Beyond The Angiography: Coronary Physiology in The Cath Lab

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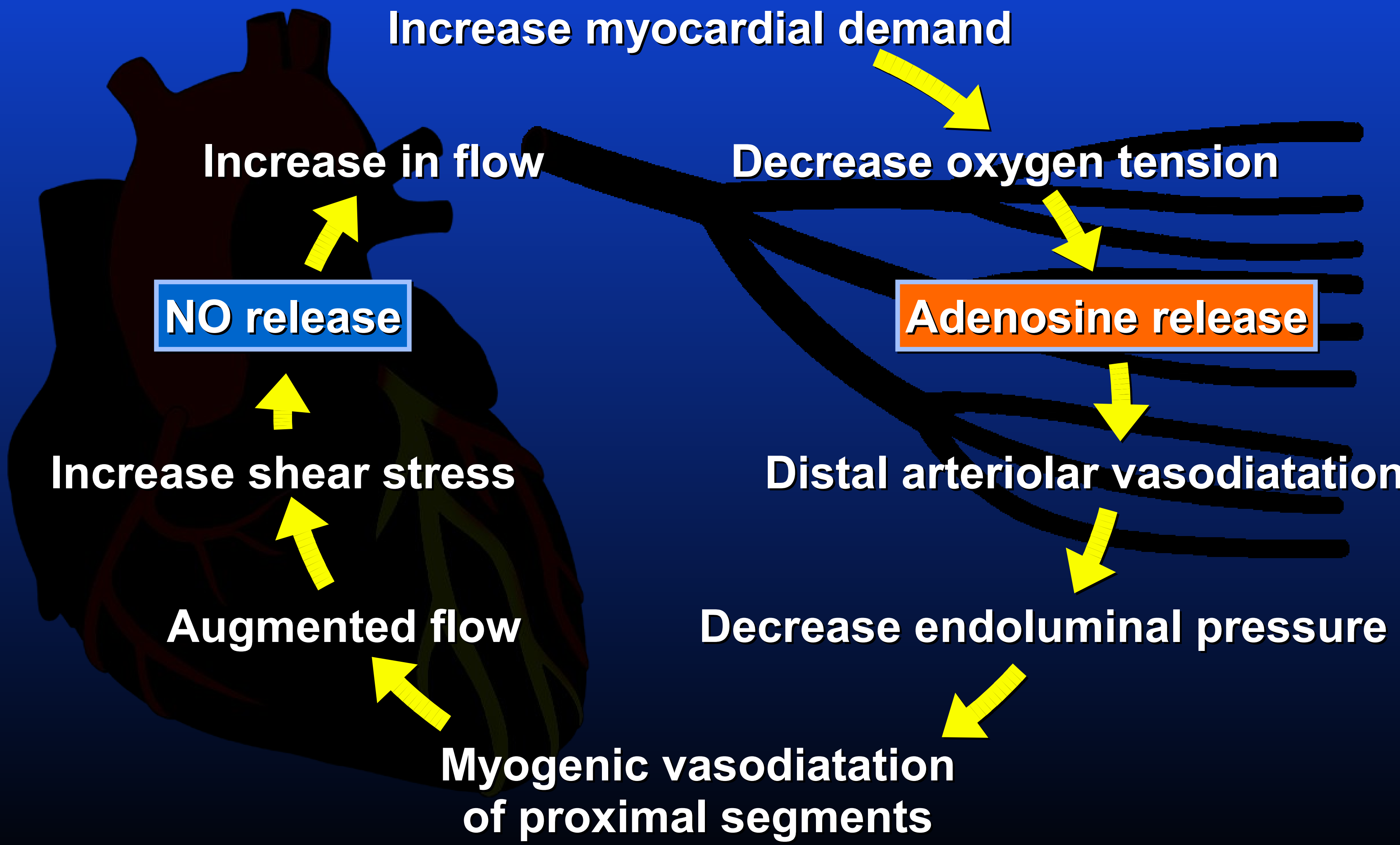
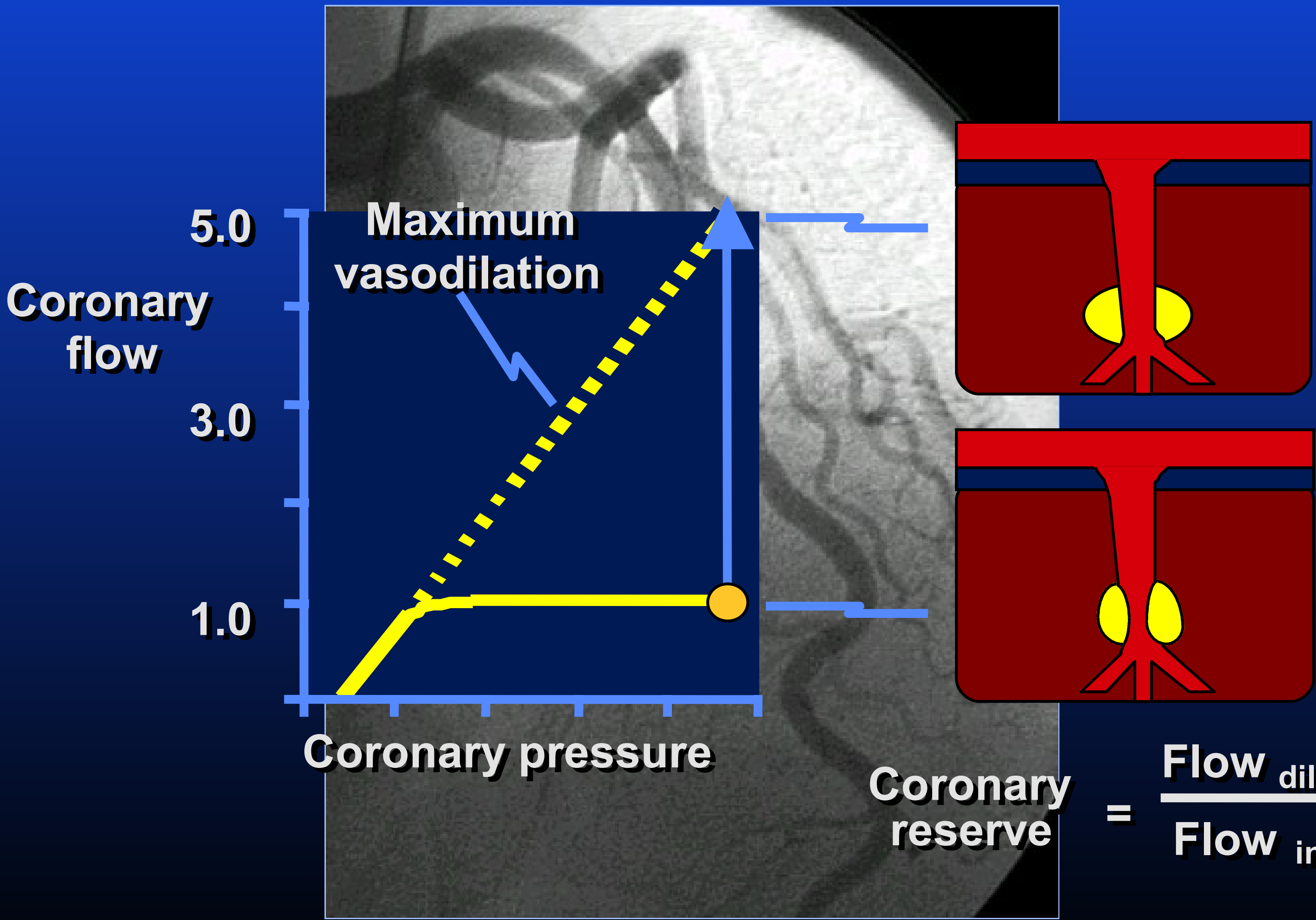
Normal Heart

Response to Increase in Demand



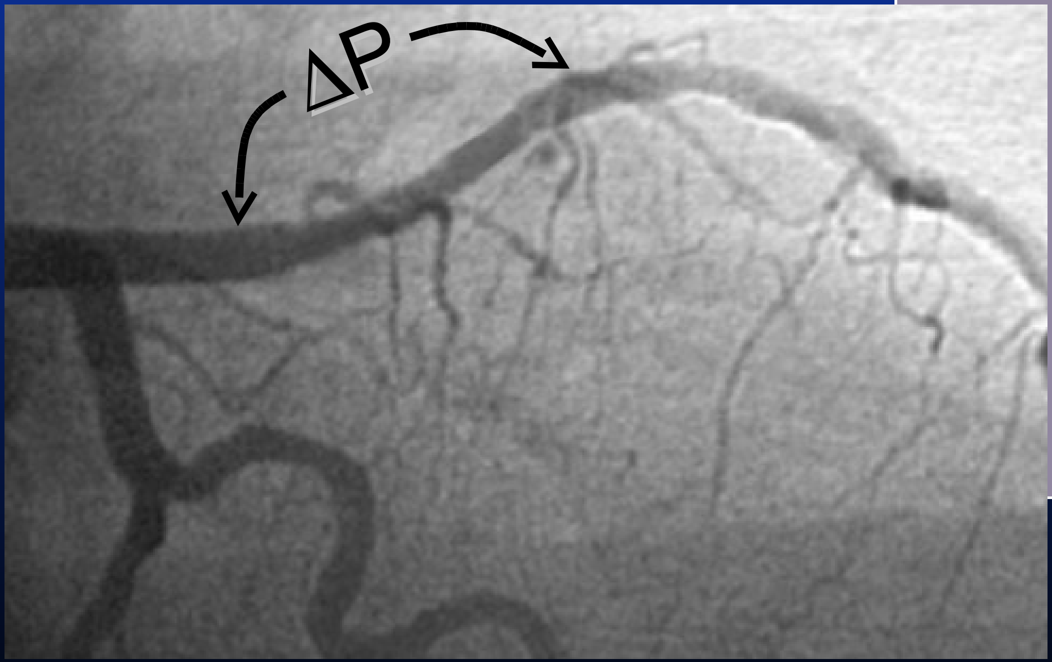
Coronary Flow Physiology

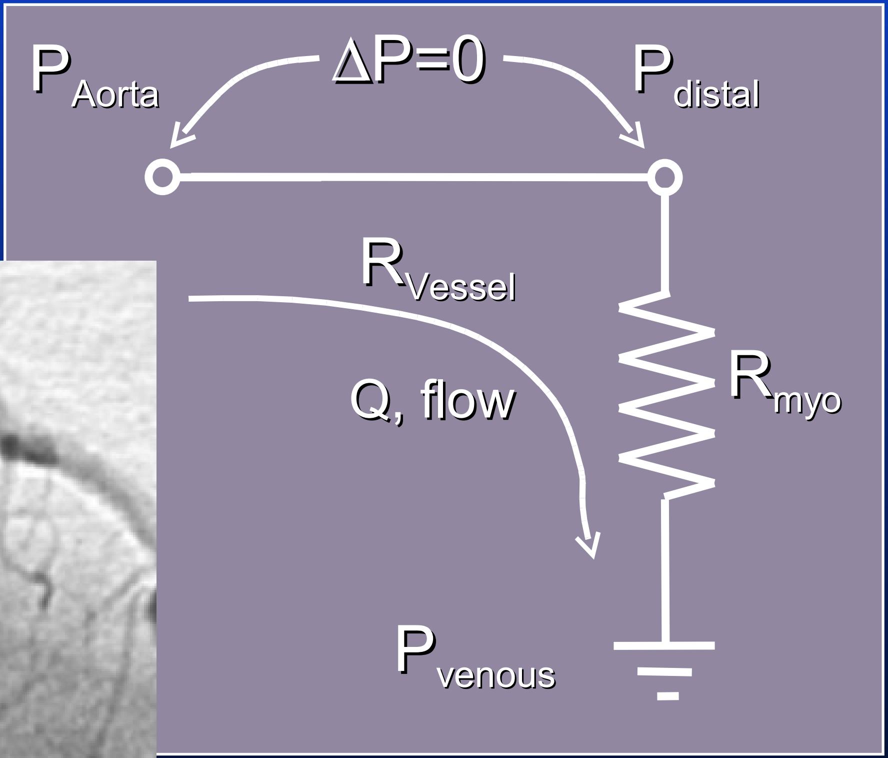


$$\text{Coronary reserve} = \frac{\text{Flow}_{\text{dilated}}}{\text{Flow}_{\text{initial}}}$$

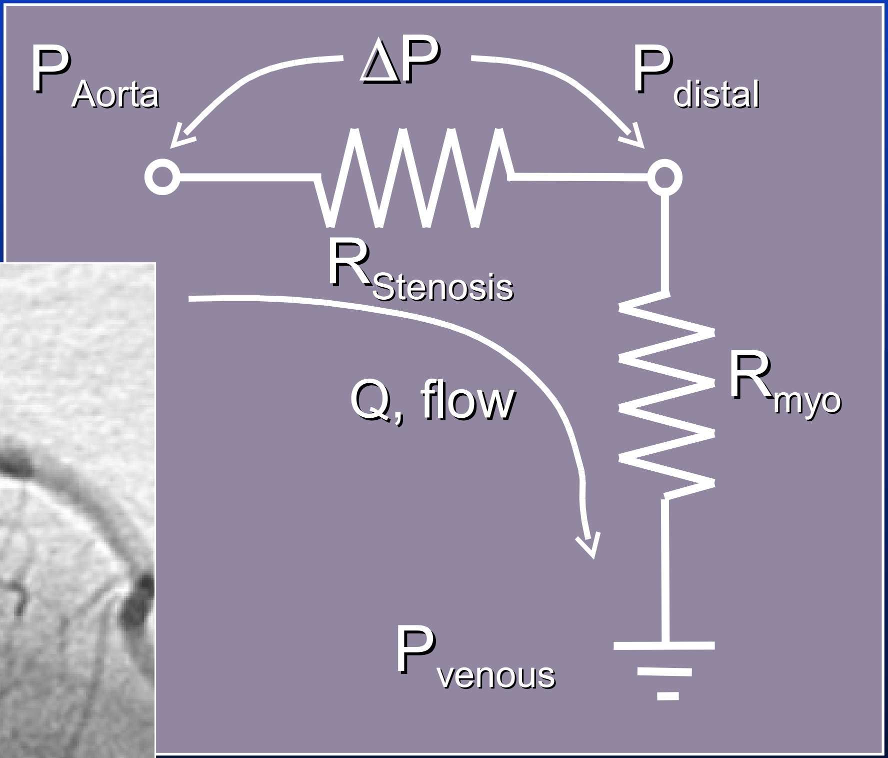
Klocke, 1990

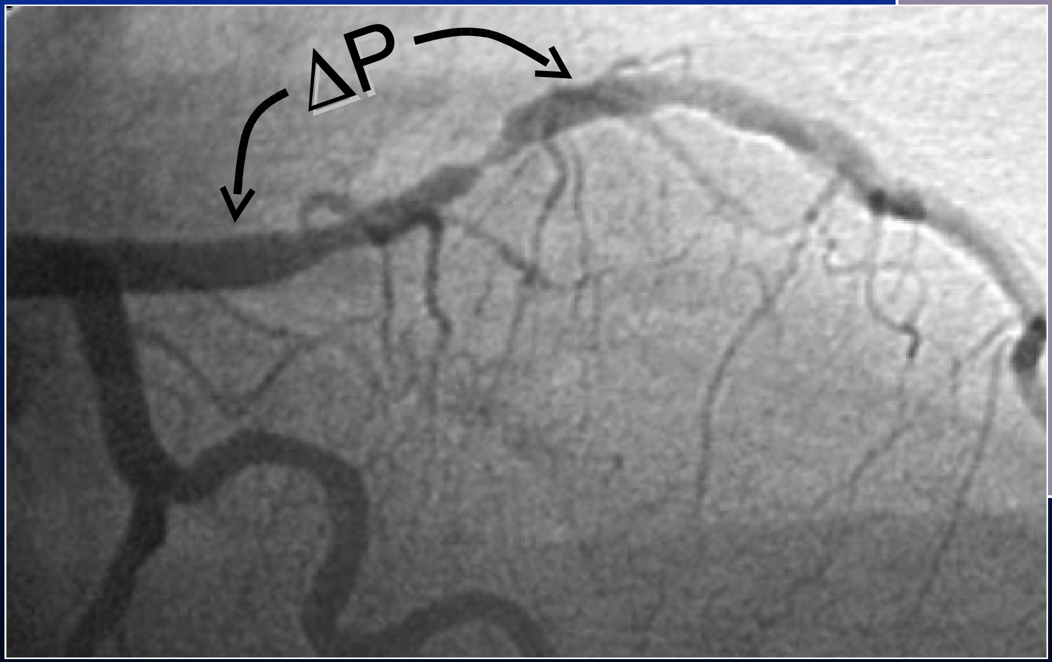
Coronary Stenosis Rheology
Pressure-Flow Relationship



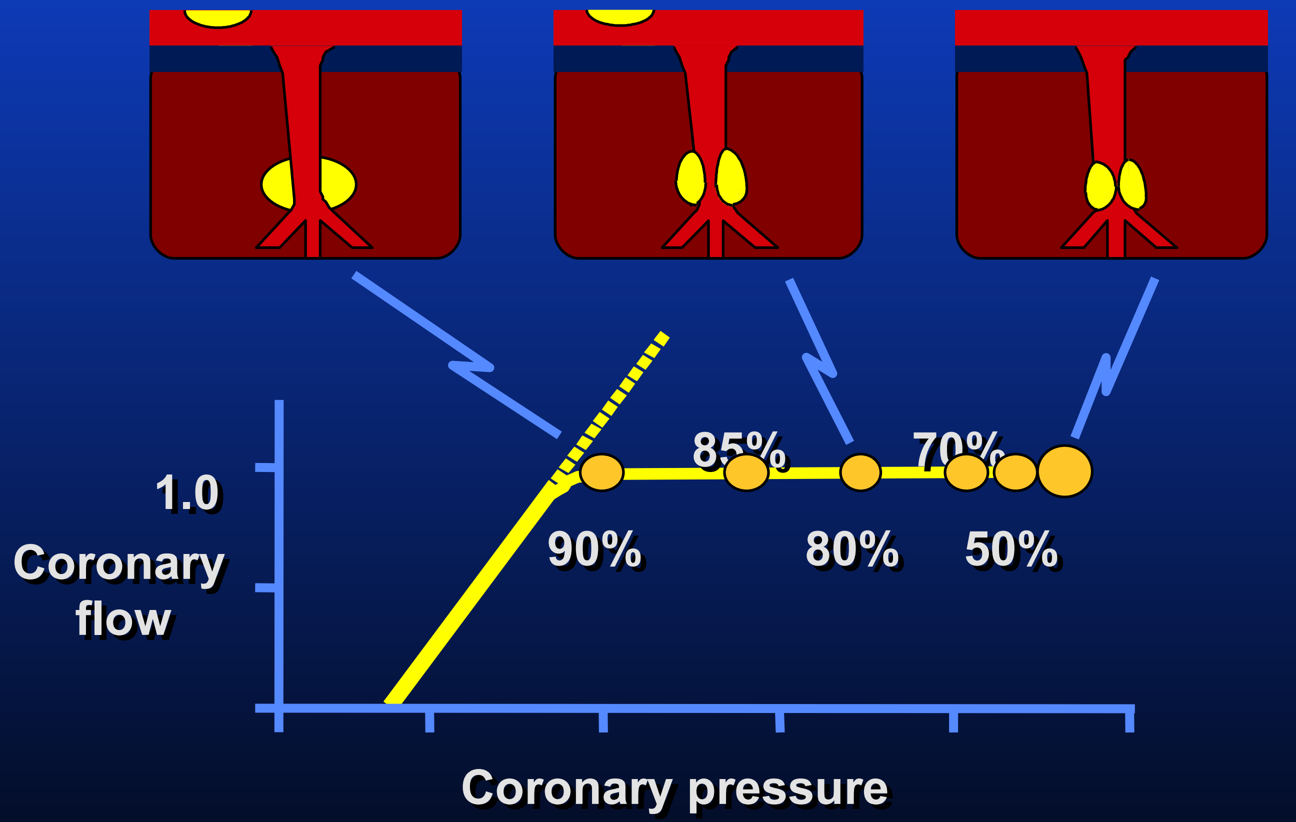


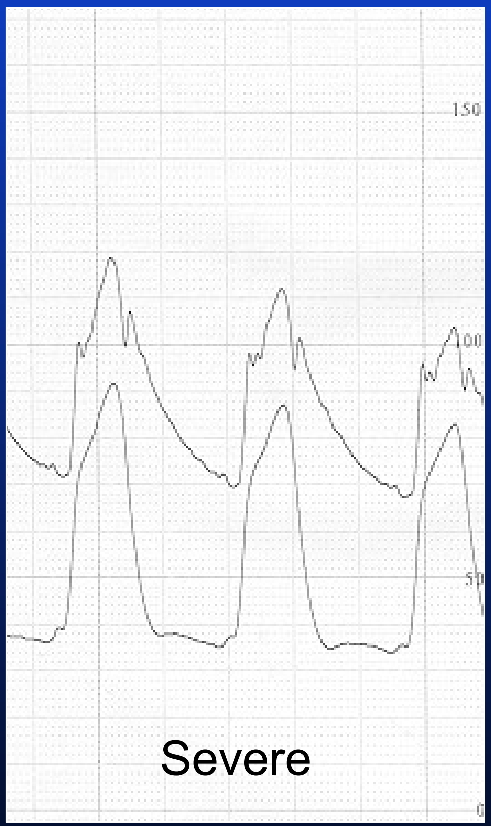
Coronary Stenosis Rheology
Pressure-Flow Relationship





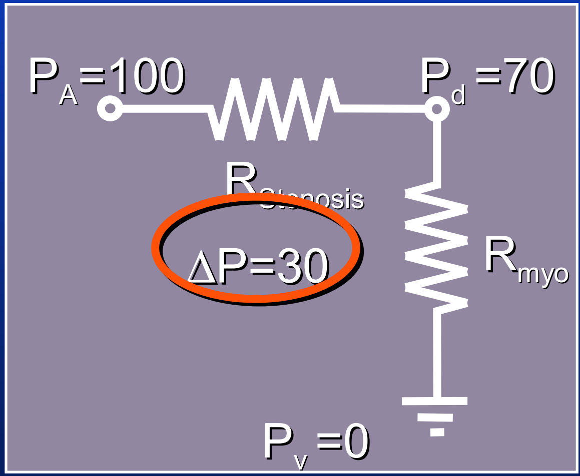
Coronary Stenoses and Resting Flow

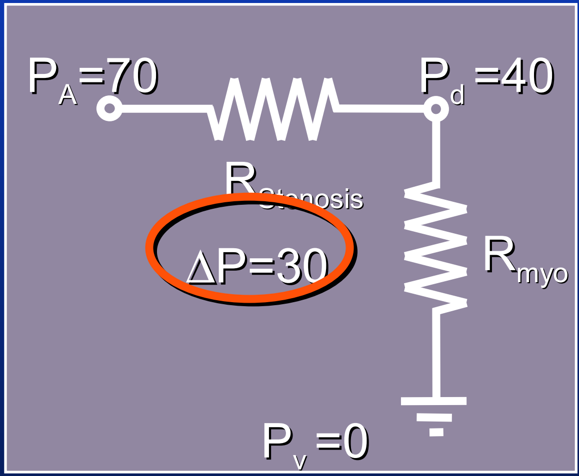


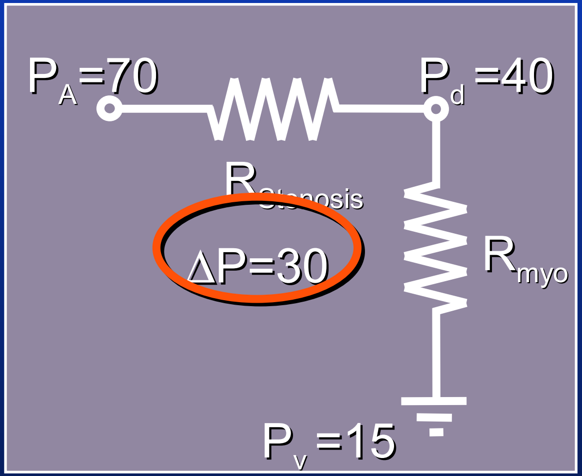


Klocke, 1990

Basic Coronary Physiology
Resting vs. Hyperemic Gradients







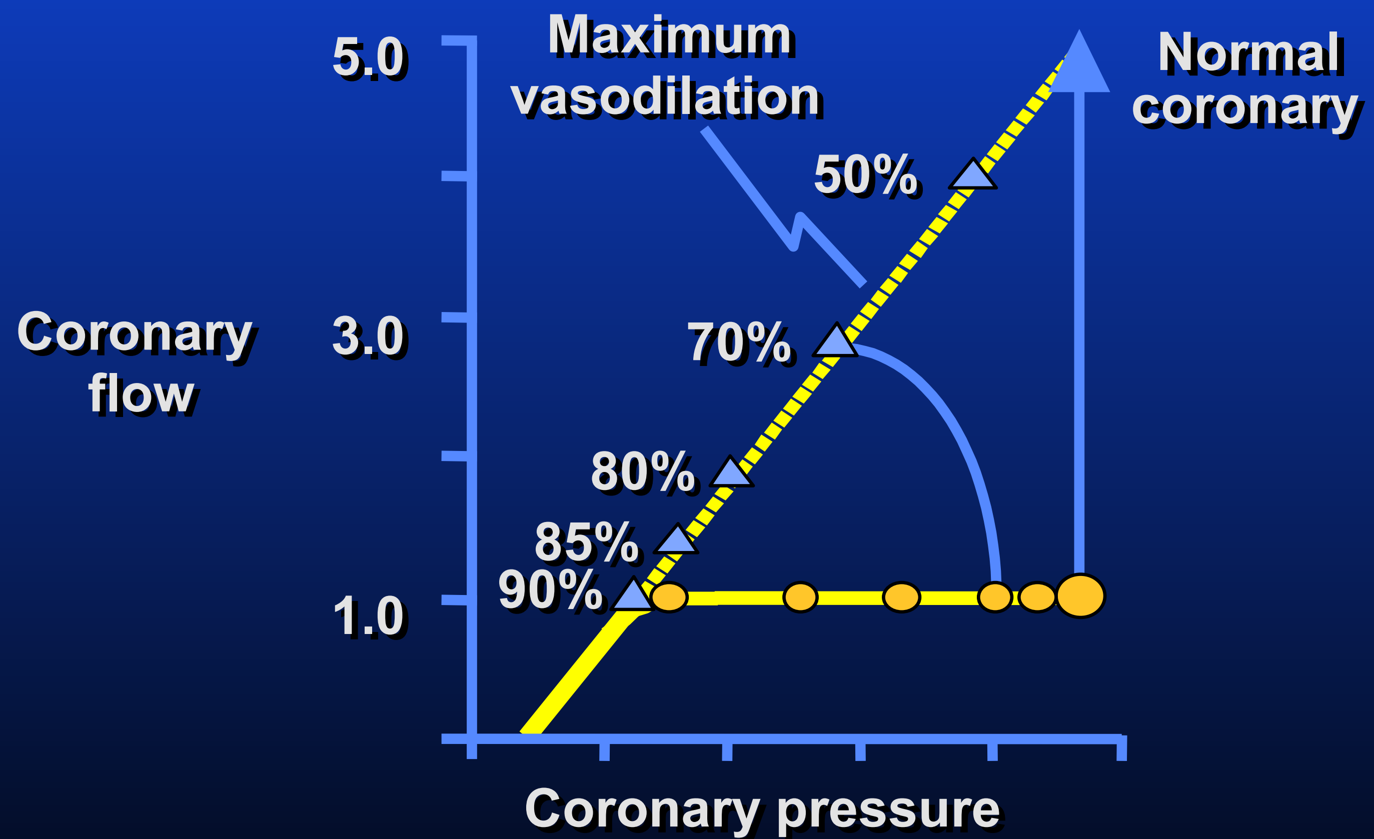
ΔP_{myo}=70

ΔP_{myo}=40

ΔP_{myo}=25

- *Equivalent resting gradients result in markedly different myocardial perfusion pressures*

Coronary Stenoses and Flow Reserve



Klocke, 1990

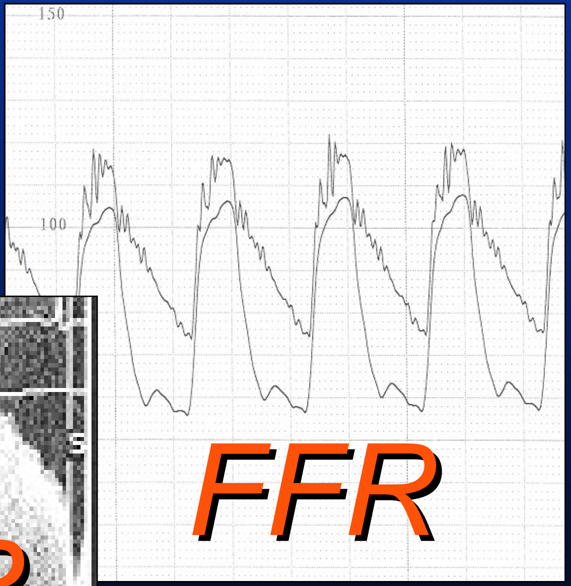
Basic Coronary Physiology
Types of Flow Reserve

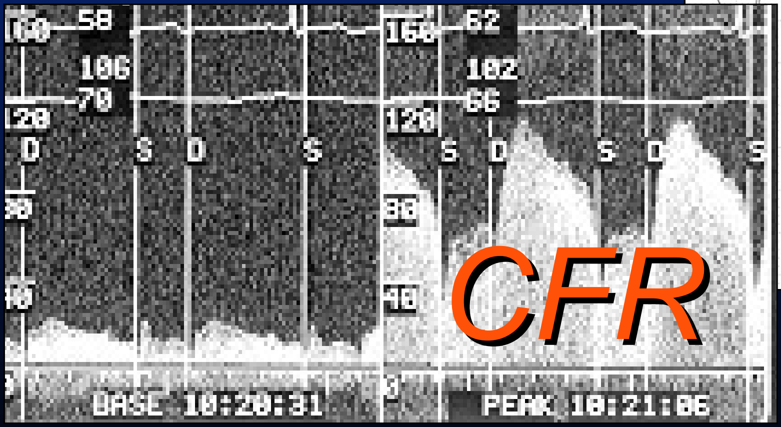
- Coronary flow reserve (CFR)
- Relative coronary flow reserve (rCFR)
- Myocardial fractional flow reserve (FFR_{myo})

Doppler Velocity and Pressure Measurements

Physiologic Guidewire Technology

- Doppler guidewire
- Pressure guidewire





rCFR

Fractional Flow Reserve Concepts

Comparison of CVR and FFR_{myo}

	Hemodynamic Independence	Independent of microcirculation abnomalities	Unequivocal normal values	Use in MVD	Assessment of collateral flow
CVR	-	-	Range >2.0	+	+
rCVR	+	+	1.0	-	-
FFR_{myo}	+	+	1.0	+	+

Fractional Flow Reserve Concepts
Definition of FFR_{myo}

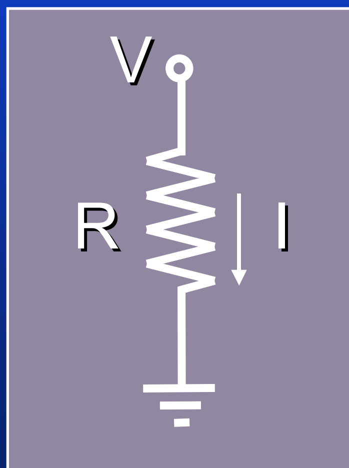
The amount of hyperemic flow that a vessel can supply when a stenosis is present

compared to

The amount of hyperemic flow that the vessel can supply without the stenosis

$$FFR_{myo} = \frac{\text{Hyperemic CBF}_{\text{Lesion}}}{\text{Hyperemic CBF}_{\text{No Lesion}}}$$

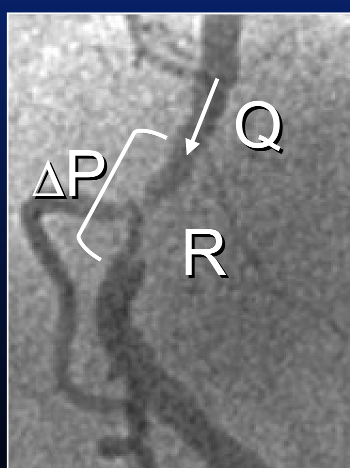
Fractional Flow Reserve Concepts



Ohm's Law

$V = I \times R$

Voltage = Current x Resistance

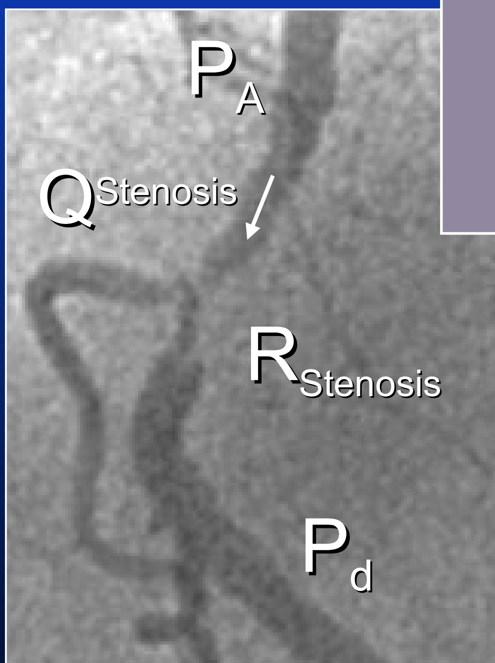


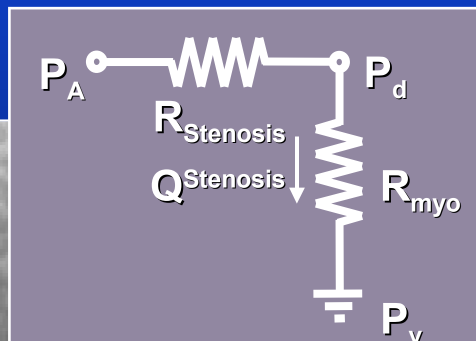
Hydraulic Equation

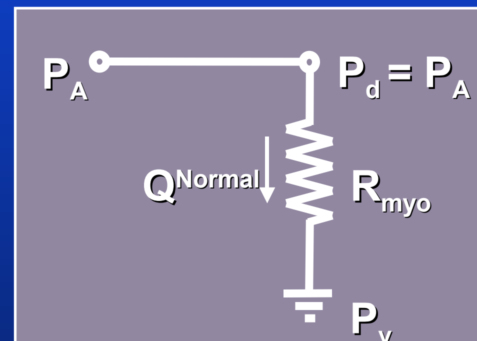
$\Delta P = Q \times R$

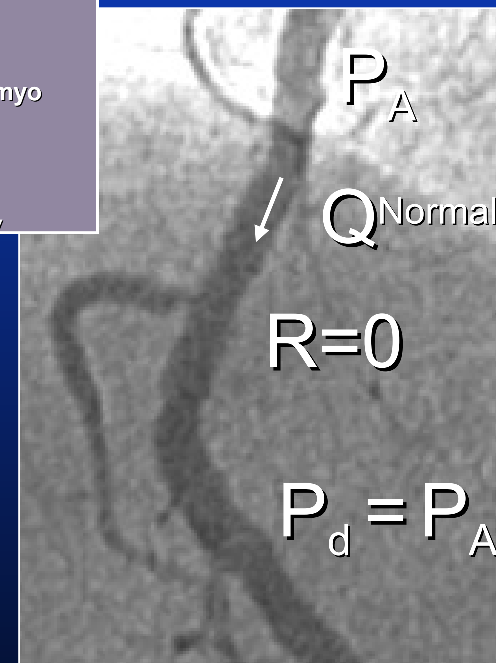
Pressure Gradient = Blood flow x Resistance

Fractional Flow Reserve Concepts









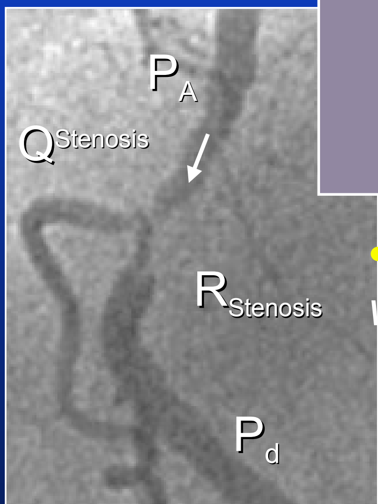
- *Myocardial blood flow during hyperemia with a stenosis*

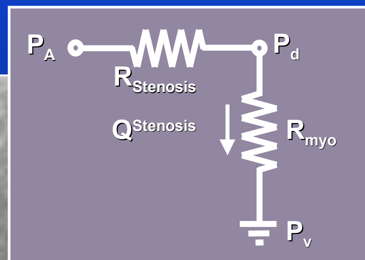
Myocardial blood flow during hyperemia without a stenosis

$$Q^{Stenosis} = (P_d - P_v) / R_{myo}$$

$$Q^{Normal} = (P_A - P_v) / R_{myo}$$

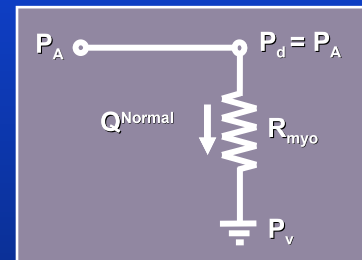
Fractional Flow Reserve Concepts

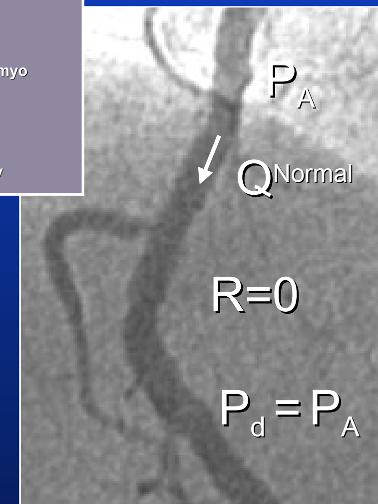




- *Hyperemic flow with a stenosis*

$$Q^{Stenosis} = (P_d - P_v) / R_{myo}$$





- *Hyperemic flow without a stenosis*

$$Q^{Normal} = (P_A - P_v) / R_{myo}$$

- *Myocardial Fractional Flow Reserve:*

$$FFR_{myo} = \frac{Q^{Stenosis}}{Q^{Normal}} = \frac{(P_d - \cancel{P_v}^{\,0}) / R_{myo}}{(P_A - \cancel{P_v}^{\,0}) / R_{myo}} = \frac{P_d}{P_A}$$

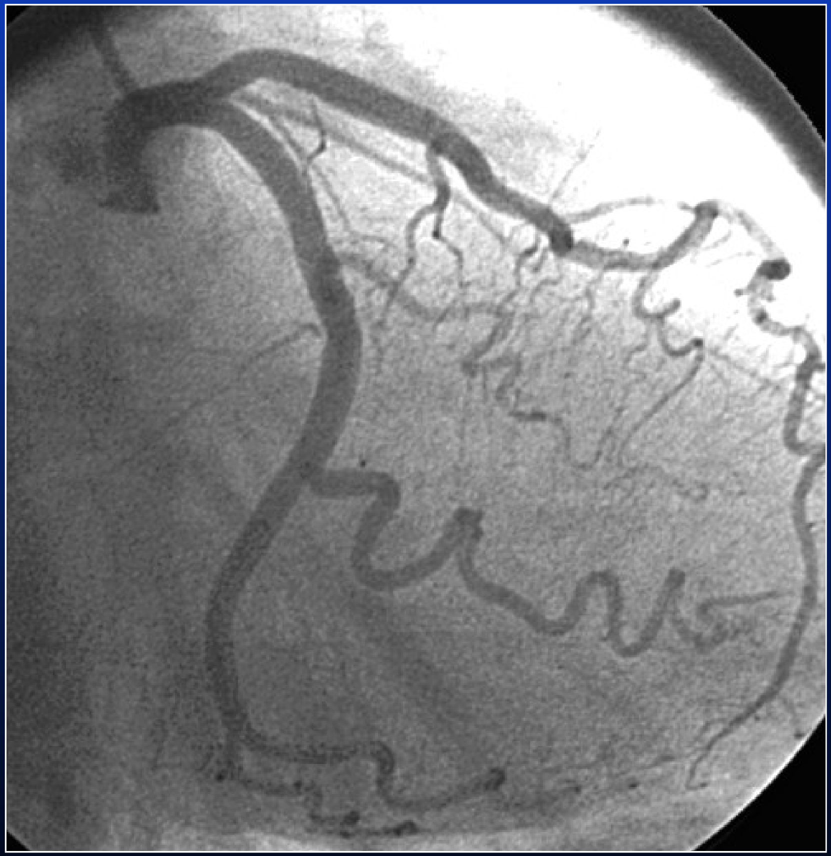
$$FFR_{myo} = \frac{\text{Hyperemic CBF}_{Lesion}}{\text{Hyperemic CBF}_{No\ Lesion}}$$

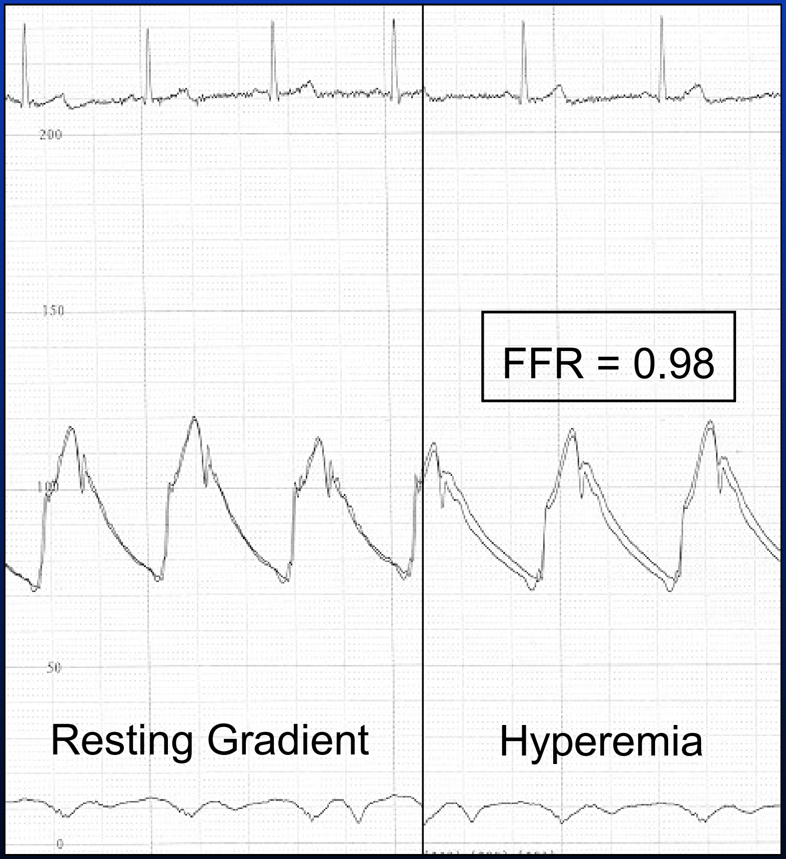
Fractional Flow Reserve Concepts
Assumptions

- *All measurements made at maximal hyperemia*
- *The microcirculation is maximally vasodilated and myocardial resistance (R_{myo}) is constant*
- *Venous pressure (right atrial) is small and can be ignored*

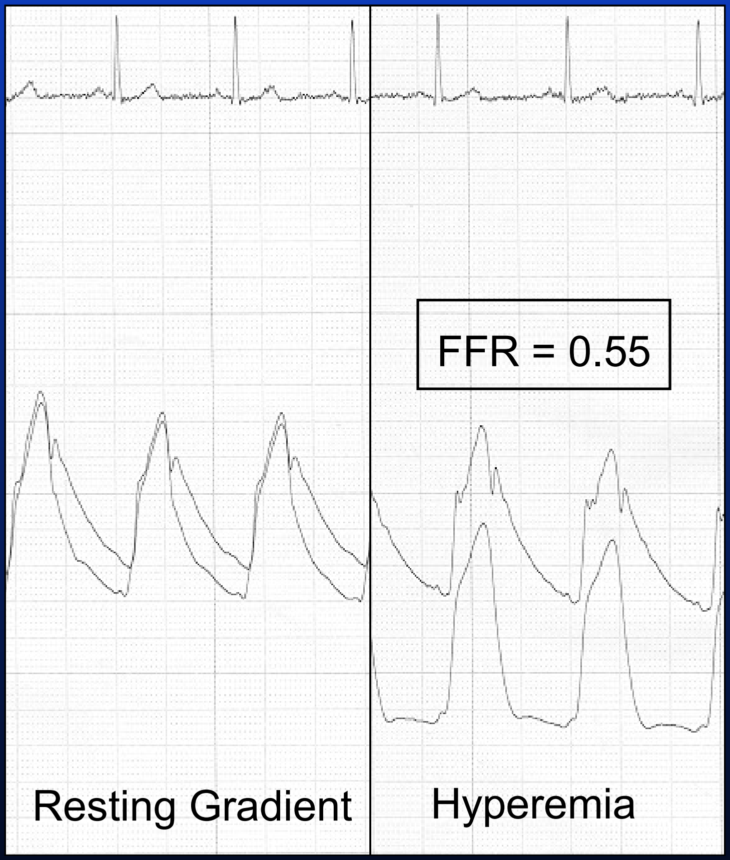
Fractional Flow Reserve Concepts

Normal FFR_{myo}

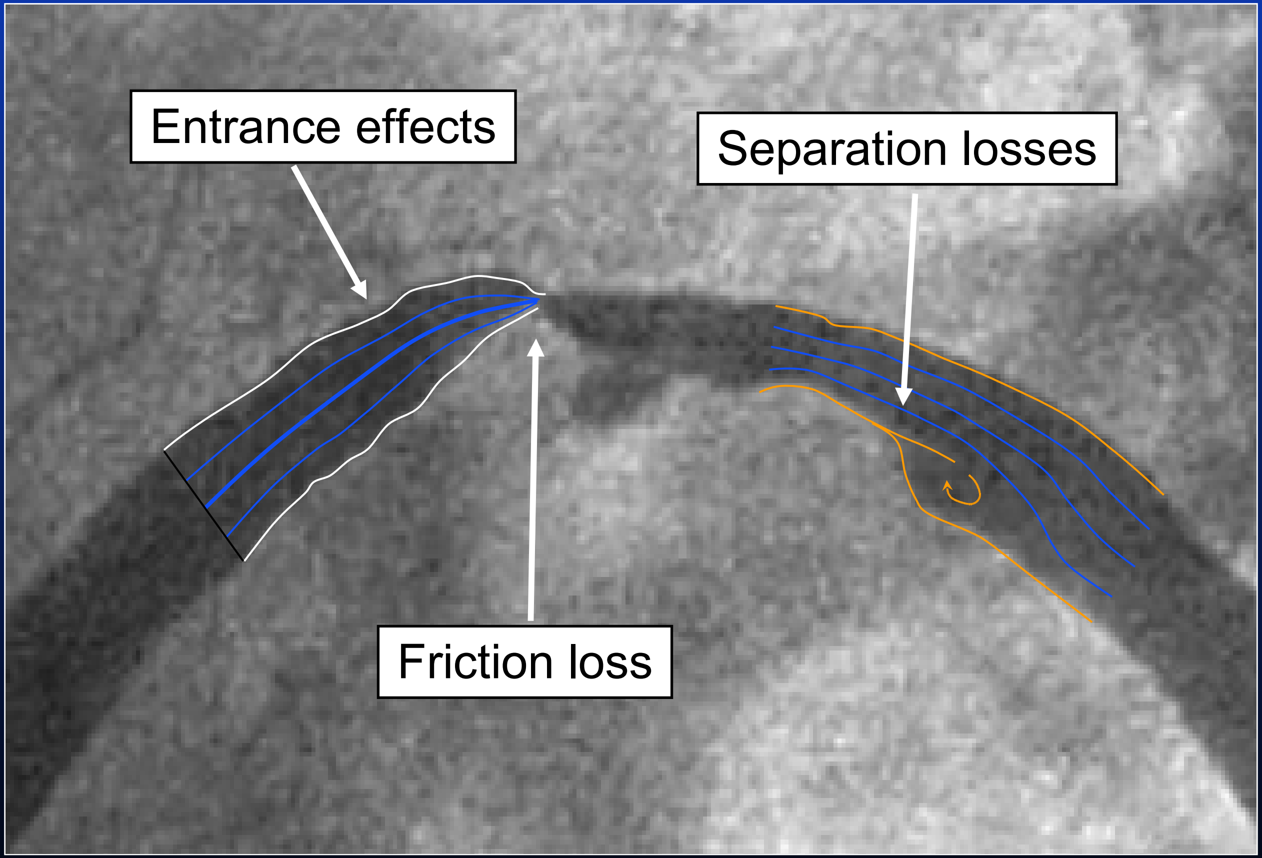




Fractional Flow Reserve Concepts
Abnormal FFR_{myo}

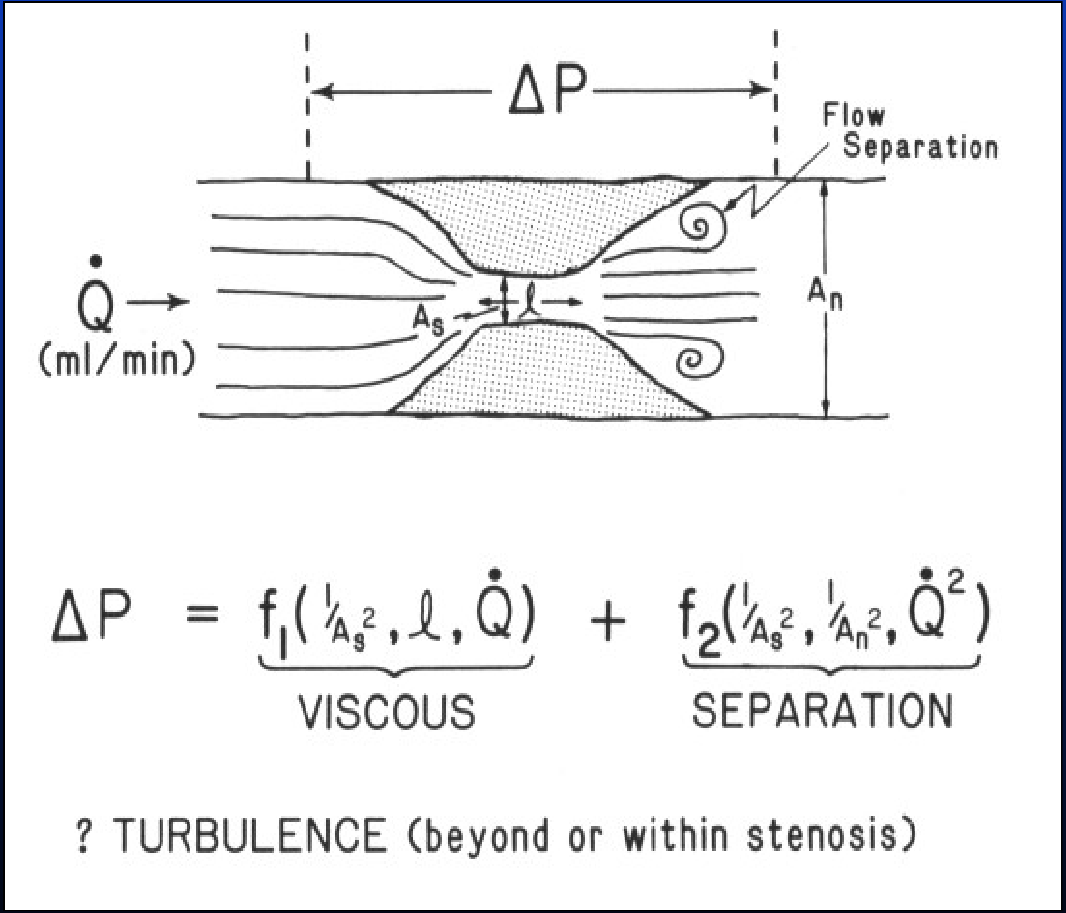


Coronary Stenosis Rheology
Pressure-Flow Relationship



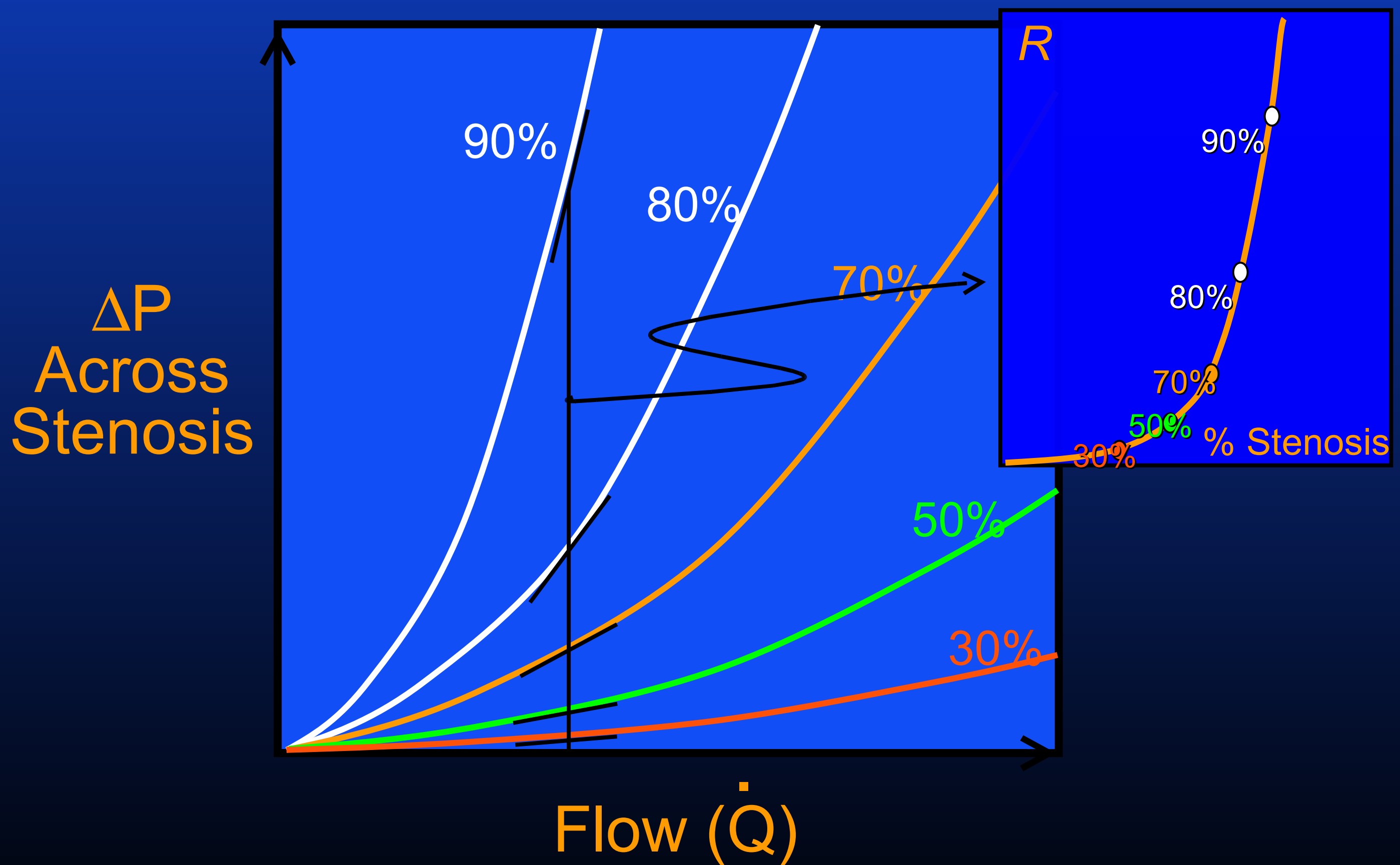
Coronary Stenosis Rheology

Pressure-Flow Relationship



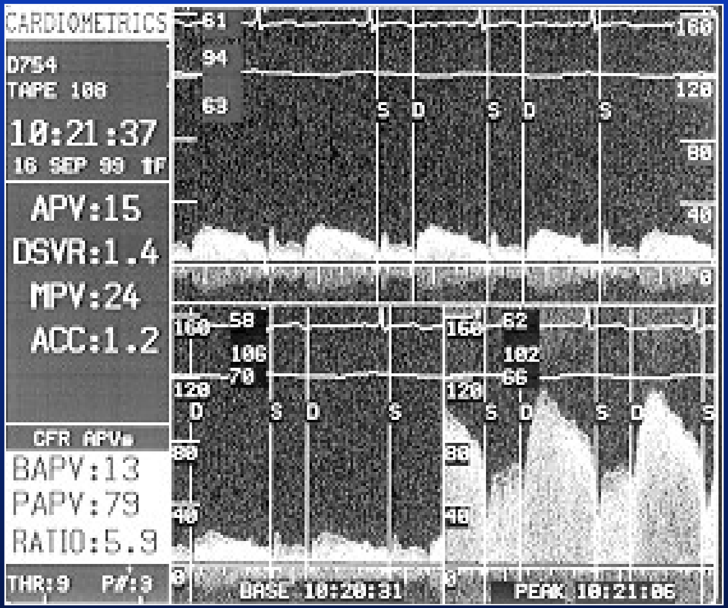
Coronary Stenosis Rheology

Pressure-Flow Relationship



Coronary Velocity Reserve

Basic Concepts

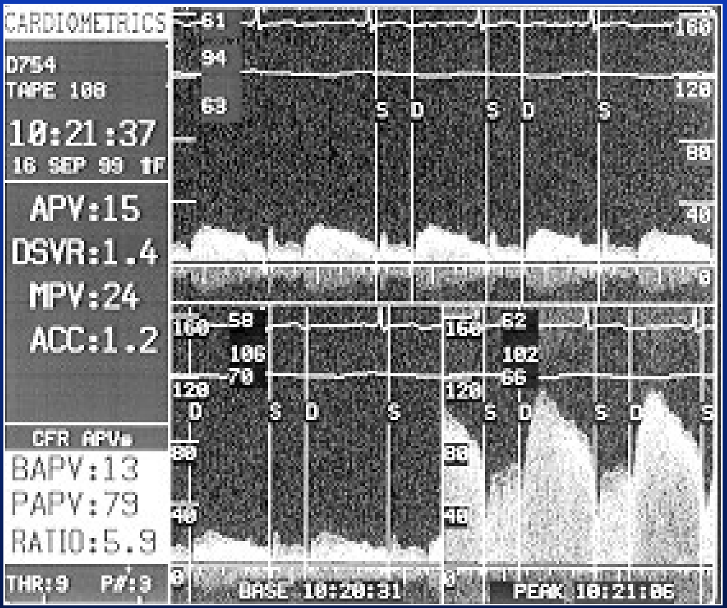


Coronary Velocity Flow Reserve:

$$CVR = \frac{Q_{Hyperemia}}{Q_{Basal}} = \frac{k_{Hyperemia} \times Area_{Hyperemia} \times APV_{Hyperemia}}{k_{Basal} \times Area_{Basal} \times APV_{Basal}}$$

Coronary Velocity Reserve

Basic Concepts



Coronary Velocity Flow Reserve:

$$CVR = \frac{Q_{Hyperemia}}{Q_{Basal}} = \frac{0.5 \times (\pi/4)\,(D_{Hyperemia})^2 \times APV_{Hyperemia}}{0.5 \times (\pi/4)\,(D_{Basal})^2 \times APV_{Basal}} = \frac{APV_{Hyperemia}}{APV_{Basal}}$$

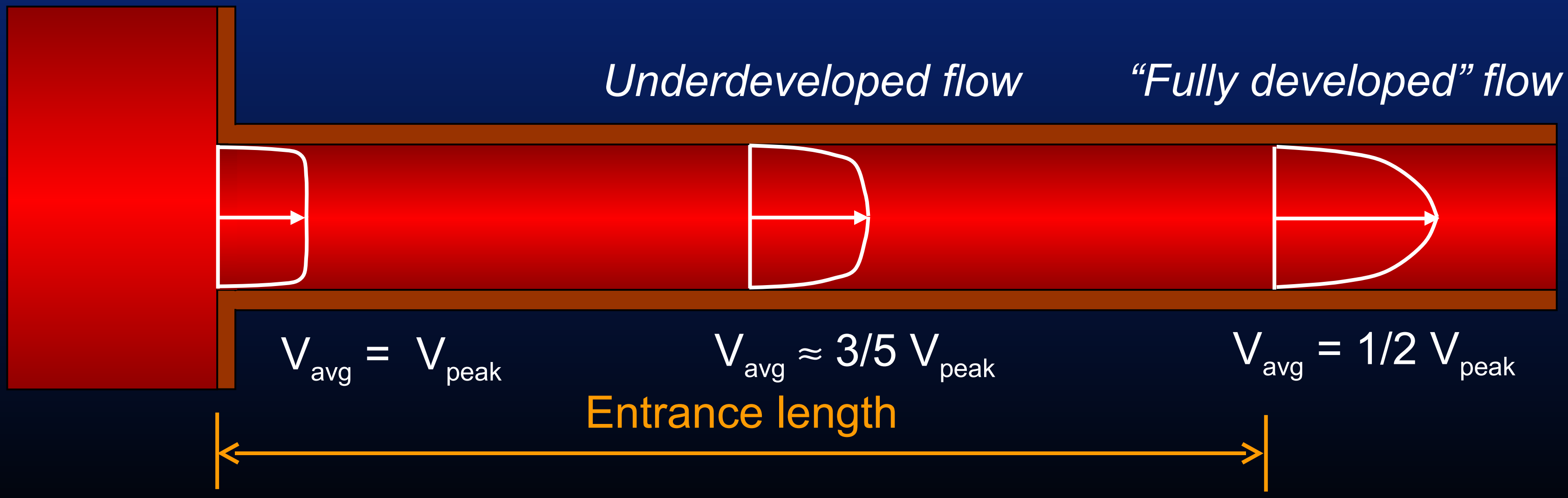
Doppler-derived CVR

Correlative Studies

Author	n	Ischemic Test	CVR	Sensitivity %	Specificity %	Accuracy %
Miller	33	Adeno/dip MIBI	<2.0	82	100	89
Joye	30	Ex-Tl^{201}	<2.0	94	95	94
Deychack	17	Ex-Tl^{201}	<1.8	94	94	96
Heller	100	Ex-Tl^{201}	<1.8	89	92	92
Danzi	30	Dip-echo	<2.0	91	84	87
Schulman	35	Exercise ECG	<2.0	95	71	86

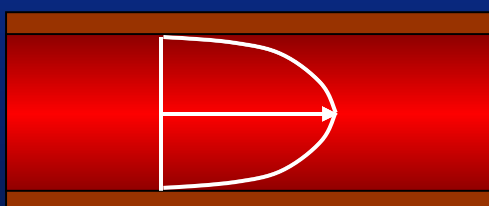
Limitations of Doppler CVR

- Velocity profile
  - Parabolic vs. non-parabolic
  - Entrance length effects
  - Varying flow area

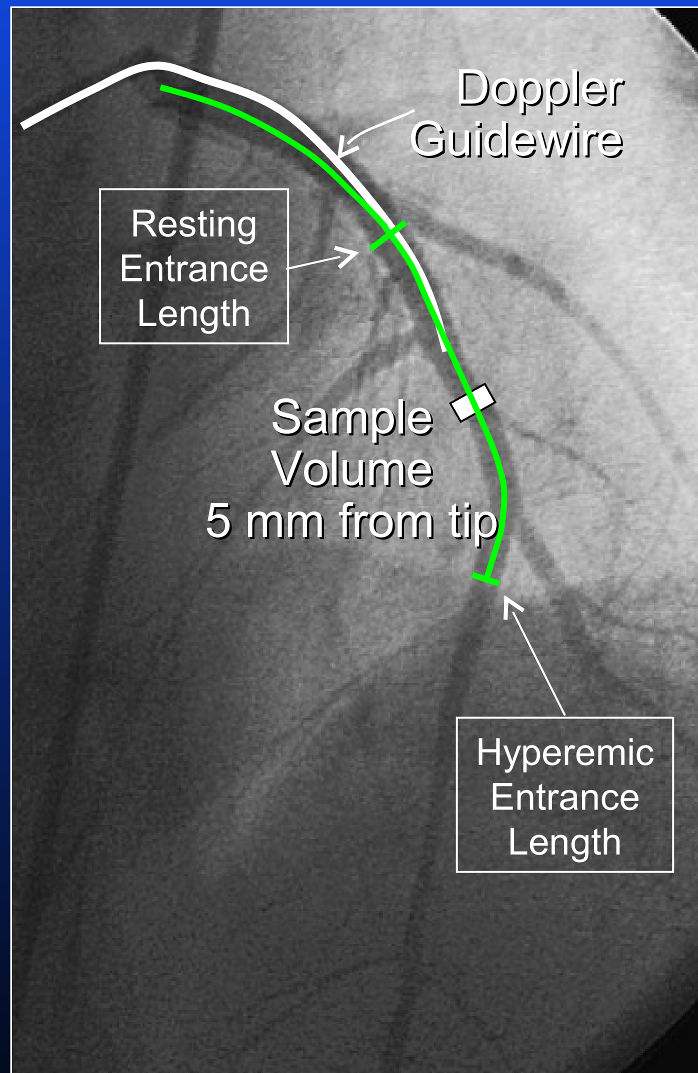


Resting Flow

“Fully developed” flow

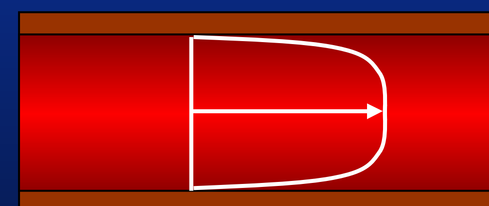


$V_{avg} = 1/2\ V_{peak}$



Hyperemic Flow

Underdeveloped flow



$V_{avg} = 4/5\ V_{peak}$

Limitations of Doppler CFR and FFR

Doppler CFR

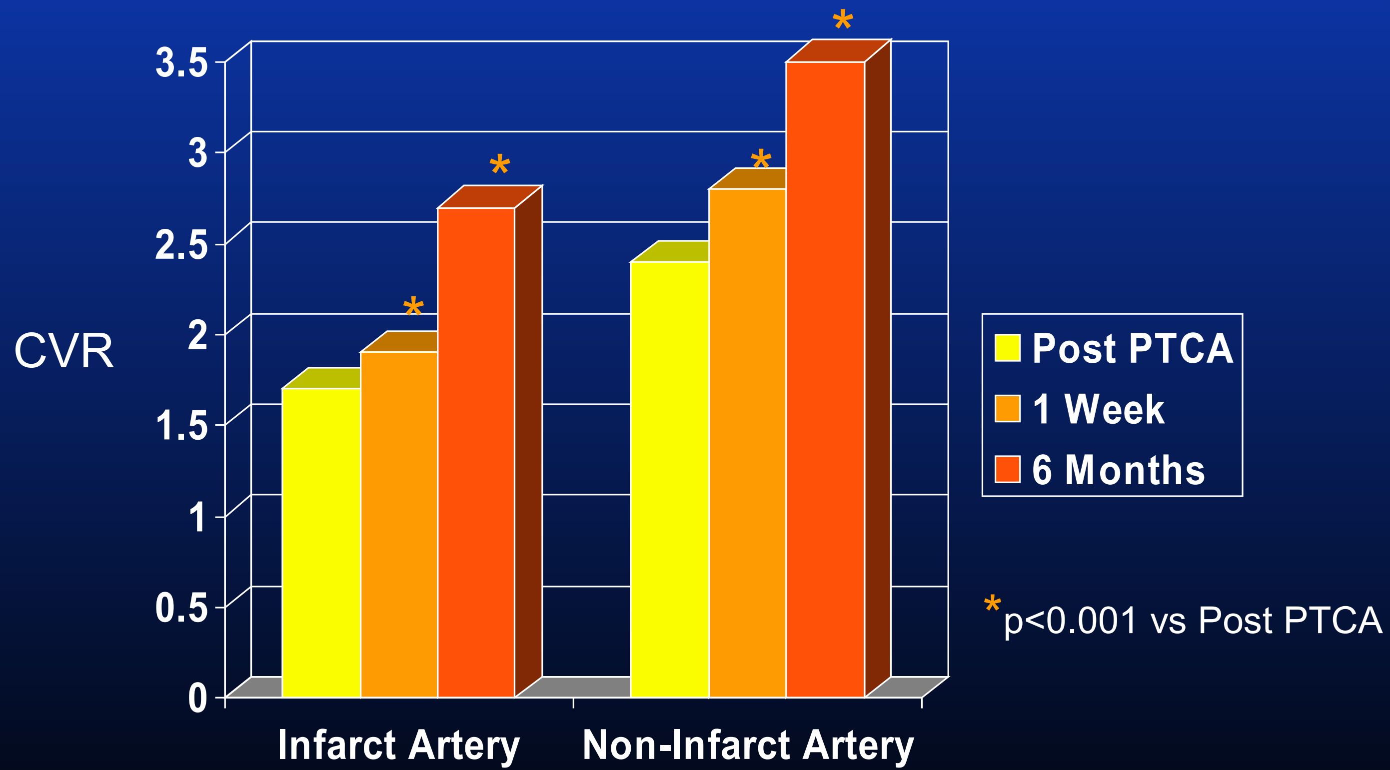
- Velocity profile
  - Parabolic vs. non-parabolic
  - Entrance length effects
  - Varying flow area
- Technical problems
  - Poor signal
- Microcirculatory disease
  - Regional heterogeneity
  - Temporal heterogeneity

Pressure-derived FFR

- Right heart failure
- Tandem, or serial, lesions
- Technical problems
  - Pressure drift
  - Guide-catheter damping
- Microcirculatory disease
  - Regional heterogeneity
  - Temporal heterogeneity

Temporal Heterogeneity in Flow
Post Myocardial Infarction

57 patients, primary PTCA for anterior MI



Bax et al, JACC 2000

MEASUREMENT OF FRACTIONAL FLOW RESERVE TO ASSESS THE FUNCTIONAL SEVERITY OF CORONARY-ARTERY STENOSES

NICO H.J. PIJLS, M.D., PH.D., BERNARD DE BRUYNE, M.D., KATHINKA PEELS, M.D., PEPIJN H. VAN DER VOORT, M.D., HANS J.R.M. BONNIER, M.D., PH.D., JOZEF BARTUNEK, M.D., AND JACQUES J. KOOLEN, M.D., PH.D.

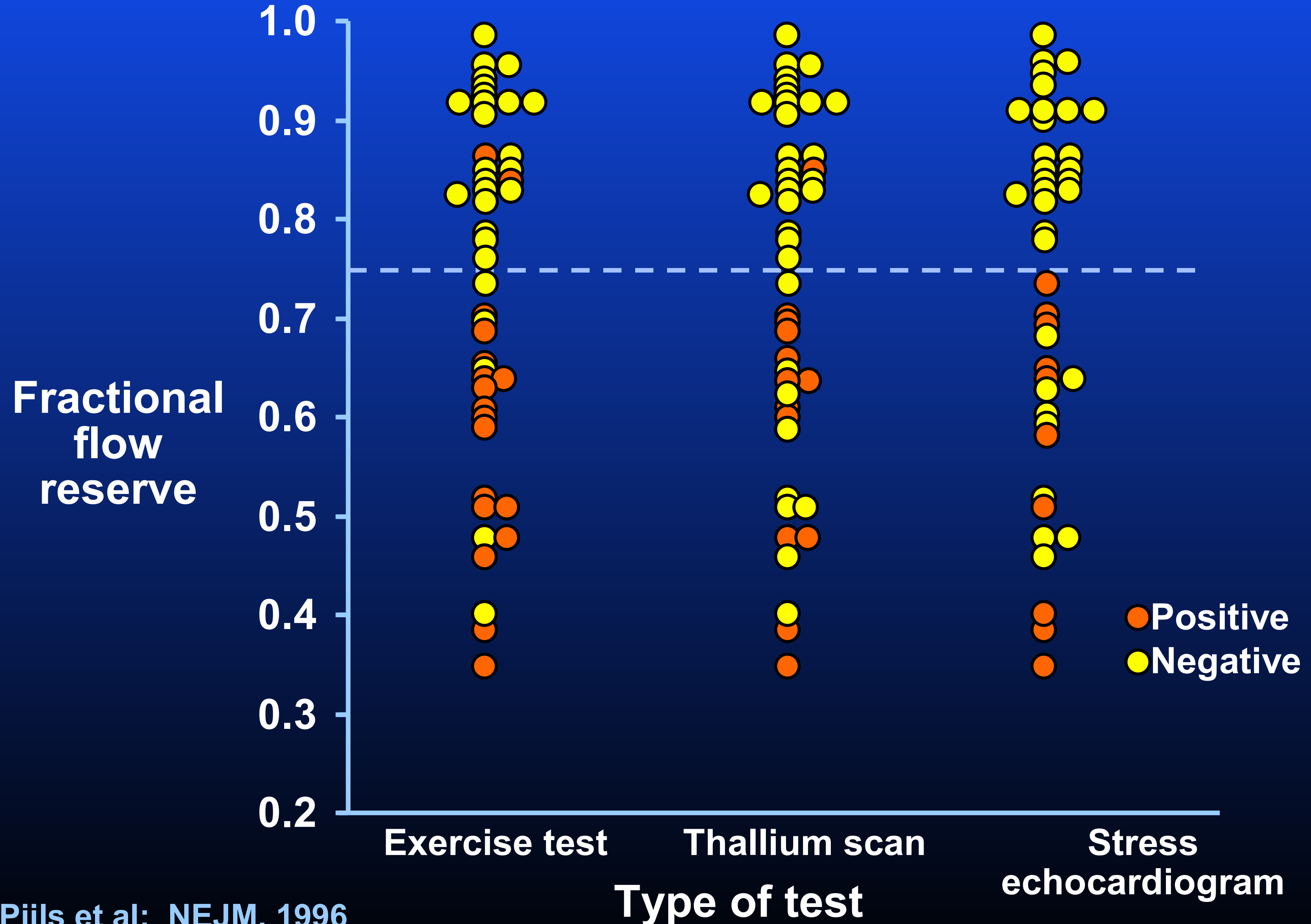
Abstract *Background.* The clinical significance of coronary-artery stenoses of moderate severity can be difficult to determine. Myocardial fractional flow reserve (FFR) is a new index of the functional severity of coronary stenoses that is calculated from pressure measurements made during coronary arteriography. We compared this index with the results of noninvasive tests commonly used to detect myocardial ischemia, to determine the usefulness of the index.

Methods. In 45 consecutive patients with moderate coronary stenosis and chest pain of uncertain origin, we performed bicycle exercise testing, thallium scintigraphy, stress echocardiography with dobutamine, and quantitative coronary arteriography and compared the results with measurements of FFR.

Results. In all 21 patients with an FFR of less than 0.75, reversible myocardial ischemia was demonstrated unequivocally on at least one noninvasive test. After coronary angioplasty or bypass surgery was performed, all the positive test results reverted to normal. In contrast, 21 of the 24 patients with an FFR of 0.75 or higher tested negative for reversible myocardial ischemia on all the noninvasive tests. No revascularization procedures were performed in these patients, and none were required during 14 months of follow-up. The sensitivity of FFR in the identification of reversible ischemia was 88 percent, the specificity 100 percent, the positive predictive value 100 percent, the negative predictive value 88 percent, and the accuracy 93 percent.

Conclusions. In patients with coronary stenosis of moderate severity, FFR appears to be a useful index of the functional severity of the stenoses and the need for coronary revascularization. (N Engl J Med 1996;334:1703-8.)

Relation Between Myocardial FFR and the Noninvasive Tests



Pijls et al: NEJM, 1996

Fractional Flow Reserve Concepts

Correlative Studies

Author	n	Ischemic Test	FFR_{mvo}	Sensitivity %	Specificity %	Accuracy %
Pijls	45	4 test standard	<0.75	88	100	93
De Bruyne	60	Exercise ECG	<0.72	100	87	-
Bartunek	37	Dobu/exer ECG	<0.68	95	94	-
Abe	46	Thallium	<0.76	96	100	96
Chamuleau	152	MIBI	<0.75	-	-	80

Results of Previous Validation Studies for Intracoronary-Derived CFVR, FFR amd rCFVR vs the Results of Noninvasive Stress Testing

Author	Year	Patients (no.)	Noninvasive stress test	Reported cut-off value
CFVR				
Miller et al	1994	33	SPECT	2.0
Joye et al	1994	30	SPECT	2.0
Deychak et al	1995	17	SPECT	1.8
Heller et al	1997	55	SPECT	1.7
Danzi et al	1998	30	Stress Echo	2.0
Verberne et al	1999	37	SPECT	1.9
FFR				
Pijls et al	1995	60	Exc-ECG	0.74
De Bruyne et al	1995	60	Exc-ECG	0.72
Pijls et al	1996	45	Exc-ECG, SPECT and stress Echo	0.75
Bartunek et al	1997	37	Stress Echo	0.68
rCFVR				

Chamuleau et al: JACC, 2001

Abnormal Epicardial Coronary Resistance in Patients With Diffuse Atherosclerosis but "Normal" Coronary Angiography

Bernard De Bruyne, MD, PhD; Ferry Hersbach, MD; Nico H.J. Pijls, MD, PhD; Jozef Bartunek, MD, PhD; Jan-Willem Bech, MD; Guy R. Heyndrickx, MD, PhD; K. Lance Gould, MD; William Wijns, MD, PhD

Background—Coronary arteries without focal stenosis at angiography are generally considered non–flow-limiting. However, atherosclerosis is a diffuse process that often remains invisible at angiography. Accordingly, we hypothesized that in patients with coronary artery disease, nonstenotic coronary arteries induce a decrease in pressure along their length due to diffuse coronary atherosclerosis.

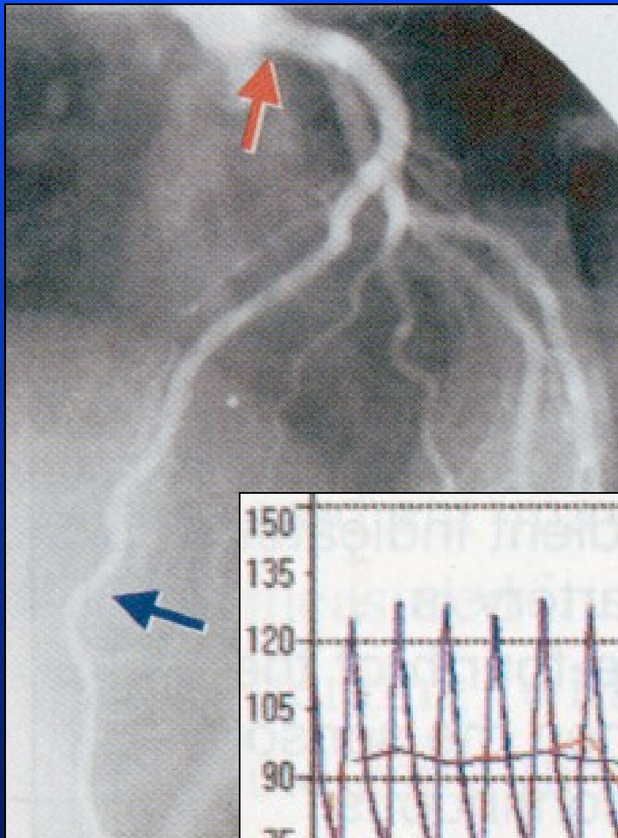
Methods and Results—Coronary pressure and fractional flow reserve (FFR), as indices of coronary conductance, were obtained from 37 arteries in 10 individuals without atherosclerosis (group I) and from 106 nonstenotic arteries in 62 patients with arteriographic stenoses in another coronary artery (group II). In group I, the pressure gradient between aorta and distal coronary artery was minimal at rest (1±1 mm Hg) and during maximal hyperemia (3±3 mm Hg). Corresponding values were significantly larger in group II (5±4 mm Hg and 10±8 mm Hg, respectively; both $P<0.001$). The FFR was near unity (0.97±0.02; range, 0.92 to 1) in group I, indicating no resistance to flow in truly normal coronary arteries, but it was significantly lower (0.89±0.08; range, 0.69 to 1) in group II, indicating a higher resistance to flow. In 57% of arteries in group II, FFR was lower than the lowest value in group I. In 8% of arteries in group II, FFR was <0.75, the threshold for inducible ischemia.

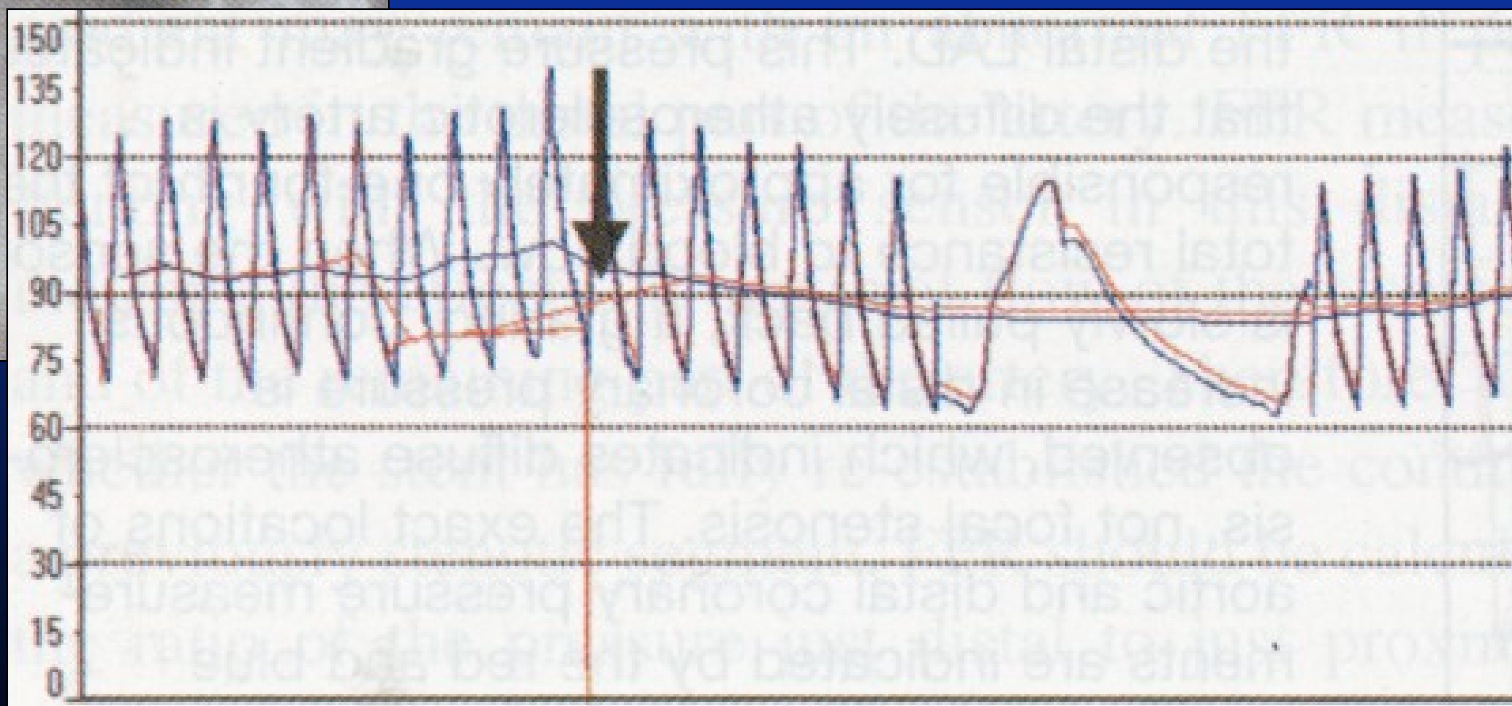
Conclusion—Diffuse coronary atherosclerosis without focal stenosis at angiography causes a graded, continuous pressure fall along arterial length. This resistance to flow contributes to myocardial ischemia and has consequences for decision-making during percutaneous coronary interventions. (***Circulation*. 2001;104:2401-2406.**)

Key Words: blood flow ■ pressure ■ coronary disease ■ atherosclerosis ■ angina ■ ischemia

Pullback record

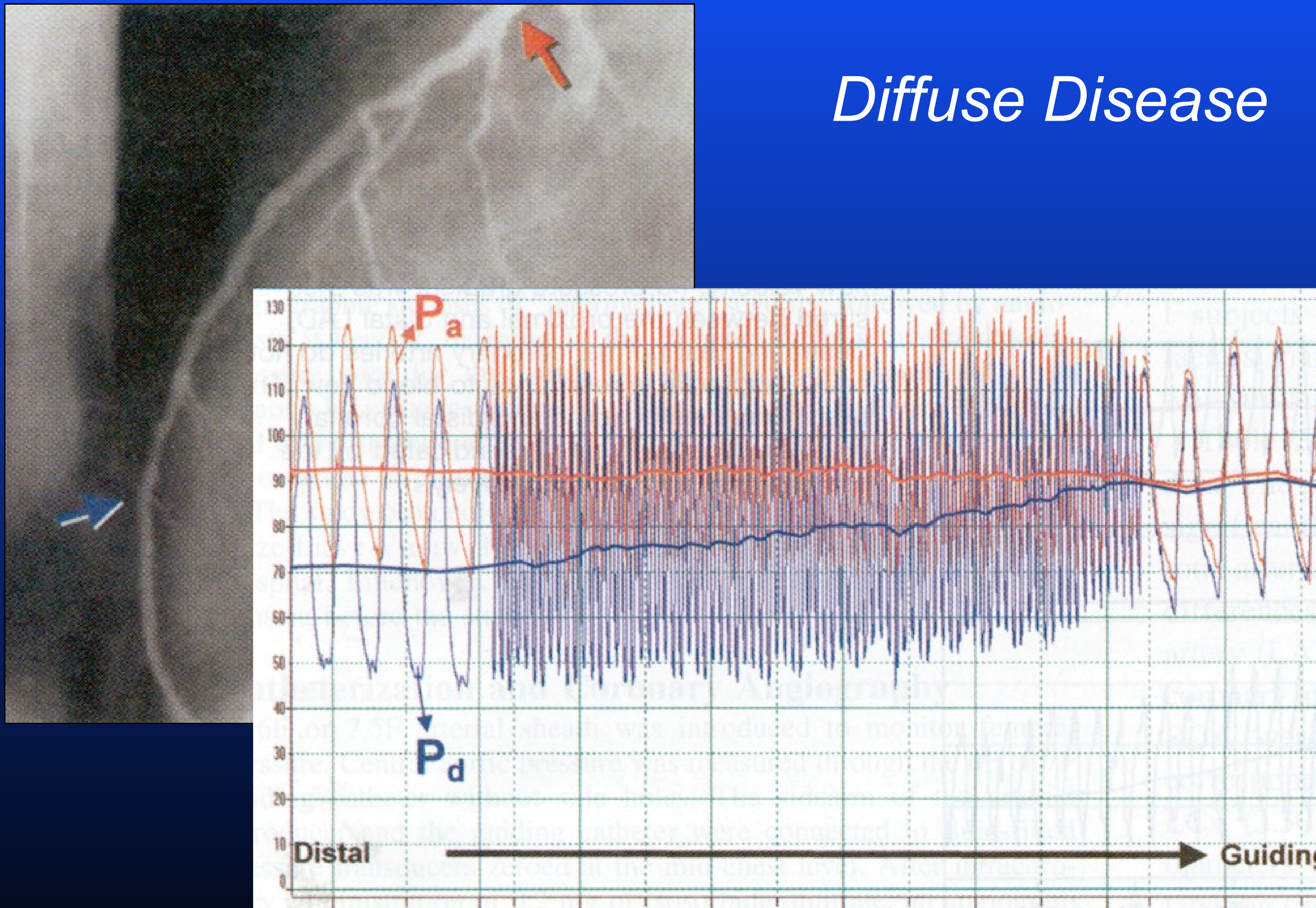
Normal Coronaries





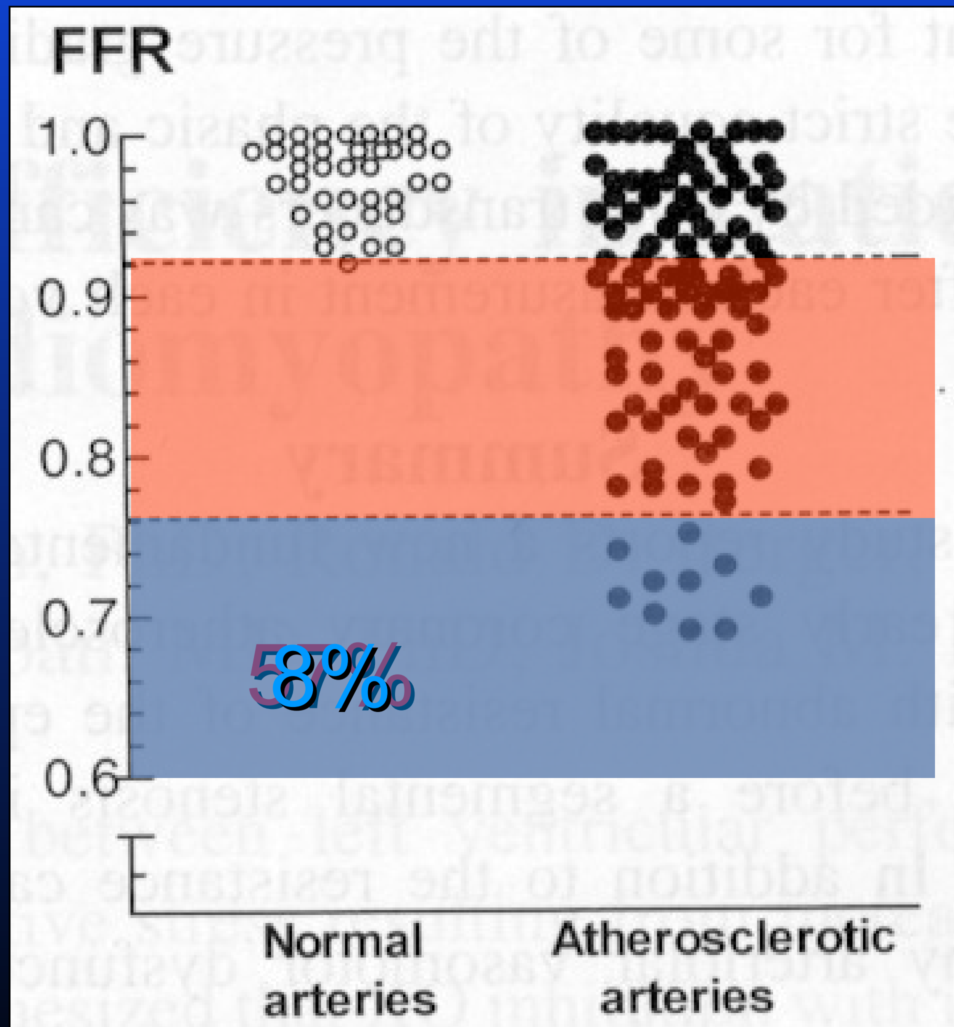
DeBruyne et al, Circulation 2001

Diffuse Disease

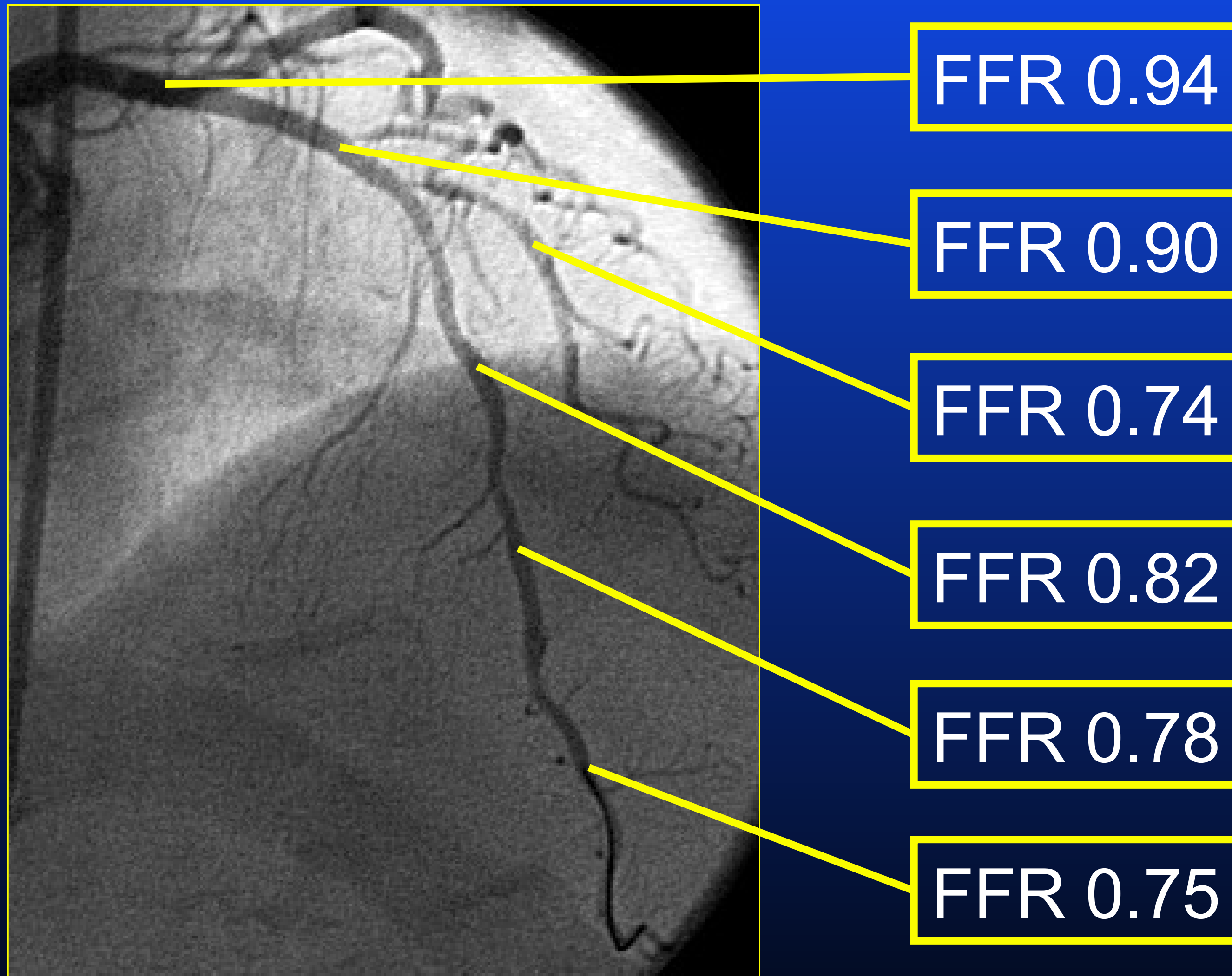


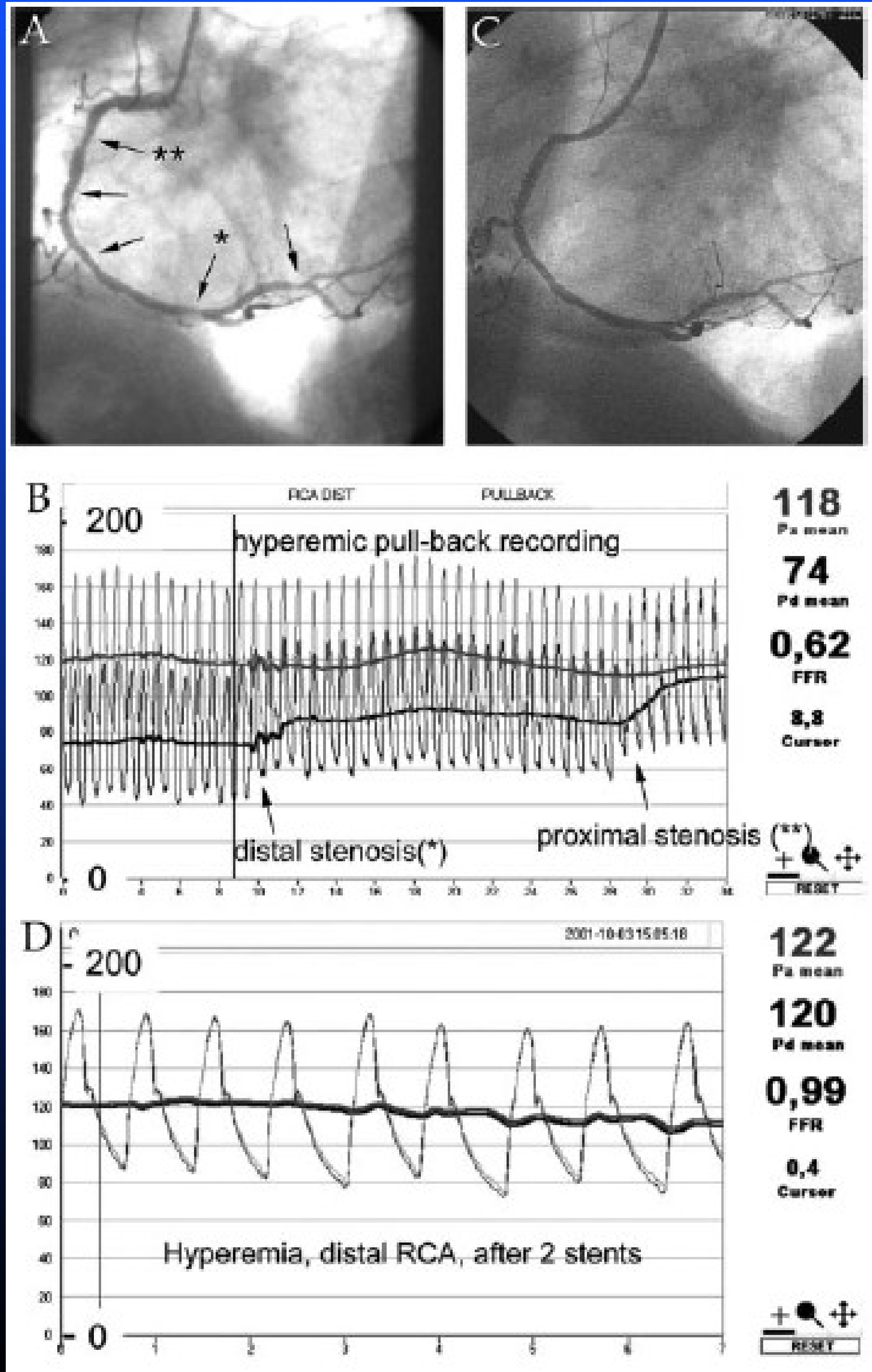
DeBruyne et al, Circulation 2001

FFR_{myo} and Diffuse Disease

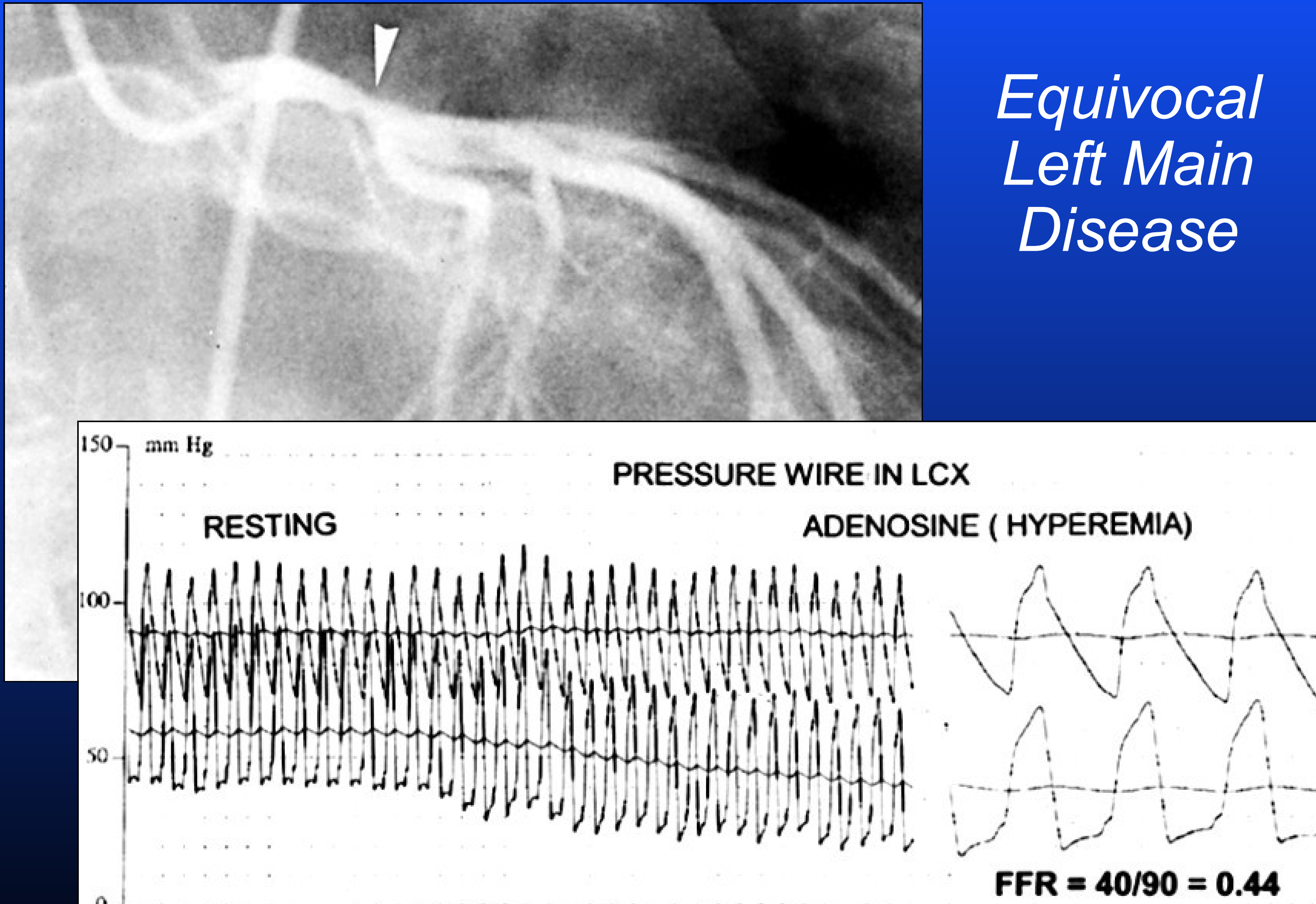


DeBruyne et al, Circulation 2001


FFR 0.94
FFR 0.90
FFR 0.74
FFR 0.82
FFR 0.78
FFR 0.75

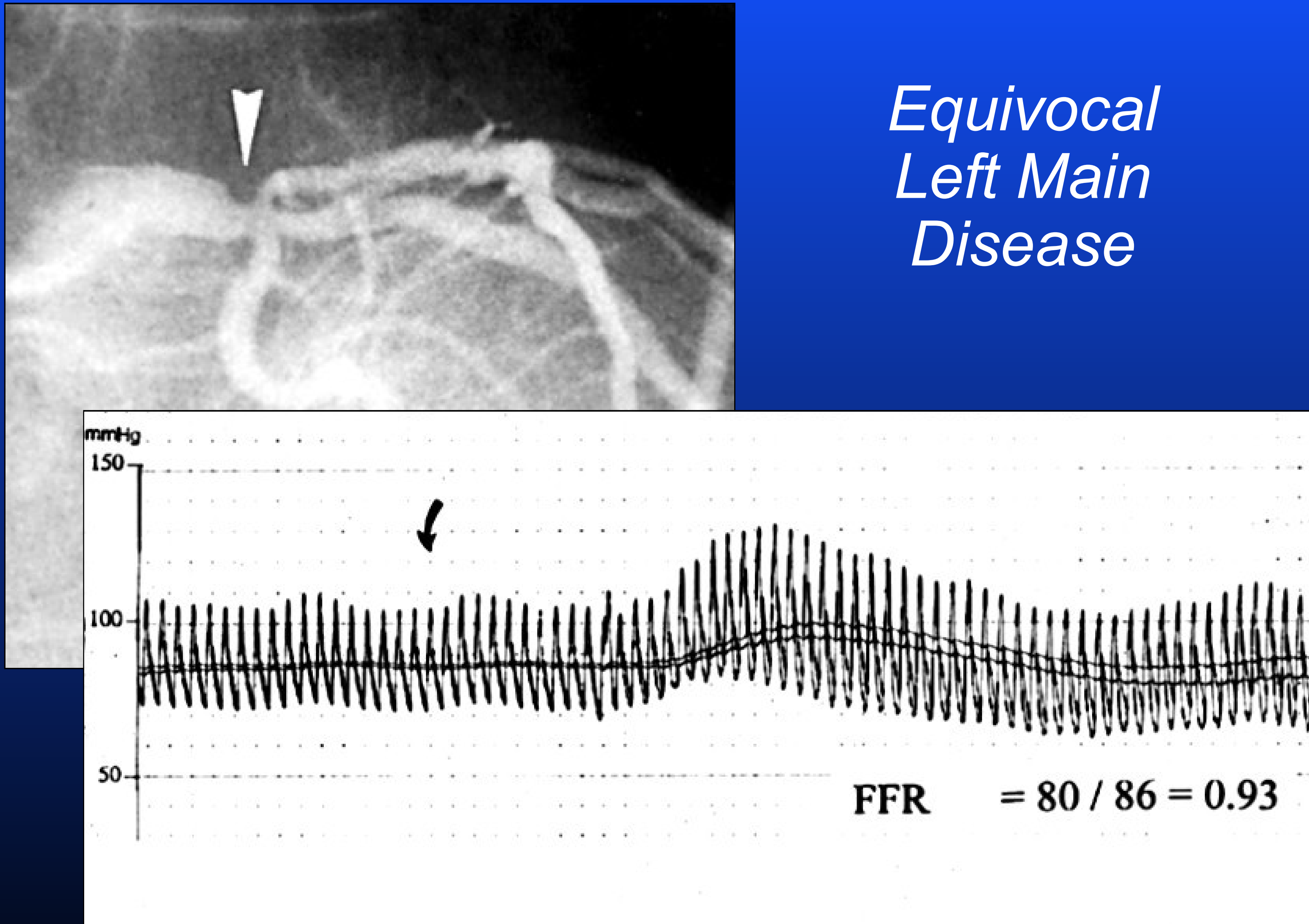

A
**
*
C
B
RCA DIST
PULLBACK
200
hyperemic pull-back recording
118
Pa mean
74
Pd mean
0,62
FFR
8,8
Cursor
distal stenosis(*)
proximal stenosis (**)
0
RESET
D
200
122
Pa mean
120
Pd mean
0,99
FFR
0,4
Cursor
Hyperemia, distal RCA, after 2 stents
0
RESET

Equivocal Left Main Disease



Bech et al, Heart 2001

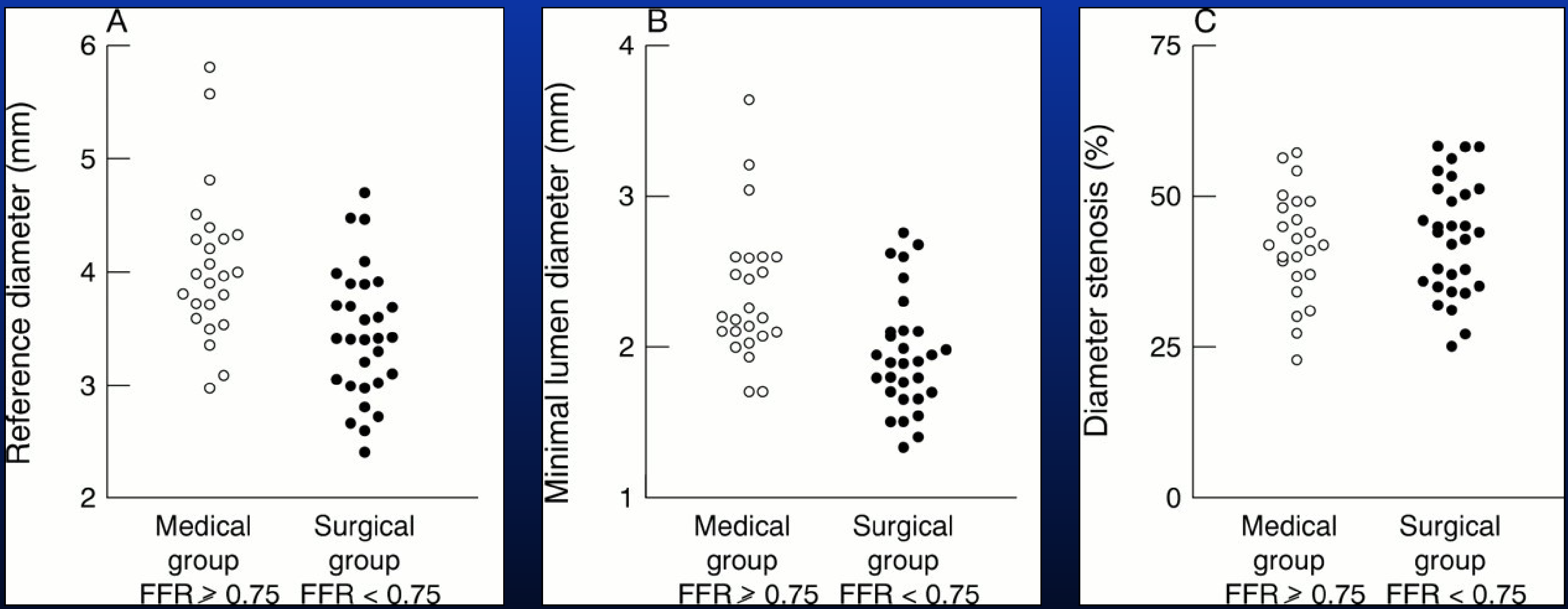
Equivocal Left Main Disease



Bech et al, Heart 2001

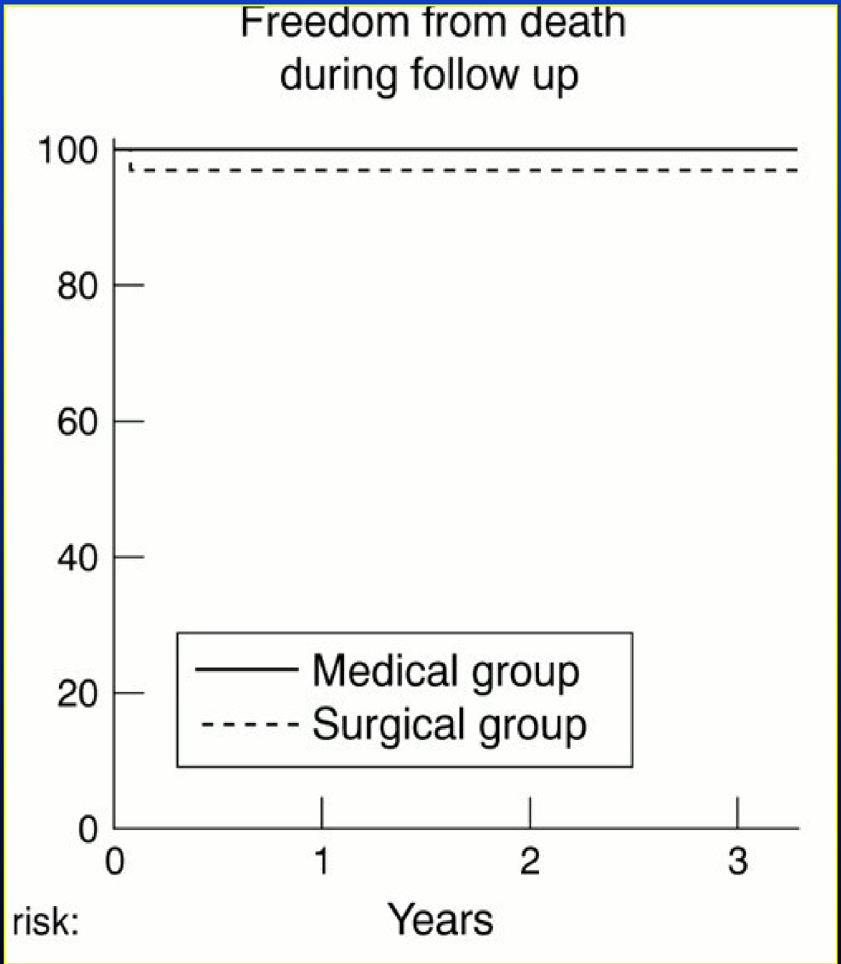
FFR$_{myo}$ and Equivocal Left Main Disease

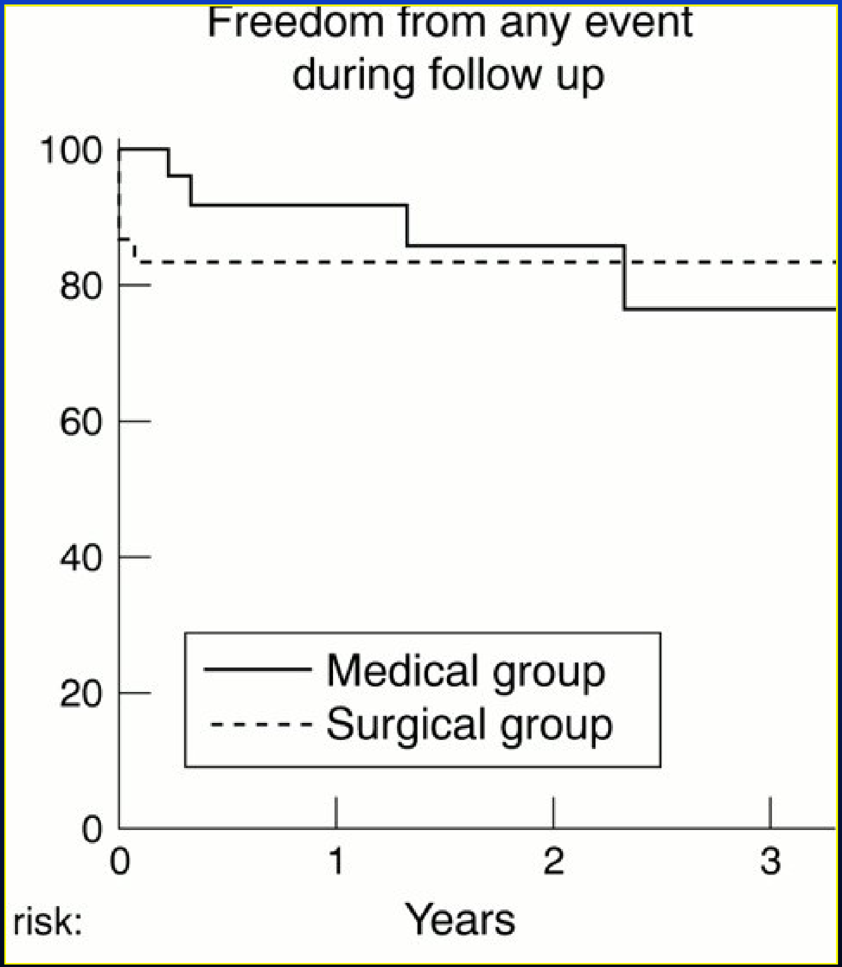
- 54 Consecutive patients with angiographically equivocal left main disease



Bech et al, Heart 2001

FFR$_{myo}$ and Equivocal Left Main Disease





Bech et al, Heart 2001

Usefulness of Fractional Flow Reserve to Predict Clinical Outcome After Balloon Angioplasty

G. Jan Willem Bech, MD; Nico H.J. Pijls, MD, PhD; Bernard De Bruyne, MD, PhD;
Kathinka H. Peels, MD; H. Rolf Michels, MD;
Hans J.R.M. Bonnier, MD, PhD; Jacques J. Koolen, MD, PhD

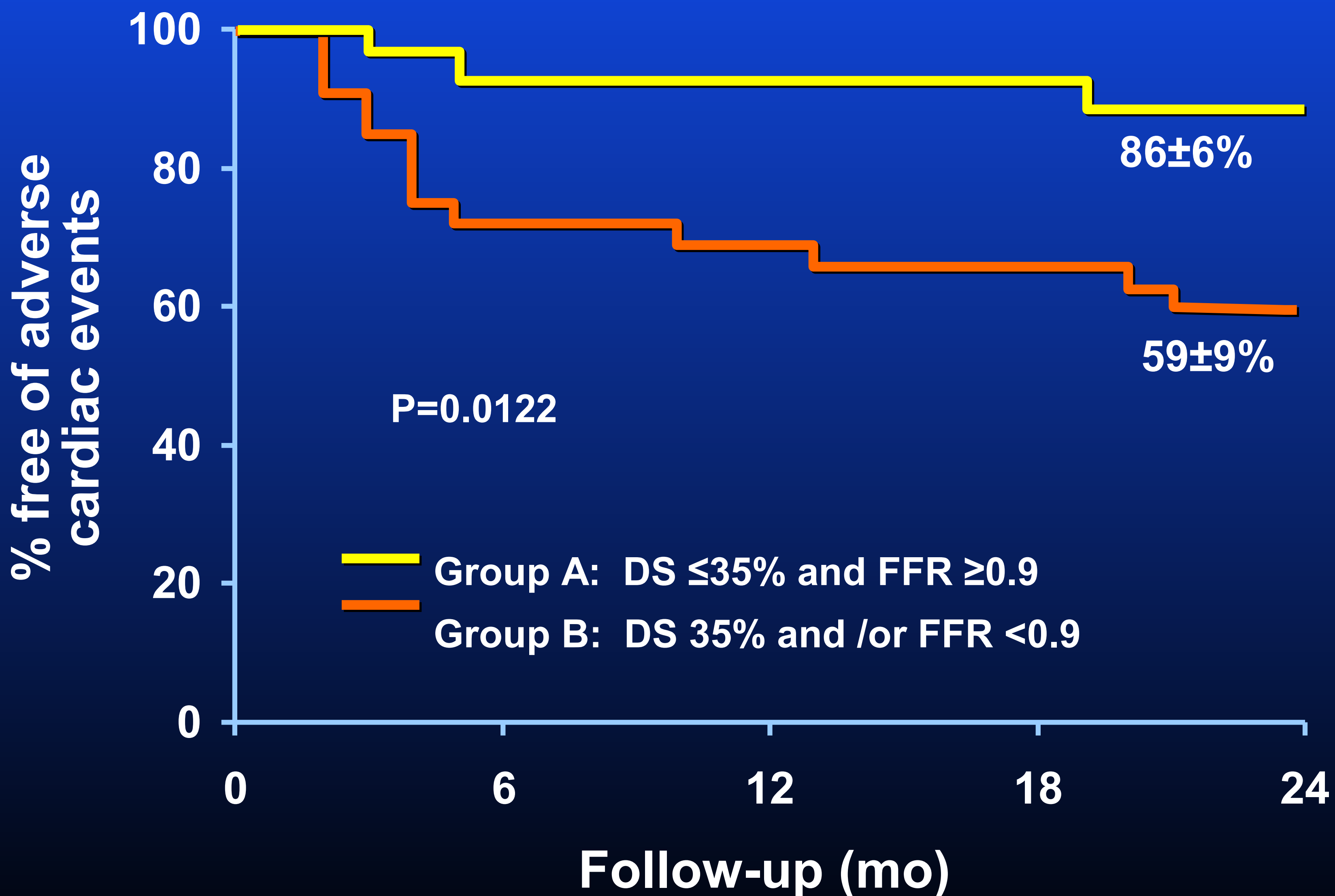
Background—After regular coronary balloon angioplasty, it would be helpful to identify those patients who have a low cardiac event rate. Coronary angiography alone is not sensitive enough for that purpose, but it has been suggested that the combination of optimal angiographic and optimal functional results indicates a low restenosis chance. Pressure-derived myocardial fractional flow reserve (FFR) is an index of the functional severity of the residual epicardial lesion and could be useful for that purpose.

Methods and Results—In 60 consecutive patients with single-vessel disease, balloon angioplasty was performed by use of a pressure instead of a regular guide wire. Both quantitative coronary angiography (QCA) and measurement of FFR were performed 15 minutes after the procedure. A successful angioplasty result, defined as a residual diameter stenosis (DS) $<50\%$, was achieved in 58 patients. In these patients, DS and FFR, measured 15 minutes after PTCA, were analyzed in relation to clinical outcome. In those 26 patients with both optimal angiographic (residual DS by QCA $\leq 35\%$) and optimal functional (FFR ≥ 0.90) results, event-free survival rates at 6, 12, and 24 months were $92 \pm 5\%$, $92 \pm 5\%$, and $88 \pm 6\%$, respectively, versus $72 \pm 8\%$, $69 \pm 8\%$, and $59 \pm 9\%$, respectively, in the remaining 32 patients in whom the angiographic or functional result or both were suboptimal ($P=0.047$, $P=0.028$, and $P=0.014$, respectively).

Conclusions—In patients with a residual DS $\leq 35\%$ and FFR ≥ 0.90, clinical outcome up to 2 years is excellent. Therefore, there is a complementary value of coronary angiography and coronary pressure measurement in the evaluation of PTCA result. (***Circulation*. 1999;99:883-888.**)

Key Words: pressure ■ balloon ■ angioplasty ■ blood flow ■ prognosis

Event-Free Survival Curve



Bech et al: Circulation, 1999

Fractional Flow Reserve to Determine the Appropriateness of Angioplasty in Moderate Coronary Stenosis

A Randomized Trial

G. Jan Willem Bech, MD; Bernard De Bruyne, MD, PhD; Nico H.J. Pijls, MD, PhD; Ebo D. de Muinck, MD, PhD; Jan C.A. Hoorntje, MD, PhD; Javier Escaned, MD, PhD; Pieter R. Stella, MD; Eric Boersma, MSc, PhD; Jozef Bartunek, MD, PhD; Jacques J. Koolen, MD, PhD; William Wijns, MD, PhD

Background—PTCA of a coronary stenosis without documented ischemia at noninvasive stress testing is often performed, but its benefit is unproven. Coronary pressure–derived fractional flow reserve (FFR) is an invasive index of stenosis severity that is a reliable substitute for noninvasive stress testing. A value of 0.75 identifies stenoses with hemodynamic significance.

Methods and Results—In 325 patients for whom PTCA was planned and who did not have documented ischemia, FFR of the stenosis was measured. If FFR was >0.75, patients were randomly assigned to deferral (deferral group; n=91) or performance (performance group; n=90) of PTCA. If FFR was <0.75, PTCA was performed as planned (reference group; n=144). Clinical follow-up was obtained at 1, 3, 6, 12, and 24 months. Event-free survival was similar between the deferral and performance groups (92% versus 89% at 12 months and 89% versus 83% at 24 months) but was significantly lower in the reference group (80% at 12 months and 78% at 24 months). In addition, the percentage of patients free from angina was similar between the deferral and performance groups (49% versus 50% at 12 months and 70% versus 51% at 24 months) but was significantly higher in the reference group (67% at 12 and 80% at 24 months).

Conclusions—In patients with a coronary stenosis without evidence of ischemia, coronary pressure–derived FFR identifies those who will benefit from PTCA. (***Circulation*. 2001;103:2928-2934.**)

Key Words: coronary disease ■ angioplasty ■ pressure ■ blood flow

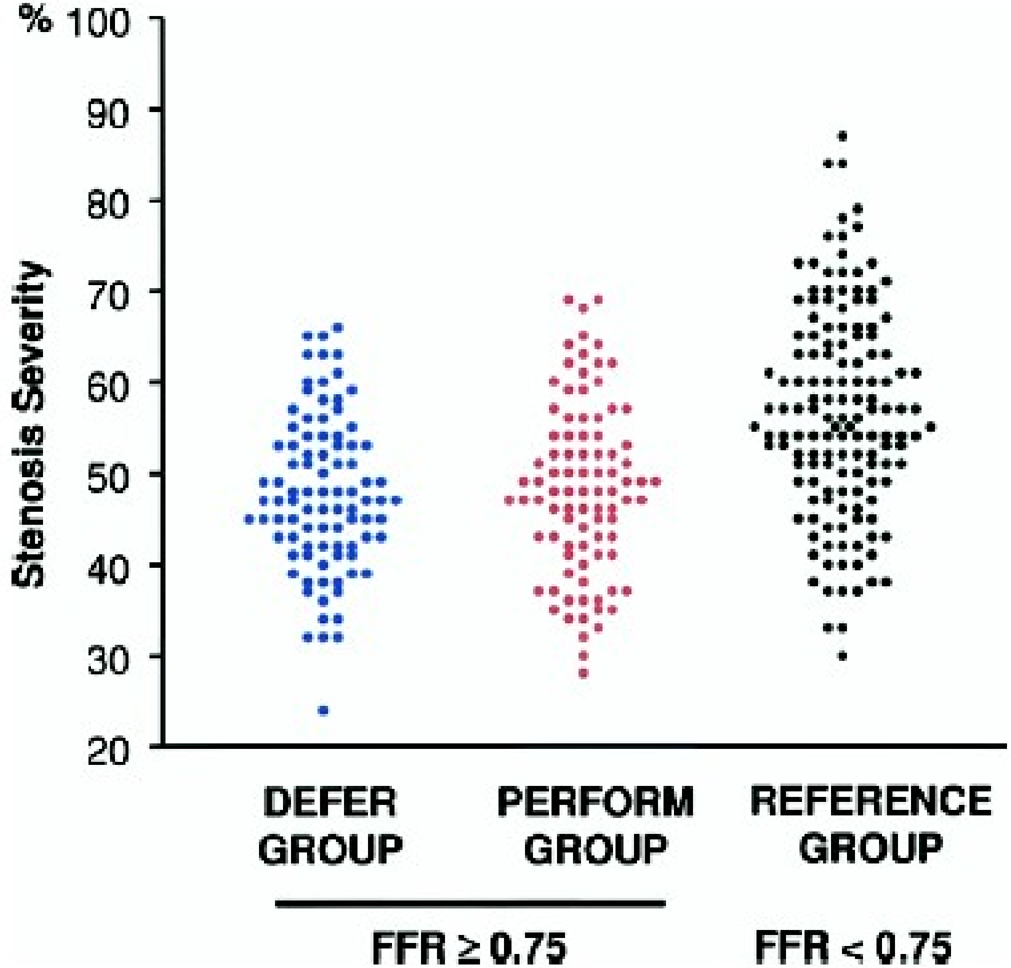


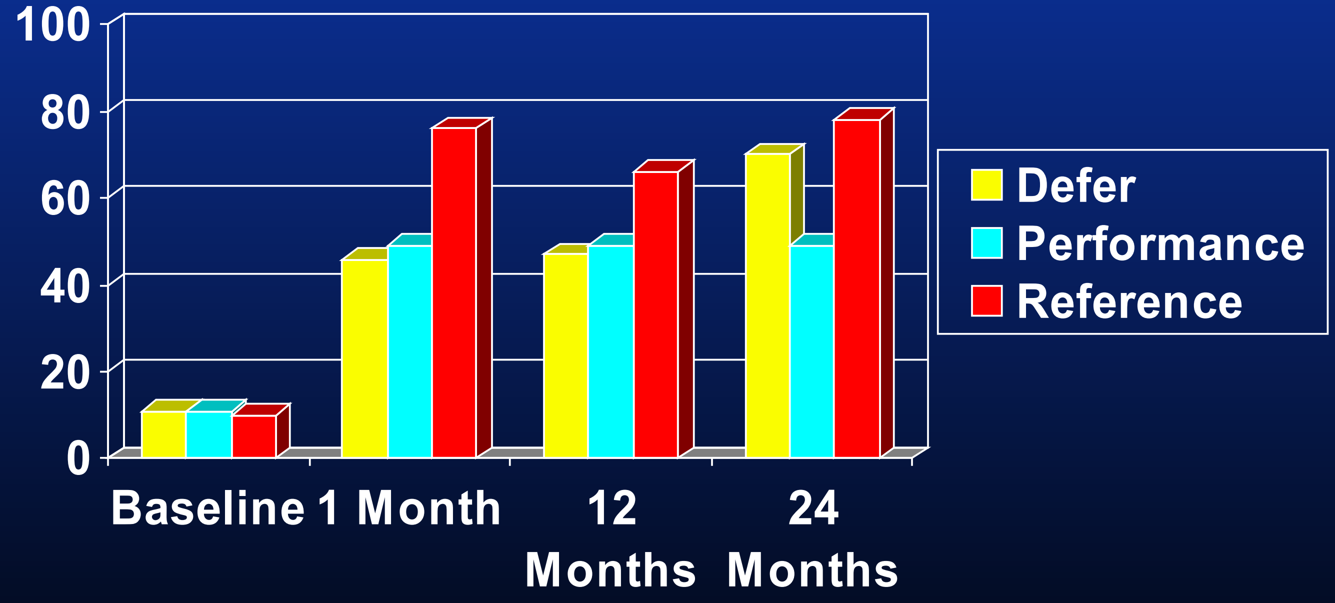
Figure 2 **Stenosis Severity at Baseline Assessed by Quantitative Coronary Angiography in the 3 Groups**

Abbreviations as in Figure 1.

Deferral of PTCA Based on FFR

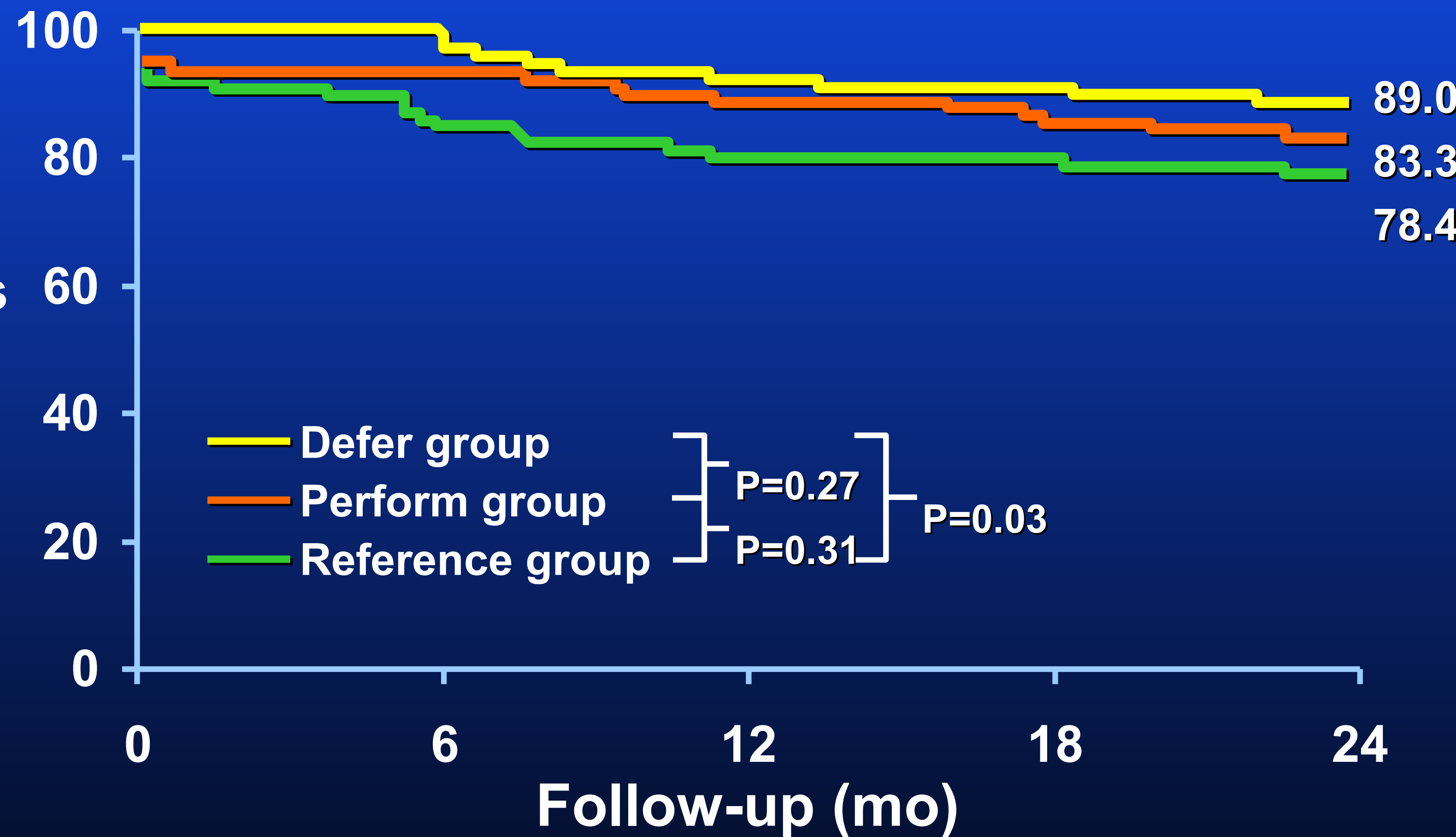
- 325 patients referred for PTCA without documented ischemia
- If FFR >0.75, randomized to Defer (91) or Performance (90) groups
- If FFR <0.75, PTCA performed, Reference group (144)

Patients free from angina (%)



Bech et al, Circulation 2001

Kaplan-Meier Survival Curves for Freedom from Adverse Cardiac Events During 24 Months of Follow-Up for 3 Groups



	91	91	85	82	80
Bech et al:	90	84	80	78	75
Circ, 2001	144	123	116	106	106

Percutaneous Coronary Intervention of Functionally Nonsignificant Stenosis

5-Year Follow-Up of the DEFER Study

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Eric Boersma, PhD,‡ Jan-Willem Bech, MD, PhD,* Marcel van't Veer, MSc,* Frits Bär, MD, PhD,§
Jan Hoorntje, MD, PhD,‖ Jacques Koolen, MD, PhD,* William Wijns, MD, PhD,†
Bernard de Bruyne, MD, PhD†

Eindhoven, Rotterdam, Maastricht, and Zwolle, the Netherlands; and Aalst, Belgium

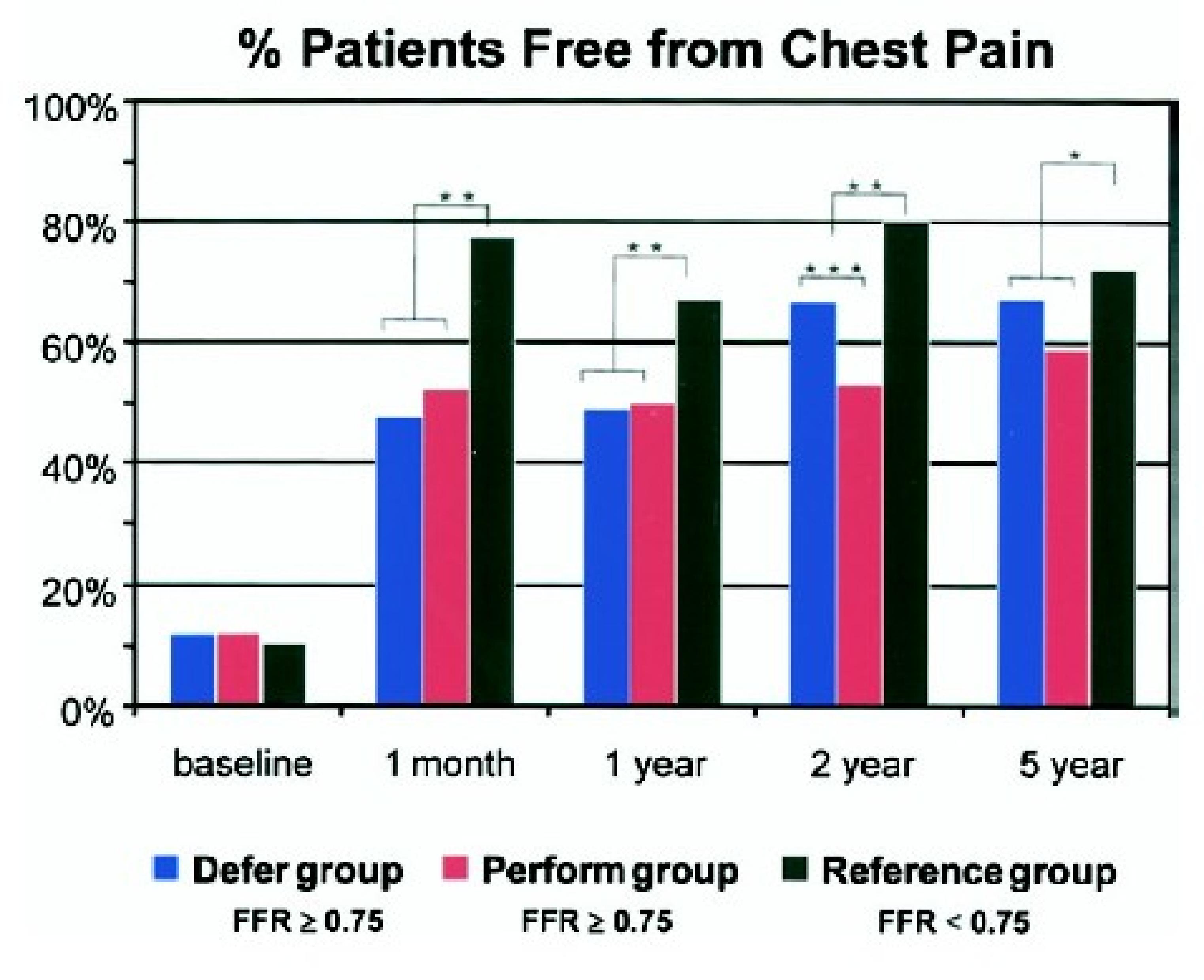
Objectives The purpose of this study was to investigate the appropriateness of stenting a functionally nonsignificant stenosis.

Background Percutaneous coronary intervention (PCI) of an intermediate stenosis without evidence of ischemia is often performed, but its benefit is unproven. Coronary pressure-derived fractional flow reserve (FFR) is an invasive index used to identify a stenosis responsible for reversible ischemia.

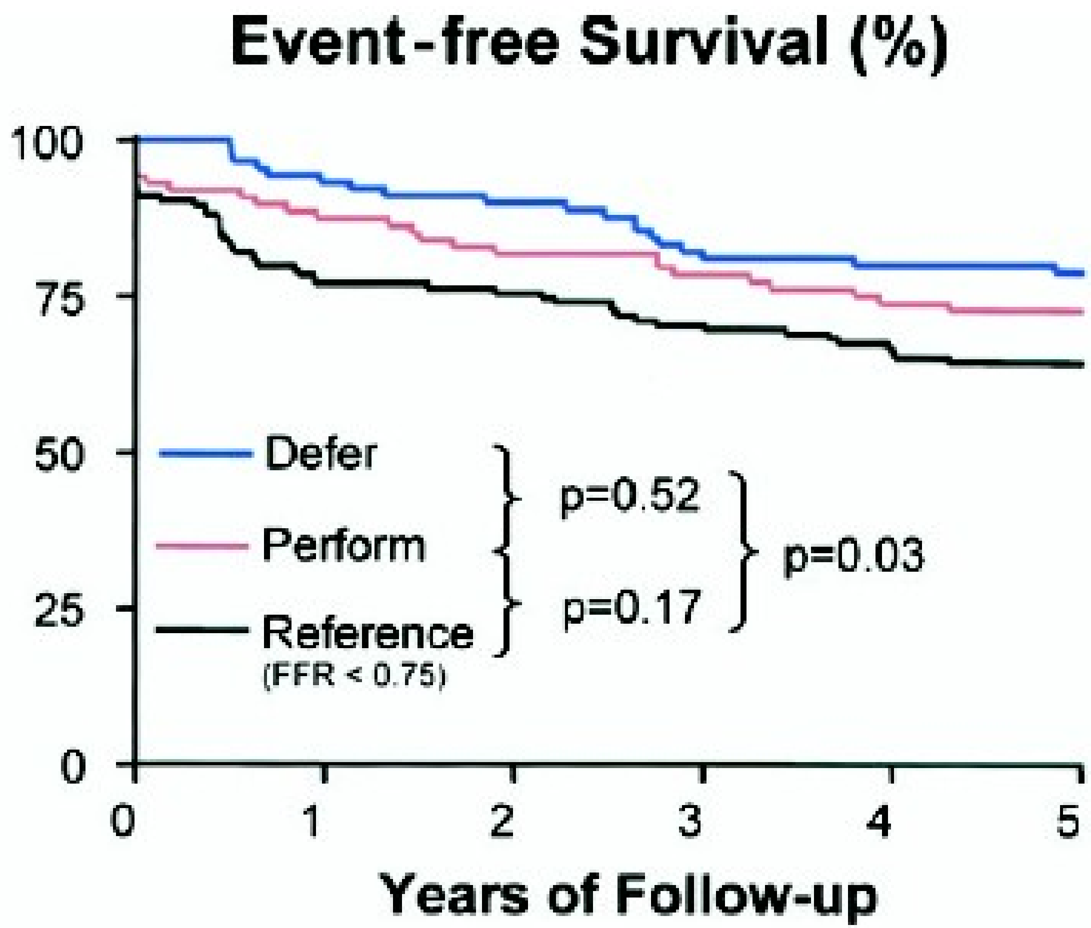
Methods In 325 patients scheduled for PCI of an intermediate stenosis, FFR was measured just before the planned intervention. If FFR was ≥ 0.75, patients were randomly assigned to deferral (Defer group; $n = 91$) or performance (Perform group; $n = 90$) of PCI. If FFR was < 0.75, PCI was performed as planned (Reference group; $n = 144$). Clinical follow-up was 5 years.

Results There were no differences in baseline clinical characteristics between the 3 groups. Complete follow-up was obtained in 98% of the patients. Event-free survival was not different between the Defer and Perform groups (80% and 73%, respectively; $p = 0.52$), but was significantly worse in the Reference group (63%; $p = 0.03$). The composite rate of cardiac death and acute myocardial infarction in the Defer, Perform, and Reference groups was 3.3%, 7.9%, and 15.7%, respectively ($p = 0.21$ for Defer vs. Perform group; $p = 0.003$ for the Reference vs. both other groups). The percentage of patients free from chest pain at follow-up was not different between the Defer and Perform groups.

Conclusions Five-year outcome after deferral of PCI of an intermediate coronary stenosis based on FFR ≥ 0.75 is excellent. The risk of cardiac death or myocardial infarction related to this stenosis is $< 1\%$ per year and not decreased by stenting. (J Am Coll Cardiol 2007;49:2105–11)



% Patients Free from Chest Pain
100%
80%
60%
40%
20%
0%
* *
* *
* * *
* *
*
baseline
1 month
1 year
2 year
5 year
Defer group
FFR ≥ 0.75
Perform group
FFR ≥ 0.75
Reference group
FFR < 0.75

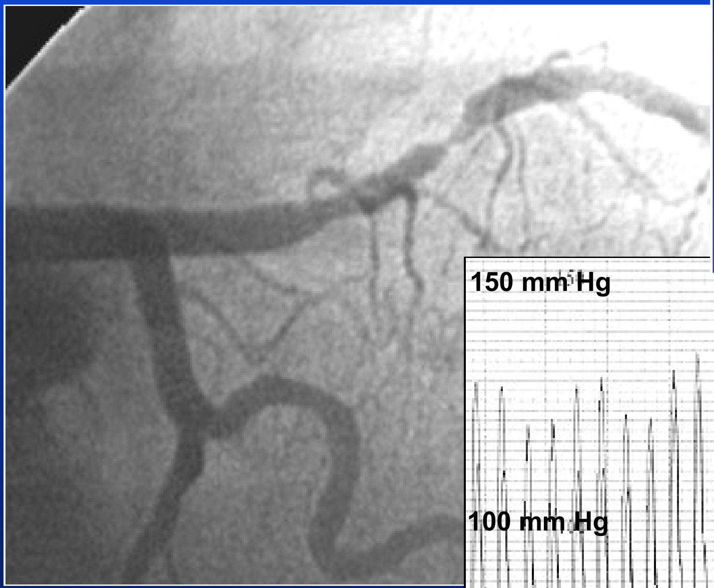


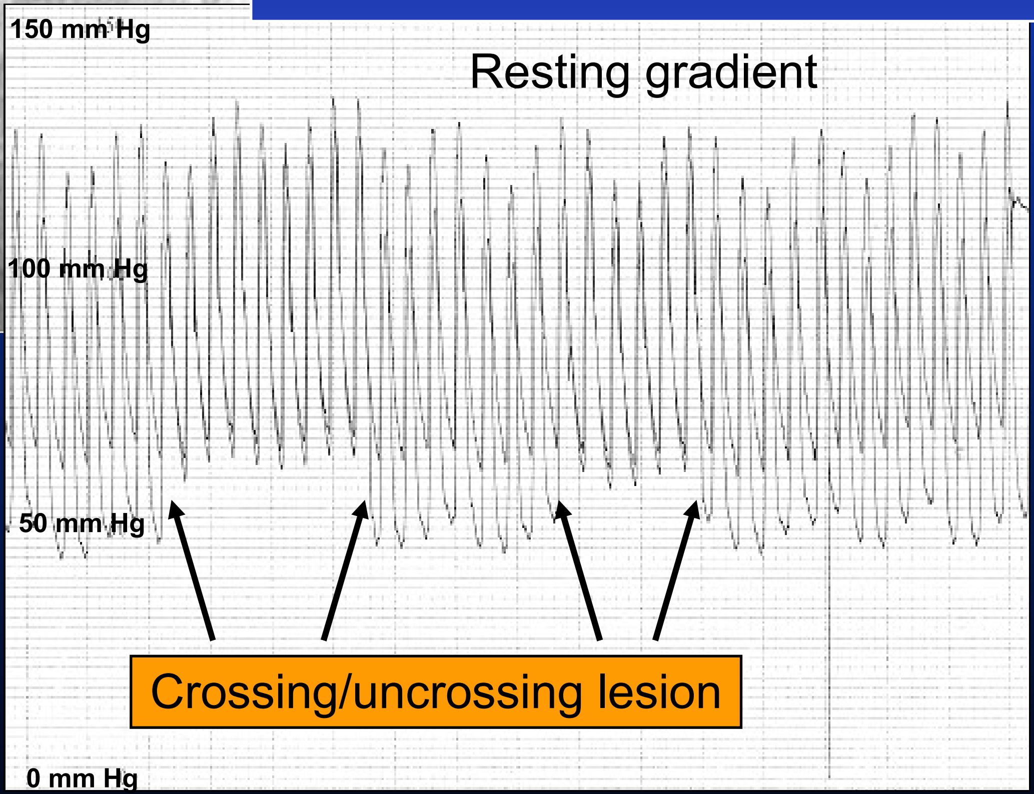
No. at risk

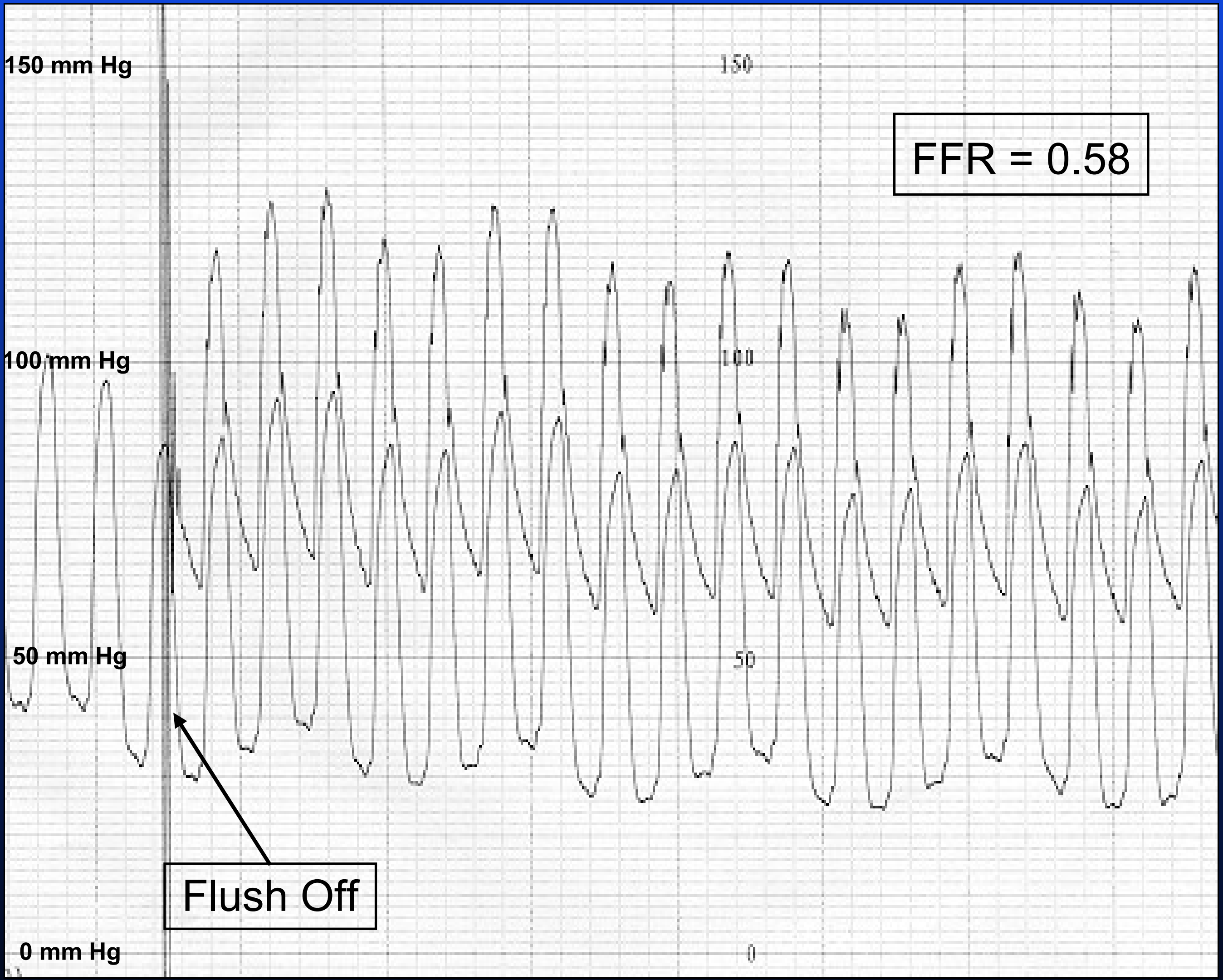
Defer group	91	85	80	74	73	72
Perform group	90	80	75	70	67	64
Reference group	144	116	106	96	90	88

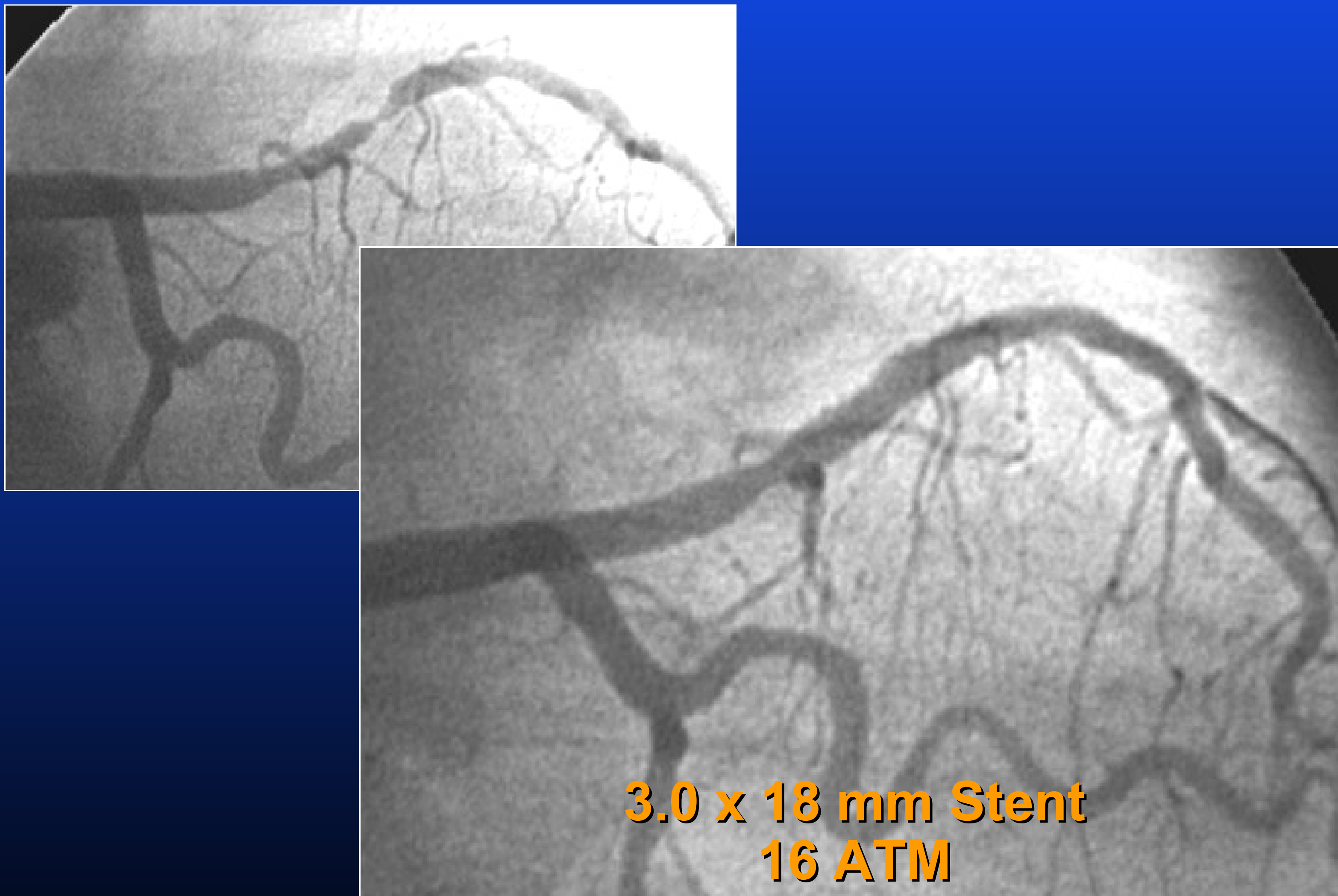
55 year old female

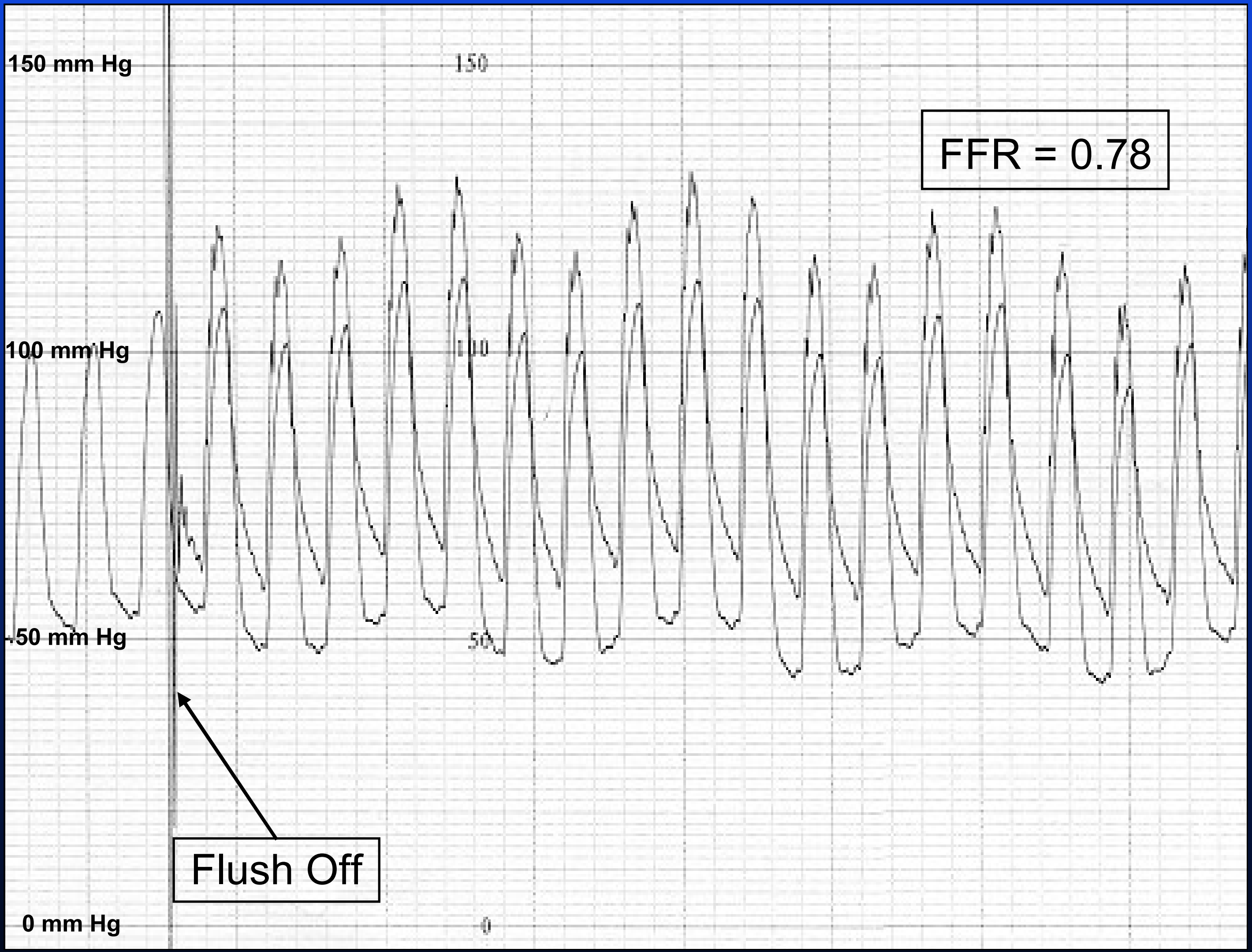
- Angina for one month
- Anterior and apical ischemia on exercise sestamibi

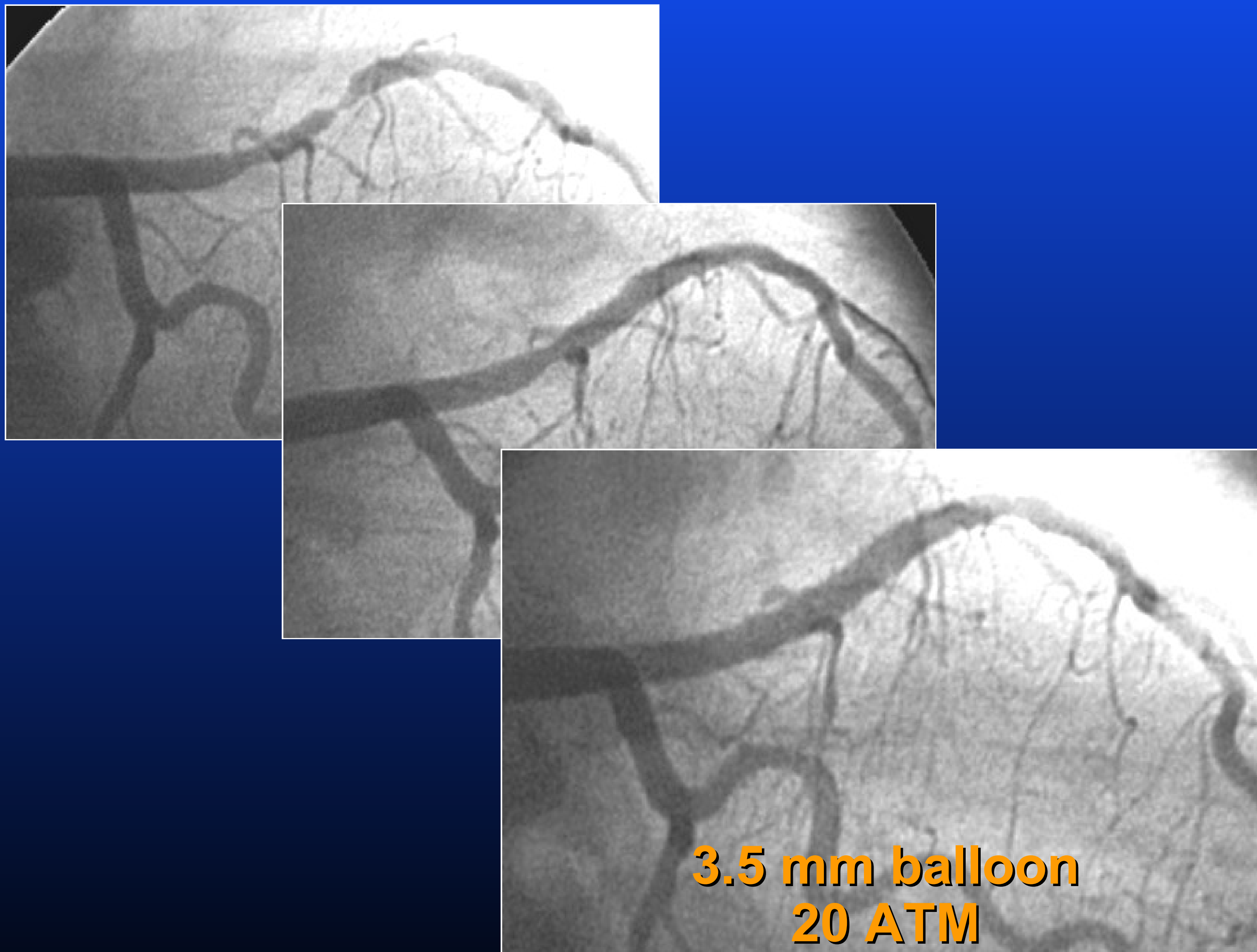


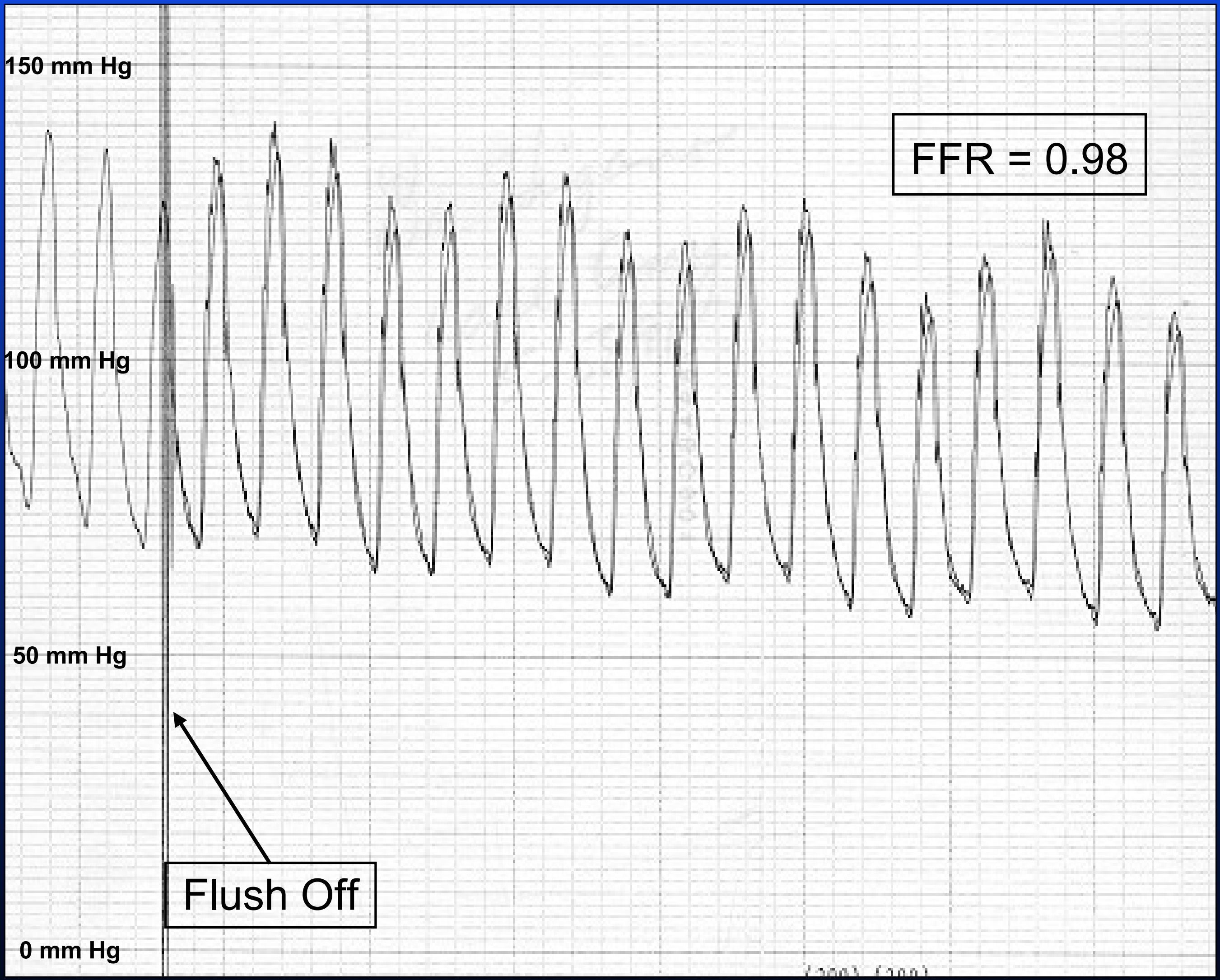



150 mm Hg
100 mm Hg
50 mm Hg
0 mm Hg
150
100
50
0
FFR = 0.58
Flush Off


3.0 x 18 mm Stent
16 ATM

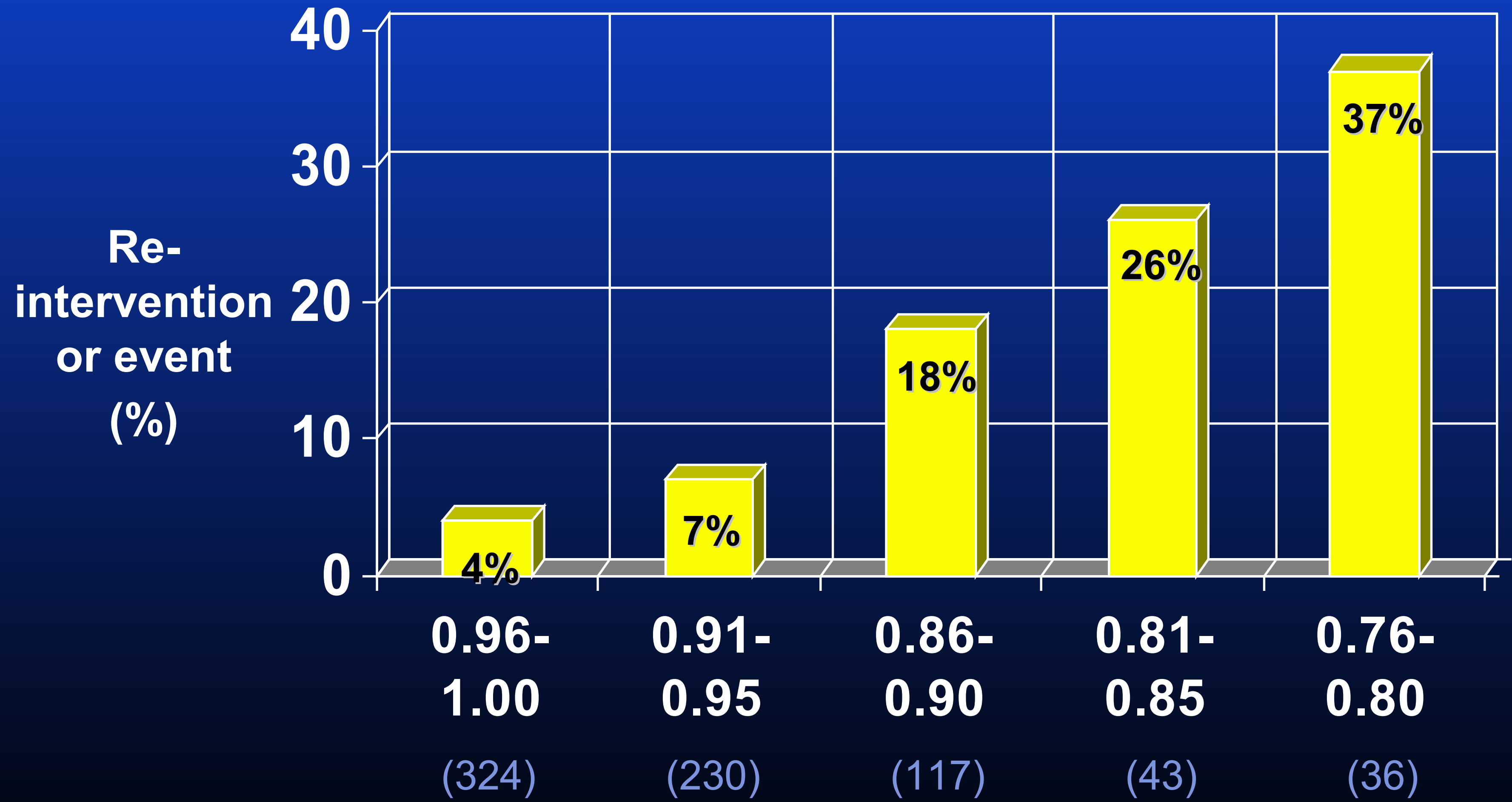

150 mm Hg
150
FFR = 0.78
100 mm Hg
50 mm Hg
50
Flush Off
0 mm Hg
0


3.5 mm balloon
20 ATM


150 mm Hg
100 mm Hg
50 mm Hg
0 mm Hg
FFR = 0.98
Flush Off

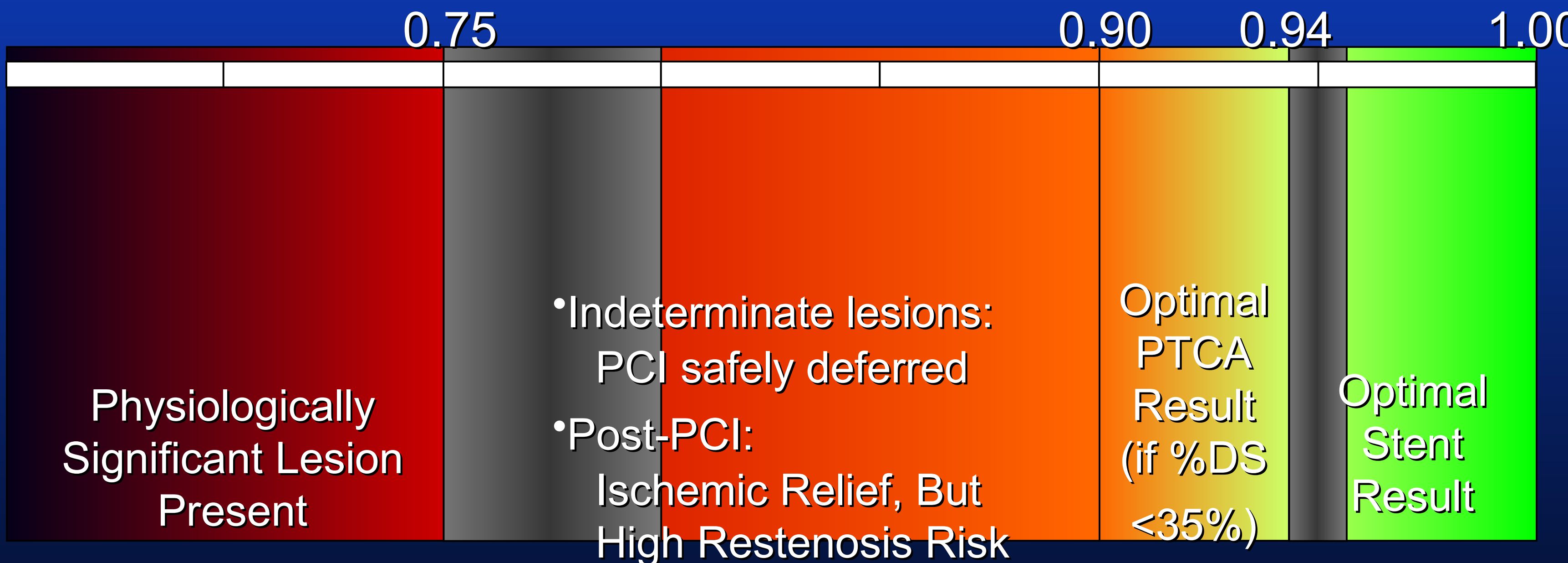
FFR-post-STENT Registry (n=750)

Multicenter European-USA-Asian



Pijls et al, ACC 2002

Assessing Coronary Physiology with FFR_{myo}



Combined CFR / FFR

The Goal

"…a real solution can only be the combination of the two sensors in the same guide wire system."

Di Mario et al, Cath. and Cardio. Diagnosis 38:189-201,1996

Coronary Thermodilution to Assess Flow Reserve

Validation in Humans

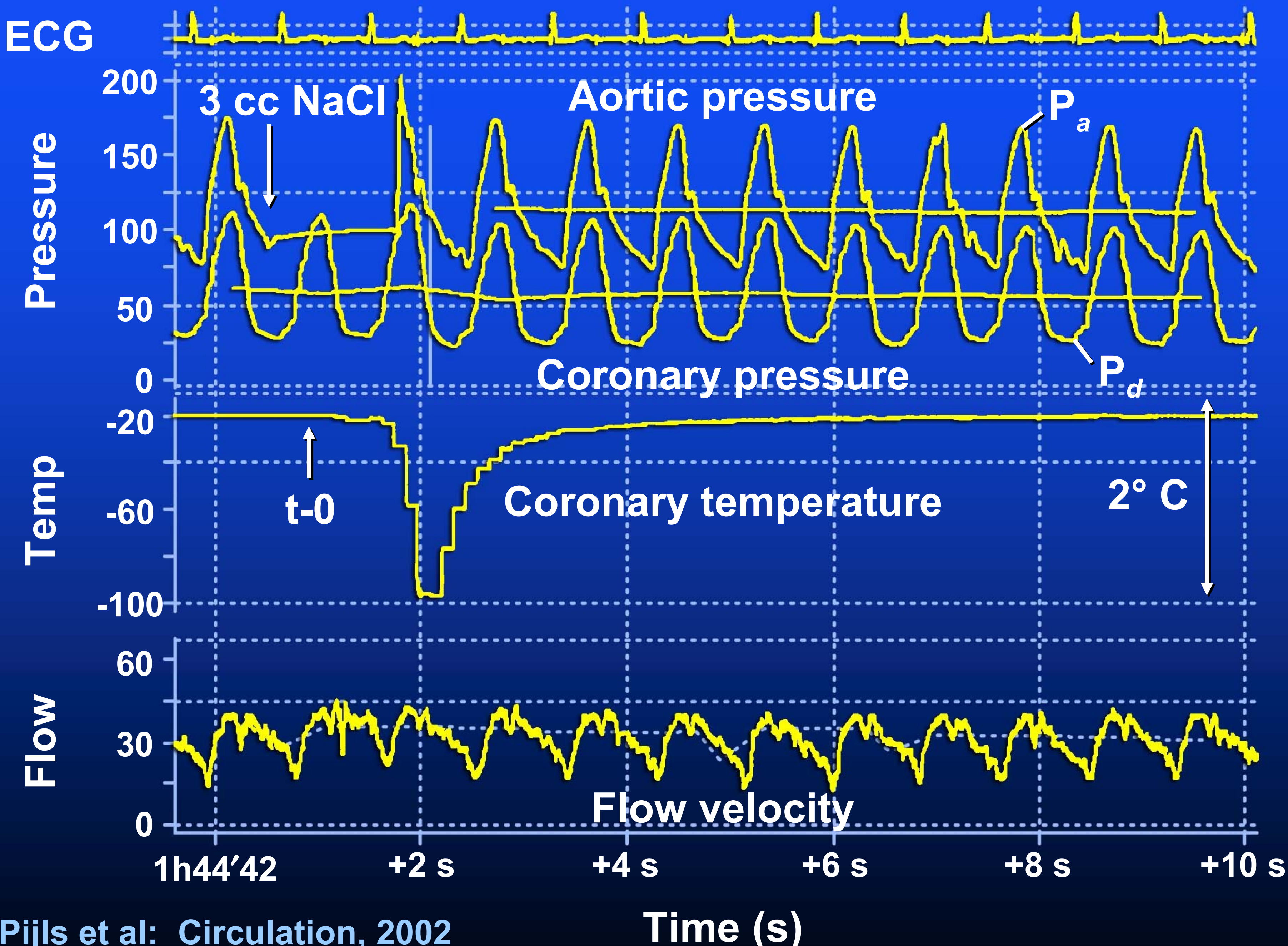
Nico H.J. Pijls, MD, PhD; Bernard De Bruyne, MD, PhD; Leif Smith, PhD;
Wilbert Aarnoudse, MD; Emanuele Barbato, MD; Jozef Bartunek, MD, PhD;
G. Jan Willem Bech, MD; Frans Van De Vosse, PhD

Background**—**Guide wire–based simultaneous measurement of fractional flow reserve (FFR) and coronary flow reserve (CFR) is important to understand microvascular disease of the heart. The aim of this study was to investigate the feasibility of simultaneous measurement of FFR and CFR by one pressure-temperature sensor-tipped guide wire with the use of coronary thermodilution and to compare CFR by thermodilution (CFR_{thermo}) with simultaneously measured Doppler CFR (CFR_{Doppl}).

Methods and Results**—**In 103 coronary arteries in 50 patients, a pressure-temperature sensor-tipped 0.014-inch floppy guide wire and a 0.014-inch Doppler guide wire were introduced. Both normal vessels and a wide range of stenotic vessels were included. With 3 mL of saline at room temperature used as an indicator, by hand-injection, thermodilution curves in the coronary artery were obtained in triplicate, both at baseline and at intravenous adenosine-induced maximum hyperemia. After adequate curve-fitting, CFR_{thermo} was calculated from the ratio of inverse mean transit times and compared with CFR_{Doppl} calculated by velocities at hyperemia and baseline. Adequate sets of thermodilution curves and corresponding CFR_{thermo} could be obtained in 87% of the arteries versus 91% for Doppler CFR and 100% for FFR. CFR_{thermo} correlated fairly well to CFR_{Doppl} ($CFR_{thermo}=0.84\ CFR_{Doppl}+0.17$; $r=0.80$; $P<0.001$), although individual differences of >20% between both indexes were seen in a quarter of all arteries.

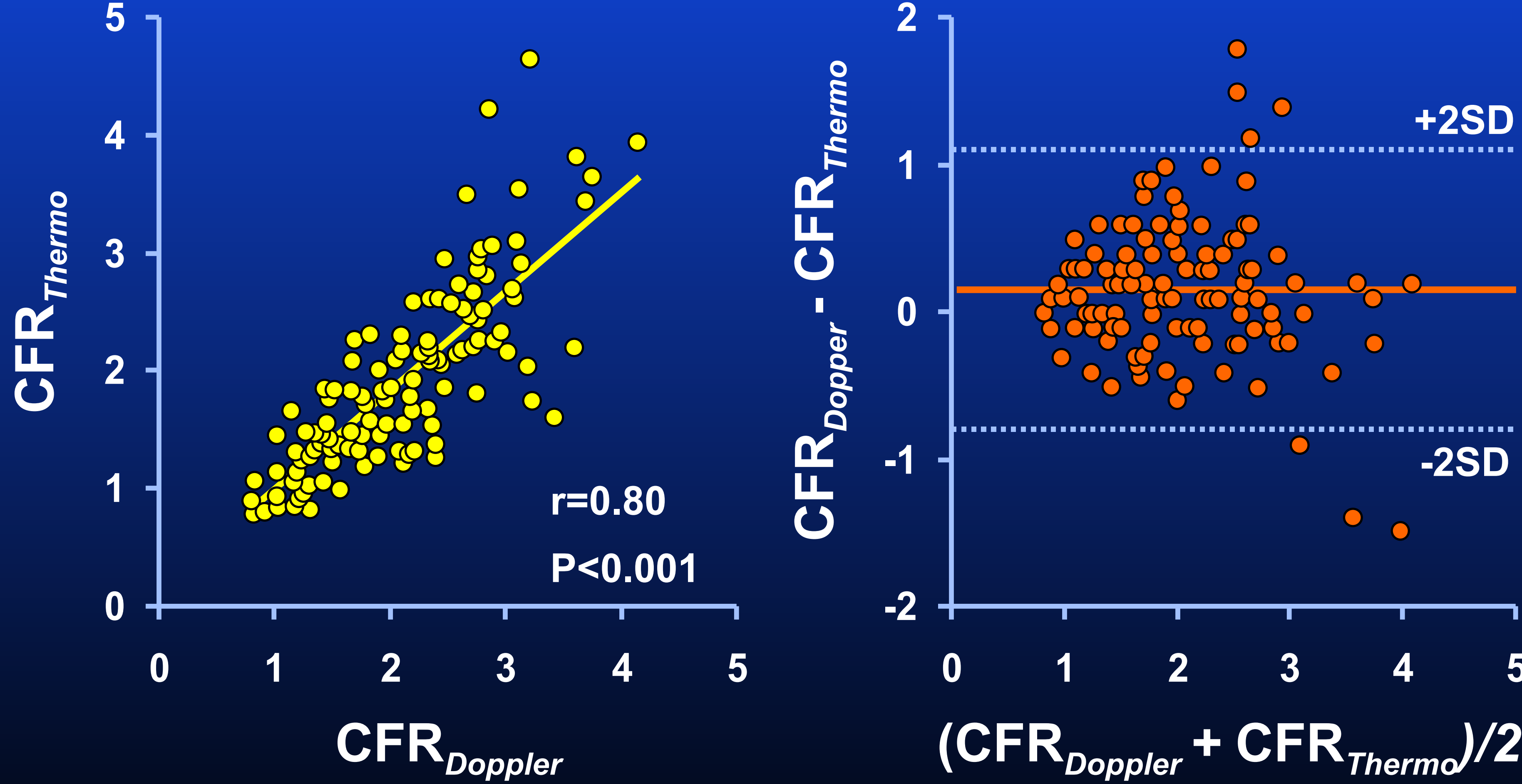
Conclusions**—**This study shows the feasibility of simultaneous measurement of FFR (by coronary pressure) and CFR (by coronary thermodilution) in humans by one single guide wire in a practical and straightforward way and will facilitate assessment of microvascular disease. (***Circulation*****. 2002;105:2482-2486.**)

Key Words: blood flow ■ stenosis ■ arteries ■ microcirculation ■ coronary artery disease



Pijls et al: Circulation, 2002

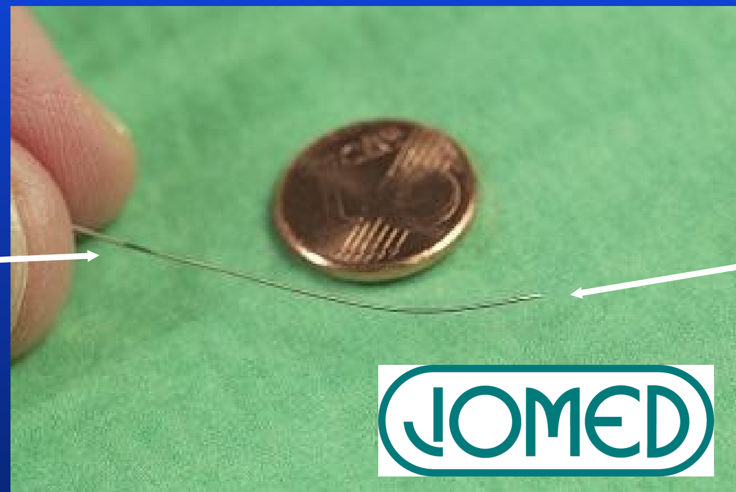
Relation Between CFR Measured by Doppler and Coronary Flow Reserve Determined by Thermodilution



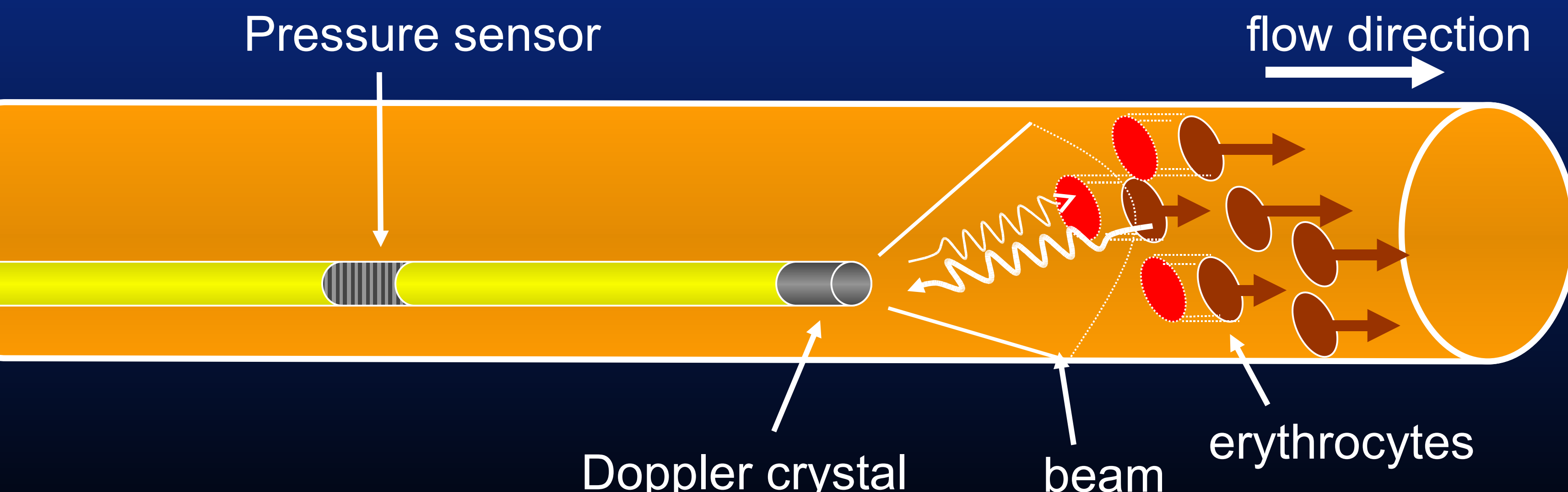
Pijls et al: Circulation, 2002

Combined guide wire

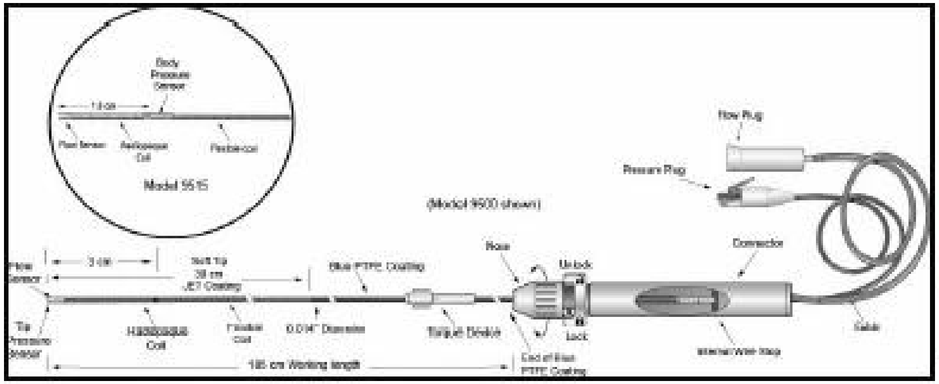
Pressure

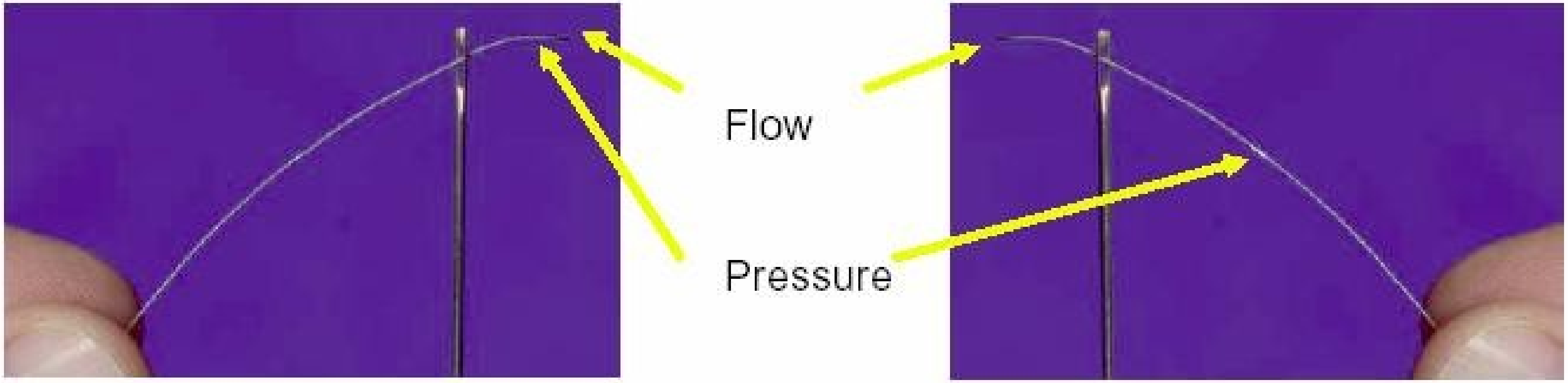


Doppler



Volcano ComboWire

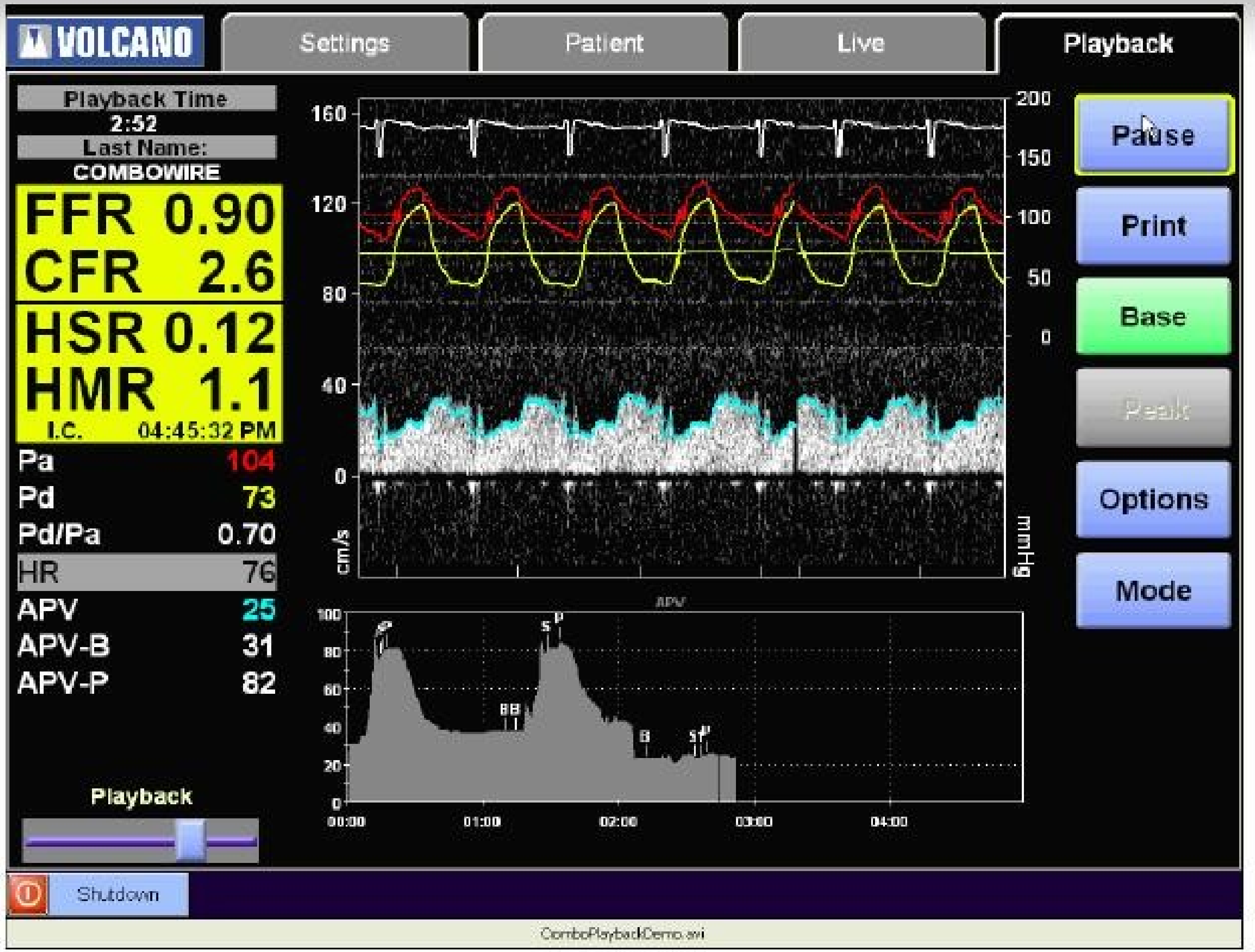




Model: 9500

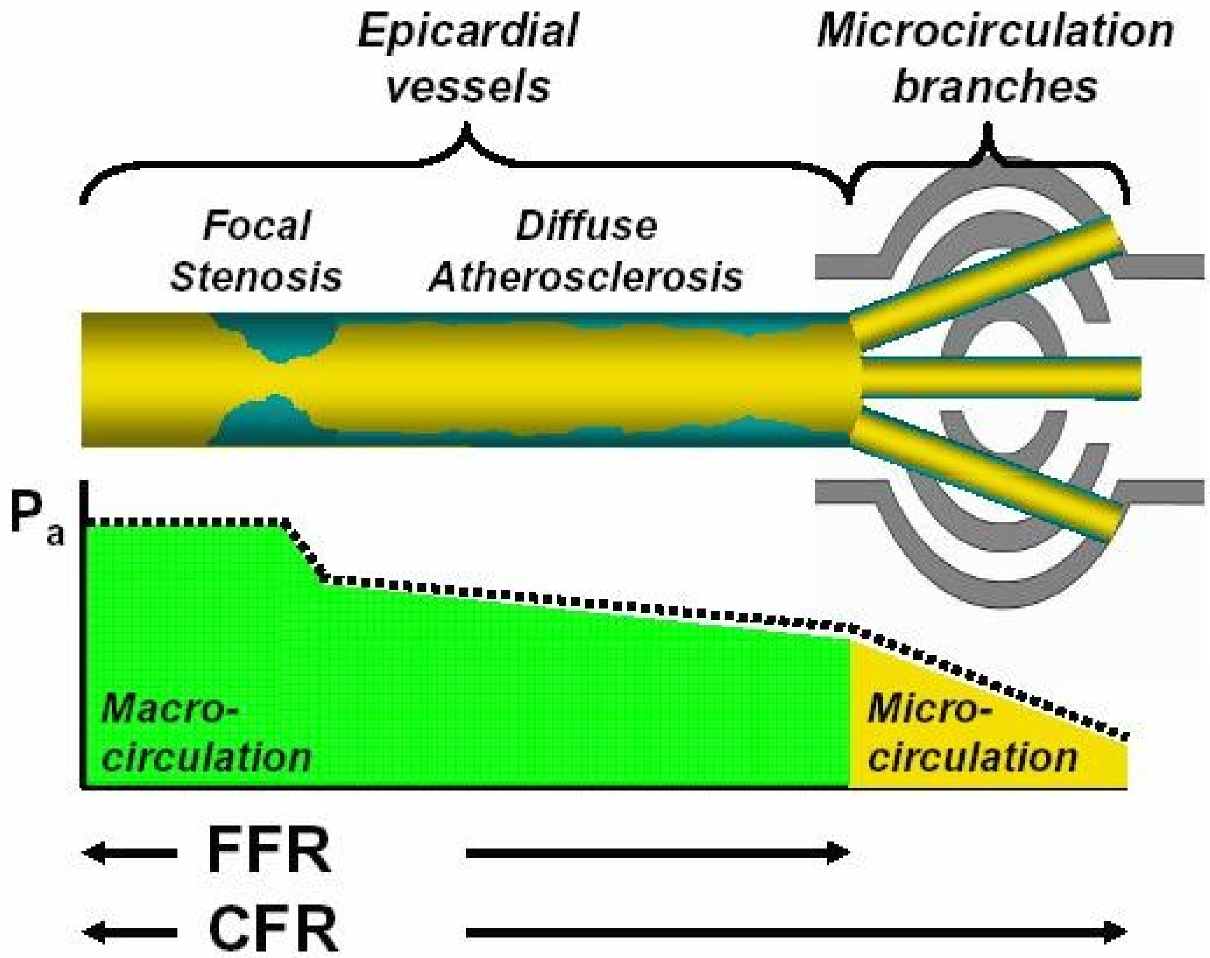
Model: 9515

VOLCANO


VOLCANO
Settings
Patient
Live
Playback
Playback Time
2:52
Last Name:
COMBOWIRE
FFR 0.90
CFR 2.6
HSR 0.12
HMR 1.1
I.C. 04:45:32 PM
Pa 104
Pd 73
Pd/Pa 0.70
HR 76
APV 25
APV-B 31
APV-P 82
Playback
Pause
Print
Base
Peak
Options
Mode
cm/s
mmHg
APV
00:00
01:00
02:00
03:00
04:00
Shutdown
ComboPlaybackDemo.avi

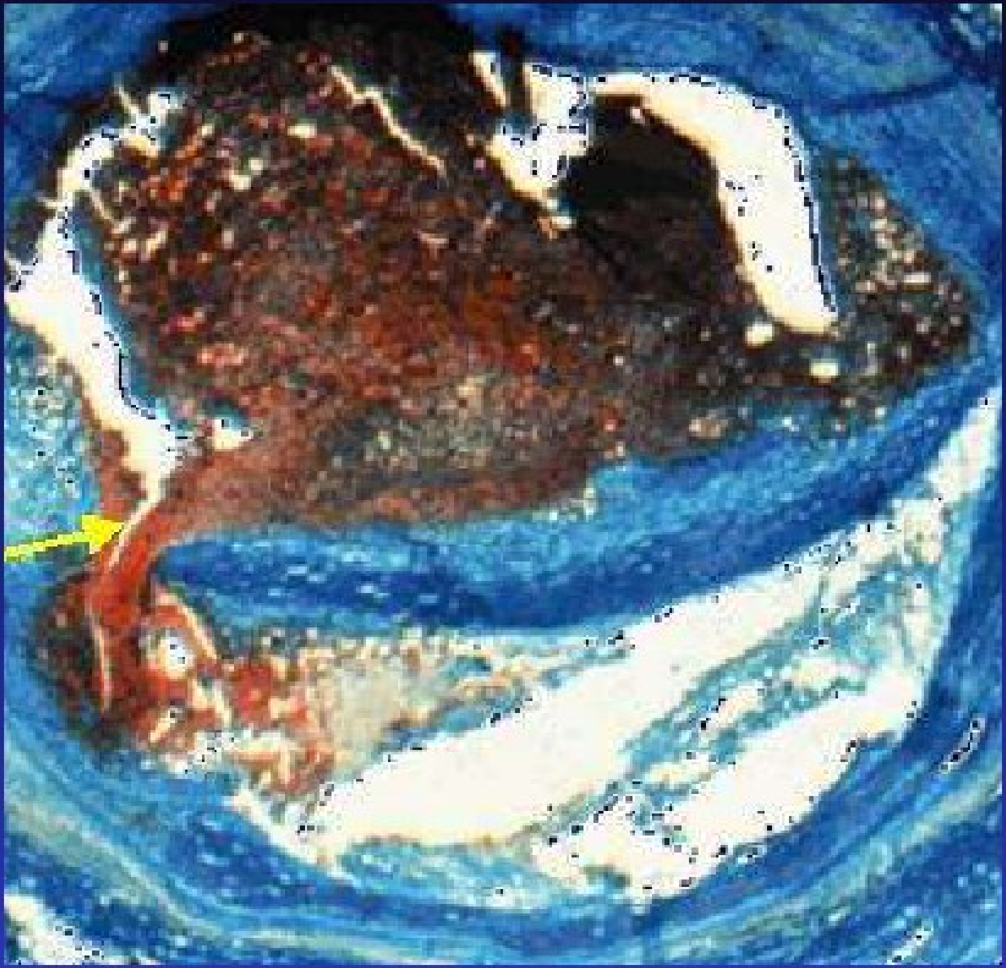
VOLCANO

ComboMap Resistance Indices



VOLCANO

What are the characteristics of a vulnerable plaque?



- thin cap
- lipid pool
- remodeling
- deformable

Constantinides P 1966;
J Atheroscler Res, 6, 1

Schaar, Muller, Falk,
Virmani et al
Eur Heart J 2004, 1007

Imaging of "vulnerable" atherosclerotic plaques

Angioscopy

Intravascular US/palpography/virtual histology

MRI-noninvasive and invasive

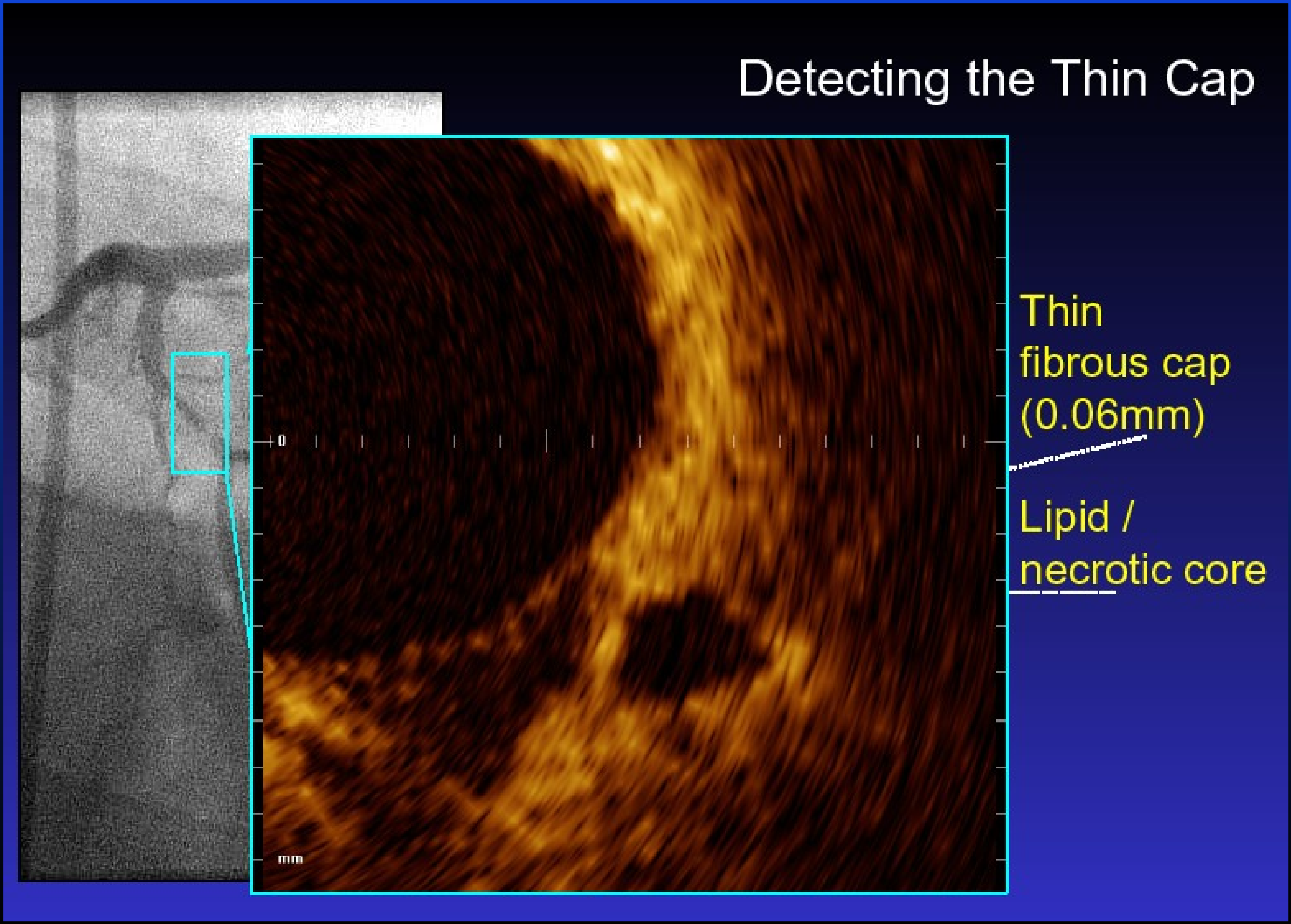
Ultrafast/Multislice CT

Near-Infared Spectroscopy

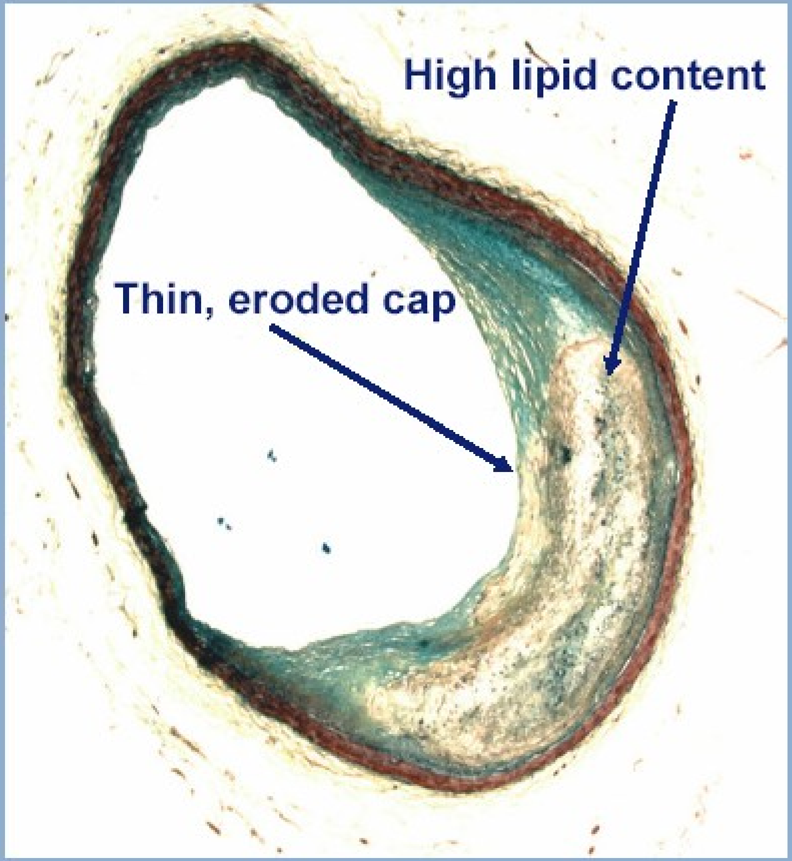
Optical Coherence Tomography

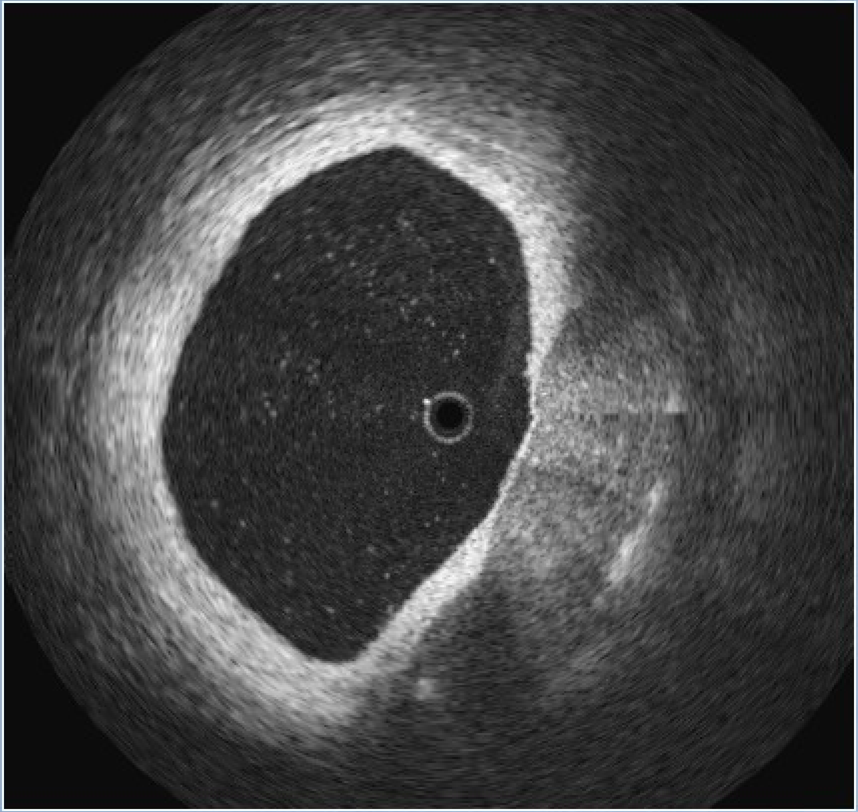
Thermography

OCT

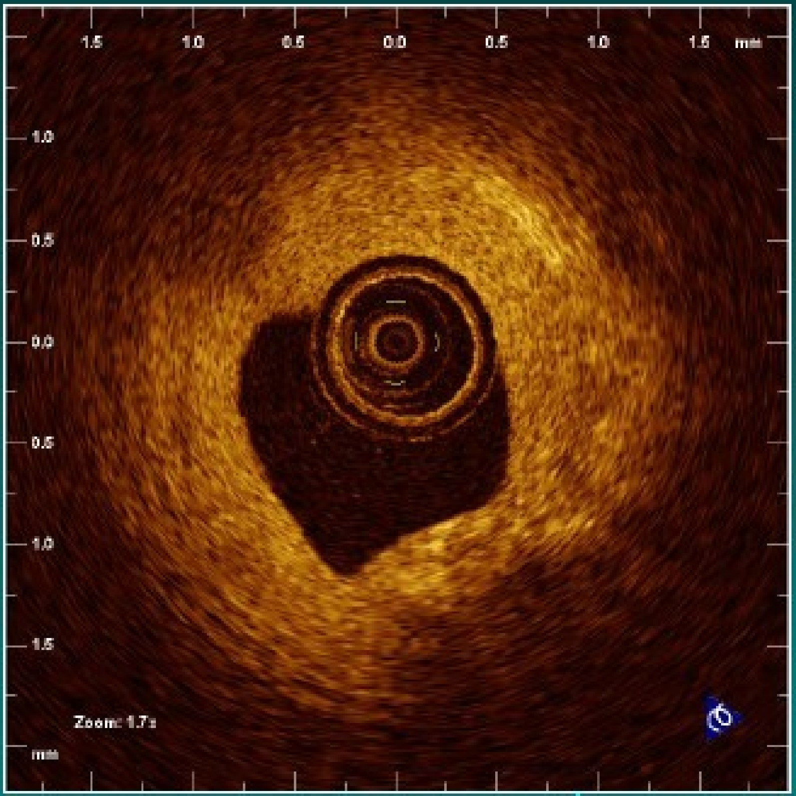

Detecting the Thin Cap
0
mm
Thin
fibrous cap
(0.06mm)
Lipid /
necrotic core

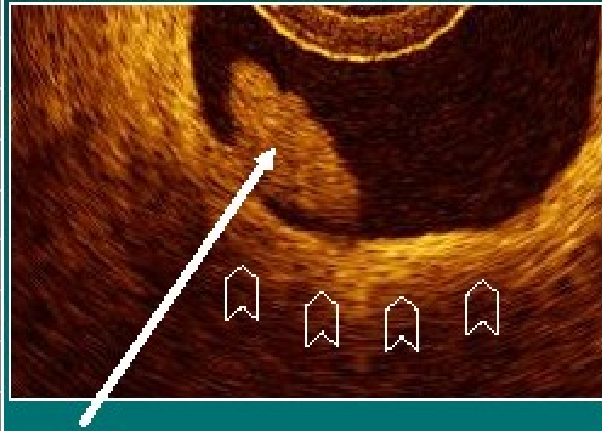
OCT - Coronary Artery Histology Comparison





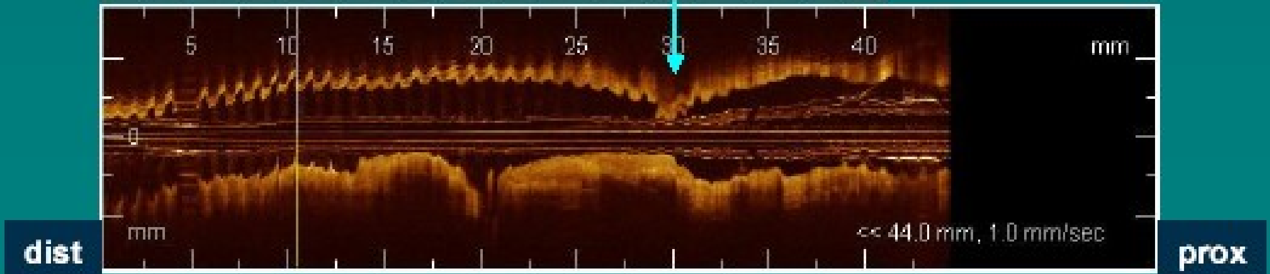
OCT Imaging: Culprit lesion



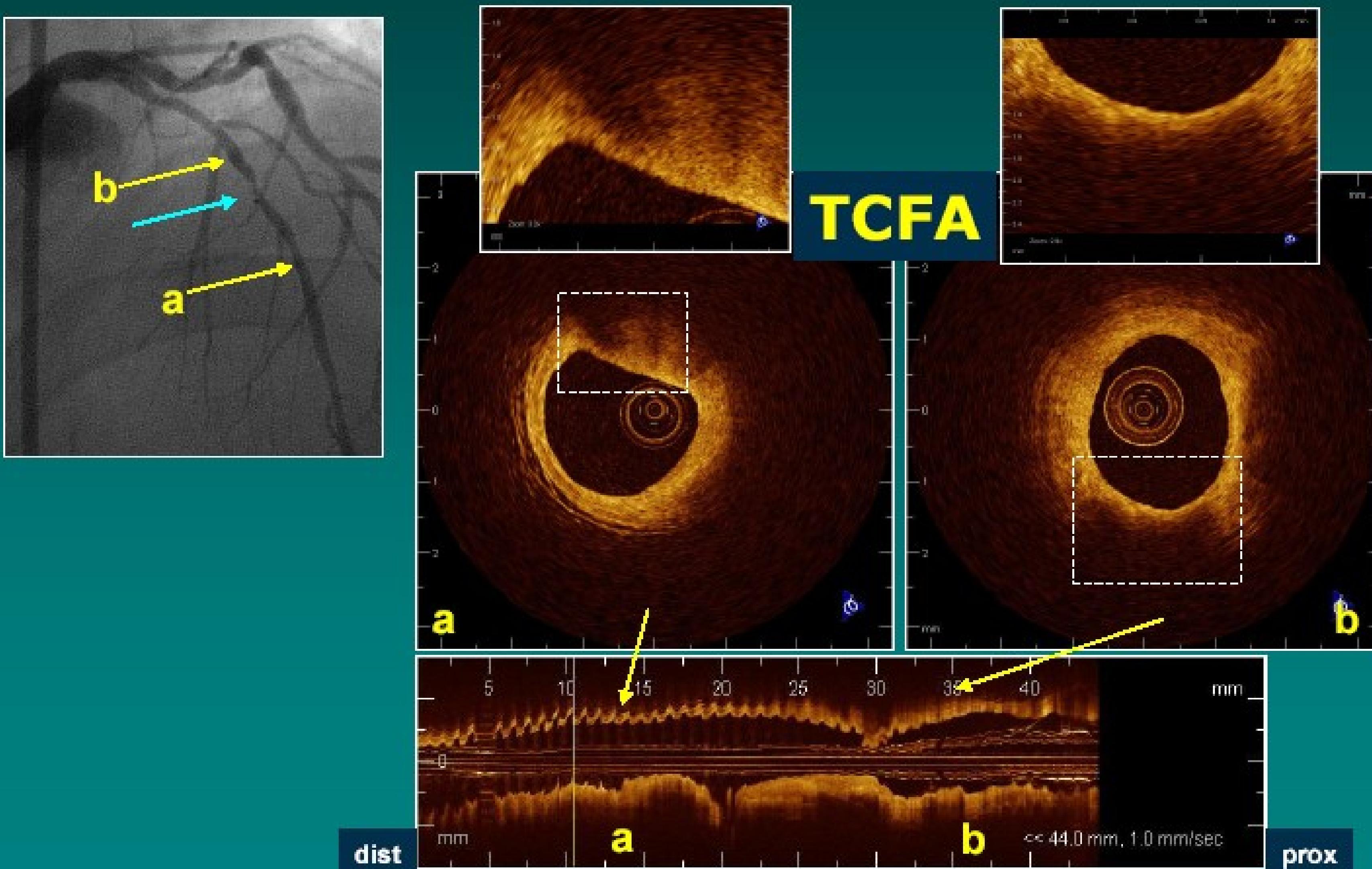


Thrombus

Plaque rupture?

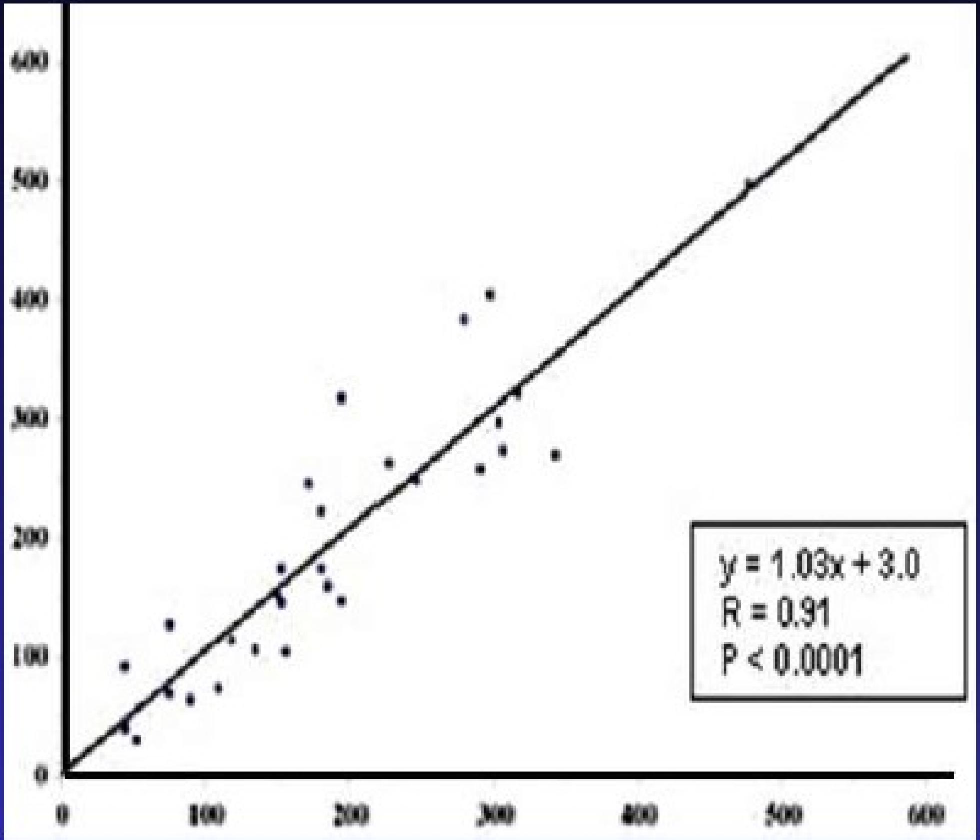


OCT Imaging: Culprit lesion



OCT

Detecting the Thin Cap

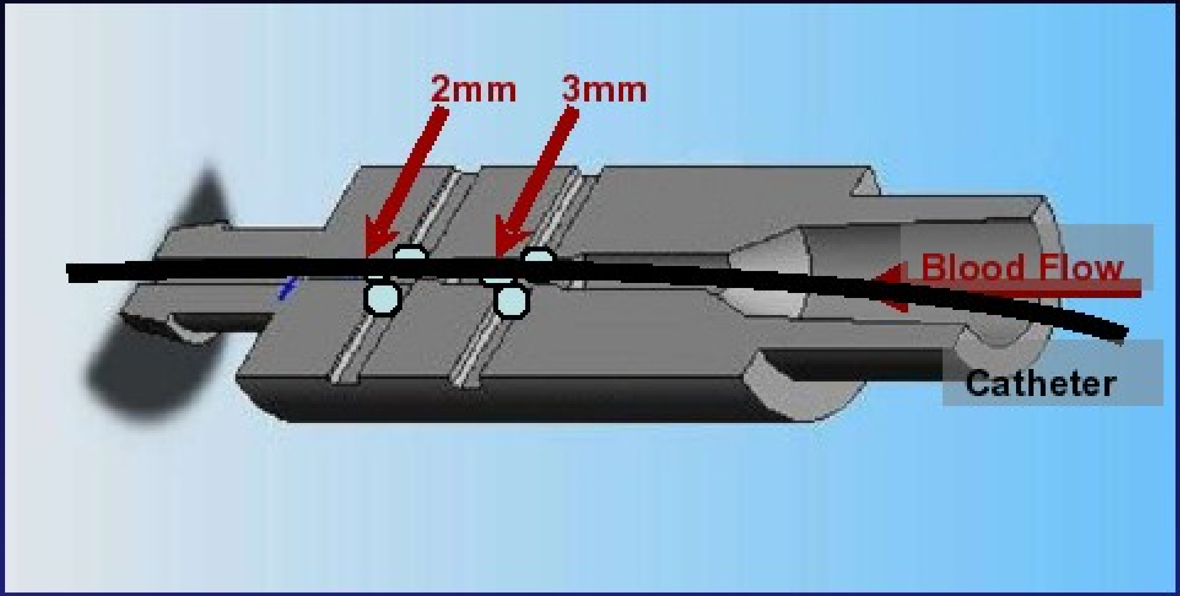


Histology (µm)

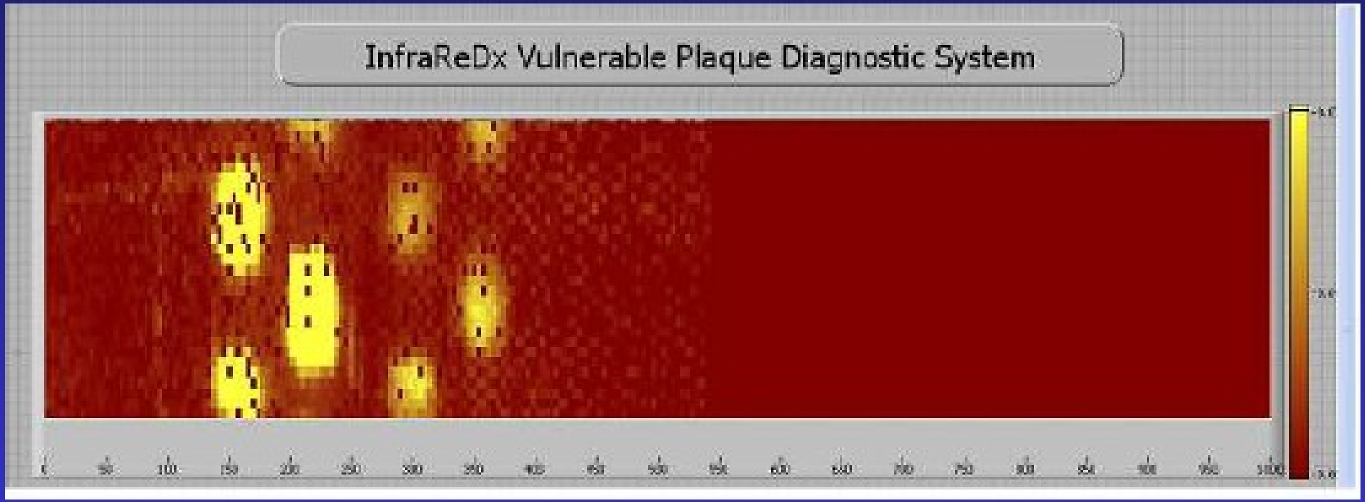
OCT measurements (µm)

Near Infrared Spectroscopy

Detecting the lipid pool/necrotic core



Scanning (Through Blood) to Detect TCFA Surrogates



All 8 Targets detected through 1 and 2 mm of blood)

Near Infrared Spectroscopy

Detecting the Lipid Pool / Inflammation

TABLE 2. NIR Detection of Plaque Composition Determined by Histology

	Lipid Pool	Inflammation
Sensitivity	90	84
Specificity	93	89
Positive predictive value	90	86
Negative predictive value	93	88

Moreno PR Circulation. 2002;105: 923

Palpography

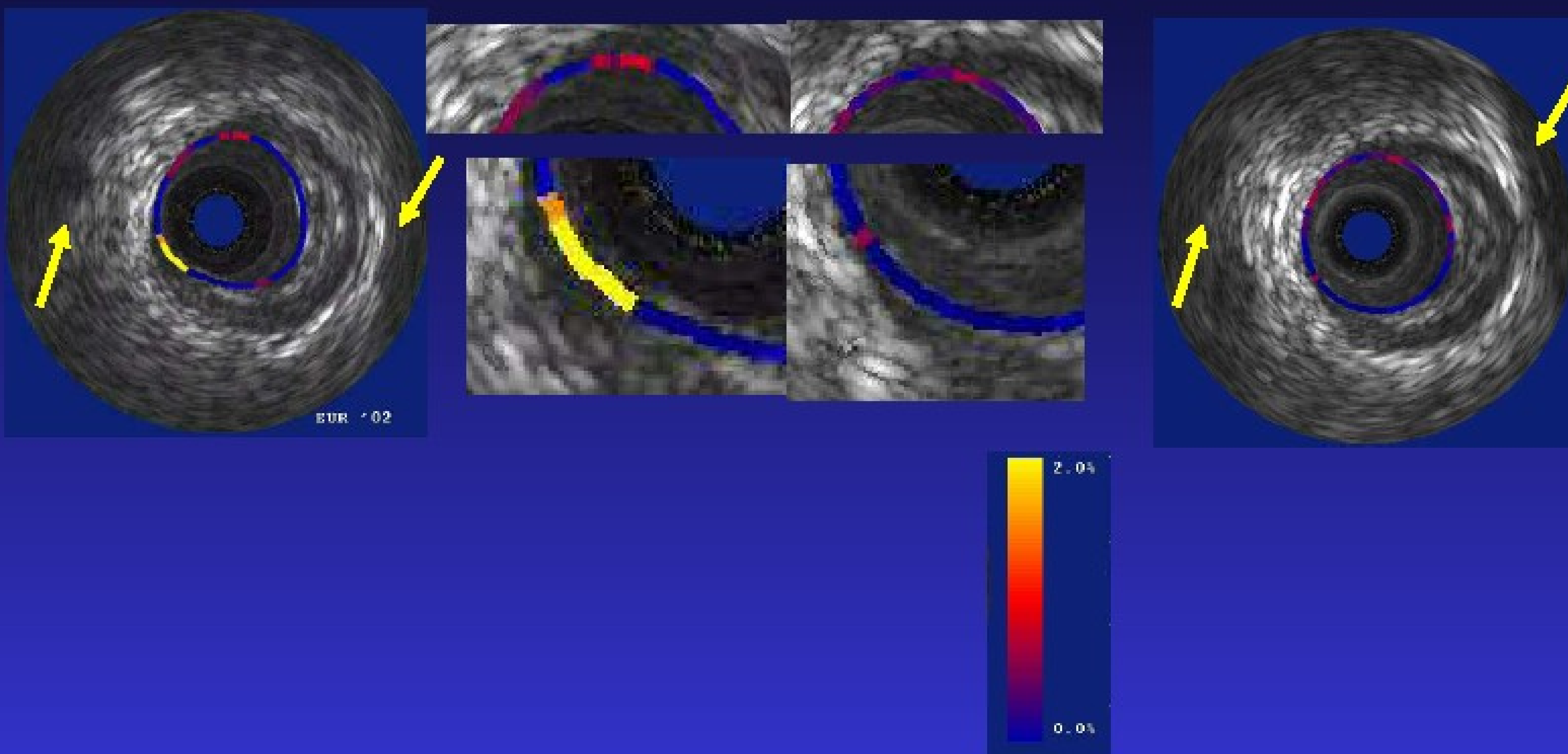
Detecting deformability

- Different tissues deform in a different way
- Deformation of tissue changes the ultrasound signals (rf-signals)

Palpography

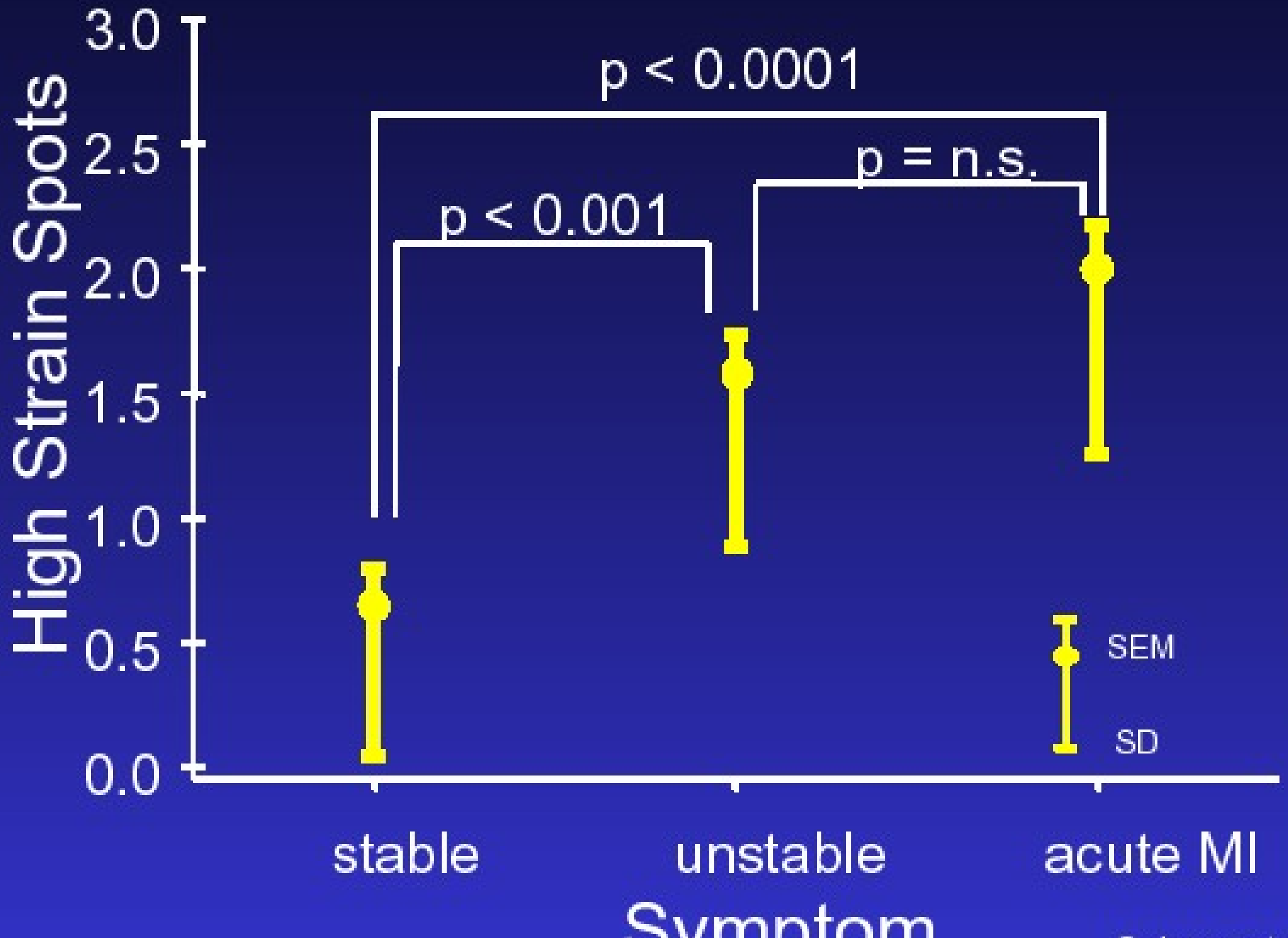
Detecting deformability

Previous   Current

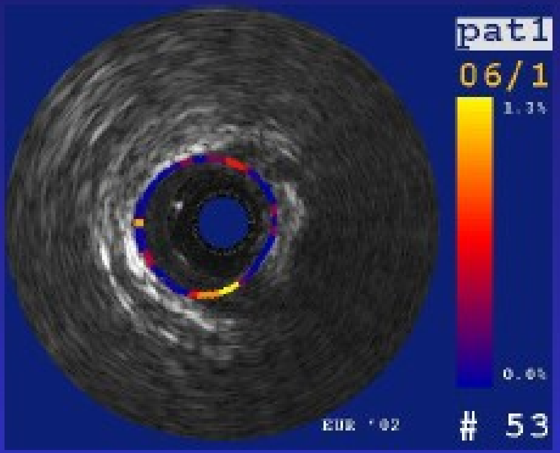


In vivo incidence of high strain spots

Symptoms vs. number of high strain spots



n = 56 coronaries
19 stable angina
19 unstable angina
18 acute MI
(contralateral
vessel)



Schaar et al, Circulation 2004

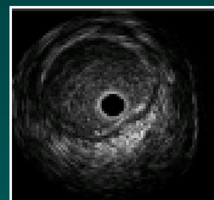
Palpography in the IBIS trial

Baseline and Follow Up – SMS index

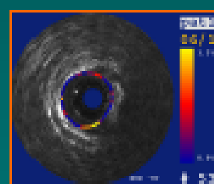
	BL	FUP	P-value
STEMI (N=12)	2.30	1.15	0.0003
Unstable (N=16)	1.78	1.41	0.29
Stable/silent (N=24)	1.21	1.17	0.56

Intravascular Imaging Modalities

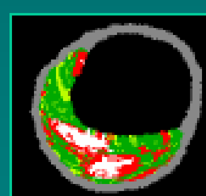
Acquired with single pull back IVUS catheter



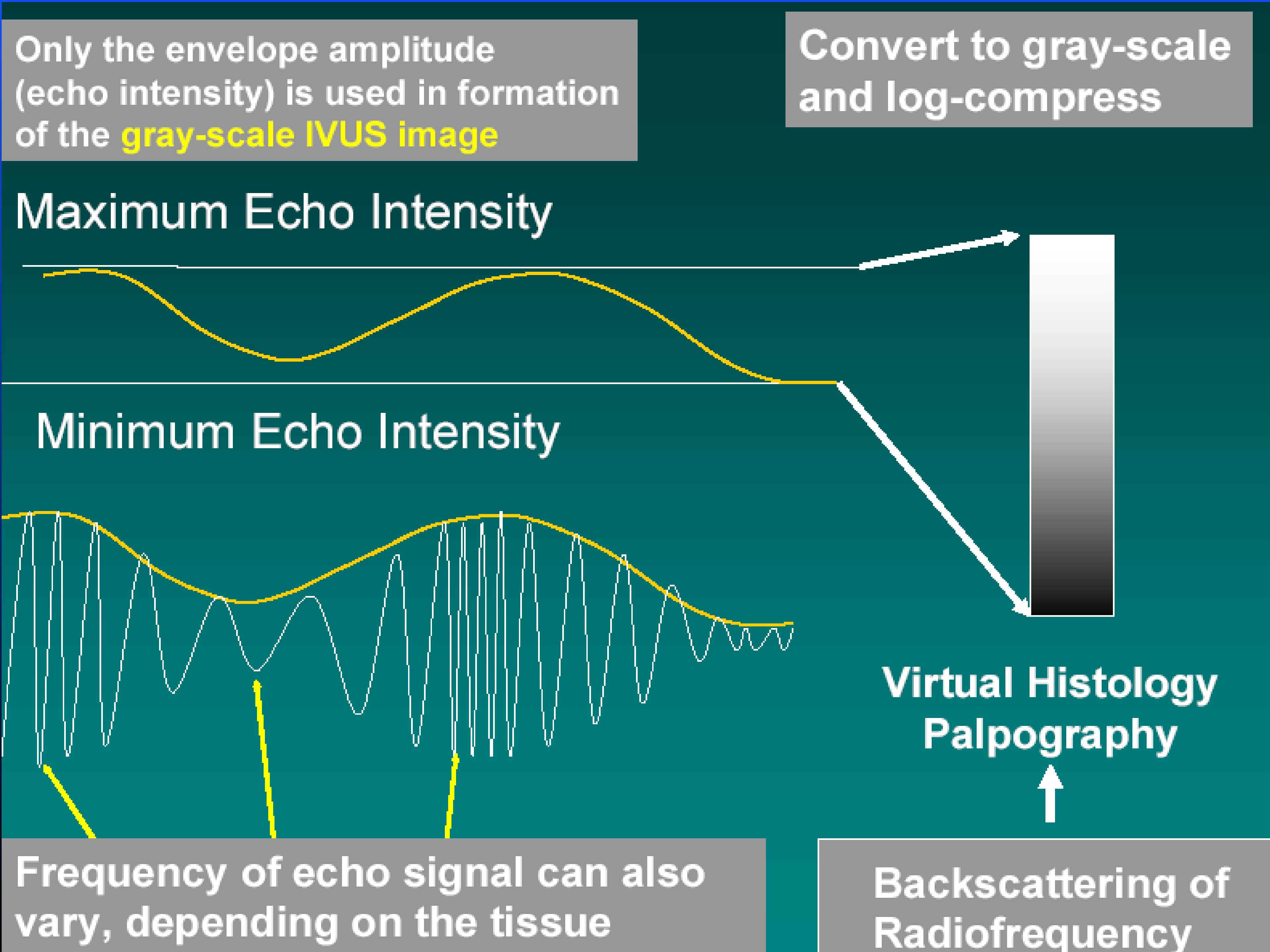
IVUS (gray scale)
(plaque burden)
(remodelling)



IVUS (backscattering RF)
Palpography
(mechanical properties)



Virtual Histology
(plaque composition)


Only the envelope amplitude (echo intensity) is used in formation of the gray-scale IVUS image
Convert to gray-scale and log-compress
Maximum Echo Intensity
Minimum Echo Intensity
Virtual Histology
Palpography
Frequency of echo signal can also vary, depending on the tissue
Backscattering of Radiofrequency

First step

identify regions

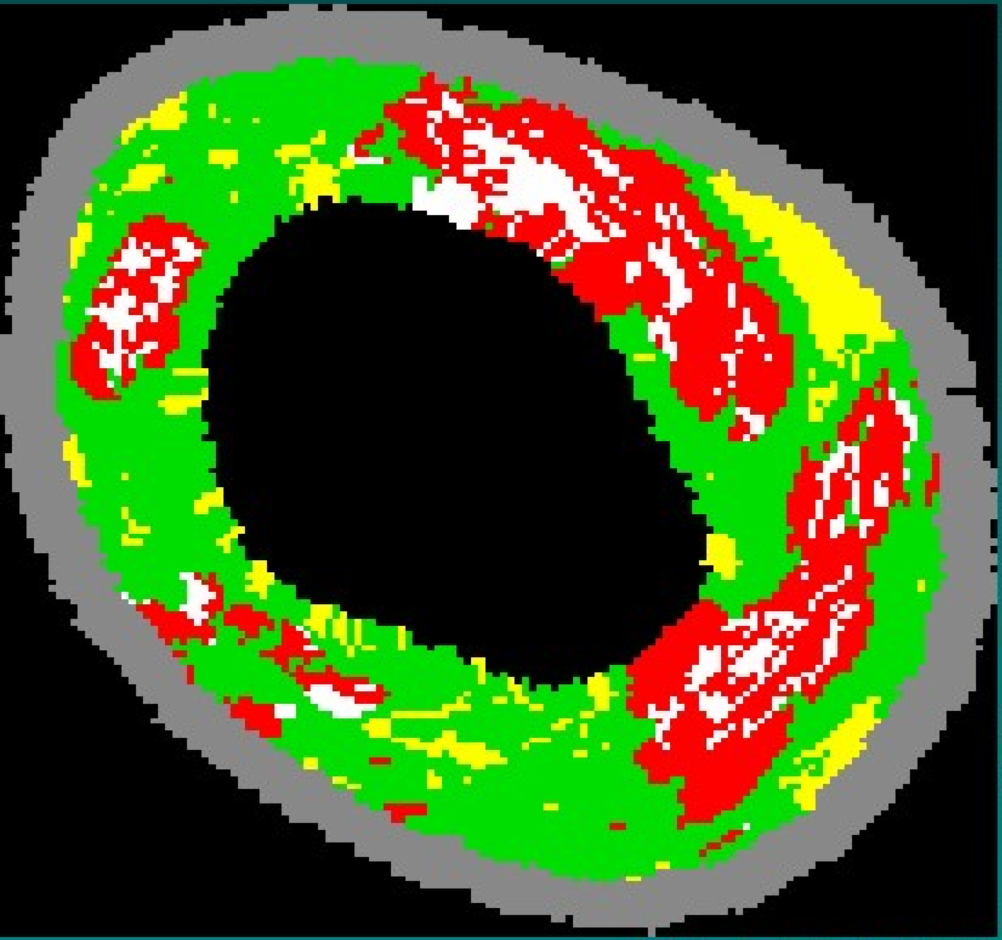
with 40 - 50 % EEM Obstruction

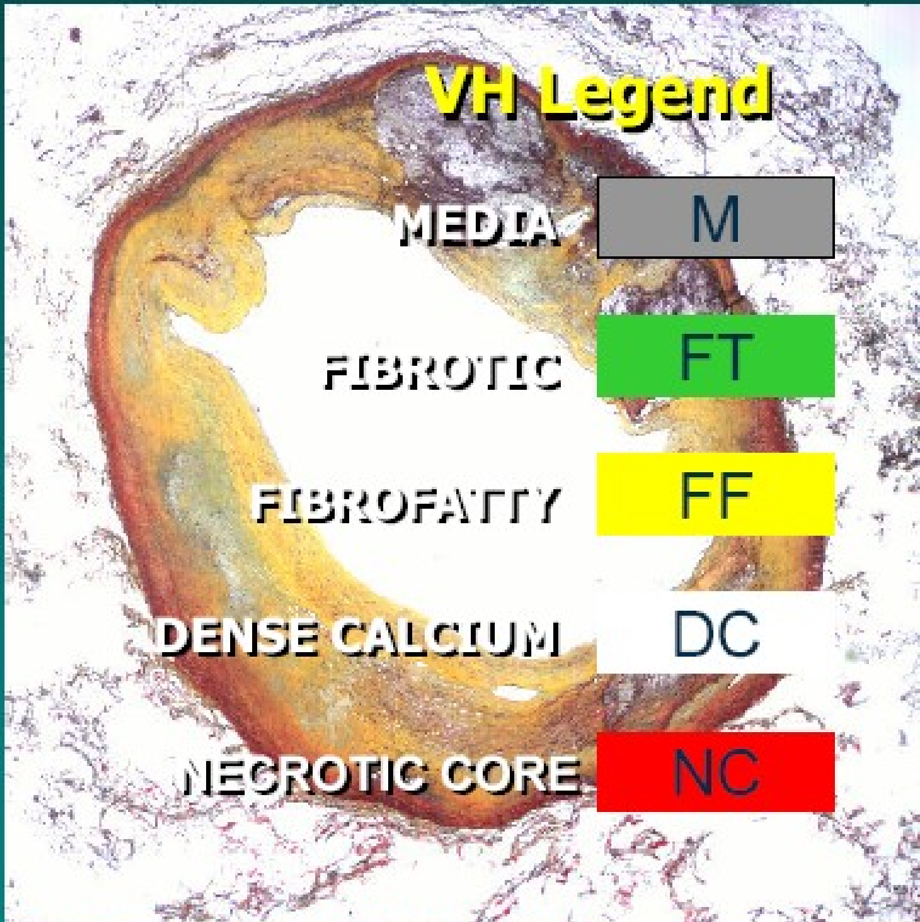
EEM: External Elastic Membrane

Second step identify regions

with Positive Remodeling Index

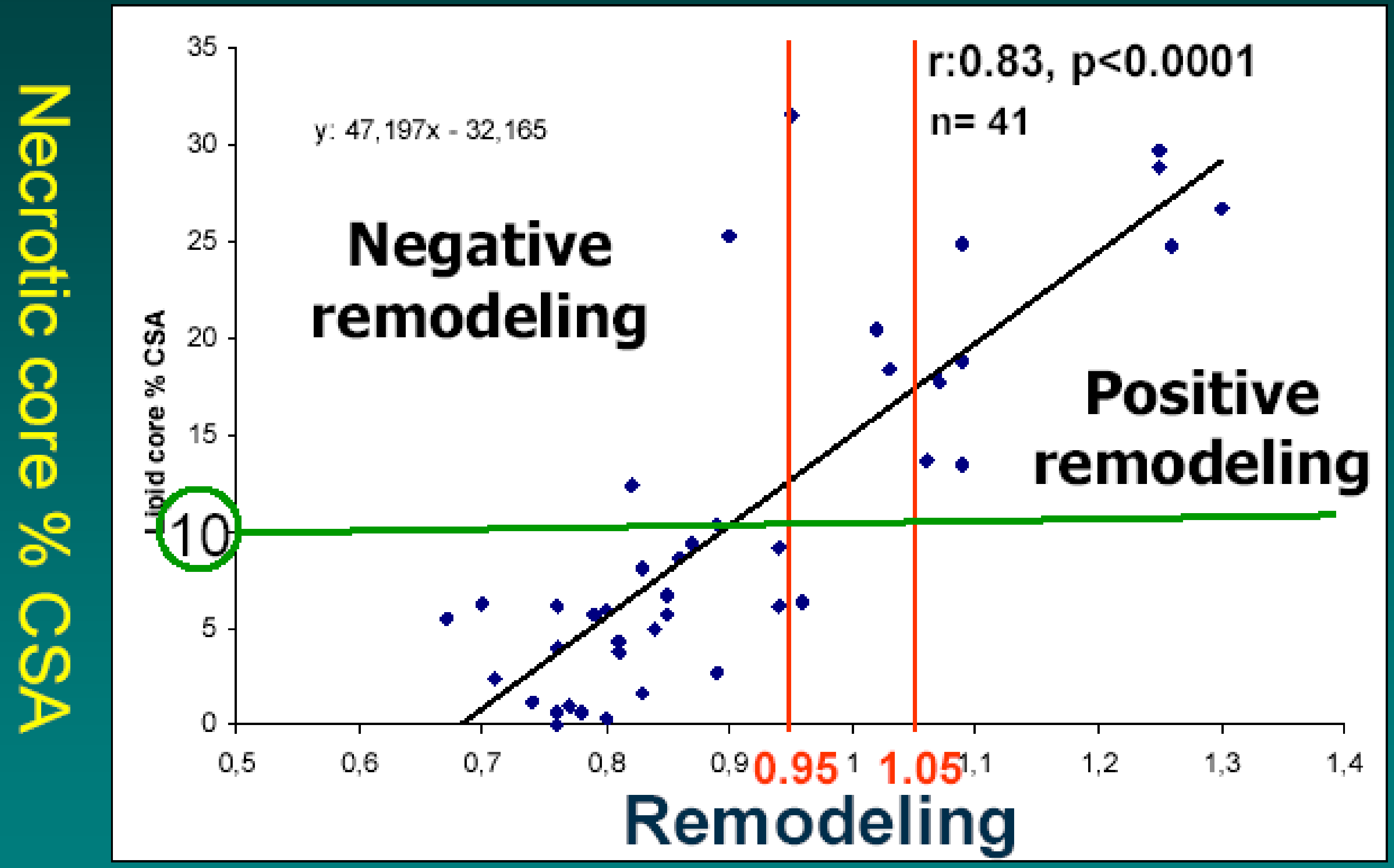
Virtual Histology or… How to convert an human ex vivo coronary IVUS image into a color coded histological cross section… by correlating backscattered radiofrequency signals with human ex vivo coronary histology





Nair A et al. Circulation. 2002;106:2200-2206

Coronary Artery Remodeling is related to plaque composition determined by IVUS-VH



Coronary artery remodeling is related to plaque composition.
Rodriguez-Granillo GA, Serruys PW, Garcia-Garcia HM, et al.. Heart 2006;92:388-91.

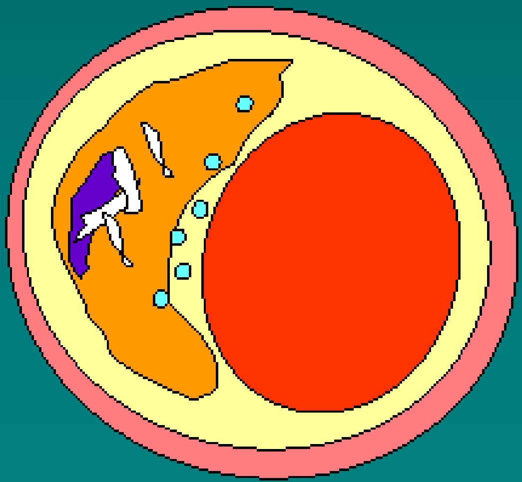
Definition of IVUS-Derived Thin-Cap Fibroatheroma (IDTCFA)

1. Focal (adjacent to non-TCFA)
2. **Necrotic core ≥10%**
3. **In direct contact with the lumen**
4. Percent area obstruction ≥40%

VH Legend

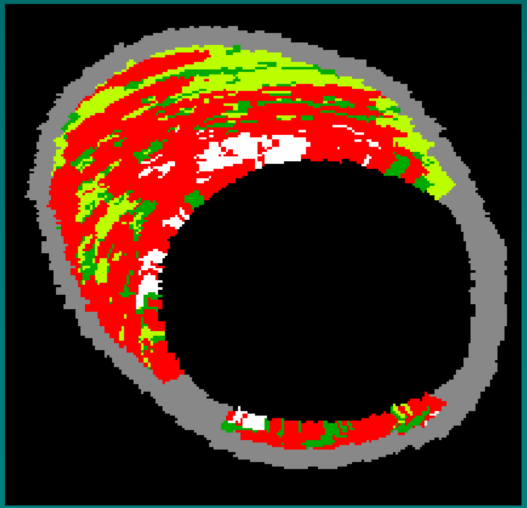
MEDIA	M
FIBROTIC	FT
FIBROFATTY	FF
DENSE CALCIUM	DC
NECROTIC CORE	NC

•Per 3 consecutive frames with four characteristics



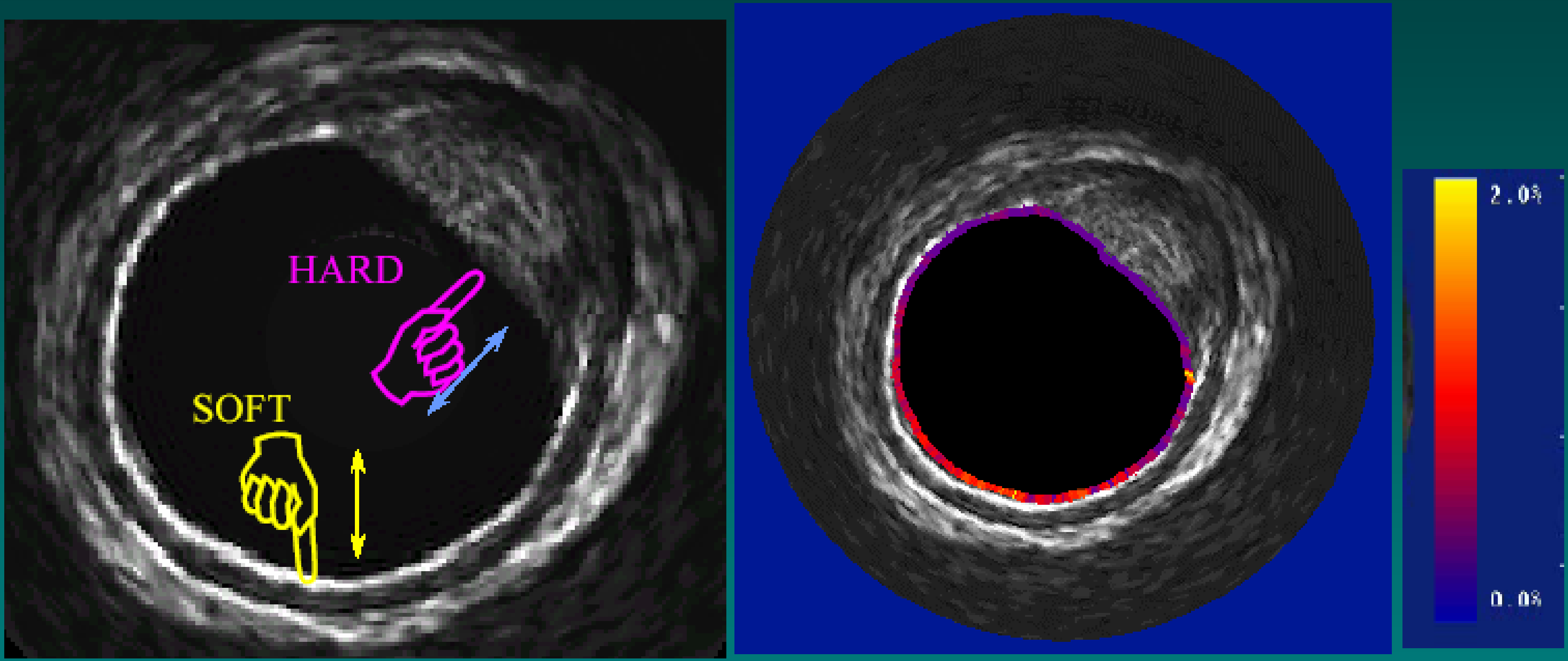
Histology legend

- NECROTIC CORE
- COLLAGEN
- CALCIFIED PLAQUE
- MACROPHAGE FOAM CELLS



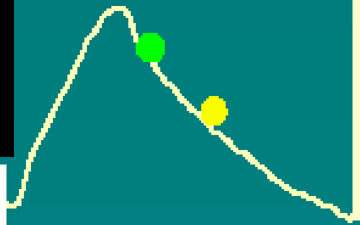
Rodriguez-Granillo GA,Serruys P W. In vivo intravascular derided thin-cap fibroatheroma detection using ultrasound radiofrequency data analysis. J Am Coll Cardiol.. 2005;46:2038-42.

Final step…Palpography: Intravascular ultrasonic palpation



High strain region = SOFT, DEFORMABLE,FRAGILE, BREAKABLE

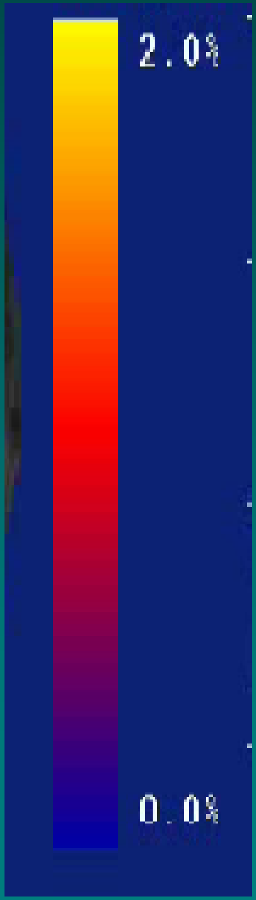
Low strain = hard,stiff,rigid



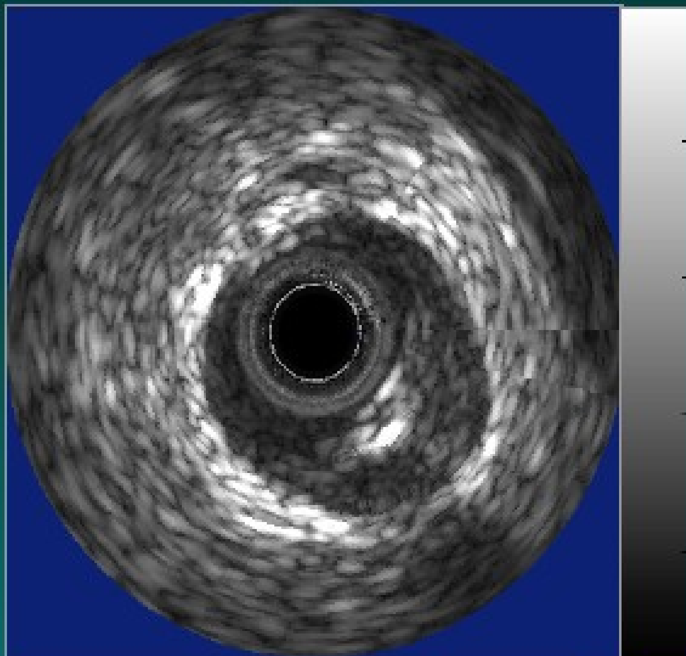
Backscattering of radiofrequency signal at 2 levels of blood pressure

ROtterdam Classification (ROC)

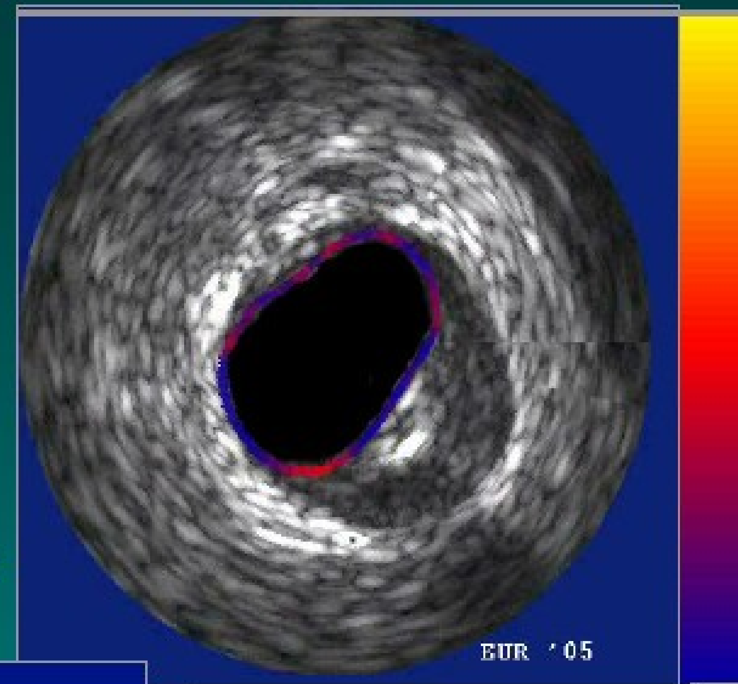
Grades (ROC)	Strain (%)
IV	>1.2
III	0.9-1.2
II	0.6-0.9
I	0-0.6



Vulnerable Plaque ? Colocalisation?



Dense calcium 10%
Fibrous 67%
Fibro-fatty 8%
Necrotic core 15%
direct lumen contact



Lumen: 8.00 mm^2
Vessel: 15.92 mm^2
Plaque burden: 50%

ROC III

“Vulnerable Plaque” ?

When non-flow limiting lesion < 50% stenosis

When EEM obstruction>40%

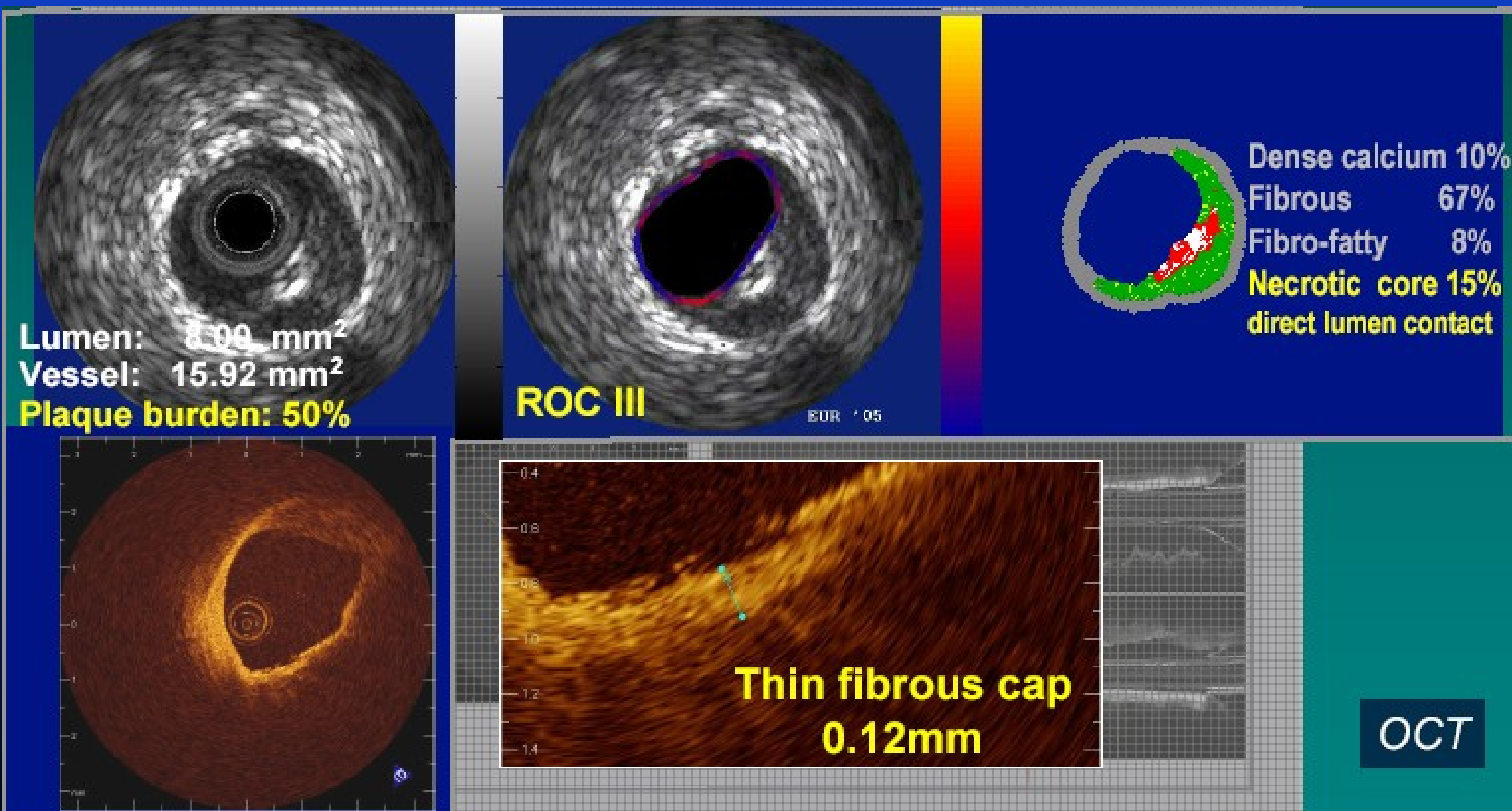
When positive remodeling index > 1.05

When large lipid core (> 10%)
in direct contact with lumen

When TCFA focal (3 slices), proximal < 30mm

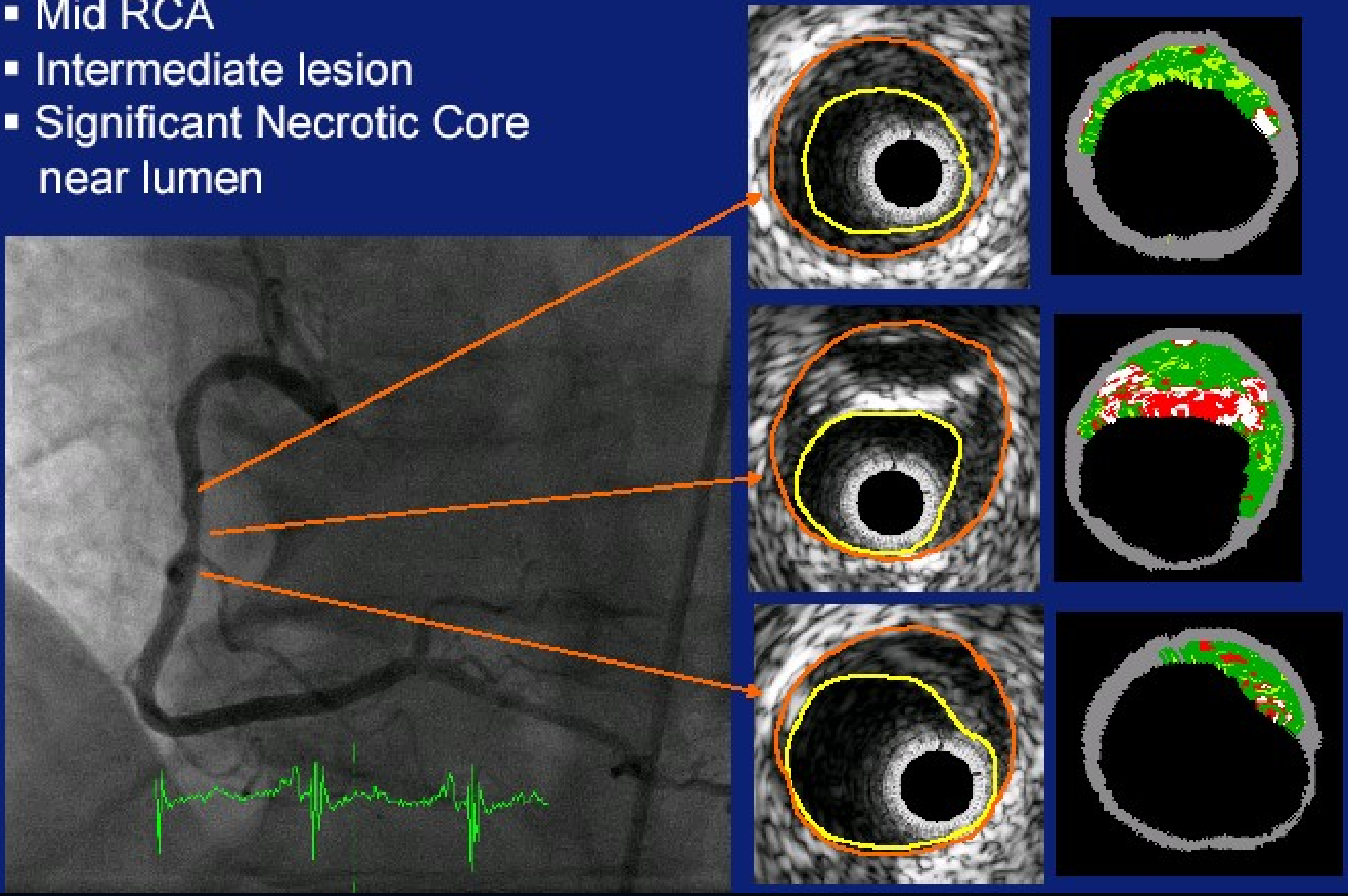
When ROC 3/4

IVUS vs VH vs Strain vs OCT

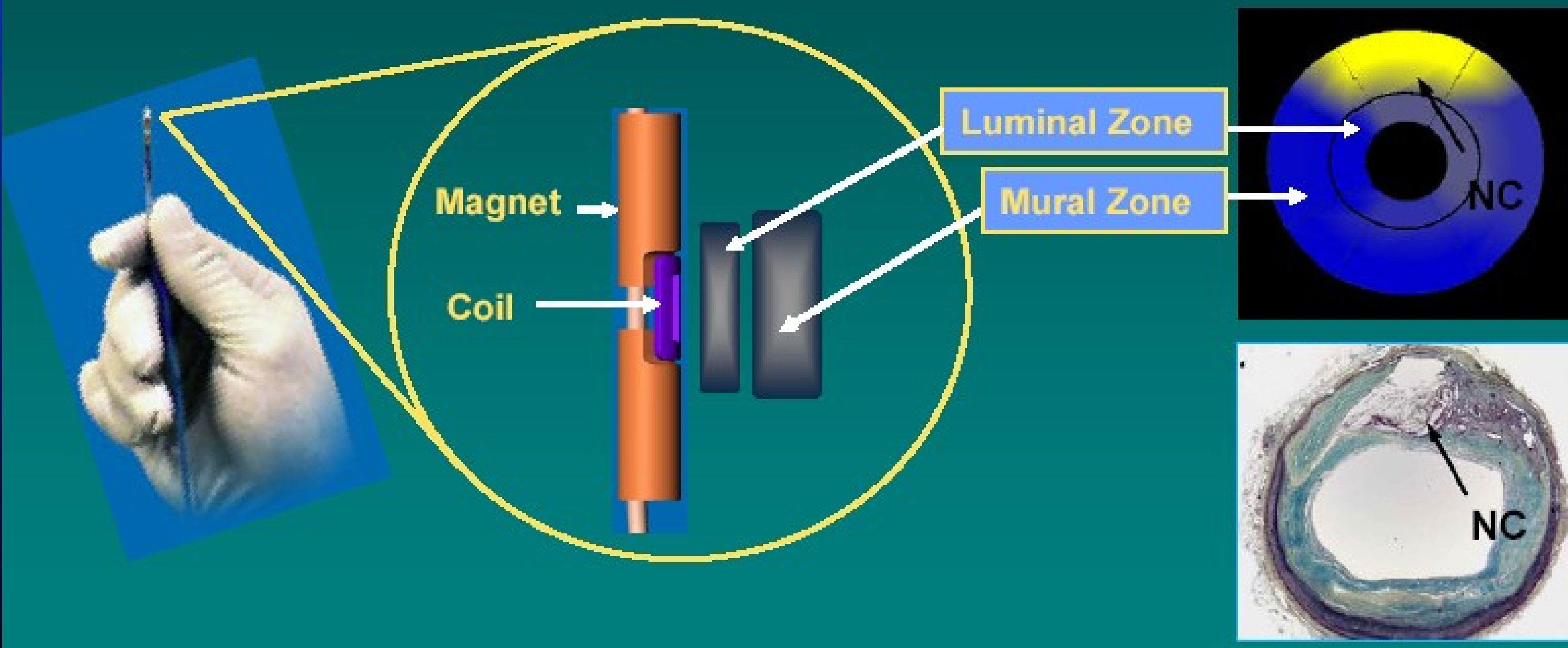


Case Example:

- Mid RCA
- Intermediate lesion
- Significant Necrotic Core near lumen



Intravascular MRI Catheter



Schneiderman J. J Am Coll Cardiol. 2005;45(12):1961-1969