

FRACTIONAL FLOW RESERVE: FROM INVESTIGATIONAL TOOL TO STANDARD OF CARE

TCT ASIA

Seoul, Korea, april 26 th, 2012



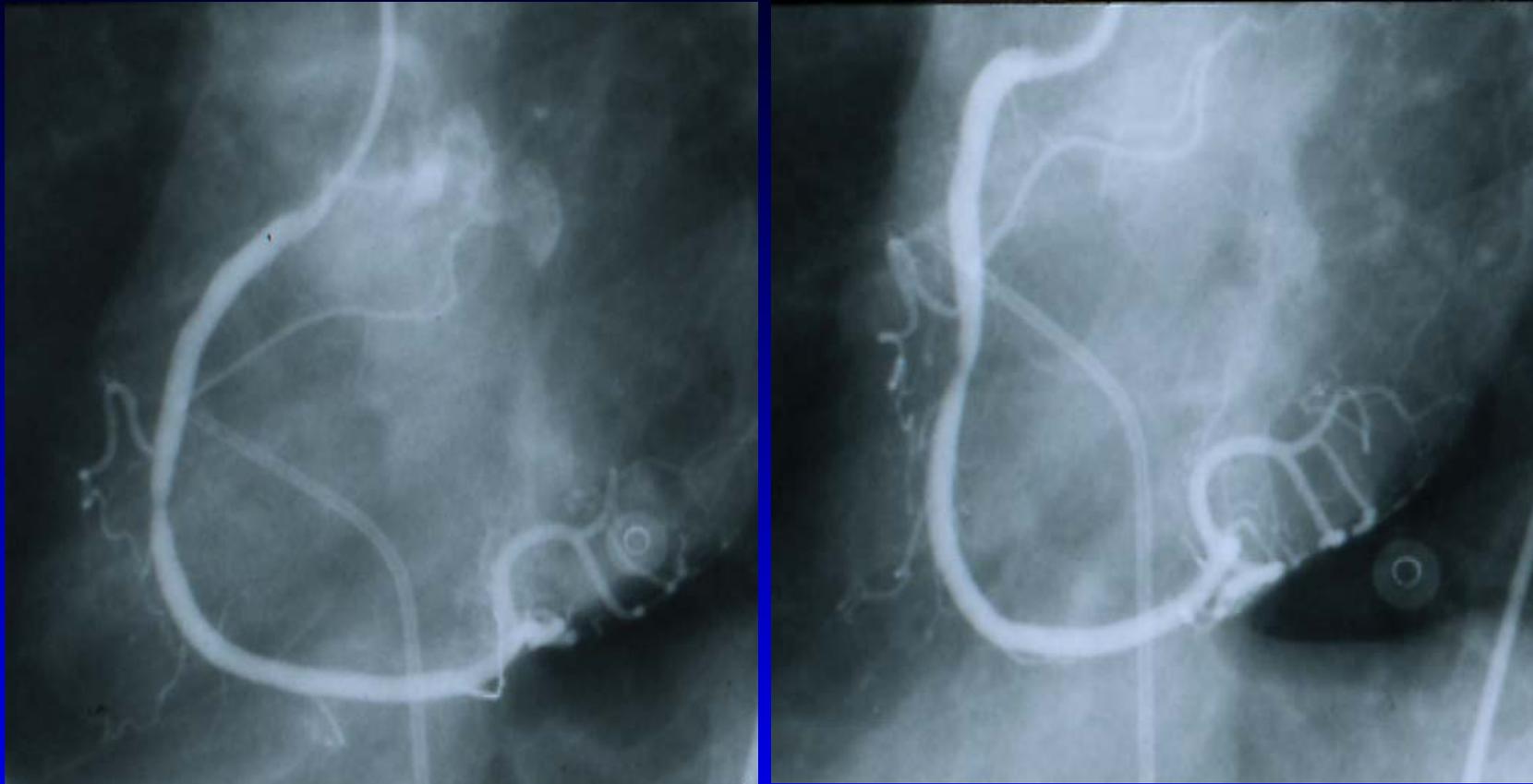
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FRACTIONAL FLOW RESERVE 1996-2012: *From Investigational Tool to Standard of Care*

- from intermediate stenosis → complex disease
- from simple diagnostic tool → improved outcome
- from adjunctive therapy → booster of PCI

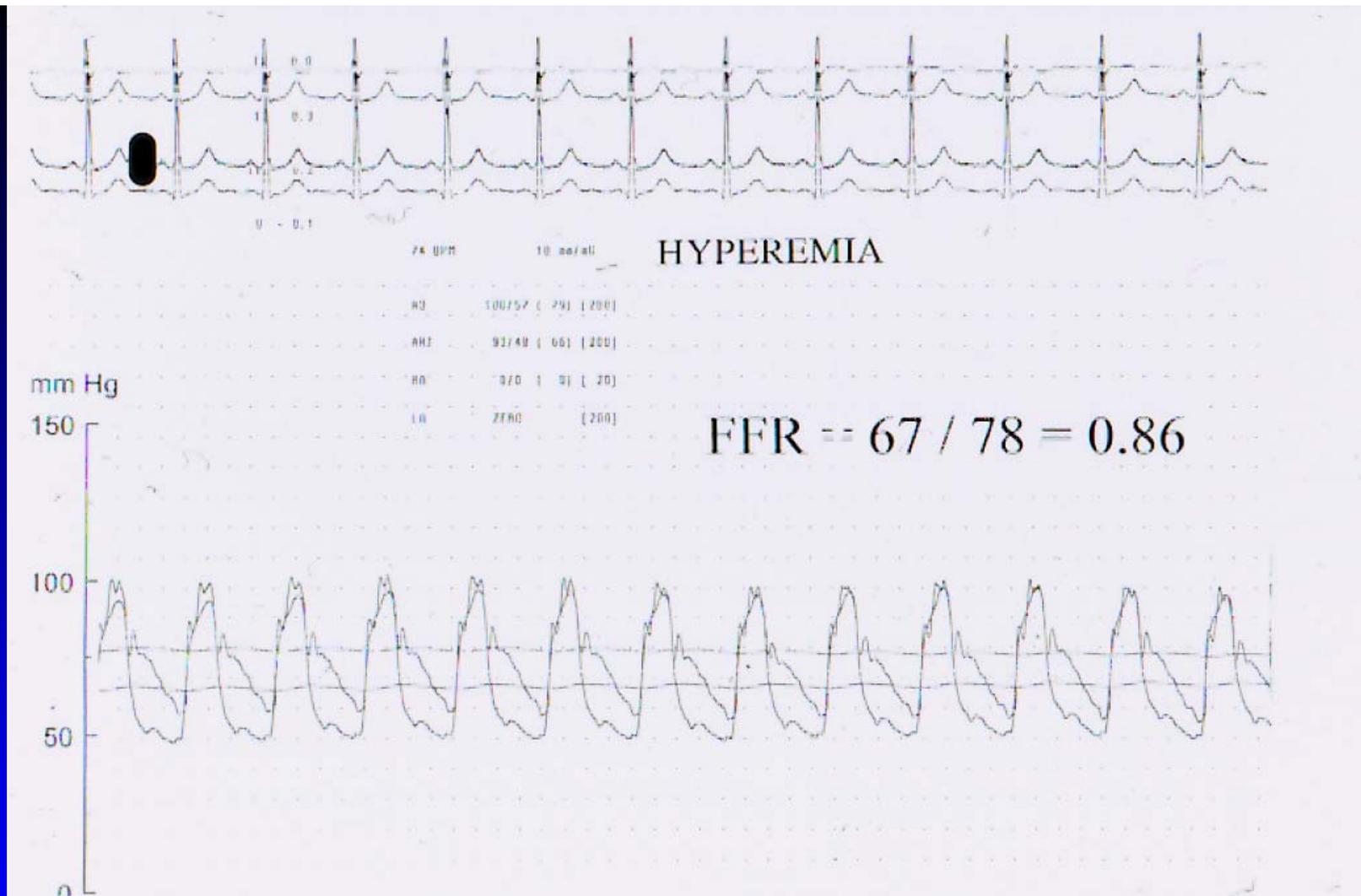
FRACTIONAL FLOW RESERVE 1996-2012:

- *from intermediate stenosis → complex disease*
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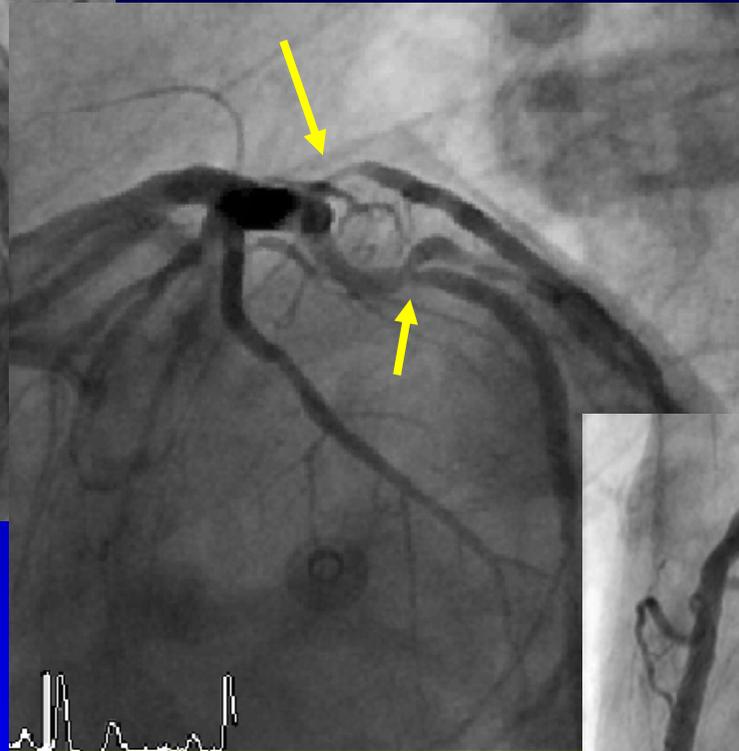
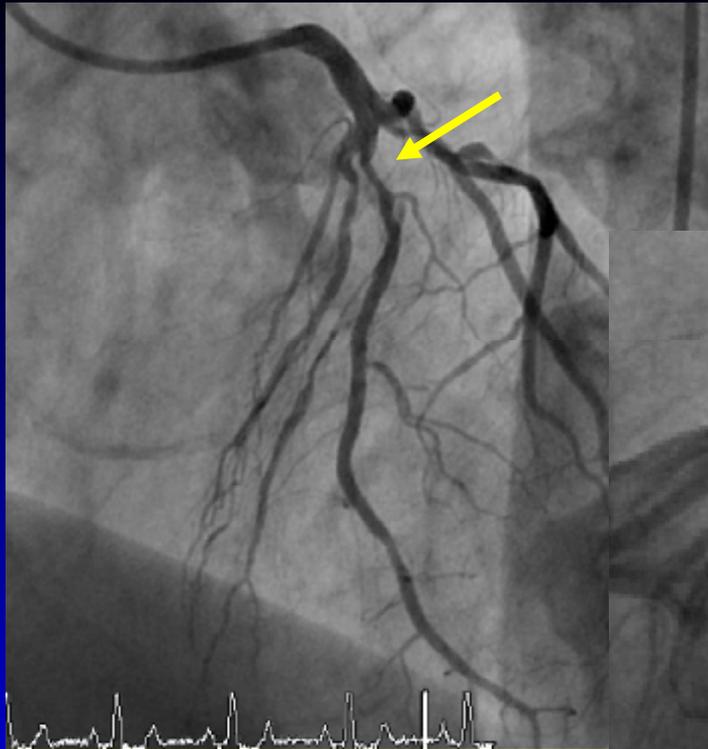
1996:
young patient with atypical chest pain and negative
exercise / MIBISpect

NEJM 1996



1996: FFR 0.86 → no intervention; asa + statin
2012: excellent condition, no complaints

2010:
Complex multivessel disease



4 of the 6 lesions were significant
by FFR and stented

2012:

FFR used to solve many complex diagnostic situations

71-year old lady with acute chest pain, positive troponin, and transient ECG-changes →

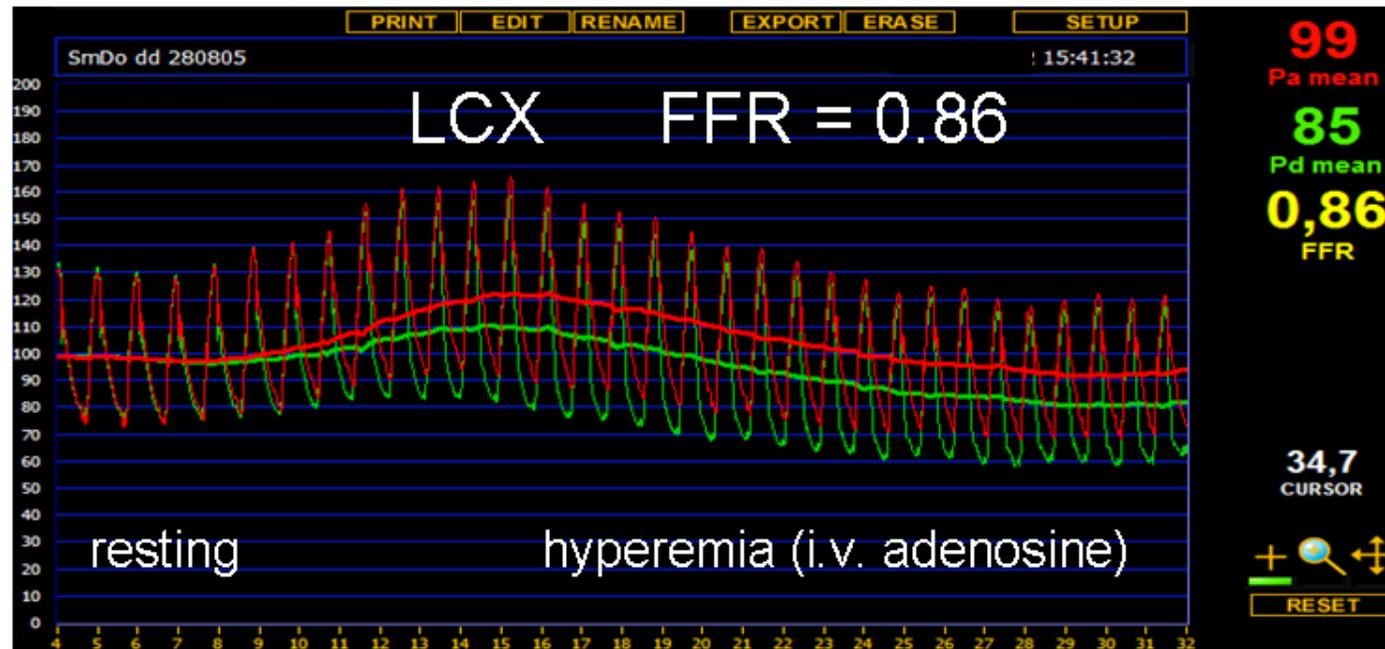
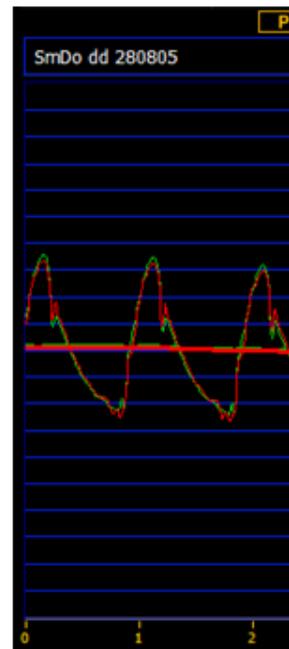
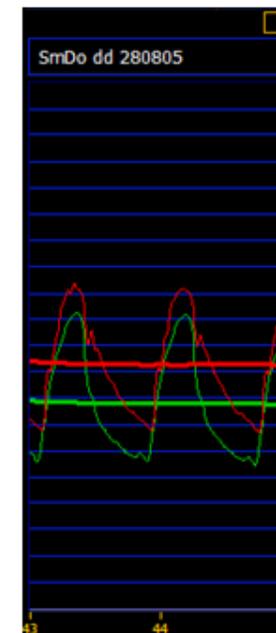
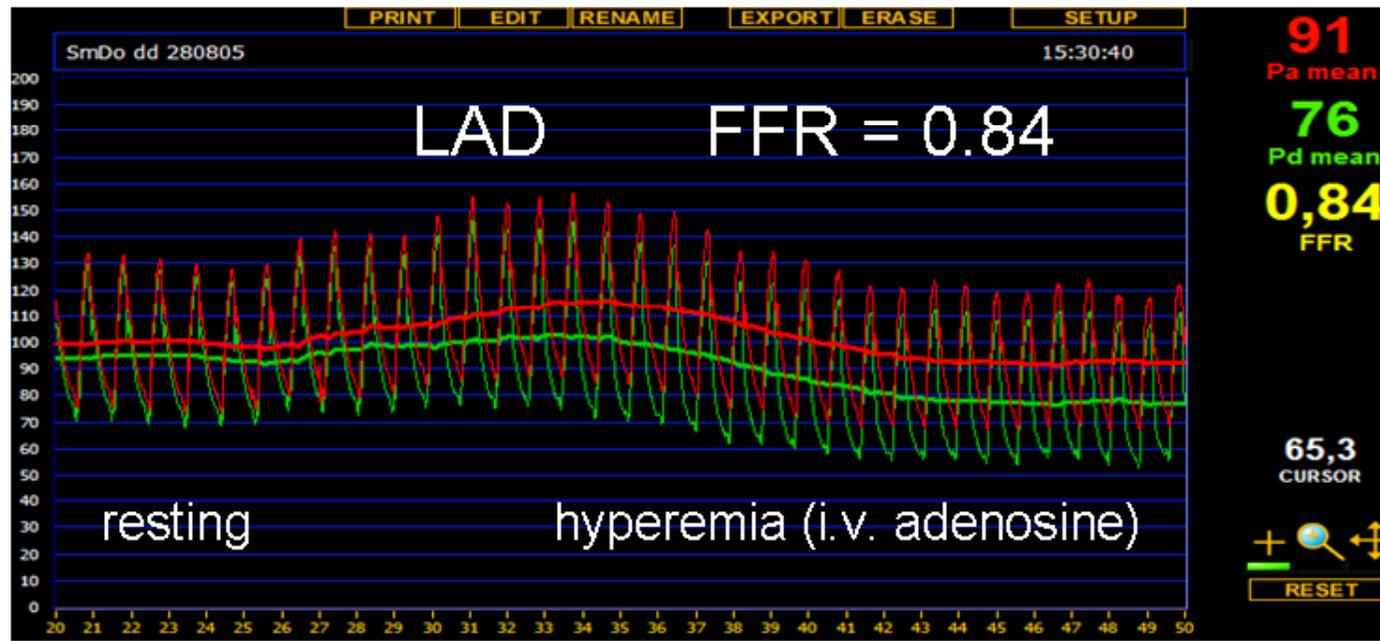
Angiogram : 50% LAD/D1 lesion and 70% CX lesion



LAD
57% stenosis
1.4 mm MLD



LCX:
71% stenosis
1.2 mm MLD

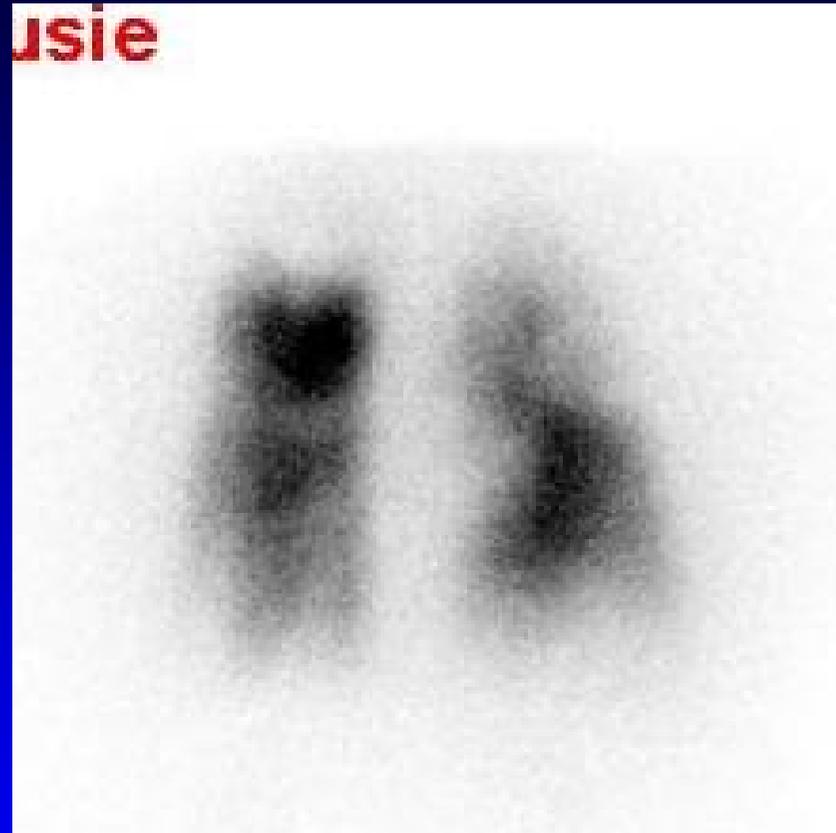


- acute chest pain
- ECG changes
- positive troponin

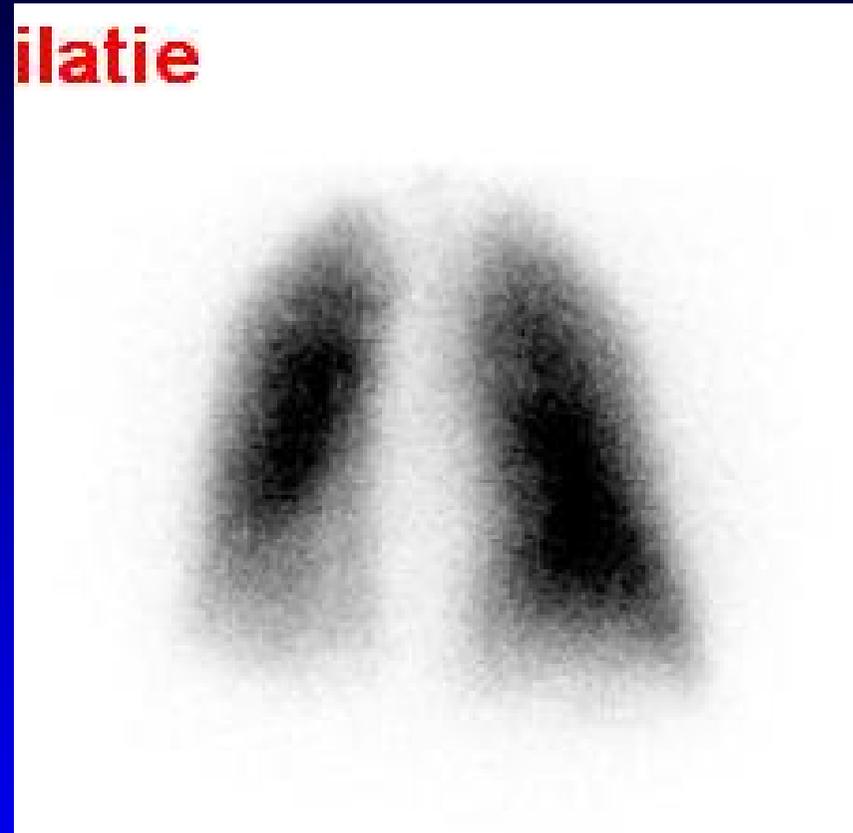
But.....only 2 intermediate lesions not fitting the ECG

→ measuring FFR prevented inappropriate stenting but warranted further exam....!!!

perfusion



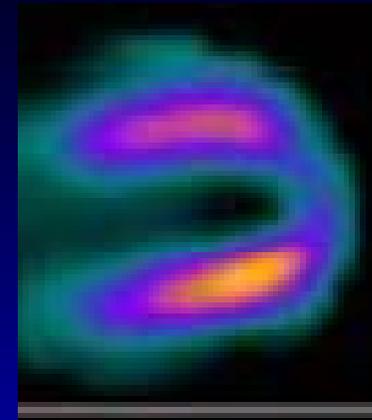
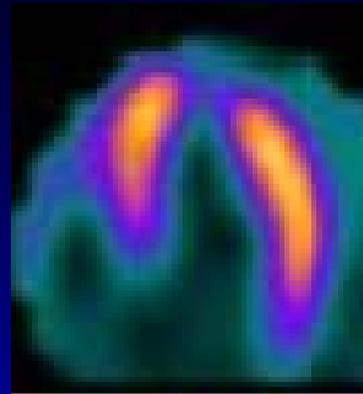
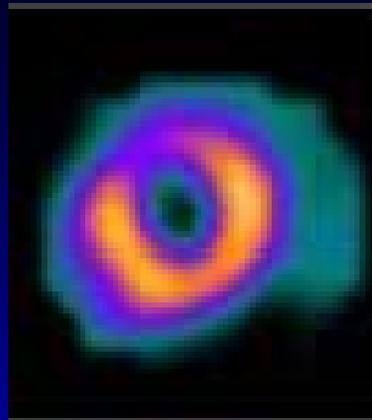
ventilation



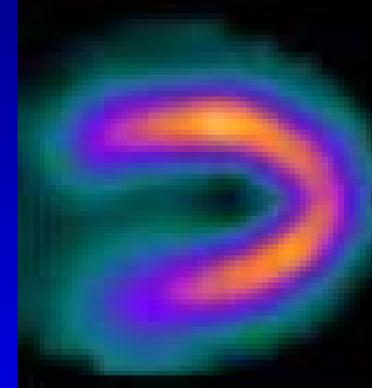
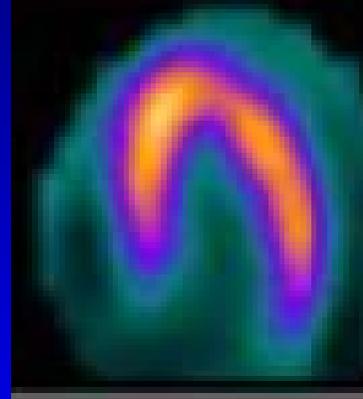
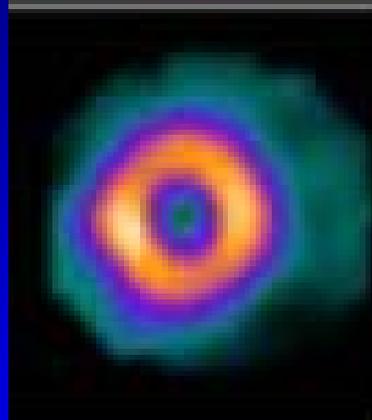
V-P scan: pathognomonic for pulmonary embolism

Also the opposite happens.....!!!

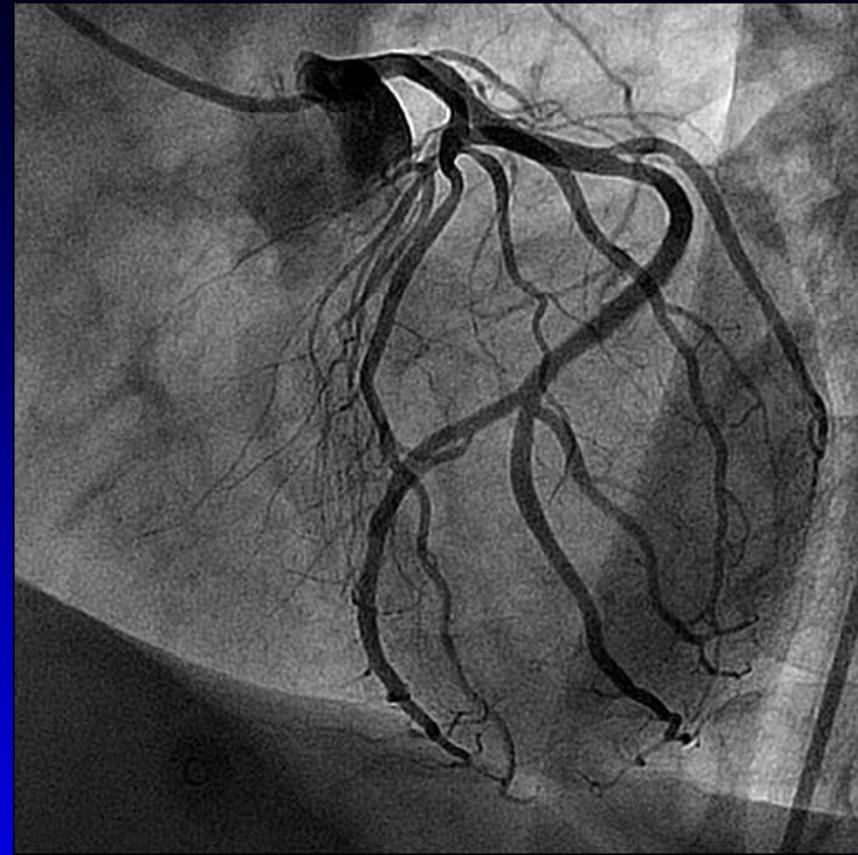
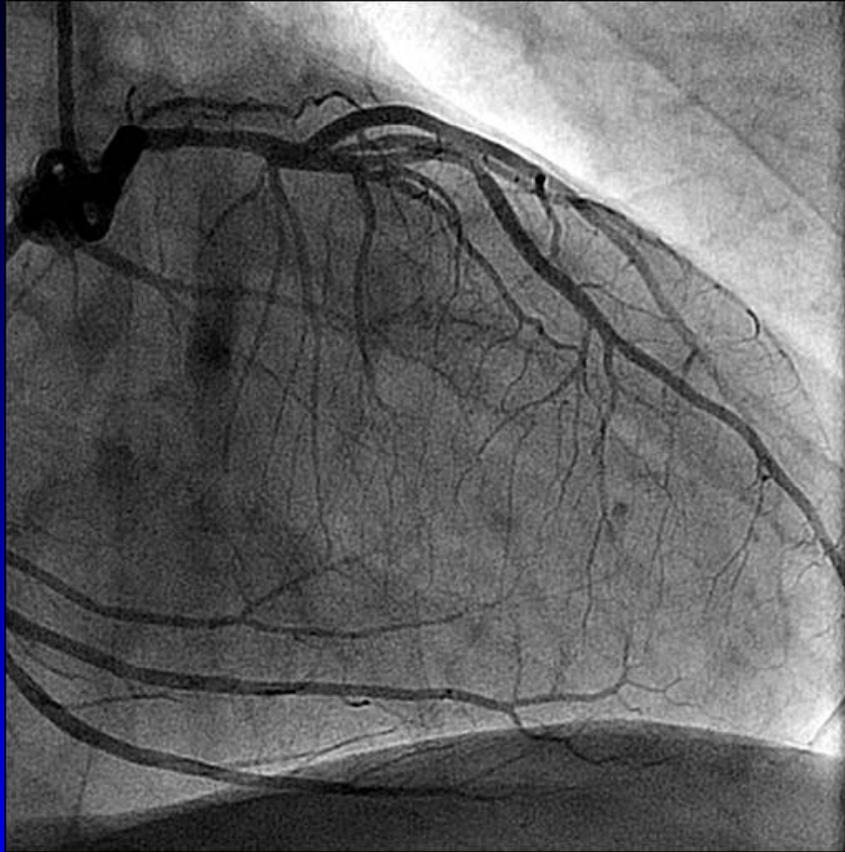
stress



resting



middle-aged male, typical chestpain at exercise,
positive stress test and MIBI.....



.....but (almost) normal coronary angiogram

COM ●



ARCHIVE CUSTOM

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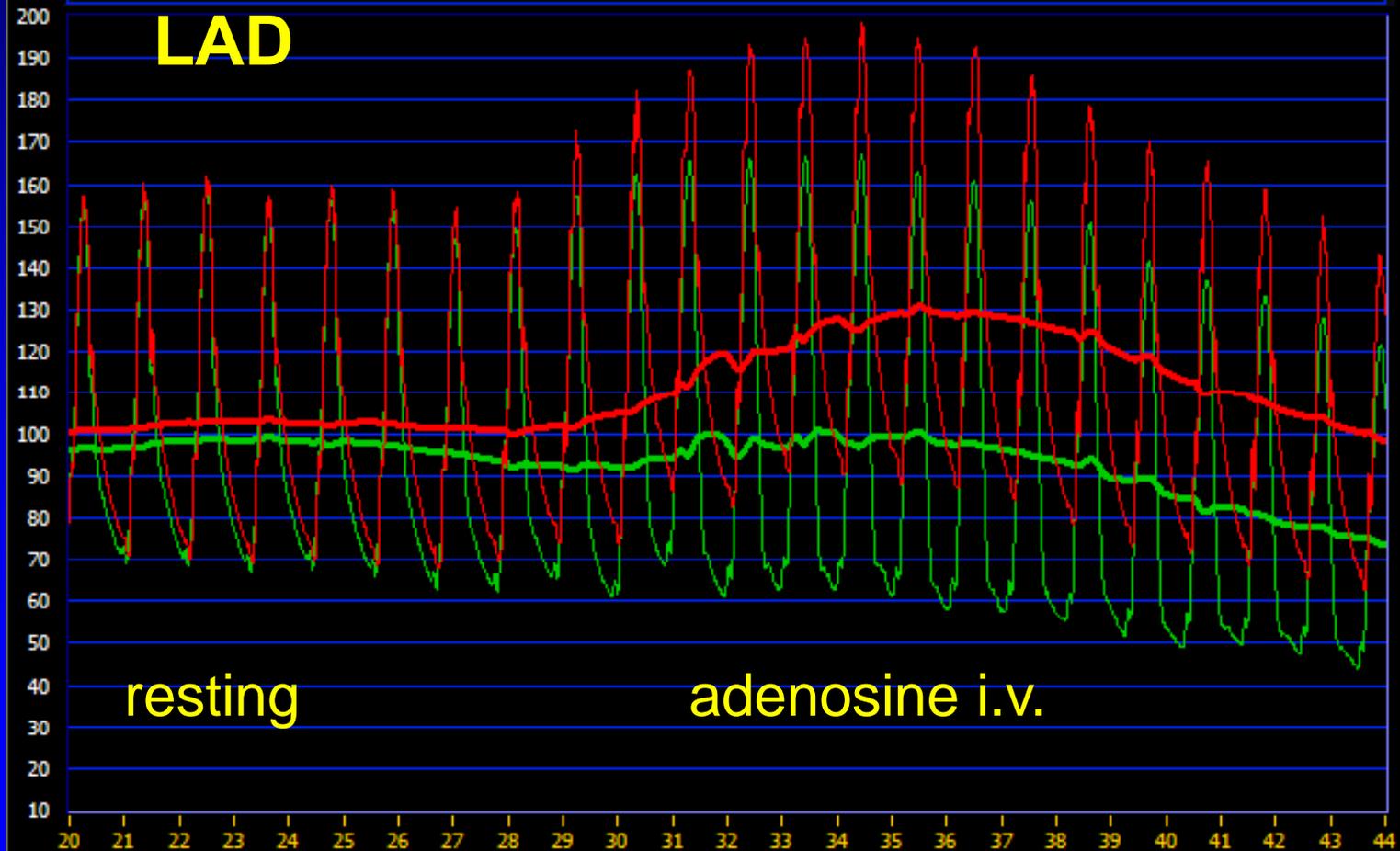
FOLDER

PATIENT ID	DATE	TIME	VESSEL	PROCEDURE	ACTION	TYPE	SIZE
	2006-11-01	16:25:23				FFR	63Kb
	2006-11-01	16:08:12				FFR	156Kb
	2006-11-01	16:00:37				FFR	3Kb

PRINT EDIT RENAME EXPORT ERASE SETUP

2006-11-01 16:08:12

LAD



100
Pa mean

74
Pd mean

0,73
FFR

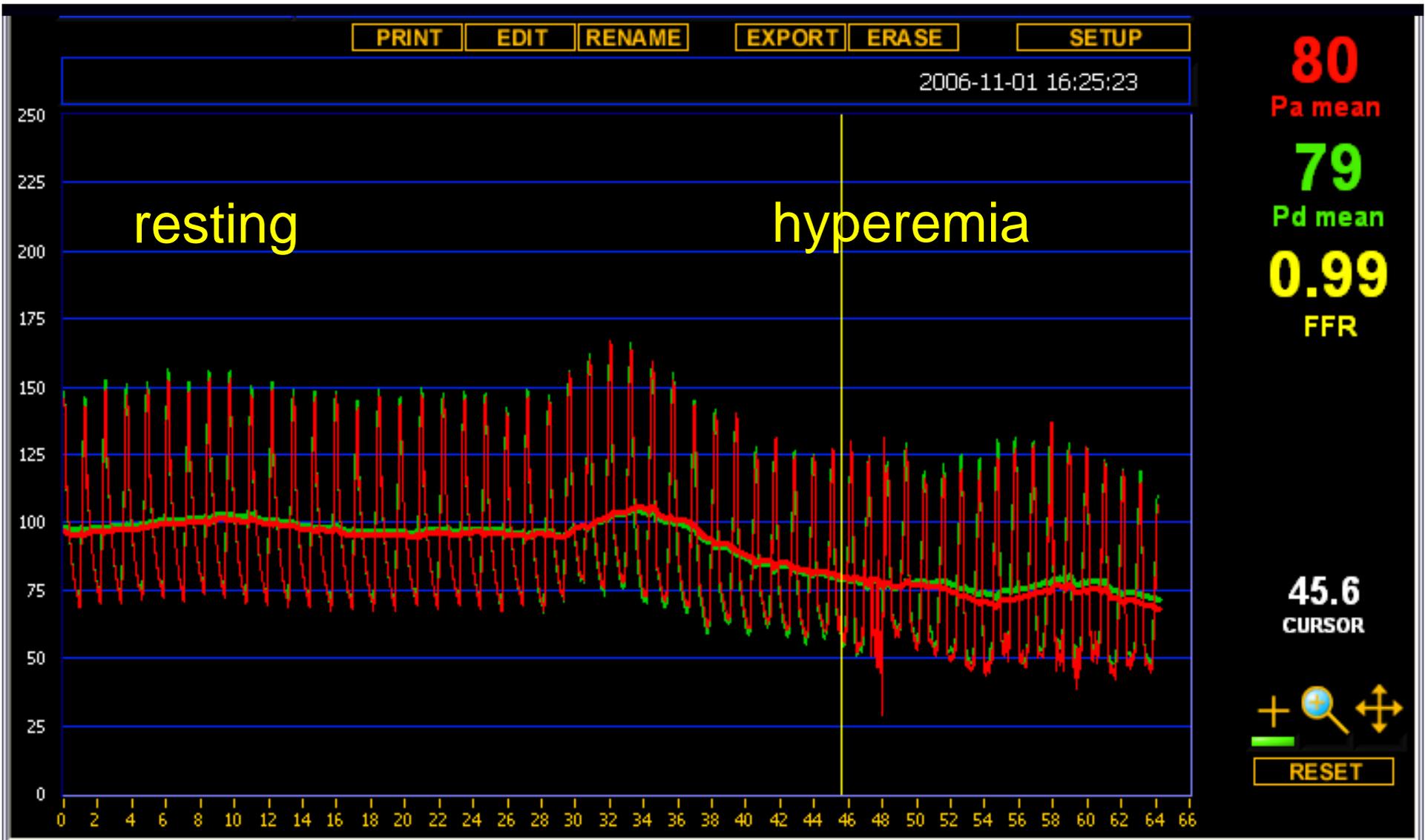
133,5
CURSOR

resting

adenosine i.v.

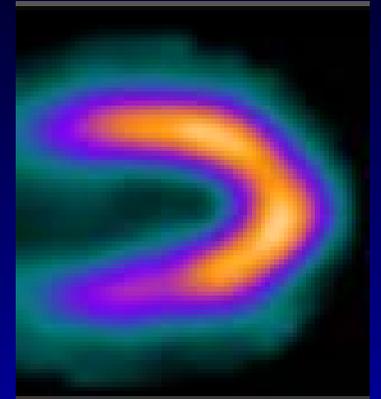
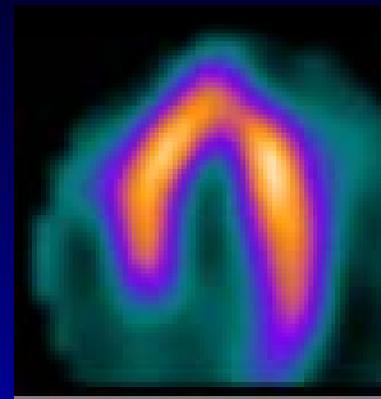
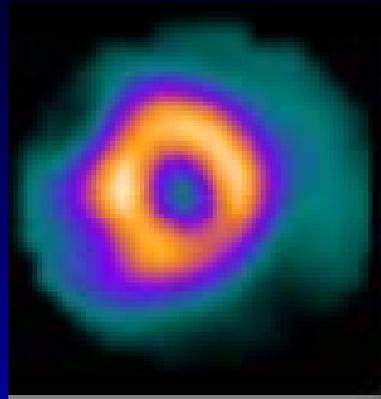


RESET

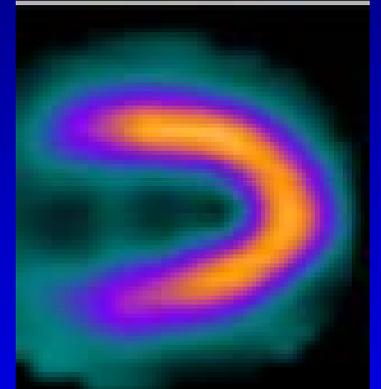
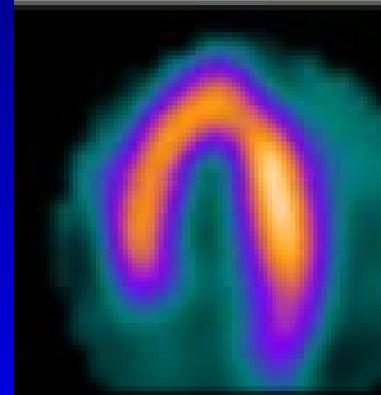
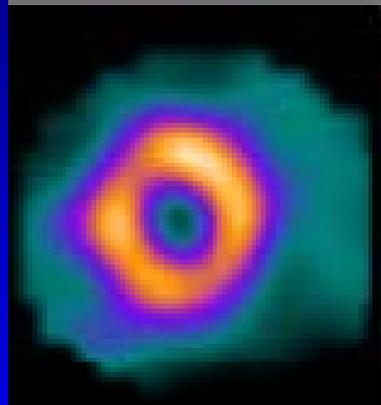


pressure measurement after stenting

stress

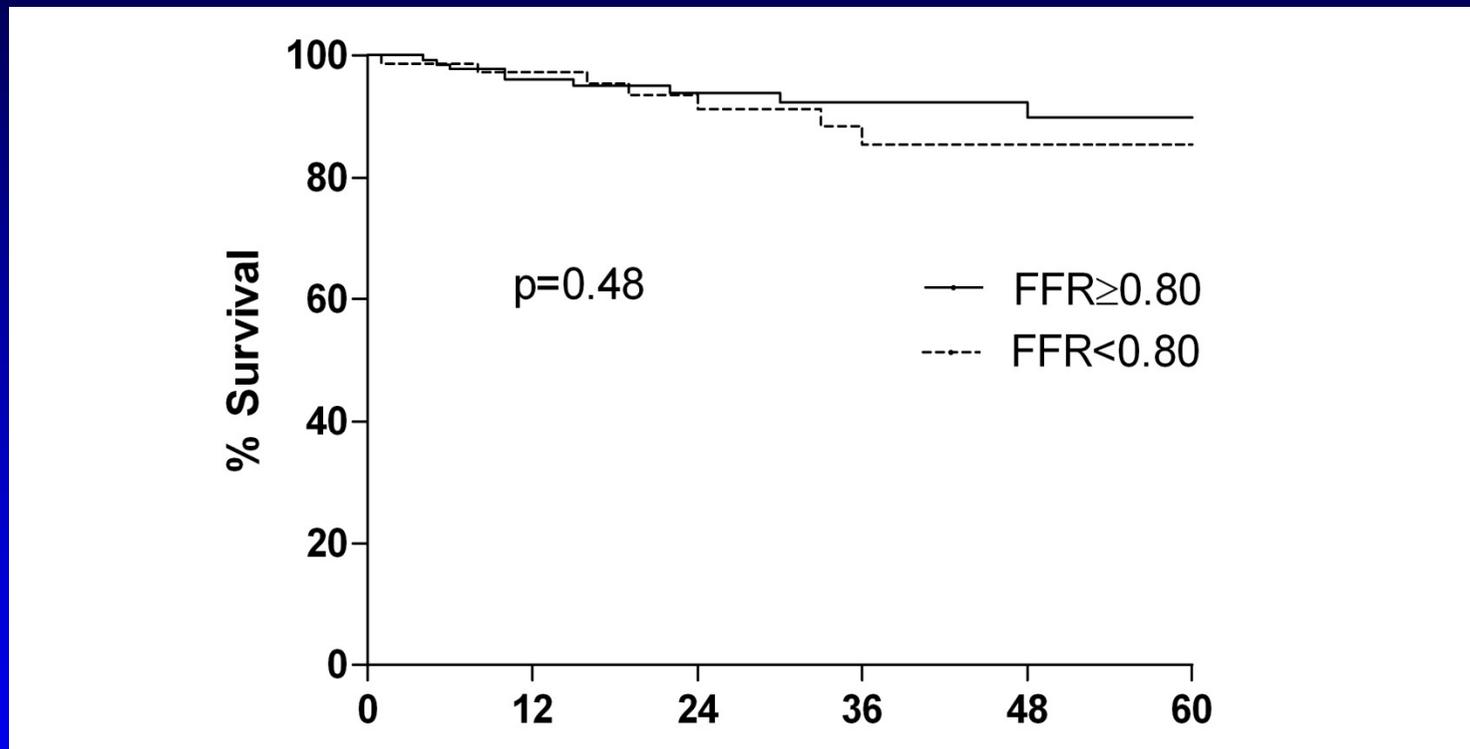


resting

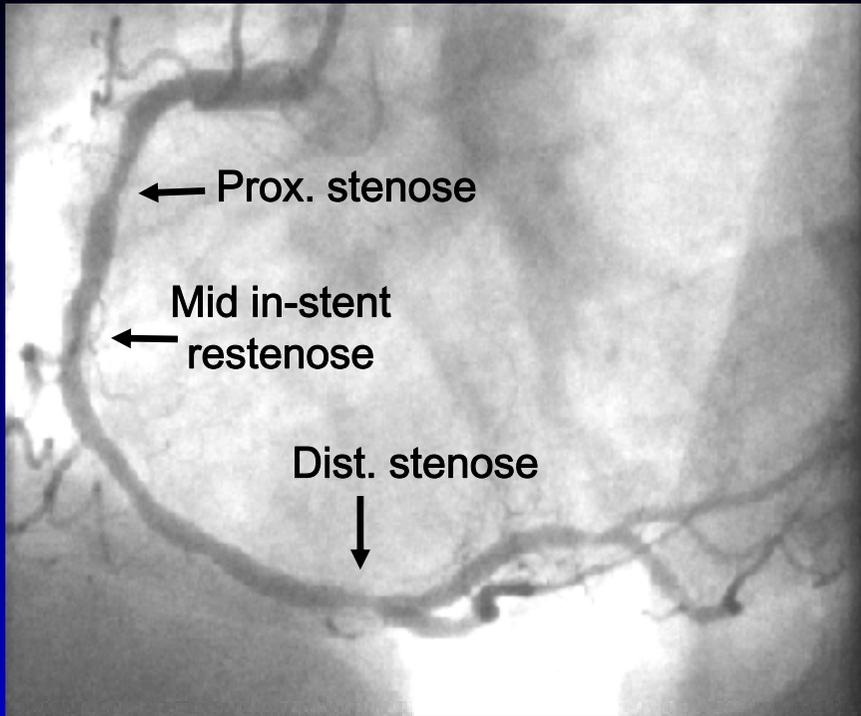


11 weeks after stent in LAD

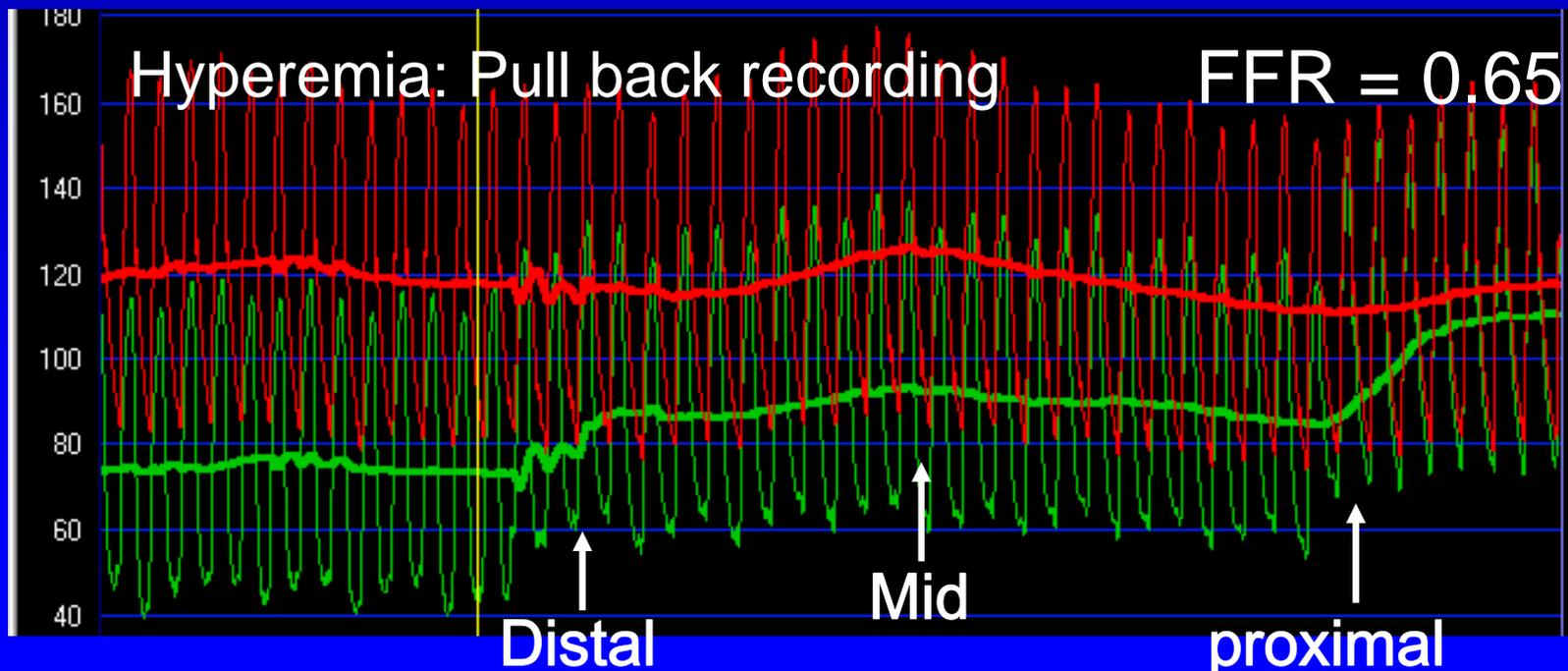
FFR & left main stenosis; 5-y f.u.



136 patients with interm. left main deferred (FFR ≥ 0.80) have the same 5 year survival and mace rate as the revascularized group! (annual mortality < 2%)



DIFFUSE DISEASE AND TANDEM LESIONS



FFR has been validated in almost all clinical and Angiographic conditions:

- multivessel disease
- left main and ostial stenosis
- diffuse disease
- bifurcation lesions
- tandem lesions
- unstable angina, NSTEMI
- previous myocardial infarction
- etc.....

- *.....but not to be used in acute STEMI*

More than 1500 papers

FRACTIONAL FLOW RESERVE 1996-2012:

- from intermediate stenosis → complex disease
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- from adjunctive therapy → booster of PCI

→ DEFER , FAME, FAME -2

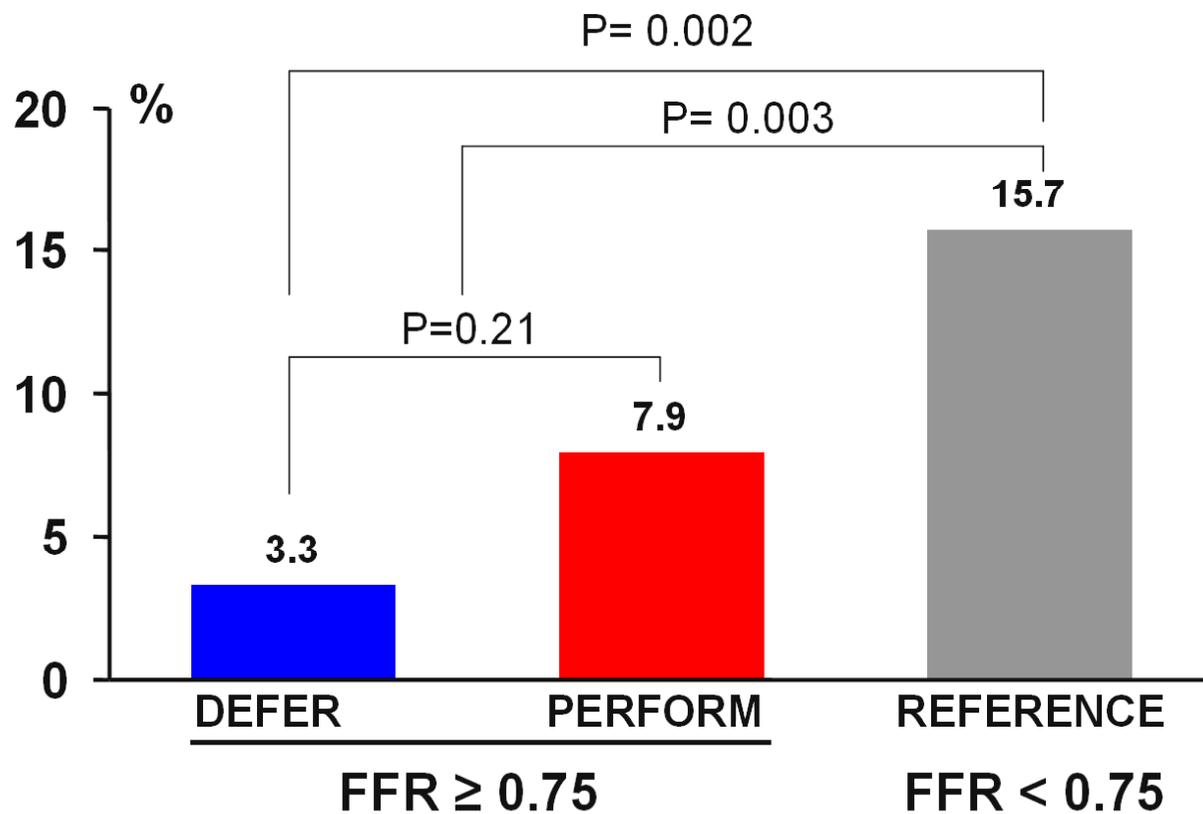
MEASURING FFR IMPROVES OUTCOME !



→ DEFER , FAME, FAME -2

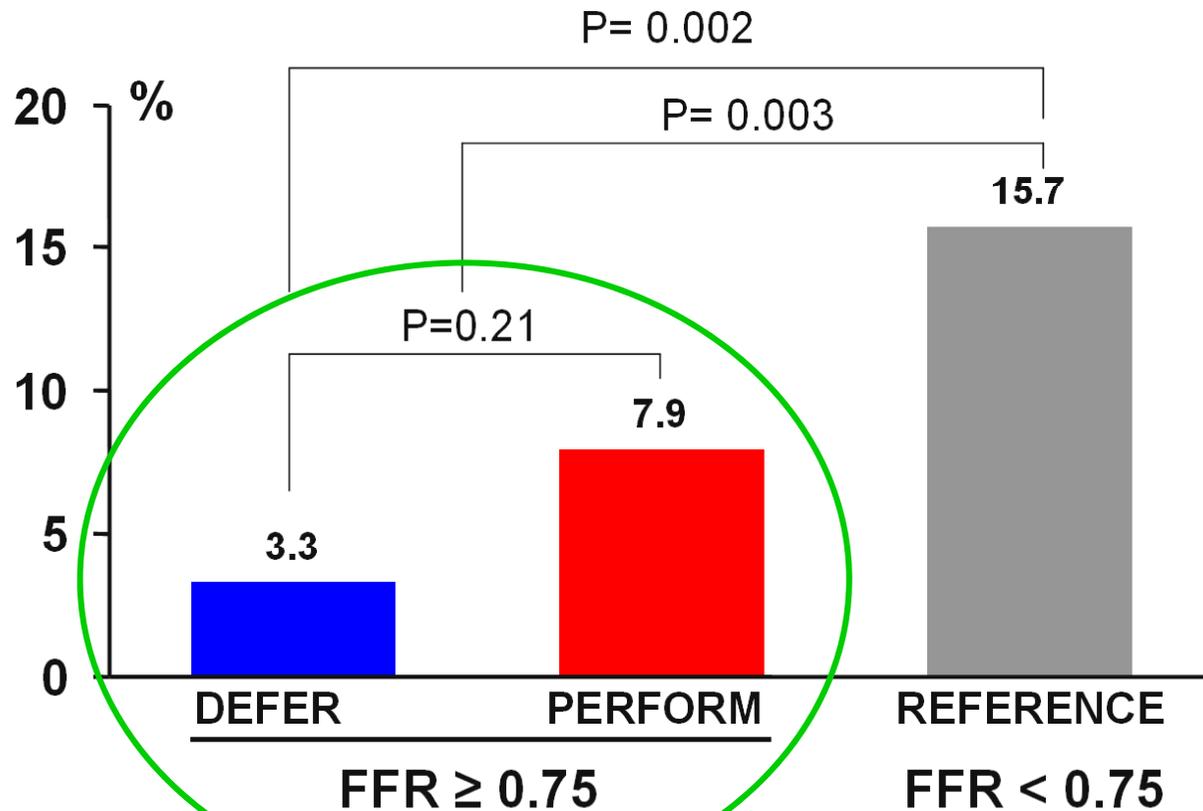
Cardiac Death And Acute MI After 5 Years

- non-ischemic stenosis, R/x
- non-ischemic stenosis, R/x + stent
- ischemic stenosis, R/x + stent



Cardiac Death And Acute MI After 5 Years

- non-ischemic stenosis, R/x
- non-ischemic stenosis, R/x + stent
- ischemic stenosis, R/x + stent



DEFER STUDY(1):

Functionally non-significant stenosis has excellent outcome with medical treatment

Stenting a functionally non-significant (FFR-negative) stenosis does NOT make any sense.

It is unnecessary, expensive, and increases the risk of death and MI without any symptomatic benefit

FUNCTIONALLY **SIGNIFICANT** STENOSIS:
CAN WE IMPROVE OUTCOME BY PCI ?

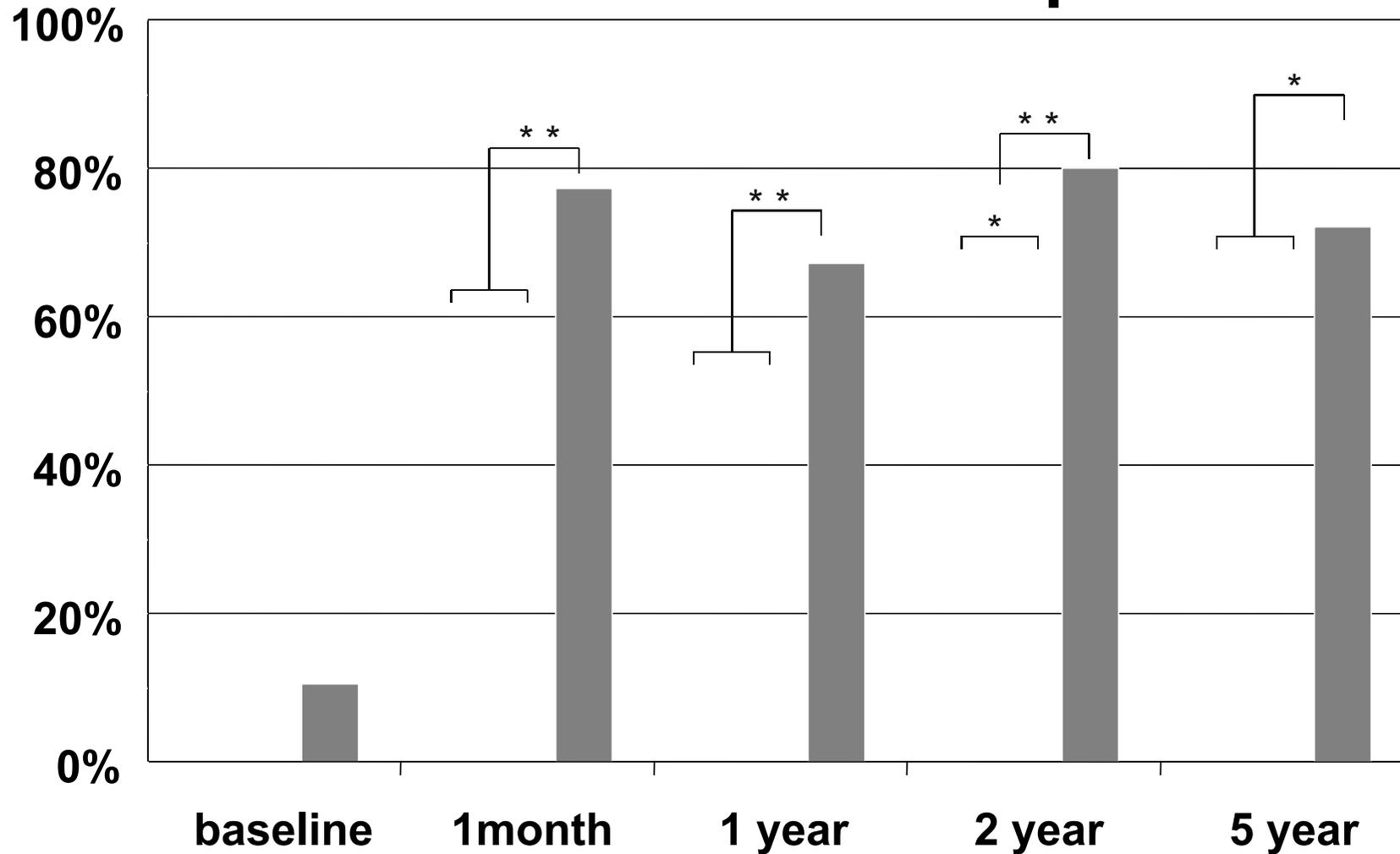
→ a **functionally significant** stenosis generally gives symptoms (angina) (*“ischemic” stenosis, hemodynamically significant stenosis*)

PCI and stenting is extremely effective in relieving symptoms (angina) in such patients

(and much more effective than medical treatment)

DEFER, COURAGE, SYNTAX, FAME

freedom from chest pain

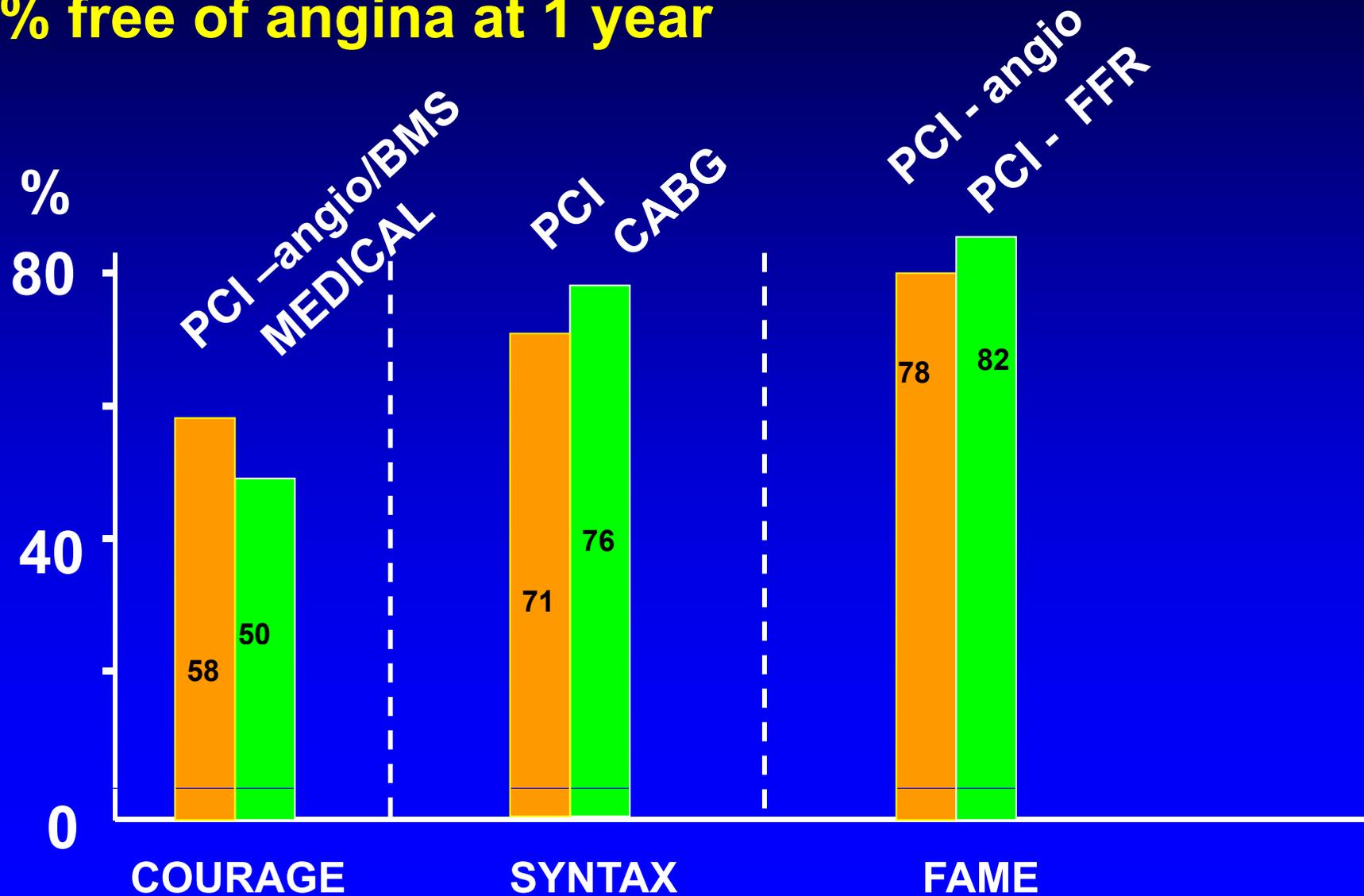


Ischemic lesions (FFR < 0.75)
treated by stenting

FUNCTIONAL CLASS

in COURAGE - SYNTAX – 3VD and FAME

% free of angina at 1 year



*Does stenting “on good indication”
(i.e. ischemic stenosis) improve outcome ?*



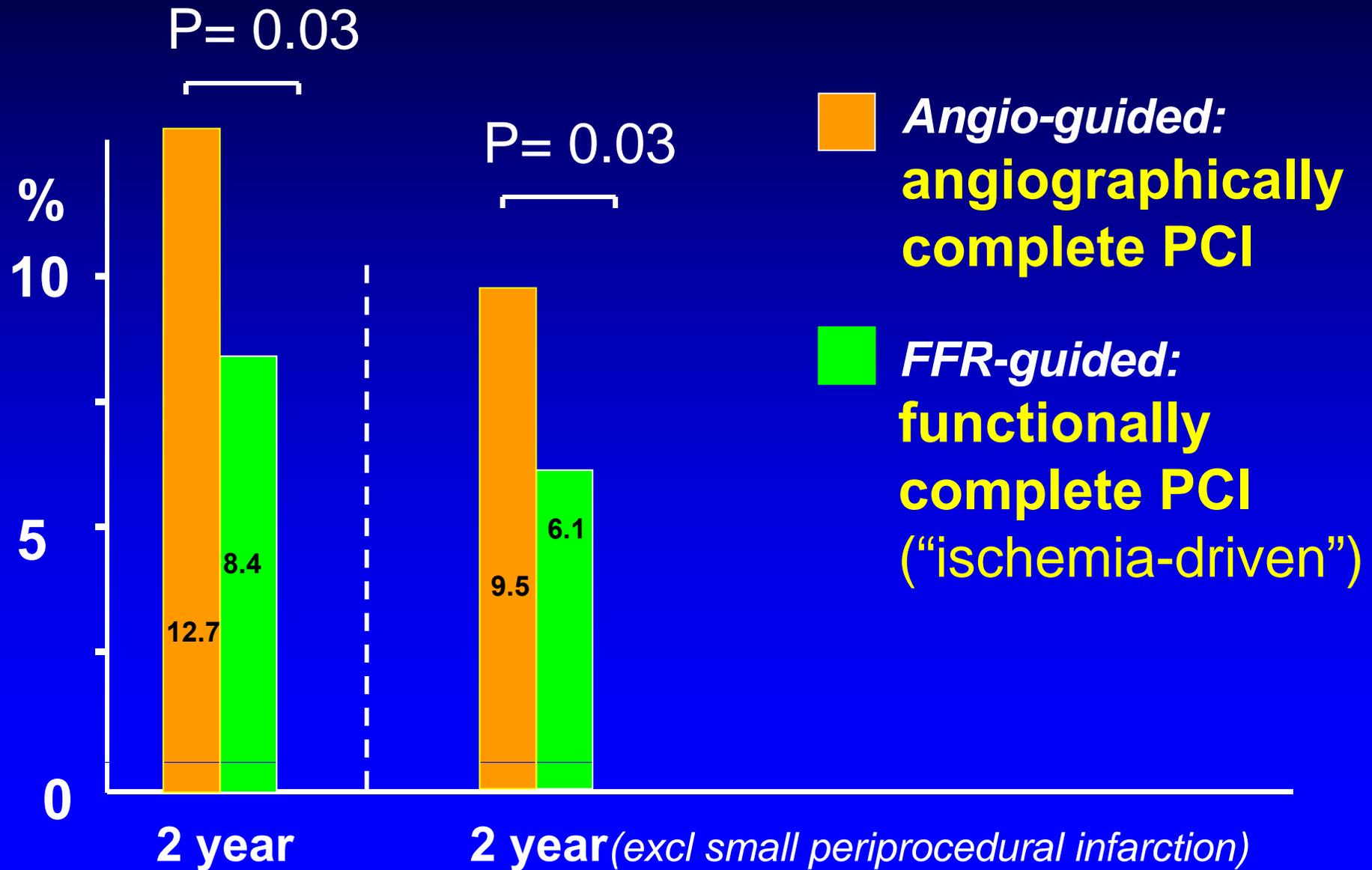
FAME STUDY



HYPOTHESIS:

- ***FFR-guided PCI in MVD is better than
angio-guided PCI***

DEATH & MI in the FAME study after 2 years



FFR –guided PCI:



- improves outcome
- improves quality of live
- is cost-saving
- reduces radiation and contrast exposure
- does not prolong time of procedure

Tonino et al, NEJM 2009; Pijls et al, JACC 2010

***IS FFR GUIDED PCI SUPERIOR TO MEDICAL
TREATMENT ?***



→ FAME -2 STUDY

COURAGE:

Medical Treatment is equivalent to angio-guided PCI

FAME:

FFR guided PCI is superior to Angio-guided PCI

FAME-2 Study:

Is FFR-guided PCI superior to Medical treatment?



FAME 2 Trial Flow Chart

Stable patients scheduled for one-,
Two- or three vessel DES stenting

FFR in all indicated target lesions

There is at least one stenosis
With an FFR ≤ 0.80

Randomisation 1:1

PCI + OMT

OMT

Cohort A

There is at no stenosis
With an FFR ≤ 0.80

OMT

Cohort B

Follow-up after 1, 6 months, 1, 2, 3, 4, and 5 years

FAME 2 Trial Flow Chart

70 % of the patients

Stable patients scheduled for one-, Two- or three vessel DES stenting

30 % of the patients

FFR in all indicated target lesions

There is at least one stenosis
With an FFR ≤ 0.80

There is at no stenosis
With an FFR ≤ 0.80

Randomisation 1:1

PCI + OMT

OMT

Cohort A

OMT

Cohort B

Follow-up after 1, 6 months, 1, 2, 3, 4, and 5 years

FAME 2 Trial Primary End-Points

The primary end-point of the FAME 2 trial is the 24-month major adverse cardiac event rate defined as:

- All cause death**
- Myocardial infarction**
- Unplanned hospitalisation leading to urgent revascularisation**

as adjudicated by the Clinical Event Committee (CEC)

On recommendation of the independent Data and Safety Monitoring Board enrollment was halted on January 15, 2012 due to a significantly increased patient risk of major adverse cardiac events (MACE) among patients randomized to OMT alone compared to patients randomized to OMT plus FFR-guided PCI

Timeline of results of FAME-2:

- *PCR may 2012 Paris: preliminary results of cohort A*
- *ESC aug 2012 Munich: late-breaking trial*
- *publication of the study : september 2012*
- *TCT oct 2012 Miami: large perspective of study*

FRACTIONAL FLOW RESERVE 1996-2012:

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TREATMENT OPTIONS FOR MVD



courage

syntax

R/x

PCI

CABG

TREATMENT OPTIONS FOR MVD



courage

syntax

R/x

PCI

CABG

FAME: improved PCI

TREATMENT OPTIONS FOR MVD



- Quality and outcome of PCI is significantly improved by FFR guidance (FAME studies)
- Therefore, it might be expected that indications for PCI as treatment of MVD, will grow into 2 directions



GUIDELINES ESC SEPTEMBER 2010

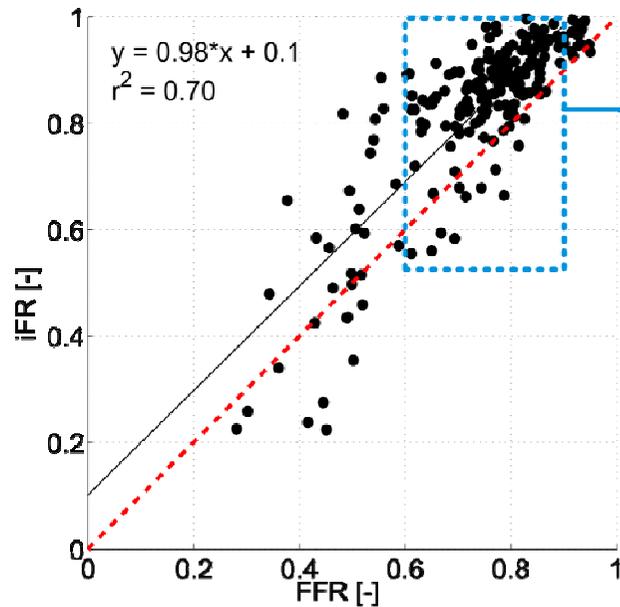
FFR UPGRADED TO LEVEL I A INDICATION

10 – Procedural aspects of PCI

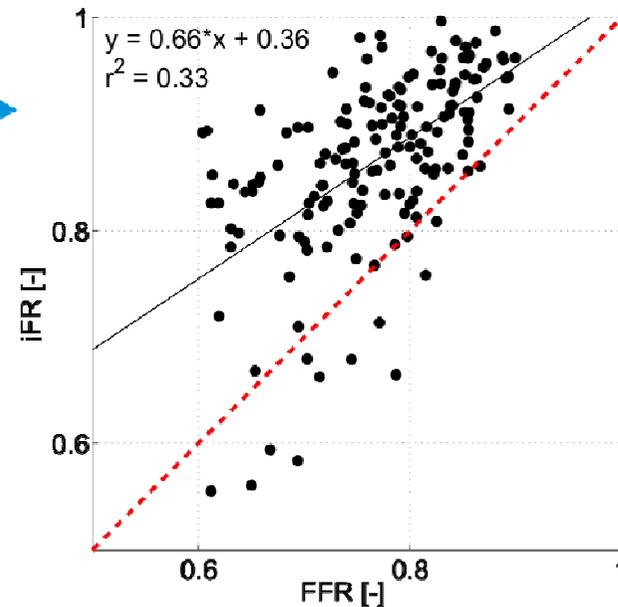
Table 28: Specific PCI devices and pharmacotherapy

	Class	Level
FFR-guided PCI is recommended for detection of ischemia-related lesion(s) when objective evidence of vessel-related ischemia is not available	I	A
DES* are recommended for reduction of restenosis/reocclusion, if no contraindication to extended DAPT	I	A
Distal embolic protection is recommended during PCI of SVG disease to avoid distal embolisation of debris and prevent MI	I	B
Rotablation is recommended for preparation of heavily calcified or severely fibrotic lesions that cannot be crossed by a balloon or adequately dilated before planned stenting	I	C

Correlation between iFR and FFR (N=206)



A

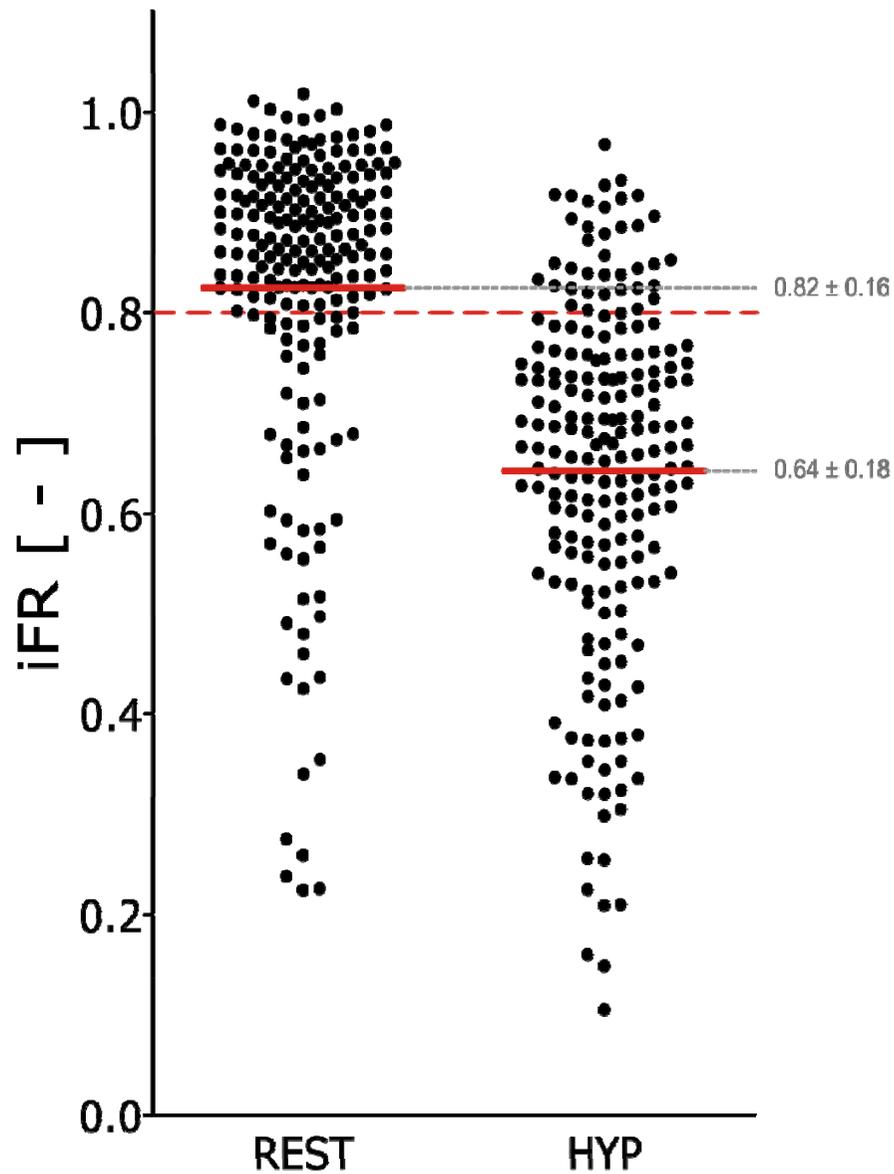


B

all data: $R^2 = 0.70$
diagn accuracy = 67 %

FFR range 0.6-0.9: $R^2 = 0.33$
diagn accuracy = 58 %

(diagnostic accuracy of flipping a coin = 50 %)



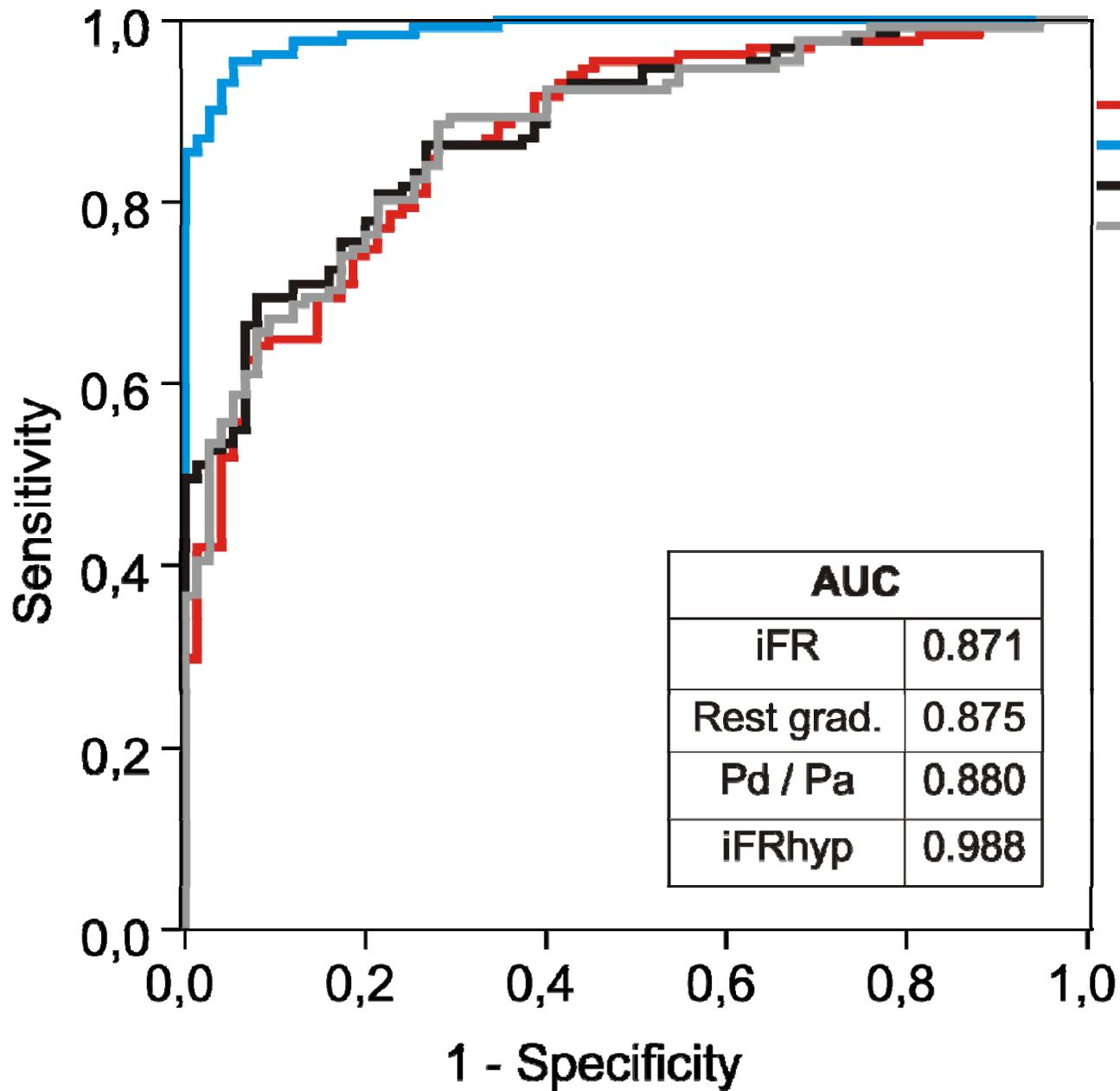
profound influence of hyperemia on iFR:

“iFRhyp” was already called diastolic FFR by Abe et al in Circulation, 1996)

estimated decrease of resistance during “wave-free period”

(1.0 – 0.64)

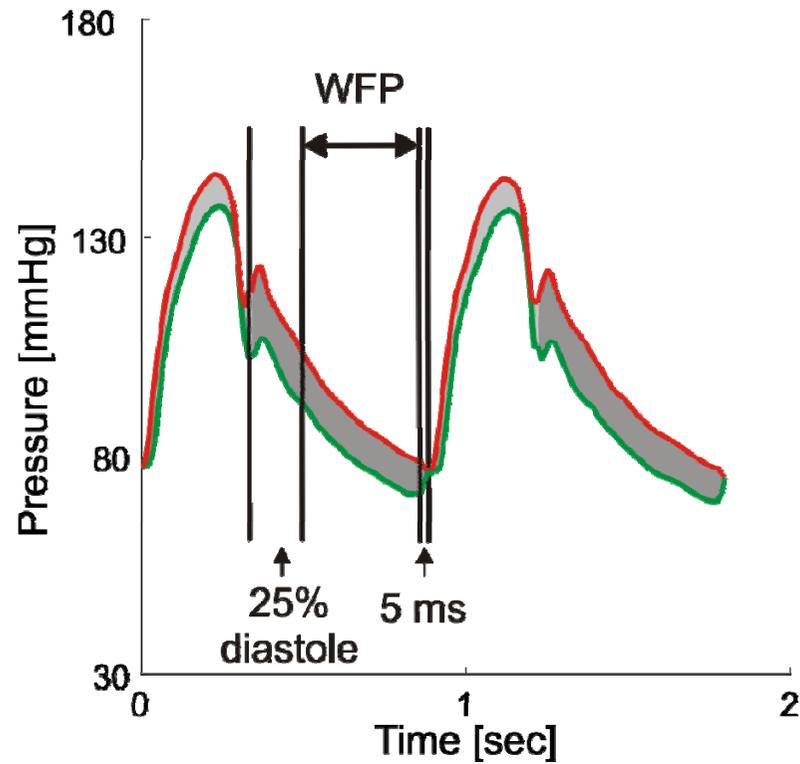
(1.0 – 0.82)



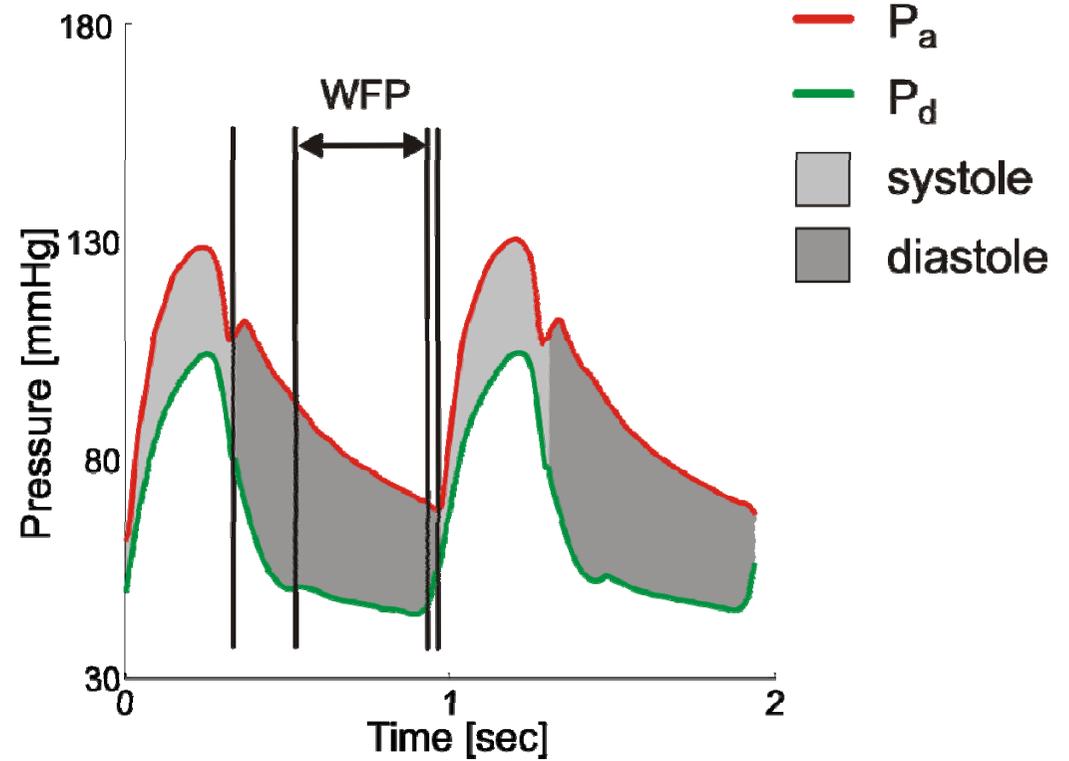
iFR
 iFRhyp
 PdPa
 Rest gradient

~ FFR_{diast}
defined by Abe,
Circulation 2000
threshold 0.76

REST

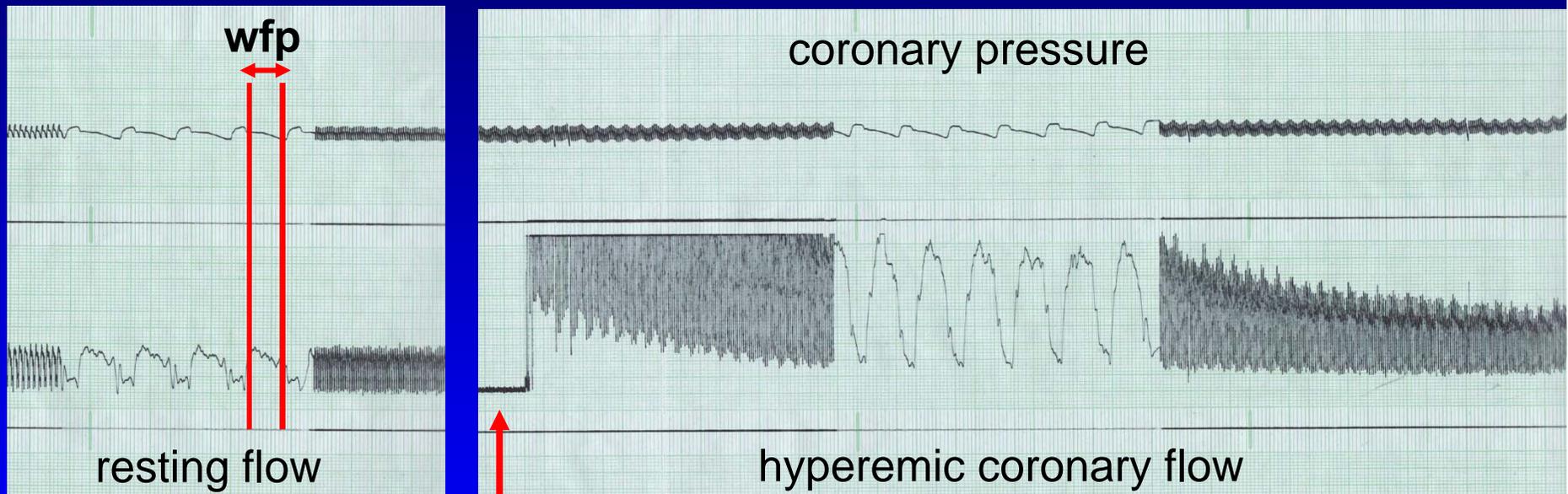


HYPEREMIA

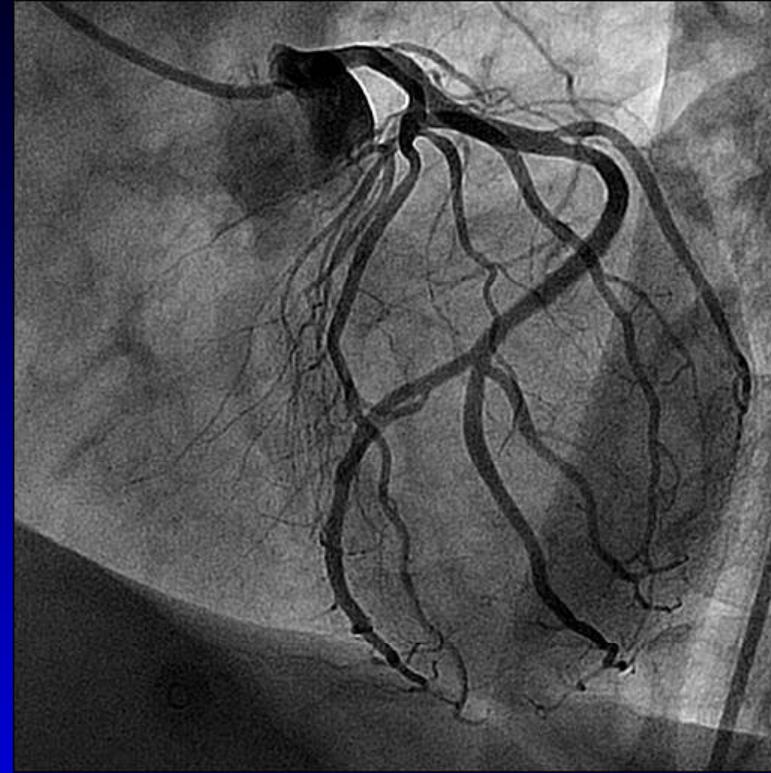
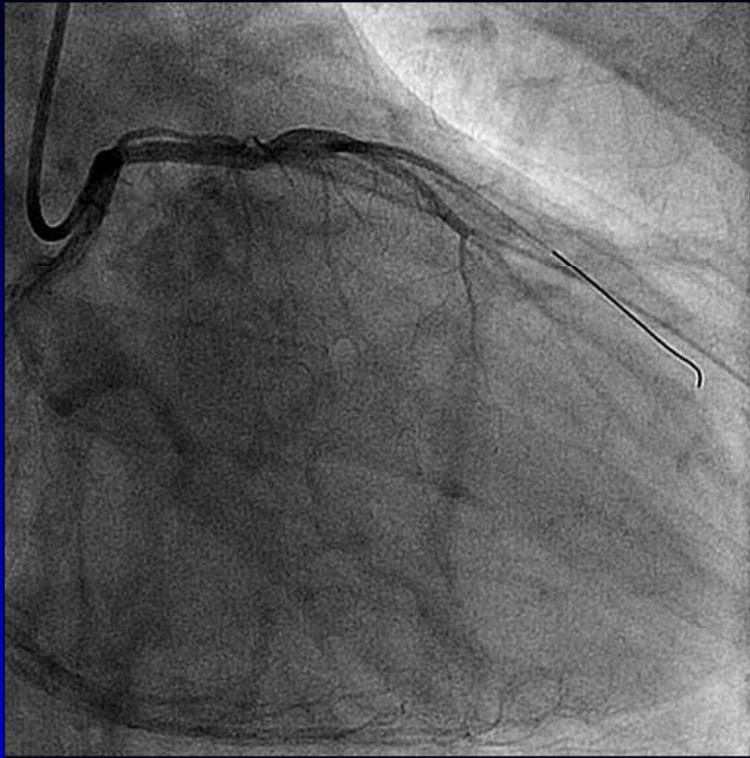


$iFR = P_d / P_a$ at rest during WFP (Sen et al)
Claimed to be independent of hyperemia

*minimal myocardial resistance during the so-called “wave-free period” is ~ 250 % higher than average myocardial resistance at maximum hyperemia in **all** dogs*



coronary occlusion



After stenting (endeavour 12 x 3.0 mm)

FAME study: DESIGN



Randomized multicenter study in 1005 patients undergoing DES-stenting for multivessel disease in 20 US and European centers

- independent core-lab
- independent data analysis
- blinded adverse event committee

Multivessel disease:

Stenoses of > 50% in at least 2 of the 3 major coronary arteries

FLOW CHART



Patient with stenoses $\geq 50\%$
in at least 2 of the 3 major
epicardial vessels

Indicate all stenoses $\geq 50\%$
considered for stenting

Randomization

Angiography-guided PCI

FFR-guided PCI

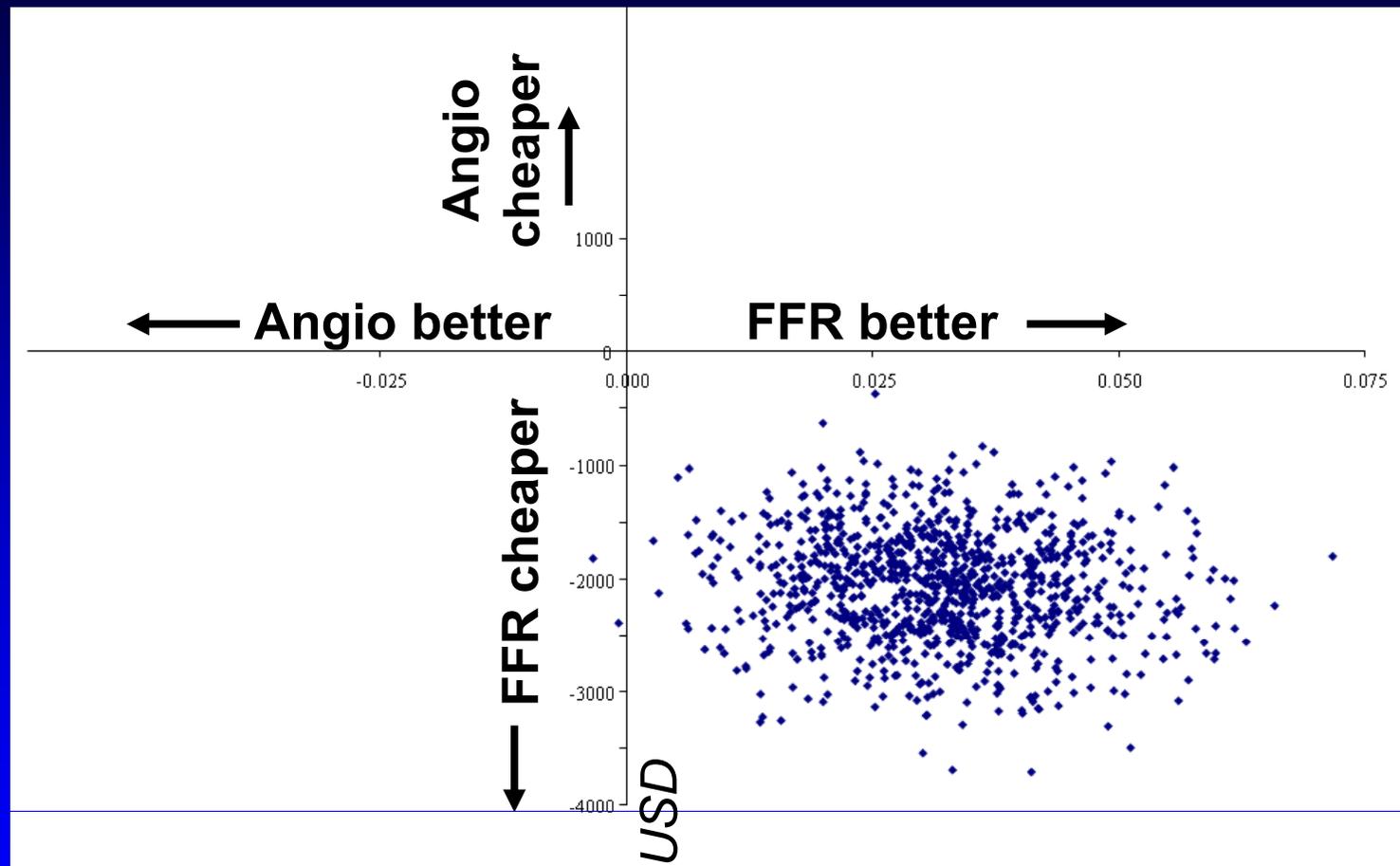
Stent all indicated
stenoses

Measure FFR in all
indicated stenoses

Stent only those
stenoses with $FFR \leq 0.80$

follow-up at 1,2,5 year

FAME study: Economic Evaluation (1)



An FFR-guided strategy to multivessel PCI is one of those rare situations in medicine in which a new innovative treatment not only improves outcome but is also cost-saving

Fearon et al, Circulation 2010

FAME-2: primary endpoints & ethical considerations

- primary endpoint is *death and infarction* at 24 month
- is it ethical to expose patients with proven ischemia to medical treatment (OMT) alone?
- substitute for death/infarction is *unstable angina with emergency PCI*
- achieved by unique *telephonic alert system* (“*FAME-telephone*”)

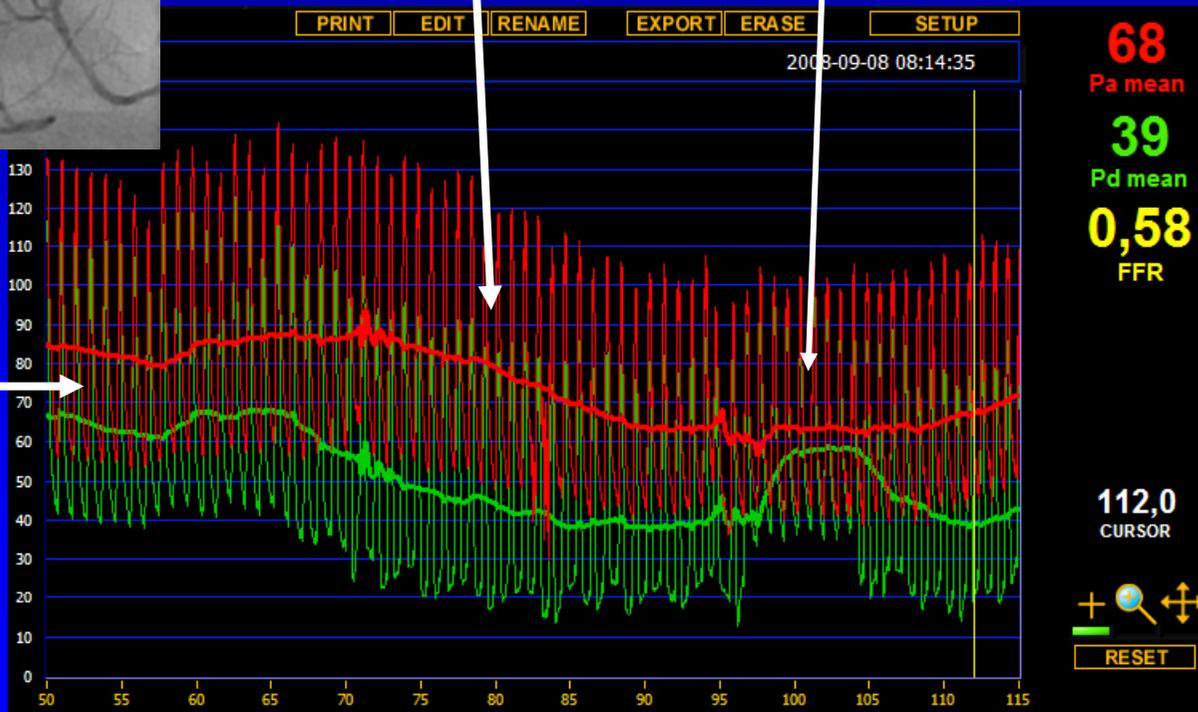


moderate LAD-stenosis with large perfusion area → *low FFR, functionally highly significant*

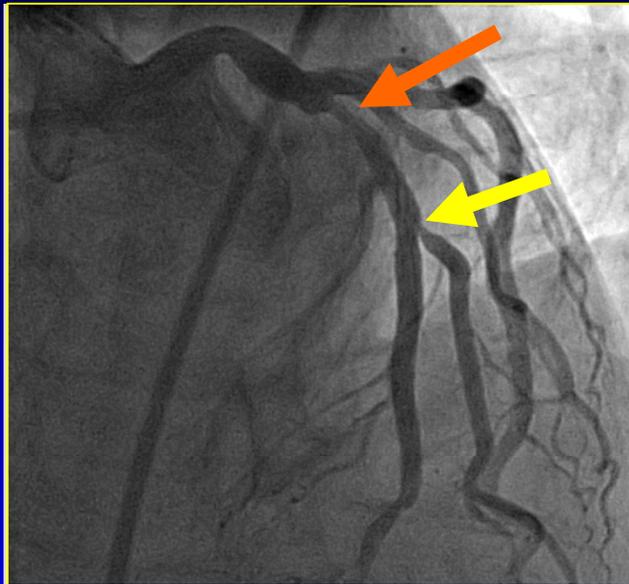
hyperemia

pull-back

resting



BIFURCATIONS



SATIE\RADIVIEW\FAM [REDACTED] COM 1

DATE	TIME	VESSEL	PROCEDURE	ACTION	TYPE	SIZE
2006-08-03	13:55:30				FFR	37Kb
2006-08-03	13:50:23				FFR	131Kb
2006-08-03	13:42:29	DIAG 1			FFR	44Kb
2006-08-03	13:40:56	LAD PROX			FFR	24Kb
2006-08-03	13:34:25	DIAG 1			FFR	36Kb
2006-08-03	13:33:10	LAD PROX			FFR	85Kb

[RENAME] [EXPORT] [ERASE] [SETUP]

G 1 2006-08-03 13:34:25

(85)
Pa mean

(64)
Pd mean

0,75
FFR

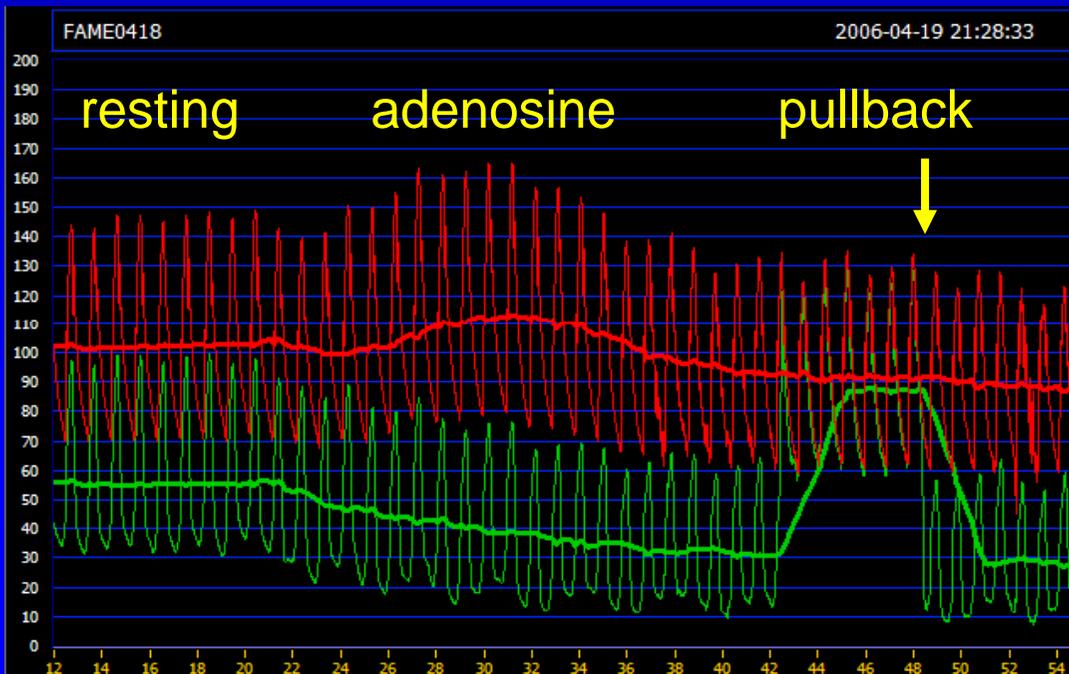
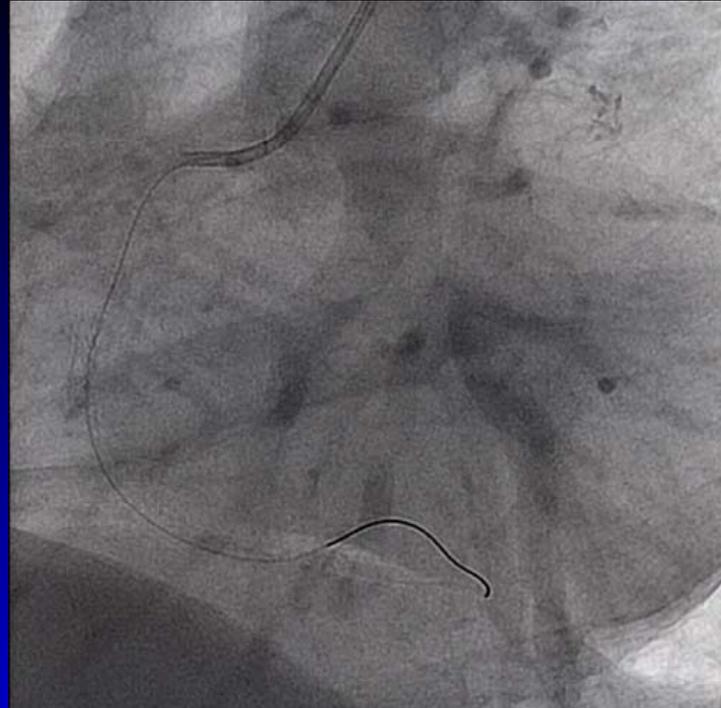
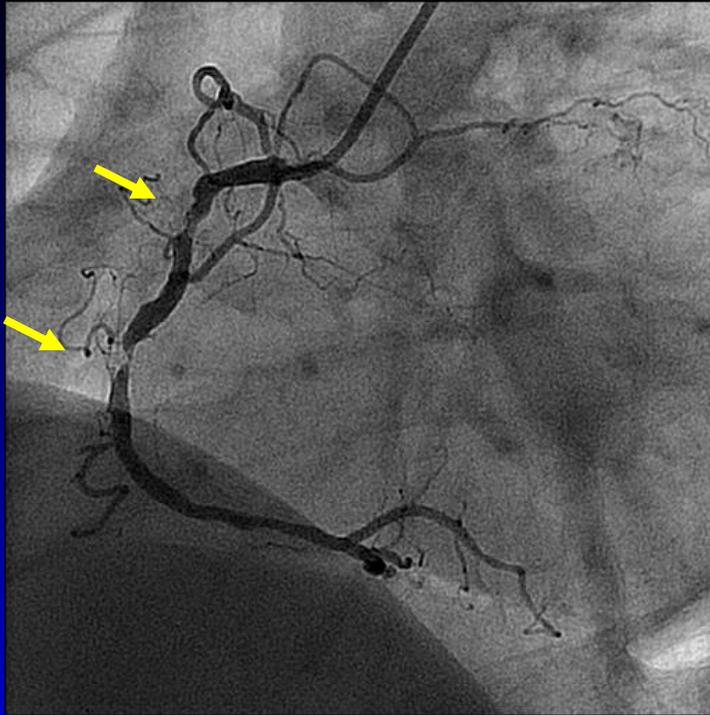
0,15
CURSOR

Ostial Diagonal

Proximal LAD

[+][magnifying glass][crosshair]

[RESET]



TANDEM LESIONS

FFR: The Pressure Pull-back Curve

Pressure pull-back curve at maximum hyperemia:

- place sensor in distal coronary artery
- induce sustained maximum hyperemia by i.v. adenosine, or i.c. papaverine
- pull back the sensor slowly under fluoroscopy
- the individual contribution of every segment and spot to the extent of disease can be studied in this way

Coronary pressure is unique in this respect and such detailed spatial information cannot be obtained by any other invasive or non-invasive method

FAME study: HYPOTHESIS



FFR – guided Percutaneous Coronary Intervention (PCI) in multivessel disease, is superior to current angiography – guided PCI

DEFER STUDY(2):

Worst Outcome With Functionally *Significant* Stenosis

Cardiac Death And Acute MI After 5 Years

- non-ischemic stenosis, R/x
- non-ischemic stenosis, R/x + stent
- ischemic stenosis, R/x + stent

