# CORONARY PHYSIOLOGY IN THE CATHLAB:

# FFR IN COMPLEX AND MULTIVESSEL DISEASE

***Educational Training Program ESC***
***European Heart House***
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catharina ziekenhuis

**In complex multivessel disease (MVD), the issue is mostly not *IF* a stent should be placed, but *WHERE exactly* and *HOW MANY* stents**

## *Fractional Flow Reserve (FFR)*

- **is a reliable index to distinguish ischemia**
- **has a high spatial resolution to detect hemodynamic important obstructions within the coronary arteries**
- **is helpful in guiding PCI**

→ ***Does routine use of FFR in MVD, result in better PCI ? (i.e., alleviate symptoms, improve outcome, save costs, etc***

**F**ractional Flow Reserve

*versus*

**A**ngiography for

**M**ultivessel

**E**valuation


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

Tonino et al, NEJM 2009

# *FAME - 1 study: HYPOTHESIS*

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

# *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

# *FAME study: 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
- At least 2 stenoses ≥ 50% in 2 or 3 major epicardial coronary artery disease, 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

Indicate all stenoses ≥ 50% considered for stenting

Randomization

Angiography-guided PCI

Stent all indicated stenoses

FFR-guided PCI

Measure FFR in all indicated stenoses

Stent only those stenoses with FFR ≤ 0.80

1-year follow-up

# *FAME study: PRIMARY ENDPOINT*

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

# *FAME study: 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

# *FAME study: 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: 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 |

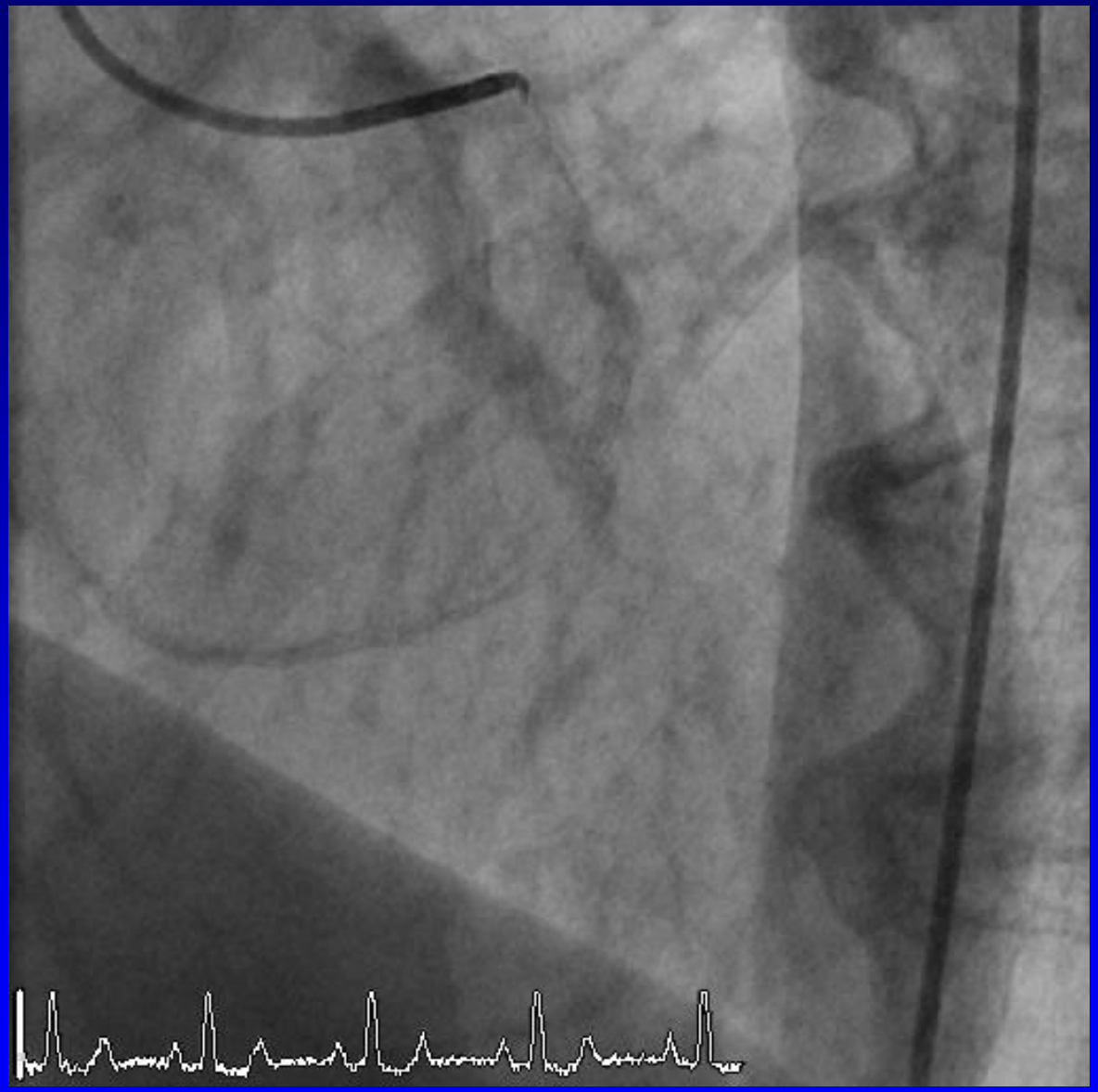
# *FAME study: Baseline Characteristics (2)*

| | ANGIO-group N=496 | FFR-group N=509 | P-value |
|---|---|---|---|
| ***# indicated lesions per patient*** | **2.7±0.9** | **2.8±1.0** | 0.34 |
| 50-70% narrowing, No (%) | **550 (41)** | **624 (44)** | - |
| 70-90% narrowing, No (%) | **553 (41)** | **530 (37)** | - |
| 90-99% narrowing, No (%) | **207 (15)** | **202(14)** | - |
| Total occlusion, No (%) | **40 (3)** | **58 (4)** | - |
| ***Patients with ≥1 total occlusion (%)*** | **7.5** | **10.6** | 0.08 |
| ***Patients with prox LAD involved, No (%)*** | **186 (38)** | **210 (41)** | 0.39 |
| % lesions in segment 1,2,6,7,or 11 | **960 (71)** | **1032 (73)** | 0.42 |

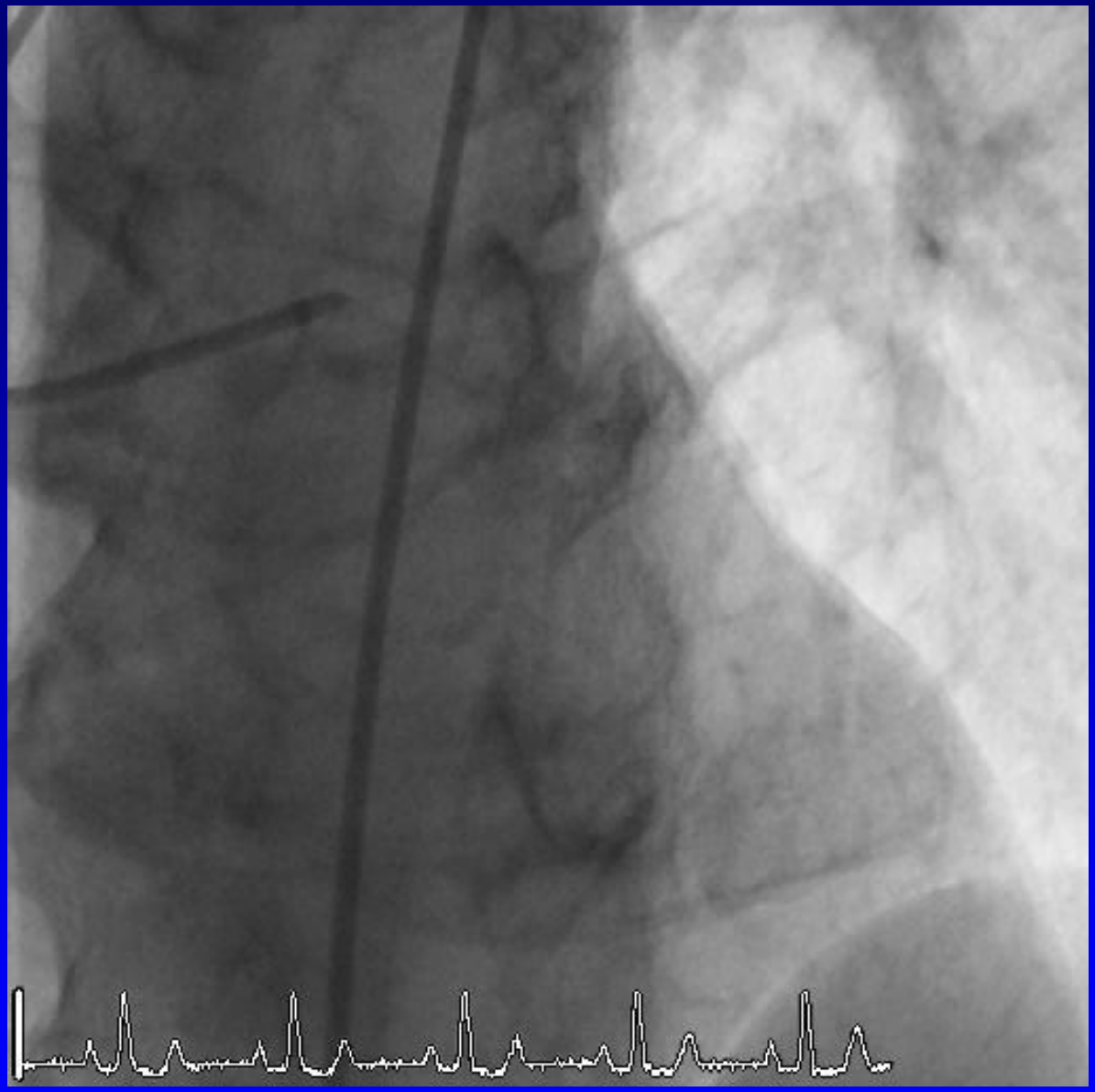
# CASE EXAMPLE:

***A rather common patient with MVD, undergoing FFR-guided PCI***

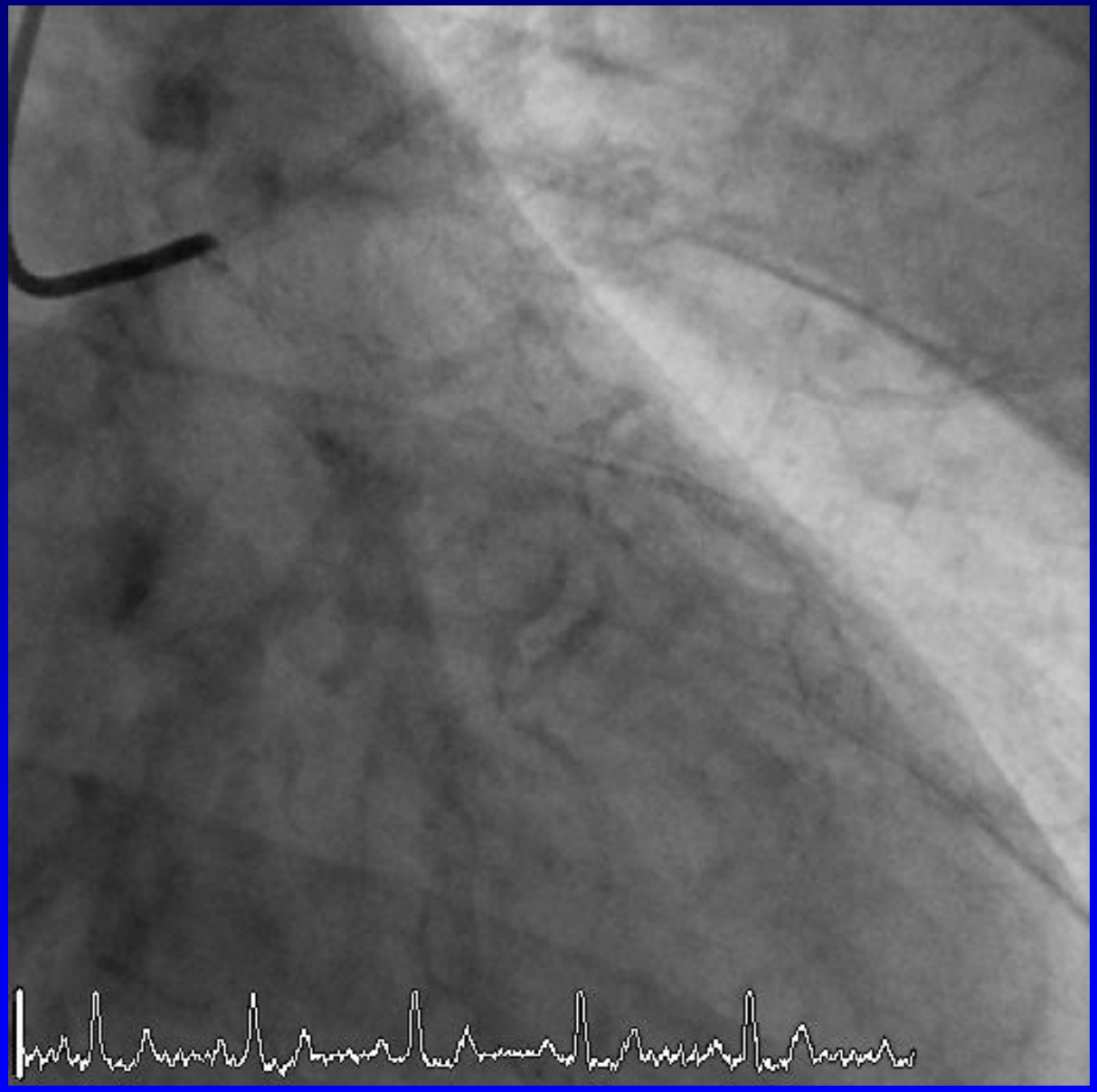
- male born 1952
- anterior wall myocardial infarction 1 month before with DES stent in mid-LAD occlusion
- post-infarction angina ⟶ further invasive analysis



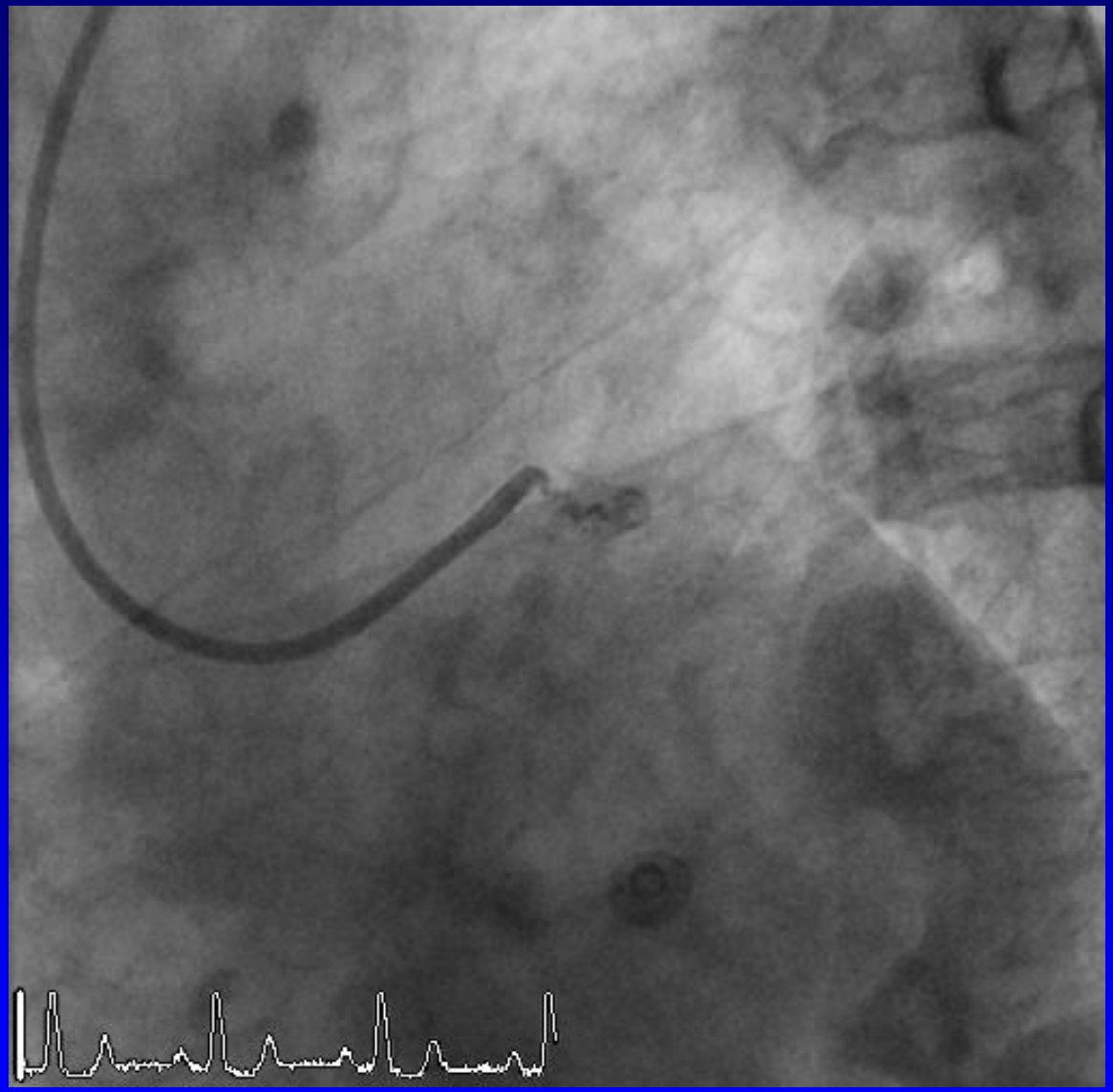
LAD lao-view



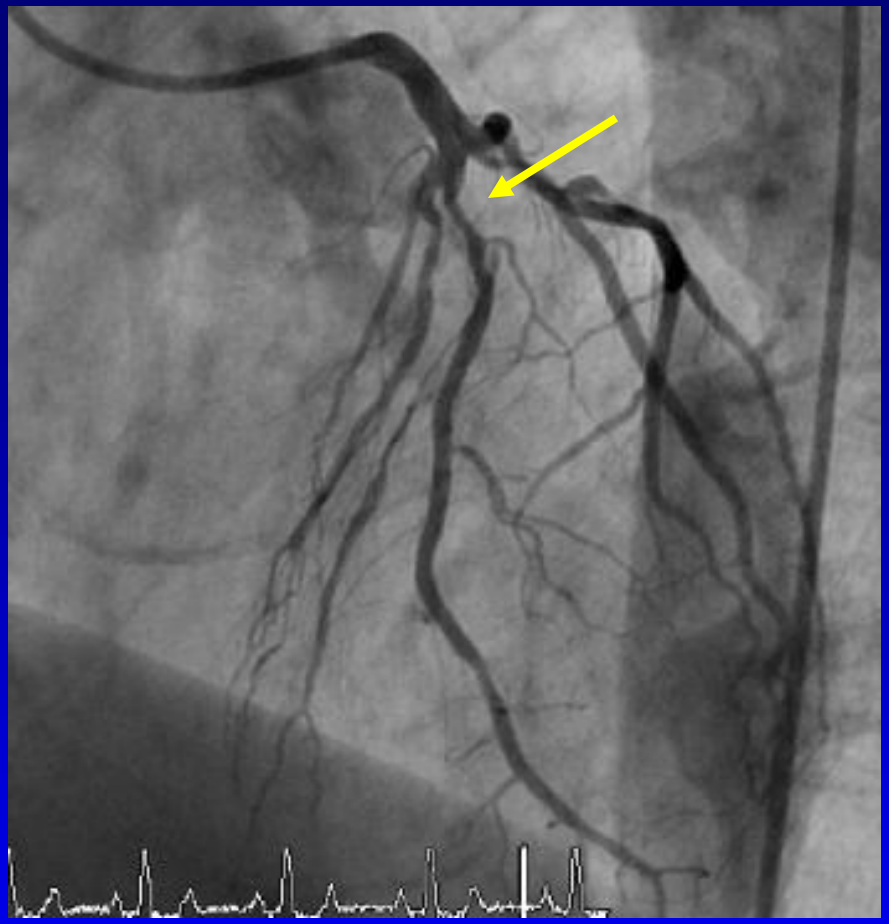
LAD Bartunek-view

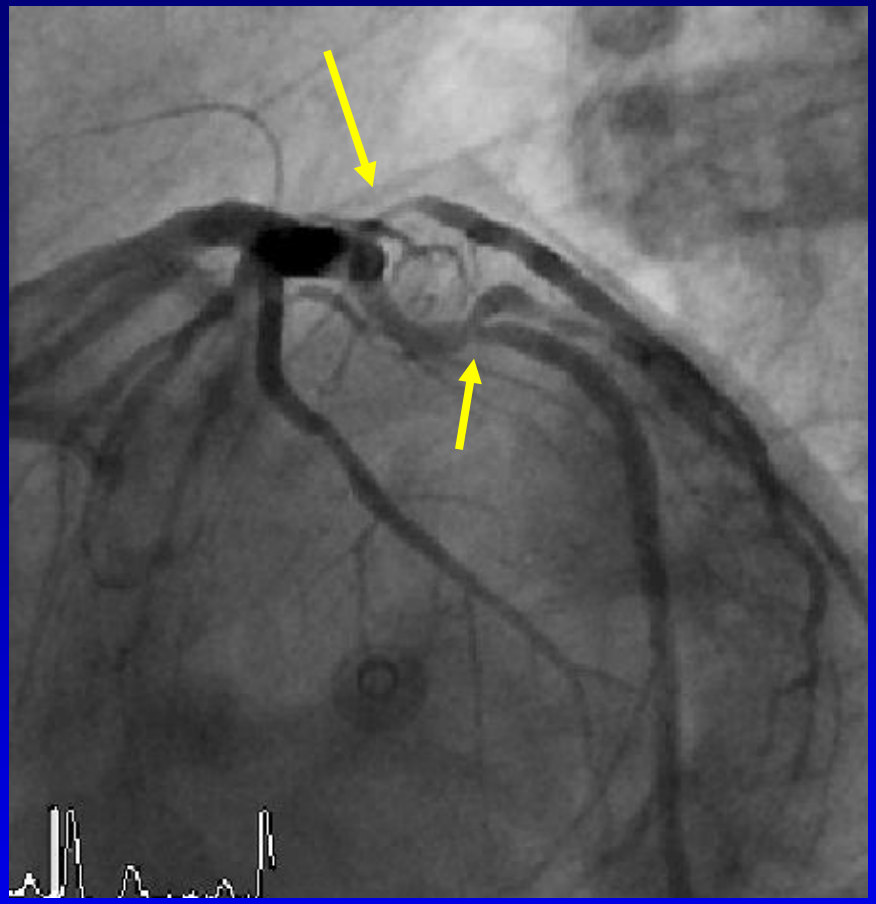


MOCX rao-view



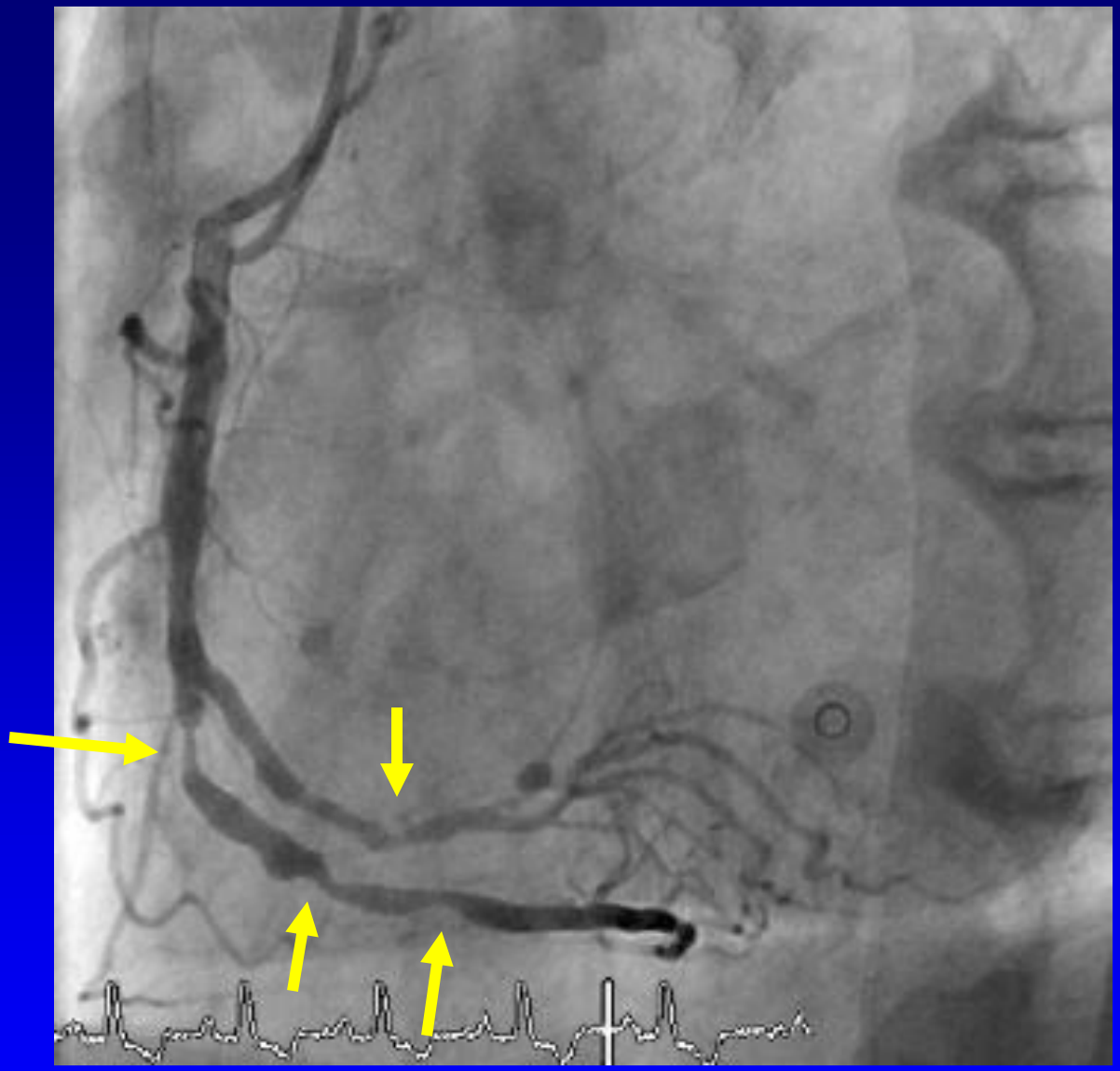
IM branch LAO view





Stent LAD is okay
70% stenosis prox LAD
70% stenosis IM branch
50% stenosis MOCX

RCA lao-view



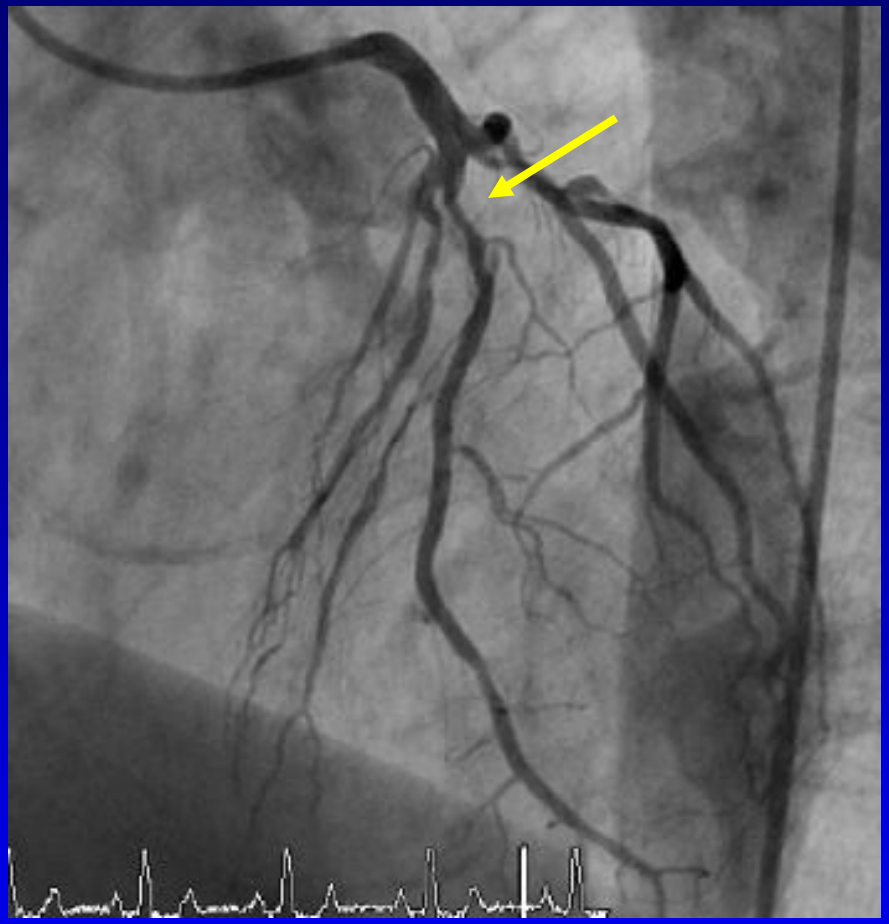
50-70% stenosis PLRCA
80% + 2x 50% stenosis in RDP

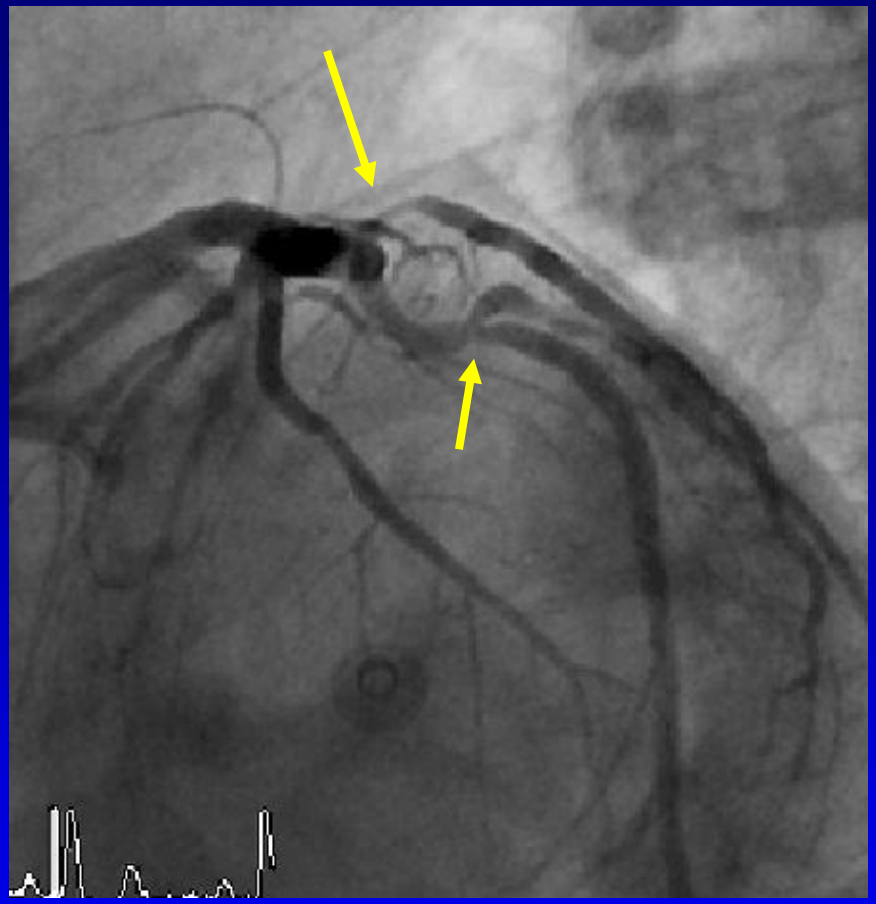
## ***A rather common patient in our cath lab today…….***

- male born 1952
- anterior wall myocardial infarction 1 month before with DES stent in mid-LAD occlusion
- post-infarction angina ⟶ further invasive analysis

  *(may 11th 2009)*

- 70% prox LAD
- 70% prox IM branch
- 50% MOCX
- 50-70% PLRCA
- 90% prox RDP
- 50% mid RDP





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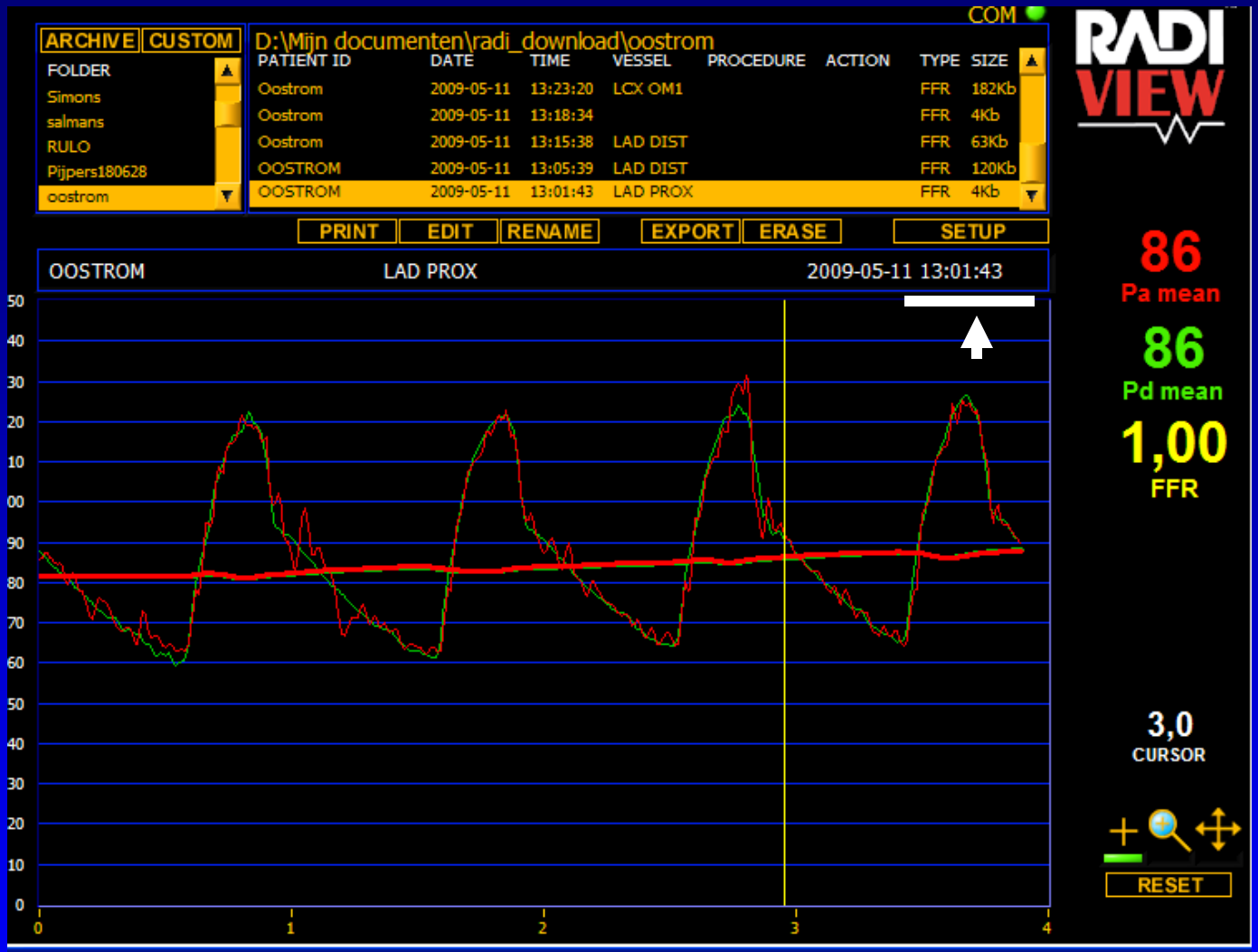
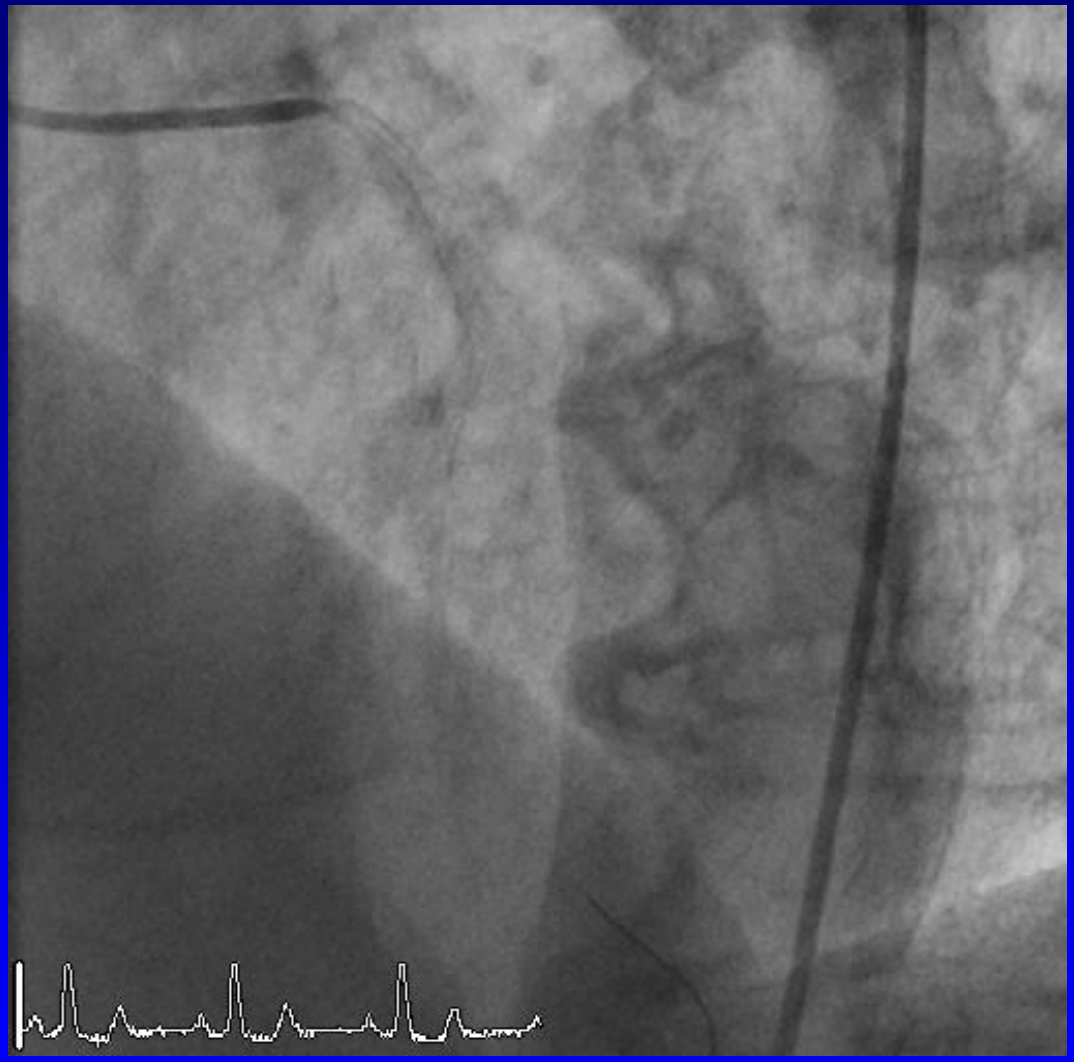
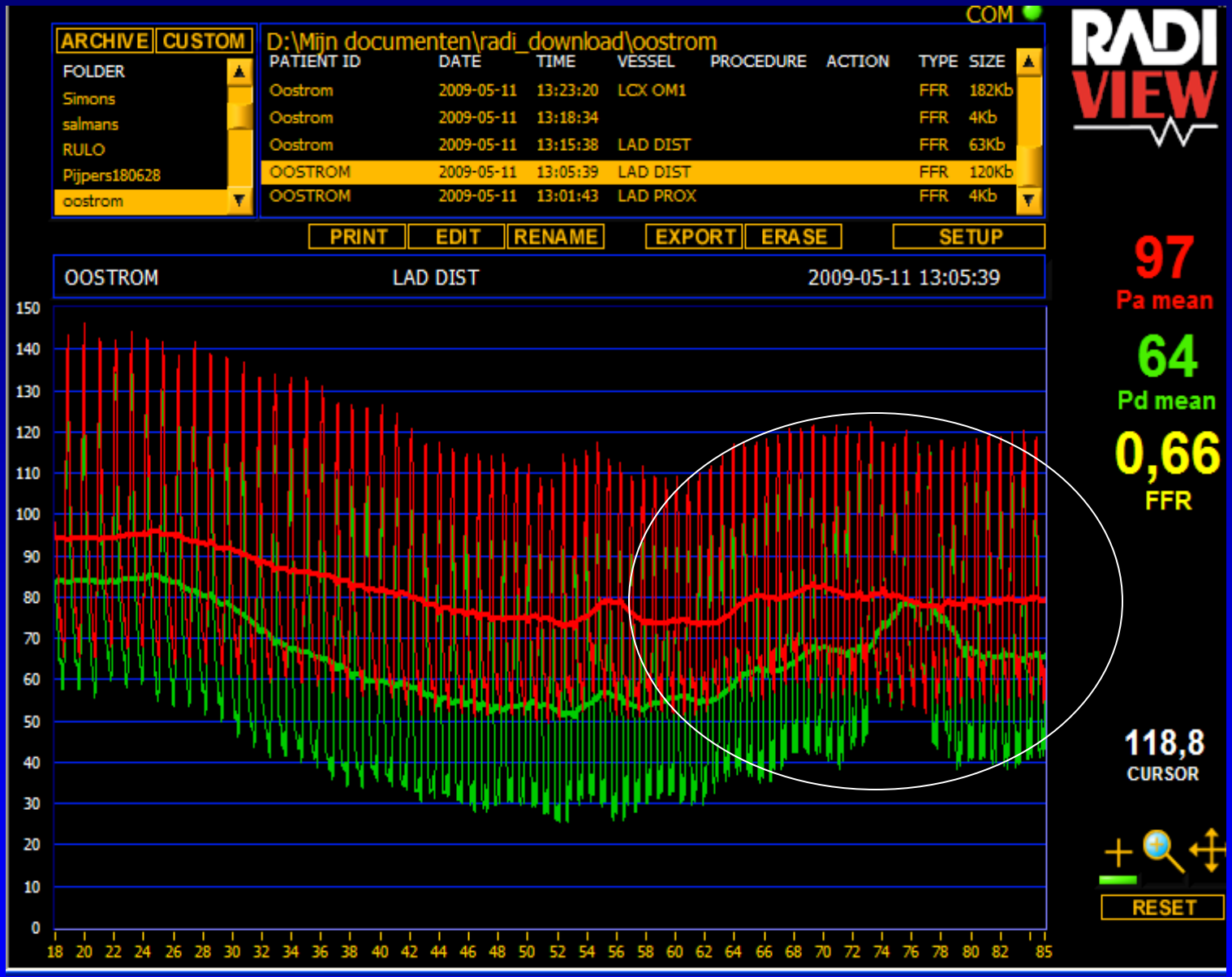



Equalization before entering LAD



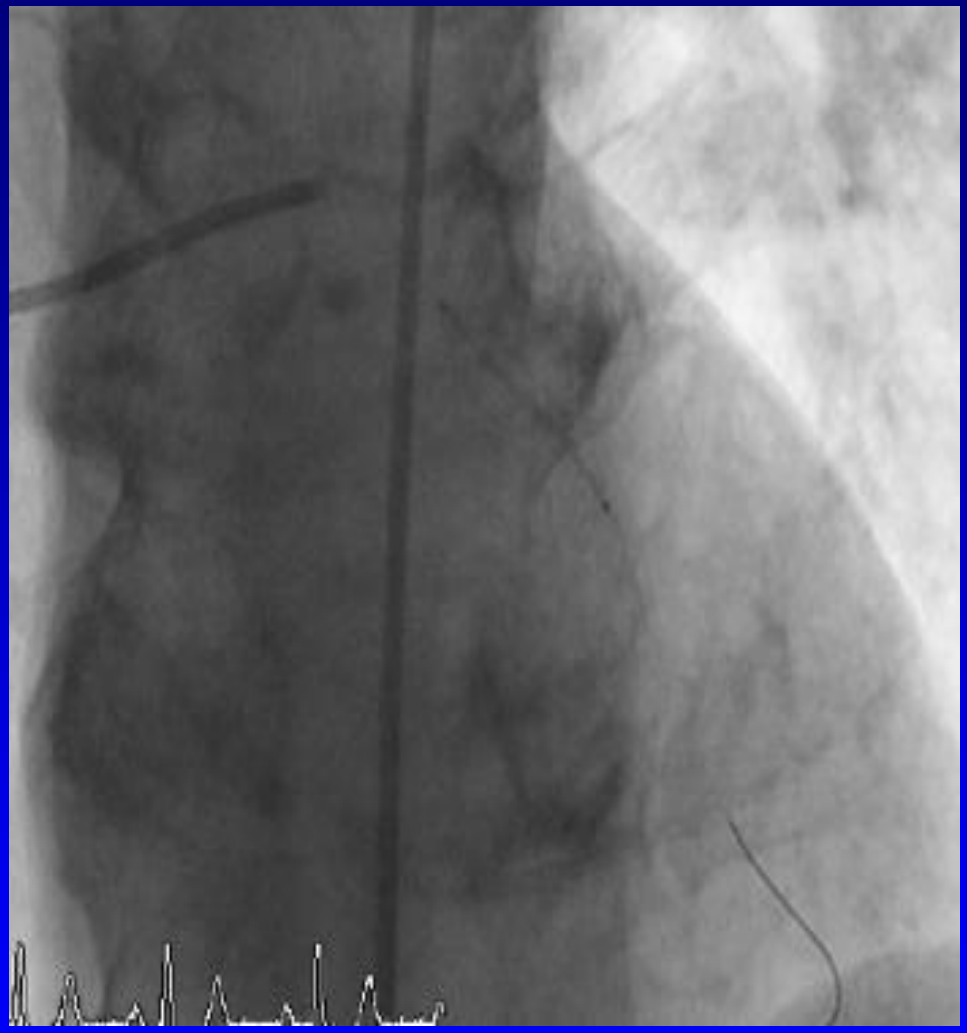
PressureWire in LAD


FFR LAD (i.v. adenosine)

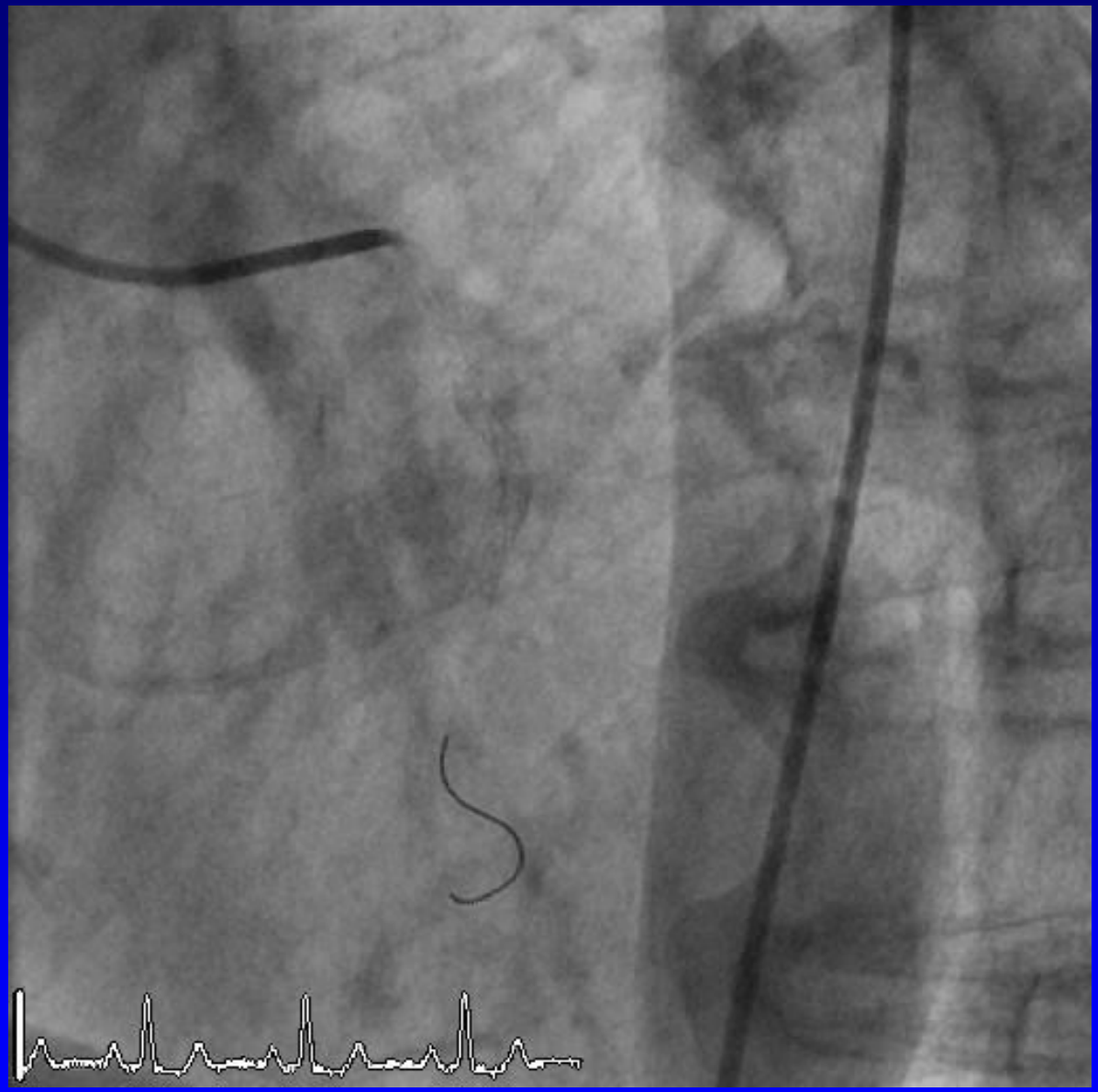



FFR LAD, pull-back &advance across prox segment

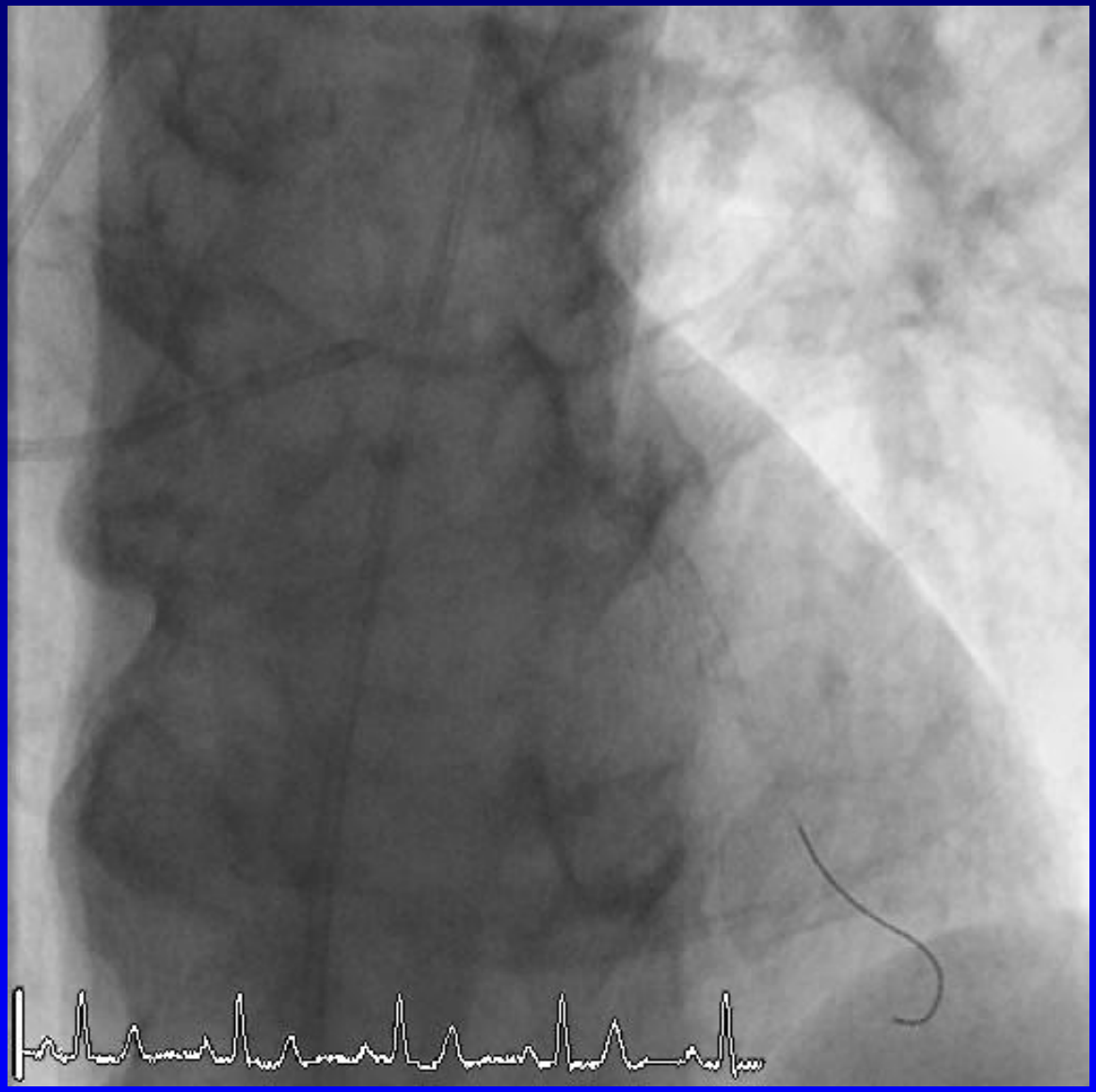

LAD hyperemic pullback detail



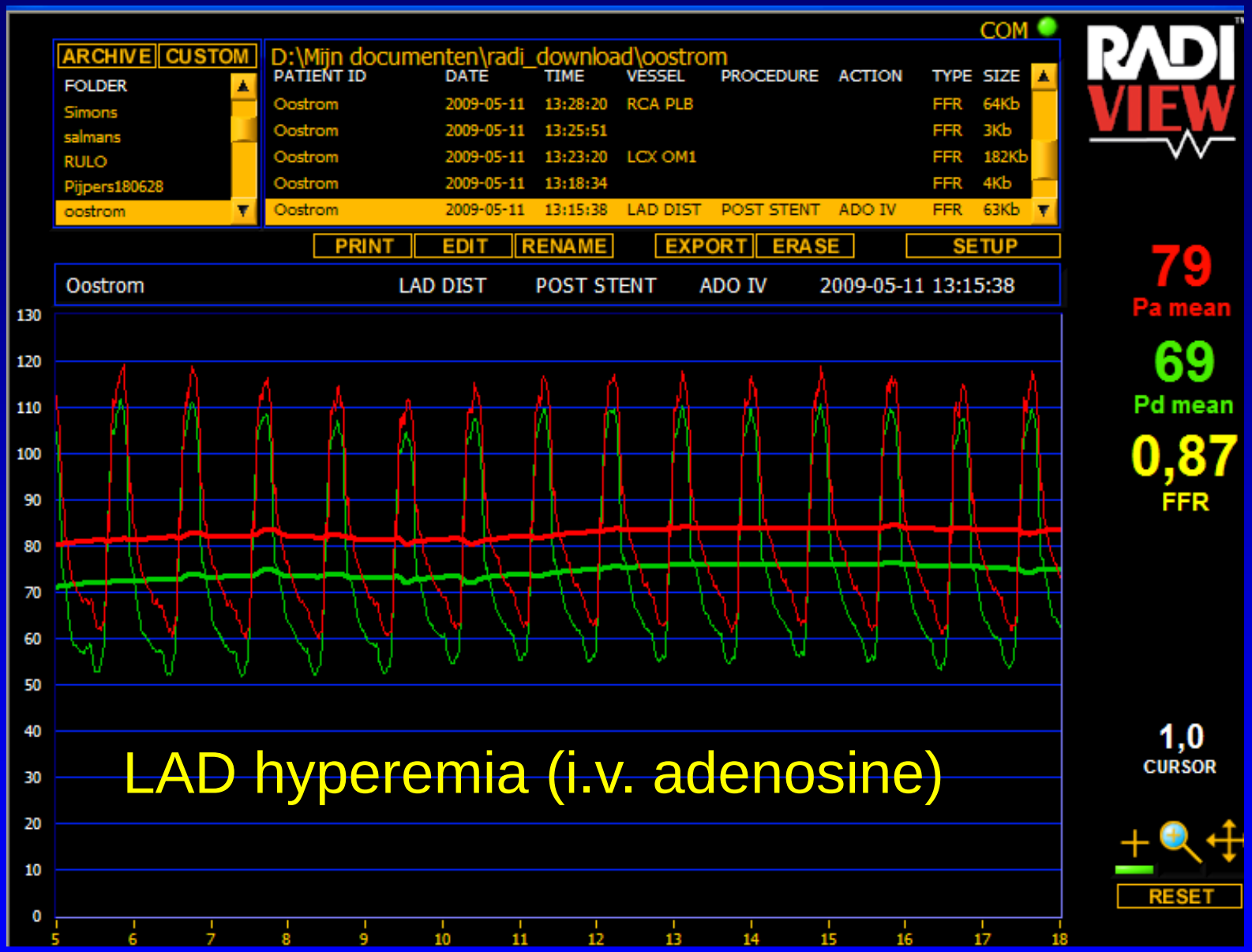
Stent in prox LAD



LAD lao after stenting



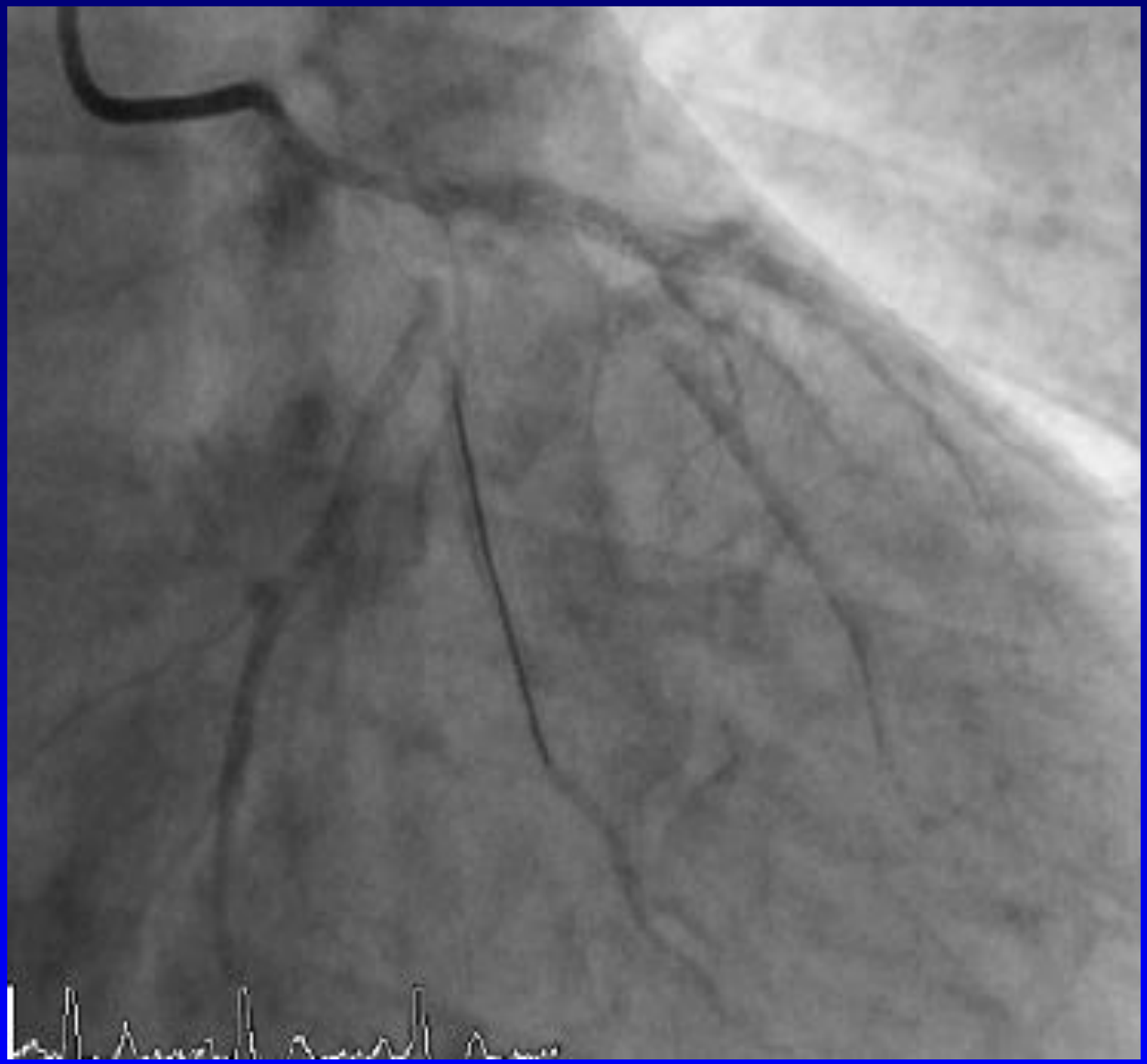
LAD Bartunek-view after stenting



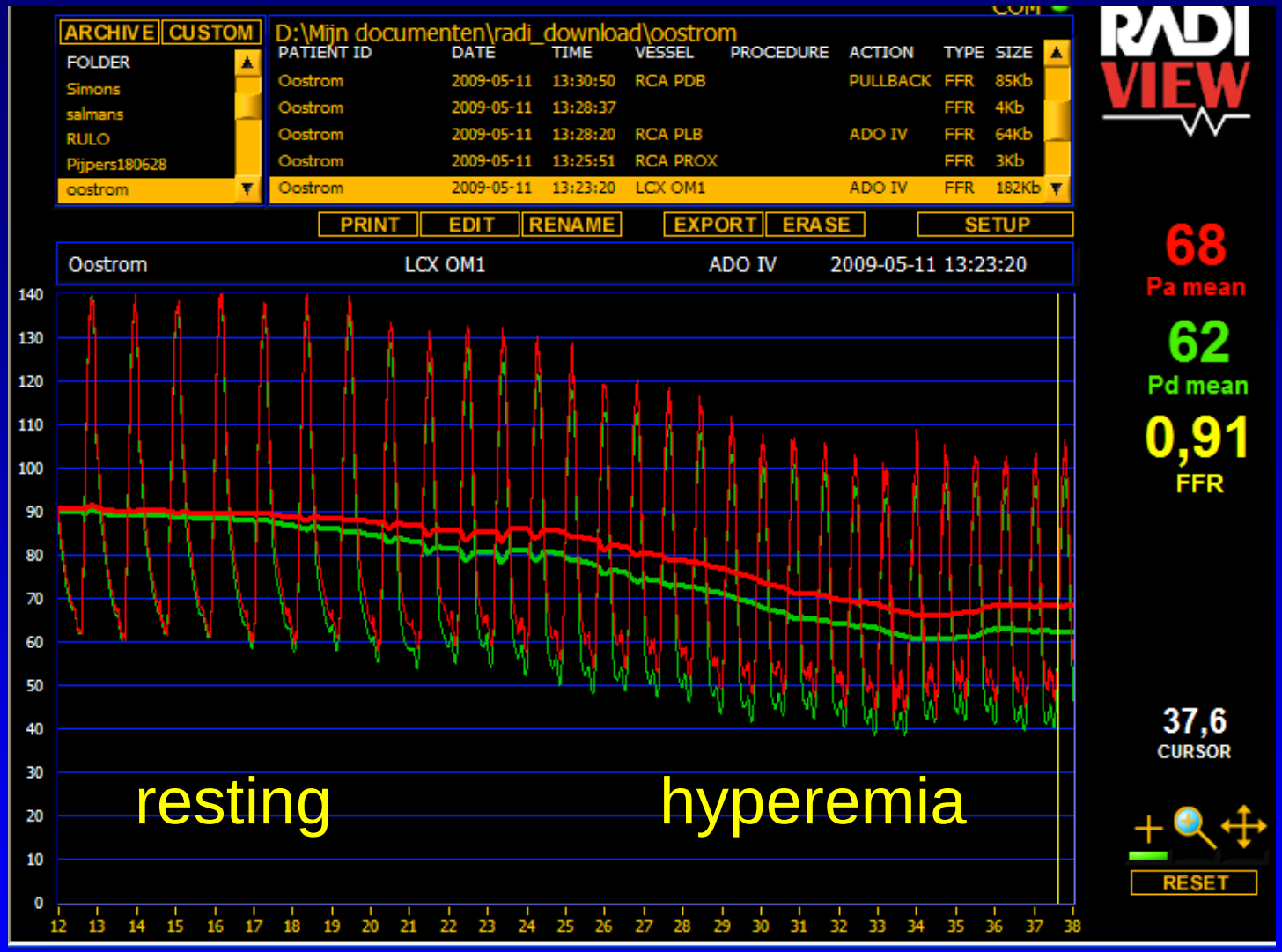

FFR measurement in LAD post stenting


Equalization after having stented LAD/

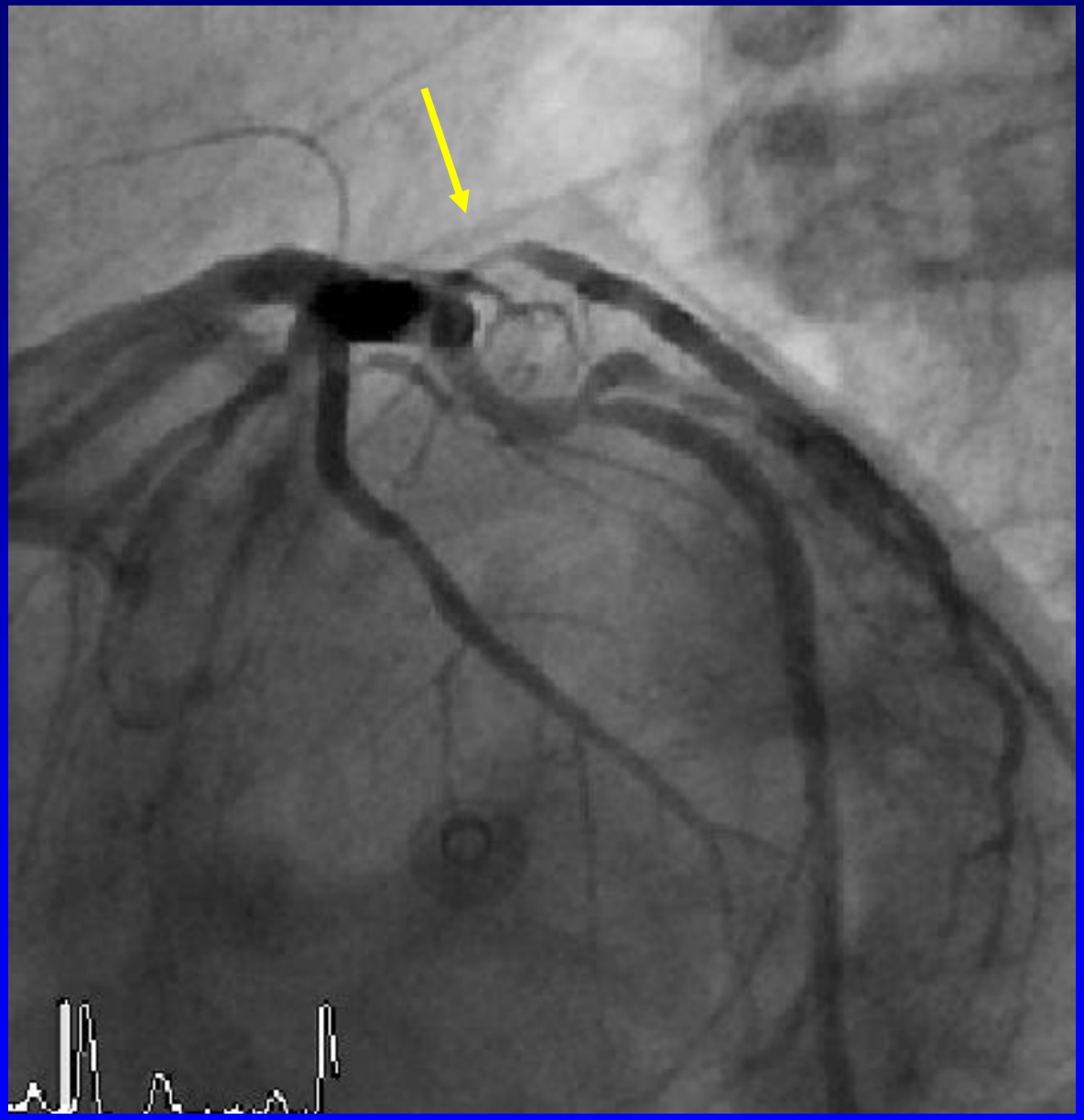
/ before entering LCX

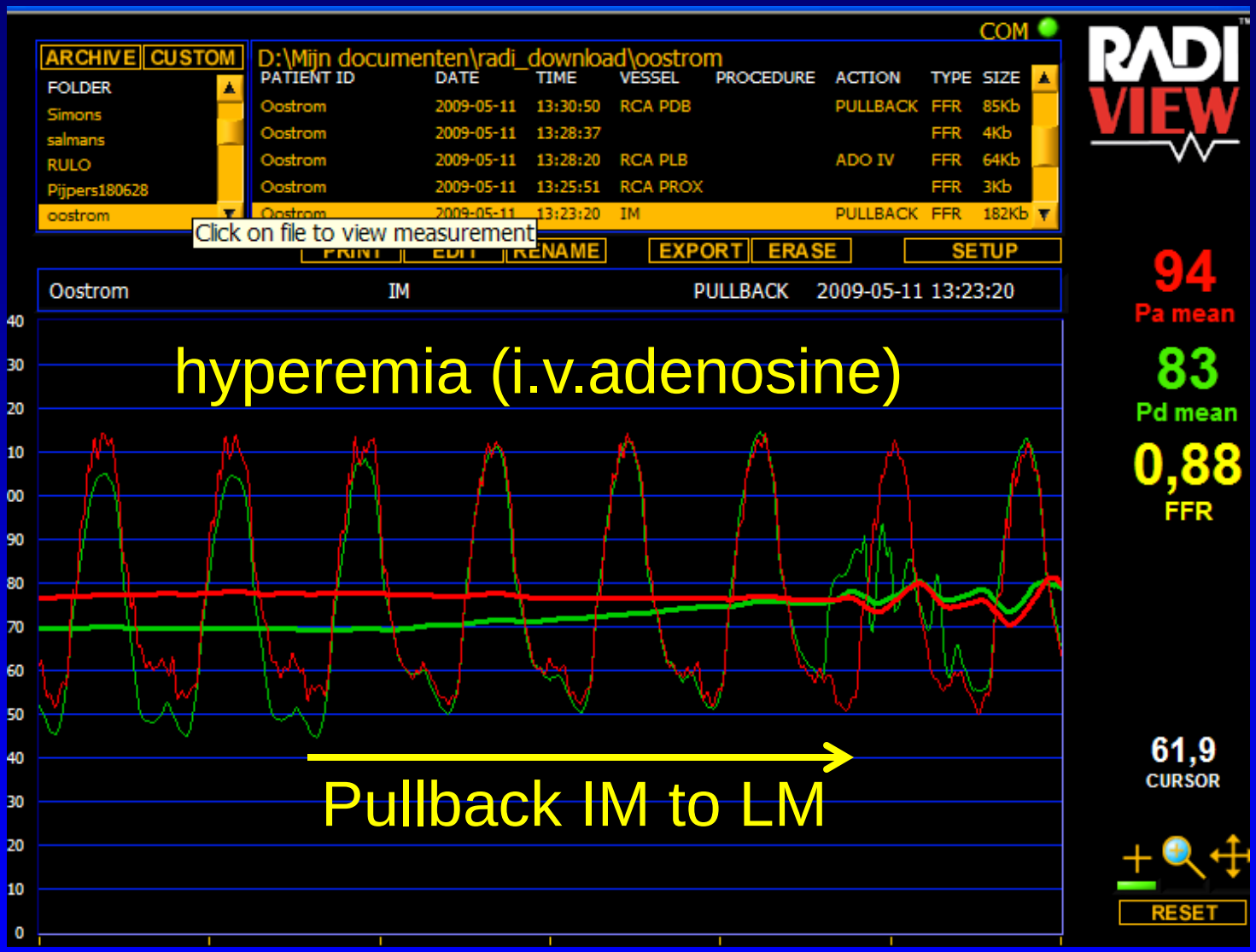


PW in MOCX


ARCHIVE
CUSTOM
FOLDER
Simons
salmans
RULO
Pijpers180628
oostrom
D:\Mijn documenten\radi_download\oostrom
PATIENT ID DATE TIME VESSEL PROCEDURE ACTION TYPE SIZE
Oostrom 2009-05-11 13:30:50 RCA PDB PULLBACK FFR 85Kb
Oostrom 2009-05-11 13:28:37 FFR 4Kb
Oostrom 2009-05-11 13:28:20 RCA PLB ADO IV FFR 64Kb
Oostrom 2009-05-11 13:25:51 RCA PROX FFR 3Kb
Oostrom 2009-05-11 13:23:20 LCX OM1 ADO IV FFR 182Kb
PRINT
EDIT
RENAME
EXPORT
ERASE
SETUP
Oostrom
LCX OM1
ADO IV
2009-05-11 13:23:20
RADI VIEW
68
Pa mean
62
Pd mean
0,91
FFR
37,6
CURSOR
RESET
resting
hyperemia

FFR MOCX

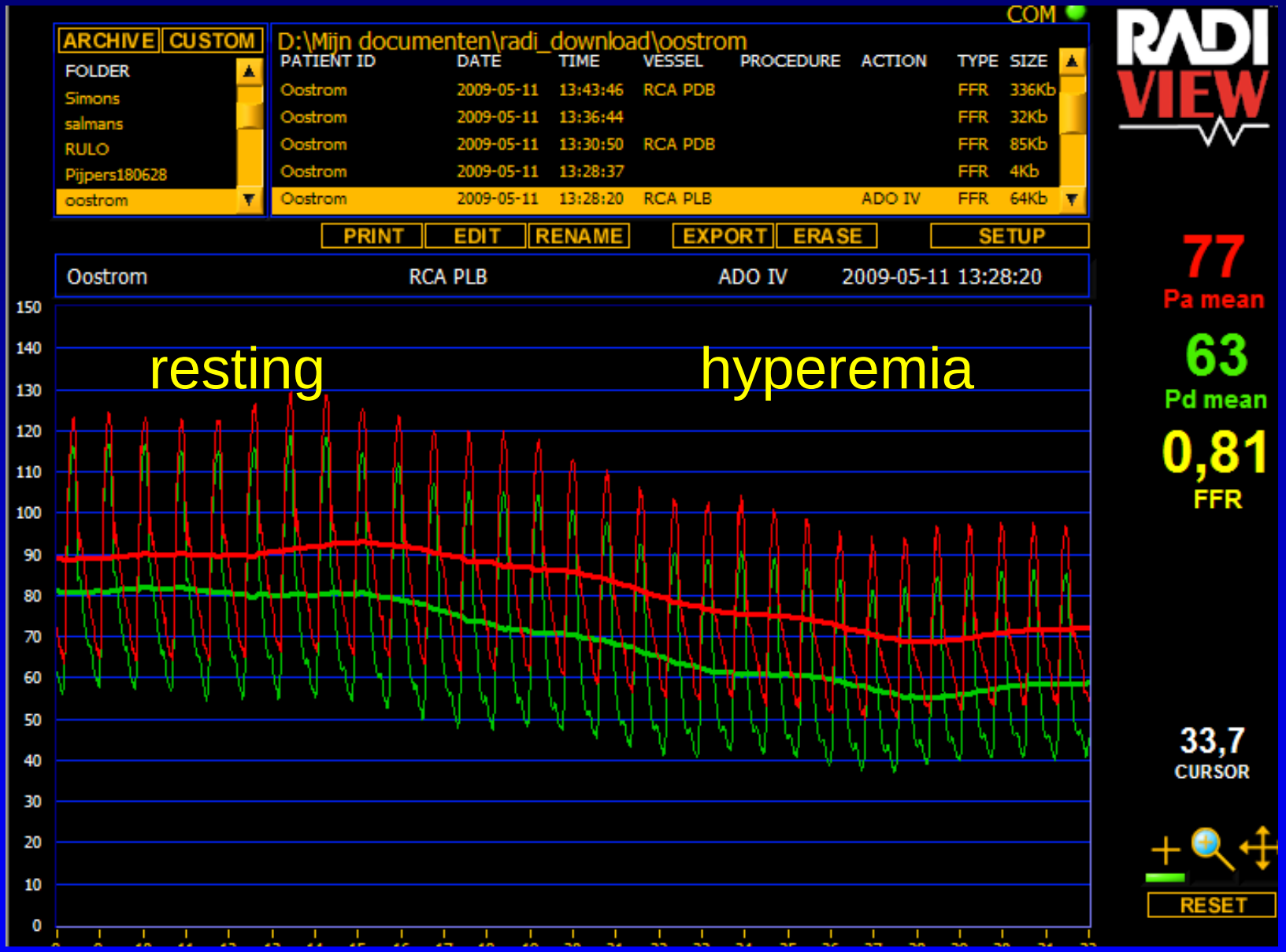




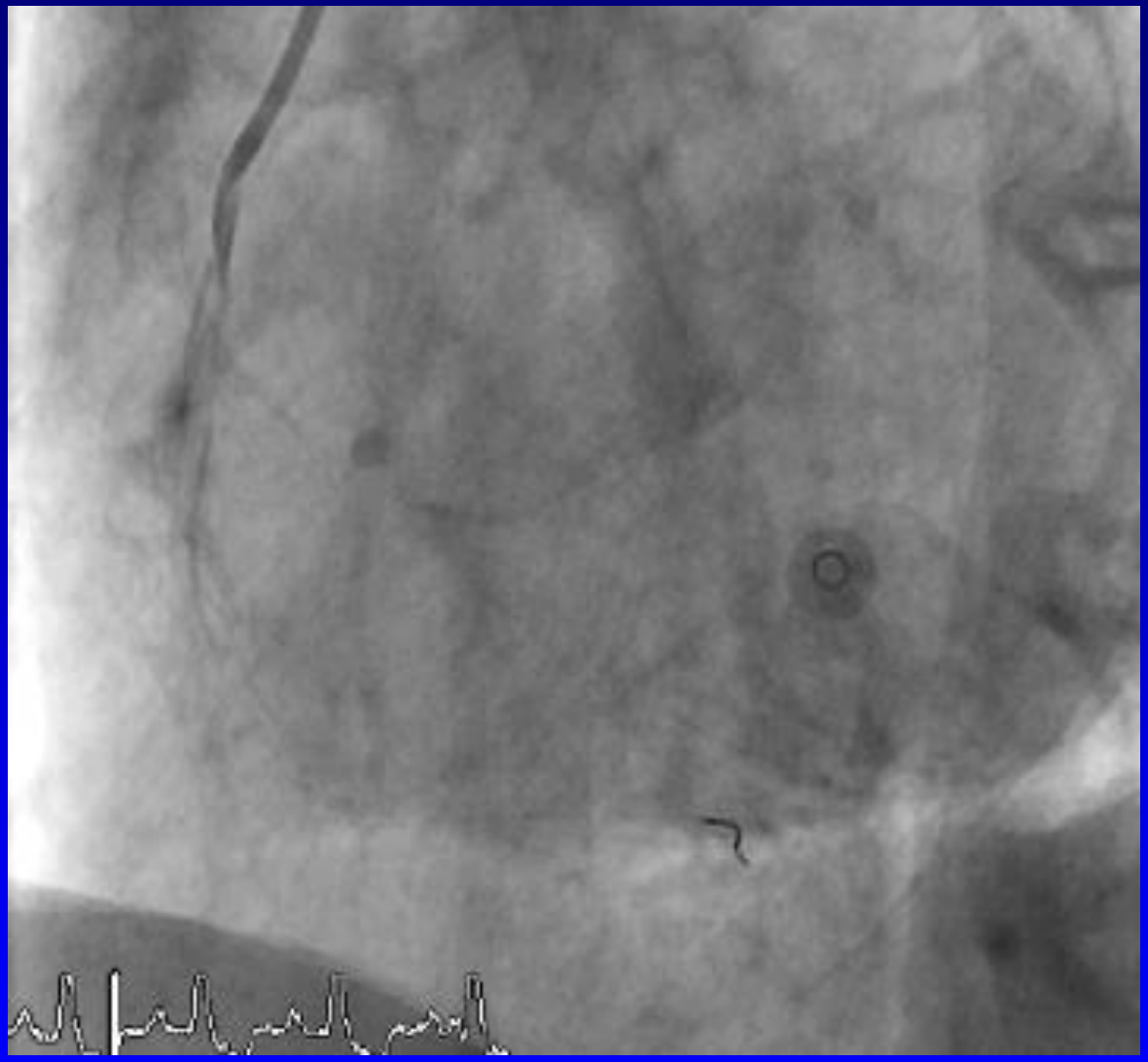

FFR IM branch


Equalizing before entering RCA

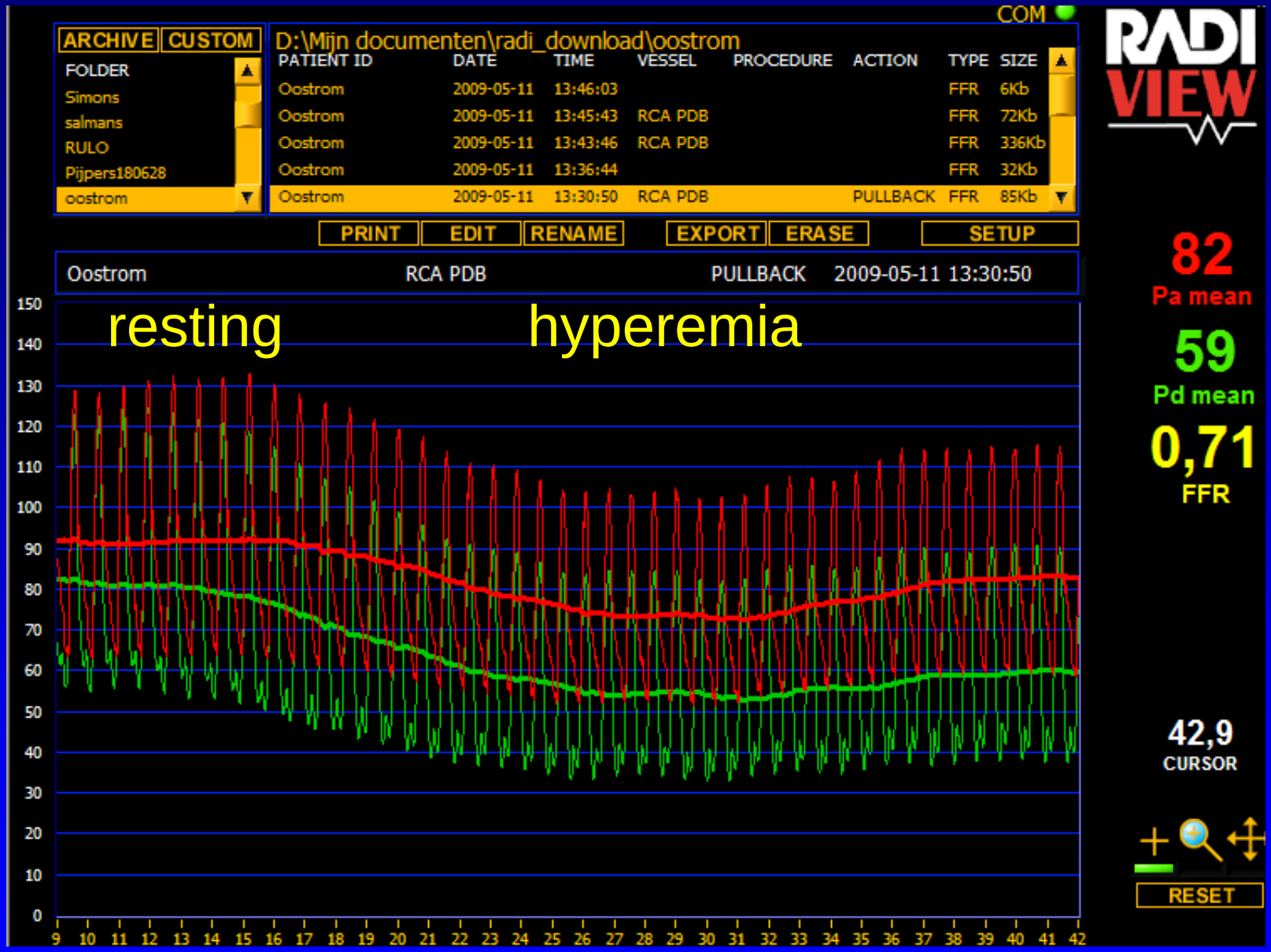
Wire in PL-RCA



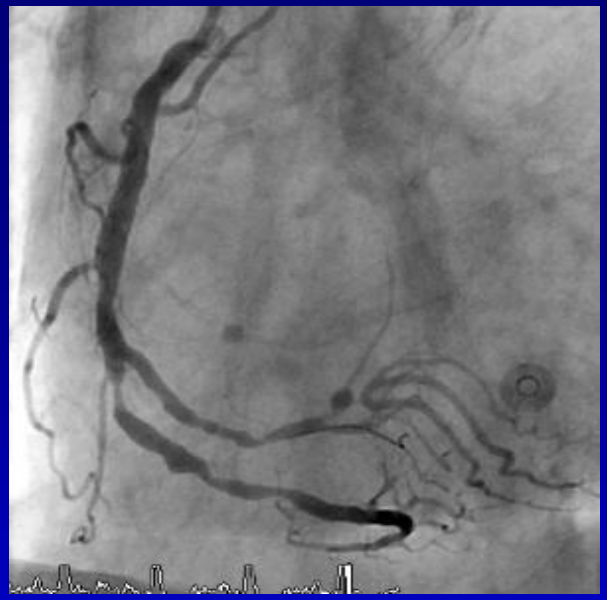

FFR measurement in PL-RCA

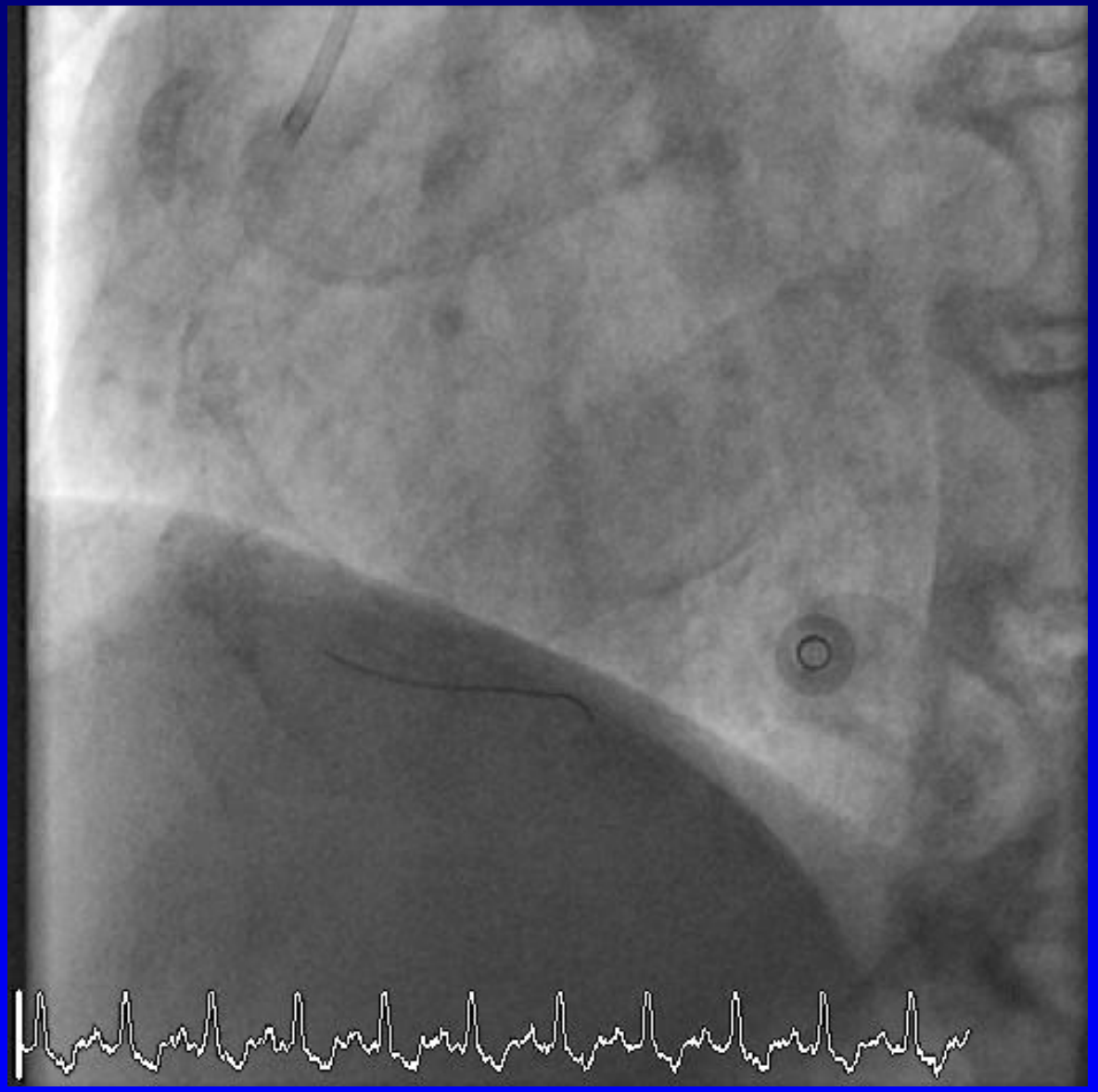


PressureWire in RDP

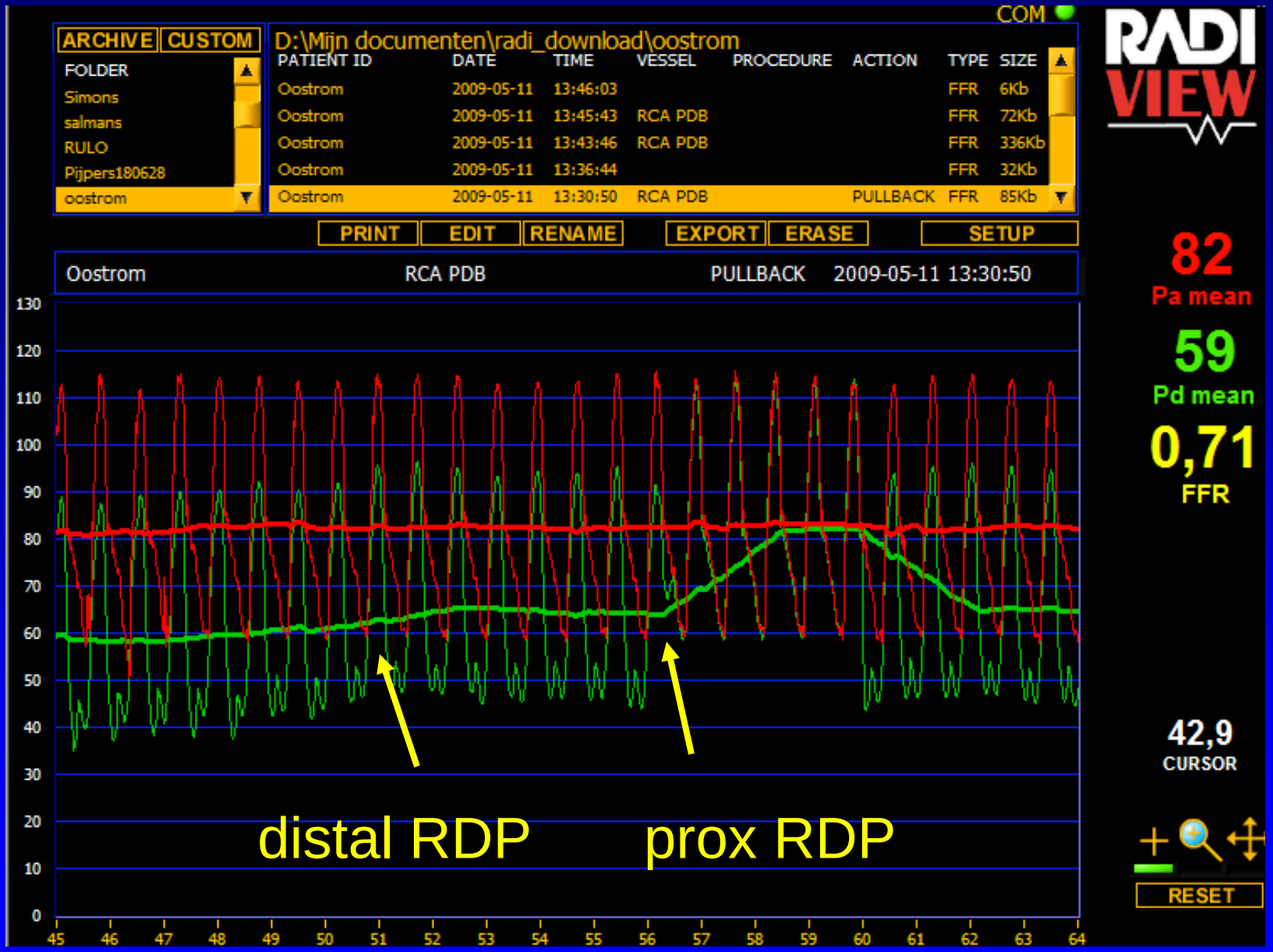



FFR measurement in RDP

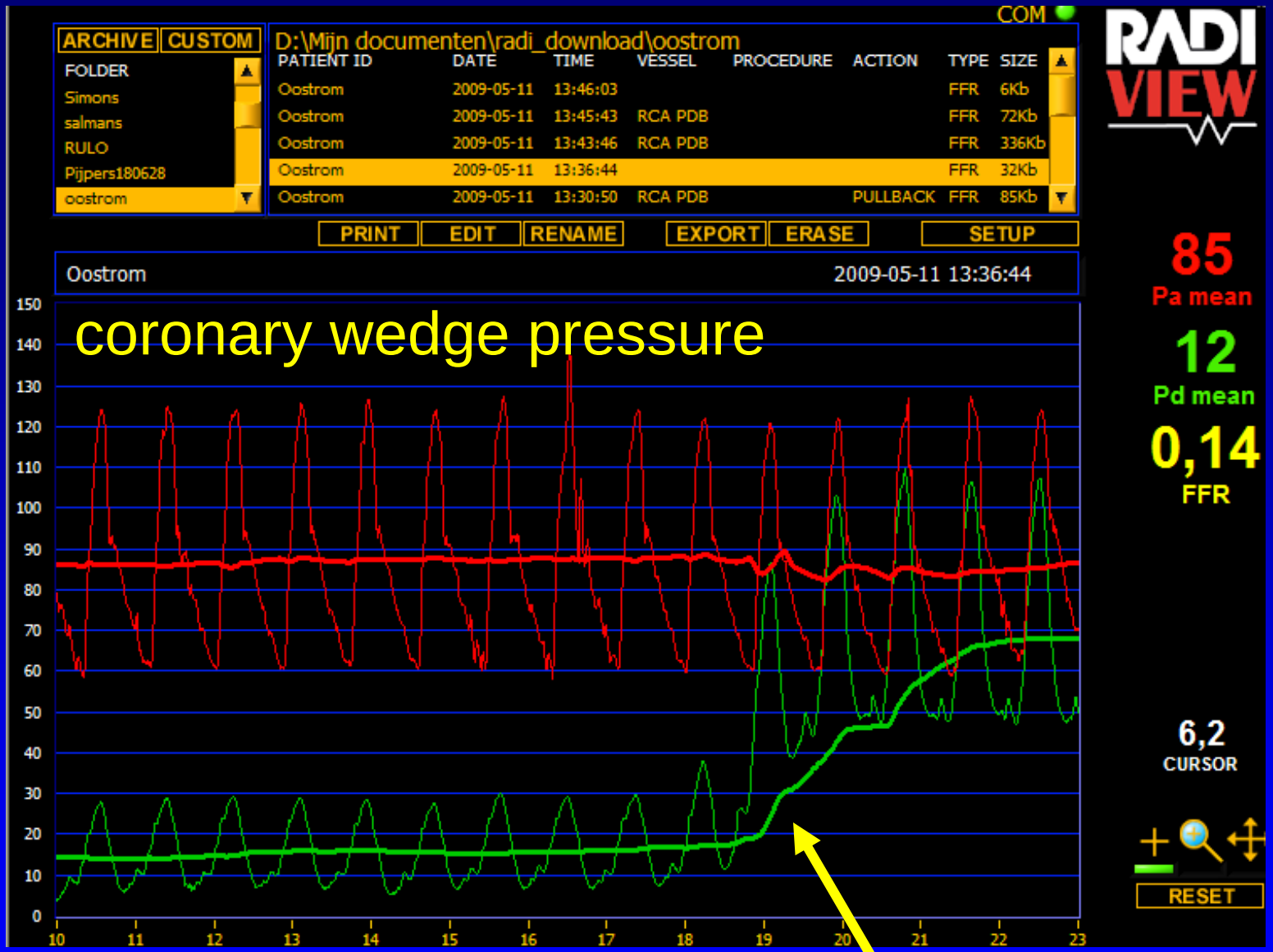




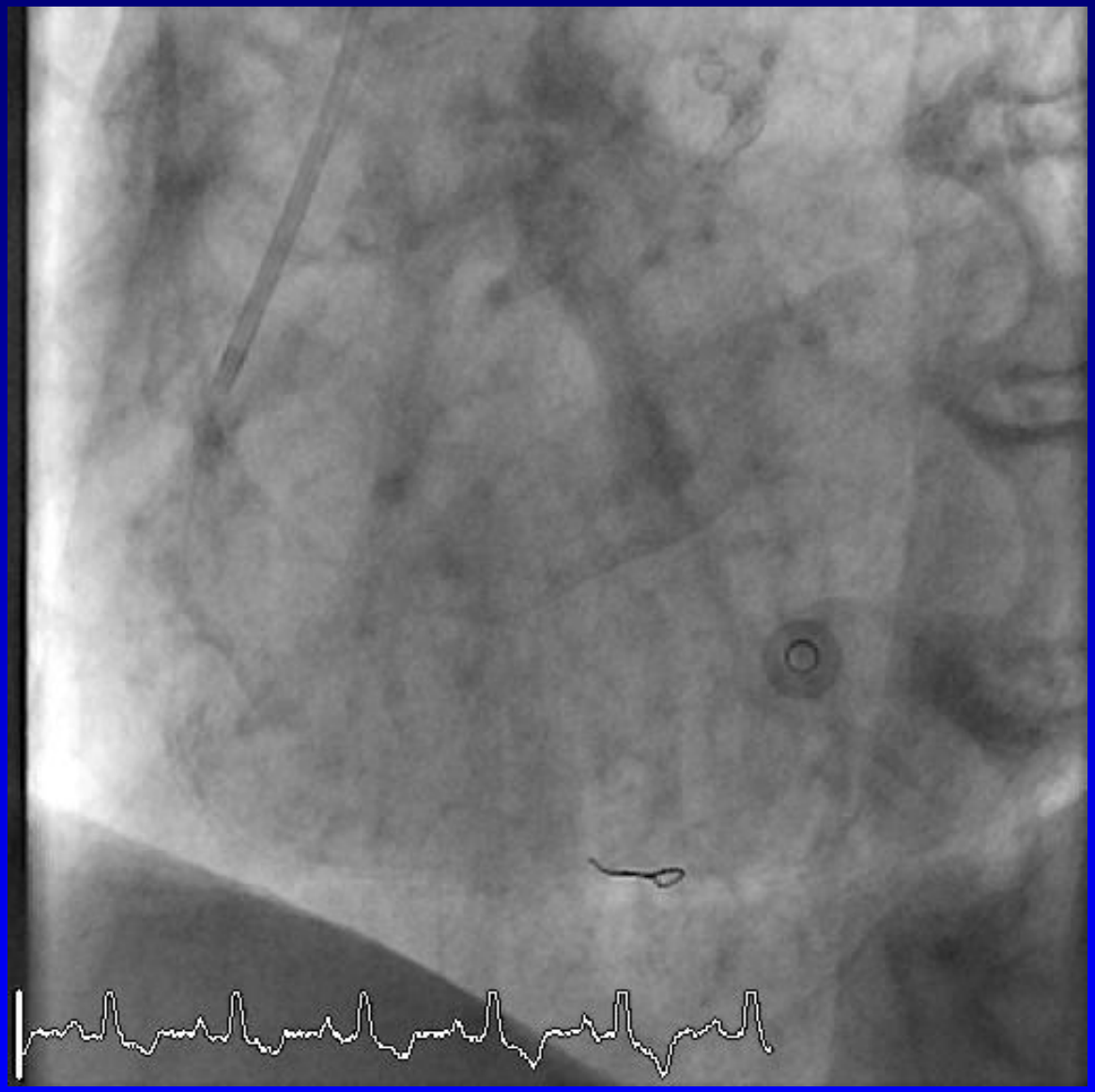
RCA RDP pull-back & push-up



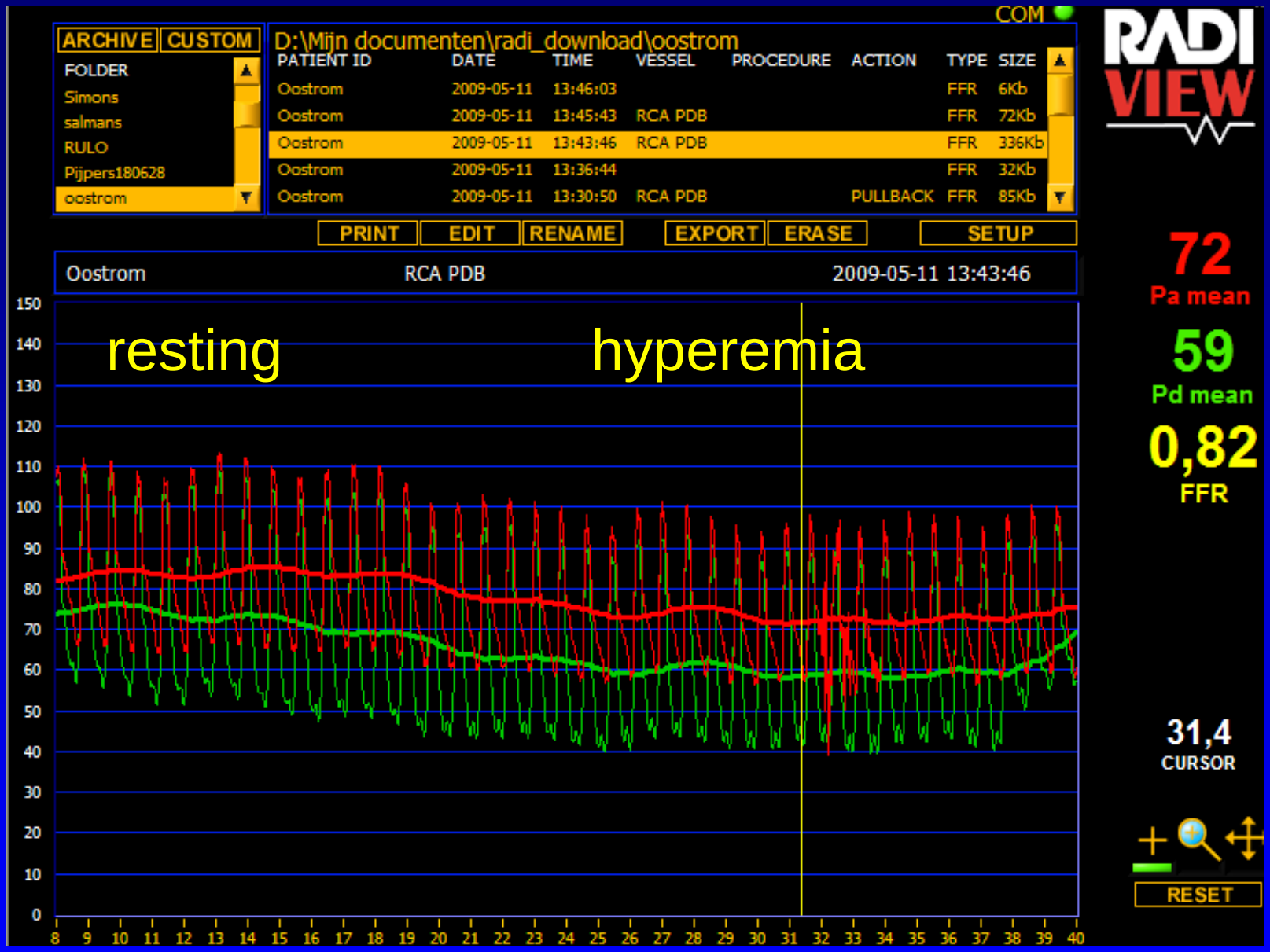

Pull back & advance sensor in RDP




Stent-Balloon inflation and deflation in RDP

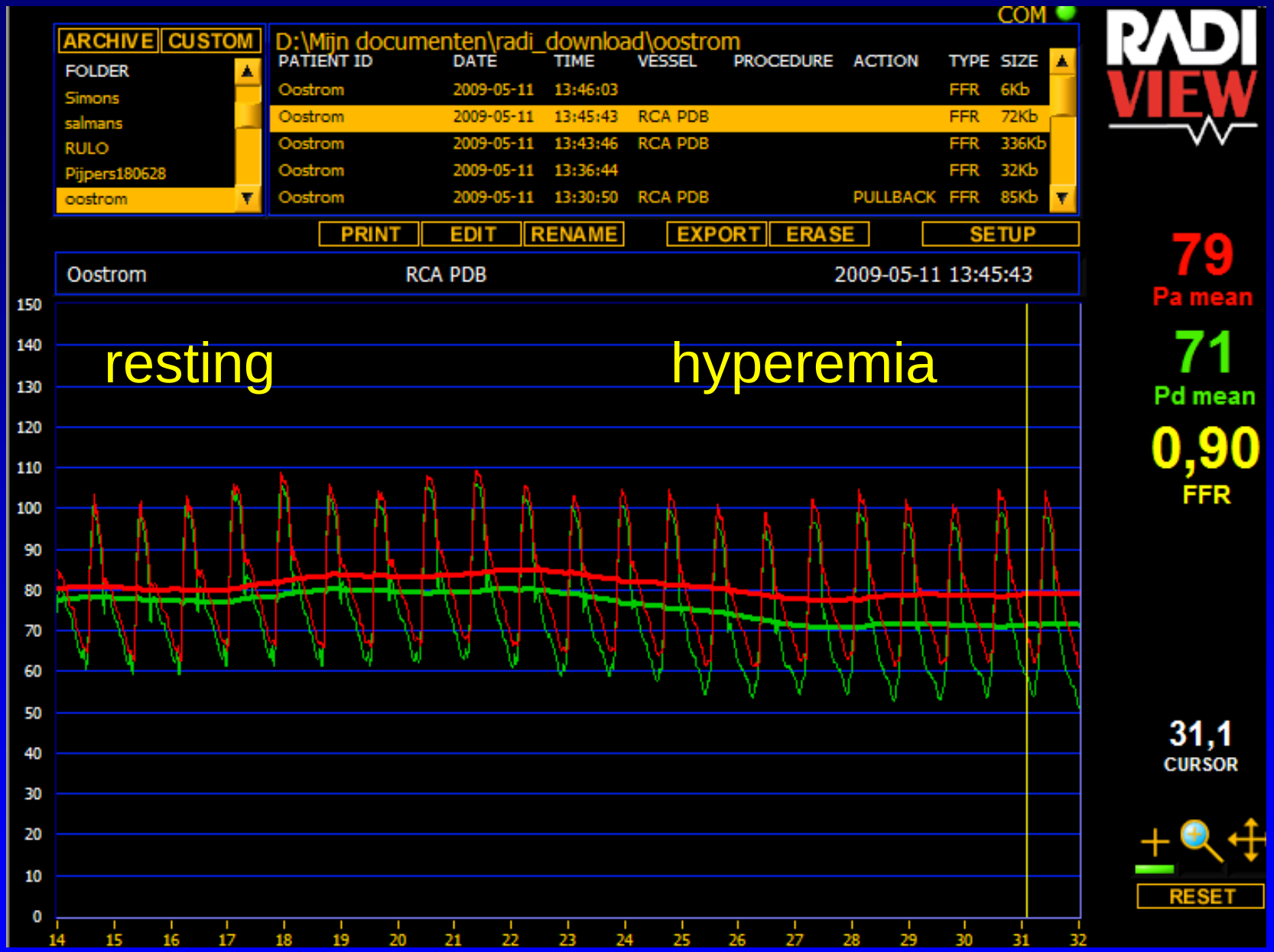


RCA after 1 stent

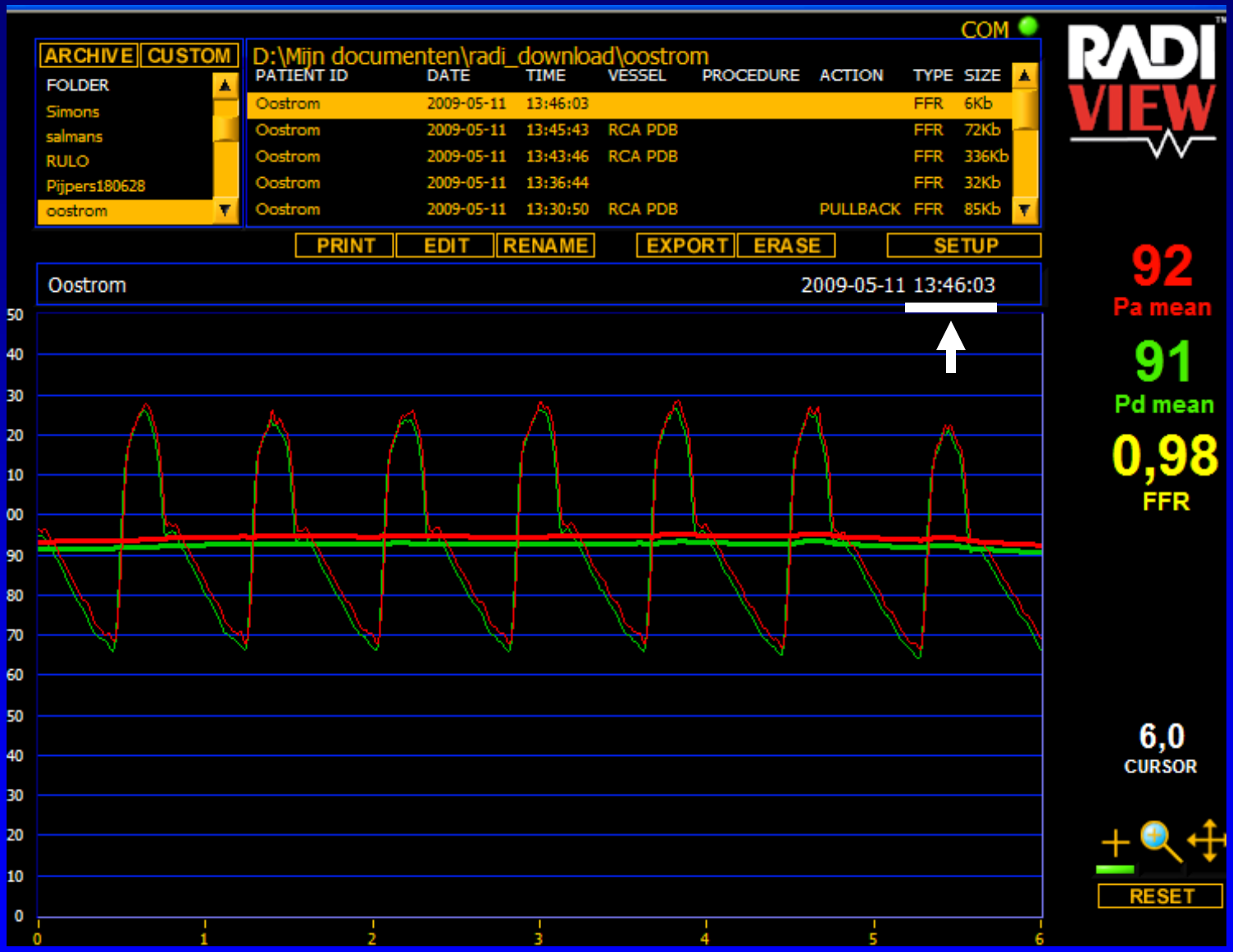



FFR in RDP after 1 stent ( 0.71 → 0.82 )

RCA after 2 stents, rao-view




FFR measurement in RDP after 2 stents




Verification of equal pressure after having stented RCA

# SUMMARY OF THIS PATIENT

- 6 stenoses in 4 arteries
- FFR indicated necessity of stenting 2 arteries ( 3 stents) with complete functional revascularization, including proximal LAD (most severe lesion !) and avoiding unnecessary stenting of IM, MO, and PL-RCA
- complete procedure including 3 stents and 8 FFR recordings with i.v. adenosine lasted 48 minutes
- guidance of decision making and treatment would not have been possible by any other modality, whether invasively or non-invasively

## *Back to the FAME study…*

# *FAME study: 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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| Lesions with FFR ≤ 0.80 ,No (%) | - | **874 (63%)** | - |
| Lesions with FFR > 0.80 ,No (%) | - | **513 (37%)** | - |
| ***Stents per patient*** | **2.7 ± 1.2** | **1.9 ± 1.3** | <0.001 |
| Lesions succesfully stented (%) | **92%** | **94%** | - |
| DES, total, No | **1359** | **980** | - |

# *FAME study: Procedural Results (2)*

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

# *FAME study: Procedural Results (2)*

| | ANGIO-group N=496 | FFR-group N=509 | P-value |
|---|---|---|---|
| Procedure time (min) | **70 ± 44** | **71 ± 43** | 0.51 |
| Contrast agent used (ml) | **302 ± 127** | **272 ± 133** | <0.001 |

# *FAME study: Procedural Results (2)*

| | ANGIO-group N=496 | FFR-group N=509 | P-value |
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| Procedure time (min) | **70 ± 44** | **71 ± 43** | 0.51 |
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| Materials used at procedure (US $) | **6007** | **5332** | <0.001 |

# FAME study: Procedural Results (2)

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| Procedure time (min) | 70 ± 44 | 71 ± 43 | 0.51 |
| Contrast agent used (ml) | 302 ± 127 | 272 ± 133 | <0.001 |
| Materials used at procedure (US $) | 6007 | 5332 | <0.001 |
| Length of hospital stay (days) | 3.7 ± 3.5 | 3.4 ± 3.3 | 0.05 |

# *FAME study: 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** | | | |

# *FAME study: 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** | **91 (18.4)** | **67 (13.2)** | **0.02** |

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| **Death, MI, CABG, or repeat-PCI** | **91 (18.4)** | **67 (13.2)** | **0.02** |
| 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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| CABG or repeat PCI | **47 (9.5)** | **33 (6.5)** | 0.08 |
| Total no. of MACE | **113** | **76** | 0.02 |

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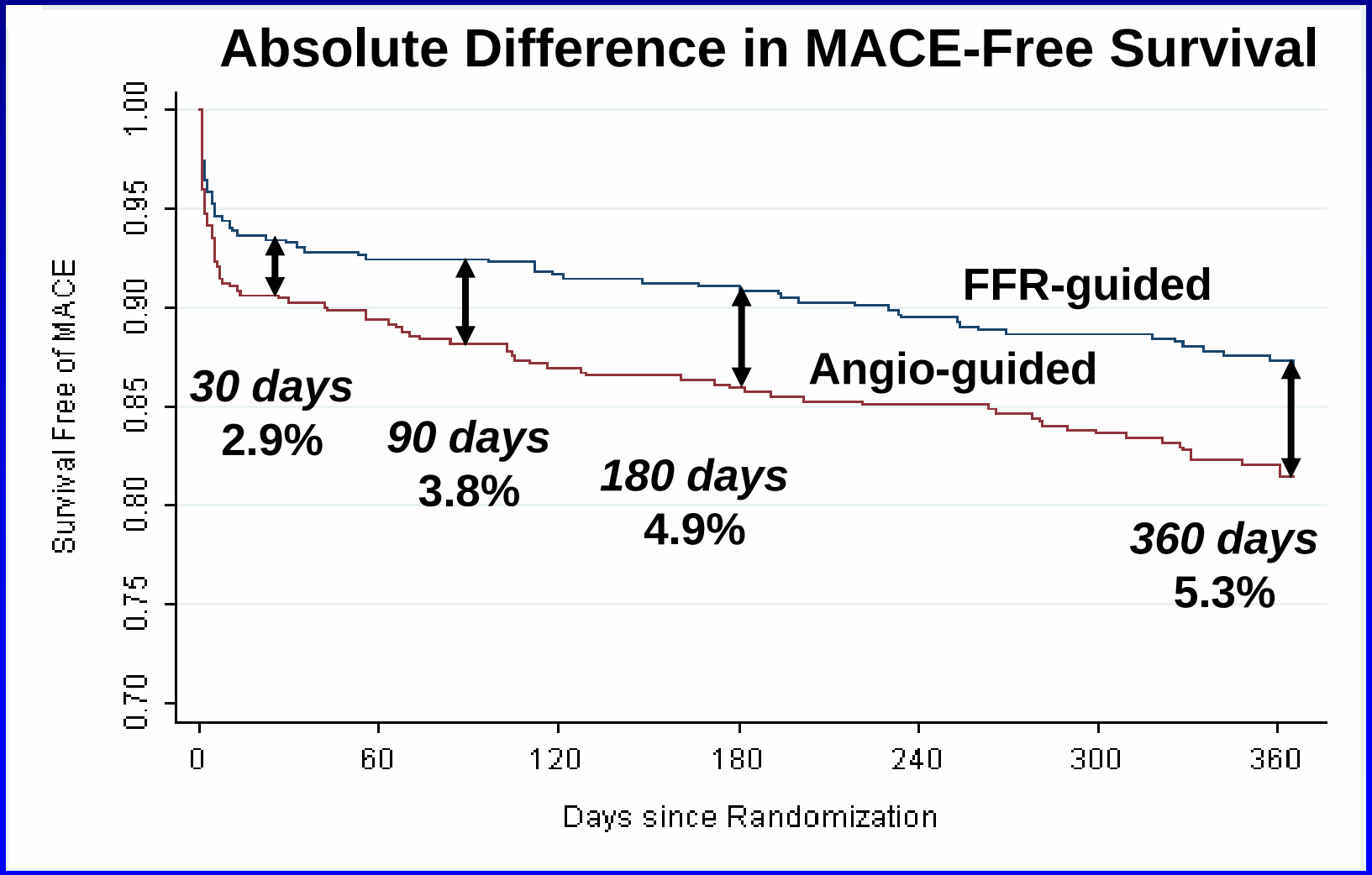
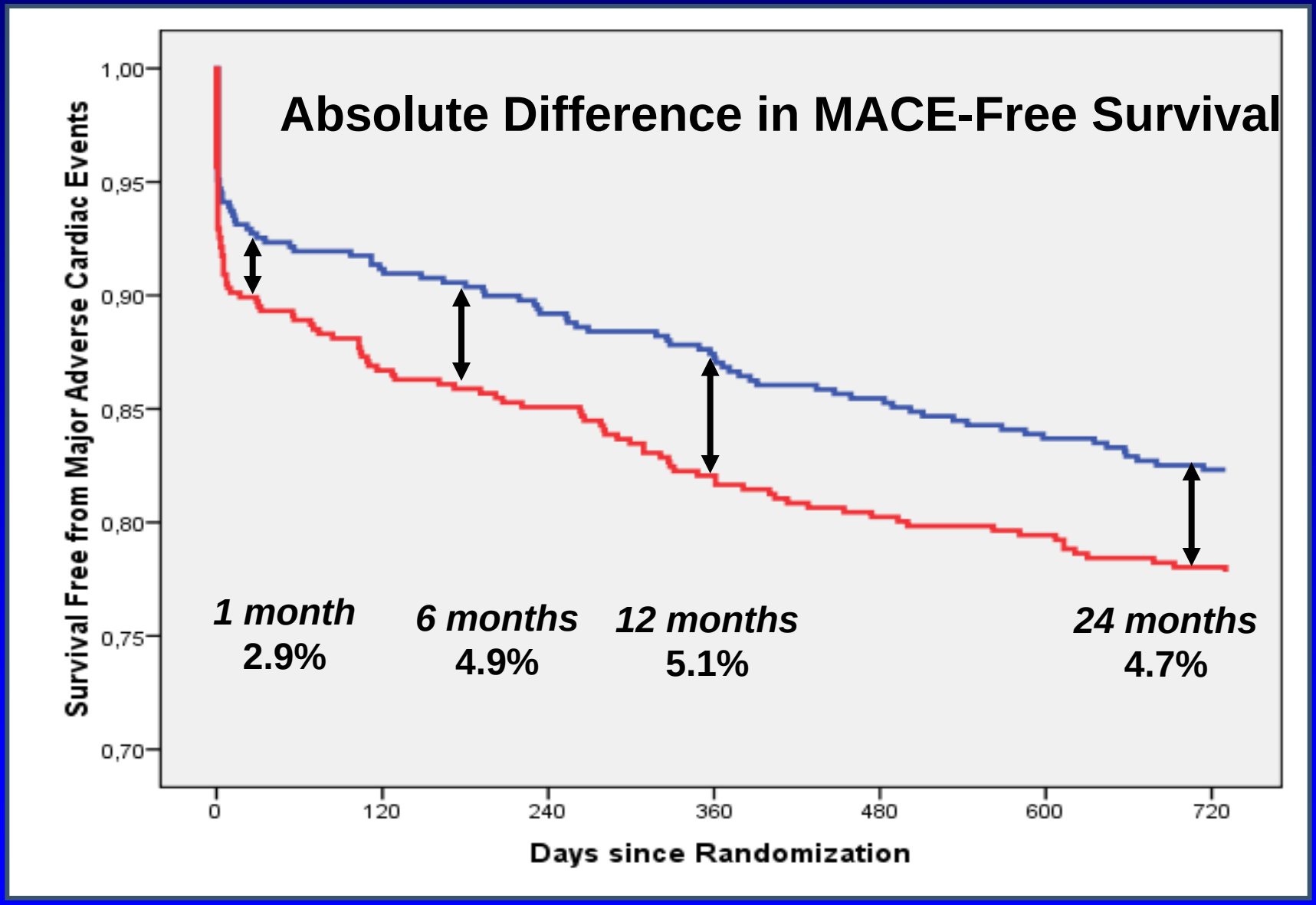
| CABG or repeat PCI | **47 (9.5)** | **33 (6.5)** | 0.08 |
| Total no. of MACE | **113** | **76** | 0.02 |
| ***Myocardial infarction, specified*** | | | |
| All myocardial infarctions | **43 (8.7)** | **29 (5.7)** | 0.07 |
| Small periprocedural CK-MB 3-5 x N | **16** | **12** | |
| Other infarctions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

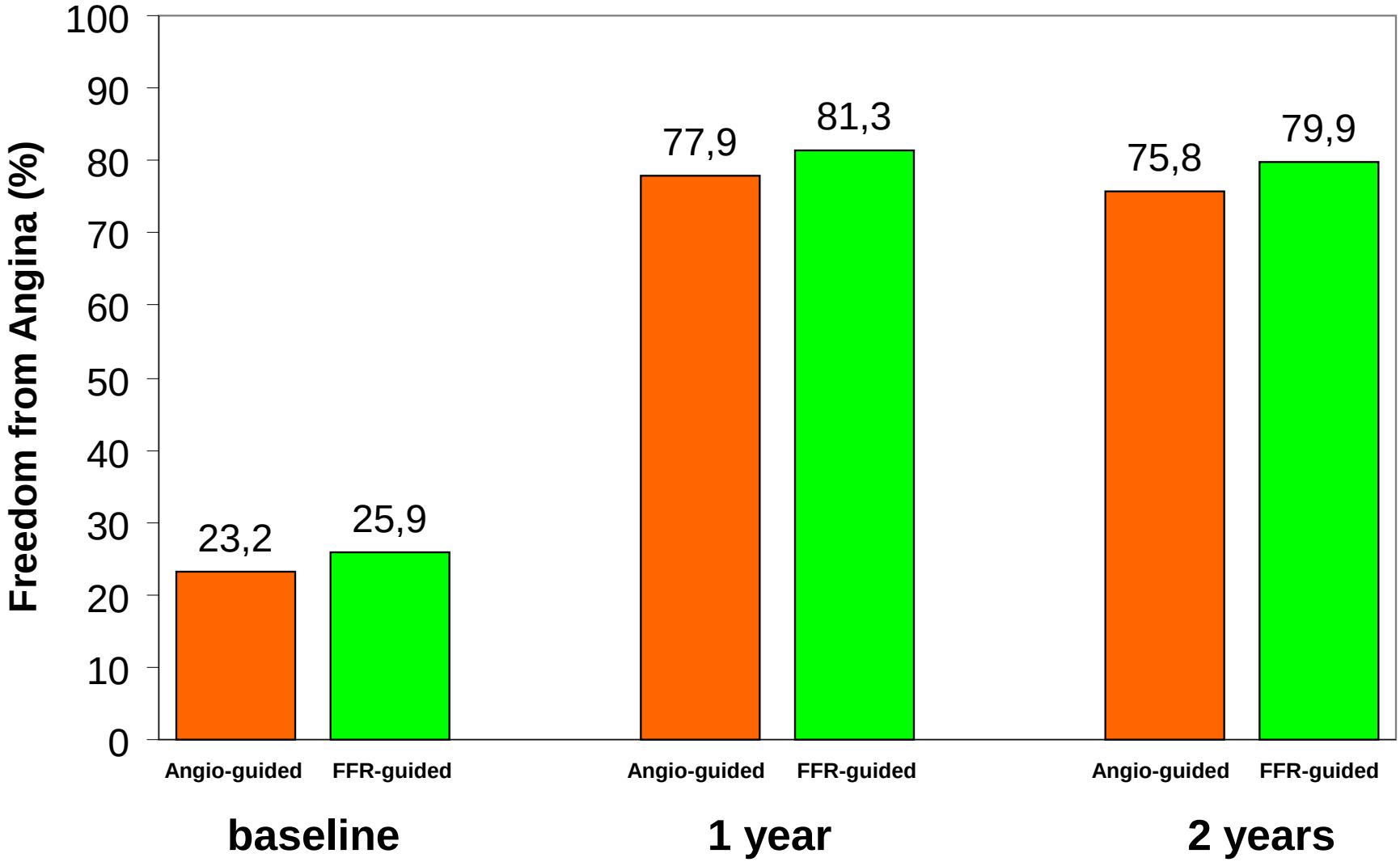
# FAME study: Event-free Survival



# FAME study: Event-free Survival 24 months



# Freedom from Angina




Angio-guided

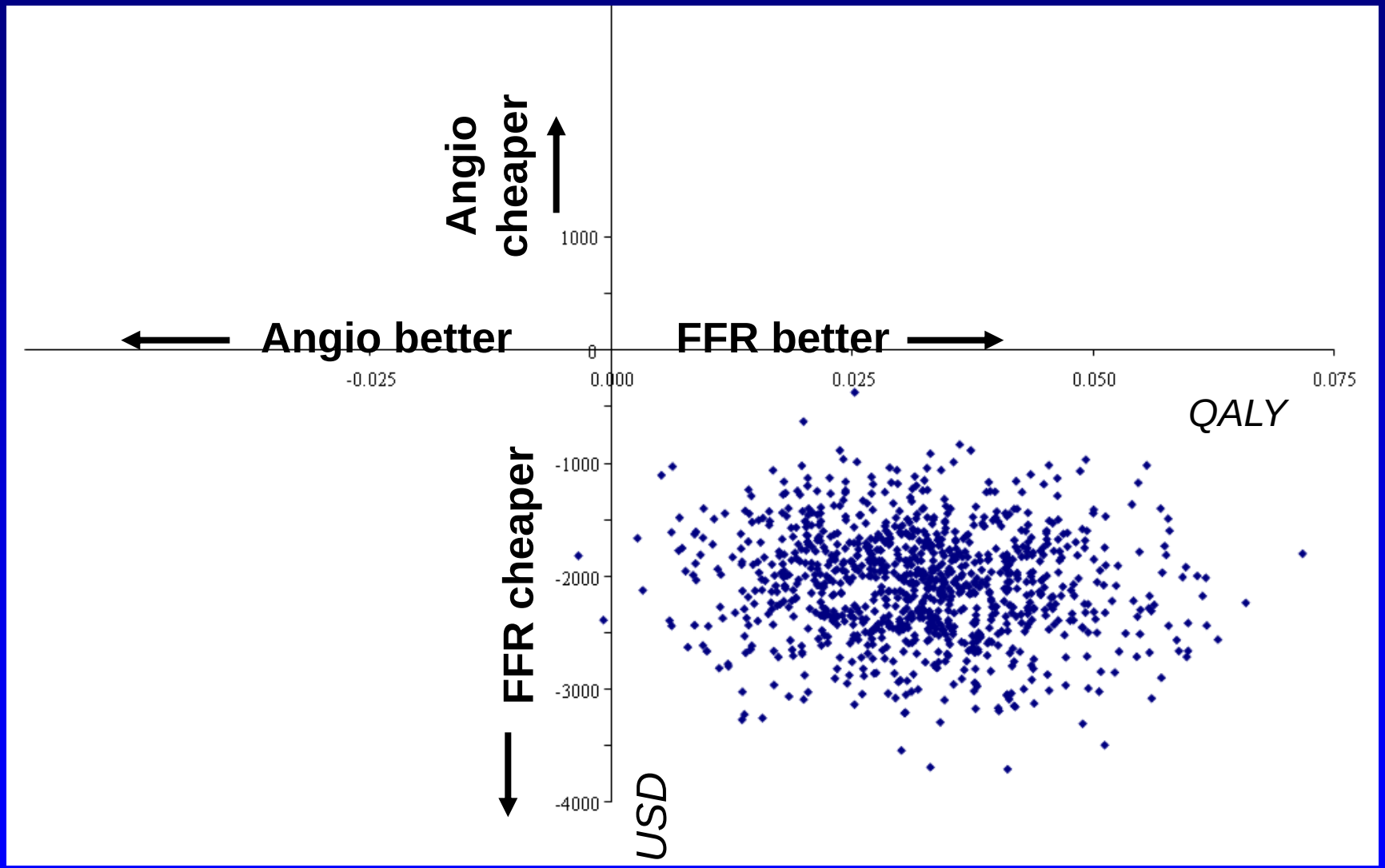
FFR-guided

**In the meantime, 5-y FU of the FAME study has been completed very recently.**

*Lokien Van Nunen, MD*
*Frederik Zimmermann, MD*

***This follow-up will be submitted as LBT to ESC***

# FAME study: Economic Evaluation (1)




Fearon et al, Circulation 2012

# *FAME study: CONCLUSIONS*

***Routine measurement of FFR during DES-stenting in patients with multivessel disease is superior to current angiography guided treatment.***

***It improves outcome of PCI significantly***

***It supports the evolving paradigm of***

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

# OPTIMUM TREATMENT OF MULTIVESSEL DISEASE

***FAME showed that PCI becomes a better and more effective treatment by FFR guidance…….but what about***

- ***PCI vs Medical treatment in MVD (FAME 2)***
- ***PCI vs CABG in 3VD (FAME 3)***

➡ **Next lectures**

# Deferral of Functionally Non-significant Stenosis

*Was it safe in the FAME study to defer functionally non-significant stenosis ?*

# Outcome of Deferred Lesions:

513 Deferred Lesions and 901 stented lesions in 509 FFR-Guided Patients

*2 Years*

**9**
Late Myocardial Infarctions

**8**
Due to a New Lesion or Stent Related

**1**
Myocardial Infarction due to an Originally Deferred Lesion

***Only 1/513 or 0.2% of deferred lesions resulted in a late myocardial infarction***

***NOTE:***

**15 (fifteen !) year follow-up of DEFER study will be presented as LBT at PCR in may in Paris**

# FFR: The Pressure Pull-back Curve

# 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*

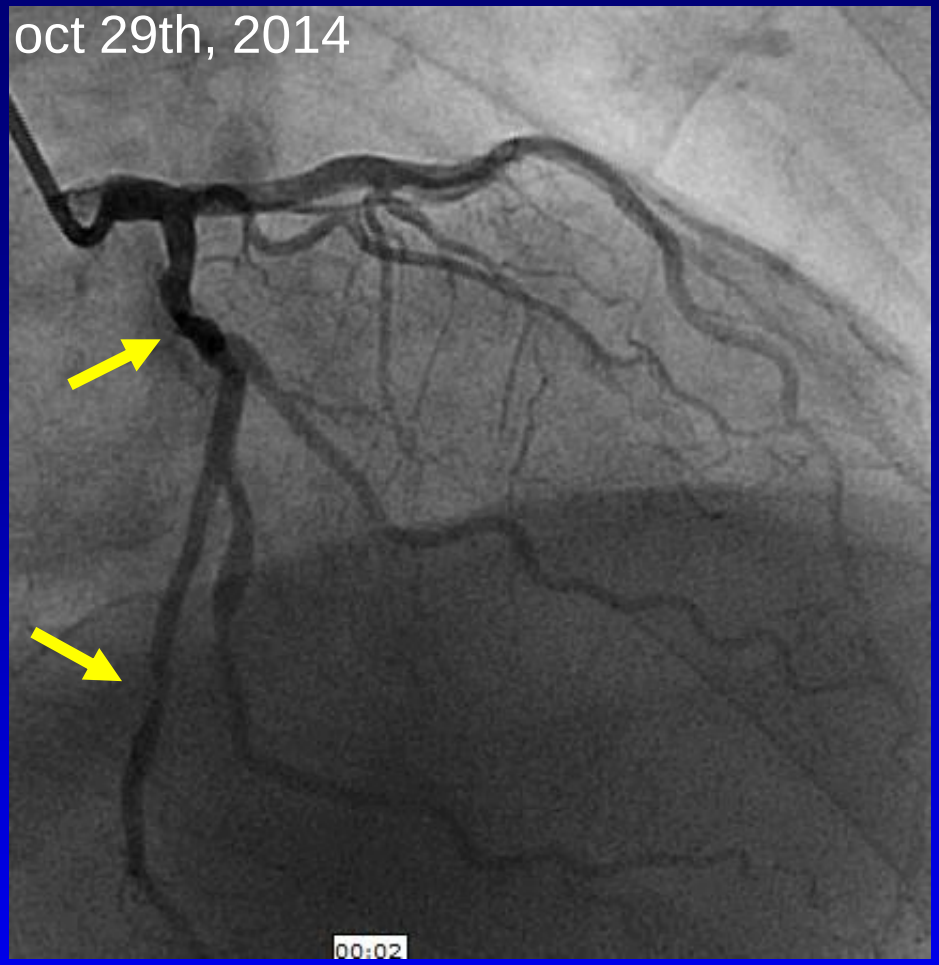
## *The Pressure Pullback Recording is Particularly Helpful in Complex Disease*

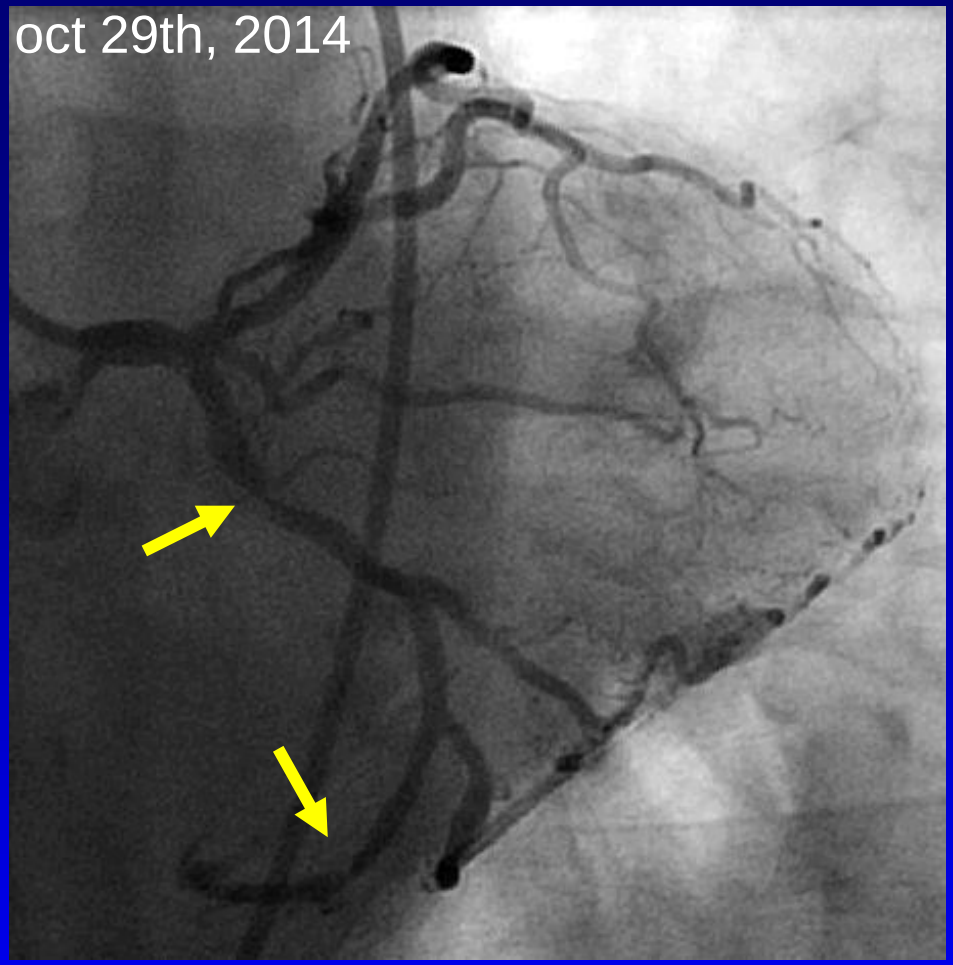
- **ostial lesions**
- **MVD**
- **left main lesions**
- **tandem lesions**
- **diffuse disease**

***Full hyperemia is necessary to guide where exactly the stent(s) should be placed !***

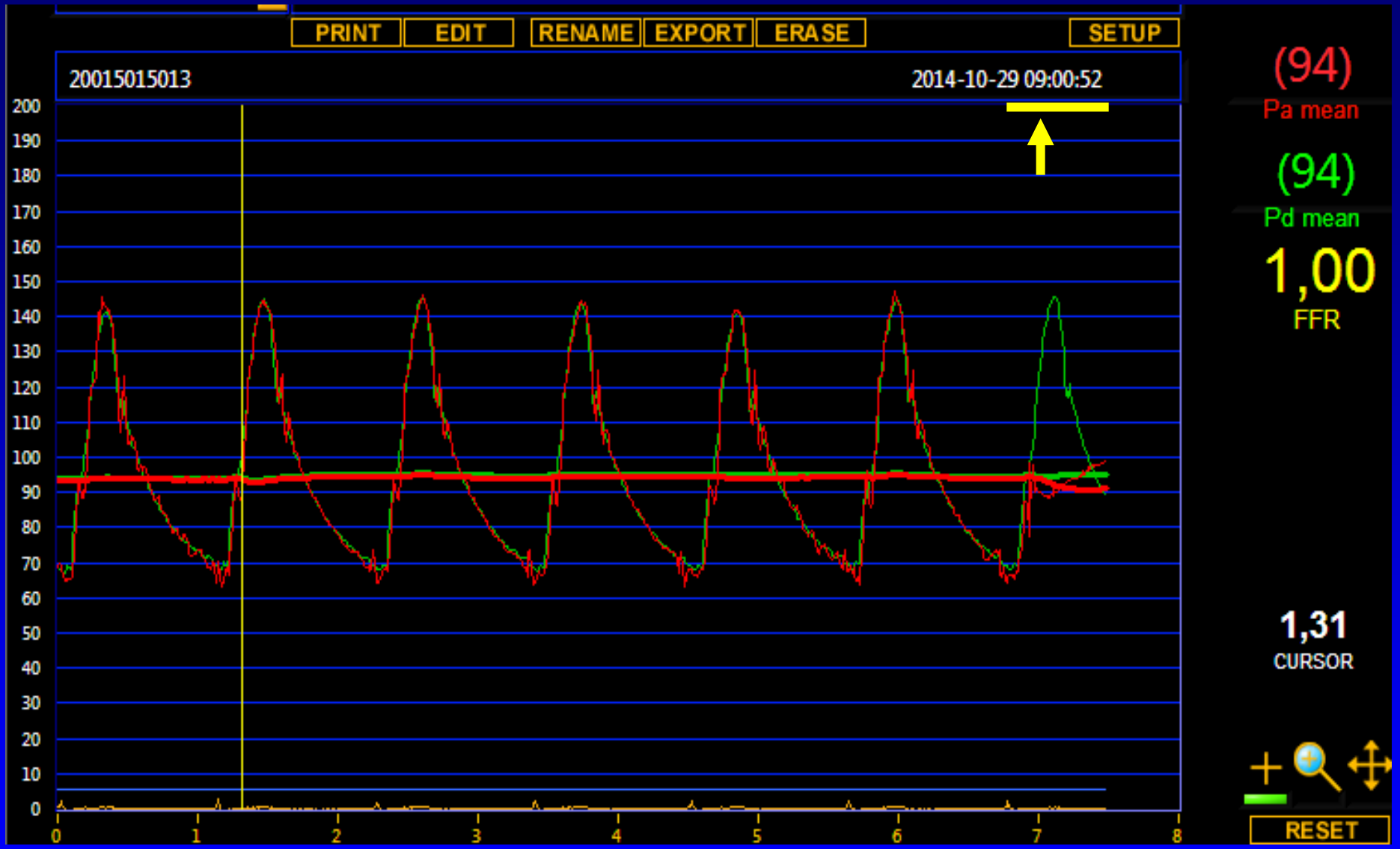
***Full hyperemia is necessary to guide where exactly the stent(s) should be placed :***

- The intrinsic error in FFR measurement is 0.01-0.02
- The total hyperemic pressure gradient within a coronary artery, is generally 2-4 x higher than the resting gradient.
- Consequently, the resolution (*signal-to-noise ratio*) of the pull-back recording, is *2-4 x higher at hyperemia*

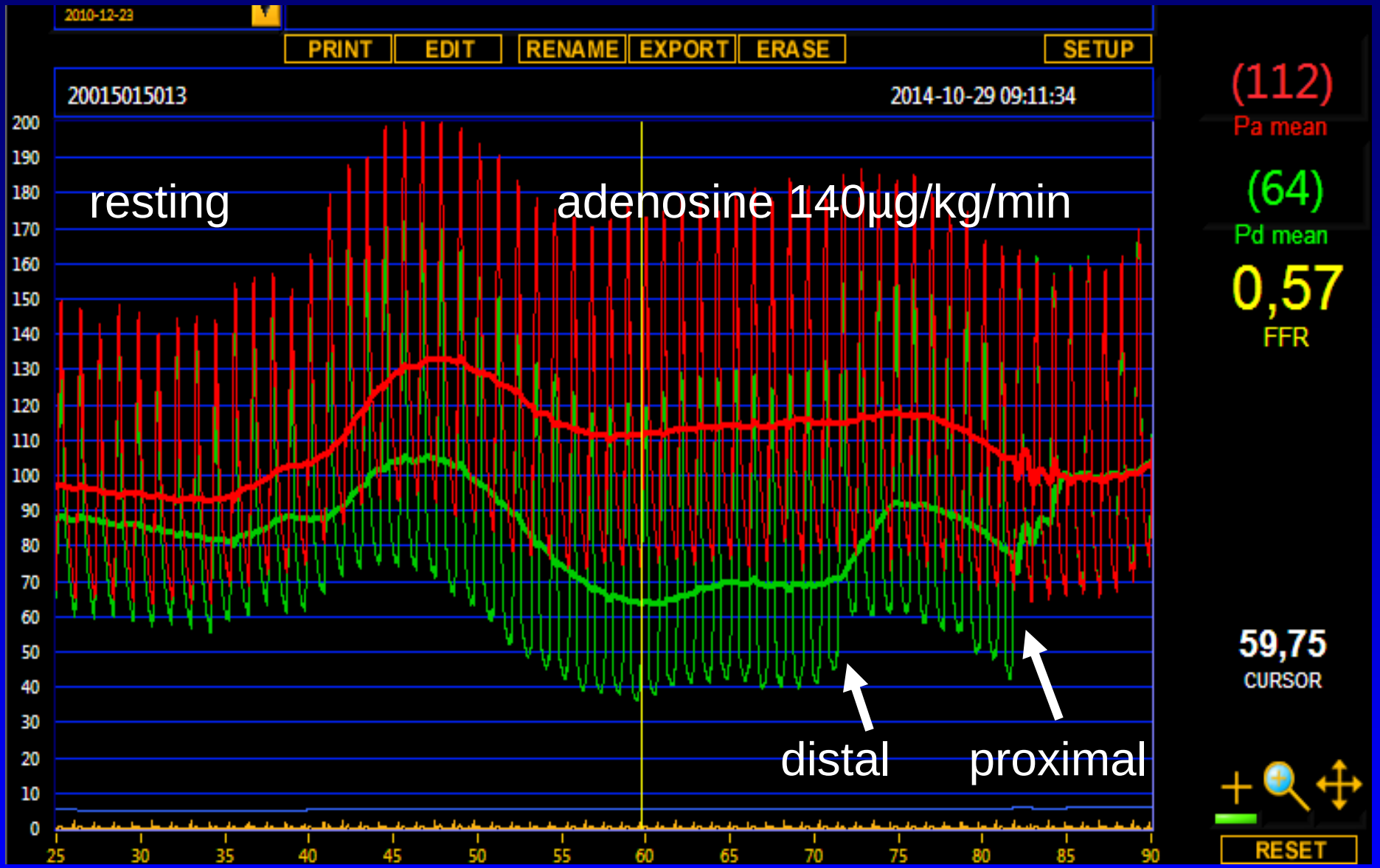



Male, 65-year-old, typical angina,
inferolateral reversible defect at MIBI-SPECT
70% lesions in proximal & distal dominant LCX

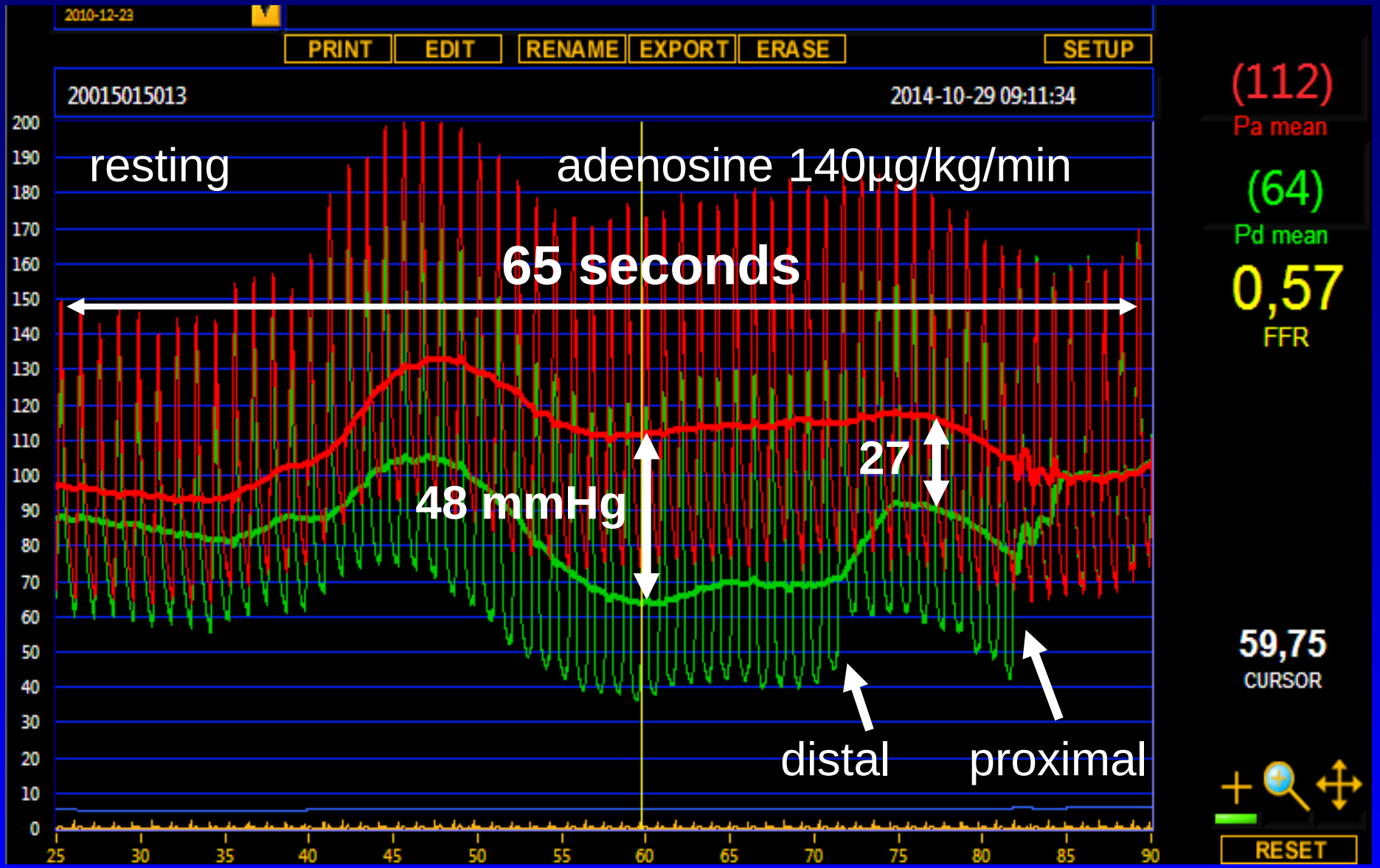



Equalization before entering LCA



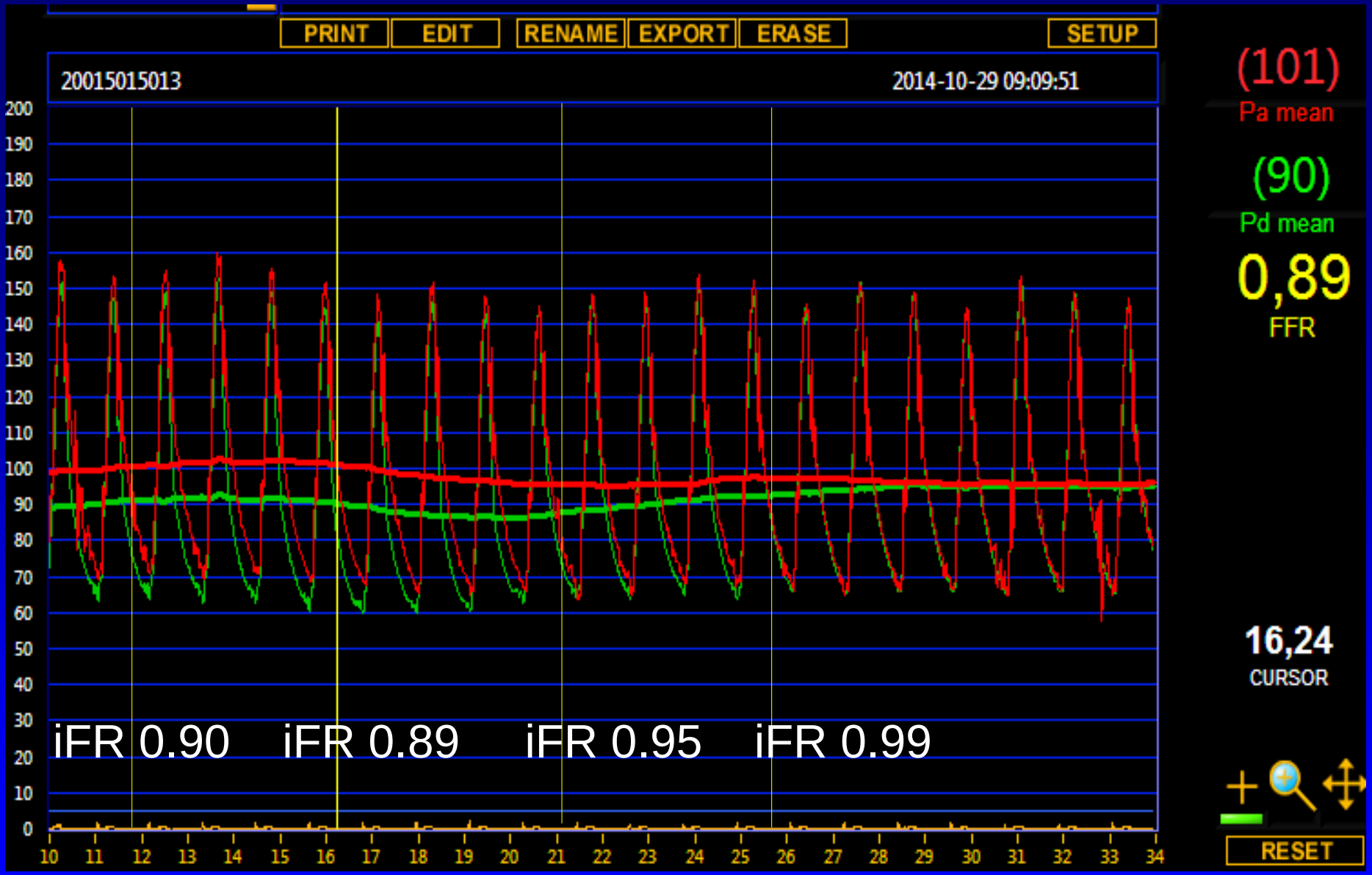

hyperemic pullback recording:

*rapid, reliable, detailed information within seconds*



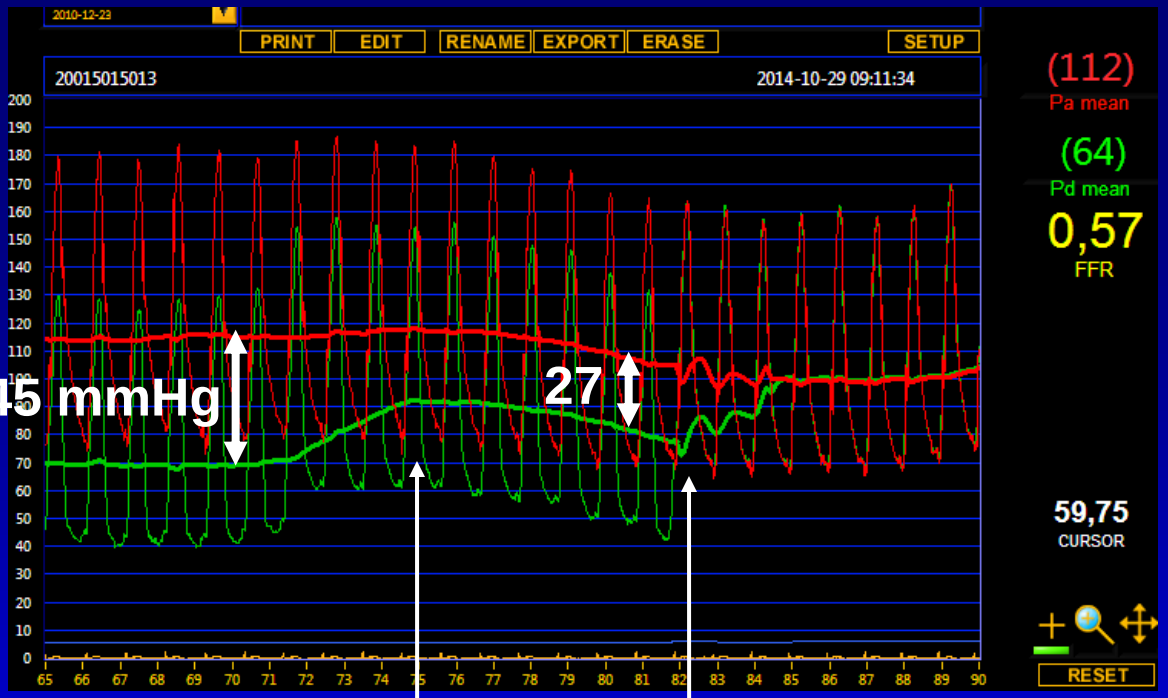

hyperemic pullback recording:

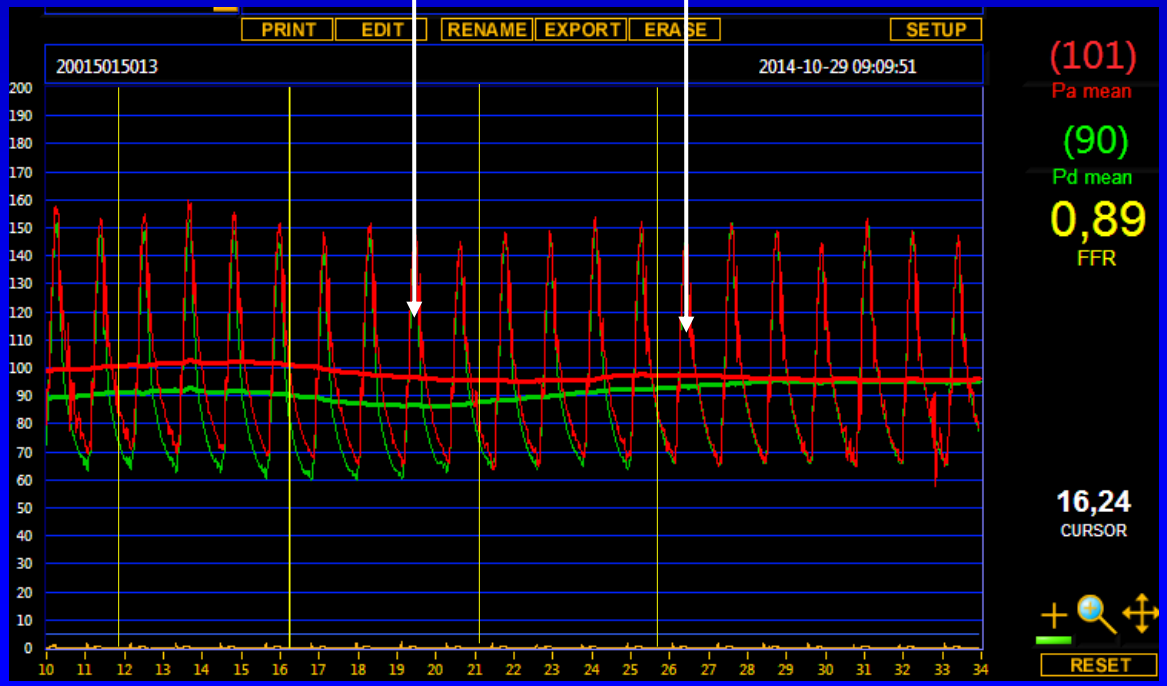
*rapid, reliable, detailed information within seconds*




"resting" pullback recording with multiple iFR:

*time-consuming, less reliable, poorly detailed information*




*as the intrinsic precision of the pressure measurement is 1-2 mmHg, the signal-to-noise ratio and resolution at hyperemia is much higher than at rest*

# *OSTIAL LESIONS*

***Caveat***: blockage of ostium by guiding catheter

↓

blood flow not as high as it really can be

↓

underestimation of gradient

↓

underestimation of stenosis severity

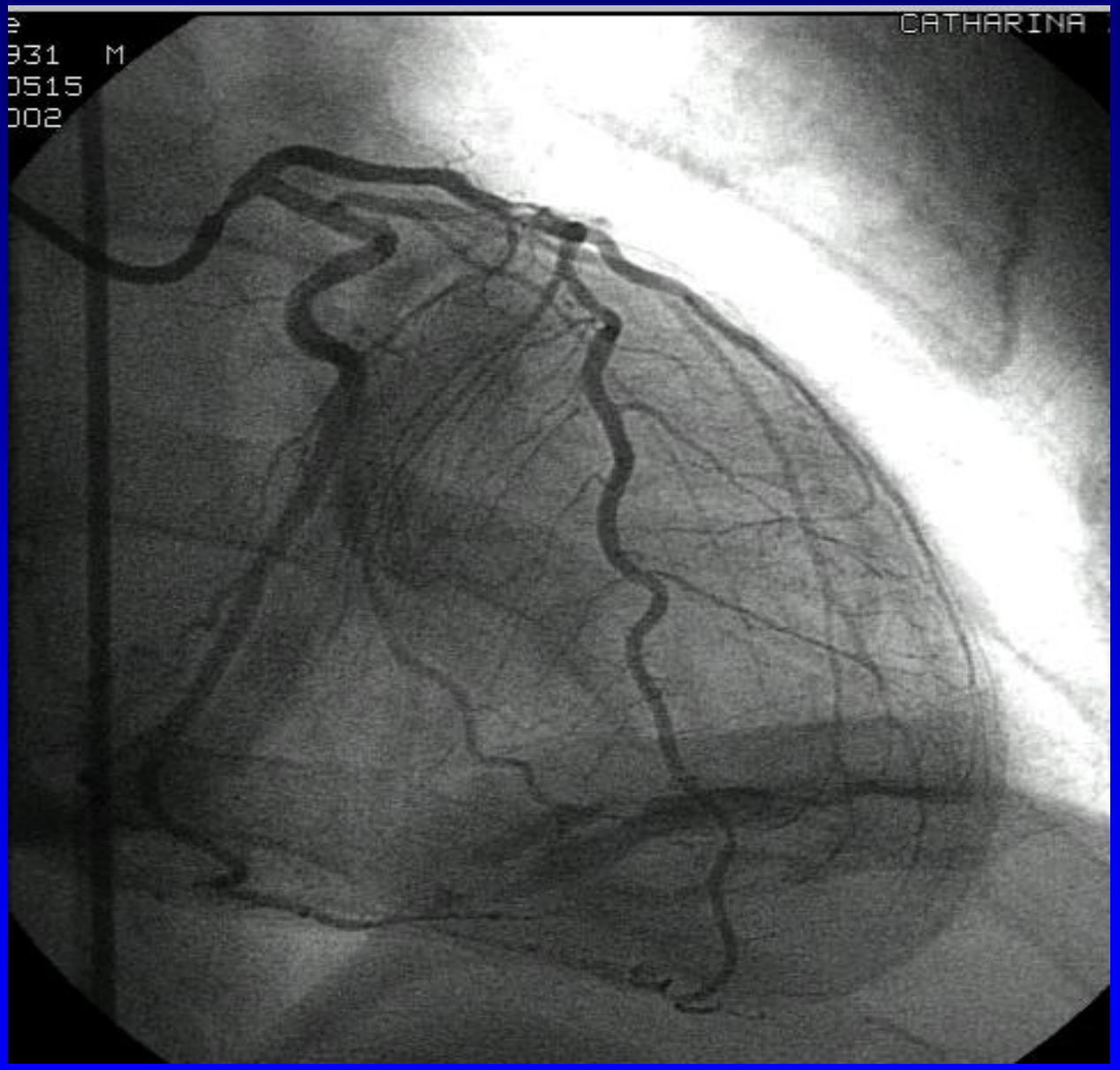
# Influence of guiding catheter on FFR in case of narrow ostium

→ *use i.v. adenosine and dislodge guiding during measurement*

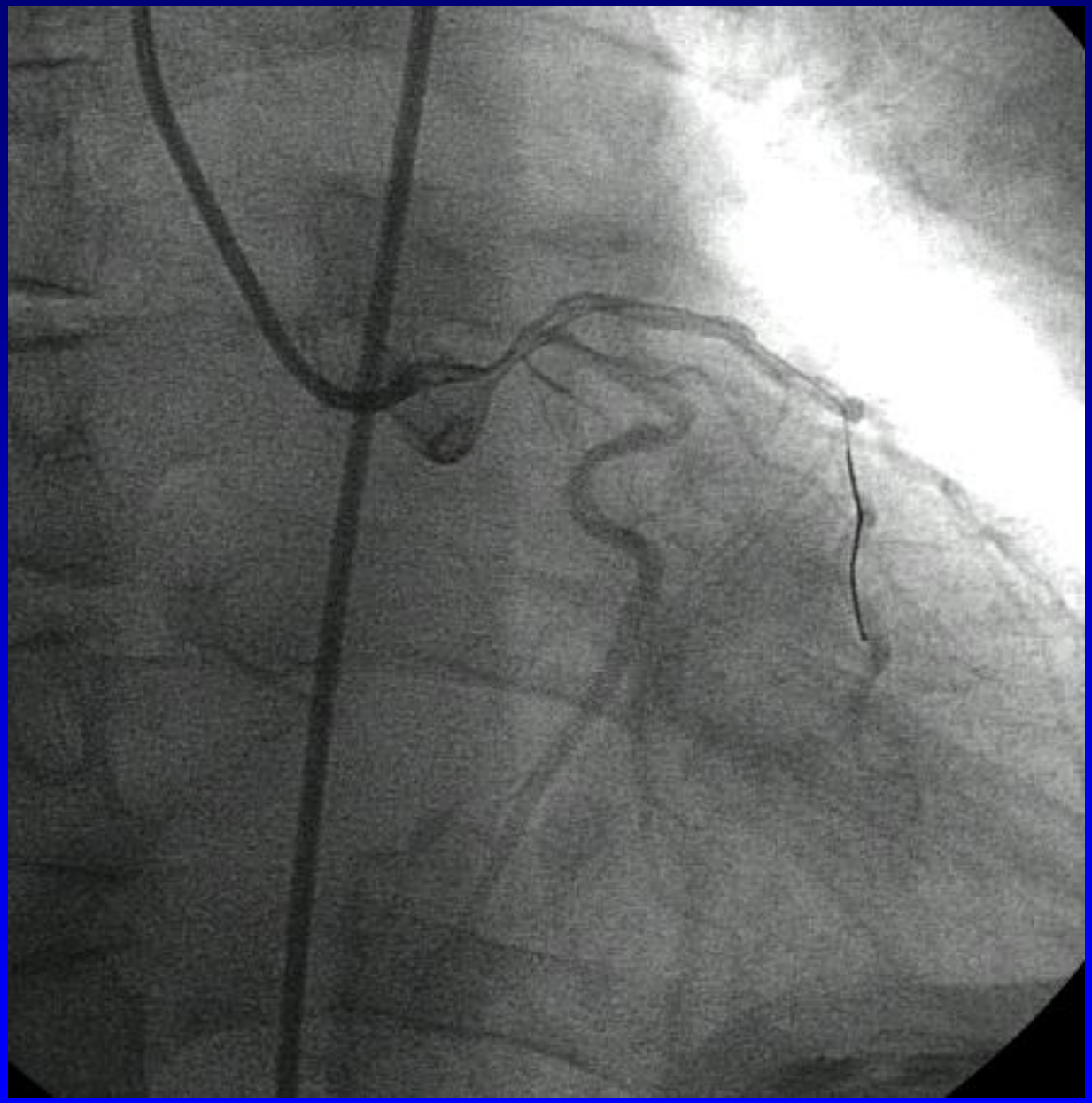

COM 1
ARCHIVE
CUSTOM
C:\RADI\DOWNLOAD\vdputten231002
PATIENT ID
DATE
TIME
VESSEL
PROCEDURE
ACTION
TYPE
SIZE
FFR 57Kb
FFR 69Kb
FFR 158Kb
FFR 98Kb
FFR 62Kb
PRINT
EDIT
RENAME
EXPORT
ERASE
SETUP
RADI VIEW
engagement of guiding into ostium
165
150
140
130
120
110
100
90
80
70
60
50
40
30
20
8
39
39
40
41
42
43
44
45
46
103
Pa mean
78
Pd mean
0,76
FFR
35,0
CURSOR
RESET

# *FFR IN OSTIAL LESIONS (including left main)*

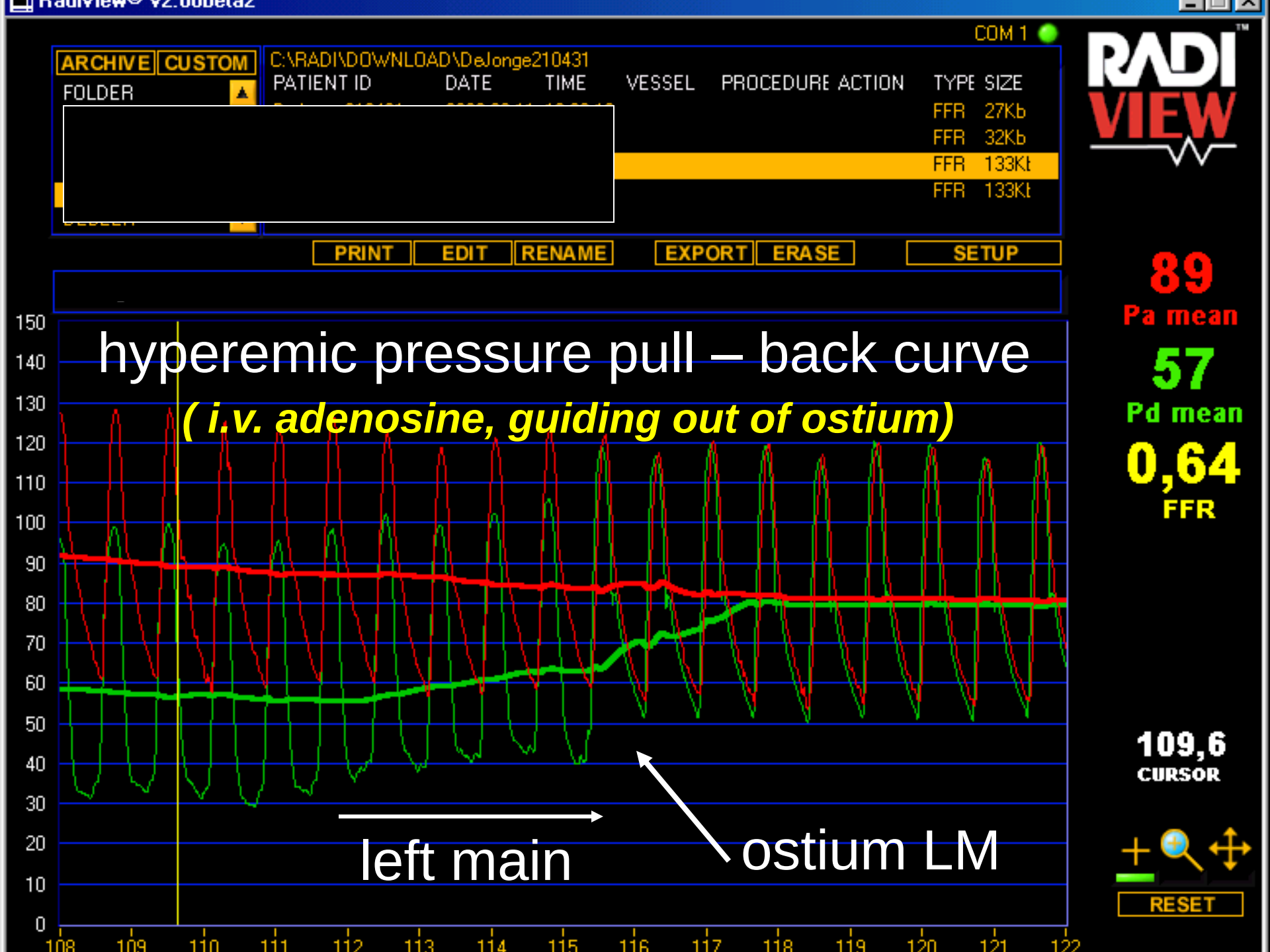
- introduce guiding catheter
- advance PW across stenosis
- start *adenosine i.v*. or *regadenoson (i.v. bolus)*
- when hyperemia is achieved, dislodge guiding catheter carefully. *Often best done by advancing PW*
- during pull-back, ask nurse to hold guiding catheter
- interpretation FFR just as usual




suspicion of left main ostial stenosis



PressureWire in LAD,  guiding catheter dis-engaged


COM 1
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PATIENT ID
DATE
TIME
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TYPE
SIZE
FFR 27Kb
FFR 32Kb
FFR 133Kb
FFR 133Kb
PRINT
EDIT
RENAME
EXPORT
ERASE
SETUP
RADI VIEW
89
Pa mean
57
Pd mean
0,64
FFR
hyperemic pressure pull – back curve
( i.v. adenosine, guiding out of ostium)
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
left main
ostium LM
109,6
CURSOR
RESET

***Notice:***

- in ostial and LM stenosis, often only a minimal gradient is present at rest, which largely increases at hyperemia (provided you dislodge the guiding adequately.)
  *This is due to the large perfusion territory*

→ **i.v. hyperemia mandatory (adenosine or regadenoson)**

# ***FFR in complex MVD: Conclusions***

- In all clinical and angiographic conditions with complex coronary artery disease, FFR (and particularly the hyperemic pull-back recording) is a useful tool to improve the quality of your PCI.

- Only exception: Acute phase of STEMI (severe microvascular dysfunction).
  Wait preferably for a few days before measuring FFR