Coronary Physiology and Imaging Summit
February 10th, 2007, Seoul, Korea

The Coronary Microcirculation:
Clinical Importance and Diagnostic Methods

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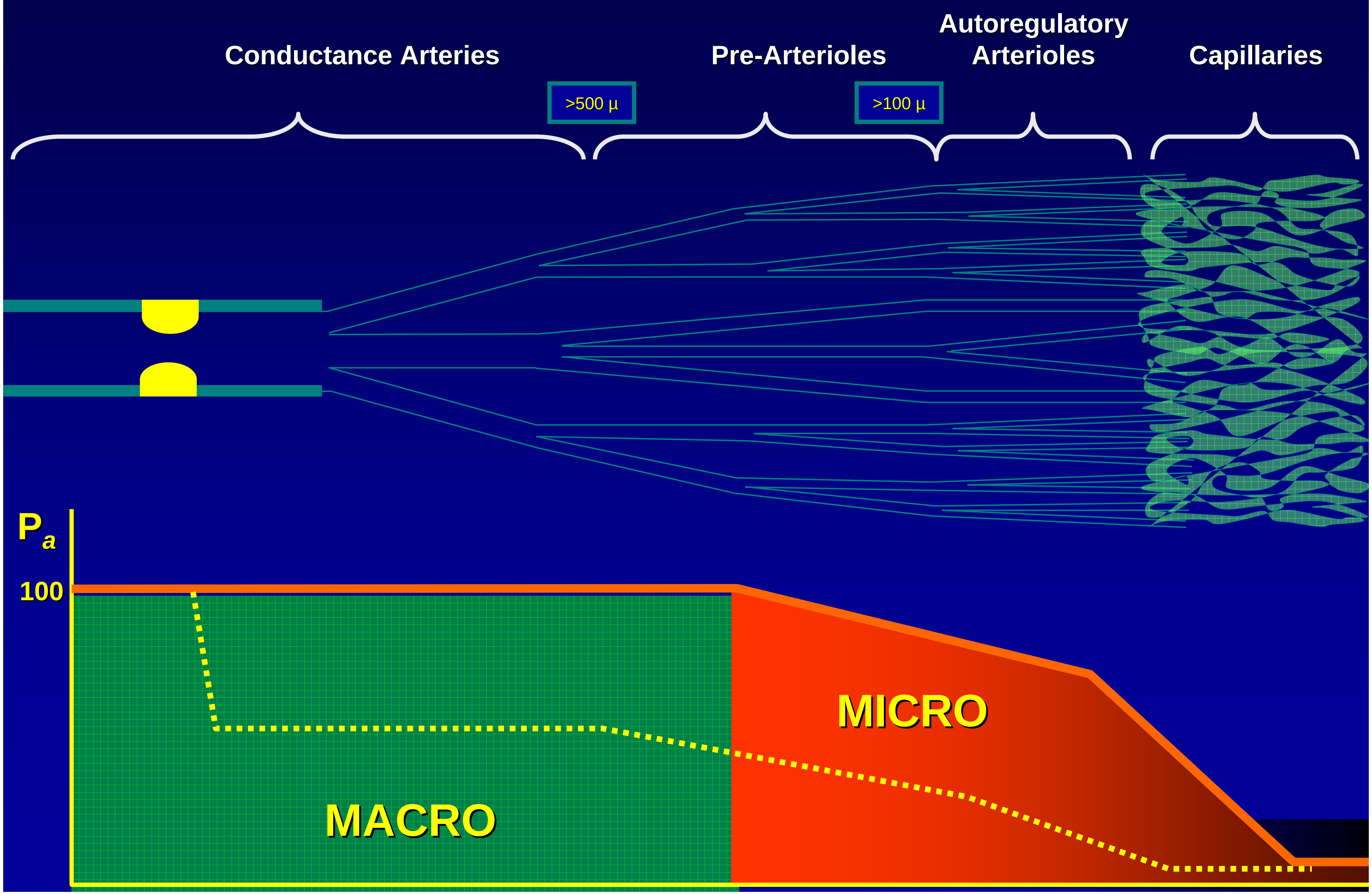
Conflict of Interest

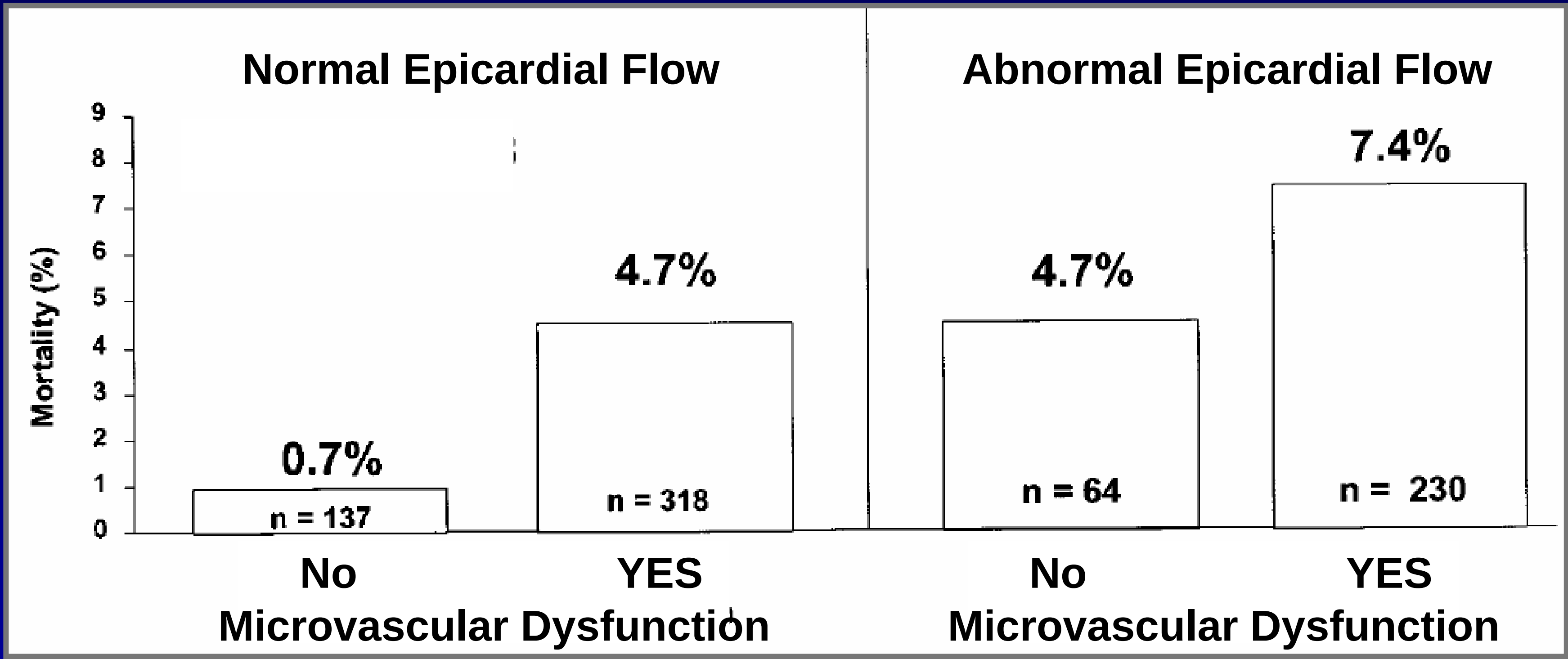
- No conflict of interest relevant to this talk

Coronary Atherosclerosis and Resistance to Myocardial Flow



Importance of the Microcirculation

30 Day Mortality in 762 AMI Patients



Gibson et al. Circulation 2000;101:125-130.

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Importance of the Microcirculation

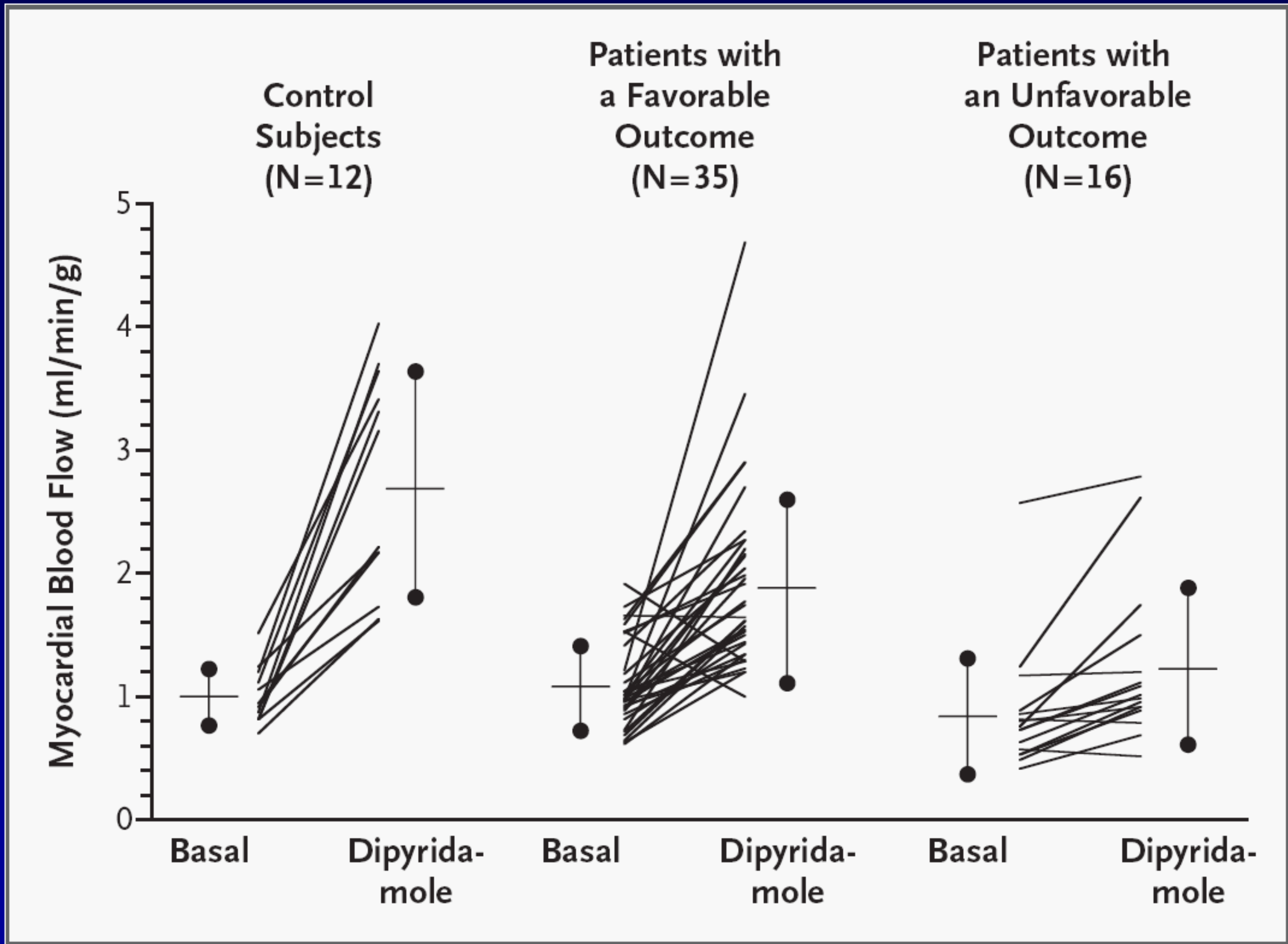
Predictors of Adverse Events in 169 Anterior AMI Patients

Variables	Odds Ratio	95% CI	χ^2	*P*
Congestive heart failure				
Microvascular injury	10.98	4.43 to 27.20	26.78	<0.001
Multivessel disease	3.76	1.44 to 9.82	7.28	0.007
Cardiac rupture				
Microvascular injury	...	...	21.05	<0.001
Cardiac death				
Microvascular injury	...	...	12.81	<0.001
Multivessel disease	13.51	1.21 to 151.4	5.70	0.017
Age ≥70 y	11.36	1.00 to 128.5	4.84	0.028

Circulation 2002;106:3051-3056.

Importance of the Microcirculation

PET-Derived CFR in 51 Patients with Hypertrophic Cardiomyopathy



New Engl J Med 2003;349:1027-1035.

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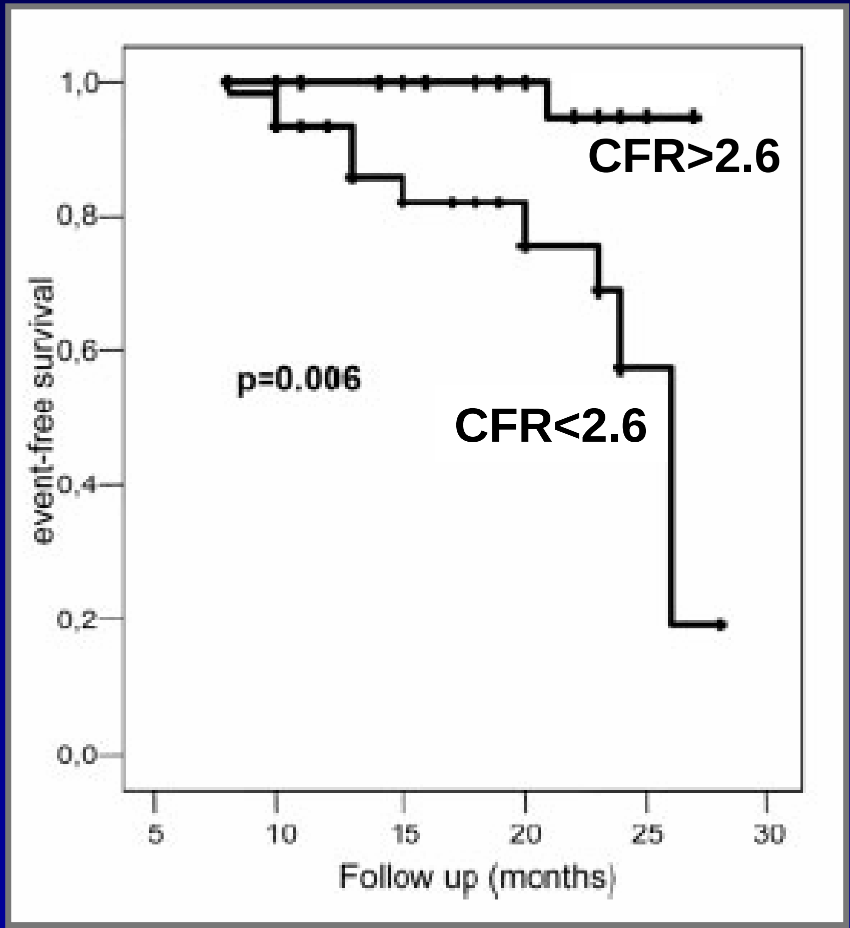
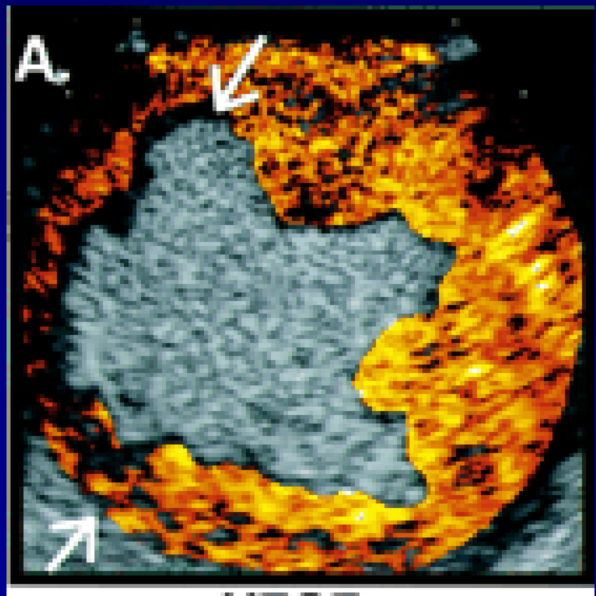
Importance of the Microcirculation

Event-Free Survival in 66 Cardiac Transplant Recipients based on CFR

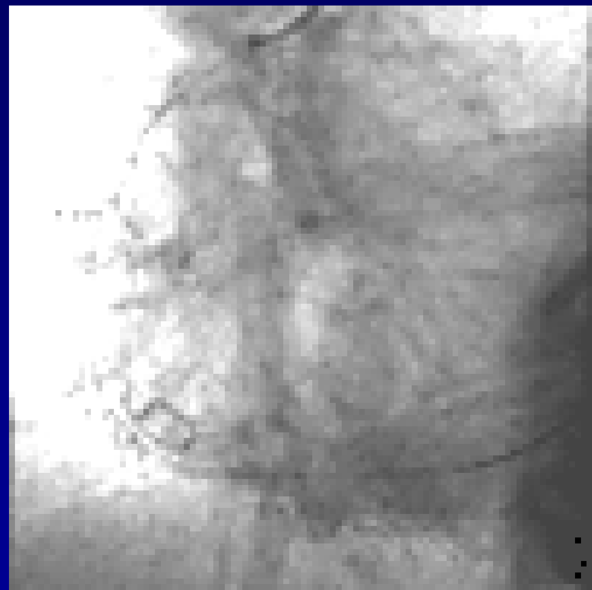


Circulation 2006;114(1 Suppl):I49-55.

Evaluating the Microcirculation

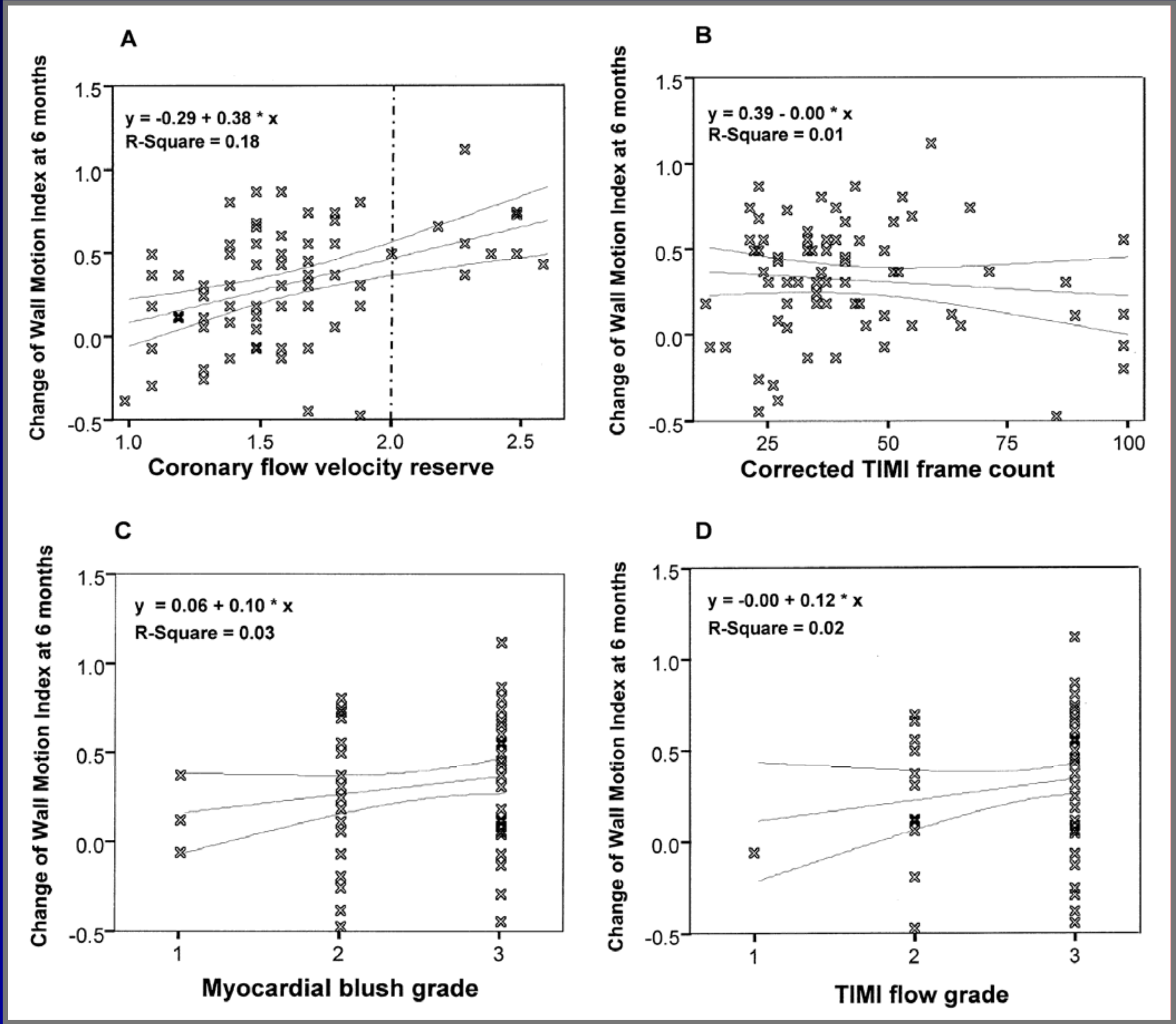


Contrast Echocardiography



Myocardial Perfusion Grade

Evaluating the Microcirculation



J Am Coll Cardiol 2004;43:534-541

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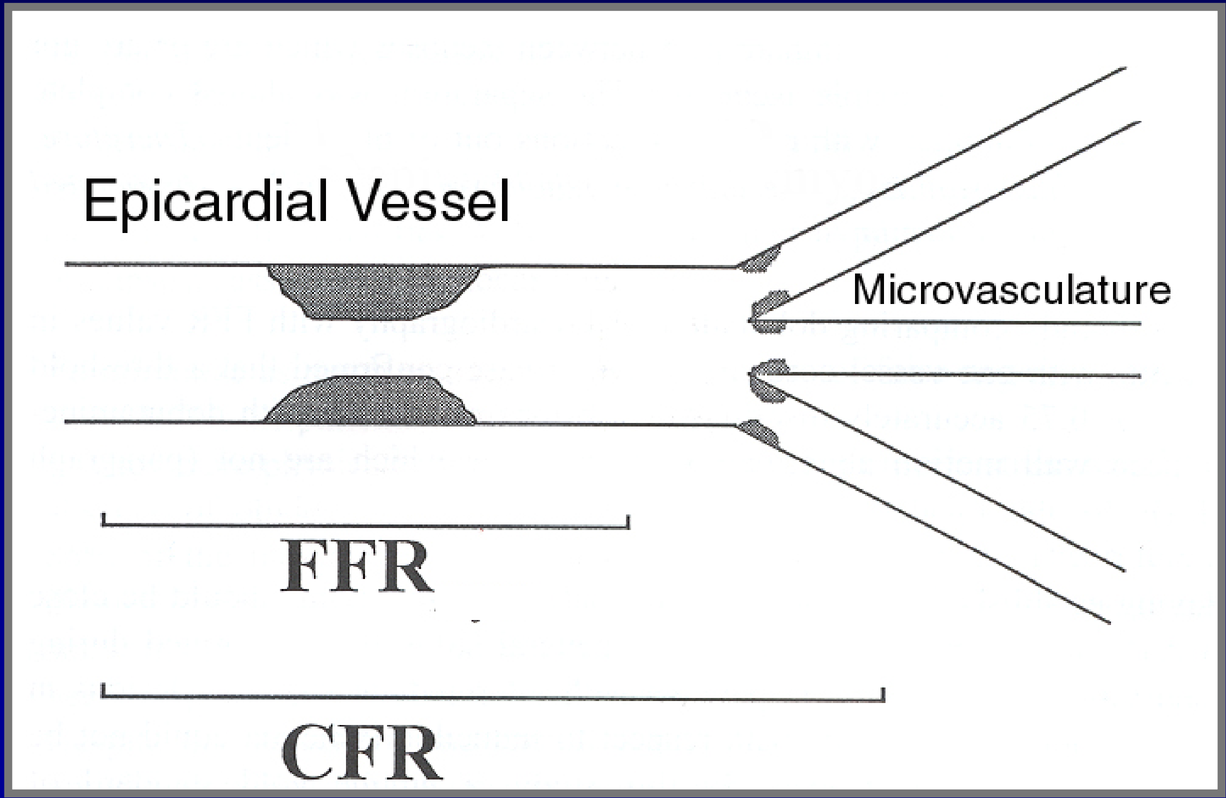
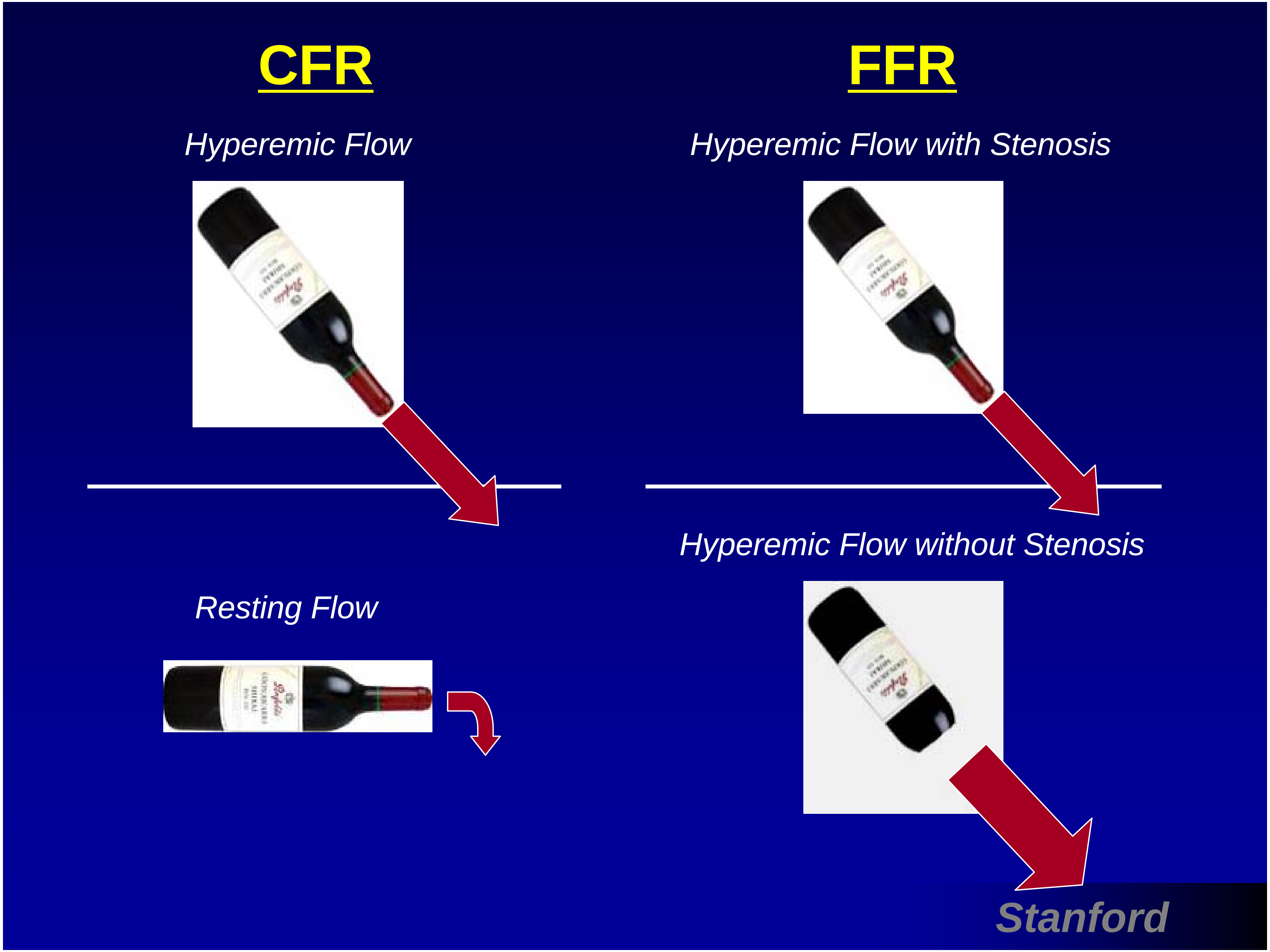
Coronary Wire-Based Evaluation of the Microcirculation



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


CFR
FFR
Hyperemic Flow
Hyperemic Flow with Stenosis
Hyperemic Flow without Stenosis
Resting Flow
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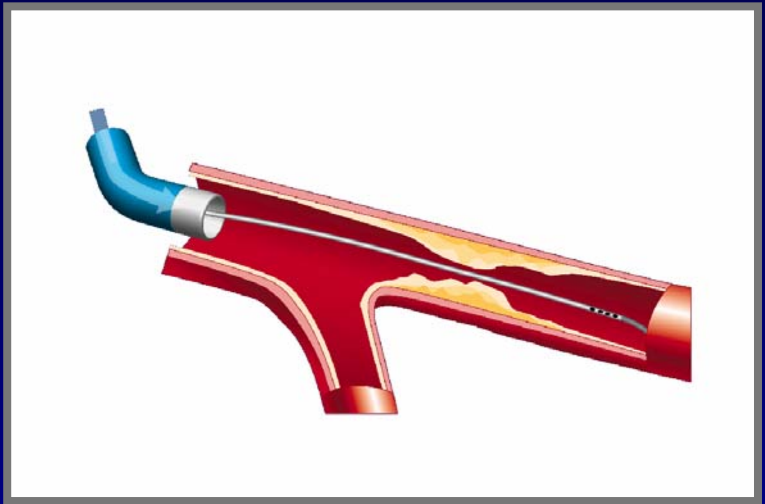
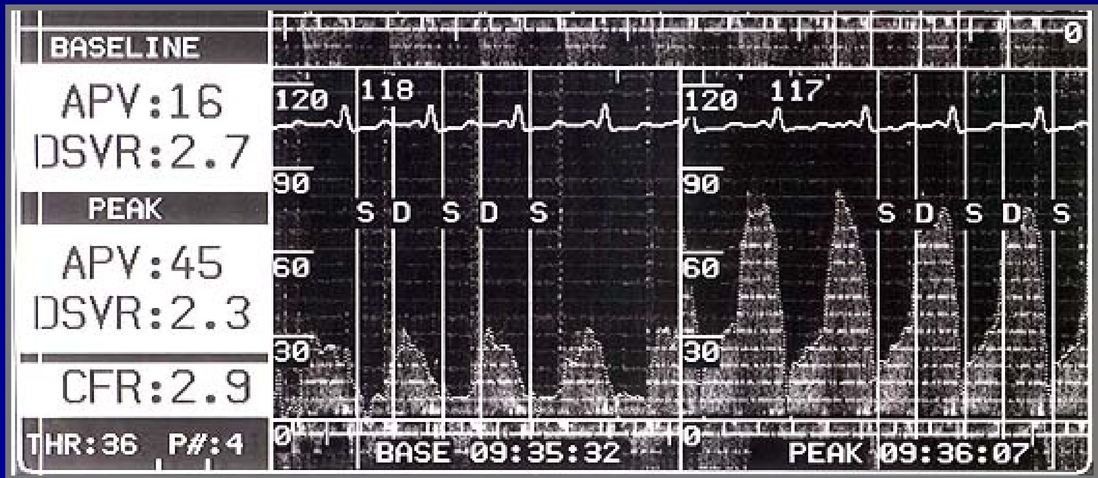
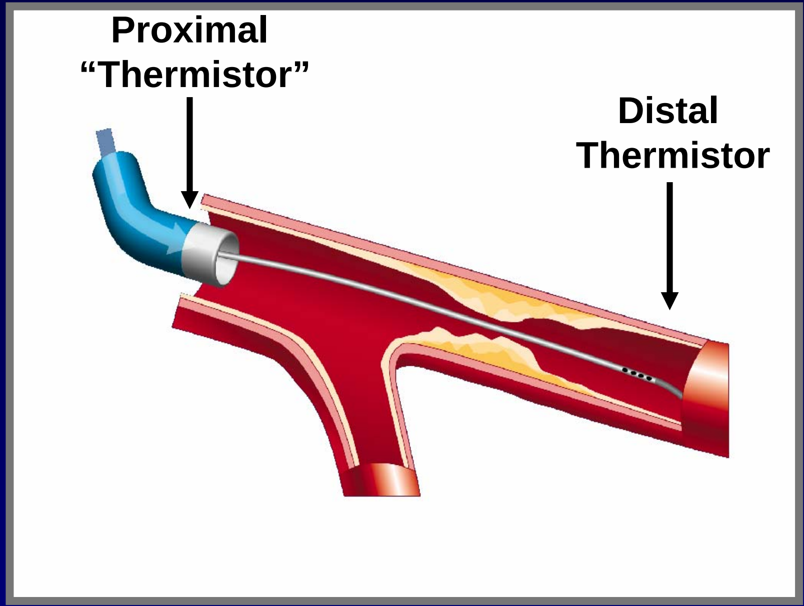
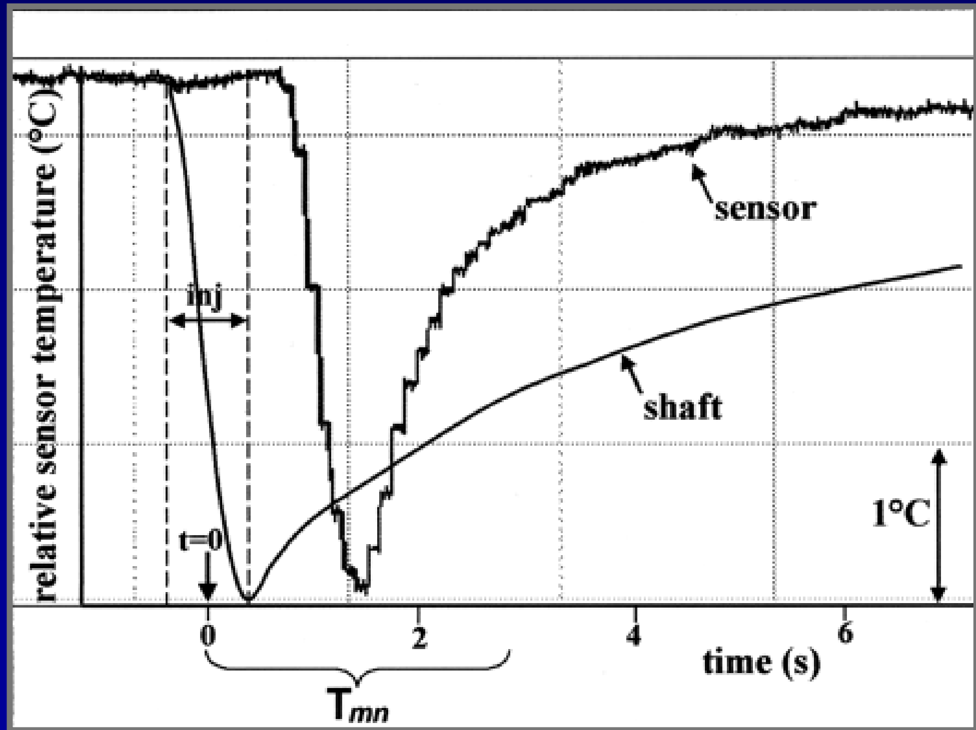
Doppler Wire CFR





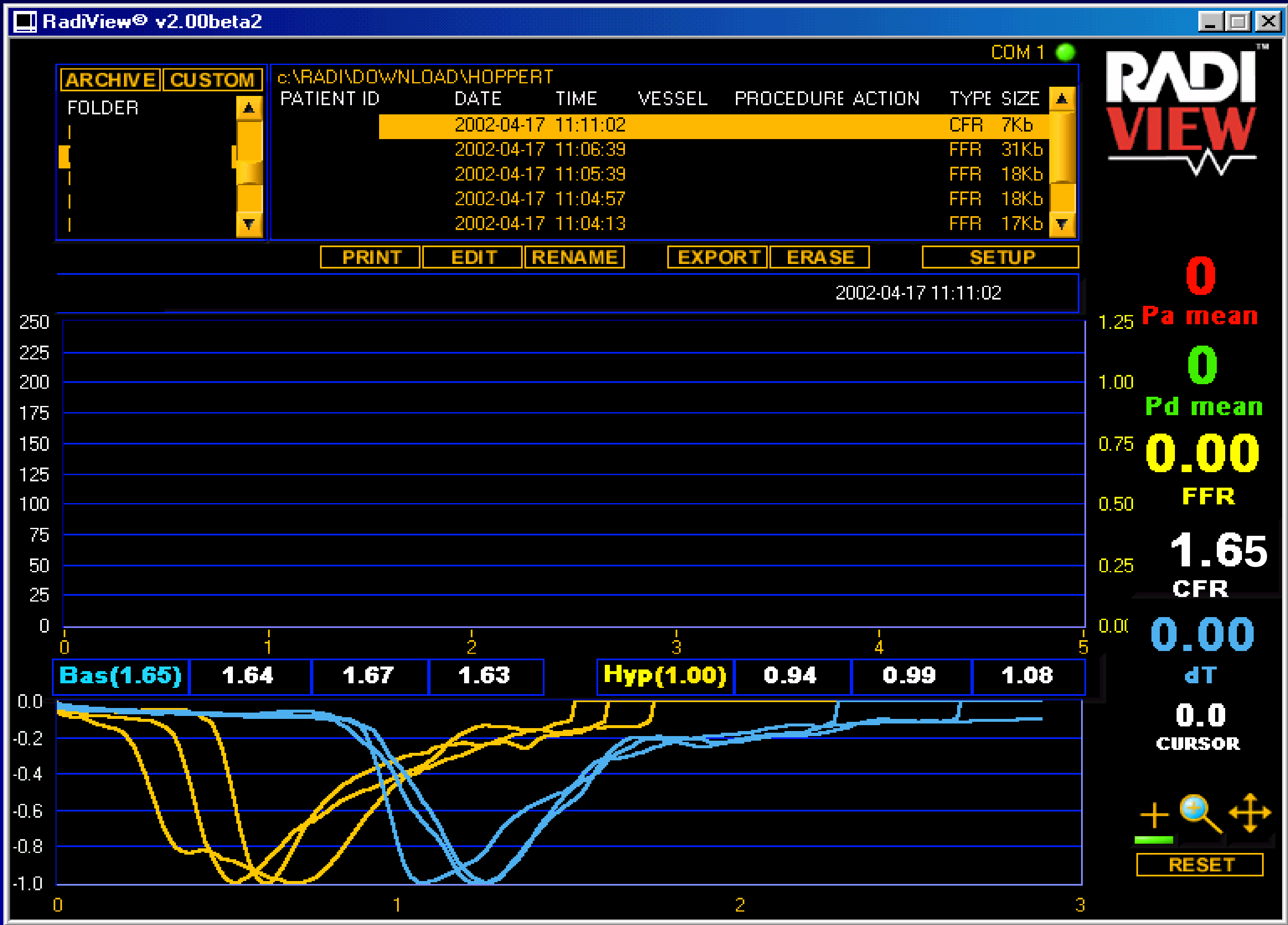
Calculation of mean transit time



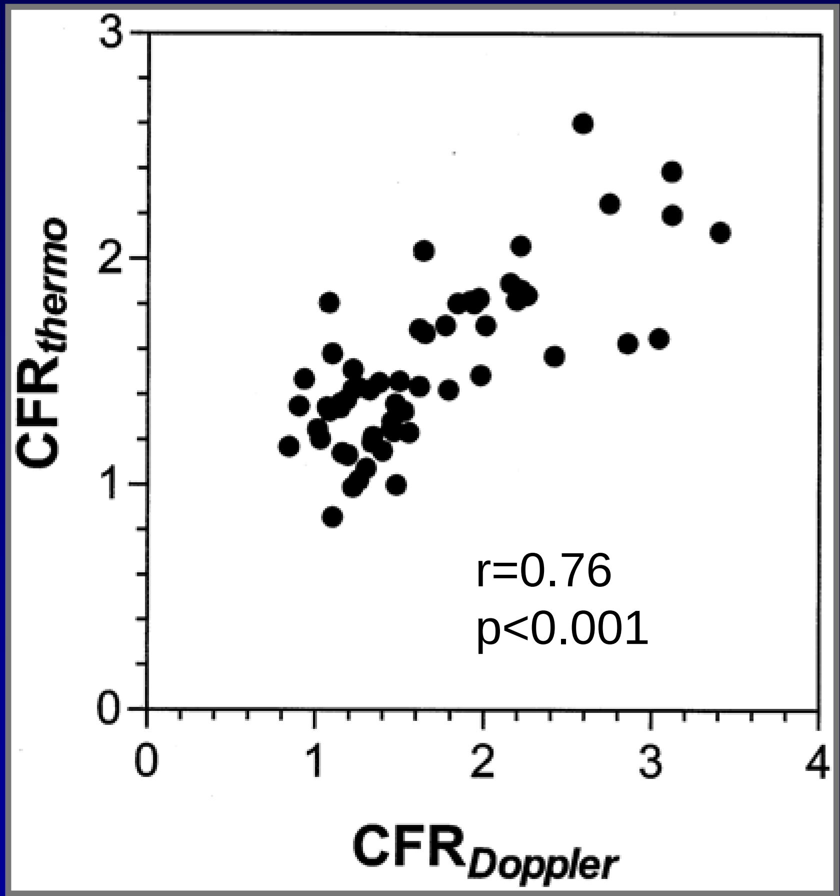


De Bruyne et al. Circulation 2002;104:2003

Thermodilution CFR

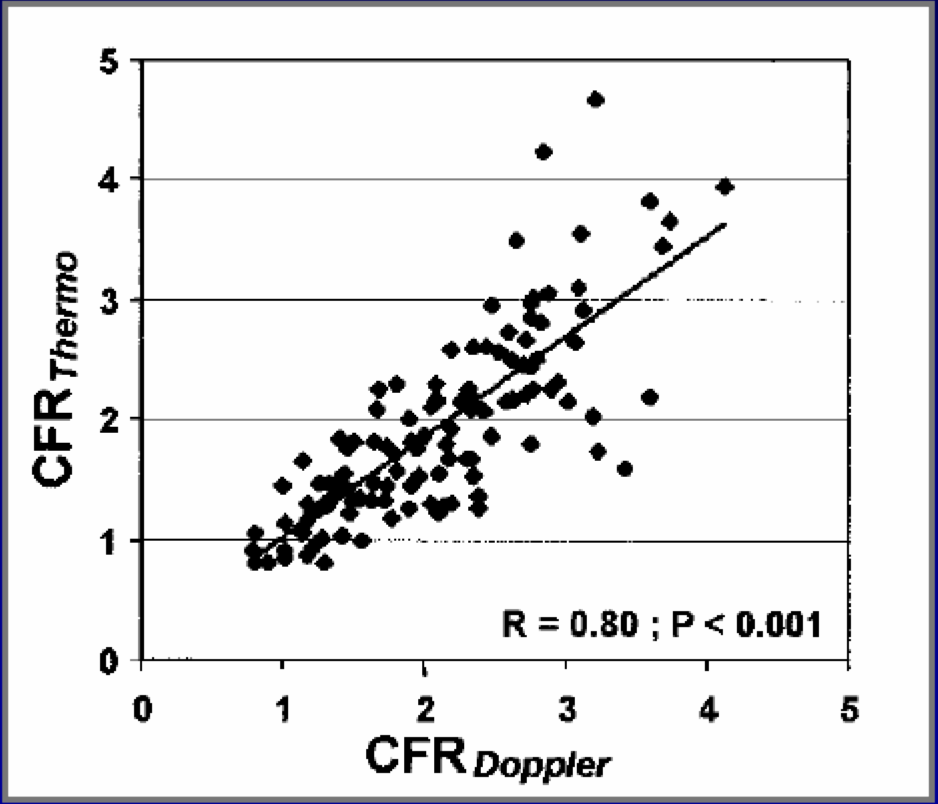


Validation of CFR_{thermo} in Dogs



De Bruyne et al., Circulation 2001;104:2003-2006

Validation of CFR_{thermo} in Humans



Pijls et al., Circulation 2002;105:2482-2486

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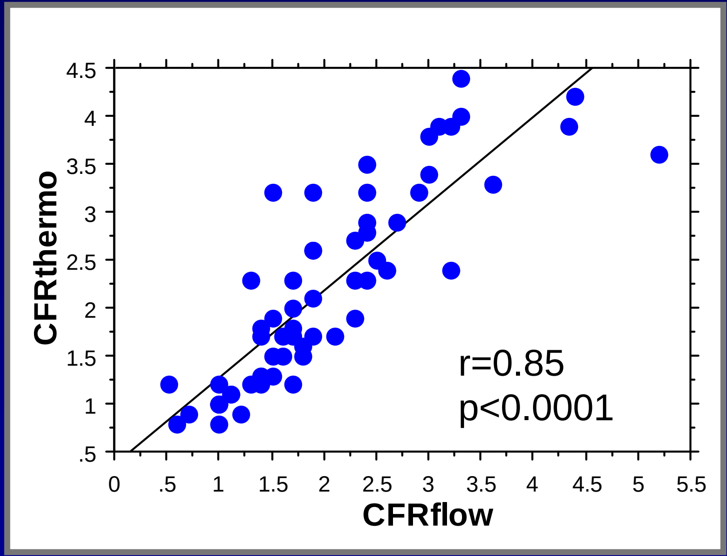
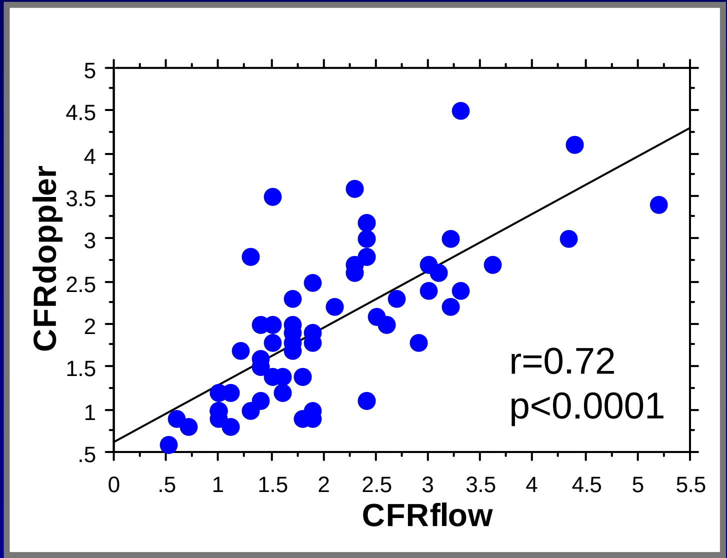
Comparison of CFR_{thermo} and $CFR_{Doppler}$





Circulation 2003;108:2198-2200

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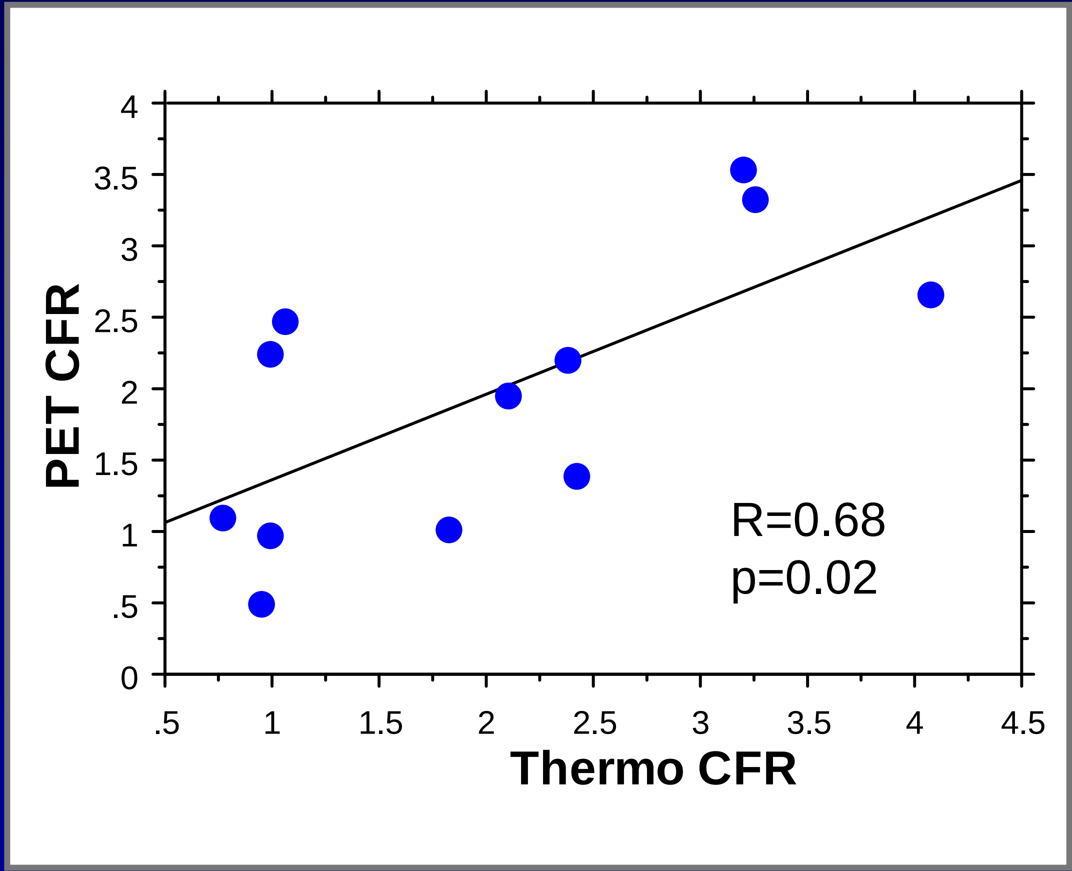
Comparison of PET CFR with Thermo CFR



Brinton et al., ACC 2007 (submitted)

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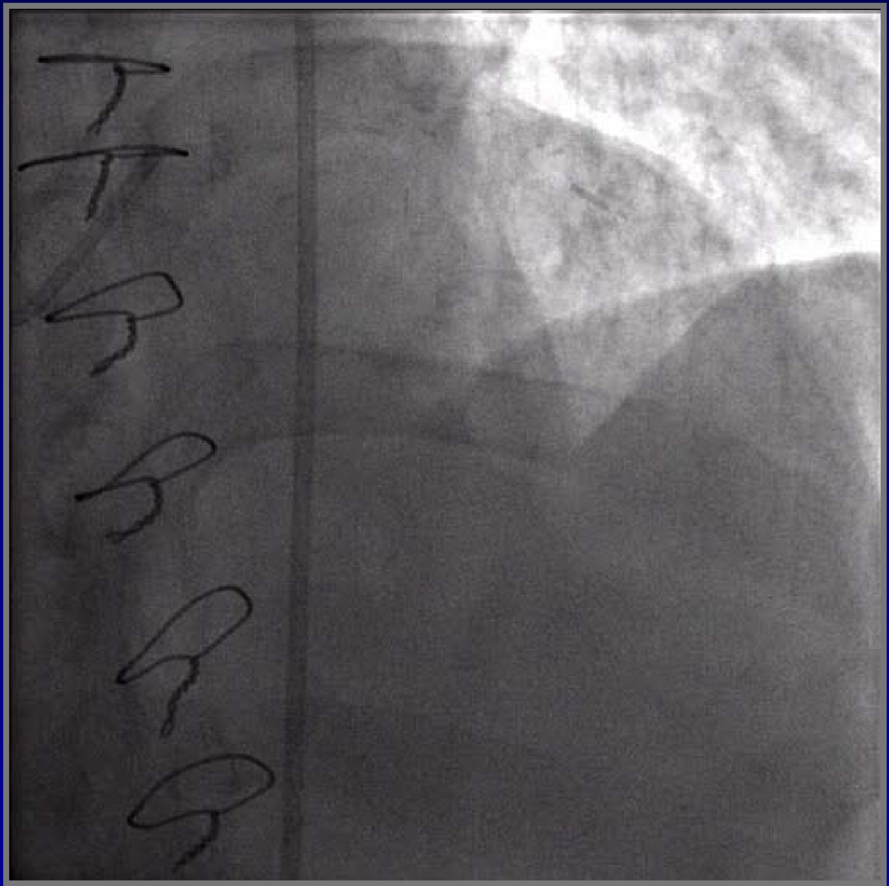
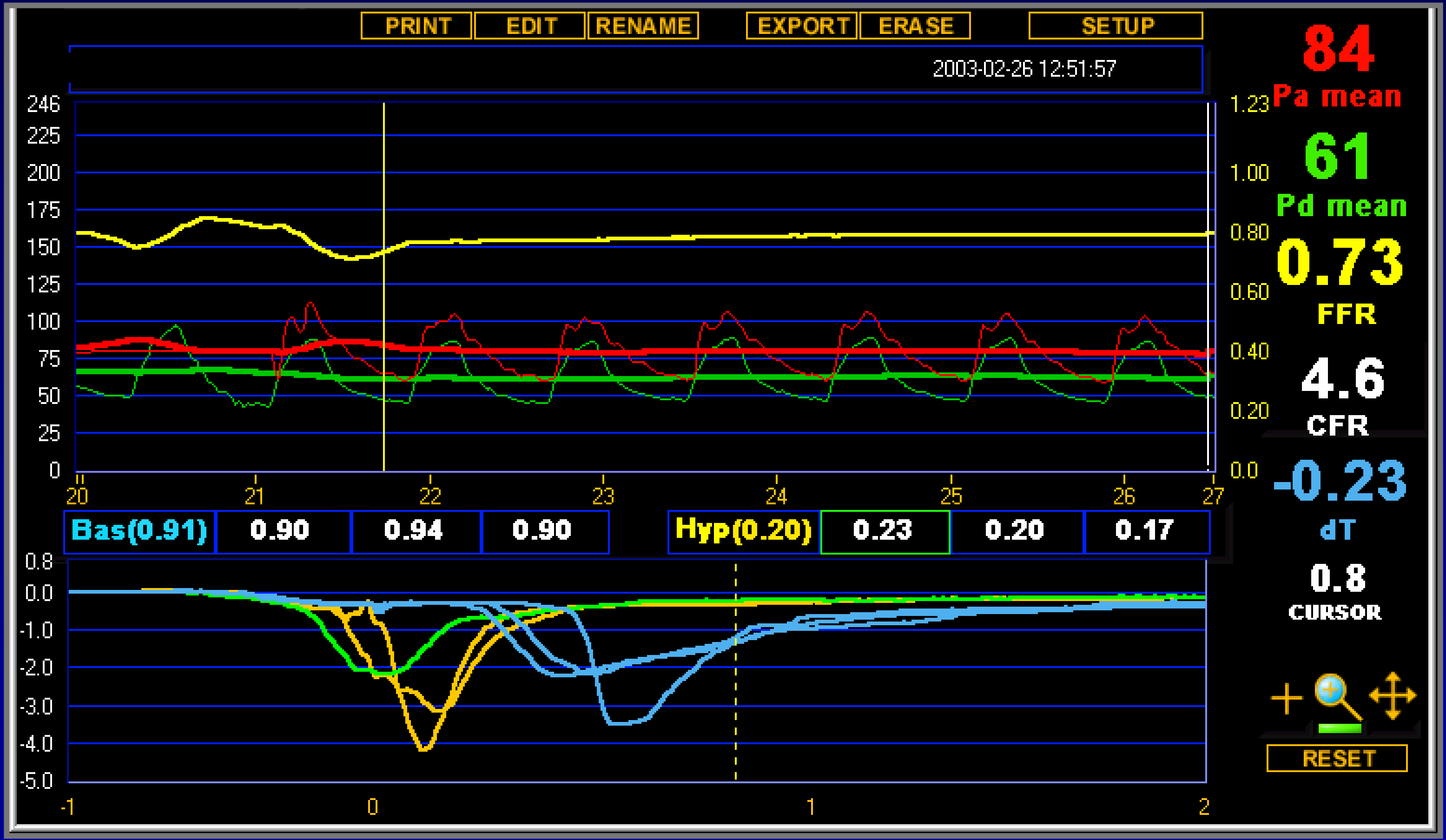
Physiologic Investigation for Transplant Arteriopathy
P.I.T.A. Study



P.I.T.A. Case 1

P.I.T.A. Case 2

P.I.T.A. Case 1: FFR-CFR



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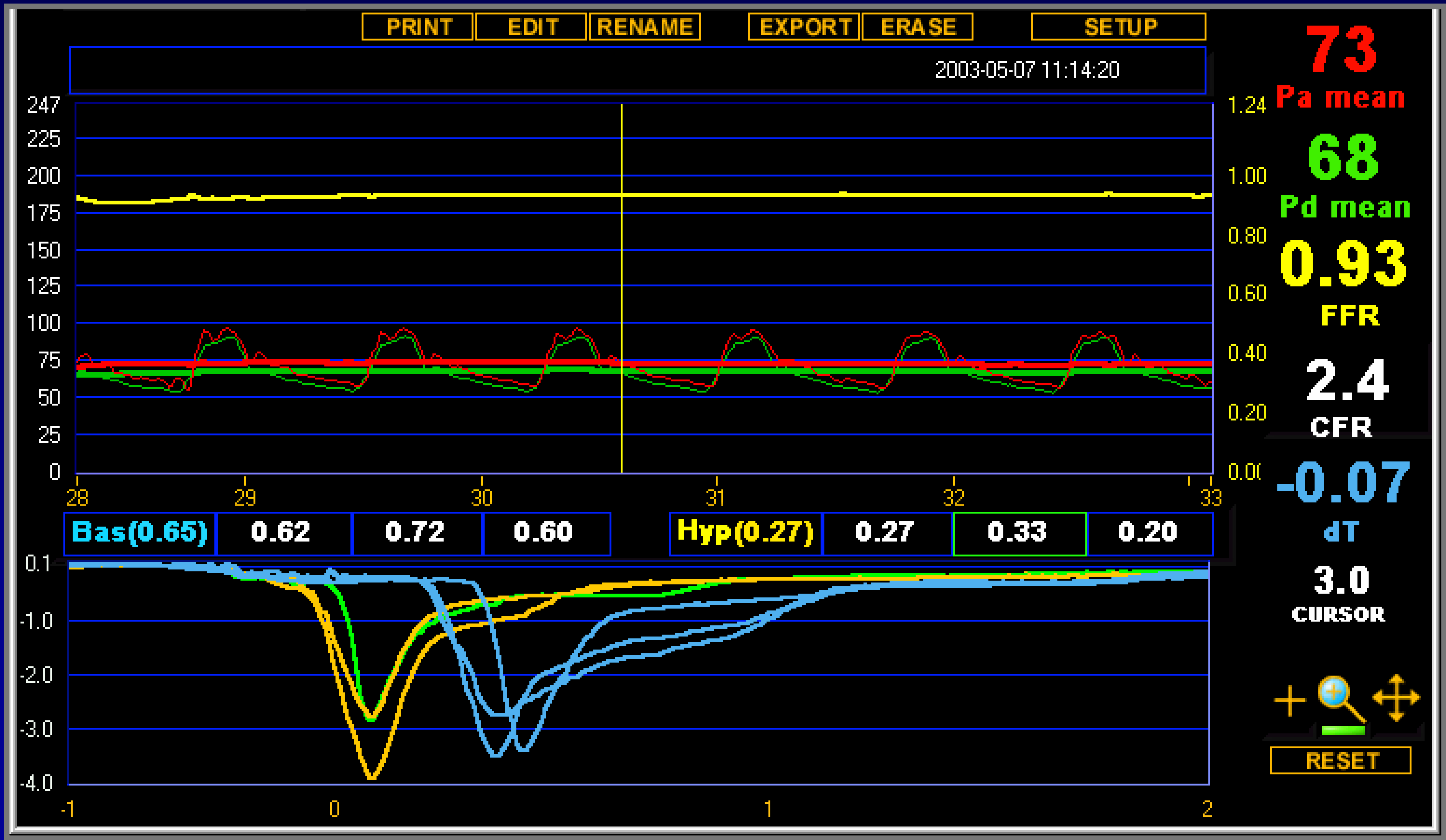
P.I.T.A. Case 1: IVUS

% Plaque Volume = 50%

P.I.T.A. Case 2: FFR-CFR



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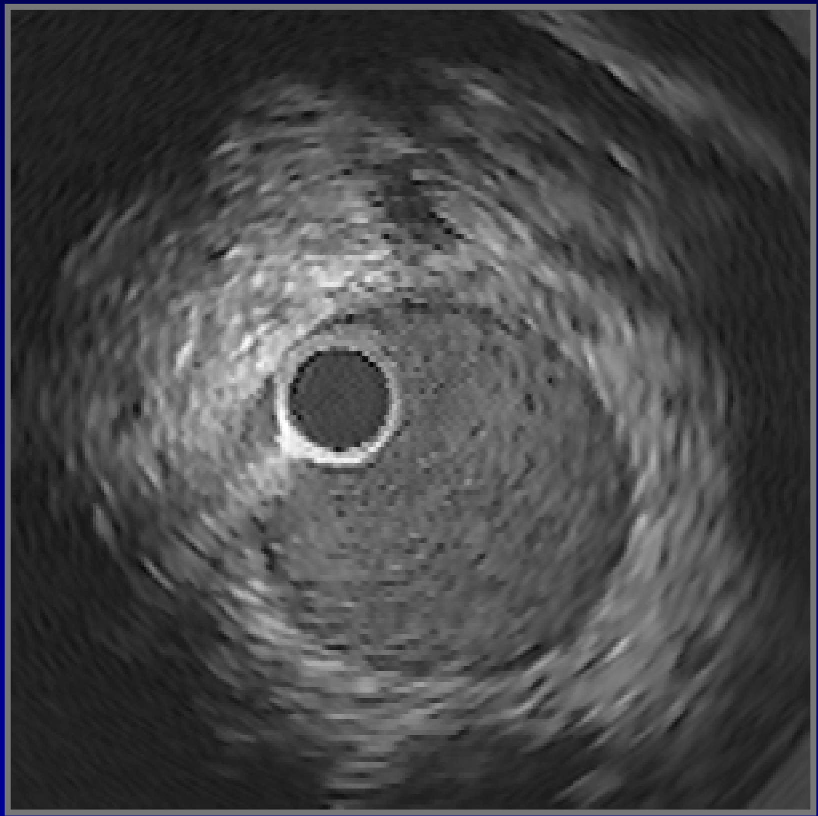
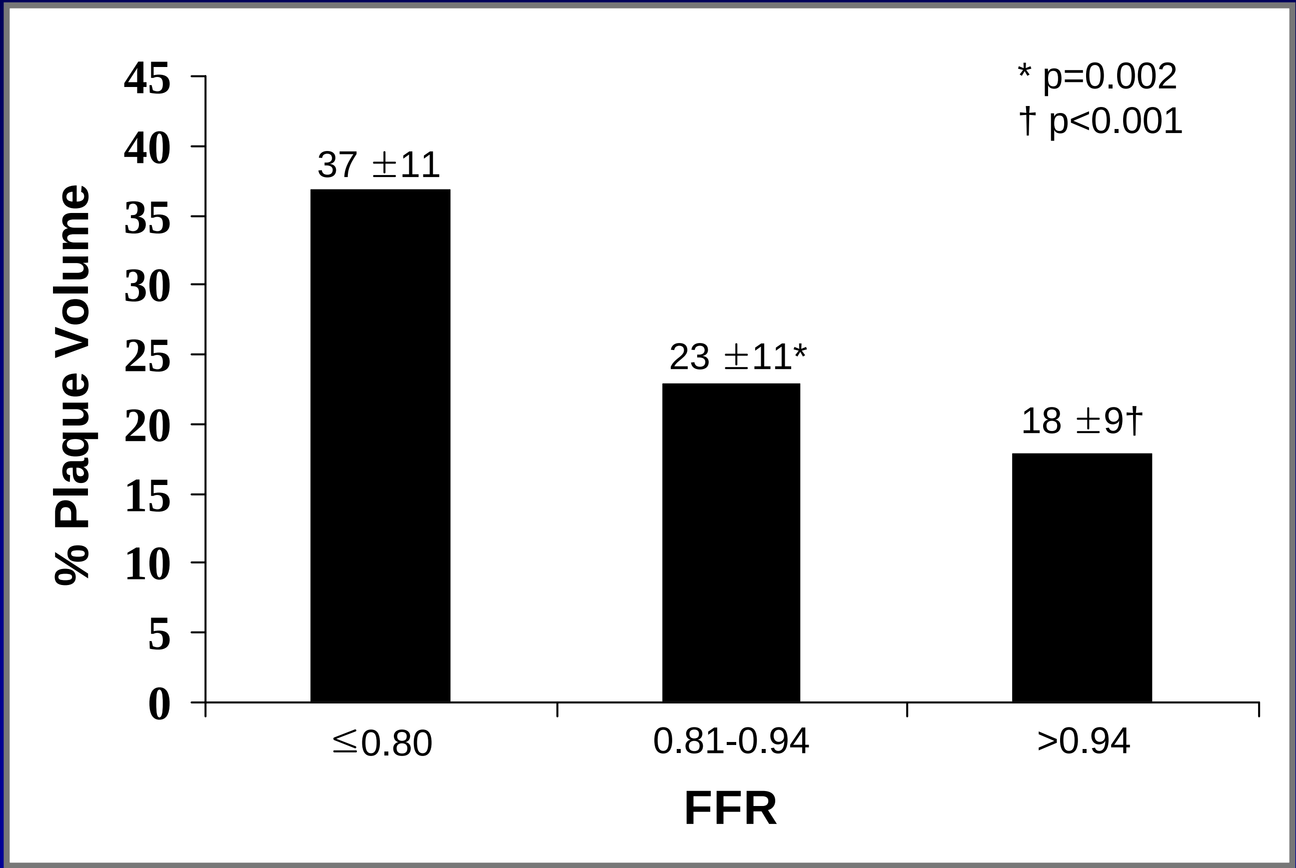
P.I.T.A. Case 2: IVUS



% Plaque Volume = 11%

Comparison of FFR and % Plaque Volume based on volumetric IVUS analysis



Circulation 2003;108:1605-1610

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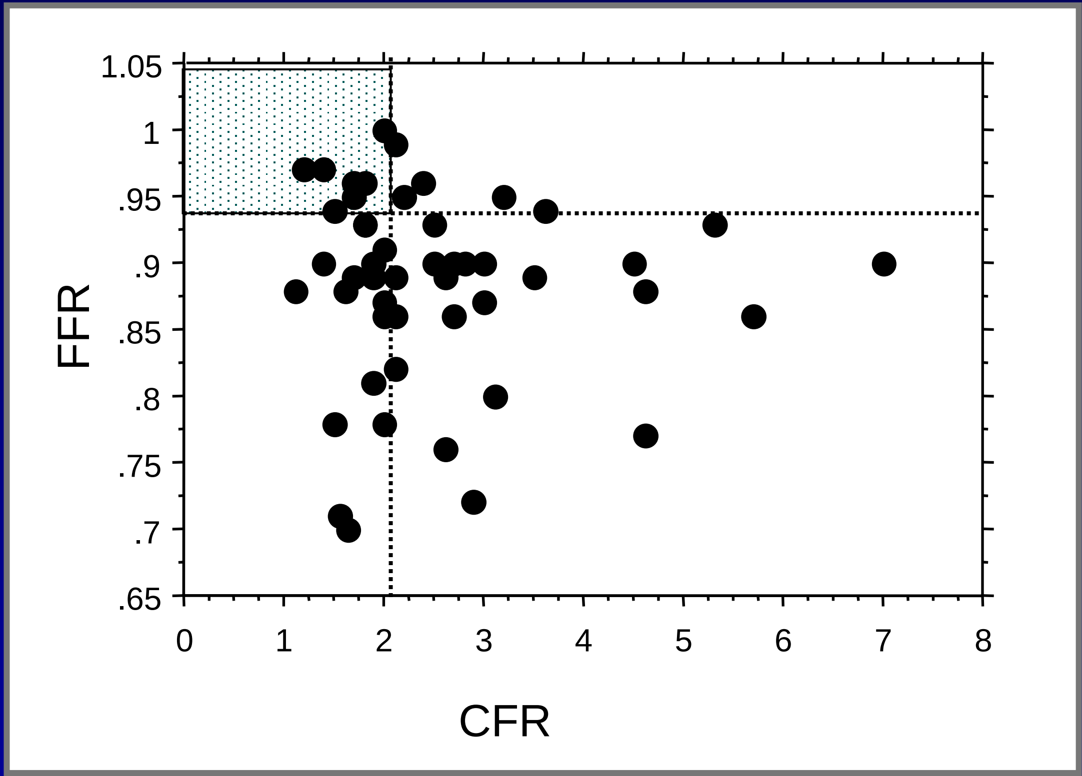
Comparison of FFR and CFR values in each P.I.T.A. case



Circulation 2003;108:1605-1610

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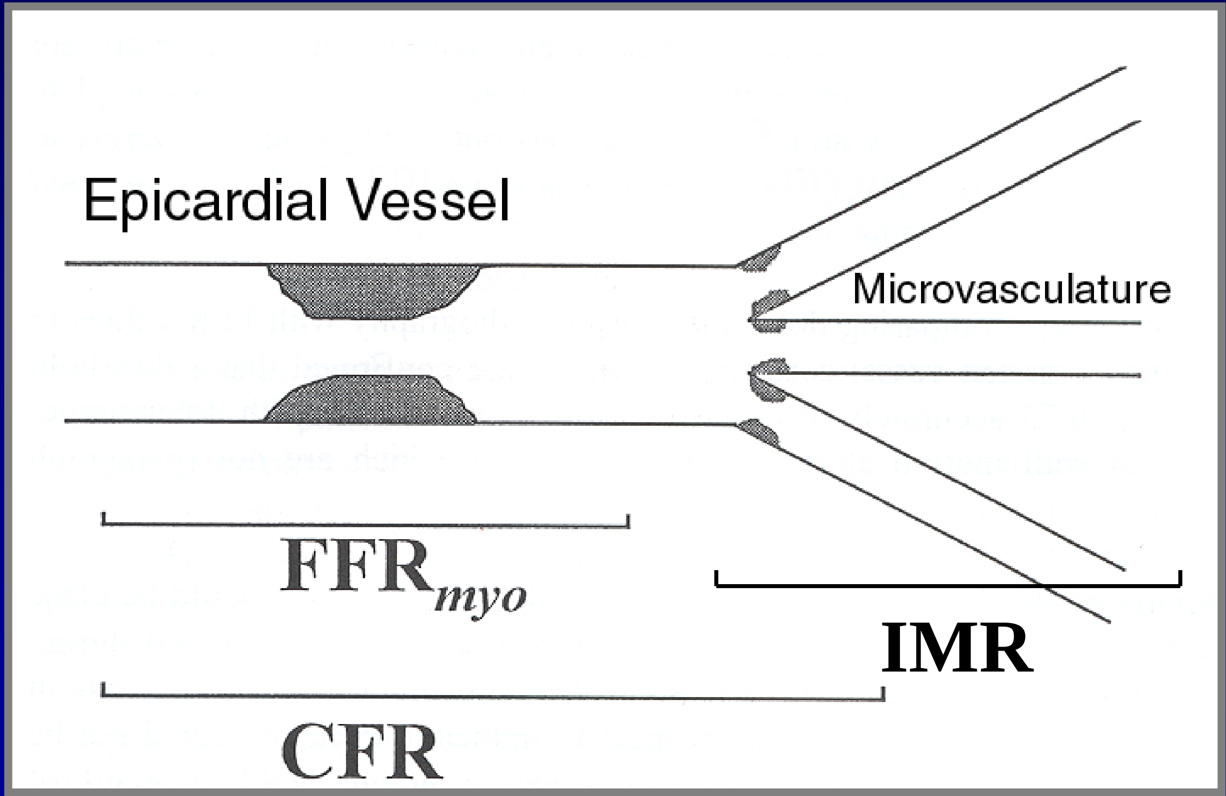
Index of Microcirculatory Resistance (IMR)



Derivation of IMR:

- Resistance = △ Pressure / Flow

- 1 / T_{mn} ≅ Flow

- IMR = Distal Pressure / (1 / T_{mn})

- **IMR = Distal Pressure x T_{mn}** ***at maximal hyperemia…***

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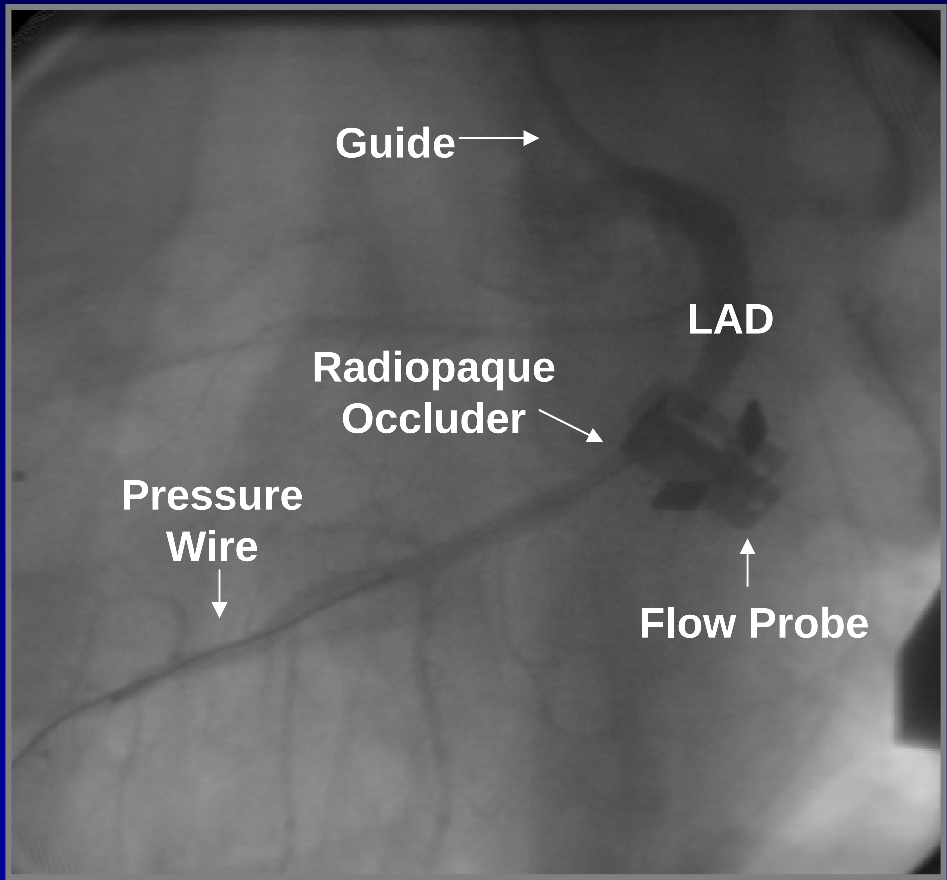
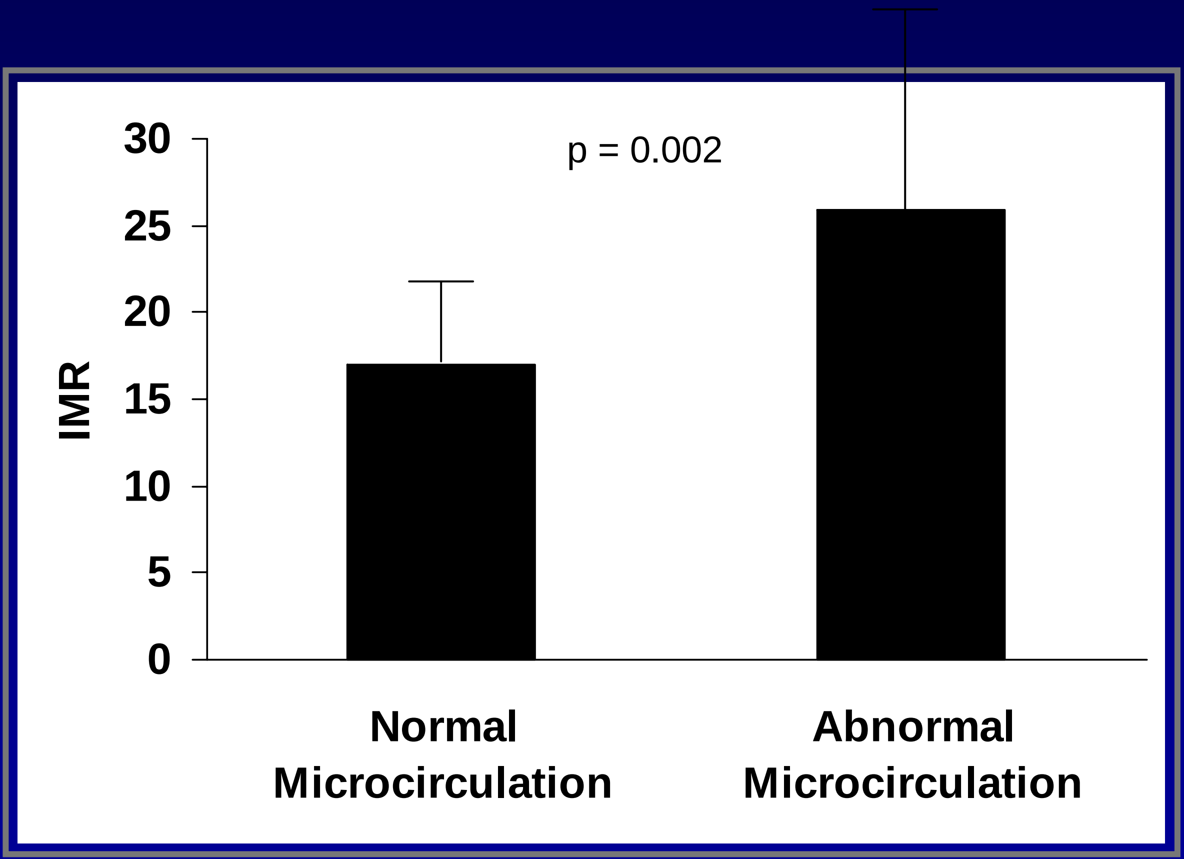
Animal Model



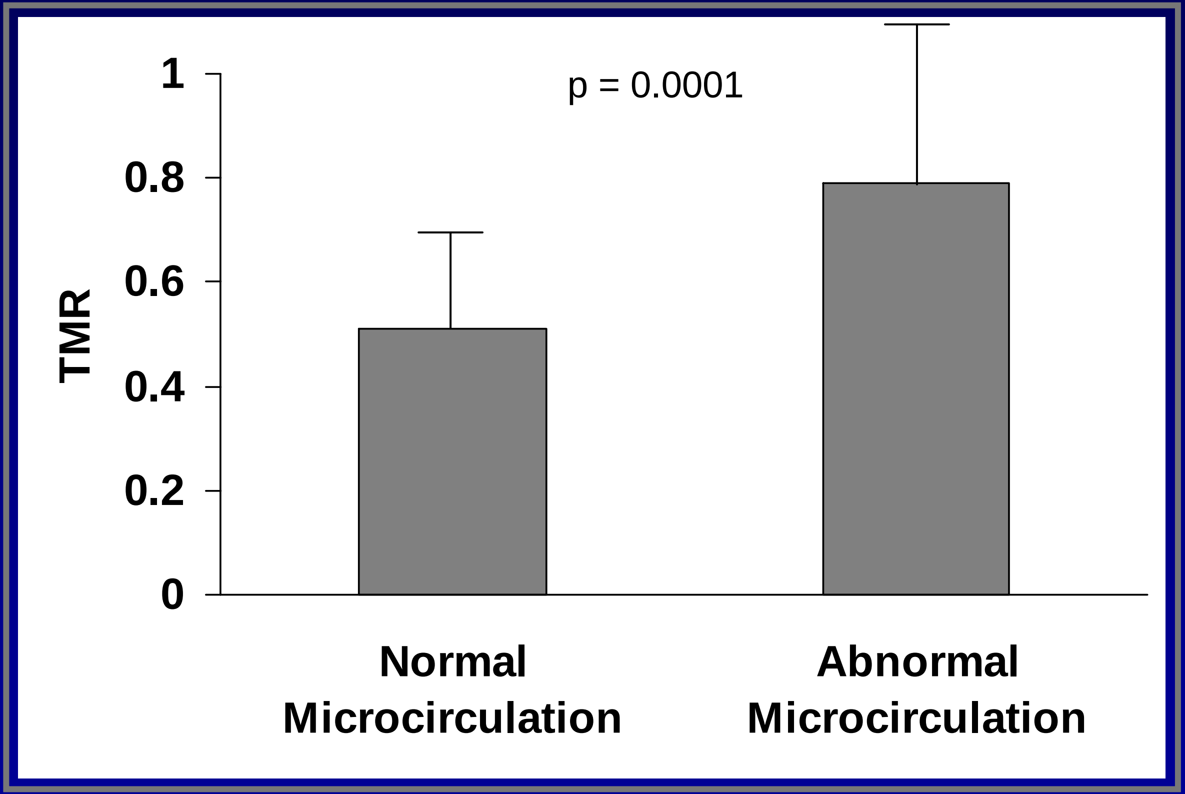
Circulation 2003;107:3129-3132.

Change in IMR after disruption of the microcirculation



Circulation 2003;107:3129-3132

Change in TMR after disruption of the microcirculation



Circulation 2003;107:3129-3132

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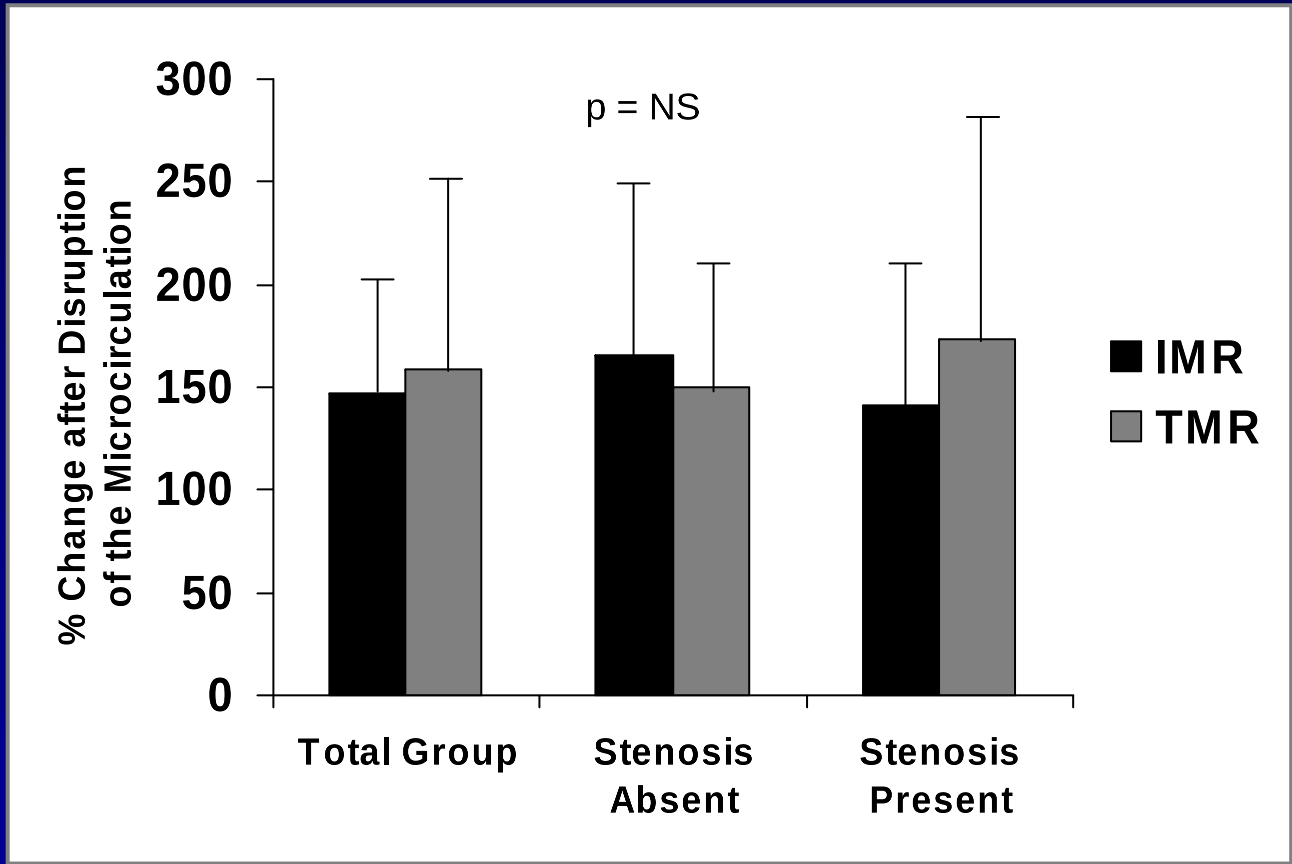
Animal Model



Circulation 2003;107:3129-3132.

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Animal Model

Comparison of IMR and TMR Values Under Various Epicardial and Microcirculatory Conditions

	Normal Microcirculation	Abnormal Microcirculation	*P*
IMR, U			
Total group	16.9±6.5	25.9±14.4	0.002
Stenosis absent	14.7±4.8	23.9±3.8	0.01
Stenosis present	19.2±7.3	28.6±14.5	<0.03
TMR, mm Hg · mL^{-1} · min^{-1}			
Total group	0.51±0.14	0.79±0.32	0.0001
Stenosis absent	0.48±0.14	0.71±0.25	0.005
Stenosis present	0.58±0.16	0.90±0.39	<0.001

Circulation 2003;107:3129-3132.

Importance of Collaterals when Measuring IMR

- Resistance = Pressure / Q_{myo}
- $Q_{myo} = Q_{cor} + Q_{coll}$
- As an epicardial stenosis increases, Q_{coll} increases, Q_{cor} decreases, and pressure decreases some, but relatively speaking not as much as Q_{cor} (e.g., total occlusion)

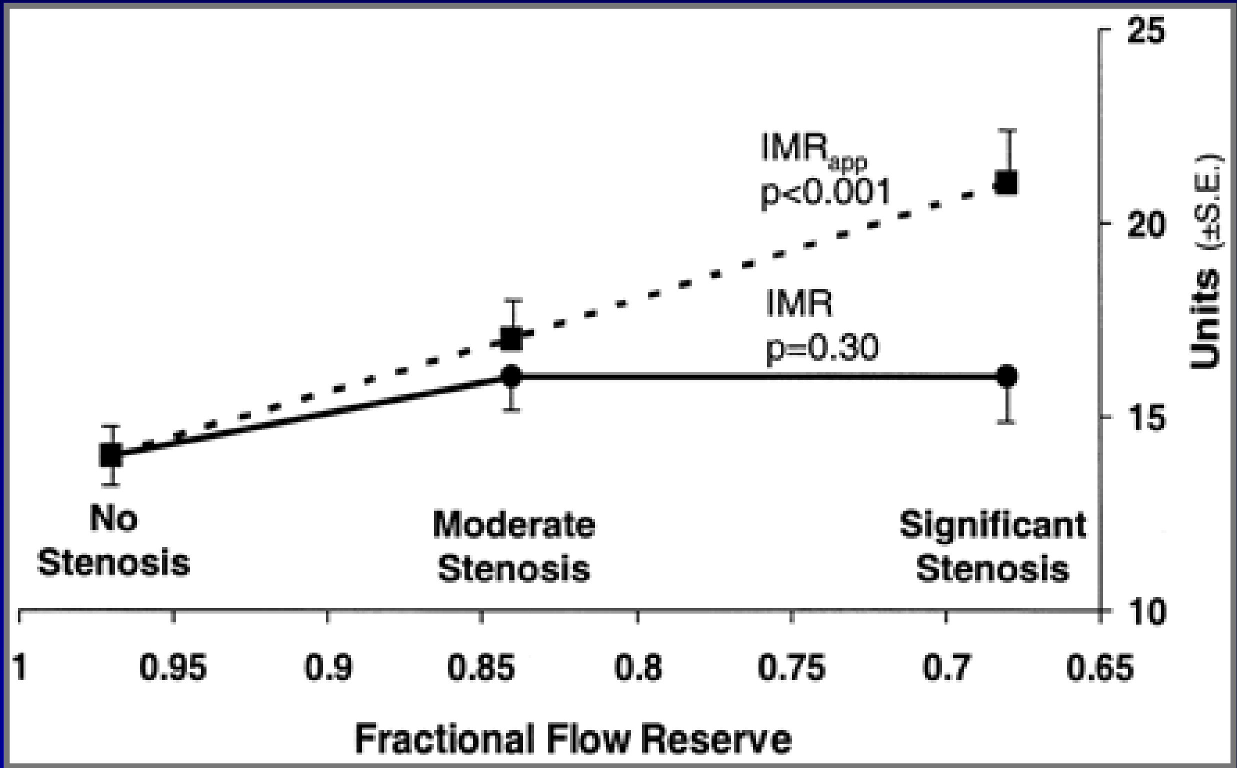
Aarnoudse et al. Catheter Cardiovasc Interv 2004;62:56-63.

Importance of Collaterals when Measuring IMR

- Simplified IMR = $P_d \times T_{mn}$
- But T_{mn} is inversely proportional to *coronary flow*
- To measure true IMR, must measure coronary wedge pressure
- $IMR = P_d \times T_{mn} \times FFR_{cor} / FFR_{myo}$

Aarnoudse et al. Catheter Cardiovasc Interv 2004;62:56-63.

IMR is not affected by epicardial stenosis severity: *Animal Validation*



Circulation 2004;109:2269-2272

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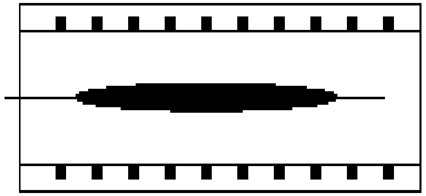
IMR is not affected by epicardial stenosis severity: *Human Validation*

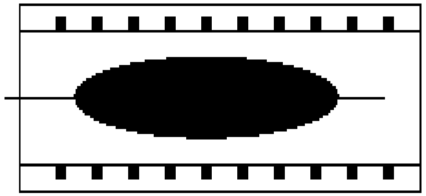
10% AS



FFR = 0.84 ± 0.08

IMR = 22 ± 15

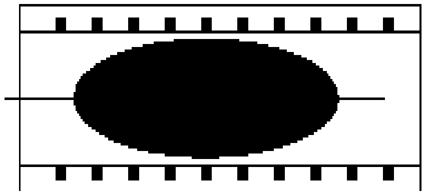
50% AS



FFR = 0.69 ± 0.09

IMR = 23 ± 14

75% AS



FFR = 0.52 ± 0.11

IMR = 23 ± 14

Aarnoudse et al. Circulation 2004;110:2137-42

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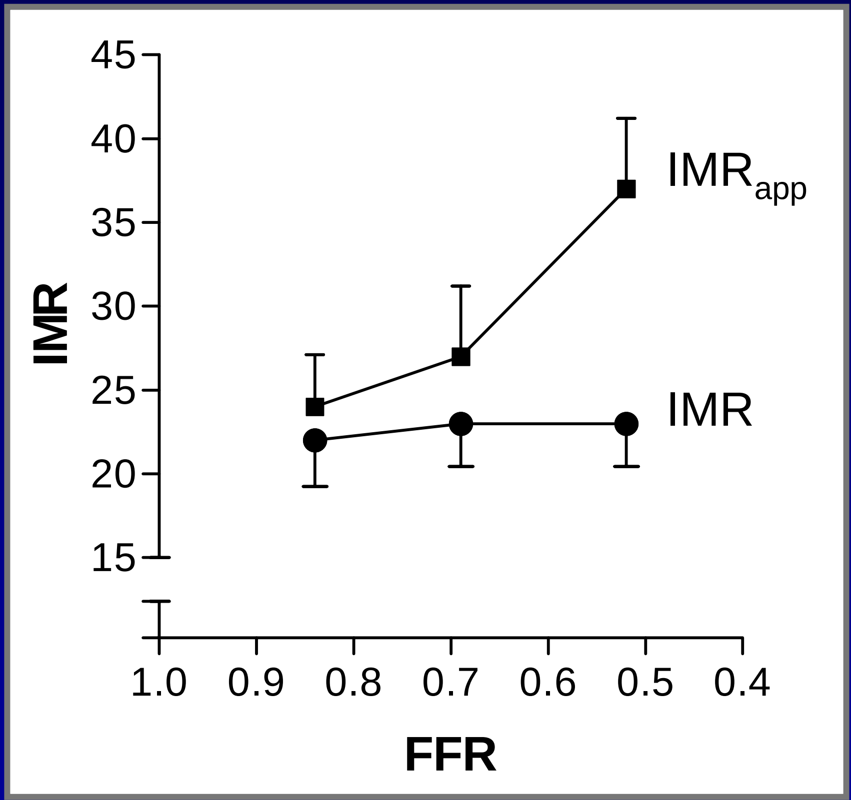
IMR is not affected by epicardial stenosis severity: *Human Validation*



Aarnoudse et al. Circulation 2004;110:2137-42

Reproducibility of IMR

Effect of Pacing on FFR/CFR/IMR

	Baseline		RV Pacing at 110 bpm	
	Rest	**Hyperemia**	**Rest**	**Hyperemia**
Mean Blood Pressure, mm Hg				
Systemic	94?7	78?1*	91?6	75?0*
Distal coronary	89?9	69?8*	86?7	66?8*
Heart rate, bpm	71?0	78?4*	110?	110?
Coronary transit time, seconds	0.97?.33	0.33?.11*	0.83?.30	0.38?.15*
Coronary Flow Reserve	**3.1?.1**		**2.3?.2**	
IMR, Units	**21.8?.5**		**22.9?.9**	
Fractional Flow Reserve	**0.88?.07**		**0.87?.07**	

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

Reproducibility of IMR

Effect of Blood Pressure on FFR/CFR/IMR

	Baseline		Nitroprusside	
	Rest	Hyperemia	Rest	Hyperemia
Mean Blood Pressure, mm Hg				
Systemic	98?3	83?9*	79?	71?0*
Distal coronary	93?2	73?4*	74?	61?*
Heart rate, bpm	73?0	82?*	78?6	84?7*
Coronary transit time, seconds	0.96?.36	0.33?.08*	0.96?.50	0.40?.13*
Coronary Flow Reserve	**2.9?.9**		**2.5?.2**	
IMR, Units	**23.85?.1**		**24.00?.9**	
Fractional Flow Reserve	**0.88?.04**		**0.87?.05**	

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

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Reproducibility of IMR

Change in LV Contractility and FFR/CFR/IMR

	Baseline		Dobutamine	
	Rest	Hyperemia	Rest	Hyperemia
Mean Blood Pressure, mm Hg				
Systemic	95?9	78?3*	99?8	79?4*
Distal coronary	90?0	69?0*	92?8	68?2*
Heart rate, bpm	71?1	79?4*	85?7	97?6*
Coronary transit time, seconds	0.99?.36	0.34?.11	0.55?.17	0.35?.13
Coronary Flow Reserve	**3.0?.0**		**1.7?.6**	
IMR, Units	**22.2?.0**		**23.6?.2**	
Fractional Flow Reserve	**0.88?.06**		**0.87?.06**	

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

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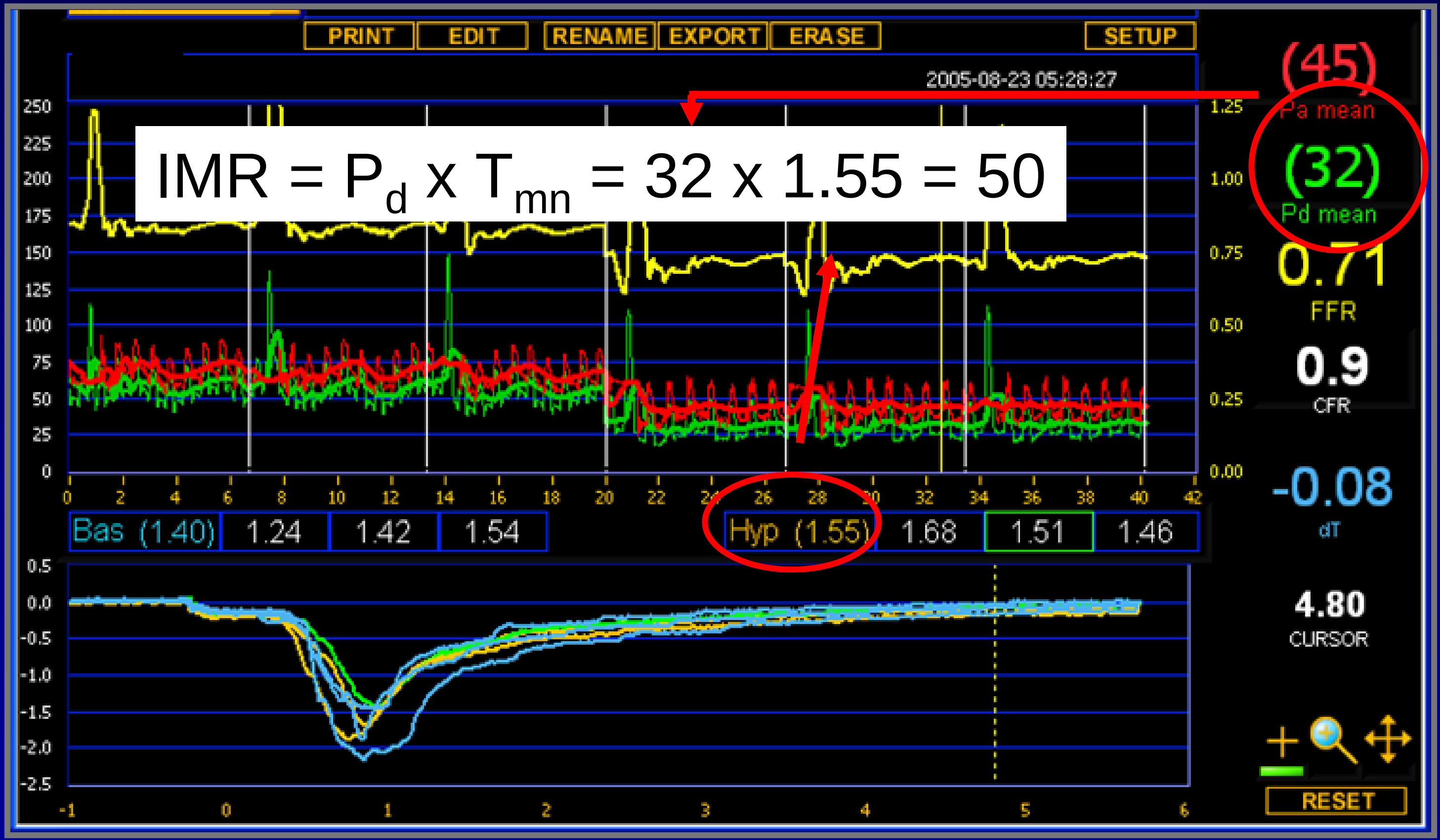
IMR in AMI

Case 1

- 65 year old man with HTN presents with chest pain and ST segment elevation in leads V_1 to V_3
- He was taken emergently to the cath lab

IMR after PCI



IMR = 50

Peak CK=3754

Initial EF=37%

F/U EF=37%

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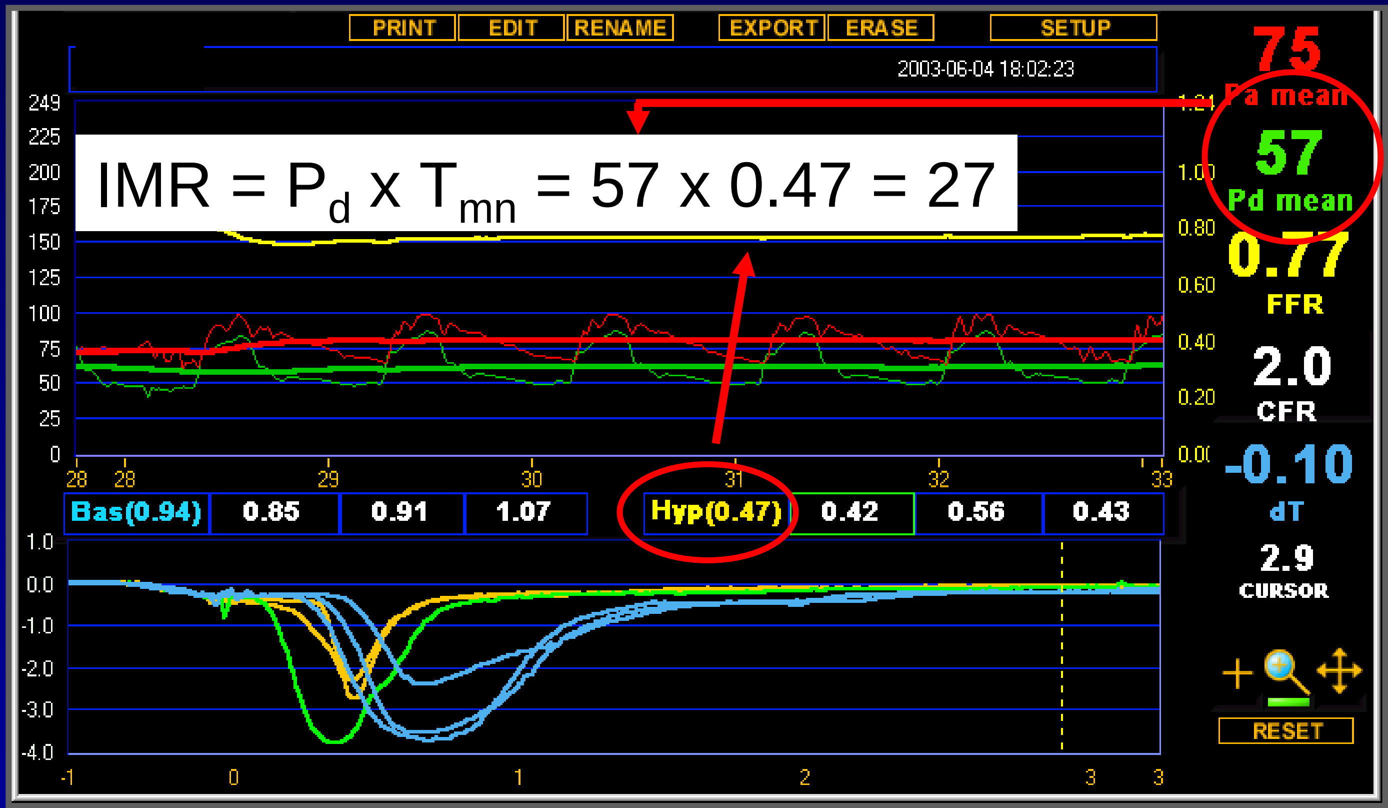
IMR in AMI

Case 2

- 52 year old man with HTN and dyslipidemia presents with chest pain and ST segment elevation in leads V_2-V_4
- He was taken emergently to the cath lab

IMR after PCI



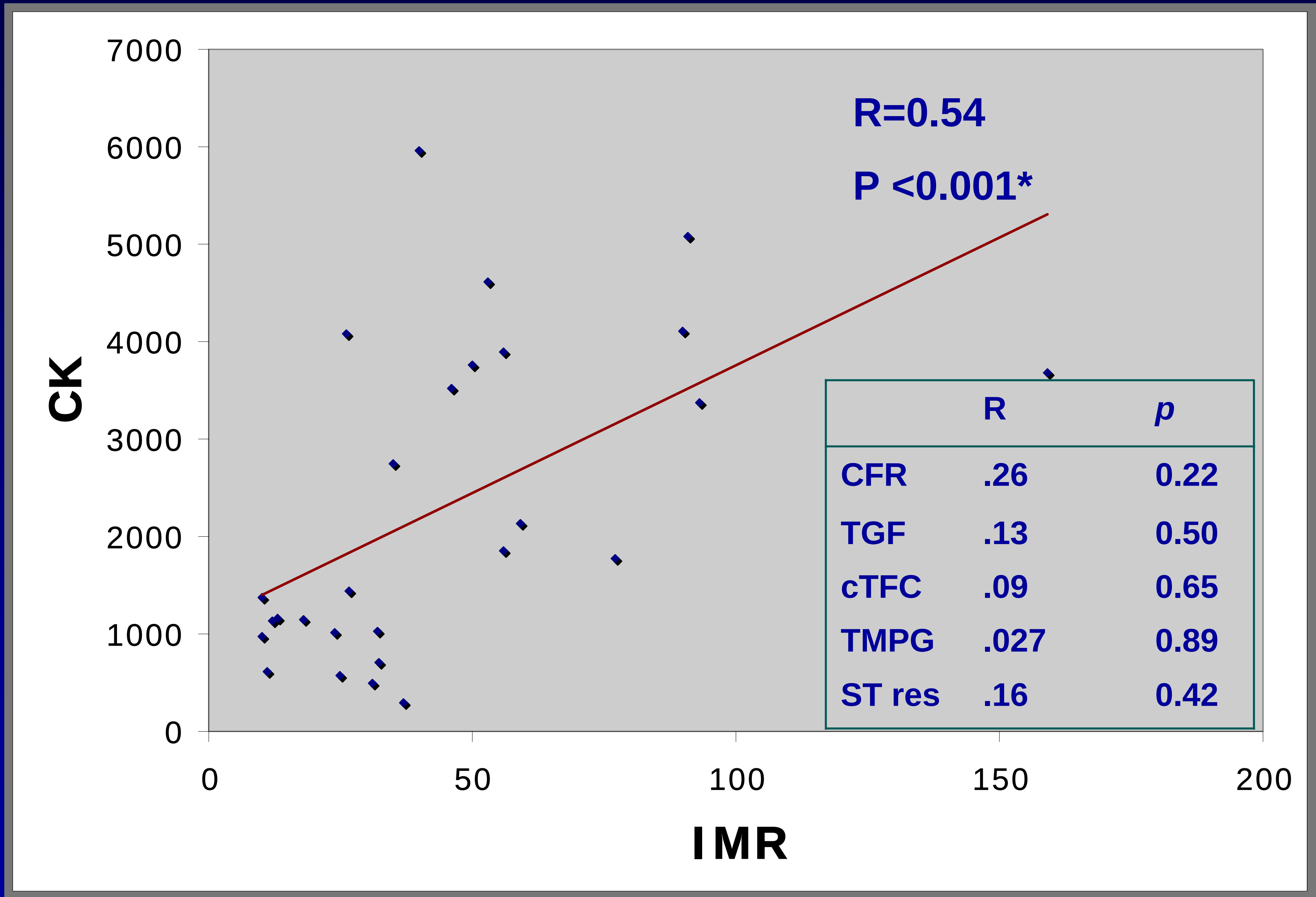
IMR = 27

Peak CK=1008

Initial EF=42%

F/U EF=62%

Correlation between IMR and Peak CK



	R	*p*
CFR	.26	0.22
TGF	.13	0.50
cTFC	.09	0.65
TMPG	.027	0.89
ST res	.16	0.42

Shah et al. AHA 2006

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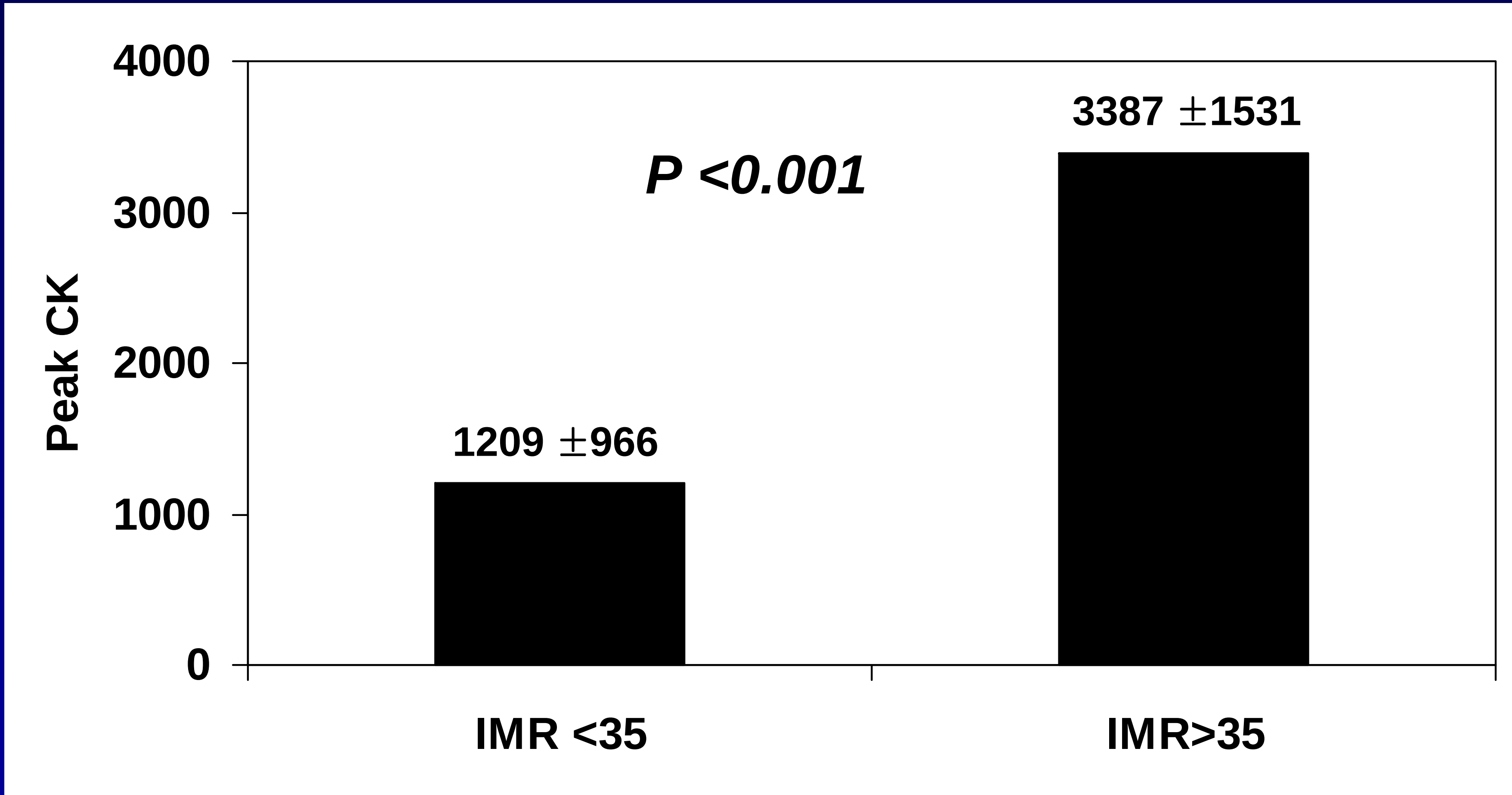
Peak CK and IMR



Shah et al. AHA 2006

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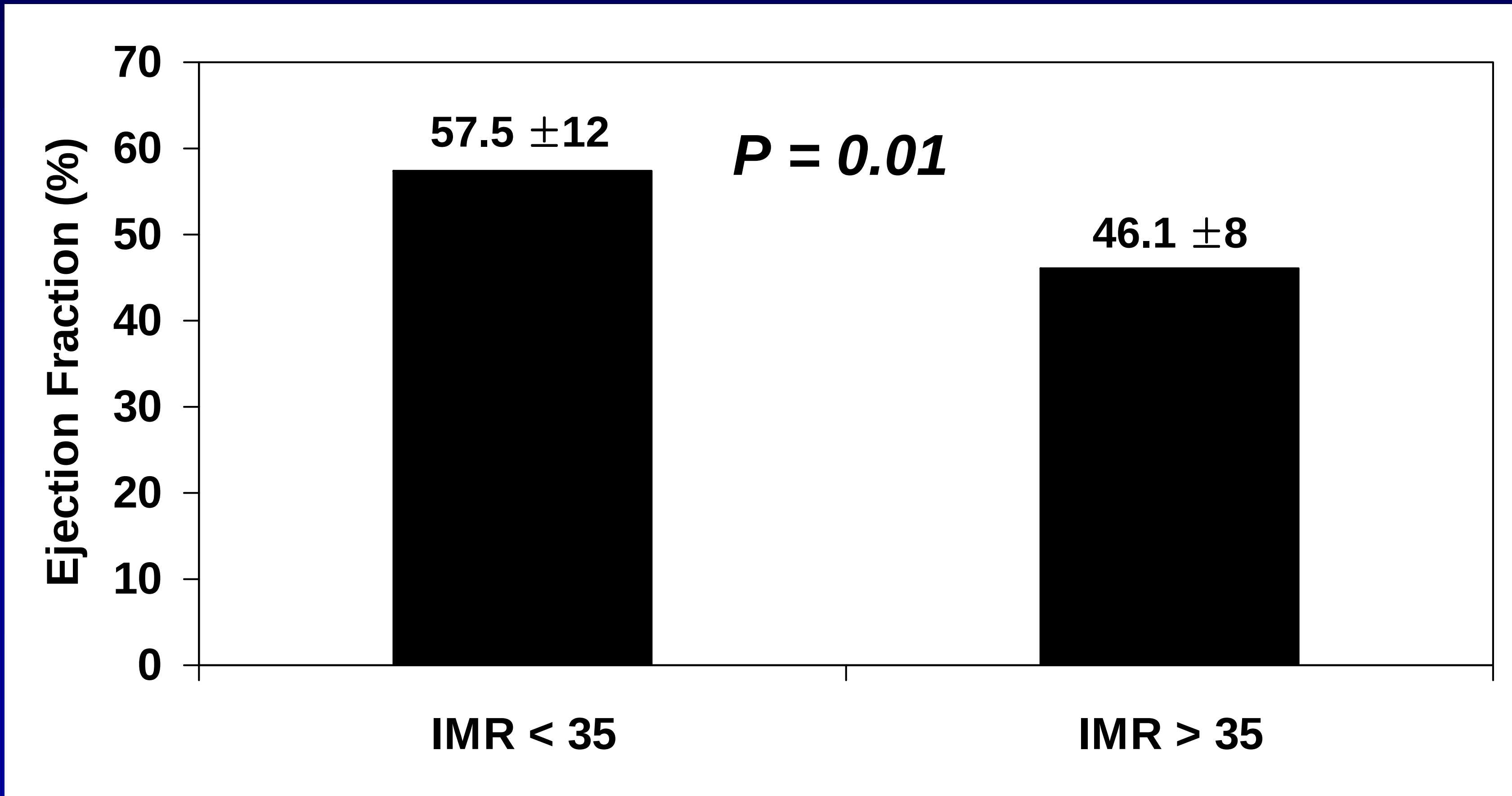
Follow-Up Ejection Fraction and IMR



Shah et al. AHA 2006

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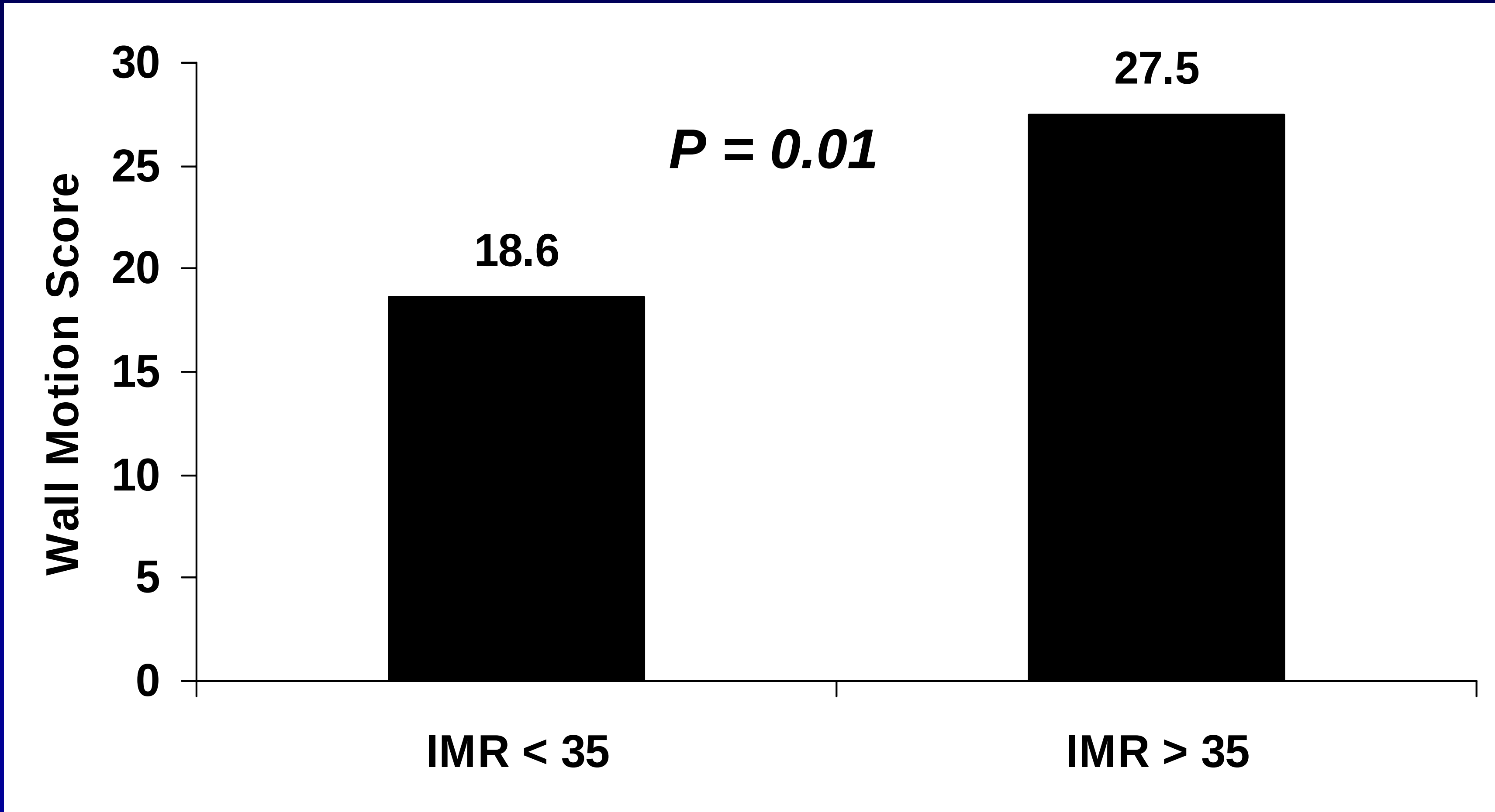
Follow-Up Echo Wall Motion Score and IMR



Shah et al. AHA 2006

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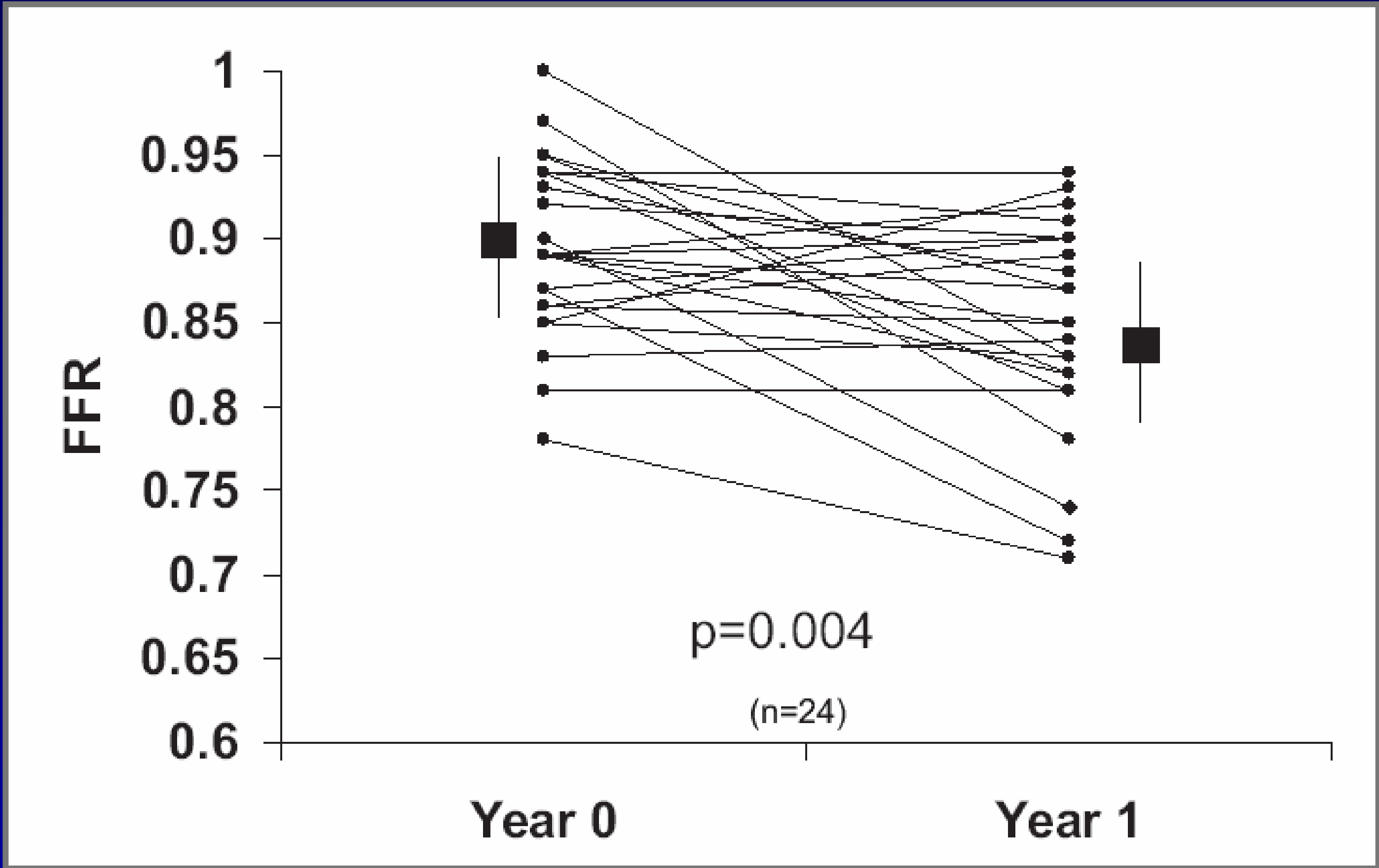
FFR, CFR, IMR Early Post Cardiac Tx

PITA II Study



J Heart Lung Transplant 2006;25:765-71

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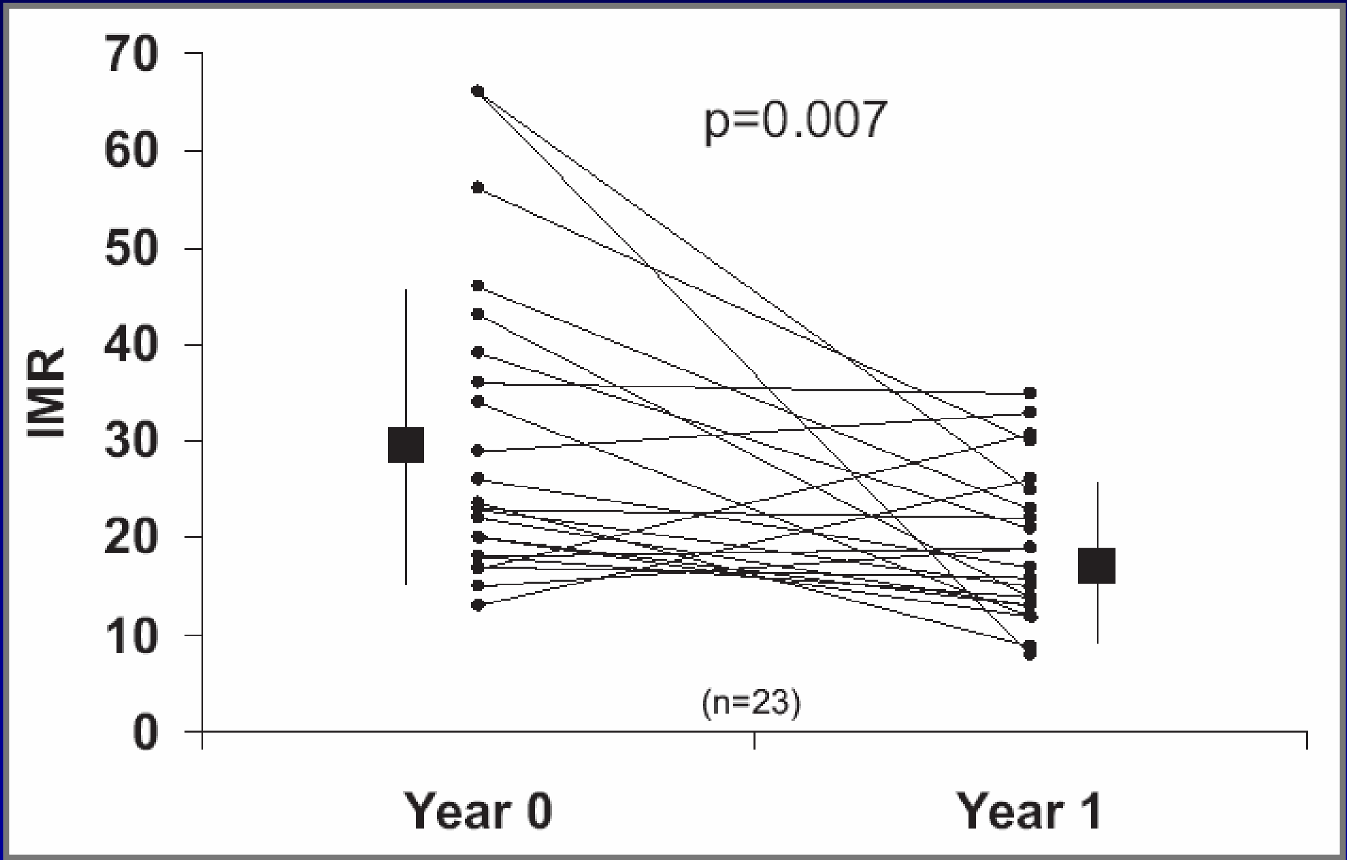
FFR, CFR, IMR Early Post Cardiac Tx

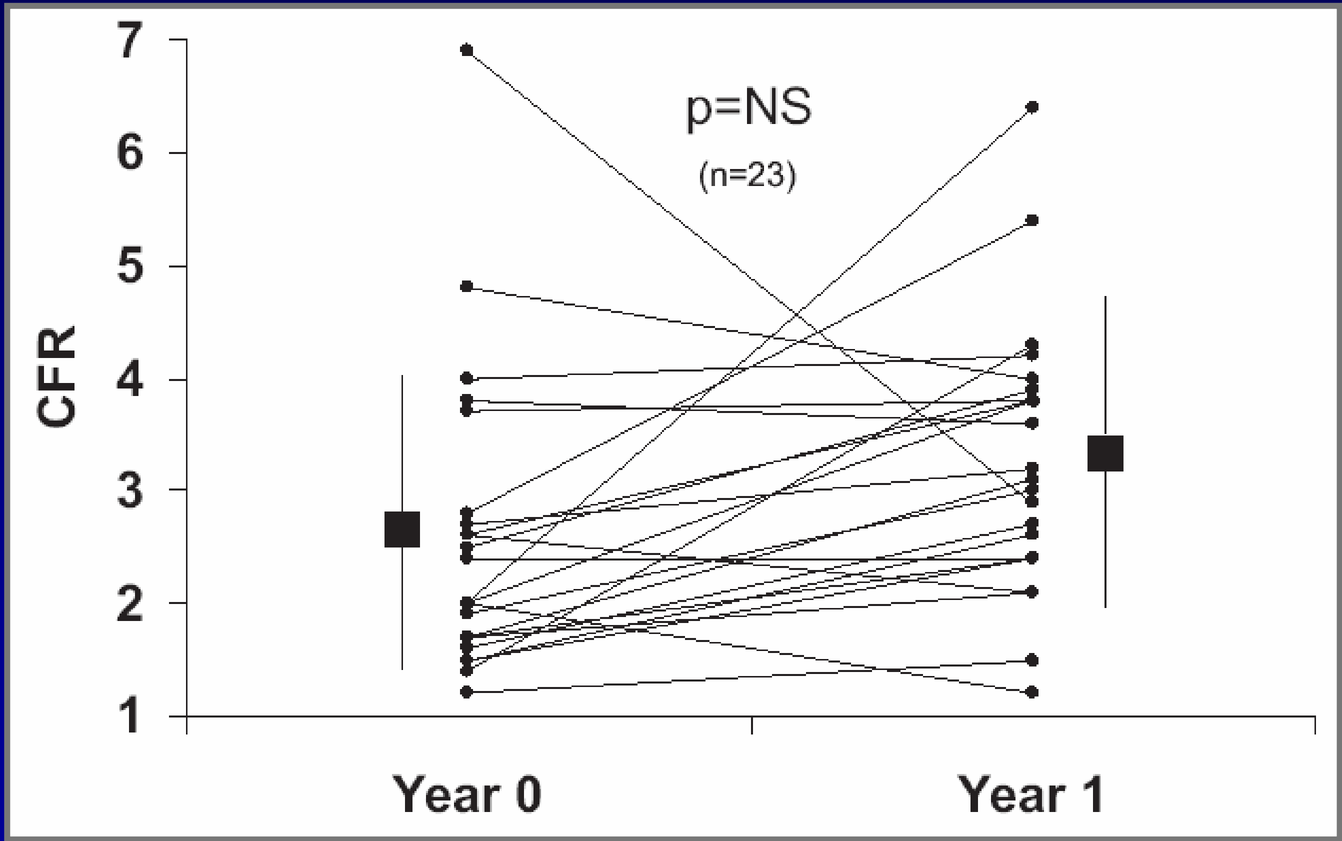
PITA II Study



J Heart Lung Transplant 2006;25:765-71

FFR, CFR, IMR Early Post Cardiac Tx

PITA II Study



J Heart Lung Transplant 2006;25:765-71

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Limitations of IMR

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

Conclusion

- The microcirculation plays an important role in patient outcomes
- Current methods for assessing the microcirculation have limitations
- IMR is an invasive, quantitative technique for evaluating the microcirculation, independent of the epicardial system