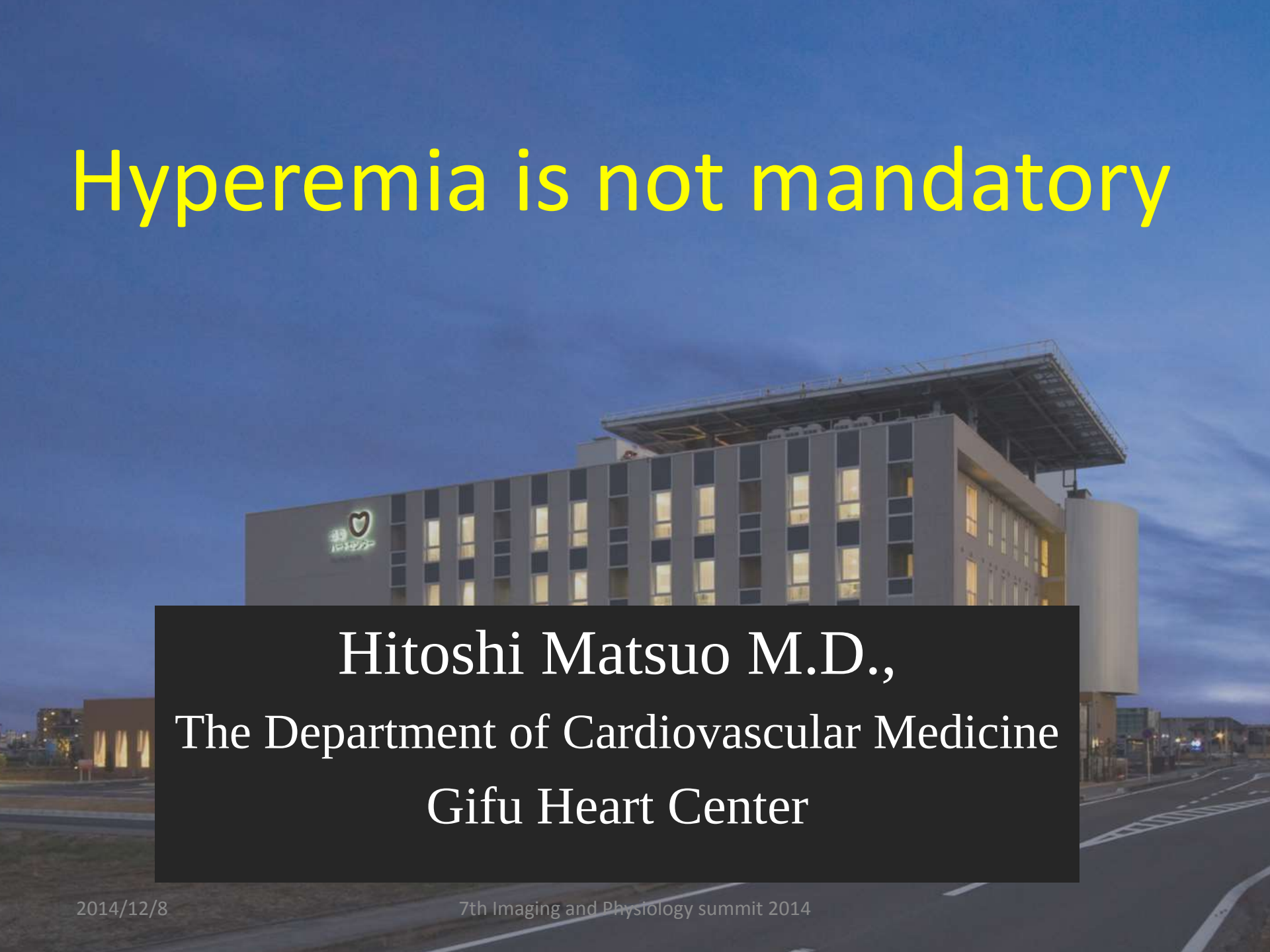
Hyperemia is not mandatory



Hitoshi Matsuo M.D.,
The Department of Cardiovascular Medicine
Gifu Heart Center

Physiological indexes in cath labo

	Resting	Hyperemic
Pressure	Whole cycle Pd/Pa	Pd/Pa (FFR)
	iFR	iFRa
Flow	APV	CFVR
		CFRthermo
Combined	stenosis resistance (BSR,HSR)	
	Myocardial resistance (MVRI, IMR)	
	Pressure flow relationship (PzF)	

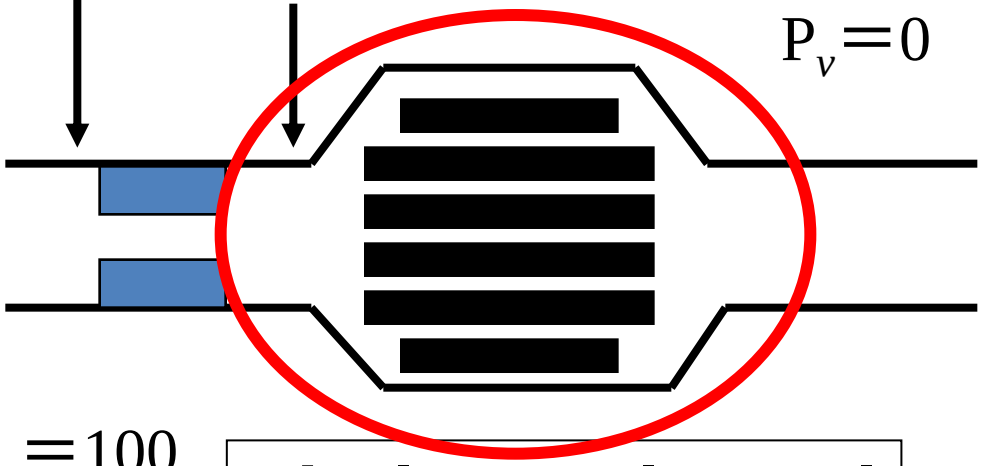
The Concept of Fractional flow reserve

$P_a = 100$

Target stenotic vessel

$P_d = 70$ **Myocardial perfusion pressure: 70mmHg**

$P_v = 0$

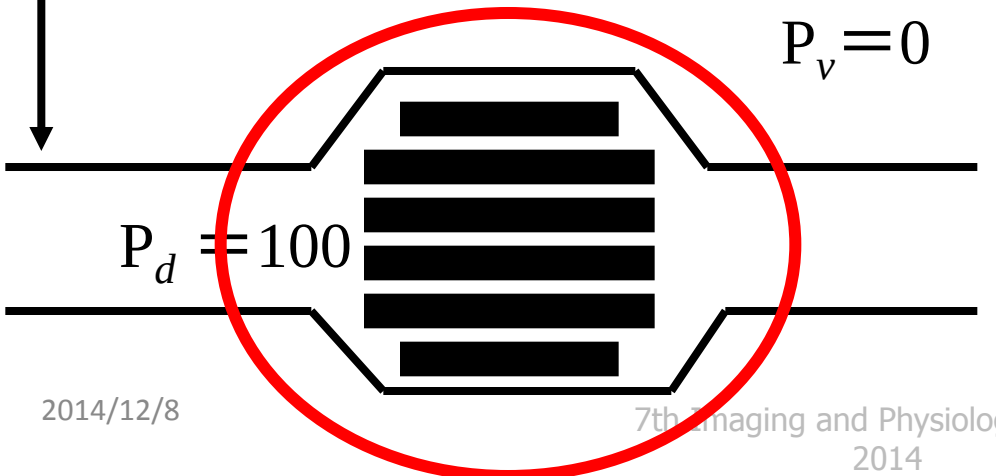


$P_a = 100$

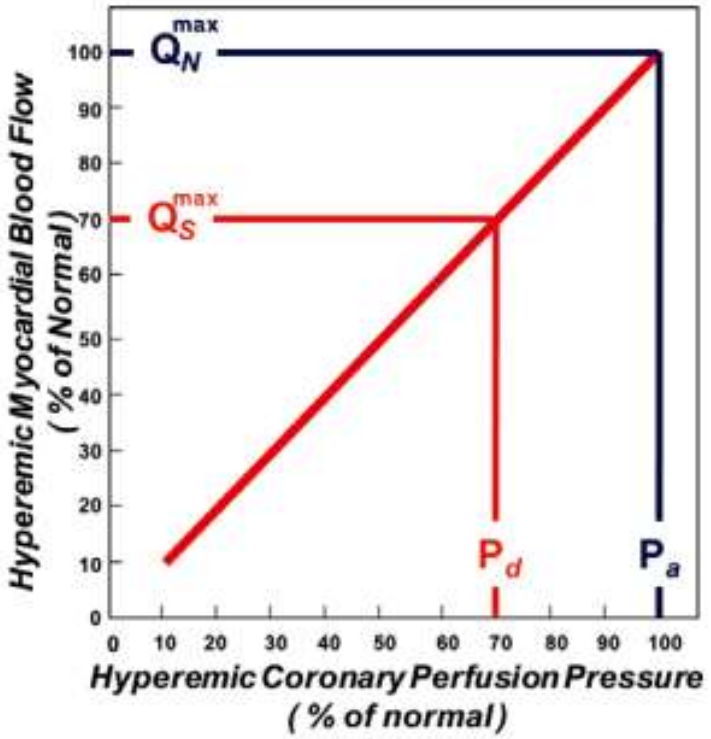
Ideal normal vessel

Myocardial perfusion pre

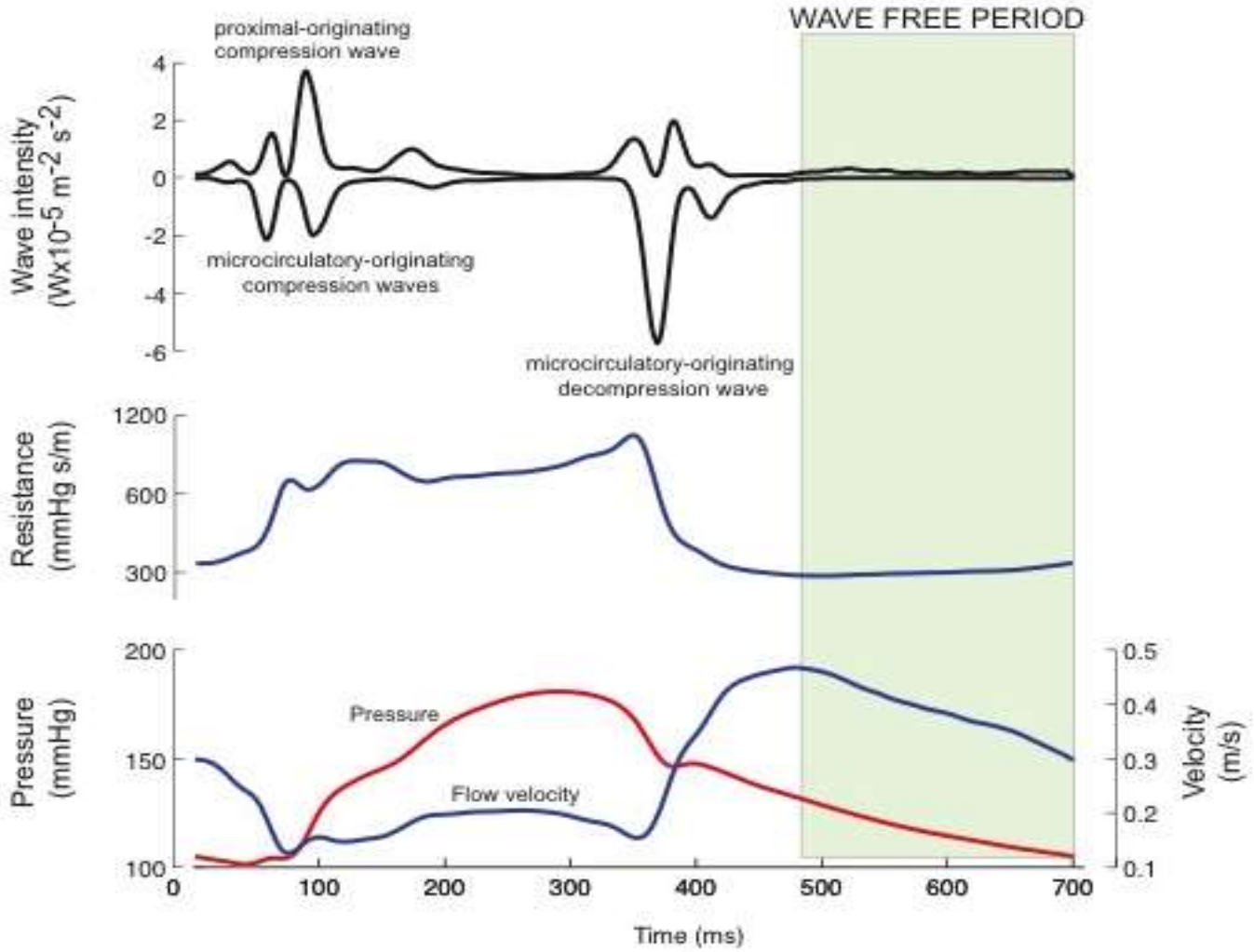
$P_v = 0$



FFR_{myo}

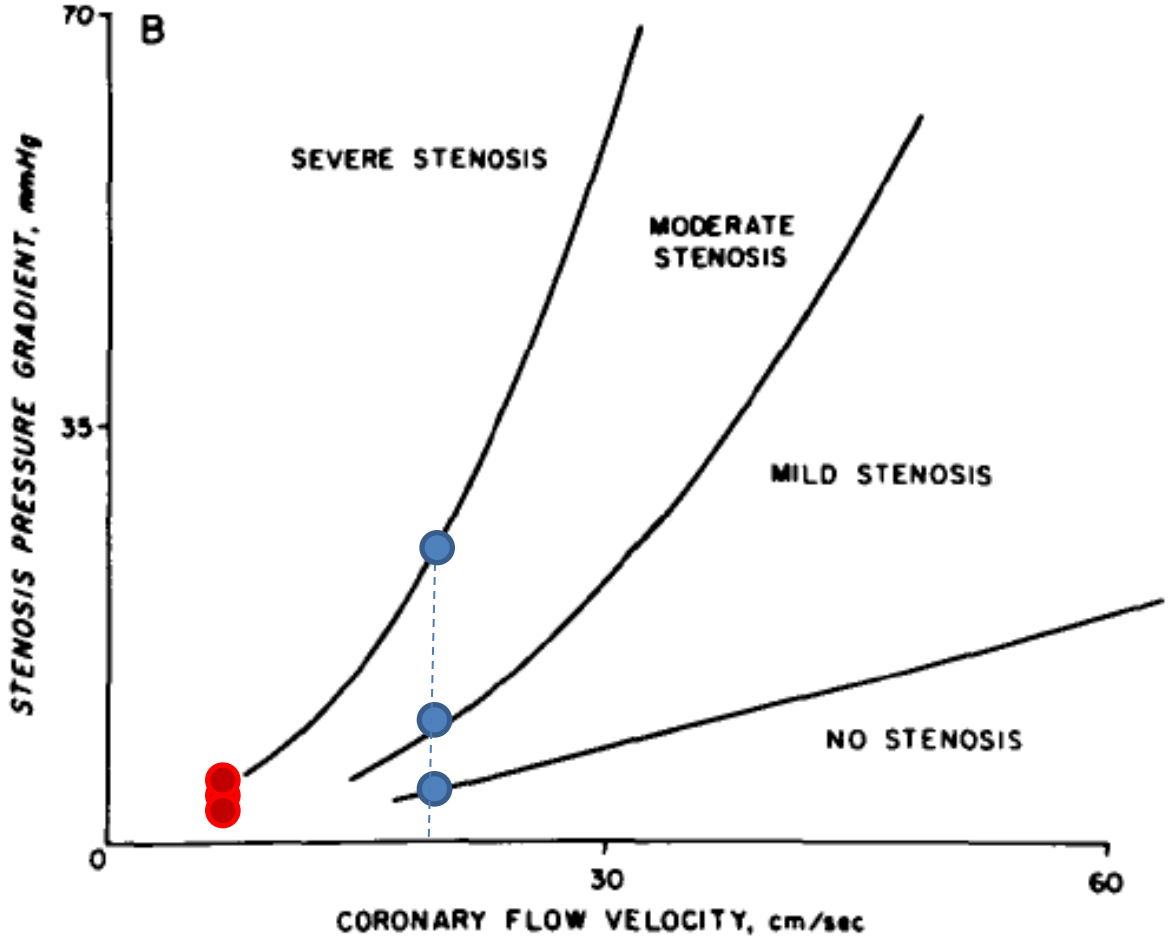


Identification of the naturally occurring diastolic wave-free period using wave intensity



Sen S, Mayet J, Davies JE et al. JACC (in press Nov 2011)
Davies JE, Francis DP, Hughes AD, Mayet J et al. Circulation 2006;113:1767-1778
Davies JE, Parker KH, Hughes AD, Mayet J et al. Circulation 2011;124:1565-1572

A minimal velocity is required for stenosis discrimination

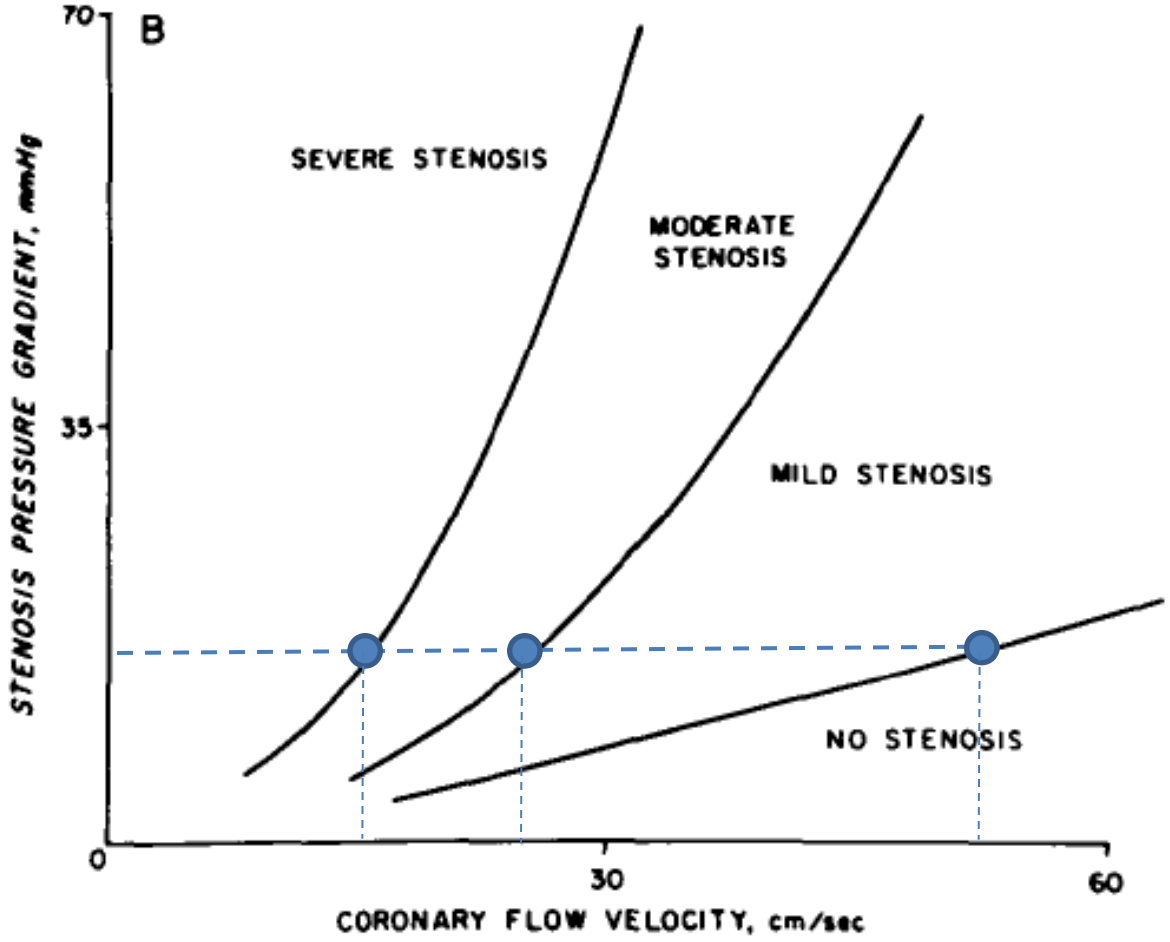


Gould, K. Circulation research 1978;43:242-253

Different stenosis severities can generate a similar low pressure drop (iFR/FFR) if interrogated with low velocities.

Therefore a minimal velocity is required

Consistent velocity is required for stenosis discrimination



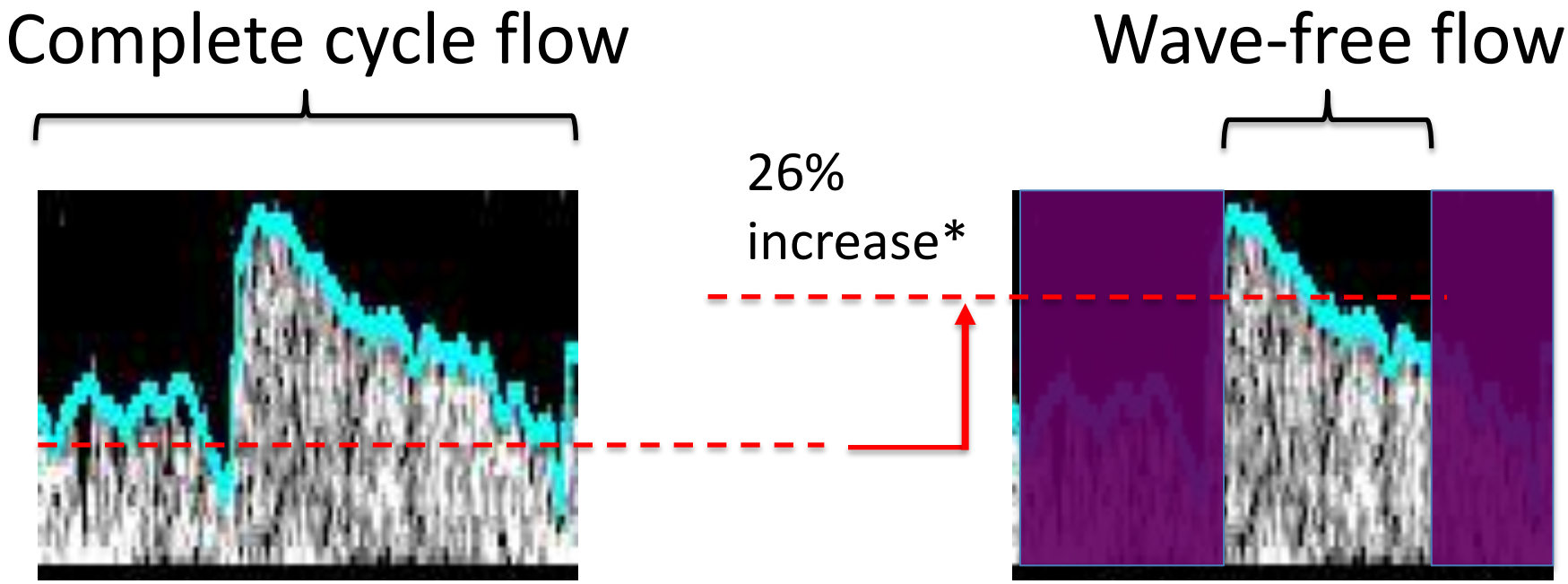
Gould, K. Circulation research 1978;43:242-253

Different stenosis severities can generate the same pressure drop (iFR/FFR) depending on the underlying velocity.

Therefore a consistent velocity is essential

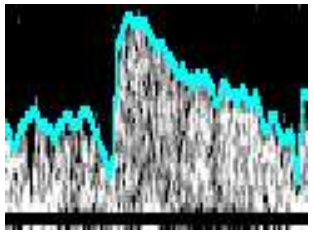
CLARIFY an ADVISE sub-study

Why does adenosine not improve diagnostic agreement?



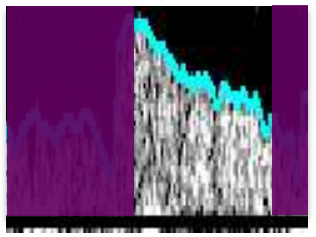
Mean velocities from ADVISE

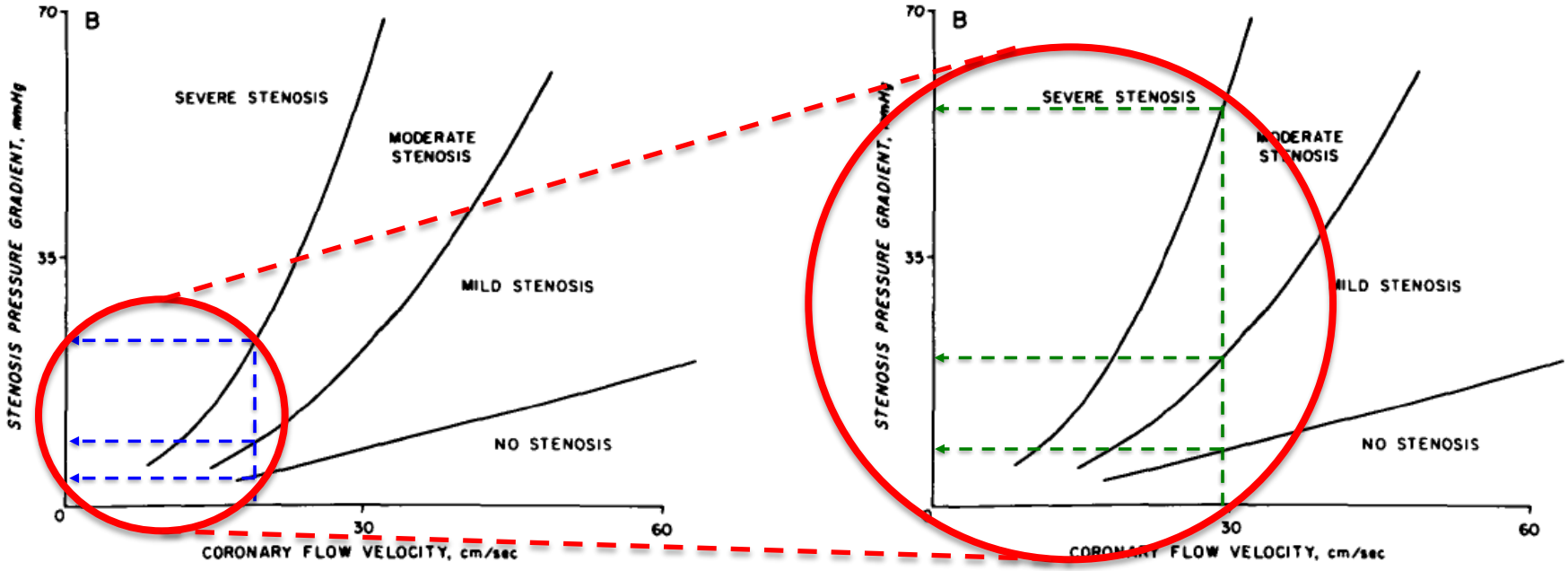
Complete cycle flow



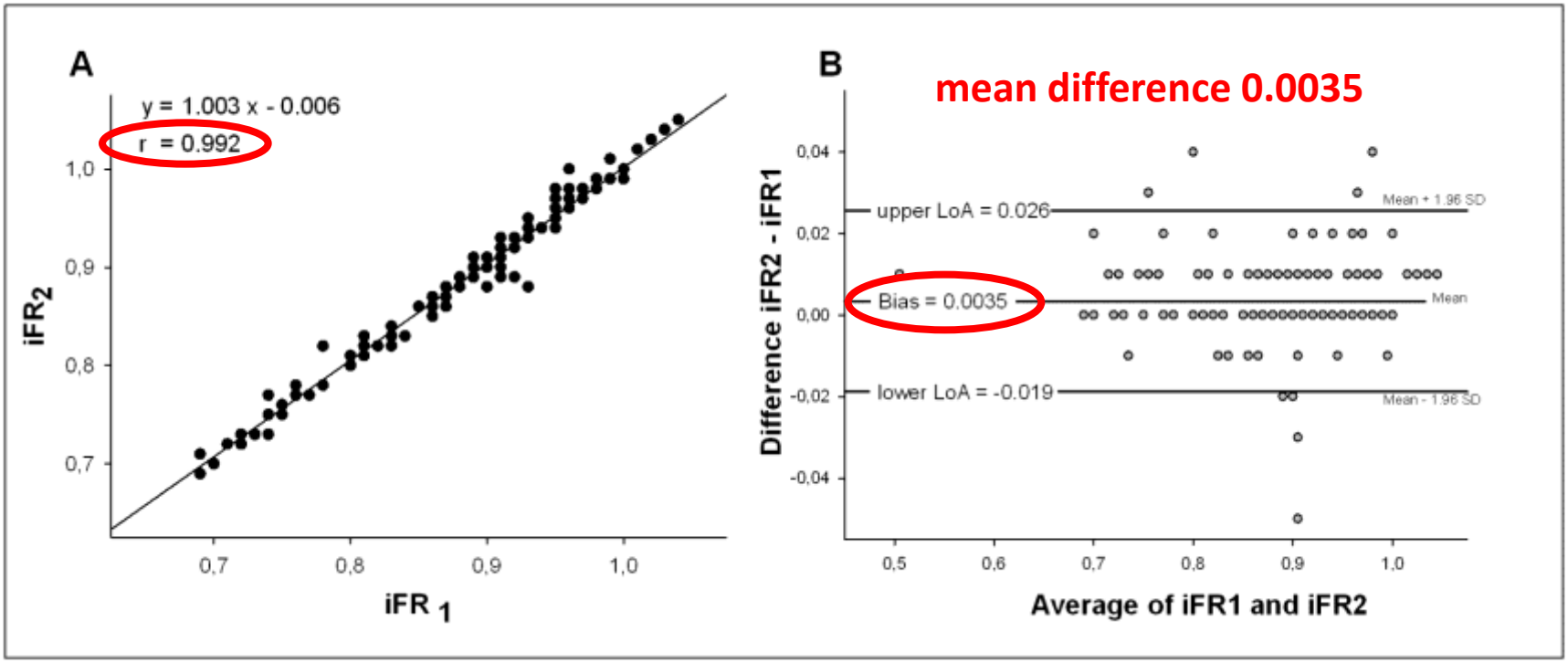
Increased sensitivity

Wave-free flow



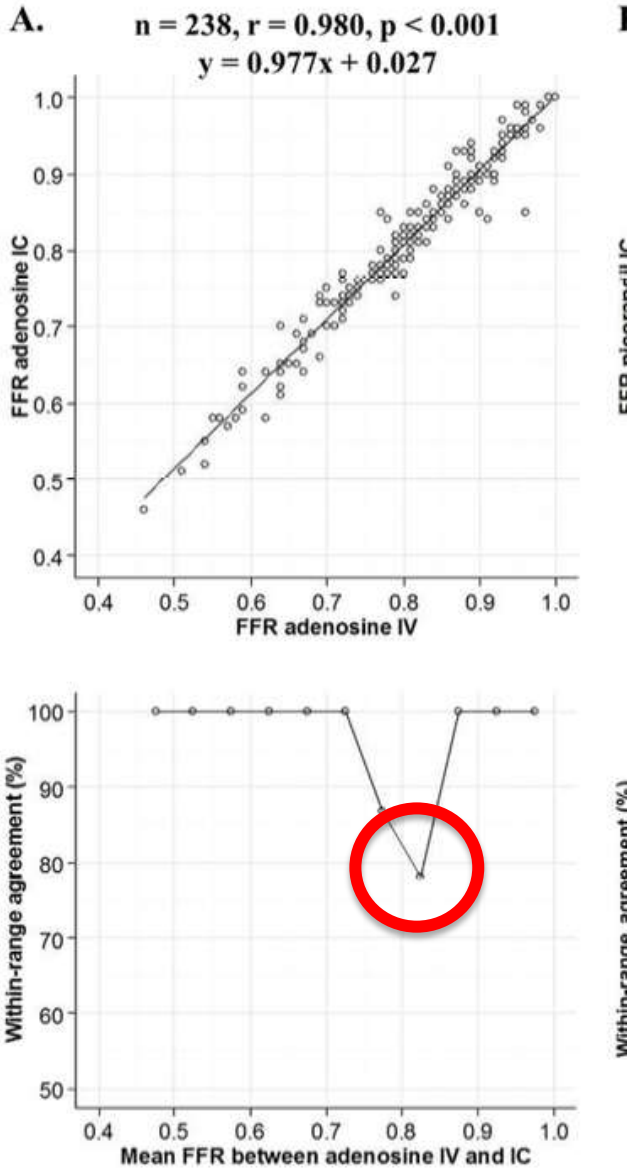


Reproducibility of iFR



iFR was measured twice in 130 lesions (86.1 %)

FFR classification changes!



Using IV adenosine and IC adenosine

FFR changes >20% around the FFR 0.80 cut-point

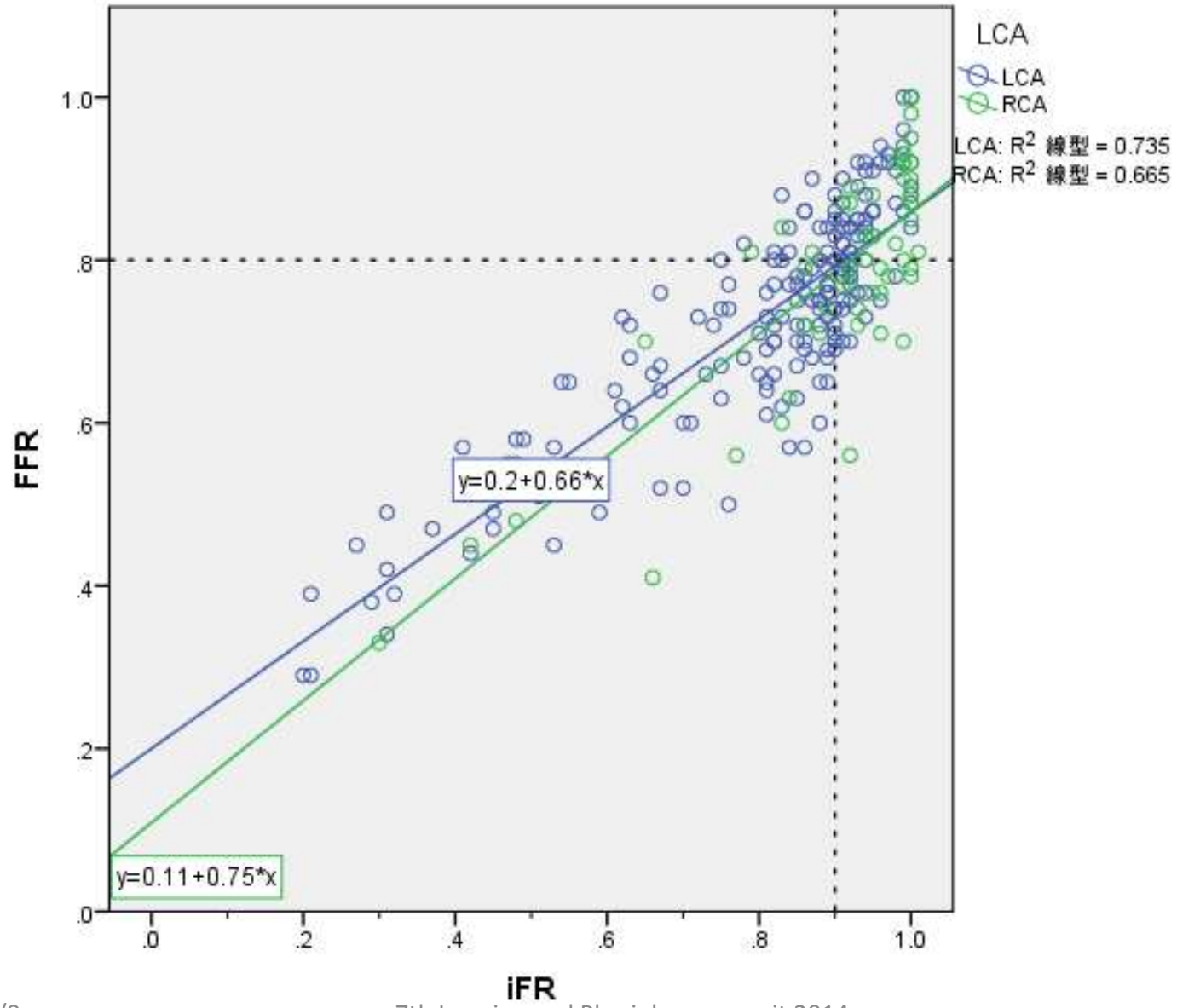
Lim WH, **Pijls NH** et al. CCI (in press)

Concordance between iFR and FFR

Lesion Characteristics

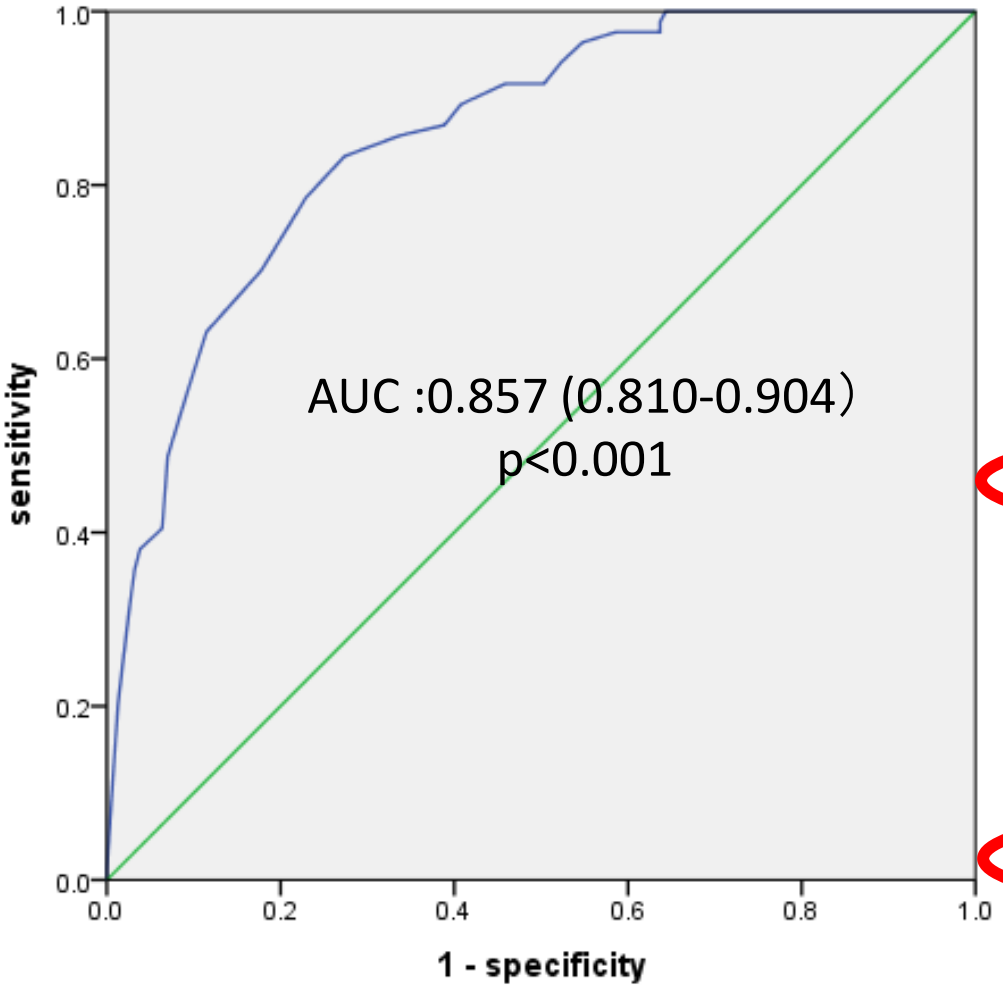
Lesion base analysis	n=241
measured vessel	RCA 58 LCA 183
MI related	12
Lesions with stable pt	155 (64.7%)
Lesions with unstable pt	85 (35.3%)
FFRmyo	0.74±0.14
FFR≦0.80	157 (65.1%)
iFR	0.83±0.18
MLD	1.20±0.40
Ref VD	2.87±0.65
LL	24.1±14.1
%DS	57.8±10.5

Correlation of iFR with FFR



Diagnostic characteristics of iFR in all

All lesions
N=241



iFR Best cutoff ：0.90
Sensitivity : 77.1%
Specificity ：79.7%
P.P.V ：87.7%
N.P.V : 65.0%
Accuracy: 78.0%

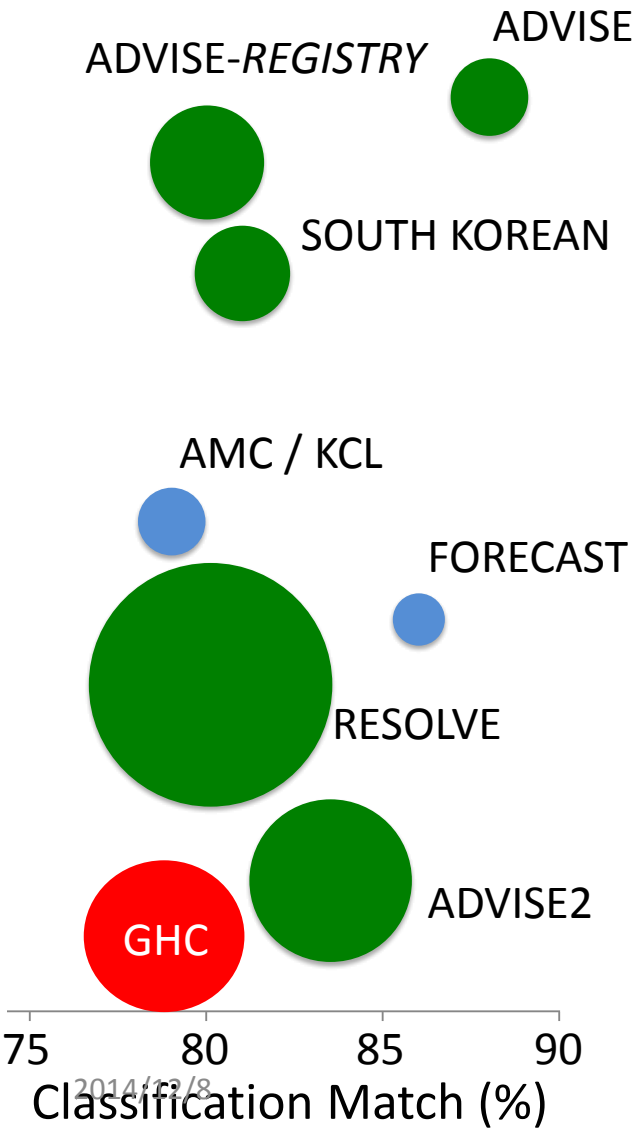
Consistent iFR cut-points

IFR value with best classification for FFR≤0.80

- ADVISE-Registry(n=339) 0.89
- South Korean Study(n=238) 0.90
- RESOLVE(n=1593) 0.90
- ADVISE-*in Practice*(n=392) 0.90
- ADVISE 2 (n=689) 0.89
- GHC (n=241) 0.90

FDA Labeling iFR = 0.89

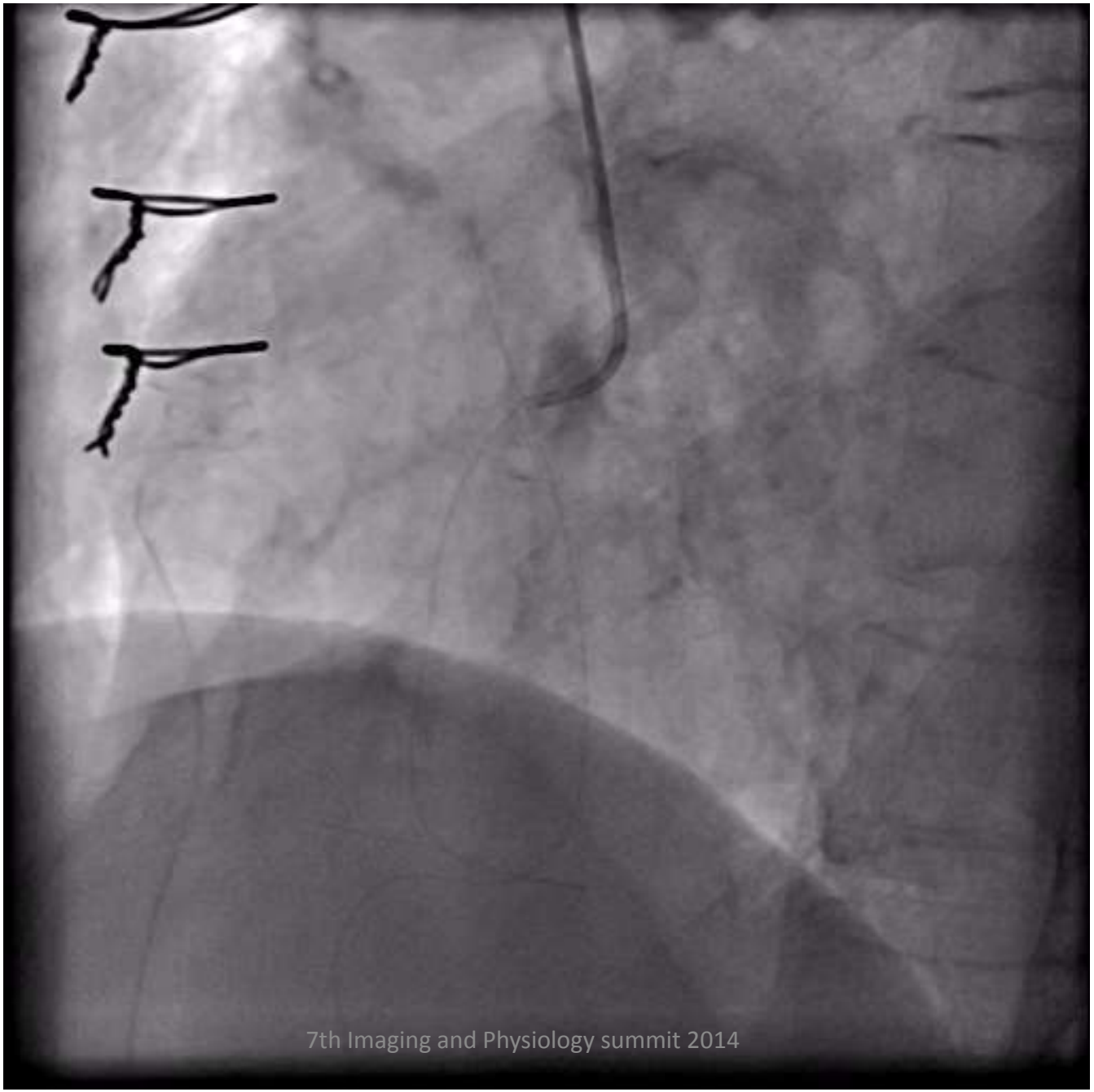
Excellent iFR-FFR classification match using independently validated algorithm

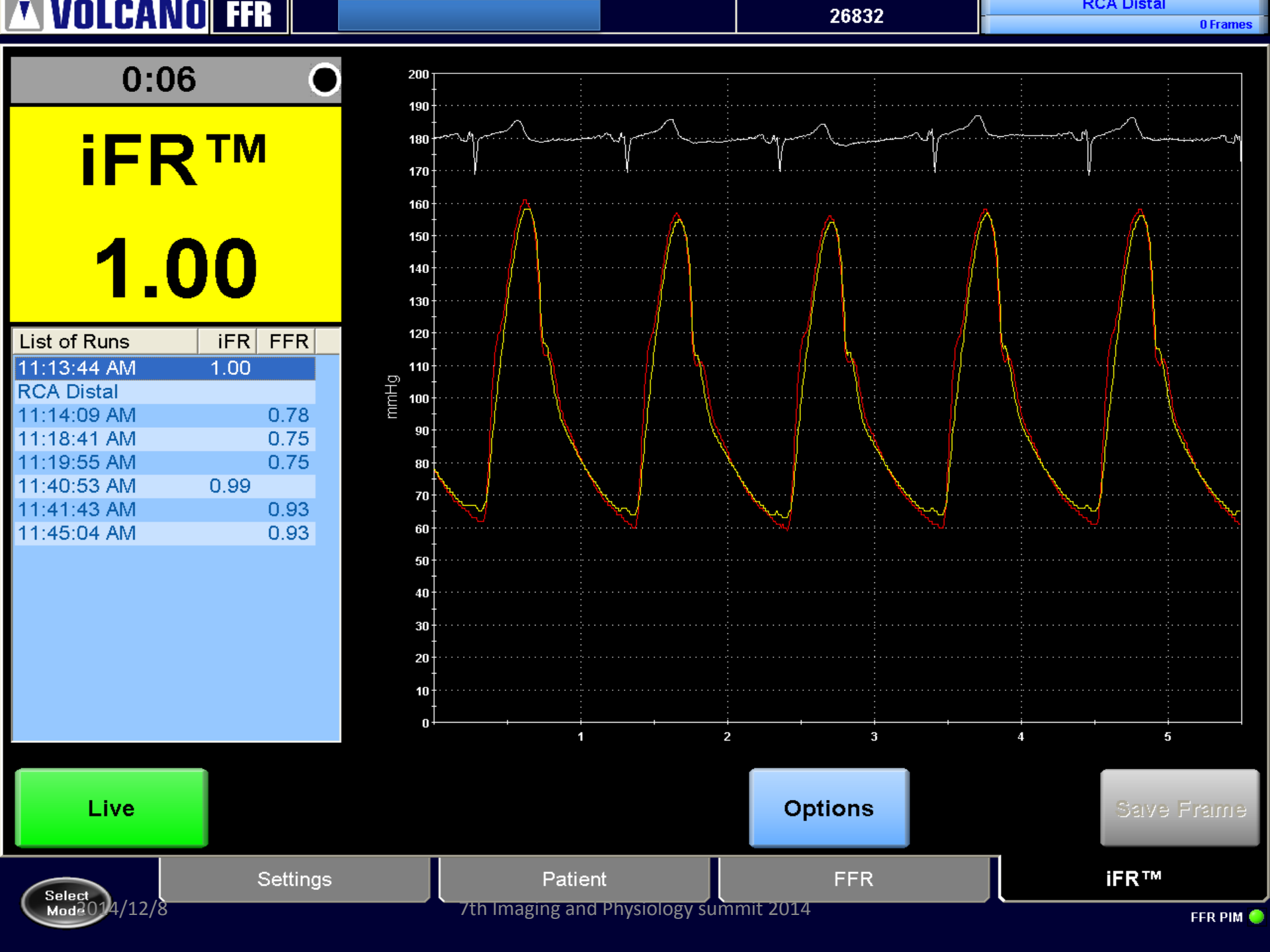


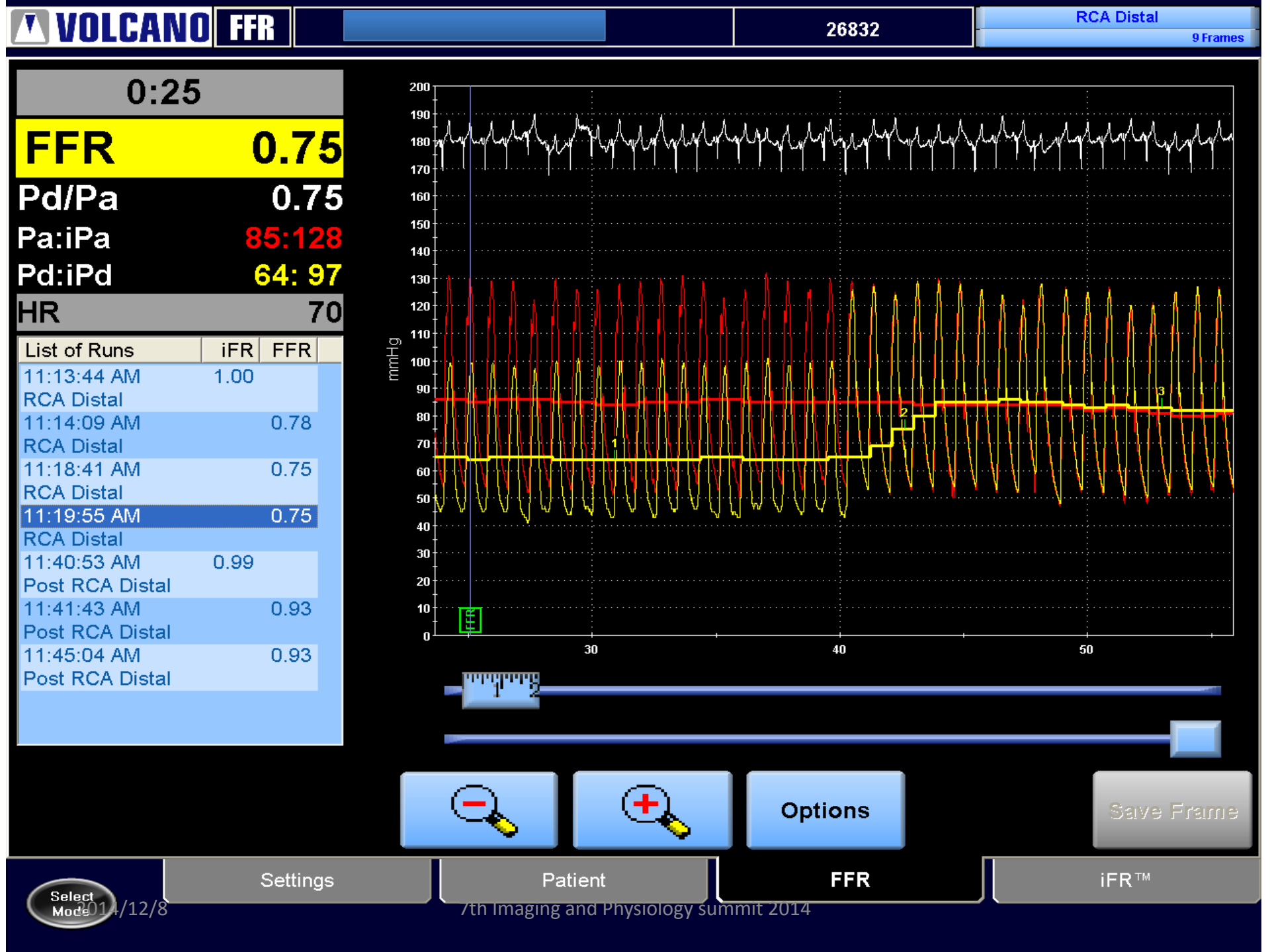
- n>3000 stenoses
- Independent core-lab blinded analyses
- Investigators studies
- Multi-centre collaborative studies

Adapted from Sen S et al. J Am Coll Cardiol. 2013;62(10):943-5

case1 : iFR and FFR Why discrepant?




VOLCANO
FFR
26832
RCA Distal
0 Frames
0:06
iFR™
1.00
List of Runs
iFR
FFR
11:13:44 AM 1.00
RCA Distal
11:14:09 AM 0.78
11:18:41 AM 0.75
11:19:55 AM 0.75
11:40:53 AM 0.99
11:41:43 AM 0.93
11:45:04 AM 0.93
mmHg
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
1
2
3
4
5
Live
Options
Save Frame
Settings
Patient
FFR
iFR™
Select Mode
FFR PIM


VOLCANO
FFR
26832
RCA Distal
9 Frames
0:25
FFR 0.75
Pd/Pa 0.75
Pa:iPa 85:128
Pd:iPd 64: 97
HR 70
List of Runs iFR FFR
11:13:44 AM 1.00
RCA Distal
11:14:09 AM 0.78
RCA Distal
11:18:41 AM 0.75
RCA Distal
11:19:55 AM 0.75
RCA Distal
11:40:53 AM 0.99
Post RCA Distal
11:41:43 AM 0.93
Post RCA Distal
11:45:04 AM 0.93
Post RCA Distal
mmHg
Options
Save Frame
Settings
Patient
FFR
iFR™
Select Mode

5 key iFR validation studies

EVIDENCE

Study 1

FFR vs iFR

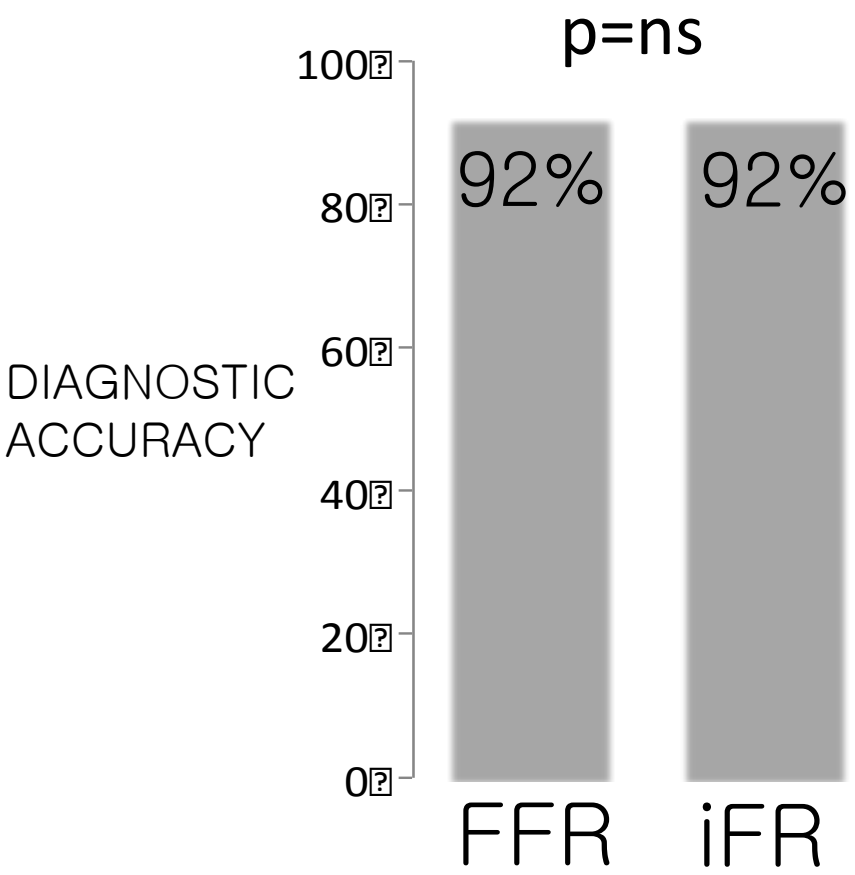
Gold Standard: Hyperaemic Stenosis Resistance (HSR)

N=51

CLARIFY

Sen et al. J Am Coll Cardiol. 2013;61(13):1409-20

iFR has similar diagnostic accuracy to FFR



CLARIFY

Sen et al. JACC 2013

EVIDENCE

Study 2

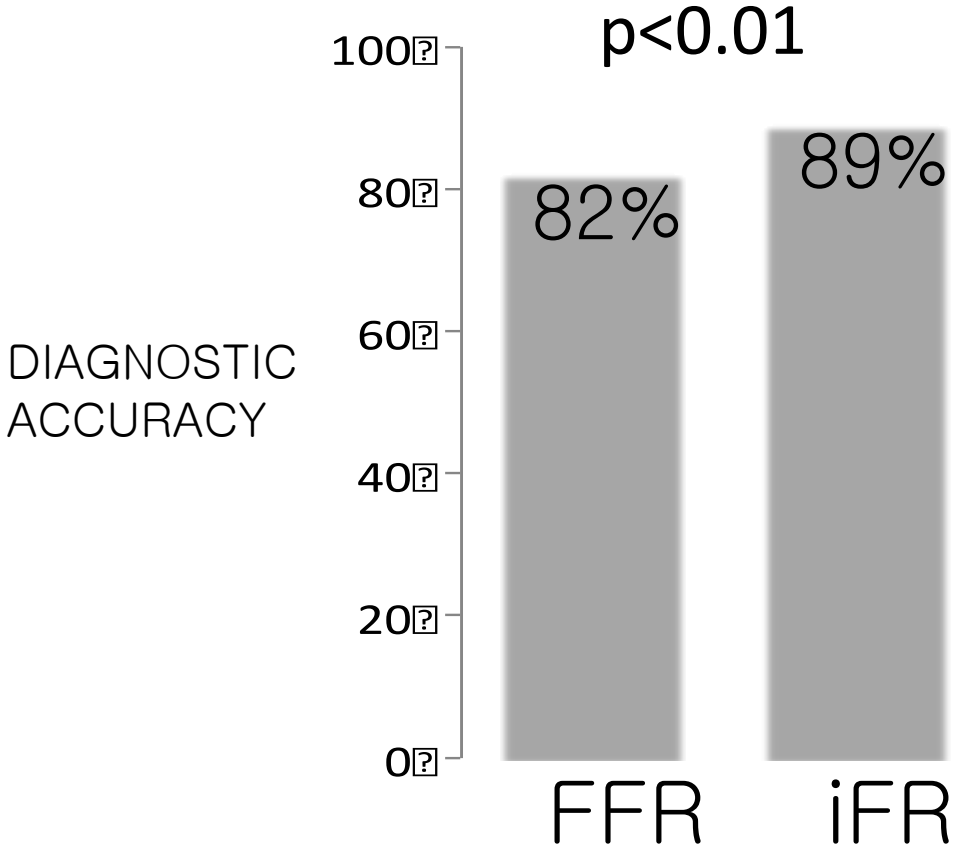
FFR vs iFR

Gold Standard: Hyperaemic Stenosis Resistance (HSR)

N=120

Sen et al. J Am Coll Cardiol. 2013;62(6):566

iFR and FFR have *similar diagnostic power* to detect ischaemia



Supplementary data courtesy of Johnson et al.
Sen S et al. J Am Coll Cardiol. 2013;62(6):566

EVIDENCE

Study 3

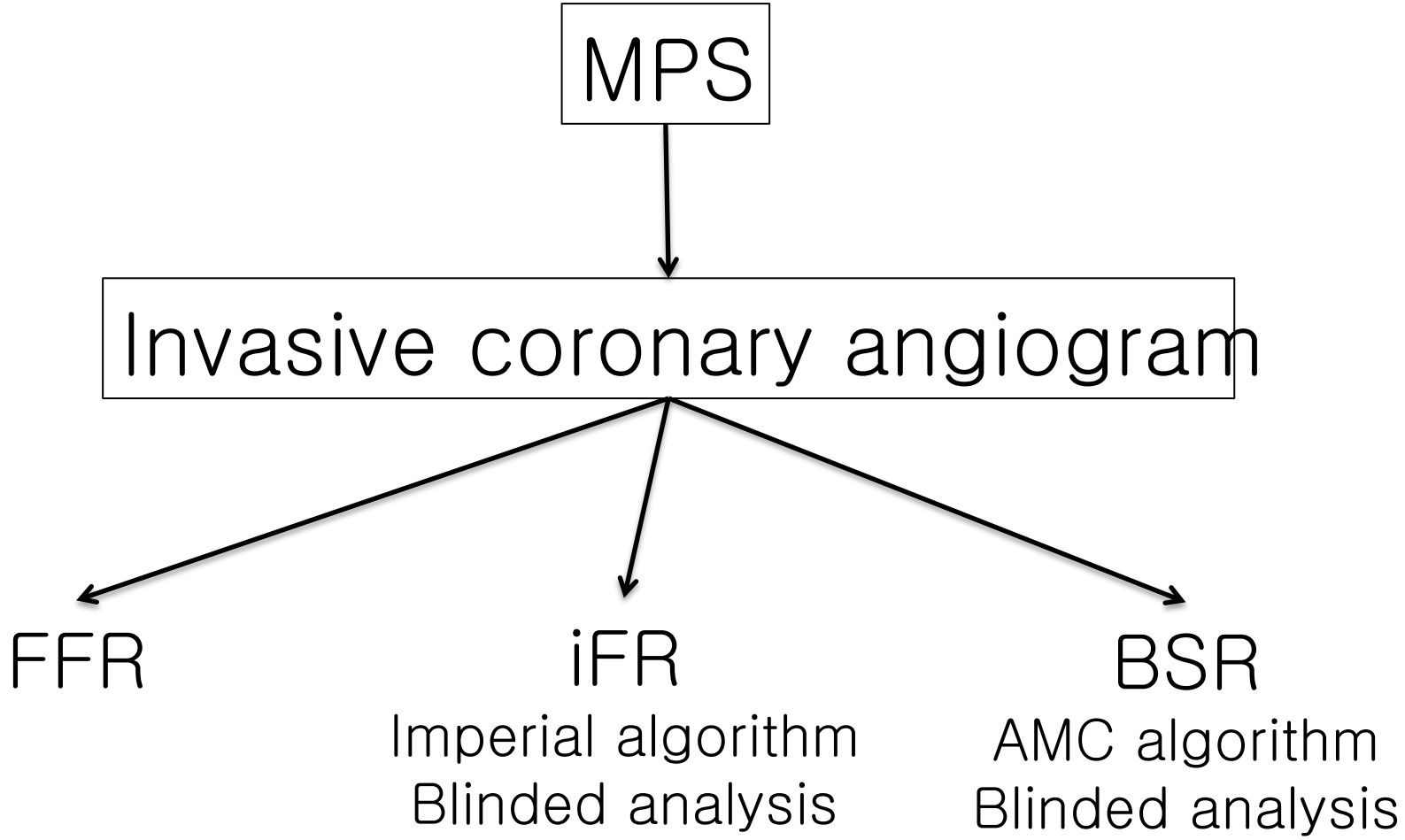
FFR vs iFR vs BSR

Gold Standard: Myocardial Perfusion Scintigraphy

N=85

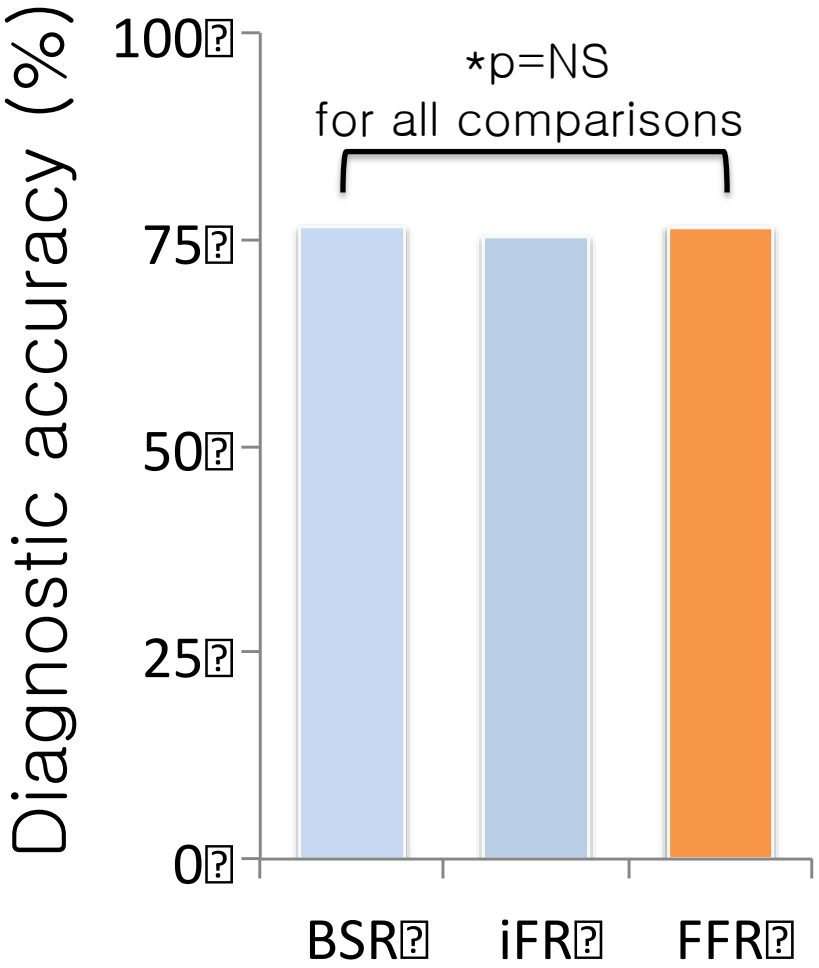
Van de Hoef et al. J Eurointervention (*in press*)

Study Design



van de Hoef et al. Eurointervention (in pres

Hyperaemia does not increase diagnostic accuracy



2014/12/8

van de Hoef et al. Eurointervention (in pres

EVIDENCE

Study 4

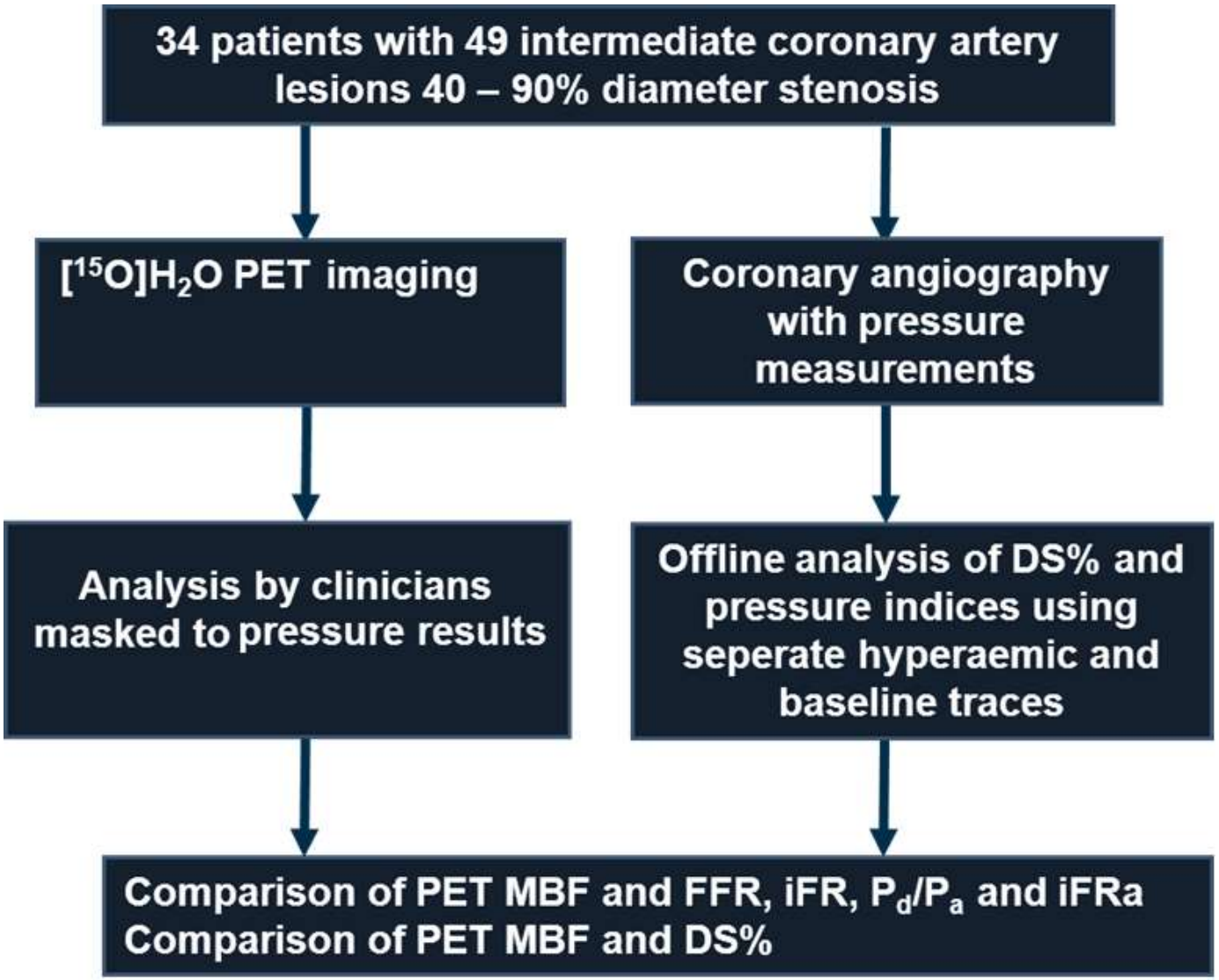
FFR vs iFR

n=49

Gold Standard: Positron Emission Tomography (PET)

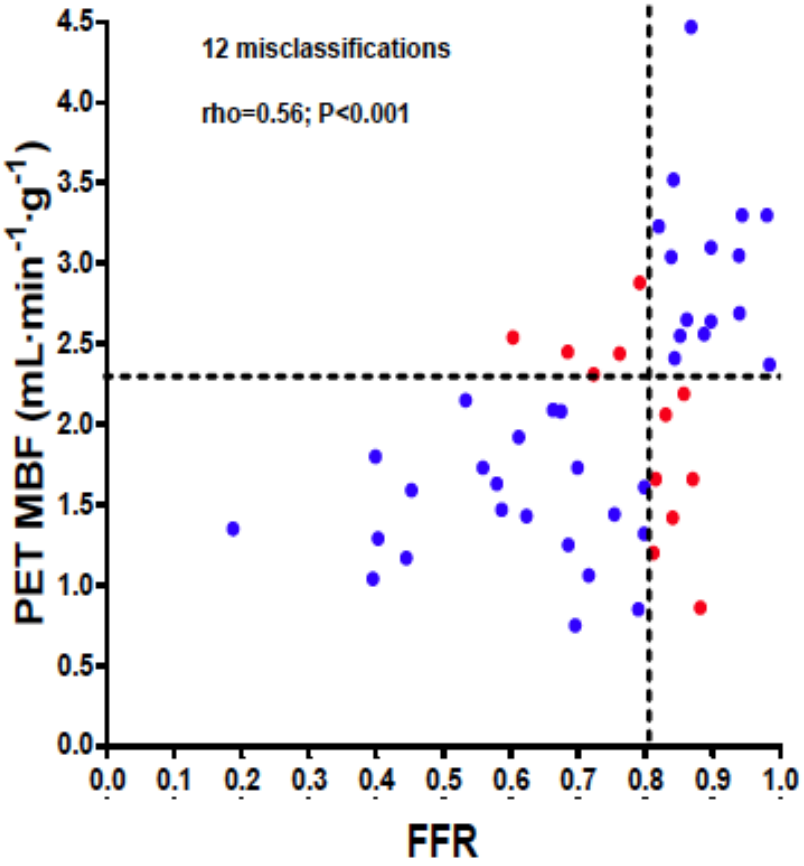
De Waard G et al. ACC 2014

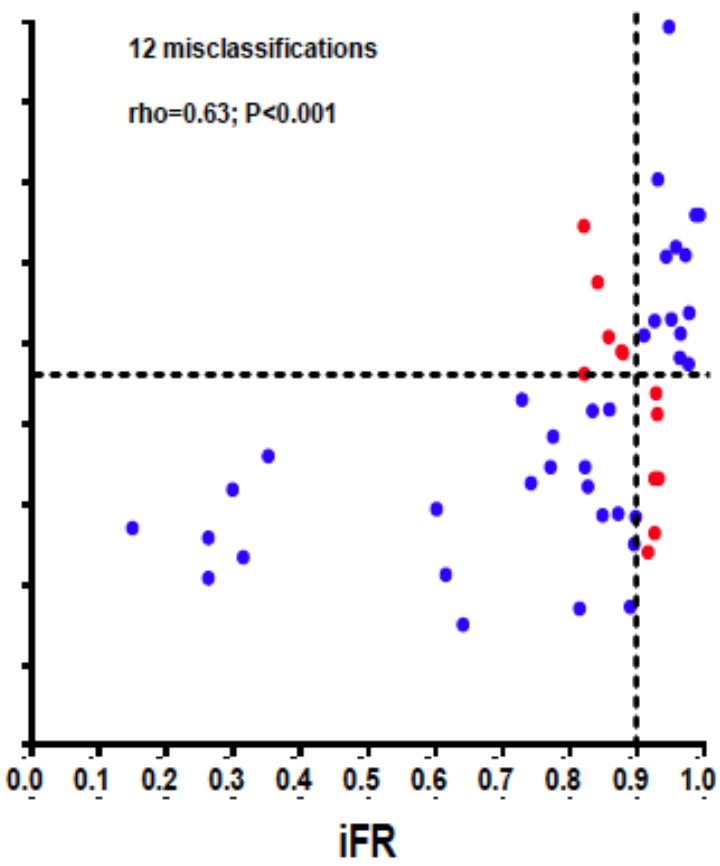
Study Protocol



De Waard G et al. ACC 2014

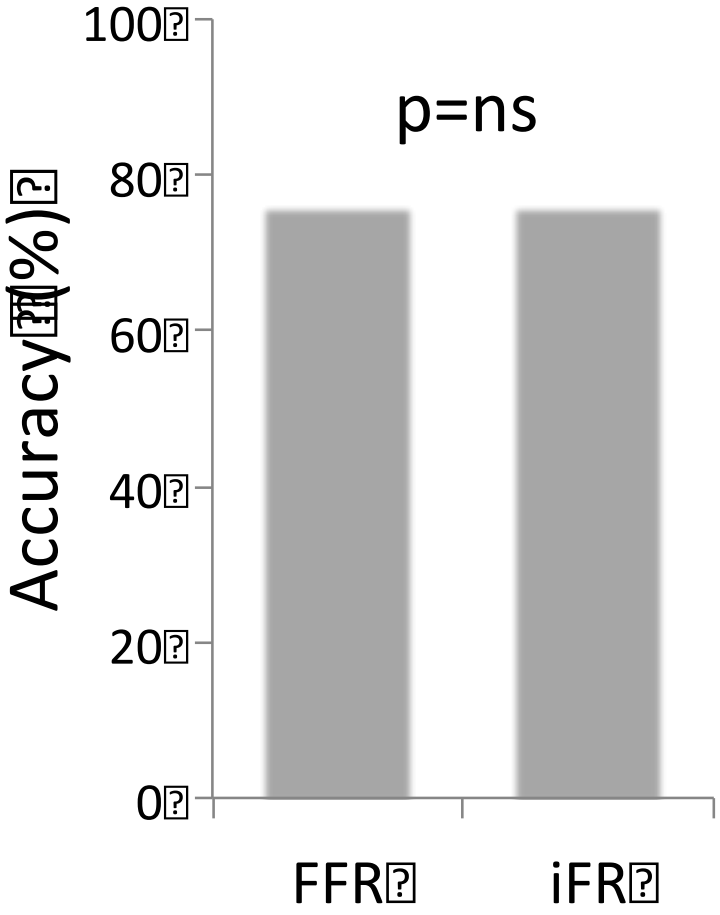
Classification between FFR / iFR and PET MBF is identical





De Waard G et al. ACC 2014

iFR and FFR have *similar diagnostic power* to detect ischaemia



De Waard G et al. ACC 2014

EVIDENCE

Study 5

FFR vs iFR

N=216

Gold Standard: Coronary Flow Reserve (CFR)

Petraco R. et al. Circ. Cardiovascular int. (*in press*)

Noninvasive Coronary Flow Reserve and Prognosis

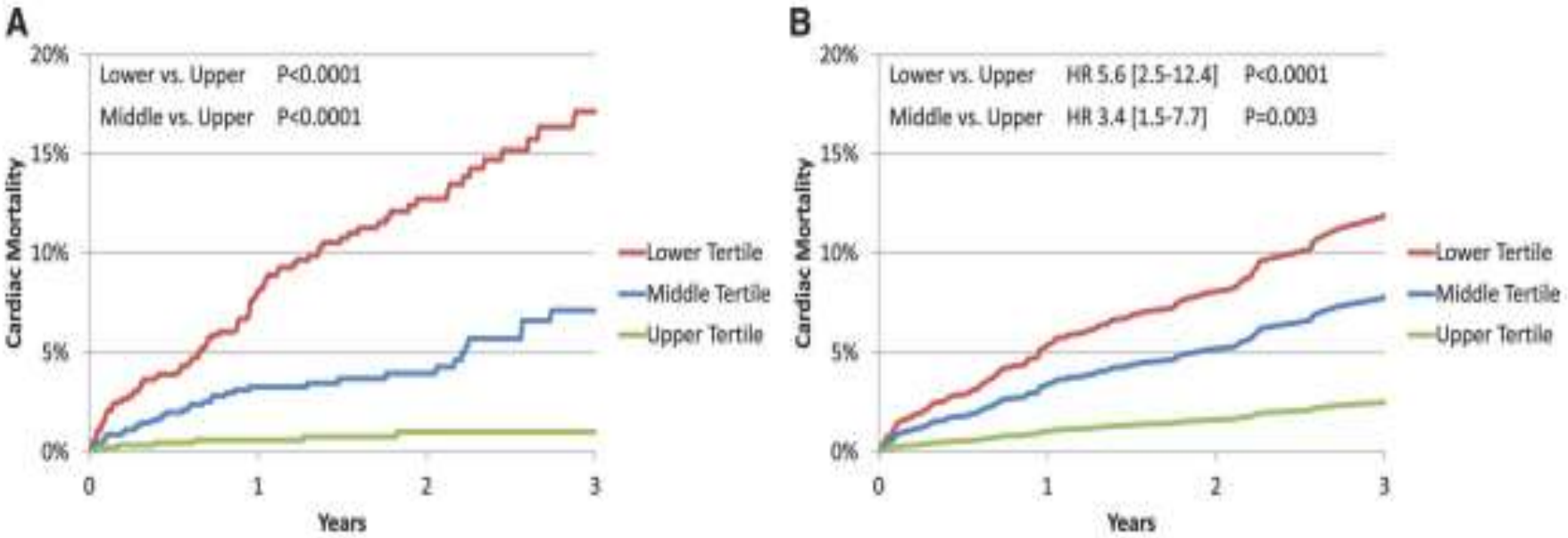
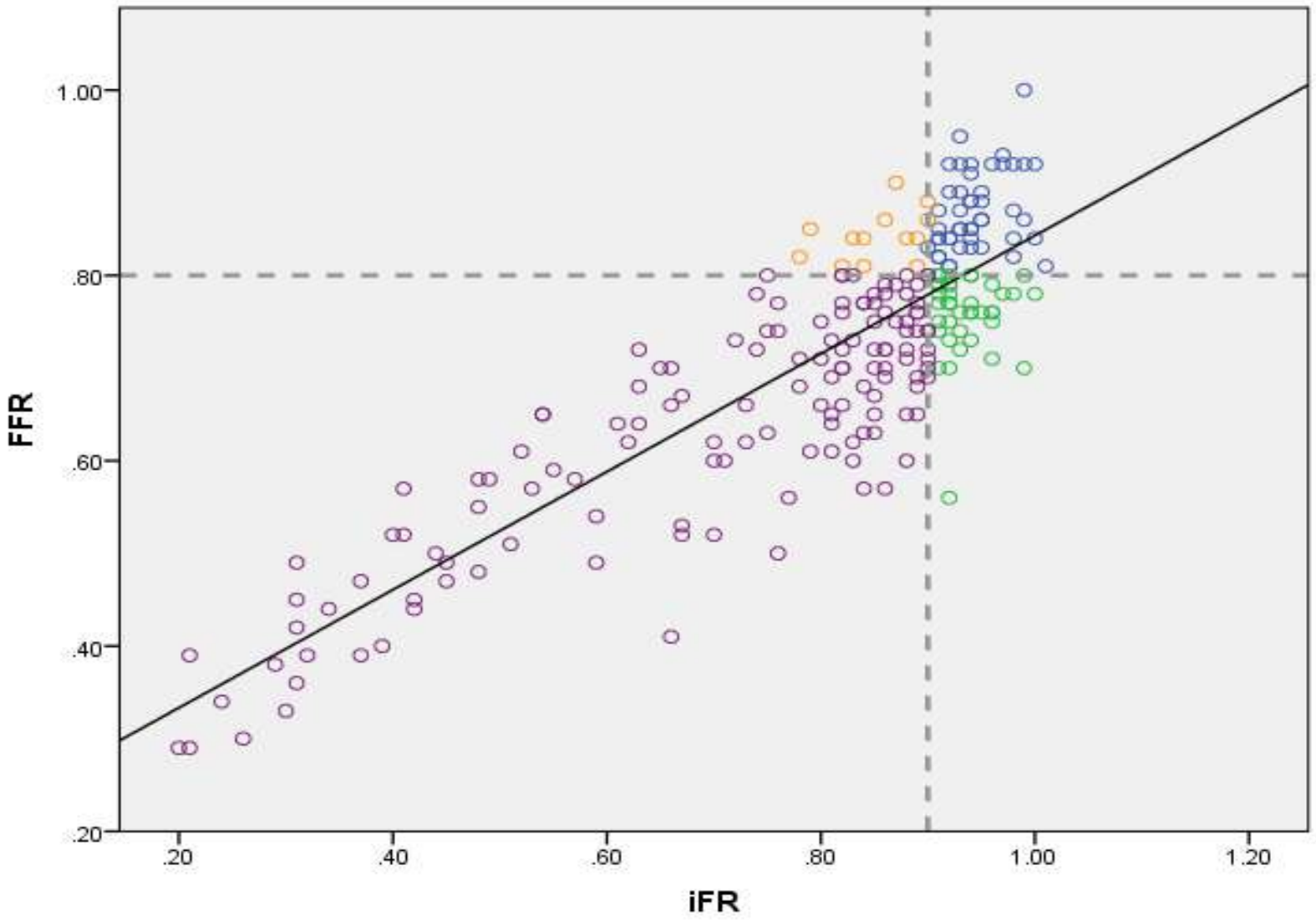
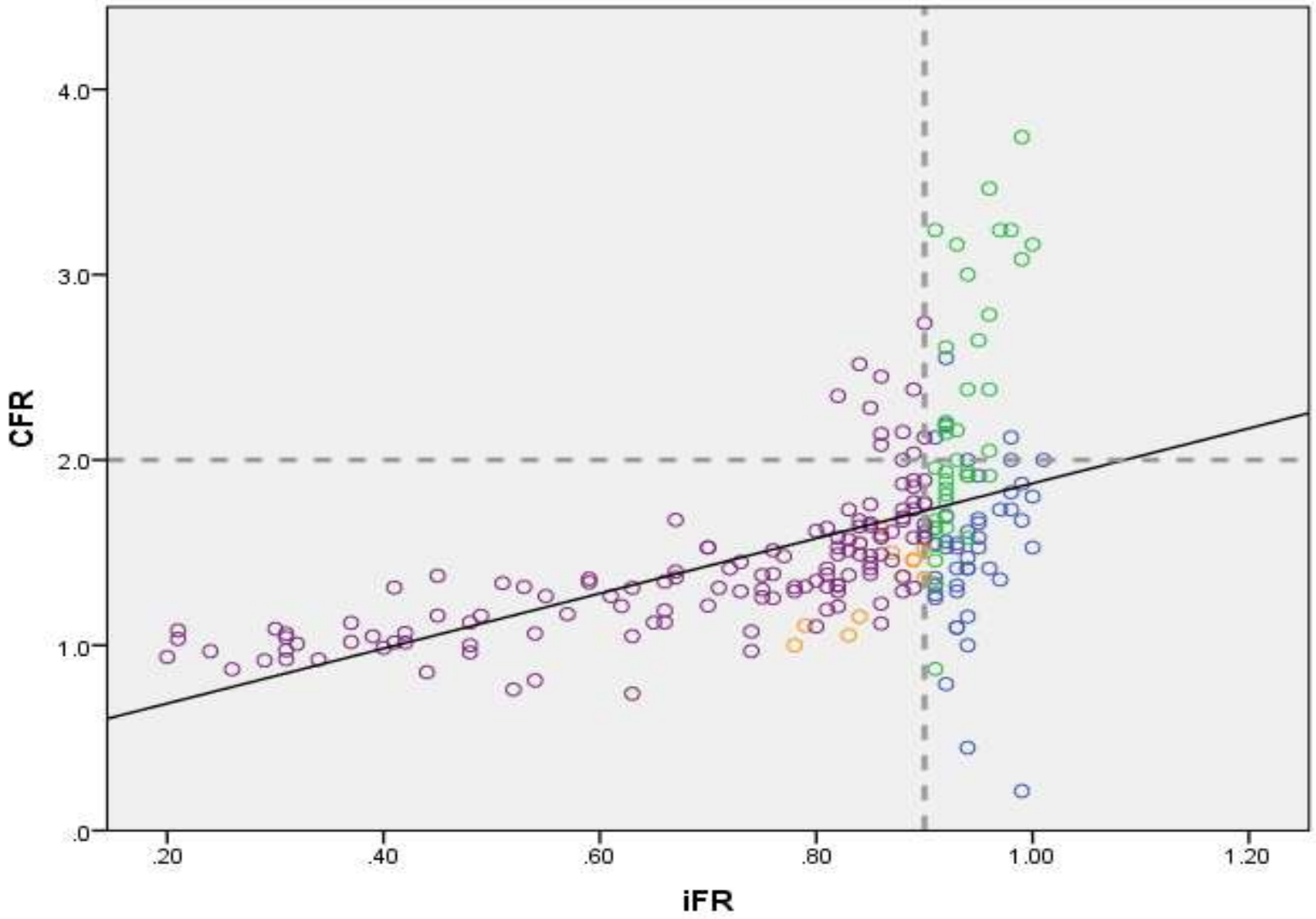


Figure 4. Cardiac mortality. Cumulative incidence of cardiac mortality for tertiles of coronary flow reserve (CFR) presented in Kaplan-Meier format (**A**) and after adjustment[18] for age, sex, body mass index, hypertension, dyslipidemia, diabetes mellitus, family history of coronary artery disease (CAD), tobacco use, prior CAD, chest pain, dyspnea, early revascularization, rest left ventricular ejection fraction (LVEF), summed stress score, and LVEF reserve (**B**), showing a significant association between CFR and cardiac mortality. HR indicates hazard ratio.

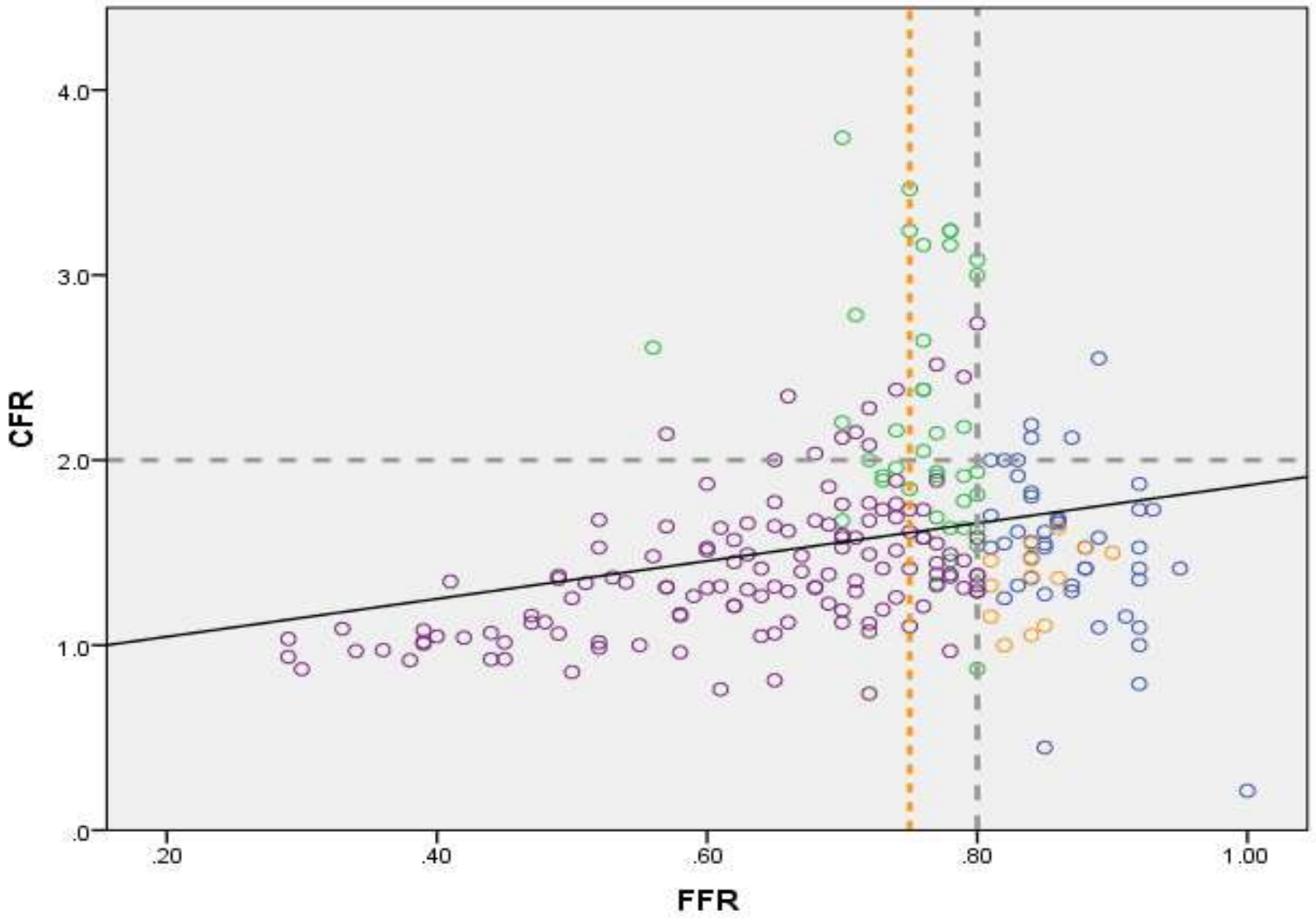
Murthy VL., et al. Circulation. 2011;124:2215-2224.



r=0.863 (95%CI: 0.589 - 0.685), p<0.001

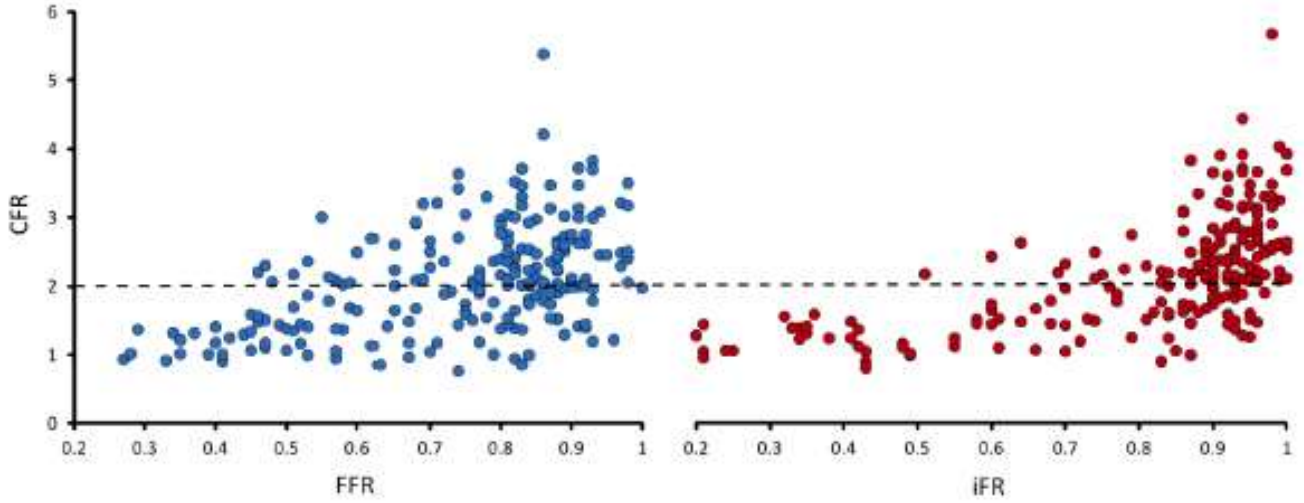


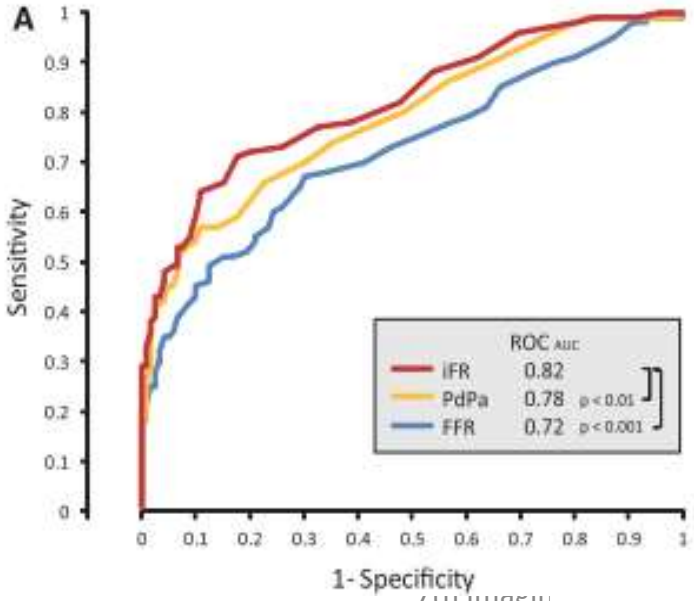
r=0.537 (95%CI: 1.183 - 1.787), p<0.001



r=0.273 (95%CI: 0.556 - 1.489), p<0.001

Resting pressure measurements provide a better estimate of hyperaemia flow





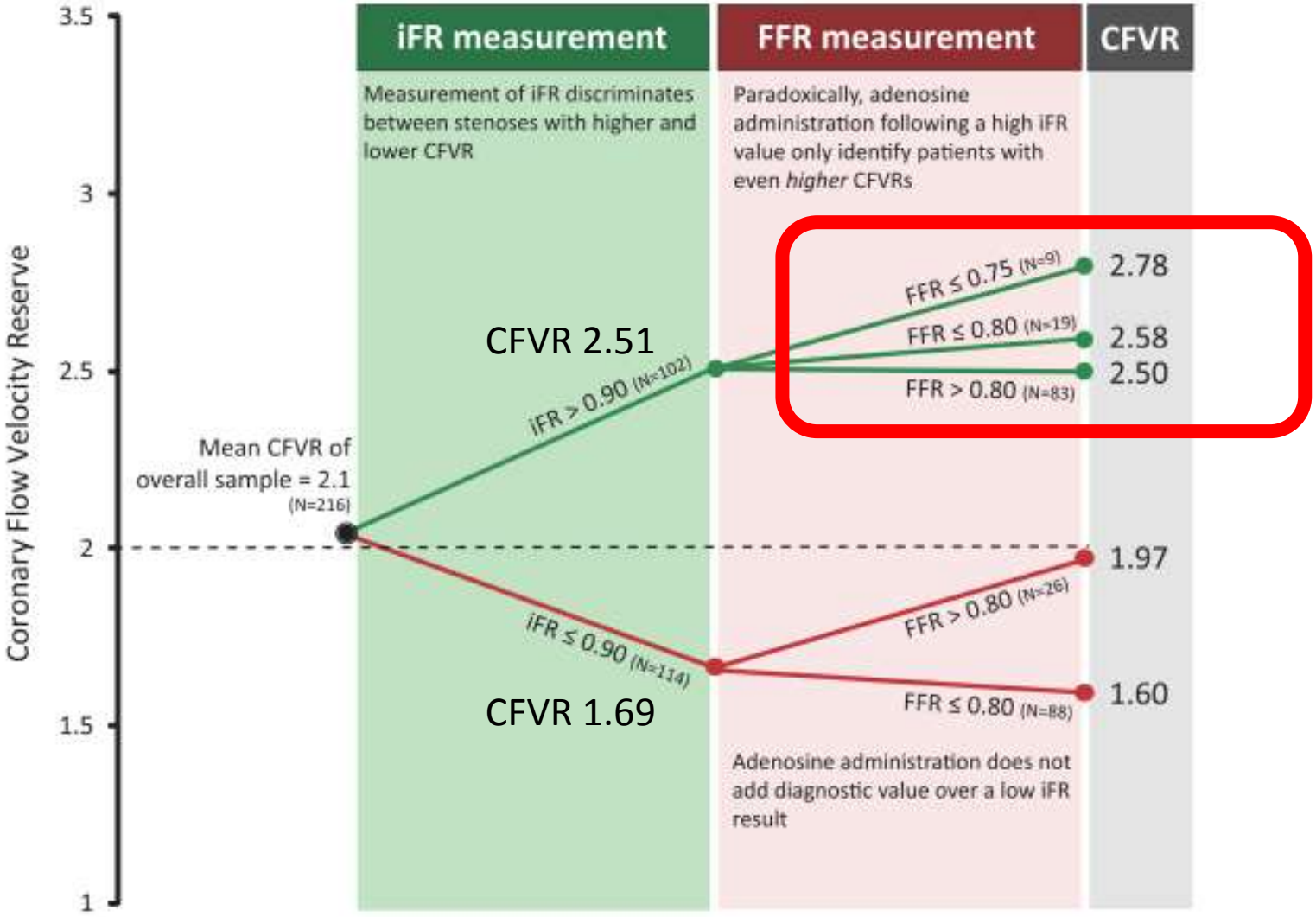
Diagnostic performance of FFR and iFR		
	FFR	iFR
Cut-off*	0.8	0.89
Diagnostic accuracy	67%	74%
Sensitivity	68%	73%
Specificity	66%	74%
PPV	62%	70%
NPV	72%	77%

* Cut-off: Highest sum of sensitivity and specificity to match a CFVR of 2.0

der review)

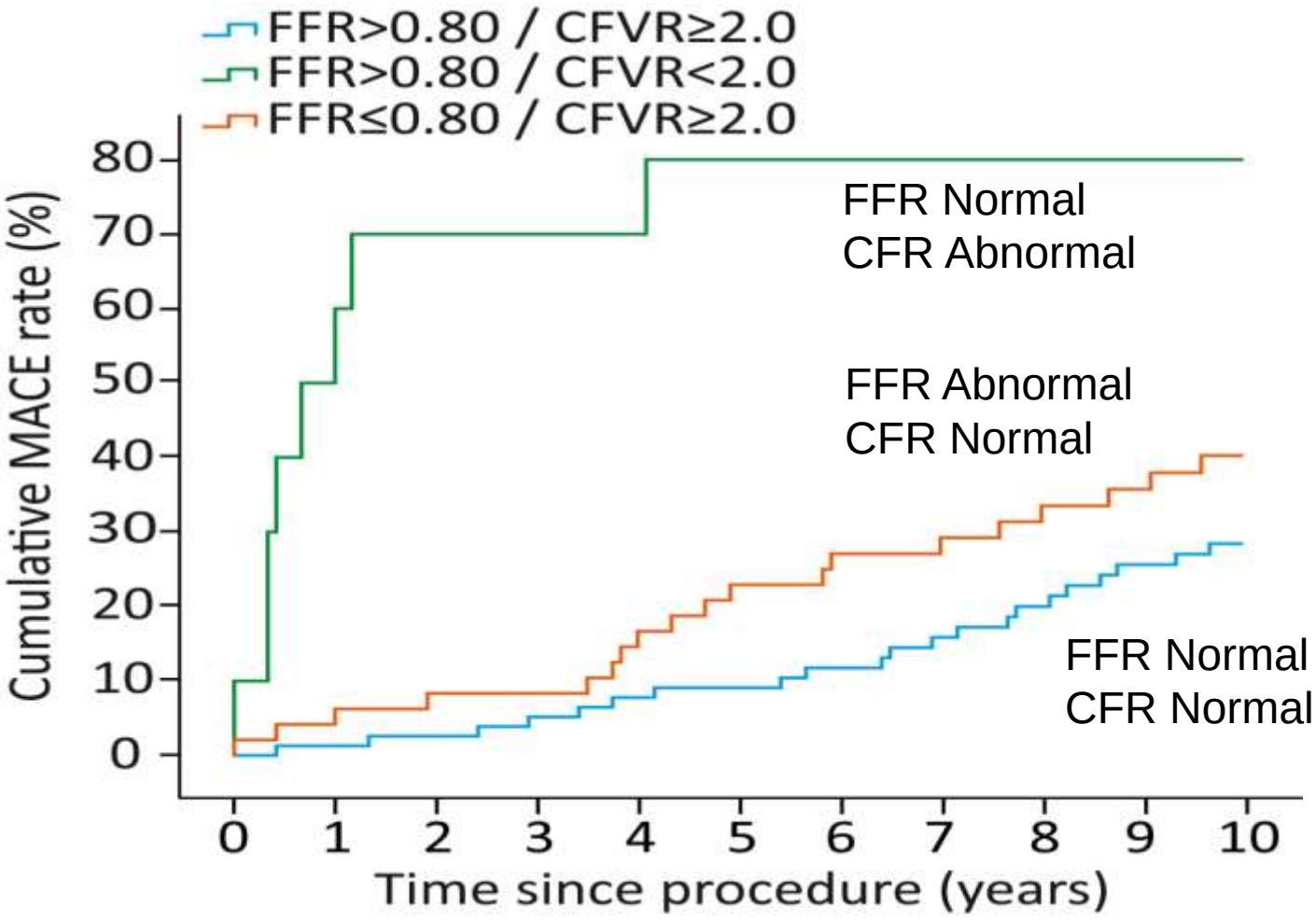
Petraco R et al. Circ Cardiovasc Interv. 2014 in press

Measurement of instantaneous wave-free ratio (iFR) and fractional flow reserve (FFR) for the identification of stenoses with abnormal coronary flow velocity reserve (CFVR)



Petraco R et al. Circ Cardiovasc Interv. 2014 in press

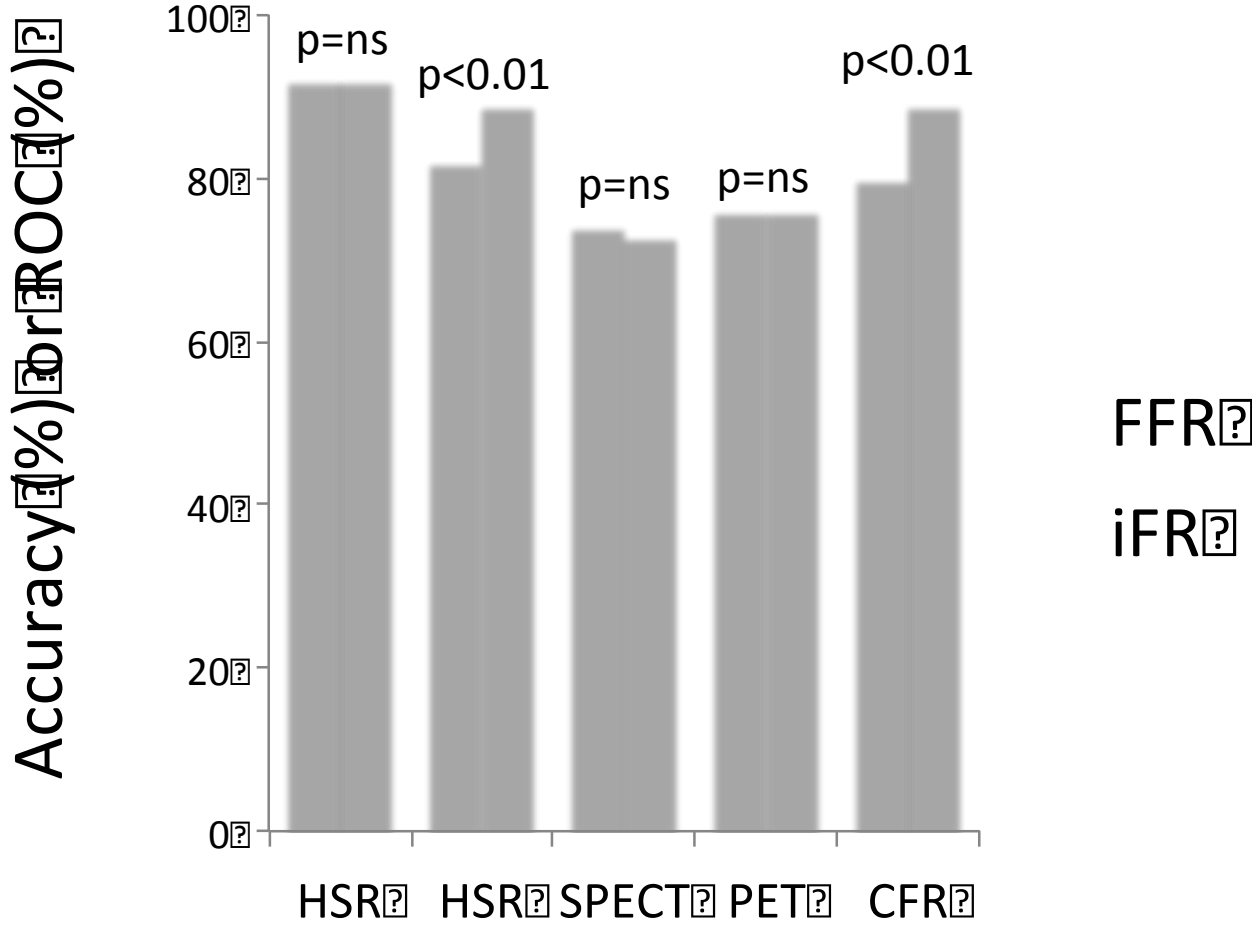
Flow adds significant benefit to FFR in predicting outcomes



FFR significance ≤0.80
CFR significance <2.0

Van de Hoef T., et al. Circ int. (in press)

Vasodilators ***do not*** improve physiological diagnostic accuracy



1. Van de Hoef et al. Circ Cardiovasc Interv. 2012;5(4):508-14
2. Sen et al. J Am Coll Cardiol. 2013;61(13):1409-20
3. Van de Hoef Euroint. (*in press*)
4. Sen et al. J Am Coll Cardiol. 2013;62(6):566
5. Petraco et al. Circ. Int. (*in press*)
6. de Waard et al. (ACC 2014)

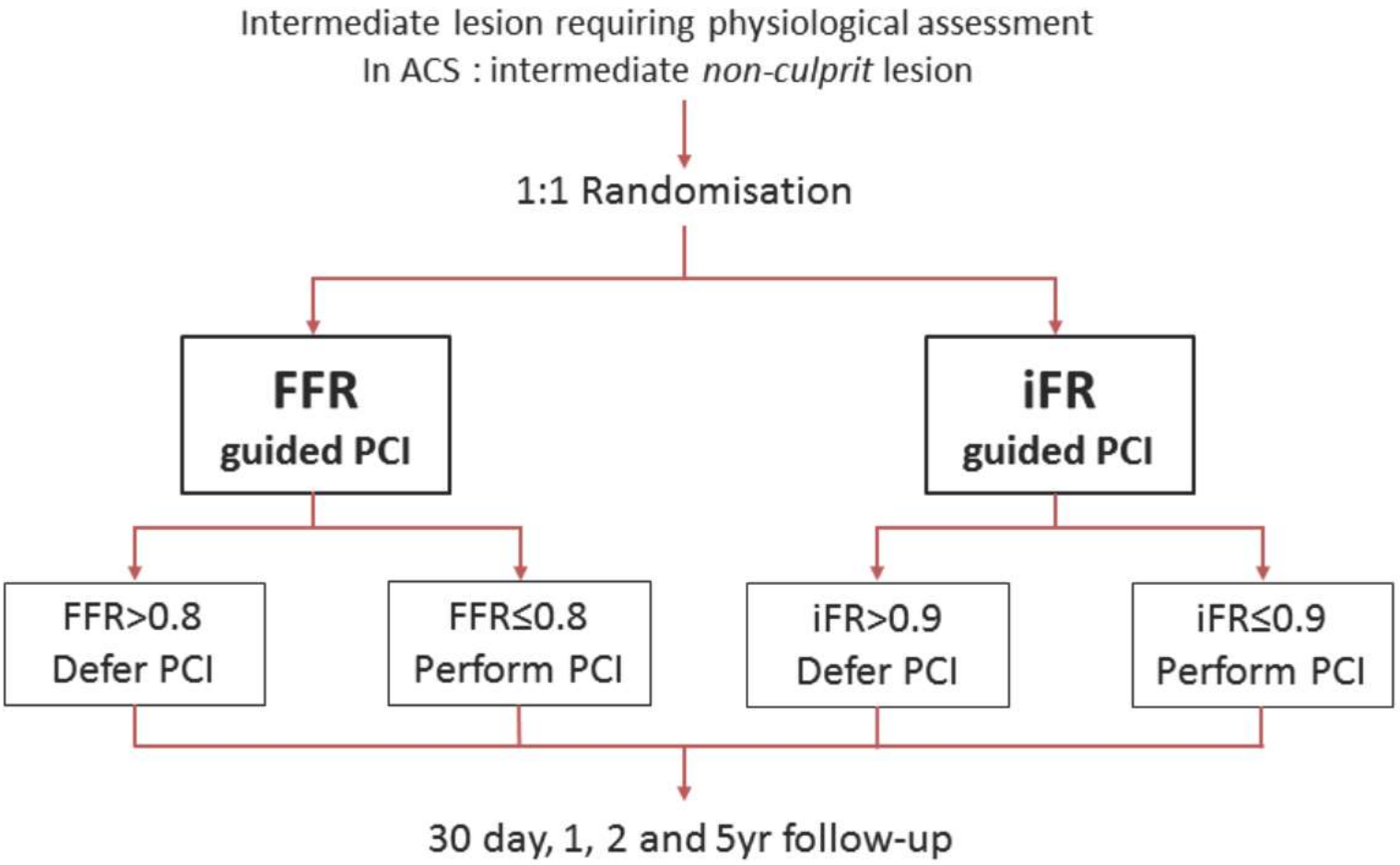
FLAIR trial

Functional Lesion Assessment of Intermediate stenosis to guide Revascularisation

Main sponsor:	**Imperial College London**
Funders:	**Unrestricted Educational grant from Volcano Corporation**
Study coordination centre:	**Imperial College London**
NRES reference:	**TBC**
Principal Investigators:	**Justin Davies & Javier Escaned**
Study Chairman:	**Manesh Patel**
Medical Lead:	**Sayan Sen**
Steering Committee:	**Eric Van Belle, Farrel Hellig, Raj Kharbanda, Martin Mates, Hitoshi Matsuo, and Nob Tanaka**

Evaluation including cost、complication、procedure time、as well aspt satisfaction

Study design



My standpoint

- Maximum hyperemia is mandatory to measure FFR .
- Diagnostic power of resting index iFR is almost equal to FFR, if both indexes are compared with another physiological golden standard.
- From above reason, maximum hyperemia is not mandatory for the discrimination of ischemia causing stenosis.
- The linkage to clinical event is also mandatory to regard iFR as the easy efficacious physiological index for decision making of revascularization in cath labo.