Angioplasty Summit, Seoul, Korea 2007

Treatment Strategies Based on Plaque Composition and Type by VH IVUS

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VP of Scientific Affairs and Medical Director, Volcano Corp.

Room for Improvement?

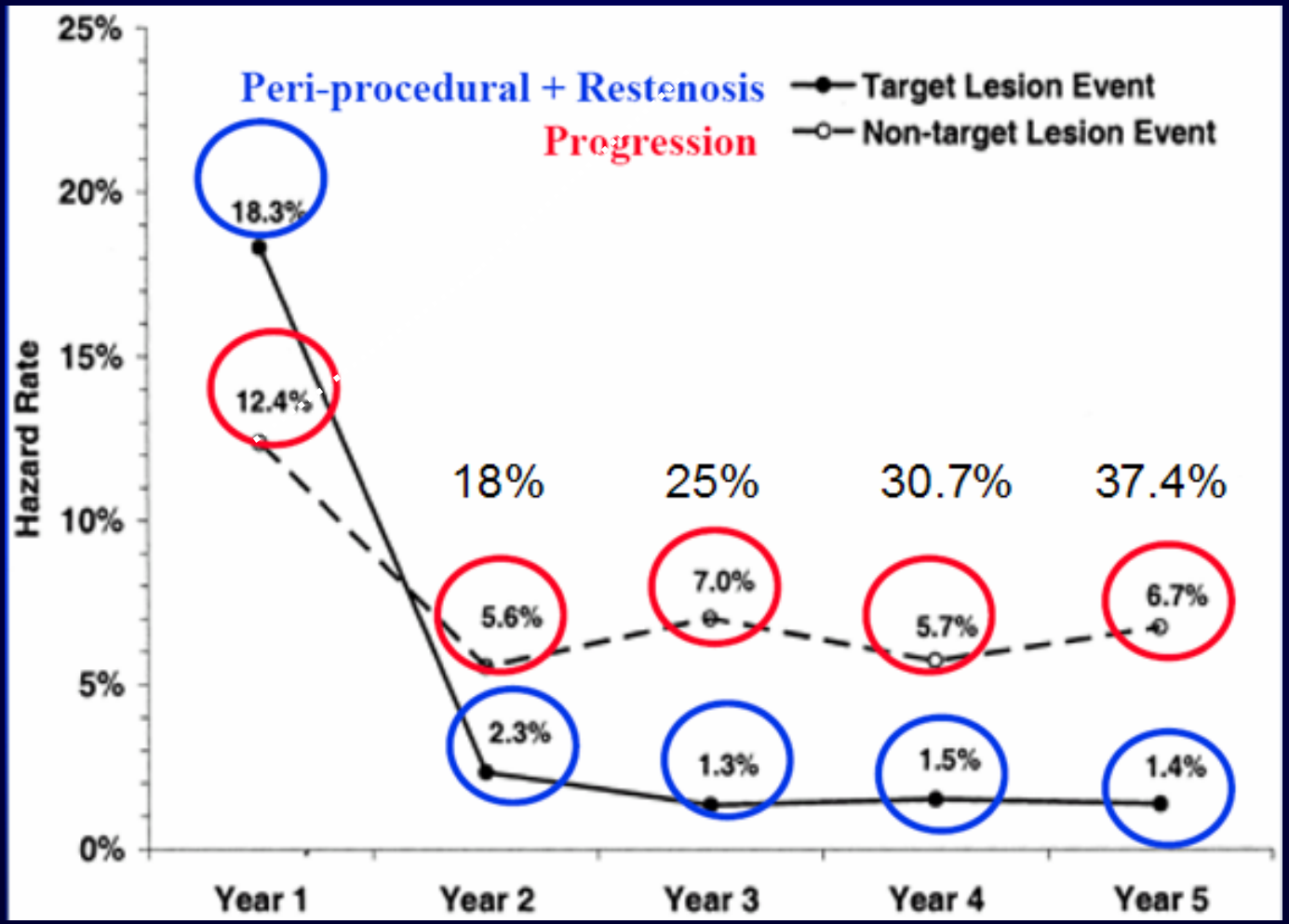
- Even during the DES era
  - Room for improvement when treating
    - Bifurcation lesions
    - Thrombotic ACS lesions
    - Ostial lesions
    - Complex lesions
  - side branch closures, plaque shift, distal embolization, acute culprit vessel closures, dissections, stent malapposition, restenosis, and LST

- Depending on patient population, coronary mortality or major cardiac event rate is still over 20 % at 2.5 years even with currently recommended systemic medication
- Non-target lesion events, unrelated to DES, and target vessel failure in 5 years is still close to 40%
- MSCT demonstrates non-invasively in increasing numbers the magnitude of angiographically silent atherosclerosis which can not be ignored anymore
  - Which lesions could be left alone and treated with systemic therapy and which ones need to be treated focally?

Optimal PCI

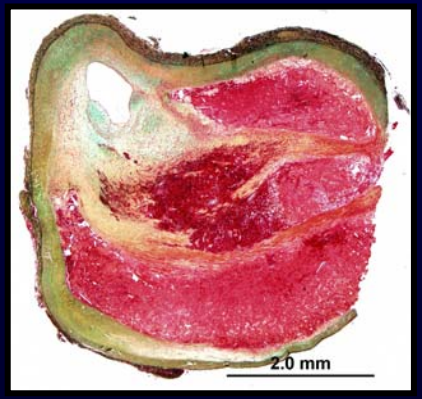
5-year outcomes after stenting: HCRI database

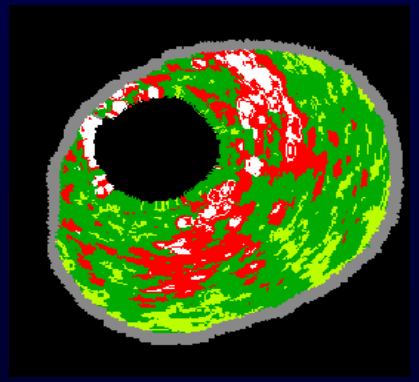
Cutlip et al. *Circulation* 2004; 110: 1226–1230.



Could Necrotic Core be the Determinant Factor we should target our attention?

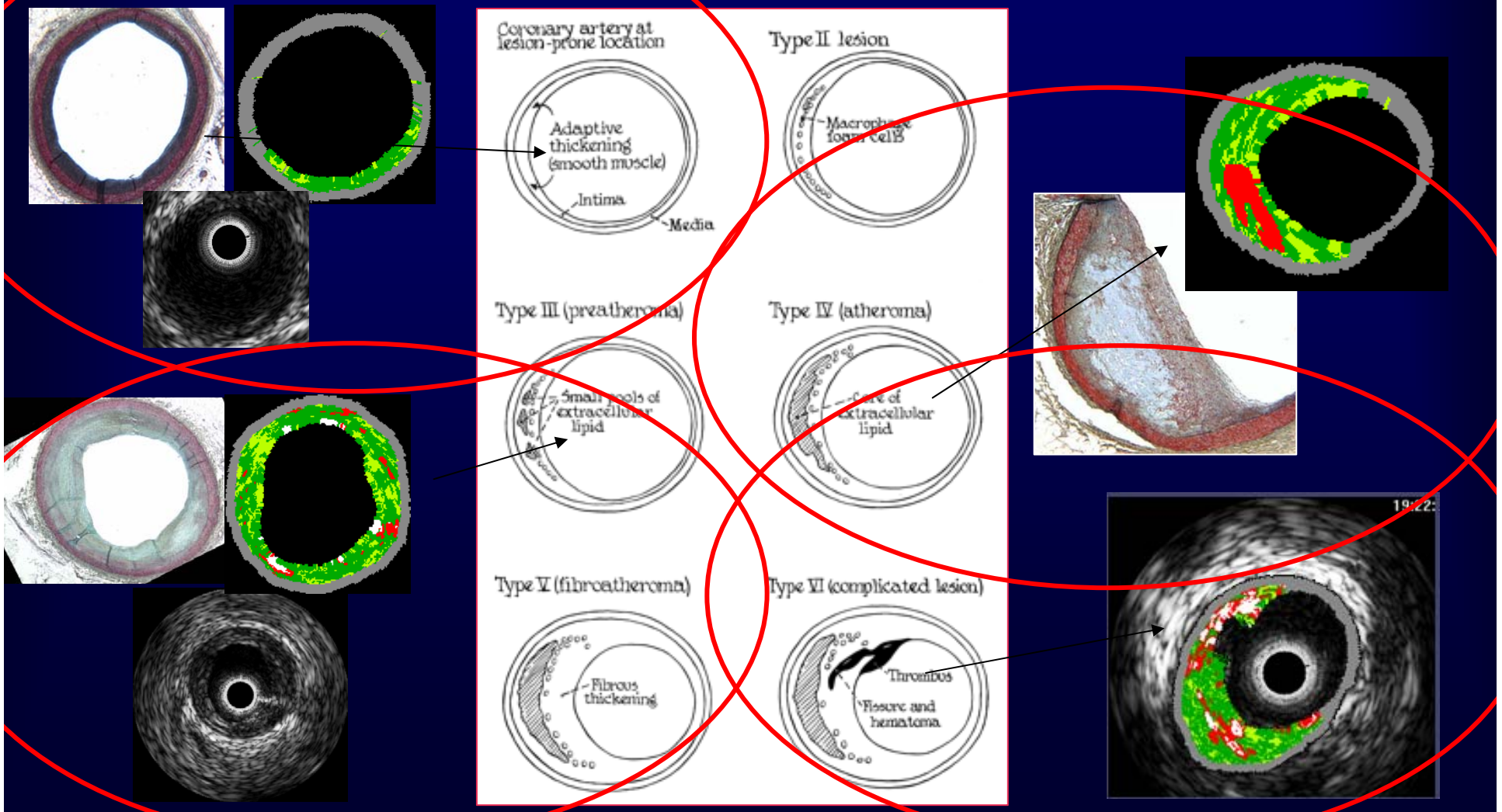
- What is necrotic core?
  - It is plaque composition filled with intracellular lipid, often inflammatory cells, and has no matrix (structure), think about bad “lasagna”
  - It is the predominant composition with or without Ca found in plaques which cause a SCD and a thrombotic event





Classic Stary Classification

Stary HC. The histological **classification** of atherosclerotic lesions in human coronary arteries. In: Fuster V, Ross R, Topol E, eds. *Atherosclerosis and Coronary Artery Disease*.



CAPITAL: VH IVUS Accuracy to Identify Different Plaque Types

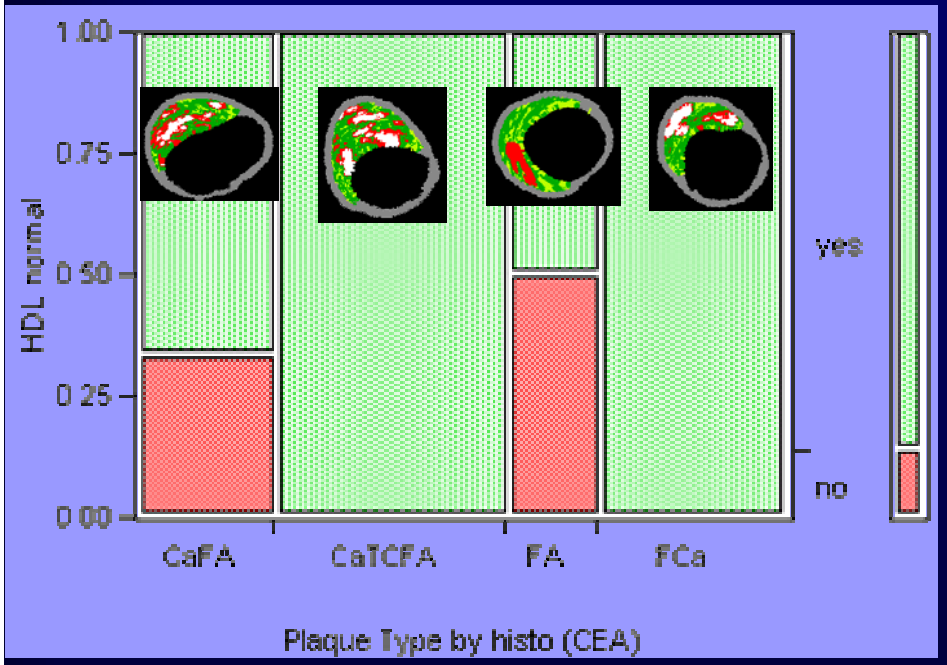
Plaque Type by VH IVUS	Predictive accuracy	Sensitivity	Specificity
CaFA	72.4%	32.5%	93.0%
CaTCFA	96.1%	90.0%	97.1%
FA	85.9%	54.1%	96.9%
FCa	85.5%	87.1%	84.5%
PIT	83.4%	88.5%	82.0%
TCFA	99.4%	75.0%	100%

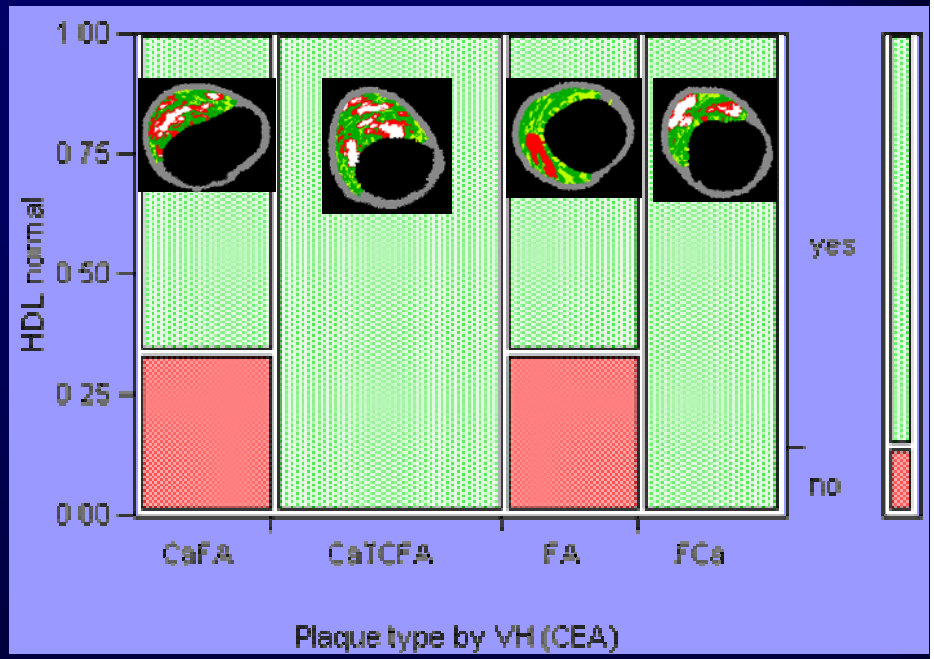
VH IVUS and the Efficacy of Systemic Therapy

- Recent data suggests strongly that the target for systemic therapy seems to be rather early stage plaque progression
- Only 11% of SCD are due to “virgin” plaque rupture (Virmani et al 2002)
- Once plaque growth has reached the level where it is more dependent on repeated plaque ruptures, lipid profile seems to play a less significant role

The Correlation between Plaque Type by Histology and VH IVUS and HDL

(14 lesions, total n of matched sites = 154, plaque type by he worst plaque type within the lesion)





By both Histology and VH IVUS, abnormal levels of HDL were associated with calcified or non-calcified fibroatheromas (FA), the advanced but less vulnerable type of plaques based on post mortem data from coronaries

Early stage Disease, Coronary Endothelial Function, ACC 2006

mayo

CP922798- 2

Diagnostic angiography

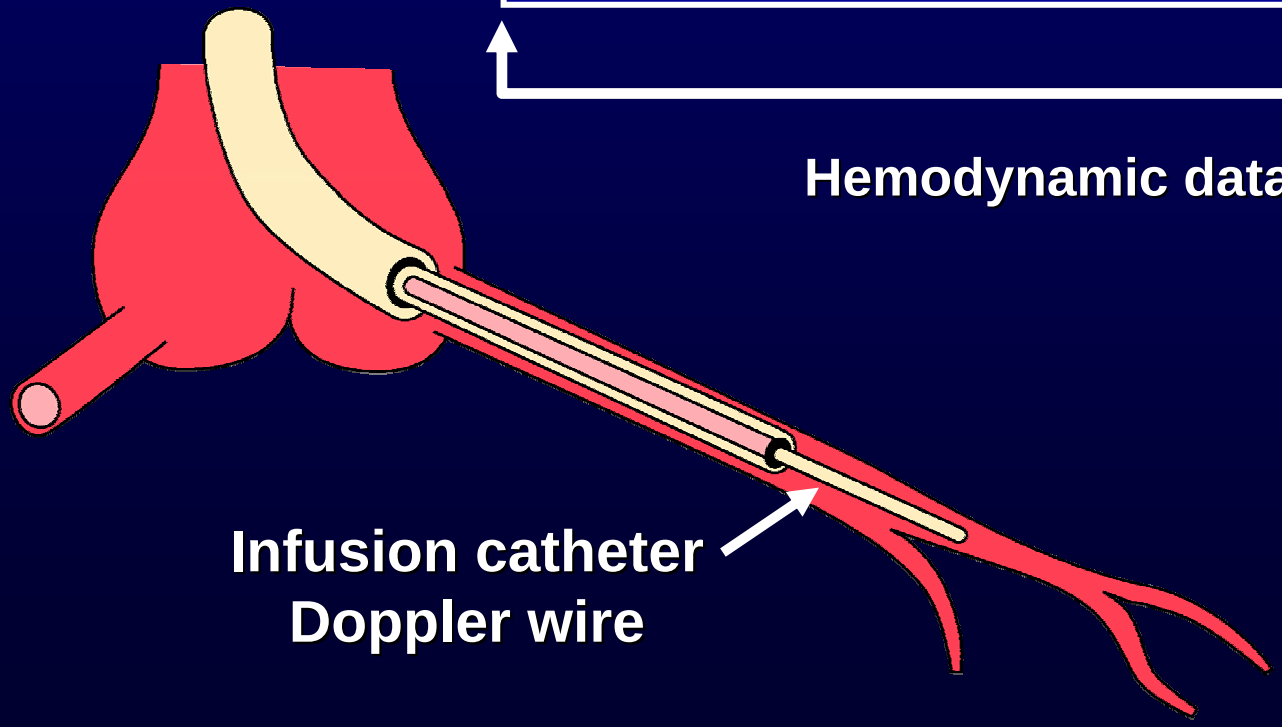
Adenosine IC

Acetylcholine

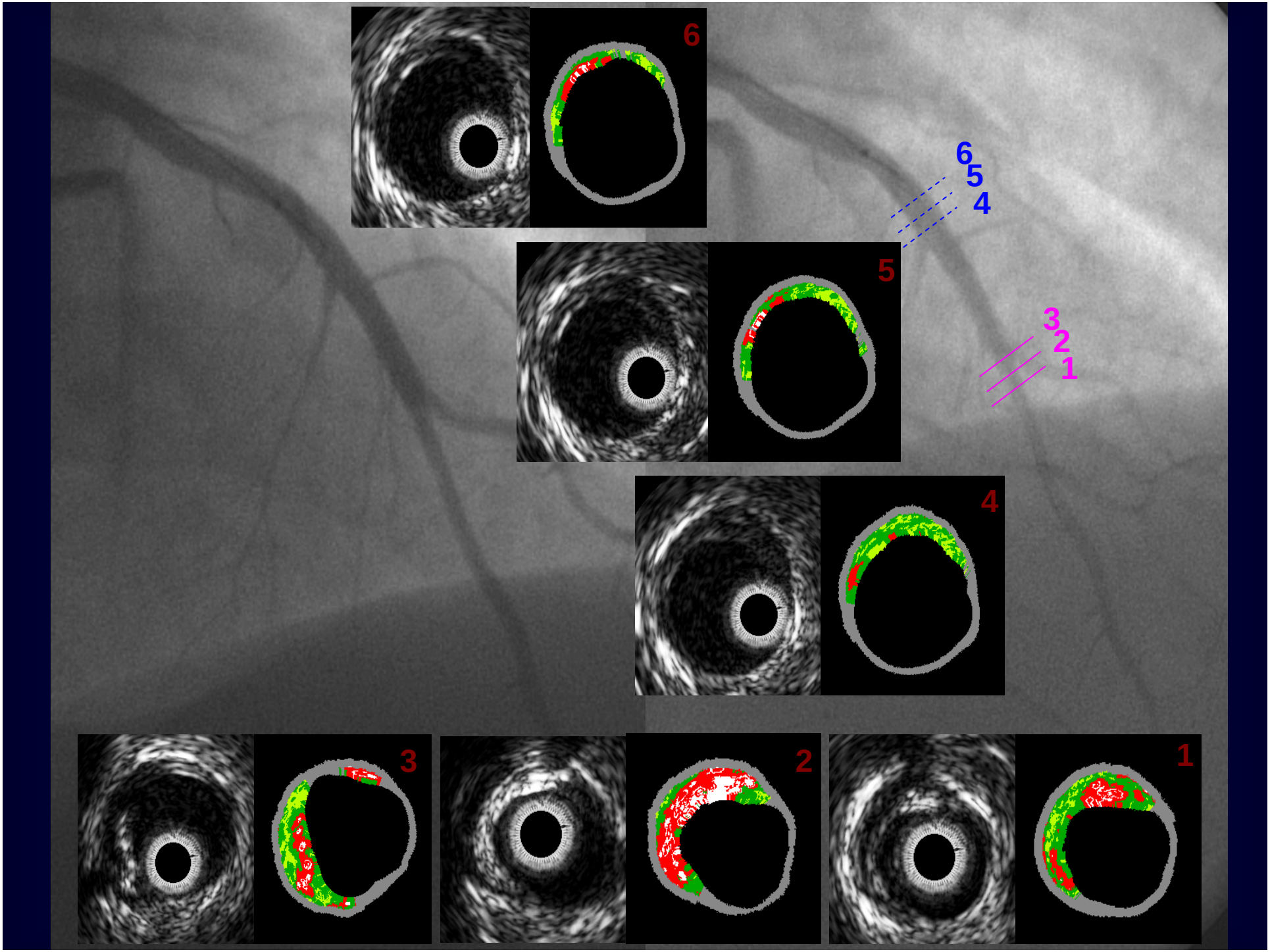
NTG

Hemodynamic data

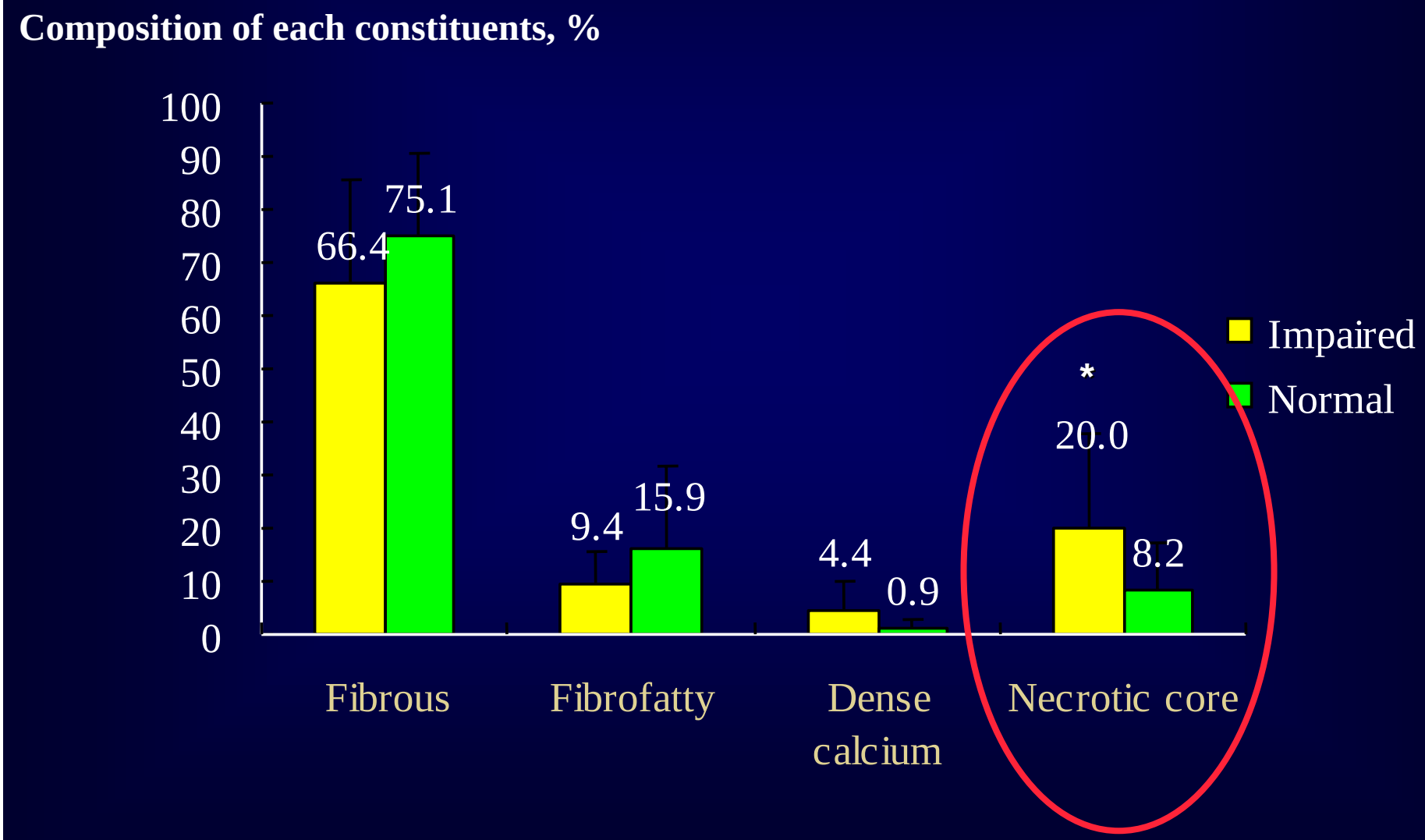
IVUS / VH



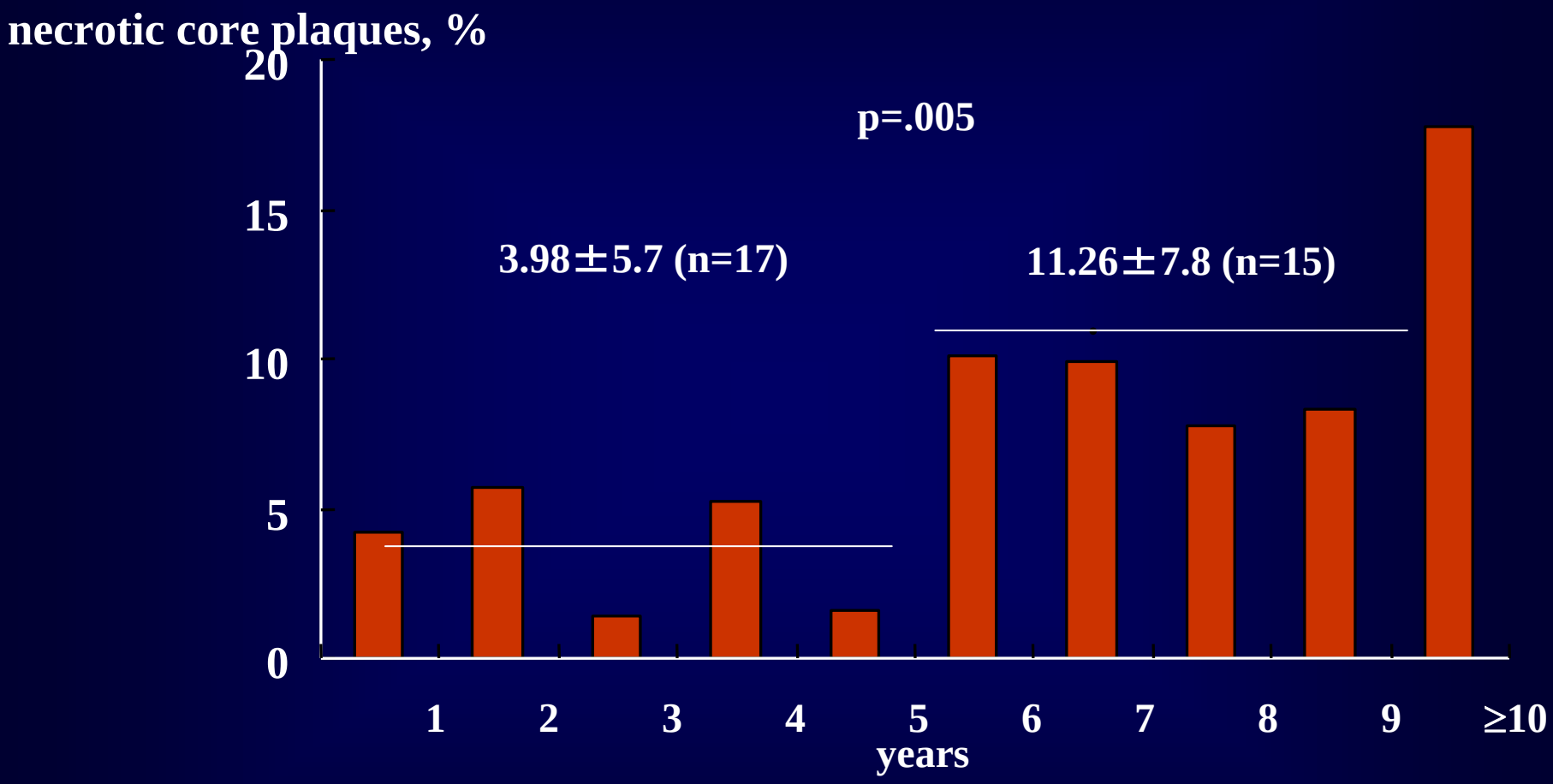
Infusion catheter
Doppler wire


6
5
4
3
2
1

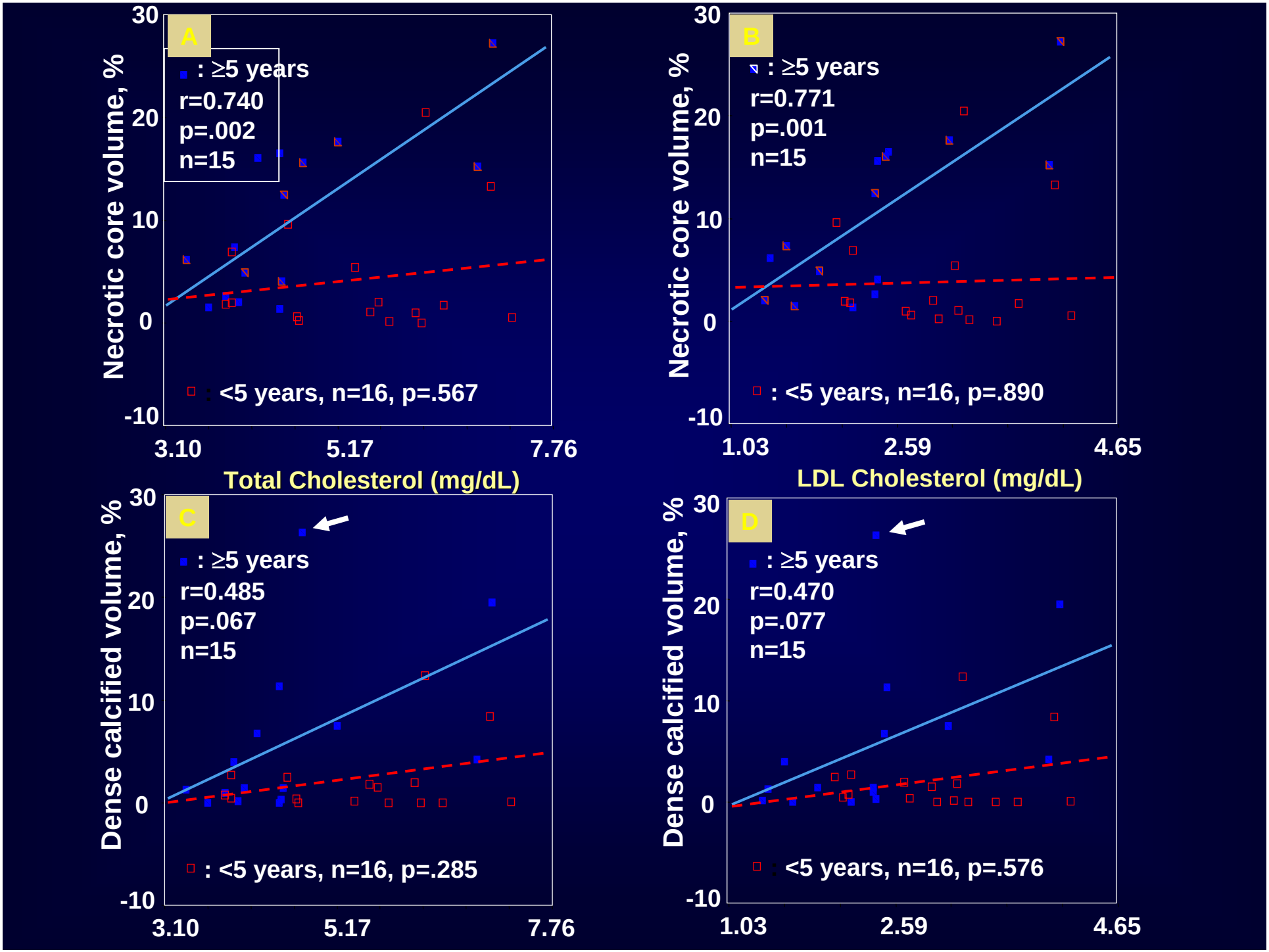
Percent each plaque constituents between the segments with and without impaired endothelial function



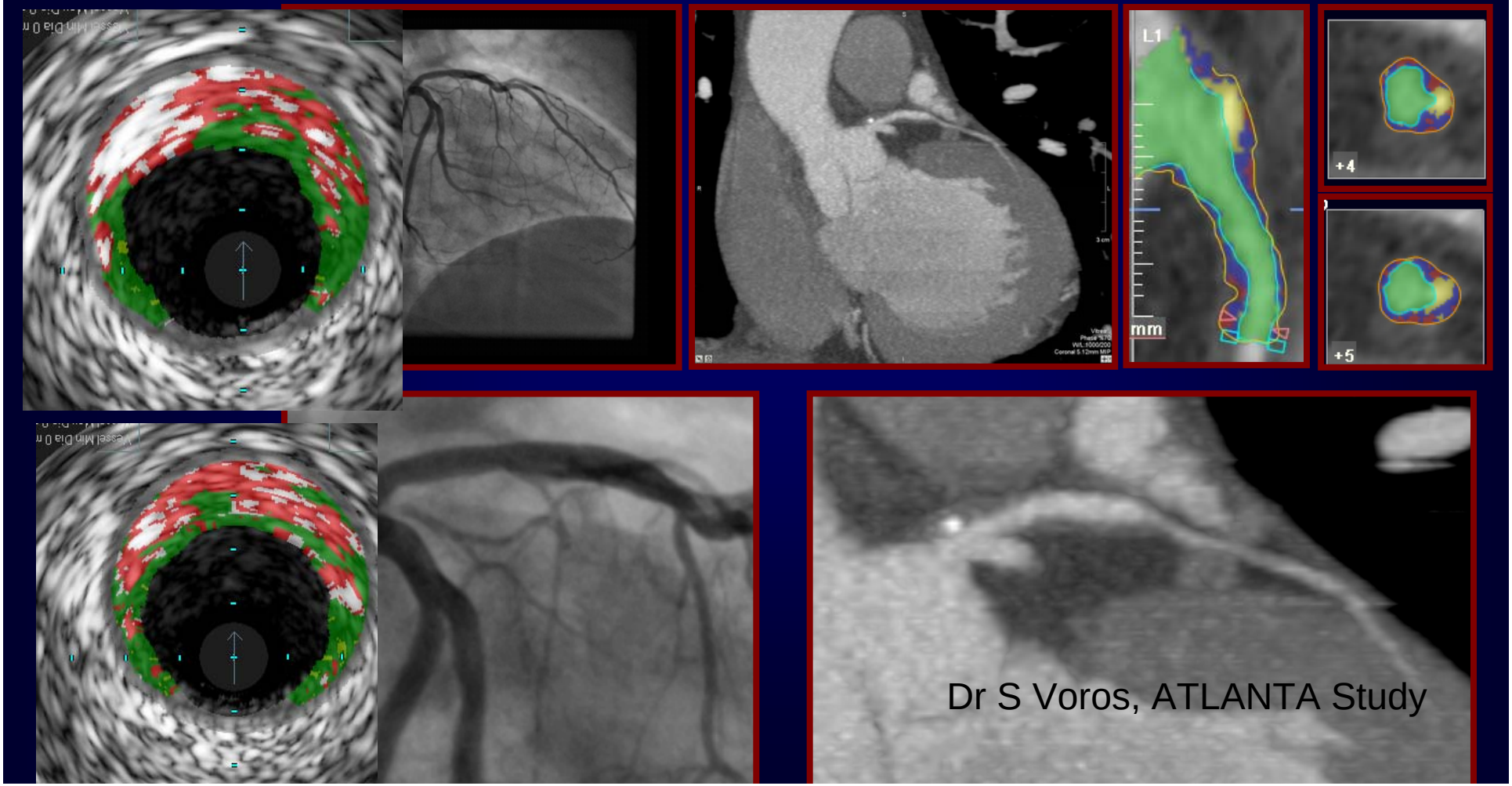
Necrotic plaque post cardiac transplantation



Total cholesterol (mmol/L)	5.41±1.09 (n=17)	4.60±1.11 (n=14)
LDL cholesterol (mmol/L)	2.95±0.70 (n=17)	2.38±0.85 (n=14)


A
: ≥5 years
r=0.740
p=.002
n=15
: <5 years, n=16, p=.567
Necrotic core volume, %
30
20
10
0
-10
3.10
5.17
7.76
Total Cholesterol (mg/dL)
B
: ≥5 years
r=0.771
p=.001
n=15
: <5 years, n=16, p=.890
Necrotic core volume, %
1.03
2.59
4.65
LDL Cholesterol (mg/dL)
C
: ≥5 years
r=0.485
p=.067
n=15
: <5 years, n=16, p=.285
Dense calcified volume, %
D
: ≥5 years
r=0.470
p=.077
n=15
: <5 years, n=16, p=.576
Dense calcified volume, %

FFR and grayscale IVUS can help to identify the MSCT detected, angiographically silent lesions which need not just systemic, but also focal therapy, the predictive accuracy of VH to improve the diagnostic power is currently under investigation



CEA

Ca or ology and VH IVUS
M Agreement

#5
Angio
Ca+

#17
Angio
Ca-

#32
Angio

#7
Angio
Ca-

#33
Angio
Ca+

#10
Angio
Ca+

#13
Angio
Ca-

VH IVUS and the Reduction of Coronary Mortality by effective systemic therapy and focal treatment of high-risk, non-ischemic lesions

- Current data supports the correlation between abnormal lipid profile and early stage atherosclerosis and the accuracy in VH IVUS to assess treatment effect
- Long term, prospective clinical trials are under way (IBIS 2)
- Capital data supports the accuracy of VH IVUS to detect also the more advanced atherosclerotic lesions which may need focal intervention

VH IVUS and the Efficacy of Focal Therapy

- Several prospective global, multicenter on-going clinical studies are currently assessing the predictive accuracy of VH IVUS to identify the focal features of high risk lesions to rupture
- All data so far indicates that VH IVUS based high risk lesions are ID CaTCFAs with or without previous plaque ruptures, with a large confluent necrotic core, positive re-modeling, and moderate plaque burden

Thin-cap Fibroatheroma Detection

Rodriguez-Granillo GA et al JACC 2005;46:2038

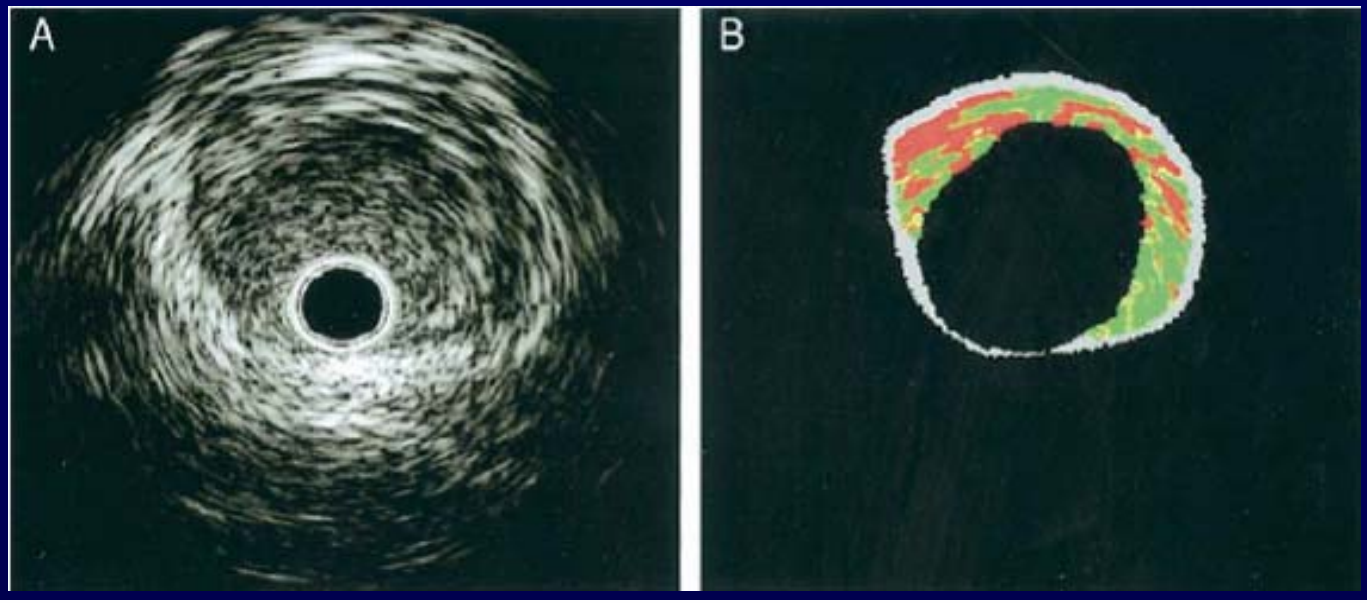


Table 2. Incidence and Characteristics of IDTCFA Lesions in Stable and ACS Patients

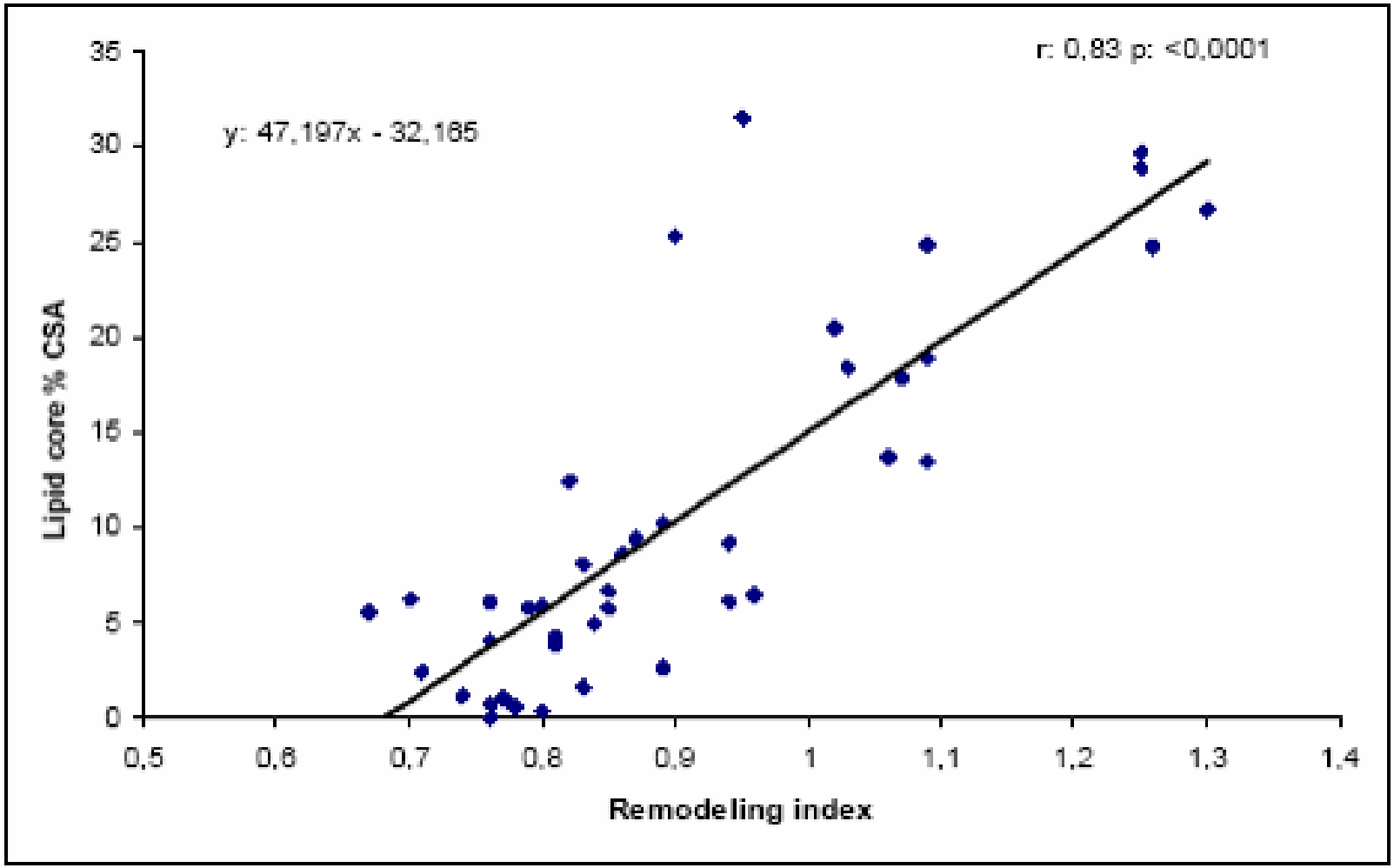
	Length of ROI	IDTCFA	IDTCFA/cm	% PAV	% NC	EI
Stable (n = 32)	35.41 ± 11.6	1.0 (0.0, 2.8)	0.2 (0.0, 0.7)	54.8 ± 6.0	18.1 ± 3.0	0.23 ± 0.1
ACS (n = 23)	33.90 ± 15.0	3.0 (0.0, 5.0)	0.7 (0.0, 1.3)	56.8 ± 7.4	19.7 ± 4.1	0.27 ± 0.2
p value	0.684	0.018	0.031	0.343	0.205	0.35

Continuous variables are presented as medians (25th, 75th percentile) or mean values ± SD when indicated.

ACS = acute coronary syndrome; EI = plaque eccentricity index (defined as minimum plaque thickness divided by maximum plaque thickness); IDTCFA = intravascular ultrasound-derived thin-cap fibroatheroma; % PAV = percent atheroma volume (defined as $EEM_{area} - lumen_{area}/EEM_{area} \times 100$, where EEM refers to external elastic membrane); ROI = region of interest; % NC = percent necrotic core of the cross-sectional area.

Plaque Composition and Coronary Remodelling

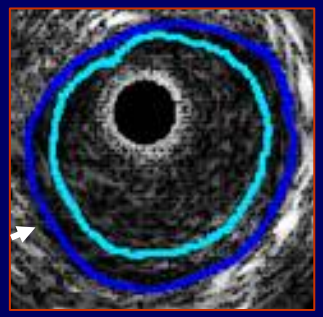
Rodriguez-Granillo GA et al. Heart 2005

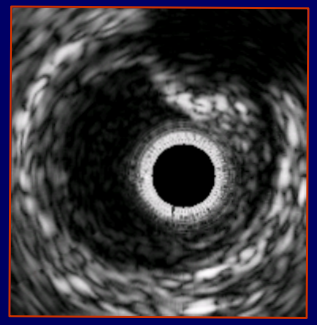


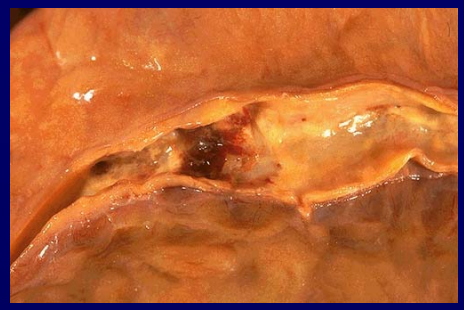
How Can Plaque Composition Guide Interventions Today

- Helps to find the “culprit of the culprit”
  - In both coronary and carotid vascular beds the site of the advanced FA is often proximal to the site of the min lumen cross sectional area (mLCSA)
  - In case of an ACS, intraluminal thrombus often obscure the angiographic view and the source for the thrombotic event can be difficult to find
  - Knowledge of plaque composition can help to have a better understanding of the possible risk of acute and long term procedural complications
    - Plaque shift
    - Distal embolization
    - LST

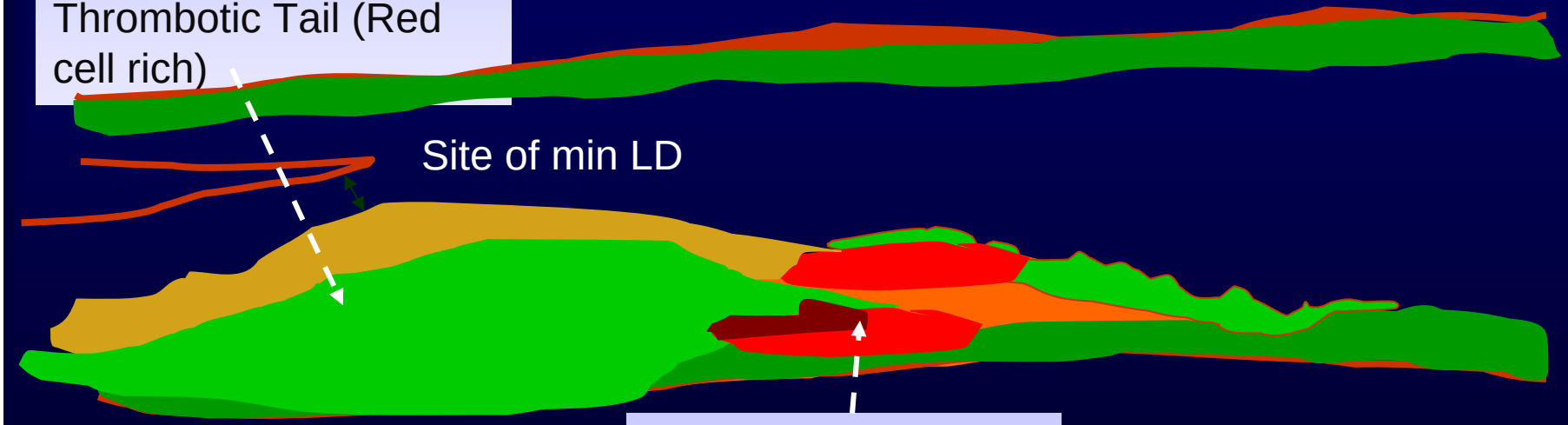
Rupture of an Eccentric ID TCFA and the Thrombotic Tails; Clinically Silent or Symptomatic







Fall Out of the problem Layers of distal Thrombotic Tail (Red cell rich)



Site of the problem Layers of healed plaque ruptures

R Virmani, CVPath and
P Margolis, Volcano Corp.

Prediction of High Risk Plaque of Distal Embolization after Percutaneous Coronary Intervention assessed by Virtual Histology Intravascular Ultrasound; A Virtual Histology IVUS Analysis from the PROSPECT Study

Tct 2006 Kaoru Tanaka, MD, PhD Cardiovascular Research Foundation

The mean distance between the MLA and NCmax was 6±10mm. Lumen and vessel areas, %Ca and %NC were greater at NCmax than MLA site (see Table). Importantly, highest risk FAs were present in 3.7% of the MLA and 6.5% of NC max (McNemars p<0.001). Of 18 highest risk FAs identified, only 10 (55%) appeared at the MLA site.

Comparison of plaque components at MLA and worst lesion

	Minimum lumen area site	Largest NC site	p value
MLA (mm^2)	6.43±3.77	7.74±4.34	<0.0001
VA (mm^2)	15.0±6.44	17.46±7.12	<0.0001
Remodeling Index	1.08±0.44	1.29±0.69	<0.0001
DC (%)	4.9±6.3	6.5±6.6	<0.0001
Fi (%)	56.5±11	54.5±10	0.0018
FF (%)	24.5±13.3	18.5±11.4	<0.0001
NC (%)	10.4±6.7	16.3±7.3	0.021

Conclusions: The highest risk FAs at non culprit sites in ACS pts are often found remote from the MLA site. VH-IVUS interrogation over long segments of the coronary arterial tree (not just at the most severe lesion) is necessary to uncover most high risk lesions.

CAPITAL Plaque type at the site of the min LCSA;

CaTCFA = 10

PIT = 8

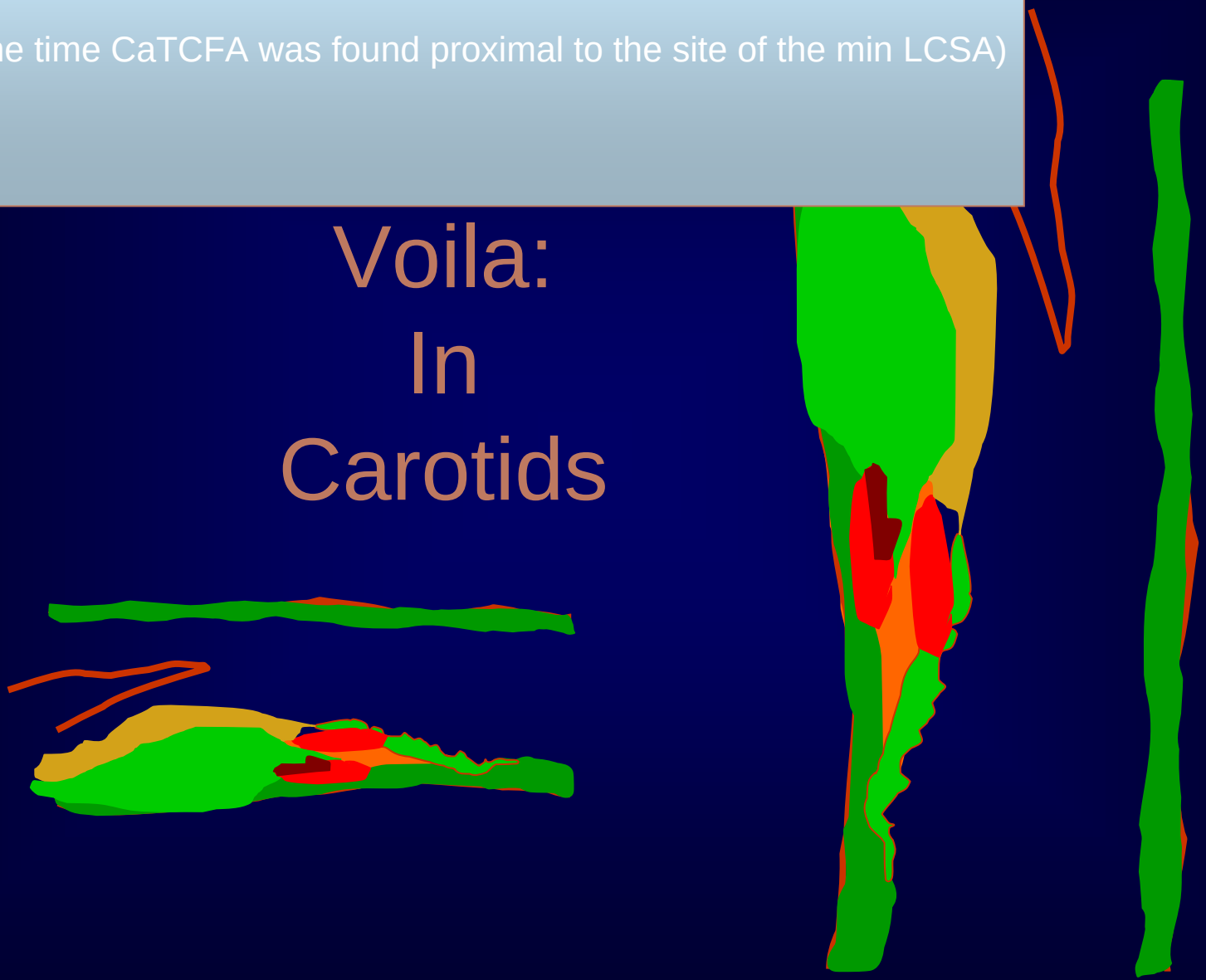
(88% of the time CaTCFA was found proximal to the site of the min LCSA)

CaFA = 4

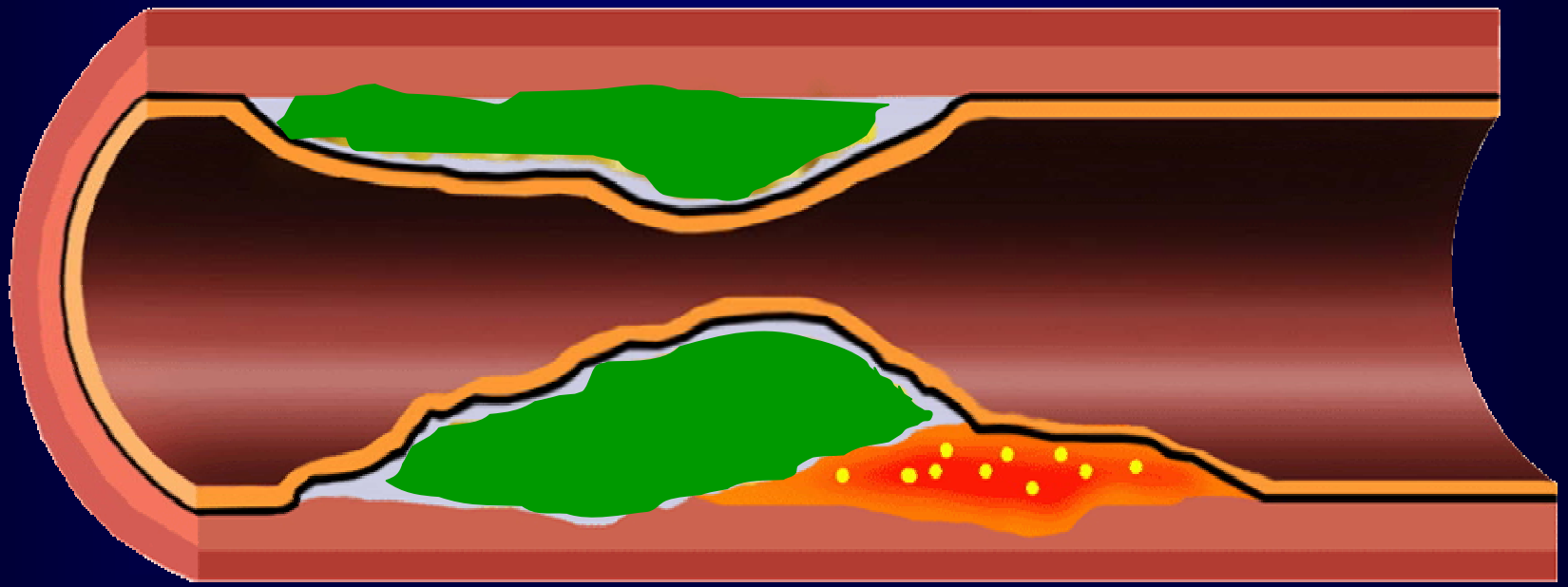
FA = 4

FCa = 3

Voila: In Carotids

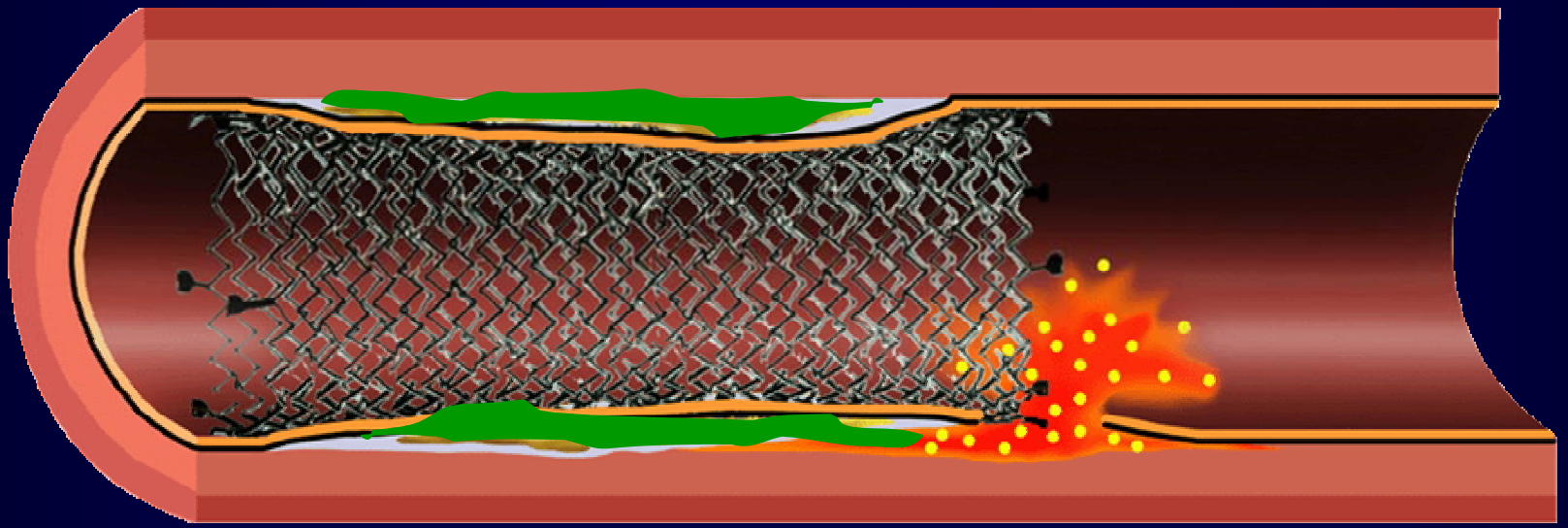


Vulnerable Plaque proximal to high grade stenosis



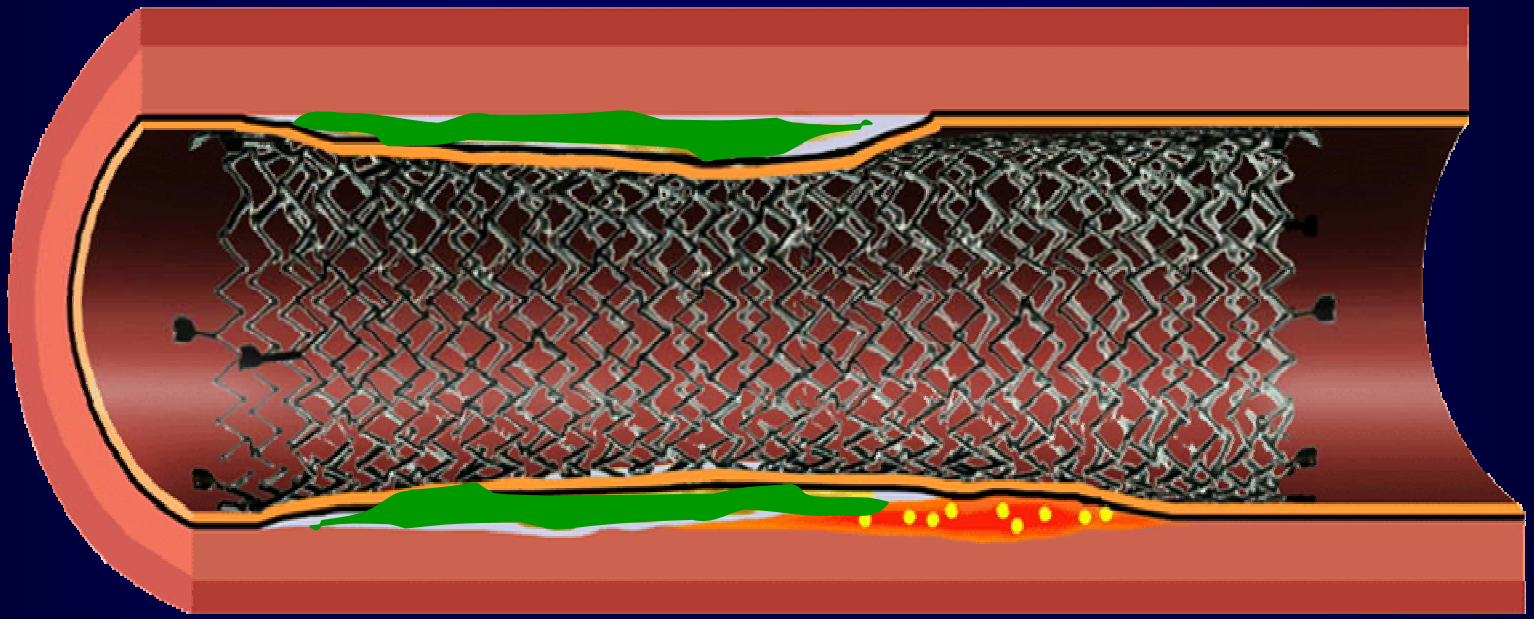
Stent Edge at the Site of Superficial FA;

Increased risk of LST with DES,
Increased risk for edge-stenosis
and re-stenosis?



Not a good Idea?

Or should we use a longer stent (on average 4-6 mm) to cover the ID TCFA and prevent possible future ruptures and further events (reduce TVF) from this lesion which has already been a problem?

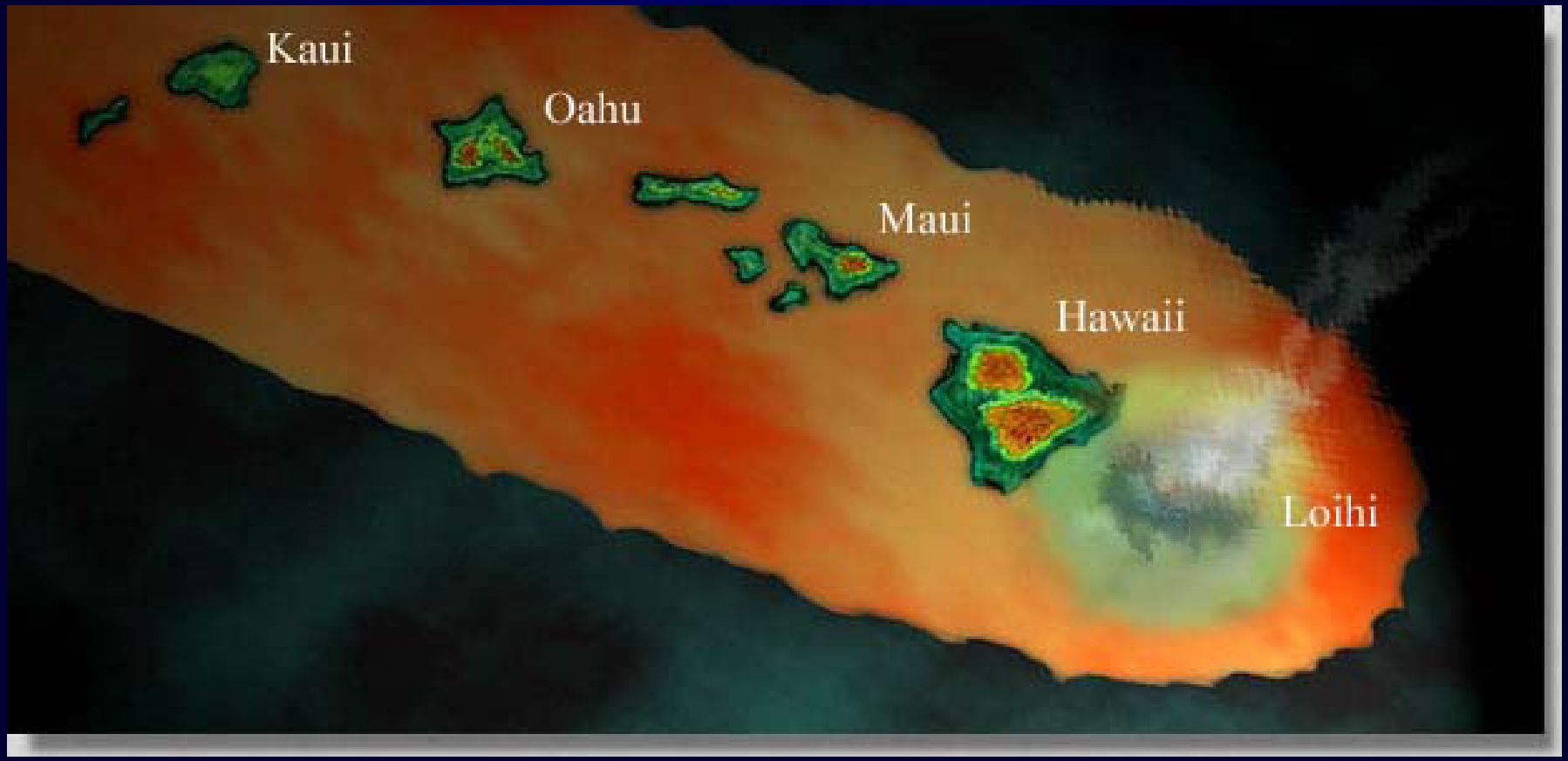


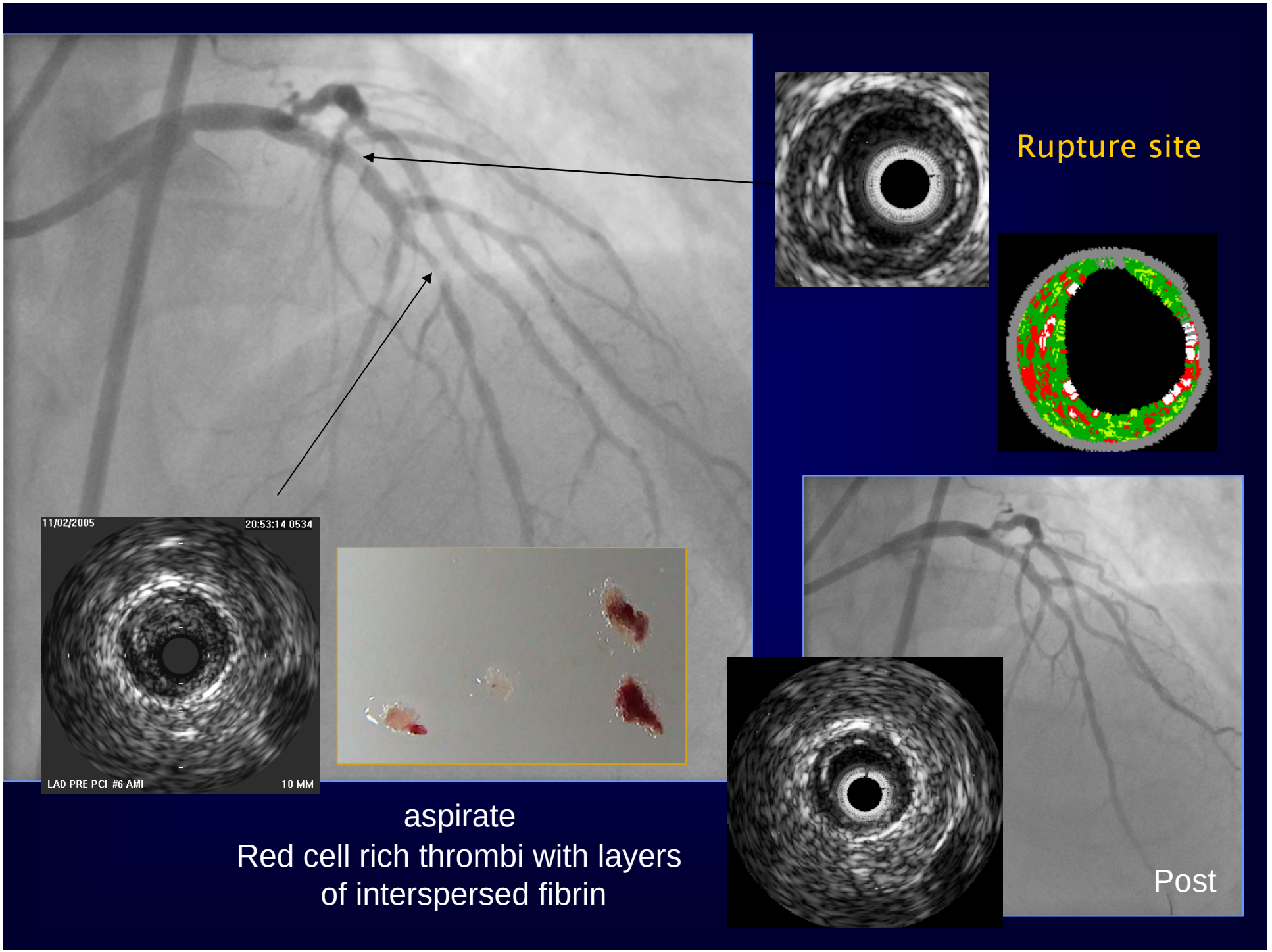
All these concepts are currently evaluated from the large set of existing clinical data with VH IVUS and prospective clinical trials are in process

How Can Plaque Composition Guide Interventions Today

- Helps to find the “culprit of the culprit”
  - In both coronary and carotid vascular beds the site of the advanced FA is often proximal to the site of the min lumen cross sectional area (mLCSA)
  - In case of an ACS, intraluminal thrombus often obscures the angiographic view and the source for the thrombotic event can be difficult to find
  - Knowledge of plaque composition can help to have a better understanding of the possible risk of acute and long term procedural complications
    - Plaque shift
    - Distal embolization
    - LST

In Case of an ACS
95 % of all ACS lesions are thrombotic




Rupture site
11/02/2005
20:53:14 0534
LAD PRE PCI #6 AMI
10 MM
aspirate
Red cell rich thrombi with layers
of interspersed fibrin
Post

Grayscale with VH IVUS can help to identify the “culprit of the culprit” and not just “STENT the SMOKE”

How Can IVUS with Plaque Composition Guide Interventions Today

- Helps to find the “culprit of the culprit”
  - In both coronary and carotid vascular beds the site of the advanced FA is often proximal to the site of the min lumen cross sectional area (mLCSA)
  - In case of an ACS, intraluminal thrombus often obscure the angiographic view and the source for the thrombotic event can be difficult to find
  - Knowledge of plaque composition can help to have a better understanding of the possible risk of acute and long term procedural complications
    - Plaque shift
    - Distal embolization
    - LST

Stent Underexpansion after High Pressure Drug-Eluting Stent Implantation

TCT 2006 Sang-Wook Kim, G Mintz, N Weissman et al

Using a standard definition (underexpansion=minimum stent area [MSA} <5mm^2), 27/148 stent subsegments (18%) were underexpanded of which 11/27 underexpanded subsegments (41%) were located in the distal third of the stent. Underexpanded stents were found in lesions with a greater percentage of dense calcium and nectoric core within the stenosis (see Table) and a smaller distal reference vessel (vessel area of 8.6±2.3 vs 14.5±5.1mm^2, p<0.0001 and lumen area of 4.0±1.0 vs 6.9±2.8mm^2, p<0.0001). Remodeling was similar in adequately vs underexpanded stents (0.91±0.17 vs 0.96±0.21, p=0.2).

	MSA > 5 mm^2 (n=121)	MSA < 5mm^2 (n=27)	p-value
Fibrous (%)	56.3±21.7	49.5±21.9	0.15
Fibro-fatty (%)	16.7±12.3	8.4±7.5	0.001
Necrotic (%)	13.2±11.8	21.4±13.7	0.007
Dense calcium (%)	4.9±6.4	9.8±10.7	0.002

Conclusions: In vivo VH-IVUS analysis indicates that stent underexpansion occurs especially at the site of increased amounts of dense calcium and necrotic core.

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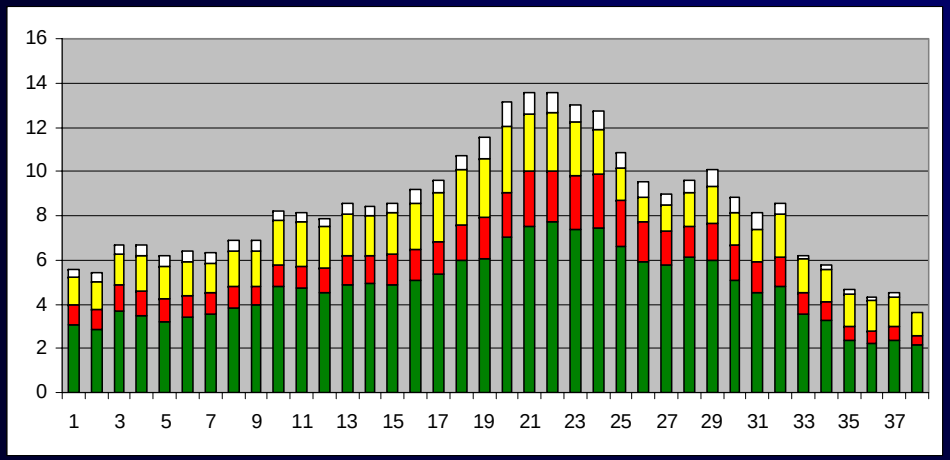
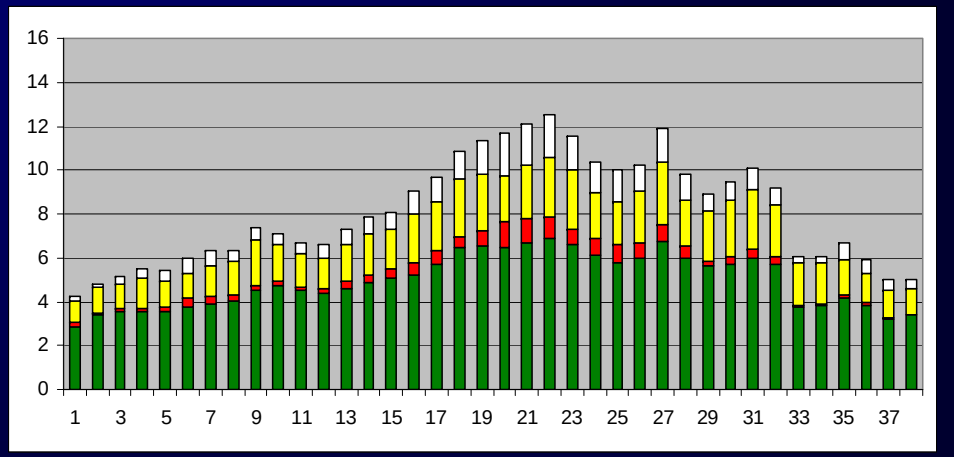
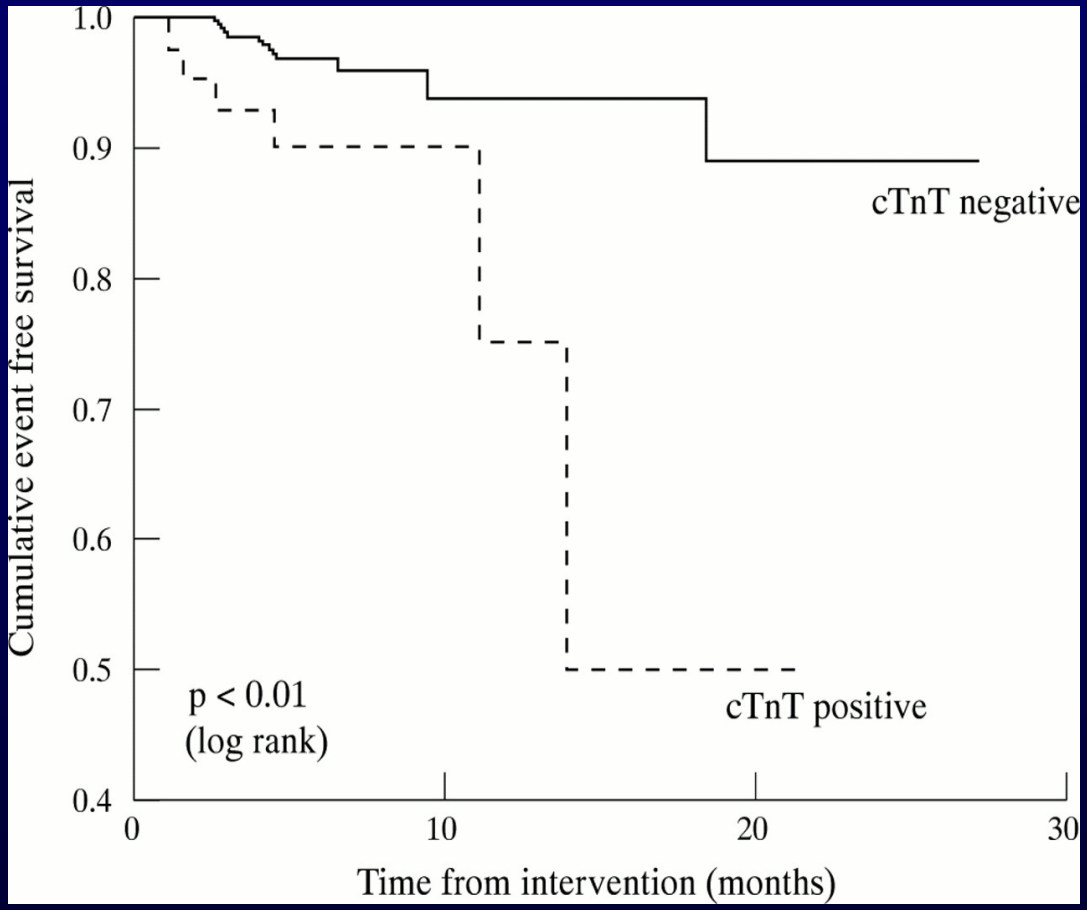
Results (5): post BA RF

	Before BA	After BA	P value
Fibrous (mm^3)	184±26 (61%)	185±29 (66%)	0.91
Fibro-fatty (mm^3)	50±12 (16%)	46±10 (16%)	0.31
Necrotic (mm^3)	45±10 (15%)	30±11 (11%)	0.002
Dense Calcium (mm^3)	21±9 (7%)	17±7 (6%)	0.12



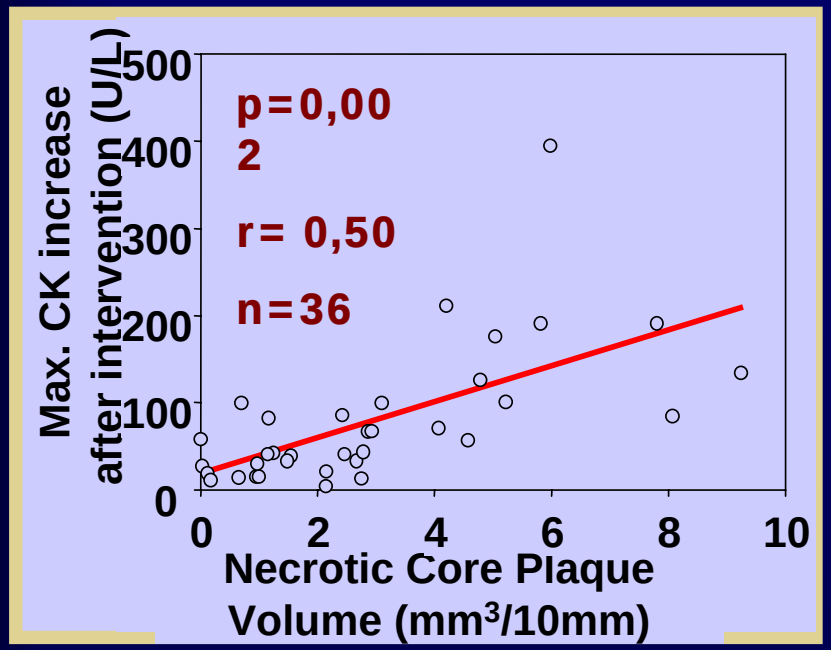


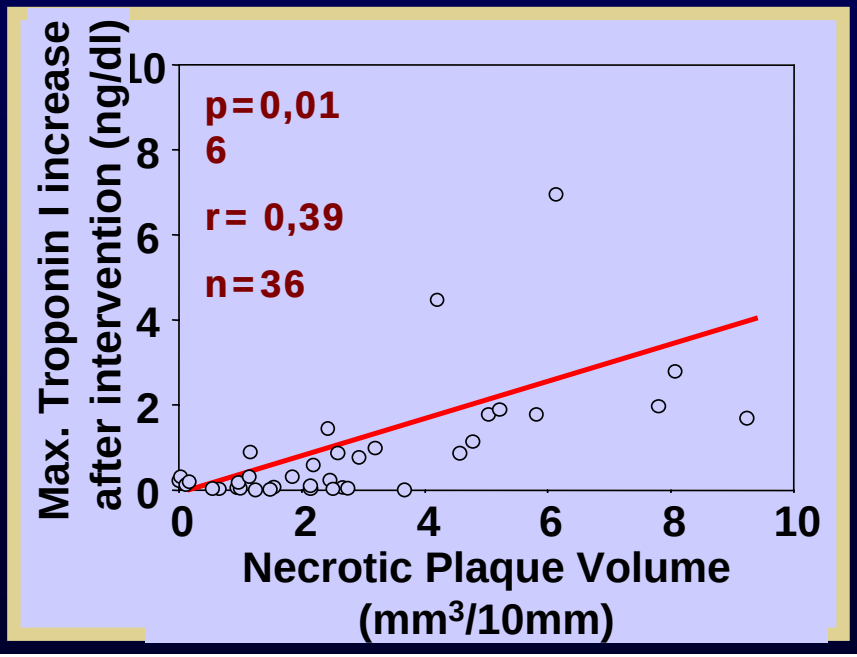
Coronary Microembolization During PCI and Cardiac Events

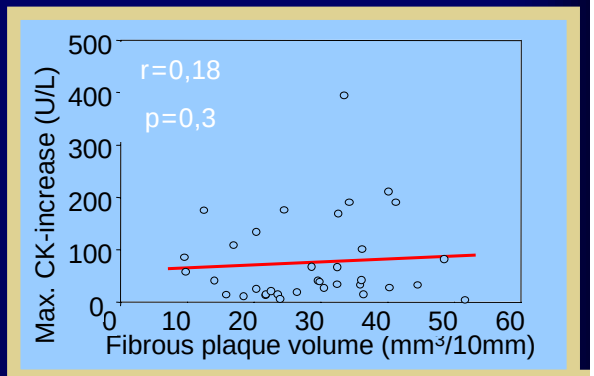


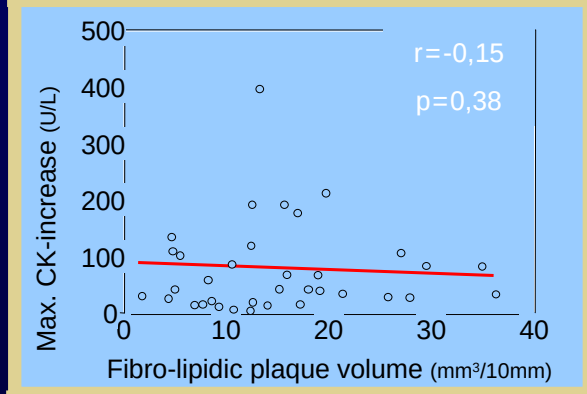
Herrmann et al. Heart 2002;87:549-553

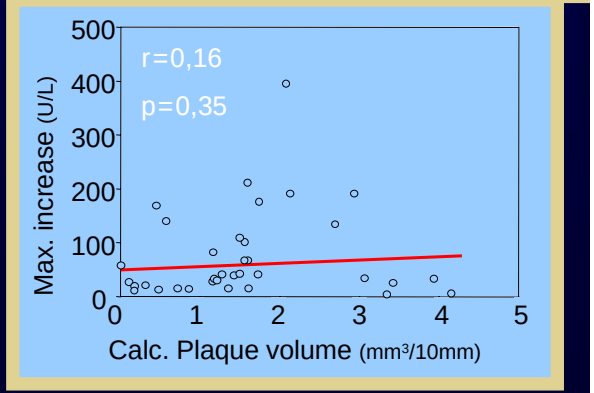
Plaque Composition and Coronary Microembolization during Standardized PCI, Prof Erbel, PCR 2006











SUMMARY:
How could we use the knowledge of *in vivo* plaque composition to reduce coronary mortality

- Angiogram is a poor dg tool to detect the amount, severity, and composition of atherosclerotic lesions but also a poor dg too to detect optimal interventional outcome
  - More accurate non-invasive and invasive dg tools need to be used to have a better understanding of the overall state of the disease

SUMMARY:
How could we use the knowledge of *in vivo* plaque composition to improve our short and long term interventional outcome

- Plaque composition can help to
  - find the origin of the problem, the “culprit of the culprit”
  - Understand the current nature and history of the lesion
    - plaque type (FA, CaFA, ID TCFA, ID CaTCFA, # of previous plaque ruptures)
    - In relation to the amount of plaque burden and positive remodeling
  - Assess the possible risk for
    - plaque protrusion,
    - plaque shift,
    - distal embolization,
    - late stent thrombosis with DES,
    - and the need for lesion preparation (densely calcified necrotic cores)

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