Torino 2012

Invasive imaging of the vulnerable plaque: embarking on a fantastic voyage

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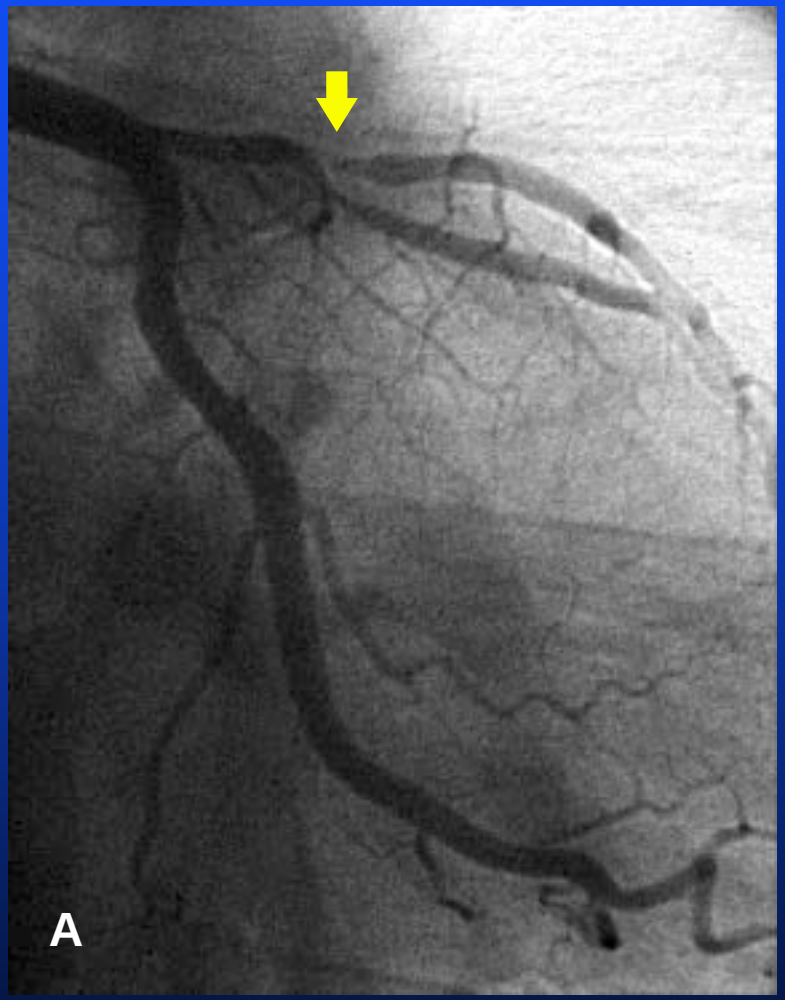
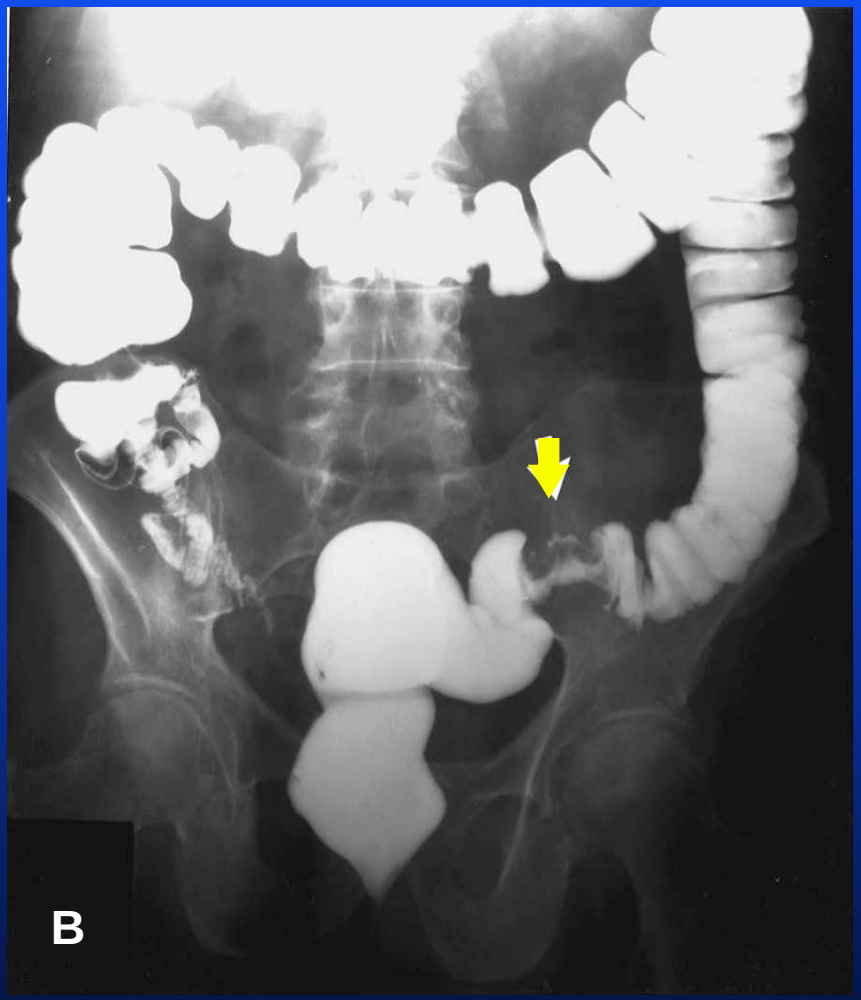
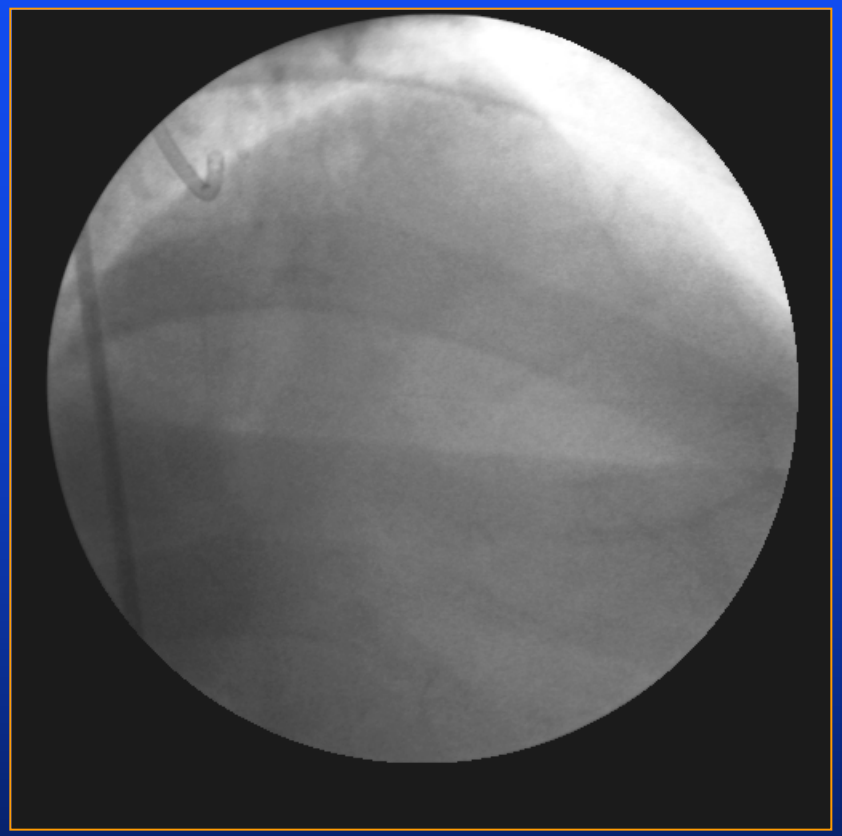
Why should we listen to the Oncologist?

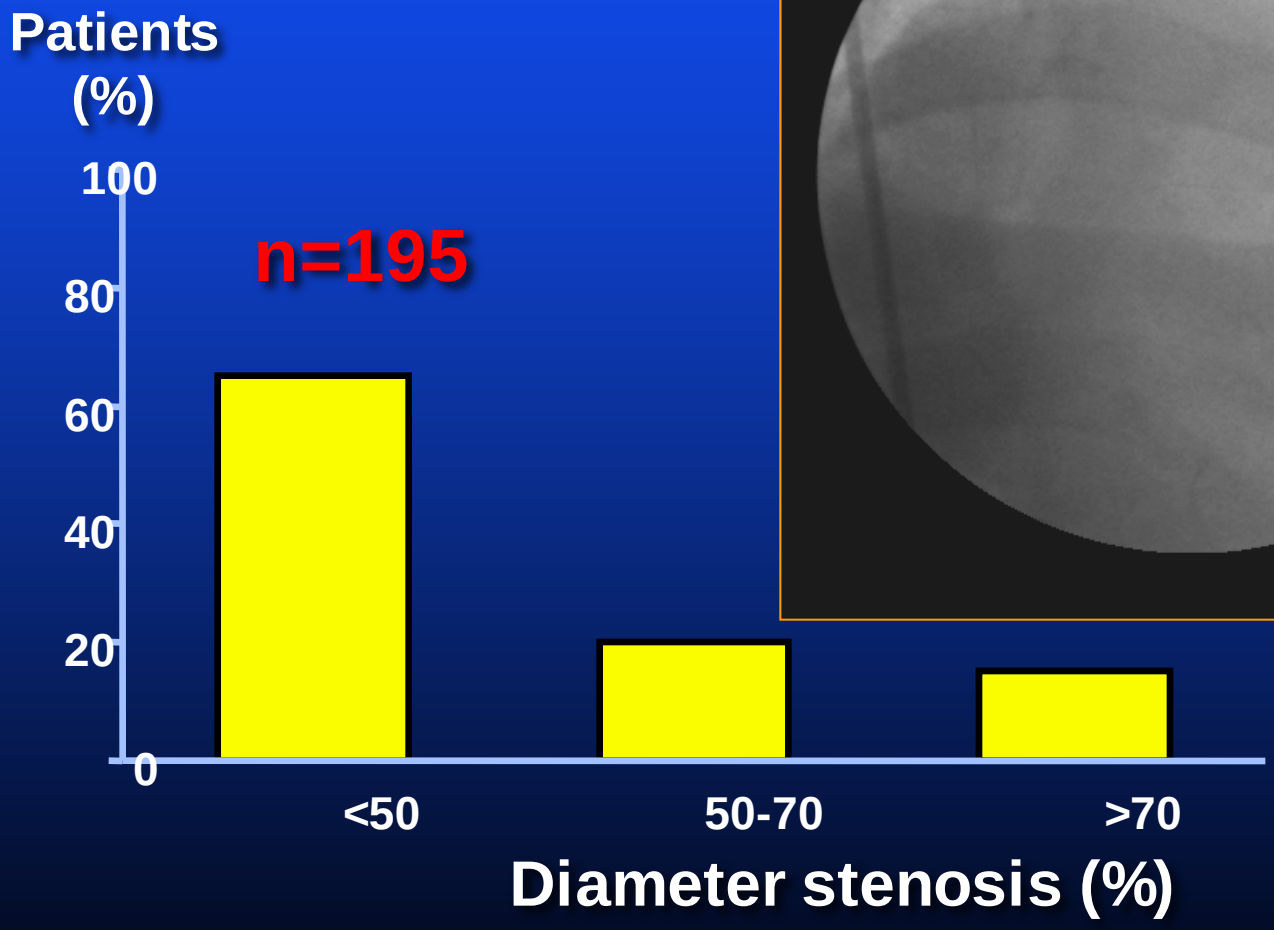




Is this ONLY a surgical disease?

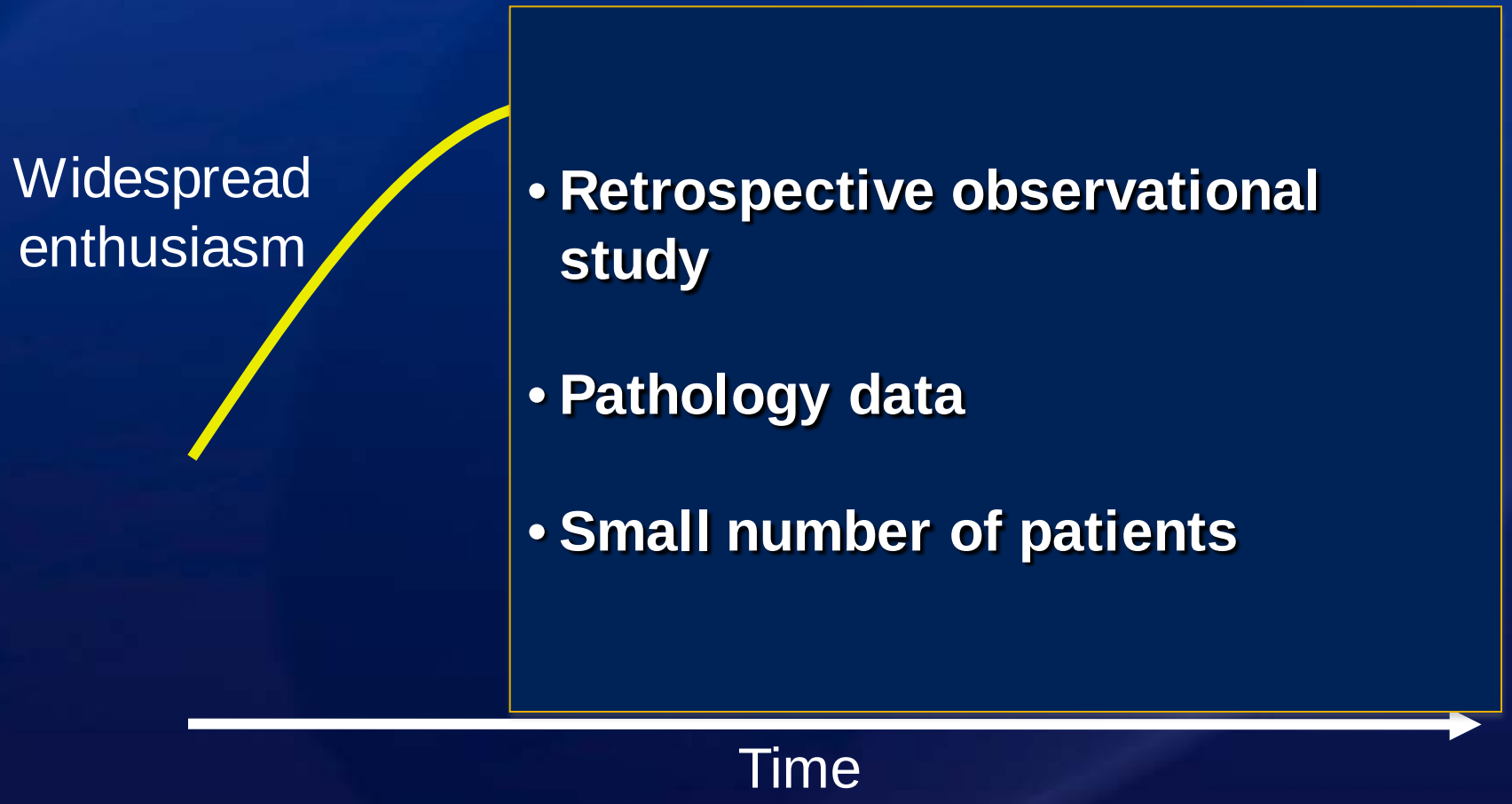
Coronary Artery Stenosis Before Acute Myocardial Infarction





Circulation, 1996 (data from four studies)

Natural history of many bio medical and theories



MAYO CLINIC

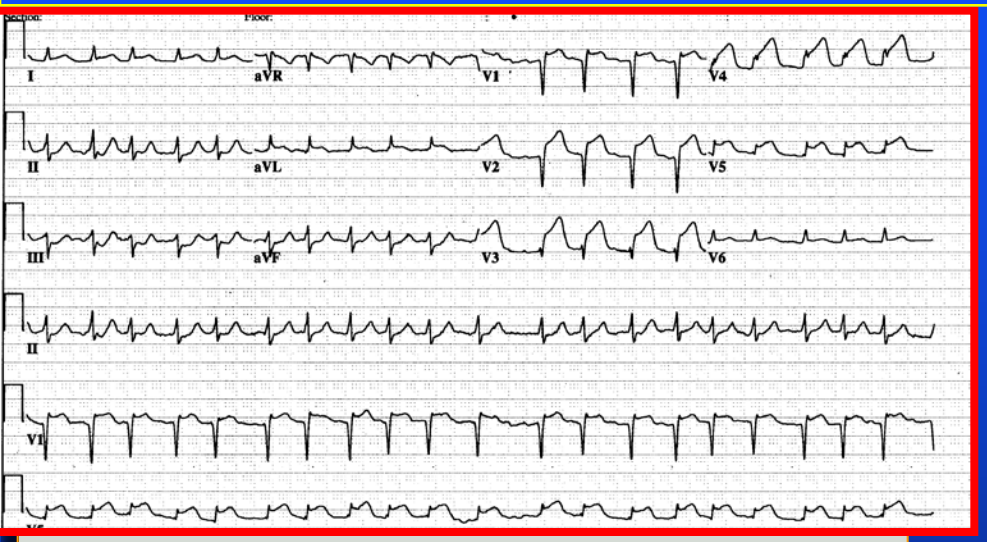
Invasive imaging of the vulnerable plaque: embarking on a fantastic voyage

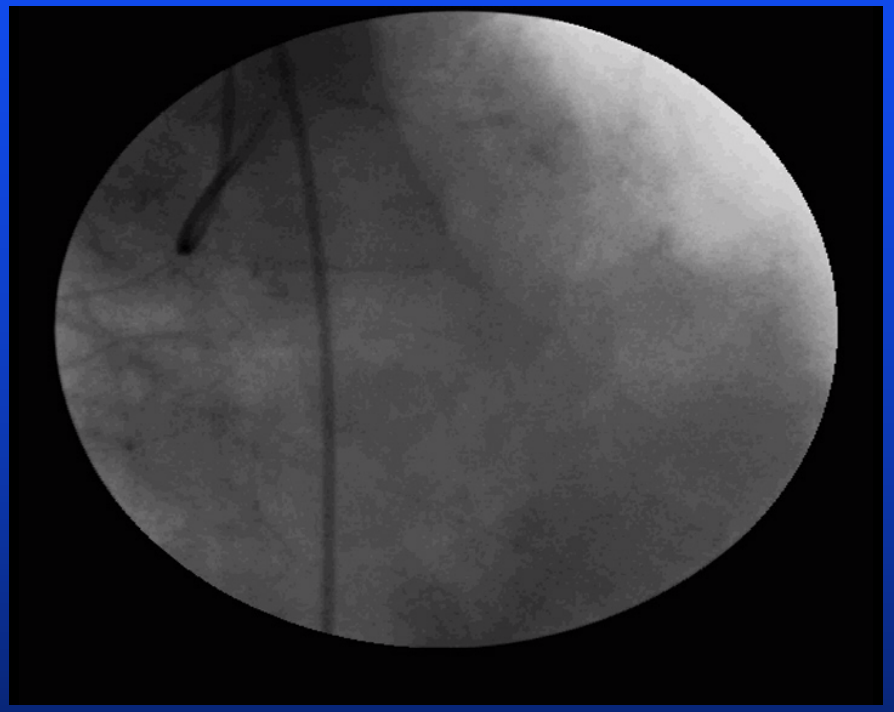
- **The vulnerable plaque theory**

Vulnerable plaque
From **Wikipedia**, the free encyclopedia
A vulnerable plaque is a kind of atheromatous plaque – a collection of white blood cells (primarily macrophages) and lipids (including cholesterol) in the wall of an artery - that is particularly unstable and prone to produce sudden major problems, such as a heart attack or stroke.

MAYO CLINIC

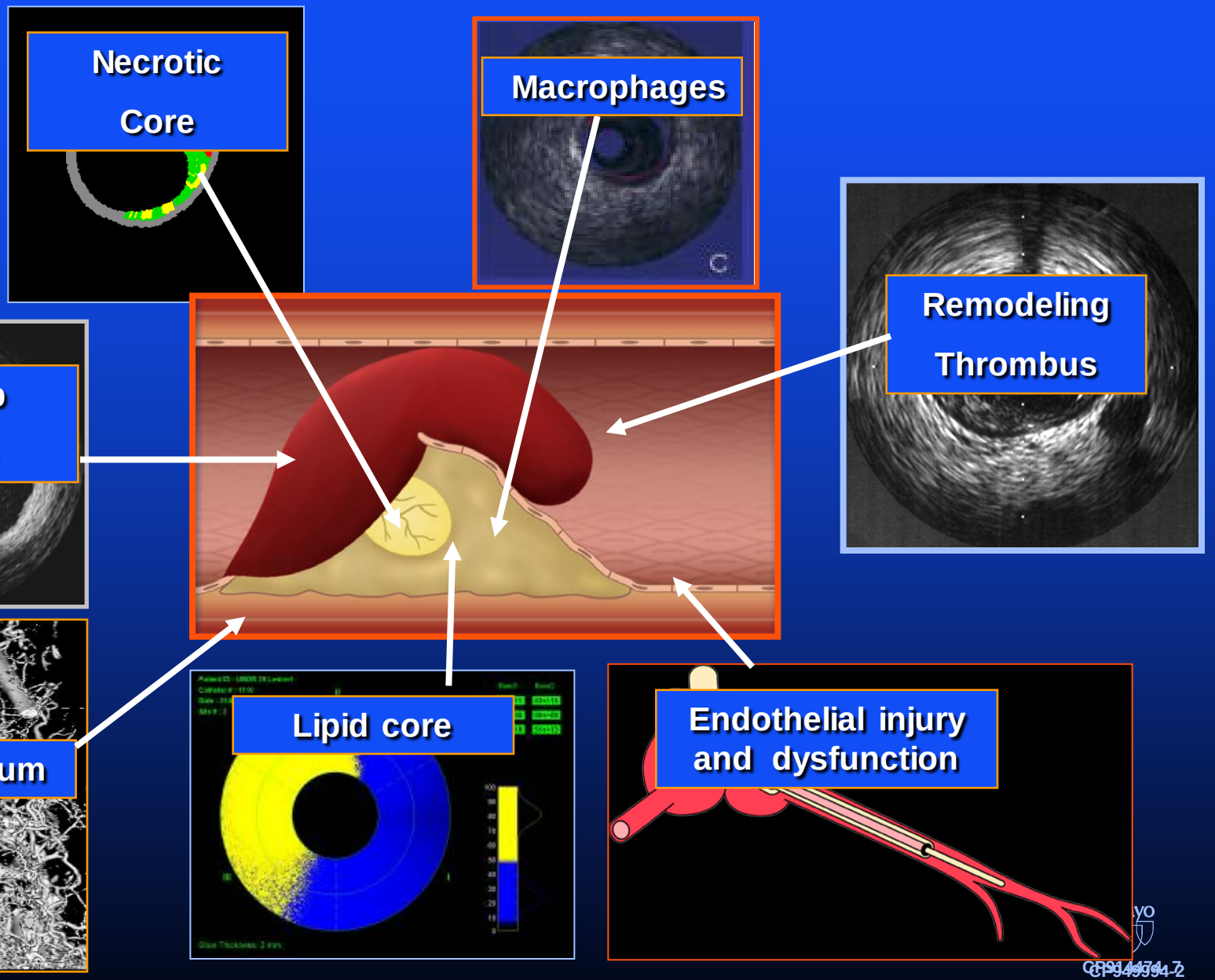
41 year old male with Ant. STEMI



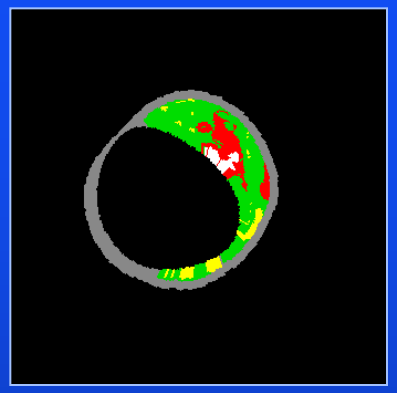


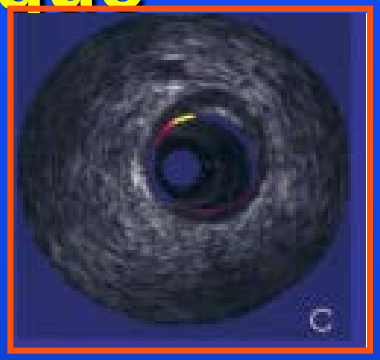
ACS is a dynamic process that occurs at the interface between the vascular wall and circulation

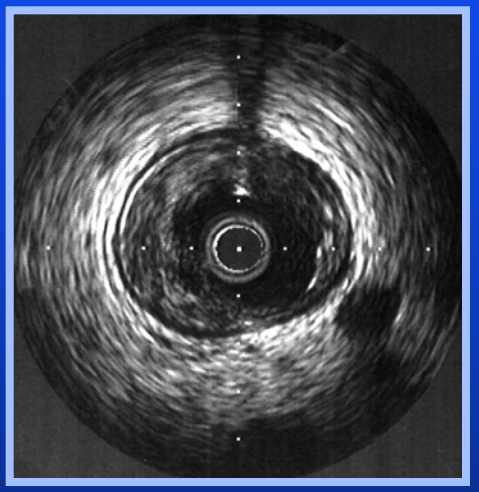
The components of the Vulnerable Plaque

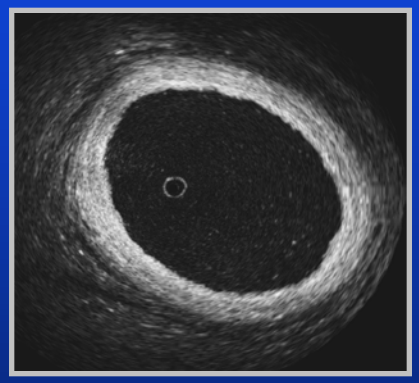


Imaging Methods for Detecting the Vulnerable Plaque

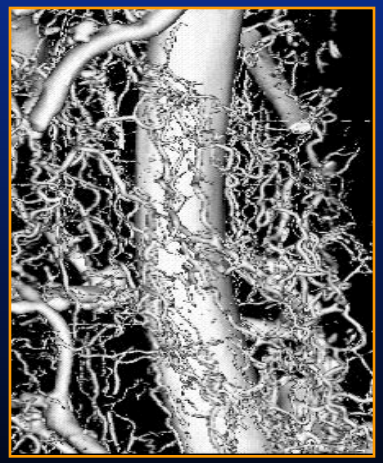


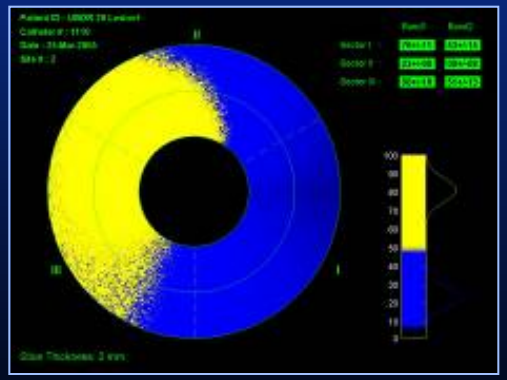


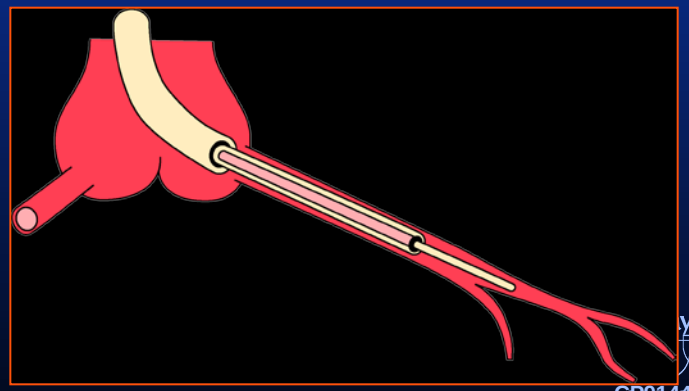




- **Functional imaging** (Endothelial function, palpography)
- **Morphologic assessment** (VH, OCT,
- **Plaque content**: (lipid scan, VV)
- Combination

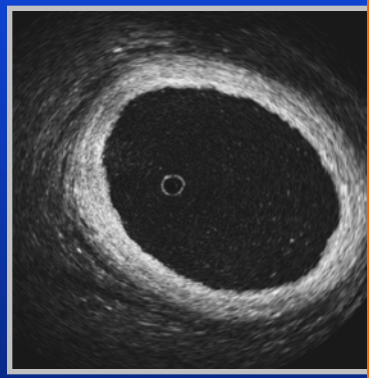


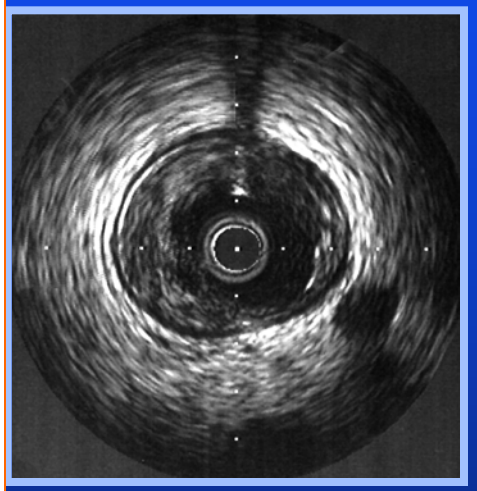


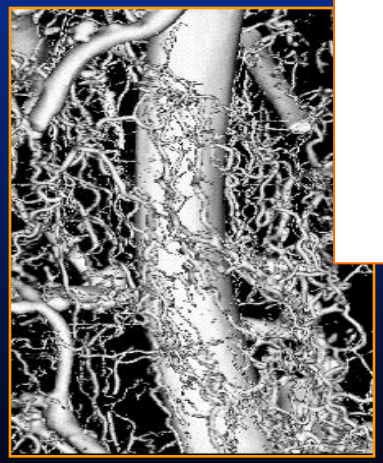


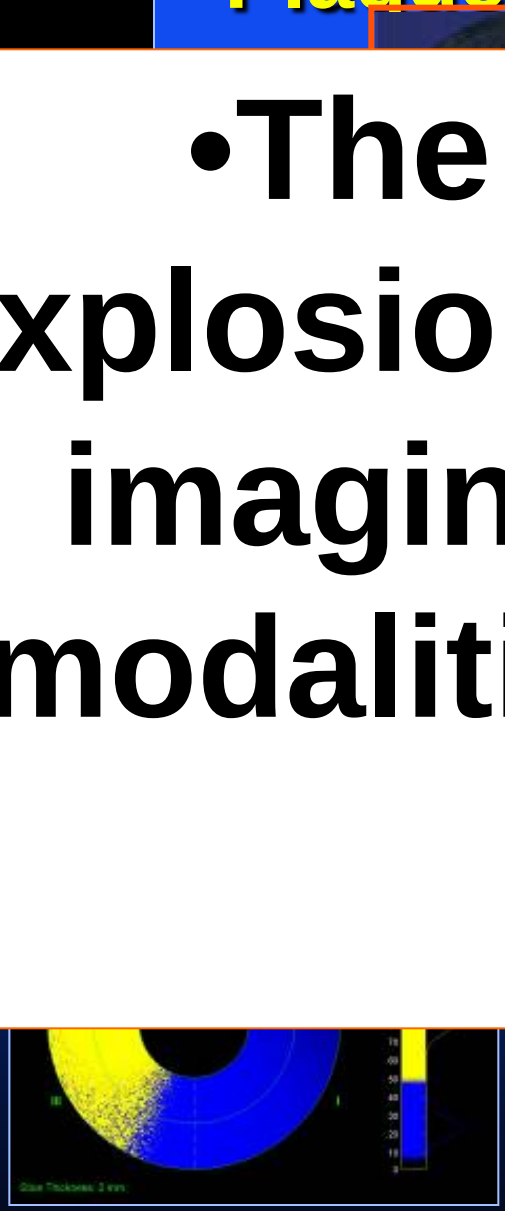
Imaging Methods for Detecting the Vulnerable Plaque

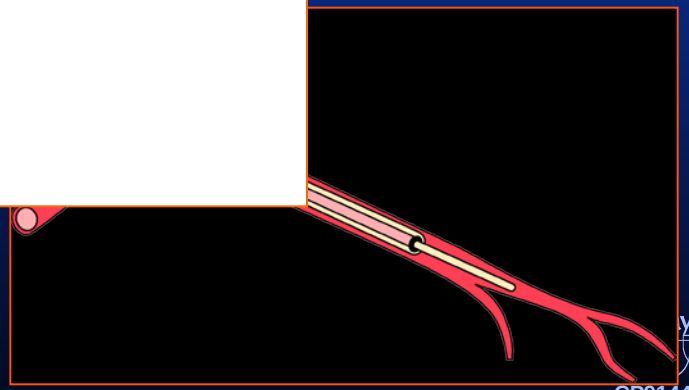
- The explosion of imaging modalities





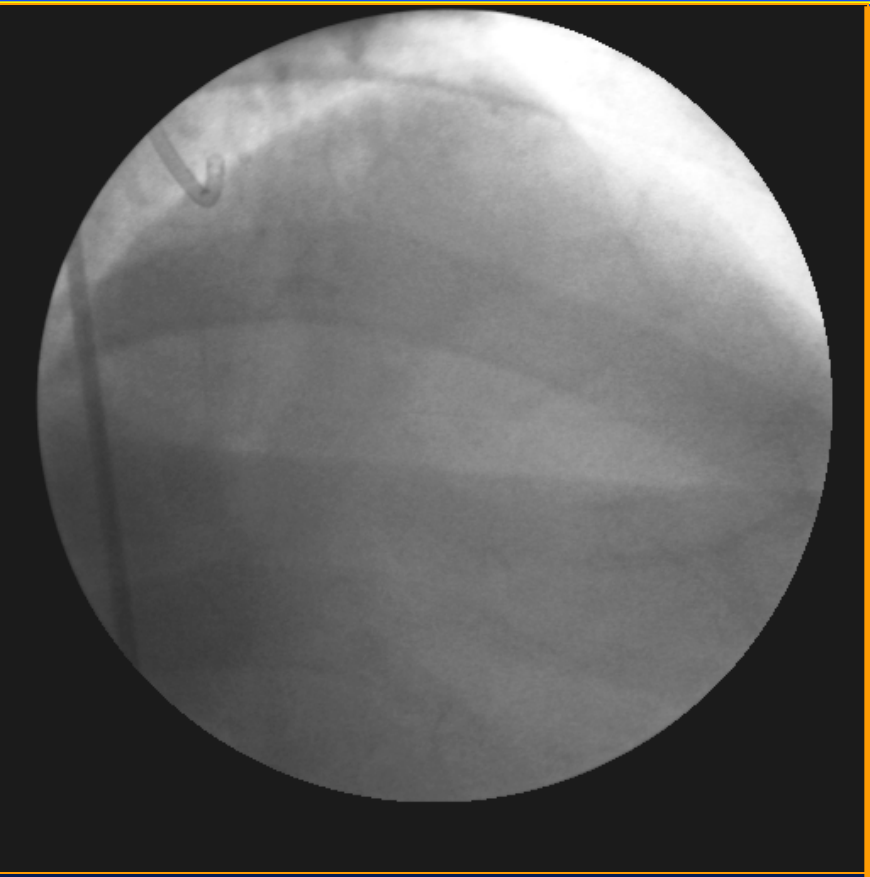


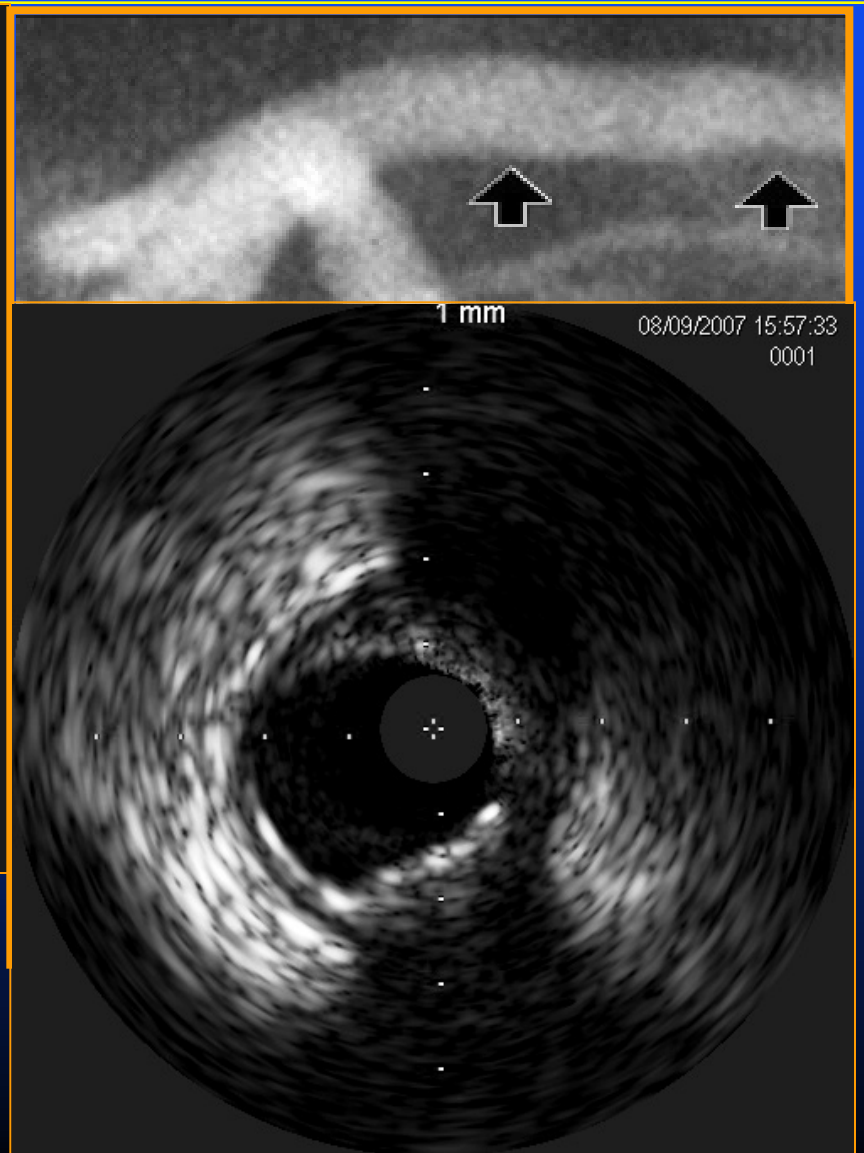




41 year old male

Vulnerable Patient

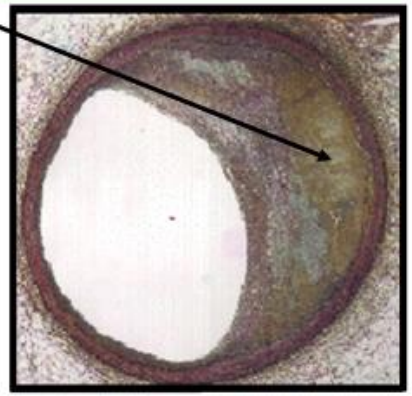




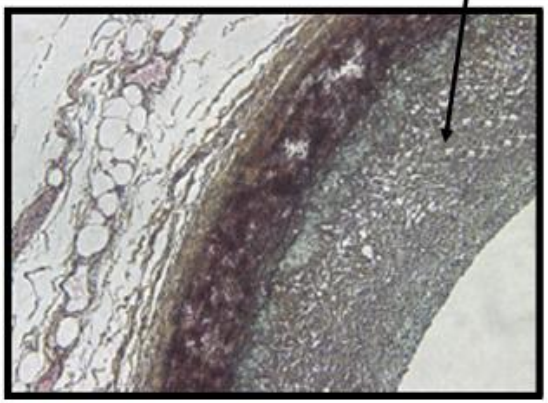
VH™ IVUS Plaque Composition

Fibrous

Densely packed bundles of collagen fibers with no evidence of intra-fiber lipid accumulation. No evidence of macrophage infiltration. Appears dark yellow on Movat stained section.

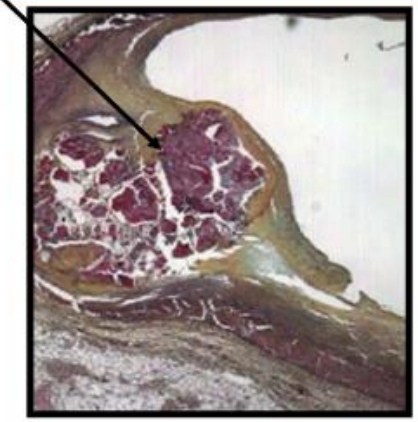


Fibro-Fatty



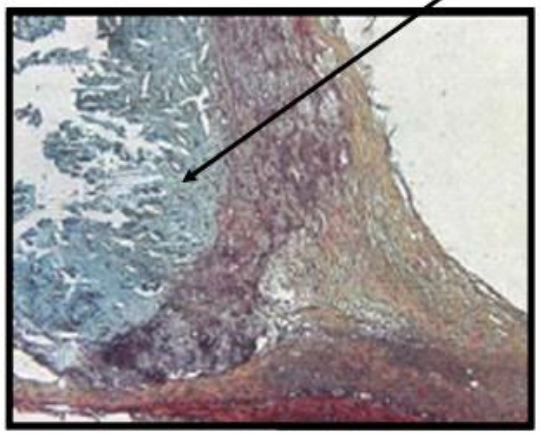
Loosely packed bundles of collagen fibers with regions of lipid deposition present. These areas are cellular and no cholesterol clefts or necrosis are present. Some macrophage infiltration. Increase in extracellular matrix. Appears turquoise on Movat stained section.

Necrotic Core



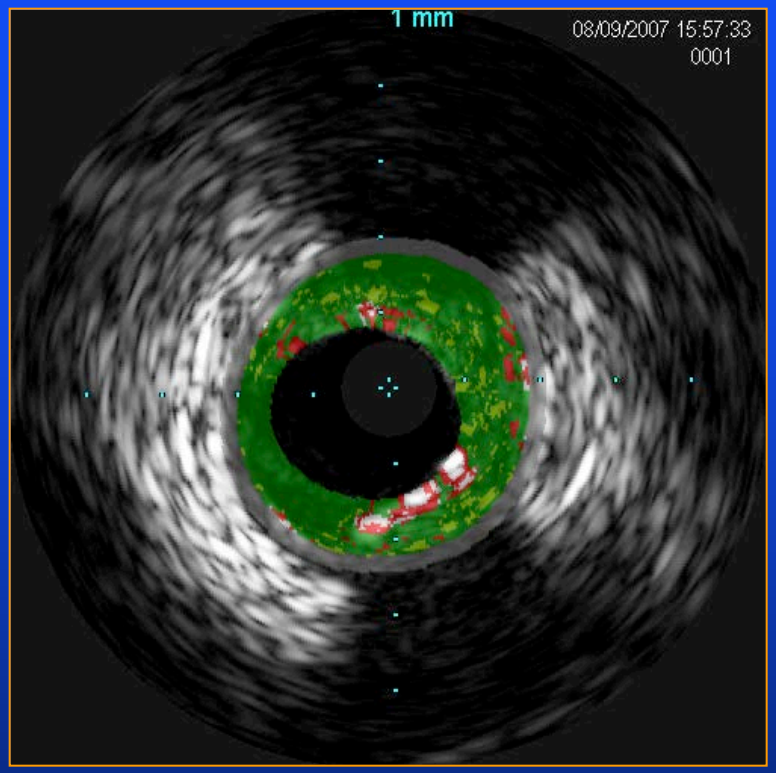
Highly lipidic necrotic region with remnants of foam cells and dead lymphocytes present. No collagen fibers are visible and mechanical integrity is poor. Cholesterol clefts and micro calcifications are visible.

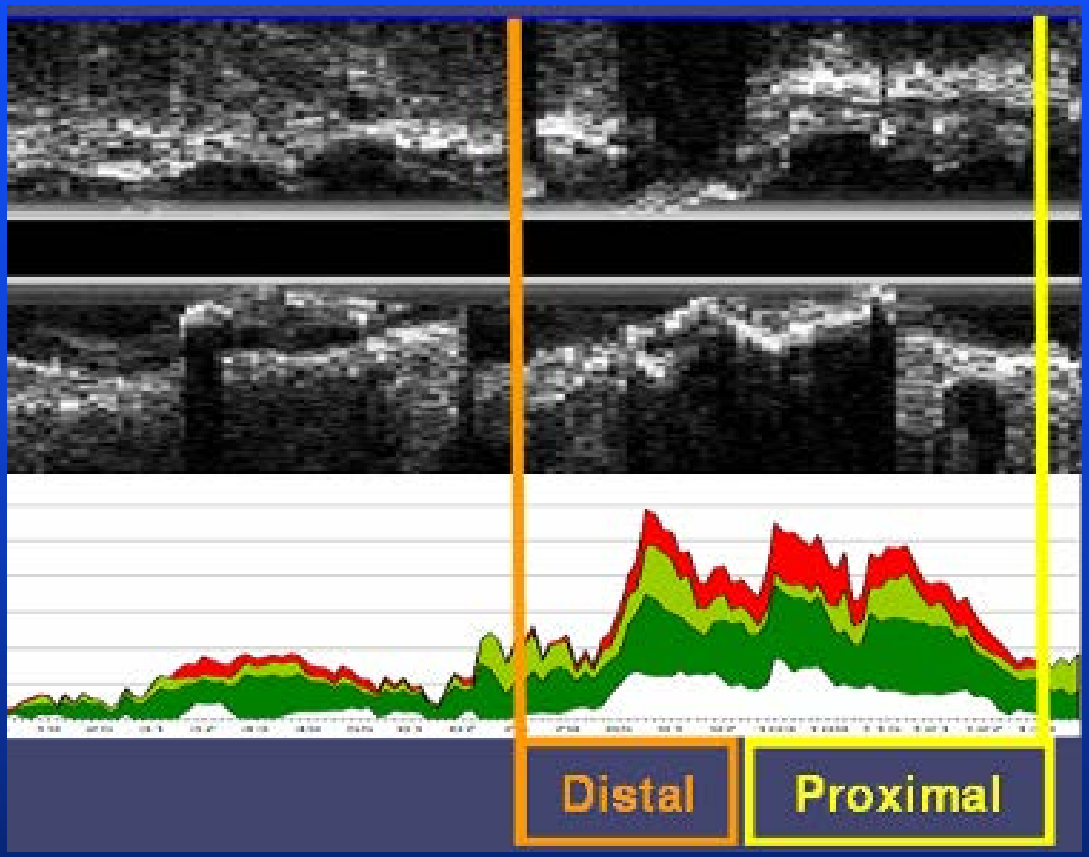
Dense Calcium



Focal area of dense calcium. Appears purple on Movat. Usually falls out of section, but calcium crystals are evident at borders.

IVUS based Virtual Histology Lesion Analysis





Fibrotic

Pathological Intimal Thickening

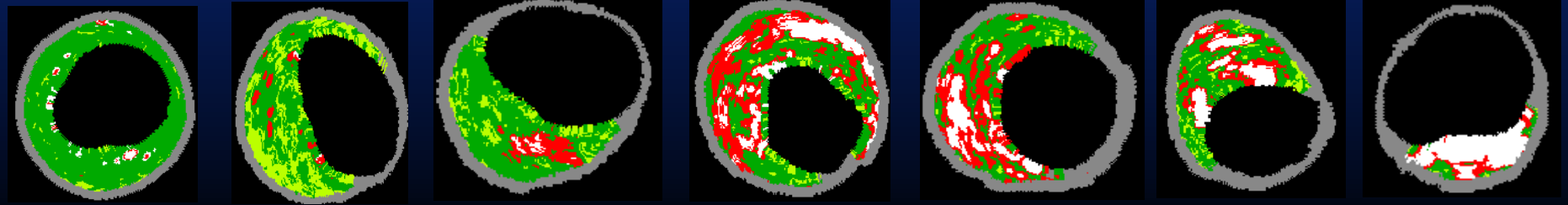
FibroAtheroma

FA Calcified

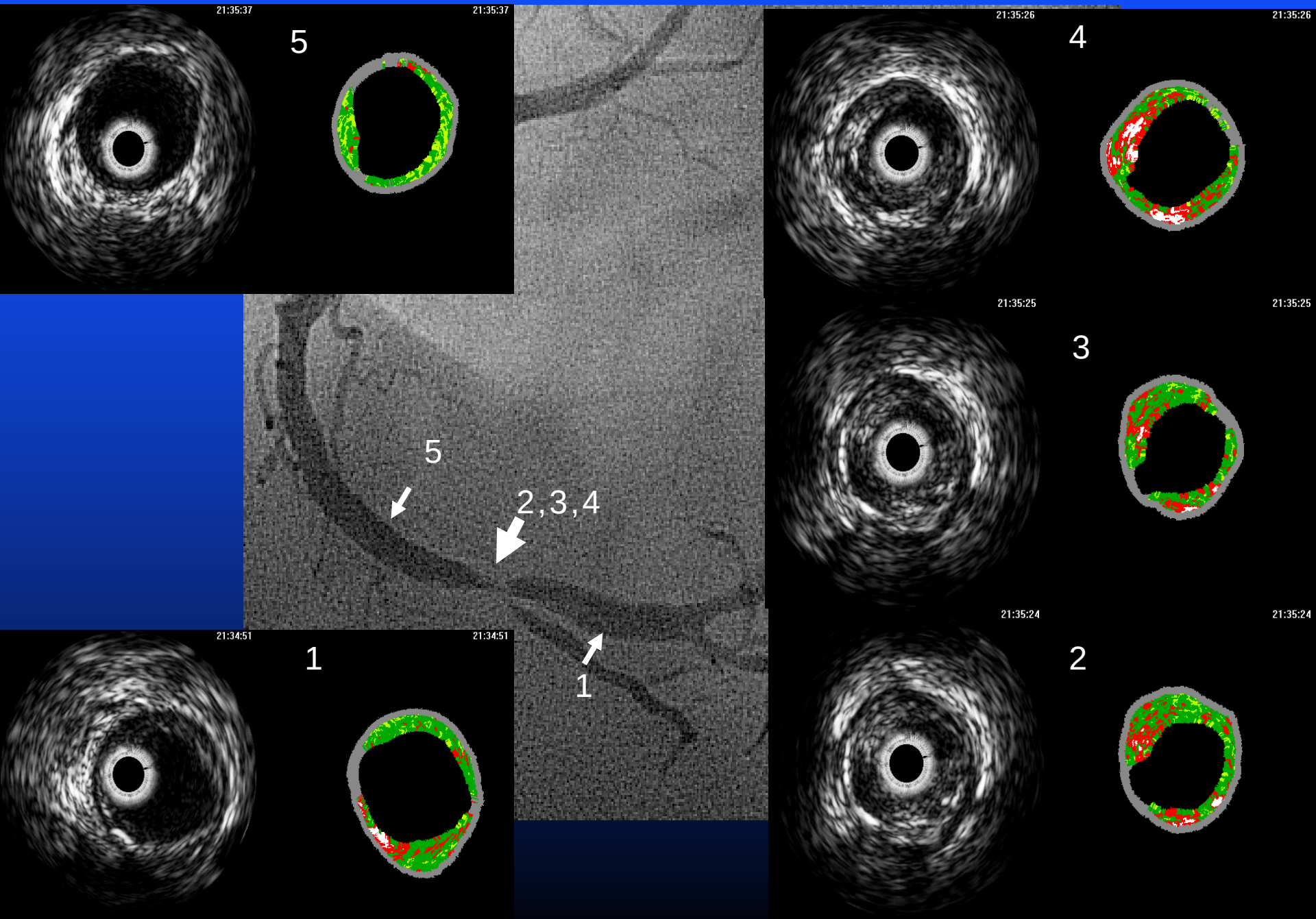
Thin Cap FA

TICFA with previous ruptures

Fibrocalcific



VH in Acute coronary syndrome



Principle of the Intravascular Palpography Measurement Procedure

Journal of the American College of Cardiology
© 2006 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 47, No. 8 Suppl C
ISSN 0735-1097/06/$32.00
doi:10.1016/j.jacc.2006.01.035

Intravascular Palpography for Vulnerable Plaque Assessment

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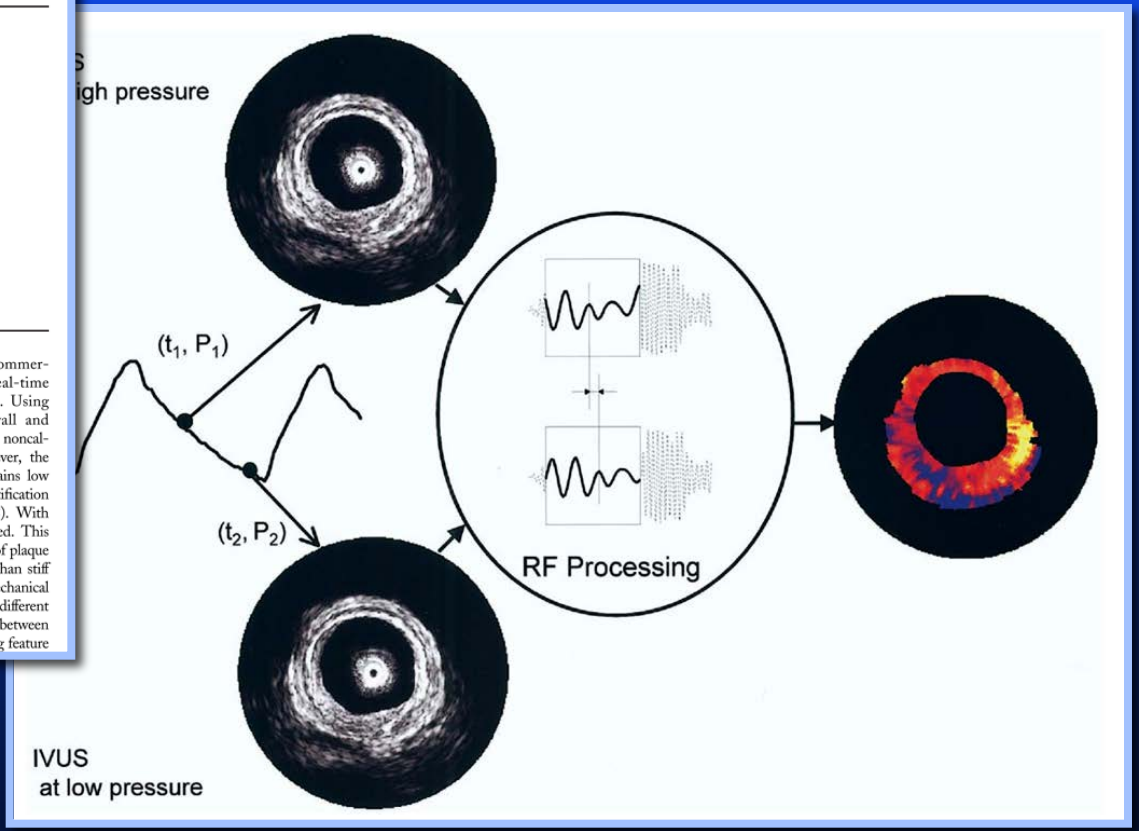
Rotterdam and Utrecht, the Netherlands

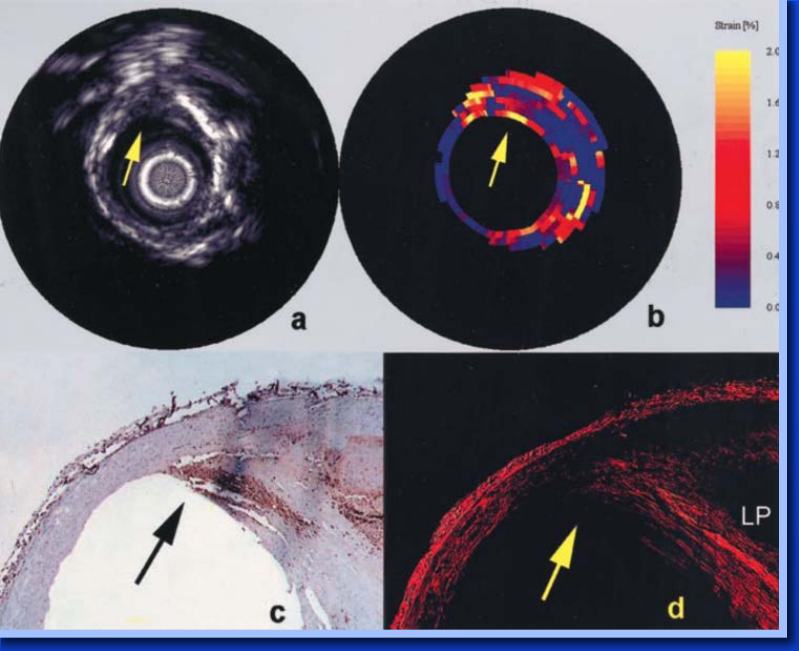
Palpography assesses the local mechanical properties of tissue using the deformation caused by the intraluminal pressure. The technique was validated in vitro using diseased human coronary and femoral arteries. Especially between fibrous and fatty tissue, a highly significant difference in strain ($p = 0.0012$) was found. Additionally, the predictive value to identify the vulnerable plaque was investigated. A high-strain region at the lumen vessel wall boundary has 88% sensitivity and 89% specificity for identifying these plaques. In vivo, the technique is validated in an atherosclerotic Yucatan minipig animal model. This study also revealed higher strain values in fatty than in fibrous plaques ($p < 0.001$). The presence of a high-strain region at the lumen-plaque interface has a high predictive value to identify macrophages. Patient studies revealed high strain values (1% to 2%) in noncalcified plaques. Calcified material showed low strain values (0% to 0.2%). With the development of three-dimensional palpography, identification of weak spots over the full length of a coronary artery becomes available. Patients with myocardial infarction or unstable angina have more high-strain spots in their coronary arteries than patients with stable angina. In conclusion, intravascular palpography is a unique tool to assess lesion composition and vulnerability. Three-dimensional palpography provides a technique that may develop into a clinically available tool for decision making to treat hemodynamically nonsignificant lesions by identifying vulnerable plaques. The clinical utility of this technique is yet to be determined, and more investigation is needed. (J Am Coll Cardiol 2006;47:C86–91) © 2006 by the American College of Cardiology Foundation

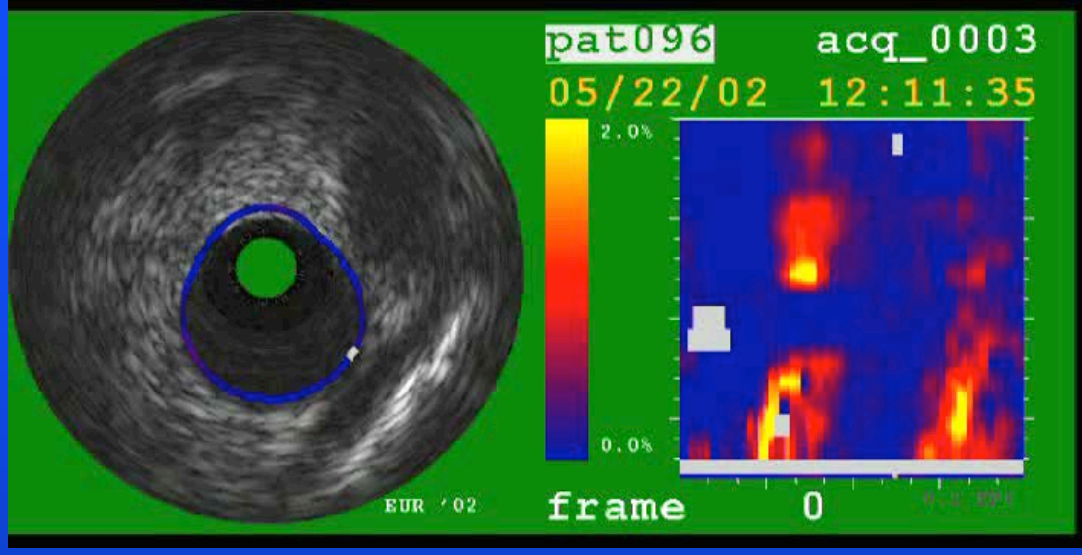
For the detection of vulnerable plaque, it is important to identify not only the composition and geometry of the plaques but also the response of the tissue to the pulsating force applied by the blood pressure. The plaque is supposed to be rupture prone if the cap is unable to withstand the stress applied on it. All the stress that is applied on the plaque by the blood pressure is concentrated in the cap, because the lipid pool is unable to withstand forces on it (1,2). During plaque development, the stress in the cap can further increase when: 1) caps become thinner; 2) lipid pools become larger; or 3) the difference in stiffness between the cap and the lipid pool increases. Furthermore, the strength of the cap is affected by inflammation: Fibrous caps with inflammation by macrophages were locally weakened (3). Therefore, the strength of a cap seems to be a more important parameter than the thickness of a cap.

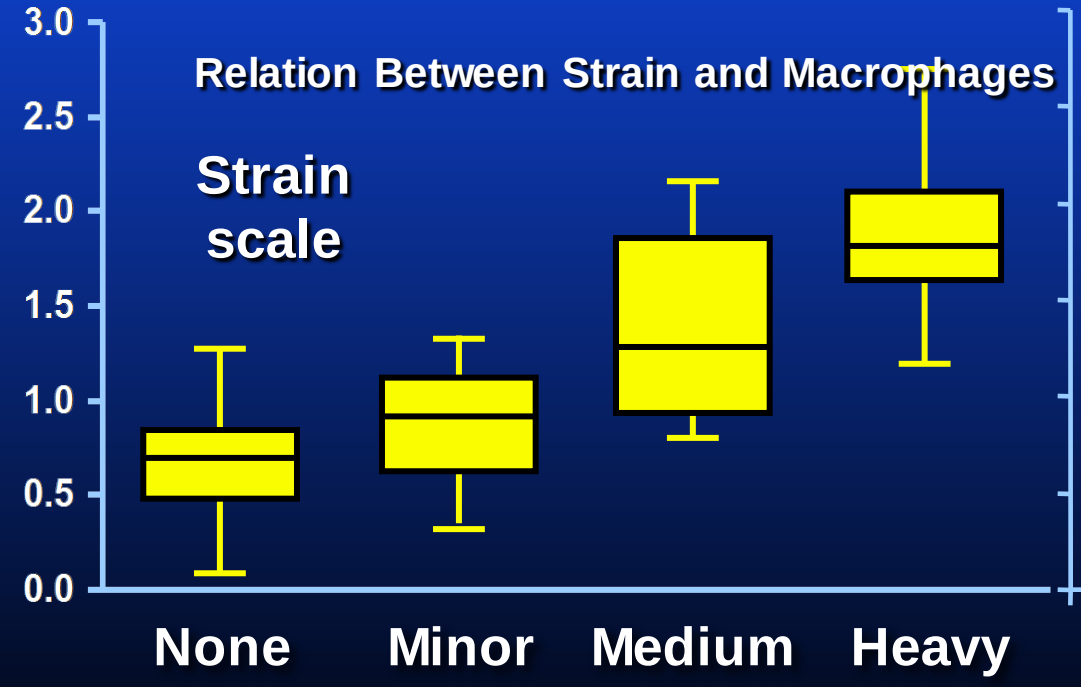
(IVUS). Intravascular ultrasound is the only commercially available clinical technique providing a real-time cross-sectional image of the coronary artery (5). Using IVUS, detailed information of the coronary wall and plaque can be obtained. Furthermore, calcified and noncalcified plaque components can be identified. However, the sensitivity to identify fatty plaque components remains low (6,7). Recent radiofrequency (RF)-based tissue identification strategies appear to have a better performance (7,8). With palpography, the local strain of the tissue is obtained. This strain is directly related to the mechanical properties of plaque components: Soft fatty tissue will be more strained than stiff fibrous tissue when equally stressed. Because the mechanical properties of fibrous and fatty plaque components are different (9–11), palpography has the potential to differentiate between different plaque components. An even more promising feature

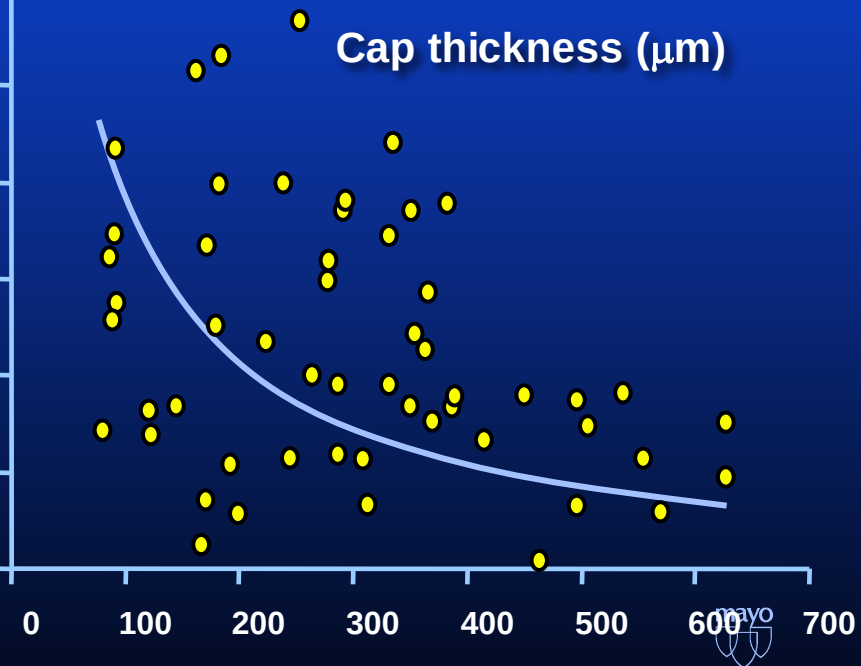


Schaar et al: JACC 47:C86, 2006



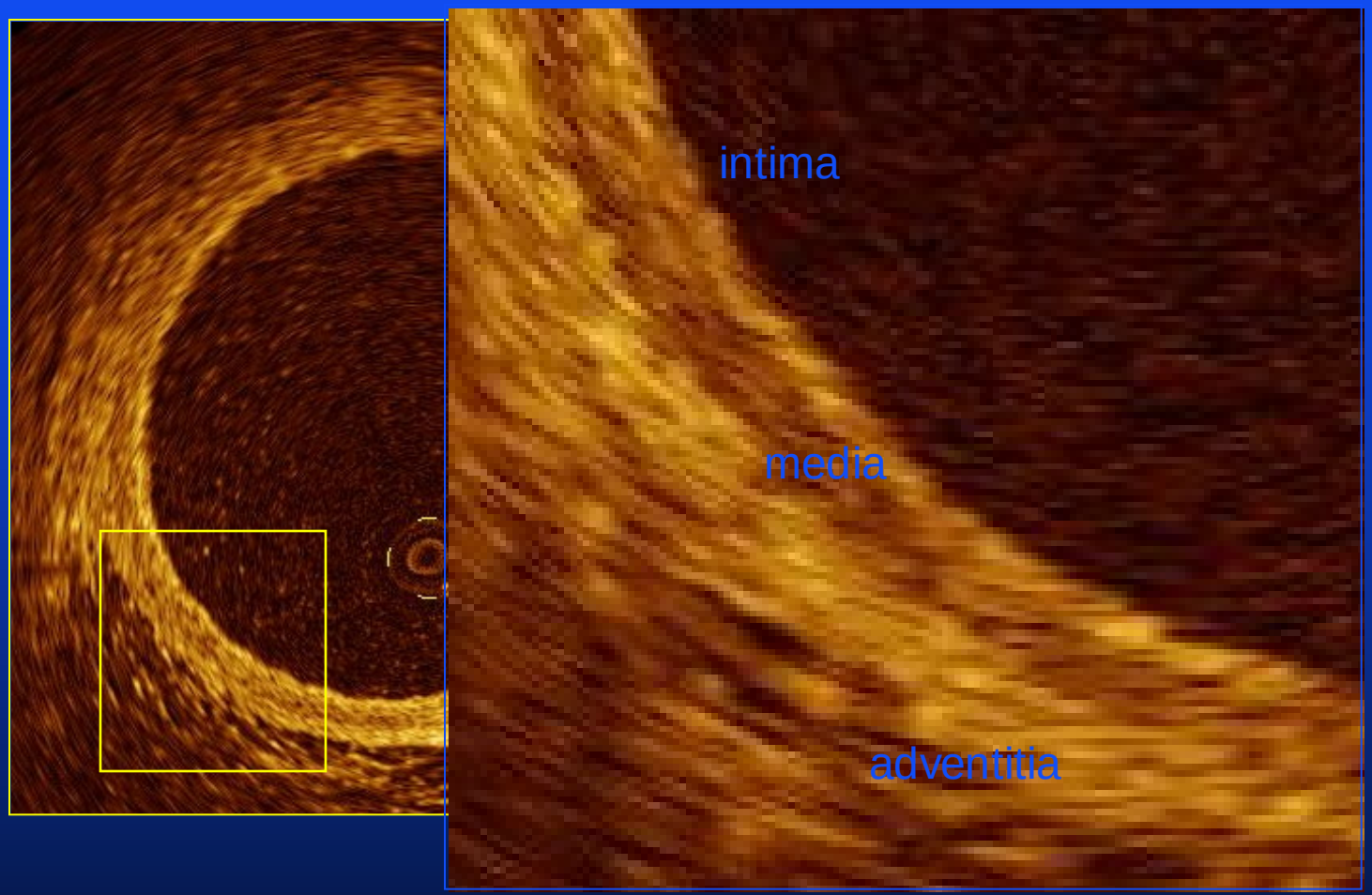






Schaar et al: Circ 108:2636, 2003

Superior resolution with OCT

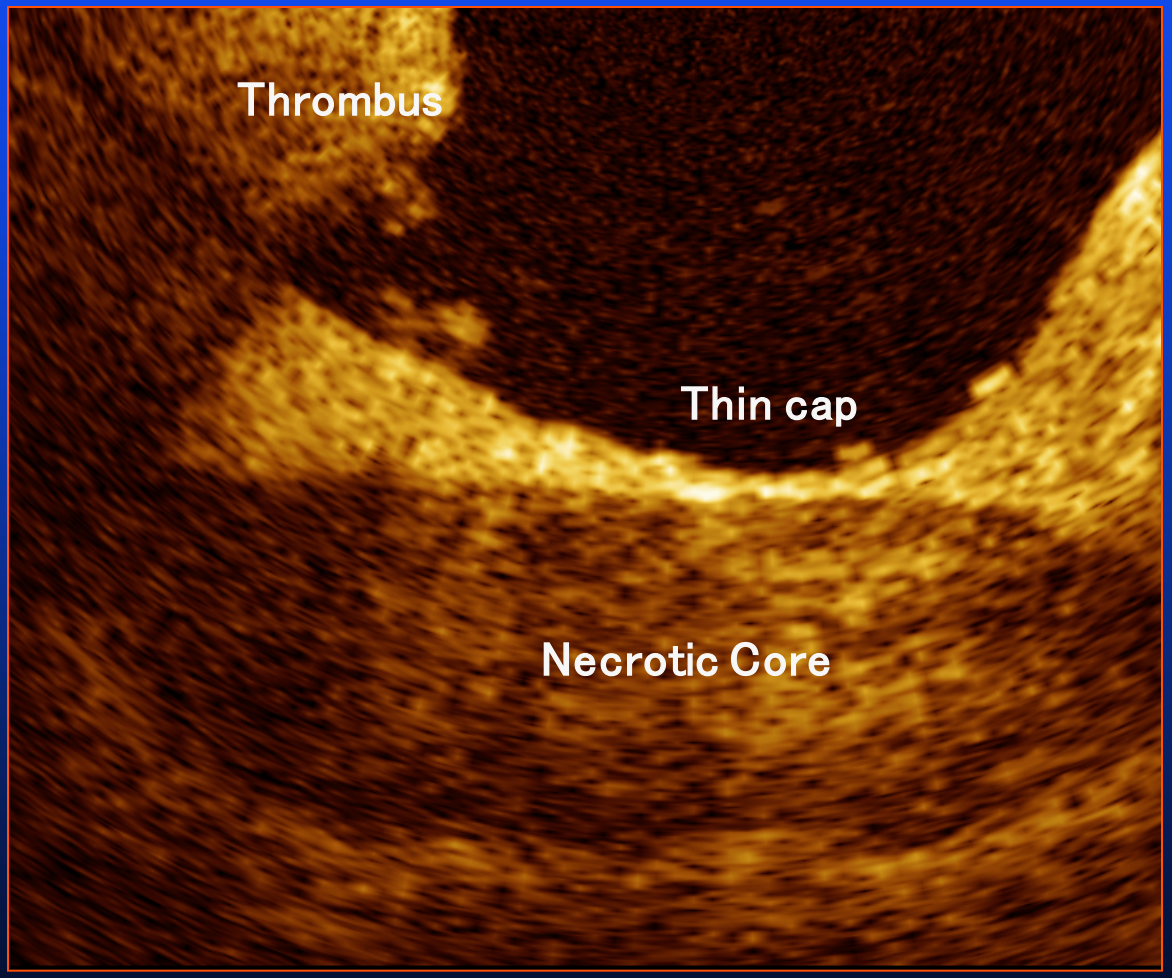


Normal native coronary artery

Strength of OCT: Visualization of the luminal border and the intimal layer

OCT for Vulnerable Plaque Detection

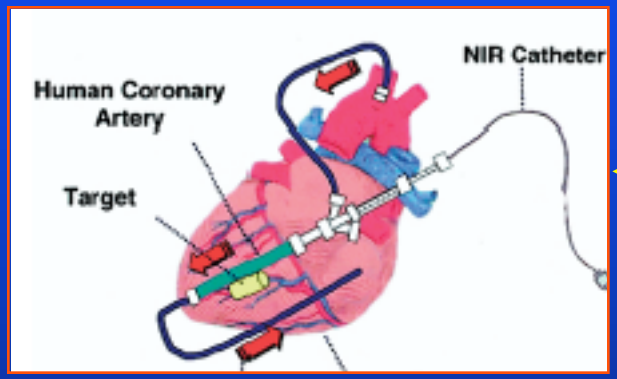
Vulnerable Plaque

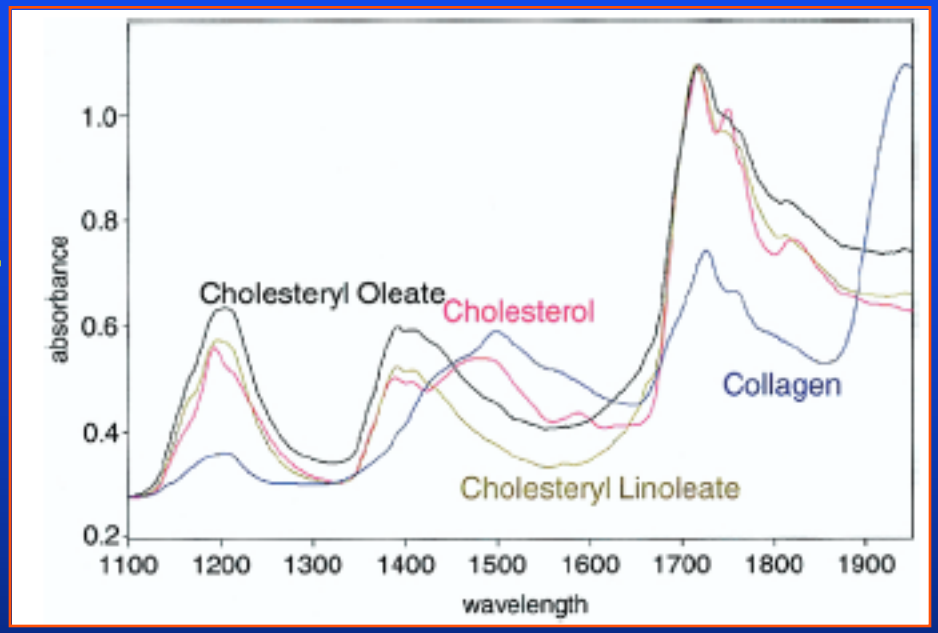


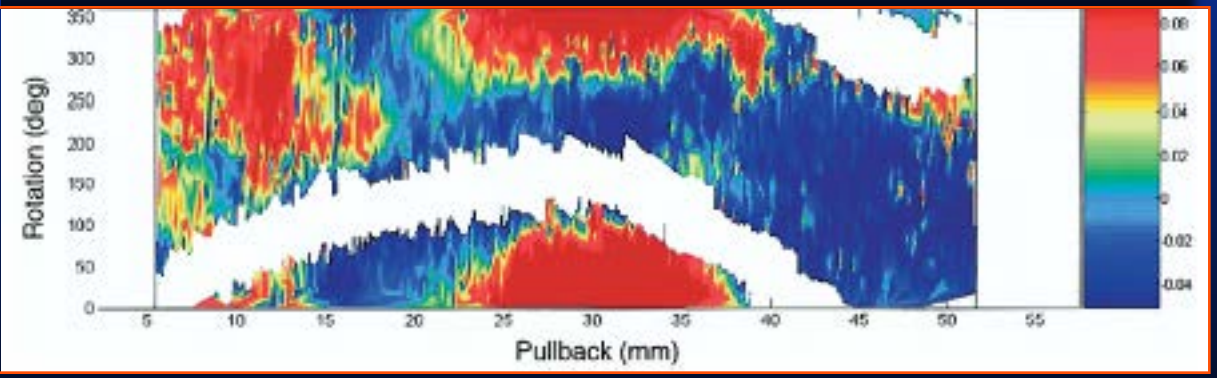
Near-Infrared Spectroscopy for the Detection of Vulnerable Coronary Artery Plaques

Jay D. Caplan, SB, MBA,* Sergio Waxman, MD,†‡ Richard W. Nesto, MD,†§ James E. Muller, MD*

Burlington and Boston, Massachusetts

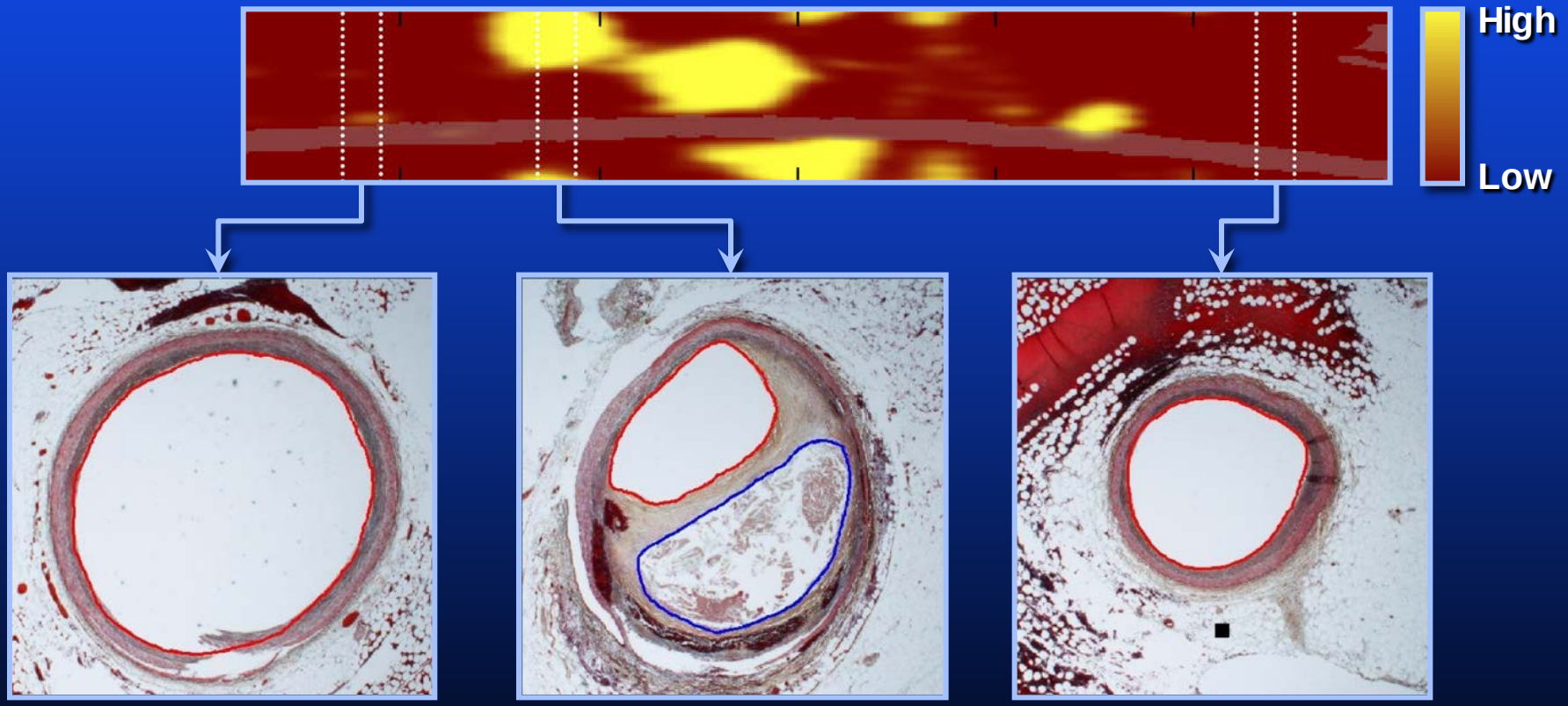






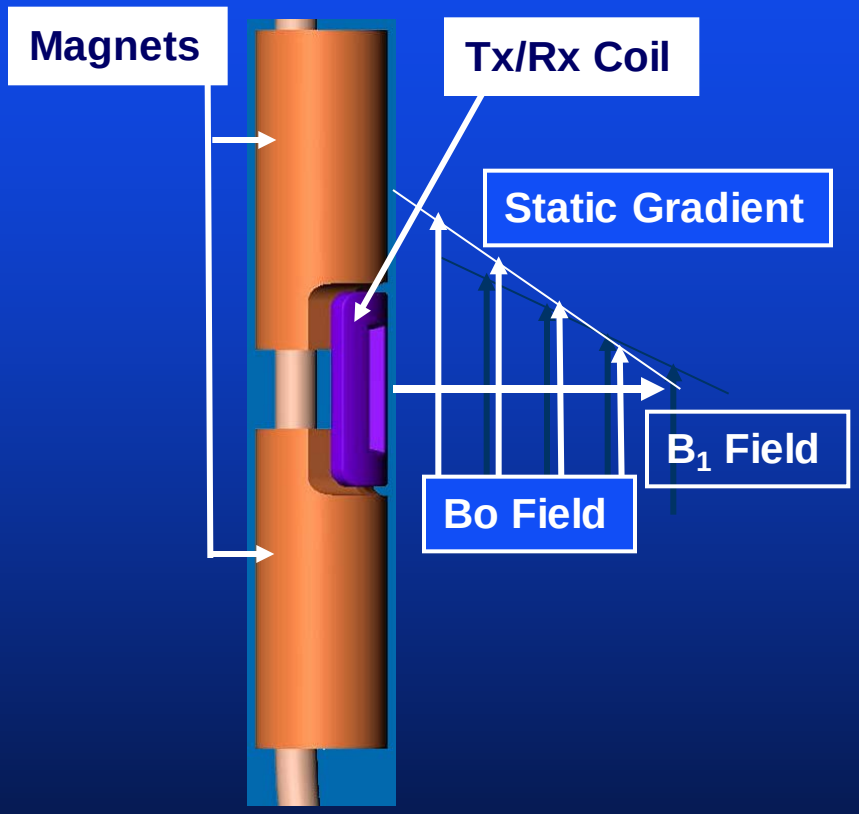
Comparison of NIR-Derived Chemogram with Histology Truth

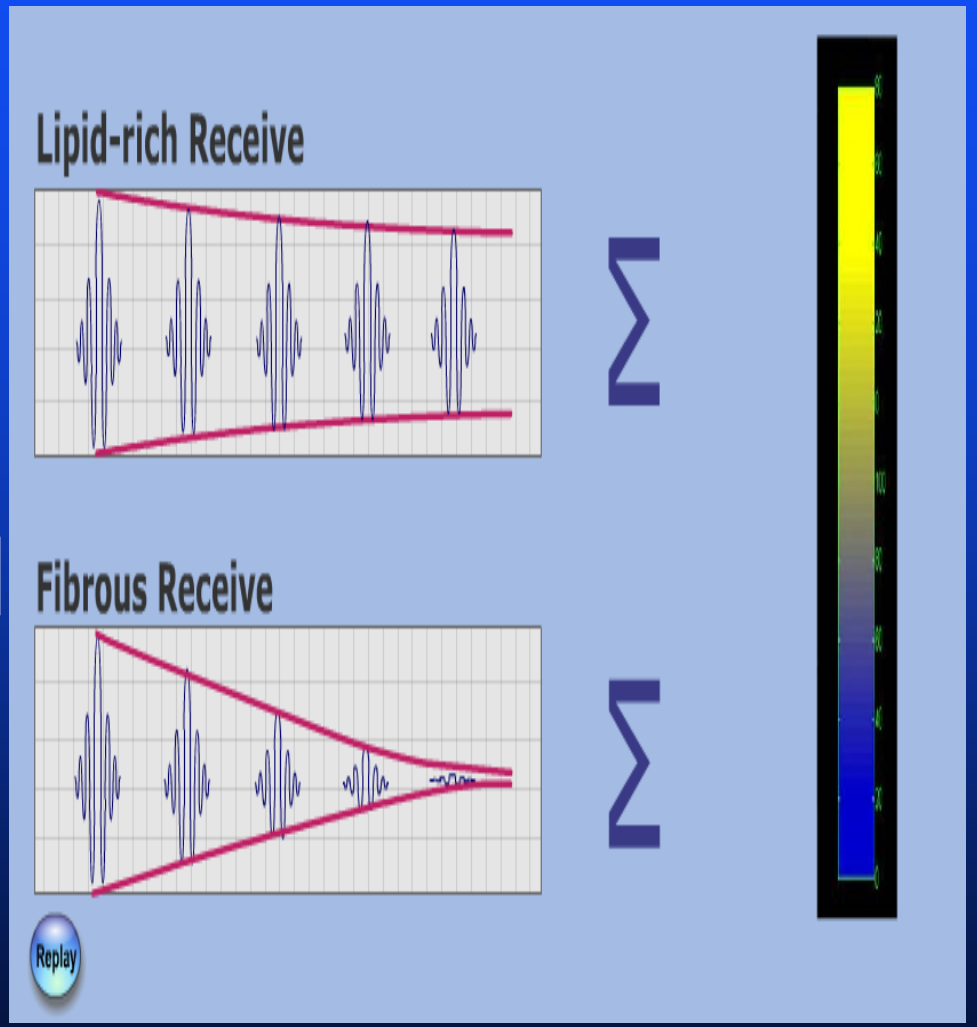
- 67-year-old male
- Cause of death: MI
- History: CAD (with previous CABG)



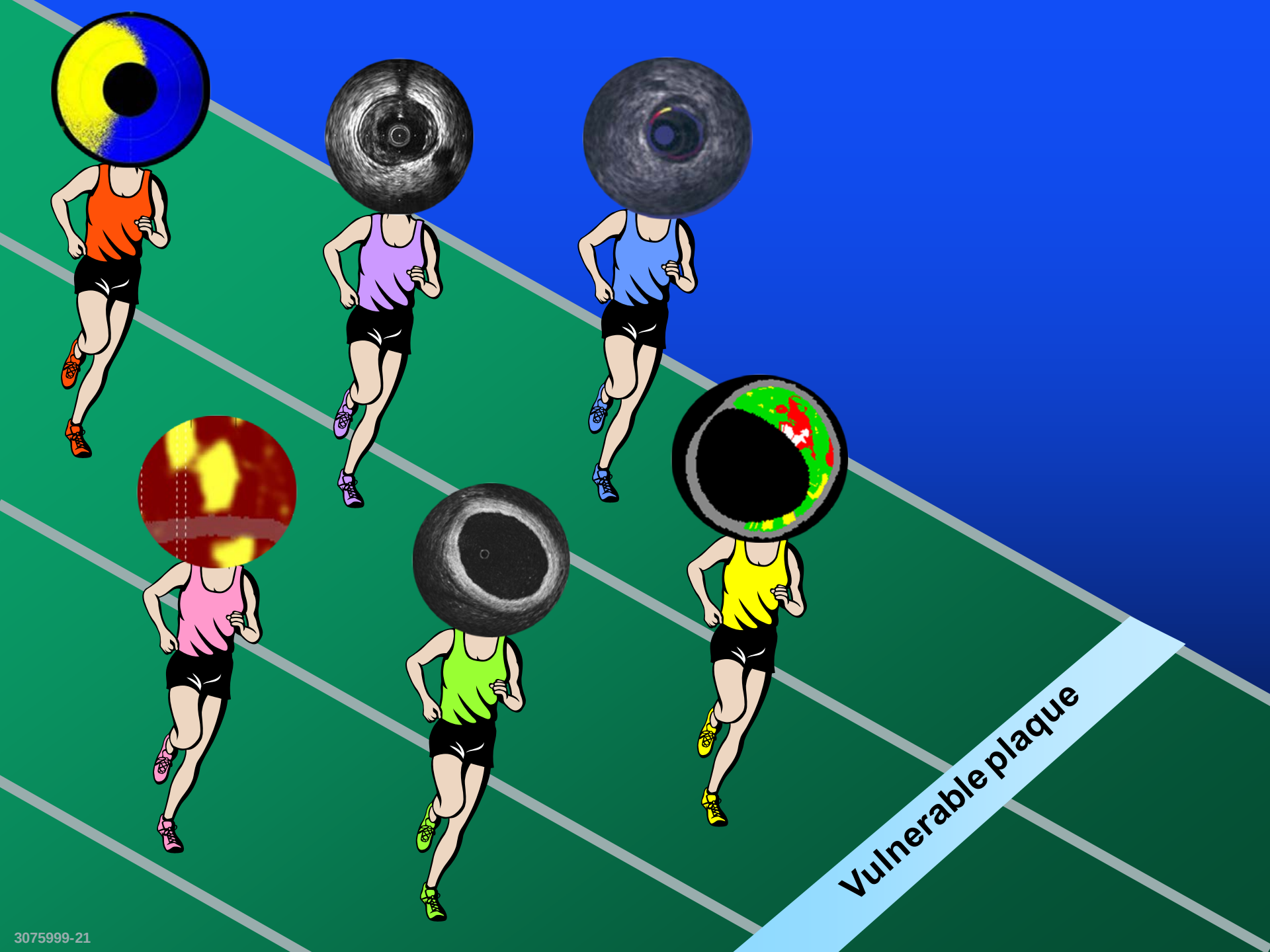
Intravascular MRI

TopSpin's IVMRI Probe





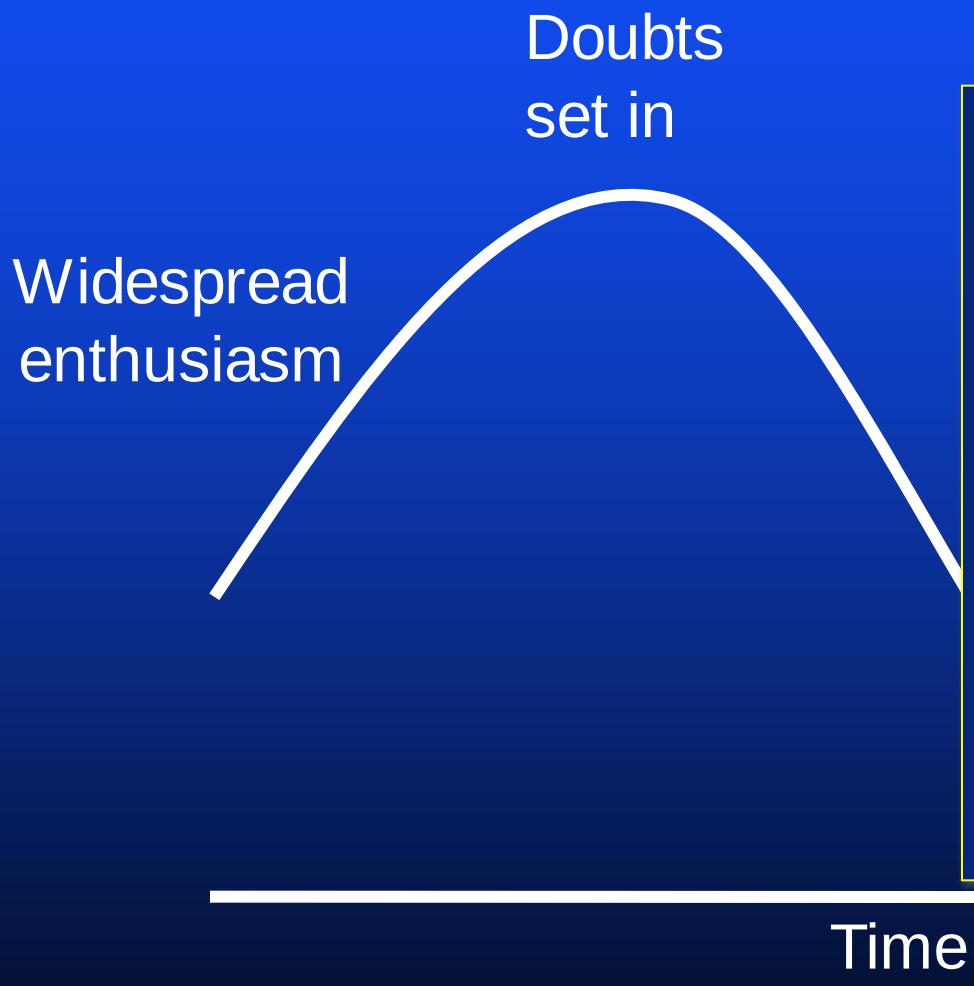
* Illustrative vis-à-vis scanner


Vulnerable plaque

What do we have so far?

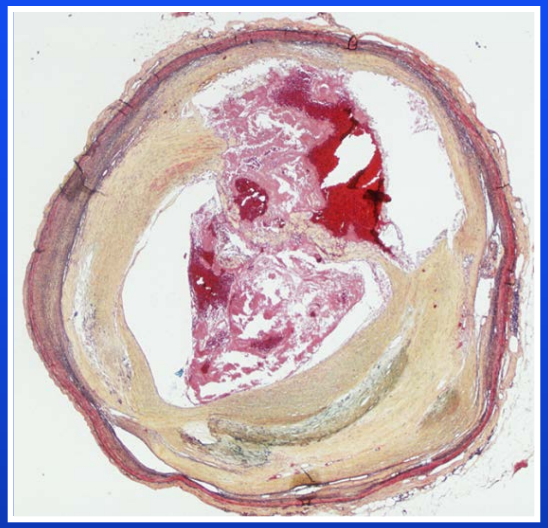
- Enhanced knowledge on the mechanism of the disease
- Multiple imaging modalities
- Many new start up companies
- Many conferences and miles traveled

Natural history of many bio medical and theories

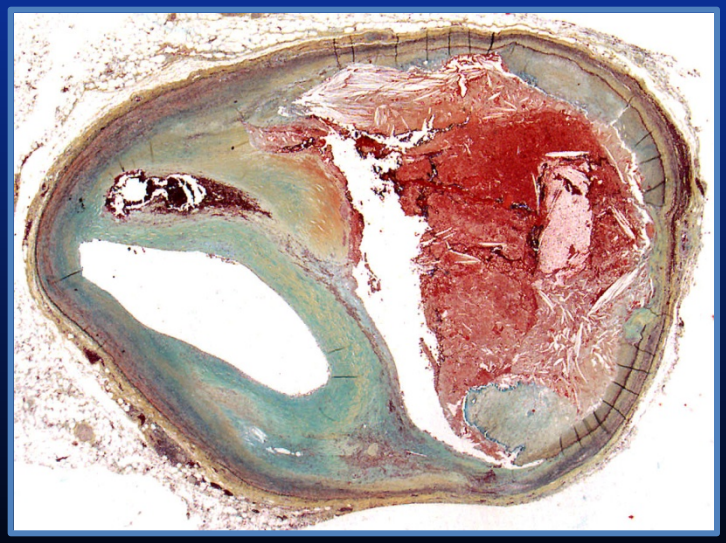


- **Not all ACS and SCD originated from VP (Pathology data)**
- **Missing elements**
- **Arithmetic**
- **Vulnerable patients: trigger**

TCFA= Thin capped Fibroatheroma with rupture

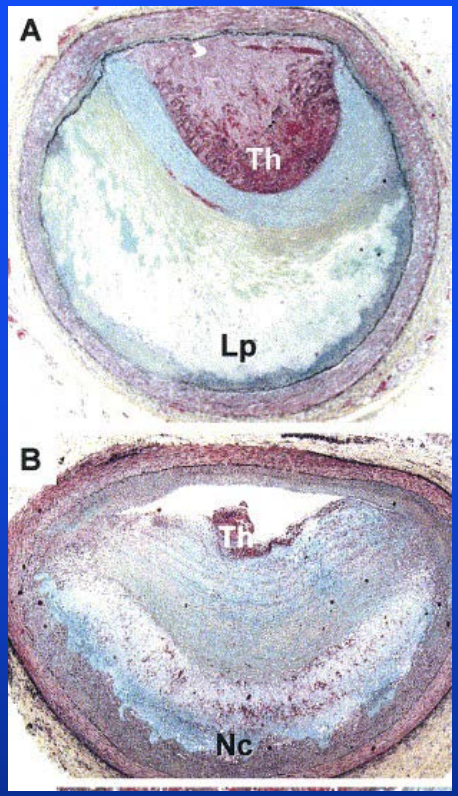


Fibroatheroma with severe Intraplaque hemorrhage

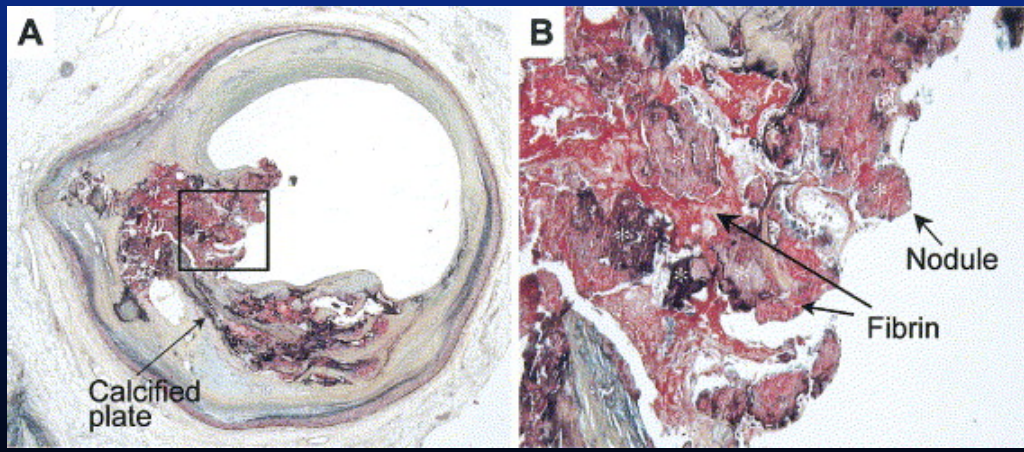


The pathology of the ACS and sudden cardiac death may demonstrate: TCFA with plaque rupture, plaque erosion. Calcium and Hemorrhage

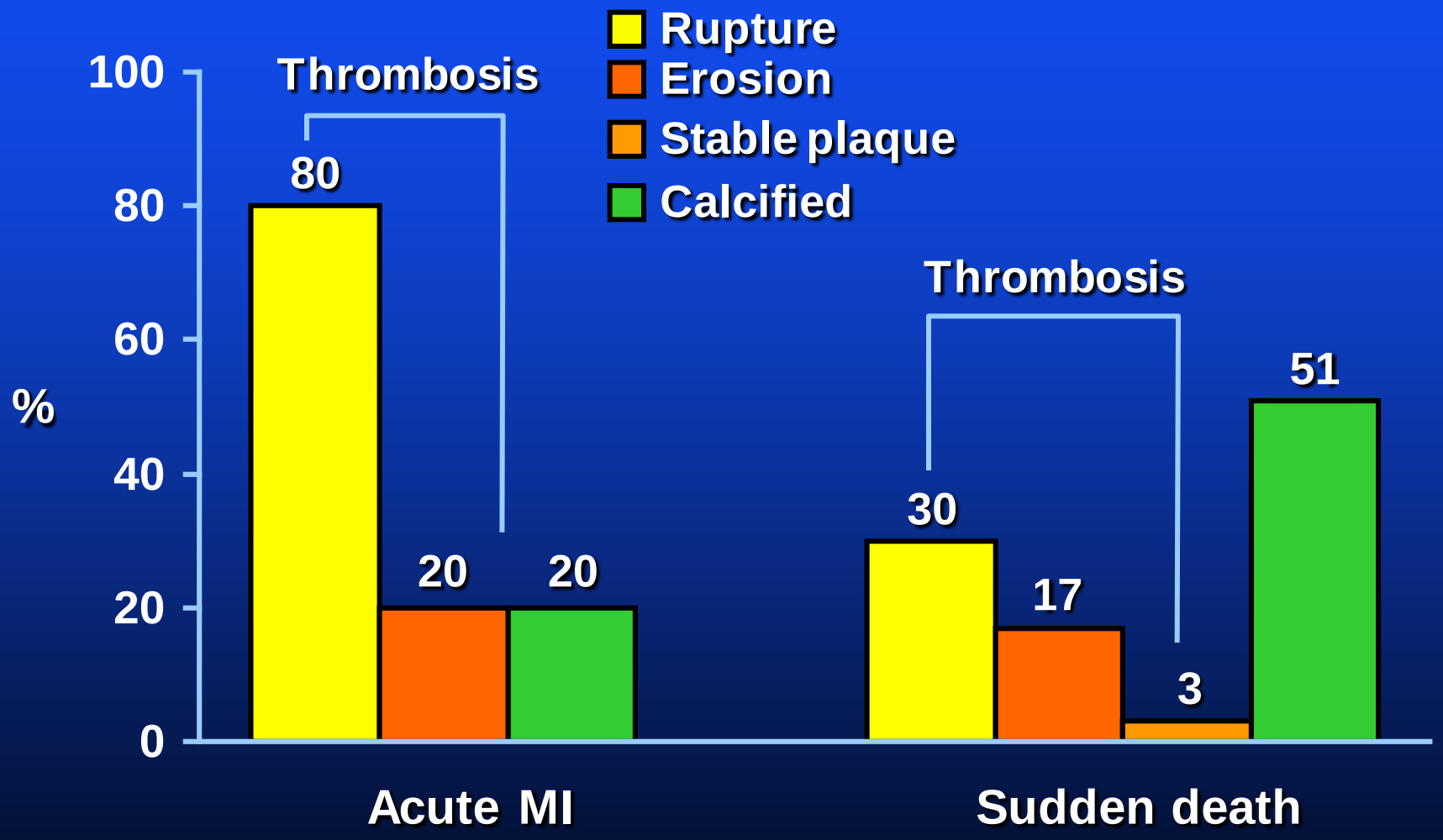
Erosion



Calcified Nodule

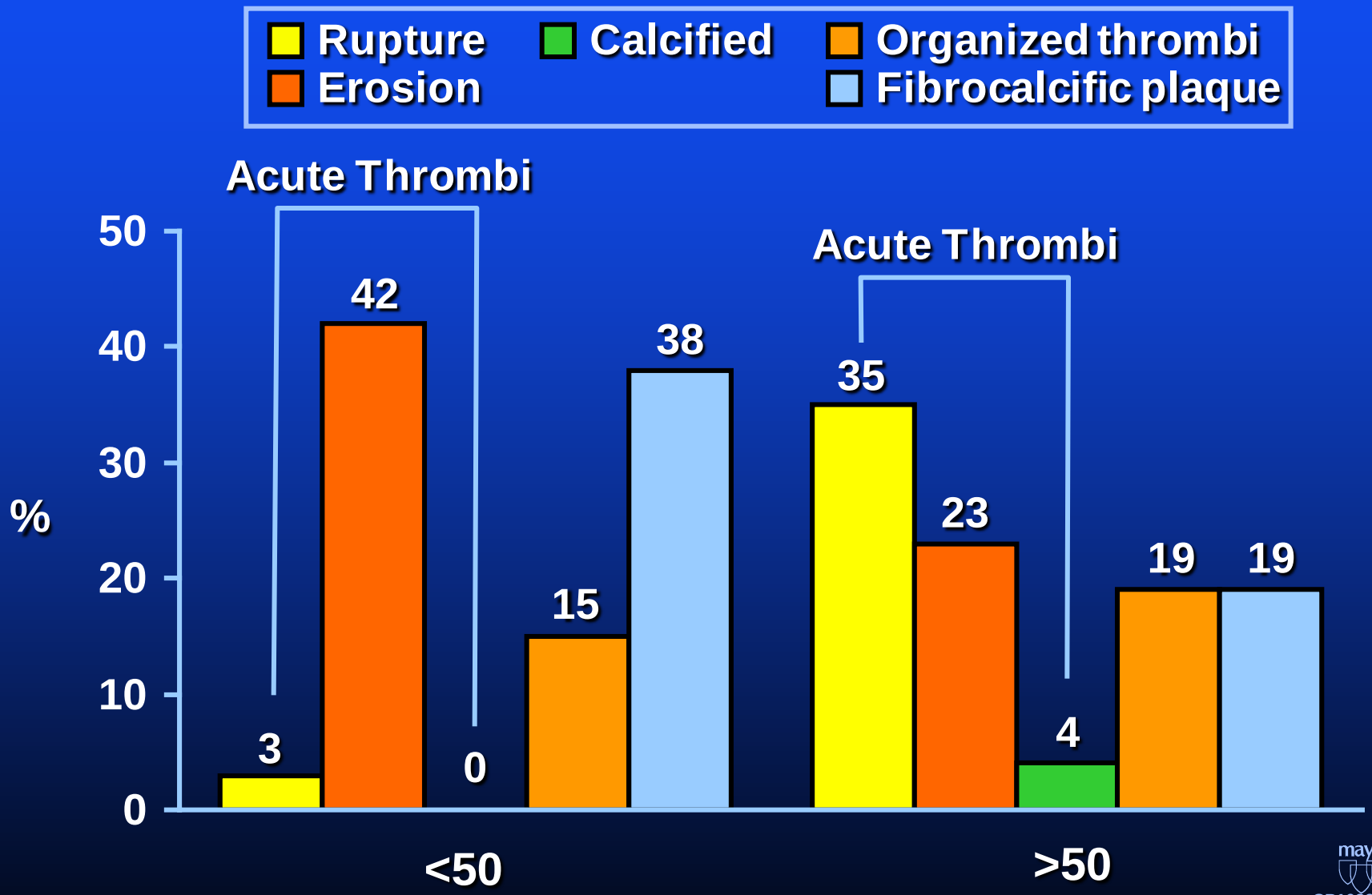


Incidence of Culprit Plaques in Varying Coronary Syndromes



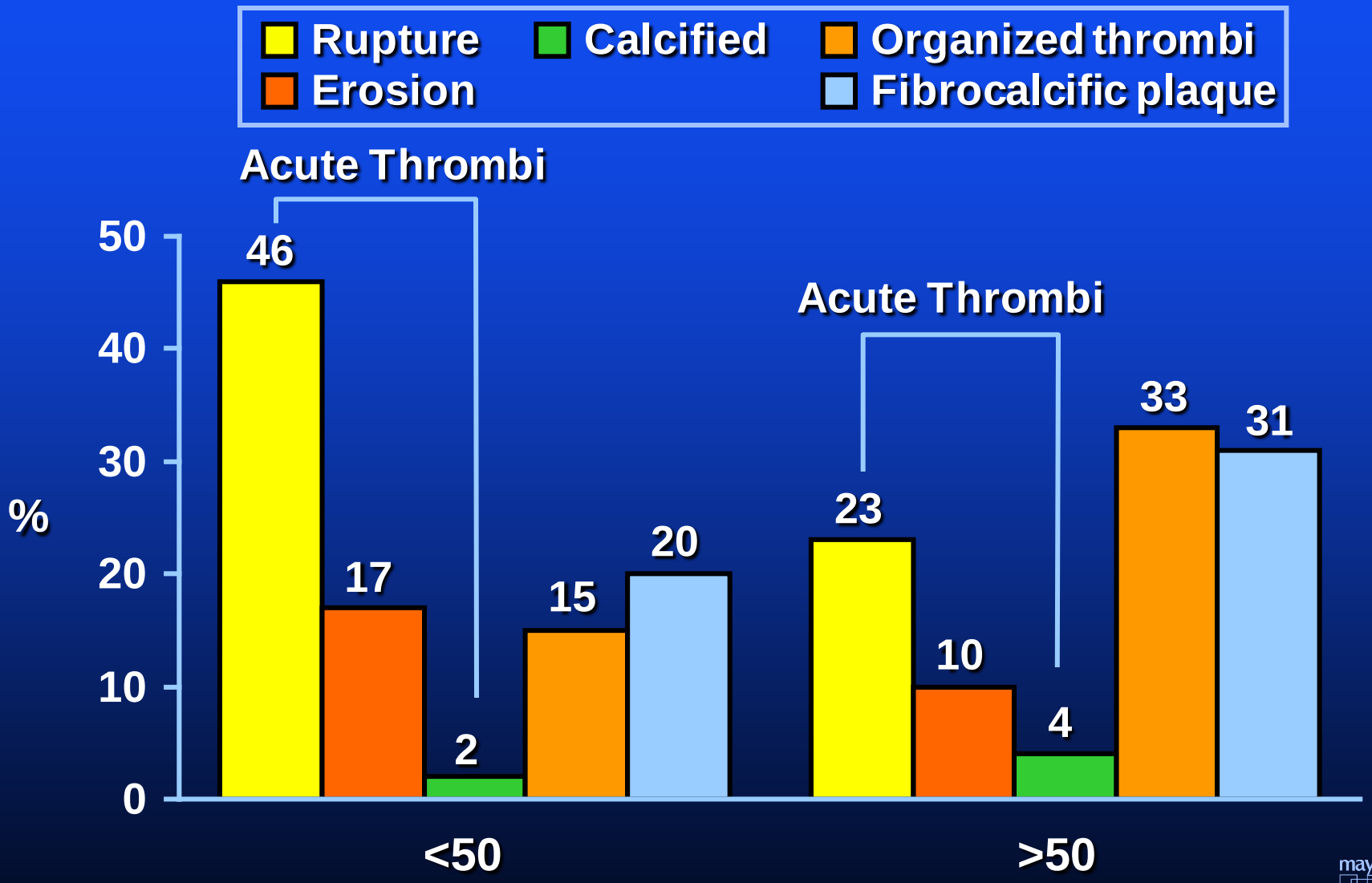
Incidence of Culprit Plaque by Sex and Age

Women

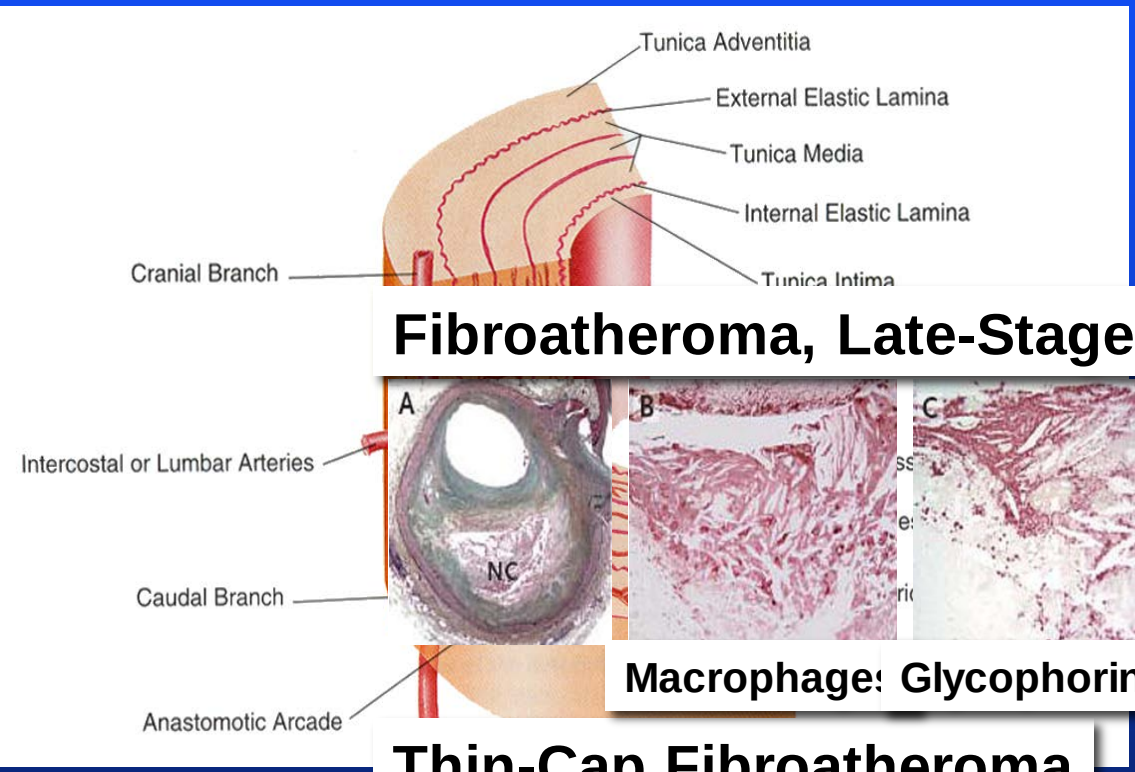


Incidence of Culprit Plaque by Sex and Age

Men



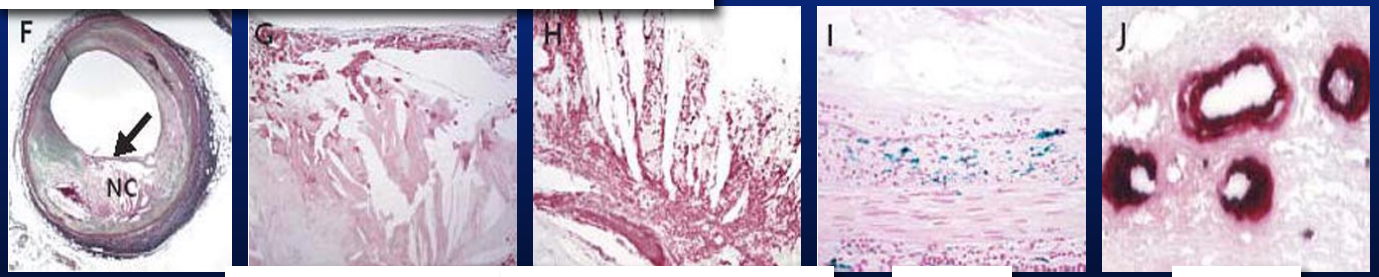
Role of intra plaque hemorrhage in plaque rupture



Fibroatheroma, Late-Stage Necrosis

Macrophages | Glycophorin A | Iron | vWF

Thin-Cap Fibroatheroma



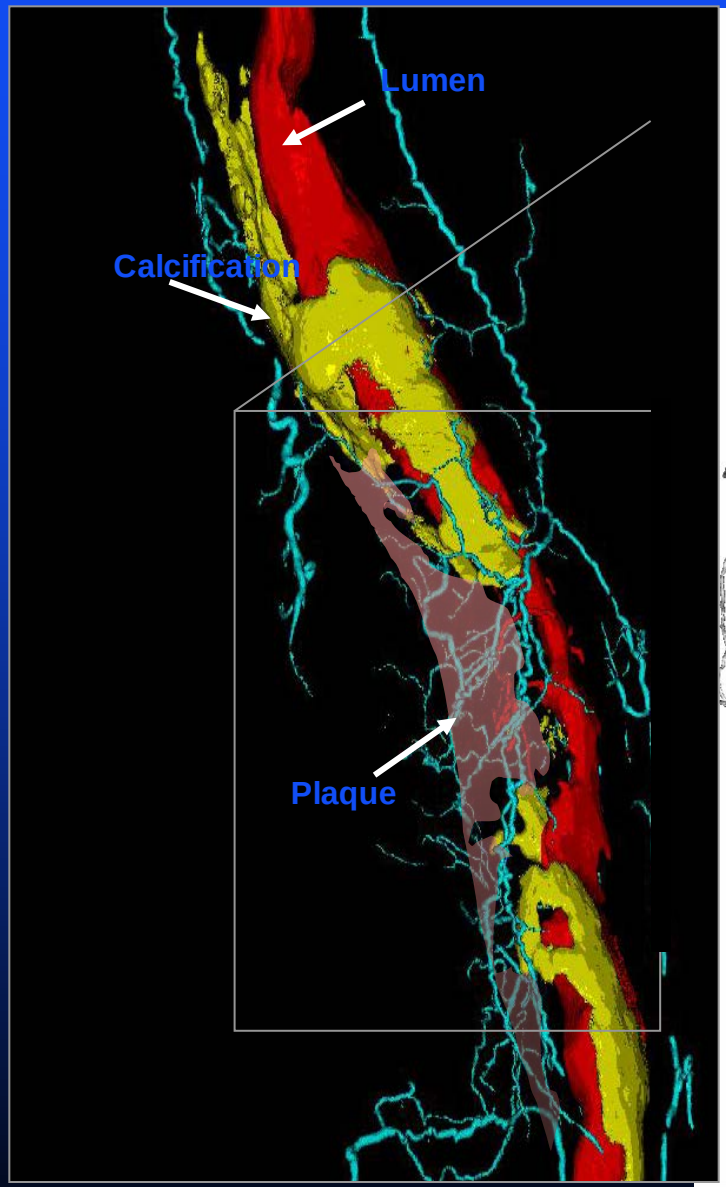
Macrophages | Glycophorin A | Iron | vWF

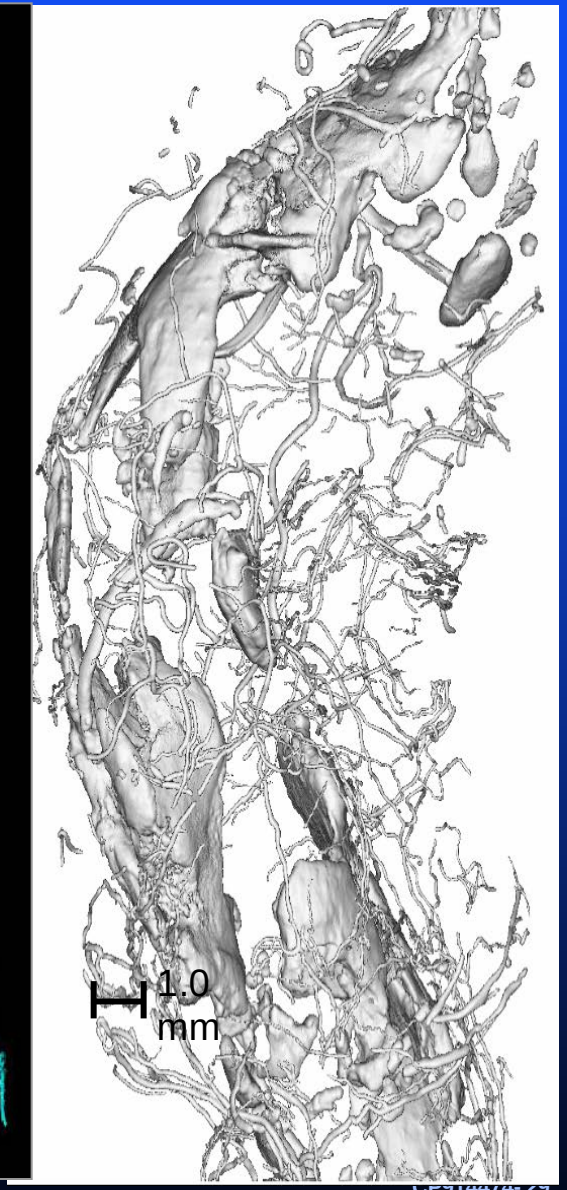
Kolodgie et al: NEJM, 2003

Vasa vasorum density and Coronary atherosclerosis

Coronary HC Pig

Coronary human





Goessl & Lerman et al:Jacc Img, 2010

Background –The objective of the present study was to investigate whether atherosclerotic plaque composition is associated with the occurrence of future vascular events.

Dominique P.V. de Kleijn, PhD; Gerard Pasterkamp, MD, PhD

Background—Identification of patients at risk for primary and secondary manifestations of atherosclerotic disease progression is based mainly on established risk factors. The atherosclerotic plaque composition is thought to be an important determinant of acute cardiovascular events, but no prospective studies have been performed. The objective of the present study was to investigate whether atherosclerotic plaque composition is associated with the occurrence of future vascular events.

Methods and Results—Atherosclerotic carotid lesions were collected from patients who underwent carotid endarterectomy and were subjected to histological examination. Patients underwent clinical follow-up yearly, up to 3 years after carotid endarterectomy. The primary outcome was defined as the composite of a vascular event (vascular death, nonfatal stroke, nonfatal myocardial infarction) and vascular intervention. The cumulative event rate at 1-, 2-, and 3-year follow-up was expressed by Kaplan–Meier estimates, and Cox proportional hazards regression analyses were performed to assess the independence of histological characteristics from general cardiovascular risk factors. During a mean follow-up of 2.3 years, 196 of 818 patients (24%) reached the primary outcome. Patients whose excised carotid plaque revealed plaque hemorrhage or marked intraplaque vessel formation demonstrated an increased risk of primary outcome (risk difference=30.6% versus 17.2%; hazard ratio [HR] with [95% confidence interval]=1.7 [1.2 to 2.5]; and risk difference=30.0% versus 23.8%; HR=1.4 [1.1 to 1.9], respectively). Macrophage infiltration (HR=1.1 [0.8 to 1.5]), large lipid core (HR=1.1 [0.7 to 1.6]), calcifications (HR=1.1 [0.8 to 1.5]), collagen (HR=0.9 [0.7 to 1.3]), and smooth muscle cell infiltration (HR=1.3 [0.9 to 1.8]) were not associated with clinical outcome. Local plaque hemorrhage and increased intraplaque vessel formation were independently related to clinical outcome and were independent of clinical risk factors and medication use.

Conclusions—The local atherosclerotic plaque composition in patients undergoing carotid endarterectomy is an independent predictor of future cardiovascular events. **(*Circulation*. 2010;121:1941-1950.)**

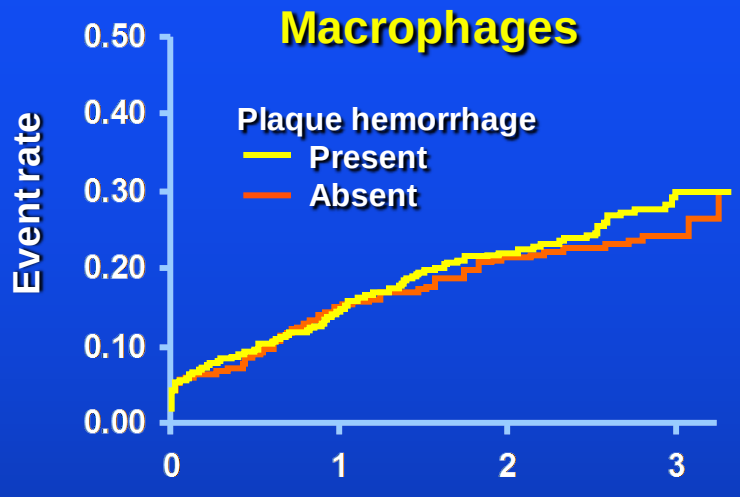
Key Words: atherosclerosis ■ cardiovascular diseases ■ outcome assessment ■ carotid arteries ■ hemorrhage ■ blood vessels

It has been recognized that clinical manifestations of atherosclerotic disease such as myocardial infarction and stroke are caused by acute thrombosis, which is triggered by atherosclerotic plaque instability rather than by gradually progressive luminal narrowing.[1–5] Pathology studies revealed that atherosclerotic plaque destabilization is related to specific "vulnerable" plaque characteristics, such as a large lipid core, thin fibrous cap, and marked inflammation.[6]

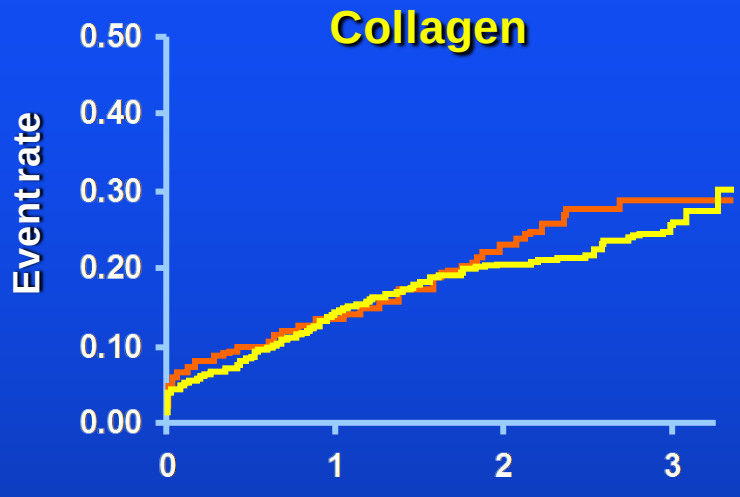
Clinical Perspective on p 1950

At present, a reliable method to predict future plaque destabilization and subsequent cardiovascular events is lack-

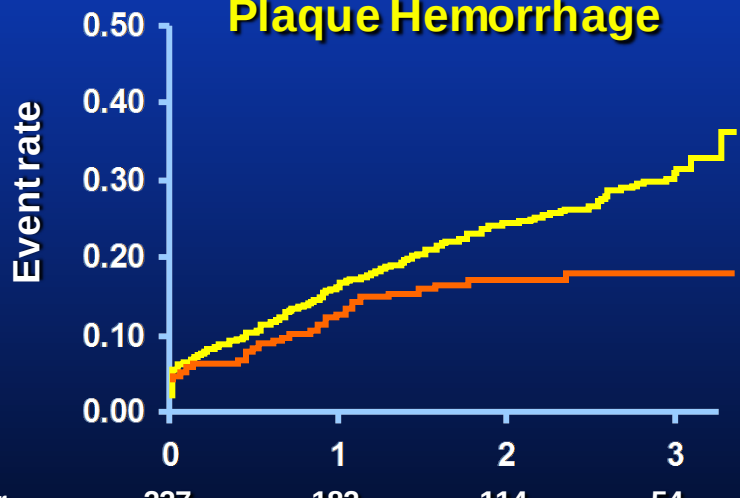
Relation Between Plaque Characteristics and Primary Outcome



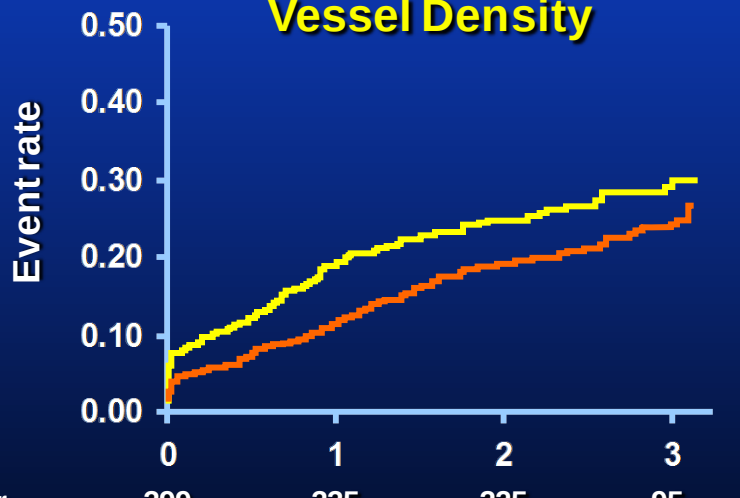
No/minor	316	257	192	89
Moderate/heavy	497	390	241	84



No/minor	146	115	85	37
Moderate/heavy	669	536	352	138



No/minor	227	182	114	54
Moderate/heavy	591	469	323	122

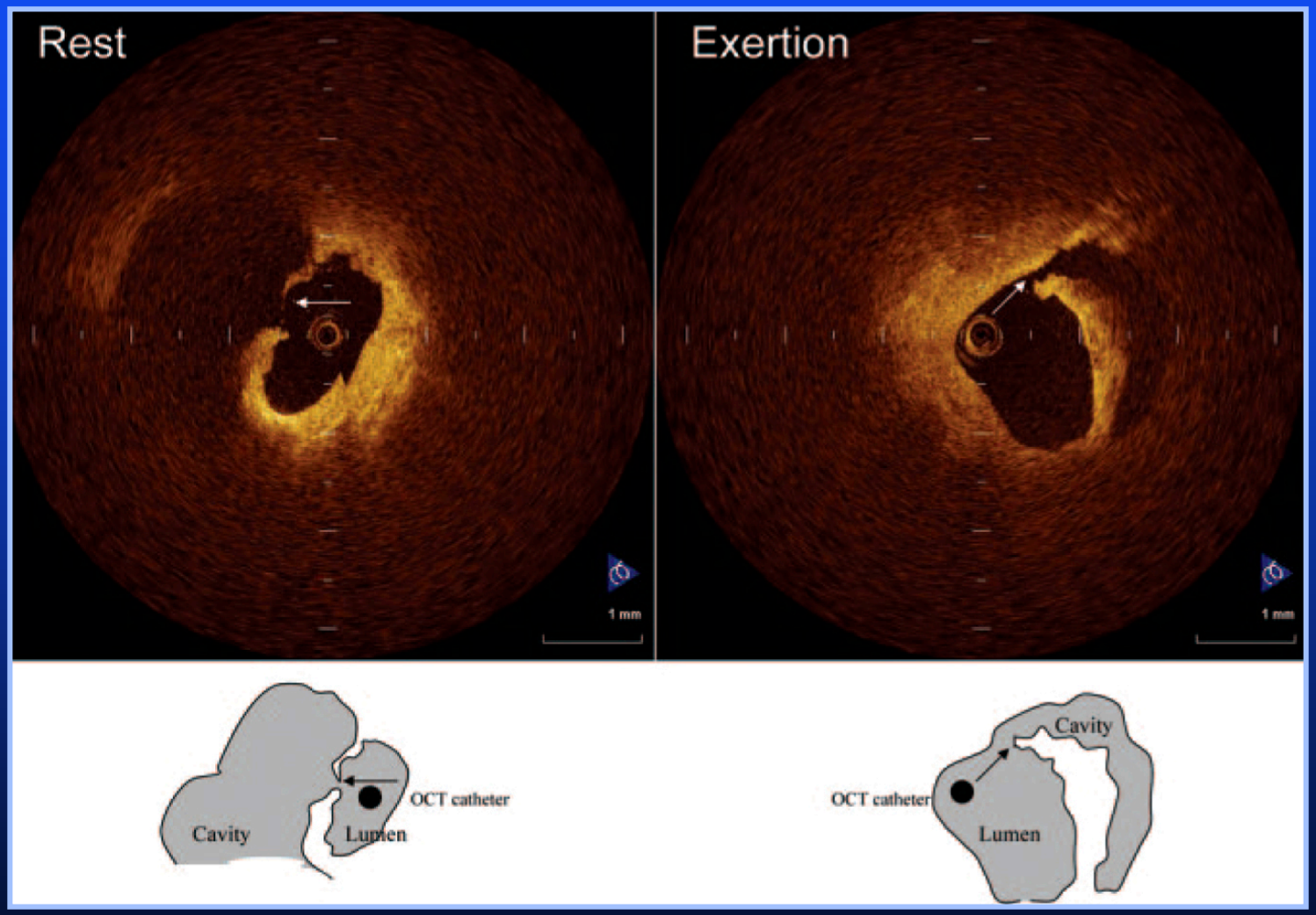


No/minor	399	335	225	95
Moderate/heavy	396	297	198	78

Hellings et al: Circ 121:1941, 2010

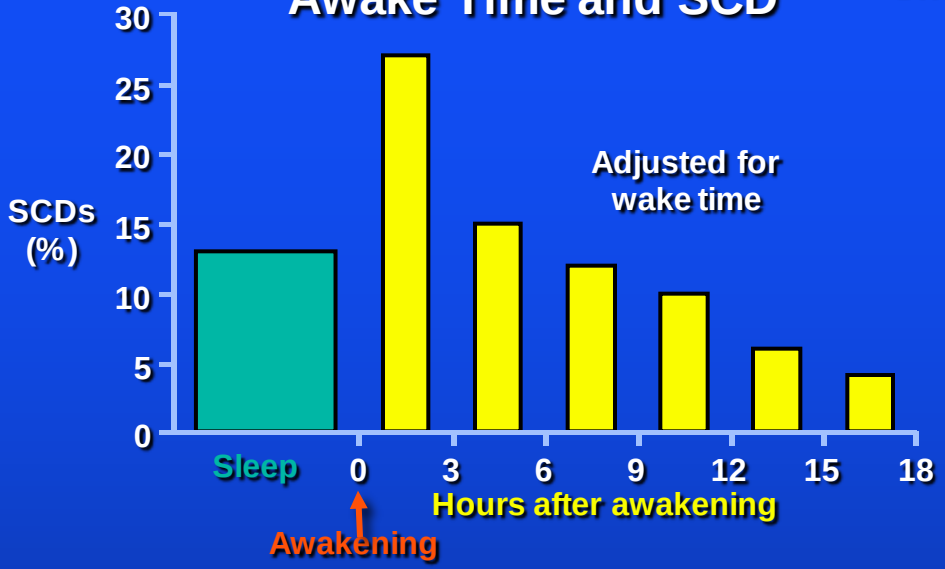
mayo

Representative Cases of Plaque Rupture Occurring at Rest or with Exertion

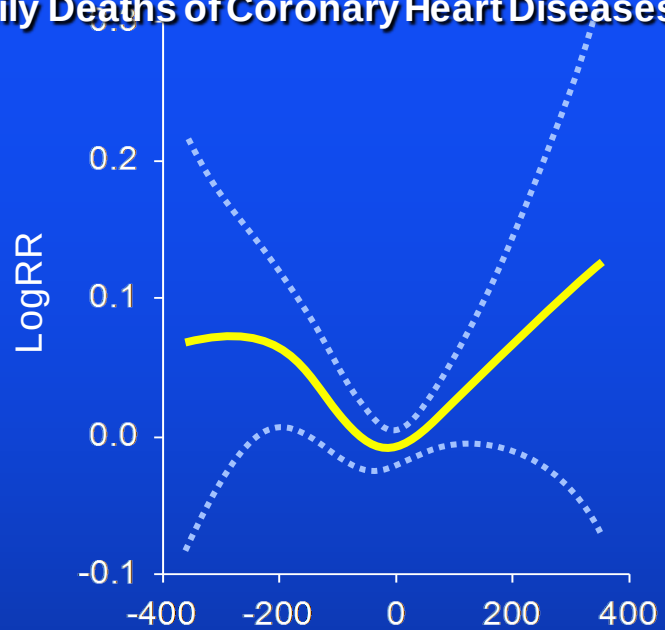


Tanaka et al: Circ 118:2368, 2008

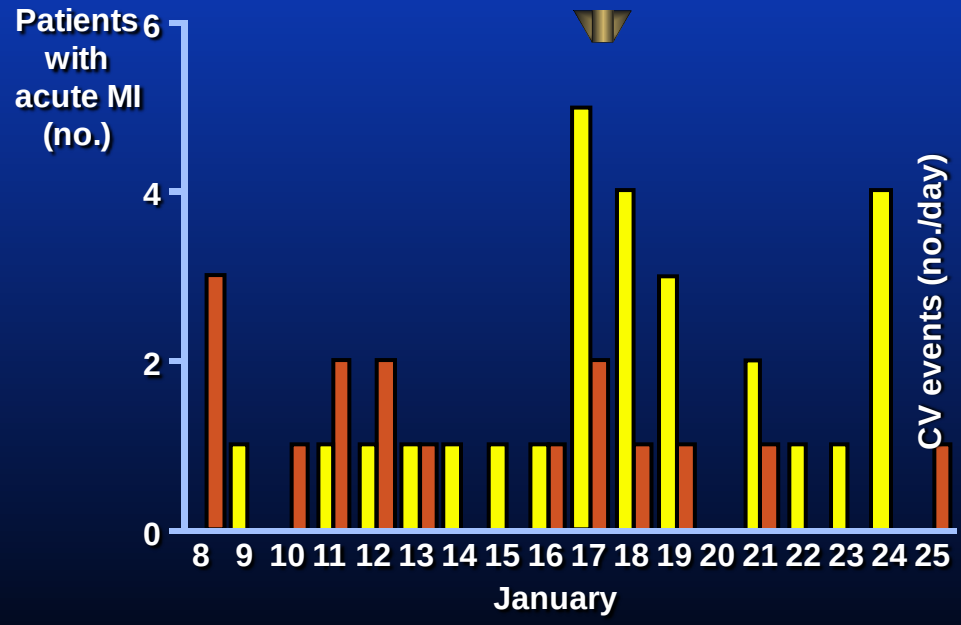
Awake Time and SCD



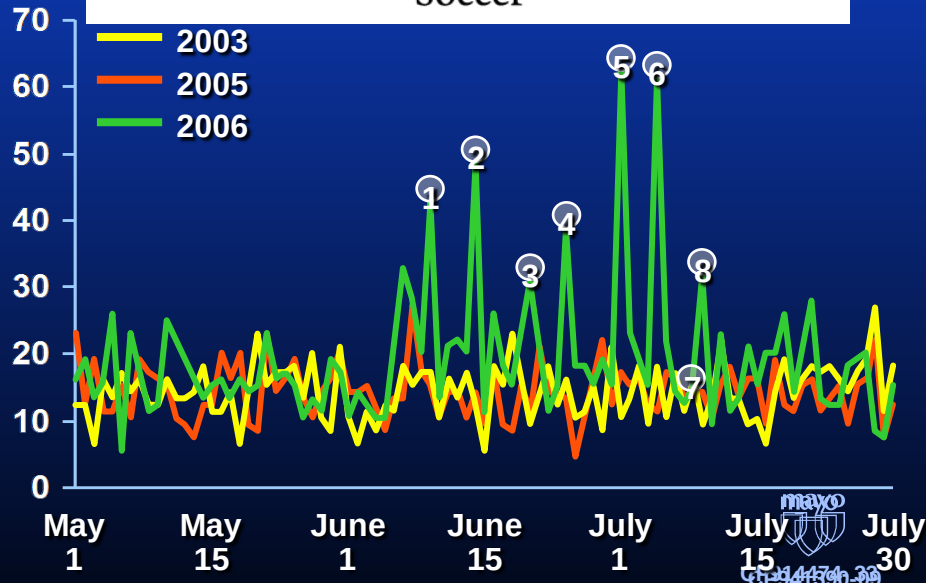
Shanghai Stock Exchange Composite Index Change with Daily Deaths of Coronary Heart Diseases



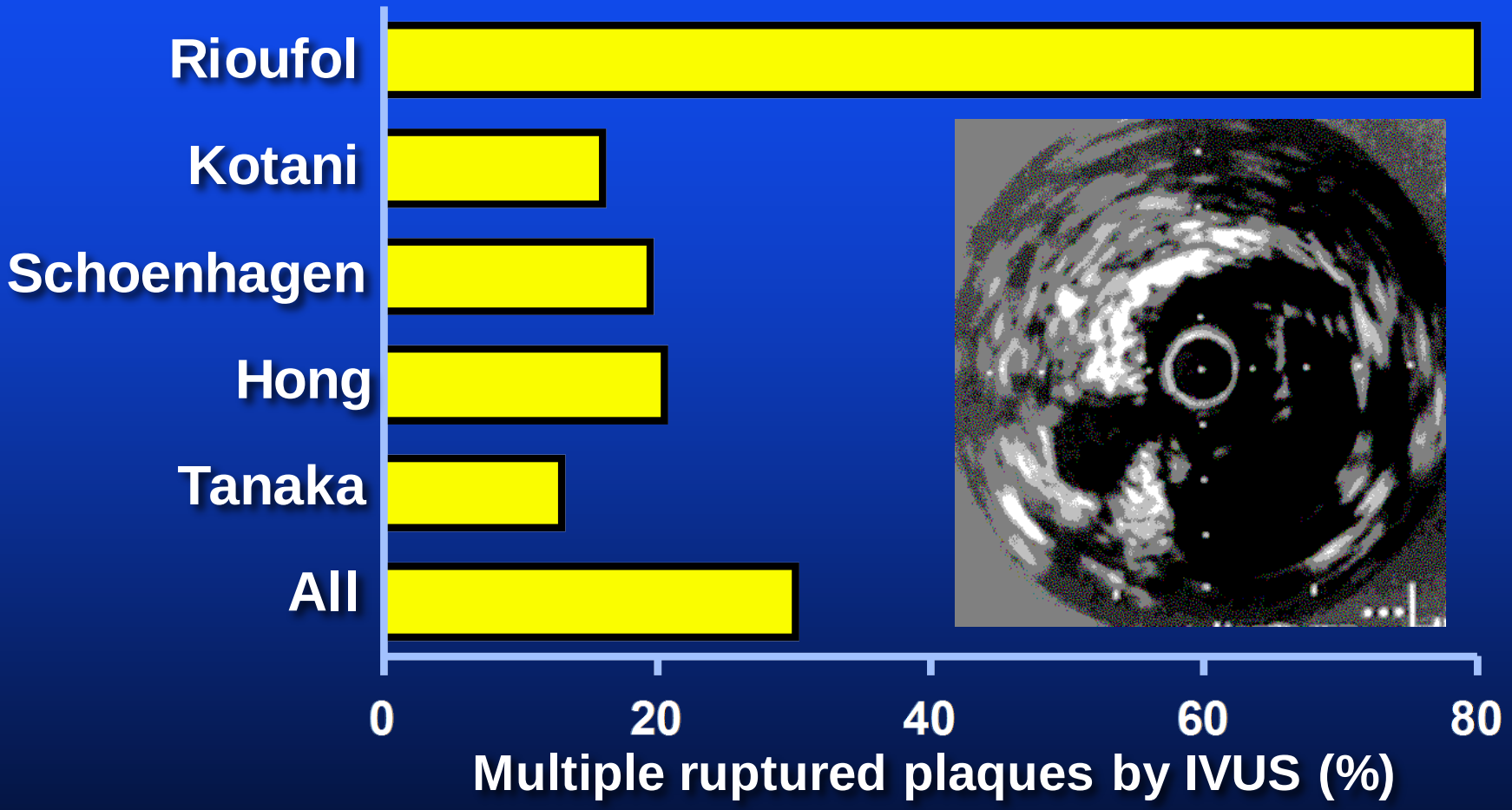
Daily Incidence of MI (Gulf War)



Cardiovascular Events during World Cup Soccer



Prevalence of Multiple Coronary Artery Plaque Ruptures Detected by Intravascular Ultrasonography in 5 Studies



Arithmetic

Autopsy series in US communities among young adults (mean age, 36 years) who died of non natural causes revealed coronary atherosclerosis in 80% of the autopsy sample, with 8% having obstructive disease

However, the annual incidence of acute coronary events in the United States for individuals 40 years of age is 0.2% to 1%,

Factors other than the mere presence of coronary atherosclerosis need to be involved for an acute coronary event to occur

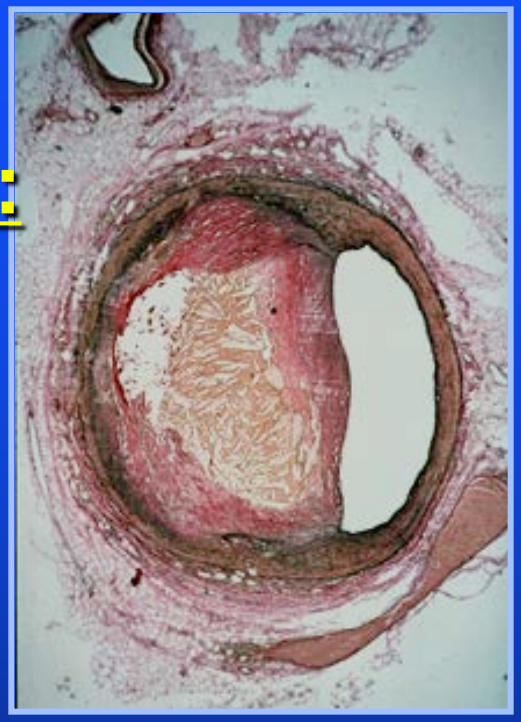
Plaque rupture and thrombus formation most often do not lead to coronary events

Acute Coronary Syndrome

a dynamic process that occurs at the inteface between the vascular wall and the circulation

Vulnerable:

- Vessel
- Mind
- Blood

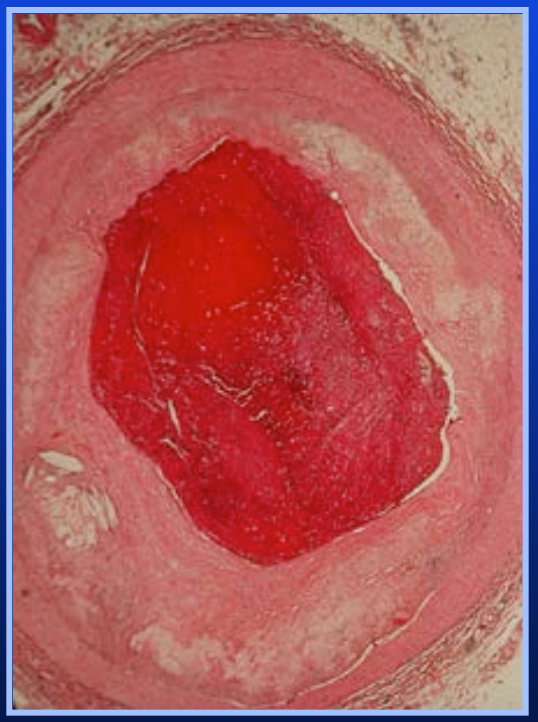


+

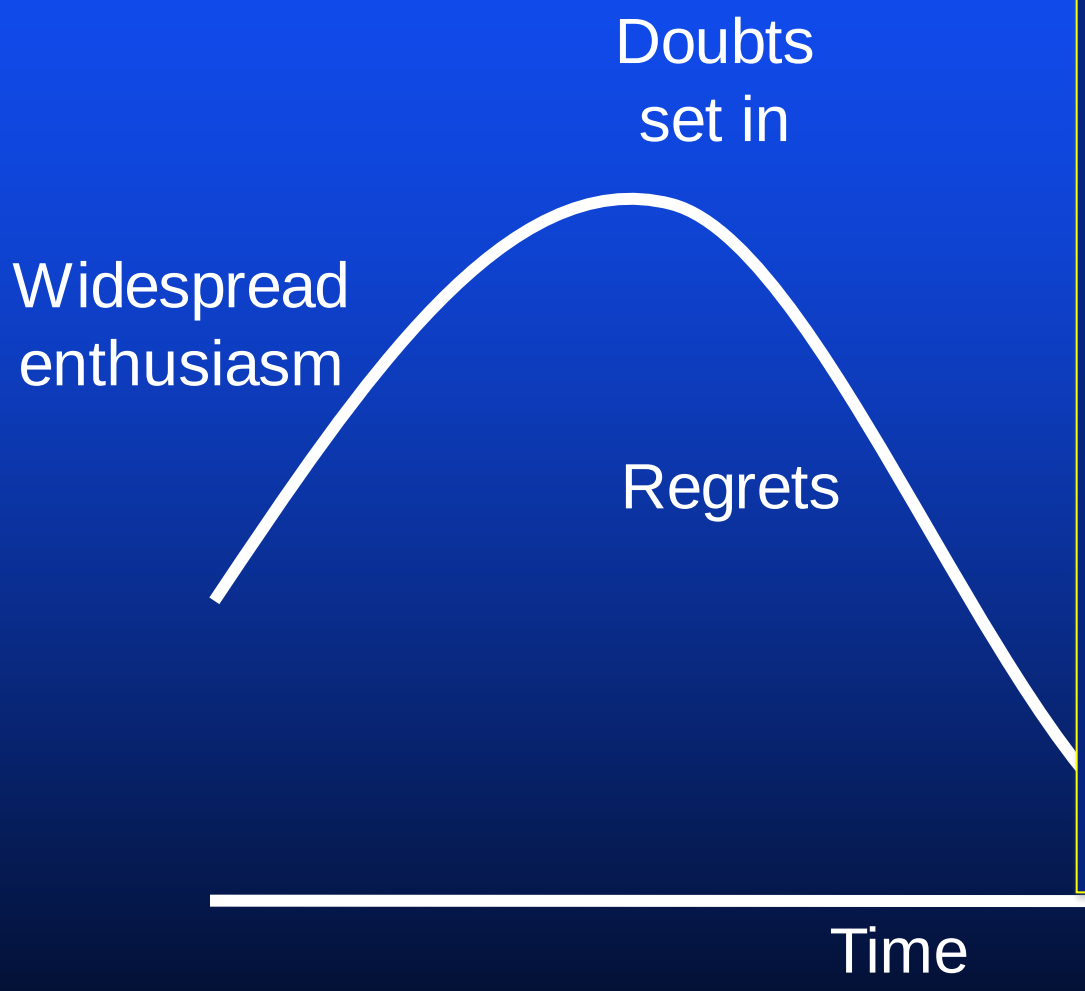
Trigger Events

- Emotional stress
- Physical stress

=



Natural history of many bio medical and theories



- **Natural history of the VP**
- **The need for a Prospective study**
- **Improve imaging modalities**
- **New theory**

Journal of the American College of Cardiology
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Vol. 45, No. 5, 2005
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2004.09.077

CLINICAL RESEARCH **Coronary Artery Disease**

Angioscopic Follow-Up Study of Coronary Ruptured Plaques in Nonculprit Lesions

Masamichi Takano, MD, Shigenobu Inami, MD, Fumiyuki Ishibashi, MD, Kentaro Okamatsu, MD, Koji Seimiya, MD, Takayoshi Ohba, MD, Shunta Sakai, MD, Kyoichi Mizuno, MD, PHD, FACC
Chiba, Japan

OBJECTIVES Changes of ruptured plaques in nonculprit lesions were evaluated using coronary angioscopy.

BACKGROUND The concept of multiple coronary plaque ruptures has been established. However, no detailed follow-up studies of ruptured plaques in nonculprit lesions have yet been reported.

METHODS Forty-eight thrombi in 50 ruptured coronary plaques in nonculprit lesions in 30 patients were identified by angioscopy. The percent diameter stenosis (%DS) at the target plaques on quantitative coronary angiographic analysis and the serum C-reactive protein (CRP) level were measured.

RESULTS The mean angioscopic follow-up period was 13 ± 9 months. Thirty-five superimposed thrombi still remained at follow-up, and the predominant thrombus color changed from red (56%) at baseline to pinkish-white (83%) at follow-up. The healing rate increased according to the angioscopic follow-up period (23% at ≤12 months vs. 55% at >12 months, $p = 0.044$). The %DS at the healed plaque increased from baseline to follow-up (12.3 ± 5.8% vs. 22.7 ± 11.6%, respectively; $p = 0.0004$). The serum CRP level in patients with healed plaques ($n = 10$) was lower than that in those without healed plaques ($n = 19$; 0.07 ± 0.03 mg/dl vs. 0.15 ± 0.11 mg/dl, respectively; $p = 0.007$).

CONCLUSIONS The present study demonstrated that: 1) ruptured plaques in nonculprit lesions tend to heal slowly with a progression of angiographic stenosis; and 2) the serum CRP level might reflect the disease activity of the plaque ruptures. (J Am Coll Cardiol 2005;45:652–8) © 2005 by the American College of Cardiology Foundation

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METHODS Forty-eight thror
identified by ang
quantitative coro
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Vol. 55, No. 15, 2010
ISSN 0735-1097/10/$36.00
doi:10.1016/j.jacc.2009.07.078

Coronary Artery Disease

The Dynamic Nature of Coronary Artery Lesion Morphology Assessed by Serial Virtual Histology Intravascular Ultrasound Tissue Characterization

Takashi Kubo, MD, PhD,* Akiko Maehara, MD,* Gary S. Mintz, MD,* Hiroshi Doi, MD, PhD,* Kenichi Tsujita, MD, PhD,* So-Yeon Choi, MD, PhD,* Osamu Katoh, MD,† Kenya Nasu, MD,† Andreas Koenig, MD,‡ Michael Pieper, MD,§ Jason H. Rogers, MD,‖ William Wijns, MD,¶ Dirk Böse, MD,# M. Pauliina Margolis, MD, PhD,** Jeffrey W. Moses, MD,* Gregg W. Stone, MD,* Martin B. Leon, MD*

New York, New York; Aichi, Japan; Munich and Essen, Germany; Kreuzlingen, Switzerland; Sacramento and San Diego, California; and Aalst, Belgium

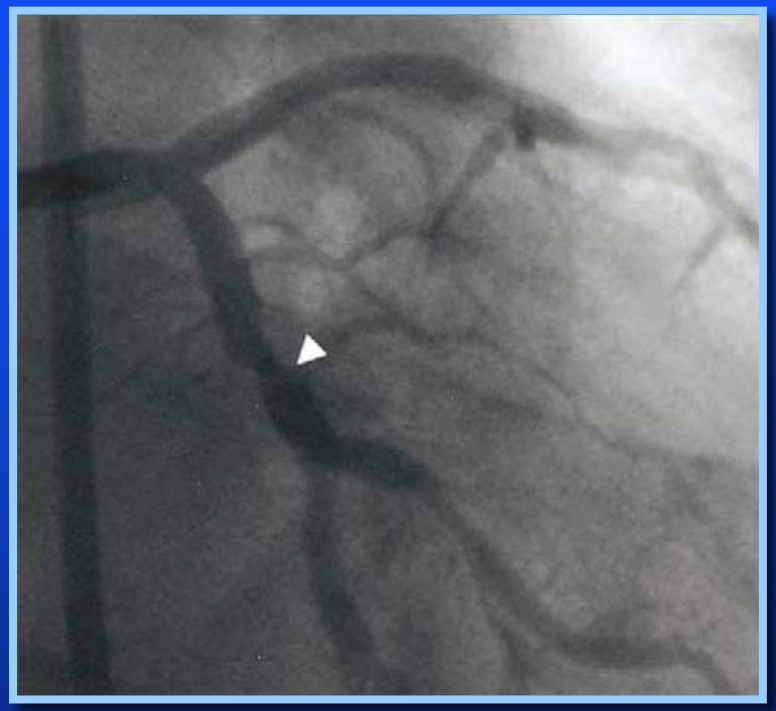
Objectives We used virtual histology intravascular ultrasound (VH-IVUS) to investigate the natural history of coronary artery lesion morphology.

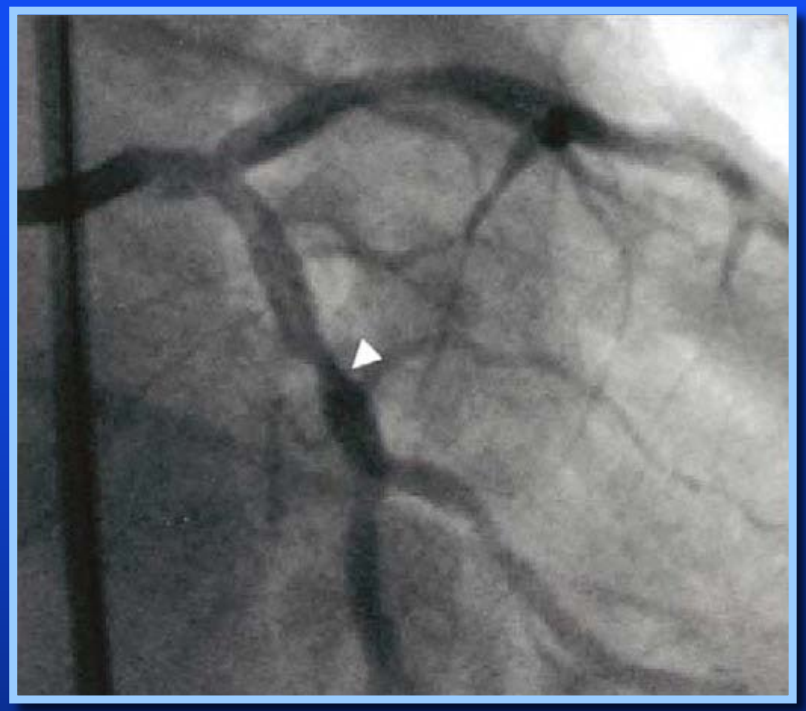
Background Plaque stability is related to its histological composition.

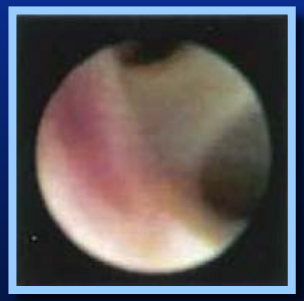
Methods We performed serial (baseline and 12-month follow-up) VH-IVUS studies and examined 216 nonculprit lesions (plaque burden ≥40%) in 99 patients. Lesions were classified into pathological intimal thickening (PIT), VH-IVUS–derived thin-capped fibroatheroma (VH-TCFA), thick-capped fibroatheroma (ThCFA), fibrotic plaque, and fibrocalcific plaque.

Results At baseline, 20 lesions were VH-TCFAs; during follow-up, 15 (75%) VH-TCFAs "healed," 13 became ThCFAs, 2

Healing of Nonculprit Plaque in Acute Coronary Syndrome

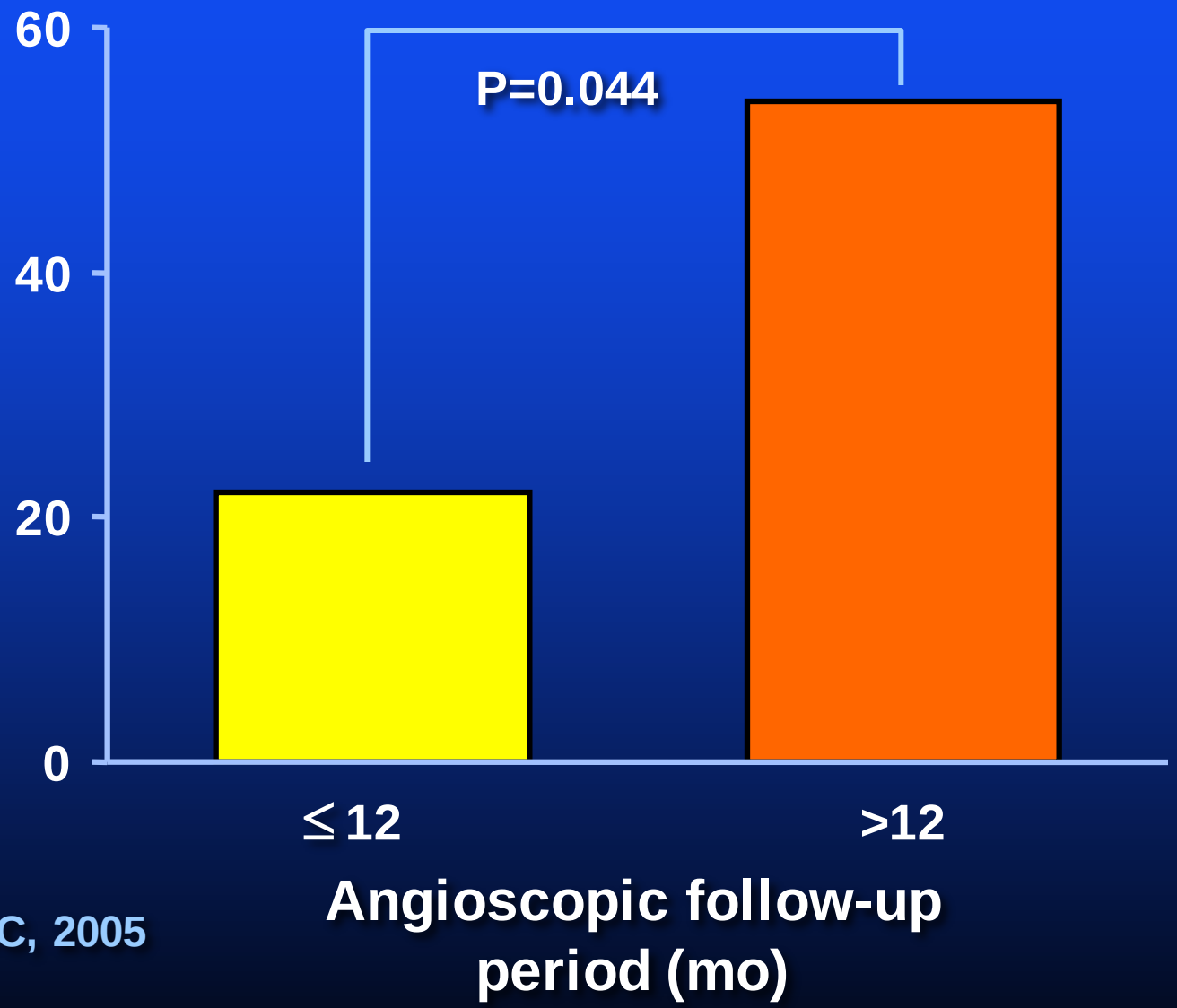






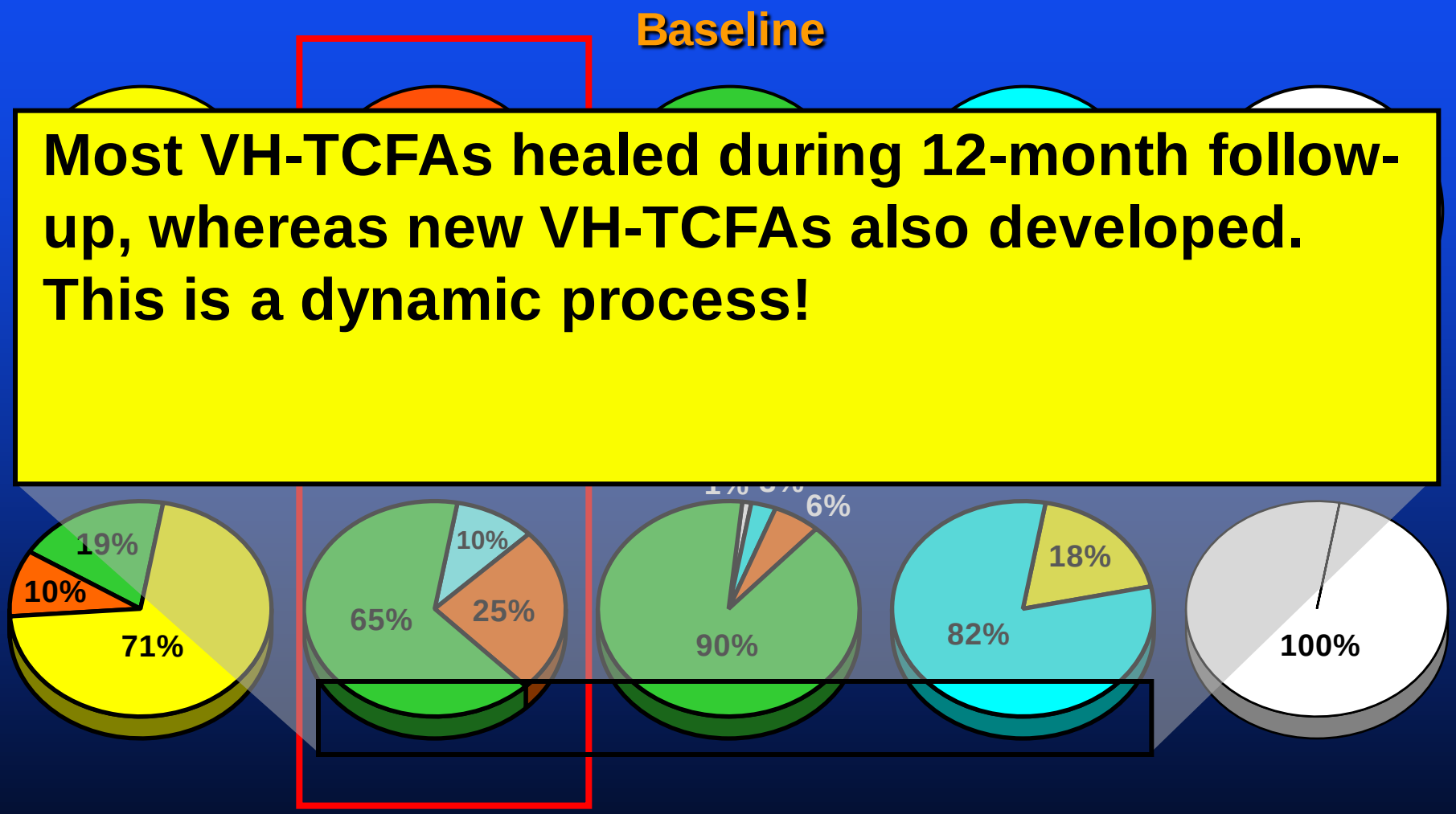
Takano et al: JACC, 2005

Relationship Between the Angioscopic Follow-Up Period and Healing Rate of the Nonculprit Ruptured Plaques



Takano et al: JACC, 2005

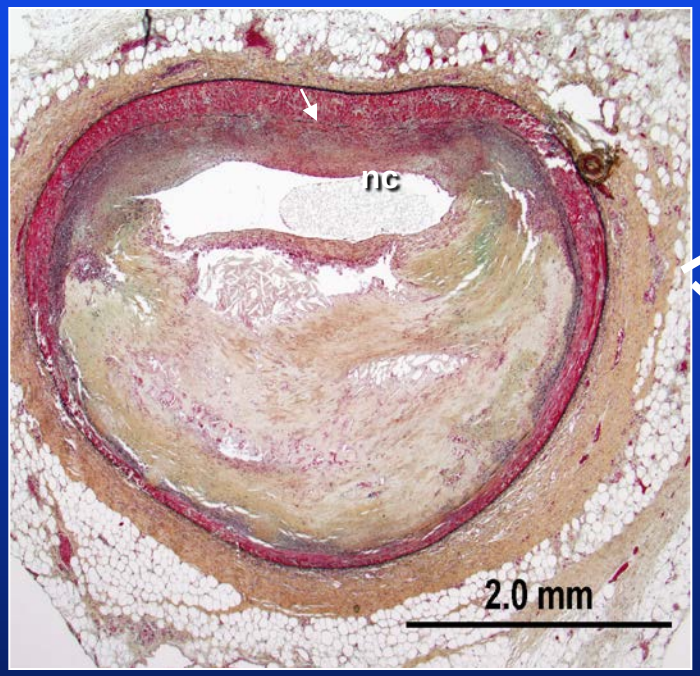
Changes in Plaque Characteristics Assessed by VH-IVUS Between Baseline and Follow-Up



Most VH-TCFAs healed during 12-month follow-up, whereas new VH-TCFAs also developed. This is a dynamic process!

Kubo T et al: JACC 55:1890, 2010

Do thin cap fibroatheromas (vulnerable plaques) go on and Rupture?

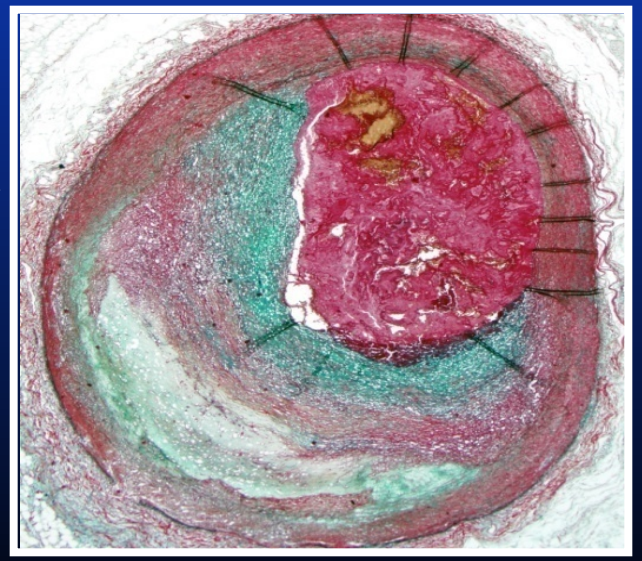


Thin cap fibroatheroma

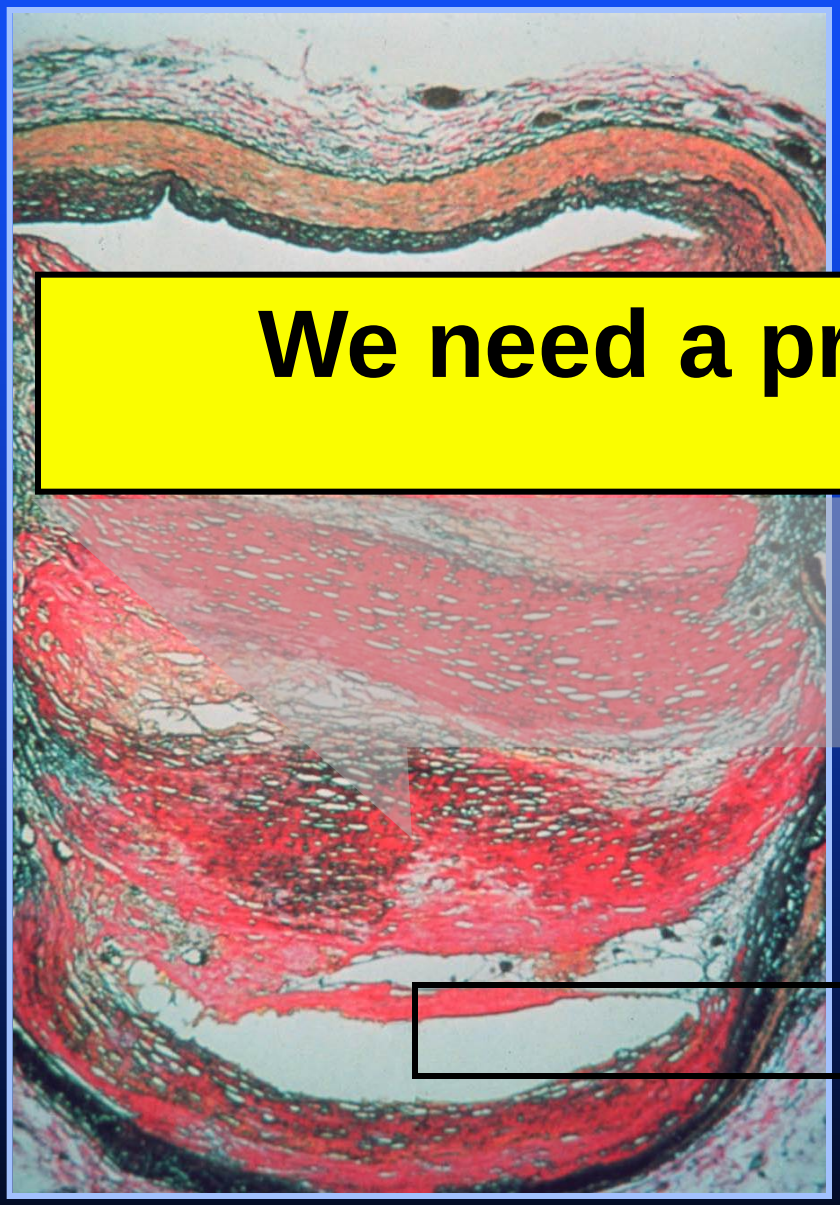
Plaque Rupture

?

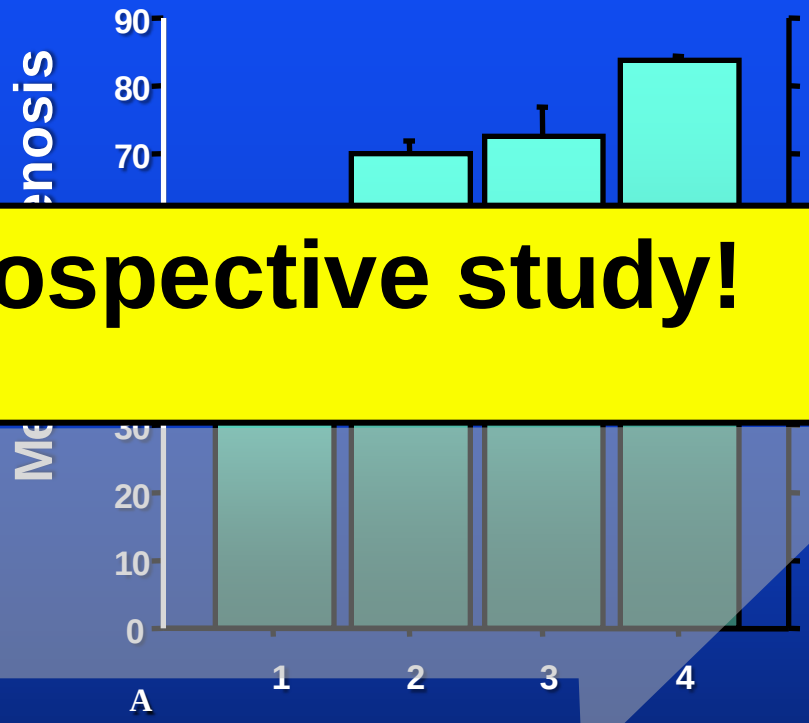
Plaque Erosion



Silent Ruptures and Erosions lead to Plaque Progression



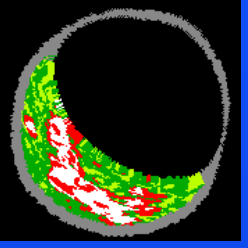
We need a prospective study!



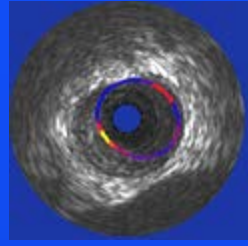
Number of prior ruptures, healed rupture sites

11% of plaque rupture are virgin

Sirius red with polarized light



The PROSPECT Trial



700 pts with ACS undergoing 1 or 2-vessel PCI followed by 3-vessel imaging

QCA of entire coronary tree

IVUS

Virtual histology

Palpography (n=~350)

Proximal 6-8 cm of each coronary artery

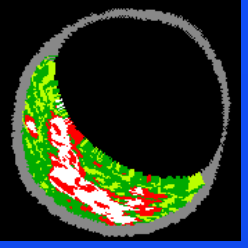
Meds rec
Aspirin
Plavix 1yr
Statin
Repeat biomarkers
@ 30 days, 6 months

F/U: Until there are 100 VP events

MSCT Substudy
N=50-100

Repeat imaging in pts with events

Sponsor: Abbott Vascular (Partner: Volcano)



PROSPECT: Imaging Summary

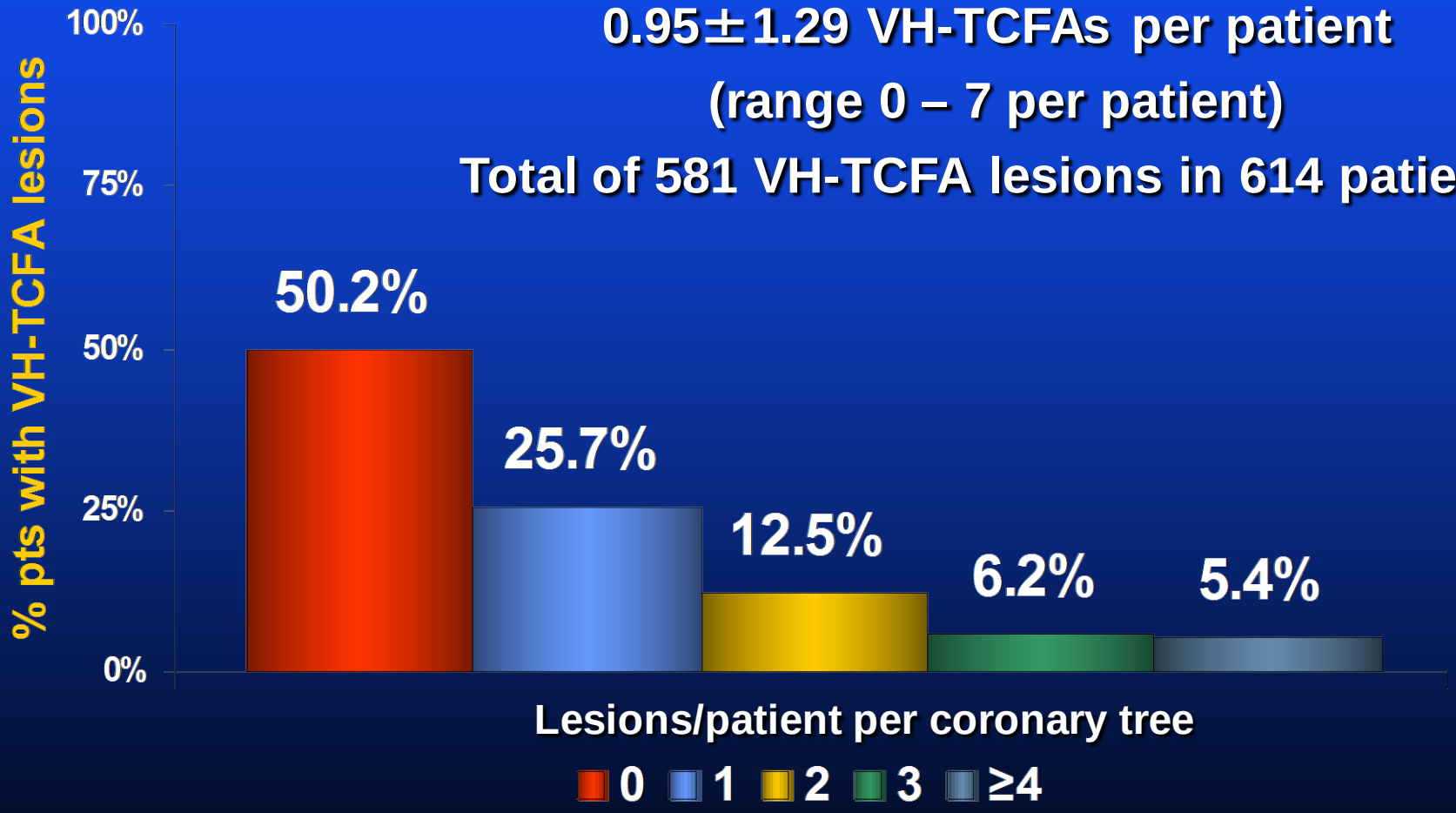
Per patient incidence of VH-TCFAs

49.8% of patients have ≥1 VH-TCFA

0.95±1.29 VH-TCFAs per patient

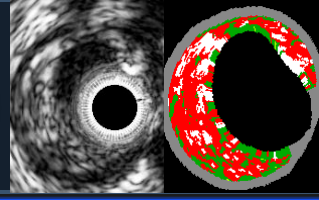
(range 0 – 7 per patient)

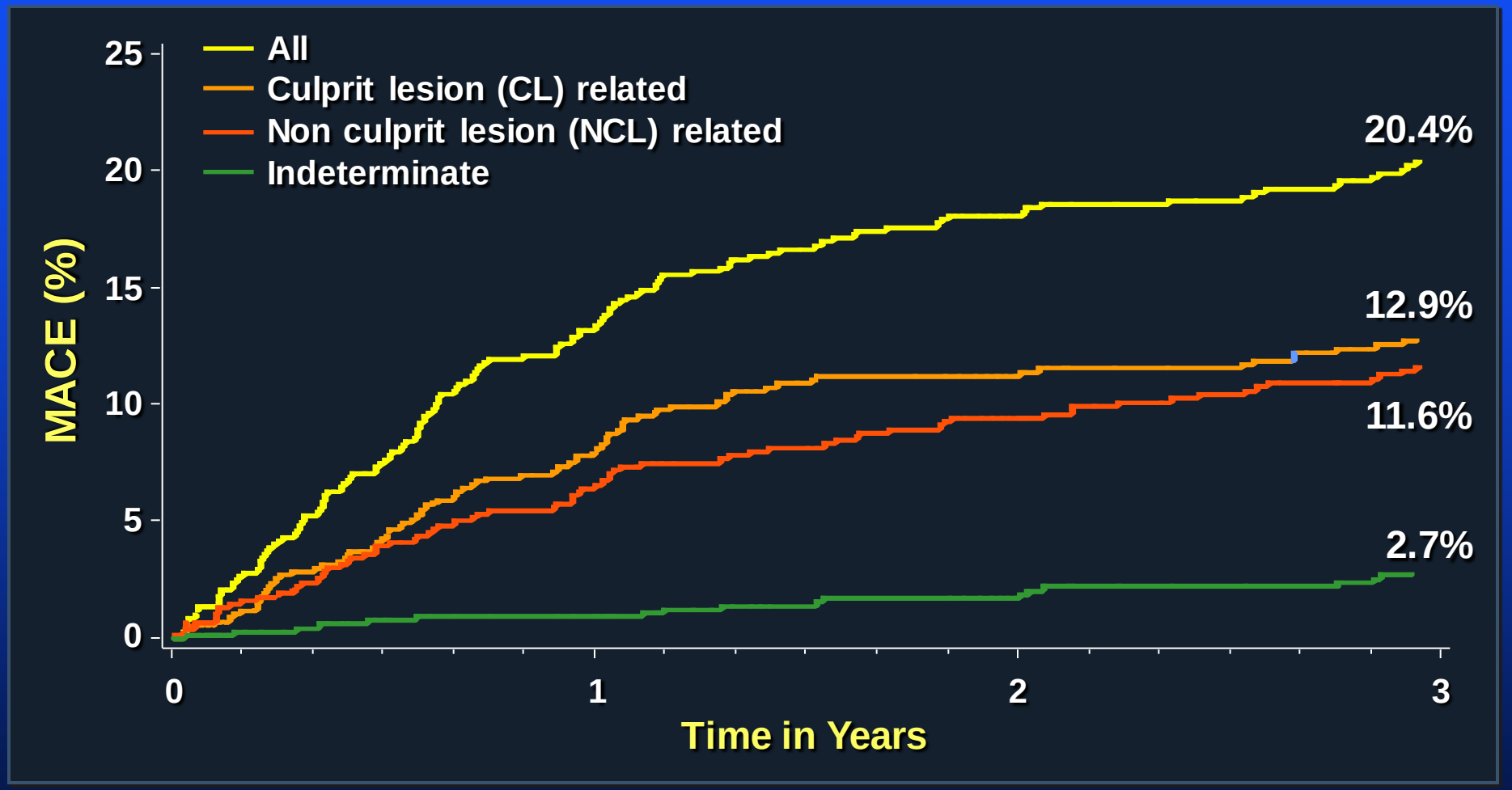
Total of 581 VH-TCFA lesions in 614 patients



mayo

PROSPECT: MACE (N=697)





Number at risk

ALL	697	557	506	480
CL related	697	590	543	518
NCL related	697	595	553	521
Indeterminate	697	634	604	583

MACE = cardiac death, cardiac arrest, MI, or rehospitalization for unstable or progressive angina

PROSPECT: MACE

3-year follow-up, hierarchical

	All	Culprit lesion related	Non culprit lesion related	Indeter-minate
Cardiac death	1.9% (12)	0.2% (1)	0% (0)	1.7% (11)
Cardiac arrest	0.3% (2)	0.3% (2)	0% (0)	0% (0)
MI (STEMI or NSTEMI)	2.7% (17)	1.7% (11)	1.0% (6)	0.2% (1)
Rehospitalization for unstable or progressive angina	15.4% (101)	10.4% (69)	10.7% (68)	0.8% (5)
Composite MACE	20.4% (132)	12.9% (83)	11.6% (74)	2.7% (17)
Cardiac death, arrest or MI	4.9% (31)	2.2% (14)	1.0% (6)	1.9% (12)

Rates are 3-yr Kaplan-Meier estimates (n of events)

PROSPECT: MACE

3-year follow-up, hierarchical

	All	Culprit lesion related	Non culprit lesion related	Indeter-minate
Cardiac death	1.9% (12)	0.2% (1)	0% (0)	1.7% (11)
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MI (STEMI or NSTEMI)	2.7% (17)	1.7% (11)	1.0% (6)	0.2% (1)
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Rates are 3-yr Kaplan-Meier estimates (n of events)

PROSPECT: Multivariable Correlates of Non-Culprit Lesion Related Events

Independent predictors of patient level events by Cox Proportional Hazards regression

Variable	HR [95% CI]	P value
Insulin dependent diabetes	3.32 [1.43, 7.72]	0.005
Prior PCI	2.03 [1.15, 3.59]	0.02

Variables entered into the model: age, gender, hypertension, insulin dependent diabetes, prior PCI, CRP at baseline, family history

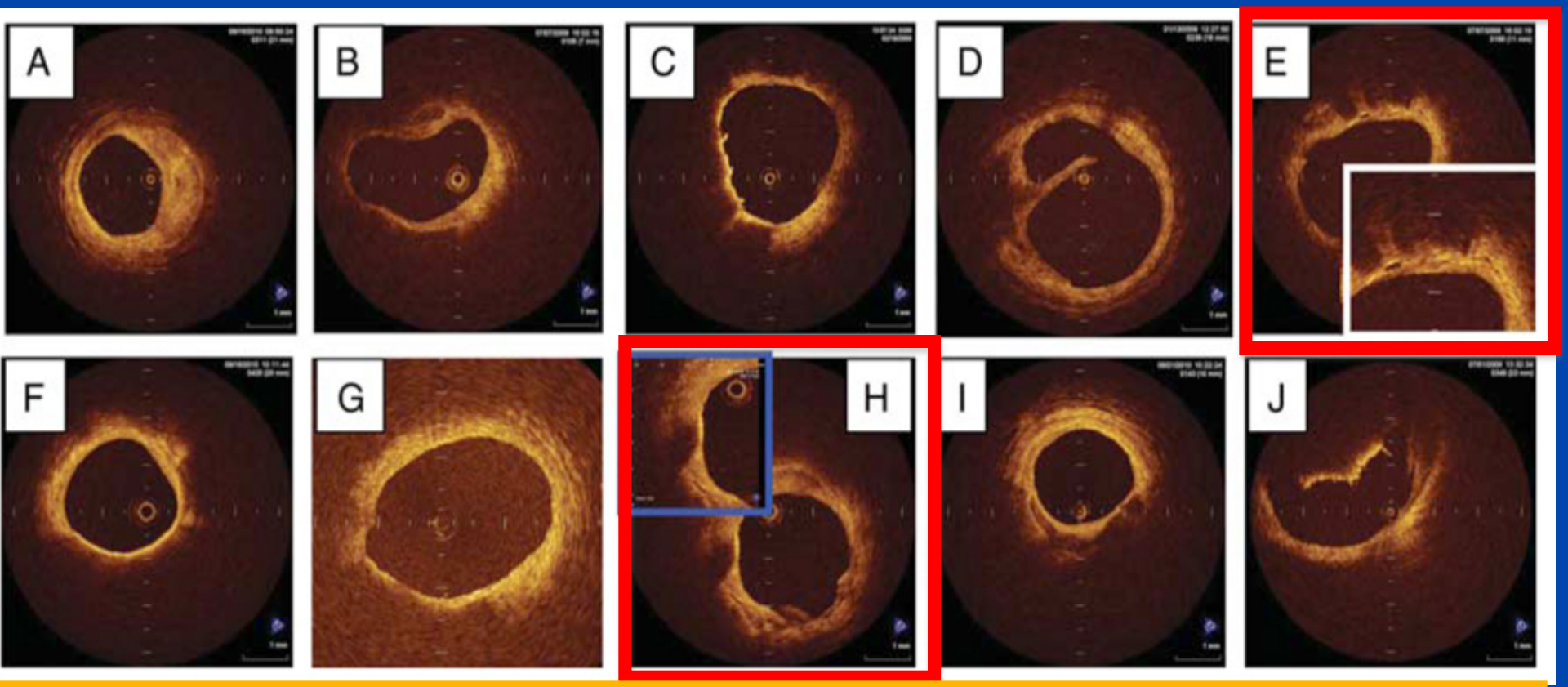
PROSPECT: Multivariable Correlates of Non-Culprit Lesion Related Events

Independent predictors of lesion level events by Cox Proportional Hazards regression

Variable	HR [95% CI]	P value
PB_{MLA} ≥70%	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
MLA ≤4.0 mm^2	3.21 [1.61, 6.42]	0.001

Variables entered: minimal lumen area (MLA), plaque burden at the MLA, external elastic membrane at the MLA, lesion length, distance from the coronary ostium to the MLA, remodeling index, thin-cap fibroatheroma, insulin-requiring diabetes and prior percutaneous coronary intervention

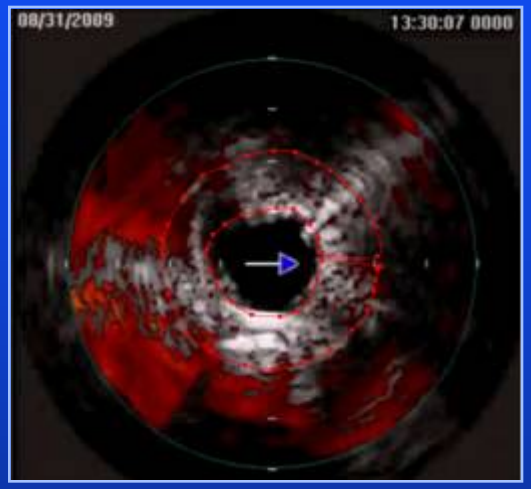
Ten Complex Optical Coherence Tomography-Based Characteristics of Non-Significant Coronary Plaques

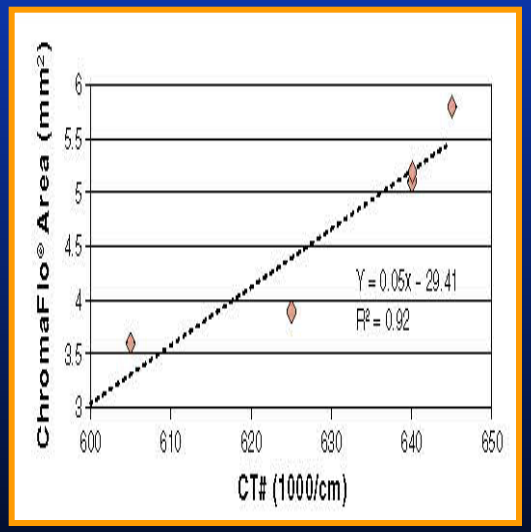


Conclusion: Optical coherence tomography-based complex characteristics of TCFA and microchannel were the potential predictors of subsequent progression of NSCPs in patients with CADs

CONCEPTS ON THE VERGE OF TRANSLATION

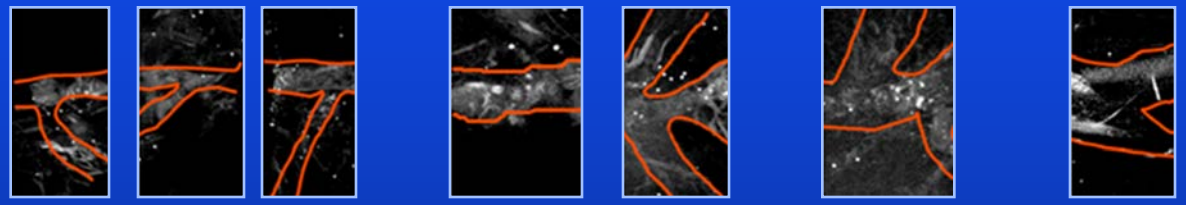
IVUS Detection of Vasa Vasorum Blood Flow Distribution in Coronary Artery Vessel Wall



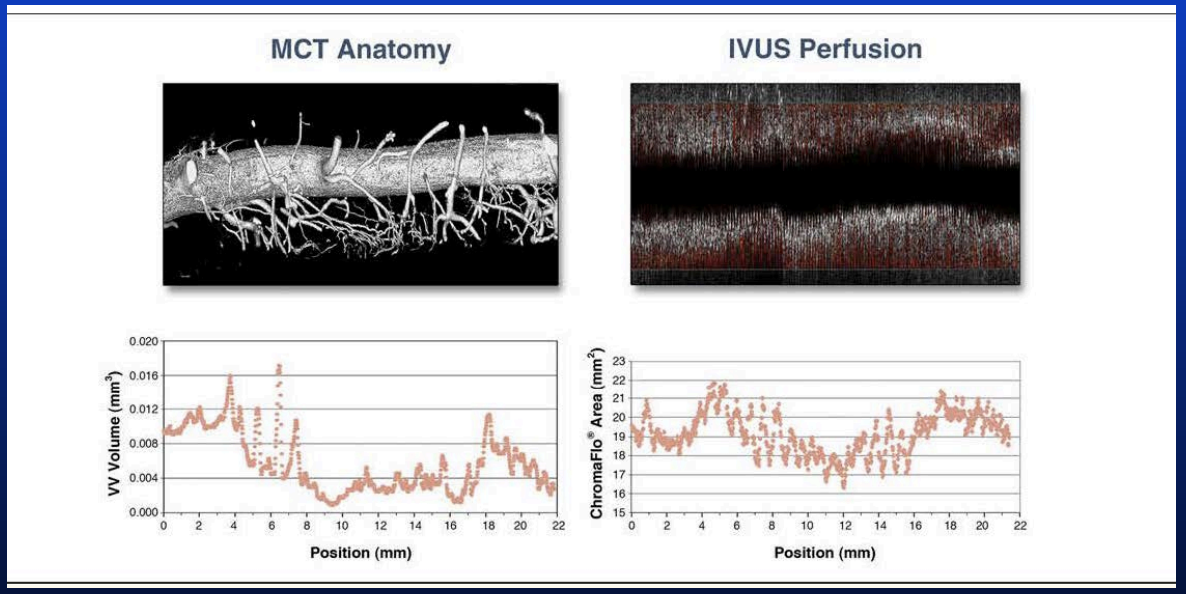


ChromaFlo®

CT



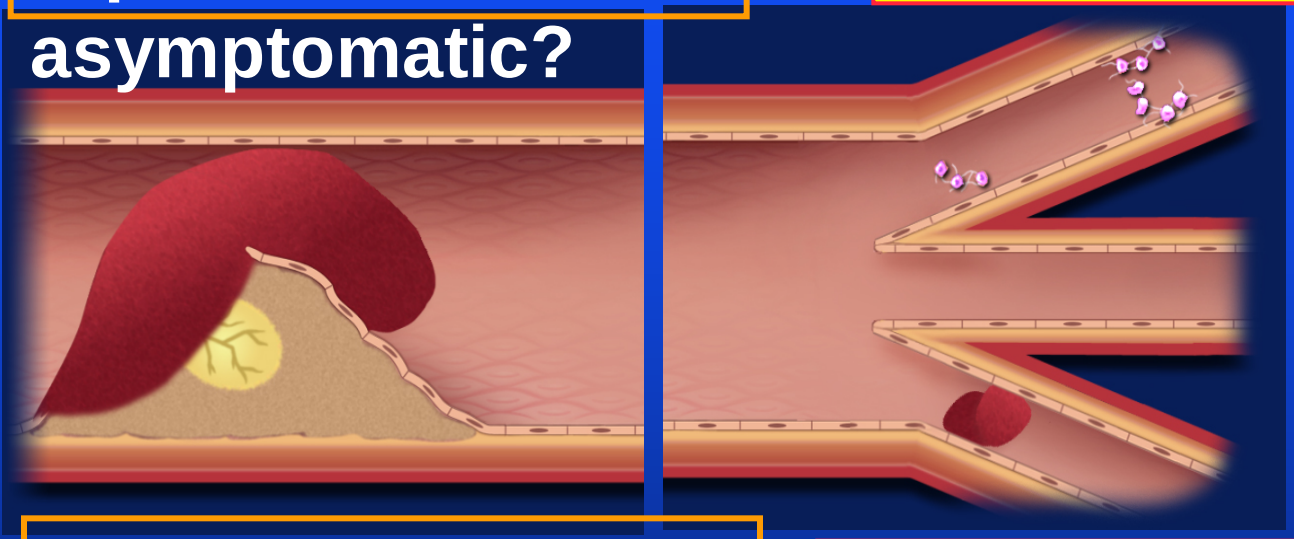
ChromaFlo® area (mm²)



CT# (1,000/mm²)

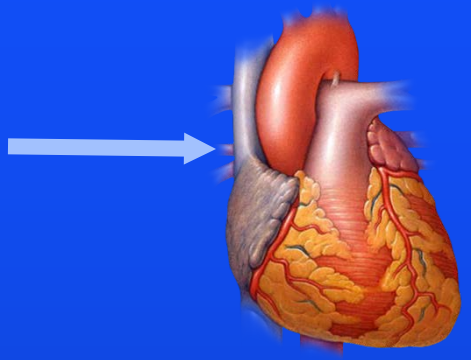
Moritz and Lerman JACC Img. 2012.

Why are most of the plaque ruptures asymptomatic?

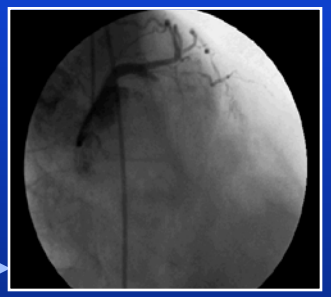


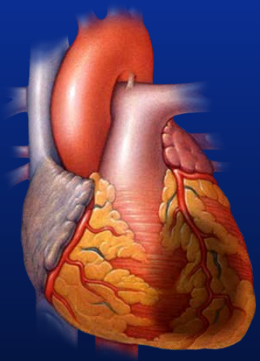
The presence of normal microcirculation serves as compensatory protective mechanism

Normal Microcirculation function



Abnormal Microcirculation function





Conclusions: These data suggest that the status of the coronary microcirculation plays a role in determining susceptibility toward periprocedural MI at the time of elective PCI. The microcirculation can predict subsequent risk of developing myocardial necrosis and may guide adjunctive prevention strategies.

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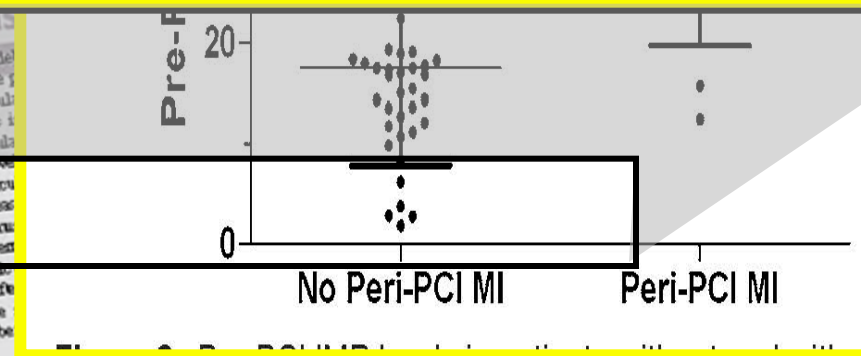
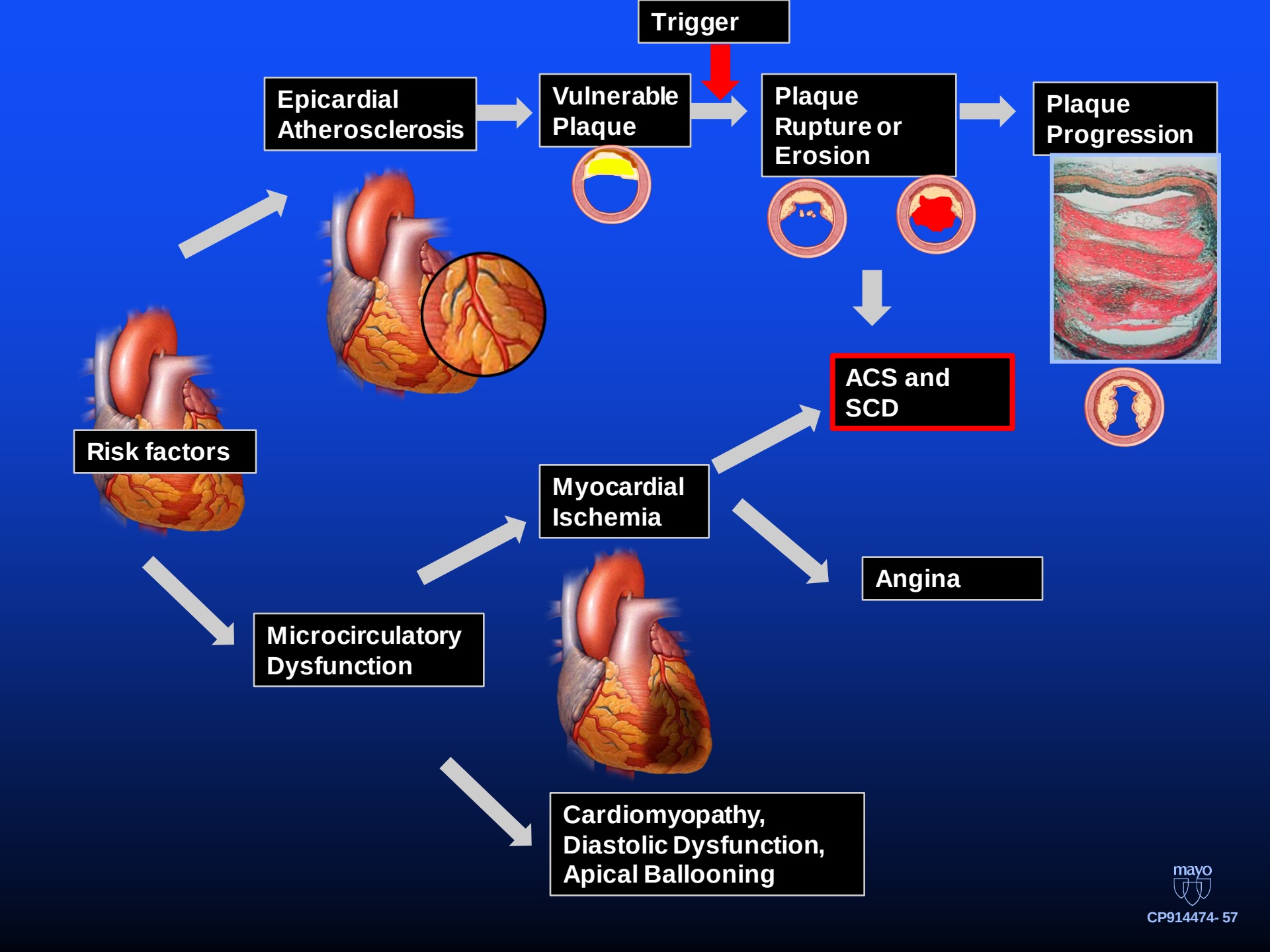
recruited.

A pressure-temperature sensor wire was used to measure IMR before PCI. Of the 50 patients studied, 10 had periprocedural MI.




Trigger
Epicardial Atherosclerosis
Vulnerable Plaque
Plaque Rupture or Erosion
Plaque Progression
ACS and SCD
Risk factors
Myocardial Ischemia
Angina
Microcirculatory Dysfunction
Cardiomyopathy, Diastolic Dysfunction, Apical Ballooning

Natural history of many bio medical and theories

Conclusion

- We make the assumption that we will be able to detect VP. After all, we are “smart” people, and a lot of money and time is being spent on this problem.

- The successful technique is the one that will predict events, not just correlate with pathology. None of the techniques that I have discussed is “there” yet.