Vulnerable Plaque Imaging By Computed Tomography

Koen Nieman, MD, PhD

Erasmus MC
University Medical Center Rotterdam

Rotterdam Thoraxcenter
Erasmus Medical Center
Departments of Cardiology & Radiology
The Netherlands

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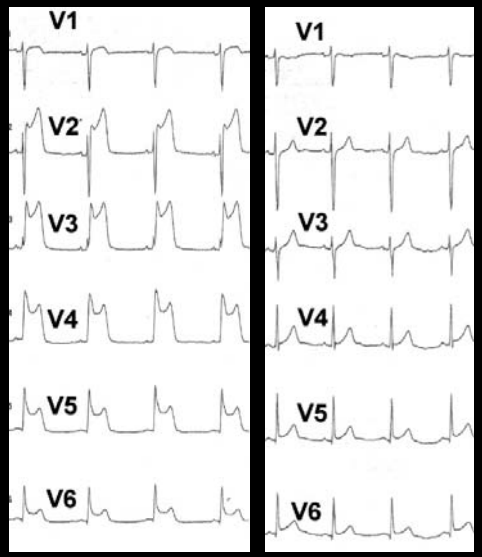
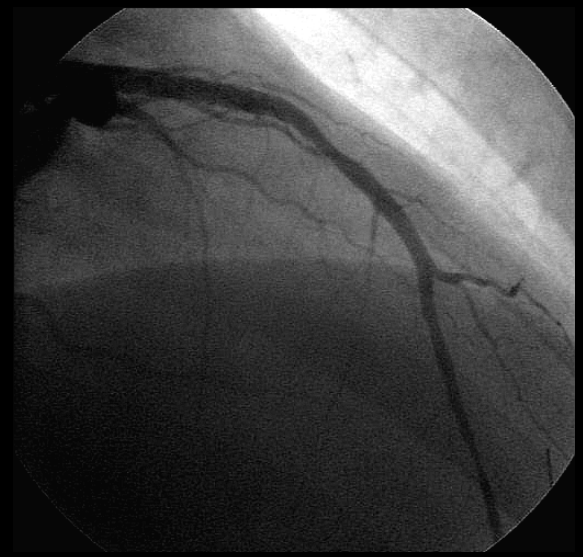
University Medical Center Rotterdam

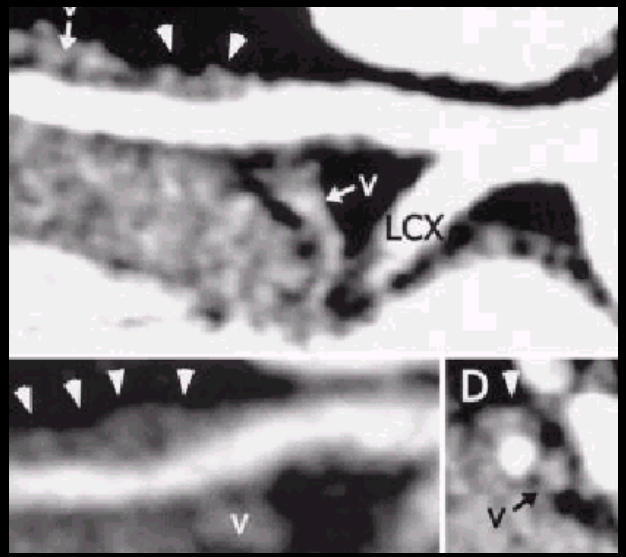
Motivation

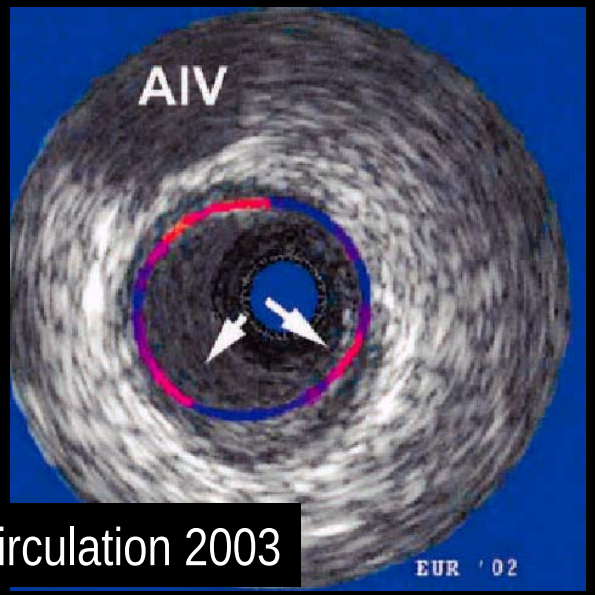
- CAD has a long subclinical course with the risk of sudden, devastating events
- More accurate, invasive techniques have practical/economic drawbacks
- CT/MRI/PET allow early detection, and perhaps identify individuals/lesions at risk

Vulnerable Plaque Imaging

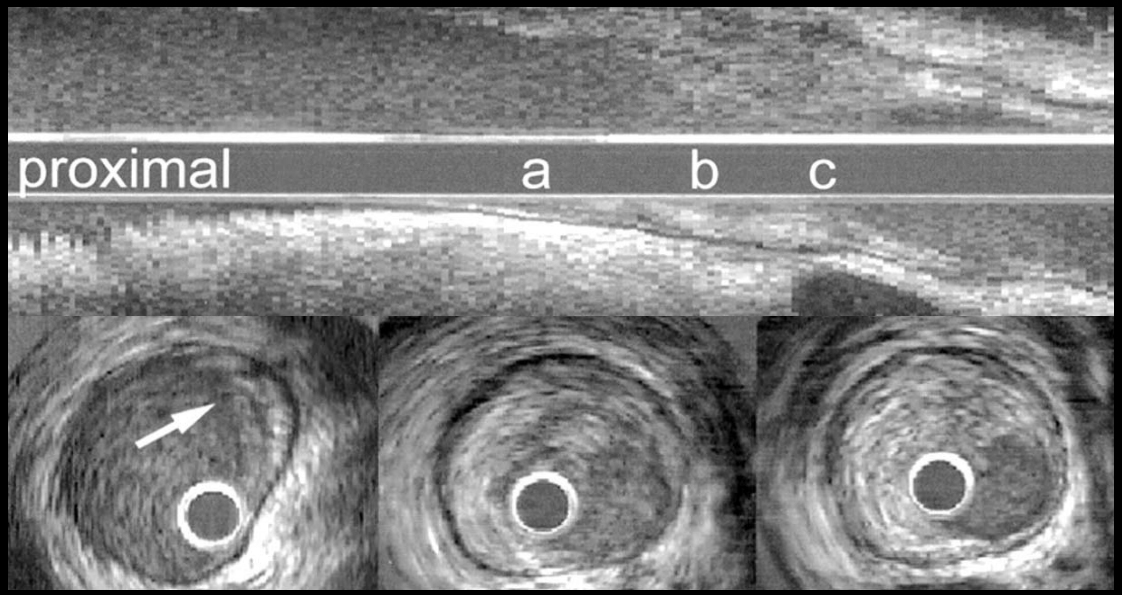








Circulation 2003



Coronary Calcium

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- Low-dose scan
- High sensitivity (IVUS)
- Calcium = atherosclerosis
- CCS ≈ total plaque burden
- CCS predicts CV events

St Francis Heart Study

Arad, et al, JACC 2005

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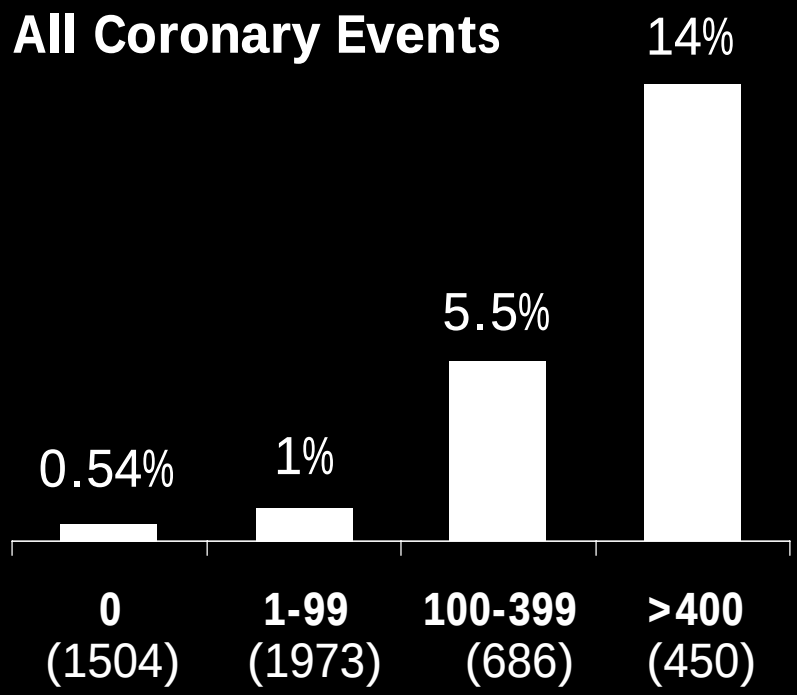
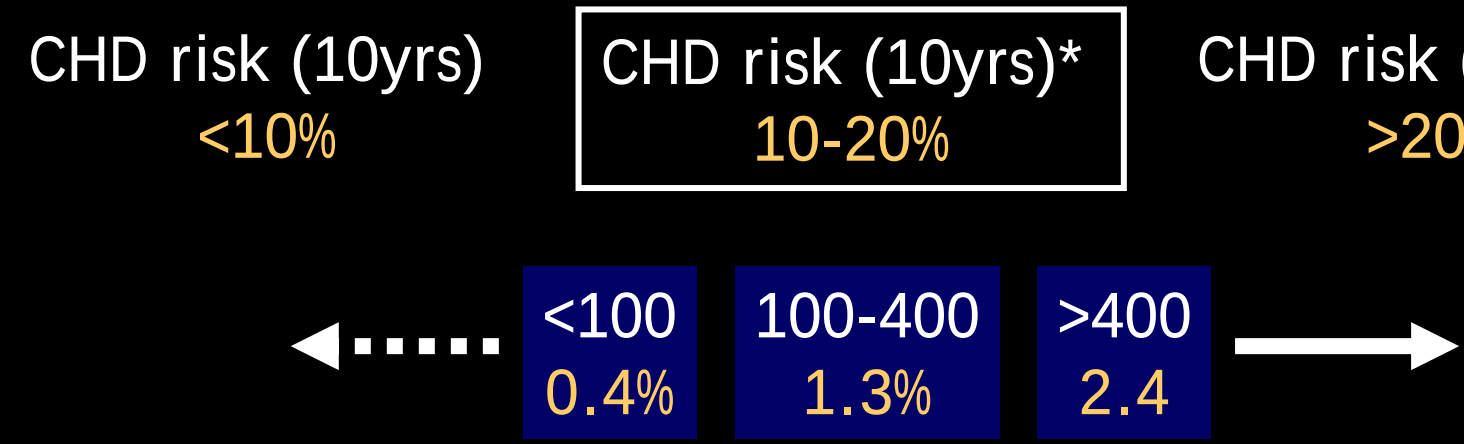
Prospective
Population-based
4613 individuals
Mean follow-up 4.3 years
50-70y Caucasians



Relative risk 9.2 for death/non-fatal MI (CCS>100)
CCS predicts CAD events independently of FRS
CCS more accurately predicts events: AUROC .79 vs .68 (FRS)

Calcium Screening (asymptomatic)



*without diabetes, history of CVD, very high single risk factor

Greenland, et al, JACC/Circulation 2007,
ACCF/AHA Expert Consensus Document on Coronary Calcium Scoring

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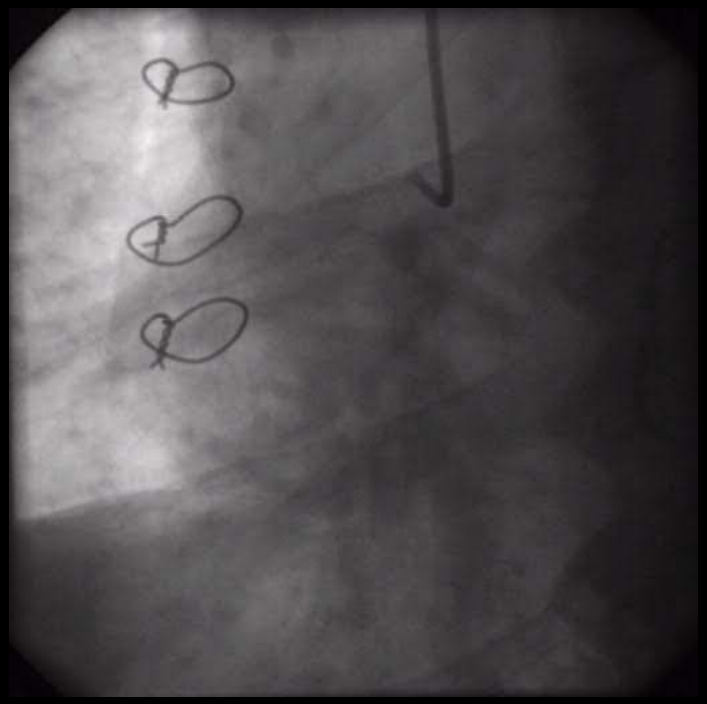

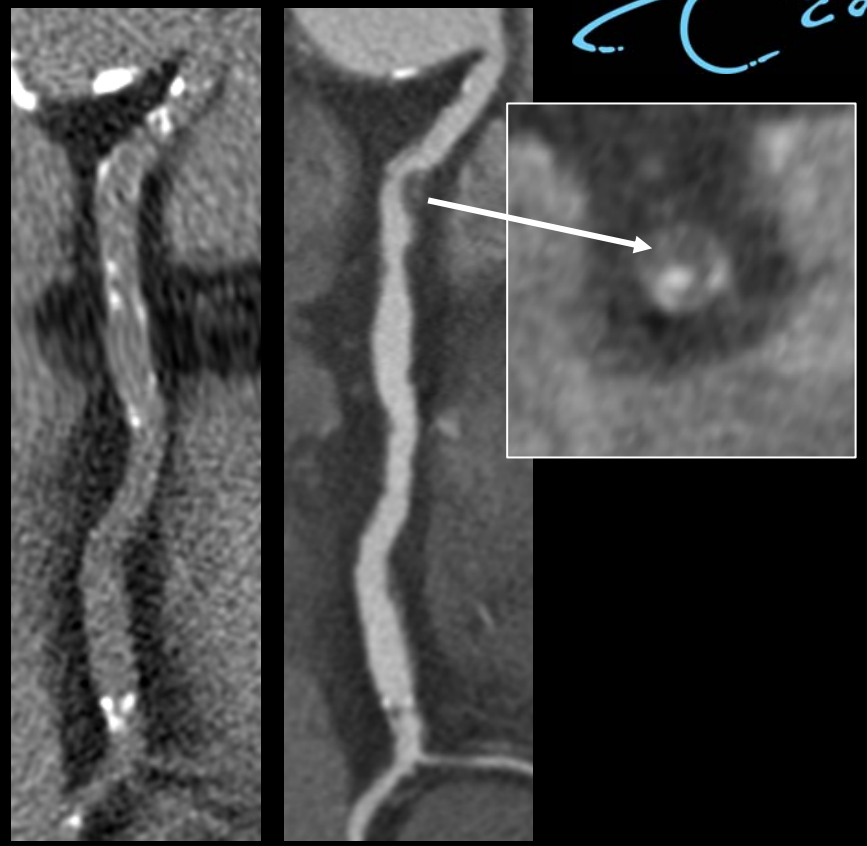

- calcium does not indicate coronary stenosis
- CCS only progresses, despite therapy
- Slowed CCS progression by treatment poorly related to events

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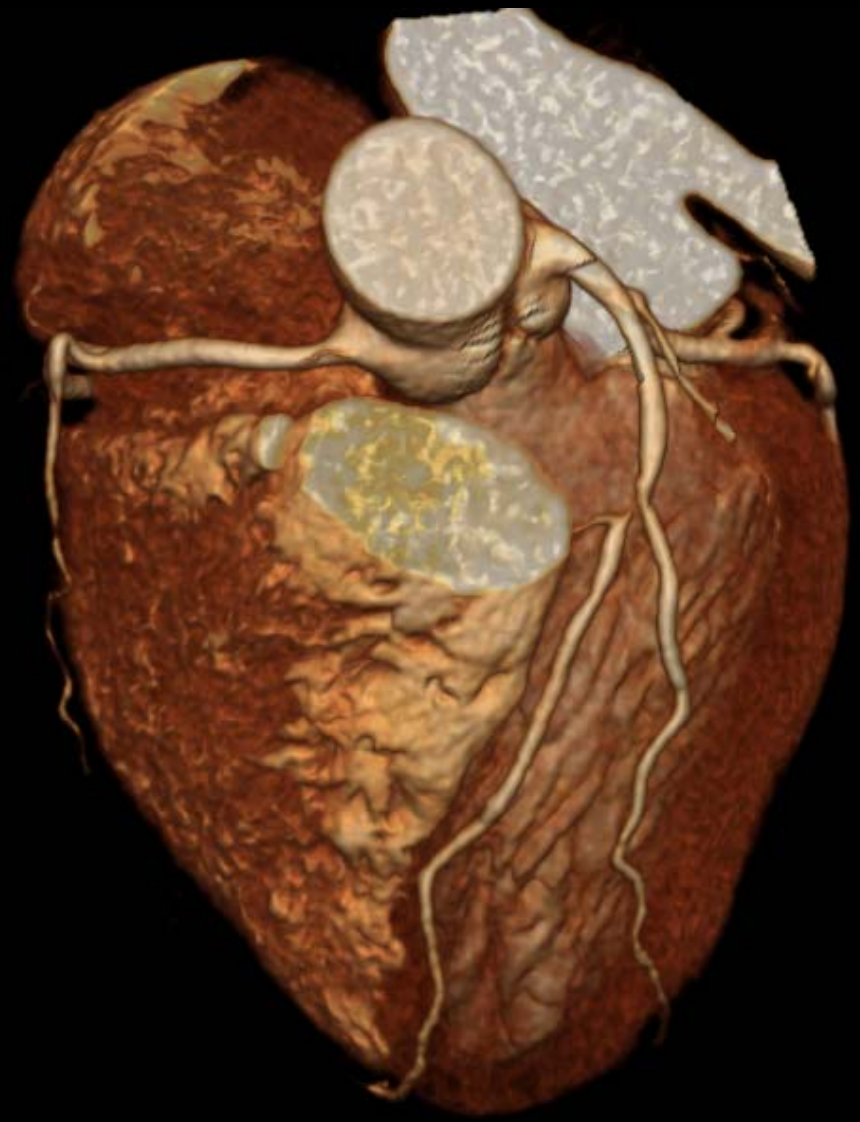
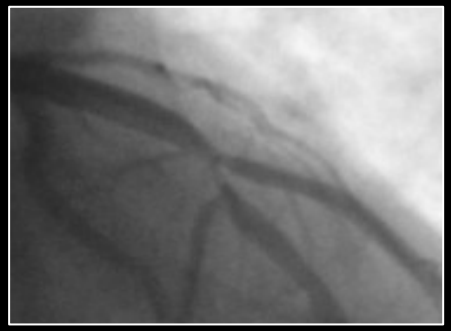
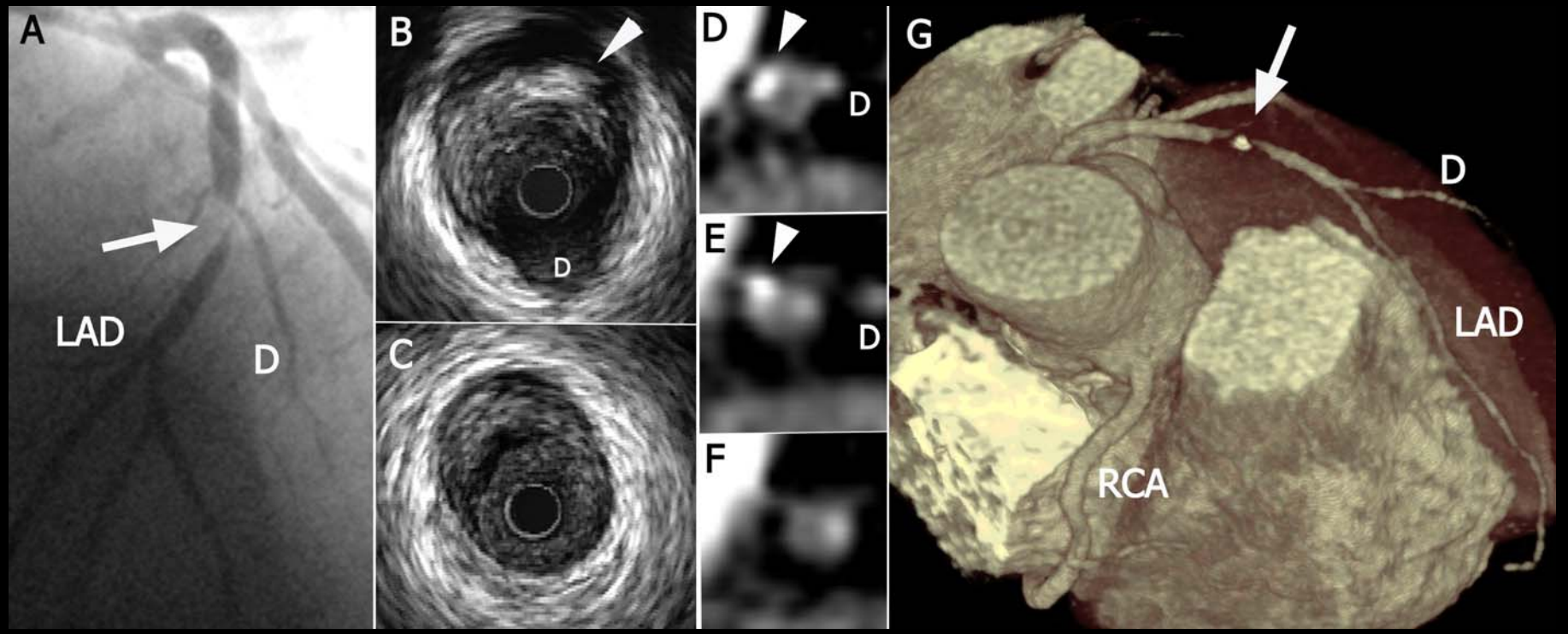


Dual-Source CT



- Rule out CAD in patients at intermediate probability (after functional tests)
- Potential replacement of cath angiography and/or ischemia testing


A
LAD
D
B
D
C
D
D
E
D
F
G
D
LAD
RCA

Coronary Plaque Detection

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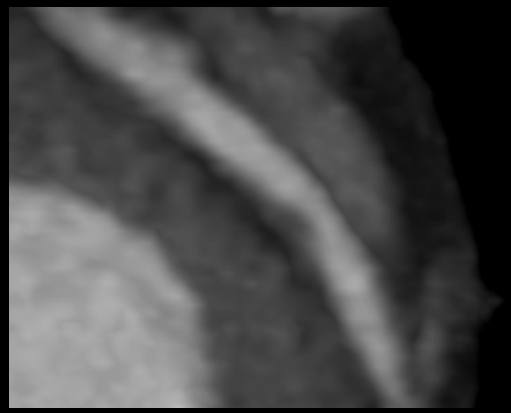
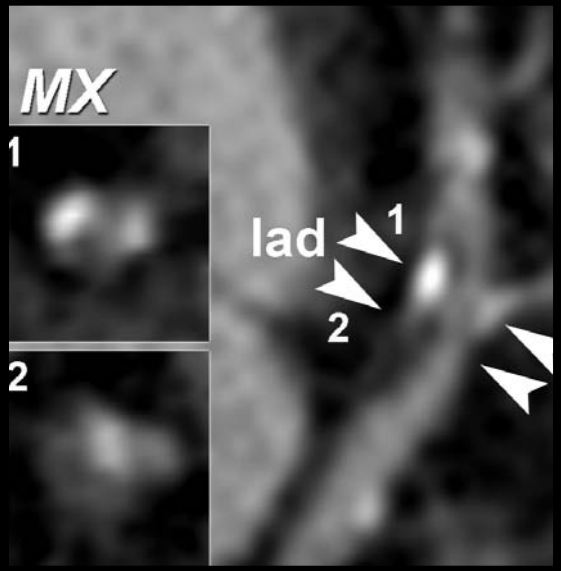
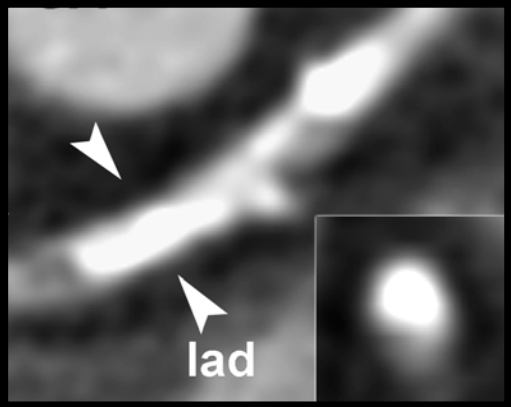
CT vs IVUS in large proximal segments



Non-calcified
Sensitivity 53%*
Sensitivity 83%**



Any Plaque
Sensitivity 82%*
Sensitivity 90%**

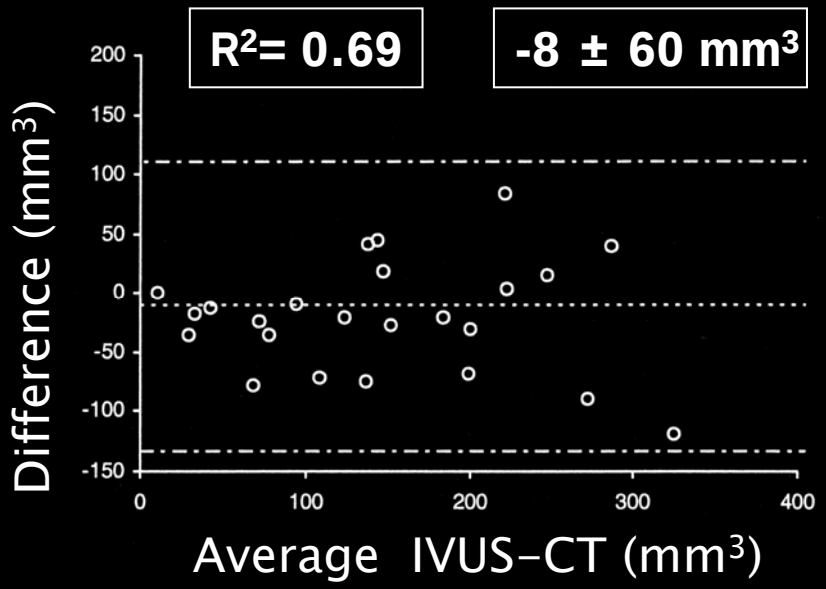


Calcified
Sensitivity 94%*
Sensitivity 95%**

**16-slice – Achenbach, Circ.'04*
***64-slice – Leber, JACC '06*

Coronary Plaque Volume

64-CT vs IVUS



N=20, 36 vessel segments

Underestimation non-calcified

Overestimation calcified plaque

Inter-observer variability 37%

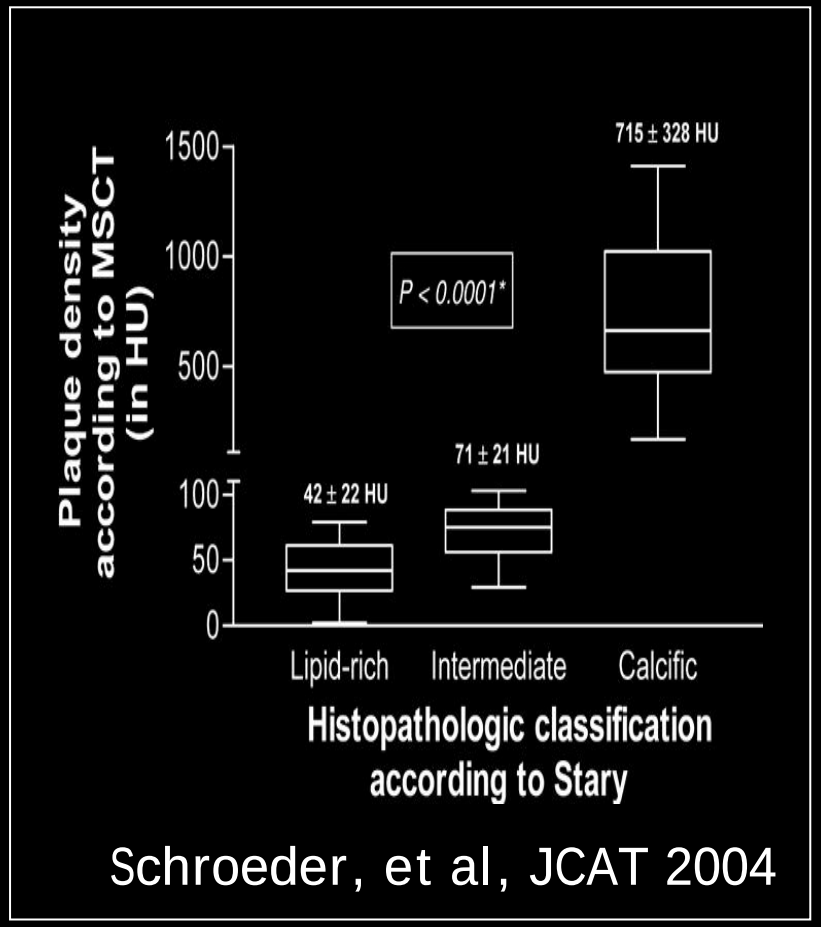
Leber et al, JACC 2006

Annual progression 24% (LM/pLAD) [Schmid '08]

No (noncalcified) plaque regression by statins [Schmid '08]

Non-calcified plaque reduction by statin: 24% [Burgstahler '07]

Plaque Characterization



Schroeder, et al, JCAT 2004

CT attenuation (HU) versus IVUS plaque classification

Author	CT	N	Soft	Intermediate	Calcified
Schroeder ‘01	4×1	15	-42 - 47	61 - 112	126 - 736
Leber ‘04	16×.75	37	14 - 82	34 - 125	162 - 820
Pohle ‘06	16×.75	32	-39 - 167	60 - 201	

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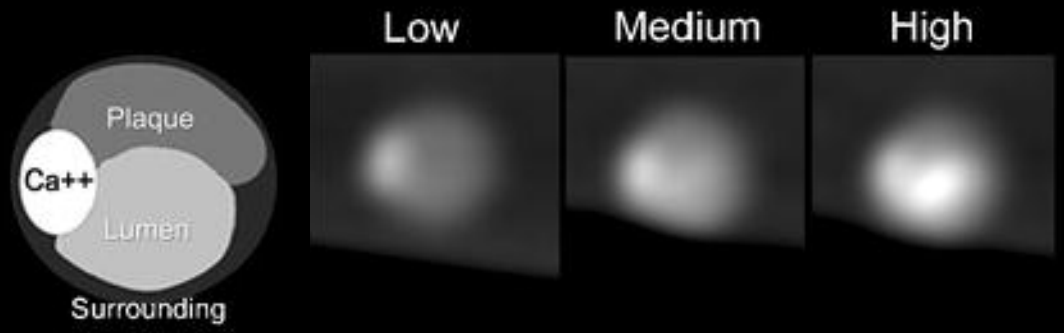
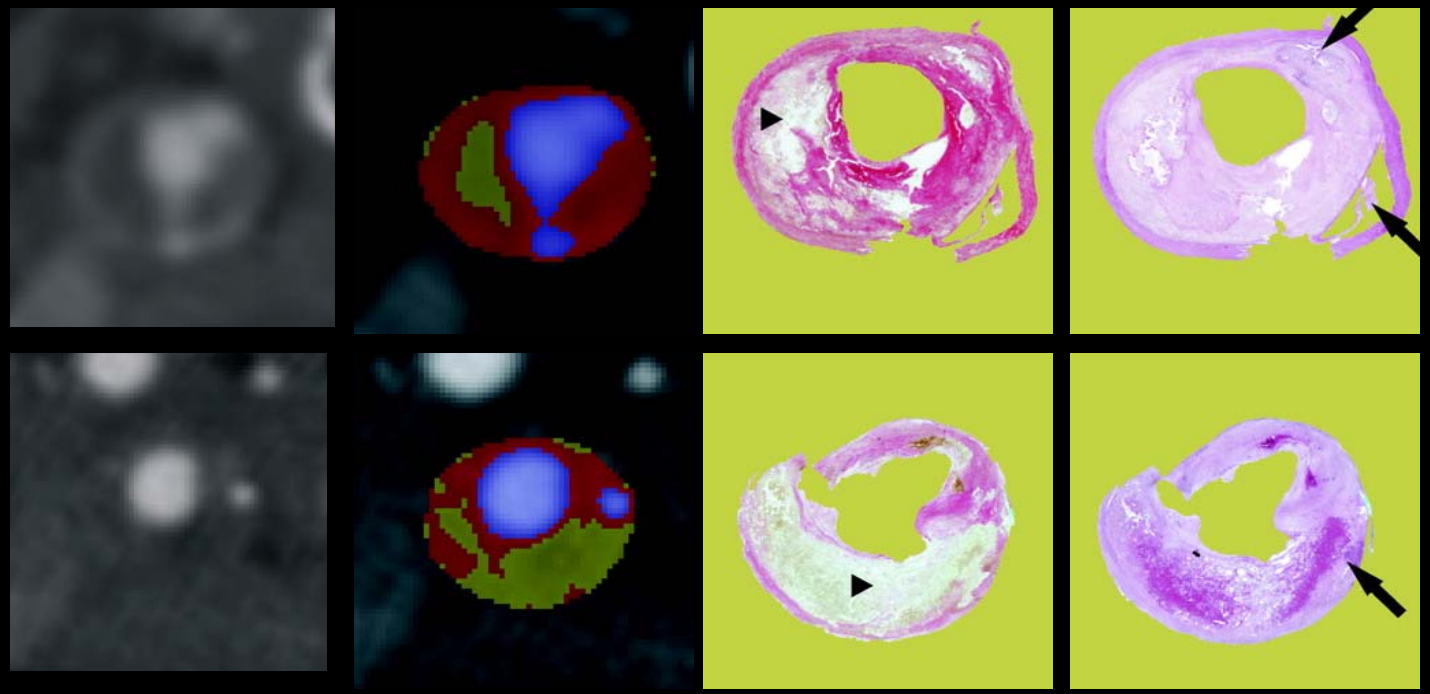


	Low	Medium	High
Lumen	120	270	502
Plaque	44	94	136
Calcium	232	239	247
Surrounding	-132	-130	-139

- Lumenal contrast effect
- Subtle motion and beam hardening
- Plaque enhancement
- Outer border differentiation

Carotid Plaque by CT

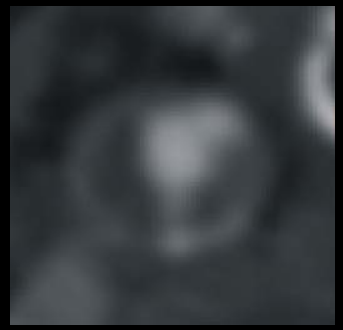


16-slice CT Grey-scale | 16-slice CT Color-coded | Sirius Red | Hematoxylin Eosin

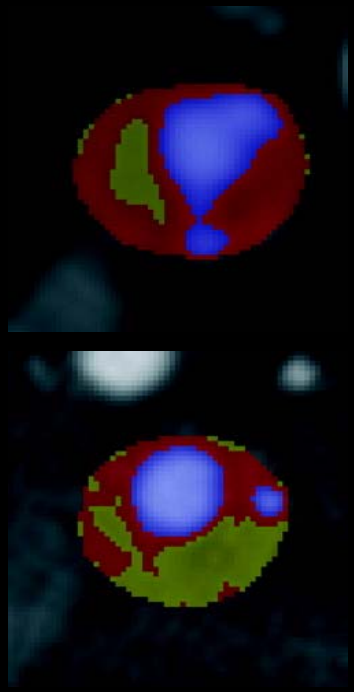
"Soft"	<60 HU	Green
Fibrous	60–130	Red
Calcified	>130 HU	Blue

De Weert, ATVB 2006

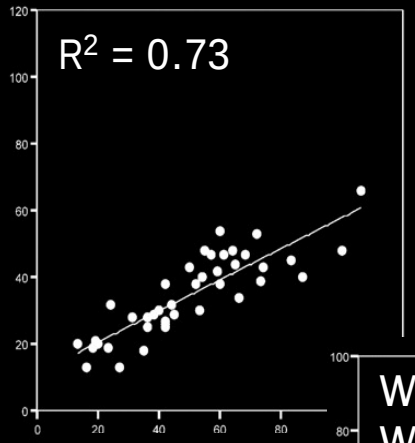
Carotid Plaque by CT



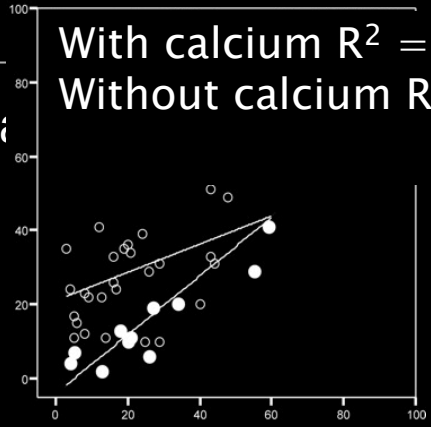
16-slice CT
Grey-scale



16-slice CT
Color-coded



plaque area



Lipid core area (%)

"Soft"	<60 HU	Green
Fibrous	60–130	Red
Calcified	>130 HU	Blue

De Weert, ATVB 2006

Vulnerable Plaque

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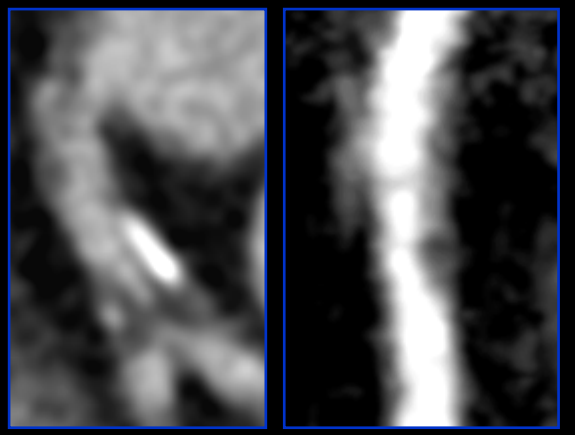
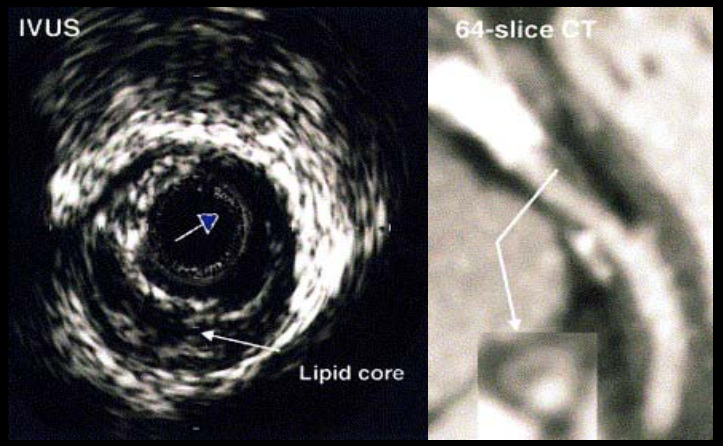
- Severe stenosis
- Plaque density
- Superficial calcified nodule
- Outward vessel remodeling
- Lipid core?
- Enough?





Leber et al, JACC 2006

Macrophage Imaging

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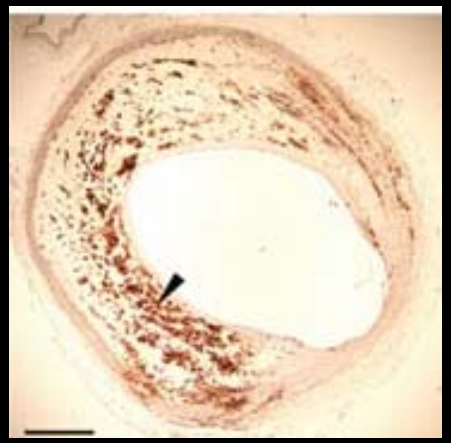
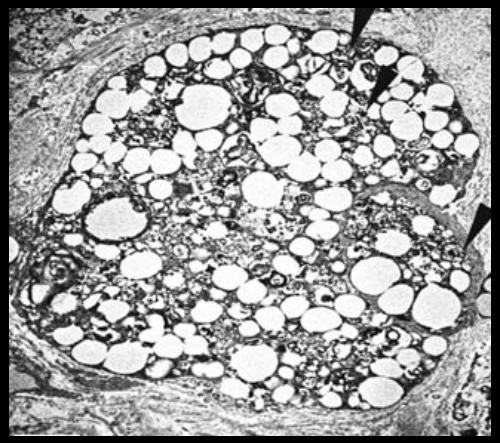
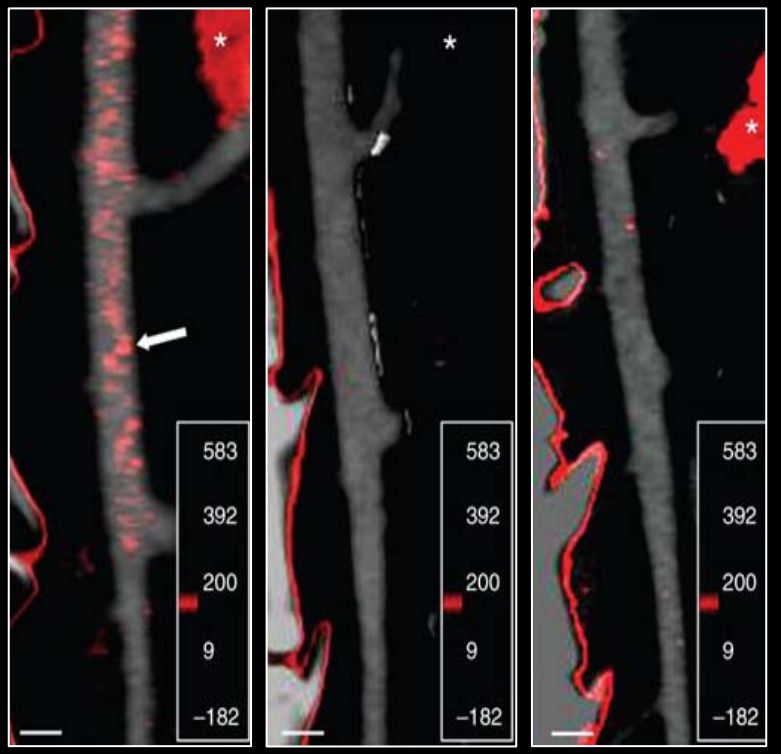


Macrophage staining



EM macrophage containing iodine



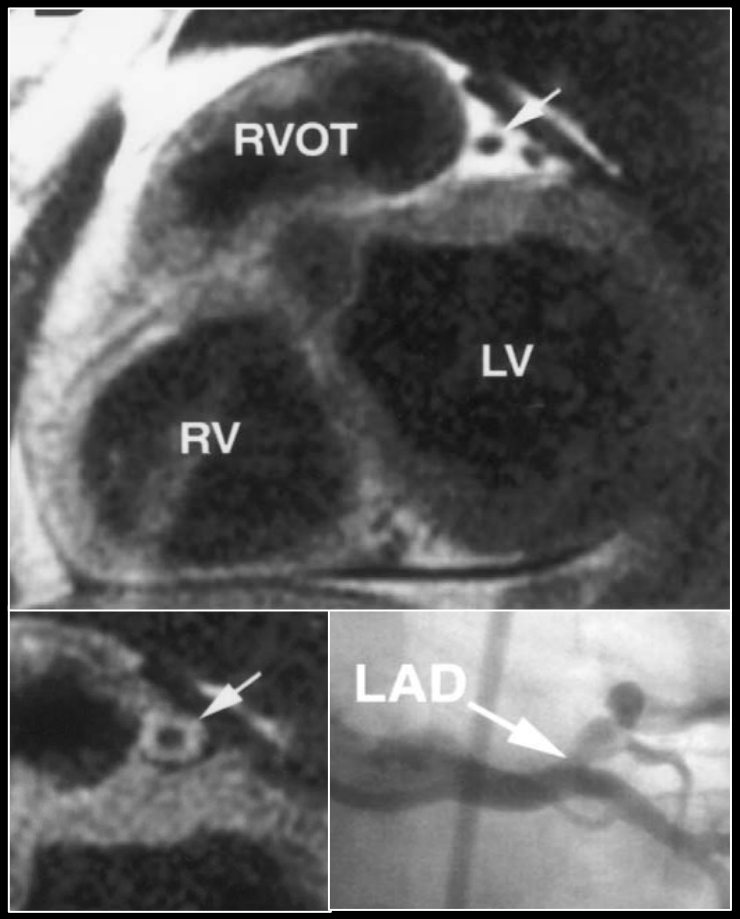
Atherosclerotic | Contro

N1177 | Convent | N1177

Iodinated particles (256nm)
Atherosclerotic rabbit aorta

Hyafil et al, Nature Med. 2007

Coronary Plaque by MRI



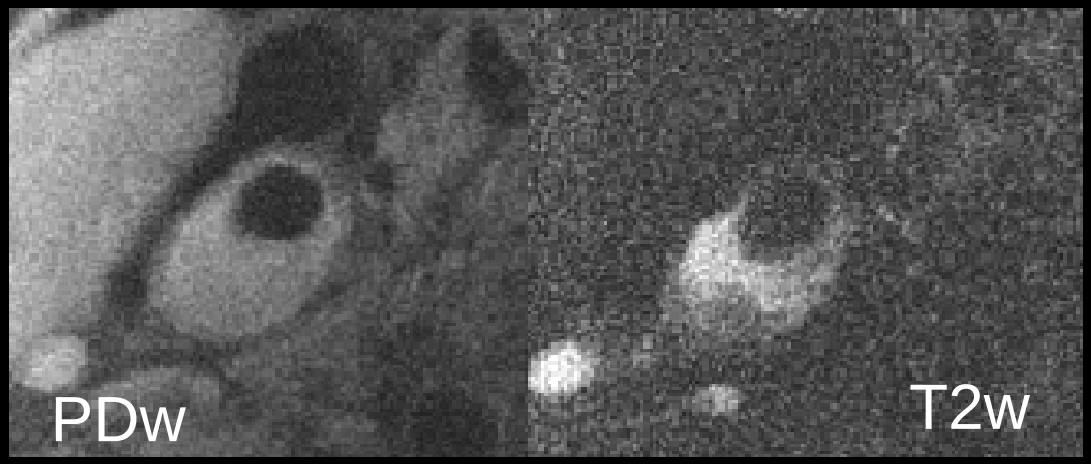
Fayad, Circulation 2000

- Versatile, but difficult
- Harmless

- Continuous trade-off:
  - Image quality
  - Scan time

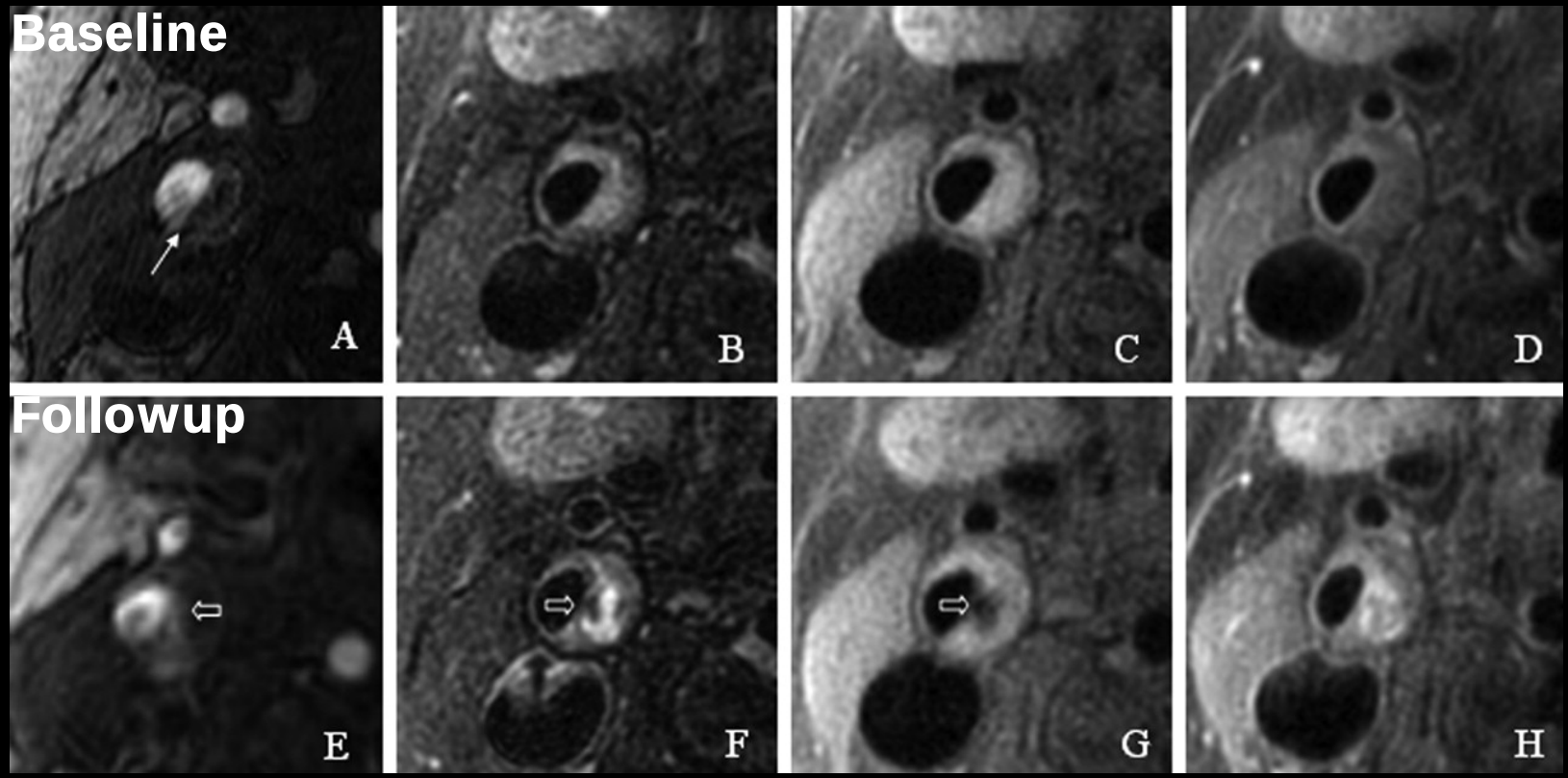
- Coronary most challenging:
  - Size & tortuosity
  - Depth
  - Pericardial fat
  - Coronary motion
  - Breathing

Multi-Contrast Plaque Imaging



T1w, T2w, proton-density weighted imaging

Multicontrast MRI Plaque Rupture



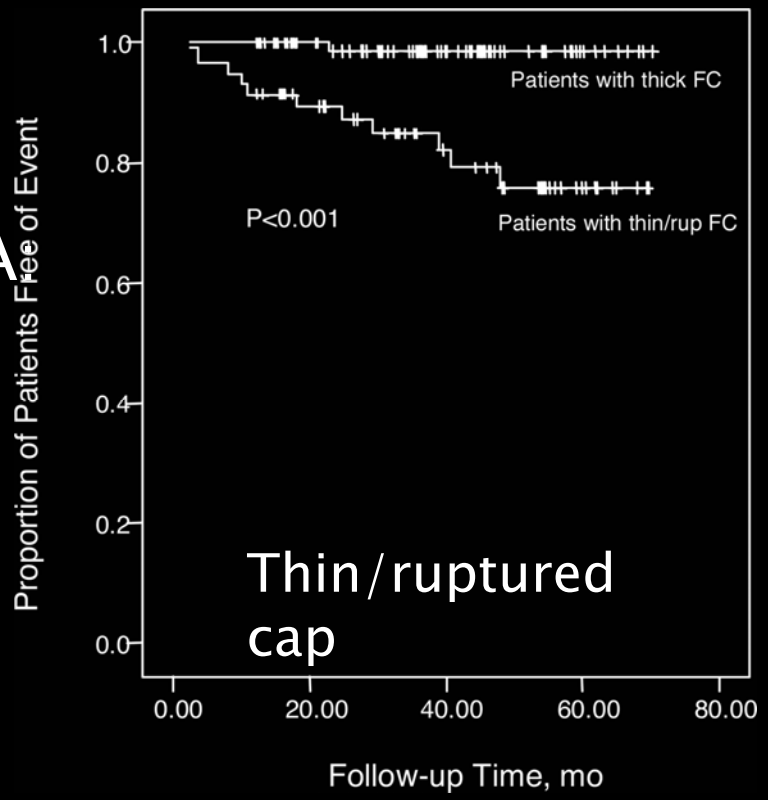
3DToF T2W T1w Pre-contrast T1w Post-contrast

Chu, Yuan, Takaya, ….Hatsukami, Circulation 2006

Predictive Value of Carotid MRI

Prospective study of 154 asymptomatic patients with a 50-79% carotid stenosis
Multicontrast MRI
38-months follow-up

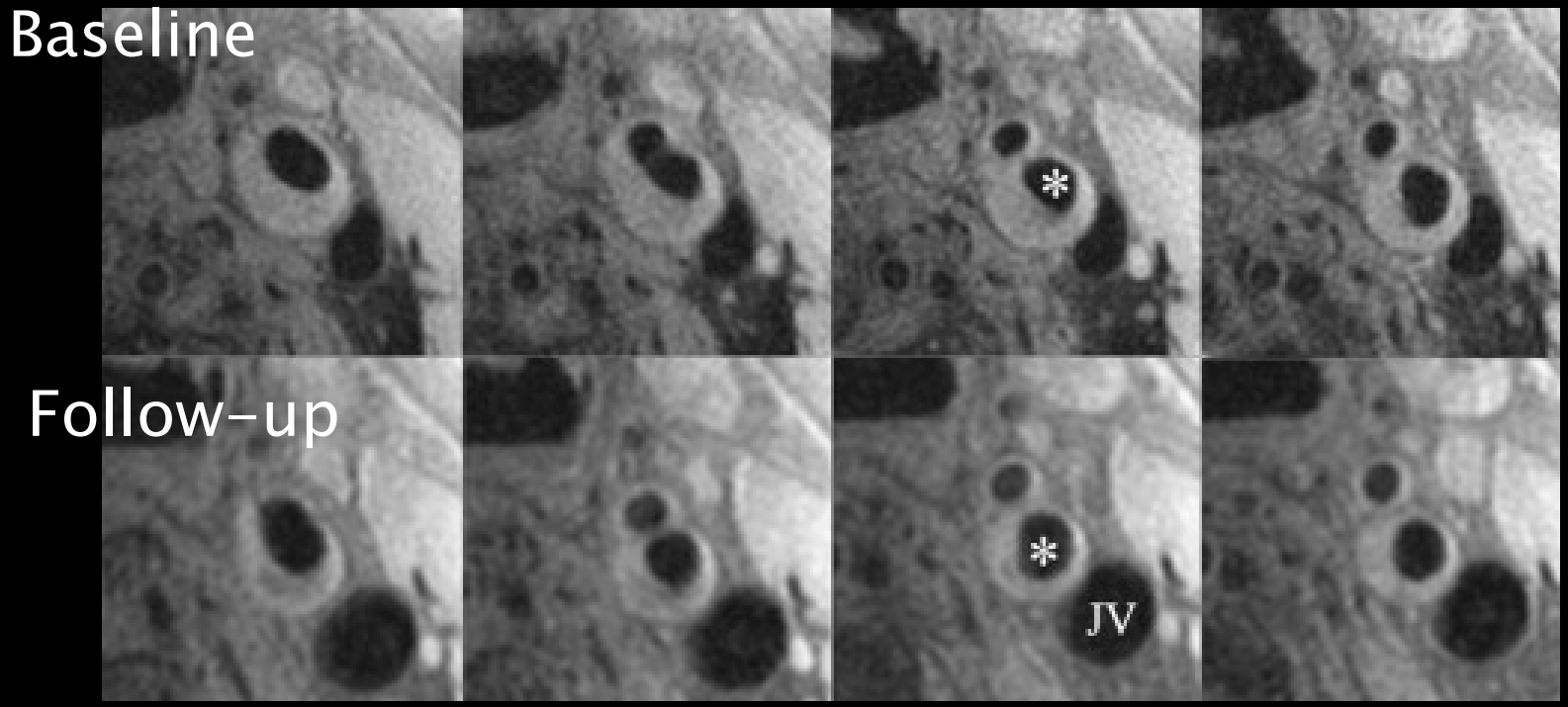
Associated with subsequent CVA
1. Thin or ruptured fibrous cap
2. Intra-plaque hemorrhage
3. Large lipo-necrotic core



Takaya, et al, Stroke 2006

Carotid Plaque Regression by Rosuvastatin

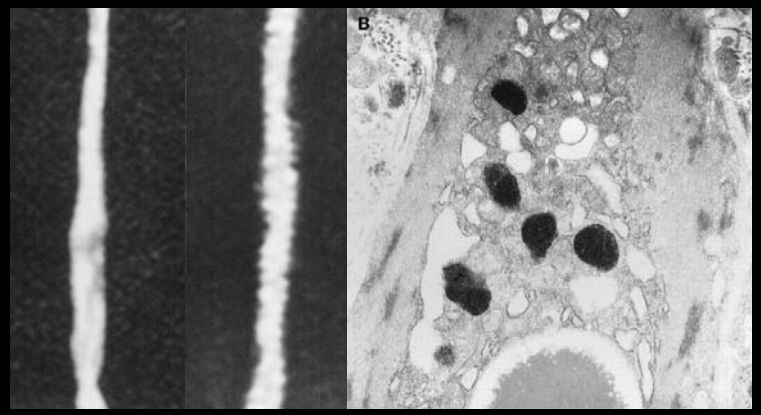
Underhill, et al, AHJ 2008



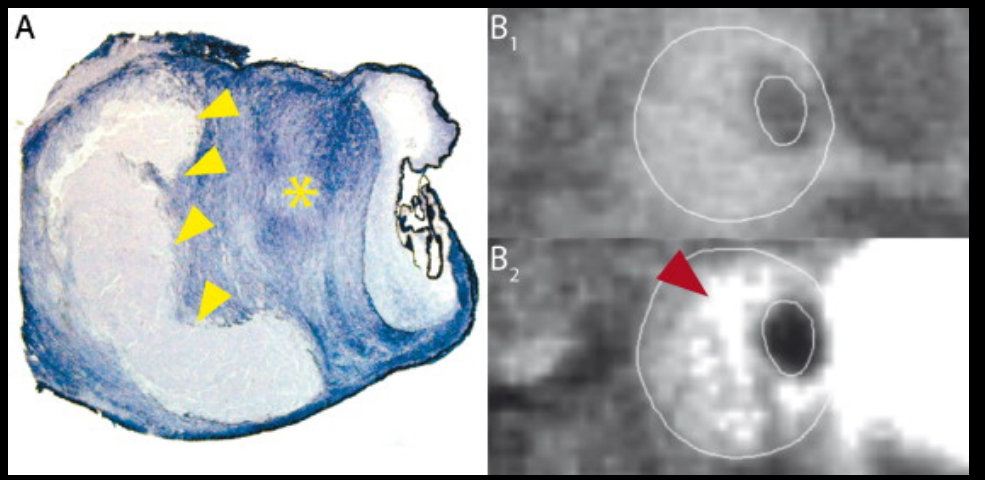
41% reduction lipid-core-containing plaque over 24 months

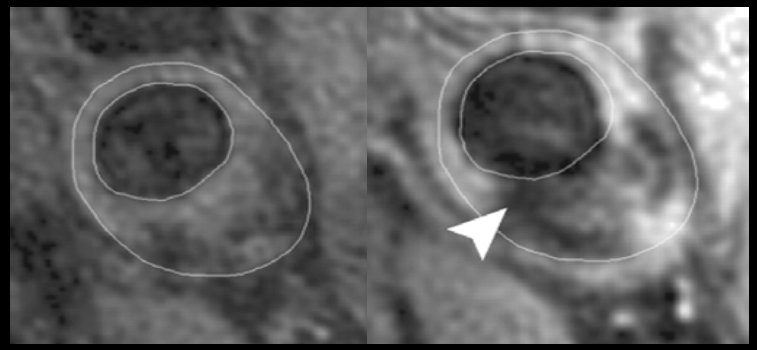
Measurement error carotid arteries 3.5% [Corti, 2001]

Macrophages by MRI



Iron oxide uptake in macrophages



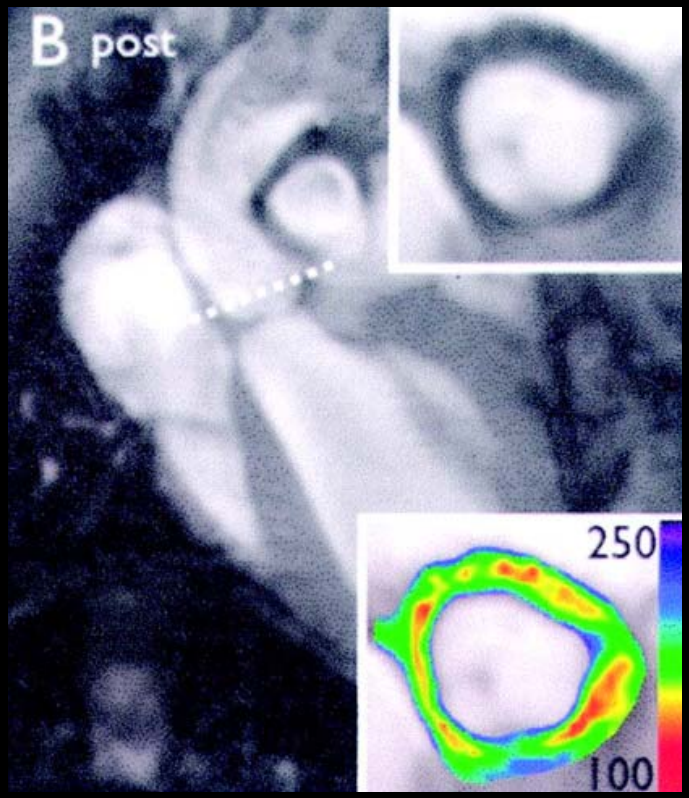


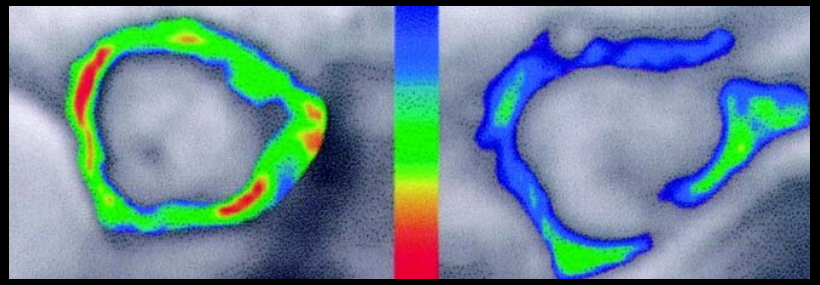
In-vivo human carotid with USPIO

Ultra-Small Super-Paramagnetic Iron Oxide (USPIO)

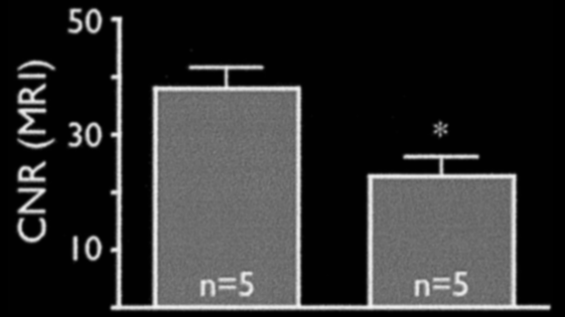
Ruehm, Circulation 2001, Tang, Stroke 2006, Howarth, EJR 2008

Imaging VCAM-1





High-cholesterol diet +/- atorvastatin



High-cholesterol diet +/- atorvastatin

^{18}FDG PET-CT

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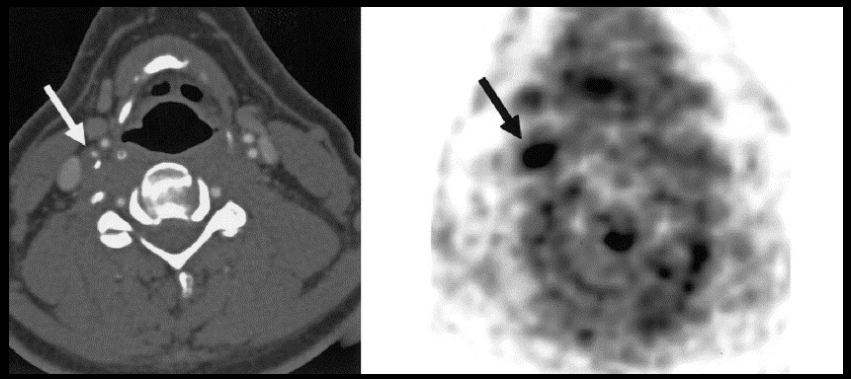
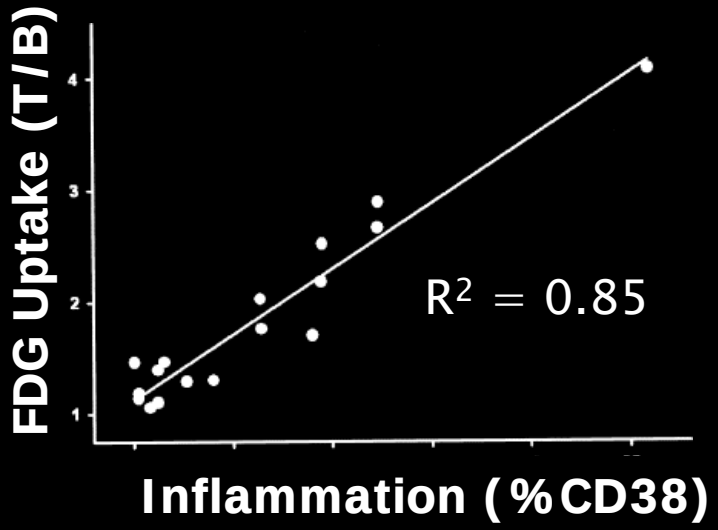
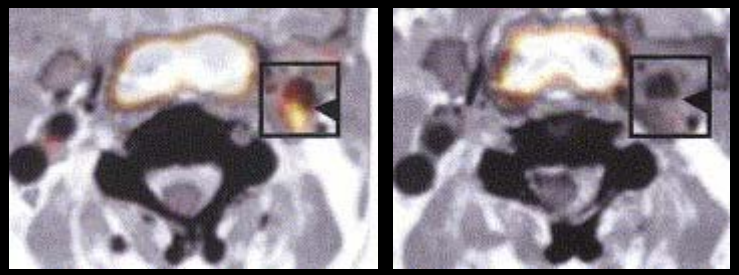


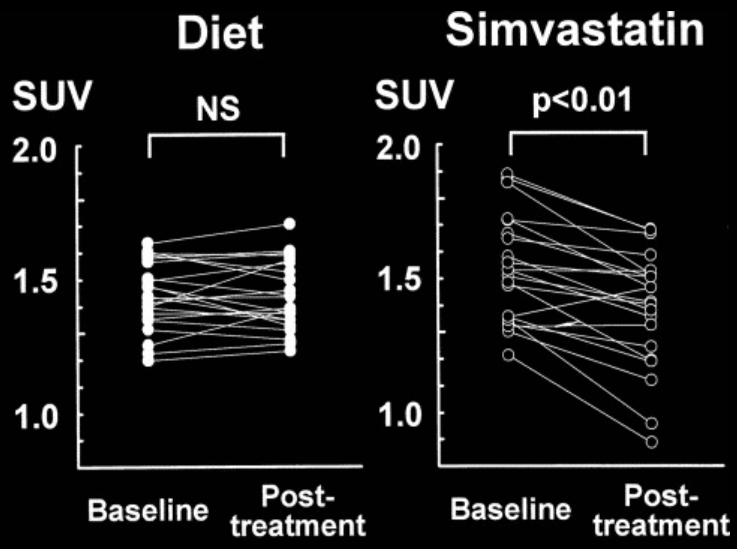


Tawakol, JACC 2006

Simvastatin treatment



Baseline and 6-months CT/PET



Tahara, et al, JACC 2006

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Conclusions

- Computed Tomography:
  - Atherosclerosis/lesion detection
  - Patient risk stratification
  - Road map for invasive imaging and PCI
- Magnetic resonance imaging:
  - Serial (non-coronary) plaque imaging
  - Promising molecular imaging
- Nuclear imaging (with CT):
  - Promising for (coronary?) inflammation imaging