FFR in the diagnostic phase

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Conflicts of Interest

- Unrestricted research funding from:
  St Jude Medical; Medtronic; Boston Scientific; Haemonetics; Heartflow
- Speaker and consultancy fees from: St Jude Medical; Haemonetics; Heartflow
- Educational grant funding from: Volcano

Diagnostic angiography without pressure wire assessment can no longer be considered to be an optimal standard of care for patients with chest pain

This talk contains 2 challenges to your conventional way of thinking

Current practice for assessment & management of angina is fundamentally flawed.....

Patient with chest pain

Test for evidence of reversible ischaemia

Diagnostic Angiogram

OMT

CABG

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What is our current philosophy for the investigation & treatment of patients with stable angina?

"Everyone with chest pain should have an angiogram"

"Only patients with objective evidence of ischaemia should have an angiogram"

"A significant stenosis is better off being treated"

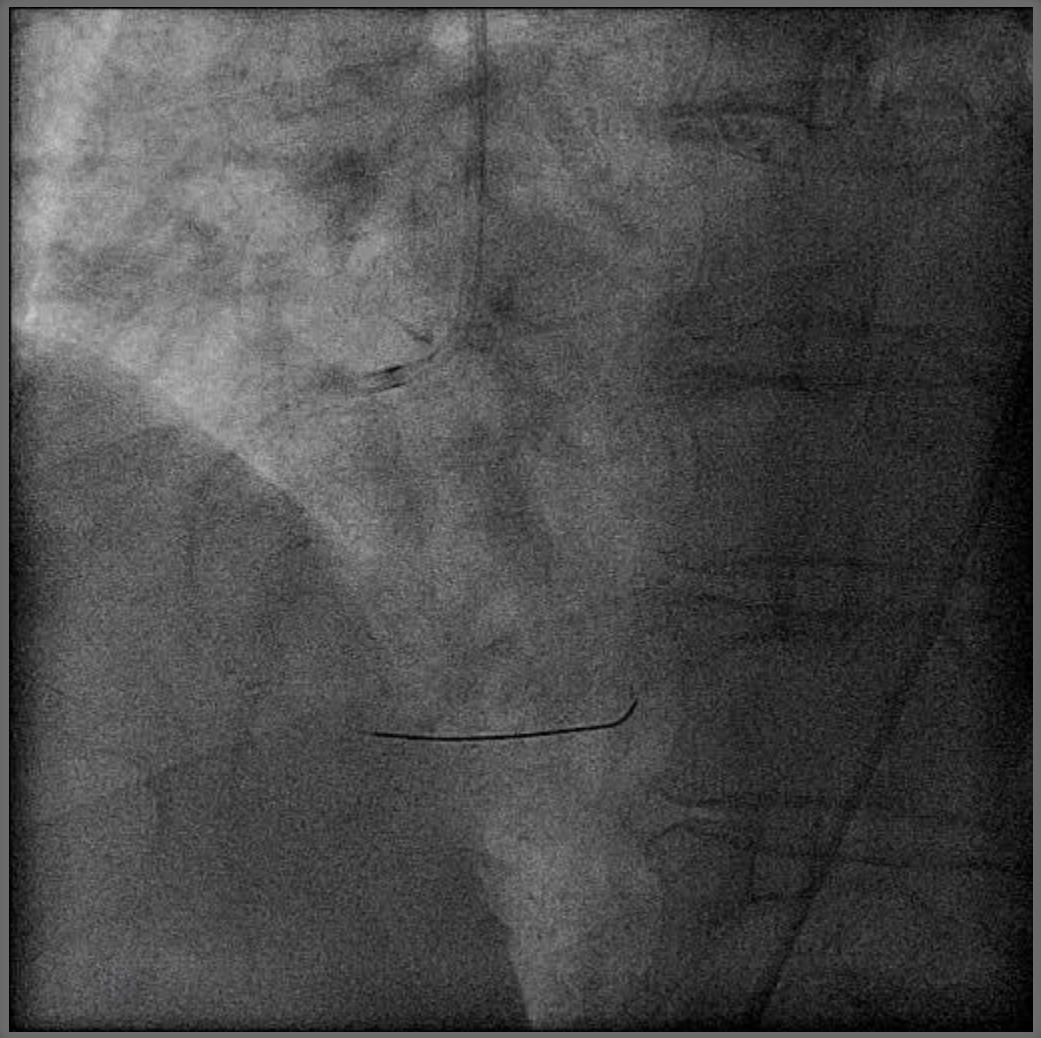
Let's ask some questions about what we are trying to do....

When someone presents with chest pain that we think is angina, what is it that we actually want to know?

Whether they have:

- ✓ Atheroma?
- ✓ "Significant" coronary artery disease?
- ✓ Impaired prognosis?

How much of this can we address by doing a coronary angiogram?



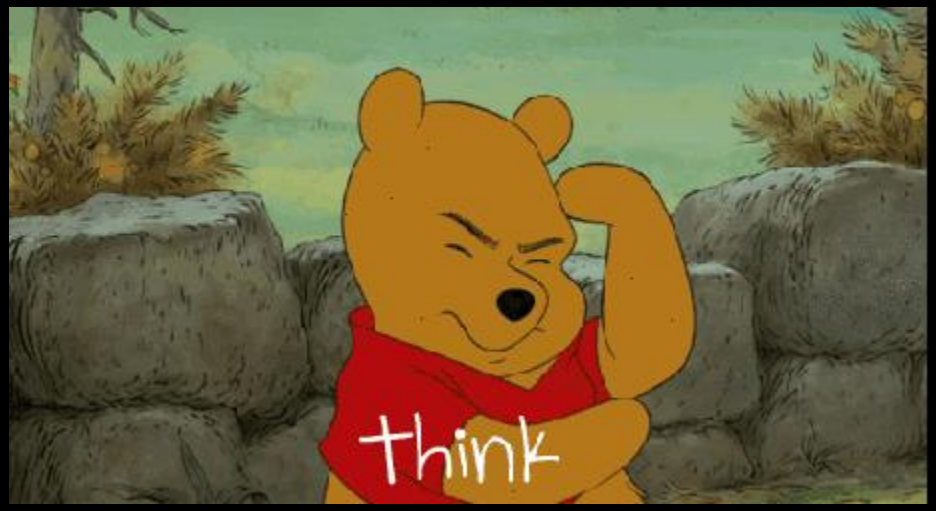
CAD present? ✓

Benefit from aspirin/statin/ramipril? ✓

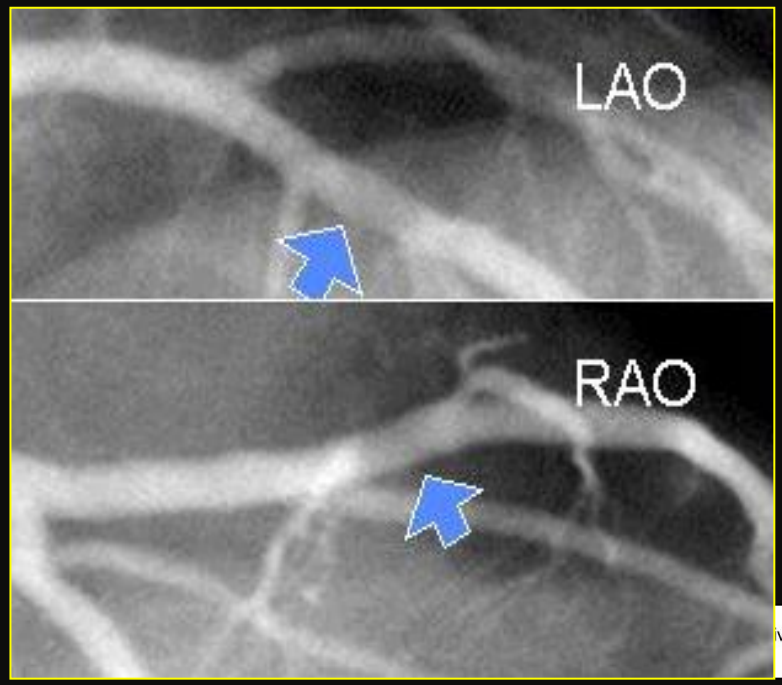
Symptoms due to this CAD? ?

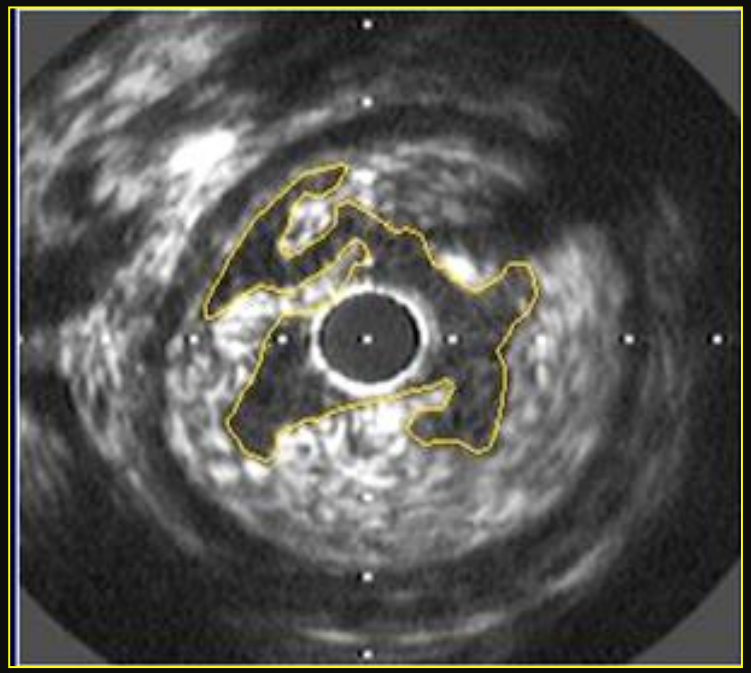
Needs revasc? ?

- ✓ Ischaemia is the dominant factor to determine clinical outcome
  - ✓ There are problems with all our NI tests for ischaemia



So... Should everyone have an angiogram?

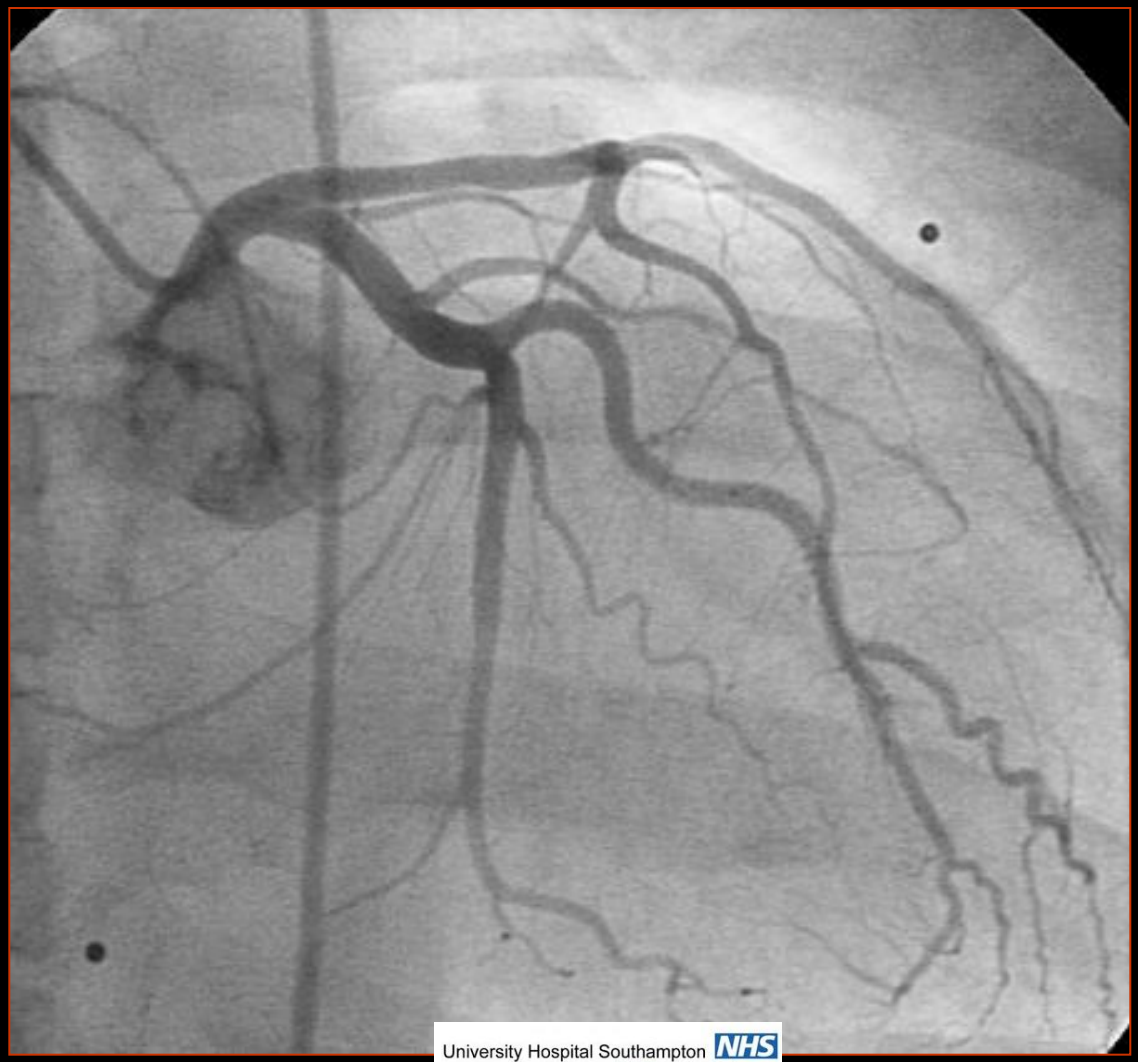


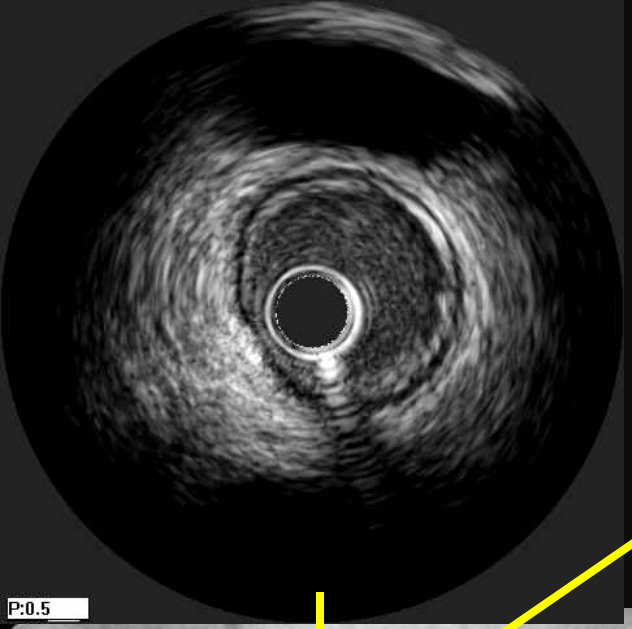


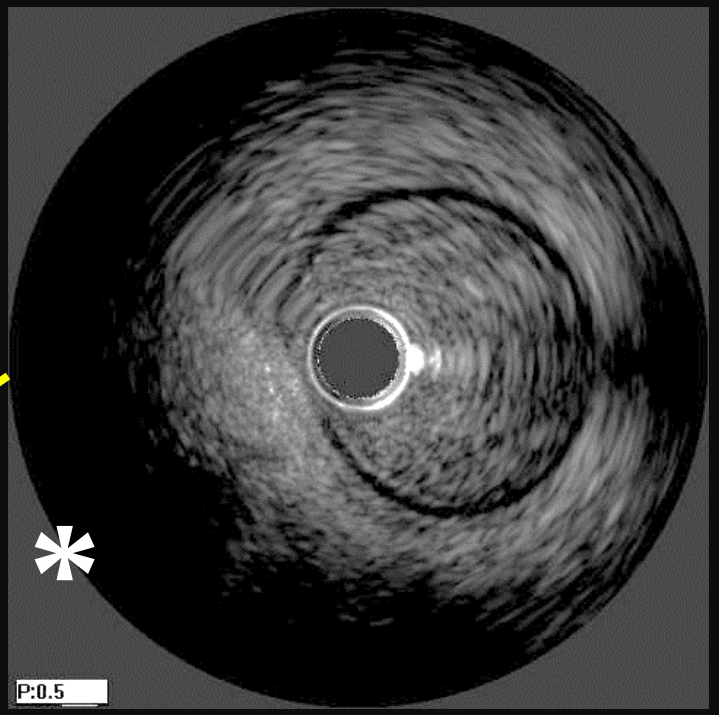
The Limitations of Coronary Angiography: Identification of a Critical Coronary Stenosis using Intravascular Ultrasound.

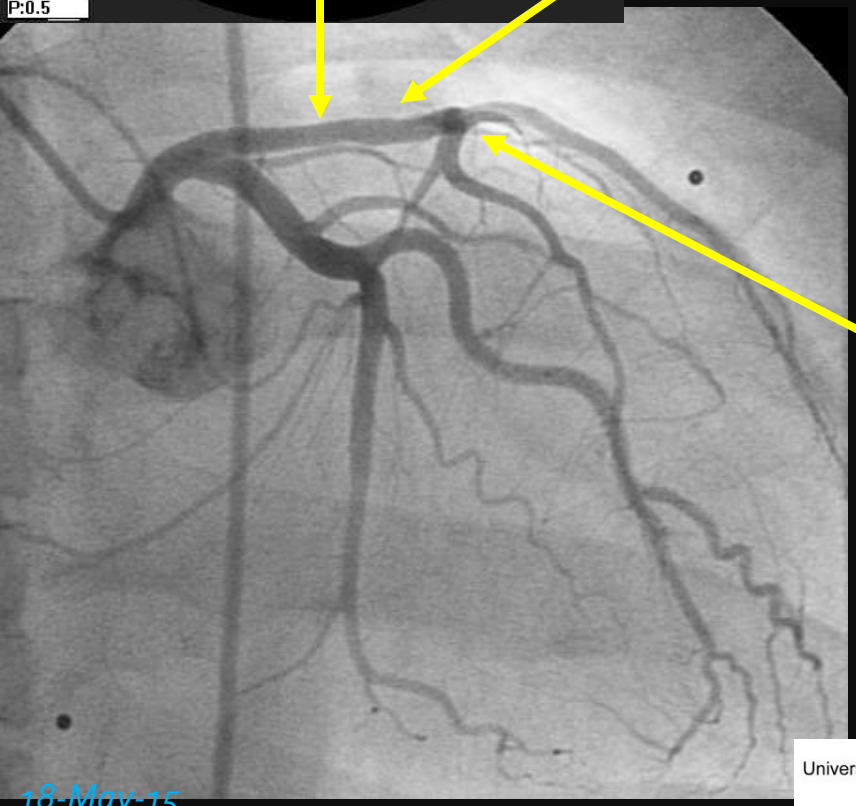
R Swallow, I Court, A Calver, N Curzen

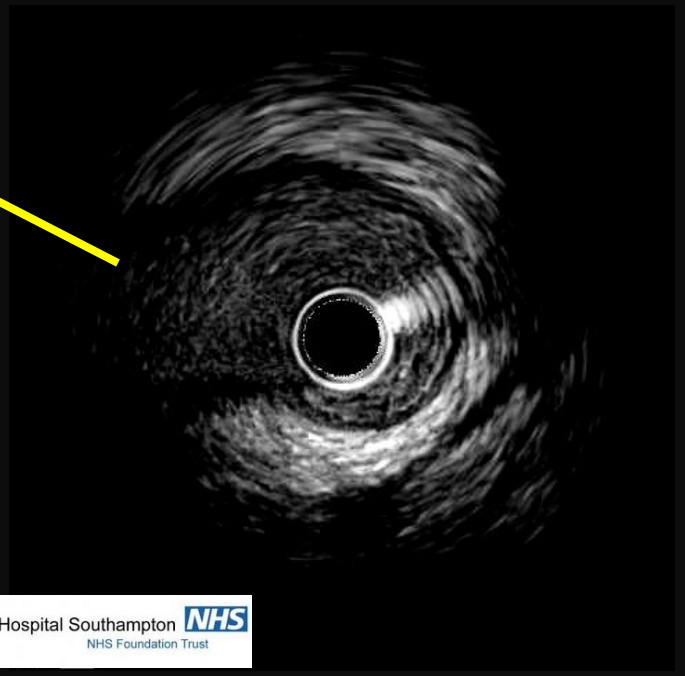
Int J Cardiol 2006;106:123-5











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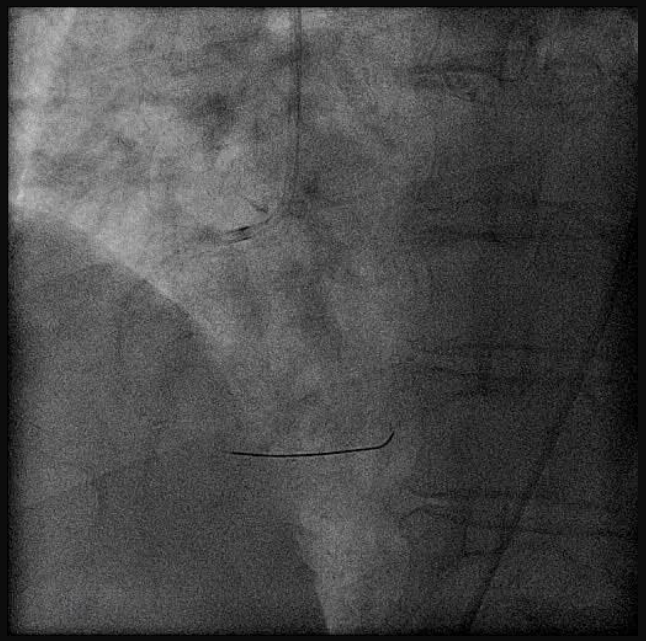
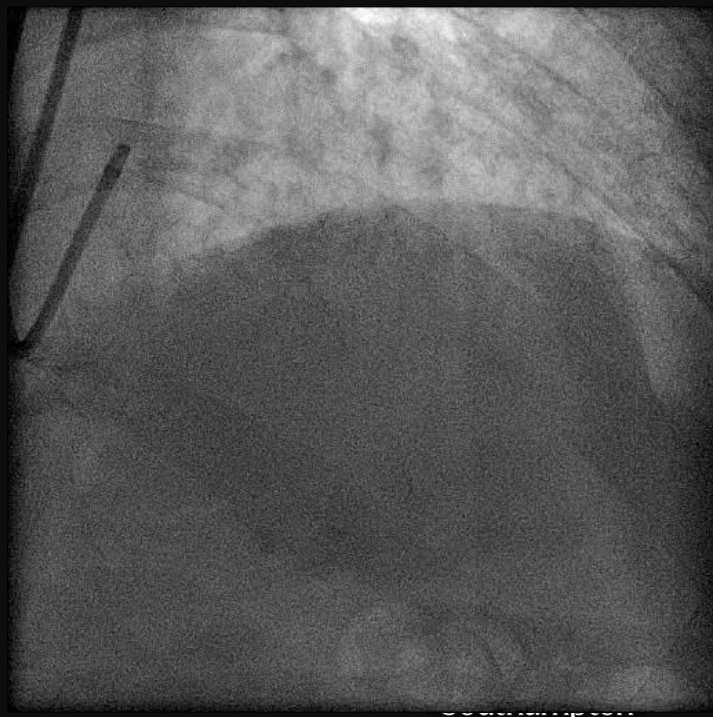


Multivessel Disease..... Stents or Surgery?



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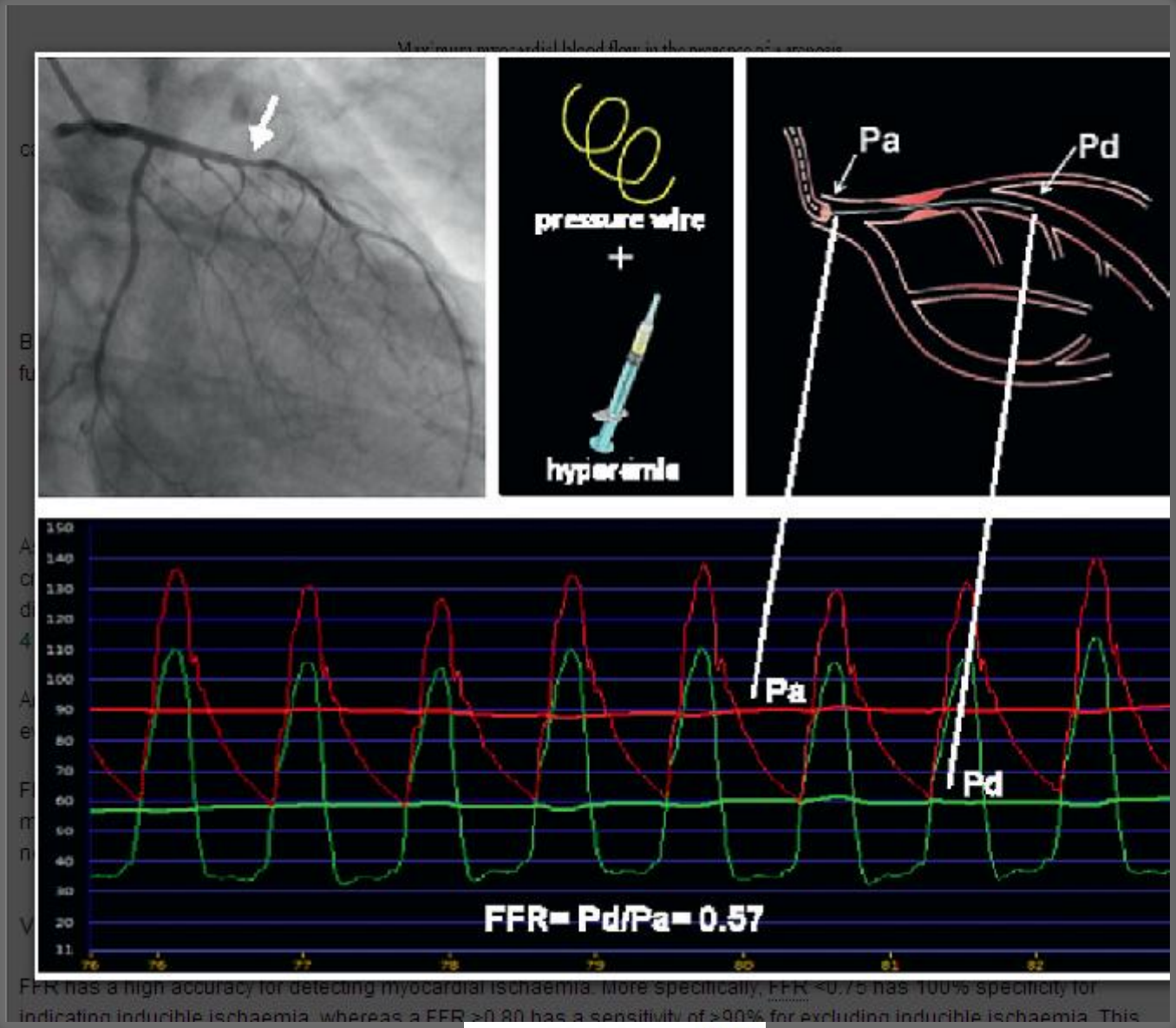
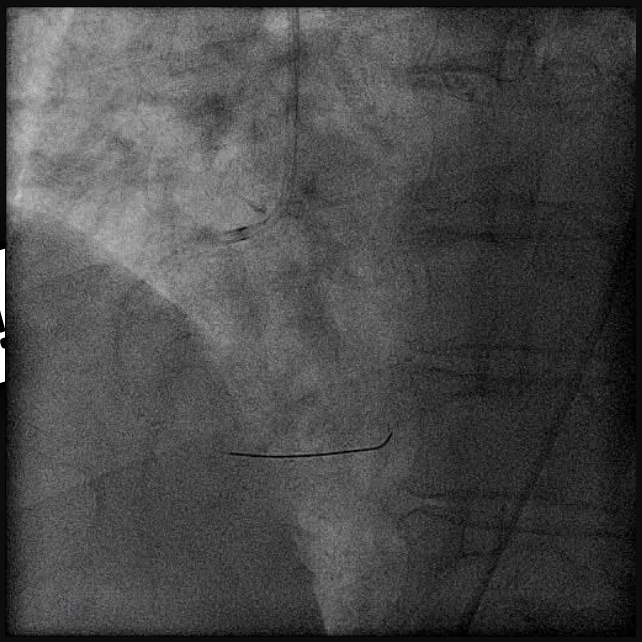
Pressure Wire: diagnostic precision in an ischaemia-directed strategy



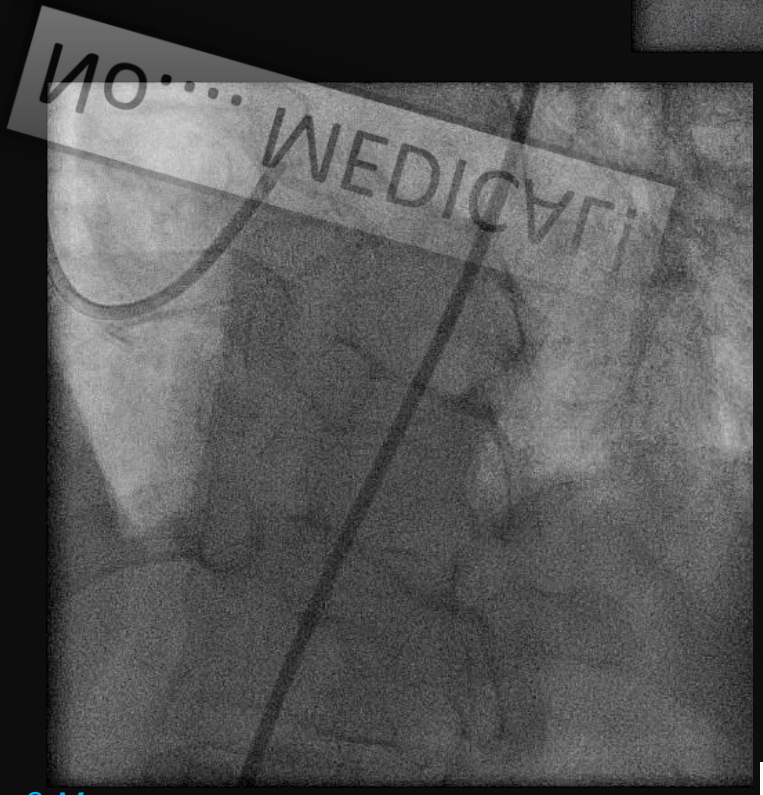
Multivessel Disease

Stents

No.... MEDICAL!



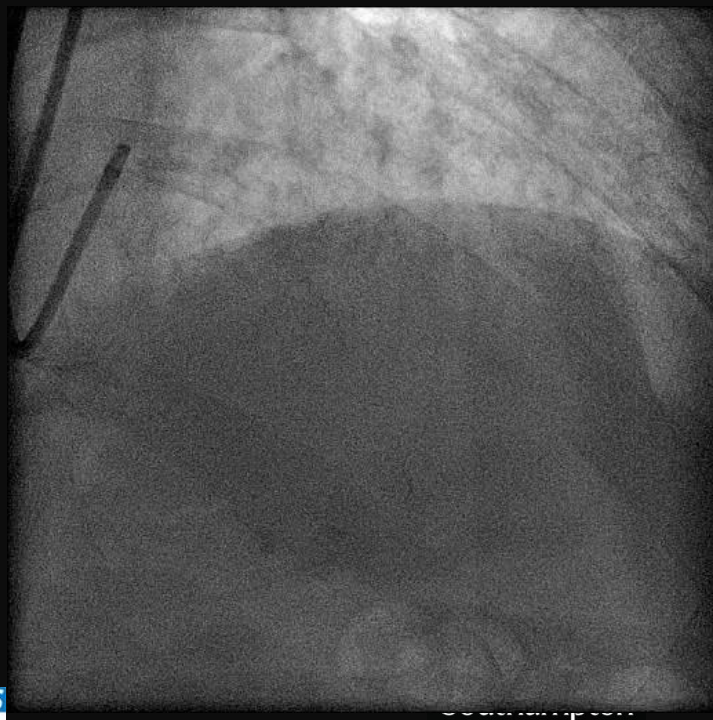
RCA:
Min FFR = 0.96



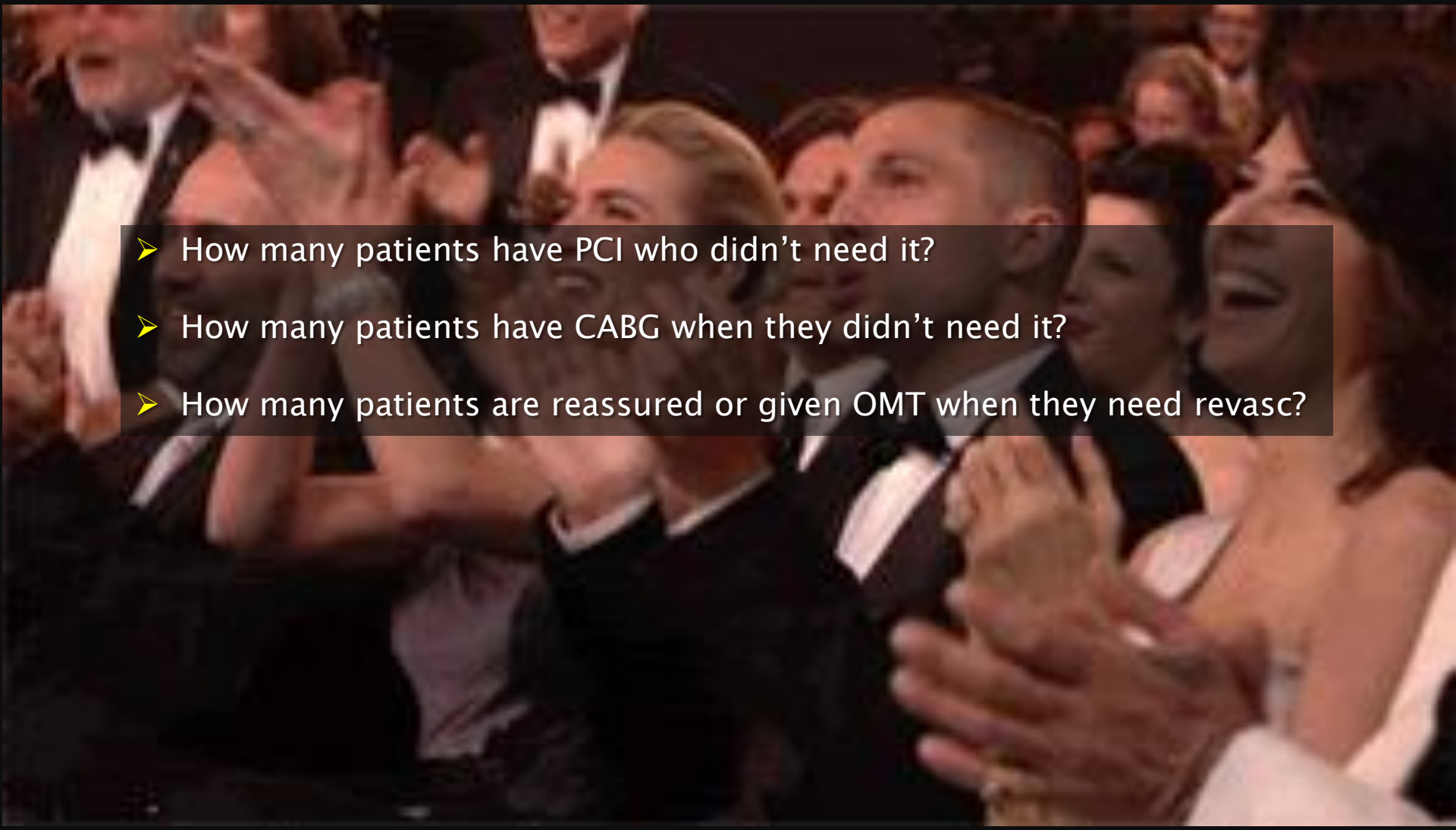
LAD:
Min FFR = 0.84

Intermediate:
Min FFR = 0.84

Diagonal
Min FFR = 0.82



What does this mean for routine angiogram-guided practice??



- How many patients have PCI who didn't need it?
- How many patients have CABG when they didn't need it?
- How many patients are reassured or given OMT when they need revasc?

Our current practice for assessment & management of angina is flawed & confused.....

You cannot rely on what you see at angiography if your currency is “significance”

Patient with chest pain

Test for evidence of reversible ischaemia

Diagnostic Angiogram

?

DEFER
FAME
FAME 2

?

OMT

CABG

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Does Routine Pressure Wire Assessment Influence Management Strategy at Coronary Angiography for Diagnosis of Chest Pain?

The RIPCORD Study

Circulation: Cardiovasc Interven 2014

Hypothesis

That, in pati… …outine assessment of FFR i… …gement strategy derived from diagnostic c…

Or, in other words……

"How different is our management with FFR compared with angio alone?"

Method

n=200

Patient being investigated for chest pain

Diagnostic Coronary Angiogram by Cardiologist 1

TREATMENT PLAN 1
Medical/PCI/CABG/more info

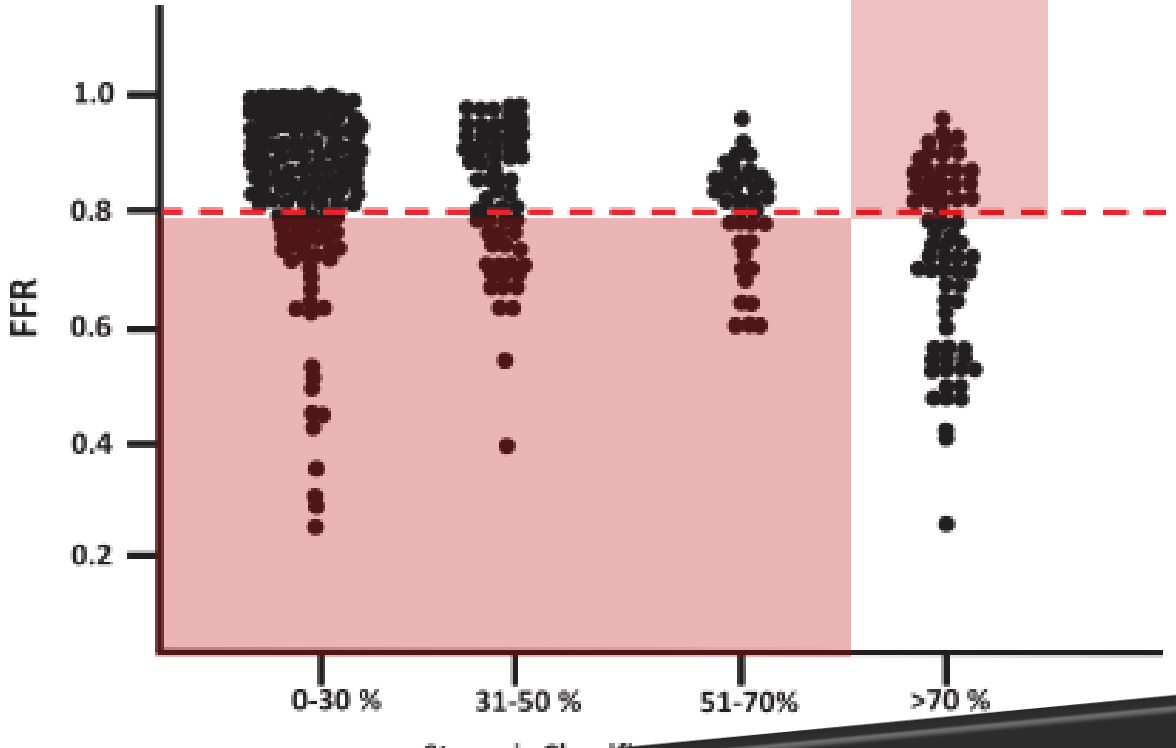
FFR* of all patent vessels of stentable (≥2.25mm) diameter by Cardiologist 2

*FFR≤0.8

Cardiologist 1 shown FFR results

TREATMENT PLAN 2
Medical/PCI/CABG/more info

Primary endpoint based upon the difference between **Plan 1** and **Plan 2**



Summary

In a total of 64 cases (32%), FFR leads to a change in the judgement as to whether a coronary artery has a "significant" lesion compared to angiogram alone

eter stenosis, the FFR reading was <0.8 in 53%. Thus, in 47% of stenoses graded >70%, the FFR indicated that there was no physiologically significant lesion. In lesions graded between 51% and 70%, 31% and 50%, and 0% and 30% diameter stenosis, the FFR value was <0.8 in 33%, 33%, and 13%, respectively.

Results: PRIMARY ENDPOINT

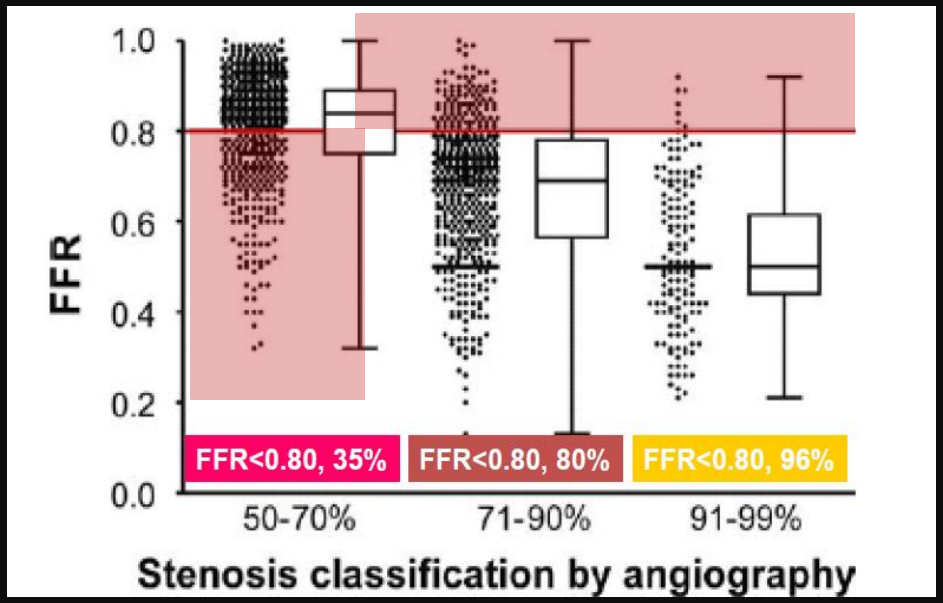
Management of population by angiogram versus FFR

		FFR PLAN 2				Total
		Medical	PCI	CABG	Further Info	
PLAN 1 ANGIO	Medical	63	6	3	0	72
	PCI	24	64	2	0	90
	CABG	1	3	19	0	23
	Further info	1	7	6	1	15
Total		89	80	30	1	200

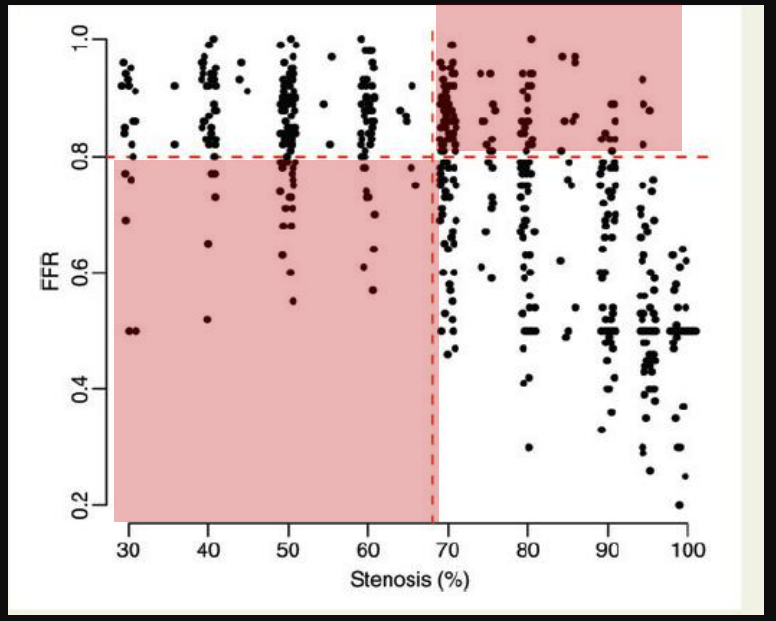
Fishers exact test p<0.0001

Summary

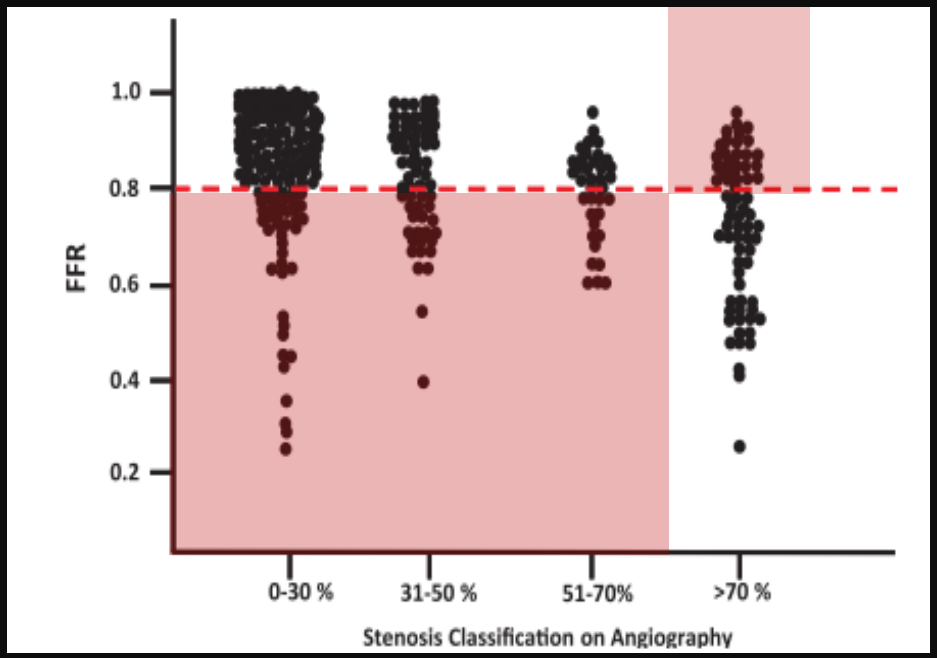
- Agreement about category of management in 147 out of 200 (74%)
  - ie after FFR management change in 26% of cases



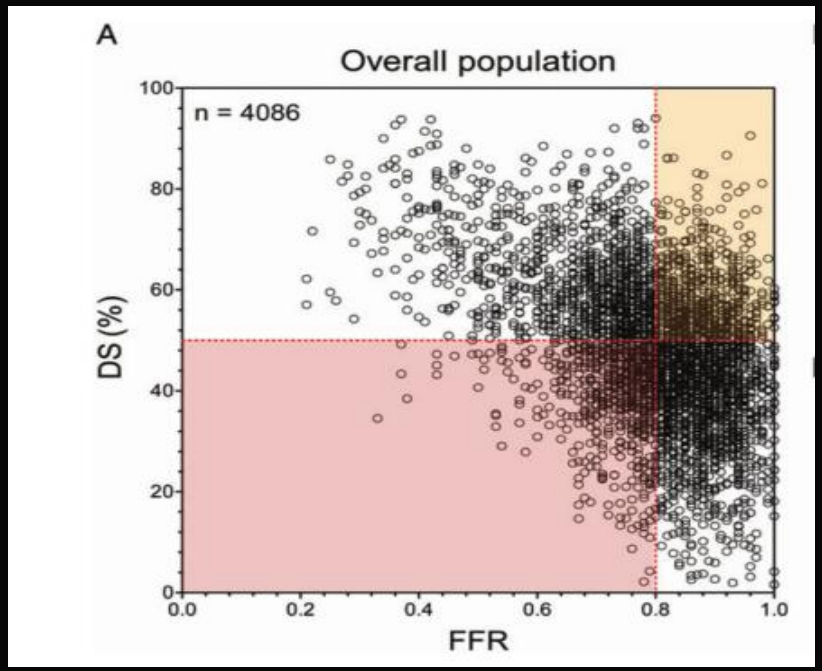
Tonino et al *JACC* 2010



Berry et al *Eur Heart J* 2014



Curzen et al *Circ Interven* 2014



Toth et al *EHJ* 2014

- No matter how experienced you are…
- No matter how "tight" the lesion looks…

<u>You will be wrong about "significance"on the angio in about 30% of lesions!</u>

And it's NOT just Intermediate lesions!!!!

IMPLICATIONS

- These results have potentially important implications for clinical practice:
  - management of patients with stable angina by angiogram alone is flawed
  - management of patients would be improved by routine use of FFR at the diagnostic stage

- A large scale randomised trial of angiographic- versus FFR-guided assessment & management of patients undergoing diagnostic angiography with stable angina is now warranted

RIPCORD 2

1100 patient randomised trial of angio-guided versus FFR-guided management in patients with chest pain

Outcome Impact of Coronary Revascularization Strategy Reclassification With Fractional Flow Reserve at Time of Diagnostic Angiography

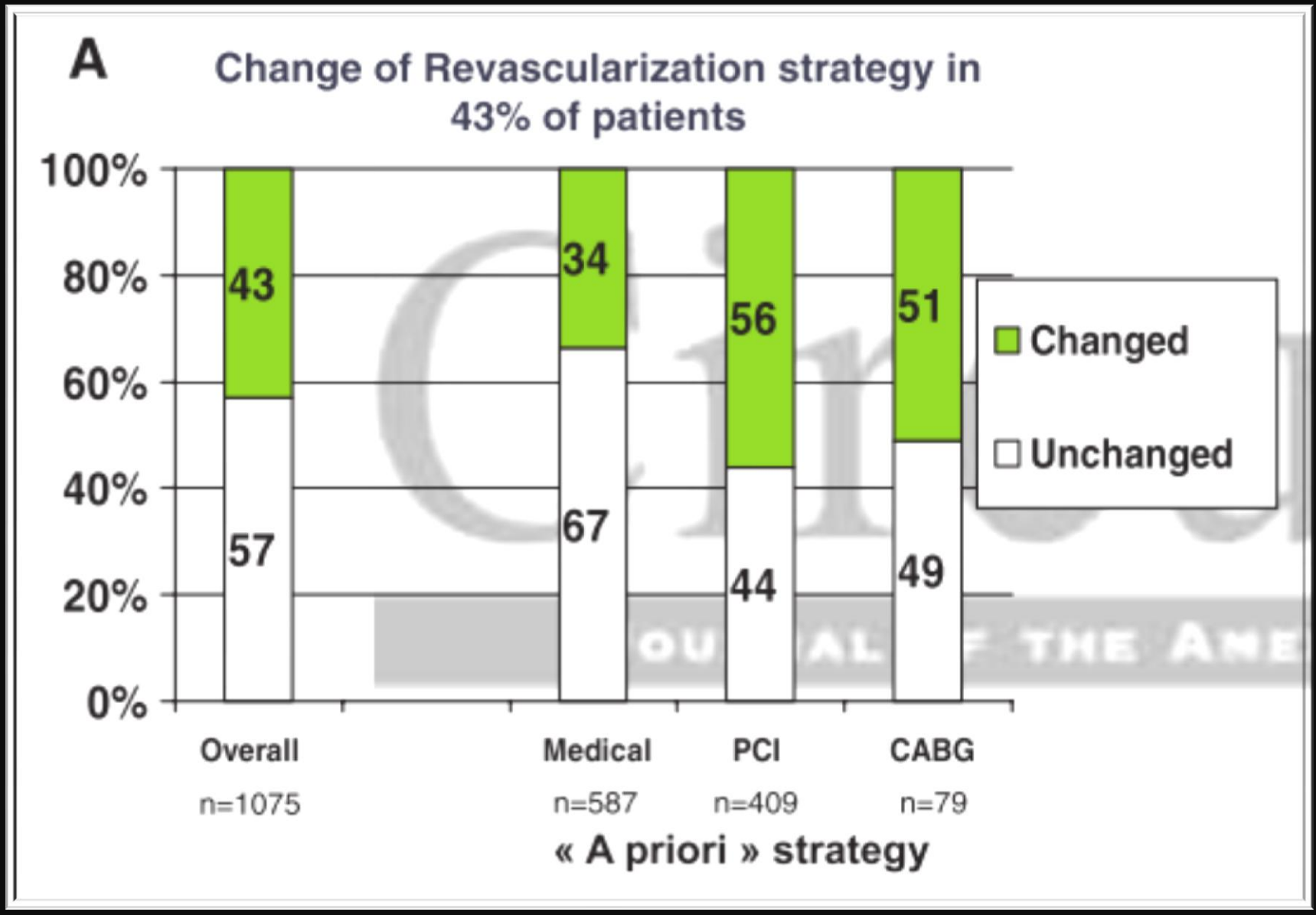
Insights From a Large French Multicenter Fractional Flow Reserve Registry

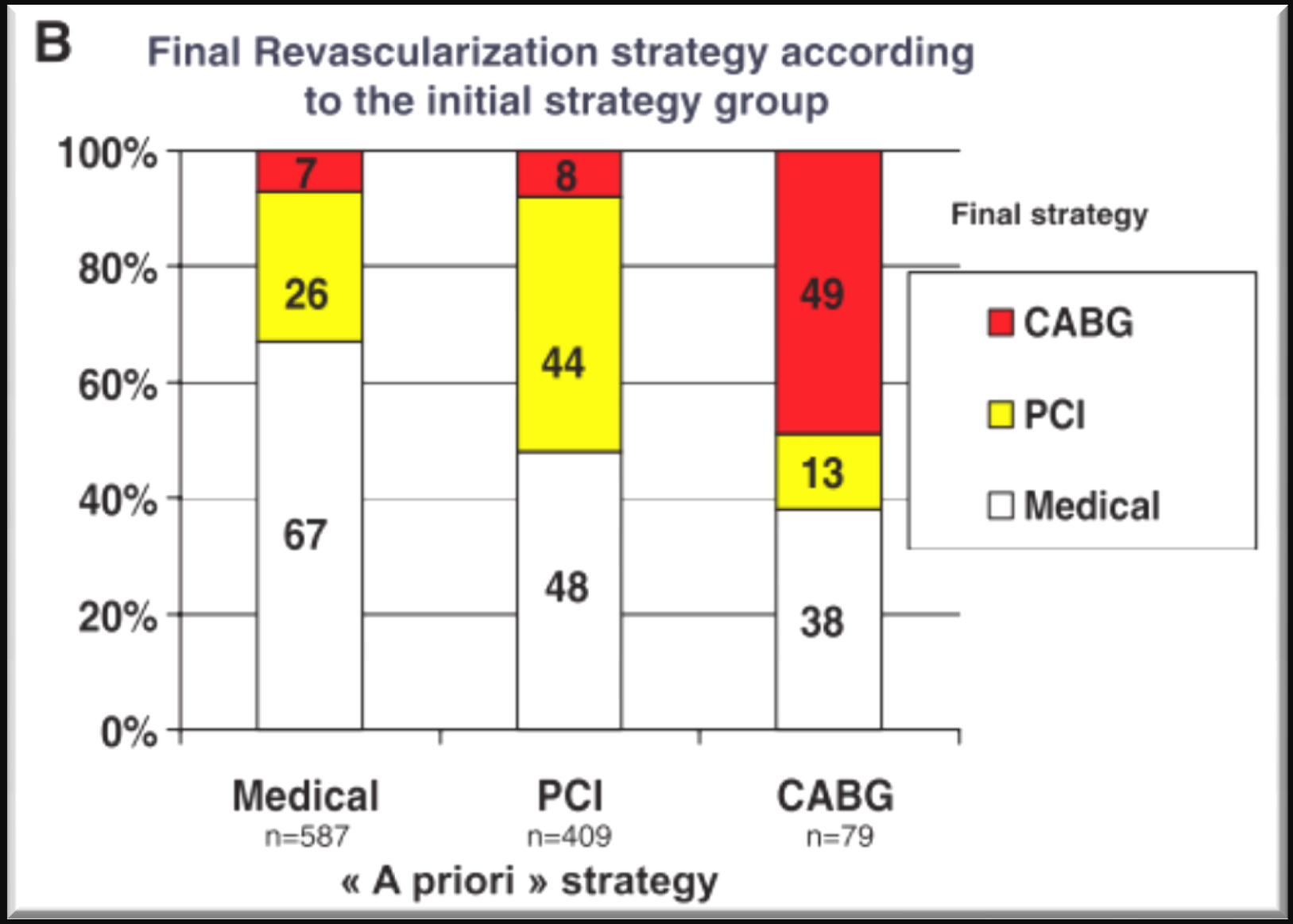
Circulation 2014

-n=1075 consecutive patients undergoing diagnostic angiography including an FFR Investigation

-Patients had to have at least 1 angiographically ambiguous lesion

-Primary objective was to describe the rate of reclassification of the patient's coronary revascularisation strategy by an intention to use FFR in patients referred for coronary angiography





"SAME TIME, SAME PLACE"

Angiogram with FFR:

(a) definitive diagnosis & (b) ischaemia-directed management

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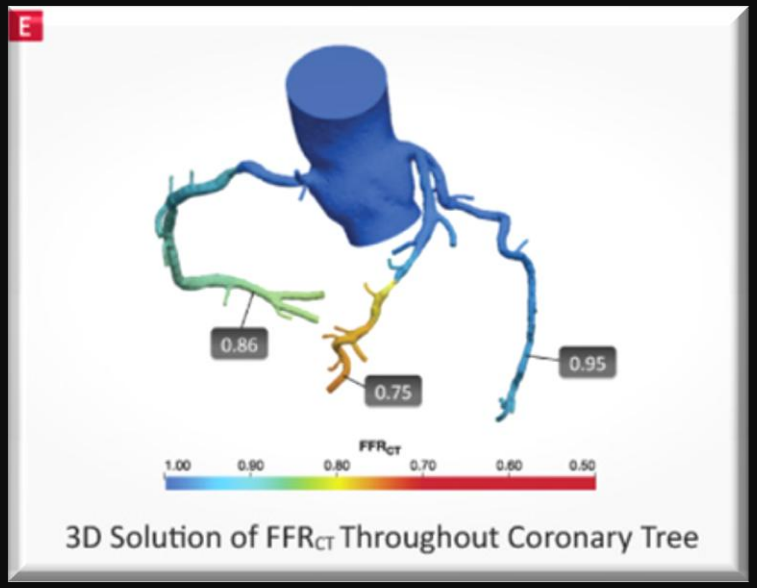
Summary

- Current strategies for diagnosis & management of chest pain are confused
- Current patient-level treatment is not ischaemia-driven in most cases
- Current lesion-level treatment is not ischaemia-driven or targeted
- Routine FFR at the coronary angiogram stage would facilitate patient-level & lesion-level tailored therapy **in the same manner as in FAME 1 & 2, but at an earlier stage of the care pathway**
- If treatment was ischaemia-tailored the results of COURAGE & SYNTAX may have been very different?
- RIPCORD 2 will help us understand this....
- USE FFR LIBERALLY IN YOUR PRACTICE: FOR THE SAKE OF YOUR PATIENTS!!

I do not think diagnostic angiography **without FFR** can any longer be considered to be an optimal standard of care for patients with chest pain…..



What if we could do all this non-invasively one day?

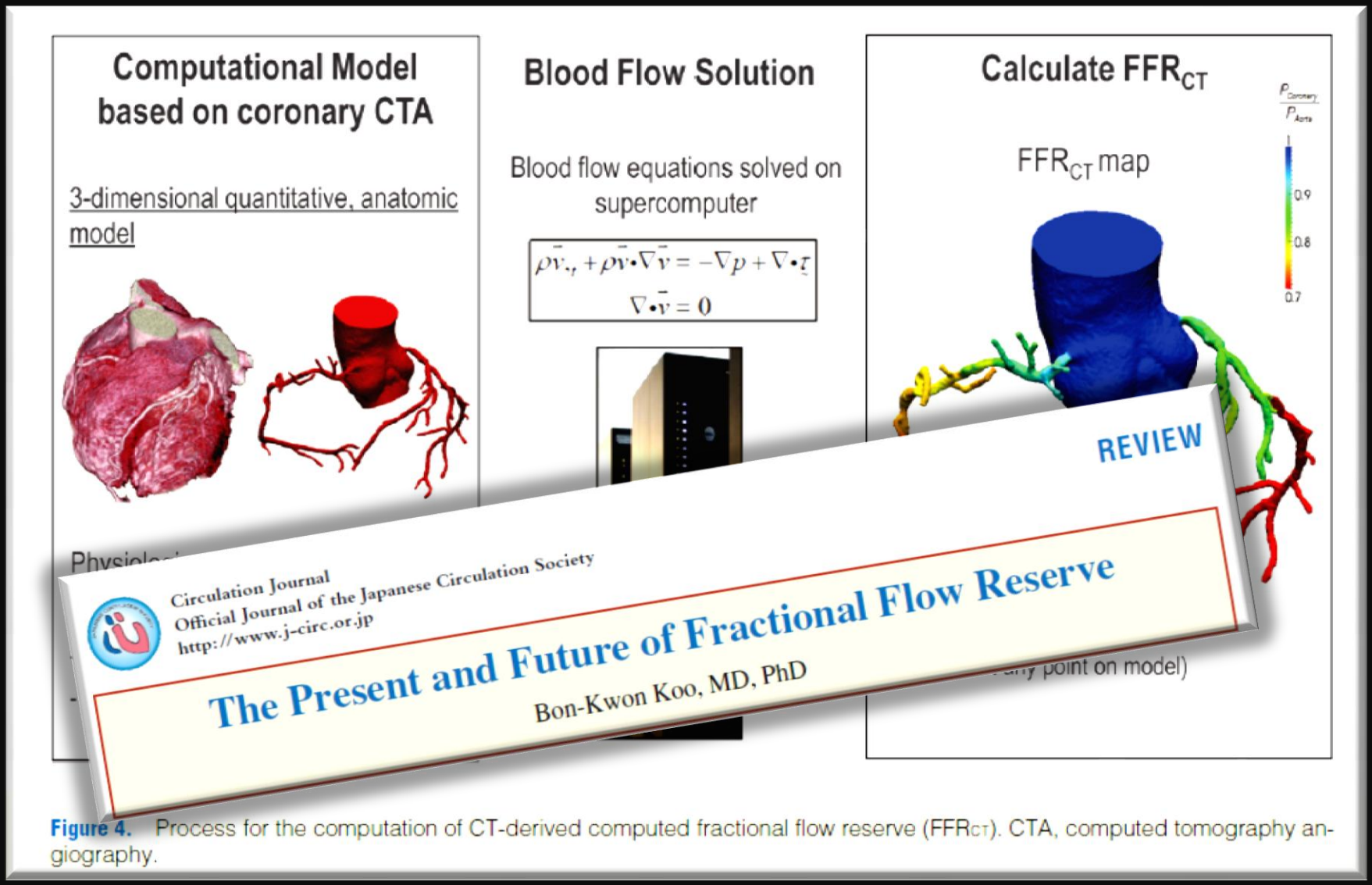
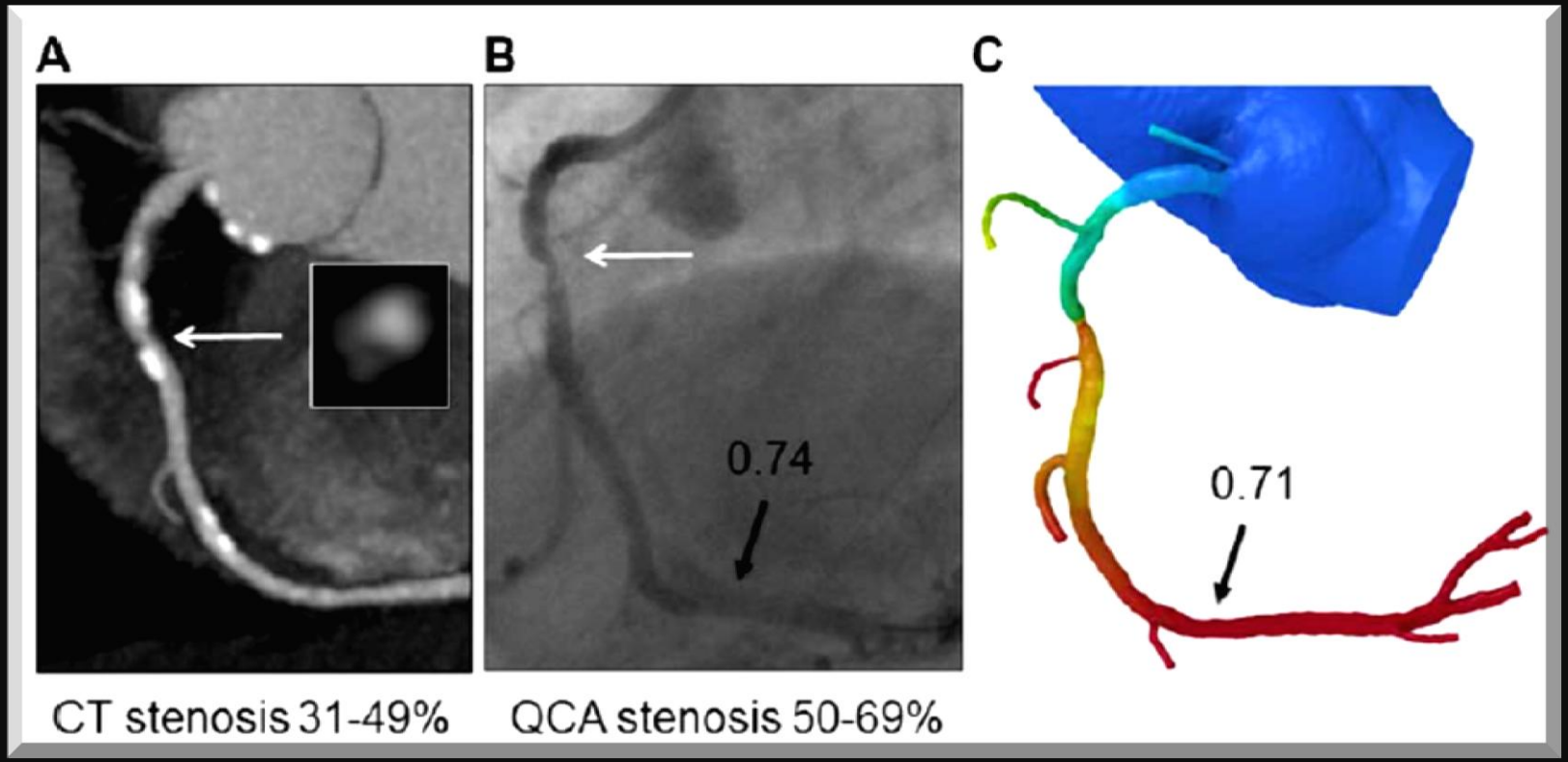


Figure 4. Process for the computation of CT-derived computed fractional flow reserve (FFR_{CT}). CTA, computed tomography angiography.

Noninvasive Fractional Flow Reserve Derived From Computed Tomography Angiography for Coronary Lesions of Intermediate Stenosis Severity

Results From the DeFACTO Study

Circ Cardiovasc Imaging 2013



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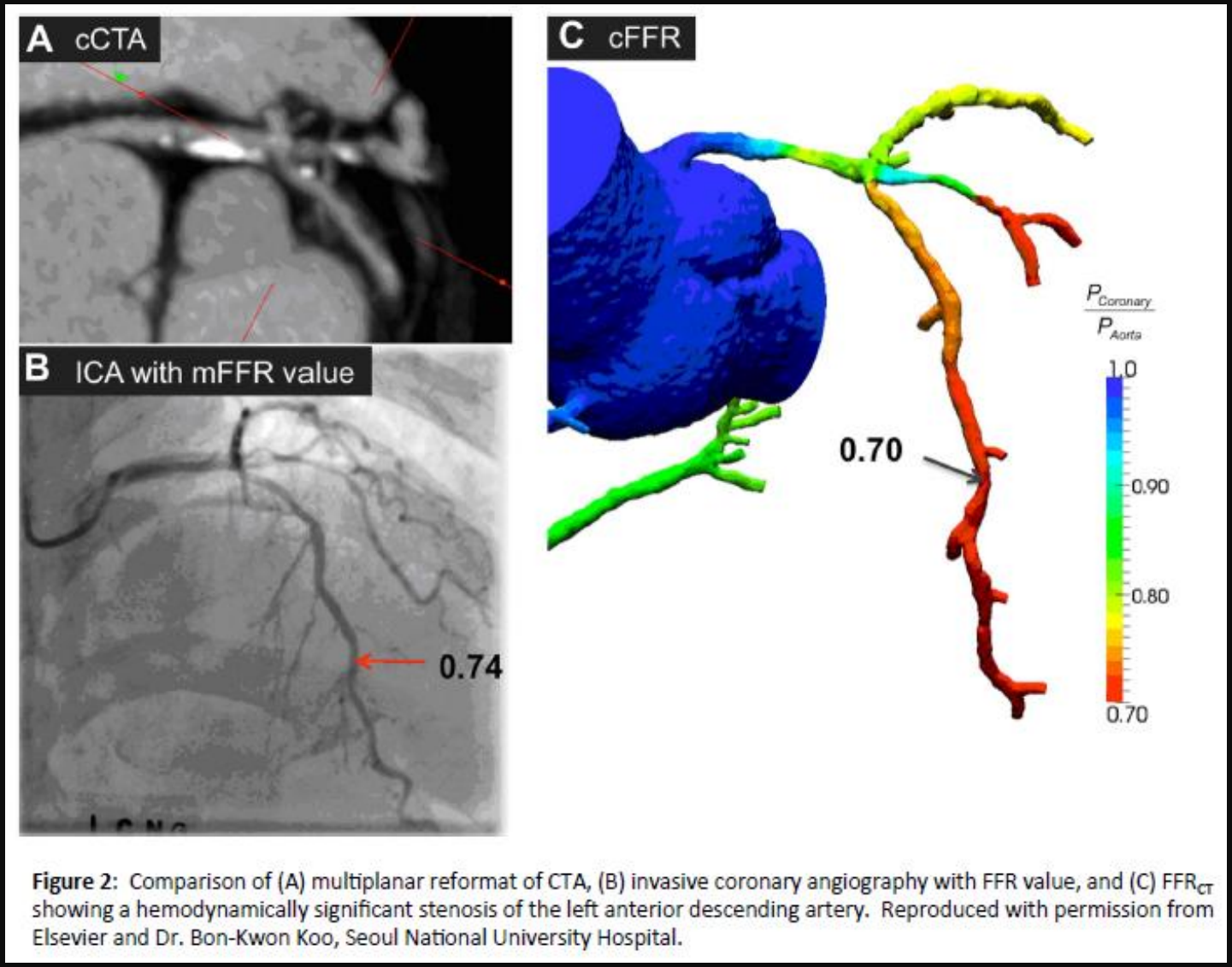
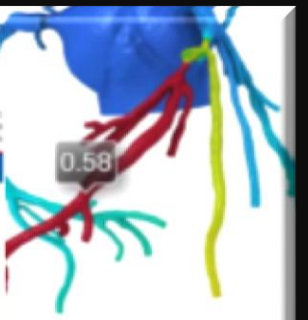


Figure 2: Comparison of (A) multiplanar reformat of CTA, (B) invasive coronary angiography with FFR value, and (C) FFR_{CT} showing a hemodynamically significant stenosis of the left anterior descending artery. Reproduced with permission from Elsevier and Dr. Bon-Kwon Koo, Seoul National University Hospital.

Clinical Validation Data



- **DISCOVER-FLOW**
  - Completed 2011
  - N=104 patients
  - First in man pilot

Cardiac Imaging

Diagnosis of Ischemia-Causing Coronary Stenoses by Noninvasive Fractional Flow Reserve Computed From Coronary Computed Tomographic Angiograms

Results From the Prospective Multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) Study

Bon-Kwon Koo, MD, PhD,* Andrejs Erglis, MD, PhD,† Joon-Hyung Doh, MD, PhD,‡ David V. Daniels, MD,§ Sanda Jegere, MD,‖ Hyo-Soo Kim, MD, PhD,* Allison Dunning, MD,¶ Tony DeFrance, MD,# Alexandra Lansky, MD,** Jonathan Leipsic, BSc, MD,†† James K. Min, MD‡‡

Seoul and Goyang, South Korea; Riga, Latvia; Palo Alto, San Francisco, and Los Angeles, California; New York, New York; New Haven, Connecticut; and Vancouver, British Columbia, Canada

- **DeFACTO**
  - Completed 2012
  - N=252 patients
  - 17 US/OUS sites

ONLINE FIRST

Diagnostic Accuracy of Fractional Flow Reserve From Anatomic CT Angiography

JAMA. 2012;308(12):doi:10.1001/2012.jama.11274

- **NXT**
  - Completed 2013
  - Focus on intermediate lesions
  - N=254 patients

Noninvasive Fractional Flow Reserve Derived From Computed Tomography Angiography for Coronary Lesions of Intermediate Stenosis Severity

Results From the DeFACTO Study

- N=407 vessels from 252 vessels
- All had invasive angio + FFR

Circ Cardiovasc Imaging 2013

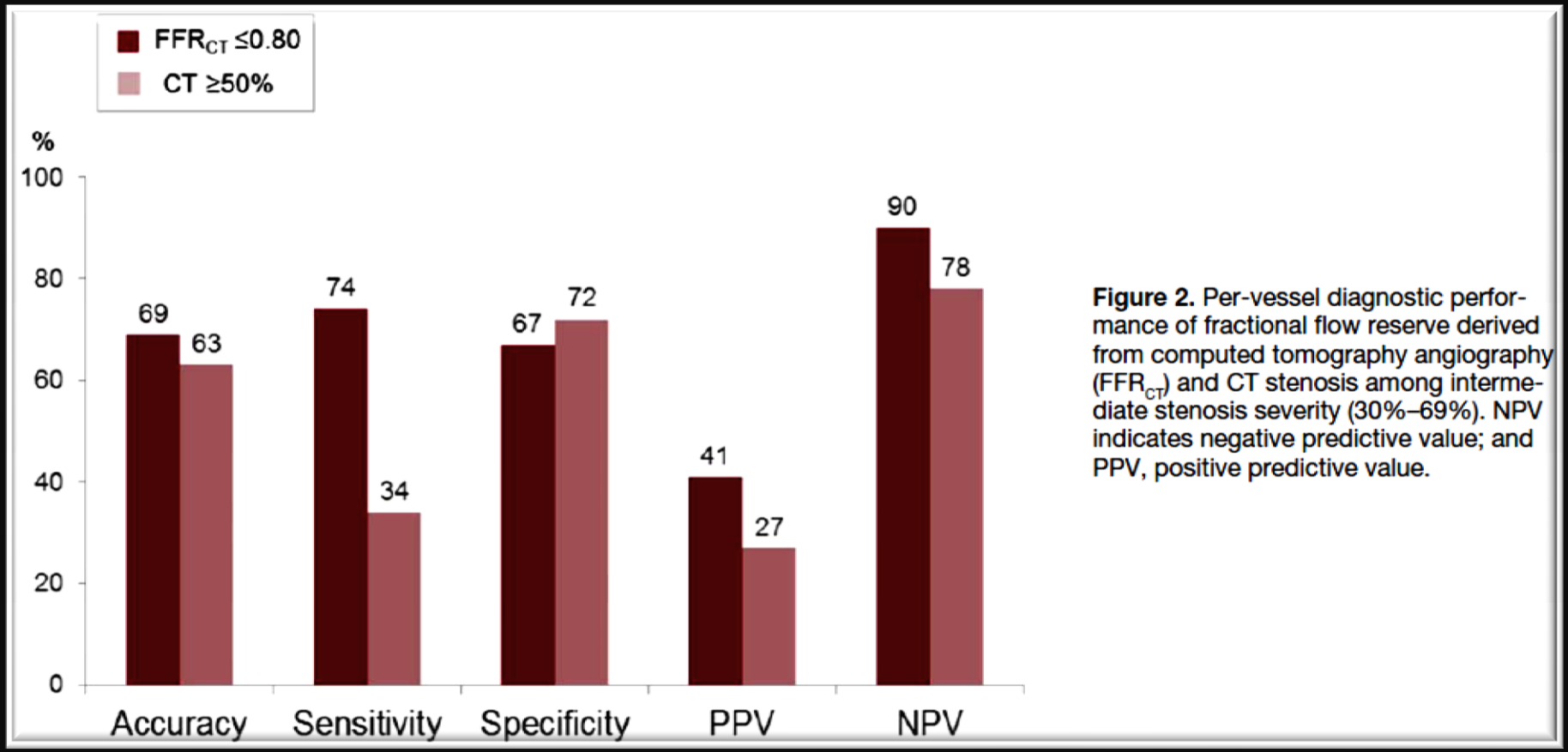


Figure 2. Per-vessel diagnostic performance of fractional flow reserve derived from computed tomography angiography (FFR$_{CT}$) and CT stenosis among intermediate stenosis severity (30%–69%). NPV indicates negative predictive value; and PPV, positive predictive value.

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Noninvasive Fractional Flow Reserve Derived From Computed Tomography Angiography for Coronary Lesions of Intermediate Stenosis Severity

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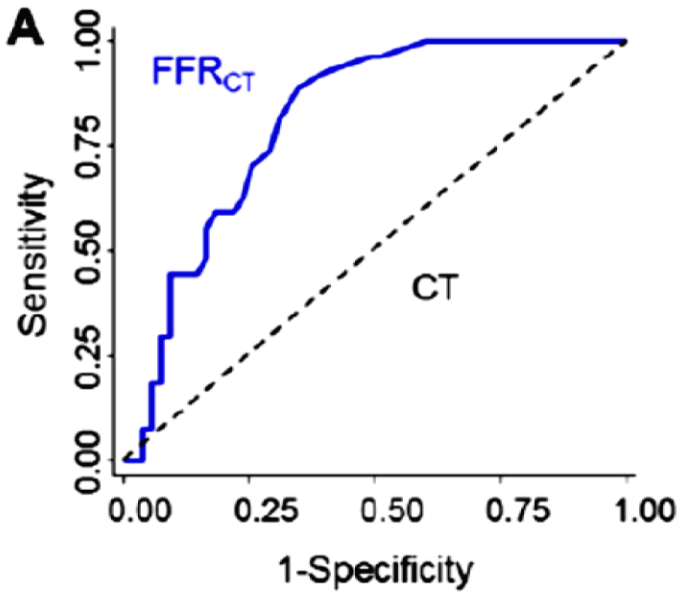
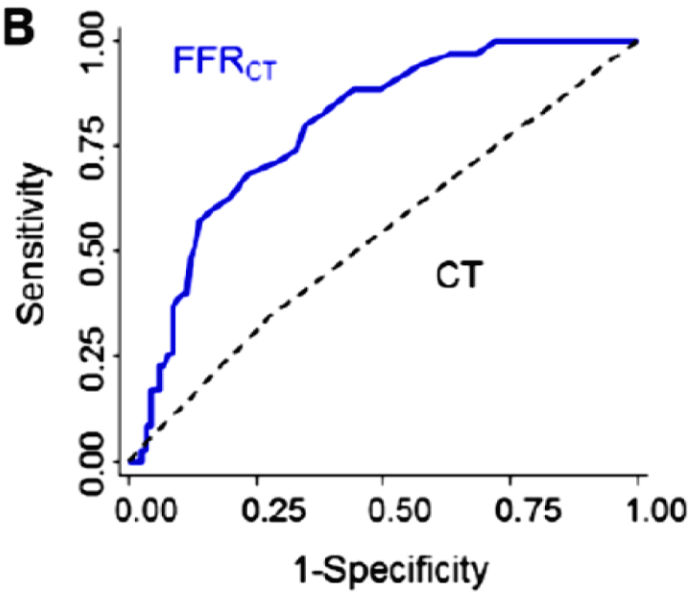




AUC	
FFR$_{CT}$	0.81 (95% CI 0.72-0.90)
CT	0.50 (95% CI 0.39-0.62)

AUC	
FFR$_{CT}$	0.79 (95% CI 0.72-0.87)
CT	0.53 (95% CI 0.44-0.62)

Diagnostic Performance of Noninvasive Fractional Flow Reserve Derived From Coronary Computed Tomography Angiography in Suspected Coronary Artery Disease

The NXT Trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps)

JACC 2014

- N=254
- CTA + FFRCT versus invasive angio + FFR

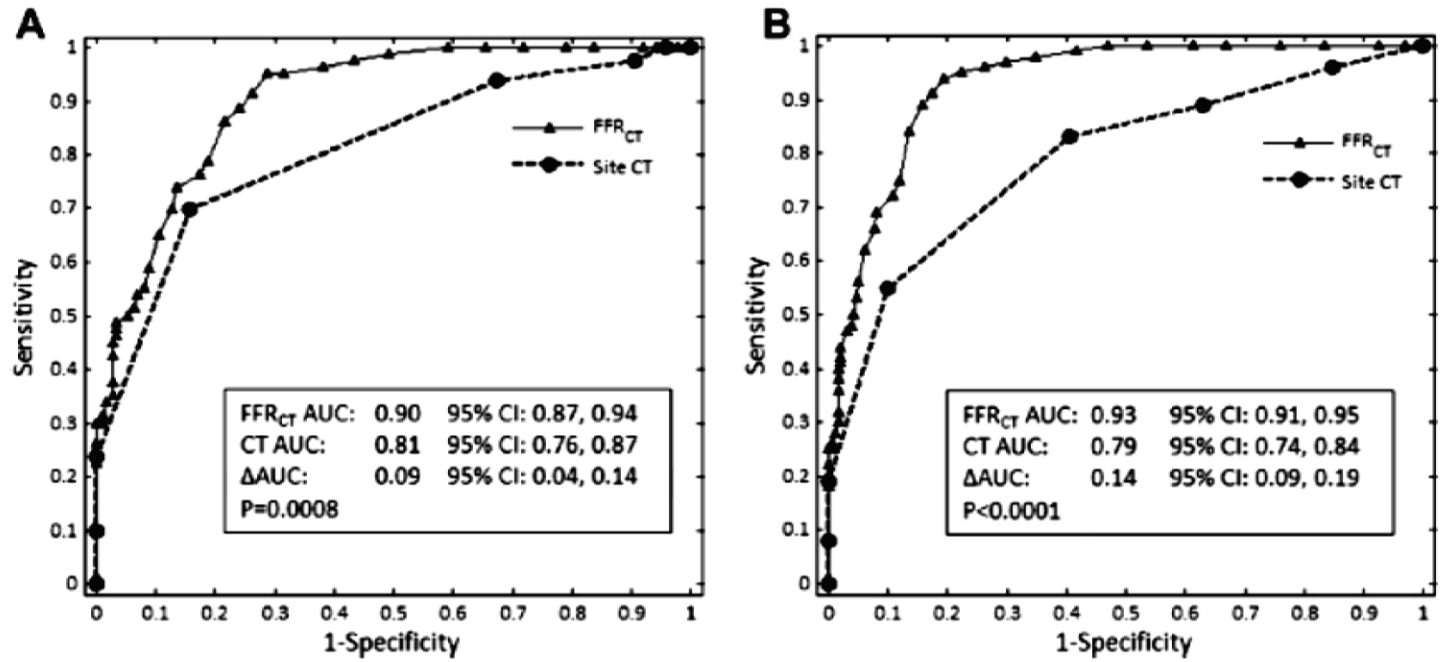


Figure 5 AUC of FFR_{CT} Versus Coronary CTA for Demonstration of Ischemia (FFR ≤0.80) on a Per-Patient and Per-Vessel Basis

(A) Per-patient; **(B)** per-vessel. In the per-patient analysis, a FFR_{CT} ≤0.80 was diagnostic of ischemia, and stenosis >50% at coronary CTA was anatomically obstructive. N = 251 for subjects and 484 for vessels. AUC = area under the receiver-operating characteristic curve; other abbreviations as in Figures 2 and 3.

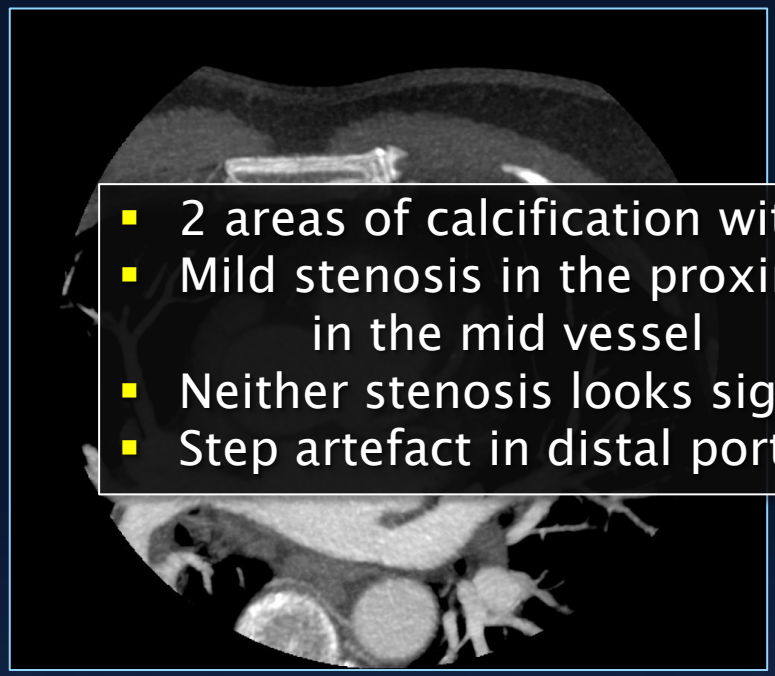
- 51 yr old male
- ↑BP; ↑cholesterol; brother MI in 50s

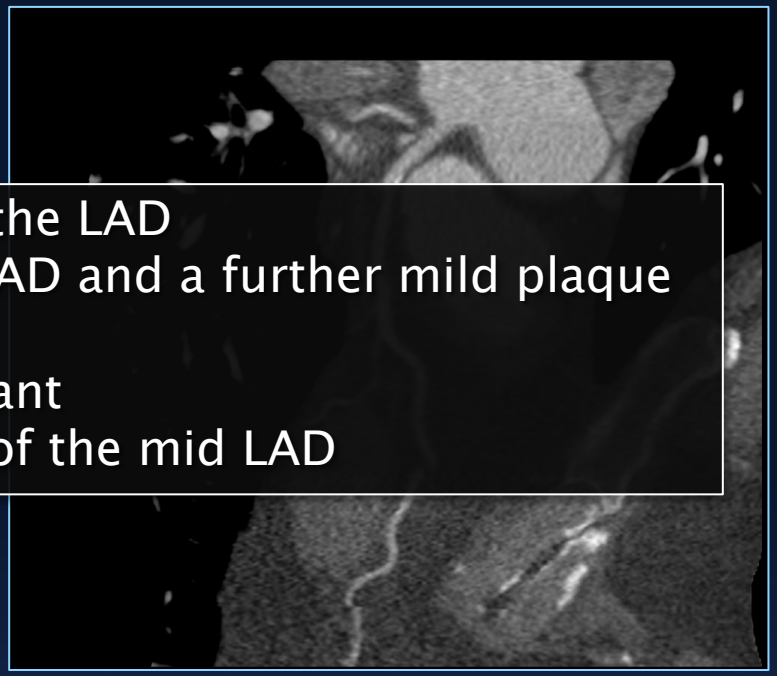
- 4 year history of SOBE… BMI 35…
- Exercise tolerance poor due to SOBE & takes little exercise
- 2 months: additional dull pain across upper chest & sharp pain R neck
- Usually exertional, occasionally at rest

What is my usual management of him?

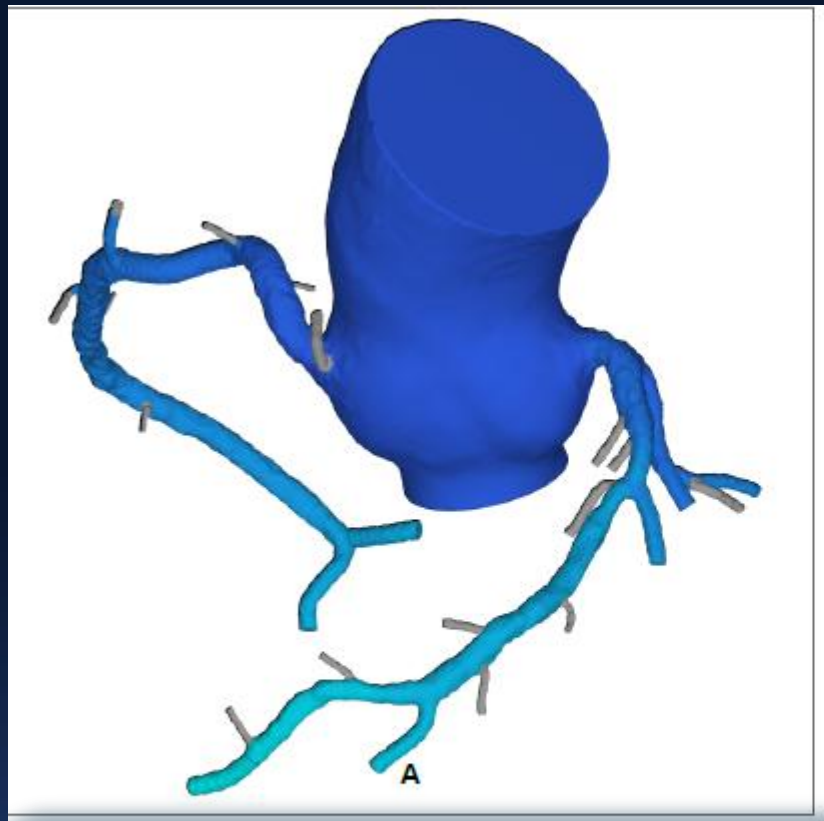
⇒Test for reversible ischaemia… ? Stress echo ?stress MRI

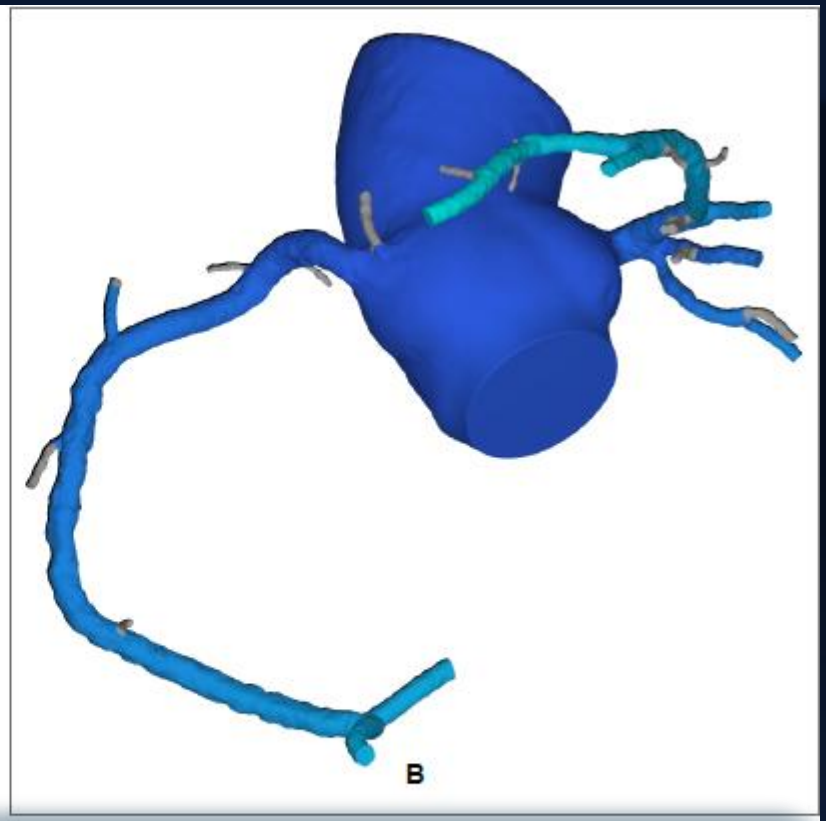
Enrolled into Cohort 2 PLATFORM Trial….





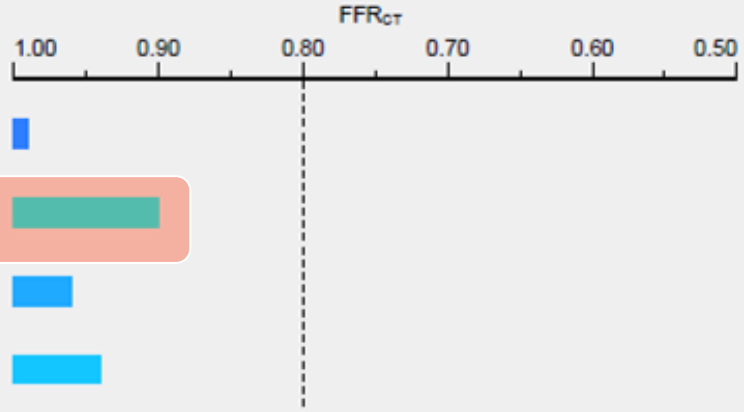
- 2 areas of calcification within the LAD
- Mild stenosis in the proxinal LAD and a further mild plaque in the mid vessel
- Neither stenosis looks significant
- Step artefact in distal portion of the mid LAD





Summary

CORONARY ARTERY		FFR_{CT}
Left Main	LM	0.99
Left Anterior Descending System	LAD	0.90
Left Circumflex System	LCx	0.96
Right Coronary Artery System	RCA	0.94



Diagnostic Performance of Noninvasive Fractional Flow Reserve Derived From Coronary Computed Tomography Angiography in Suspected Coronary Artery Disease

The NXT Trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps)

JACC 2014

- N=254
- CTA + FFRCT versus invasive angio + FFR

Negative predictive value for lesions with CTFFR >0.9 was 100%

(206 out of 206 vessels)

What's coming up…FFR CT?

“The times, they are a’changin…”

Bob Dylan