Città della Salute e della Scienza

Coronary heart disease: what's new?

Noninvasive imaging of the vulnerable plaque in 2012

Federico Conrotto

Definition of Vulnerable Plaque

The susceptibility of a plaque to rupture

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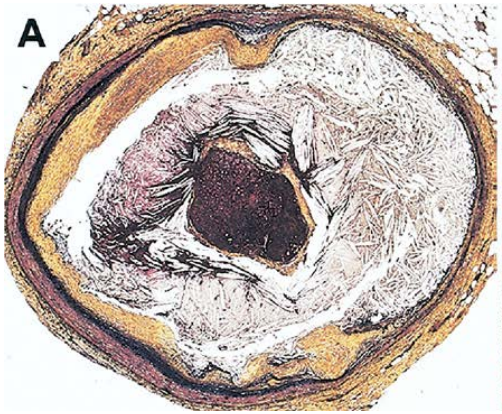
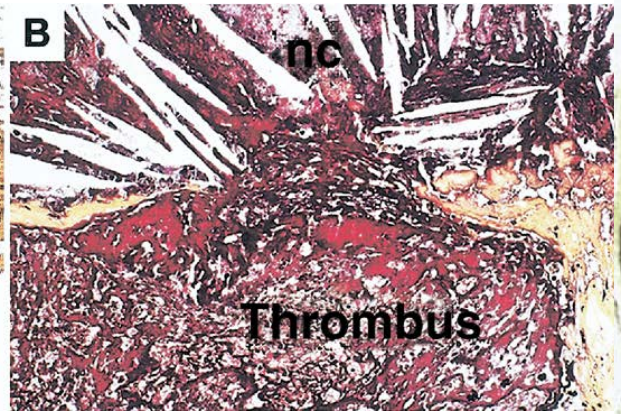
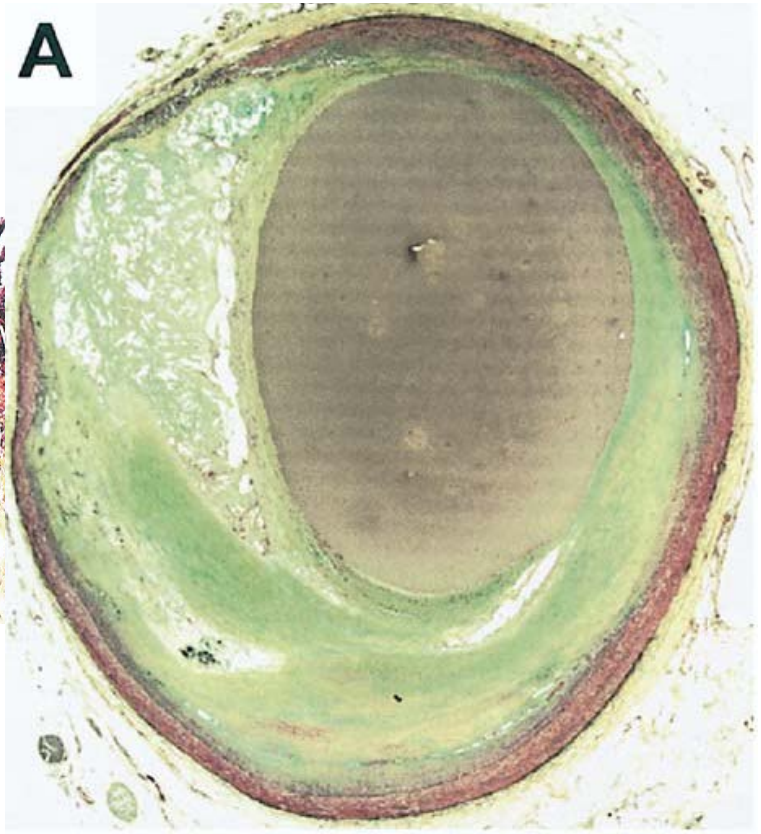
Circulation 1989; 79: 733-43

JACC 2006; 47 Suppl 8: C13-8

Plaque rupture as the basis of ACS

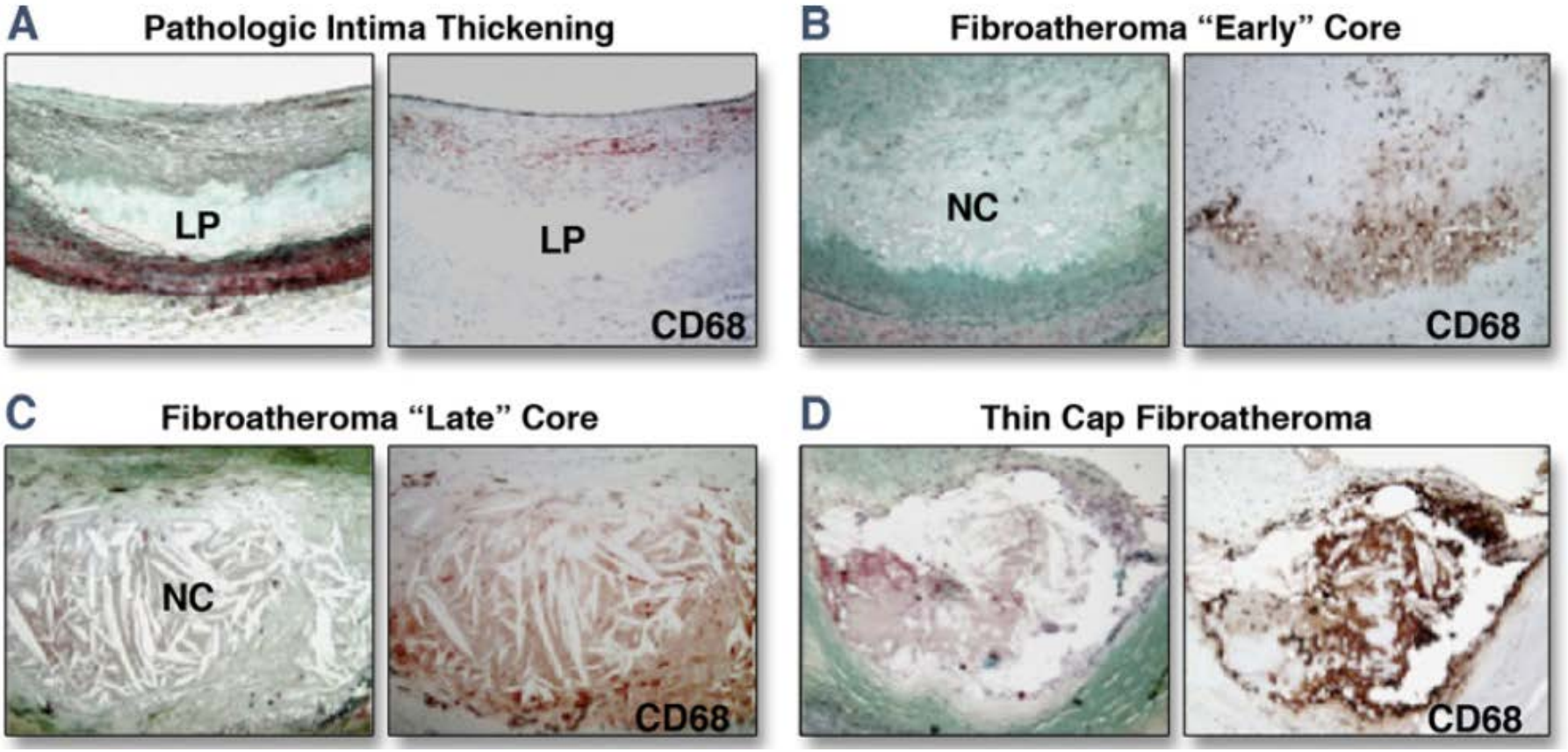






From autopsy sudies in patients who had died of cardiac causes, the most common underlying plaque morfology was a ruptured thin-cap fibroatheroma

Representative Lesion Morphologies for Progressive Human Coronary Atherosclerosis



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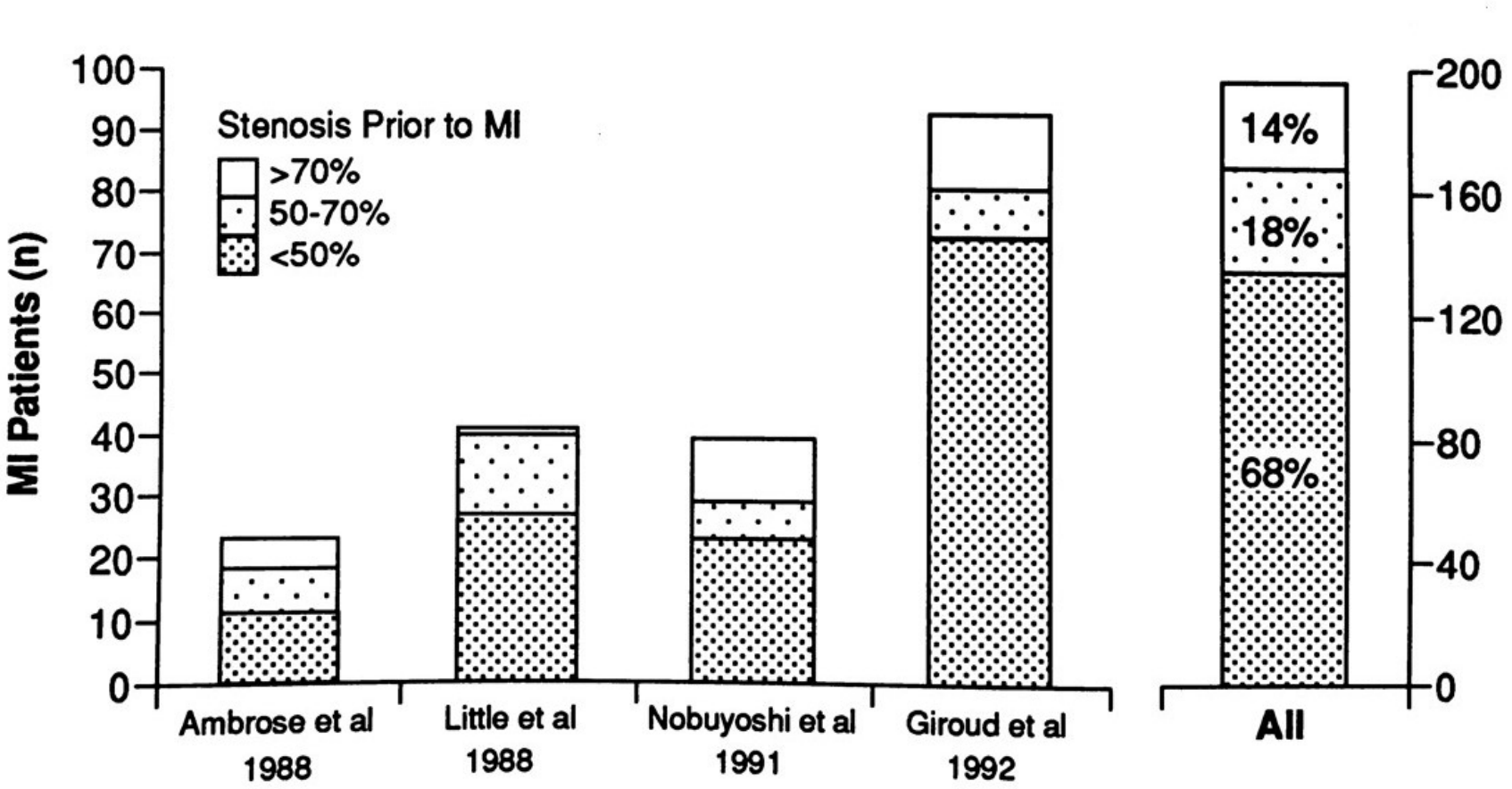
The Vulnerable Atherosclerotic Plaque: Strategies for Diagnosis and Management. Malden, MA: Blackwell Futura, 2007:37–59

Most Culprit Lesions Cause Insignificant Luminal Narrowing Prior to Onset of MI



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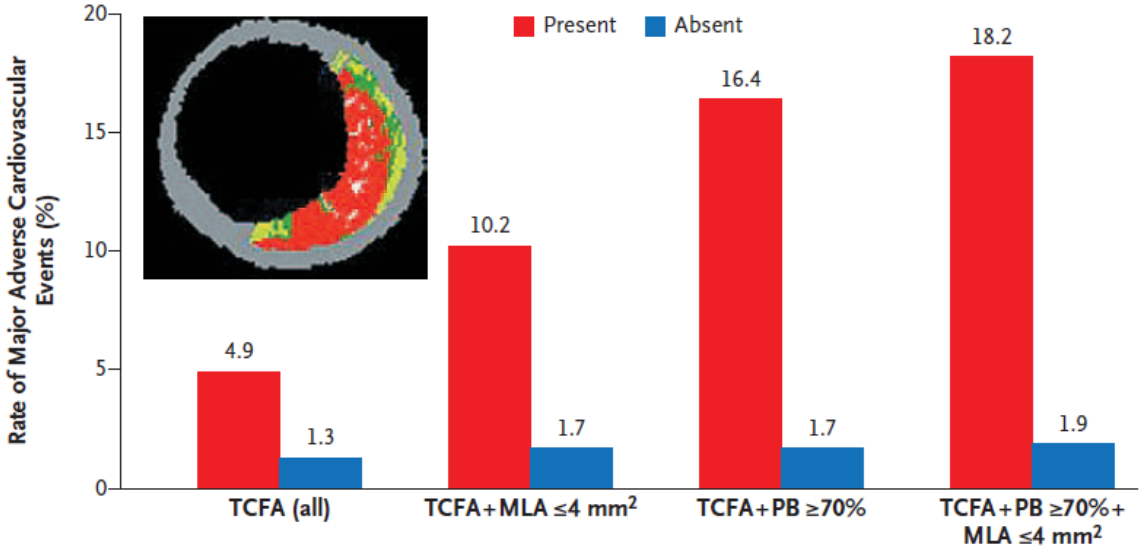
ORIGINAL ARTICLE

A Prospective Natural-History Study of Coronary Atherosclerosis



Lesion hazard ratio (95% CI)	3.90 (2.25–6.76)	6.55 (3.43–12.51)	10.83 (5.55–21.10)	11.05 (4.39–27.82)
P value	<0.001	<0.001	<0.001	<0.001
Prevalence (%)	46.7	15.9	10.1	4.2

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N Engl J Med 2011;364:226-35

Noninvasive imaging of the vulnerable plaque

Plaque morphology and plaque composition (identification of the “vulnerable plaques”)

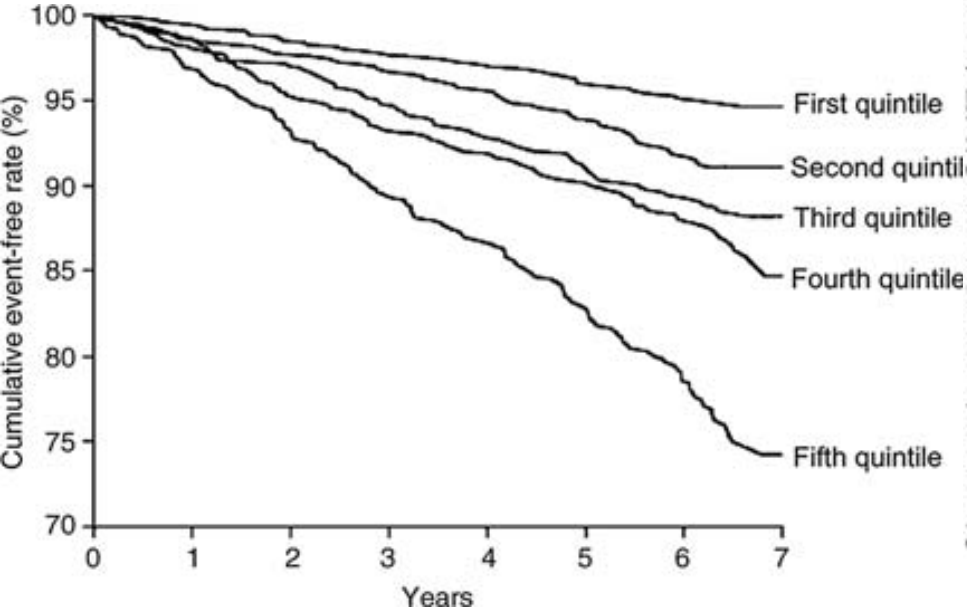
Plaque progression/regression.

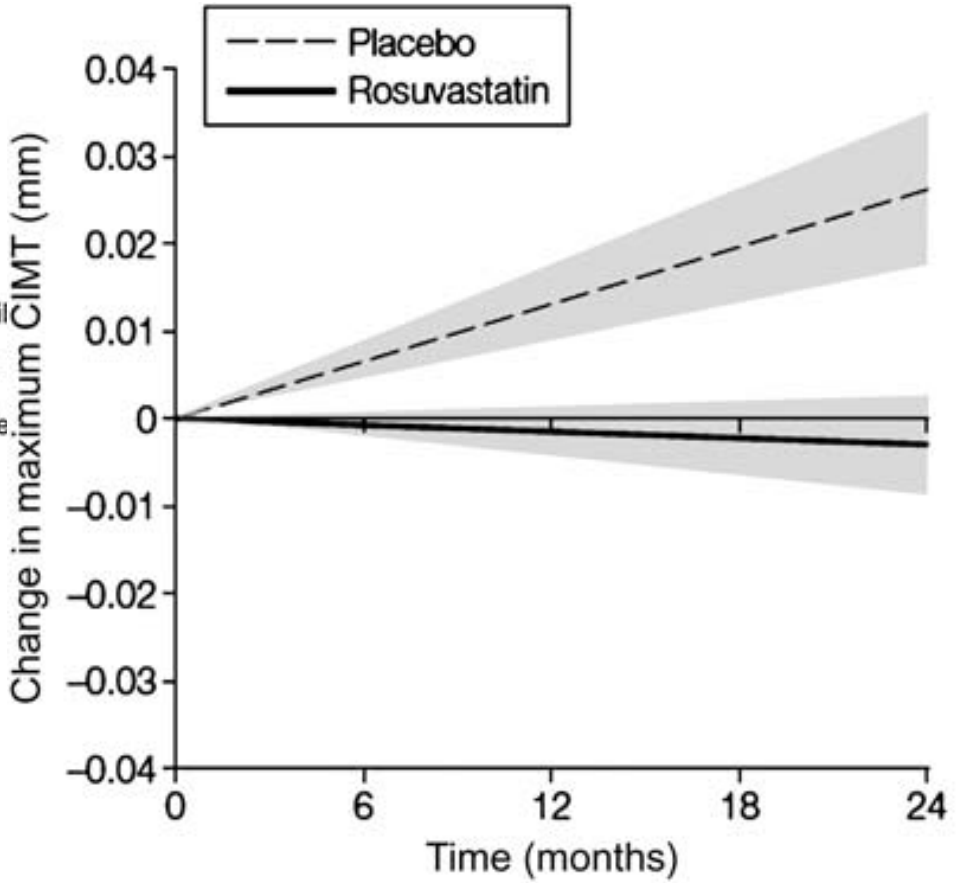
Monitor the effects of drugs on diseased arteries

European Heart Journal (2010) **31**, 1682–1689
doi:10.1093/eurheartj/ehq185

Imaging

Imaging of atherosclerosis: carotid intima–media thickness





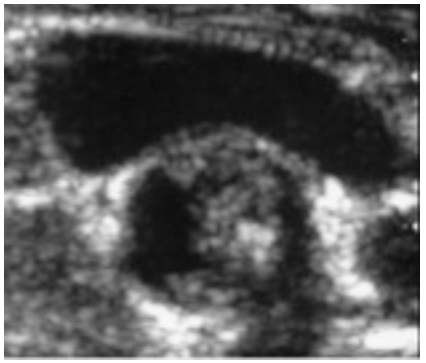
Lines were estimated from the statistical model based on 12 carotid artery sites. Gray shading indicates 95% confidence intervals.

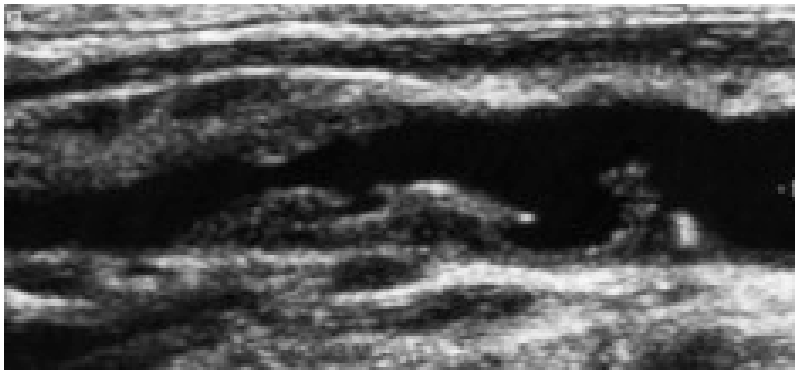
A.L. 56 aa

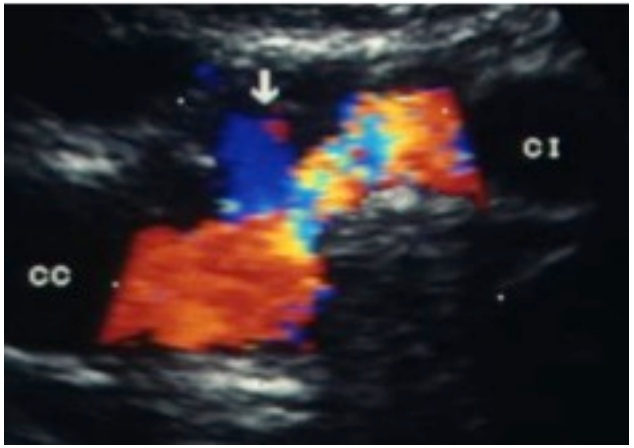
Hypertension, dislipidemia

Transient ischemic attack

Detection of carotid vulnerable plaque on doppler examination







Carotid endarterectomy

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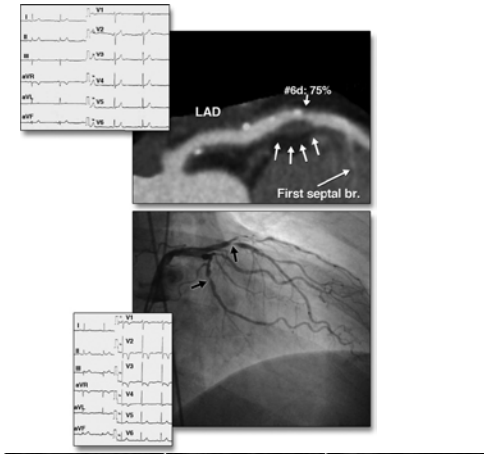
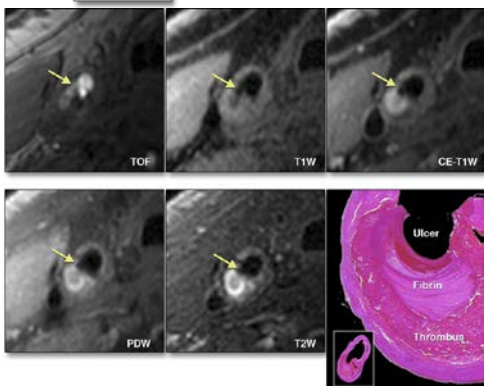
Noninvasive Characterization of Plaque Morphology

Computed tomography angiography:

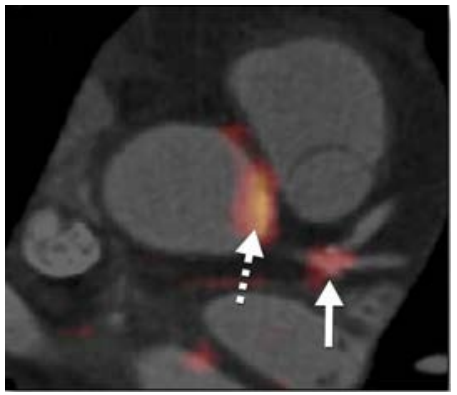
Calcium, plaque attenuation and PVR



MRI:plaque morphology and intraplaque hemorrhage



Positron emission tomography



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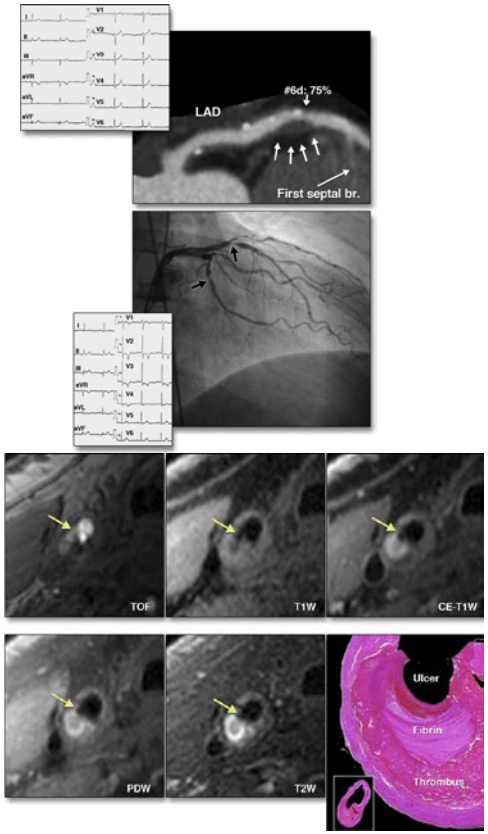
Noninvasive Characterization of Plaque Morphology

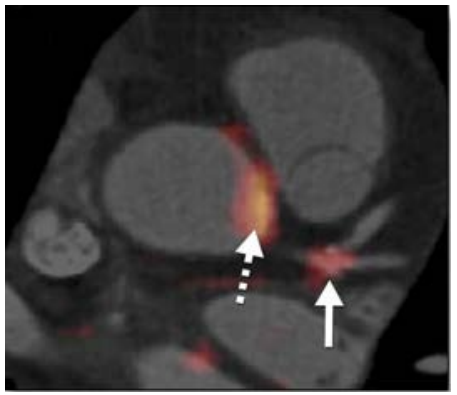
Computed tomography angiography:

Calcium, plaque attenuation and PVR



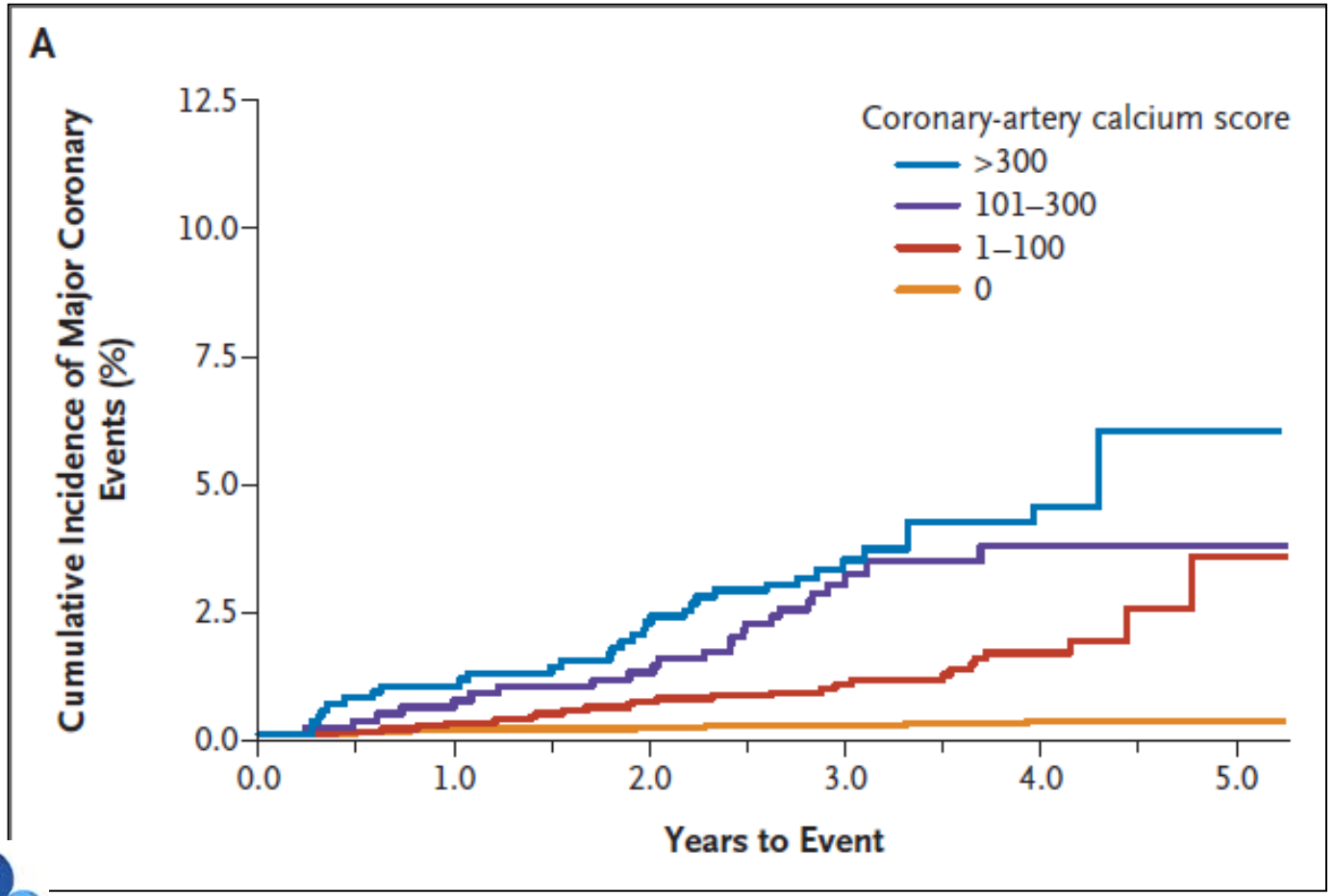
MRI:plaque morphology and intraplaque hemorrhage

Positron emission tomography



ORIGINAL ARTICLE

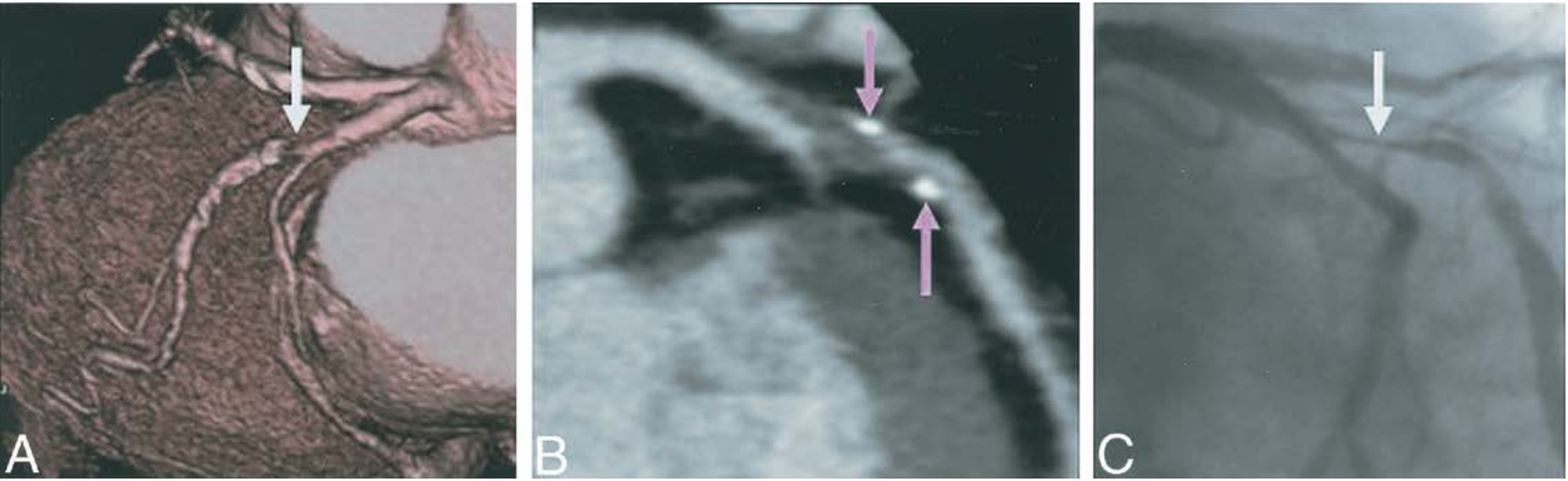
Coronary Calcium as a Predictor of Coronary Events in Four Racial or Ethnic Groups



N Engl J Med 2008;358:1336-45.

Multislice Computed Tomographic Characteristics of Coronary Lesions in Acute Coronary Syndromes

Acute Coronary Syndrome



Positive remodeling

NCP plaque (also including areas of 30 HU)

Spotty calcification (pink arrows)

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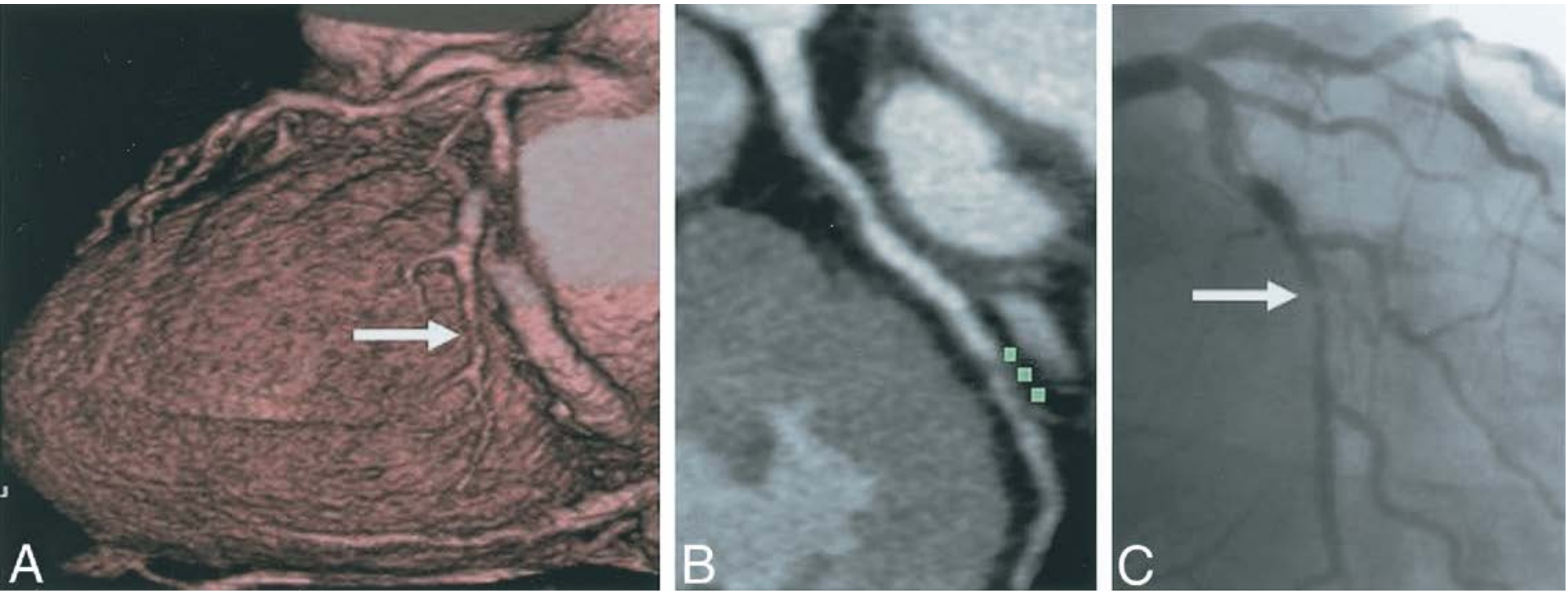
J Am Coll Cardiol 2007;50:319–26

Multislice Computed Tomographic Characteristics of Coronary Lesions in Acute Coronary Syndromes

Stable Angina



Negatively remodeled

No NCP 30 HU or spotty calcification

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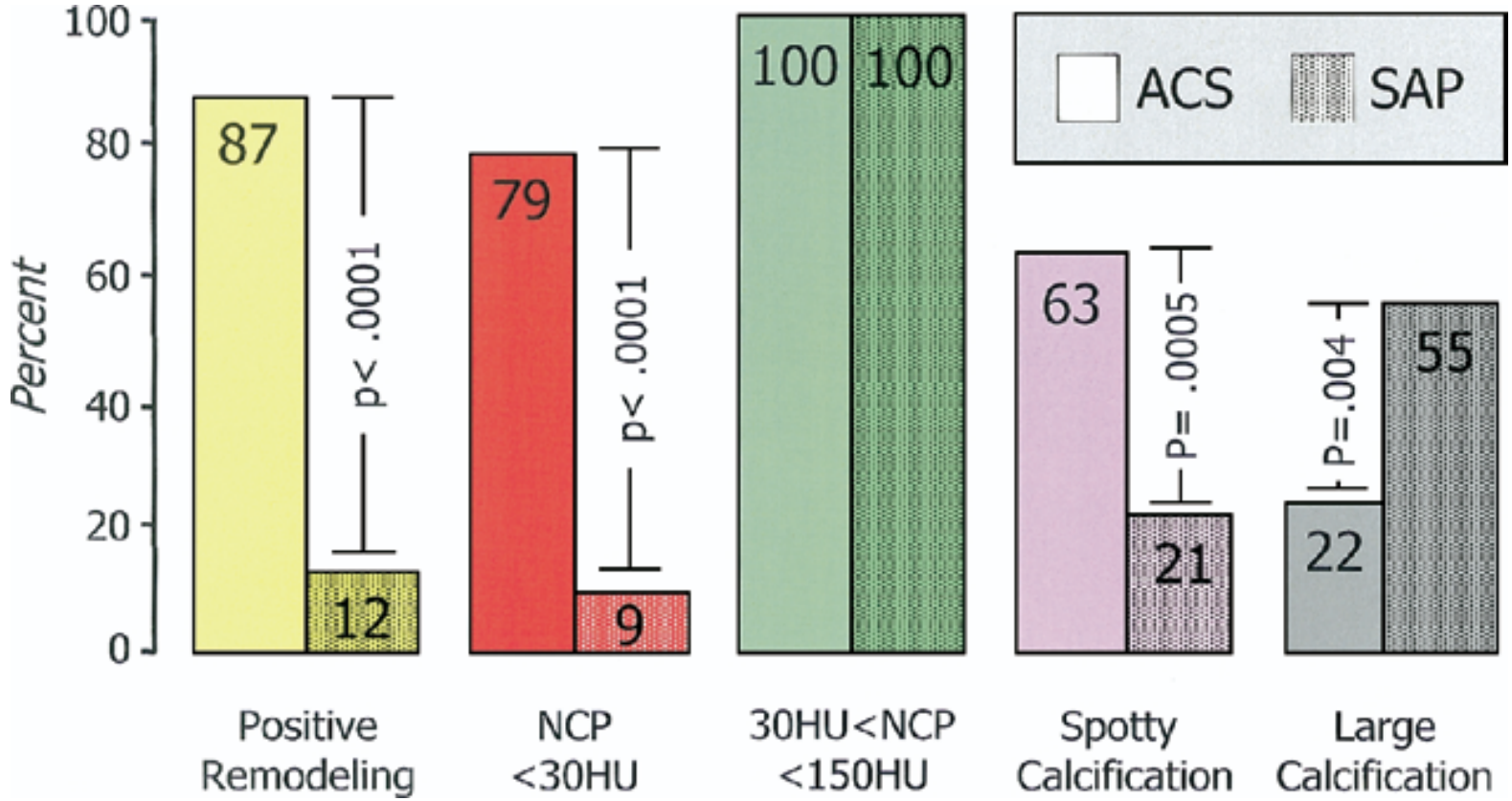
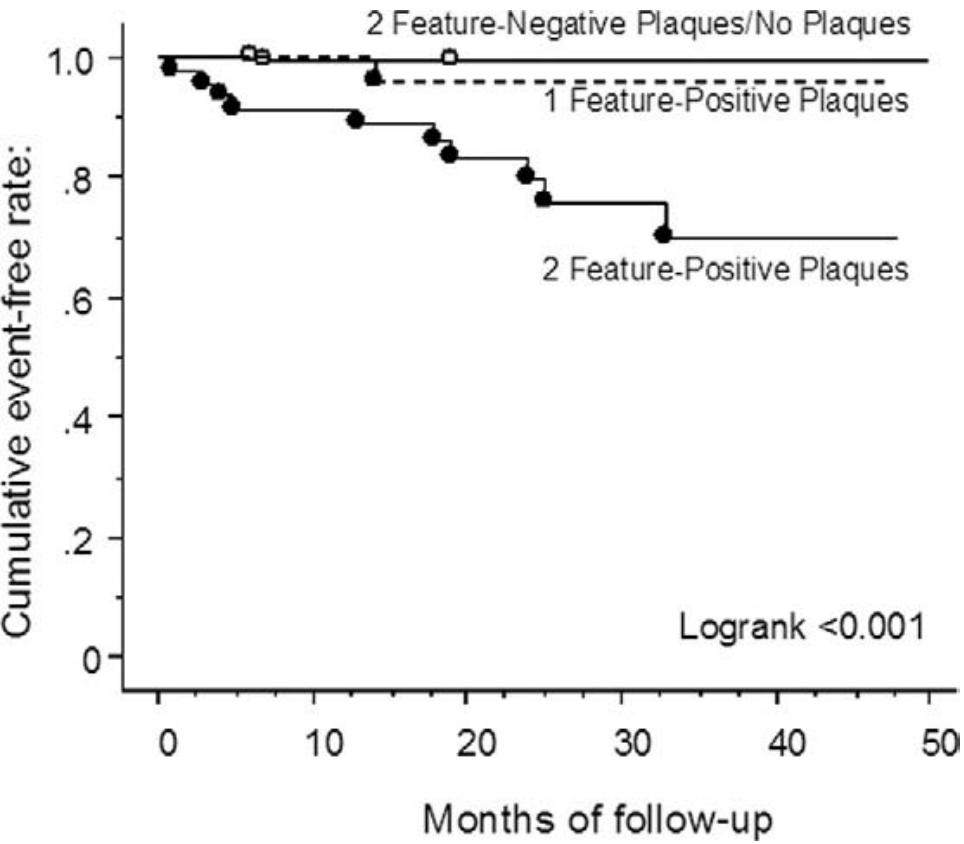
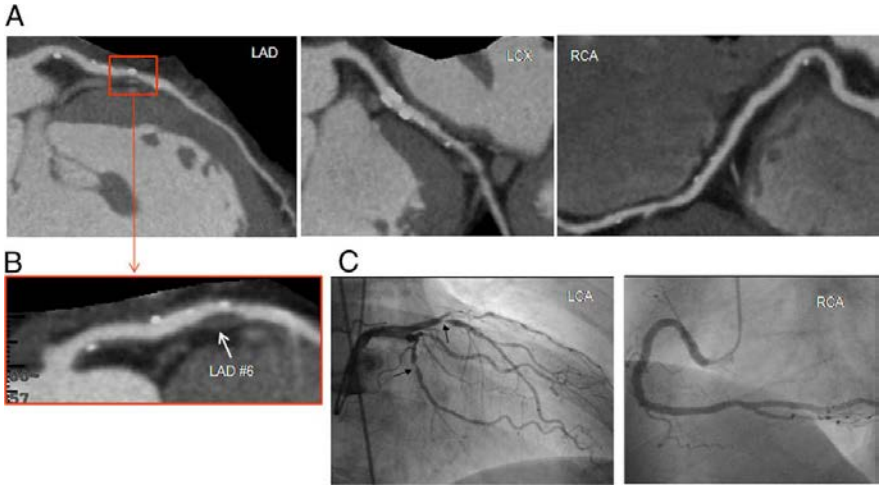
Multislice Computed Tomographic Characteristics of Coronary Lesions in Acute Coronary Syndromes



Plaque Characteristics in ACS and SAP

Computed Tomographic Angiography Characteristics of Atherosclerotic Plaques Subsequently Resulting in Acute Coronary Syndrome





2-year ACS Risk

22% PVR + LAP

Vs

0.5% No PVR nor LAP

J Am Coll Cardiol 2009;54:49–57

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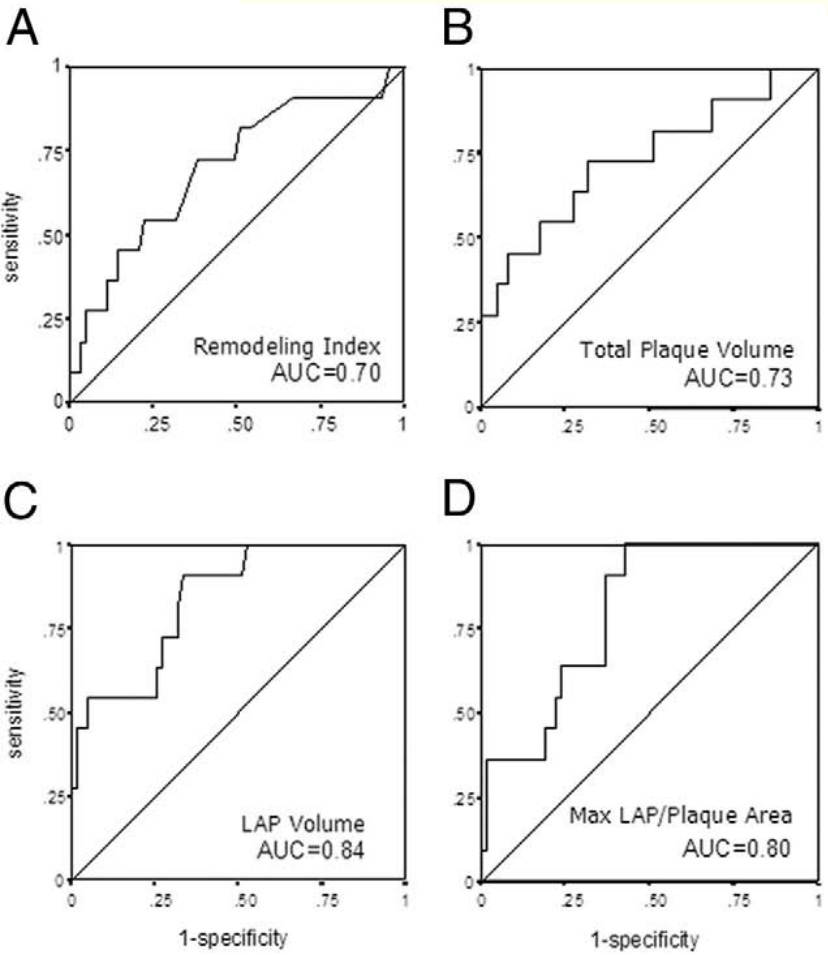
Computed Tomographic Angiography Characteristics of Atherosclerotic Plaques Subsequently Resulting in Acute Coronary Syndrome



	Cutoff Value	Sens (%)	Spec (%)	PPV (%)	NPV (%)
Remodeling Index (%)	116.5	72.7	61.9	25.0	69.0
Total Plaque Volume (mm^3)	63.13	72.7	68.3	28.6	93.5
LAP Volume (mm^3)	0.99	90.0	66.7	32.3	97.7
Max LAP Area/ Plaque Area (%)	11.39	63.6	76.2	31.8	92.3

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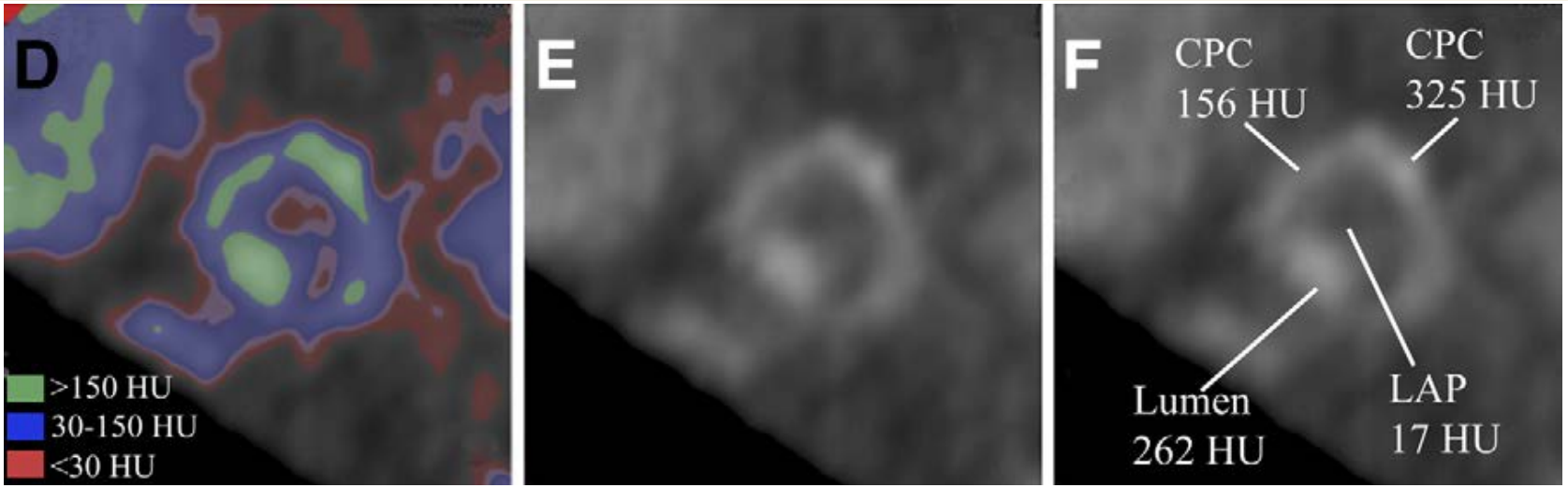
J Am Coll Cardiol 2009;54:49–57

Computed Tomographic Angiography–Verified Plaque Characteristics and Slow-Flow Phenomenon During Percutaneous Coronary Intervention

Variable	All Patients (N = 80)	Control Group (n = 40)	SF Group (n = 40)	p Value
CCTA findings				
Positive remodeling index	1.4 (1.2–1.6)	1.2 (1.0–1.5)	1.5 (1.3–1.8)	<0.001
Minimum CT value, HU	34 (18–75)	45 (29–86)	23.5 (9.5–40)	0.001
% Stenosis	69 ± 11	69 ± 12	69 ± 11	NS
CPC	27 (34)	2 (5)	25 (63)	<0.001
ULA	9 (11)	5 (13)	4 (10)	NS



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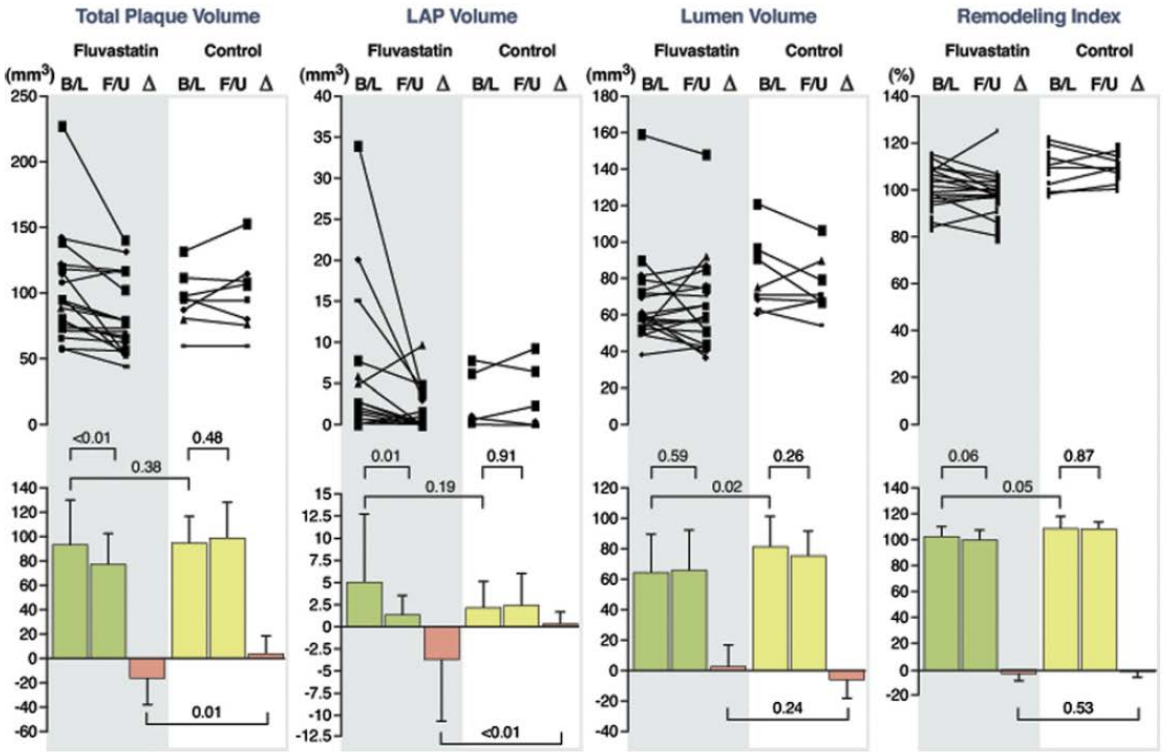
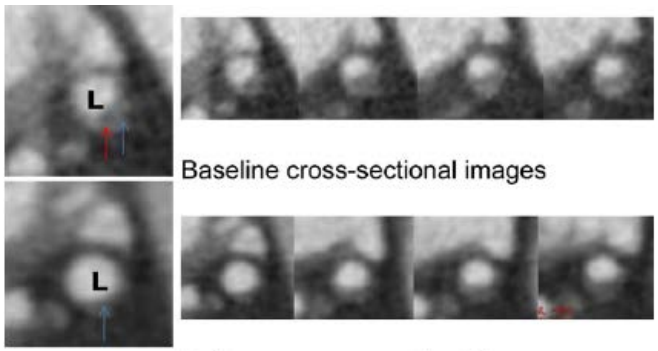
J Am Coll Cardiol Intv 2012;5:636–43

Serial Coronary CT Angiography–Verified Changes in Plaque Characteristics as an End Point

Evaluation of Effect of Statin Intervention





Baseline cross-sectional images

Follow-up cross-sectional images

JACC: CARDIOVASCULAR IMAGING, VOL. 3, NO. 7, 2010
JULY 2010:691–8

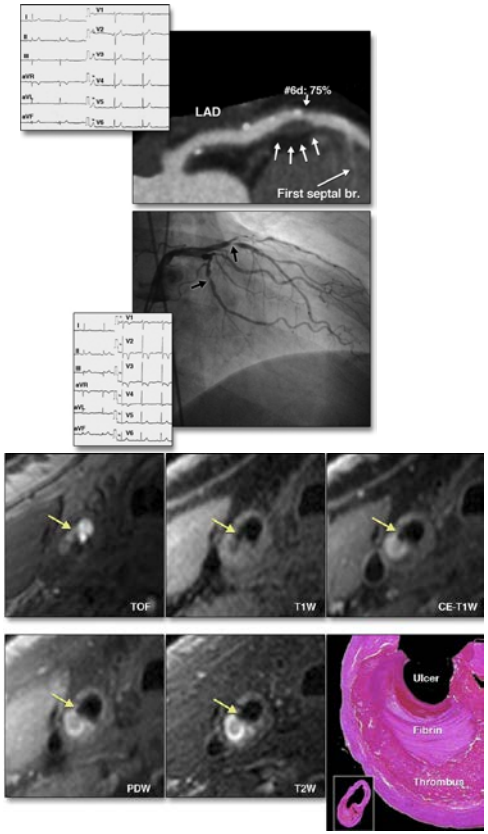
CT LIMITATIONS

1. Suboptimal resolution
2. Various imaging or technical parameters may significantly influence the soft plaque measurements
3. Heavy plaque calcification
4. No characterization of plaque erosions
5. Radiation burden
6. No Primary prevention studies

Noninvasive Characterization of Plaque Morphology

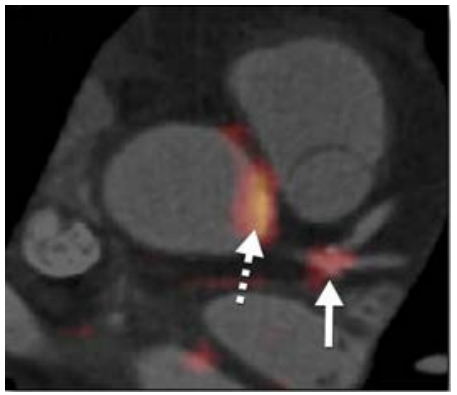
Computed tomography angiography:

plaque attenuation and PVR



MRI:plaque morphology and intraplaque hemorrhage

Positron emission tomography



Noninvasive Characterization of Plaque Morphology

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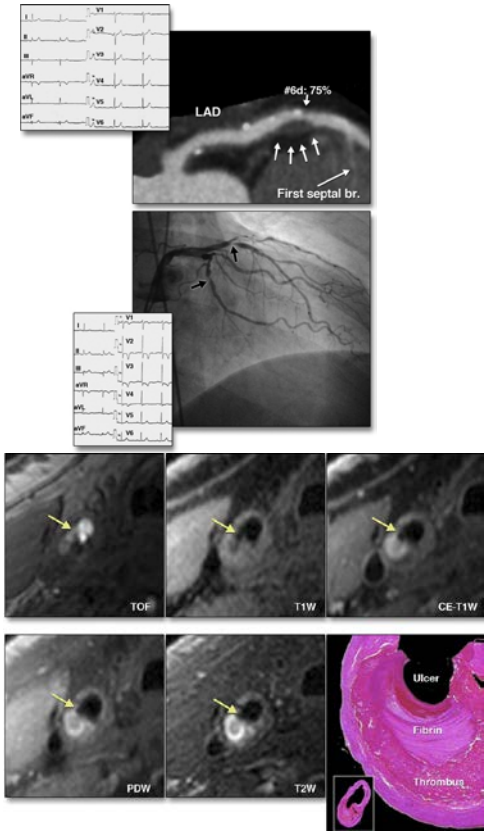
plaque attenuation and PVR



MRI:plaque morphology and intraplaque hemorrhage

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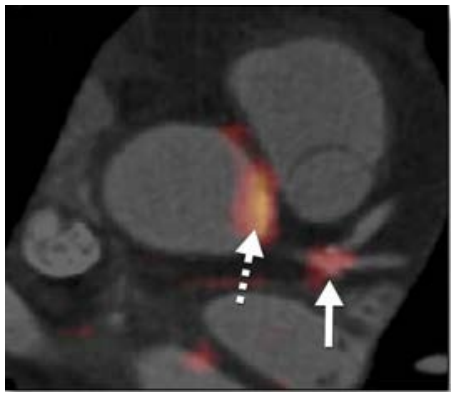
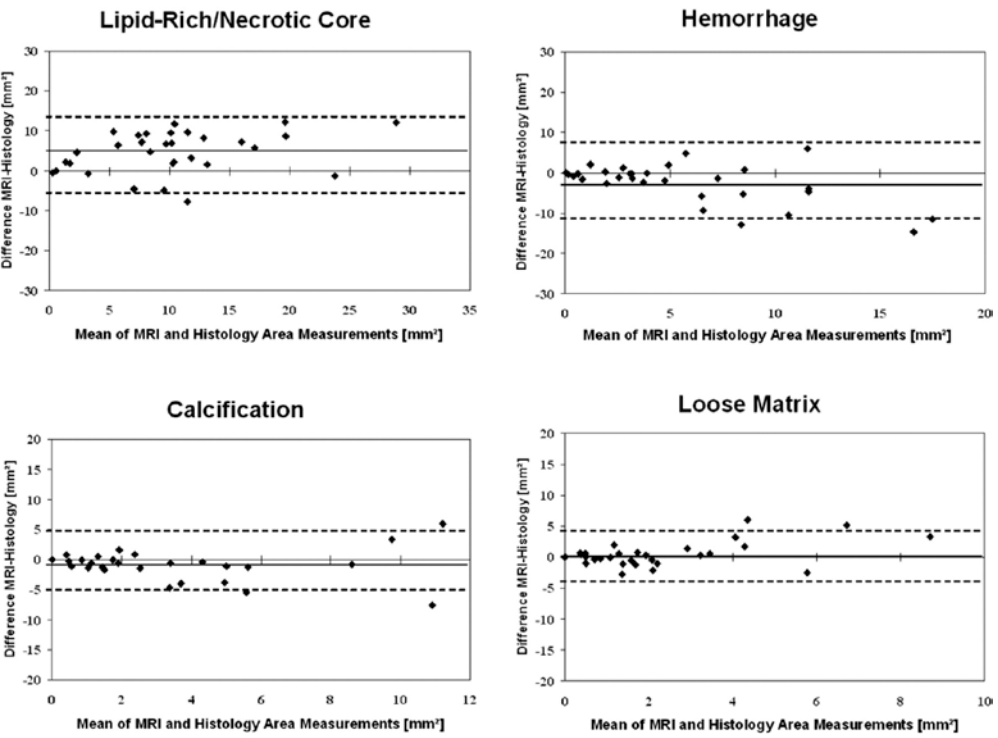
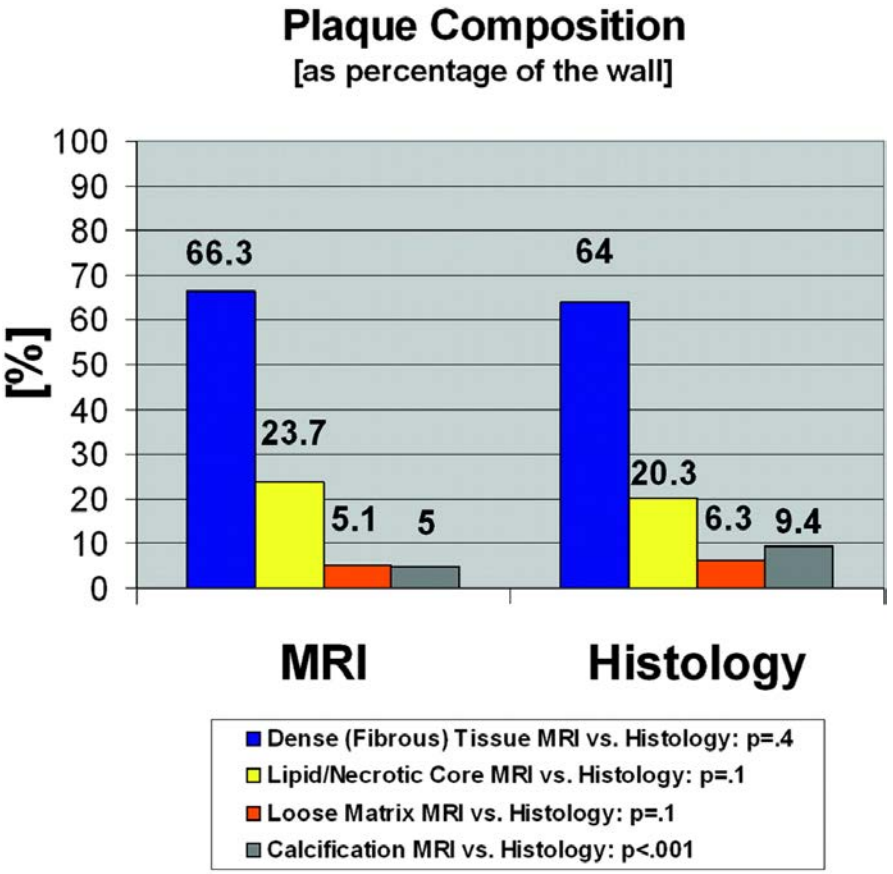


Quantitative Evaluation of Carotid Plaque Composition by In Vivo MRI

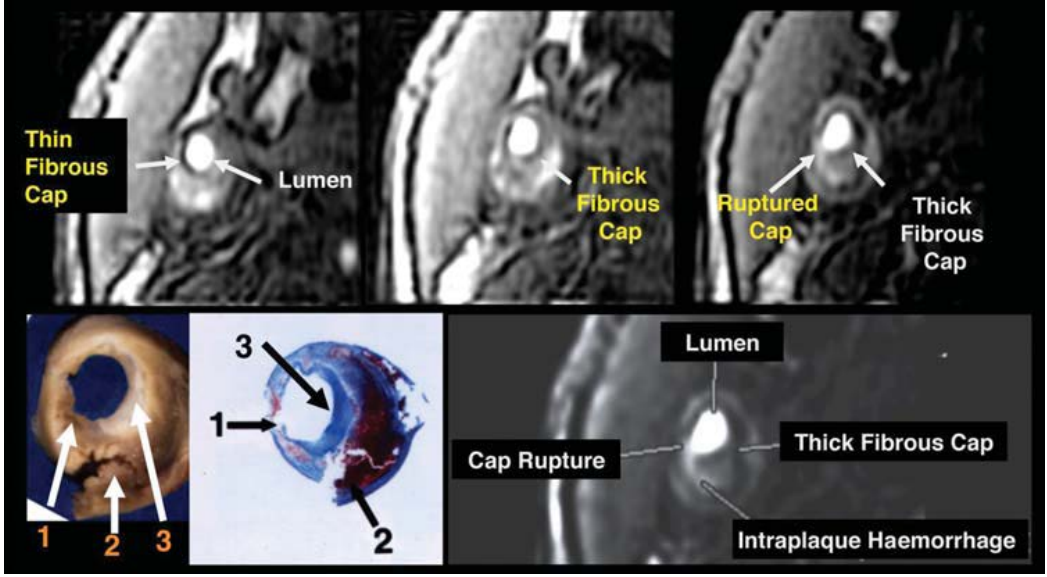
Arteriosclerosis, Thrombosis, and Vascular Biology
Journal of the American Heart Association





Arterioscler Thromb Vasc Biol 2005;25:234-239

1. severity of stenotic lesions
2. spatial distribution
3. composition



154 asymptomatic patients

50% to 80% carotid stenosis

Thin or ruptured fibrous cap (HR: 17.0; p 0.001)

IPH (HR: 5.2; p 0.005)

Larger mean necrotic core area (HR: 1.6; p 0.01 per 10-mm2 increment)

Plaque features predictive of subsequent transient ischemic attack or stroke during a mean follow-up of 3 years

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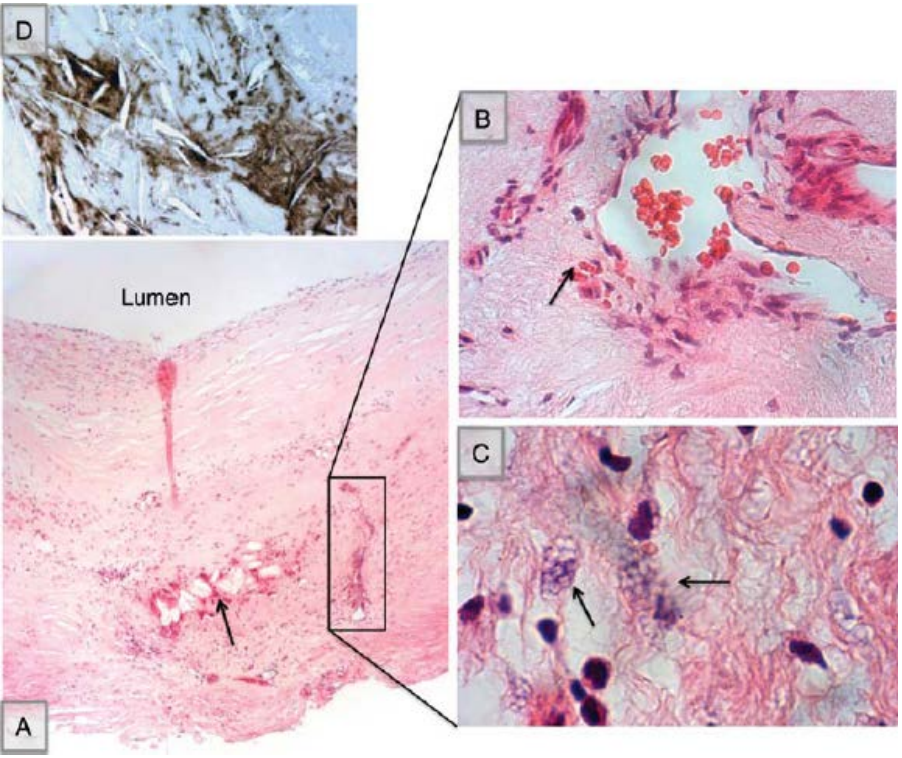
Stroke 2006;37:818 –23.

European Heart Journal (2011) 32, 1977–1985
doi:10.1093/eurheartj/ehr054

REVIEW

Intraplaque haemorrhages as the trigger of plaque vulnerability

Jean-Baptiste Michel[1]*, Renu Virmani[2], Eloïsa Arbustini[3], and Gerard Pasterkamp[4]



From centripetal neo-angiogenesis to intraplaque haemorrhages

These microvessels are fragile because of lack of support by smooth muscle cells and focal discontinuity of the endothelial lining

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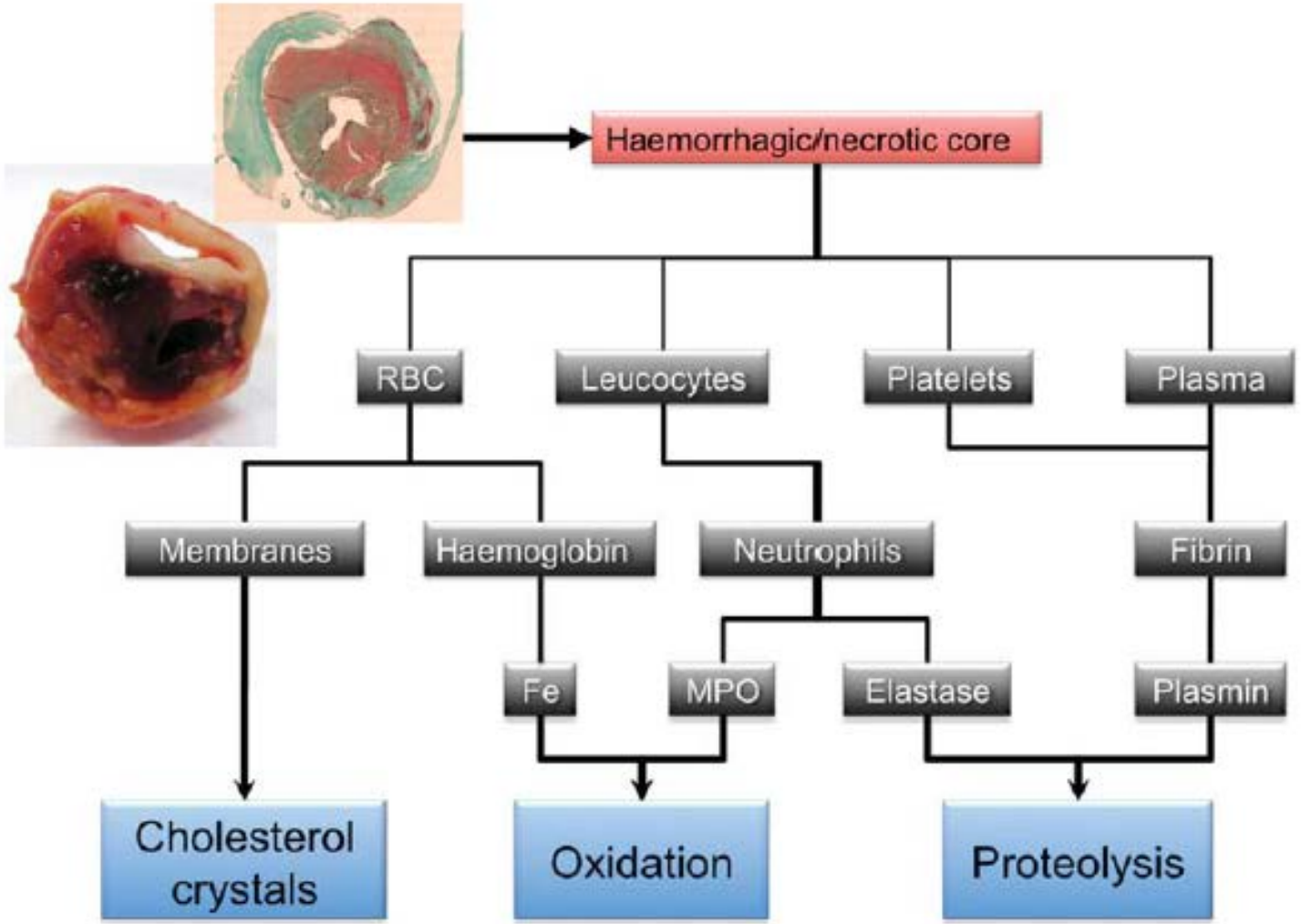

Haemorrhagic/necrotic core
RBC
Leucocytes
Platelets
Plasma
Membranes
Haemoglobin
Neutrophils
Fibrin
Fe
MPO
Elastase
Plasmin
Cholesterol crystals
Oxidation
Proteolysis

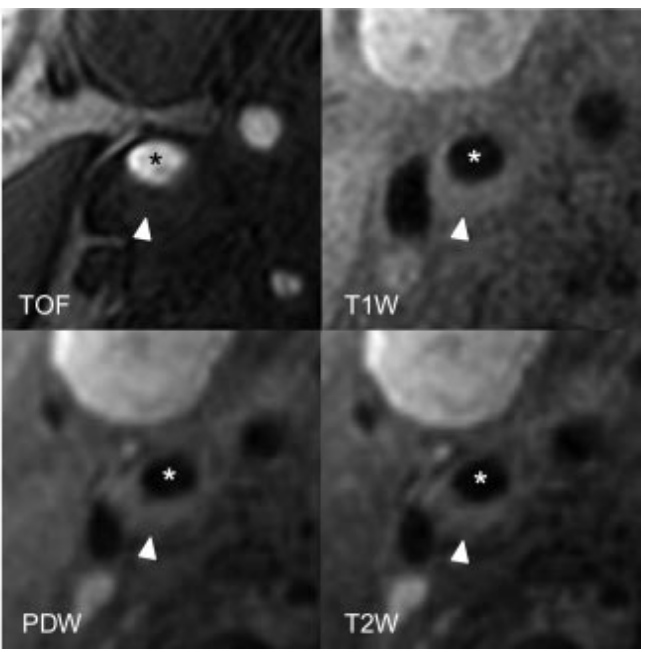
Presence of Intraplaque Hemorrhage Stimulates Progression of Carotid Atherosclerotic Plaques : A High-Resolution Magnetic Resonance Imaging Study

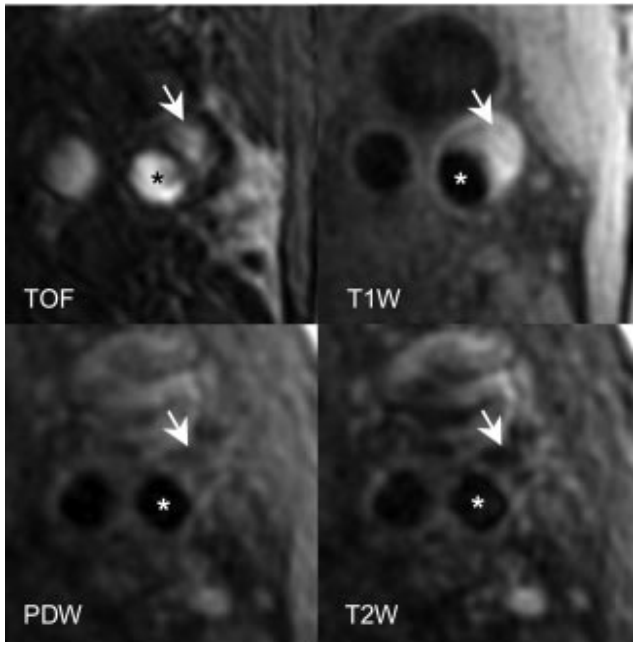
Norihide Takaya, Chun Yuan, Baocheng Chu, Tobias Saam, Nayak L. Polissar, Gail P. Jarvik, Carol Isaac, Judith McDonough, Cynthia Natiello, Randy Small, Marina S. Ferguson and Thomas S. Hatsukami

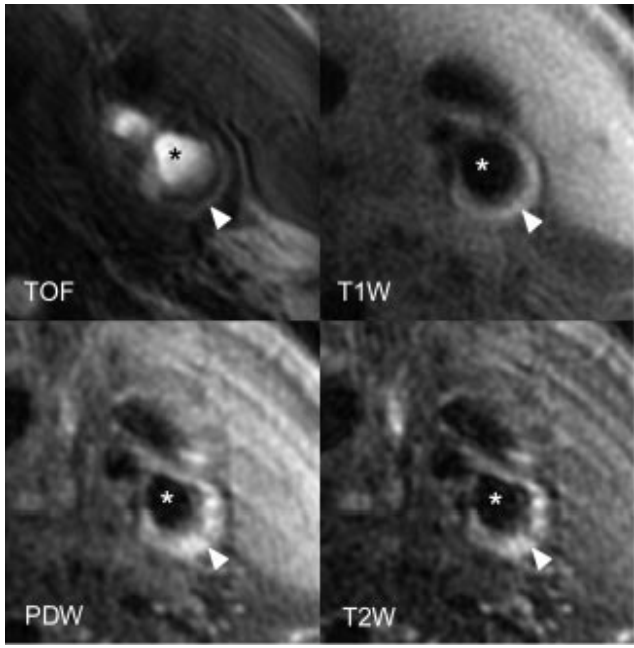
Lipid-rich necrotic core without hemorrhage

Type I hemorrhage

Type II hemorrhage







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Takaya N et al. Circulation 2005;111:2768-2775

Images of progression of atherosclerosis with intraplaque hemorrhage in right carotid artery.

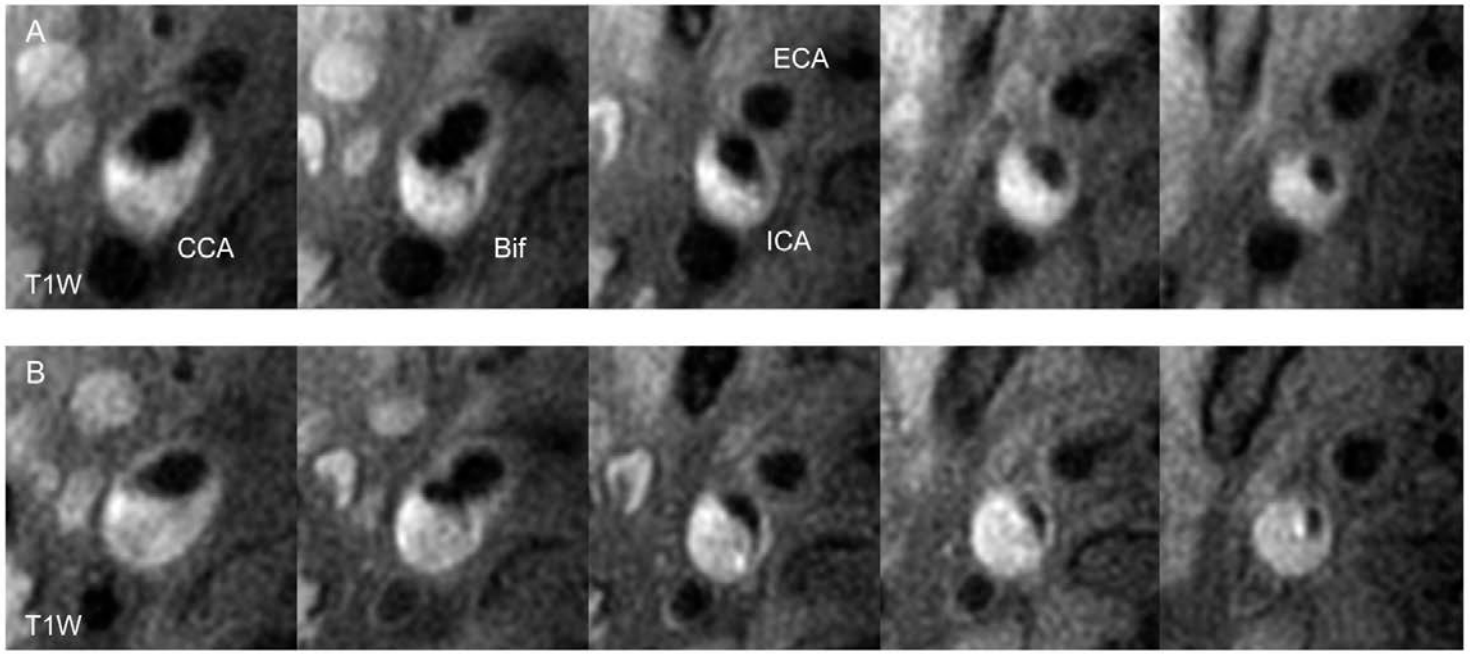

TABLE 3. Percent Change of Volume and Wall Thickness

	Hemorrhage Group (n=14)	Control Group (n=15)	*P*
Lumen volume	−8.5±12.2	1.5±7.9	0.014
Wall volume	6.8±7.9	−0.15±5.1	0.009
Outer wall volume	1.5±6.2	0.2±4.6	0.5
Lipid-rich necrotic core volume	28.4±29.7	−5.2±17.3	0.001
Calcium volume	0.3±38.4	3.4±26.1	0.8
Maximum wall thickness	8.3±11.3	−3.2±10.7	0.009
Minimum wall thickness	3.9±21.3	−5.6±23.4	0.3
Mean wall thickness	8.5±8.8	−1.6±4.74	0.001

Values are mean±SD.

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Takaya N et al. Circulation 2005;111:2768-2775

Advantages

- ✓ Technique Non-invasive
- ✓ Any exposition to radiation
- ✓ Adequate spatial resolution for large vessels (i.e. aorta, carotid, and femoral arteries

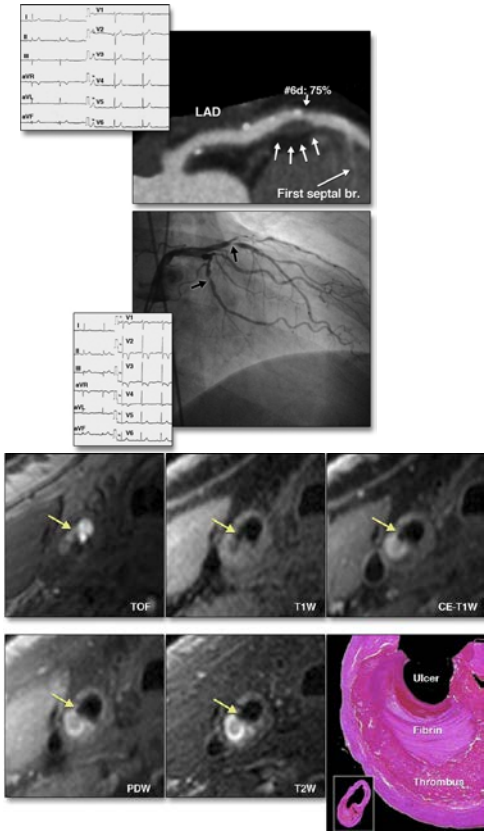
Limitations

- ✓ Limited temporal resolution hampering its application in the coronary circulation

Noninvasive Characterization of Plaque Morphology

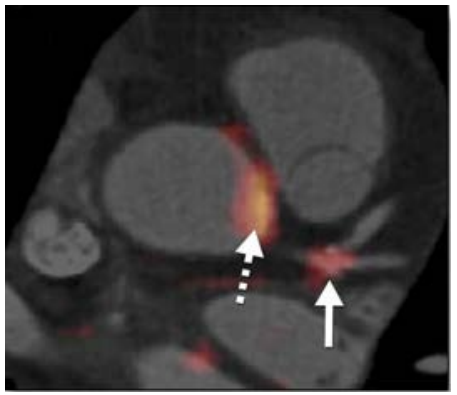
Computed tomography angiography:

plaque attenuation and PVR



MRI:plaque morphology and intraplaque hemorrhage

Positron emission tomography



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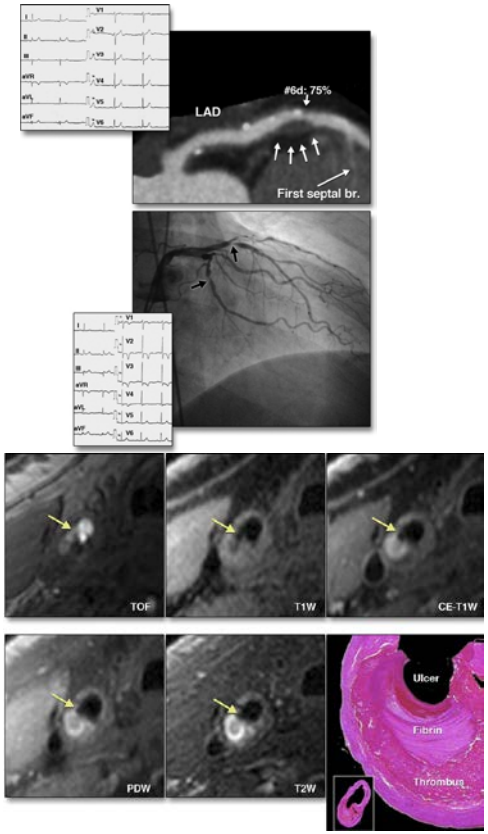

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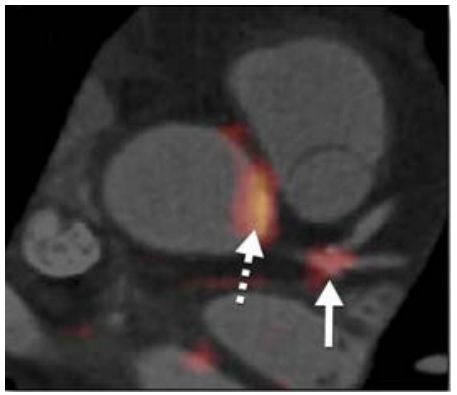


Increased FDG Uptake in Vascular Inflammatory Diseases

Increased FDG uptake has been reported in:

-Takayasu's arteritis,

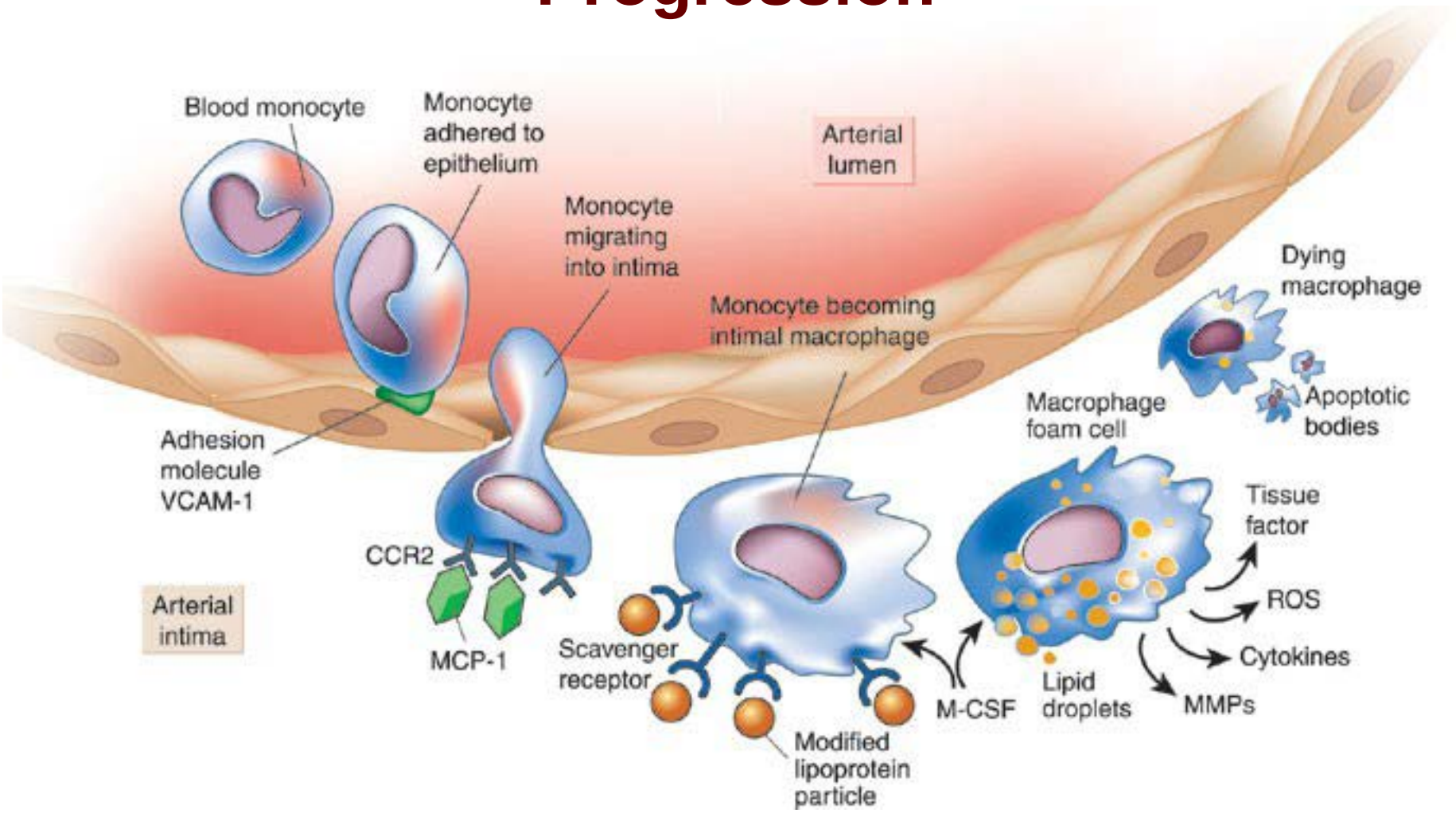
-Giant cell arteritis,

-Polymyalgia rheumatica

-Nonspecific aortitis

-Patients with atherosclerosis

Inflammation and Plaque Progression



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Nature 2002,:420, 868 - 874

Basis for FDG-PET Imaging of Inflamed Atherosclerotic Plaques

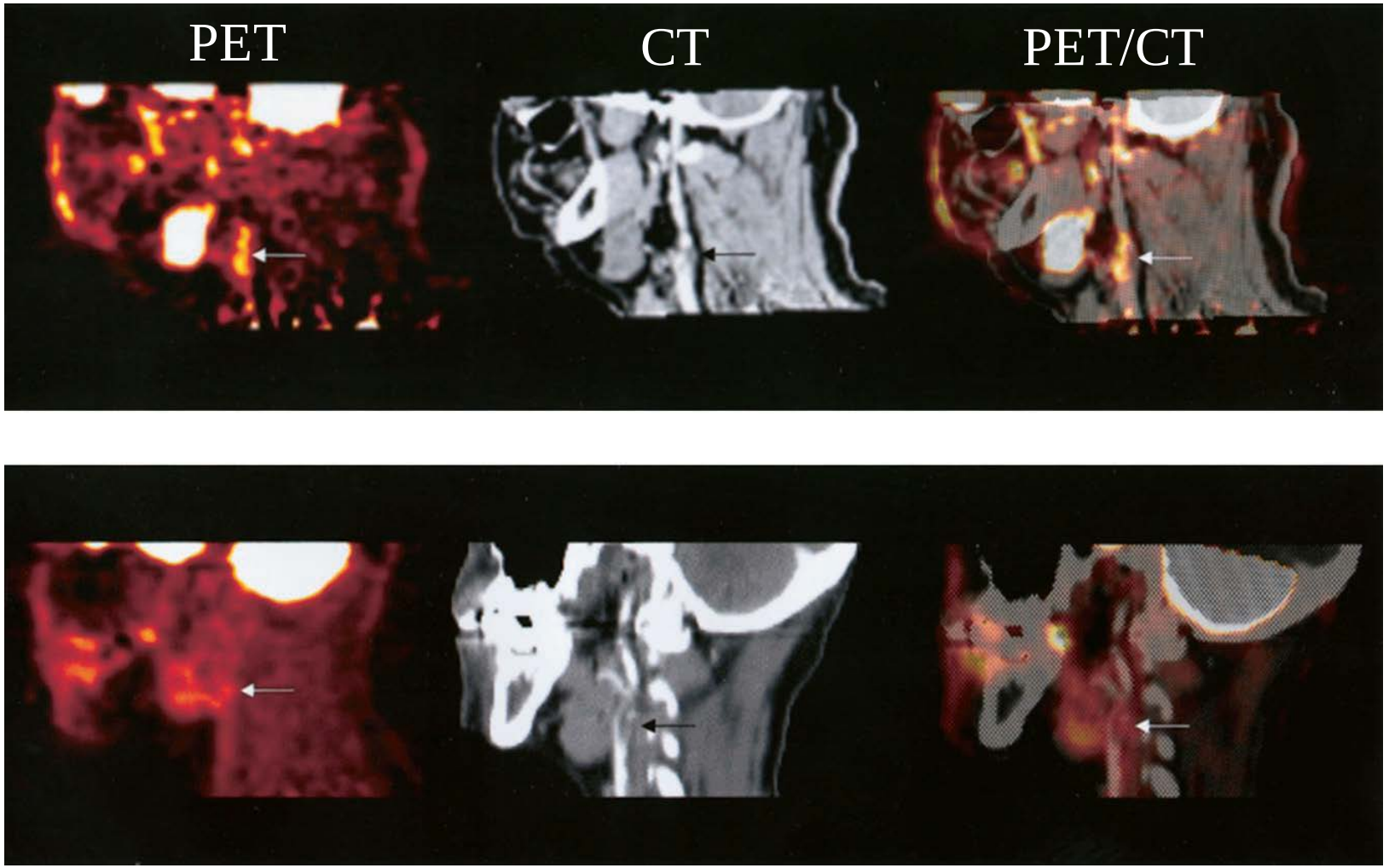
Macrophages:

- Have high basal metabolic rates
- Rely on external glucose source as fuel (macrophages do not store glycogen)
- Increase glucose consumption further when activated.

FDG uptake by inflamed tissues is 10-20 times that of most other tissues.

FDG uptake is often higher in inflammatory tissue than in tumor cells.

Increased FDG Uptake Observed in symptomatic Carotid Disease



Circulation. 2002;105:2708-2711

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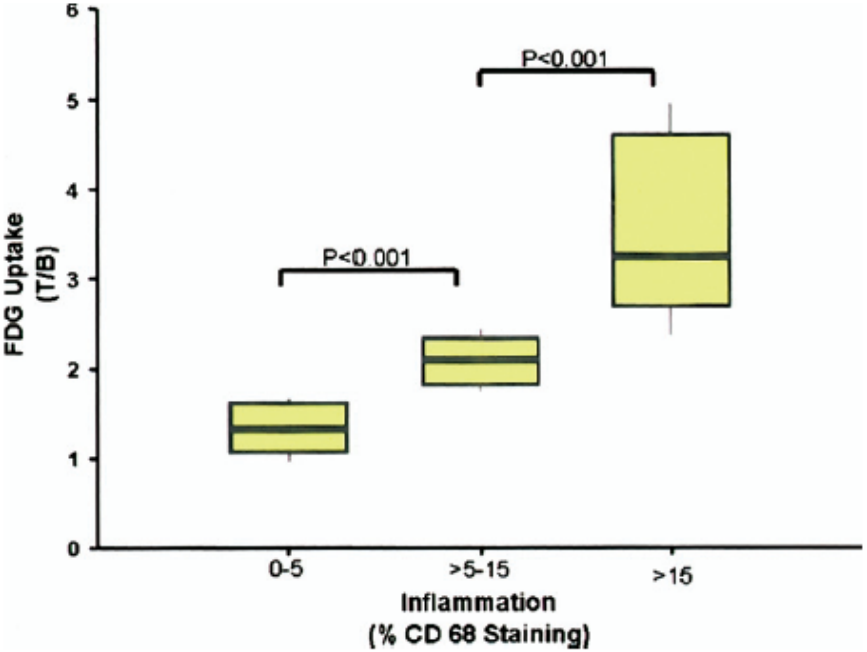
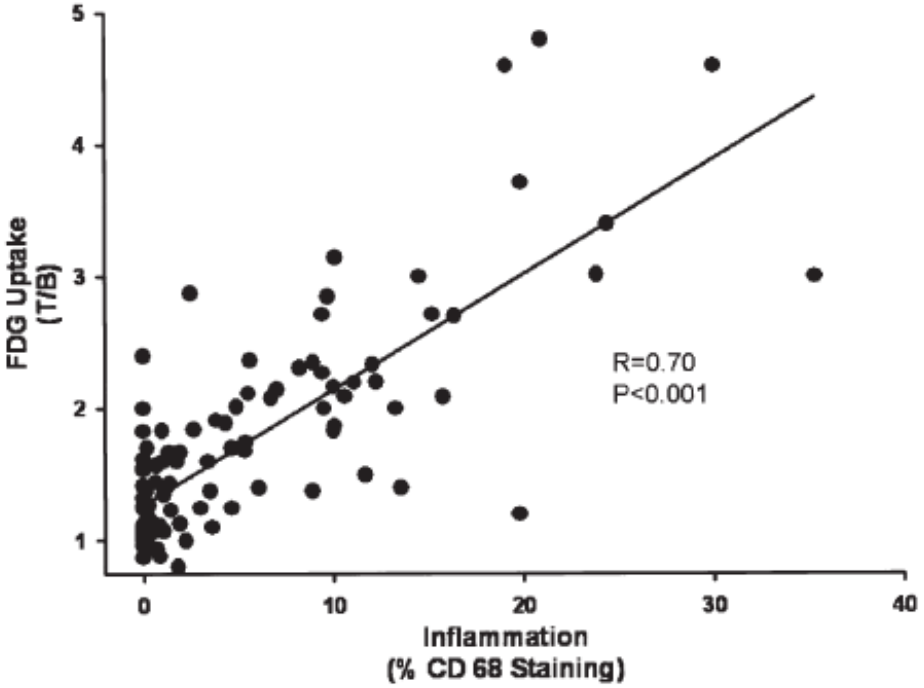
In Vivo 18F-Fluorodeoxyglucose Positron Emission Tomography Imaging Provides a Noninvasive Measure of Carotid Plaque Inflammation in Patients





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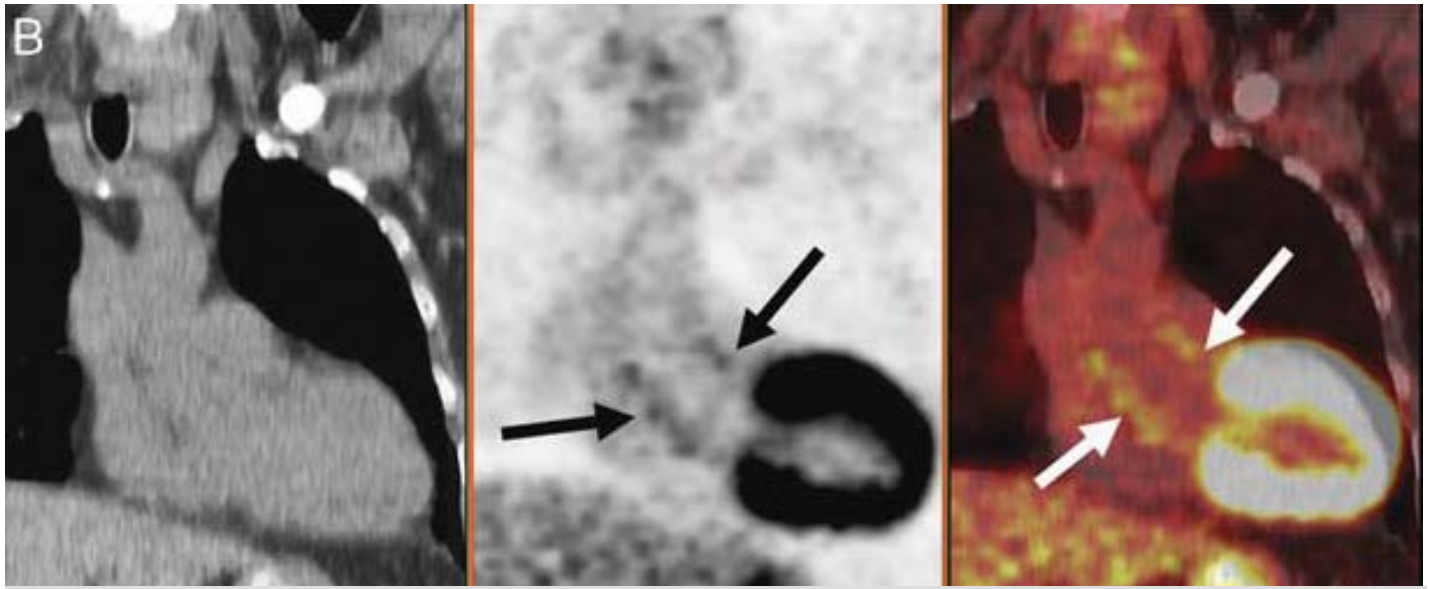
J Am Coll Cardiol 2006;48:1818–24

18F-FDG Uptake and Calcifications in the Thoracic Aorta on Positron Emission Tomography/Computed Tomography Examinations Frequency and Stability on Serial Scans



-Aortic 18F-FDG uptake 70% of the patients
- Calcifications were often seen in patients
- Calcification and 18F-FDG uptake were present at the same site in only 2%

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J Thorac Imaging 2011;26:54–62

Arterial wall uptake of fluorodeoxyglucose on PET imaging in stable cancer disease patients indicates higher risk for cardiovascular events.

Abstract

BACKGROUND:

We aimed to evaluate the additional information of 18 fluorodeoxyglucose (FDG) arterial uptake with respect to other conventional cardiovascular risk factors and arterial calcifications in patients with stable cancer.

METHODS AND RESULTS:

We compared the rate of cardiovascular events in 2 groups of patients with (n = 45) and without (n = 56) enhanced arterial 18FDG uptake, matched for the main clinical parameters. The extent and intensity of 18FDG uptake were quantified. A calcification index was also determined. About one third of the selected patients had a history of cardiovascular events and thus could be defined as "vulnerable patients." Old cardiovascular factor related to old events (P = .004 and P = .002, respectively).

The extent of 18FDG arterial uptake was the unique factor significantly related to the occurrence of a recent event by either logistic regression or discriminant analysis (P = .004 for all).

CONCLUSIONS:

Extensive arterial 18FDG uptake might be an indicator of an evolving atherosclerotic process and should be mentioned in PET/computed tomography reports.

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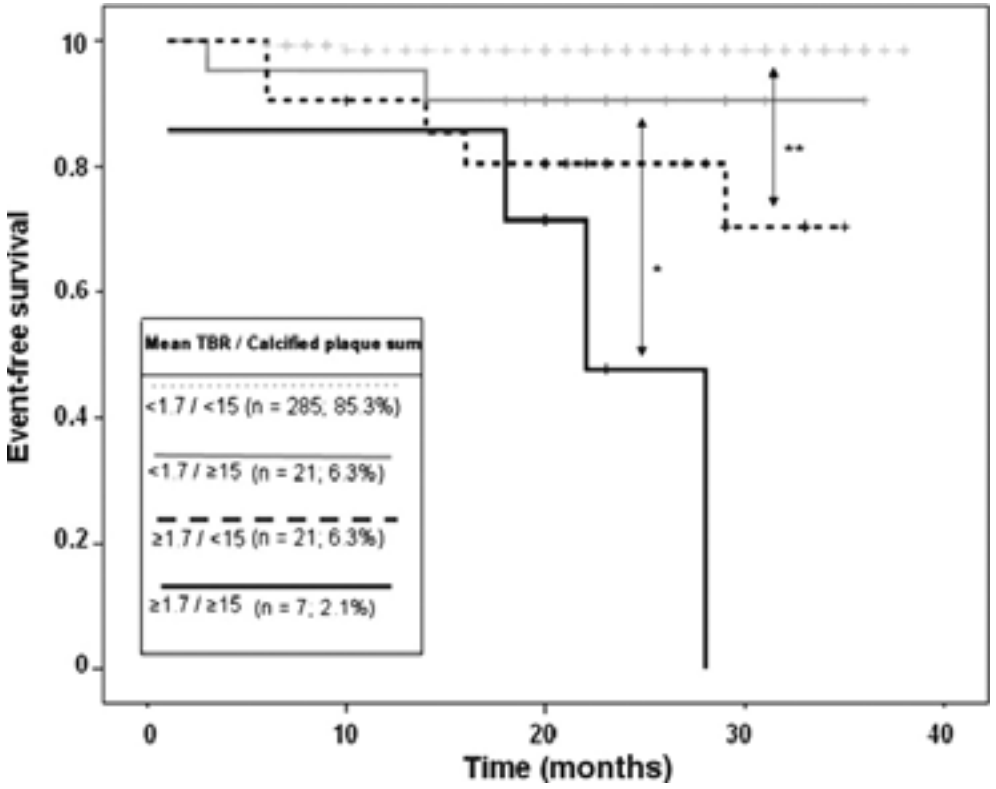
J Nucl Cardiol 2008 Mar-Apr;15(2):209-17.

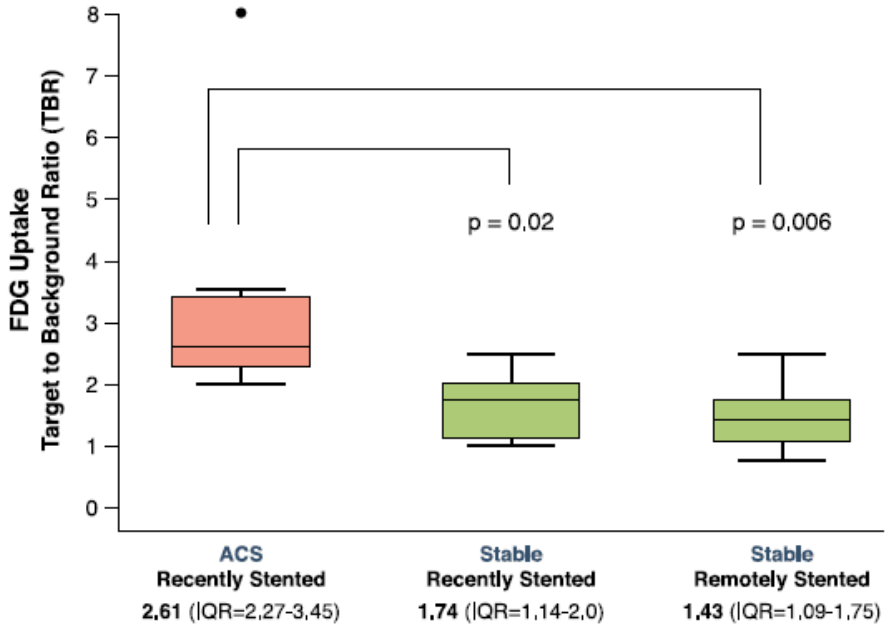
18F-FDG PET / CT identifies patients at risk for future vascular events in an otherwise asymptomatic cohort with neoplastic disease

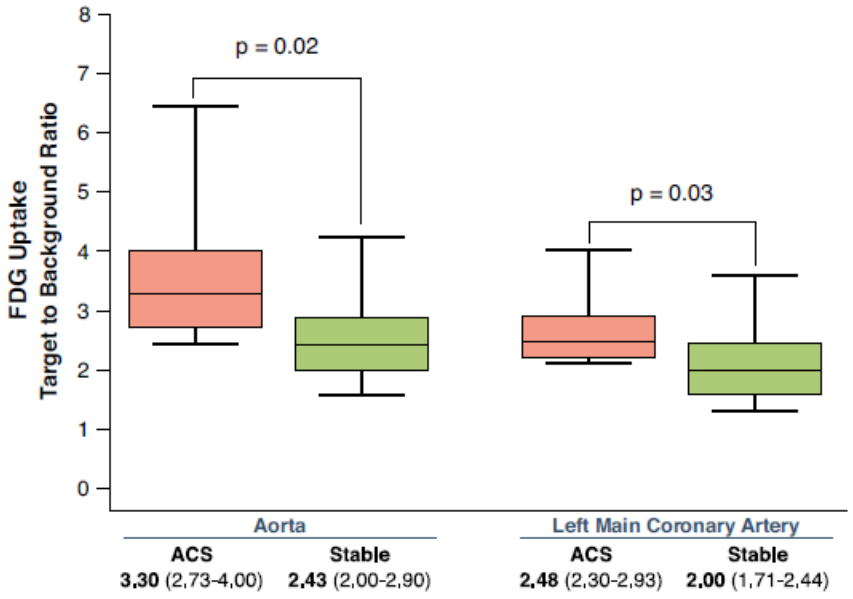


JNuclMed2009; 50:1611–20

Feasibility of FDG Imaging of the Coronary Arteries

Comparison Between Acute Coronary Syndrome and Stable Angina





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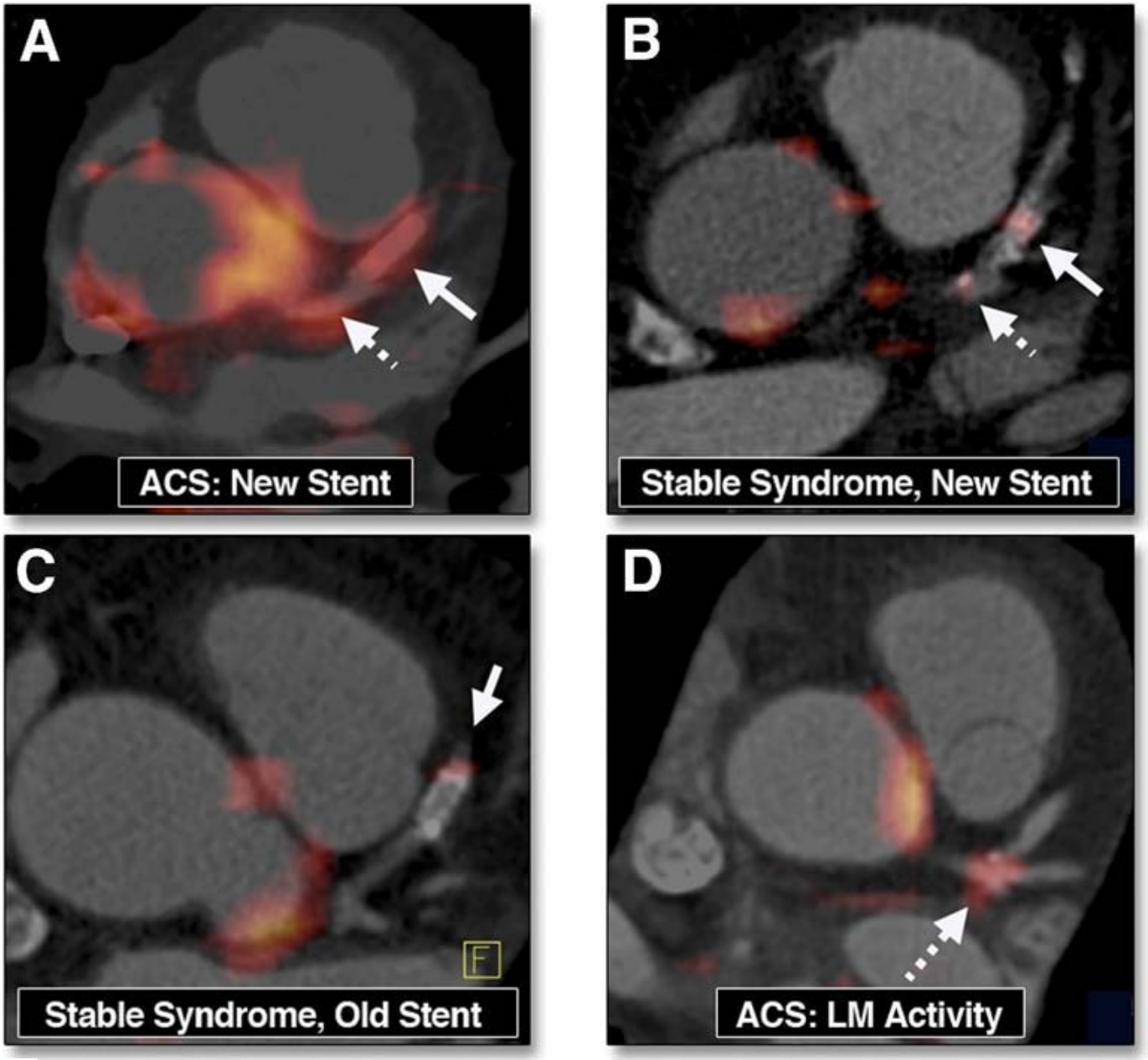
J Am Coll Cardiol Img 2010;3:388 –97

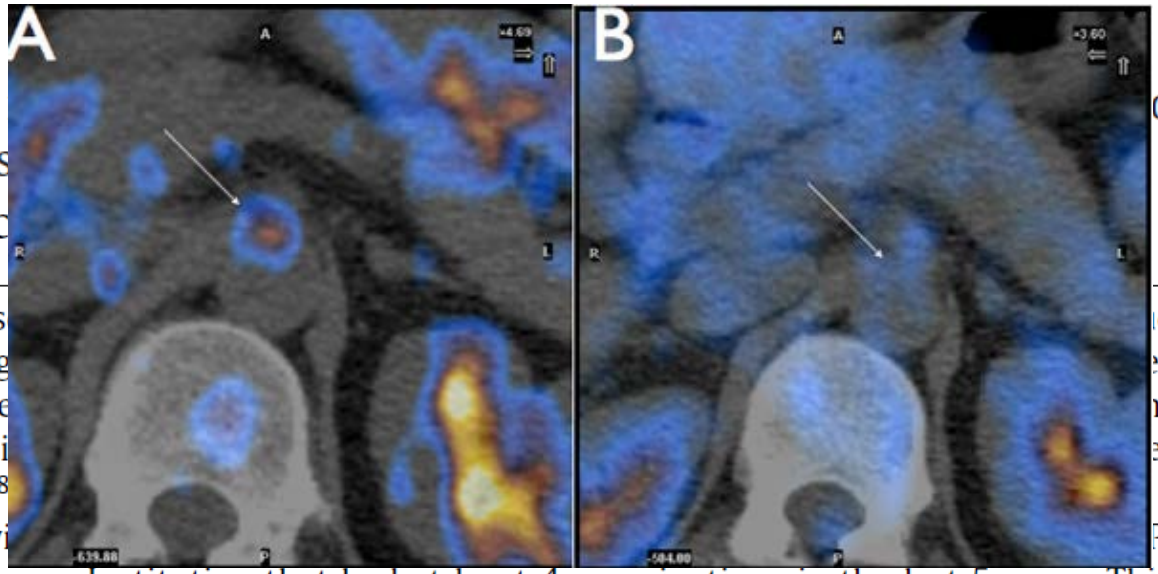


Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

What is the ...on PET/CT? Implications



A B S T R A C

Purpose: Increas...e on Positron Emission Tomog... PET signal is reproducible ove...natural history of these lesions i...eased vascular wall uptake of 18...

Methods: Followi...PET/CT images of patients from our Institution that had at least 4 examinations in the last 5 years. This represented 205 studies in total, from 50 patients (29 men, 21 women, mean age 49.4 ± 12.1 years, mean 5.1 ± 1.7

Conclusions: Arterial lesions with increased 18F-FDG uptake represent transient phenomena. This data is important for the interpretation of findings of clinical trials using arterial 18F-FDG uptake as an imaging biomarker to monitor pharmacological intervention.

biomarker to monitor pharmacological intervention.

18F-FDG Uptake and Calcifications in the Thoracic Aorta on Positron Emission Tomography/Computed Tomography in TAVI patients

BACKGROUND
Unstable, vulnerable plaques are associated with increased microembolisation during interventions (carotid or coronary)

Has been shown that trans femoral TAVI is associated with >70% incidence of new cerebral lesion following the procedure as evaluated by diffusion-weighted magnetic resonance imaging

Imaging modalities able to identify aortic high risk plaque could select high risk patients

In this subset of patients anti embolic system device could be used

J Am Coll Cardiol 2010; 55: 1427-32
Circulation 2010; 121: 870-8
Circulation. 2012;126(10):1245-55.

Città della Salute e della Scienza

Aim

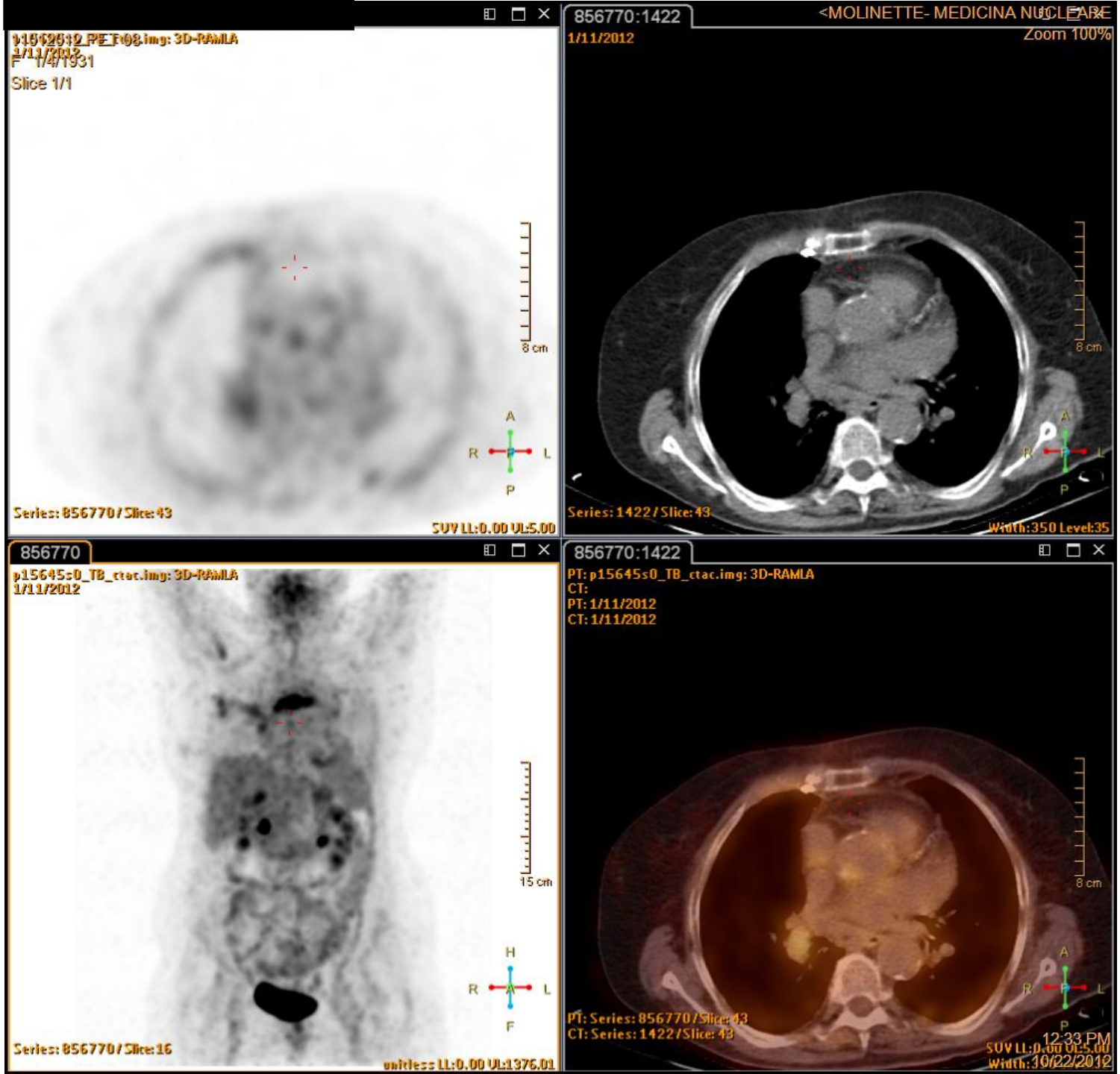
Detection of vulnerable plaque using 18FDGPET/CT and correlation with aortic calcification in patients scheduled for transcatheter aortic valve implantation

METHODS

Eight patients scheduled for Trans Cathether Aortic Valve Implantation underwent 18FDG PET/CT.

16 patients without aortic stenosis who underwent 18FDG PET/CT for neoplasm were reviewed.

PET/CT images of the aorta were reviewed for focal 18F-FDG activity that followed arterial contours on the fused images in 3 orthogonal planes. The intensity of 18 F-FDG uptake was quantified by measuring the maximum standardized uptake value (SUVmax). We consedered significant a SUV max > 2.5
The thoracic aorta was divided into 3 segments of analysis:
ascending (extending from the aortic root to the origin of the innominate artery), arch (from the origin of the innominate artery to the origin of the left subclavian artery), and descending (from the origin of the left subclavian artery to the level of the diaphragm).
The presence of calcifications was identified in a quantitative manner; calcifications were defined as regions with multiple attenuation greater than 130 Hounsfield units in the thoracic aortic wall on CT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PT: 1/11/2012
CT: 1/11/2012
PT: Series: 856770 / Slice: 43
CT: Series: 1422 / Slice: 43
12:33 PM
10/22/2012

Population characteristics

	TAVI
	n=8
Female	4/8
Age	82.4 (69-87)
Hypertension	4/8 (50%)
Diabetes	2/8 (25%)
Dyslipidemia	1/8 (12.5%)

TAVI Patients n=8

	18F-FDG			Calcifications		
	Asc	Arch	Disc	Asc	Arch	Disc
CS♀, 87y	-	-	-	+	+	+
MT♀, 81y	-	-	-	-	+	+
CG♀, 84y	-	-	-	+	+	+
GS♂, 85y	-	-	-	+	+	+
CC♂, 69y	+	-	-	+	+	+
VA♀, 83y	-	-	-	+	+	+
MR♂, 83 y	-	-	-	-	+	+
LB♂, 84y	-	-	-	-	+	+

No TAVI Patients n=16 Age: 81.1

	18F-FDG			Calcifications		
	Asc	Arch	Disc	Asc	Arch	Disc
VV ♂, 81y	-	-	-	-	+	-
CF ♂, 81y	-	-	-	-	-	-
RG ♂, 80y	-	-	-	-	+	+
BP♂, 84y	-	-	-	-	-	-
AM ♂, 83y	-	-	-	-	+	+
DG ♂, 69y	+	-	-	-	-	-
GA ♂, 70y	+	-	-	-	-	+
RG ♀, 81y	+	-	-	-	+	-
PR♀, 87y	-	-	-	-	+	+
AR ♀, 82y	-	-	-	-	+	-
MI ♀, 87y	-	-	-	-	+	+
MC ♀, 84y	-	-	-	+	+	+
CM ♀, 81y	-	-	-	-	-	-
GR ♀, 82y	-	-	-	-	+	-
CG ♀, 84y	-	-	-	-	+	+
FG ♀, 81y	+	-	-	+	-	-

Analyisis per segment

	TAVI N=8 (%)	No TAVI N=16 (%)	*p*
FDG			
Asc	1 (12.5)	4 (25)	*0.85*
Arch	0	0	-
Disc	0	0	-
Tot	1 (4.1)	4 (8.3)	*0.75*
Calcification			
Asc	5 (62.5)	2 (6.2)	*0.039*
Arch	8 (100)	10 (62.5)	*0.13*
Disc	8 (100)	7 (43.7)	*0.025*
Tot	21 (87.5)	19 (39.6)	*<0.001*

Conclusion

Aortic 18F-FDG uptake is rare in patients> 80y

No relationship between arterial 18F-FDG uptake and calcification

High calcification rate

(TAVI patients>No TAVI patients)

Advantages

- ✓Morphological and metabolic information
- ✓FDG is widely available
- ✓FDG uptake reflects atherosclerotic plaque inflammation

Limitations

- ✓Limited spatial resolution (Requires CTorMRI for co-registration)
- ✓Radiation burden
- ✓Cost
- ✓Meaning of FDG uptake?

Conclusions

Non invasive detection of plaque vulnerability in vivo is becoming a reality.

There is an ongoing evidence that the presence of vulnerable plaques is associated with an increased risk of subsequent acute ischemic events

Therefore, before these methods can be implemented into daily clinical routine, their diagnostic and predictive accuracy need to be evaluated in large groups of patients.

We need to learn which of the different morphological, molecular, biological features of vulnerable plaques are clinically relevant to the outcome of patients.

Thanks for your attention

"Le seul véritable voyage, ce ne serait pas d'aller vers de nouveaux paysages, mais d'avoir d'autres yeux"

" The real voyage of discovery consists not in seeking new landscapes, but in having new eyes."

Marcel Proust

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