Imaging the Vulnerable Plaque

David A. Dowe, MD

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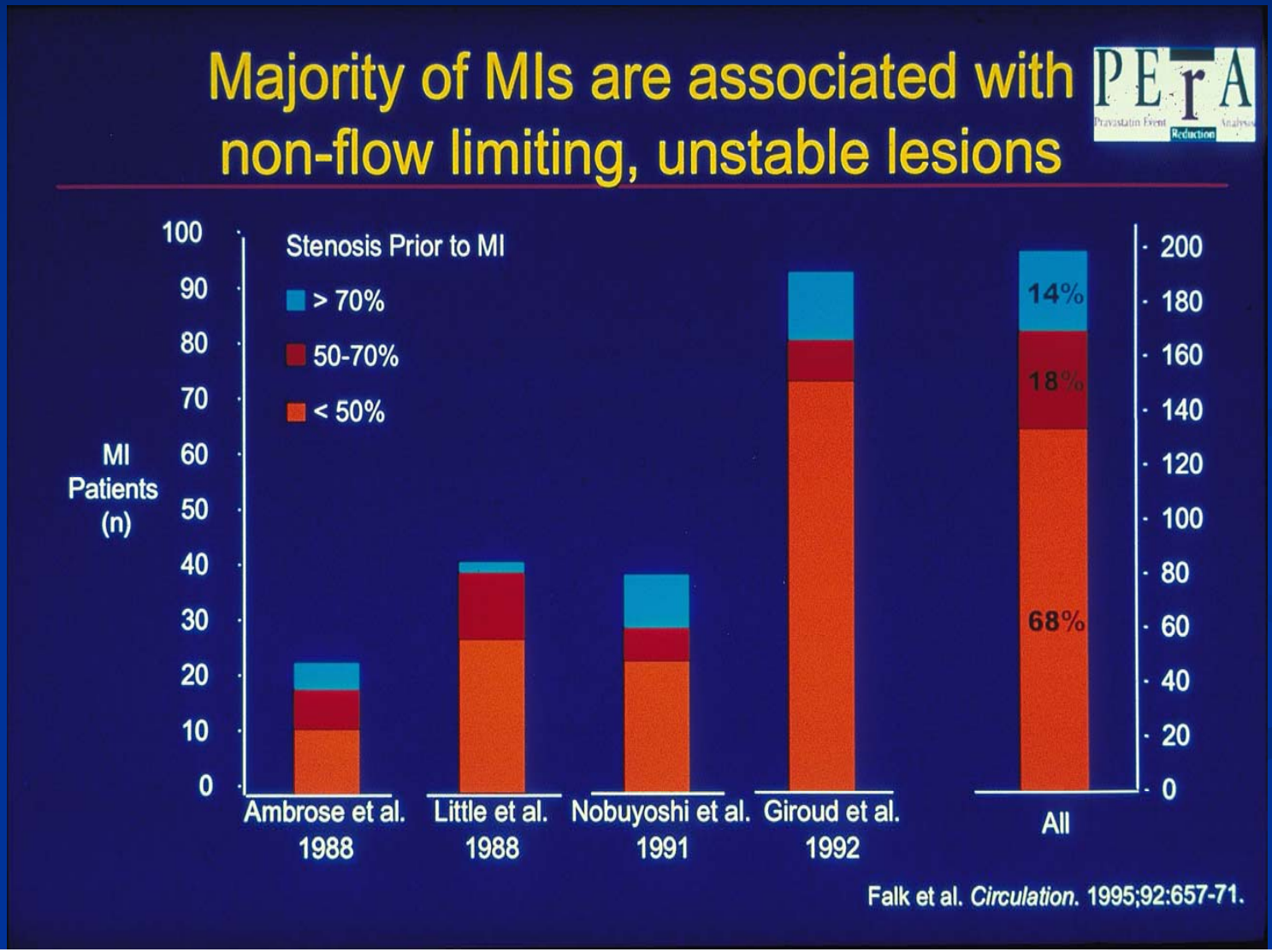
Why is this so important?

The Acute Situation



Coronary disease-Important

- Diagnosis of cardiovascular disease cost $148 billion in 2006
- 5 million patients visit emergency department with chest pain/year.
- Commonest cause for medicolegal litigation within the emergency department

AHA. Heart & stroke statistics-2006 update Dallas 2006

Traditional CAD Risk Factors

- Traditional CAD risk factors are incomplete in predicting CAD events.
- 50% of patients with an acute MI have normal cholesterol profiles.
- Sudden death is the FIRST (and last) sign of CAD in 150,000 people/year.

Traditional Clinical Risk Assessment Tools Do Not Accurately Predict Coronary Atherosclerotic Plaque Burden: A CT Angiography Study

Johnson KM, Dowe DA, Brink JA.

AJR 2009; 192: 235-243.

Traditional Clinical Risk Assessment Tools Do Not Accurately Predict Coronary Atherosclerotic Plaque Burden: A CT Angiography Study

- 26% of patients had no plaque but were already on statins for life.
- 21% had no need for statins yet had plaque at as high or higher than the median for patients with known CAD.
- 20% of plaque is calcified and 18% of patients with plaque have no calcium.

Lowering Cholesterol with Statin Medication

- Statins reduce blood cholesterol, risk of MI by 33%.
- 25-50 million in US could benefit.
- 4-5 million on statin therapy in US (costs $2000/year/patient)

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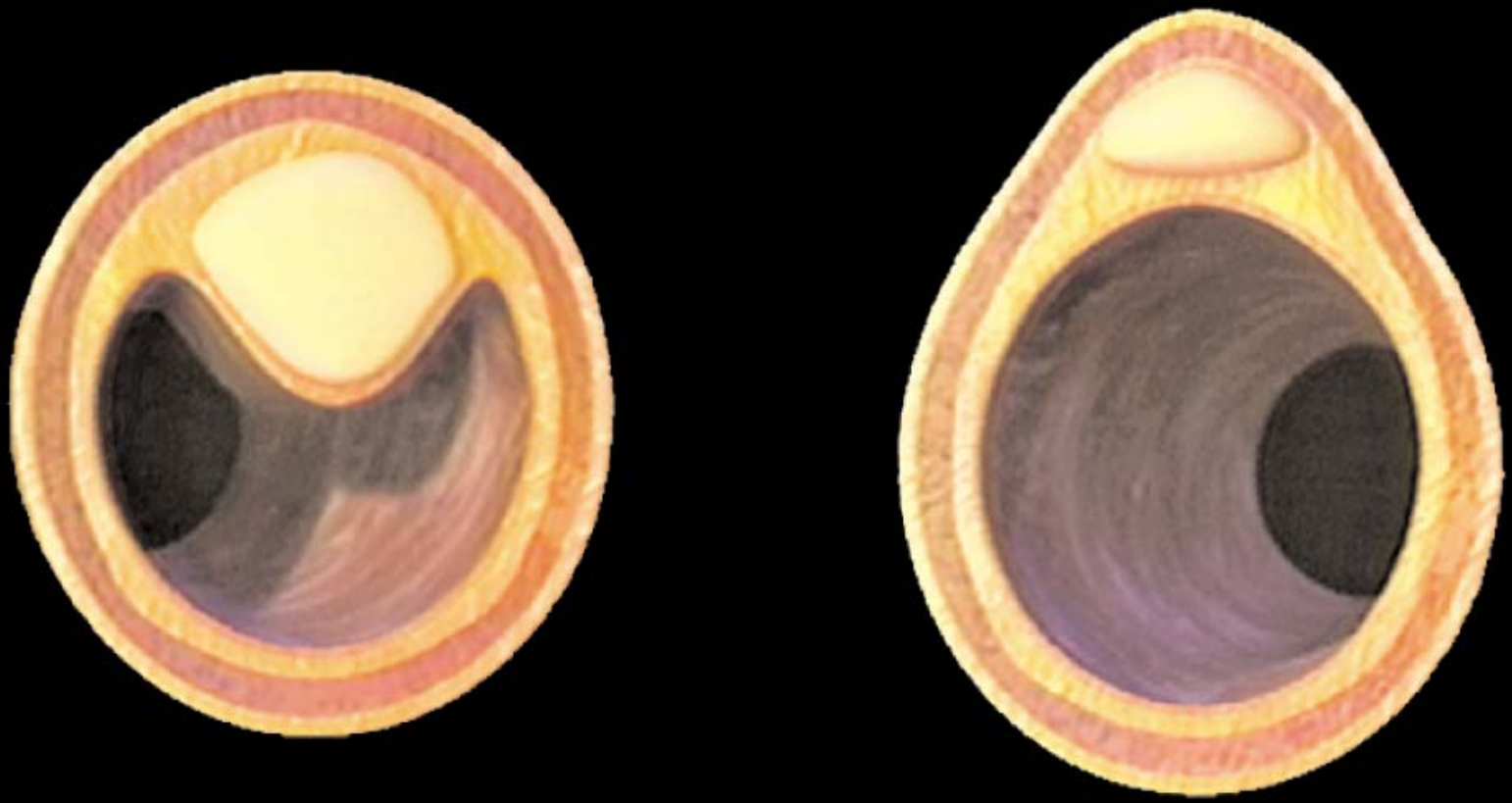
VBWG

Atherosclerosis: Traditional vs contemporary model



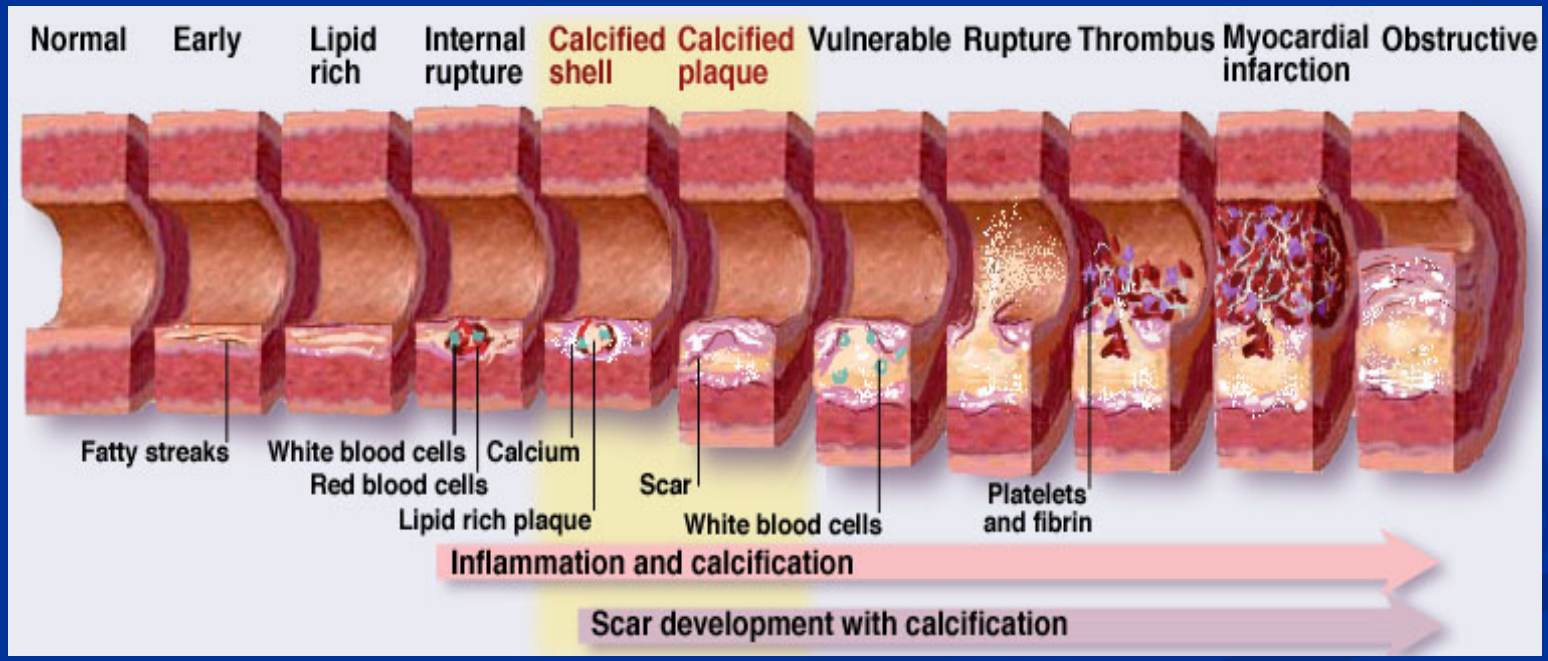
Traditional

Contemporary

Thanks to Carl Roobottom, MD

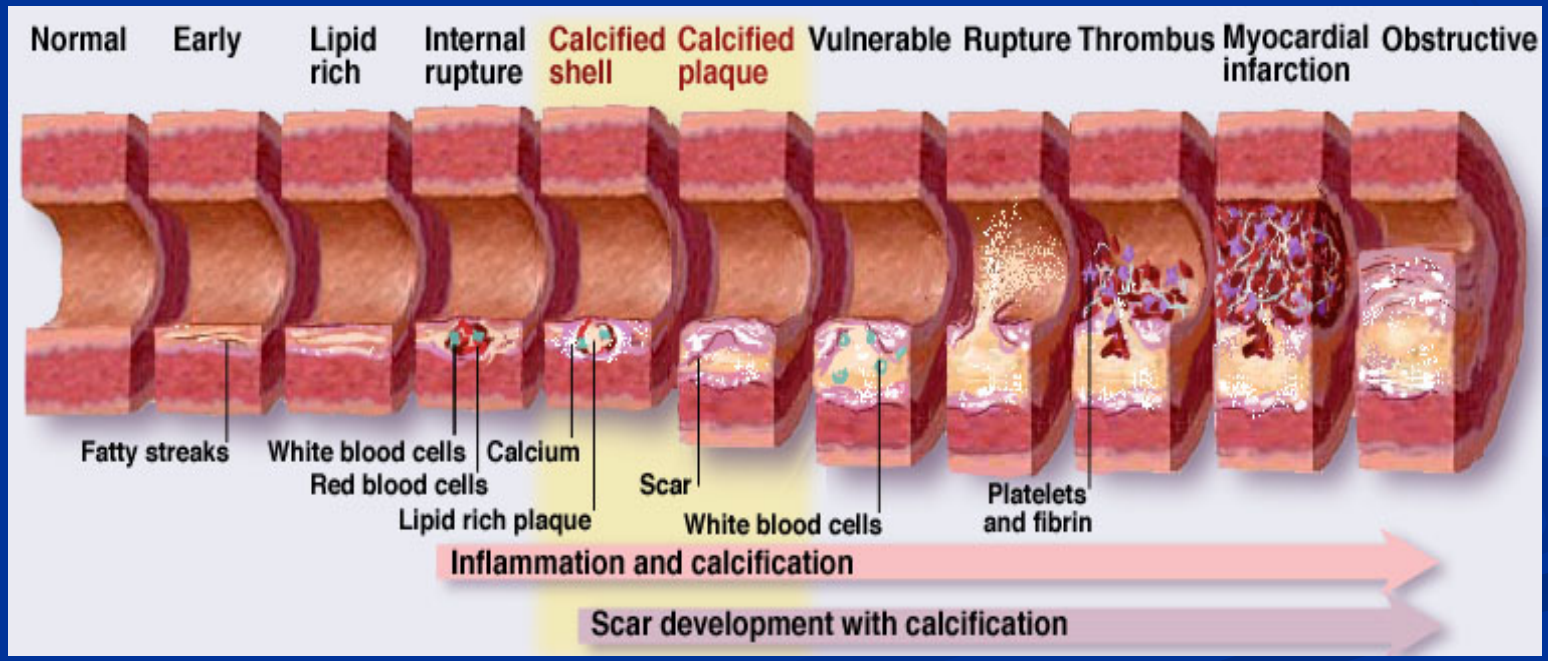
Pathophysiology of coronary atheroma

- Starry classification 1995



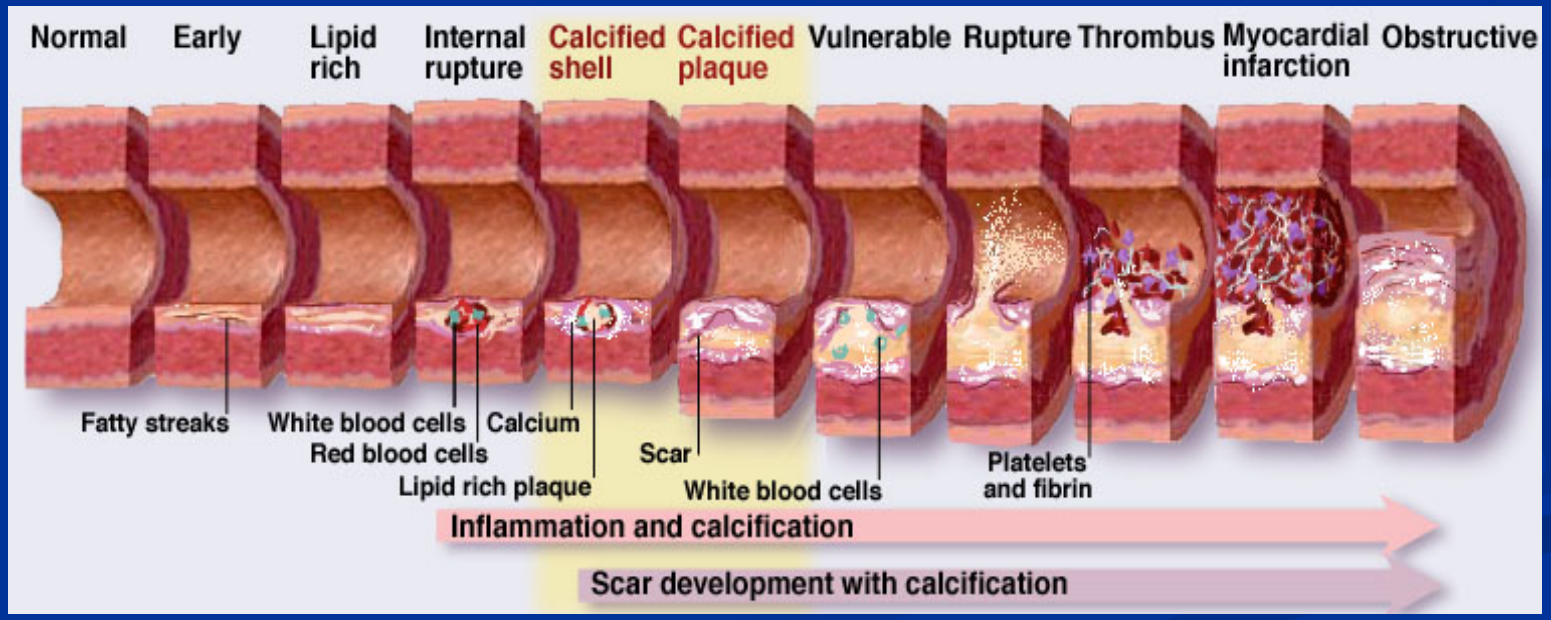
Pathophysiology of coronary atheroma

- Fatty streaks deposited in 20's



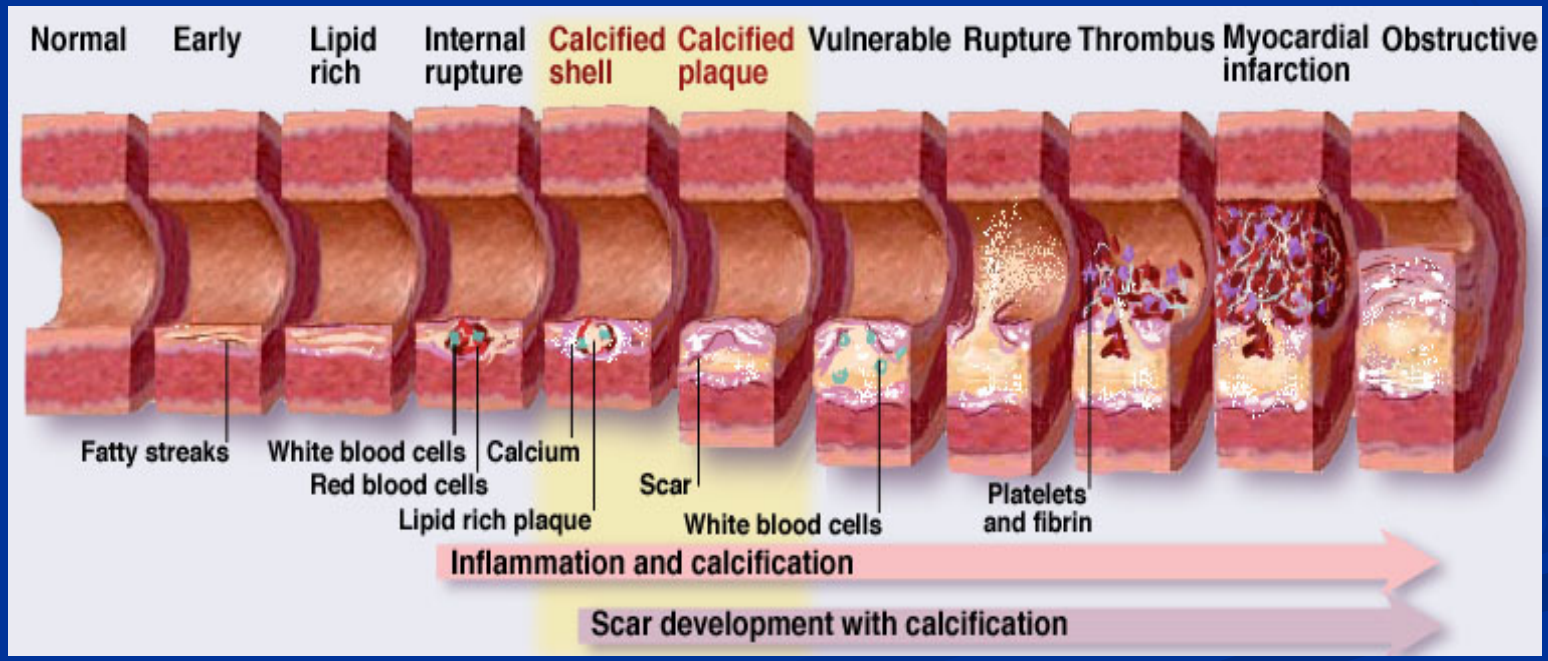
Pathophysiology of coronary atheroma

- Further deposition results in vessel expansion = positive remodelling



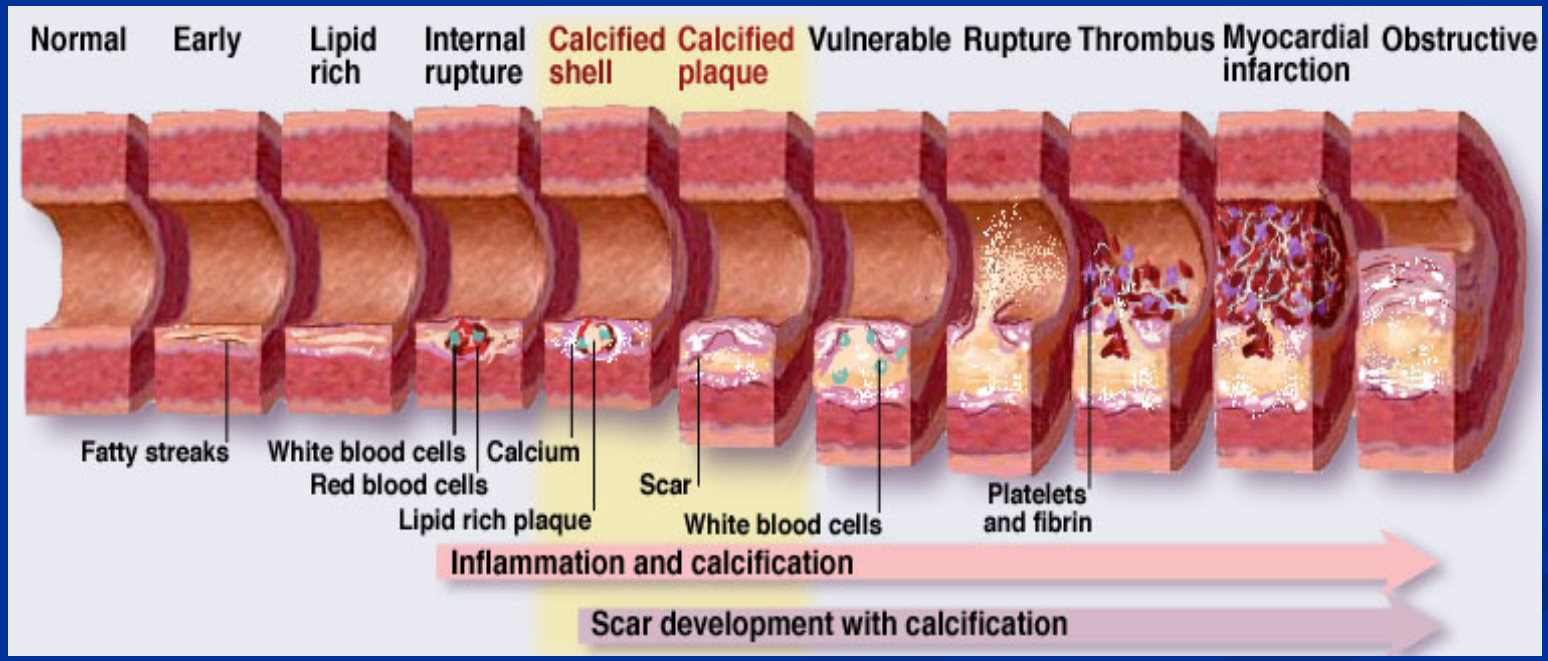
Pathophysiology of coronary atheroma

- Deposition within wall = inflammation



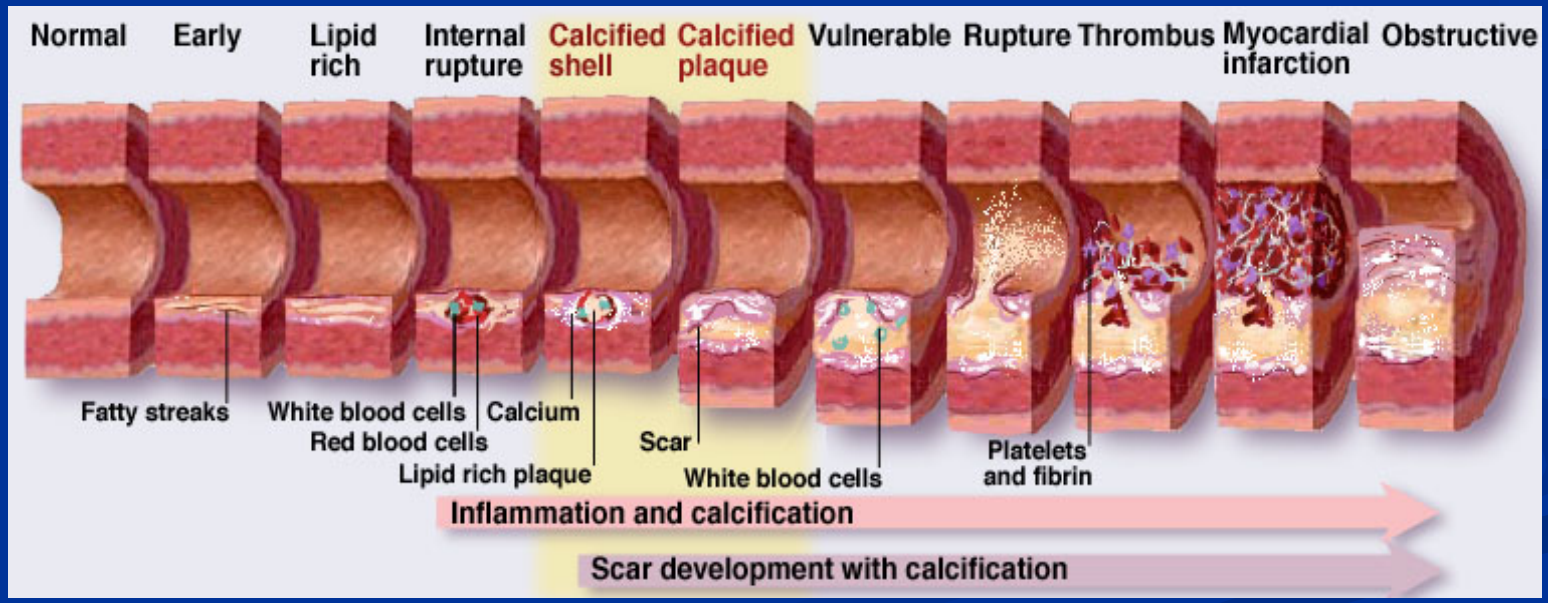
Pathophysiology of coronary atheroma

- Interspersed with episodes of plaque rupture



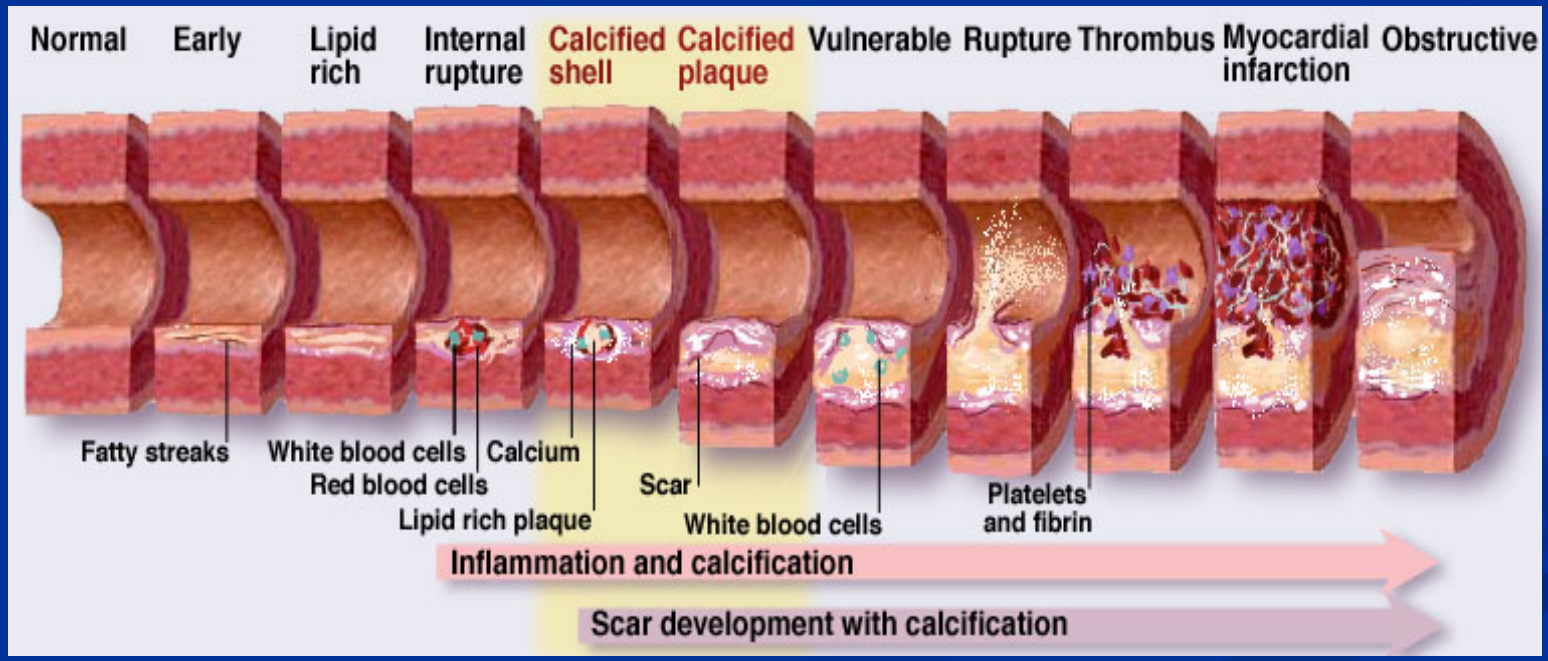
Pathophysiology of coronary atheroma

- Repeated plaque rupture and inflammation causes fibrosis +/- luminal narrowing



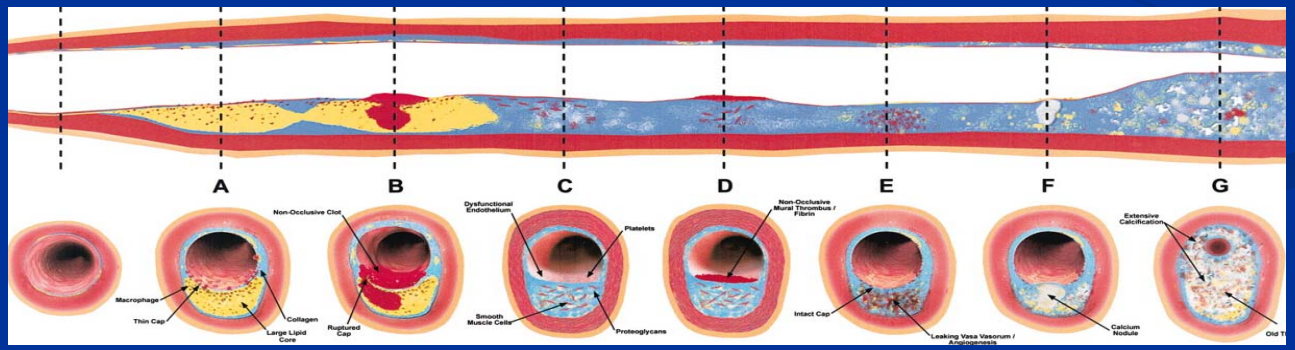
Pathophysiology of coronary atheroma

- Stabilized plaque is formed in 10-20 years



Summary Points:

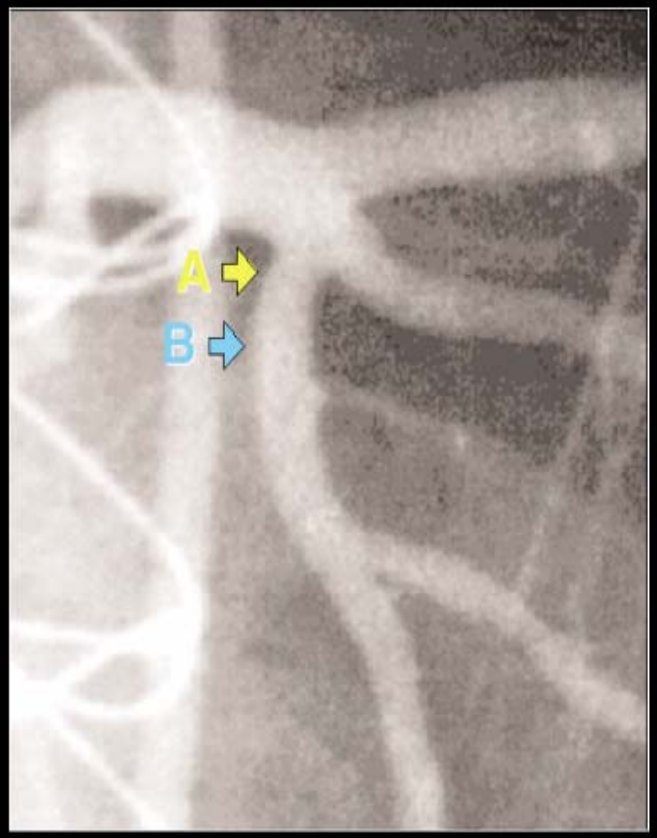
- Atheroma is a disease of the vessel wall
- The process of positive remodelling means luminal diameter is maintained for a long period of its natural history and are therefore undetectable by stress tests and caths.
- Coronary stenosis (and coronary calcium) are end stage consequences of repeated inflammation

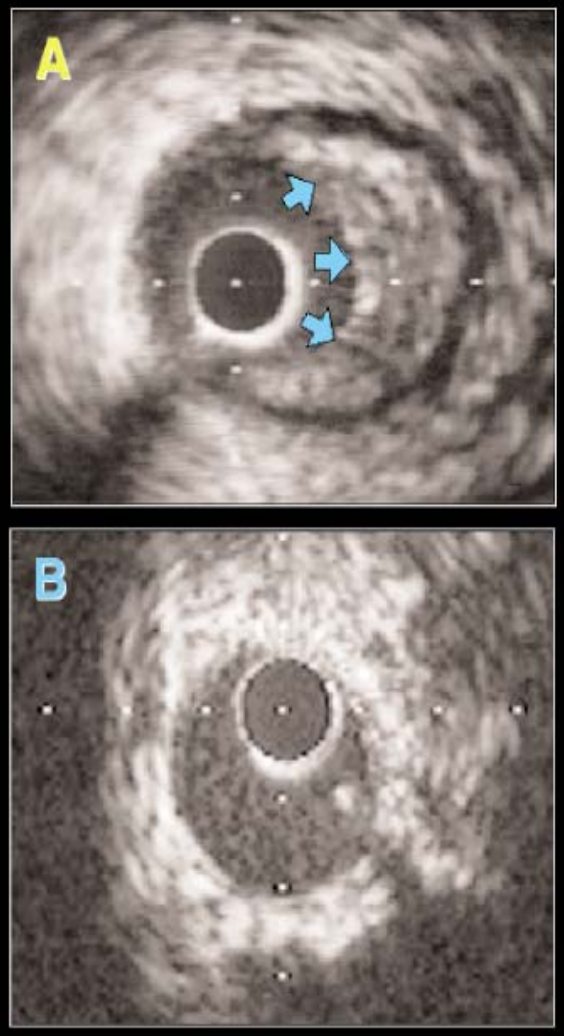


How do we currently diagnose coronary disease?

By looking at the lumen!

Remodeling in an angiographically "normal" artery



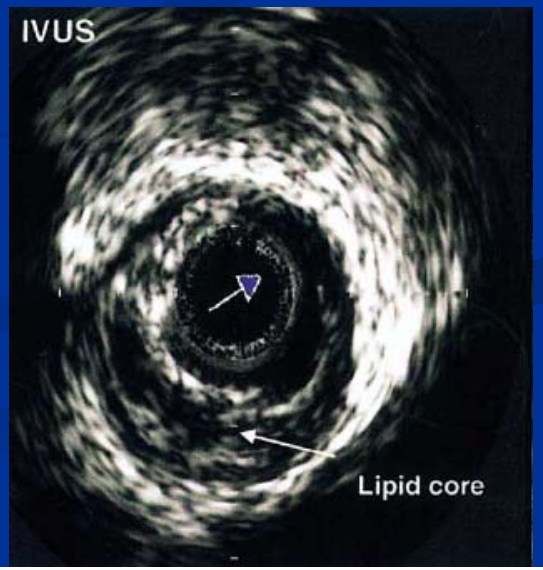


Topol EJ, Nissen SE. *Circulation*. 1995;92:2333-2342.

IVUS is the gold standard

- Invasive
- Expensive
- Only assesses proximal vessels
- Carries risk
- Changes groin management
- THEREFORE NOT

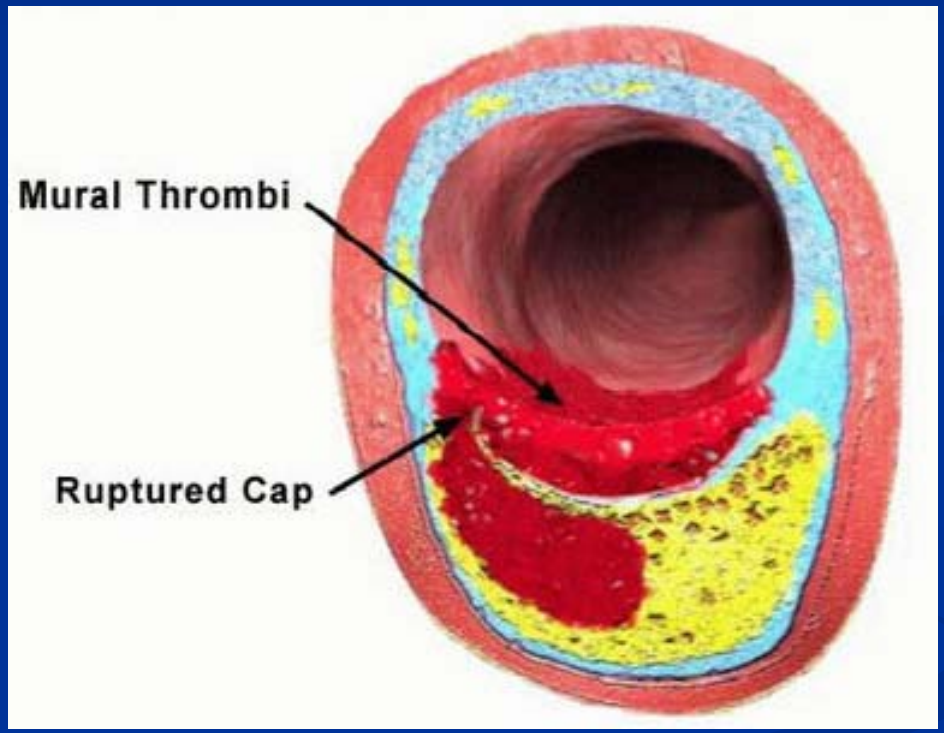
WIDELY APPLICABLE



The Incremental Value of Coronary Catheterization

- With the exception of left main stem disease and severe 3 vessel disease intervention has no prognostic benefit
- Intervention is for symptomatic disease-providing their symptoms are related to CAD.
- It does not stop patients from dying!
- Why?

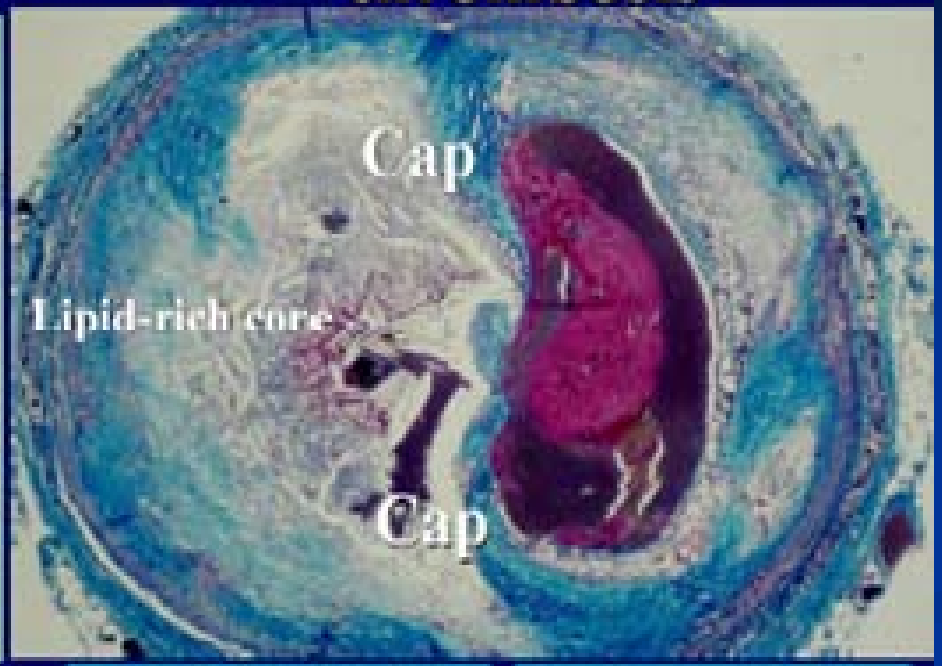
Cath does not detect the lesions that cause 86% of ACS

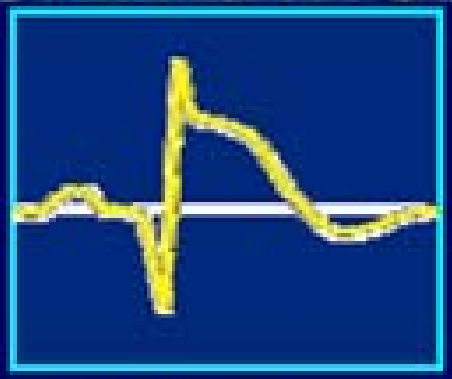


thrombosis⇒ sudden death, MI, unstable angina

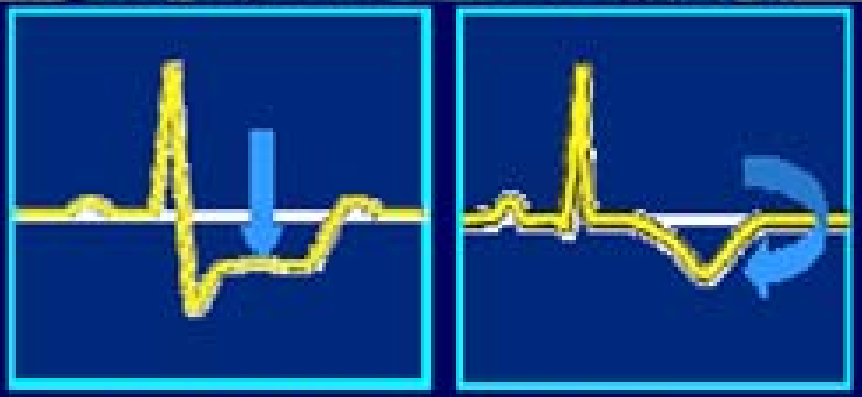
Occlusive thrombosis

Non-occl. thrombosis





CK- MB or Troponin ↑

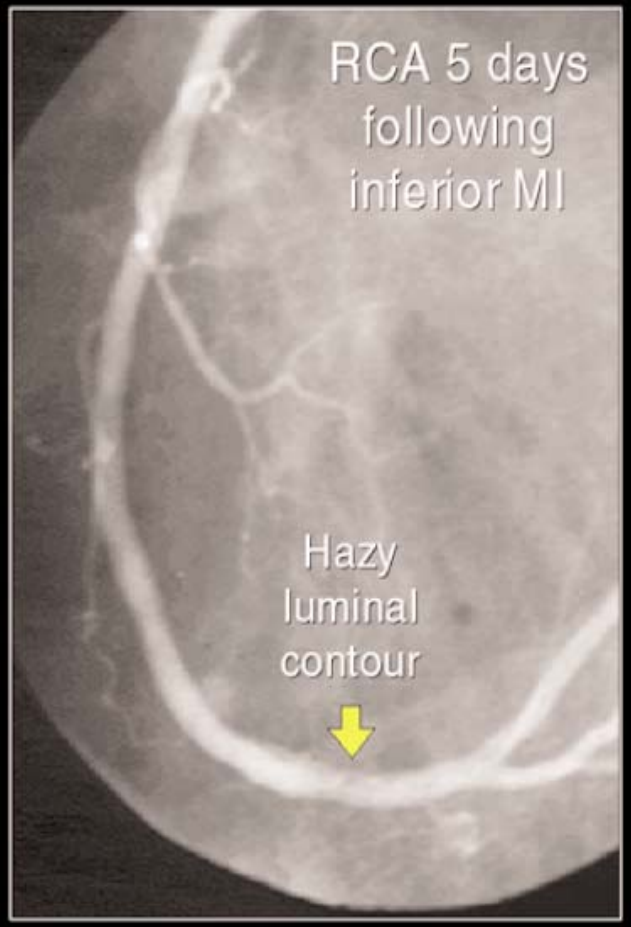


Troponin elevated or not

Courtesy Dr E. Falk

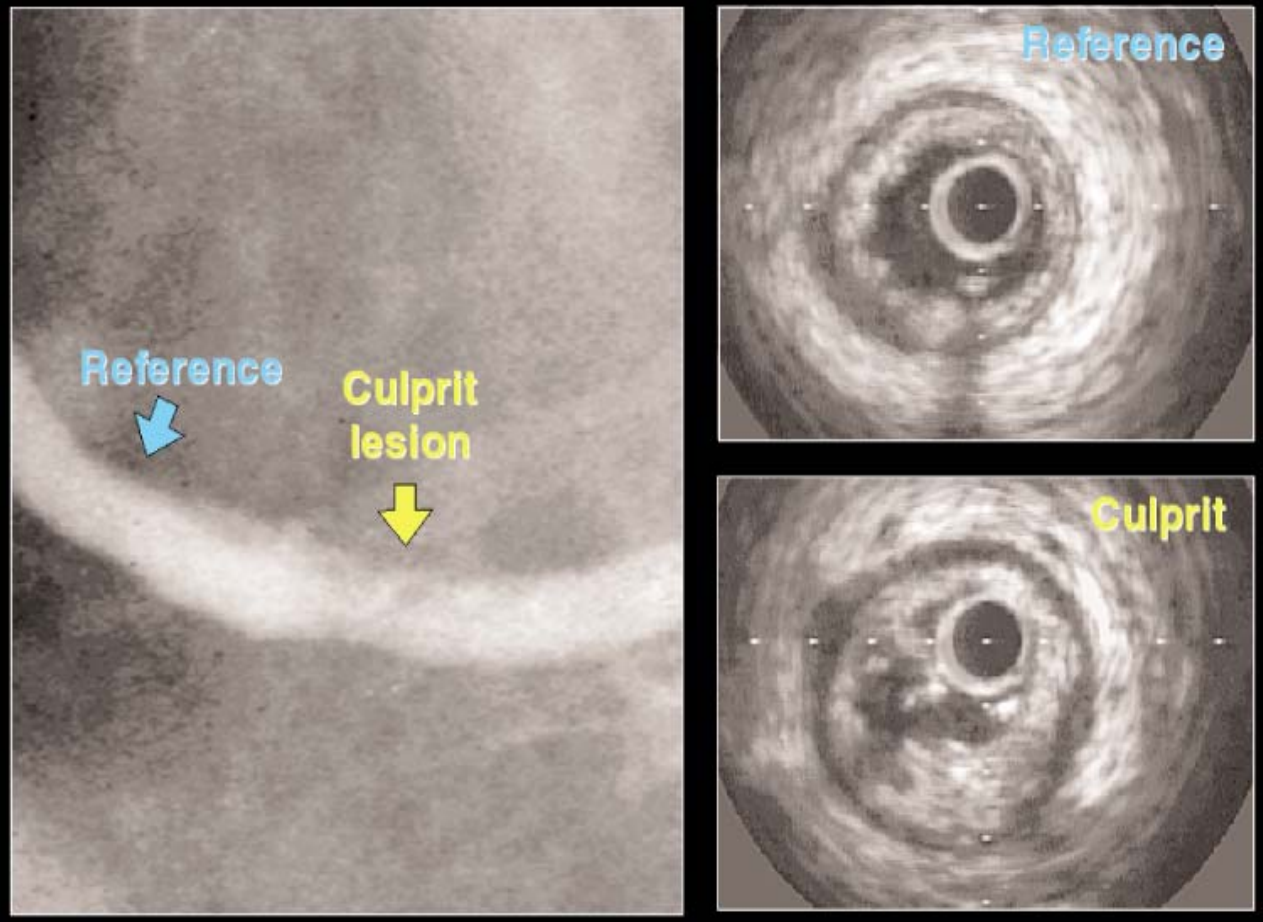
“It’s the doughnut, not the hole.”

Rupture in bulky, remodeled atheroma: Angiographic findings



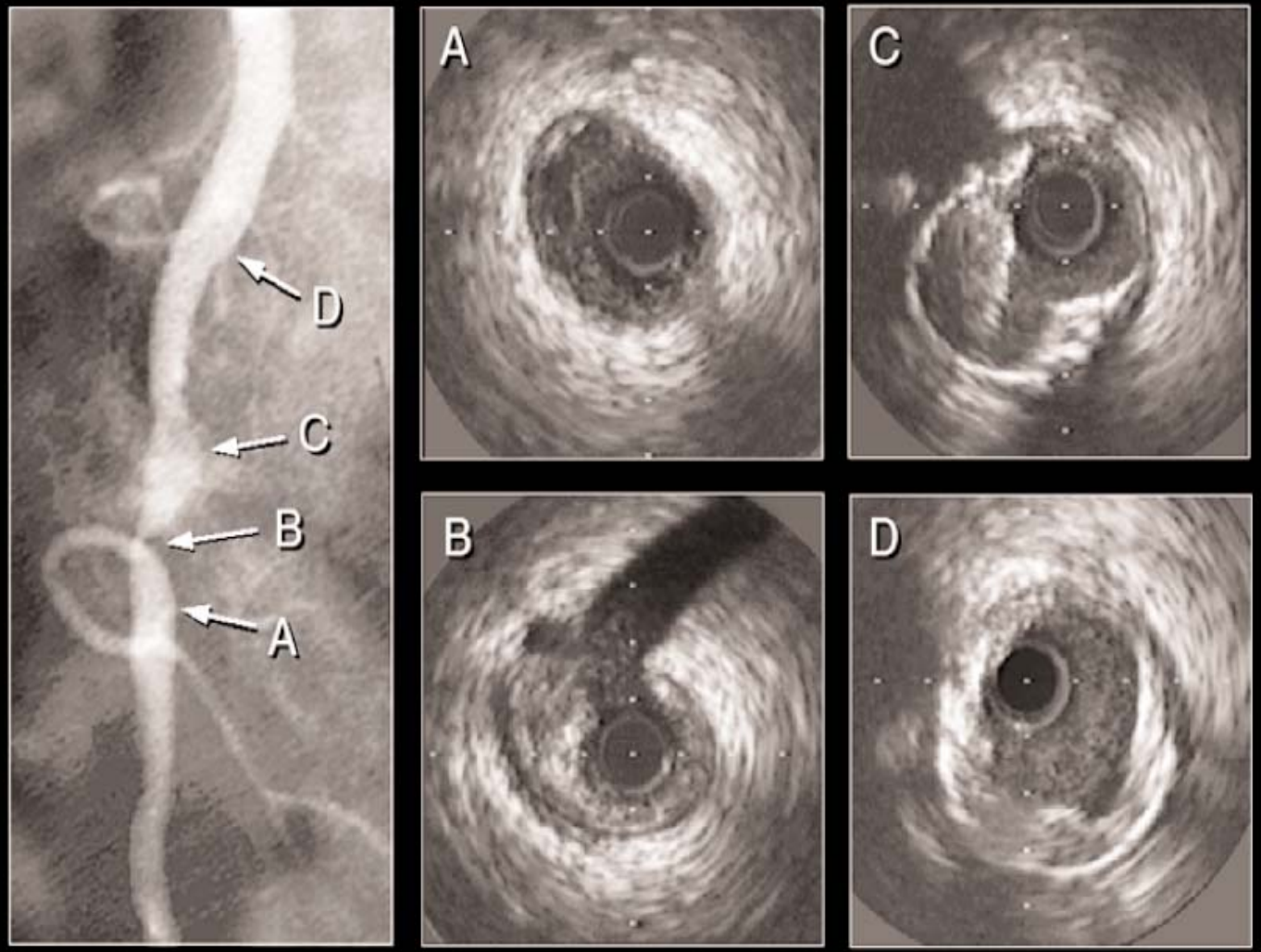
The Cleveland Clinic Intravascular Ultrasound Research Laboratory.

Rupture in bulky, remodeled atheroma: IVUS findings



The Cleveland Clinic Intravascular Ultrasound Research Laboratory.

Plaque rupture proximal to a severely stenotic lesion



The Cleveland Clinic Intravascular Ultrasound Research Laboratory.

Clinical Reality

- Non invasive tests look for end organ ischemia or damage, not vulnerable plaque
- Intravascular ultrasound is expensive, invasive and not without risk
- Angiography is the best test we have got!

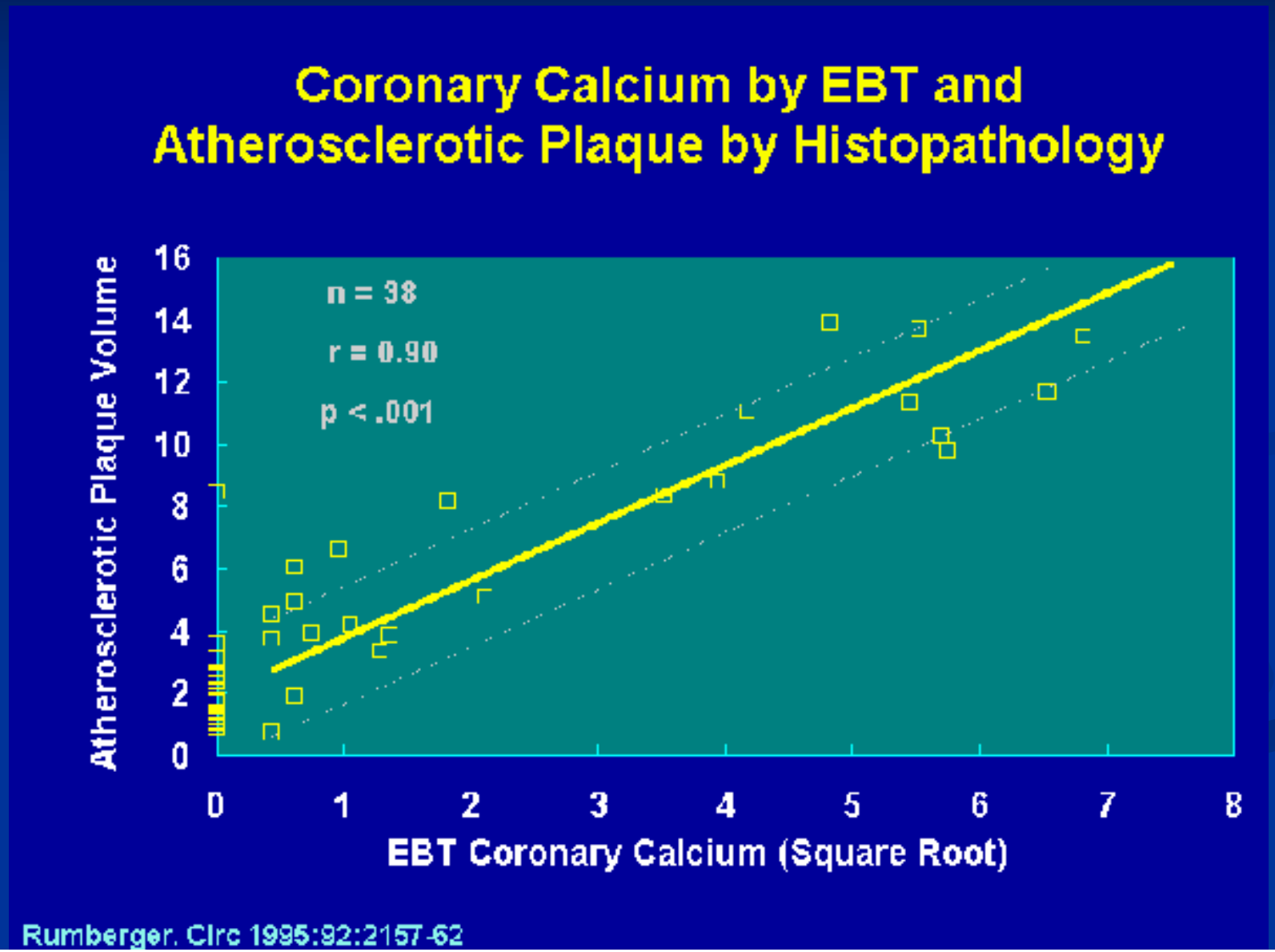
Calcium scoring

- EBCT has been around for over 25 years
- EBCT is (only!) good for calcium scoring
- There are large amounts of data on coronary calcium
- Calcium scoring can be performed with MDCT

Good news!

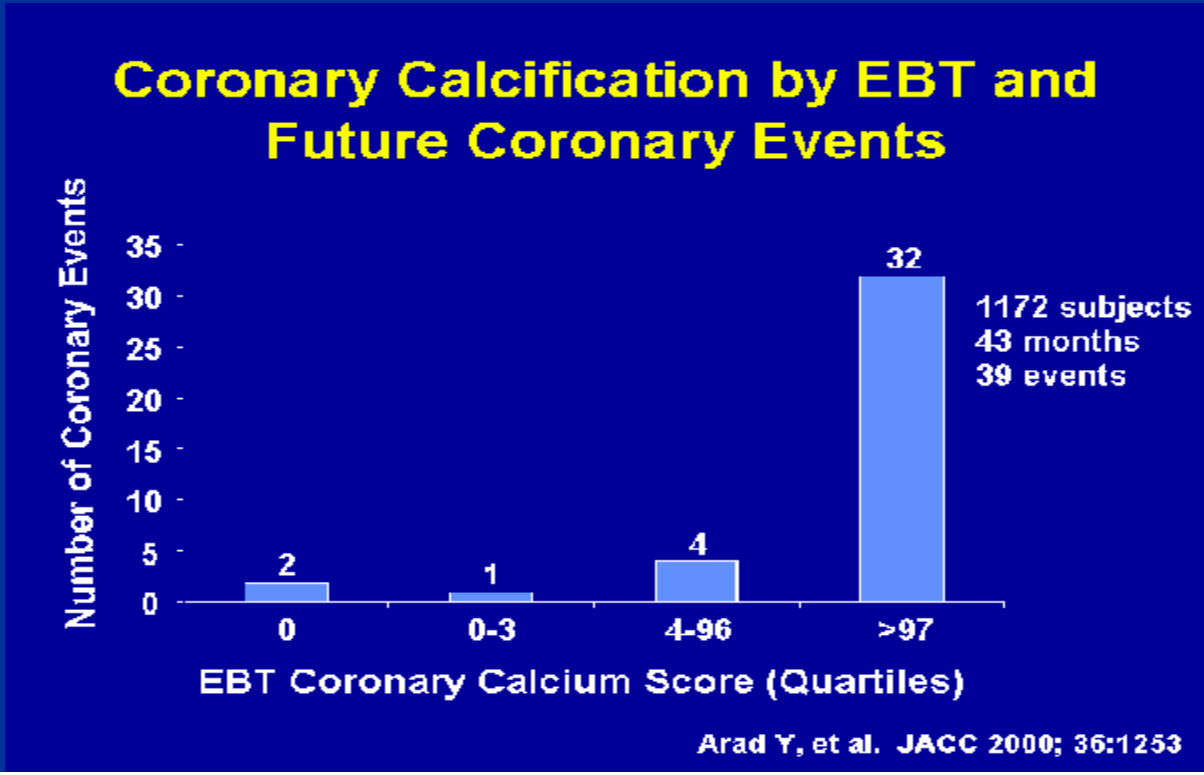
- Calcification of the coronary arteries is a specific marker of atherosclerosis.

Calcium = Atheroma



Mixed News

- There is a close relationship between coronary calcium and coronary disease but ACS can happen across the entire spectrum of calcium scores.



The Real Good News

"With a calcium score=0 you have a 0.4% risk of ACS over the next 5 years."

Why I do not stop CCTA with a Calcium Score=0

30 yo wm, asymptomatic. Three male family members have had MI before the age of 55.

Proximal LAD "Widow maker" atheromatous plaques

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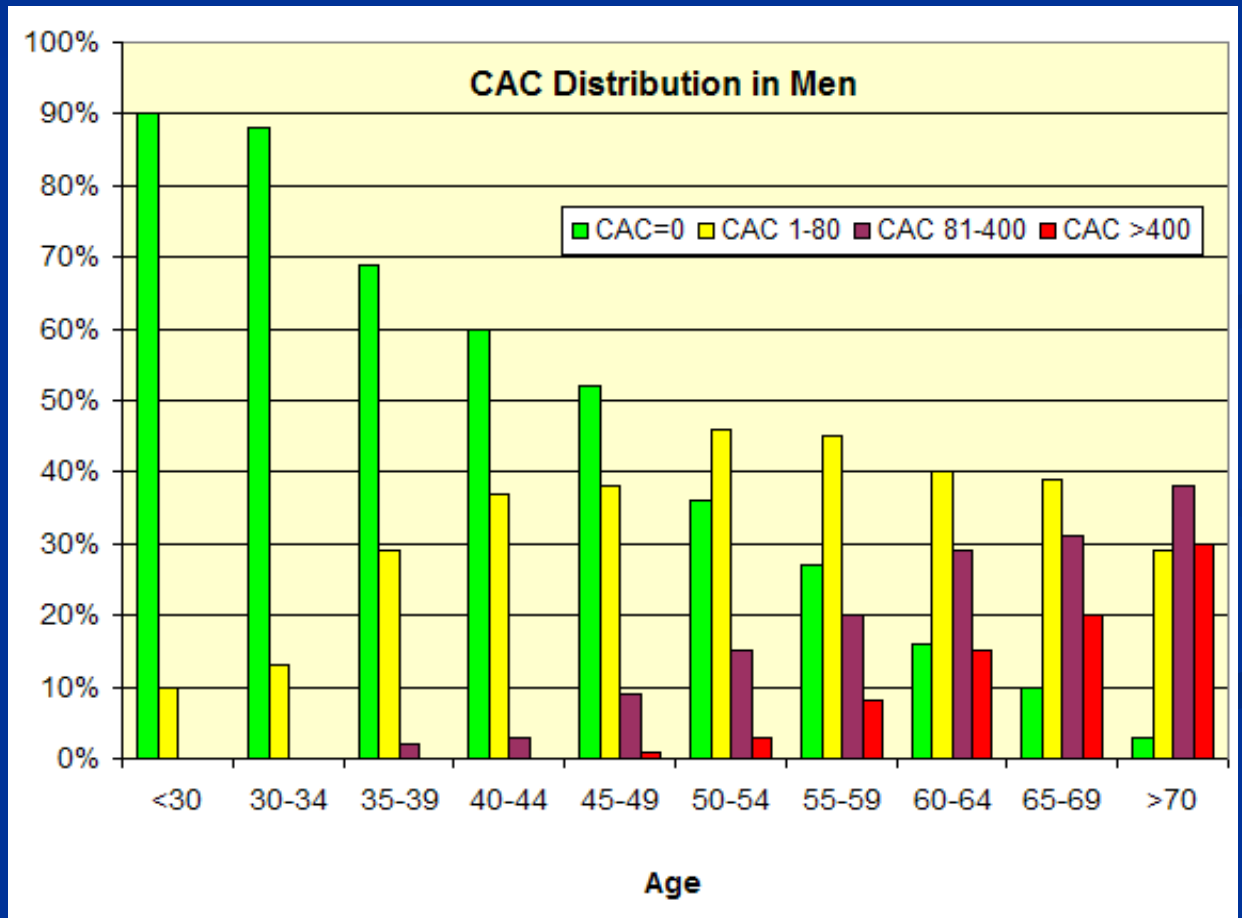
Bad News!

- While calcium indicates coronary atheroma it is not necessarily related to stenotic disease
- There is little relationship between the location of stenotic disease and calcification (no big deal).
- There is little correlation between the site of calcium and vulnerable plaque
- *Calcium is merely the gravestone of previous episodes of coronary inflammation*

Bad News

- Coronary calcium is very common!



Calcium alone is the tip of the iceberg and you are the Titanic

ACCF/AHA consensus document JACC Jan 2007

- May be useful in intermediate CHD risk patients in reclassification to high/low risk
- May be useful in helping rule out obstructive coronary disease in atypical chest pain (no calcium has 0.4% risk of MI)

EXPEDITED REVIEW

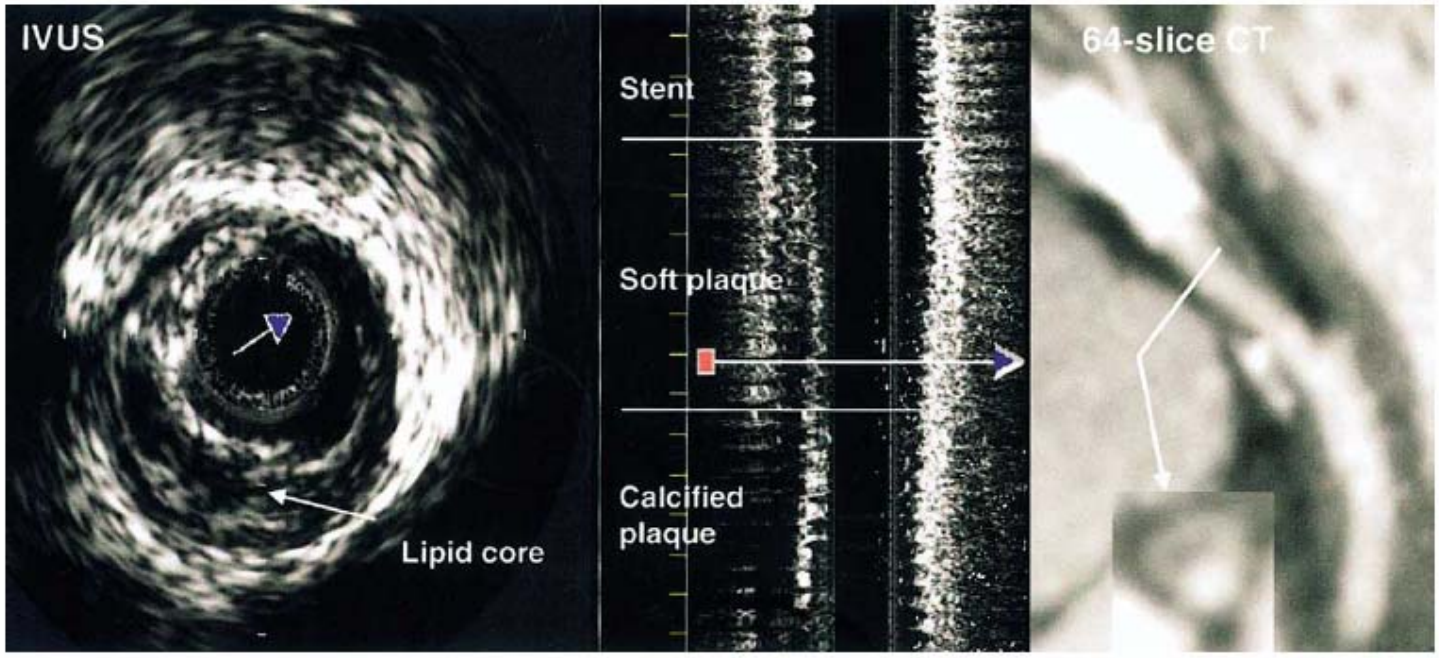
Accuracy of 64-Slice Computed Tomography to Classify and Quantify Plaque Volumes in the Proximal Coronary System

A Comparative Study Using Intravascular Ultrasound

Alexander W. Leber, MD,*§ Alexander Becker, MD,* Andreas Knez, MD,* Franz von Ziegler, MD,* Marc Sirol, MD,§ Konstantin Nikolaou, MD,† Bernd Ohnesorge, PHD,‡ Zahi A. Fayad, PHD,§ Christoph R. Becker, MD,† Maximilian Reiser, MD,† Gerhard Steinbeck, MD,* Peter Boekstegers, MD*

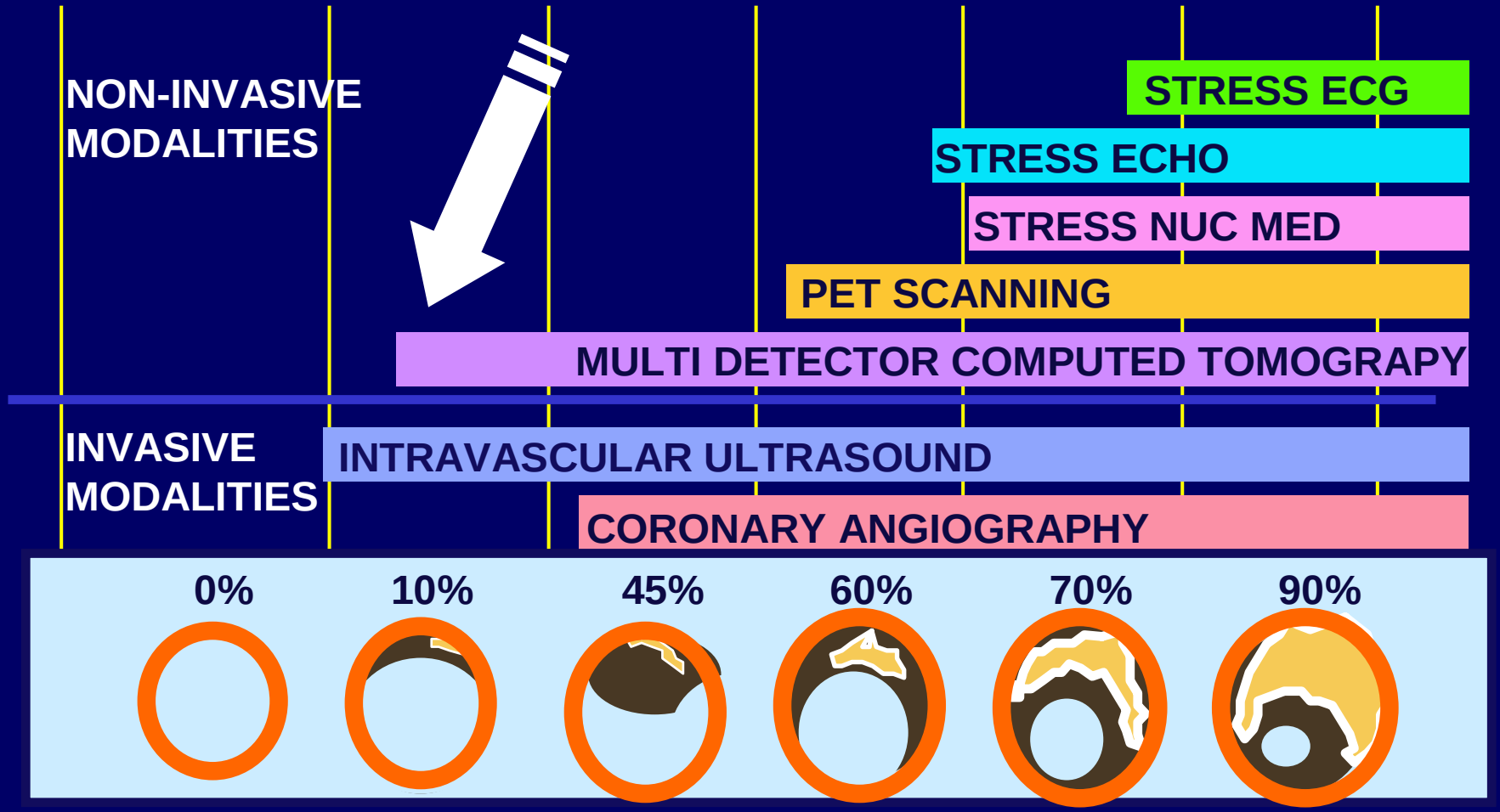
Munich and Forchheim, Germany; and New York, New York

JACC 2006



3. Noncalcified section with an embedded lipid core indicated by echolucency on intravascular ultrasound (IVUS) and hypodensity on 64-slice ted tomography (CT).

DIAGNOSTIC SENSITIVITY



So is it worth us finding "early" disease?

Can we do anything about it?

Statin effect

- REVERSAL Trial
- 34 centers, 18 month FU, 654 pts
- Assessment of atheroma with IVUS
- Aggressive statin therapy halted disease progression whereas moderate therapy was associated with significant disease progression

Am J Cardiol 2005 Sept 61-68

Effects of Very High-Intensity Statin Therapy on Regression of Coronary Atherosclerosis. The ASTEROID Trial.

Nissen SE, Nicholls SJ, Sipahi I, et.al. JAMA March 2006.

The ASTEROID Trial

- N=349
- All patients received rosuvastatin 40mg/day.
- After 24 months patient serial IVUS comparison
- Mean LDL decrease from 130.4 to 60.8 mg/dl.
- Mean HDL increase from 43.1 to 49.0 mg/dl.

The ASTEROID Trial Conclusion

High intensity statin therapy resulted in significant regression of atheroslcerosis as specified by IVUS.

Effect of Rosuvastatin Therapy on Coronary Artery Stenosis Assessed by Quantitative Coronary Angiography

Ballantyne CM, Raichlen JS, Nicholls SJ, et.al. Circulation. 2008; 117: 2458-2466

Rosuvastatin/Serial QCA

- N=507
- Blinded QCA analysis of % diameter stenosis and minimum lumen diameter for up to 10 segments of coronary arteries and major branches with >25% diameter stenosis at baseline.

Rosuvastatin/QCA Results

- Decreased mean LDL by 53.3% and increased mean HDL by 13.8%.
- Mean decrease in diameter stenosis by 37.3% ($P<0.001$)
- Minimum lumen diameter increased from 1.65mm to 1.67mm ($P<0.001$)

CCTA Study of Plaque Progression

- Fluvastatin Reduces Coronary Plaque and Increases Lumen Volume: Assessment by MDCT.
- Sato, et. al.- ACC, 2006
- MDCT performed on 16, 32 and 64 MDCT in 12 patients with CAD.

Sato et.al. Fluvastatin and MDCT Progression

- Plaque volume and lumen volume was measured before and after 12 month Rx with Fluvastatin 20mg qd.
- Fluvastatin significantly reduced plaque volume (104.3+/- 47.8 to 91.2 +/- 36.1 mm3, p=0.045)
- And increased Lumen Volume (97.7 +/- 45.9 to 108.3 +/- 47.0 mm3, p=0.010)

Sato et.al. Fluvastatin and MDCT Progression

- There was no significant change in the lipid profile.
- Total chol 202 to 197.
- LDL 119 to 119.
- HDL 50 to 49.
- TG 168 to 147.

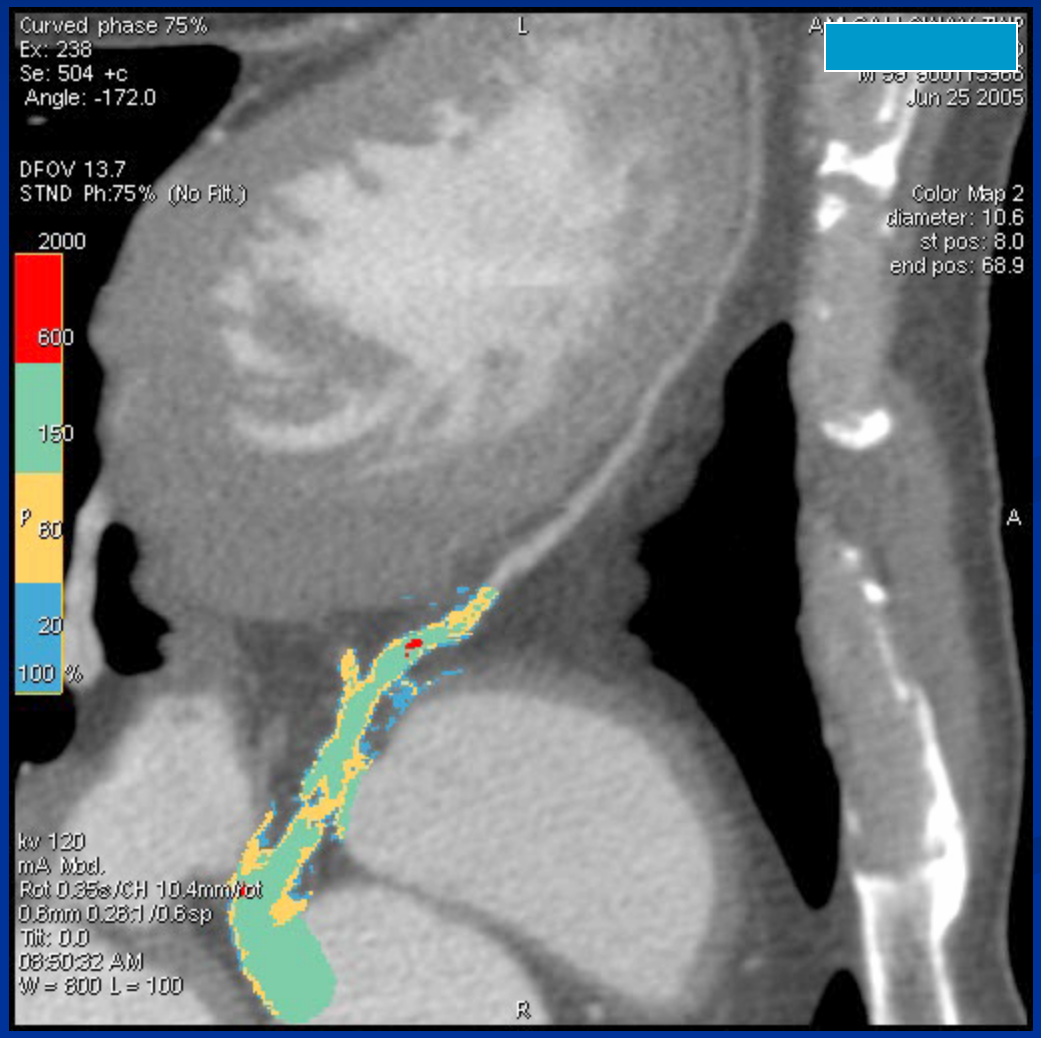
Fibro-atheromatous Plaque

Calcium

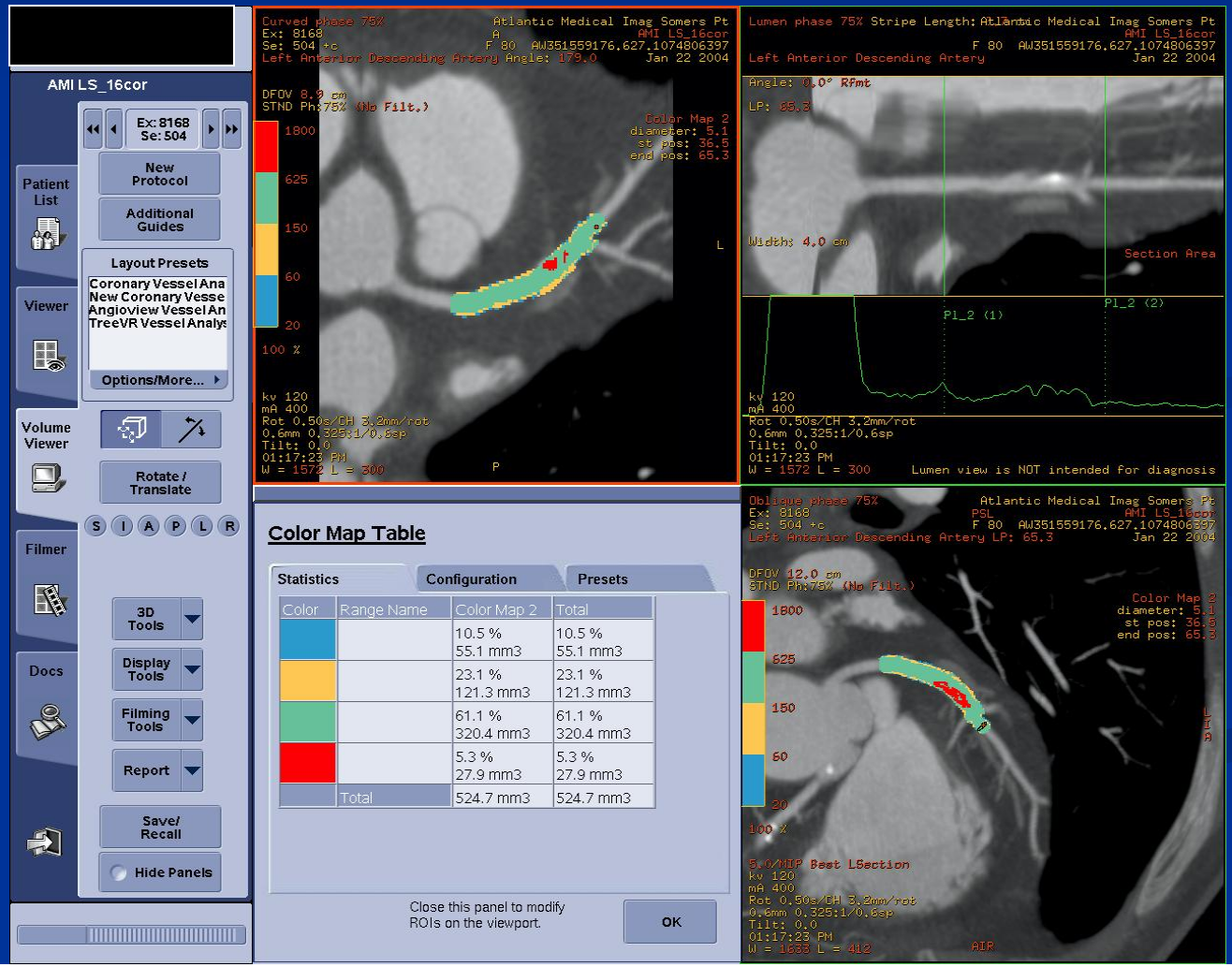
Contrast

Fibrosis

Atheroma

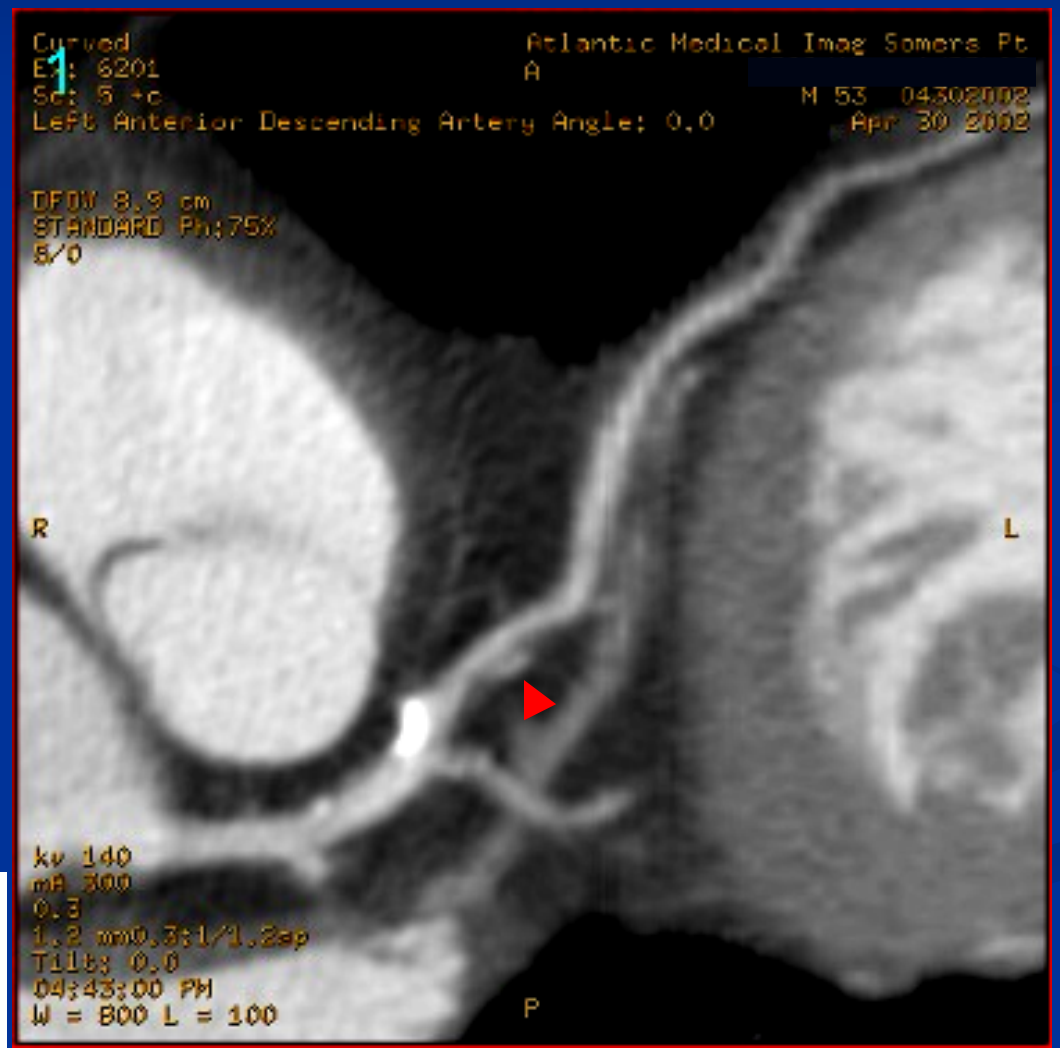


The Cholesterol Test of the Future



53 y.o. wm with positive family history. High cholesterol =190 on Lipitor. Asymptomatic.

ULCERATED PROX. LAD PLAQUE



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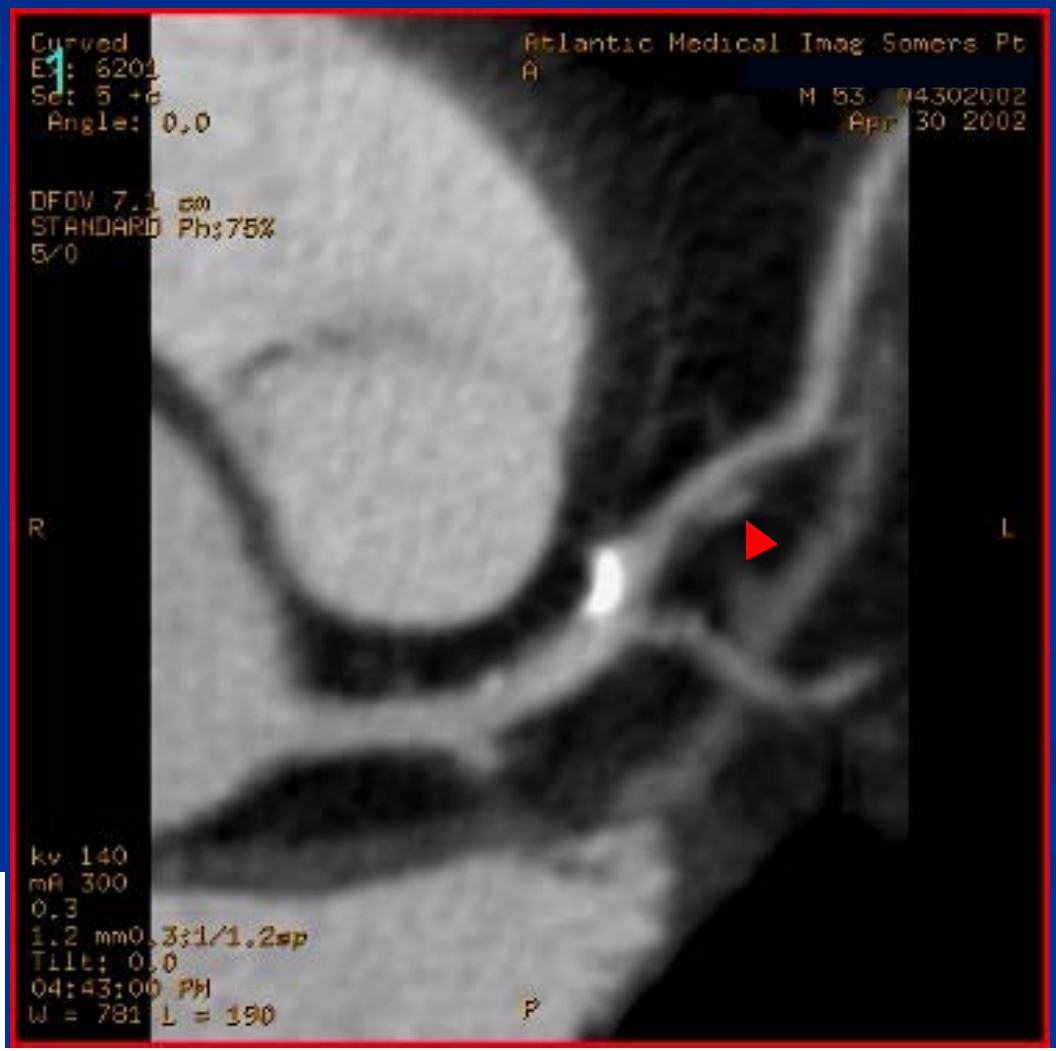
ULCERATED PROX. LAD PLAQUE



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4/30/02

- Total chol.=190
- Lipitor 10 mg.
- Asymptomatic

6/09/03

- Total chol=165
- Lipitor 40mg.
- Asymptomatic

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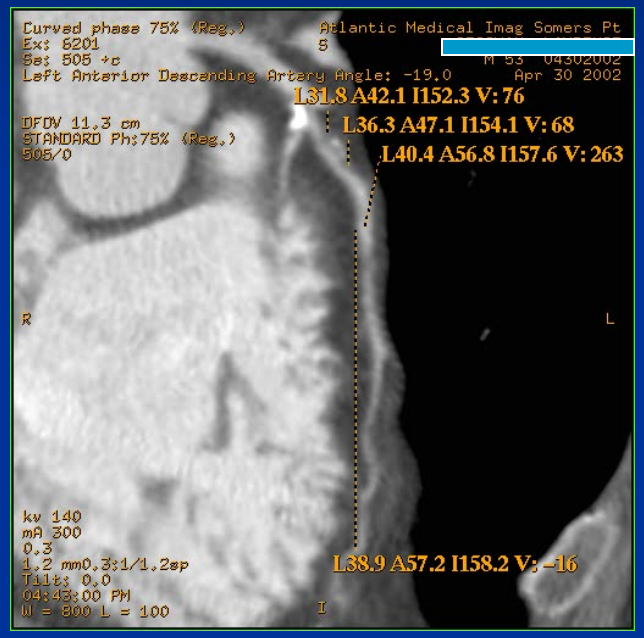
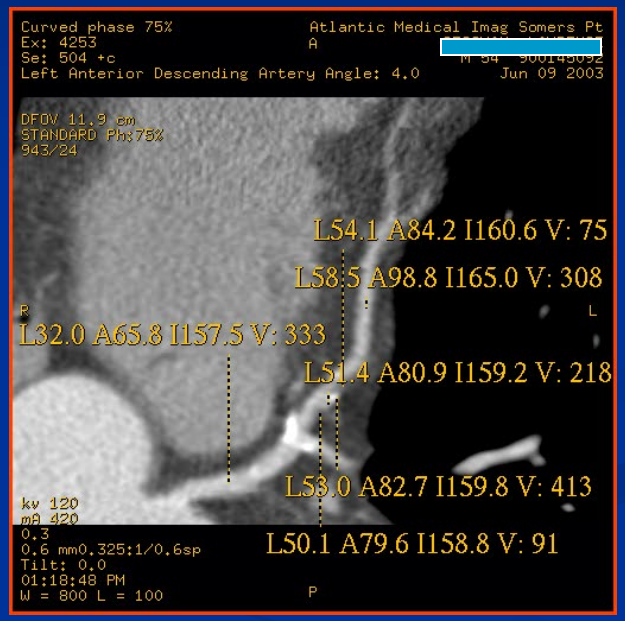
Follow up 14 months later…

Ulcerated Plaque LAD





- Assess plaque size, plaque area, HU at relevant plaque components and degree of stenosis.

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4/30/02

- Plaque = 13.6mm long
- Long area=19.8sq.mm
- Tr. Area=5.0sq.mm.
- Prox. Fornix= 79 HU
- Dist. Fornix=73 HU
- Prox. Crater=221 HU
- Dist. Crater=403 HU

6/09/03

- Plaque= 13.2mm long
- Long area=13.7sq.mm
- Tr. Area=4.5sq.mm
- Prox.Fornix= 91 HU
- Dist. Fornix=87 HU
- Prox. Crater= 218 HU
- Dist. Crater= 413 HU

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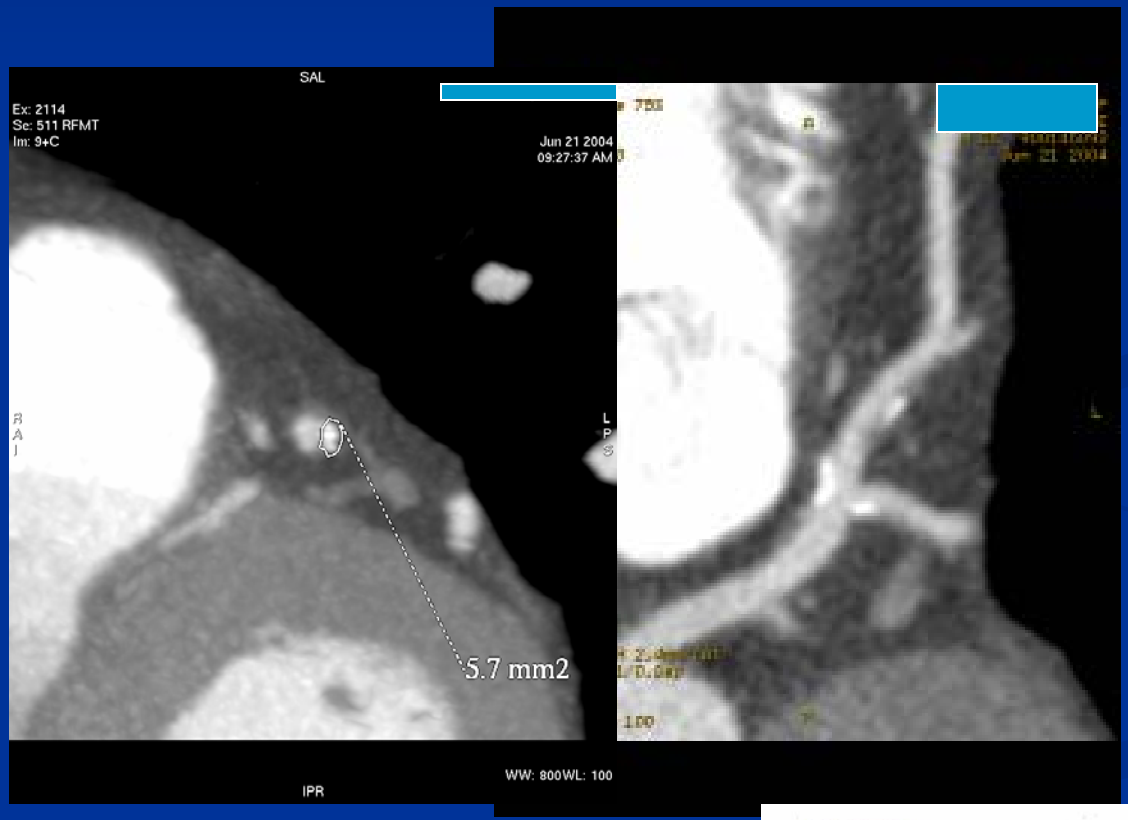
Same patient develops "angina like" chest pain and gets his third CCTA on 6/26/04.

Ulcerated Plaque LAD



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4/30/02, 6/09/03, 6/26/04

- Plaque length= 13.6, 13.2, 13.2 mm
- Long. Area= 19.8, 13.7, 10.8 sq. mm.
- Tr. Area= 5.0, 4.5, 5.4 sq. mm.
- Prox. Fornix= 79, 91, 98 HU
- Dist. Fornix= 73, 87, 99 HU
- Prox. Crater= 221, 218, 606 HU
- Dist. Crater= 403, 413, 578 HU

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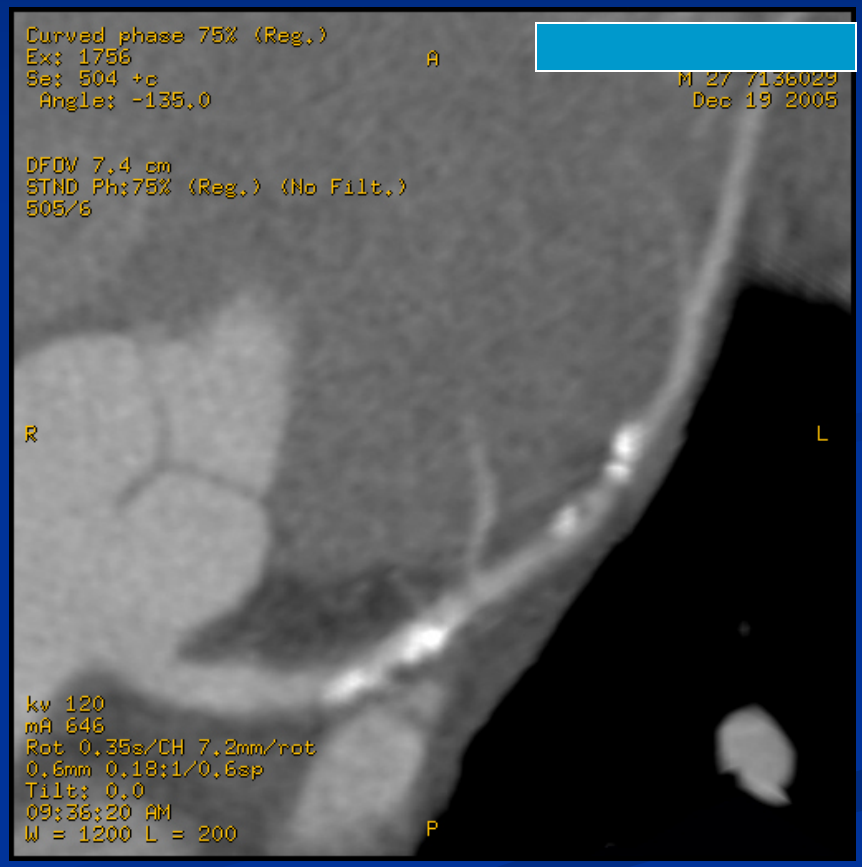
Coronary Artery Disease is a Reversible Disease!

Save the Lives of those too Young to have CAD.

27 yo wm with chest pain at rest radiating to the left arm, dyspnea at rest. Risk factors- hyperchol, FHx, smoking and HTN.

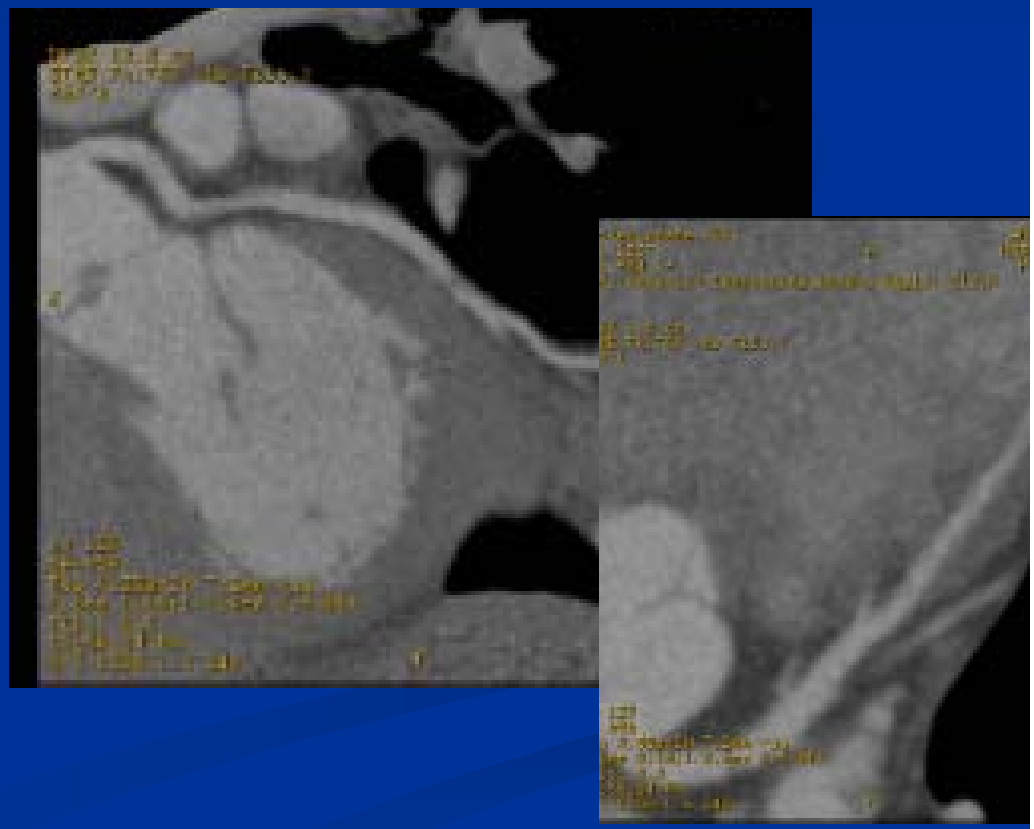
Diffuse LAD plaque without stenosis



Mild plaque in the RCA and LCX

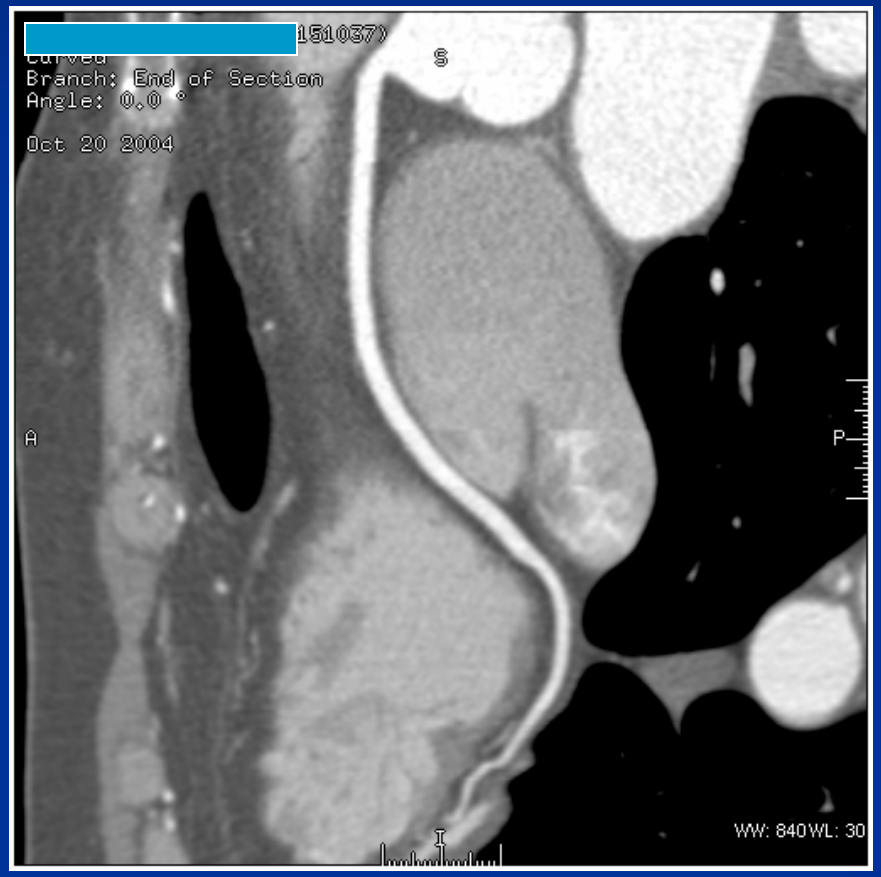
His 30 yo brother….+FHx, ex-smoker, asymptomatic.

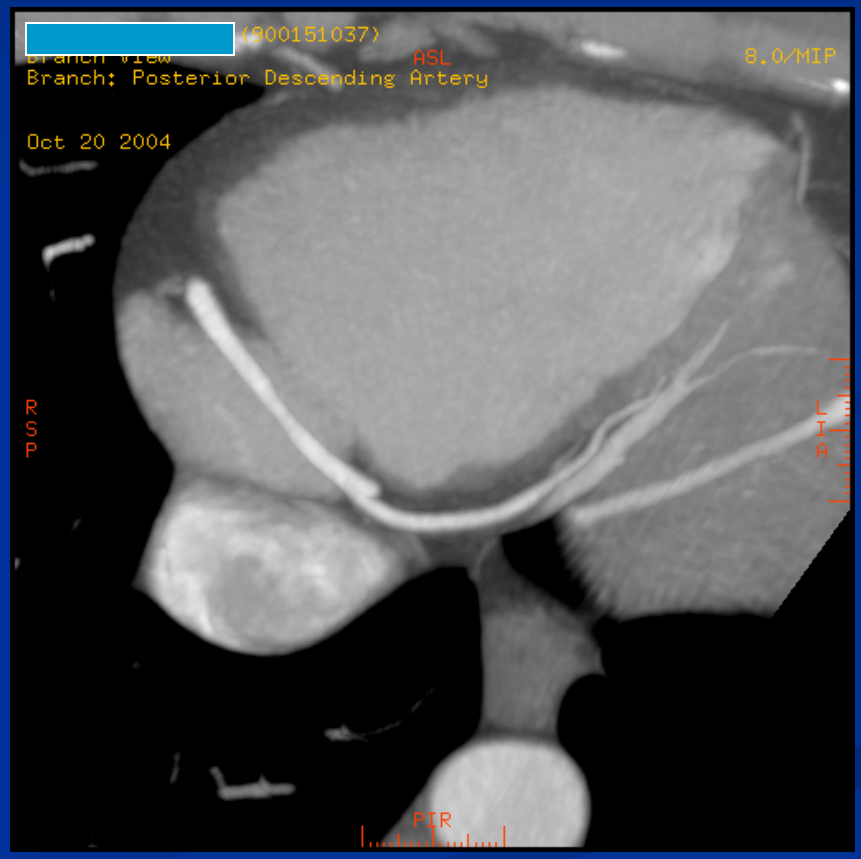
Normal CCTA



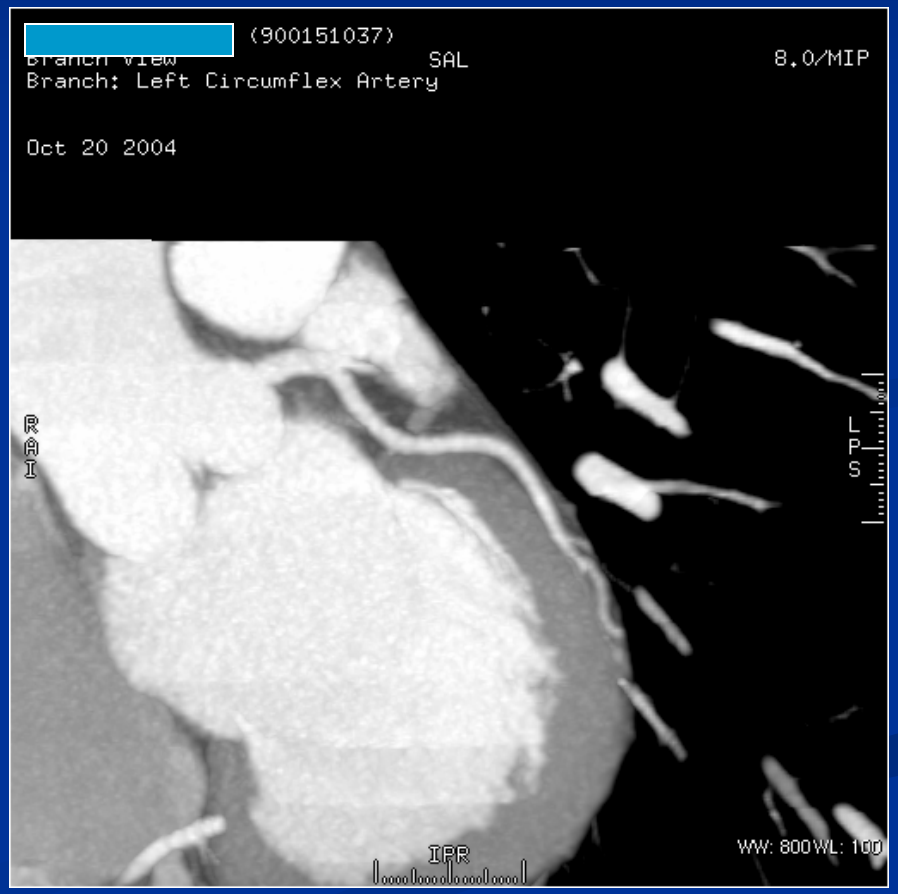
44 yo white female with chest pain and total cholesterol = 350.

Normal RCA and PDA





Normal LAD and LCX



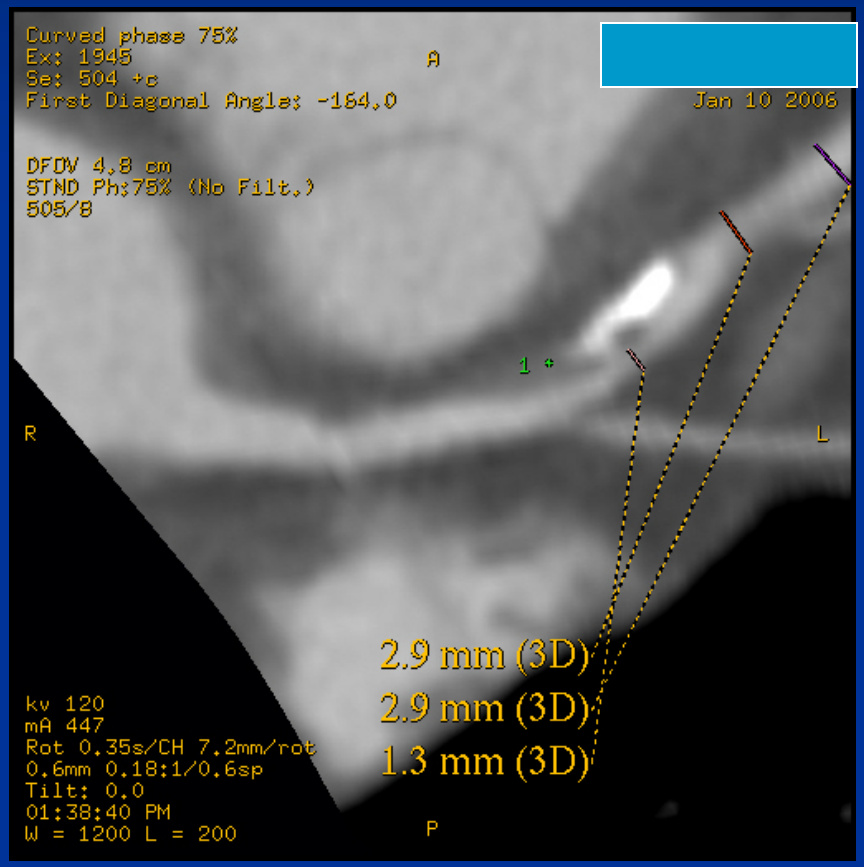
39 yo wm with chest pain. Stress test normal. +Fhx, hypercholesterolemia and HTN.

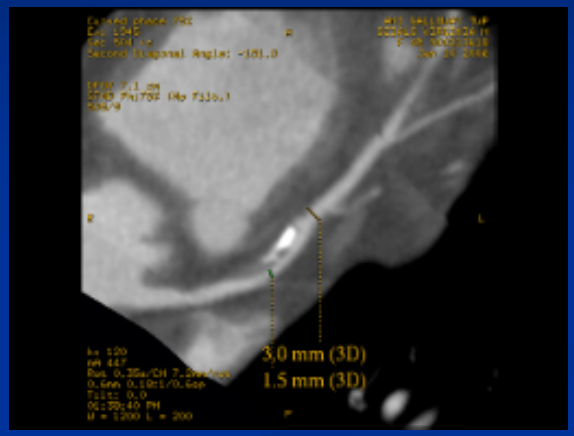
High grade LAD stenosis

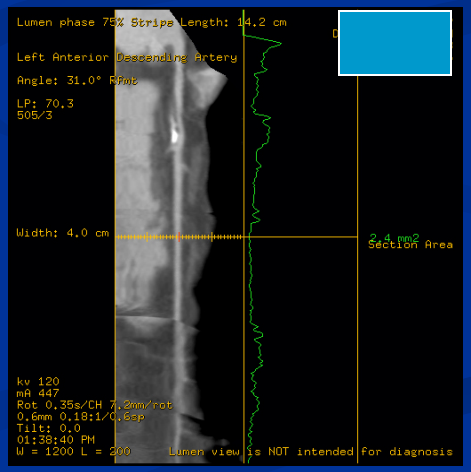
High grade LAD stenosis. Normal LCX and RCA.

45 yo wf with chest pain. +FHx, ex-smoker. SPECT stress negative 5 months prior. Pain persists.

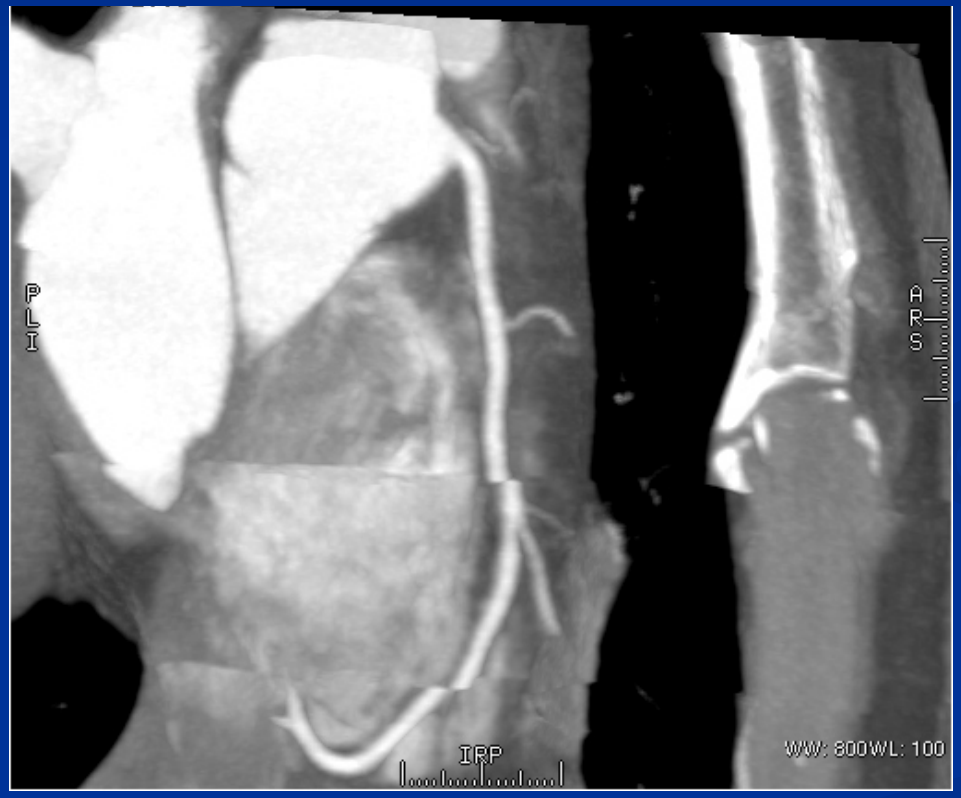
50-70% LAD stenosis







Normal RCA, Plaque LCX



For the asymptomatic?

Risk Assessment: General Population. Asymptomatic.

- Low risk CAD

  Neither

- Moderate risk CAD

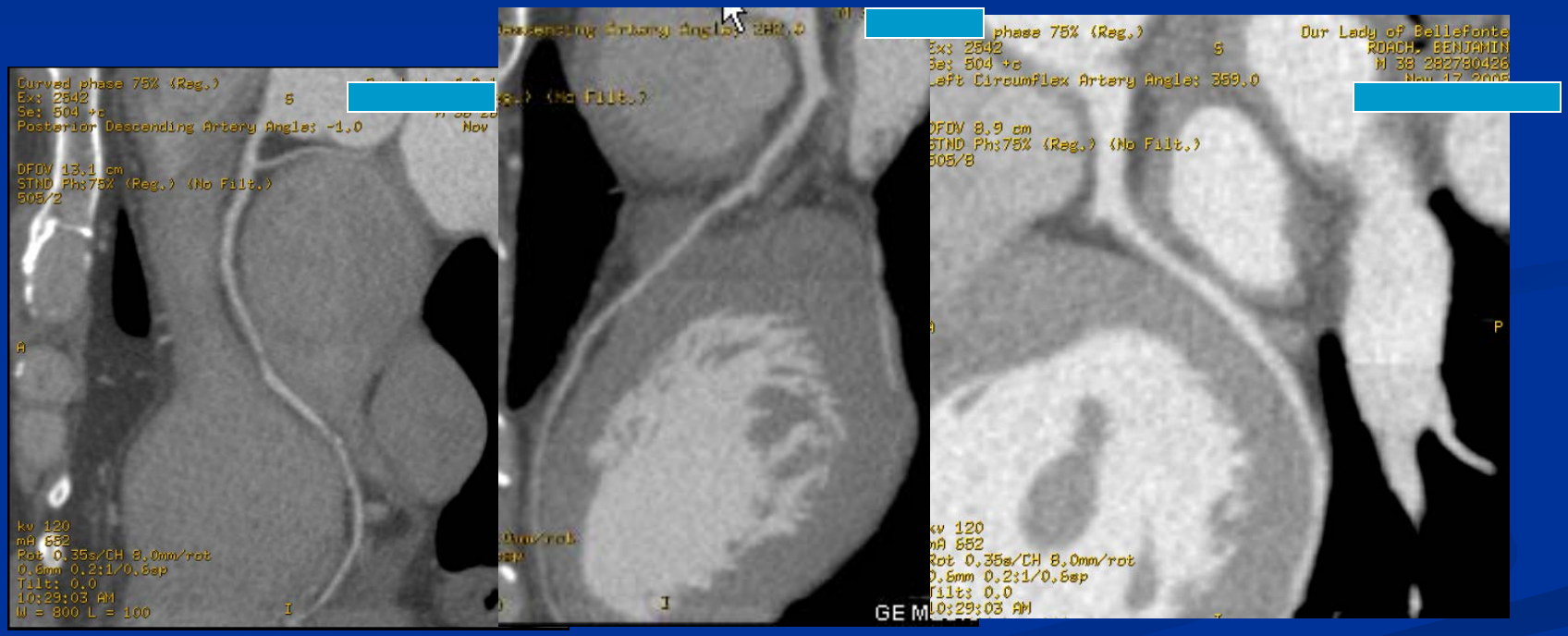
  CCTA- the stress test negative, CCTA positive patient. Value of statins in this population. Prior to CCTA would you have ordered a stress test here?

- High risk CAD

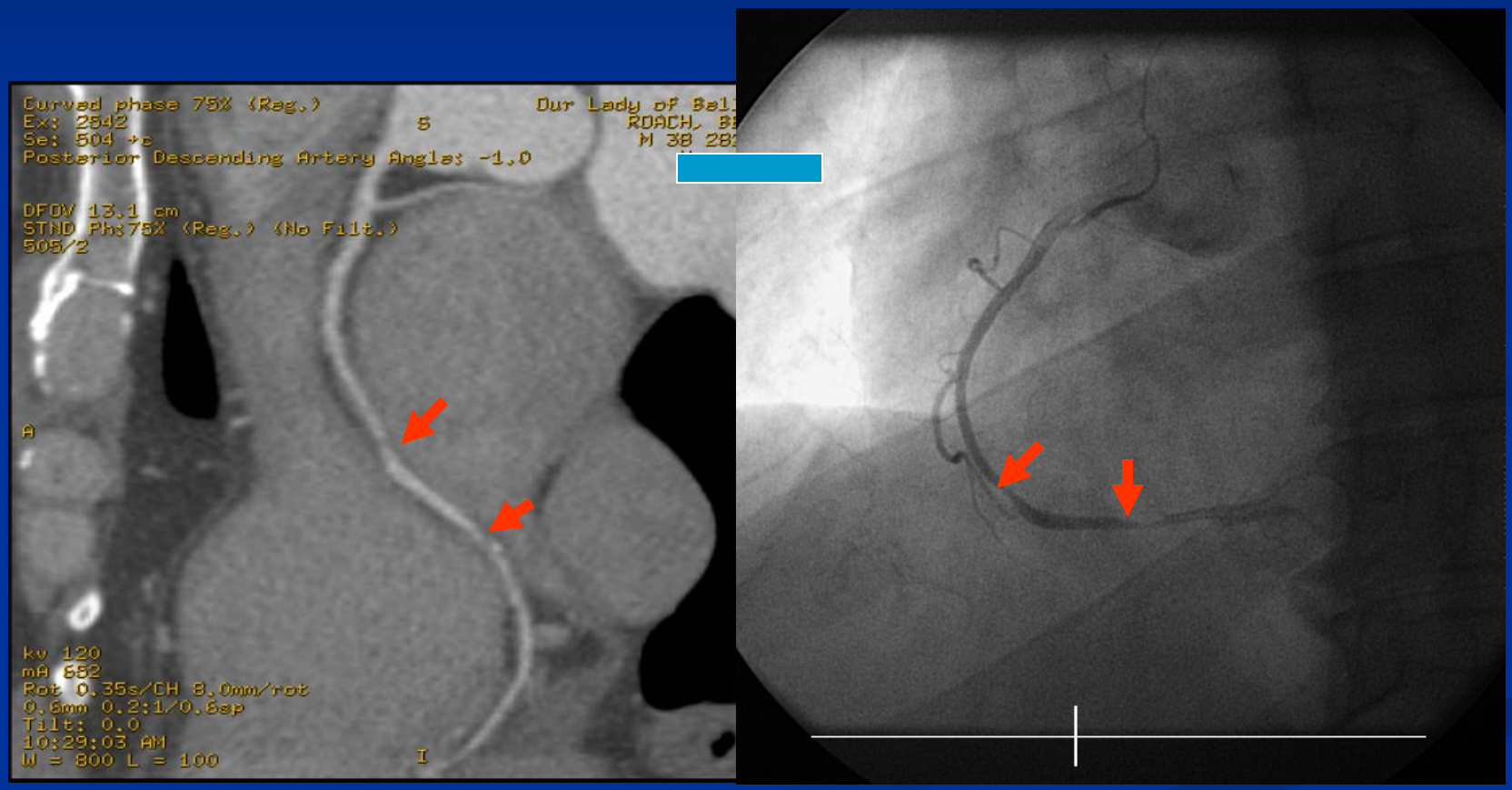
  CCTA. Very often these patients will have a negative CCTA and at the very least may be encouraged to maintain medical management.

38 yo wm, HTN, Hypercholesterolemia, +FHX. Asymptomatic, high performance athlete.

High grade tandem RCA stenoses, LAD plaque, normal LCX.



Tandem RCA Stenoses



HISTORY

55 year old male, asymptomatic, with no family history. Serum cholesterol 205. Runs 3.5 miles per day.


AIR
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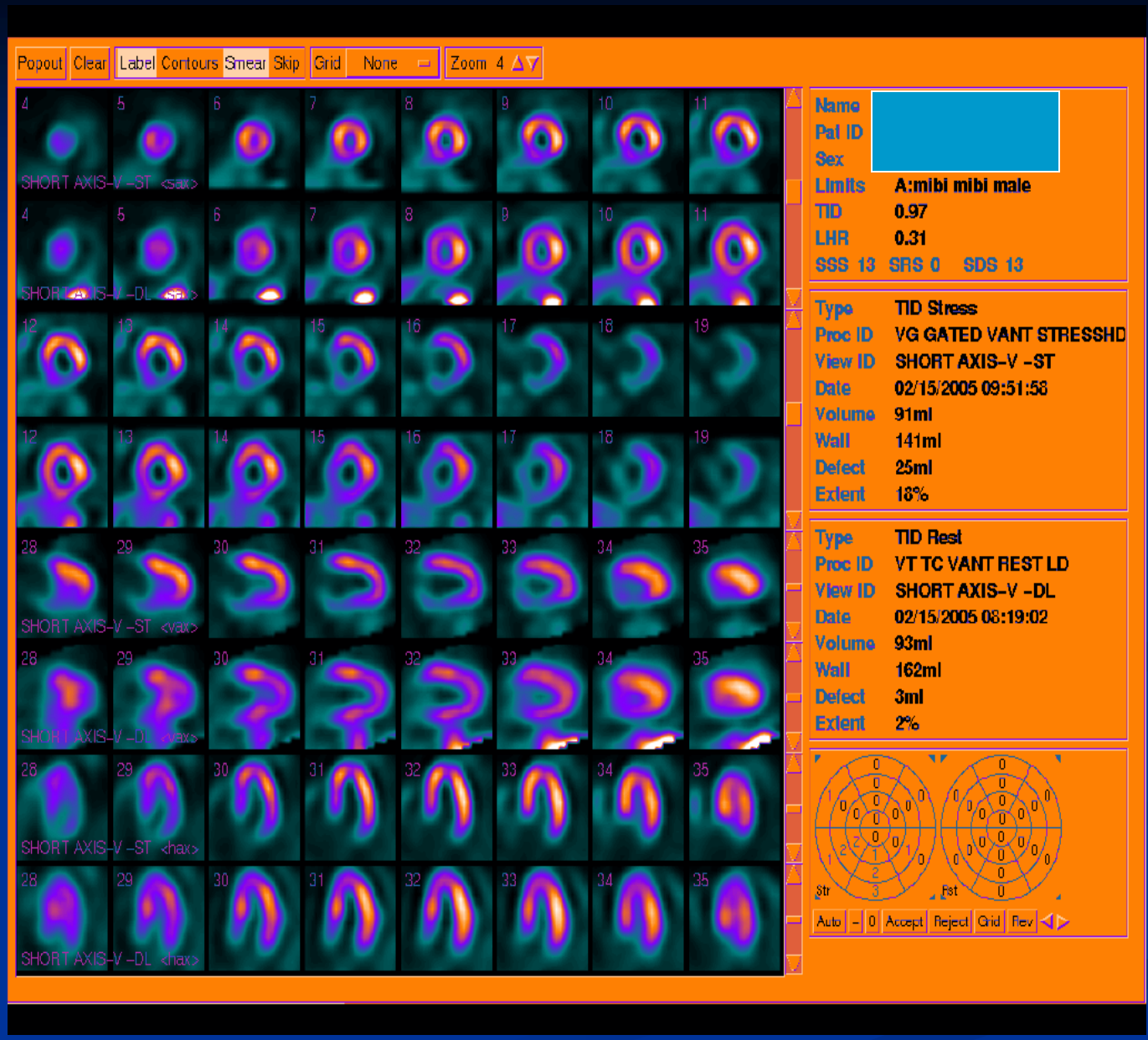
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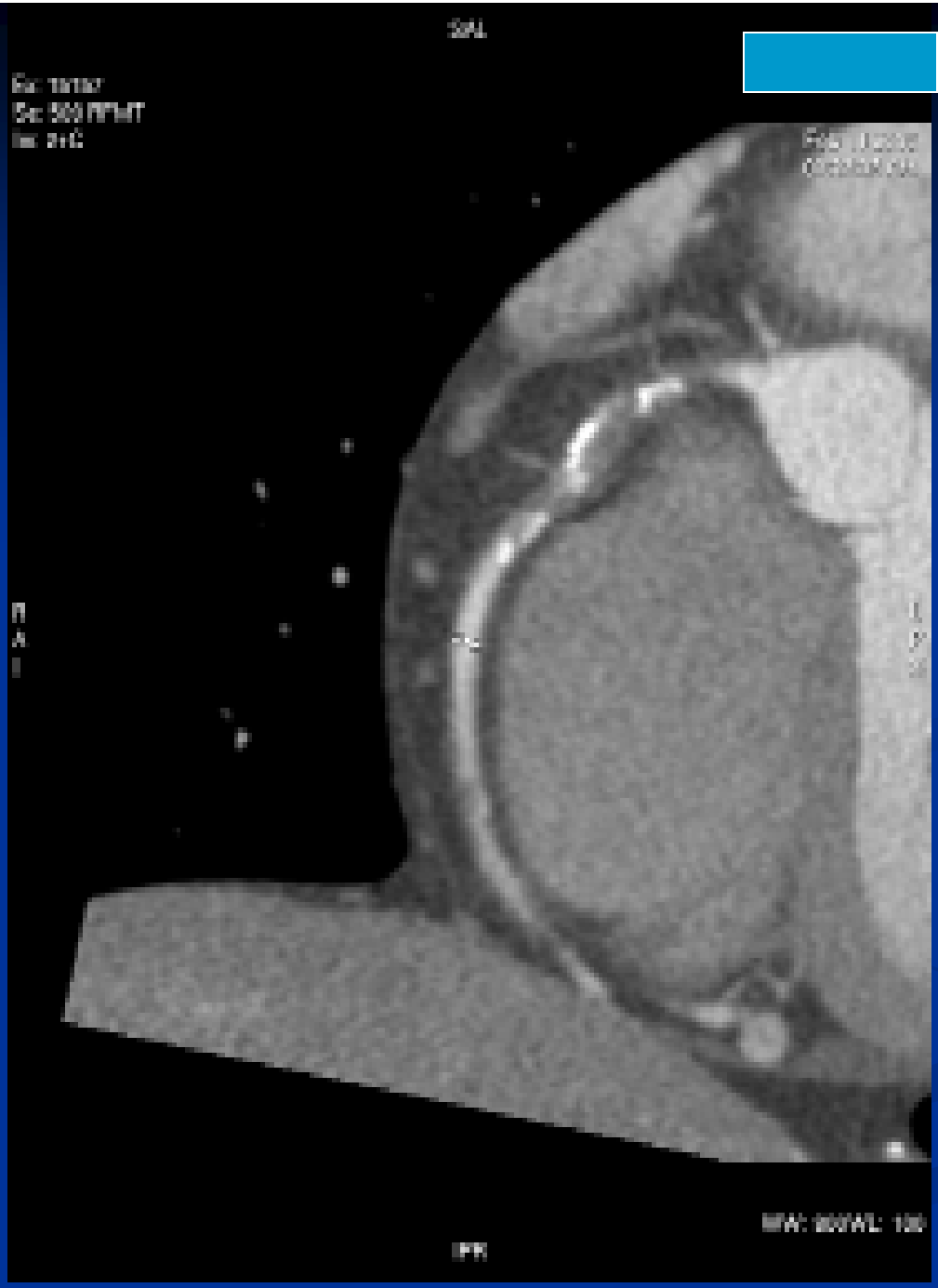

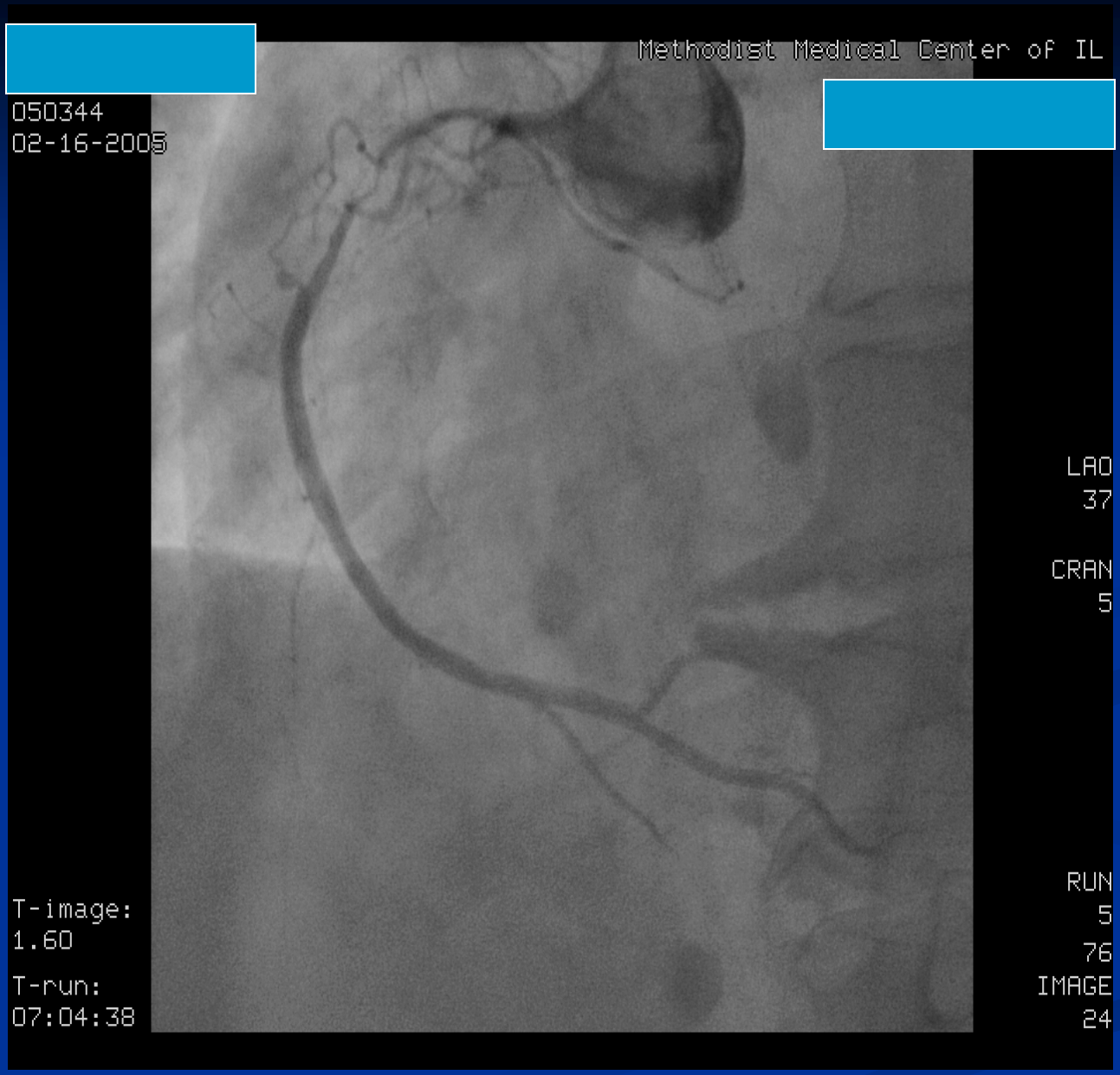
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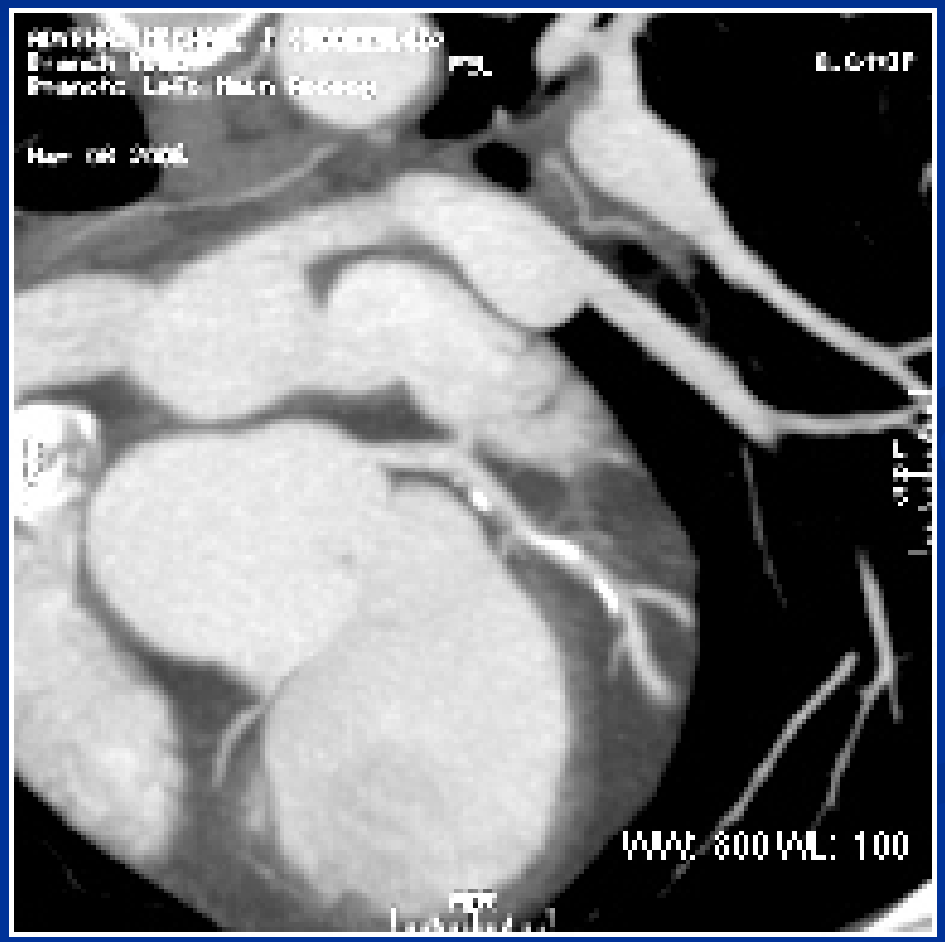
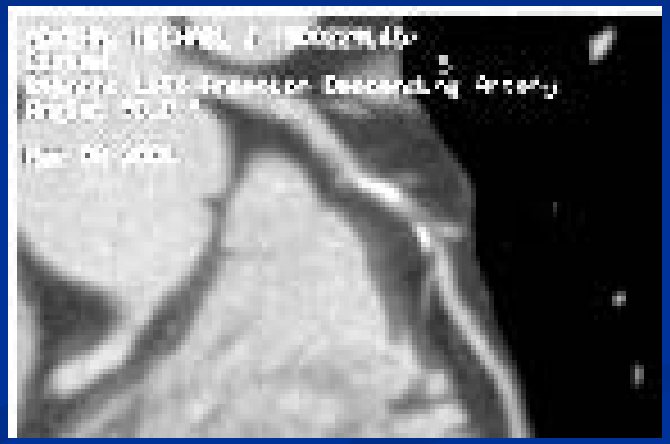
41 yo wm with erectile dysfunction. No risk factors for CAD.

Single Vessel LAD Disease



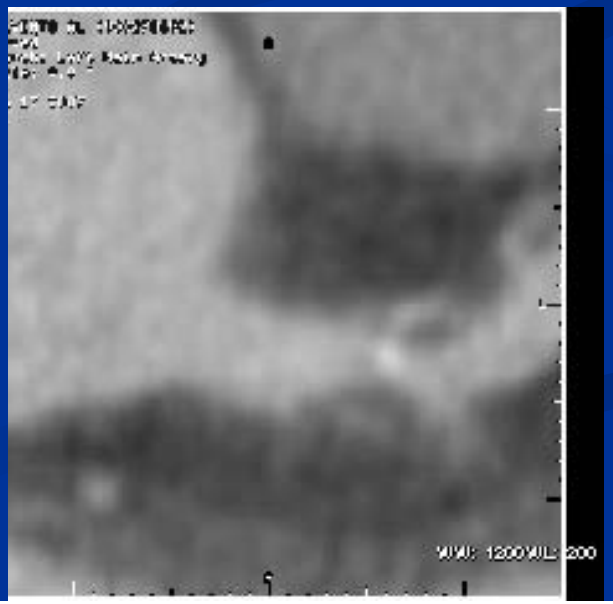


Is erectile dysfunction the first sign of CAD in males <50 yo?

Is the treatment for ED statin therapy (regardless of cholesterol level) rather than a viagra bandaid?

52 yo, wm asymptomatic. Hypercholesterolemia.

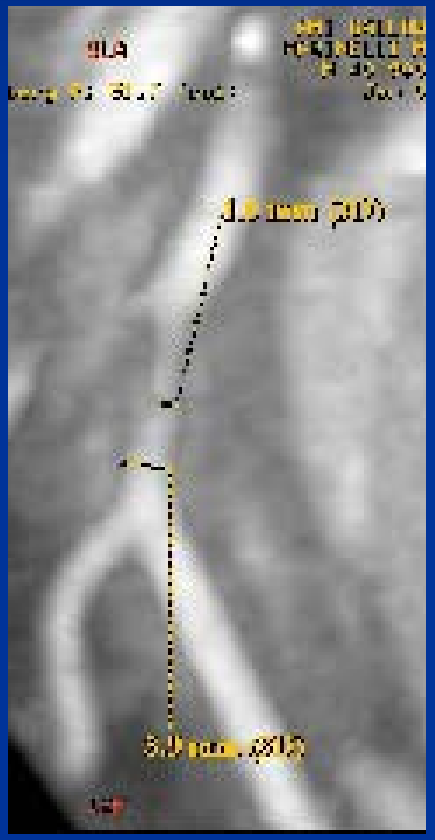
Left Main Equivalent



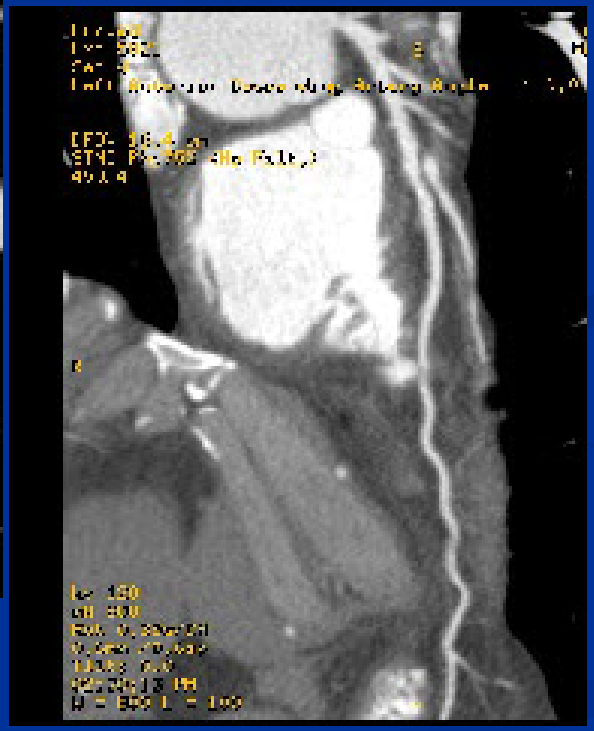
Left Main Equivalent

39 yo, wm asymptomatic, helicopter pilot. +FHx, mild hypercholesterolemia.

>70% Stenosis mid-RCA

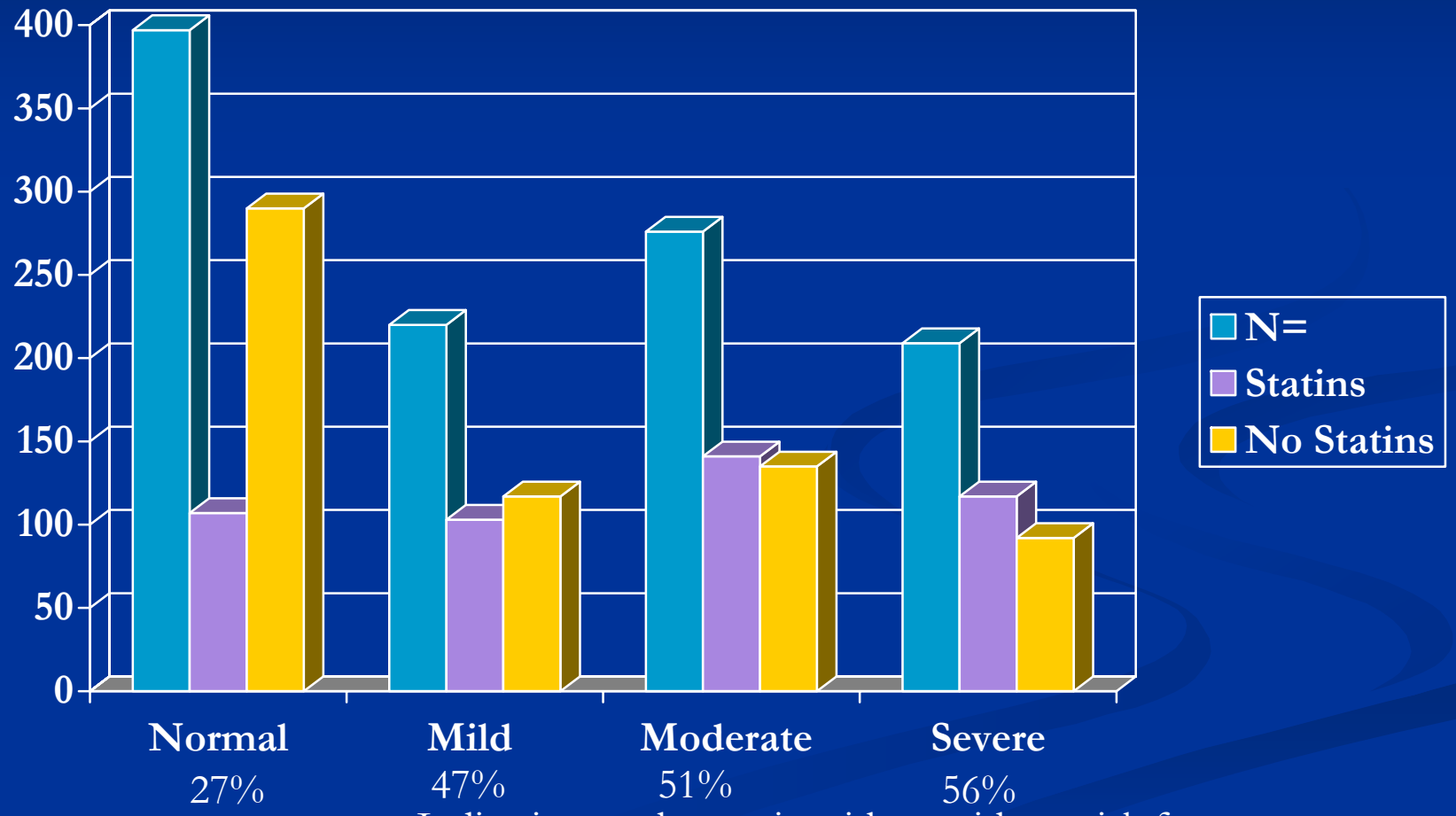


Normal LCX and LAD



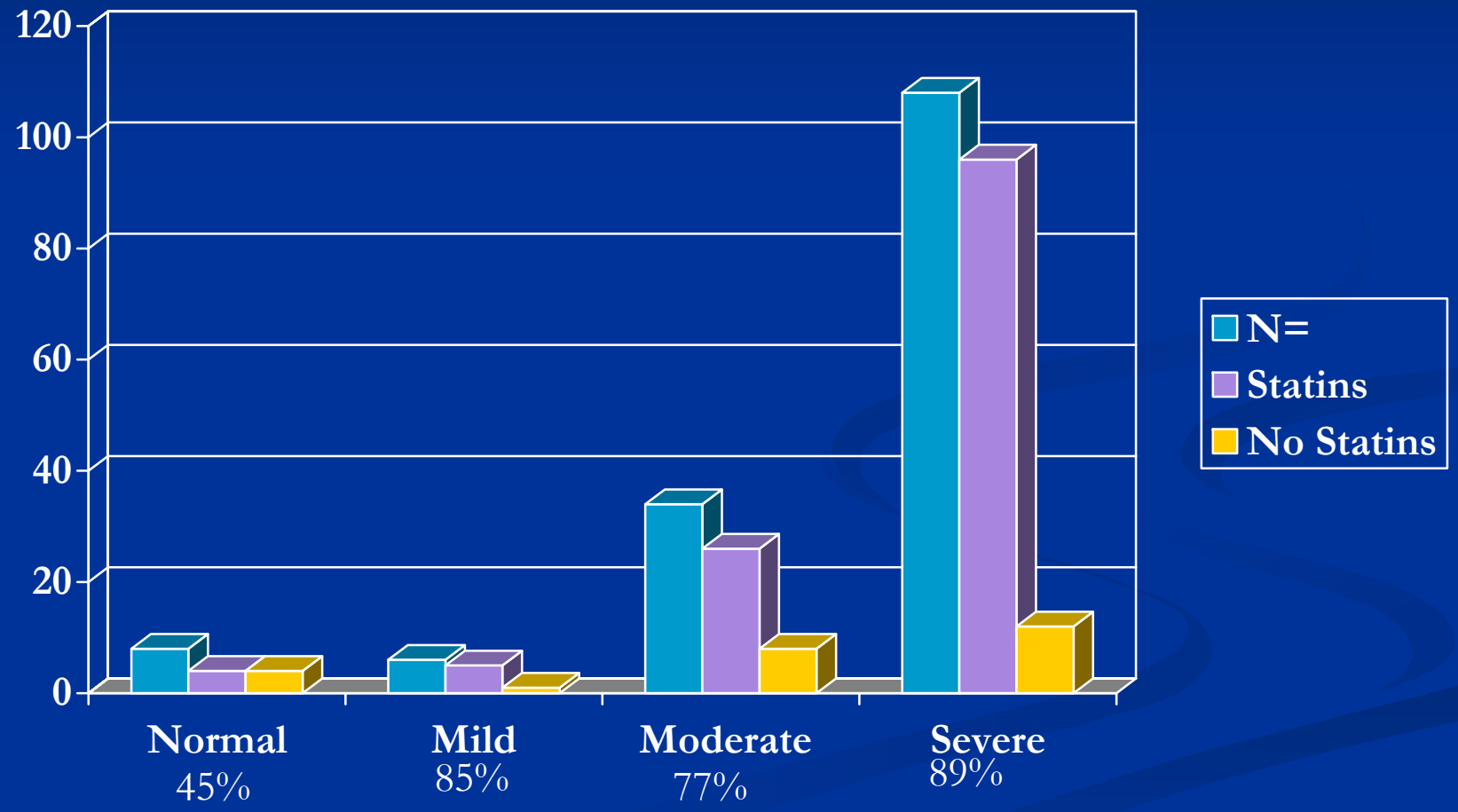
Who is getting statins?

Patients without Hx of CAD (n=1102)



Indications= chest pain with or without risk factors, asymptomatic patients with risk factors (low to intermediate probabilty of CAD +FHx.

Patients with a Hx of CAD (n=156)



Hx= CABG, stents, angioplasty, MI, "heart artery blockage."

Non-obstructive Coronary Plaque is a Predictor of all cause Mortality

Min J, et. Al., Cornell University

- N=5018
- Excluded patients with a significant stenosis
- 50.6% had no plaque
- 49.4% had nonobstructing plaque= 3.39x increased risk of all cause mortality.
- Increased risk of 10% mortality over a 10 year period in patients with NO DM, HCO or HTN!

"Coronary CTA Tops Other tests for Long Term Prognosis"

Haamitsky M, et.al. Munich, Germany

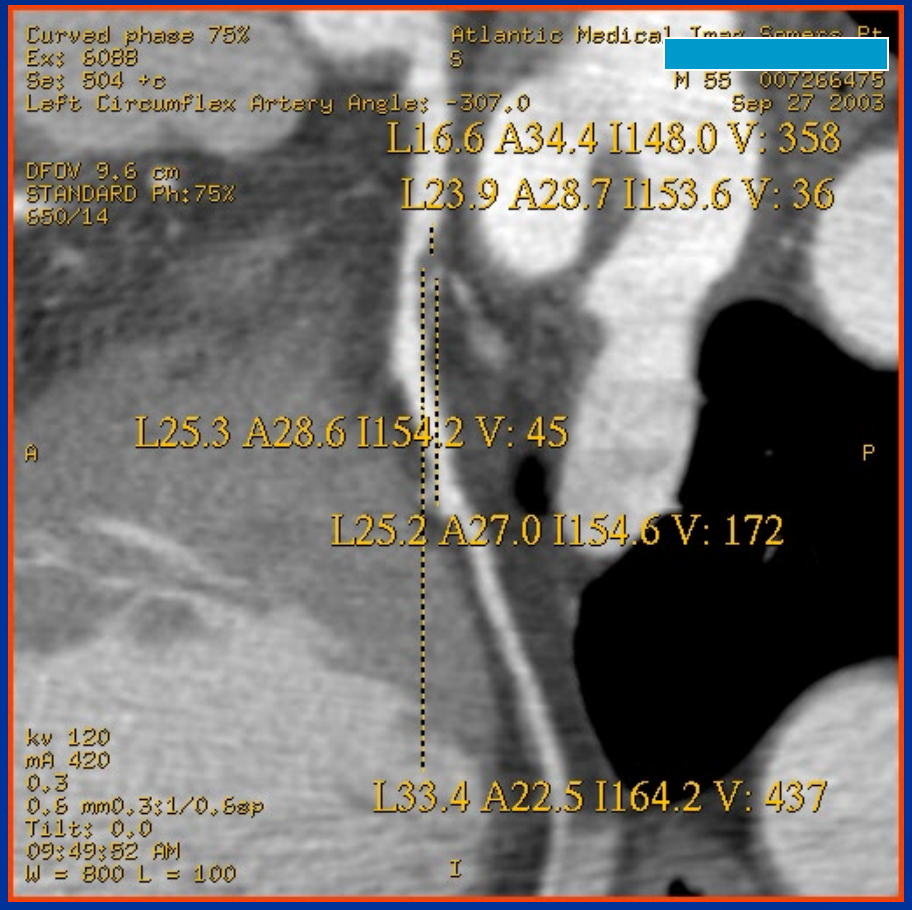
- N=1916. Patient had both CCTA and CAC.
- Excluded vessels <1.5mm.
- End point=MACE >90 days after CCTA.
- 36 late events.
- ROC-CCTA=.88, CAC=.75, FRE=.70

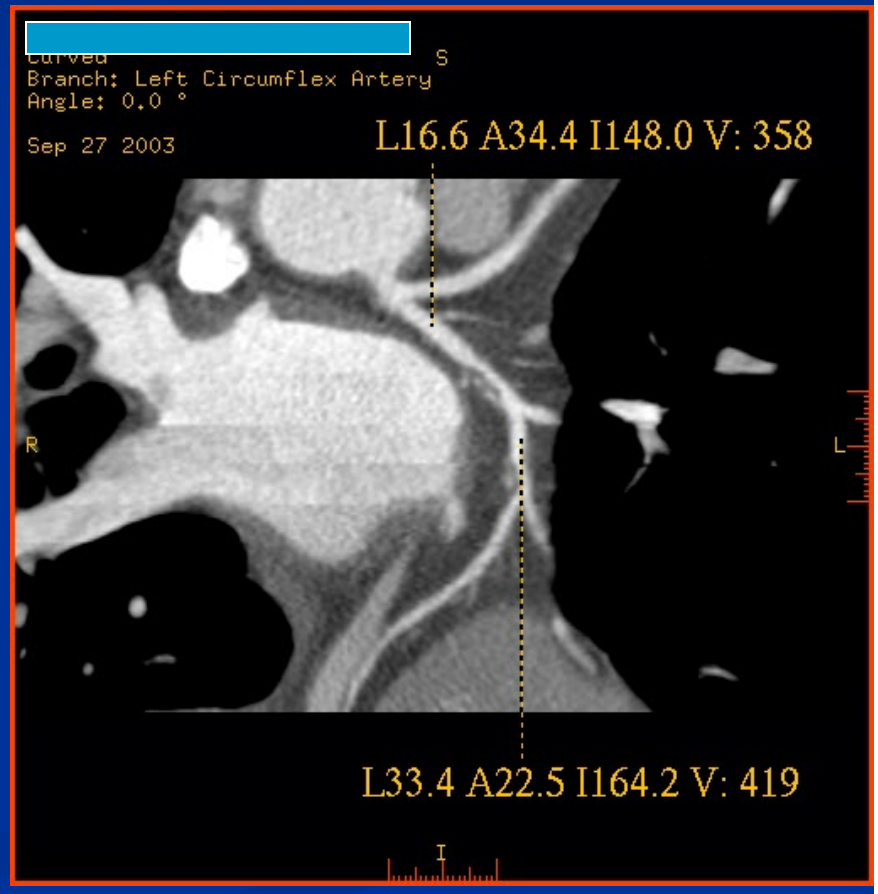
CCTA

- Has the potential to demonstrate disease before other non invasive tests
- May be able to allow targeting of therapy for non stenotic soft plaque
- This could reduce sudden death & MI from coronary disease.

How reliable is CCTA at detecting soft plaque?

Atheromatous Plaque





CCTA v. IVUS

- 58 vessels
- 78% sensitive for hypoechoic plaque (HU 49 +/-22)
- 78% sensitive for hyperechoic plaque (HU 91 +/- 22)
- 95% sensitive for calcified plaque (HU 391 +/- 156)
- Leber et.al., J Am Coll Cardiol, 2004; 43(7): 1241-7.

CCTA v. IVUS

- 83 coronary segments
- Any plaque = 78% sens, 87 spec.
- Ca++ plaque = 94% sens, 94% spec.
- NonCa++ plaque = 78% sens, 87% spec.
- But….

CCTA v. IVUS

- If limited to proximal vessels:
- Any plaque = 92% sens, 88% spec.
- Ca++ plaque = 95% sens, 91% spec.
- NonCa++ plaque = 91% sens, 89% spec.
- Achenbach, et.al., Circulation, 2004; 109:14-7.

These studies were NOT done on a high mA, EKG dose modulated system.

Does it matter? Does it change patient management?

Yes!!!

Physicians will initiate or maximize statin therapy and perhaps add an ACE Inhibitor in response to the detection of atheromatous plaques!

When you refer to an atheromatous plaque as a “fresh plaque” patients tune in. How long will their motivation last?

Percentage of individuals maintaining statin therapy at 3.6 years according to various levels of baseline CAC

- 0 = 44%
- 1-99 = 63%
- 100-399 = 75%
- >400 = 90%

- Budoff, May 22, 2004

MDCT screening?

- With new dose reduction techniques this is becoming a feasible option
- We can't put the whole world on statins!

Coronary CTA as a Screening Tool in an At Risk Occupation Population

Johnson KM, Dowe DA, Min J.

Submitted for Publication

53 yo wm with IDDM, HTN, active smoker and chest pain.

But we can't put the whole world on statins?

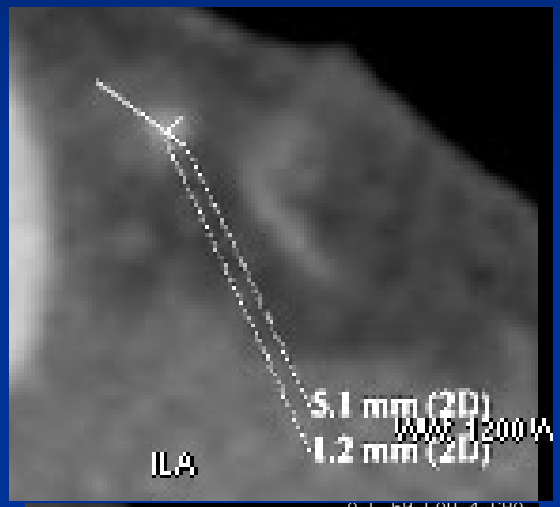
Remodeling Index

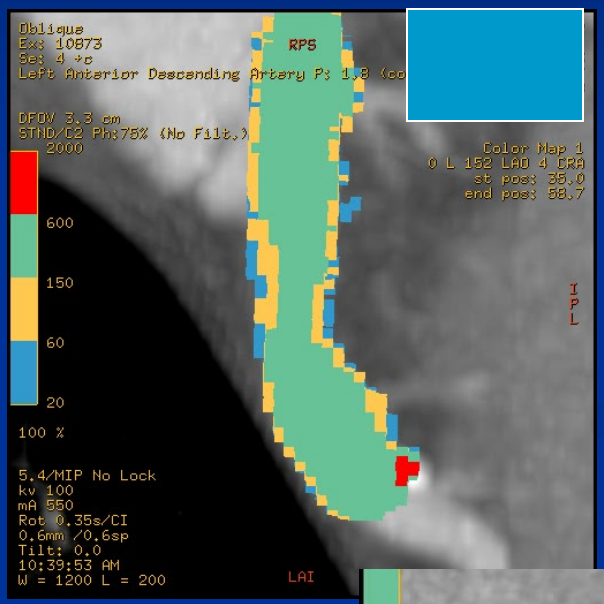
>1.4

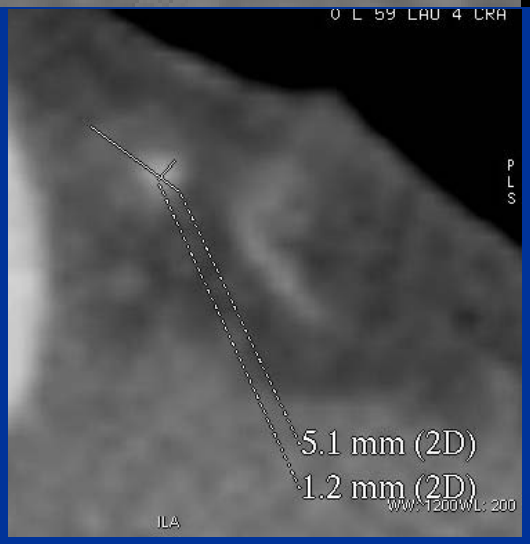
50yo, wf with chest pain.
Normal SPECT.
NIDDM, HCO and
HTN.

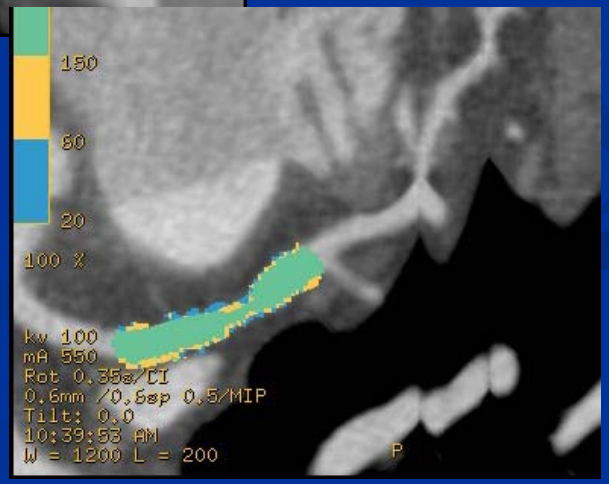
80% LAD stenosis

High Remodeling Index and High Grade Stenosis









But I can't get a precert?

The William Reilly Coronary CTA Program

William Reilly CCTA Program

- Needs based assessment.
- Applies to those with income <70k.
- Takes number of dependents into account.
- Fill need to submit paystubs, etc., to Susan Christopher, Administrator.
- Final price between $0 and $650.
- Call Susan at 609-653-6708.

Conclusion

- Cardiac CT is the only non invasive technique that can assess atheromatous burden in the vessel wall and luminal narrowing
- It has the only noninvasive study that detects the vulnerable plaque. This carries prognostic significance.
- ***It has the potential to alter the natural history of CAD***

Thank you.