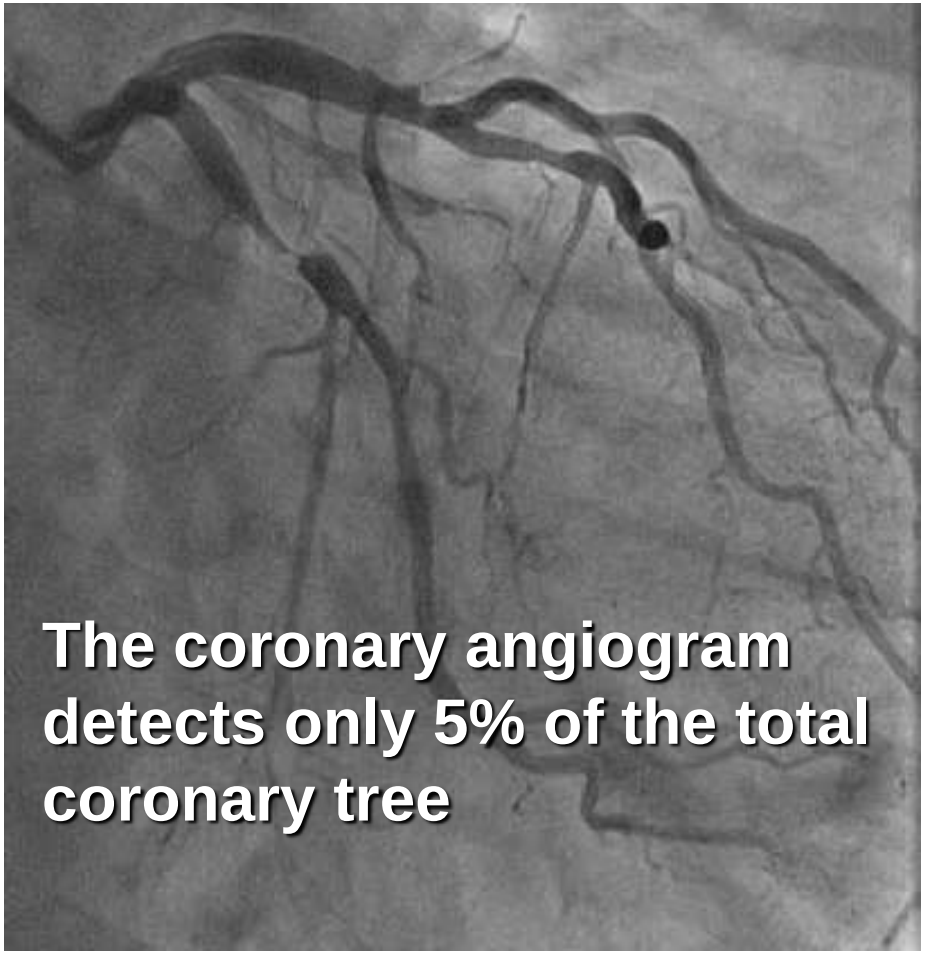
Evaluating the Microvasculature in the Cath Lab:

William F. Fearon, MD
Associate Professor of Medicine
Director, Interventional Cardiology
Stanford University Medical Center

Coronary Microvasculature



Courtesy of Bernard De Bruyne, MD,PhD

Why is Microvascular Dysfunction Important?

- Up to 30% of patients continue to have angina despite successful coronary revascularization

- ~20% of patients with chest pain are found to have no angiographic apparent CAD

- Microvascular dysfunction predicts adverse outcomes in a variety of clinical settings

Assessment of the Microvasculature

- Extremely challenging diagnosis
  - Heterogeneous patient population
  - Variety of pathogenetic mechanisms
  - Poor anatomic resolution
  - Potentially patchy nature of the disease

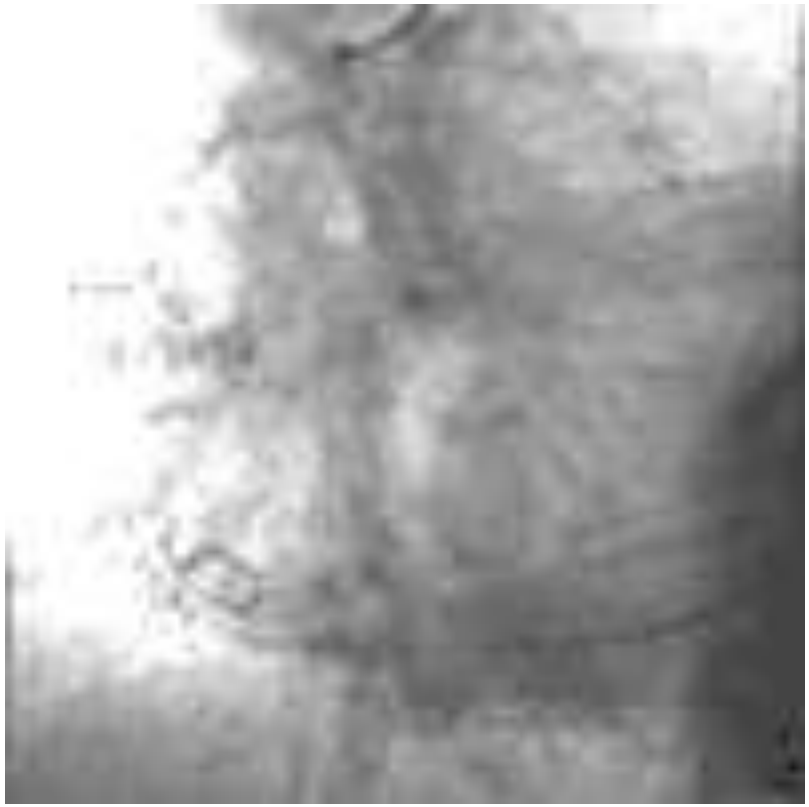
Assessment of the Microvasculature

- Extremely challenging diagnosis
  - Heterogeneous patient population
  - Variety of pathogenetic mechanisms
  - Poor anatomic resolution
  - Potentially patchy nature of the disease

- Therefore, assessment of the microvasculature is primarily *functional* and not *anatomic*

Evaluating the Microcirculation…
…in the Cath Lab

TIMI Myocardial Perfusion Grade:



Evaluating the Microcirculation…
…in the Cath Lab

TIMI Myocardial Perfusion Grade:

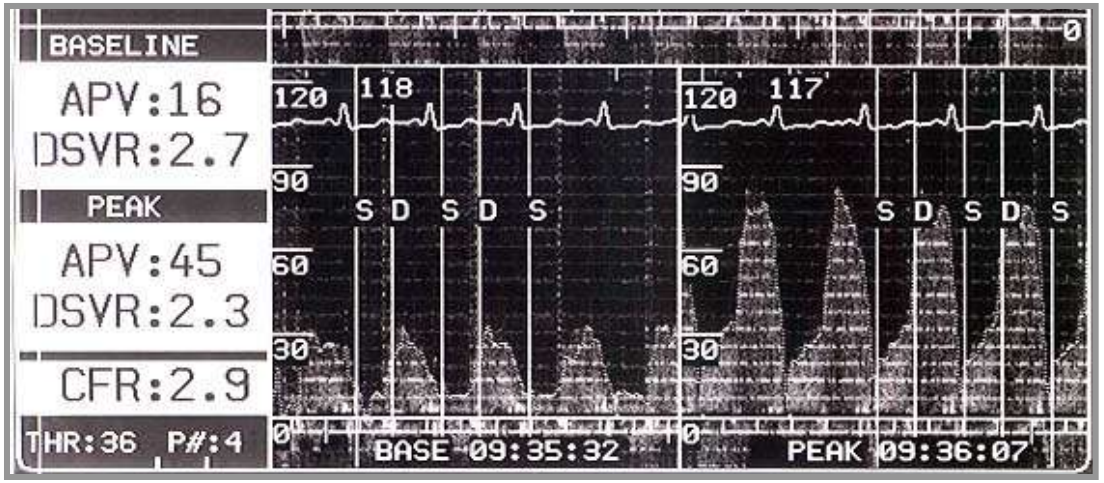
- Easy to obtain
- Specific for microvasculature
- Predictive of outcomes in large studies

Drawbacks:

- Qualitative
- Mainly useful in STEMI
- Interobserver variability
- Not as useful in smaller studies

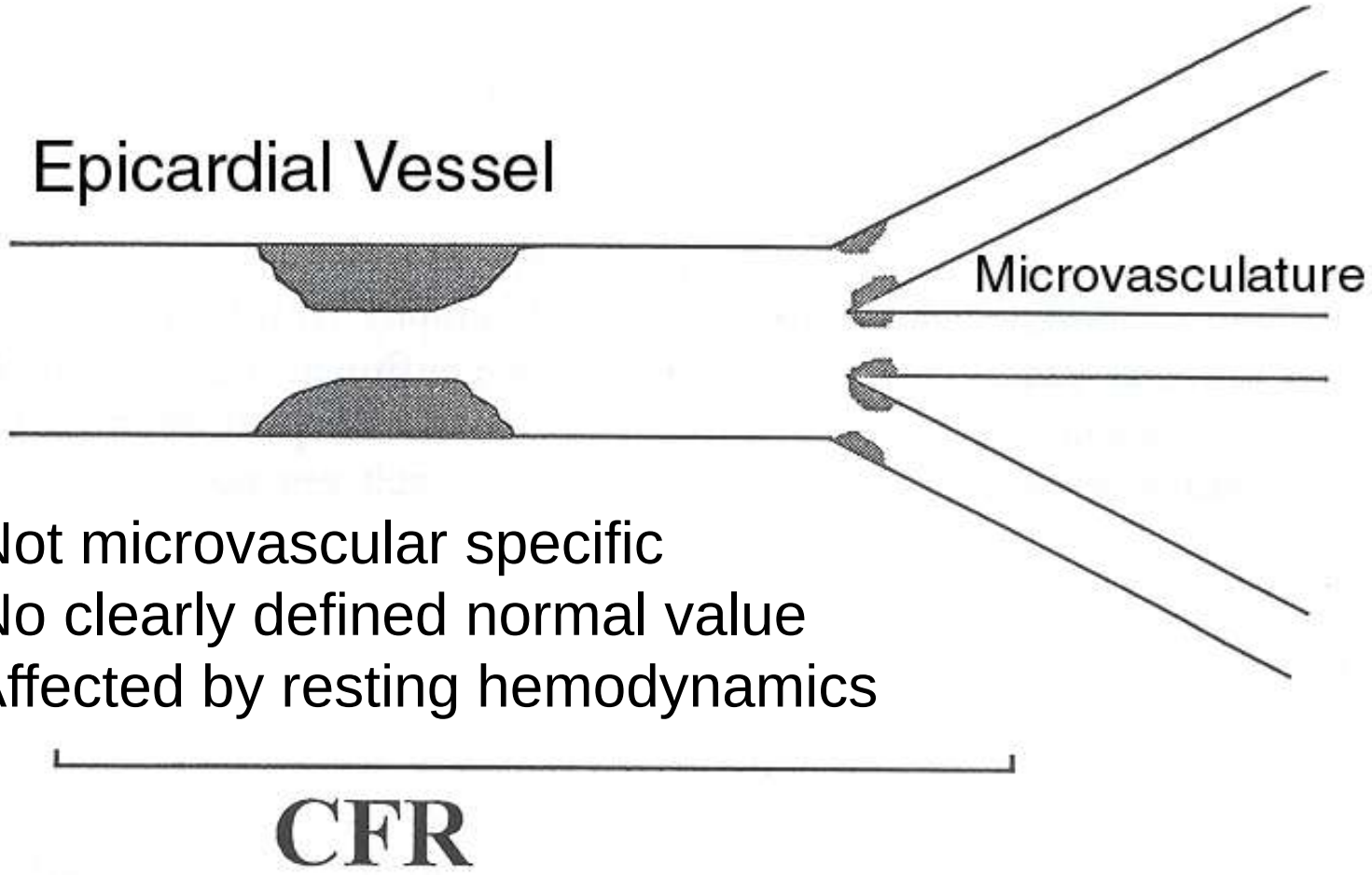
Doppler Wire Coronary Flow Reserve

$$CFR = \frac{Hyperemic\ Flow}{Resting\ Flow}$$



Coronary Wire-Based Assessment

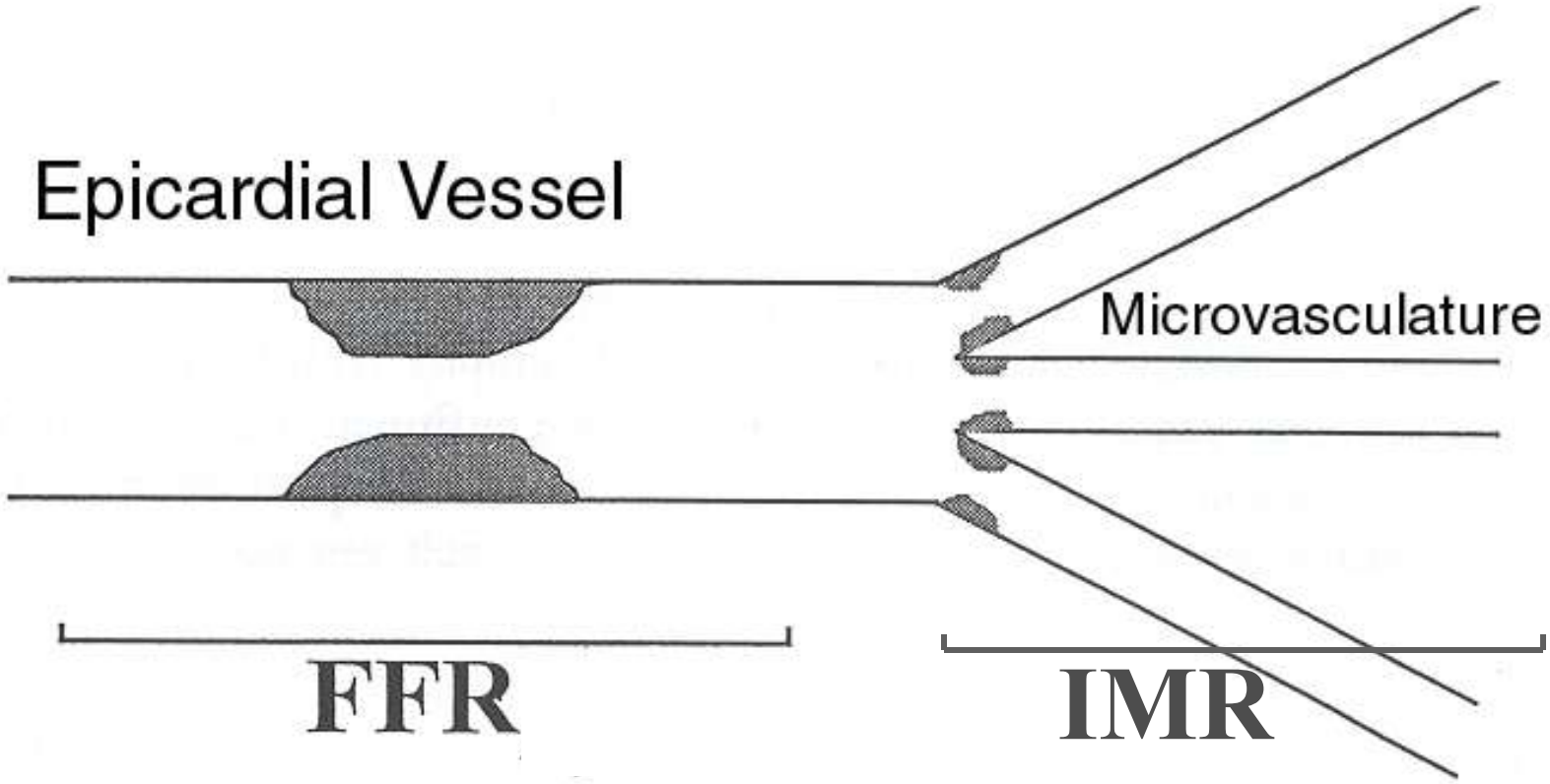
Coronary Flow Reserve



- Not microvascular specific
- No clearly defined normal value
- Affected by resting hemodynamics

Pijls NHJ and De Bruyne B, Coronary Pressure
Kluwer Academic Publishers, 2000

Index of Microcirculatory Resistance

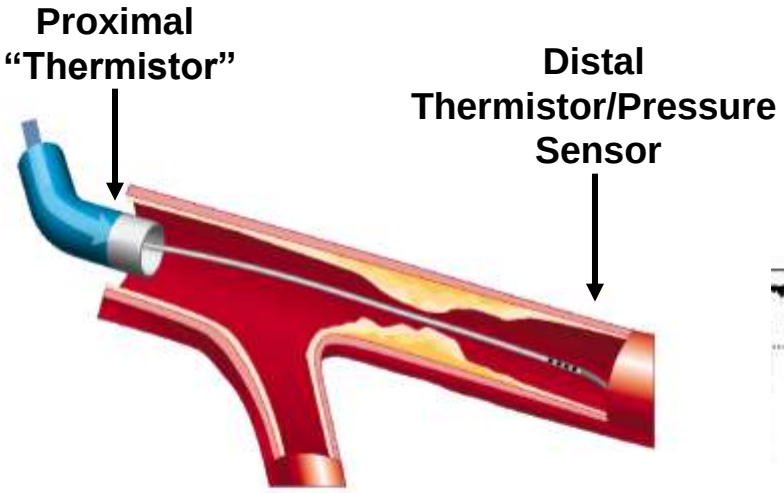


Index of Microcirculatory Resistance

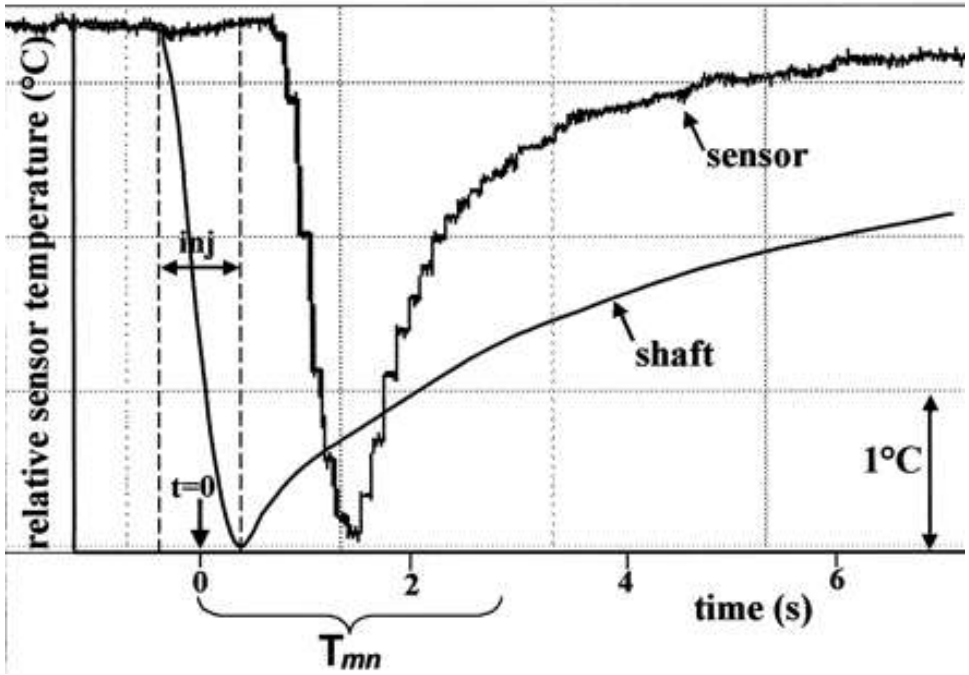
Potential Advantages:

- Readily available in the cath lab
- Specific for the microvasculature
- Quantitative and reproducible
- Predictive of outcomes

Estimation of Coronary Flow



Calculation of mean transit time



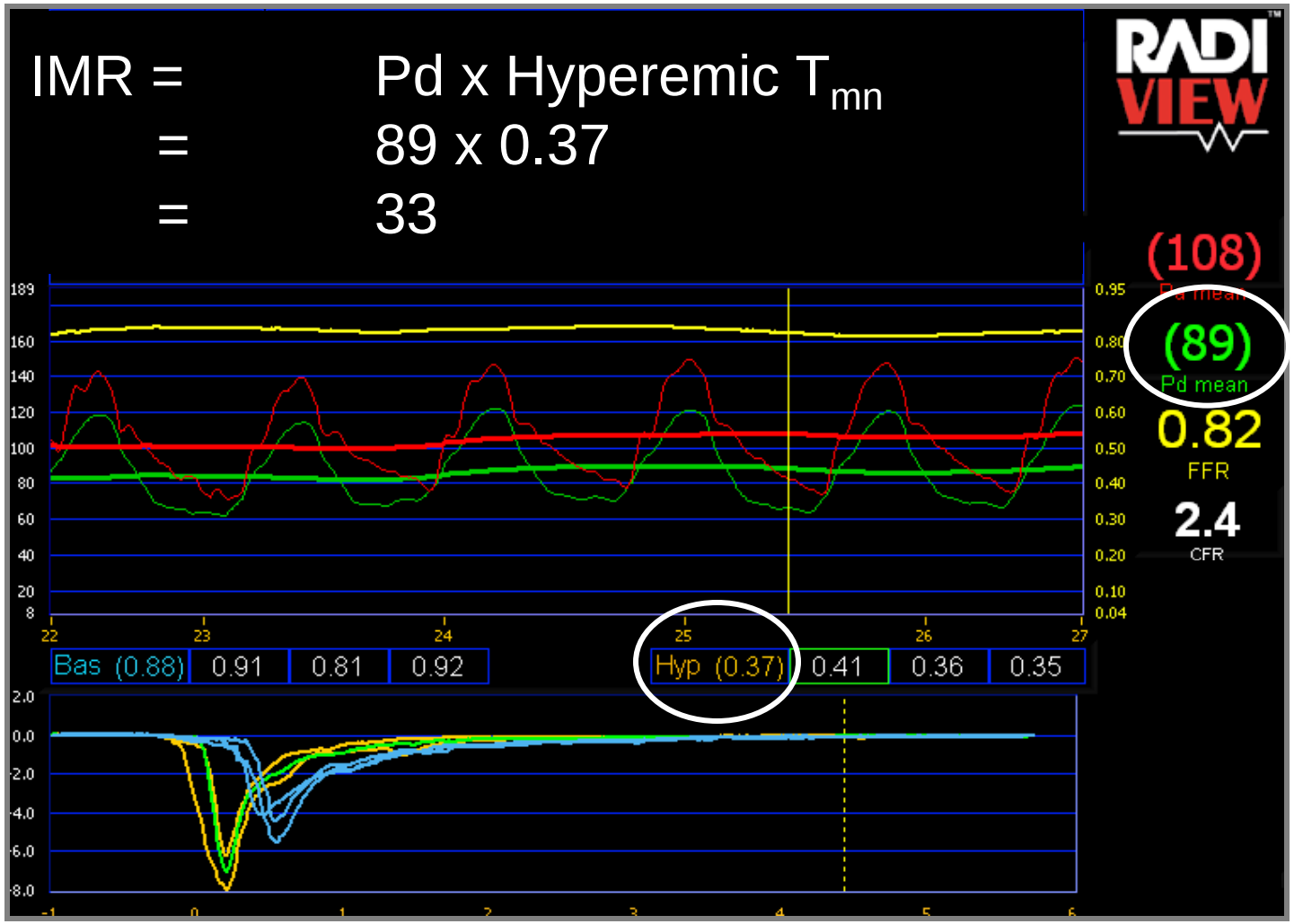
De Bruyne, et al. Circulation 2002;104:2003

Derivation of IMR:

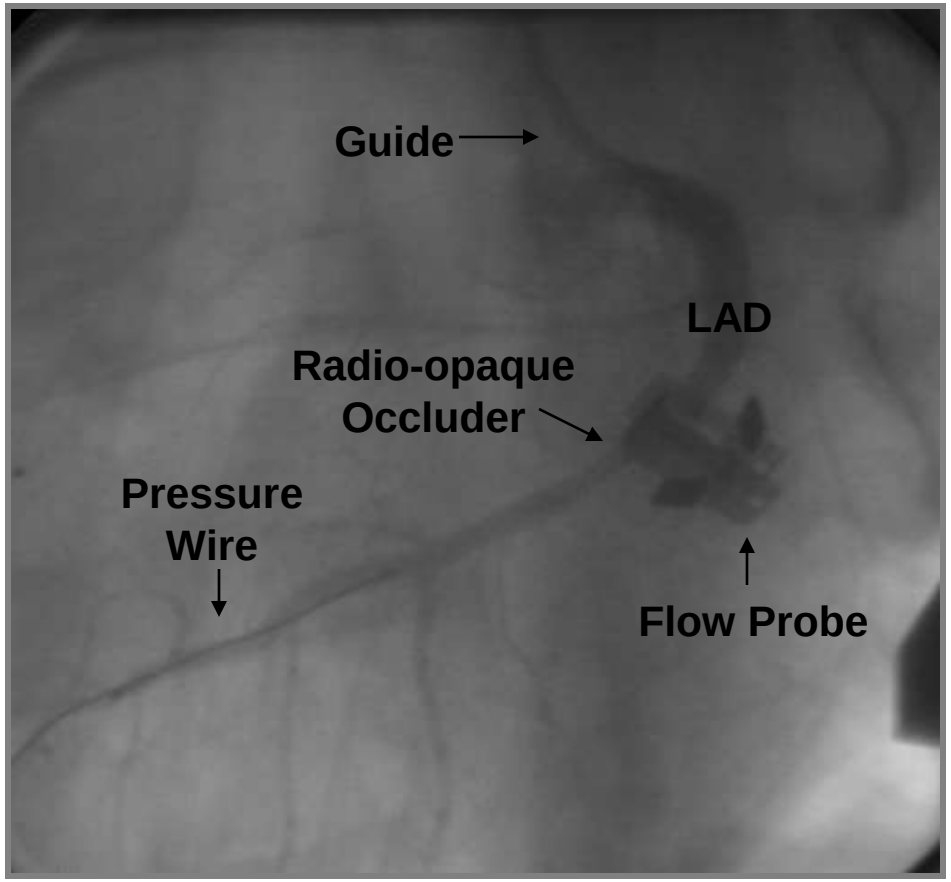
- Resistance = Δ Pressure / Flow
- Δ Pressure = P_d-P_v Flow $\cong$ 1 / T_{mn}
- IMR = P_d-P_v / (1 / T_{mn})
- IMR = P_d x T_{mn} ***at maximal hyperemia…***

Circulation 2003;107:3129-3132.

Practical Measurement of IMR

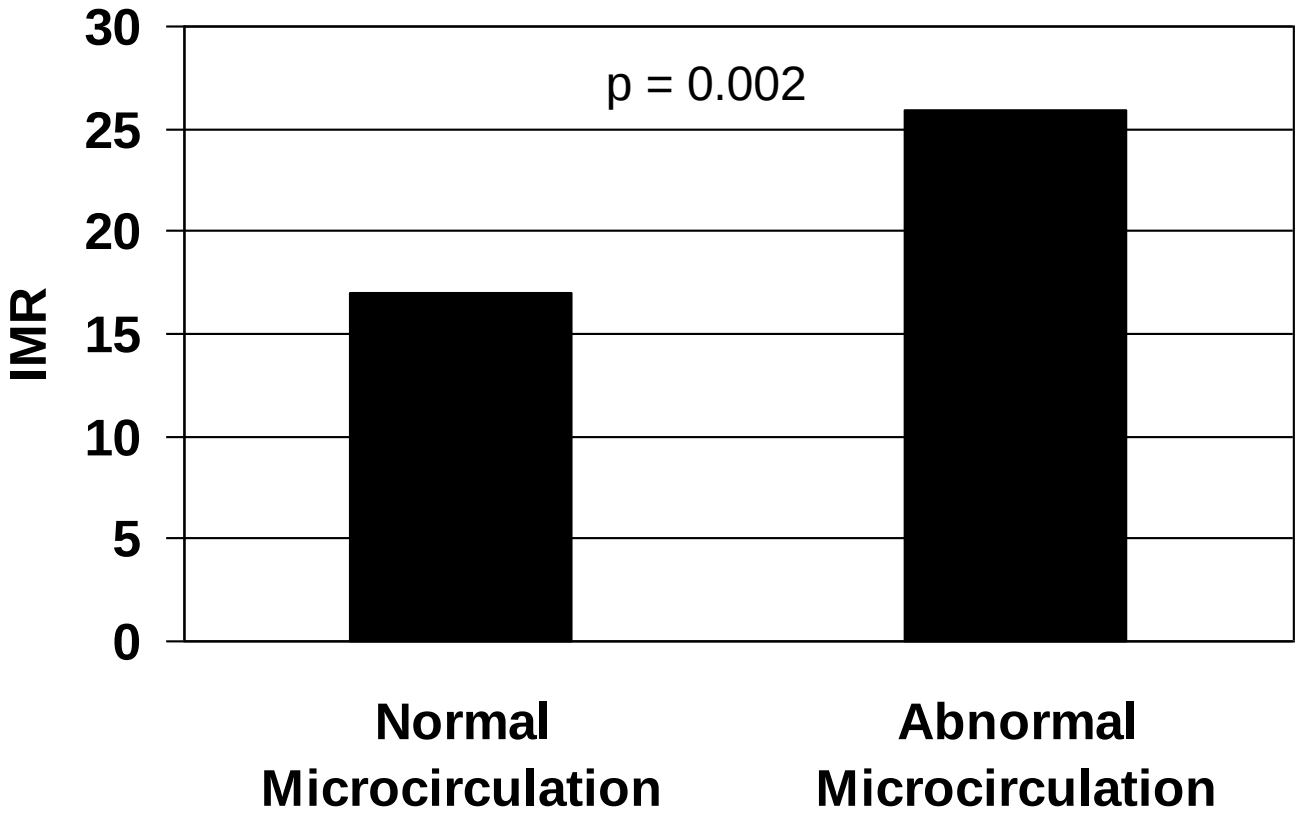


Animal Validation of IMR



Circulation 2003;107:3129-3132.

Animal Validation of IMR



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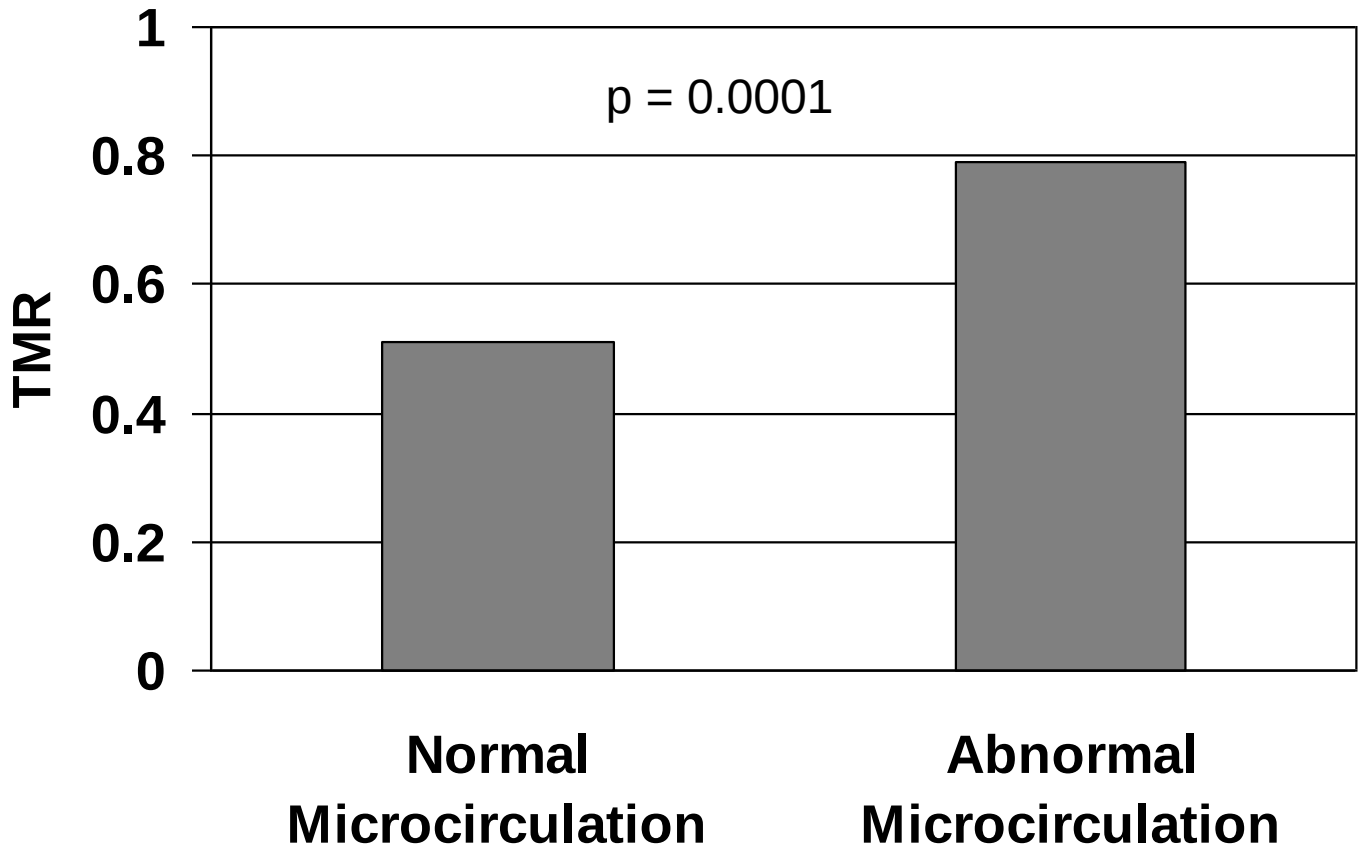

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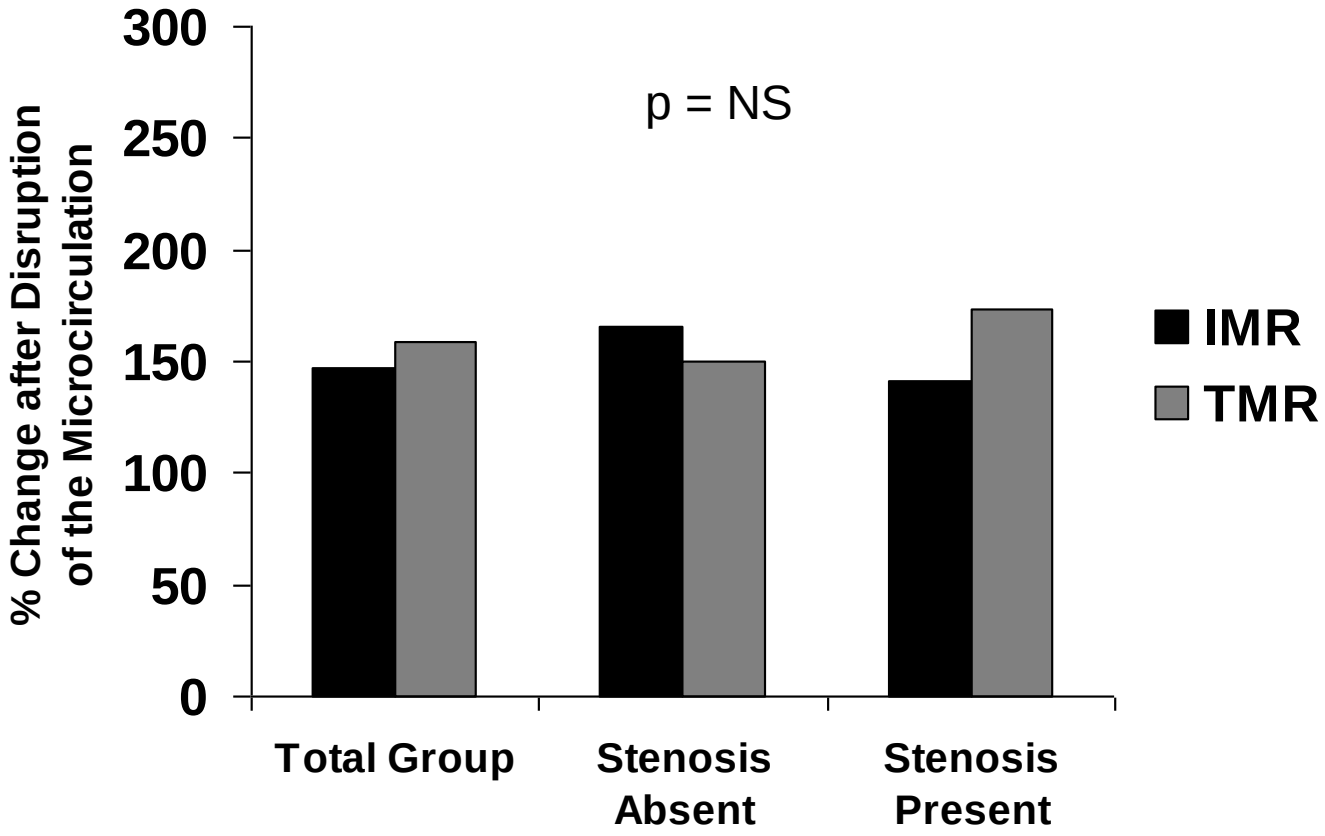
Animal Validation of IMR



Circulation 2003;107:3129-3132.

Reproducibility of IMR

Effect of Pacing on FFR/CFR/IMR

	Baseline	RV Pacing at 110 bpm
CFR	3.1±1.1	2.3±1.2†
IMR, U	21.8±6.5	22.9±6.9
FFR	0.88±0.07	0.87±0.07

Effect of Blood Pressure on FFR/CFR/IMR

	Baseline	Nitroprusside
CFR	2.9±0.9	2.5±1.2
IMR, U	23.85±6.1	24.00±7.9
FFR	0.88±0.04	0.87±0.05

Change in LV Contractility and FFR/CFR/IMR

	Baseline	Dobutamine
CFR	3.0±1.0	1.7±0.6†
IMR, U	22.2±6.0	23.6±8.2
FFR	0.88±0.06	0.87±0.06

Ng, et al. Circulation 2006;113:2054-61.

Why should we assess the coronary microvasculature?

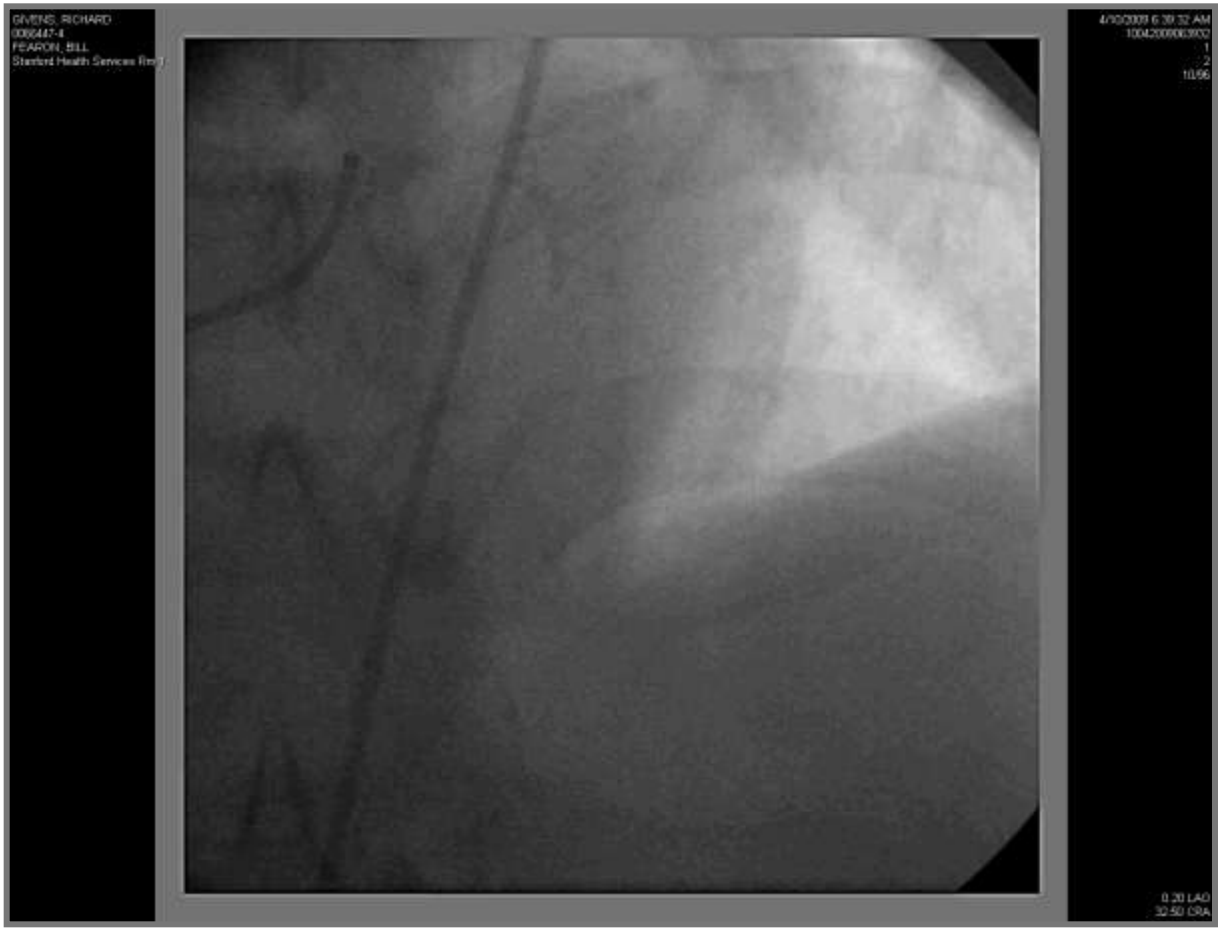
- **In stable patients with "normal" coronary arteries, abnormal microvascular function predicts adverse outcome.**

- In stable patients undergoing PCI, abnormal microvascular resistance may predict adverse outcome.

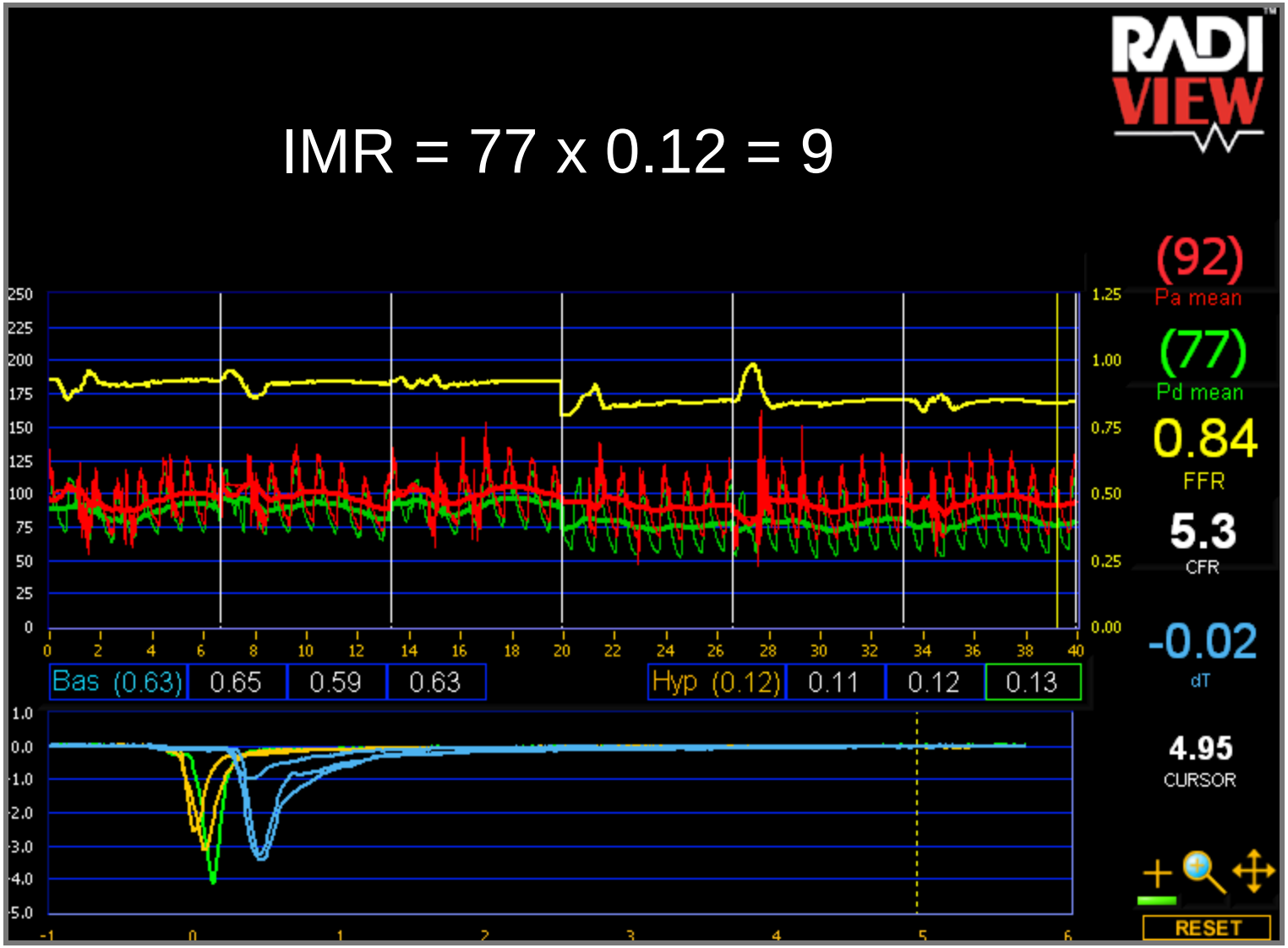
- Immediately after STEMI, impaired microvascular function predicts adverse outcome.

Clinical Application of IMR

65 year old man with HTN, ↑Chol, and chest pain with anterior ischemia on ETT-Echo

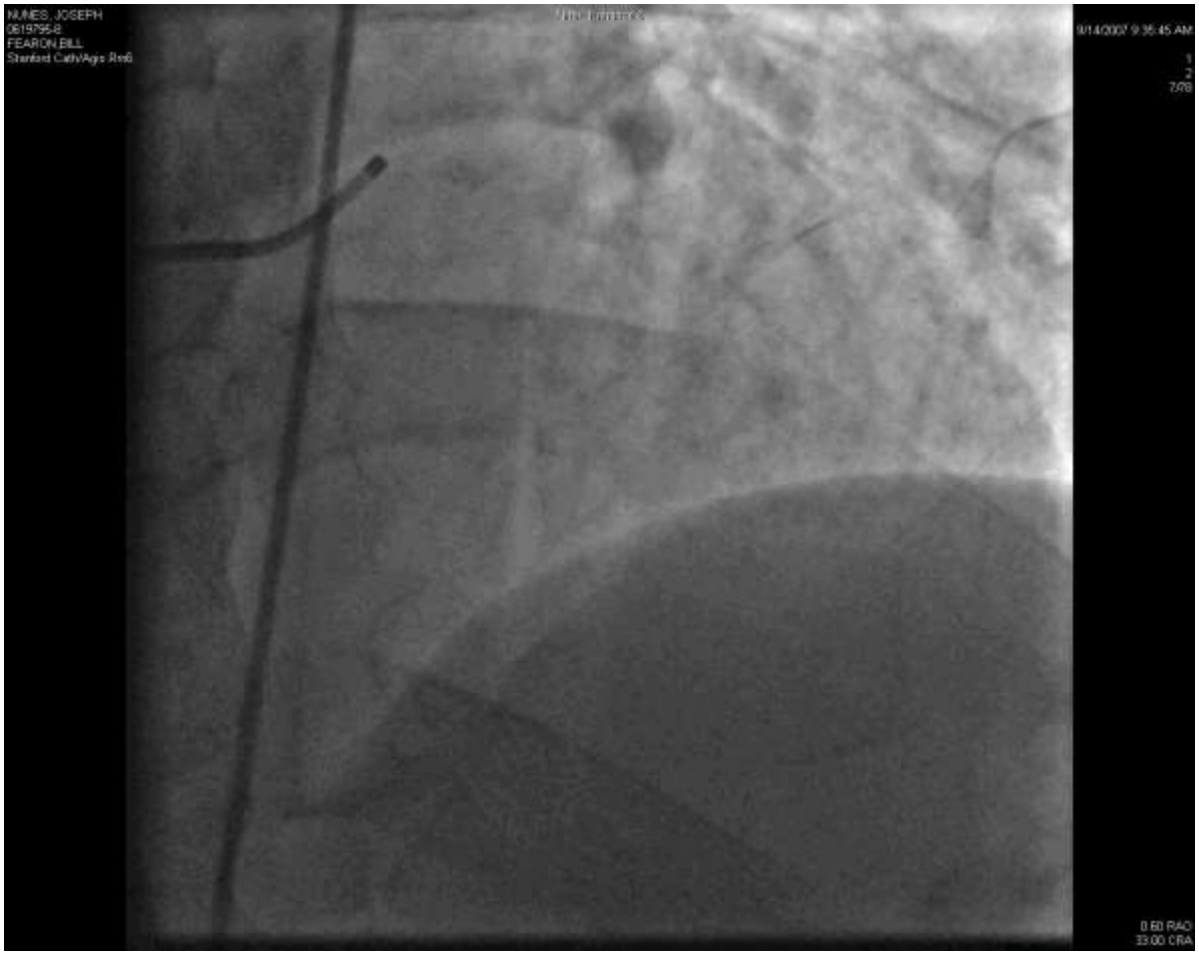


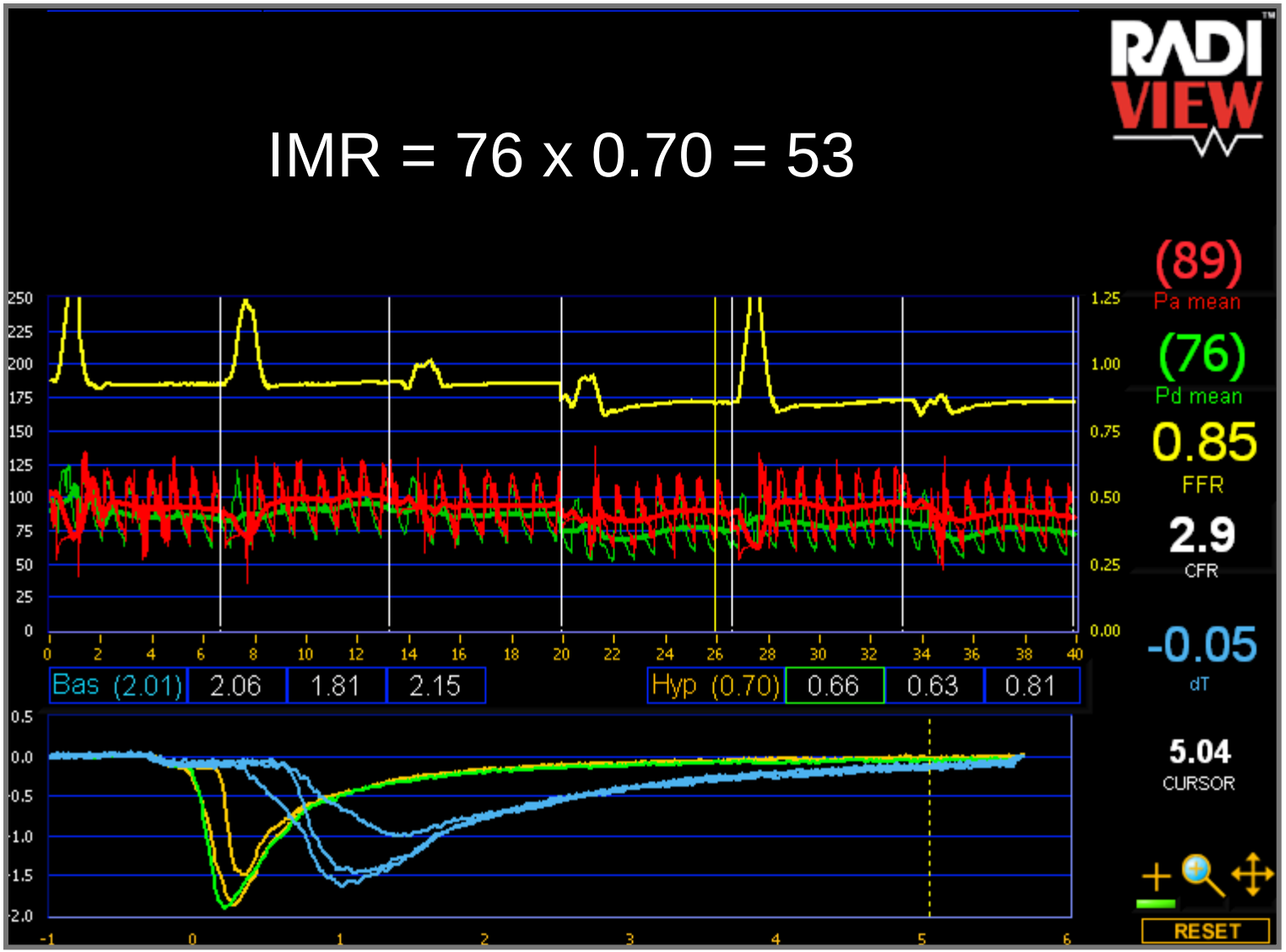
IMR = 77 x 0.12 = 9


RADI VIEW
(92)
Pa mean
(77)
Pd mean
0.84
FFR
5.3
CFR
-0.02
dT
4.95
CURSOR
RESET
Bas (0.63) 0.65 0.59 0.63
Hyp (0.12) 0.11 0.12 0.13

Clinical Application of IMR

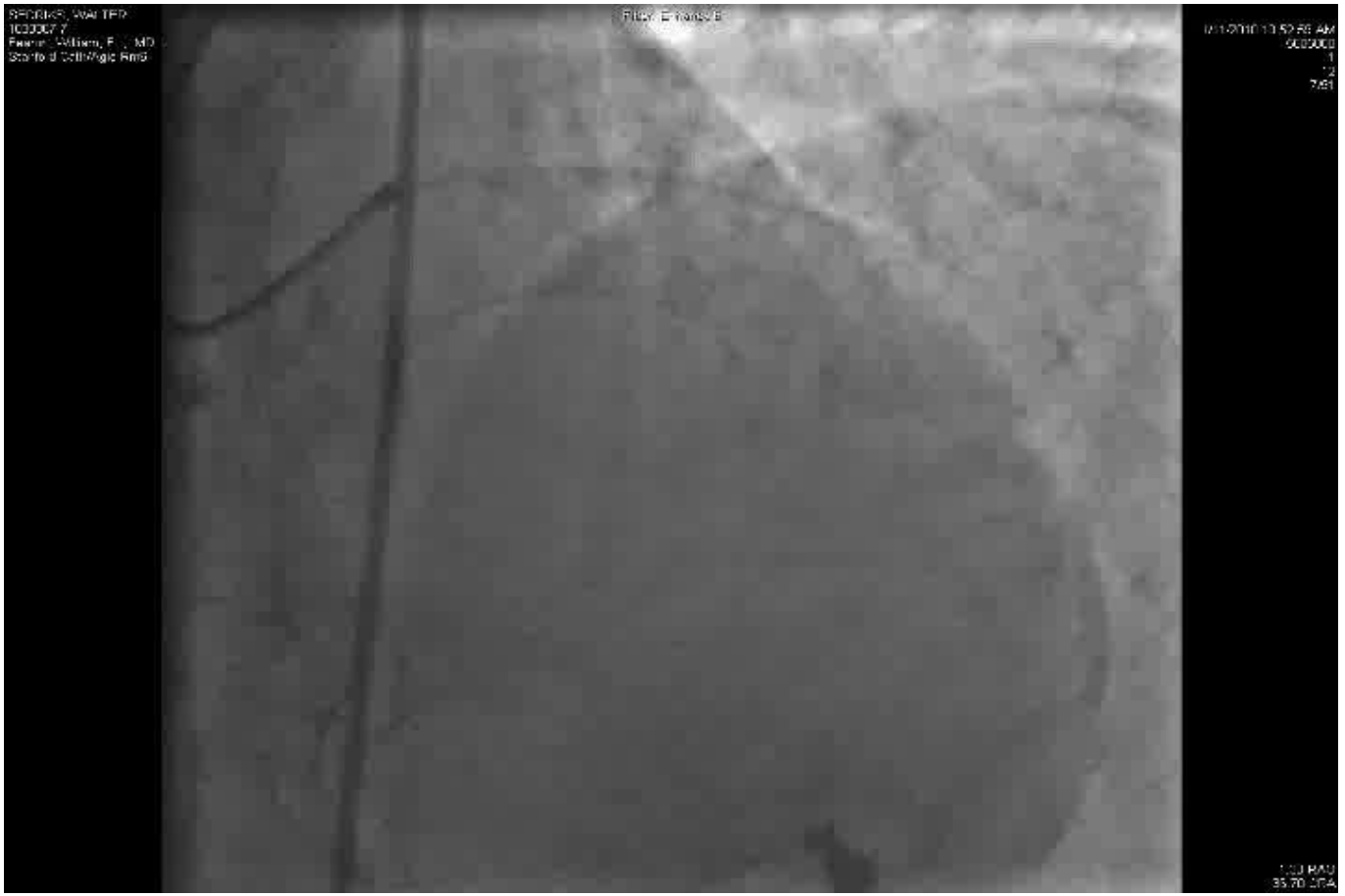
59 year old man with HTN, dyslipidemia and chest pain with emotional stress and septal ischemia on Nuclear Scan



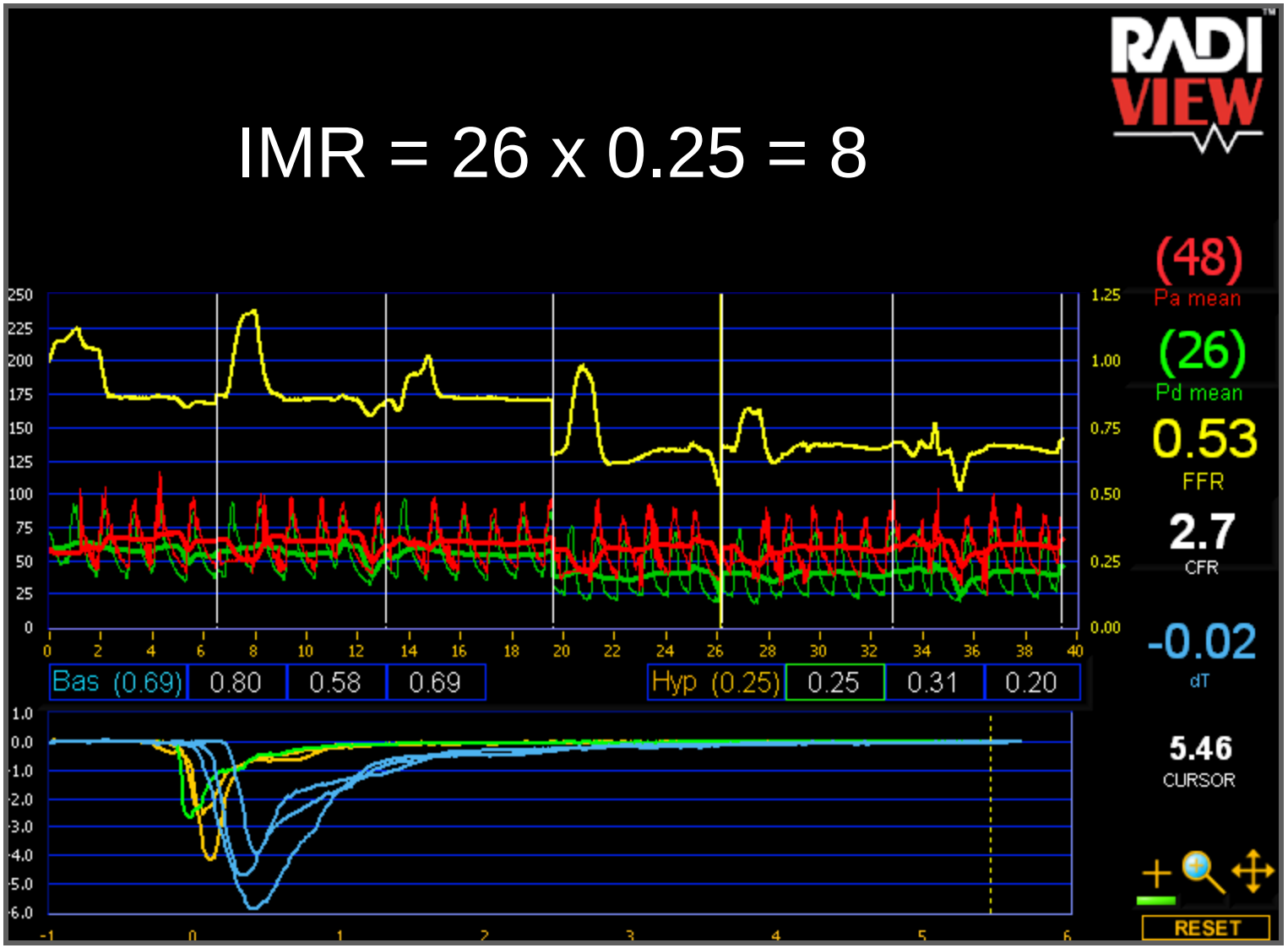

IMR = 76 x 0.70 = 53
RADI VIEW
(89)
Pa mean
(76)
Pd mean
0.85
FFR
2.9
CFR
-0.05
dT
5.04
CURSOR
RESET
Bas (2.01) 2.06 1.81 2.15
Hyp (0.70) 0.66 0.63 0.81

Clinical Application of IMR

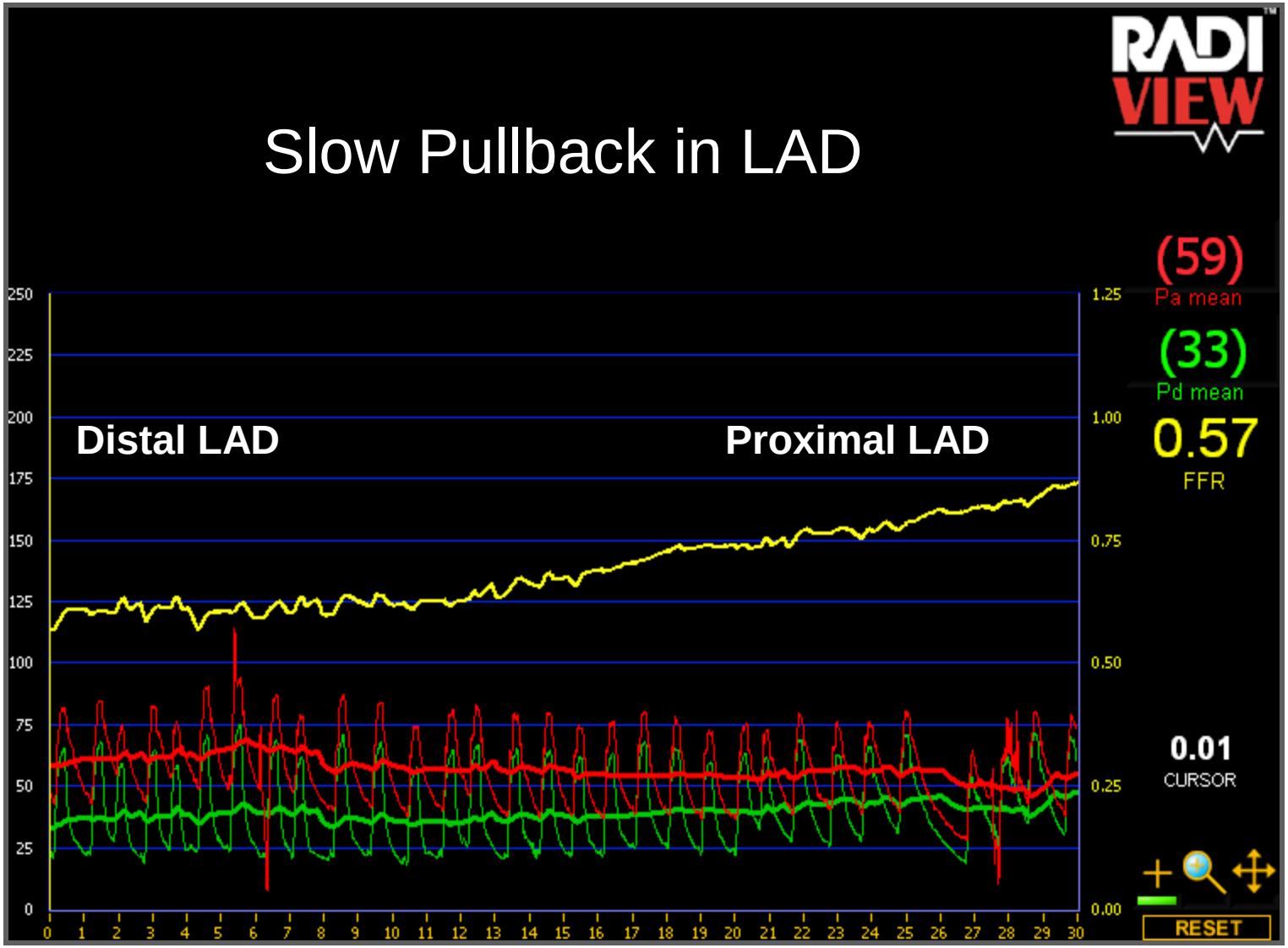
68 year old man HTN and tobacco use with negative stress echo 4 months ago, but increasingly severe classic exertional angina



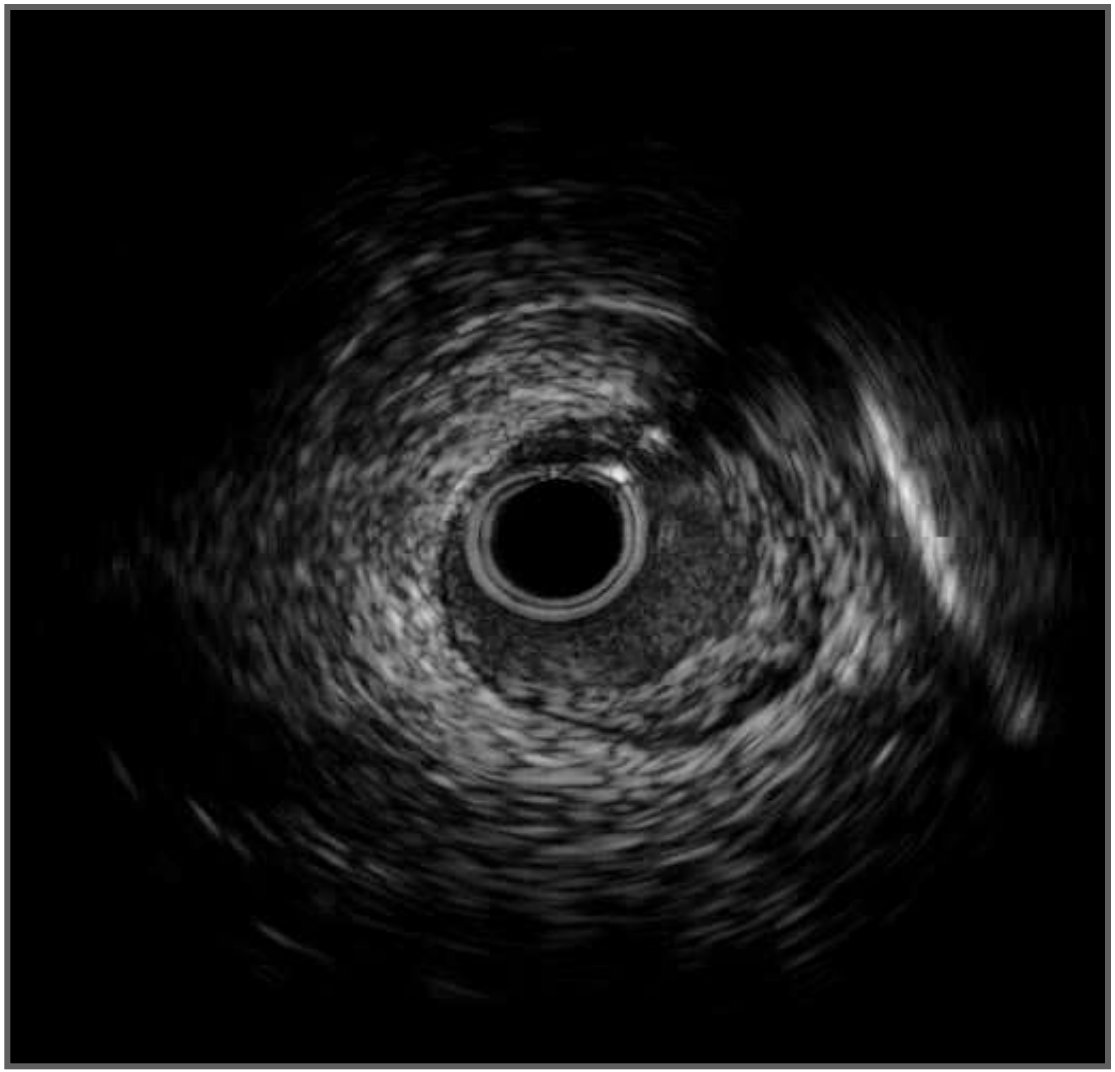
IMR = 26 x 0.25 = 8


RADI VIEW
(48)
Pa mean
(26)
Pd mean
0.53
FFR
2.7
CFR
-0.02
dT
5.46
CURSOR
RESET
Bas (0.69) 0.80 0.58 0.69
Hyp (0.25) 0.25 0.31 0.20

Slow Pullback in LAD



IVUS of LAD



Chest Pain and “Normal Coronaries”

- 139 patients referred for coronary angiography because of symptoms and/or abnormal stress test and found to have “normal” appearing coronaries

- FFR, IMR, CFR, IVUS and acetylcholine challenge were performed down the LAD

Lee BK, et al. Circulation. 2013;128:A19113

Chest Pain and “Normal Coronaries”

Patient Characteristic	n=139
Age (years)	54 ±11
Female	77%
Hypertension	53%
Diabetes	23%
Dyslipidemia	63%
Tobacco Use	8%

Lee BK, et al. Circulation. 2013;128:A19113

Chest Pain and "Normal Coronaries"

- The mean IMR was 19.6 ±9.1
- Microvascular dysfunction was present in 21% (defined as IMR ≥ 25)
- Predictors of microvascular dysfunction were age, diabetes, HTN, and BMI

Lee BK, et al. Circulation. 2013;128:A19113

Chest Pain and "Normal Coronaries"

- 5% of patients had an FFR of the LAD ≤ 0.80
- 44% had epicardial endothelial dysfunction
- 58% had a myocardial bridge

- 24% had nonischemic FFR, normal IMR, no endothelial dysfunction and no "bridge"

Lee BK, et al. Circulation. 2013;128:A19113

Why should we assess the coronary microvasculature?

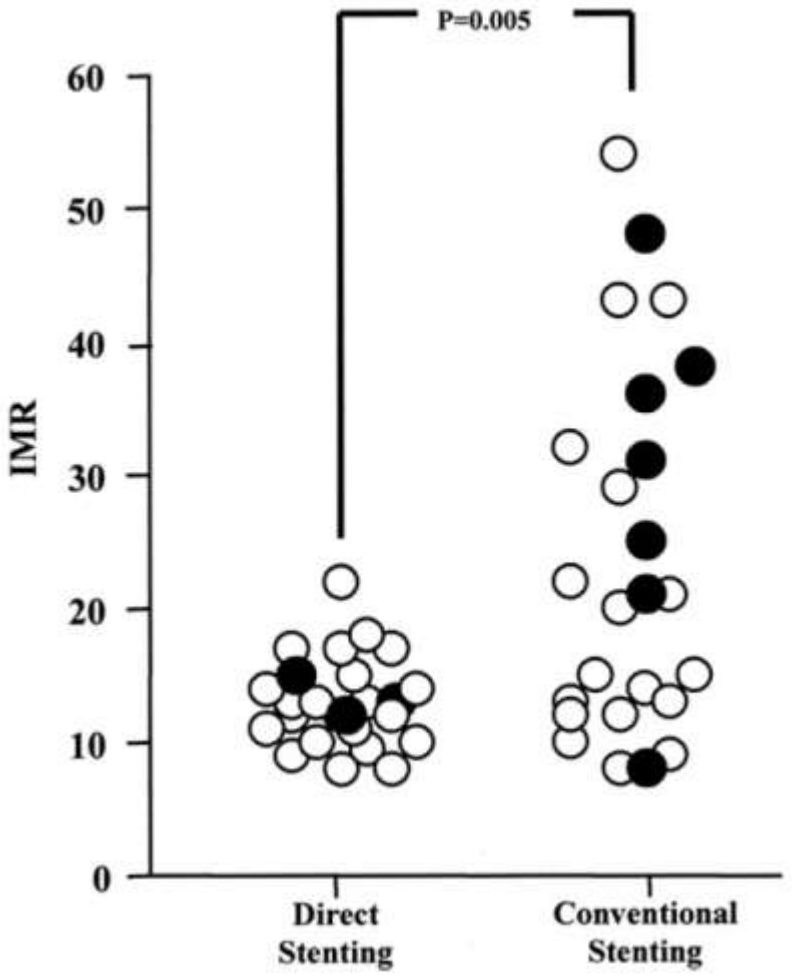
- In stable patients with “normal” coronary arteries, abnormal microvascular function predicts adverse outcome.

- **In stable patients undergoing PCI, abnormal microvascular resistance may predict adverse outcome.**

- Immediately after STEMI, impaired microvascular function predicts adverse outcome.

IMR after PCI in Stable Patients

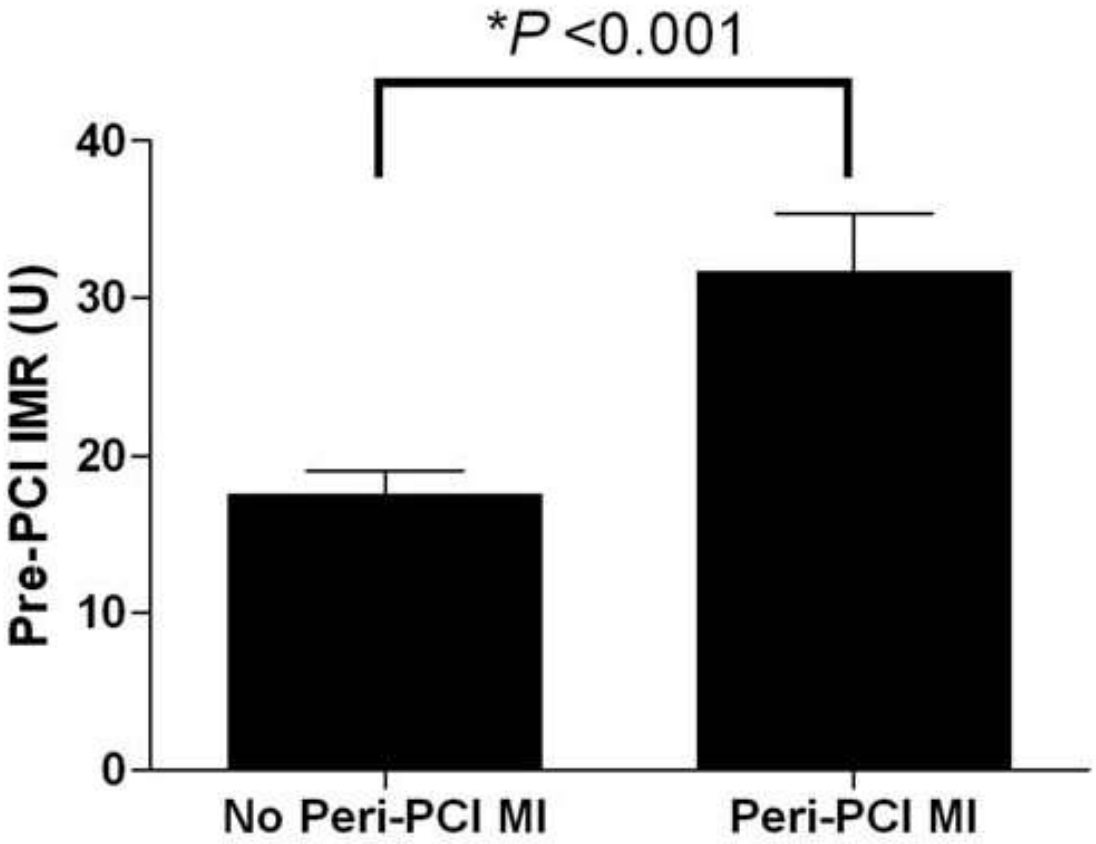
- **50 patients randomized to conventional stenting with predilatation versus direct stenting**
- **IMR measured after PCI and correlated with troponin release**
- **In the 10 patients with elevated Tn post PCI, IMR was 24.7 ±13.3 vs. 16.9 ±10.2, p=0.04.**



Cuisset, et al. J Am Coll Cardiol;2008:51:1060

IMR *Before* PCI in Stable Patients

IMR measured before PCI in 50 stable patients undergoing LAD PCI



Ng, et al. Circ Cardiovasc Interv 2012;5:515-22.

IMR *Before* PCI in Stable Patients

IMR measured before LAD PCI in 50 stable patients

Multivariable Regression Analysis

Variable	*P*	Odds ratio	95% Confidence interval
IMR	0.002	1.25	1.08 – 1.43
Beta-blocker	0.064	13.97	0.97 – 200.56
Post-dilation	0.072	0.09	0.01 – 1.24
Total inflation time	0.115	1.01	0.99 – 1.03
Stent length	0.35	1.08	0.92 – 1.27

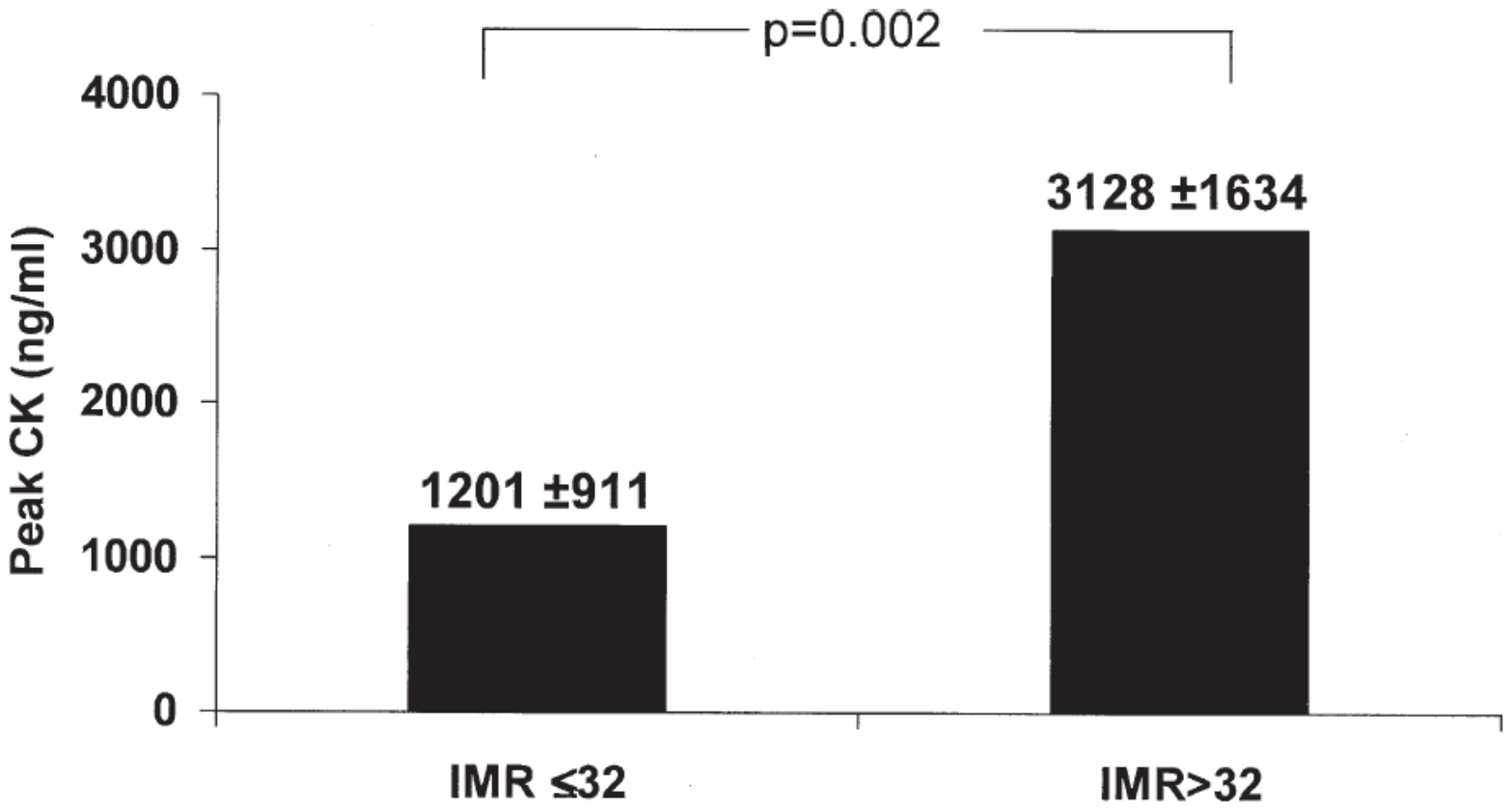
Ng, et al. Circ Cardiovasc Interv 2012;5:515-22.

Why should we assess the coronary microvasculature?

- In stable patients with “normal” coronary arteries, abnormal microvascular function predicts adverse outcome.
- In stable patients undergoing PCI, abnormal microvascular resistance may predict adverse outcome.
- **Immediately after STEMI, impaired microvascular function predicts adverse outcome.**

Predictive Value of IMR after PCI for STEMI

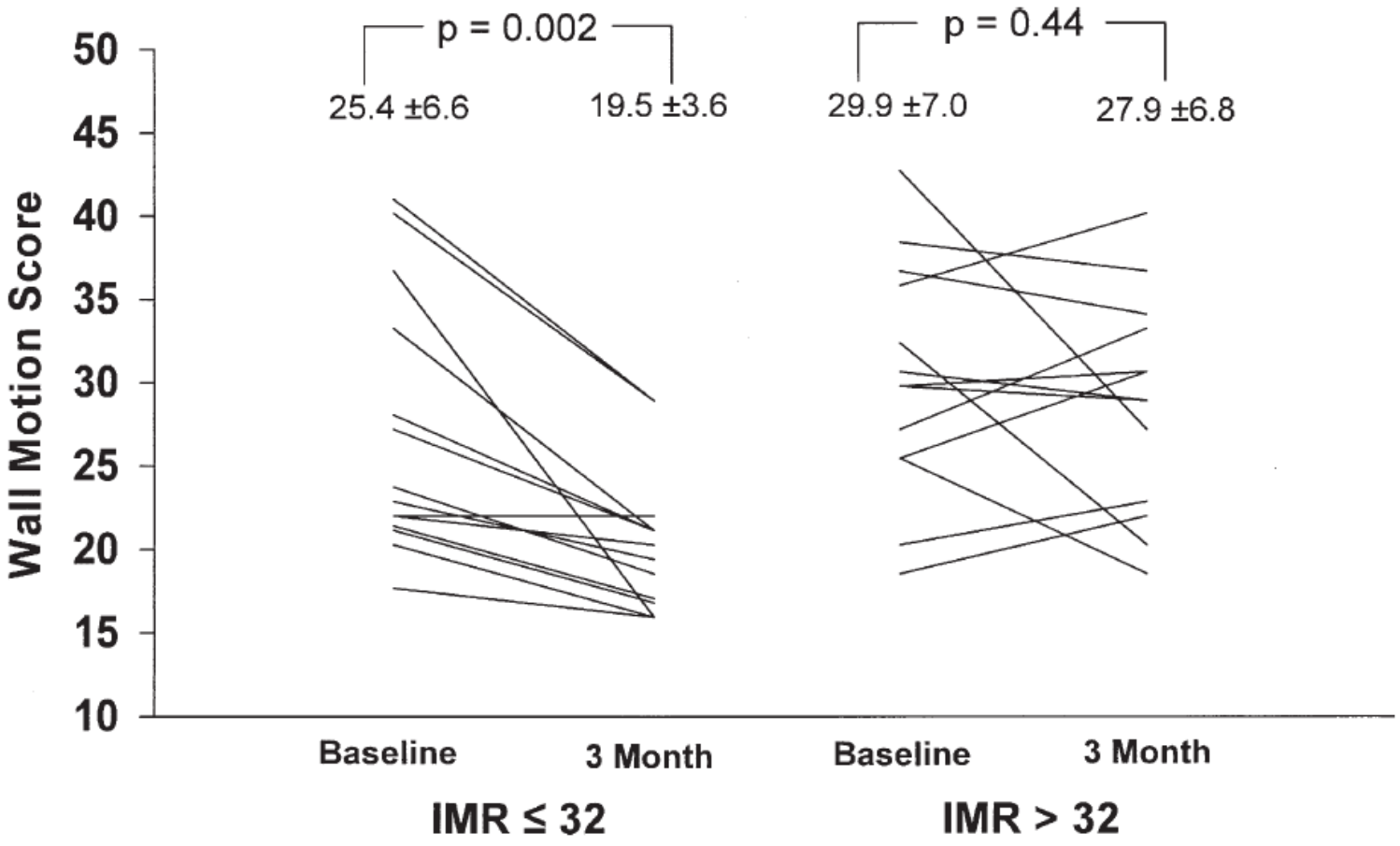
IMR predicts peak CK in patients with STEMI



J Am Coll Cardiol 2008;51:560-5

Predictive Value of IMR after PCI for STEMI

IMR predicts which patients will have improved LV function after STEMI



J Am Coll Cardiol 2008;51:560-5.

Predictive Value of IMR after PCI for STEMI

Correlation between measures of microvascular function and peak CK and 3-month wall motion score

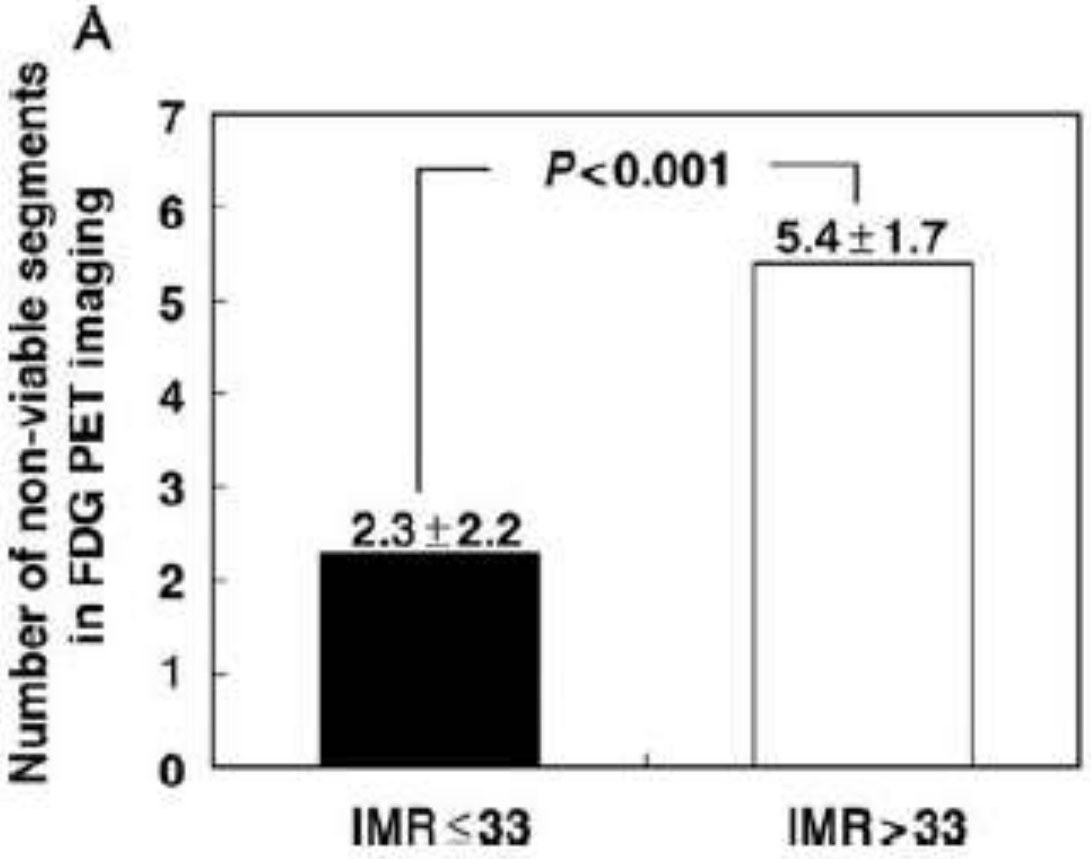
Variable	Peak CK	3-Month WMS
IMR	0.61*	0.59†
TMPG	0.05	0.12
CFR	−0.32	−0.35
ST-segment resolution	−0.35	−0.34
cTFC	−0.02	0.06

*p = 0.0005, †p = 0.002, p = NS for all others.

J Am Coll Cardiol 2008;51:560-5.

Predictive Value of IMR after PCI for STEMI

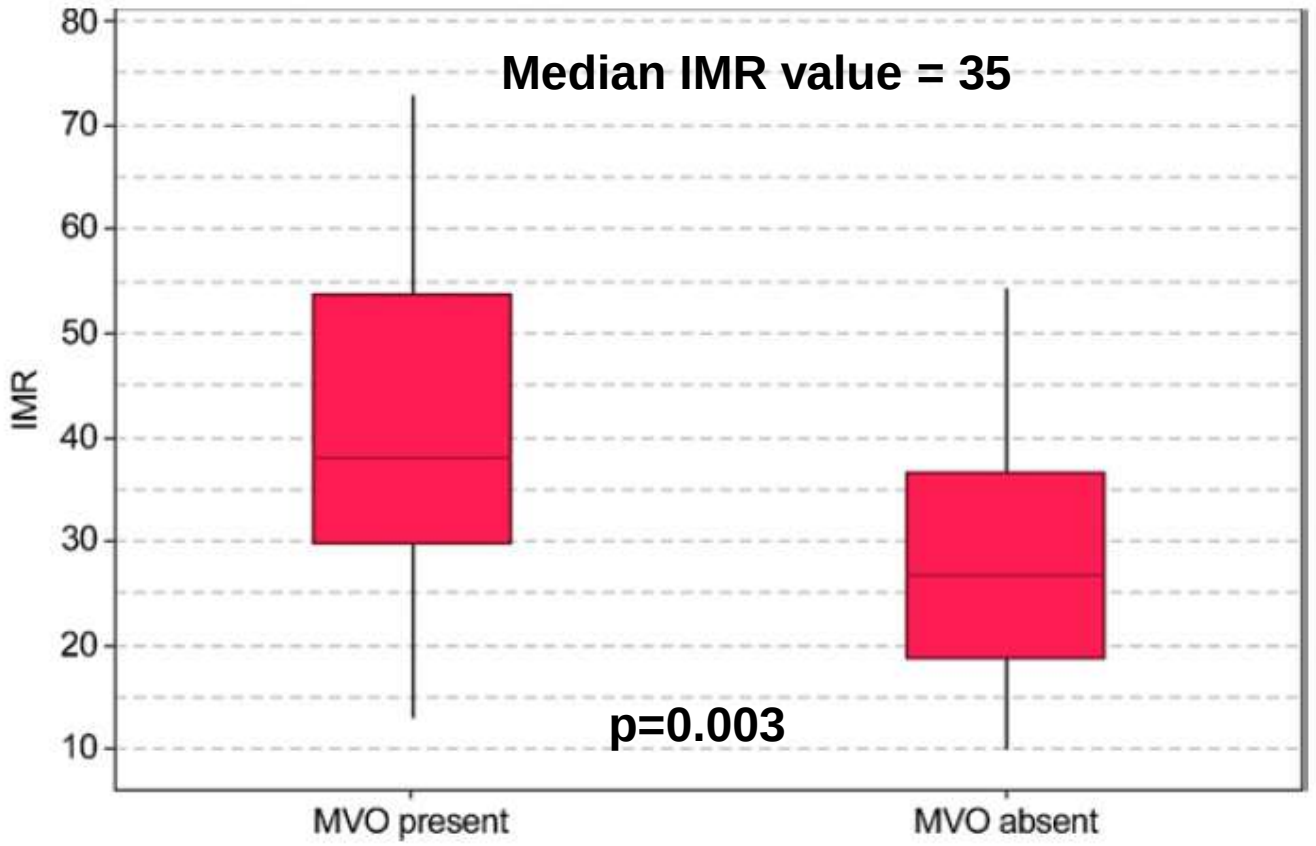
Relation between IMR and PET viability in 40 STEMI patients



Lim HS, et al Eur Heart J 2009;30:2854-60.

Predictive Value of IMR after PCI for STEMI

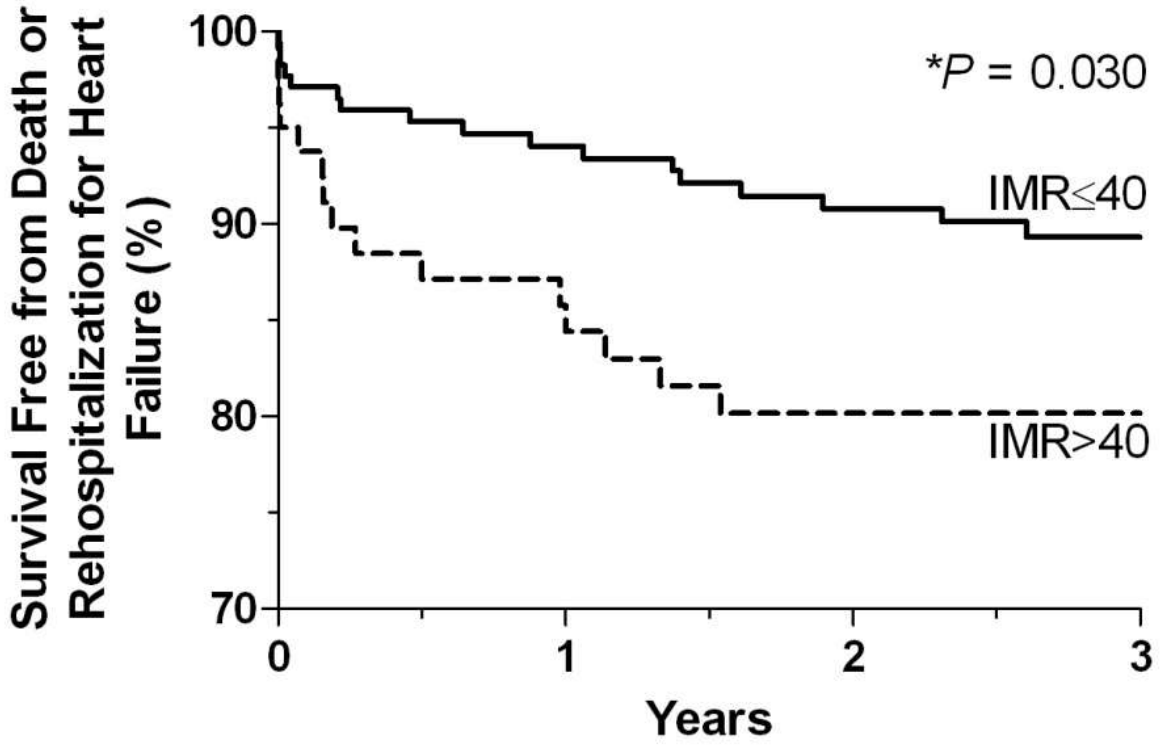
Correlation between IMR and cardiac MR assessment of Microvascular obstruction in 57 patients after STEMI



McGeoch, et al. J Am Coll Cardiol Intv 2010;3:715-22.

IMR and Outcomes post STEMI

Multicenter study evaluating relationship between IMR and longer-term outcomes in 253 STEMI patients

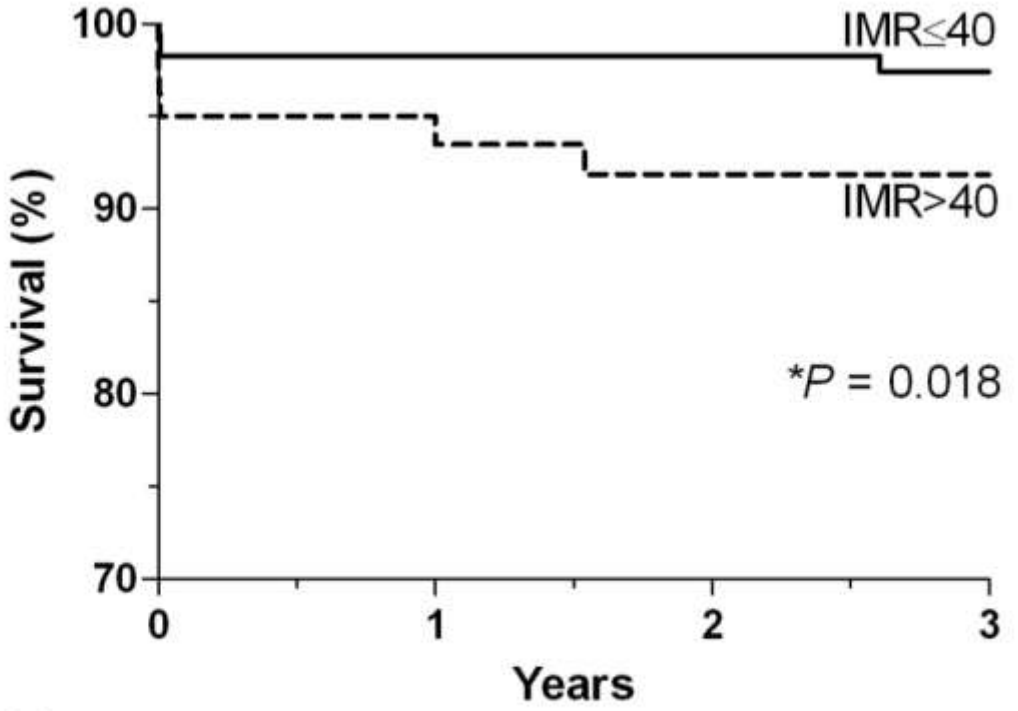


No. at risk:				
IMR ≤40	173	148	138	76
IMR >40	80	63	55	28

Circulation 2013; 127:2436-2441.

IMR and Outcomes post STEMI

Multicenter study evaluating relationship between IMR and longer-term outcomes in 253 STEMI patients



No. at risk:				
IMR ≤40	173	154	149	84
IMR >40	80	69	63	33

Circulation 2013; 127:2436-2441.

Limitations of IMR

- Invasive
- Interpatient and intervessel variability?
  - Sensor distance
- Independent of epicardial stenosis
  - Coronary wedge pressure

Conclusion

Take Home Messages:

- The microvasculature is a complex entity, which is challenging to investigate.
- In the cardiac catheterization laboratory, measurement of IMR may help guide treatment in patients with “normal coronaries” and chest pain.
- IMR predicts outcomes in acute MI; emerging data suggest its utility in stable PCI patients, as well.