FFR State of the Art:

Clinical Applications and New Technologies

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Disclosure Statement of Financial Interest

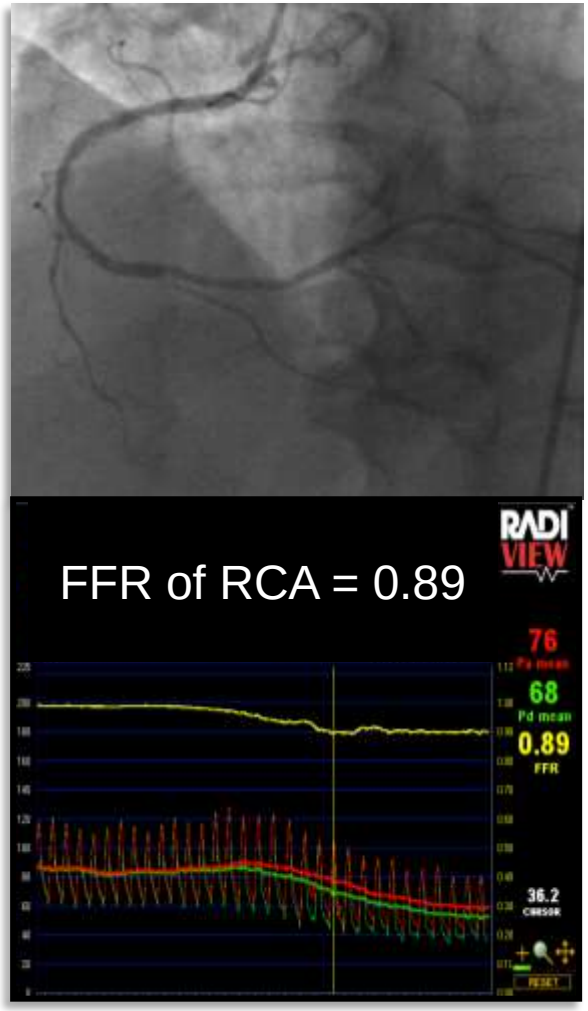
Within the past 12 months, I or my spouse/partner have had a financial interest /arrangement or affiliation with the organization(s) listed below

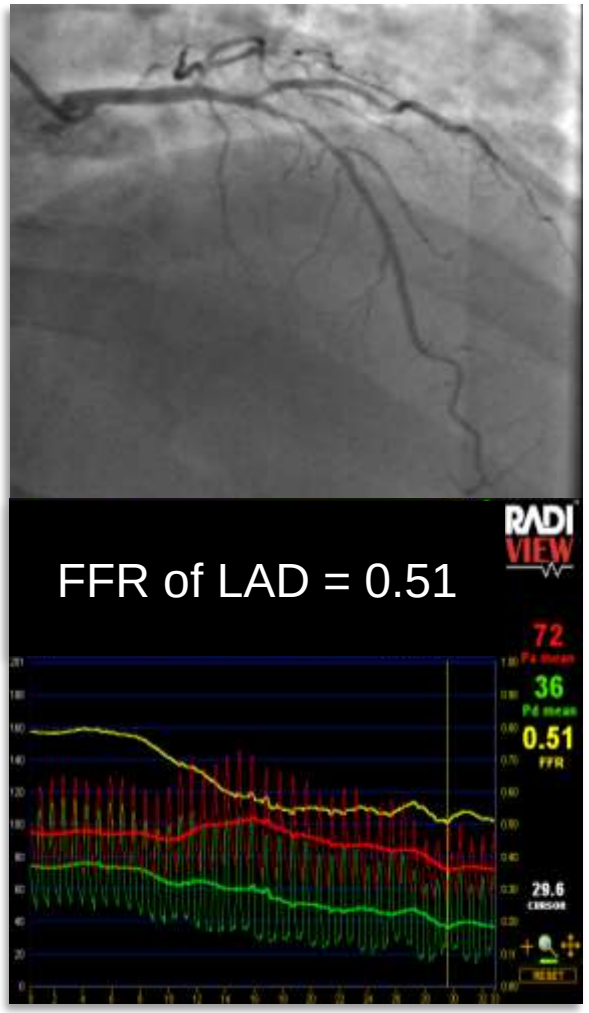
Affiliation/Financial Relationship	Company
Grant/ Research Support:	**St. Jude Medical/Medtronic**
Grant/ Research Support:	**NIH-R01 HL093475 (PI)**
Consulting Fees/Honoraria:	**Medtronic**
Major Stock Shareholder/Equity Interest:	
Royalty Income:	
Ownership/Founder:	
Salary:	**NIH-R01 HL093475 (PI)**
Intellectual Property Rights:	
Other Financial Benefit (minor stock options):	**HeartFlow**

FFR State of the Art:

- Evolving clinical applications
- New techniques/technologies

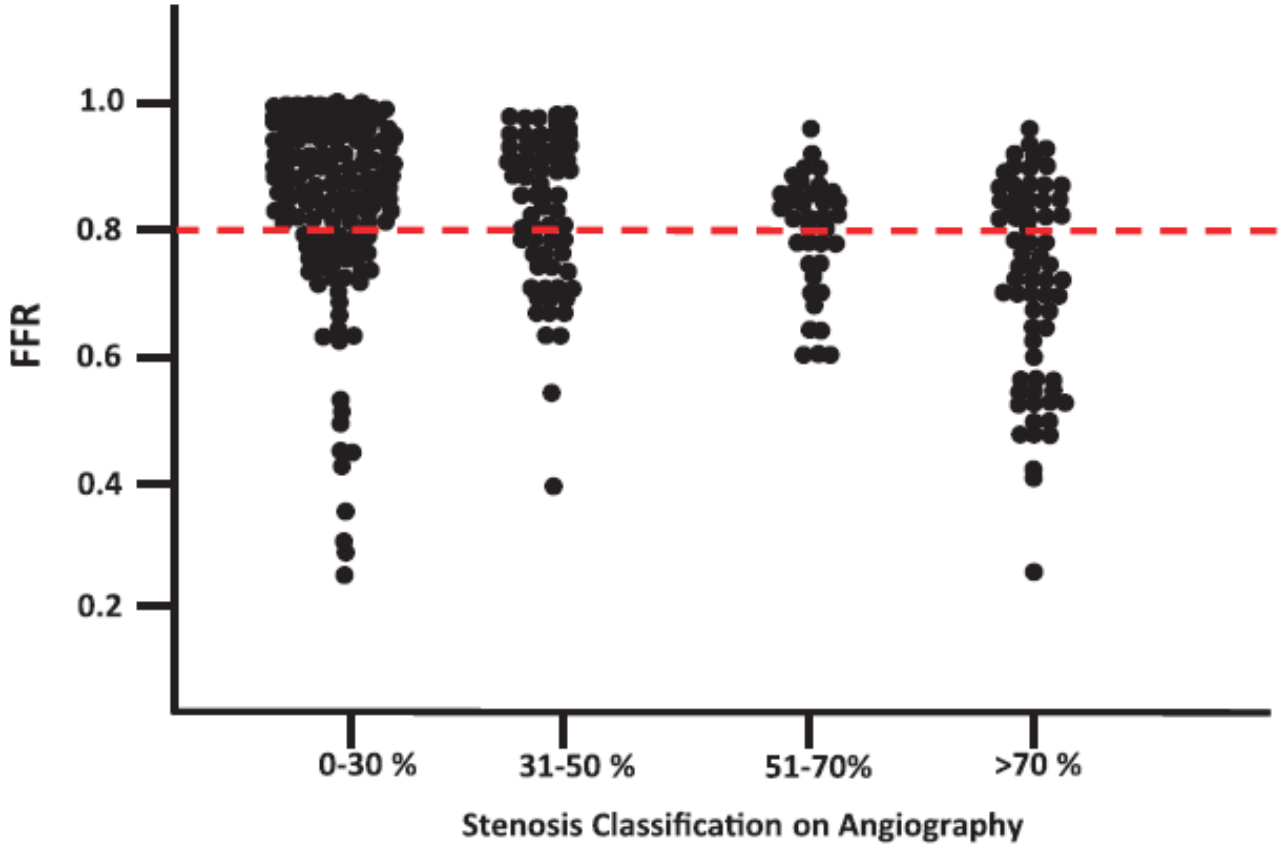
DEFER and FAME





FFR for *All* Angiograms?

200 stable patients referred for coronary angiography underwent routine FFR in all patent vessels. Treatment plan pre and post FFR compared.



Curzen, et al. Circ Cardiovasc Interv 2014;7:248-55.

FFR for *All* Angiograms?

200 stable patients referred for coronary angiography underwent routine FFR in all patent vessels. Treatment plan pre and post FFR compared.

	Post–FFR Decision				
Post–Angiogram Decision	Medical	PCI	CABG	Further Info	Total
Medical	63	6	3	0	72
PCI	24	64	2	0	90
CABG	1	3	19	0	23
Further info	1	7	6	1	15
Total	89	80	30	1	200

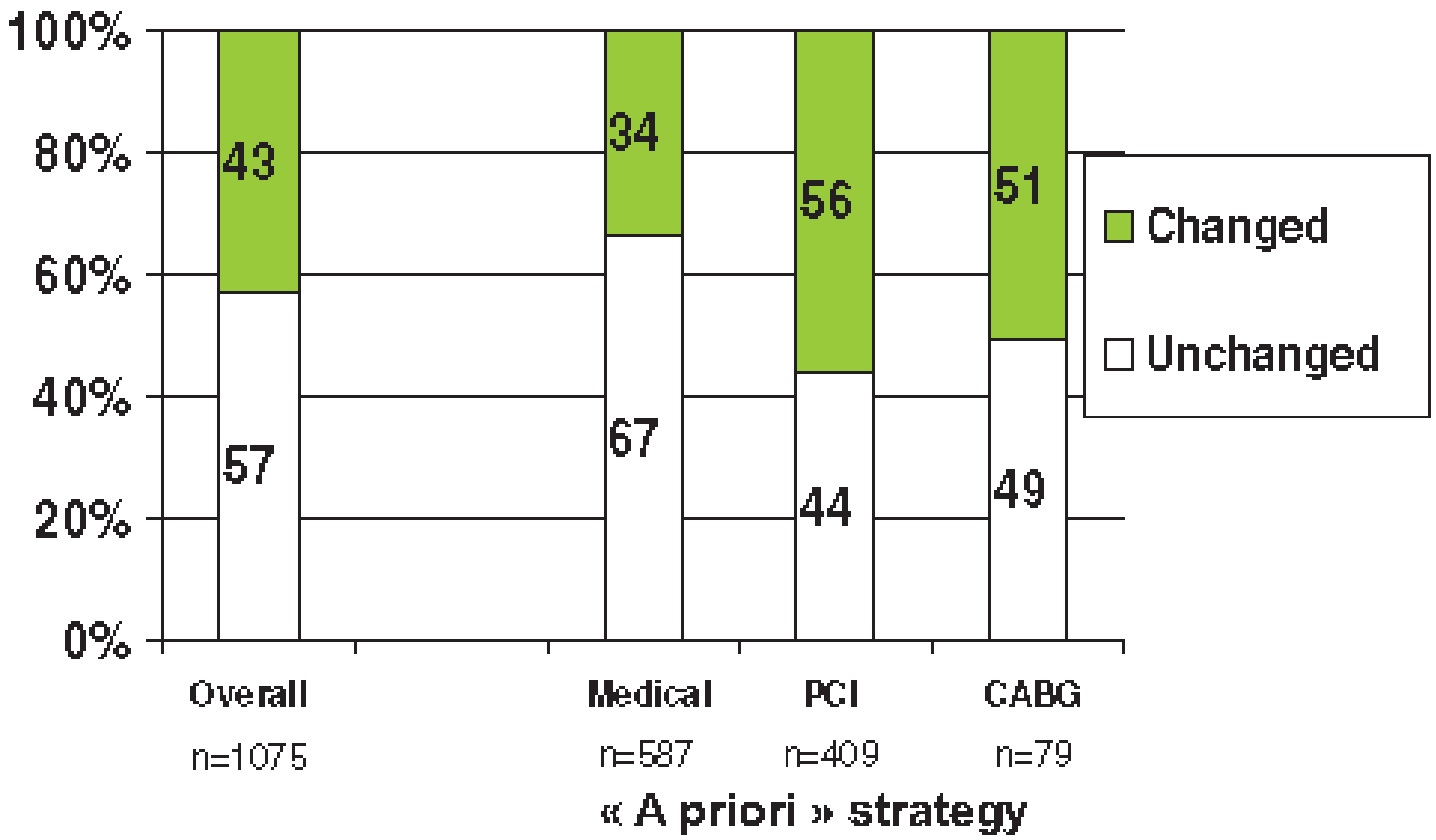
$P<0.001$ by McNemar test. CABG indicates coronary artery bypass grafting; FFR, fractional flow reserve; and PCI, percutaneous coronary intervention.

Overall the management plan was changed in 26% of cases.

Curzen, et al. Circ Cardiovasc Interv 2014;7:248-55.

FFR for *All* Angiograms?

1,075 consecutive patients undergoing FFR at 20 French centers

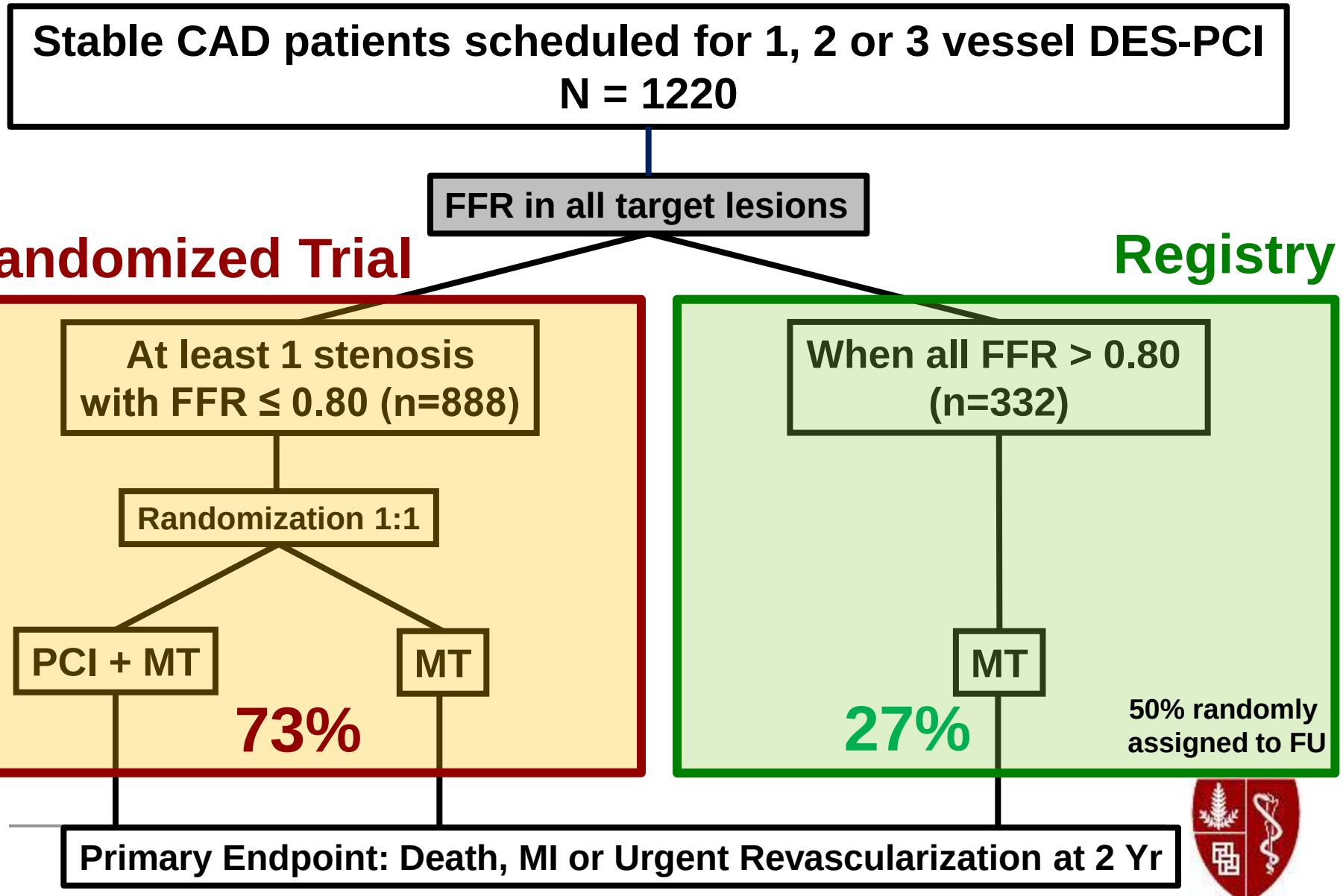


Van Belle, et al. Circulation 2014;129:173-185.

FFR for *All* Angiograms?

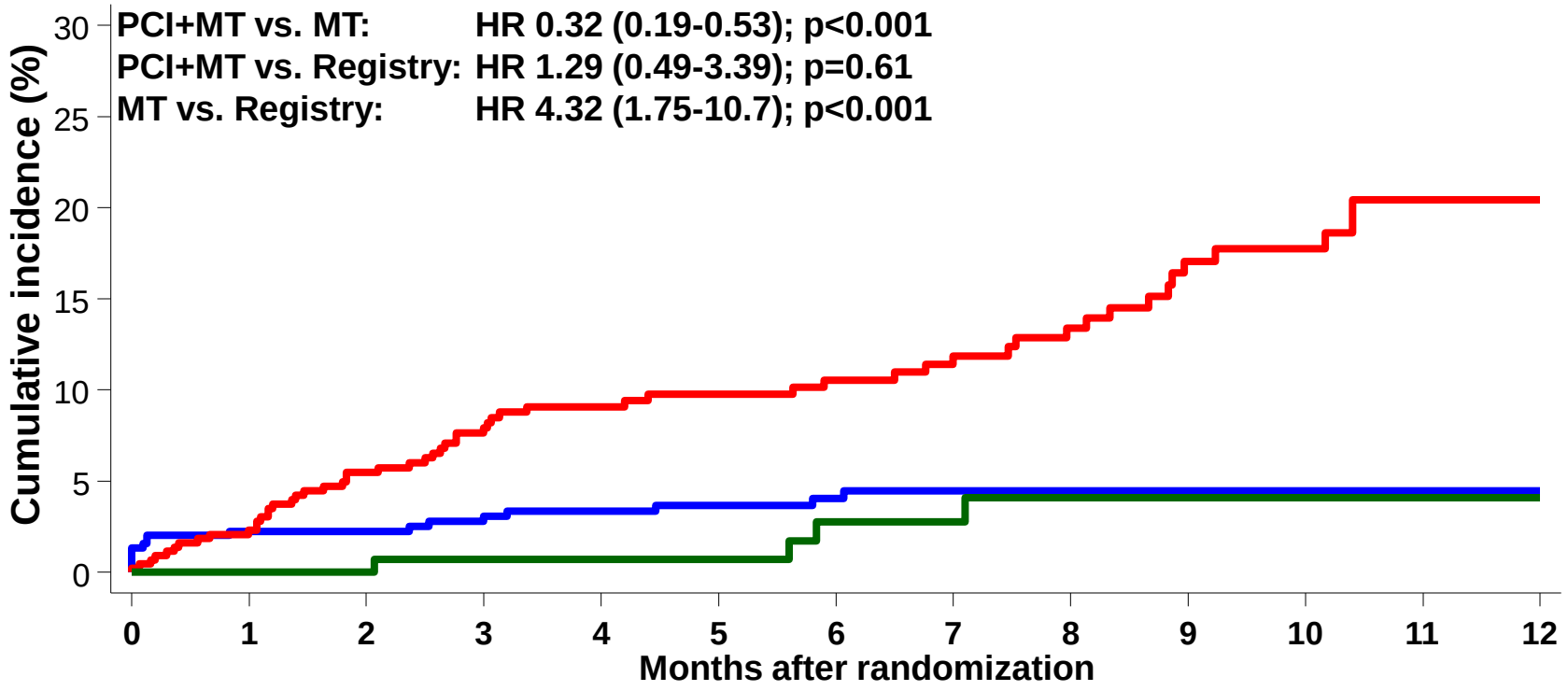
- These studies suggest that even broader application of FFR measurement is warranted.

FAME 2


Stable CAD patients scheduled for 1, 2 or 3 vessel DES-PCI
N = 1220
FFR in all target lesions
Randomized Trial
Registry
At least 1 stenosis with FFR ≤ 0.80 (n=888)
Randomization 1:1
PCI + MT
MT
73%
When all FFR > 0.80 (n=332)
MT
27%
50% randomly assigned to FU
Primary Endpoint: Death, MI or Urgent Revascularization at 2 Yr

FAME 2: *Initial Results*

Primary Endpoint: Death, MI, Urgent Revascularization



No. at risk

MT	441	414	370	322	283	253	220	192	162	127	100	70	37
PCI+MT	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

De Bruyne, et al. New Engl J Med 2012;367:991-1001

FAME 2: *Two Year Follow-Up*

Variable	PCI (N=447)	Medical Therapy (N=441)	Hazard Ratio (95% CI)†	P Value‡
	no. (%)			
Primary end point	36 (8.1)	86 (19.5)	0.39 (0.26–0.57)	<0.001
Death from any cause	6 (1.3)	8 (1.8)	0.74 (0.26–2.14)	0.58
Myocardial infarction	26 (5.8)	30 (6.8)	0.85 (0.50–1.45)	0.56
Urgent revascularization	18 (4.0)	72 (16.3)	0.23 (0.14–0.38)	<0.001
Death or myocardial infarction	29 (6.5)	36 (8.2)	0.79 (0.49–1.29)	0.35

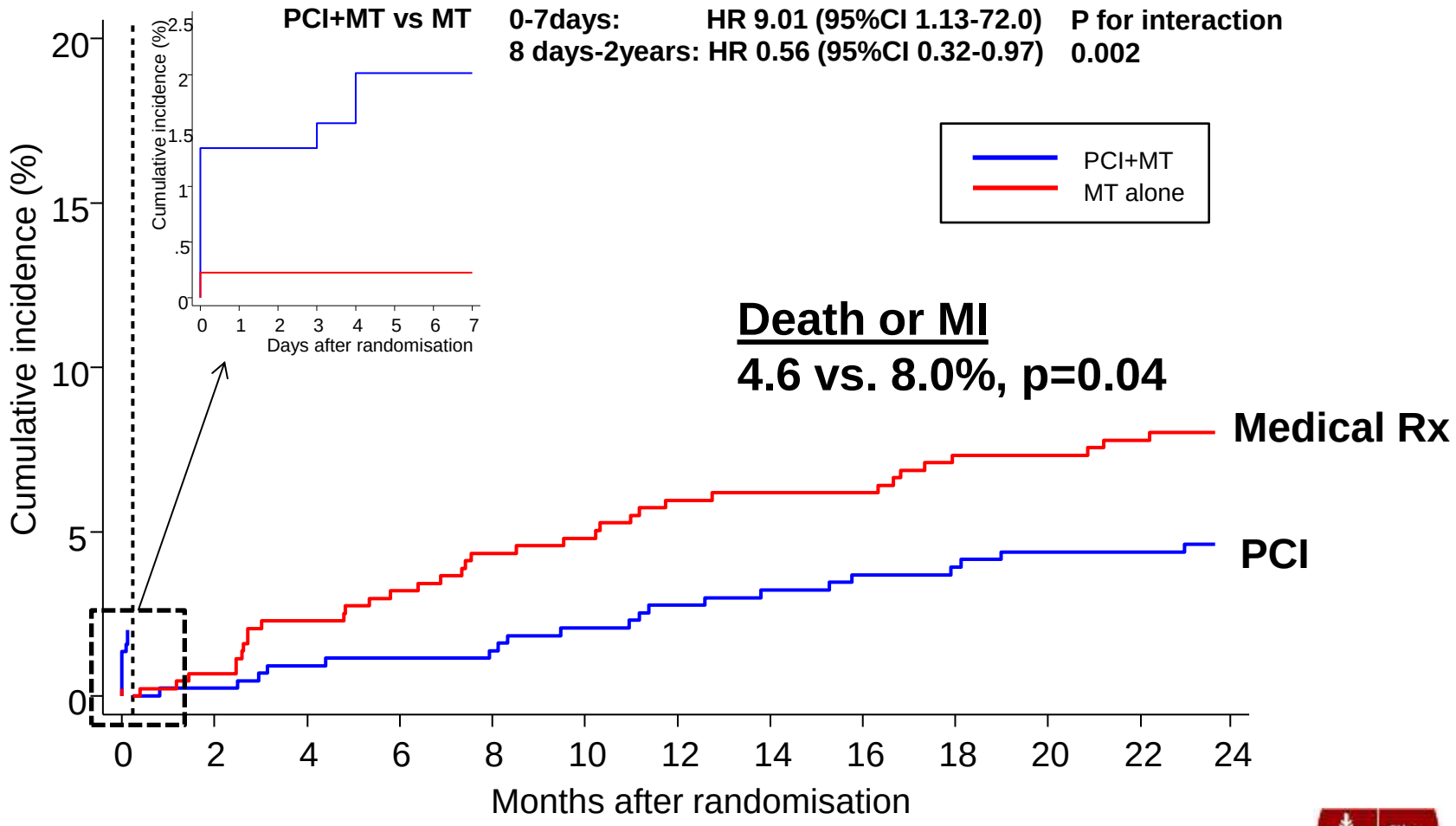
51% of urgent revascularizations were triggered by myocardial infarction or ischemic ECG changes (3.4 vs 7.0%, p=0.01, PCI vs OMT)

>80% of urgent revascularizations were triggered by myocardial infarction, ischemic ECG changes, or Class IV angina

De Bruyne, et al. New Engl J Med 2014;371:1208-17.

FAME 2: *Two Year Follow-Up*

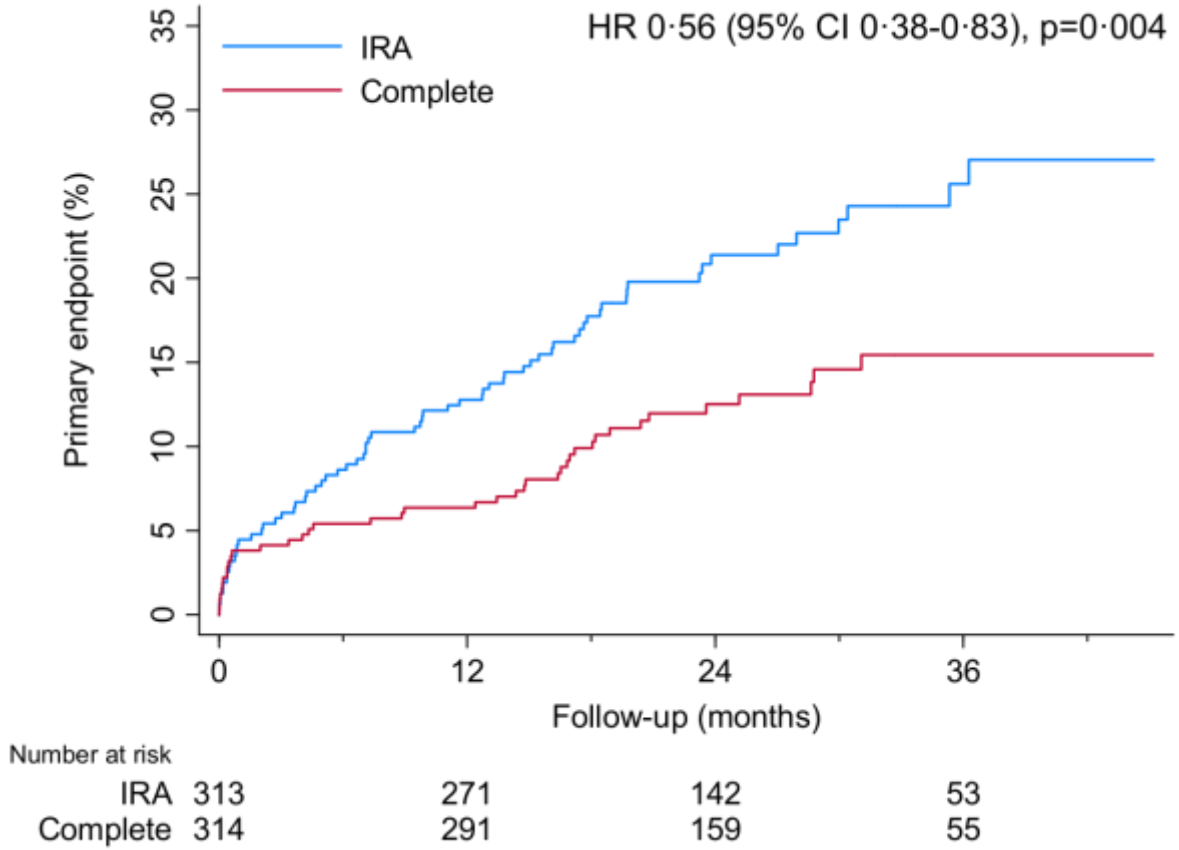
Landmark Analysis of Death/MI after 7 days



De Bruyne, et al. New Engl J Med 2014;371:1208-17.

Non-Culprit PCI in STEMI?

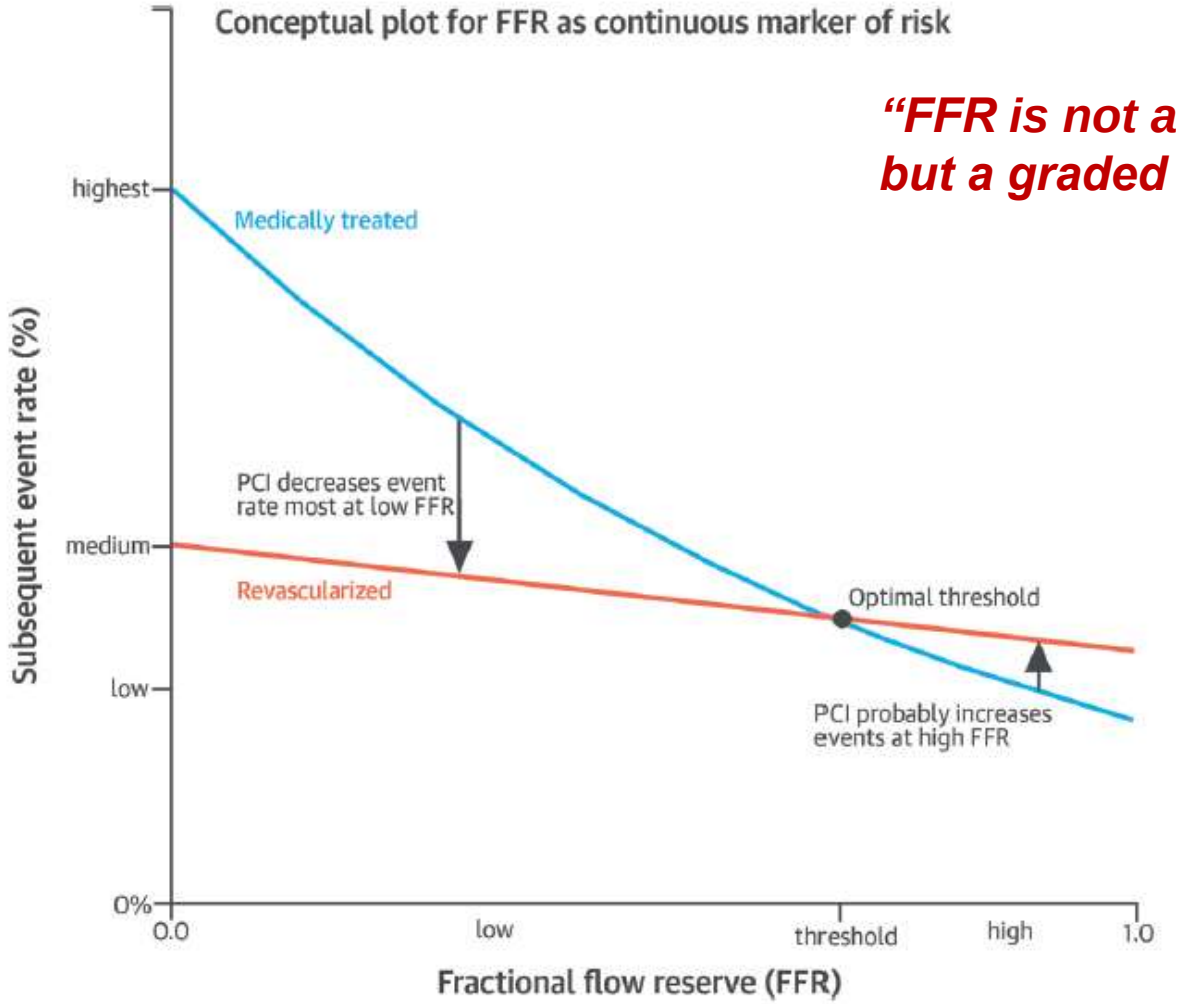
DANAMI-3-PRIMULTI Trial: 627 STEMI patients with MVD randomized to culprit only PCI vs. culprit PCI and FFR-guided non-culprit PCI



Composite of death, MI, ischemia driven revascularization of non-culprit

Engstrom T, et al. ACC 2015

FFR Meta-Analysis



"FFR is not a dichotomous state, but a graded continuum"

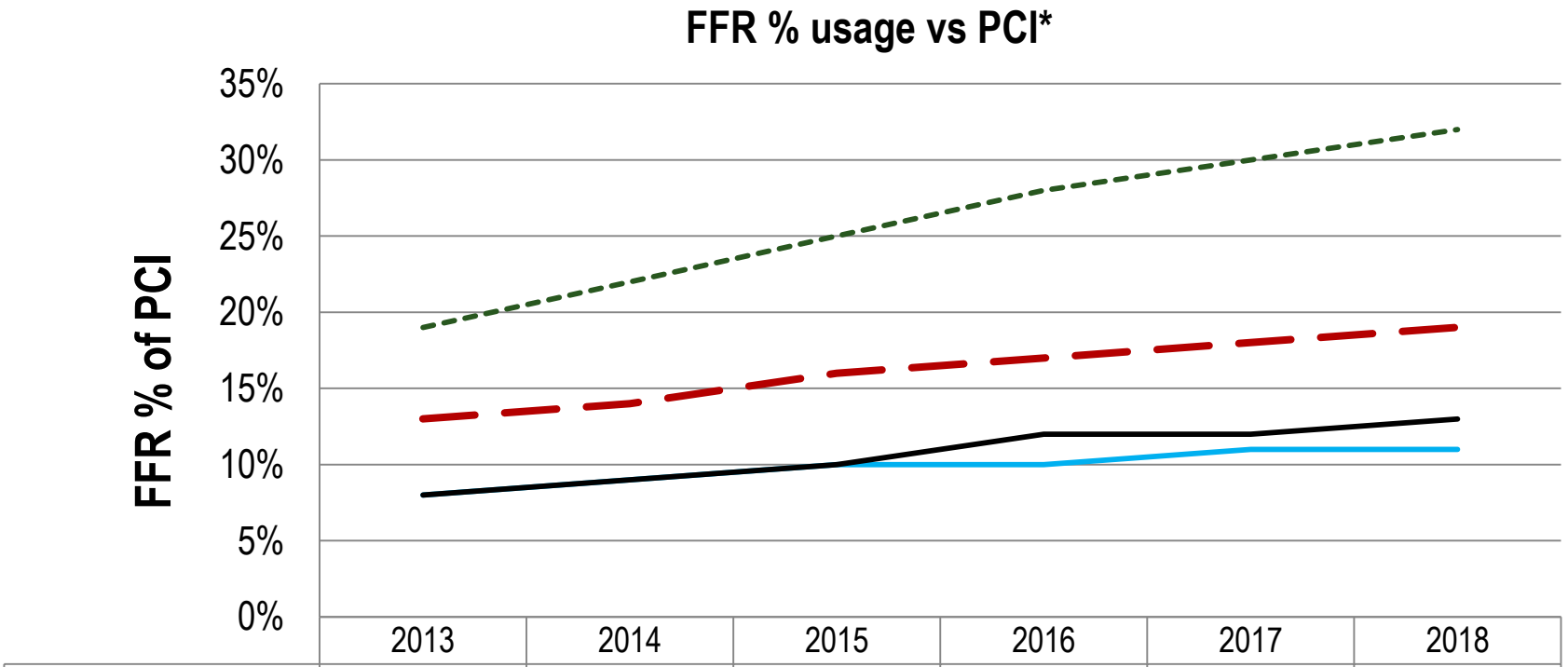
Johnson, et al. J Am Coll Cardiol 2014;64:1641-54.

FFR State of the Art:

- Evolving clinical applications
- New techniques/technologies

FFR Adoption

Worldwide Annual Coronary Pressure Wire Use

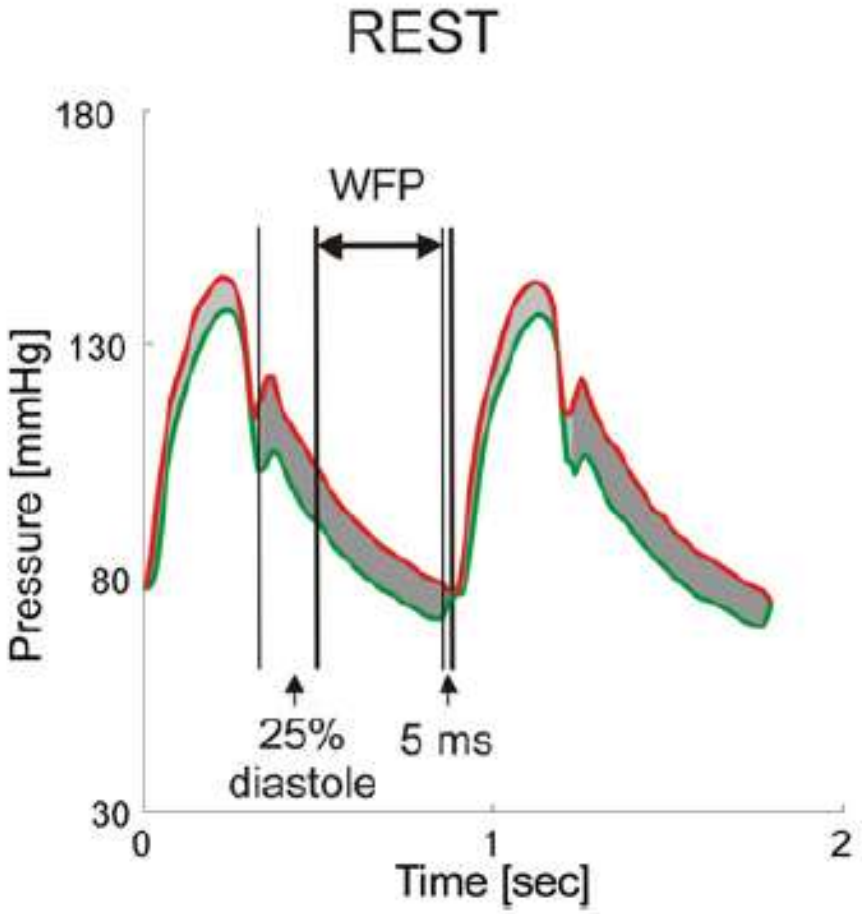


	2013	2014	2015	2016	2017	2018
US	19%	22%	25%	28%	30%	32%
Europe	8%	9%	10%	10%	11%	11%
Japan	8%	9%	10%	12%	12%	13%
WW (US,JPN,EU)	13%	14%	16%	17%	18%	19%

Total number of FFR Procedures divided by number of PCI
Source: Millennium Research Group (2013-2015)

Eliminating Adenosine:

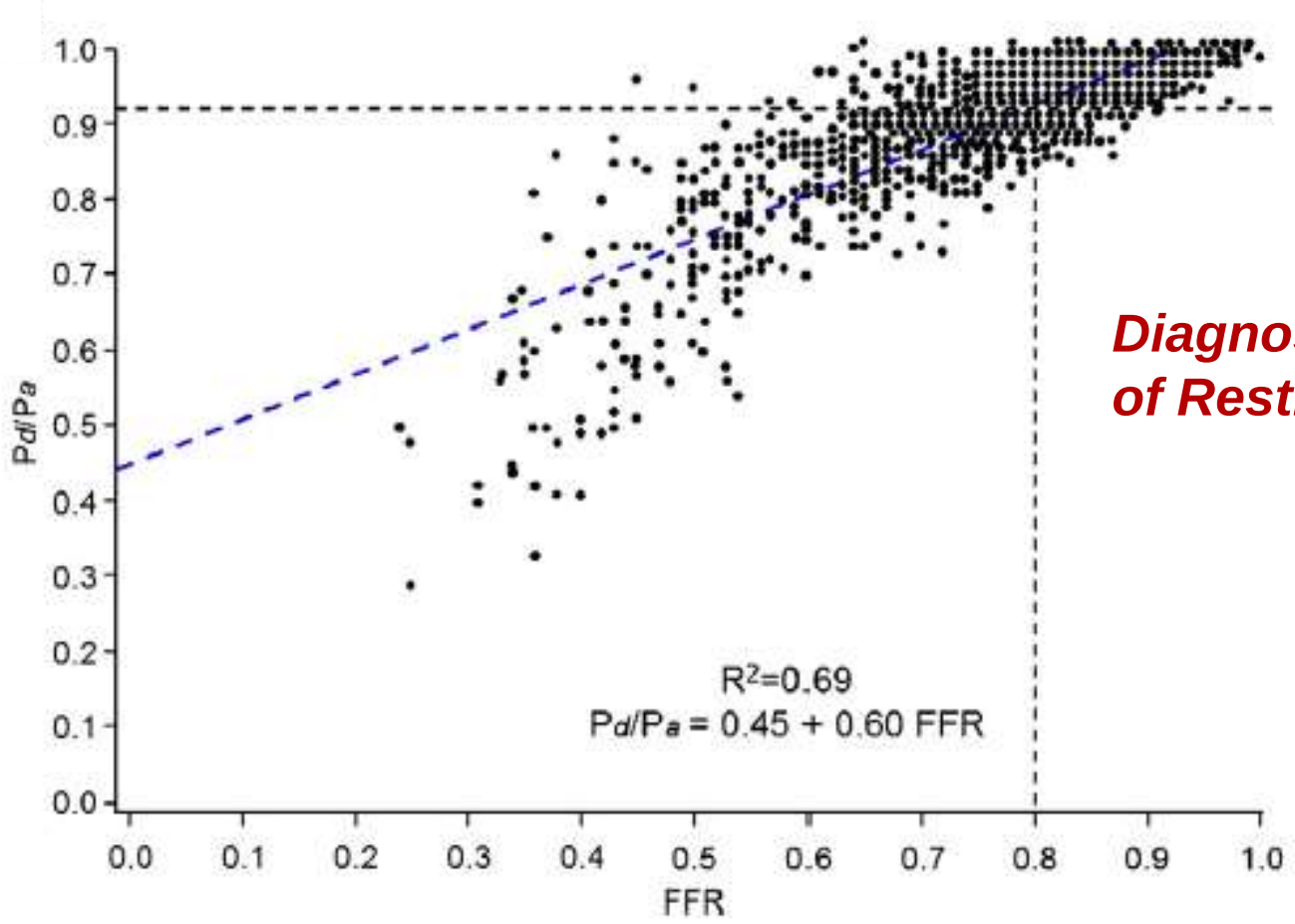
iFR and Resting P_d / P_a



Berry, et al. J Am Coll Cardiol 2013;61:1421-7.

RESOLVE Study:

Resting P_d/P_a, iFR and FFR were measured in 1,678 patients



Diagnostic Accuracy of Resting P_d/P_a = 81.5%

Jeremias, et al. J Am Coll Cardiol 2014;63:1253-61.

RESOLVE Study:

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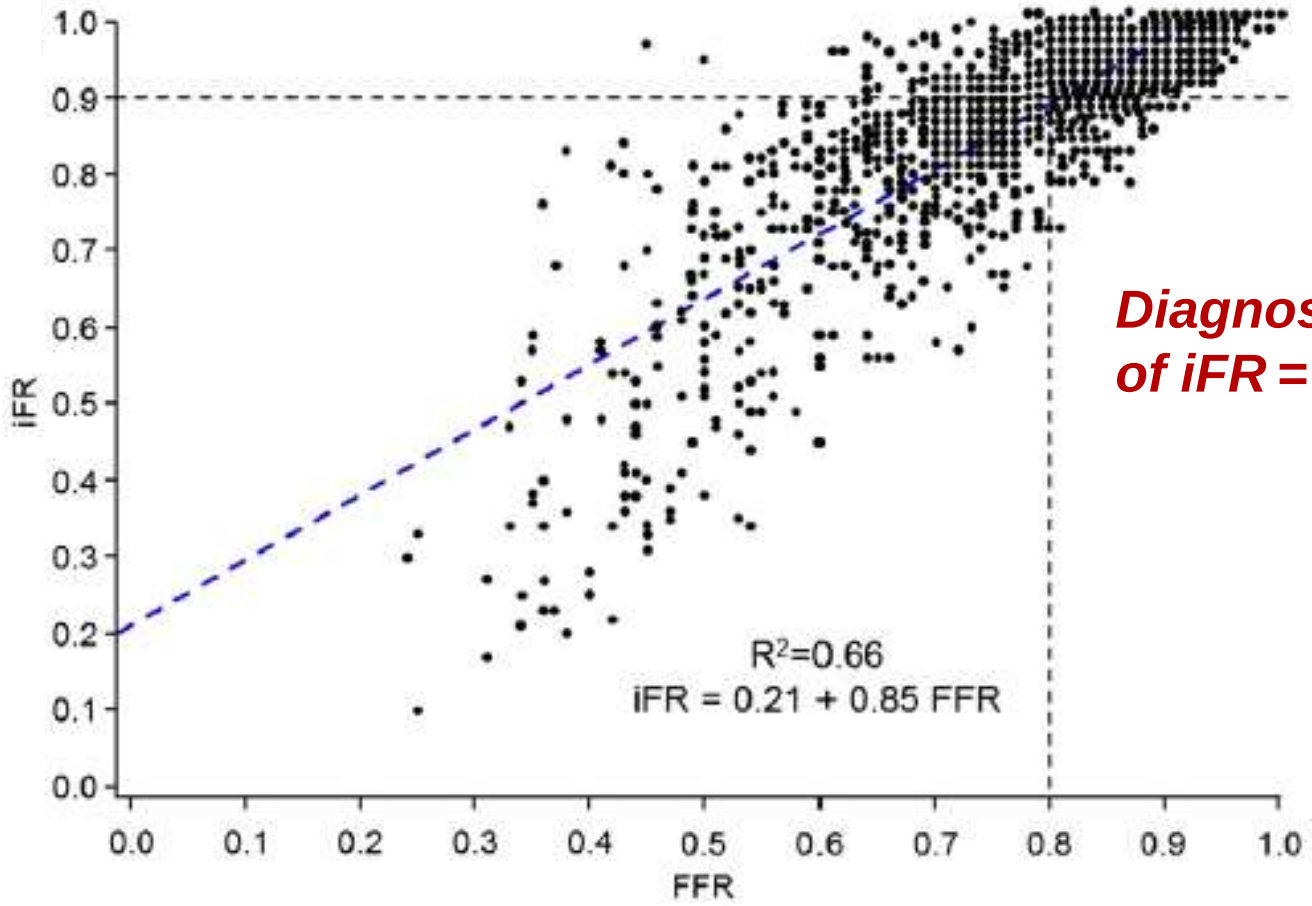


Diagnostic Accuracy of iFR = 80.4%

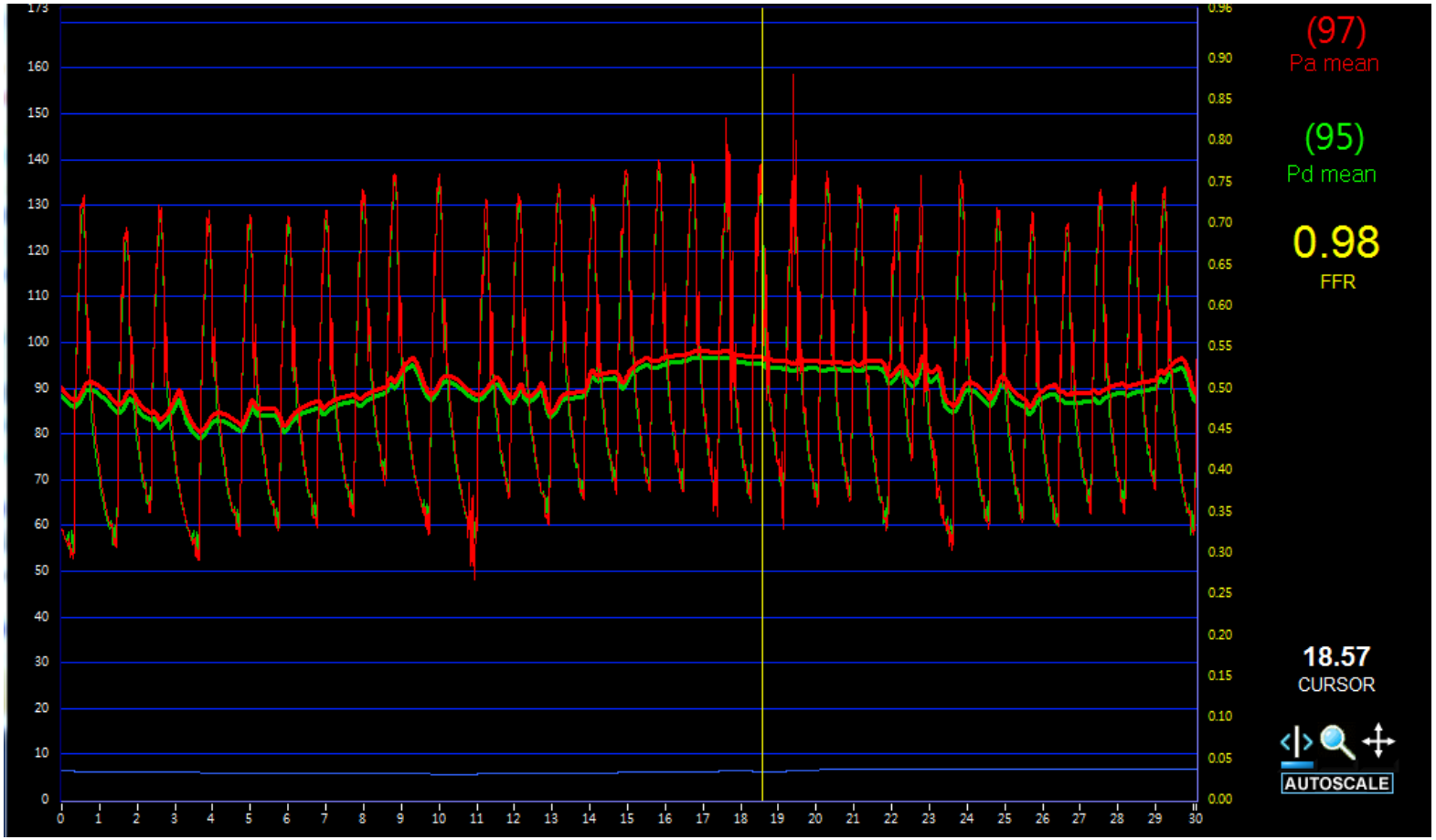
Jeremias, et al. J Am Coll Cardiol 2014;63:1253-61.

How about “contrast” FFR (cFFR)?

Can contrast media replace adenosine for FFR measurement?

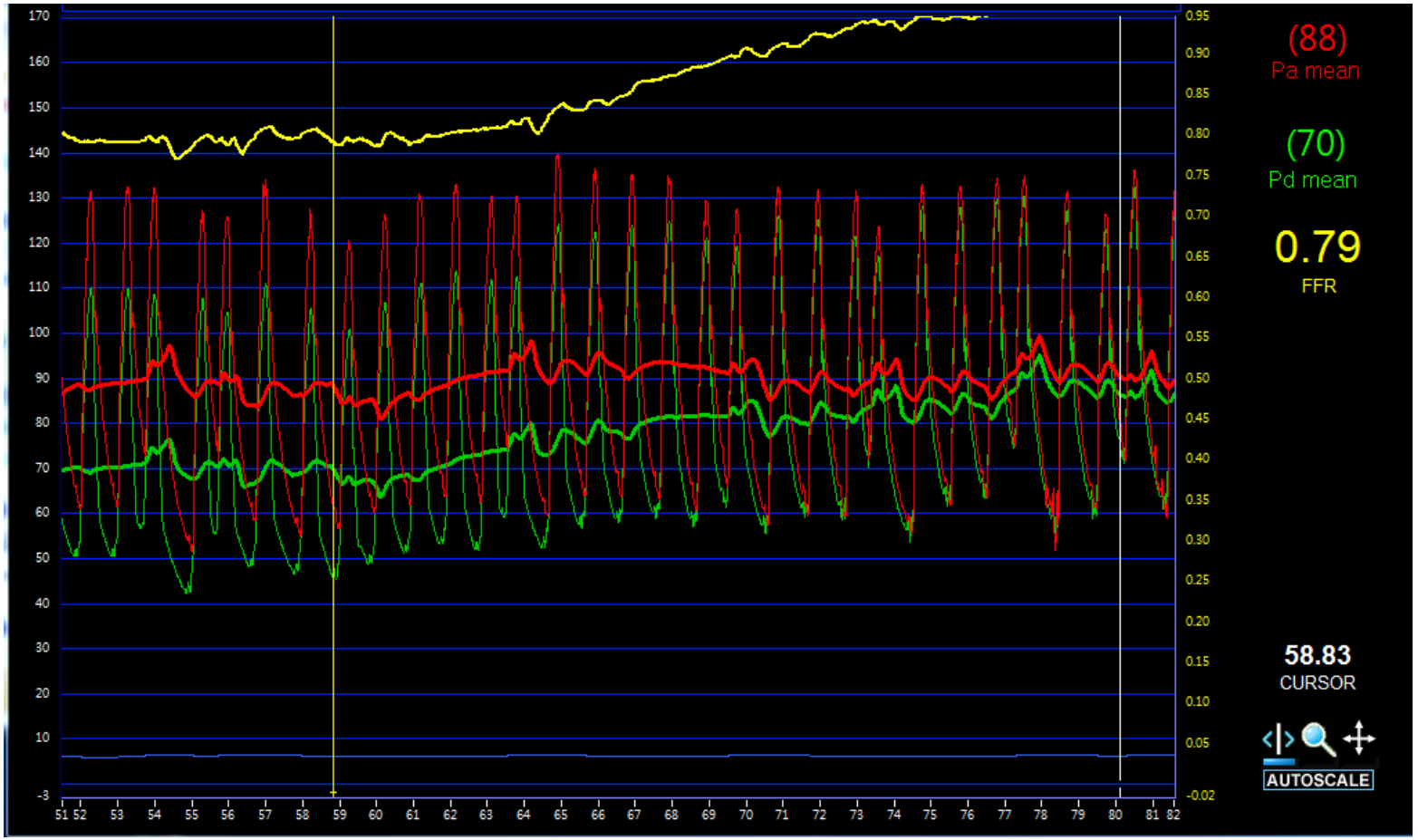
How about “contrast” FFR (cFFR)?

Resting P_d/P_a = 0.98 and iFR ≈ 0.95 across moderate circumflex lesion



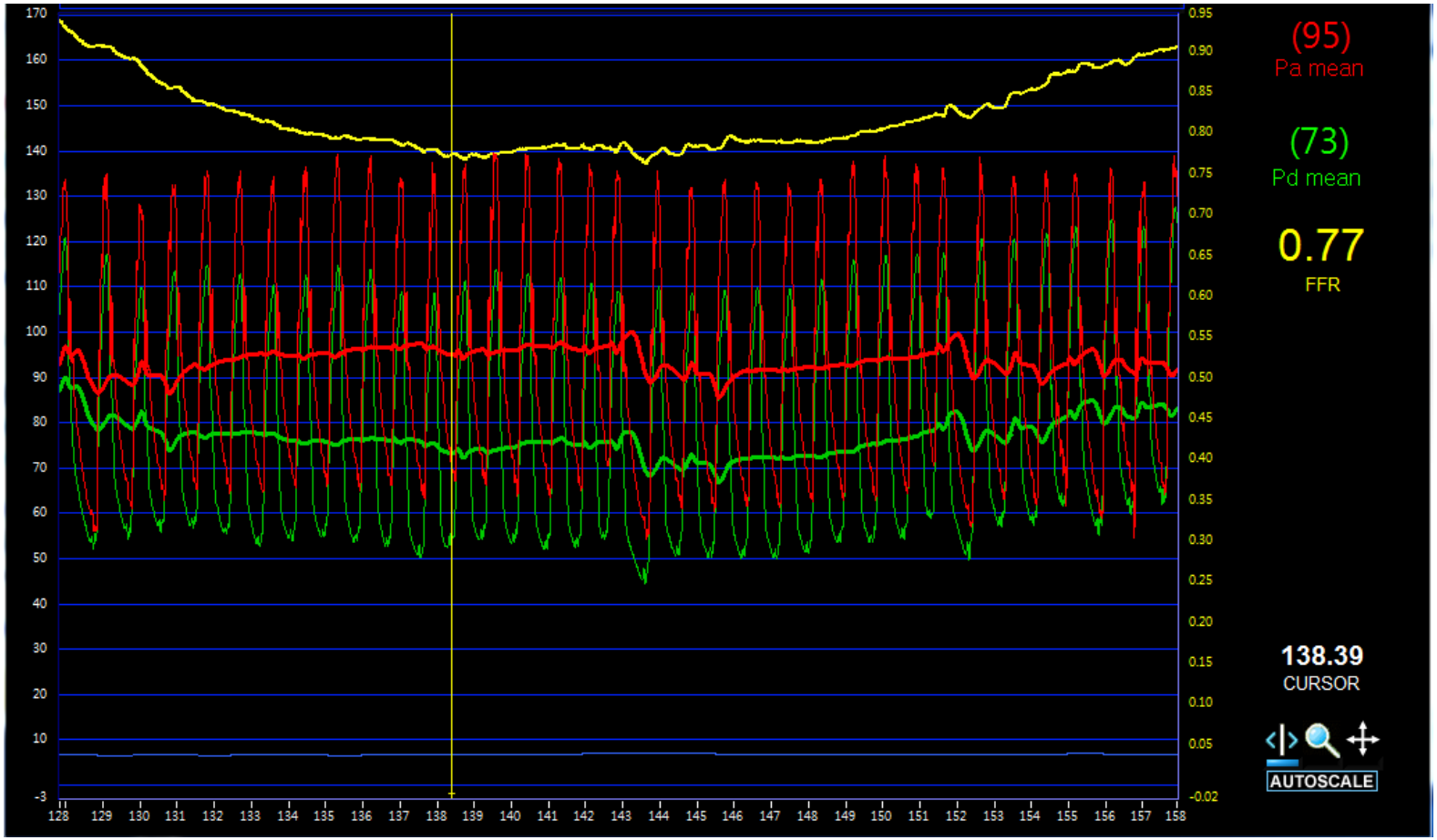
How about “contrast” FFR (cFFR)?

cFFR = 0.79 (6 ml Isovue) across moderate circumflex lesion



How about “contrast” FFR (cFFR)?

FFR = 0.77 (240 mcg IC Adenosine) across moderate circumflex lesion

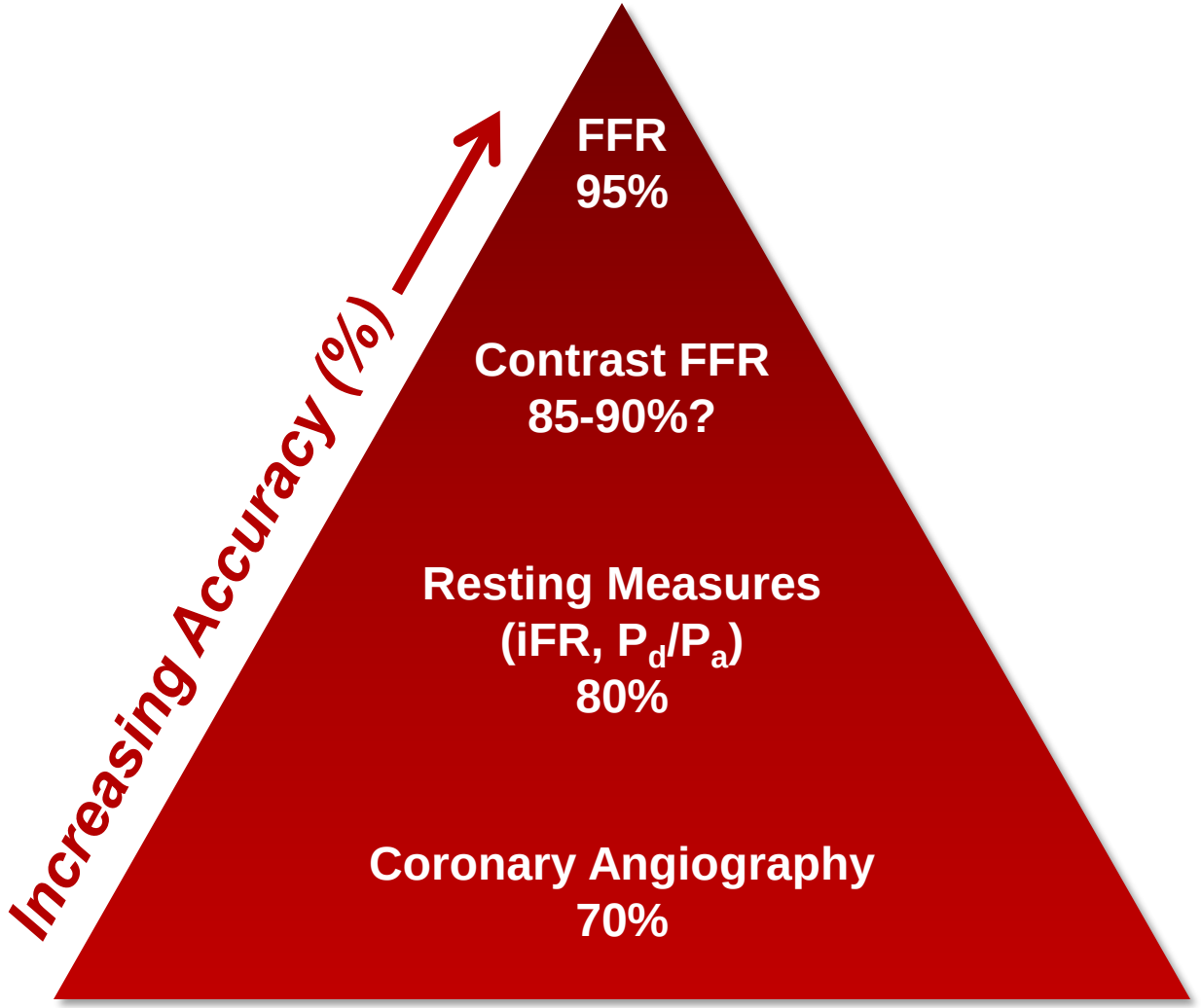


CONTRAST Study:

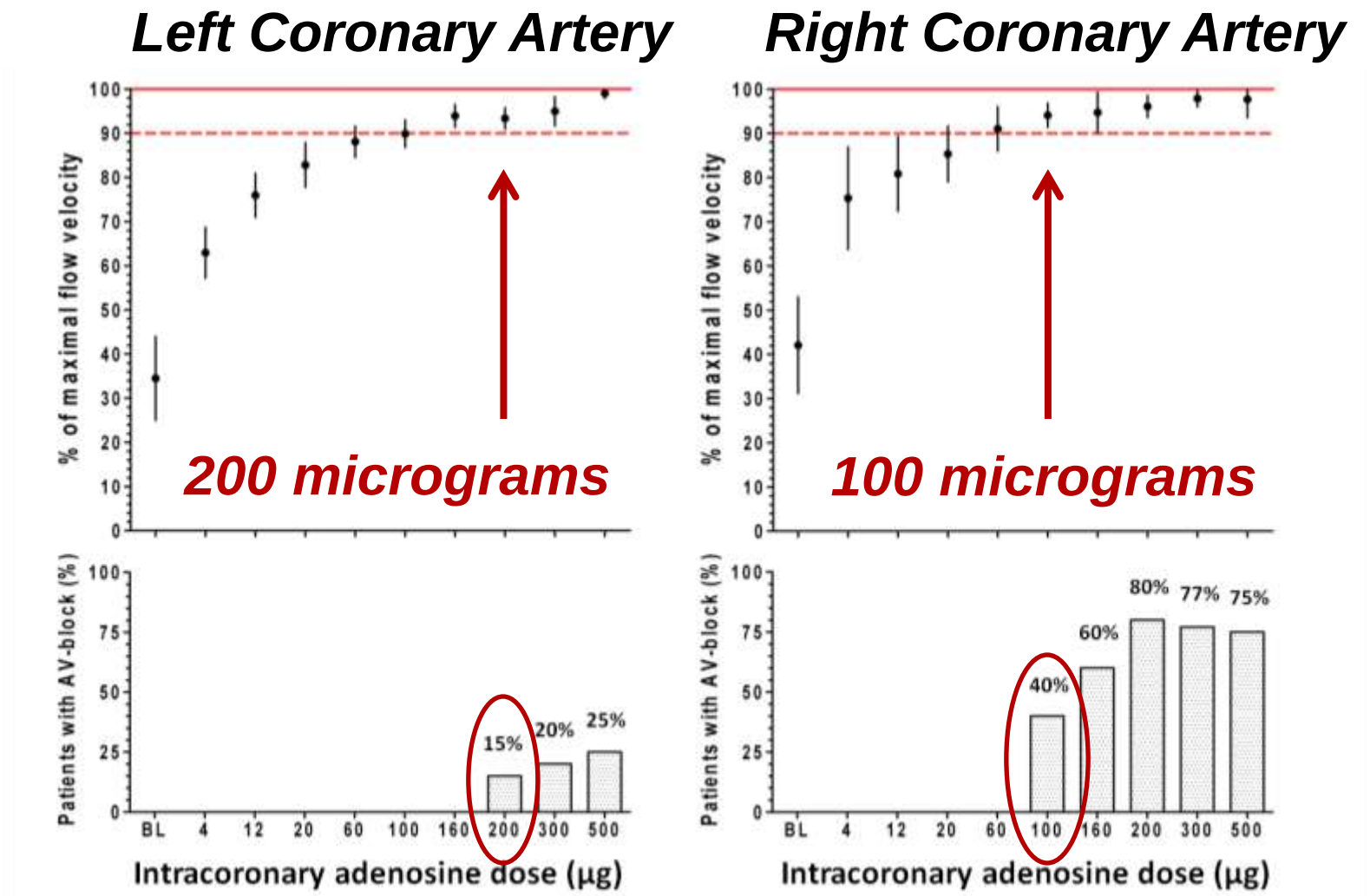
- Comparison of FFR with IV or IC adenosine to: cFFR, Resting P_d/P_a and iFR
- Multicenter, international trial including 750 patients (1 lesion/patient)
- Blinded, independent core lab
- Results to be presented at the Late Breaking Trial session at EuroPCR, May 2015

ClinicalTrials.gov Identifier: NCT02184117

Diagnosing Ischemia in the Cath Lab



Optimal Intracoronary Adenosine Dose?



Adjedj, et al. JACC Intervent 2015;in press.

New FFR Devices:

POLARIS Display

Wireless Bedside

Disposable Cable

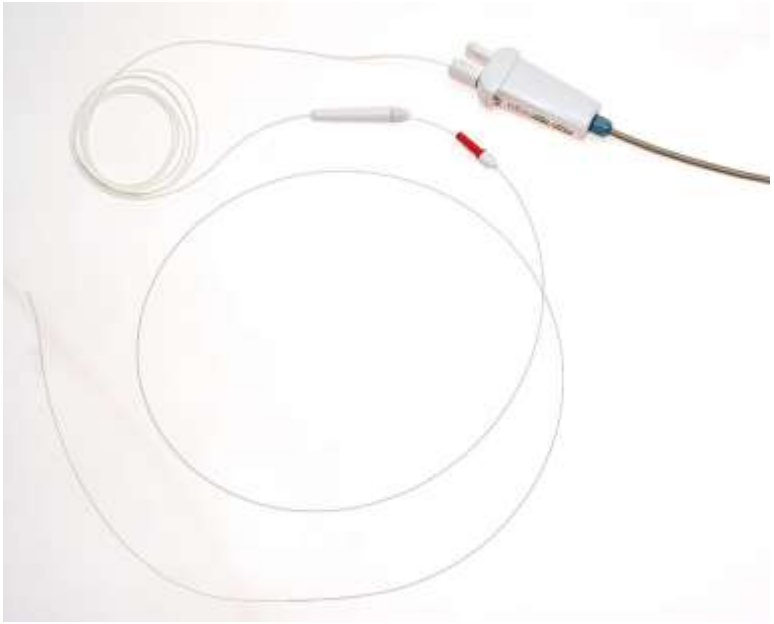
FFR Wire

Design Goals

- Integrated POLARIS display
- Wireless from bed-to-POLARIS
- Targeting improved wire performance
  - Workhorse-like feel
  - "Invisible" connection
  - Accurate (no drift)
  - Reliable (re)connection

Courtesy: Boston Scientific

New FFR Devices:

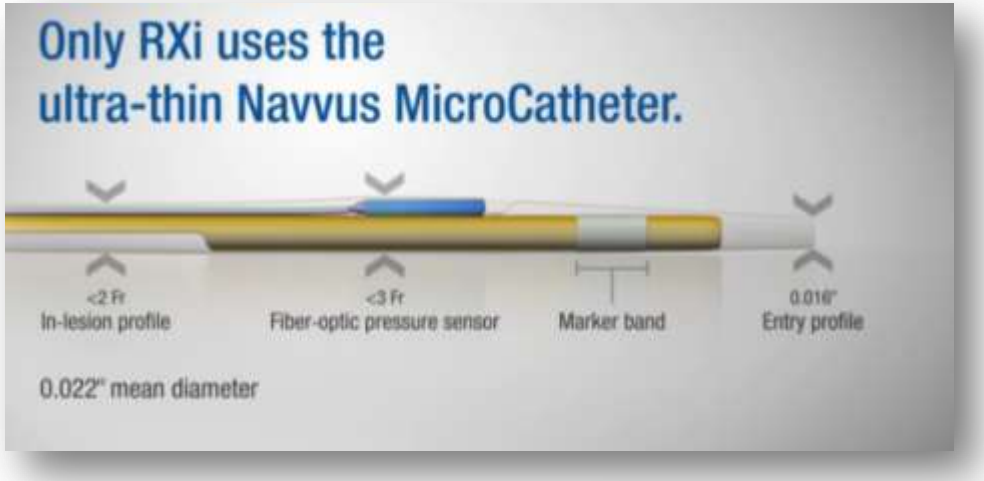


Optowire

Optomonitor

Opsensmedical.com

New FFR Devices:



Conclusions:

- Indications for fractional flow reserve measurement continue to evolve to include more routine assessment and to include ACS patients.

- Evolving techniques and new technology aim to simply and streamline FFR measurement.