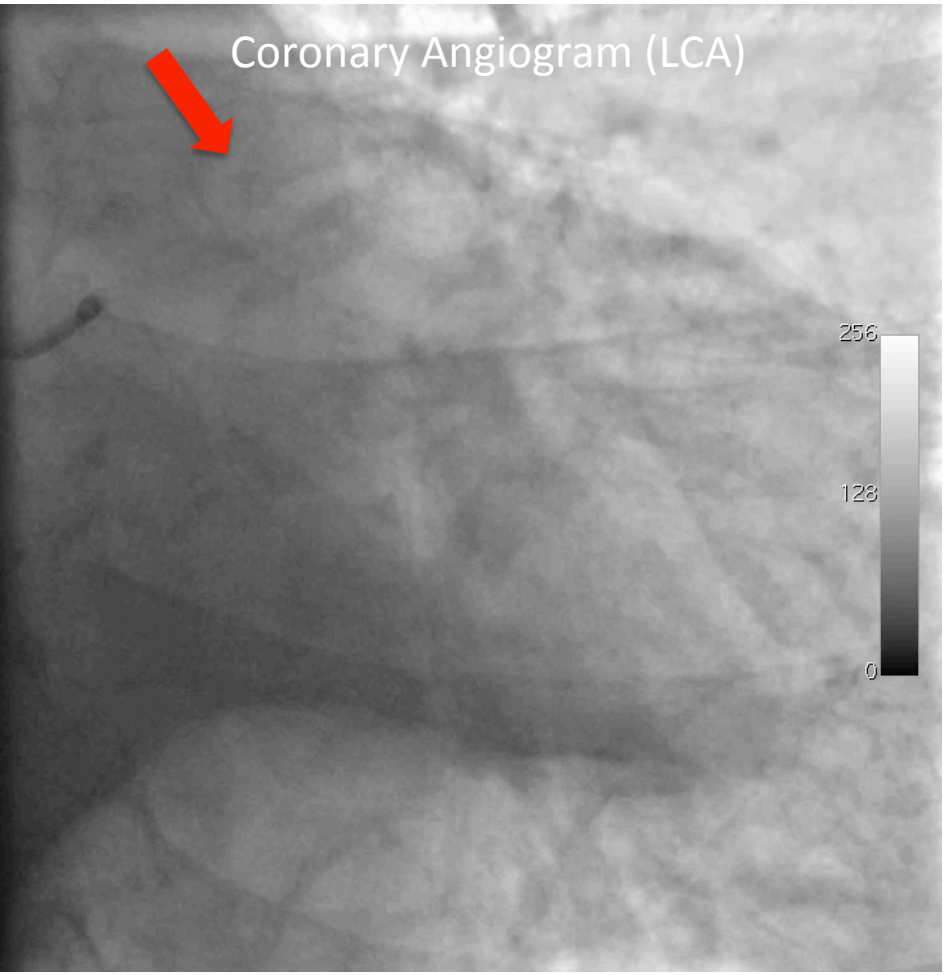
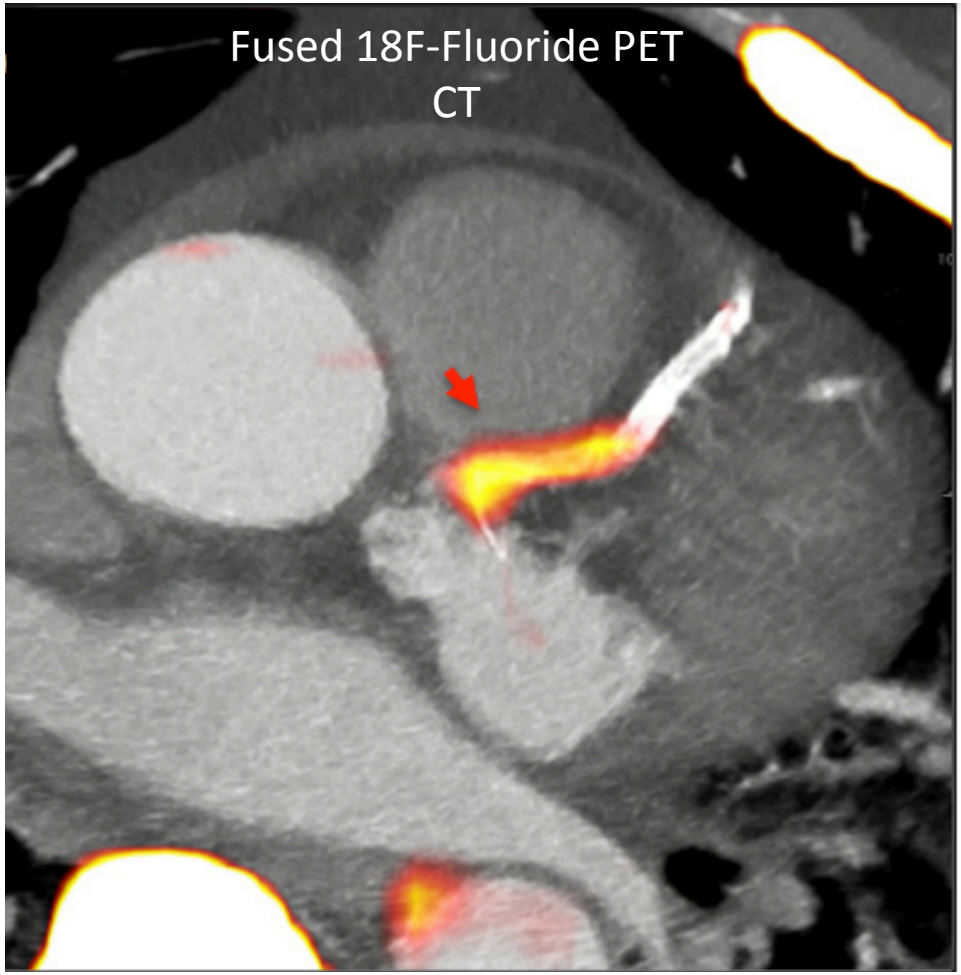
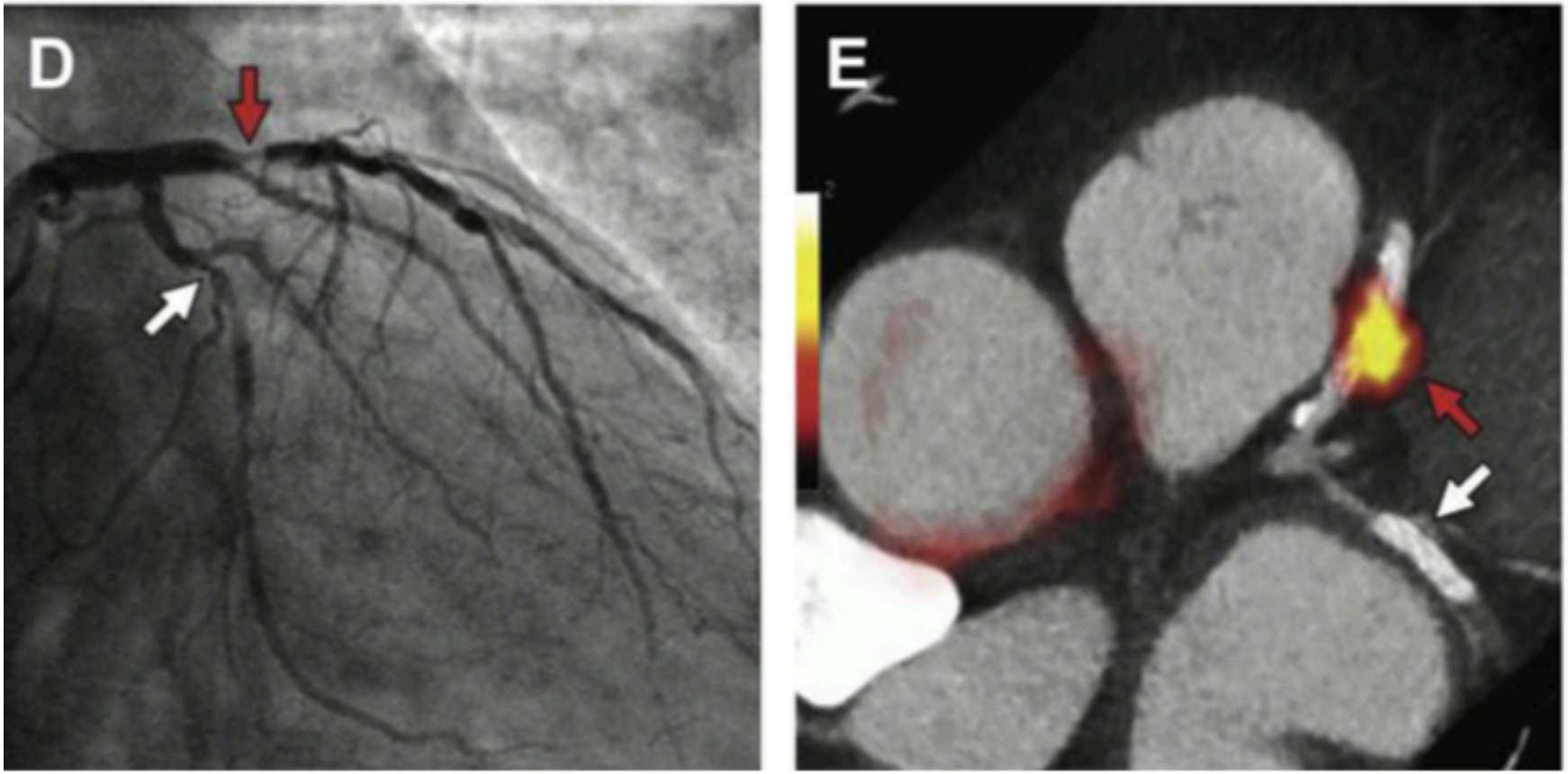
18F-Fluoride post STEMI



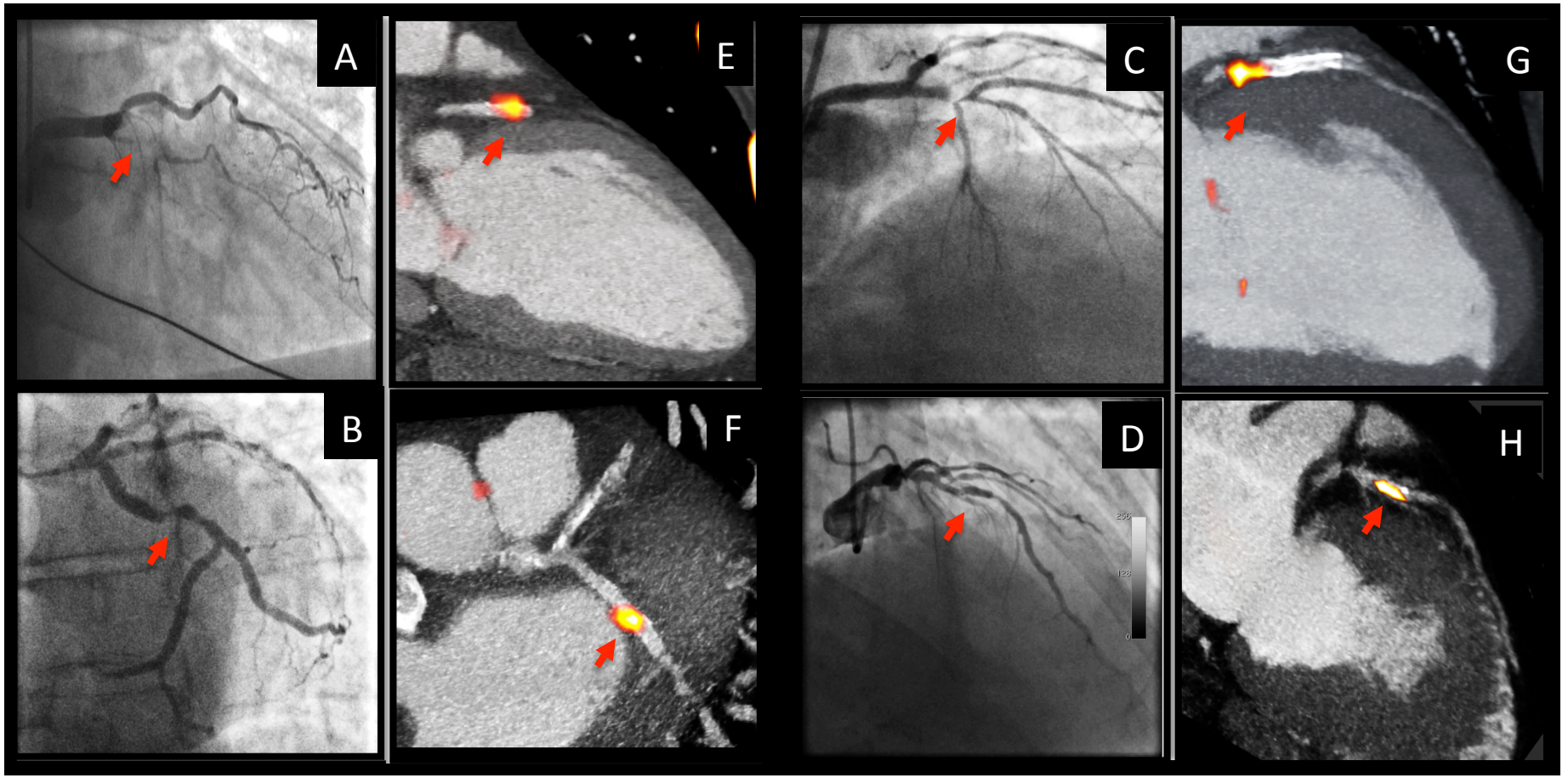


Joshi, Dweck, Newby. The Lancet. 2014

18F-Fluoride post STEMI



Patients with Myocardial Infarction
18F-Fluoride *Identifies Culprit Plaque*



Joshi, Dweck, Newby. The Lancet. 2014

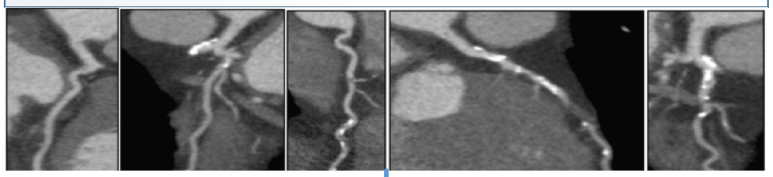
Will 18F-Fluoride Predict Events?

Patients with Myocardial Infarction and Multi-Vessel Disease (n=700)

Baseline ^{18}F-NaF PET, CTCa^{2+} + CT-Coronary Angiogram <21days from MI

Telephone follow-up at 12 monthly intervals until study end

CTCa^{2+} + CT-Coronary Angiogram at 2 years → Disease Progression

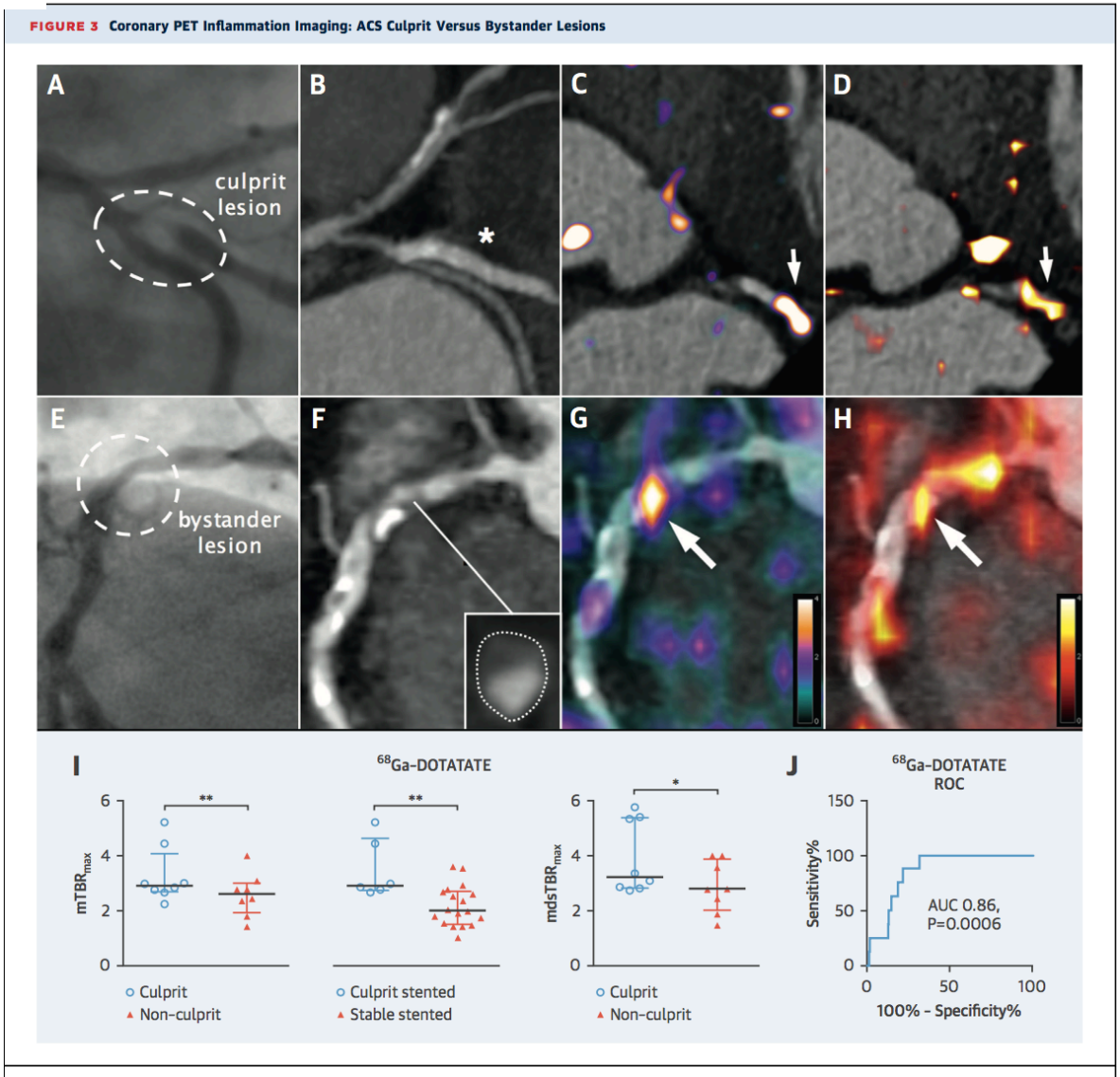


Electronic Health Record Review for 5 years after study end → Clinical Events (Cardiac Death or MI)

The PRE18FFIR Study

New Tracers

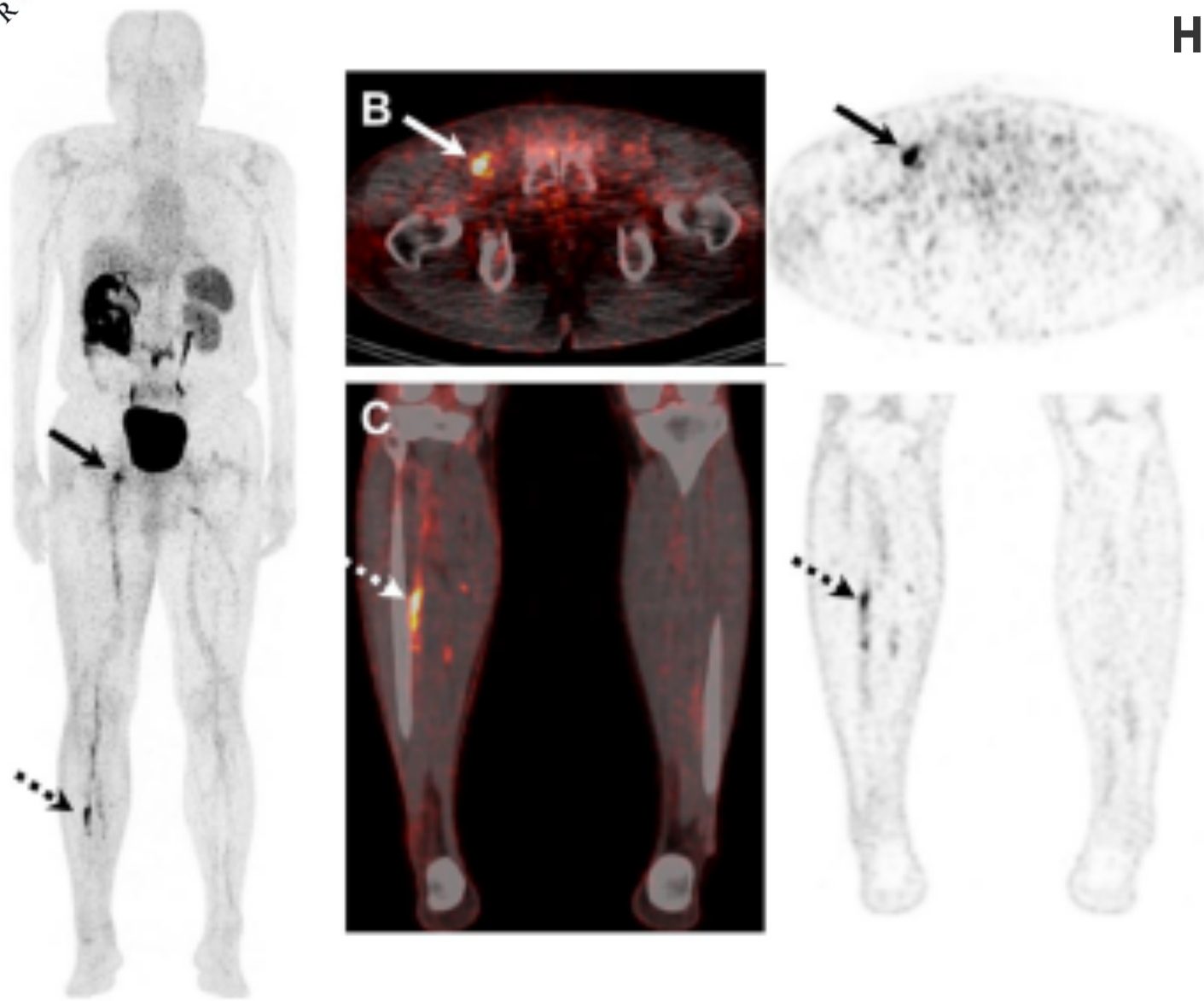
Macrophages
68-Gallium Dotatate



Tarkin JACC 2017

18F-GP1 THROMBUS TRACER

Edinburgh Heart Centre



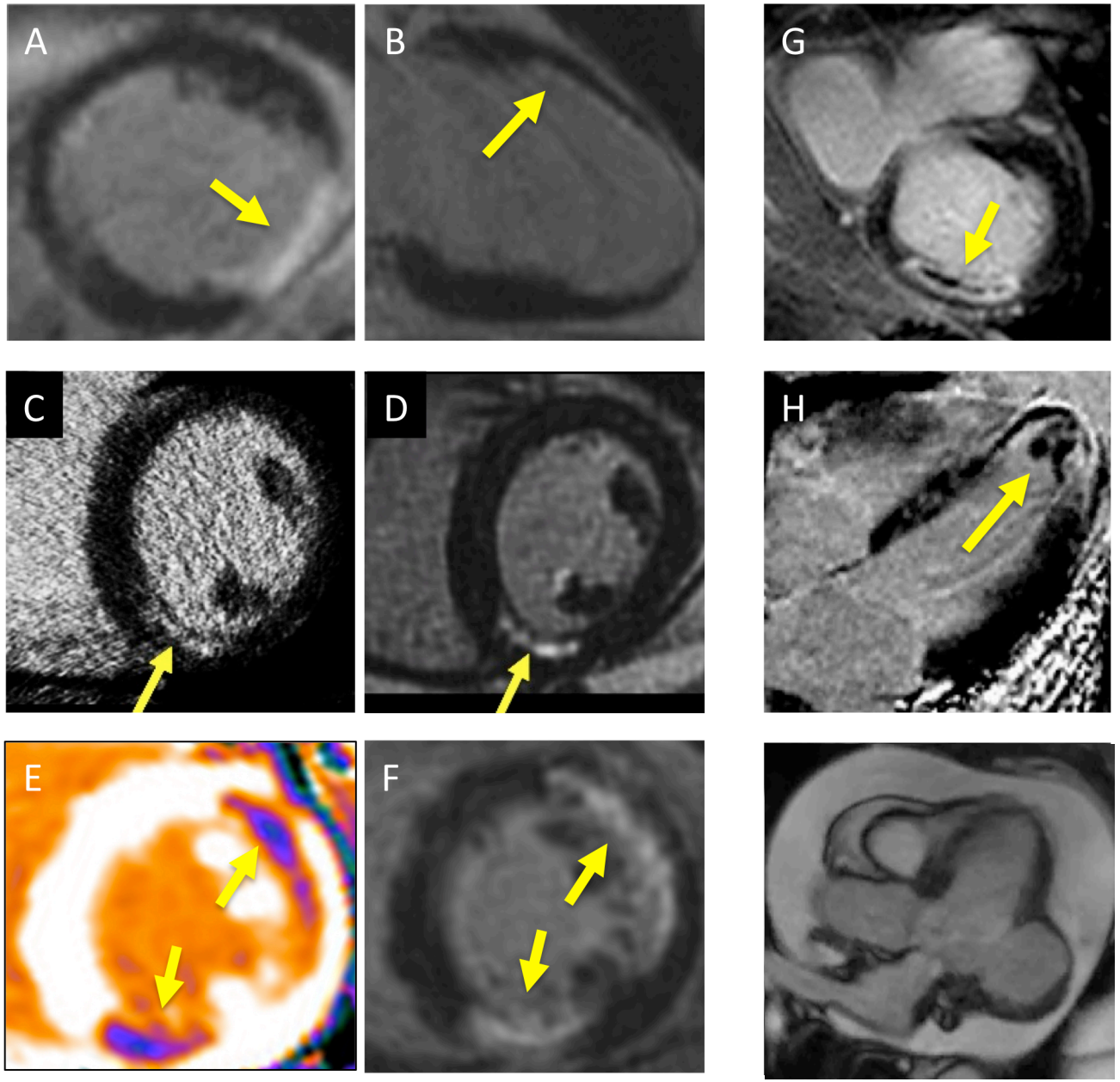
18F-GP1 THROMBUS TRACER

Kim, C., Lee, J. S., Han, Y., Chae, S. Y., Jin, S., Sung, C., et al. (2018). Glycoprotein IIb/IIIa receptor imaging with 18F-GP1 positron emission tomography for acute venous thromboembolism: an open-label, non-randomized, first-in-human phase 1 study. *Journal of Nuclear Medicine : Official Publication, Society of Nuclear Medicine*, jnumed.118.212084. http://doi.org/10.2967/jnumed.118.212084

Cardiac MRI

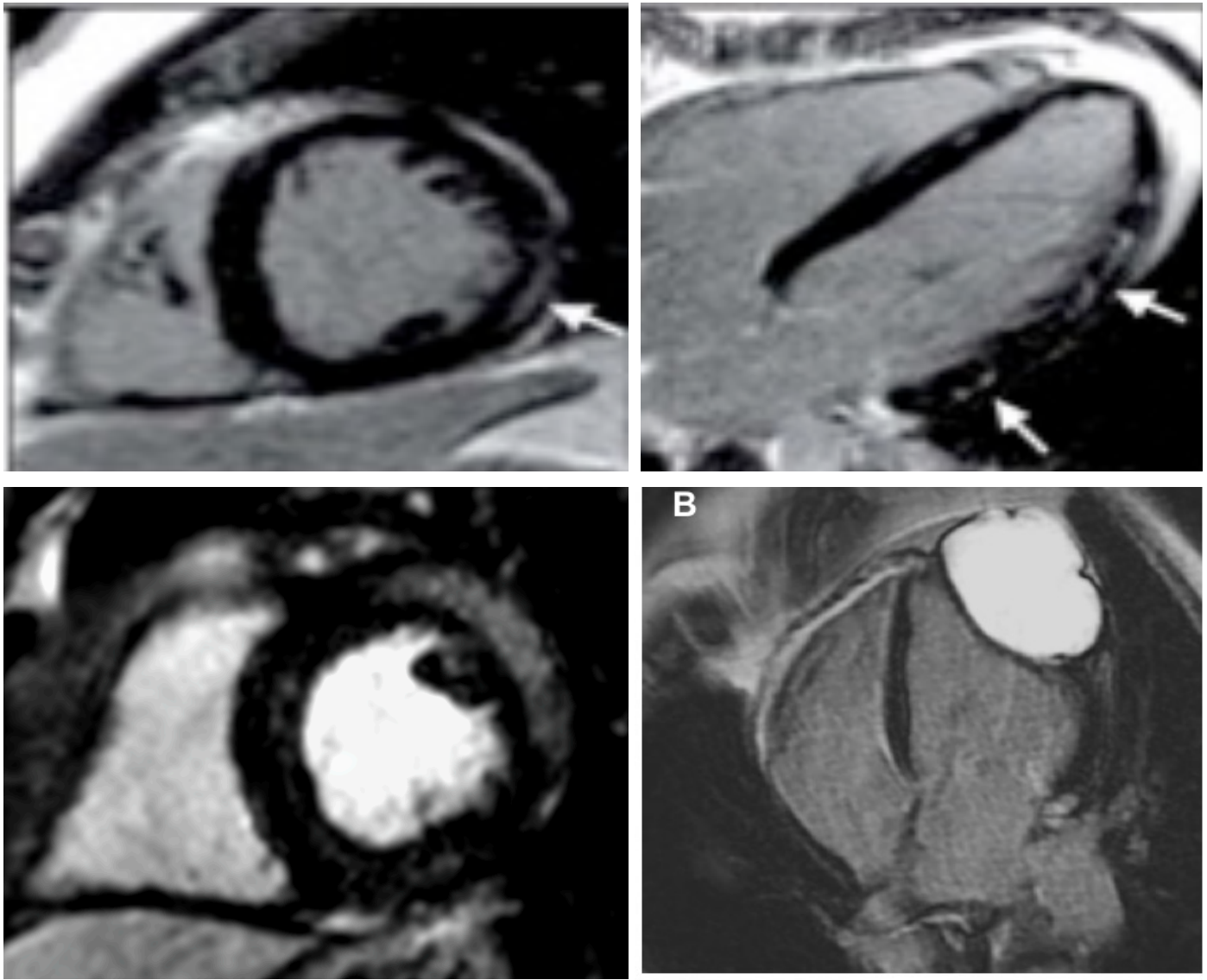
Myocardial scar imaging post MI

Complications post MI



Dweck et al. CT & MR imaging in Ischemic Heart Disease. JACC 2016

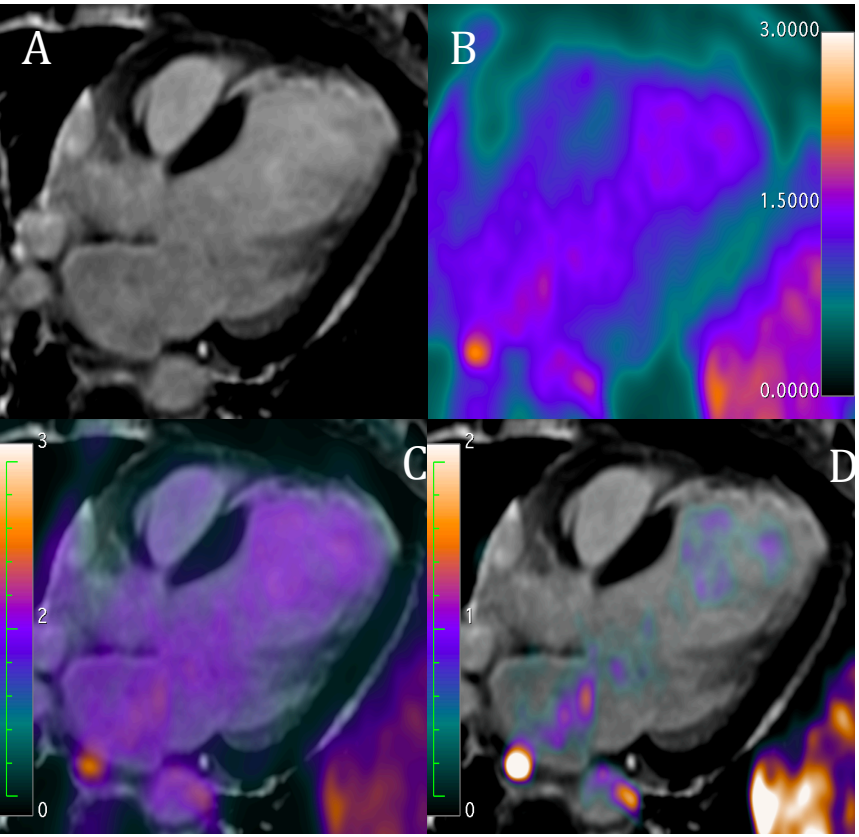
DIFFERENTIAL DIAGNOSIS

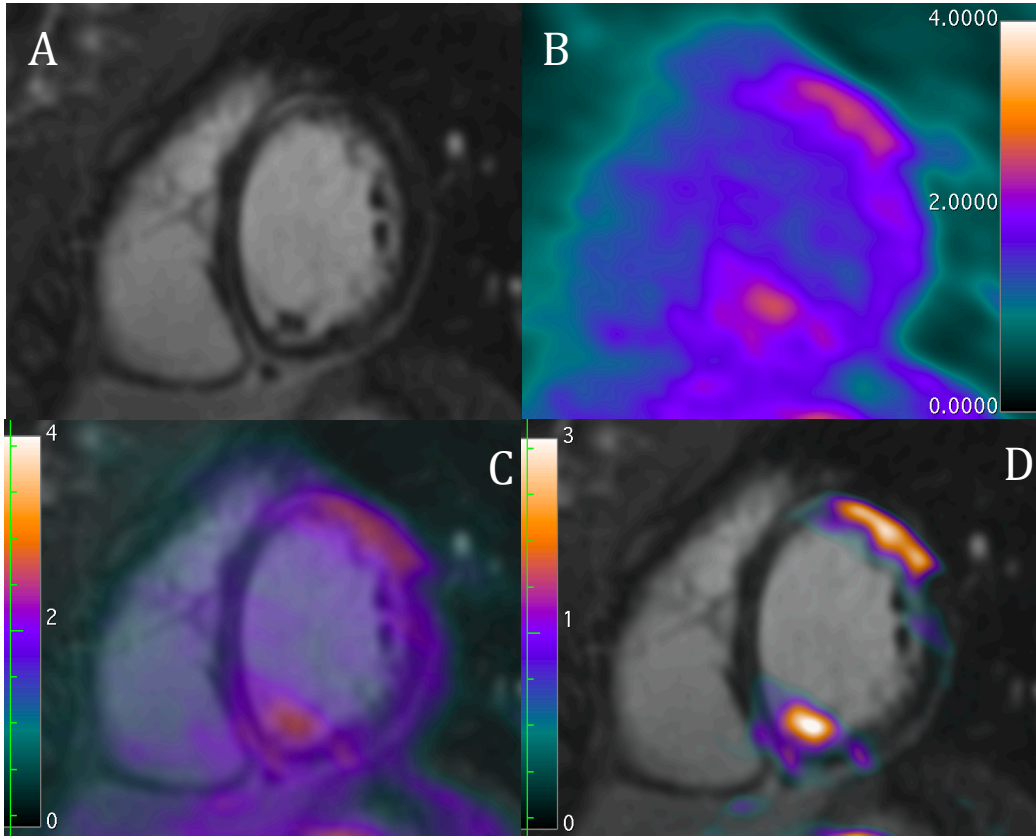


MI vs Myocarditis & Disease Activity

Old Infarct

Acute Myocarditis





Dweck Abgral JACC Imaging 2015

Acknowledgements

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Dr Jack Andrews
Dr Tim Cartlidge
Dr Chris Tuck
Dr Alastair Moss
Dr Phil Adamson

University of Cambridge
Dr James Rudd
Dr Anthony Davenport
Prof Martin Bennett
Dr Agnese Irkle
Dr Patrick Calvert

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- Extension to Clinical Research Training Fellowship (FS-10/026)
- BHF Clinical Research Training Fellowship (FS/12/84/29814)
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- BHF Programme Grant (RG/16/10/32375).
- BHF Centre of Research Excellence Award.

The Chief Scientist Office
Wellcome Trust
Sir Jules Thorn Award for Biomedical Research 2015

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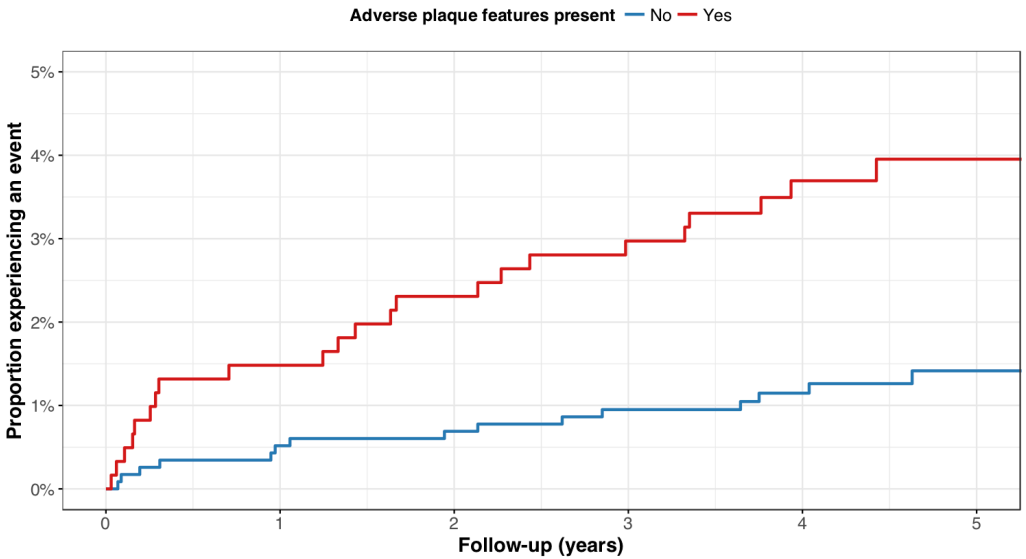
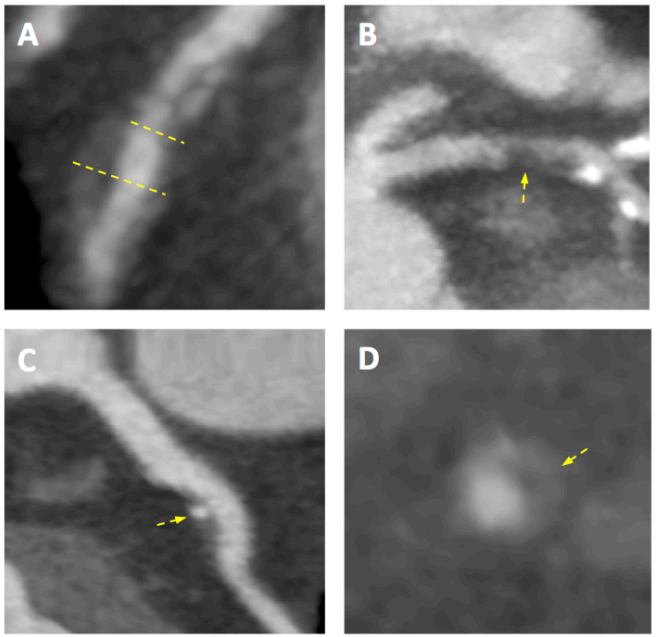
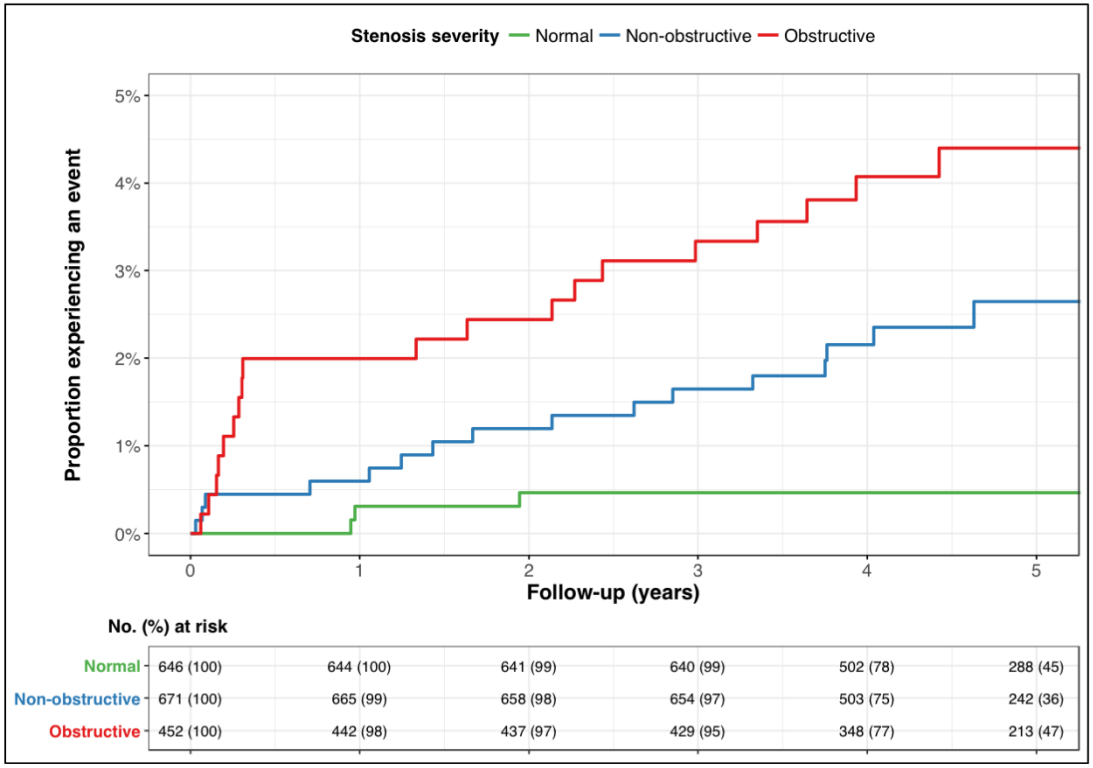
High Risk Plaque



Adverse plaque features present						
No	1161 (100)	1153 (99)	1146 (99)	1141 (98)	886 (76)	488 (42)
Yes	608 (100)	598 (98)	590 (97)	582 (96)	467 (77)	255 (42)

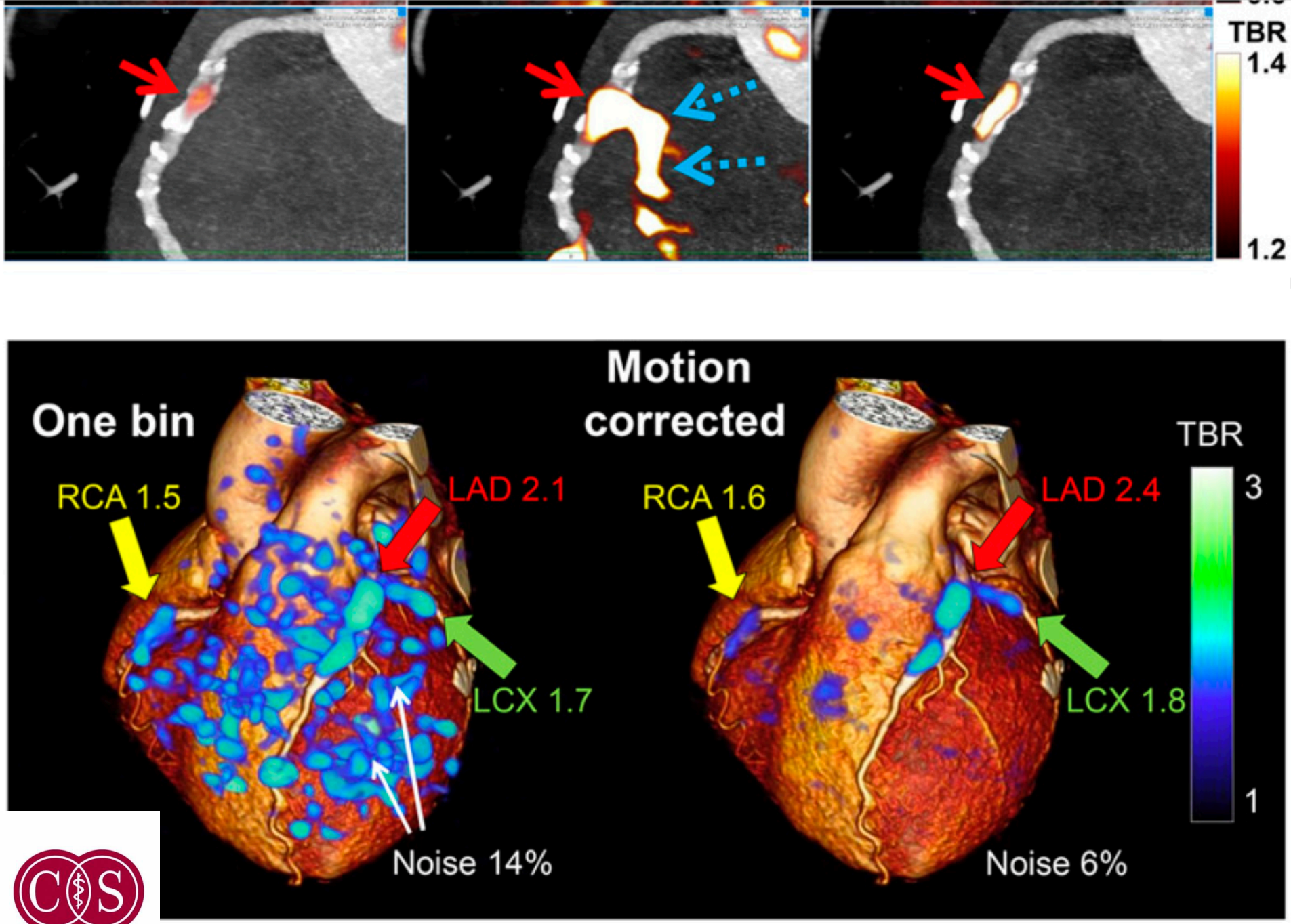


Obstructive & Non-obstructive Plaque



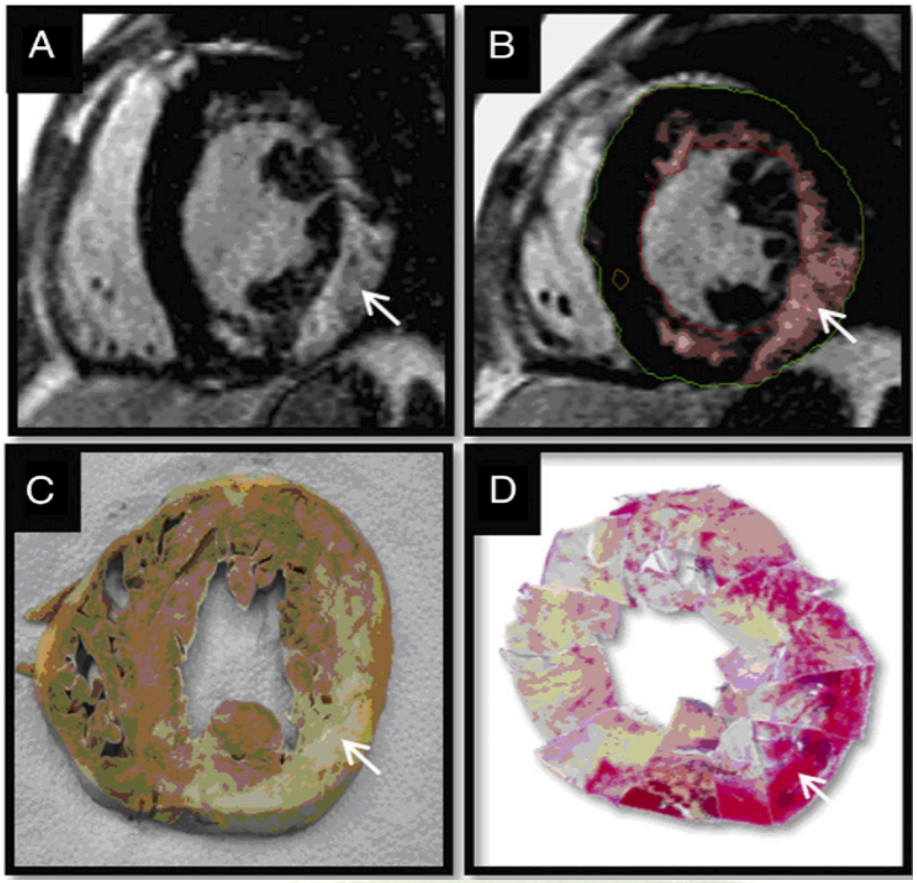
Plaque Burden is the Only Independent Predictor

	Univariable analysis	Multivariable analysis [#]
Adverse plaque *	3.00 (1.60, 5.63) p=0.001	1.15 (0.54, 2.47) p =0.714
Coronary Artery Calcium Score **	1.99 (1.49, 2.68) p <0.001	1.72 (1.16, 2.56) p=0.007
Obstructive coronary artery disease	3.35 (1.81, 6.19) p <0.001	1.36 (0.63, 2.95) p=0.431
Male Gender	2.12 (1.06, 4.24) p=0.033	1.21 (0.58, 2.53) p=0.610
Cardiovascular Risk score [$]	1.00 (0.98, 1.03) p=0.861	-



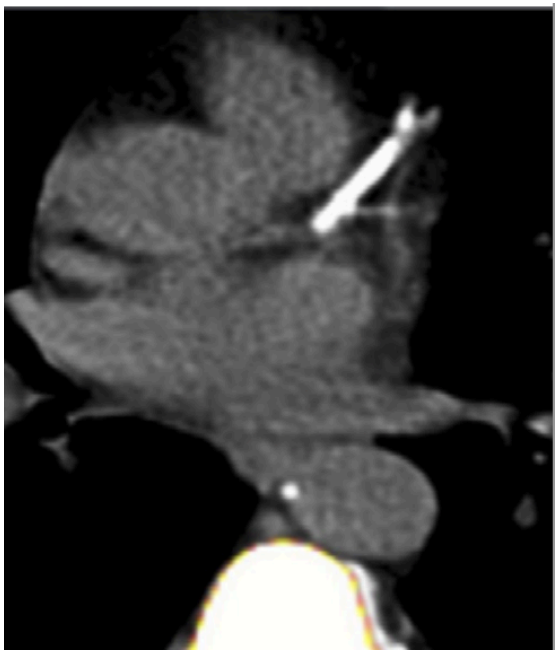
Rubeaux JNM 2016

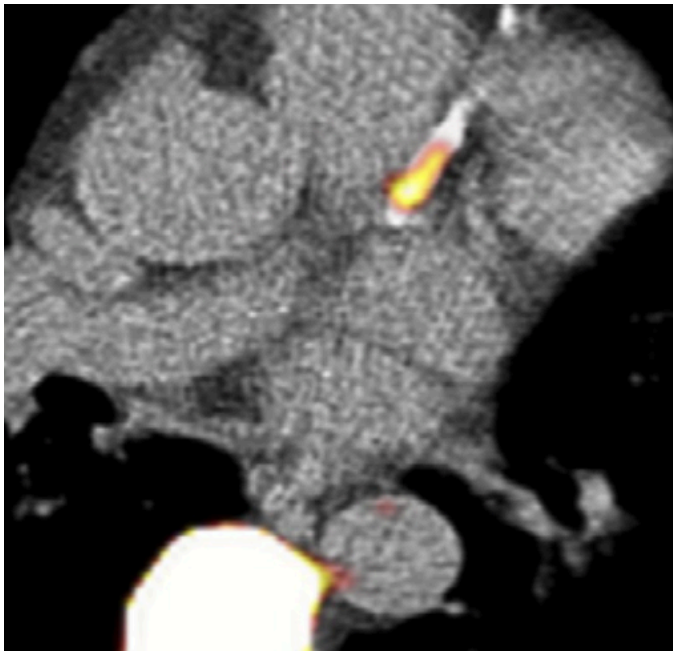
Detecting Scar in Heart Muscle



How Will We Use It?

- In patients with advanced atheroma
- Differentiating patients with stable burnt out disease and patients with active atheroma

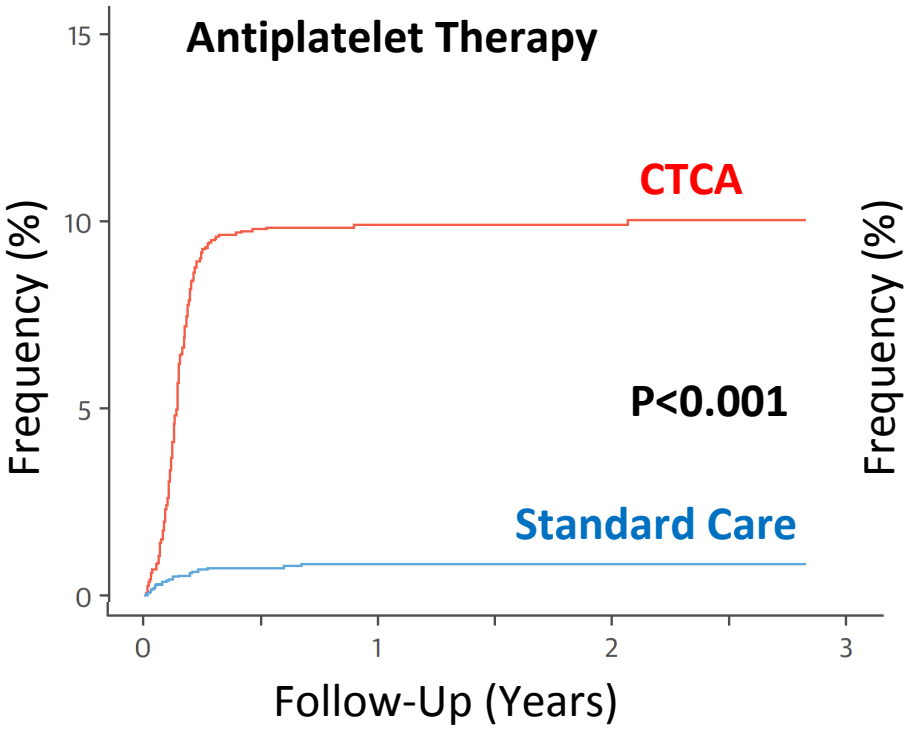


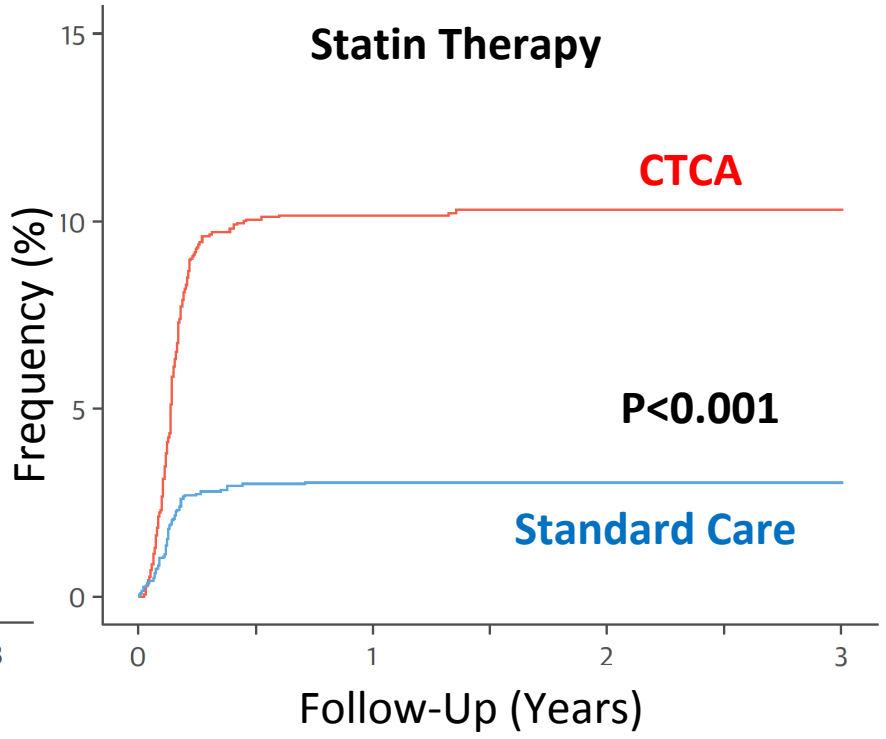


40% patients with calcium score >1000 have normal 18F-fluoride uptake

Dweck JACC 2012

National Prescribing Data
Anti-platelet and Statin Therapy





Median 46 [30-64] days from clinic to prescription

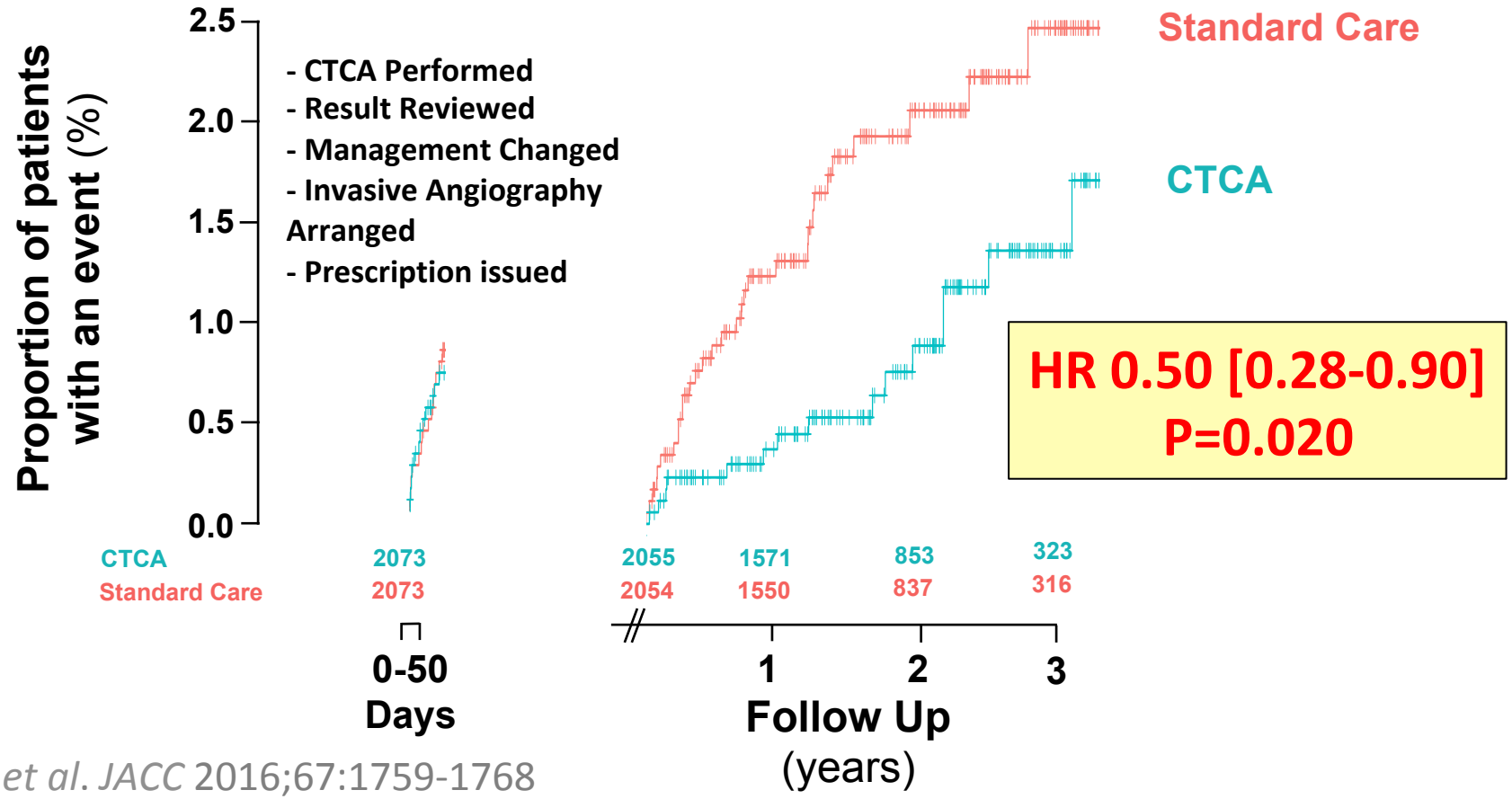
Median 50 [30-70] days from clinic to prescription

Williams *et al*. *JACC* 2016;67:1759-1768

CHD Death and Non-fatal MI

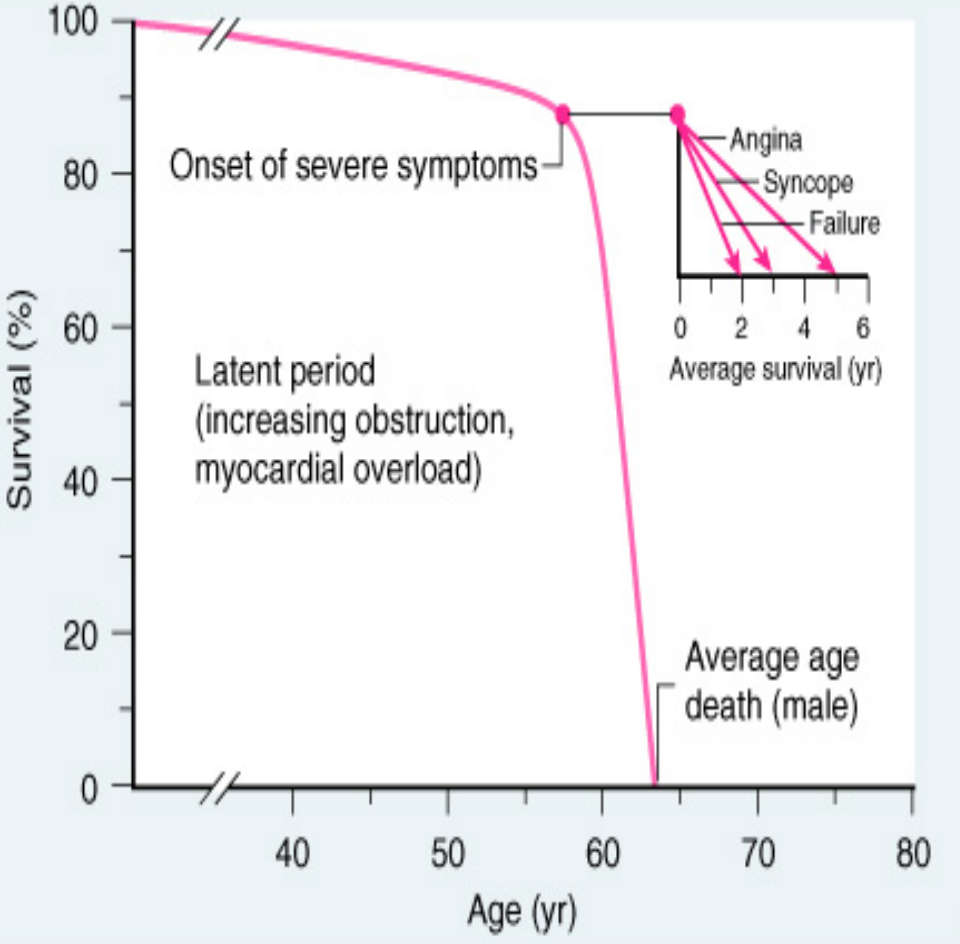
Post-hoc 50-Day Landmark Analysis

Implementation Delay	Impact of Alterations in Therapy

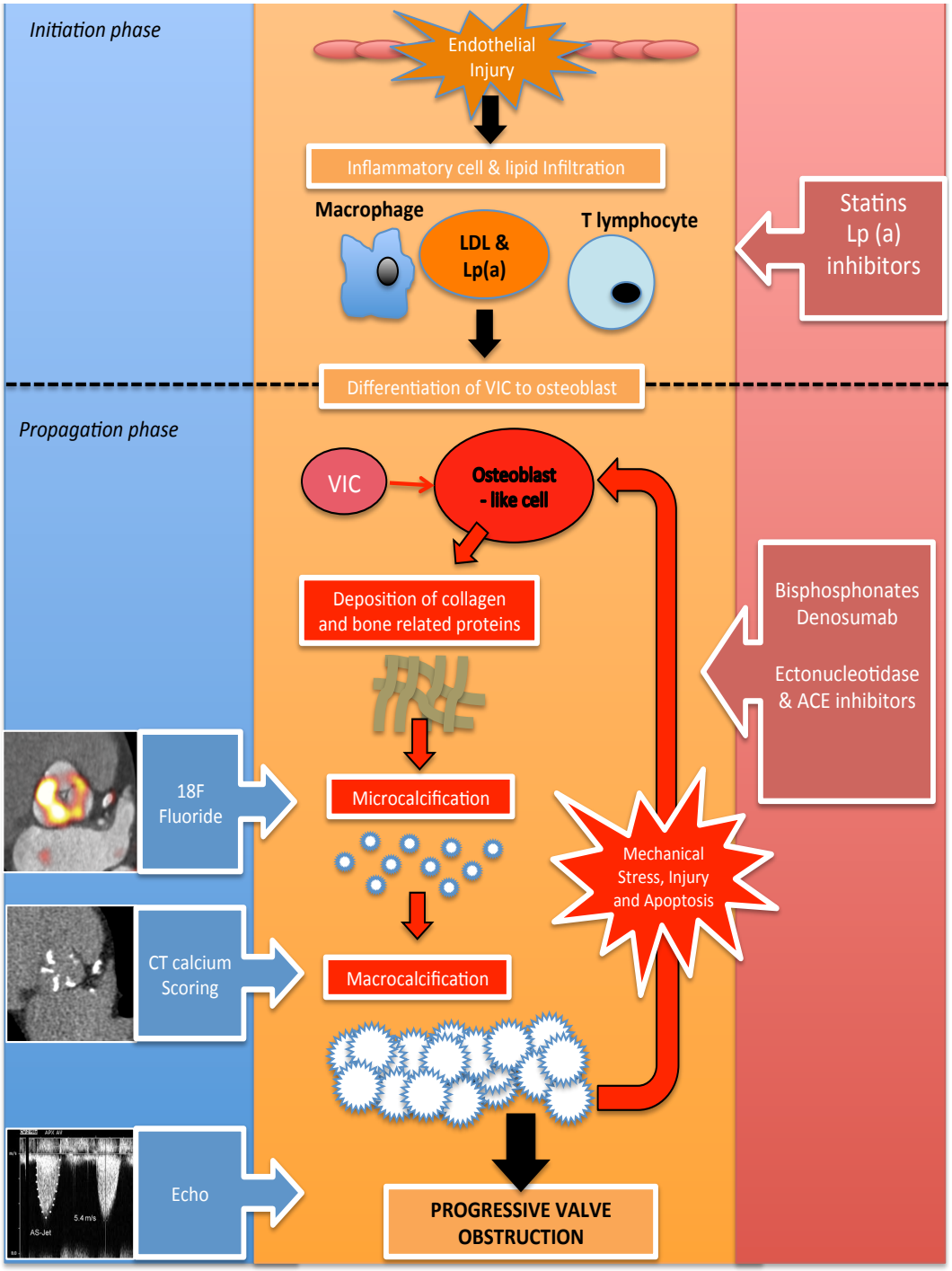


Williams *et al*. *JACC* 2016;67:1759-1768

Symptoms & Aortic Stenosis



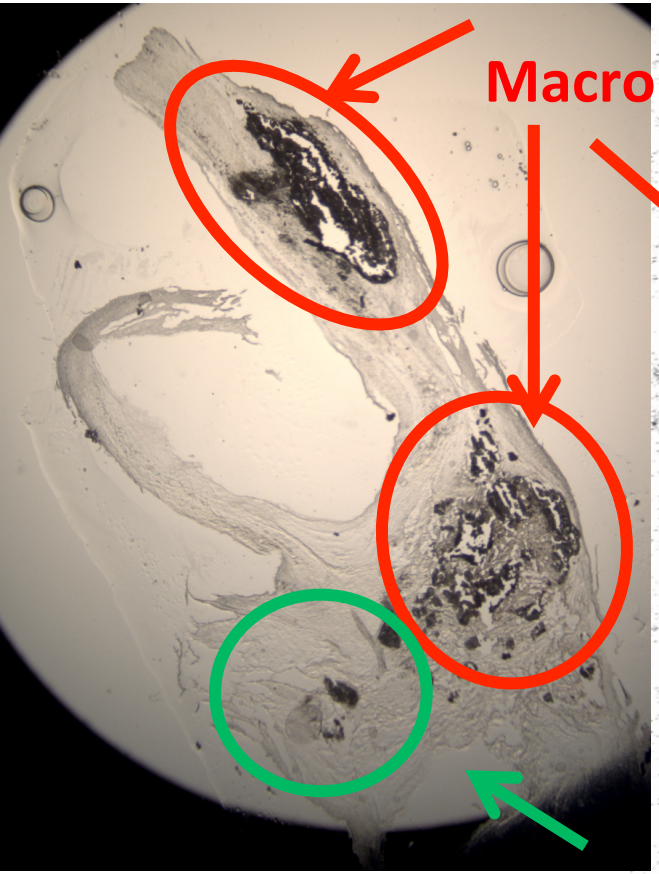
Ross J Jr, Braunwald E: Aortic stenosis. Circulation 38[Suppl

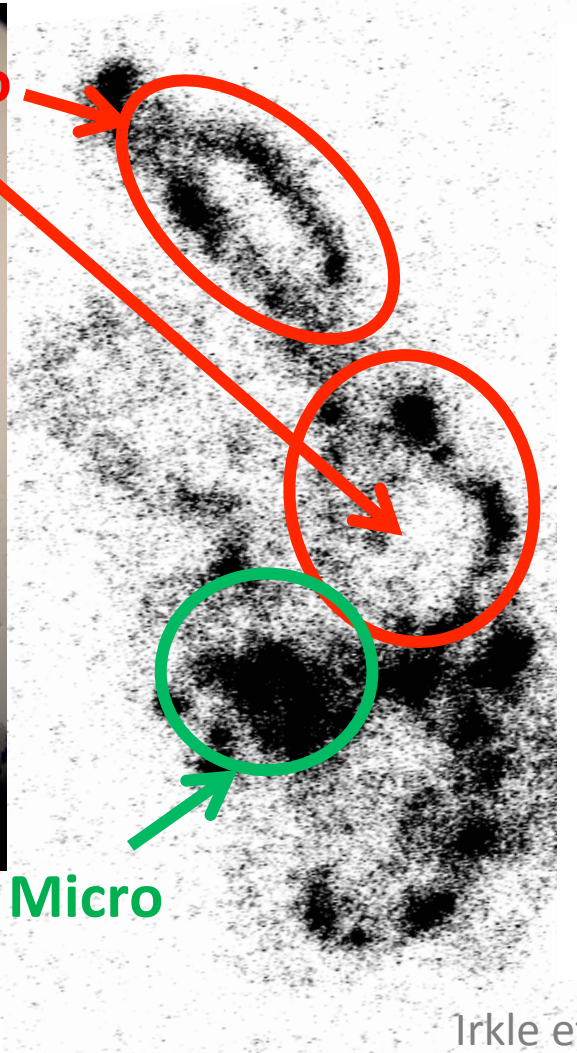


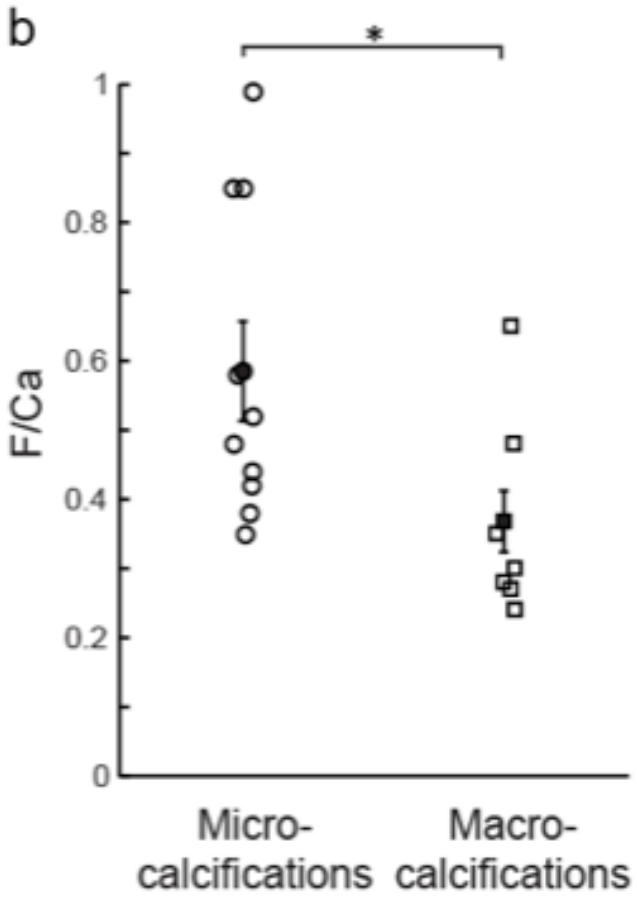
Pawade, Newby, Dweck. Calcification in aortic stenosis: the skeleton key JACC. 2015

$^{18}F^-$Fluoride Preferentially Binds areas of Microcalcification

Light Microscopy **Autoradiography**







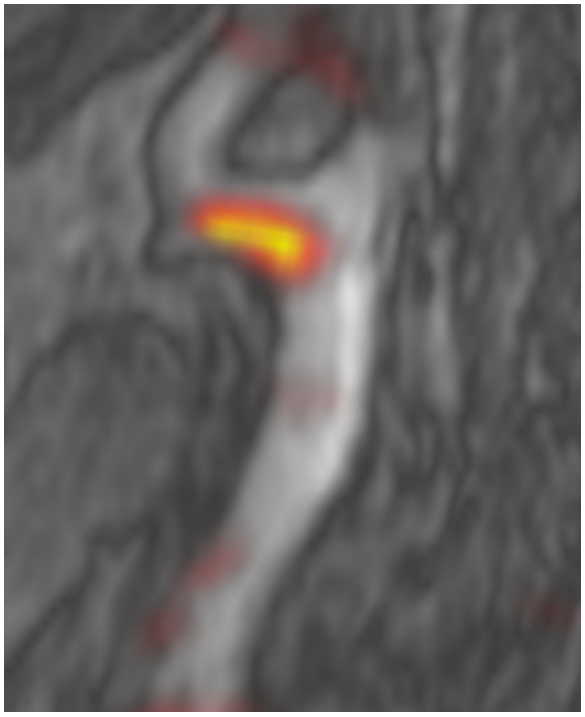
Irkle et al. Nature Communications. 2015

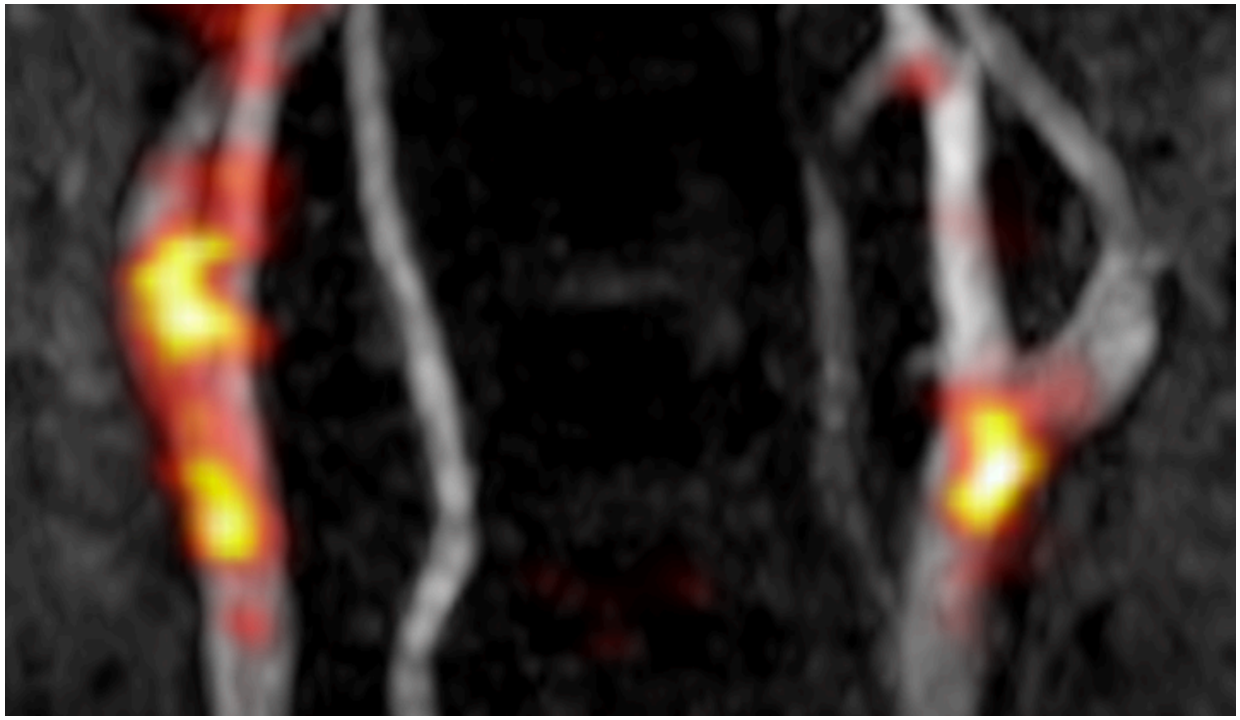
Why MR PET not PET CT?

- What is MR good at?
  - Myocardial disease
  - Carotid atherosclerotic plaque

- Low radiation doses
  - Multi-time point imaging (e.g. drug trials)
  - Multiple different tracers
  - Multiple remote organ systems

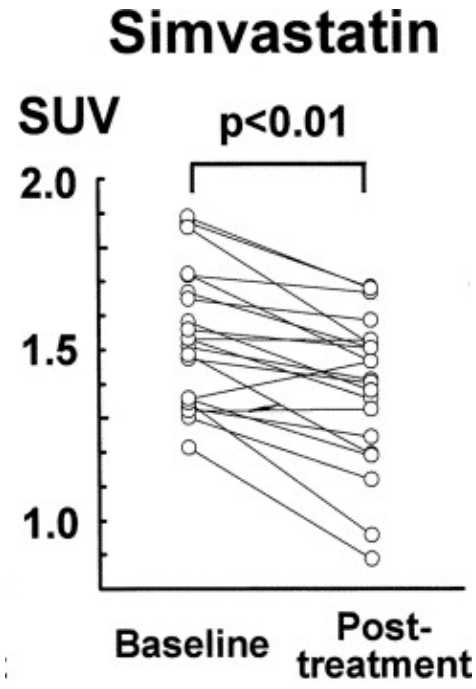
Carotid FDG PET/MR



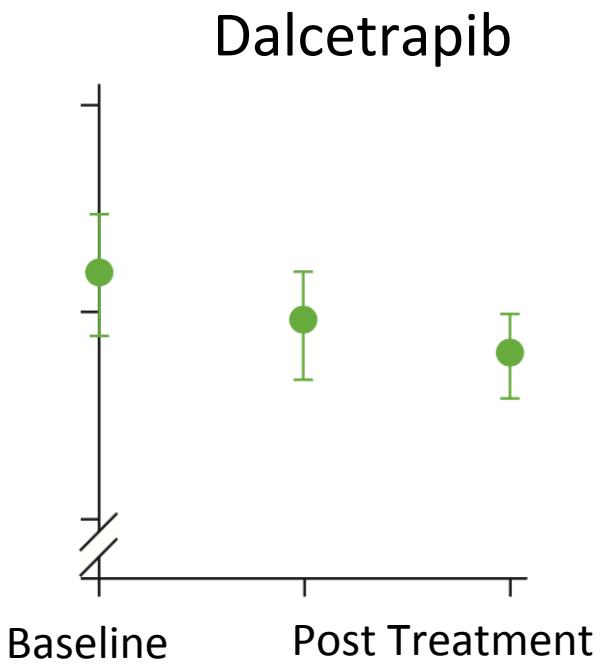


Phase 2 Drug Trials

PET/MR 1 → NEW THERAPY → PET/MR 2



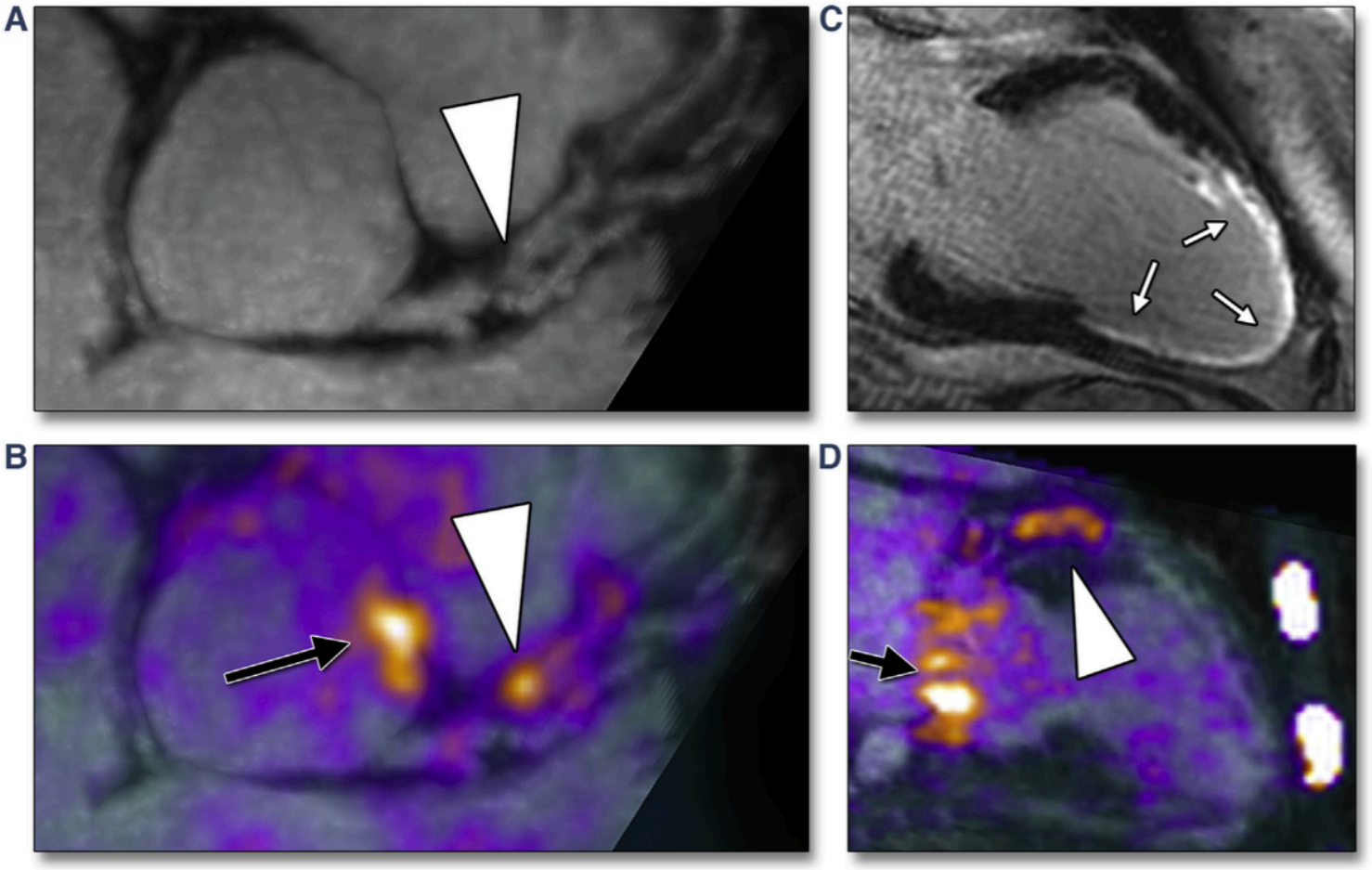
Tahara et al JACC 2006



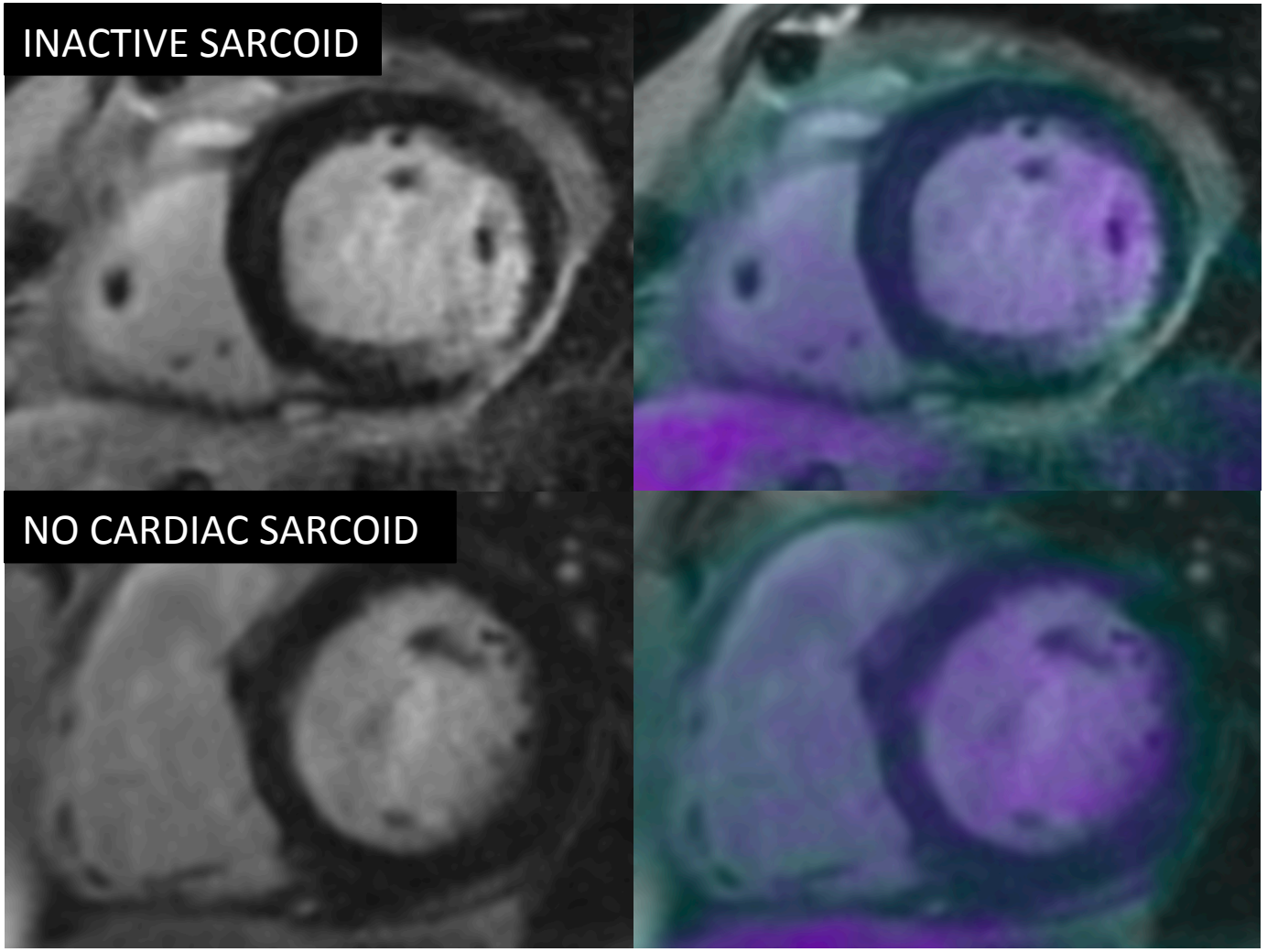
Fayad et al. Lancet 2011

Low Radiation PET/MR Imaging

FIGURE 3 Examples of Increased Coronary ^{18}F-Sodium Fluoride Uptake on Positron Emission Tomographic/Magnetic Resonance Images

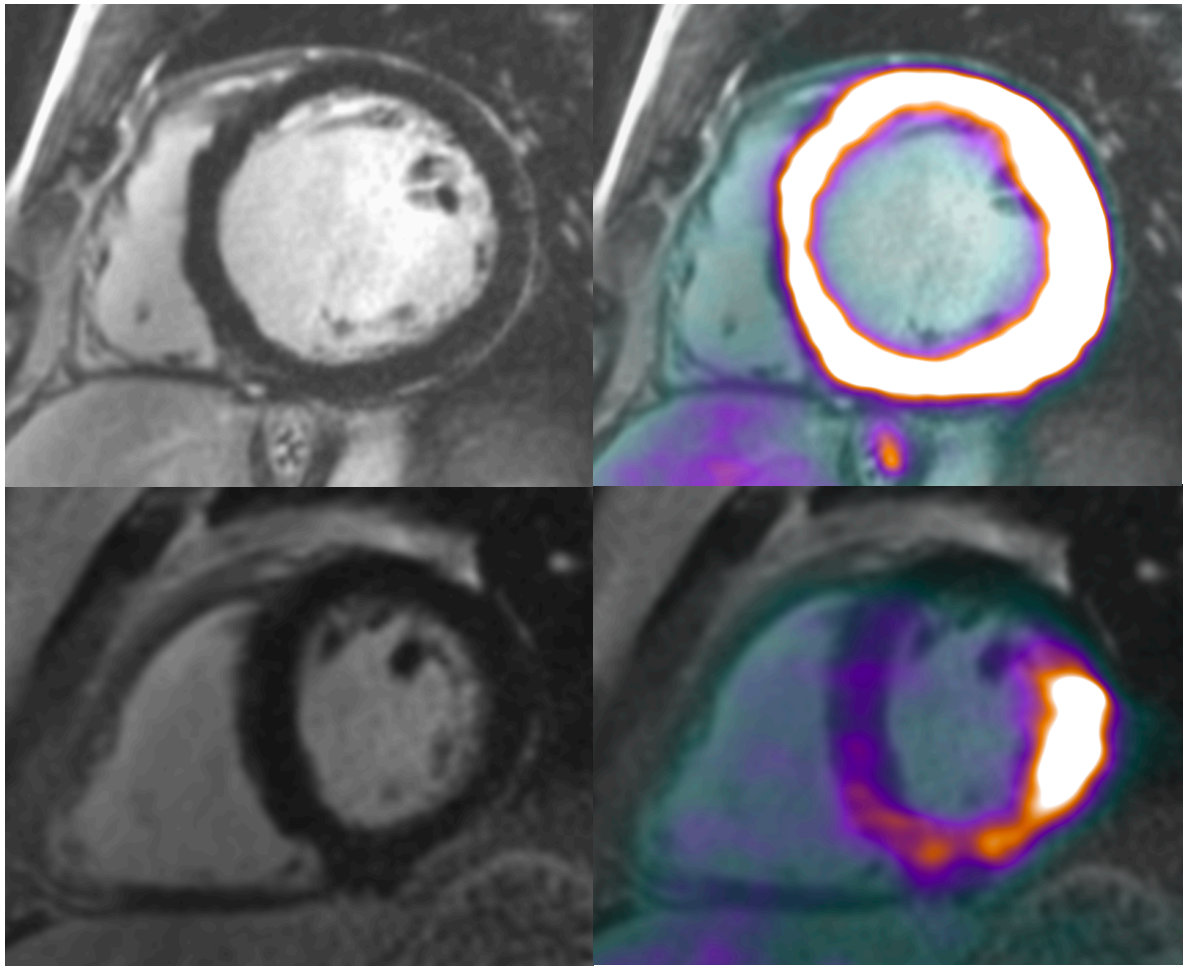


Robson, Dweck, Fayad JACC Imaging 2017



Dweck JACC CVS Imaging 2017

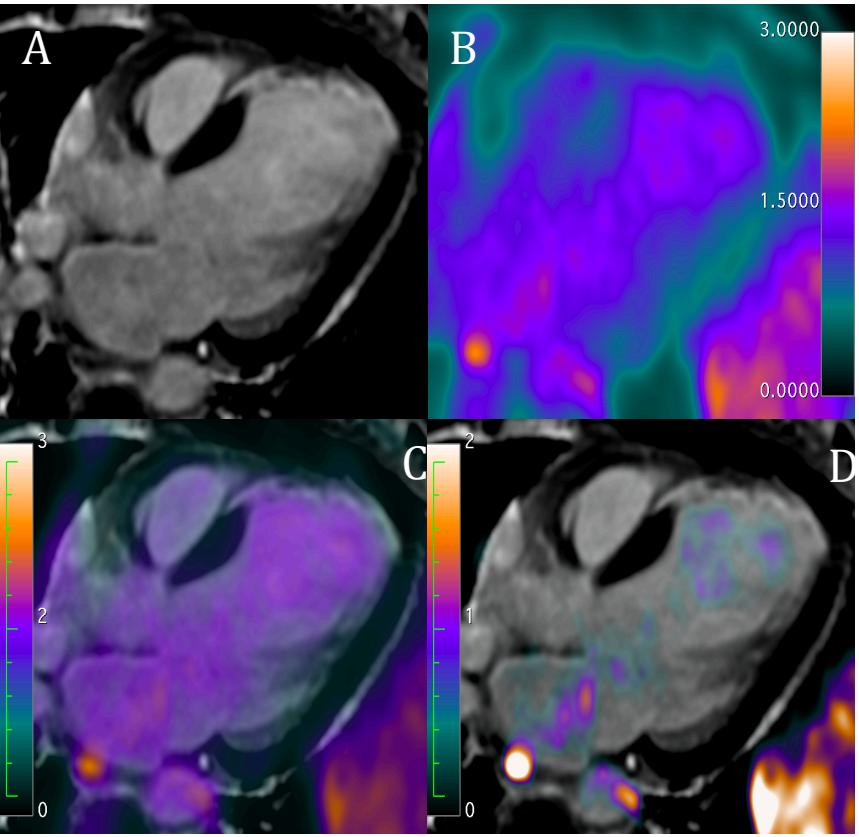
False Positive 18F-FDG PET



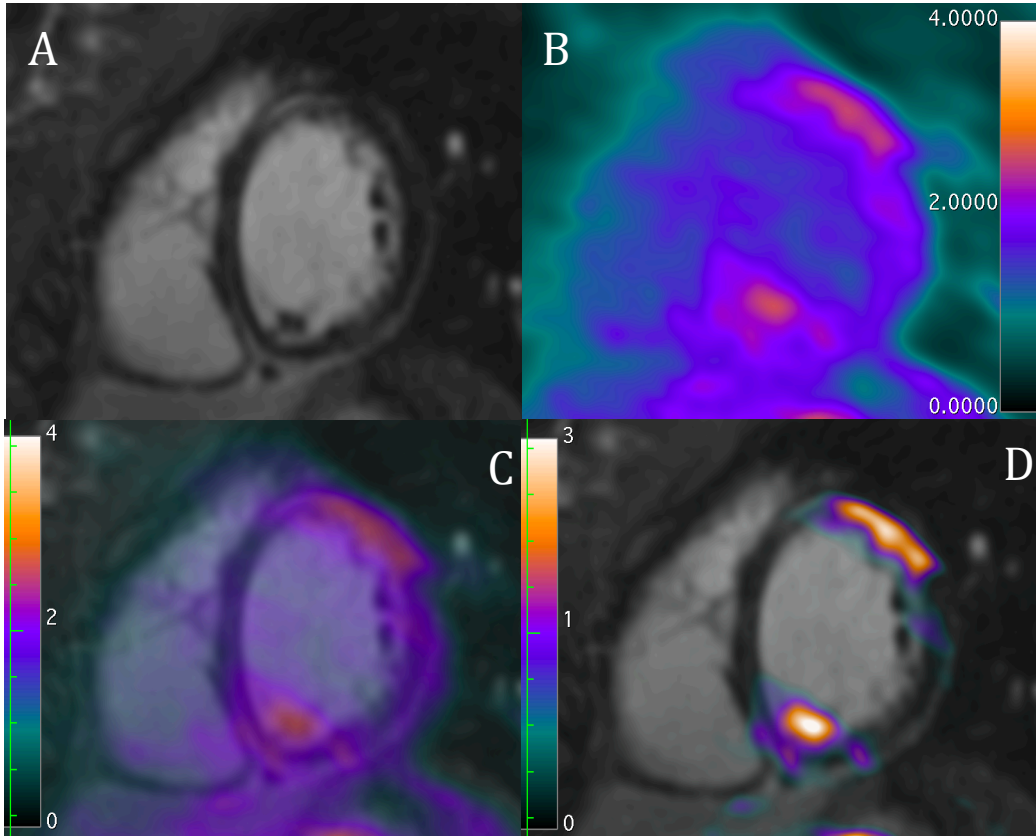
Dweck JACC CVS Imaging 2017

PET/MR & Disease Activity

Old Infarct



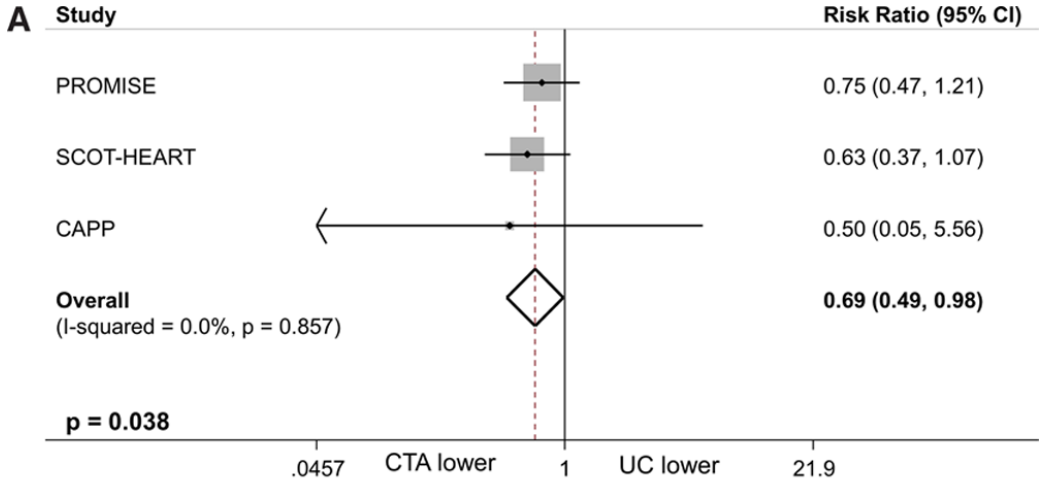
Acute Myocarditis



Dweck Abgral JACC Imaging 2015

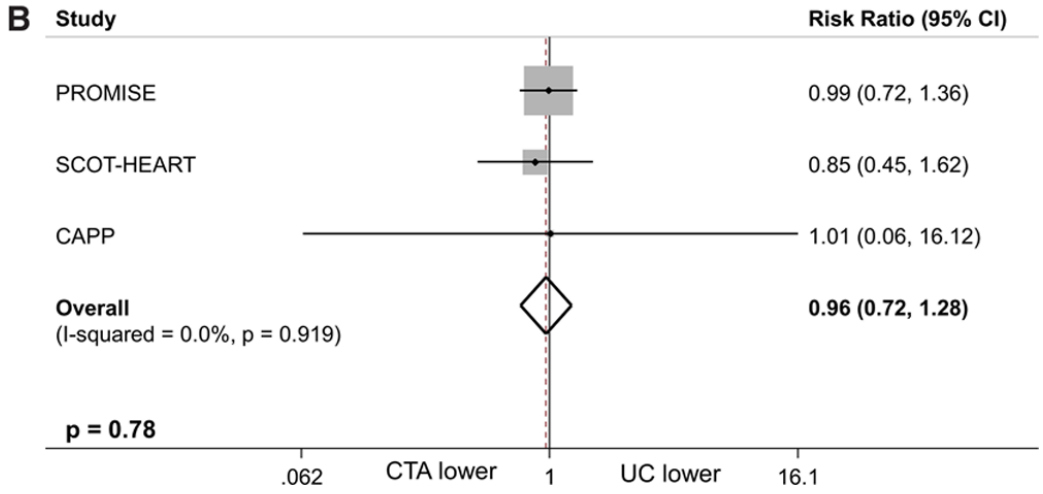
Meta-analysis

Myocardial infarction



Significant reduction in the annual rate of myocardial infarction

All cause death



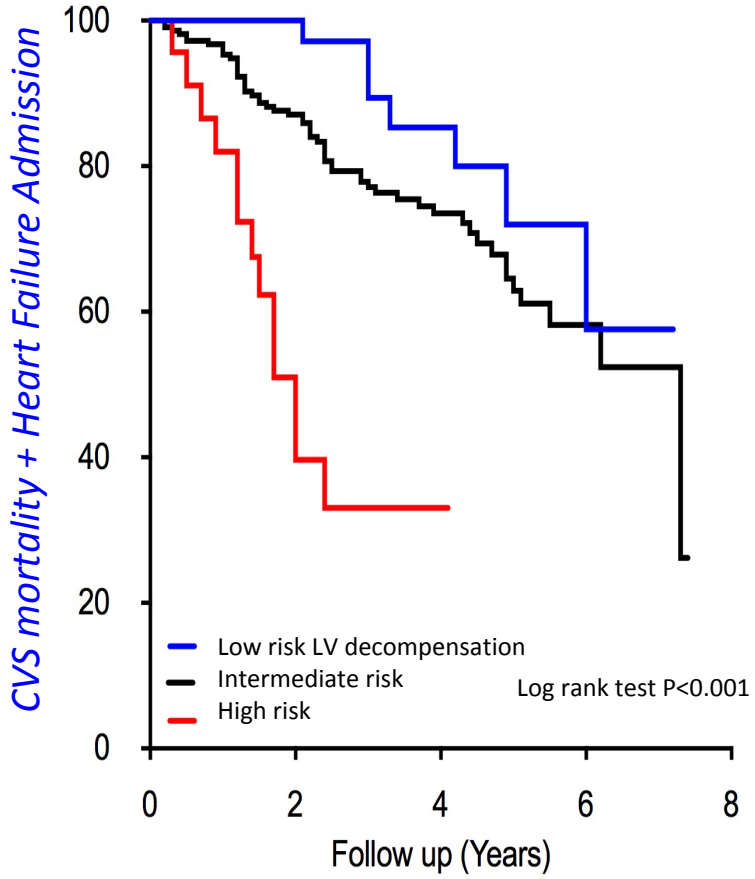
No difference in all cause mortality

Bittencourt et al. Circulation CVI 2016

Clinical Outcomes Often Poor Following AVR

Edinburgh Heart Centre

Kaplan-Meier Curve



Chin et al. EHJ. 2015