Imaging and Physiology Summit
Seoul, Korea, November 22, 2008

Fractional Flow Reserve and the 1 Year Results of the FAME Study

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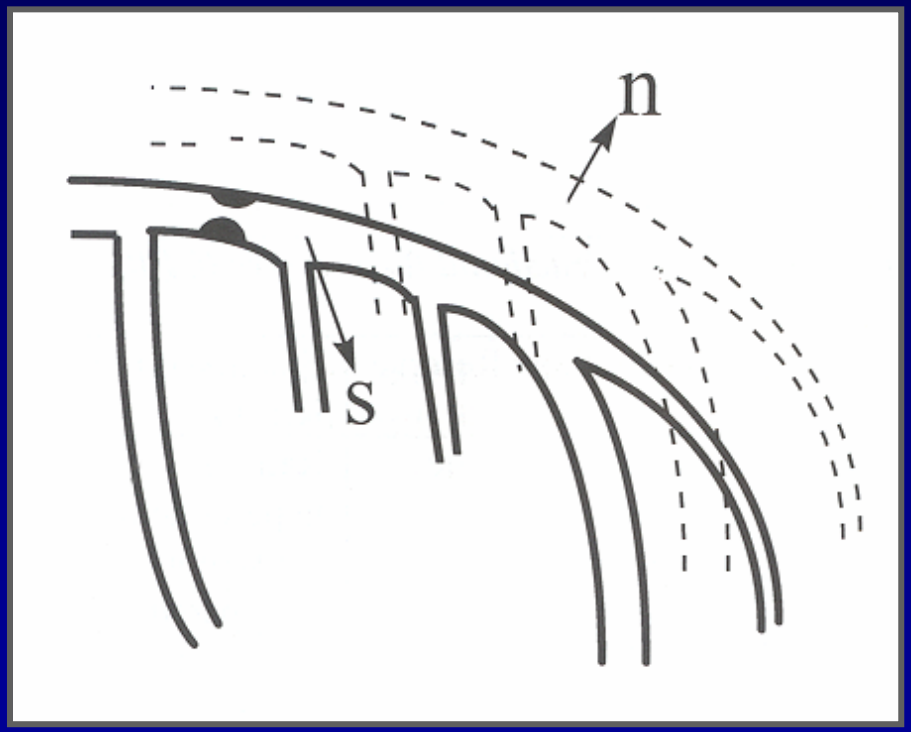
Fractional Flow Reserve (FFR)

Maximum flow down a vessel in the presence of a stenosis…

…compared to the maximum flow in the hypothetical absence of the stenosis



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

Derivation of FFR

- $\text{FFR} = \dfrac{\text{Coronary Flow (Stenosis)}}{\text{Coronary Flow (Normal)}}$
- $\text{Coronary Flow} = \dfrac{\text{Pressure}}{\text{Resistance}}$
- *at maximal hyperemia* $\text{Coronary Flow} \approx \text{Pressure}$

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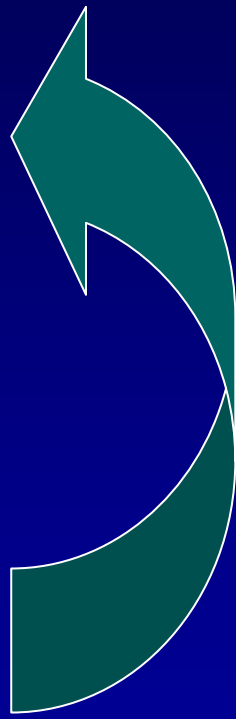

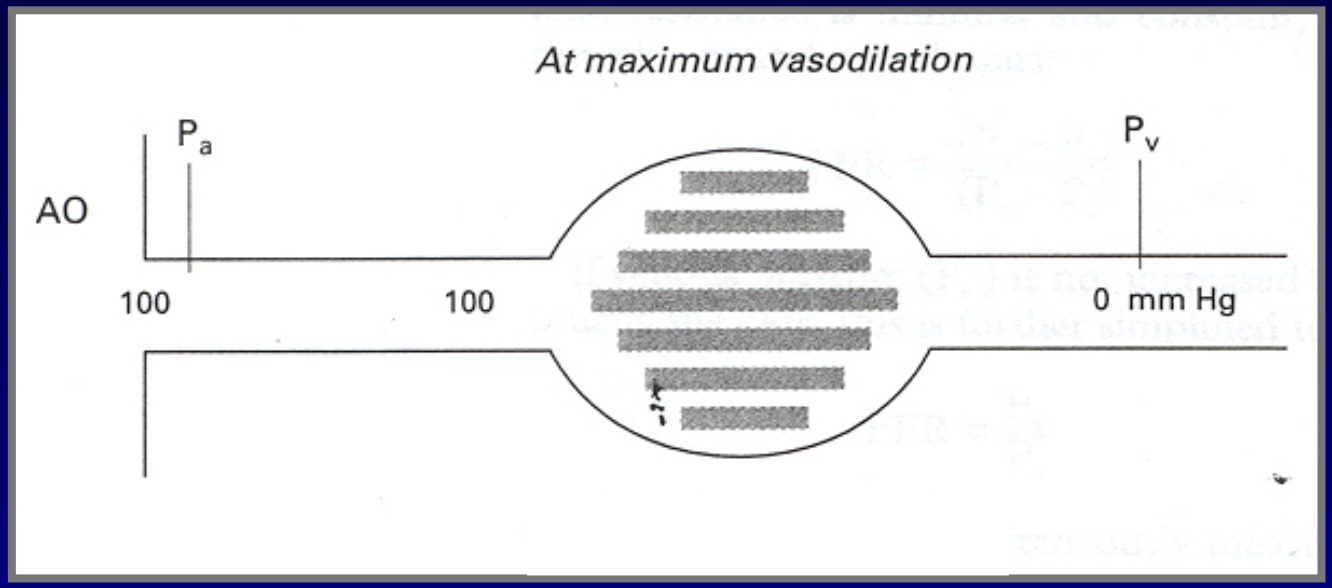

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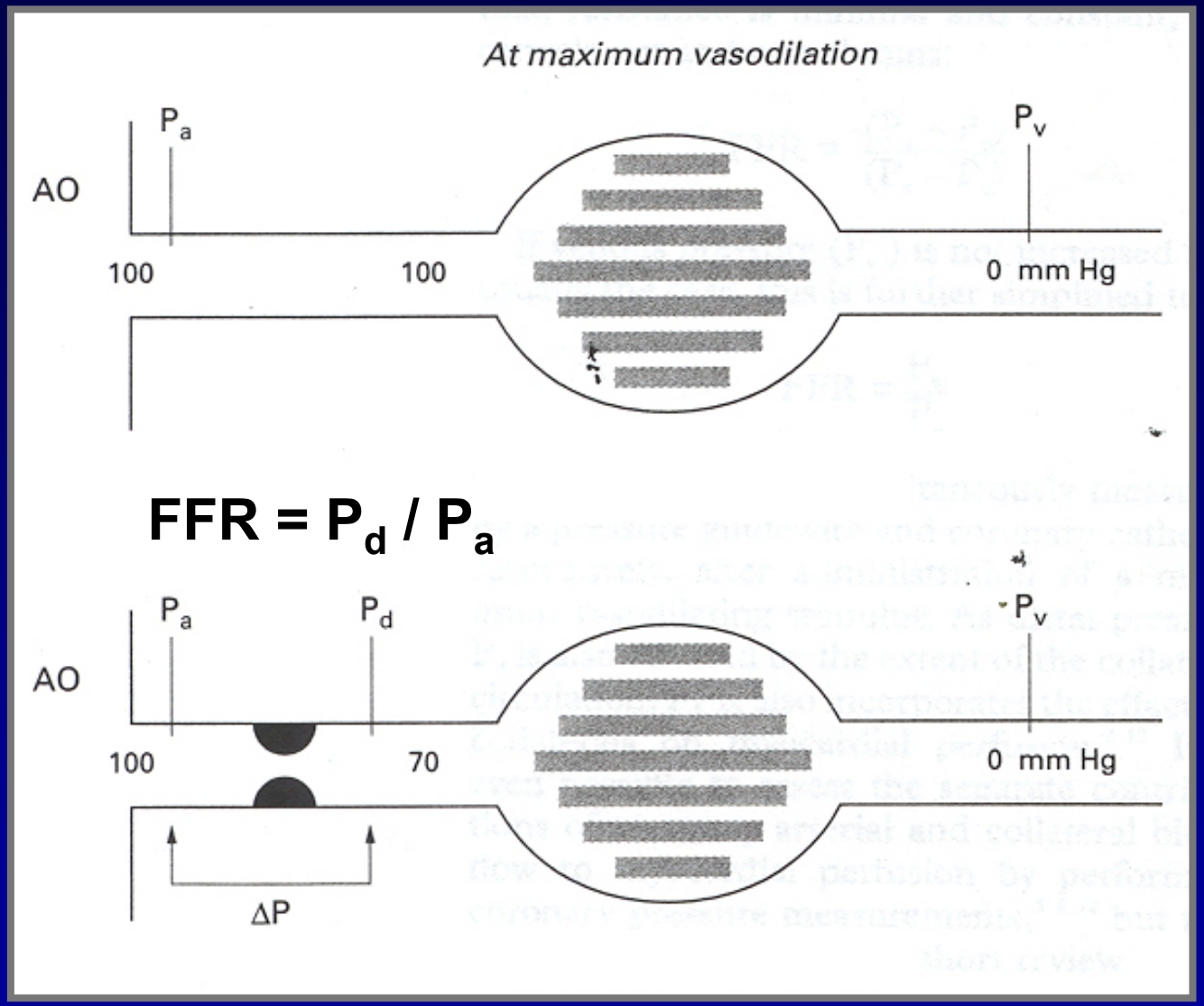

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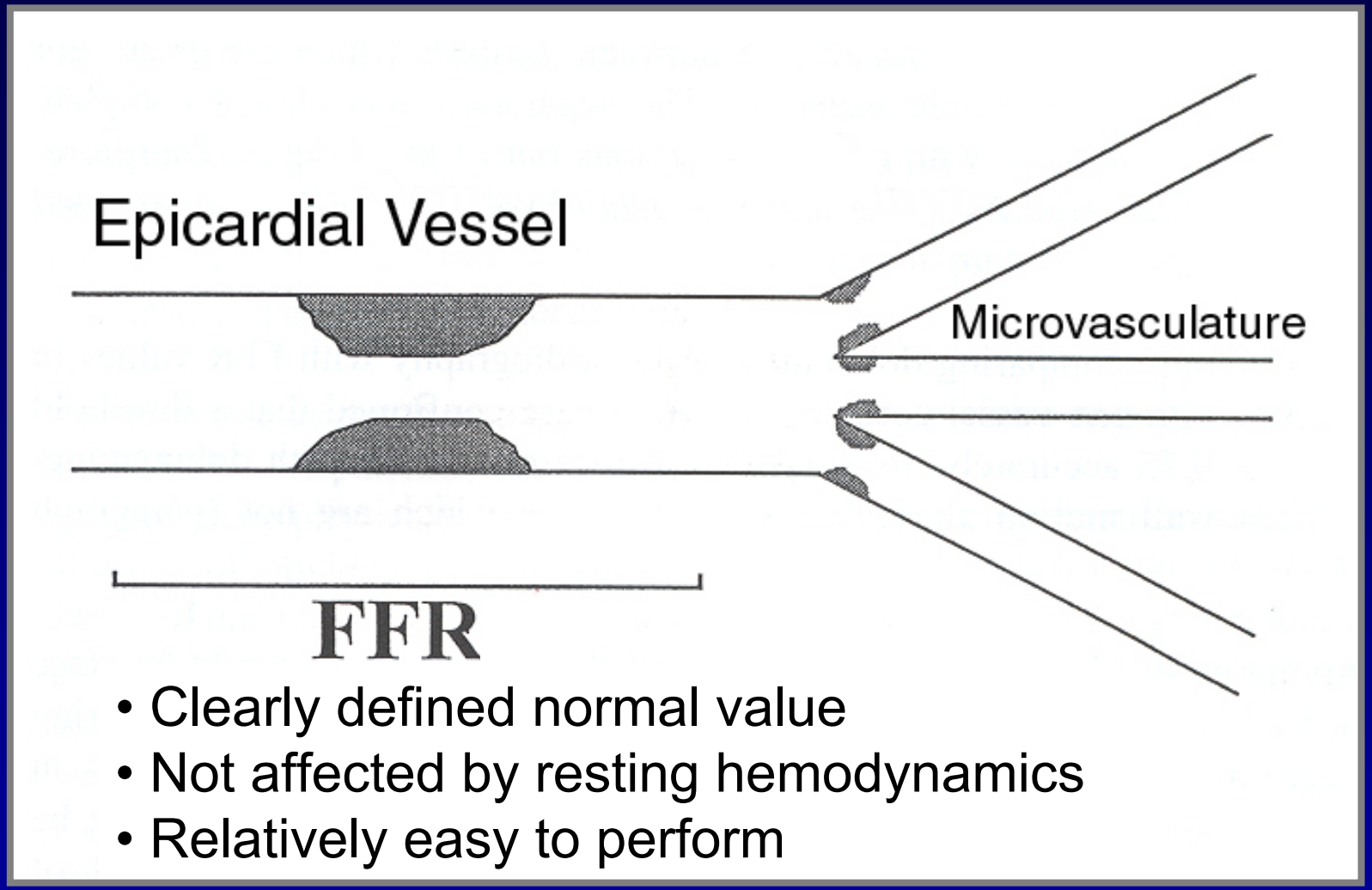


- Clearly defined normal value
- Not affected by resting hemodynamics
- Relatively easy to perform

Adapted from: Pijls and De Bruyne, Coronary Pressure
Kluwer Academic Publishers, 2000

Fractional Flow Reserve

versus

Angiography for

Multivessel

Evaluation

FRACTIONAL FLOW RESERVE *versus* ANGIOGRAPHY FOR GUIDING PCI IN PATIENTS WITH MULTIVESSEL CORONARY ARTERY DISEASE

Late Breaking Trial at
TCT, October 14th , 2008

Nico H.J.Pijls, MD, PhD
Catharina Hospital, Eindhoven
The Netherlands,
on behalf of the ***FAME investigators***

Stanford

BACKGROUND (1)

- Stenting of non-ischemic stenoses has no benefit compared to medical treatment only
- Stenting of ischemia-related stenoses improves symptoms and outcome
- In multivessel coronary disease (MVD), identifying which stenoses cause ischemia is difficult:

  Non-invasive tests are often unreliable in MVD and coronary angiography often results in both under- or overestimation of functional stenosis severity

BACKGROUND (2)

- Fractional Flow Reserve (FFR) is an accurate and selective index which indicates whether a stenosis is responsible for inducible ischemia
- FFR can be easily determined in the cath lab just prior to stenting

Therefore:

- *FFR guidance of PCI in patients with multivessel disease may improve outcome*

Study Population

The FAME study was designed to ***reflect daily practice*** in performing PCI in patients ***with multivessel disease***

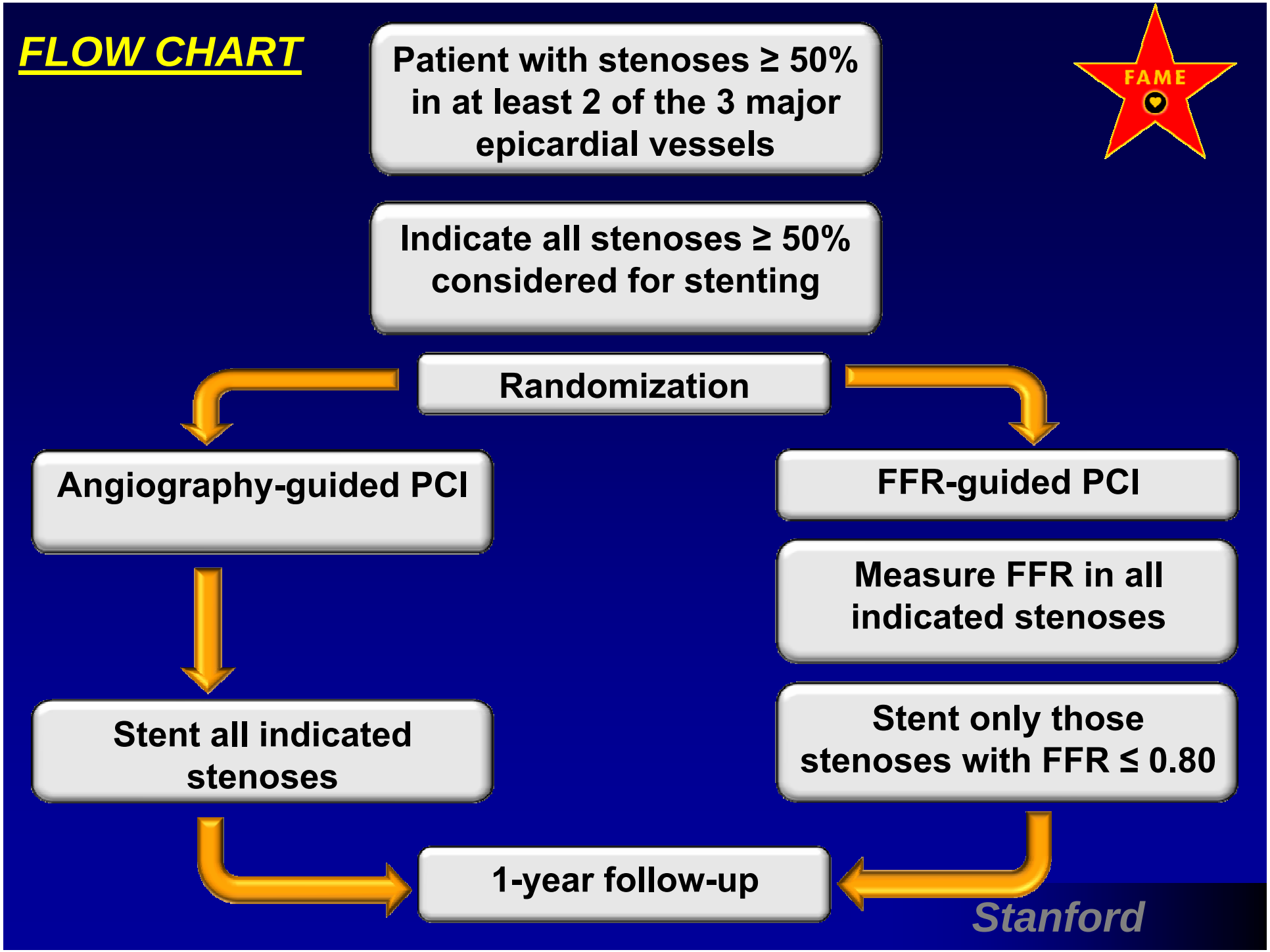
Inclusion criteria:

- ***ALL*** patients with multivessel disease
- Stenoses ≥ 50% in 2 or 3 major epicardial coronary arteries, which are amenable for stenting

Exclusion criteria:

- Left main disease or previous bypass surgery
- Acute STEMI
- Extremely tortuous or calcified coronary arteries

Note: Patients with previous PCI were not excluded


FLOW CHART
Patient with stenoses ≥ 50% in at least 2 of the 3 major epicardial vessels
FAME
Indicate all stenoses ≥ 50% considered for stenting
Randomization
Angiography-guided PCI
FFR-guided PCI
Measure FFR in all indicated stenoses
Stent all indicated stenoses
Stent only those stenoses with FFR ≤ 0.80
1-year follow-up
Stanford

PRIMARY ENDPOINT

Composite of death, myocardial infarction, or repeat revascularization ("MACE") at 1 year

SECONDARY ENDPOINTS

- Individual components of MACE at 1 year
- Functional class
- Use of anti-anginal drugs
- Health-related quality of life (EuroQOL-5D)

- Procedure time
- Amount of contrast agent used during procedure
- Cost of the procedure

Treatment

- PCI according to local routine
- Only drug-eluting stents (DES)
- FFR measured by Pressure Wire
  (***Certus wire, RADI Medical Systems***)
- Hyperemia induced by i.v. adenosine 140 µg/kg/min in femoral vein
- EKG, CK, CK-MB, etc during hospital stay
- Follow-up at 1 month, 6 months, 1 year

FAME study

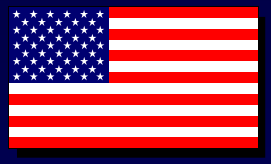
Steering Committee:
Nico H.J. Pijls, Eindhoven, Netherlands (PI)
William F. Fearon, Stanford, CA, USA (PI)
Bernard De Bruyne, Aalst, Belgium
Pim A.L. Tonino, Eindhoven, Netherlands

Data analysis:
Uwe Siebert, Boston, MA, USA and Hall iT, Austria

Clinical Events Committee:
Eric Eeckhout, Lausanne, Switzerland
Morton Kern, Irvine, CA, USA
Mamdouh El Gamal, Eindhoven, NL
John Hodgson, Phoenix, AZ, USA
Emanuele Barbato, Naples, Italy

Funding Source:
Radi Medical Systems, Medtronic Corporation

Participating Centers



EUROPE (14)

Cardiovascular Center Aalst *(B. De Bruyne)*

Catharina Hospital Eindhoven *(N.Pijls)*

Rigshospitalet, Copenhagen (*T.Engstrom*)

Klinikum der Universitat Munchen *(V.Klauss)*

Aarhus University Hospital *(O. Frobert)*

University Hosp Bergmannsheil *(W. Bojara)*

Sodersjukhhuset, Stockholm *(I Herzfeld)*

Helsingborgs Lasarett *(F Schersten)*

Klinikum Darmstadt *(Gerald Werner)*

Bristol Royal Infirmary *(A.Baumbach)*

Staedt. Krankenhaus, Bogenhausen *(G.Riess)*

Glasgow Western Infirmary *(K Oldroyd)*

Royal Victoria Hosp, Belfast *(G. Manoharan)*

King´s College Hosp, London *(P.MacCarthy)*

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(Peter N. Ver Lee)

Stanford University
(William F. Fearon)

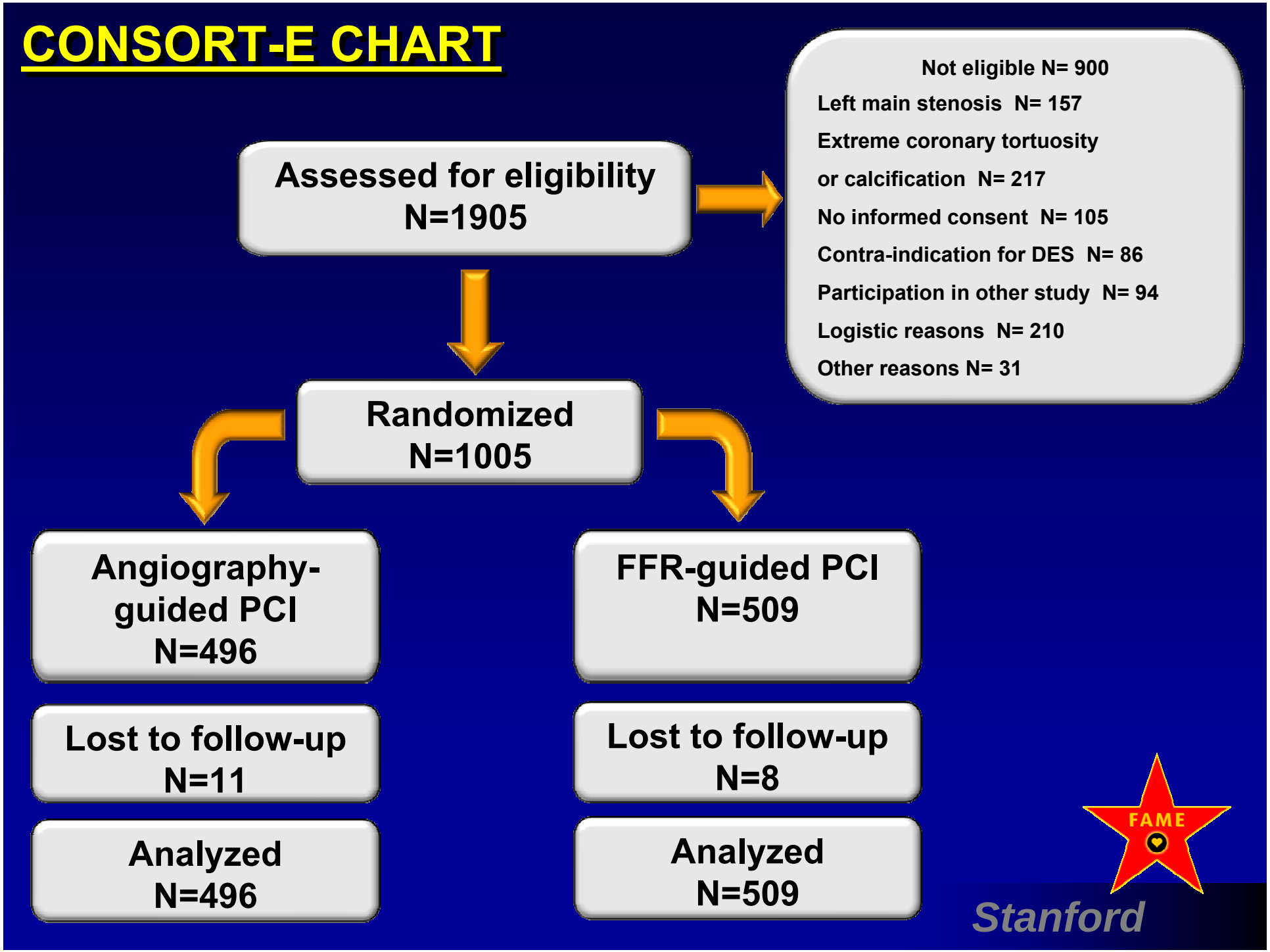
St Louis University
(Michael Lim)

University of Louisville
(Massoud Leesar)

University of South Carolina
(Eric Powers)

University of Virginia
(Michael Ragosta)

CONSORT-E CHART



Baseline Characteristics (1)

	ANGIO-group N=496	FFR-group N=509	P-value
Age, mean±SD	64±10	65±10	0.47
Male, %	73	75	0.30
Diabetes, %	25	24	0.65
Hypertension, %	66	61	0.10
Current smoker, %	32	27	0.12
Hyperlipidemia, %	74	72	0.62
Previous MI, %	36	37	0.84
Unstable angina, %	36	29	0.11
Previous PCI , %	26	29	0.34
LVEF, mean±SD	57±12	57±11	0.92
LVEF < 50% , %	27	29	0.47

Baseline Characteristics (2)

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# indicated lesions per patient	2.7±0.9	2.8±1.0	0.34

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Reference diameter (mm)	**2.5±0.6**	**2.5±0.7**	0.81
% stenosis severity	**61±17**	**60±18**	0.24
MLD (mm)	**1.0±0.4**	**1.0±0.5**	0.35

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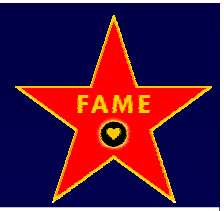
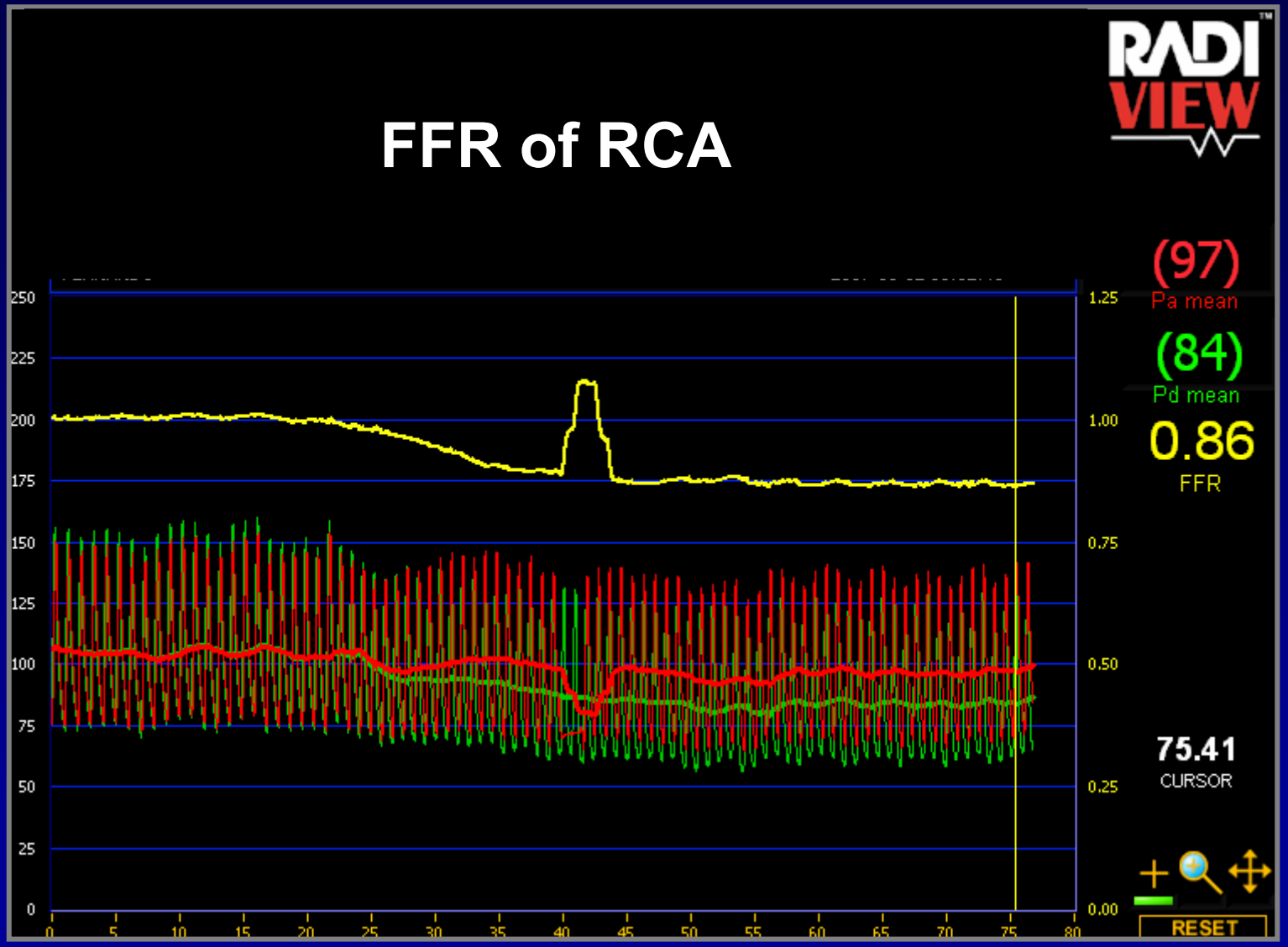
MLD (mm)	**1.0±0.4**	**1.0±0.5**	0.35
50-70% narrowing, No (%)	**550 (41)**	**624 (44)**	-
70-90% narrowing, No (%)	**553 (41)**	**530 (37)**	-
> 90% narrowing, No (%)	**247 (18)**	**260 (18)**	-
Patients with ≥1 total occlusion (%)	**7.5**	**10.6**	0.08

Case Example:



- 71 year old woman with increasing symptoms of exertional dyspnea ± chest pain
- Coronary angiography 2 years prior revealed 60% LAD and 60% RCA lesions…treated medically
- Recent stress echo without ischemia, normal EF
- Because of worsening symptoms referred for cath, moderate 3 vessel disease noted and CABG considered.
- Referred back to the cath lab for FFR assessment and possible PCI

FFR of RCA



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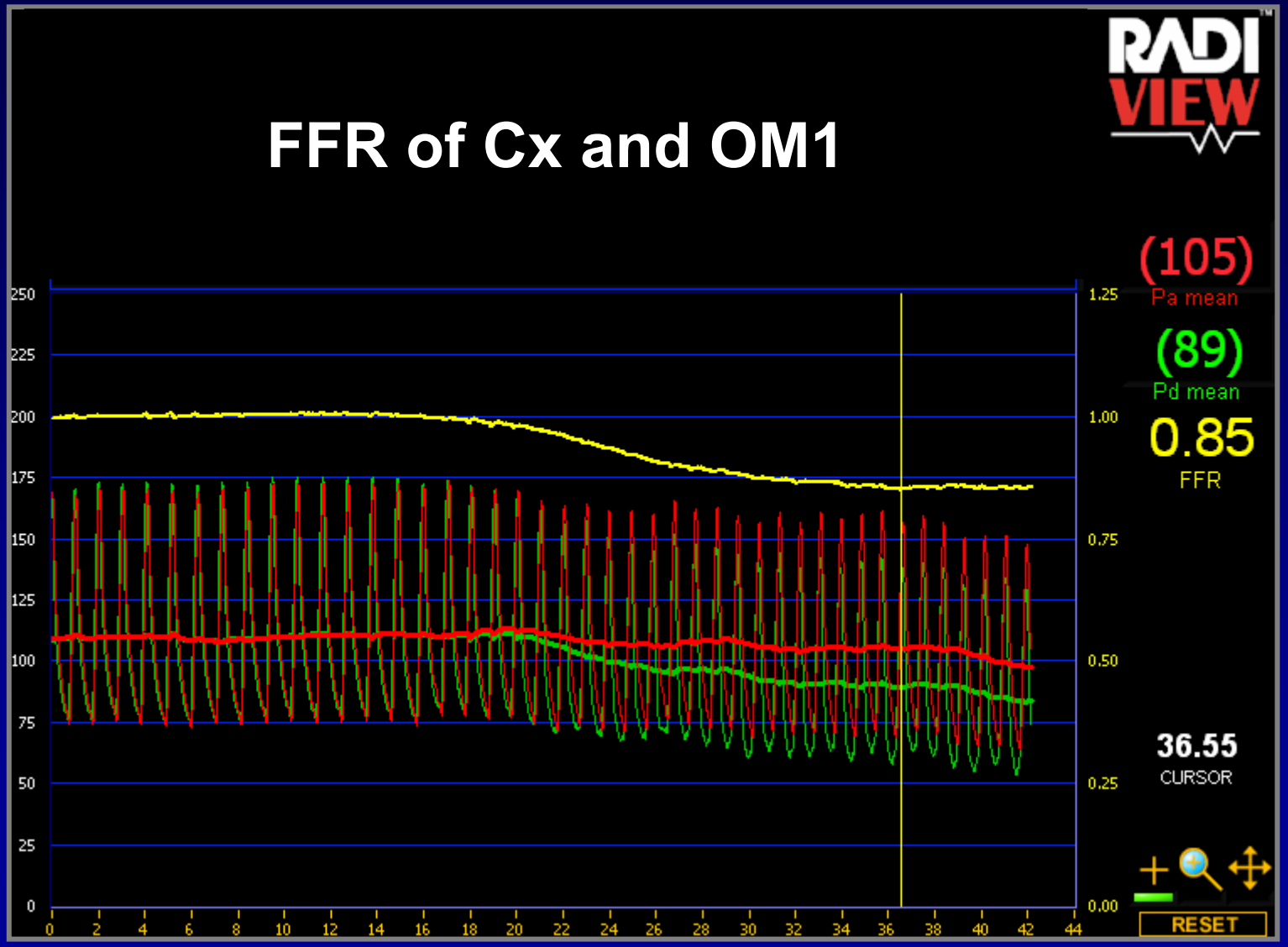
FFR of Cx and OM1



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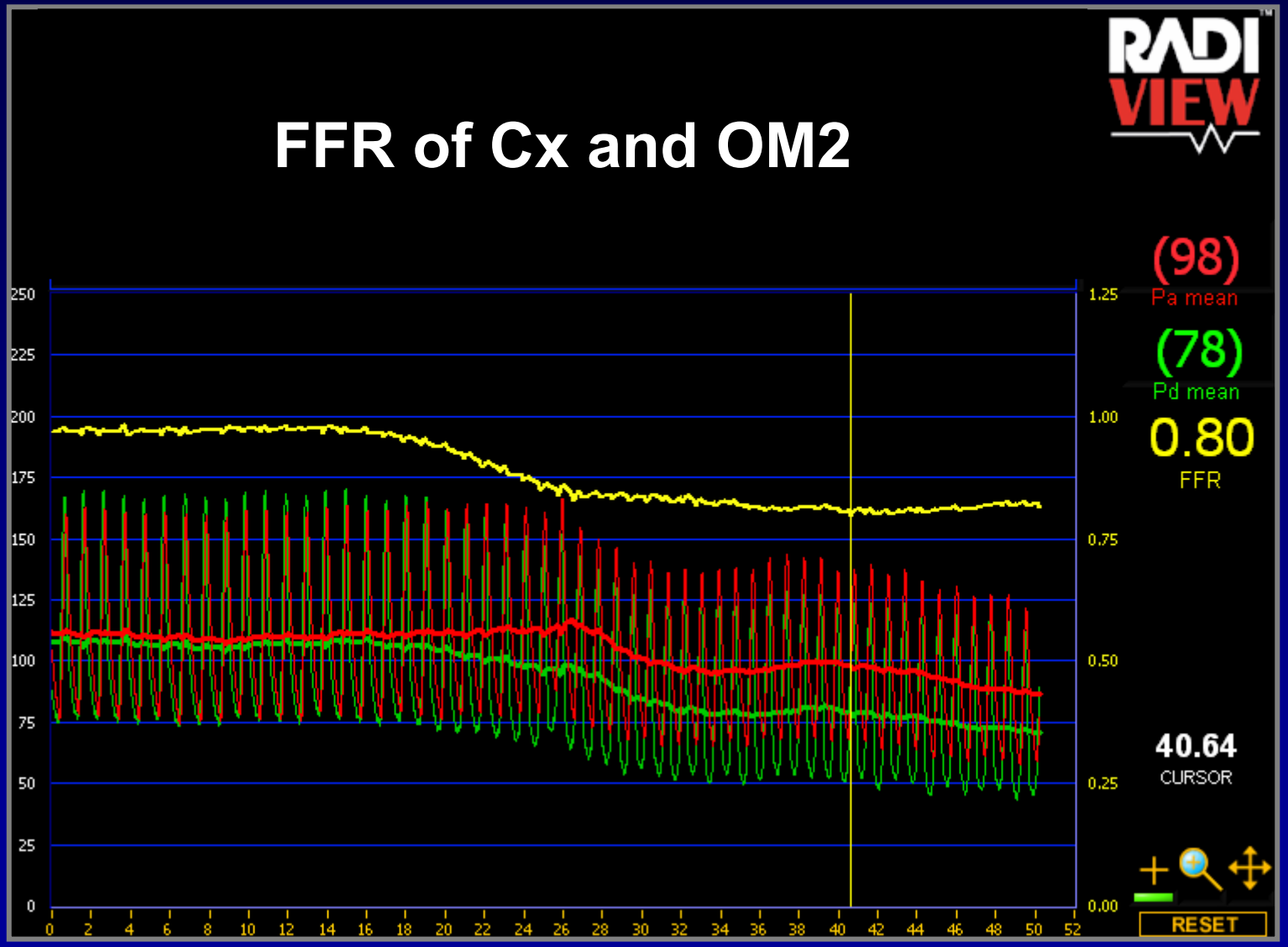
FFR of Cx and OM2



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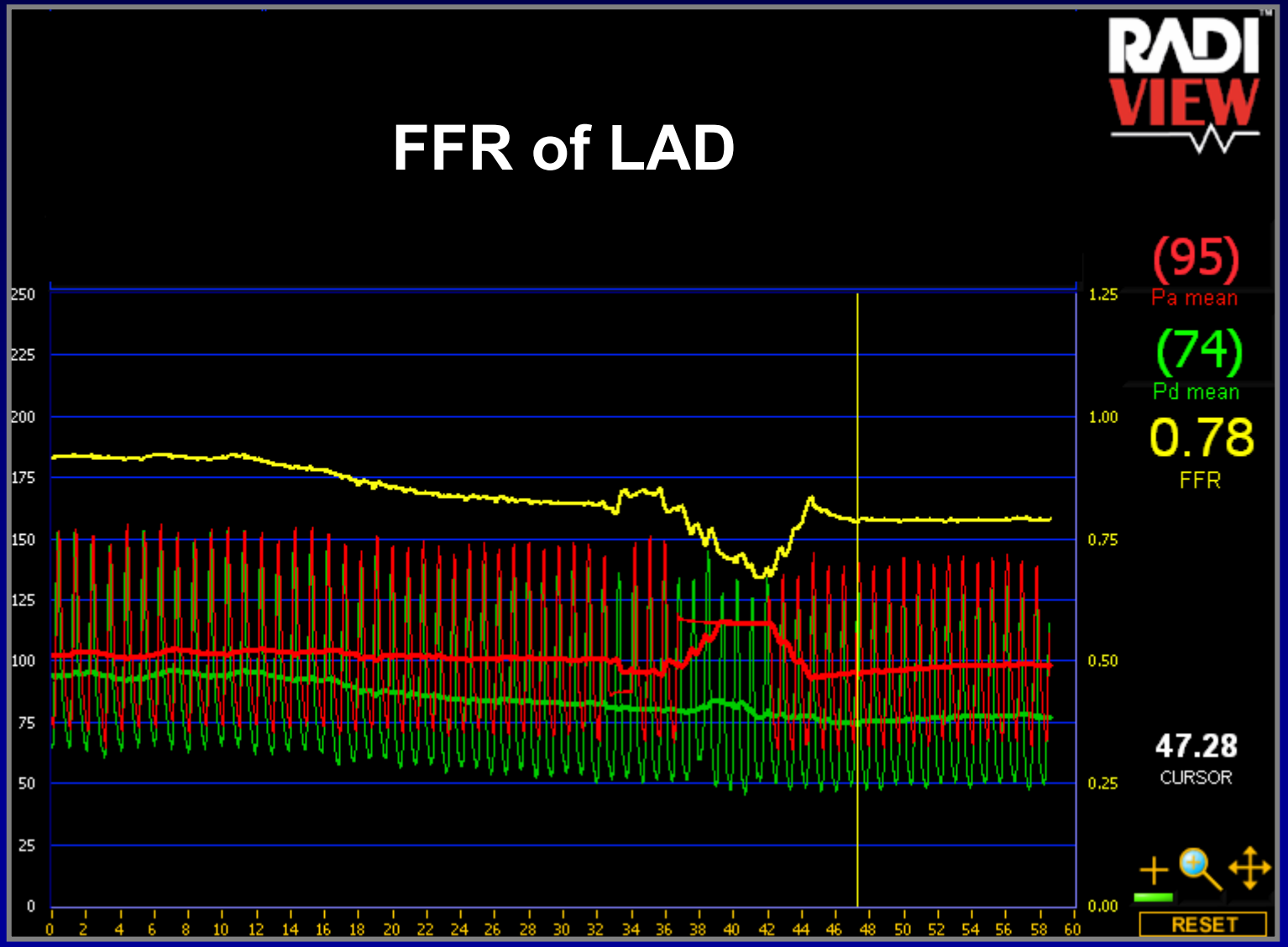
FFR of LAD



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Procedural Results (1)

	ANGIO-group N=496	FFR-group N=509	P-value
# indicated lesions per patient	2.7 ± 0.9	2.8 ± 1.0	0.34
FFR results			
Lesions succesfully measured, No (%)	-	1329 (98%)	-
Lesions with FFR ≤ 0.80 ,No (%)	-	874 (63%)	-
Lesions with FFR > 0.80 ,No (%)	-	513 (37%)	-
FFR in ischemic lesions	-	0.60 ± 0.14	-
FFR in non-ischemic lesions	-	0.88 ± 0.05	-

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Stents per patient	**2.7 ± 1.2**	**1.9 ± 1.3**	<0.001
Lesions succesfully stented (%)	**92%**	**94%**	-
DES, total, No	**1359**	**980**	-

Procedural Results (2)

	ANGIO-group N=496	FFR-group N=509	P-value
Procedure time (min)	70 ± 44	71 ± 43	0.51

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Procedure time (min)	70 ± 44	71 ± 43	0.51
Contrast agent used (ml)	302 ± 127	272 ± 133	<0.001

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Length of hospital stay (days)	3.7 ± 3.5	3.4 ± 3.3	0.05

Adverse Events at 1 year

	ANGIO-group N=496	FFR-group N=509	P-value
Events at 1 year, No (%)			
Death, MI, CABG, or repeat-PCI			

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Death	**15 (3.0)**	**9 (1.8)**	0.19
Death or myocardial infarction	**55 (11.1)**	**37 (7.3)**	0.04
CABG or repeat PCI	**47 (9.5)**	**33 (6.5)**	0.08

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Total no. of MACE	**113**	**76**	0.02

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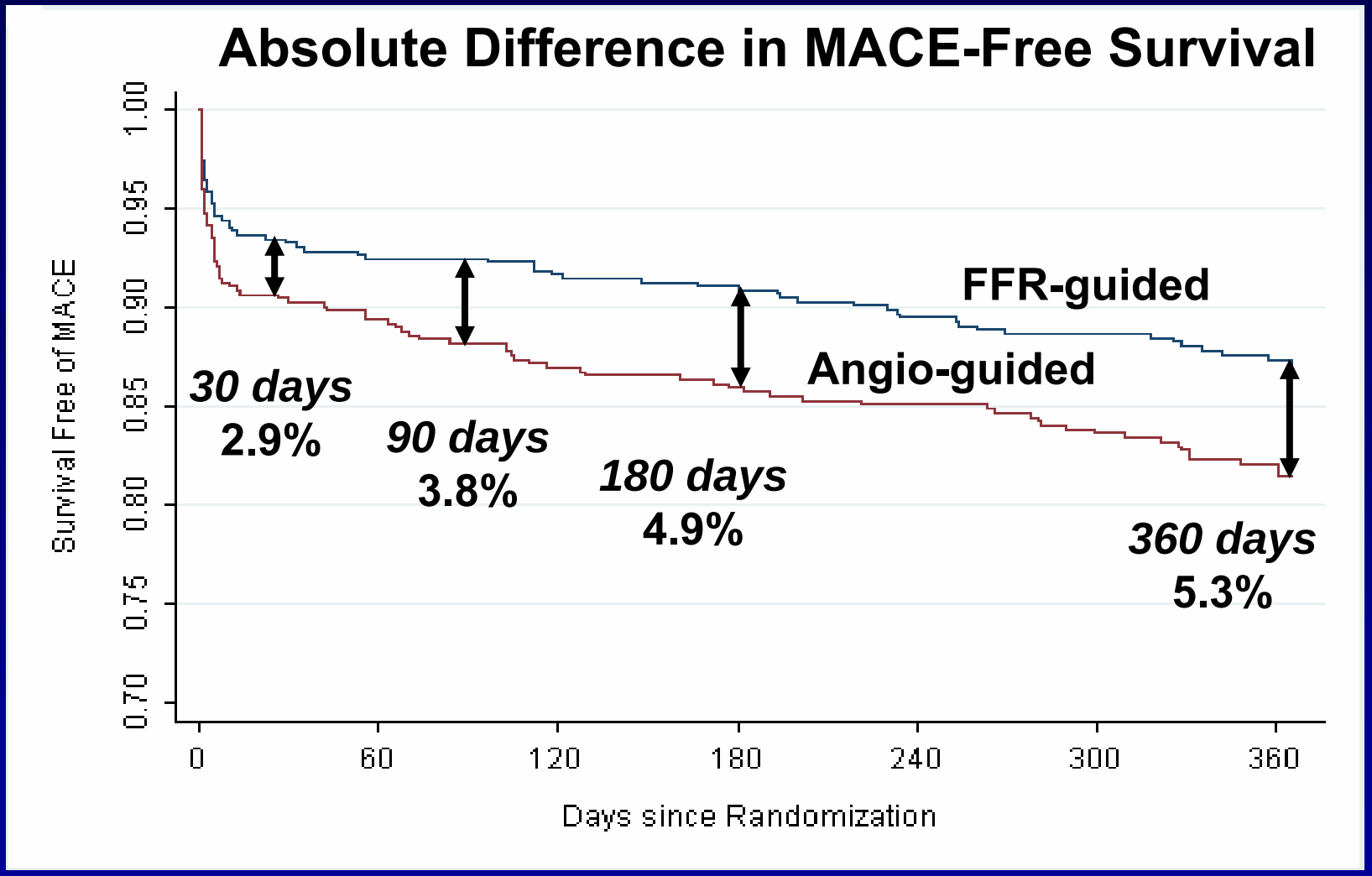
CABG or repeat PCI	**47 (9.5)**	**33 (6.5)**	0.08
Total no. of MACE	**113**	**76**	0.02
Myocardial infarction, specified			
All myocardial infarctions	**43 (8.7)**	**29 (5.7)**	0.07
Small periprocedural CK-MB 3-5 x N	**16**	**12**	
Other infarctions (“late or large”)	**27**	**17**	

Event-free Survival



Functional Class at 1 Year

	ANGIO-group N=496	FFR-group N=509	P-value
Patients without event and free from angina	326 (68)	360 (73)	0.07
Patients free from angina, No. (%)	374 (78)	399 (81)	0.20
Number of anti-anginal meds, No.	1.2 ± 0.7	1.2 ± 0.8	0.48
EQ-5D visual analogue scale	74 ± 16	75 ± 16	0.65

CONCLUSIONS (1)

Routine measurement of FFR during PCI with DES in patients with multivessel disease, when compared to current angiography guided strategy

- *Reduces the rate of the composite endpoint of death, myocardial infarction, re-PCI and CABG at 1 year by ~ 30%*

- *Reduces mortality and myocardial infarction at 1 year by ~ 35 %*

CONCLUSIONS (2)

Routine measurement of FFR during PCI with DES in patients with multivessel disease, when compared to current angiography guided strategy

- *Is cost-saving and does not prolong the procedure*
- *Reduces the number of stents used*
- *Decreases the amount of contrast agent used*
- *Results in a similar, if not better, functional status*

CONCLUSIONS (3)

Routine measurement of FFR during PCI with DES supports the evolving paradigm of:

"Functionally Complete Revascularization", i.e. revascularization of ischemic lesions and medical treatment of non-ischemic ones.