Imaging & Physiology Summit

CORONARY HYPEREMIA IS MANDATORY ?

YES ! RESTING INDEX IS NOT ENOUGH

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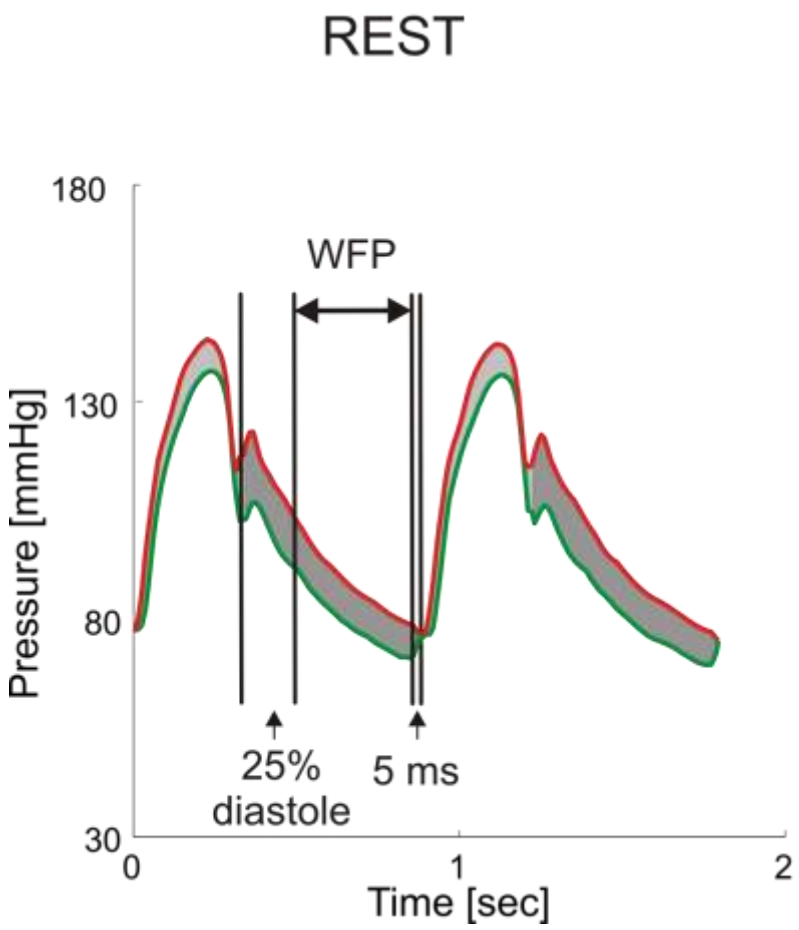
Why Do I Need Hyperemia ?

- *Limited Clinical Significance of resting indices*
- *iFR is at odds with experimental validation*
- *resting gradients poorly predict hyperemic gradients*
- *Resting Conditions Are Hard to Obtain*
- *Large gray zone without hyperemia*
- *no independent outcome data for iFR or cFFR*
- *decreased signal to noise ratio without hyperemia*



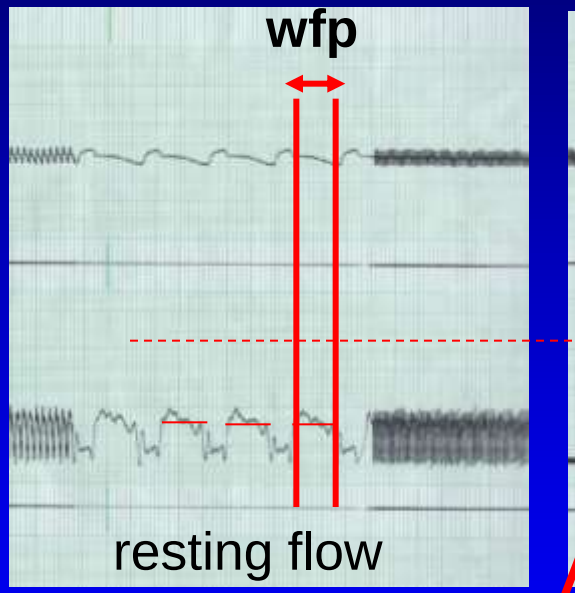
iFR = Pd / Pa at rest during WFP ***(Sen et al, JACC 2012)***

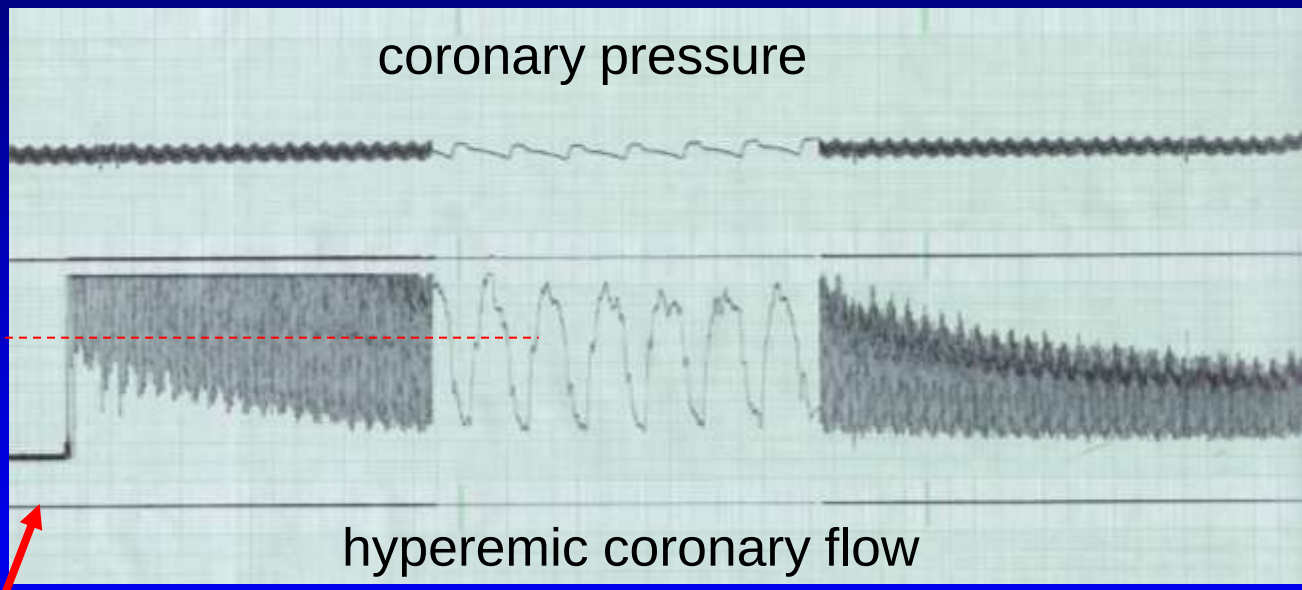
basic assumptions:

1. resistance during WFP at rest equals average hyperemic resistance
2. iFR is claimed to be “hyperemia-free”

Review from 27 dogs and 12 swine exper performed between 1986 and 2003

minimal myocardial resistance during the so-called "wave-free period" is ~ 250 % higher than average myocardial resistance at maximum hyperemia in all dogs and swine, and varies a lot



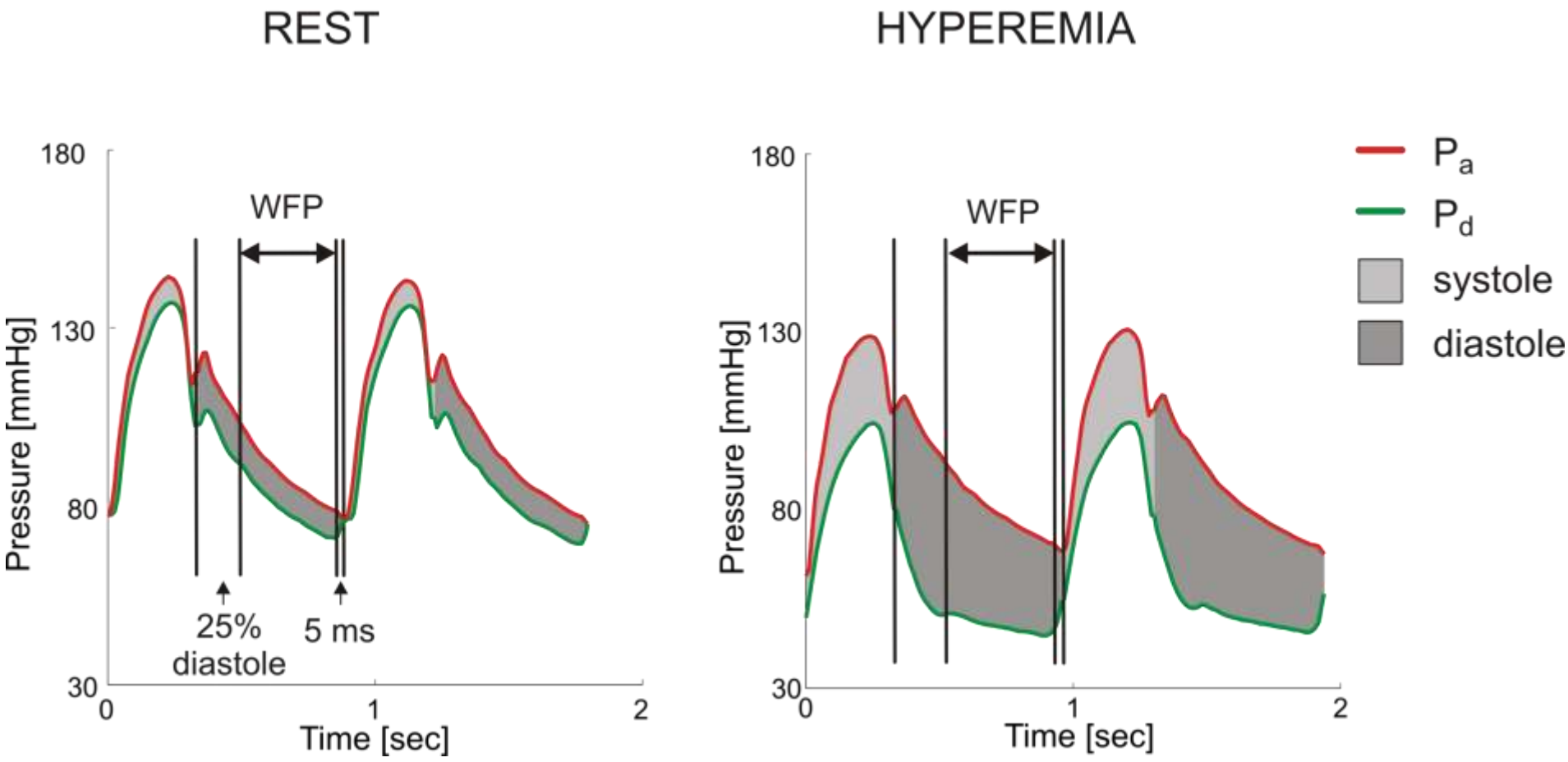


coronary occlusion

iFR is:

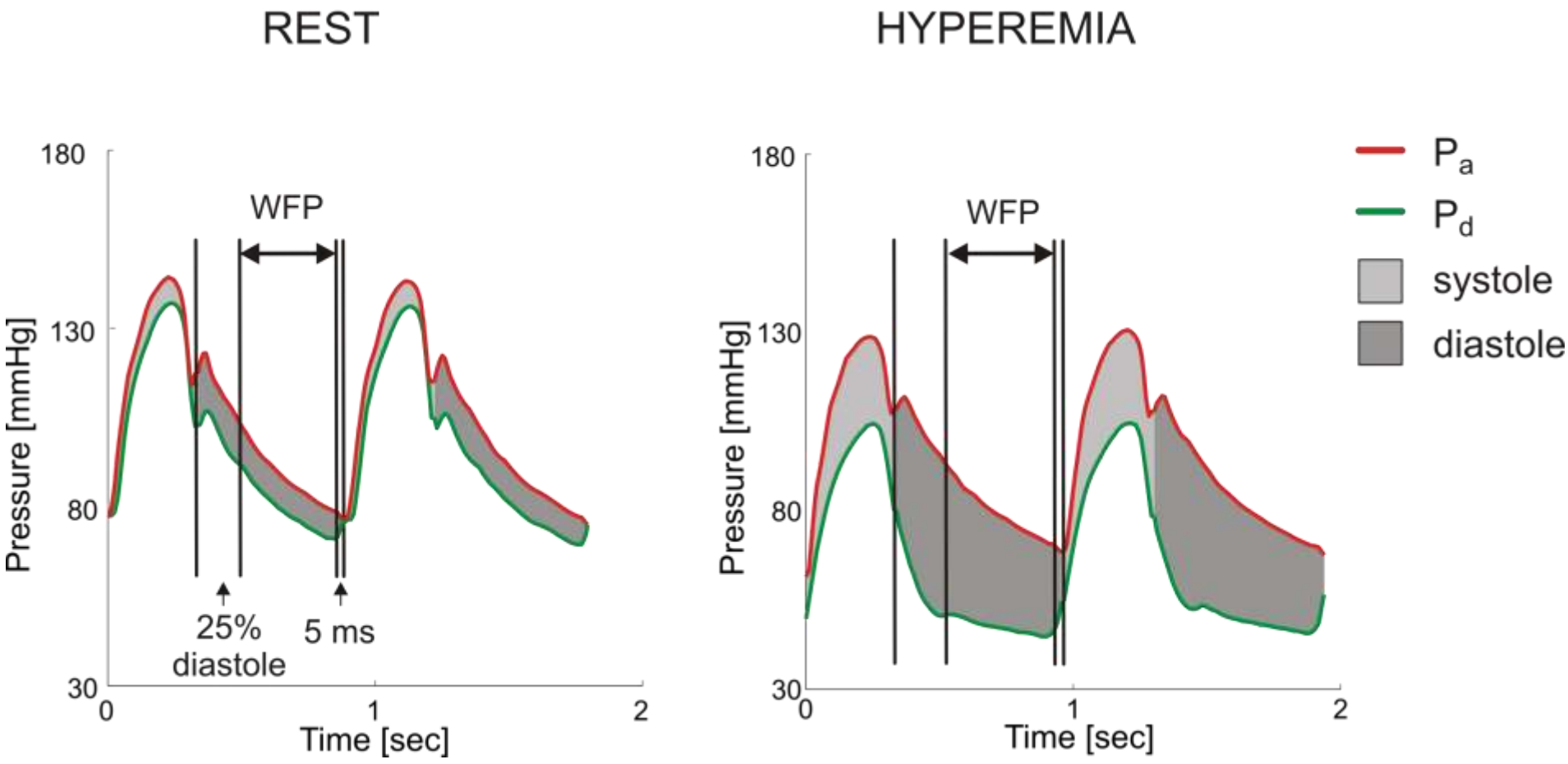
- ***not instanteneous***,
- ***not "wave-free"***,
- ***strongly dependent on hyperemia***,
- ***and not different from diast Pd/Pa*** $_{rest}$

VERIFY study, Berry et al, JACC 2013: N= 200 patients



iFR = Pd / Pa during WFP → strongly dependent on hyperemia

Colin et al, JACC 2013,
Johnson et al JACC 2013



iFR = Pd / Pa during WFP → strongly dependent on hyperemia

…….and by slight manipulations of the wire, giving a little bit of contrast, or even just saline, you can get any iFR or Pd/Pa value you like

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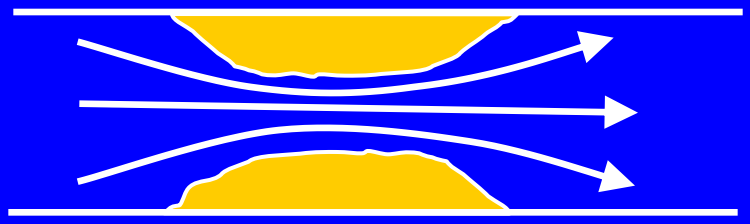
$\Delta P = f.Q + s.Q^2$

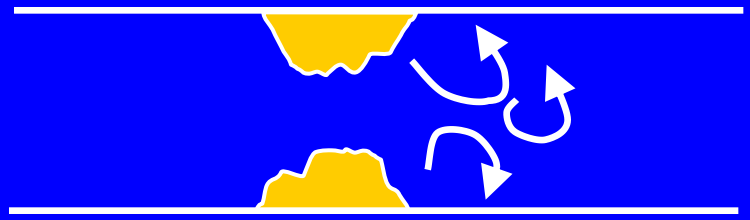
f = friction coefficient



Moderate gradient at rest

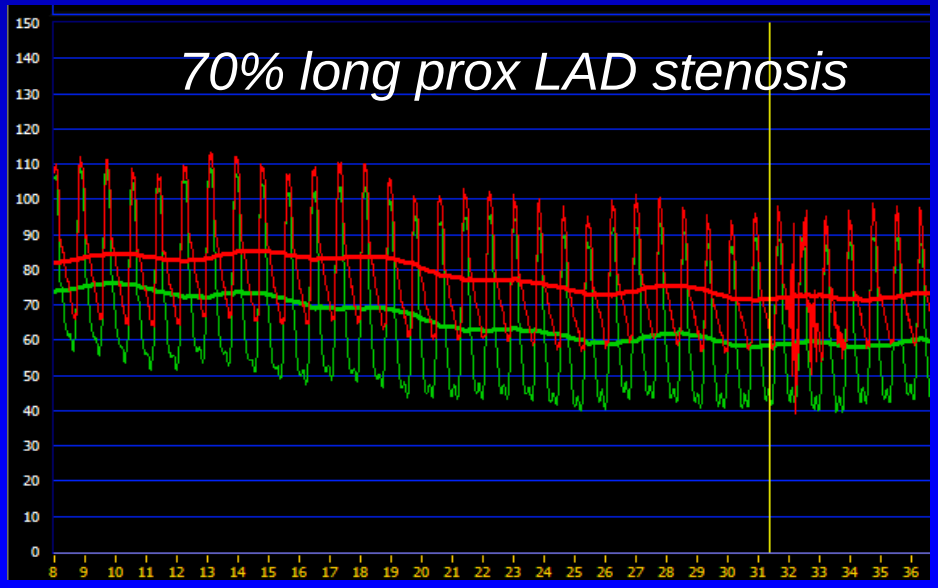
Moderate increment at hyperemia

S = separation coefficient

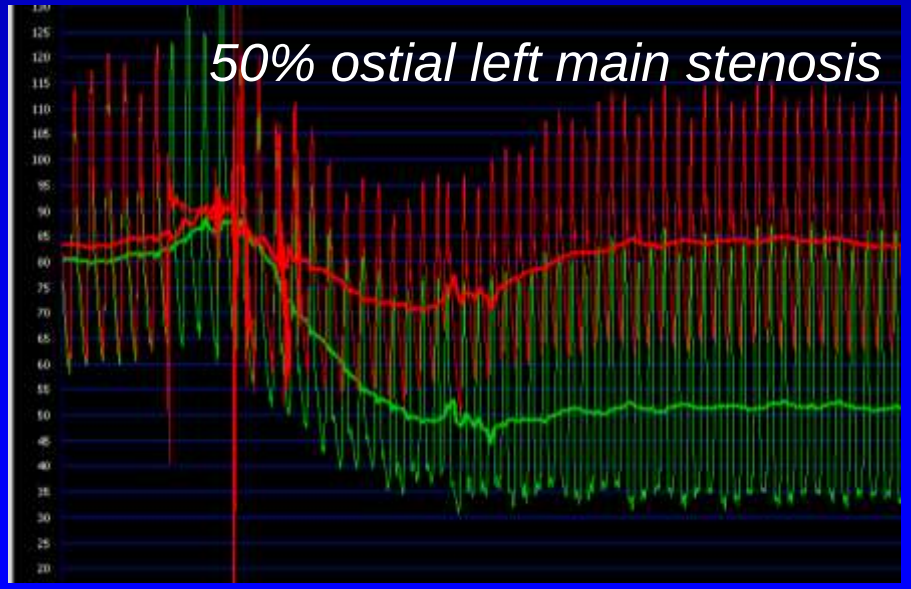


Small gradient at rest

Large gradient at hyperemia



iFR = 0.89 FFR = 0.85



iFR = 0.94 FFR = 0.57

In general:

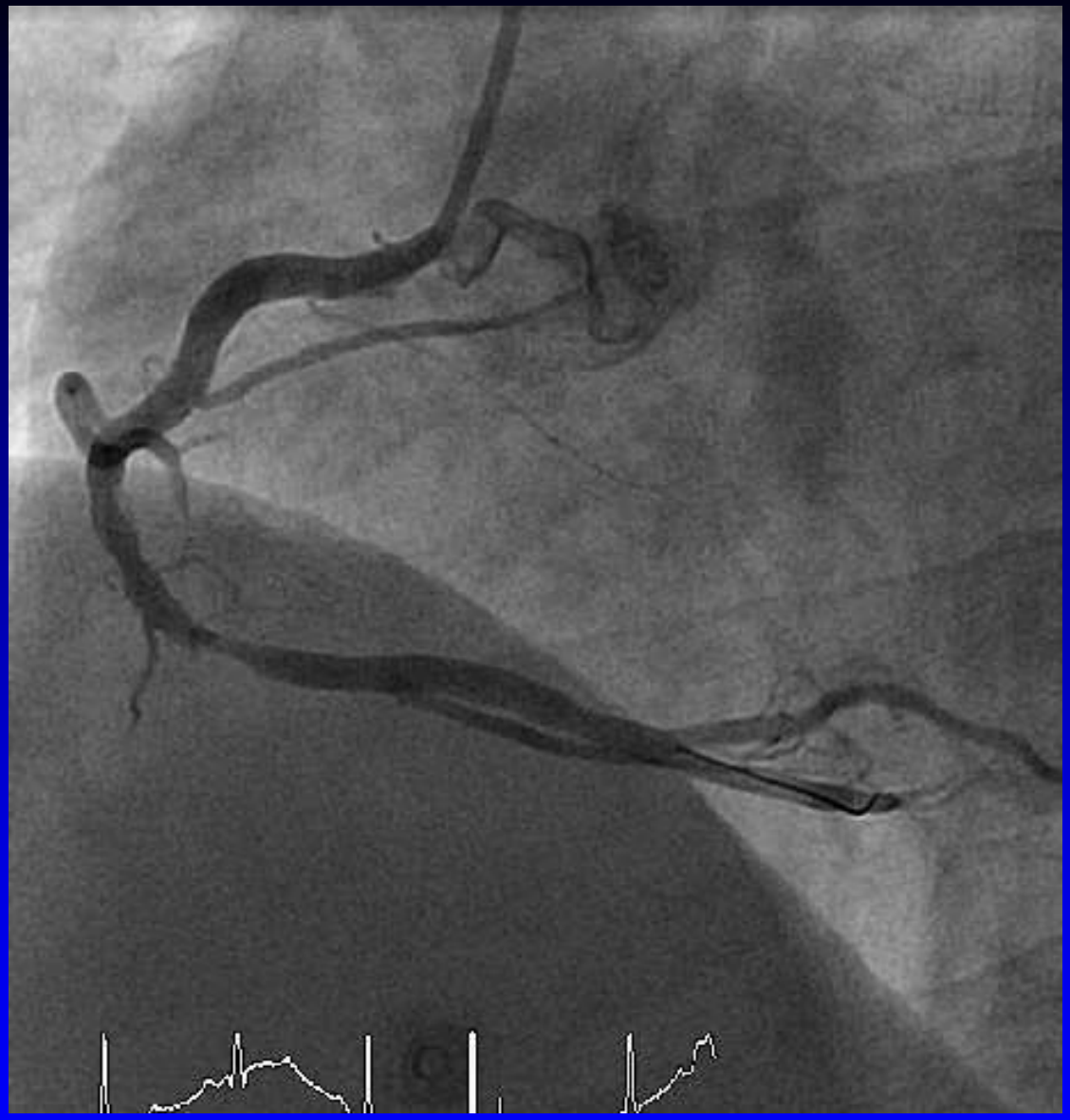
- small perfusion territory, distal stenosis, older patient, moderate long lesion, small artery, microvascular disease:

  → *often moderate gradient at rest with little increase at hyperemia*

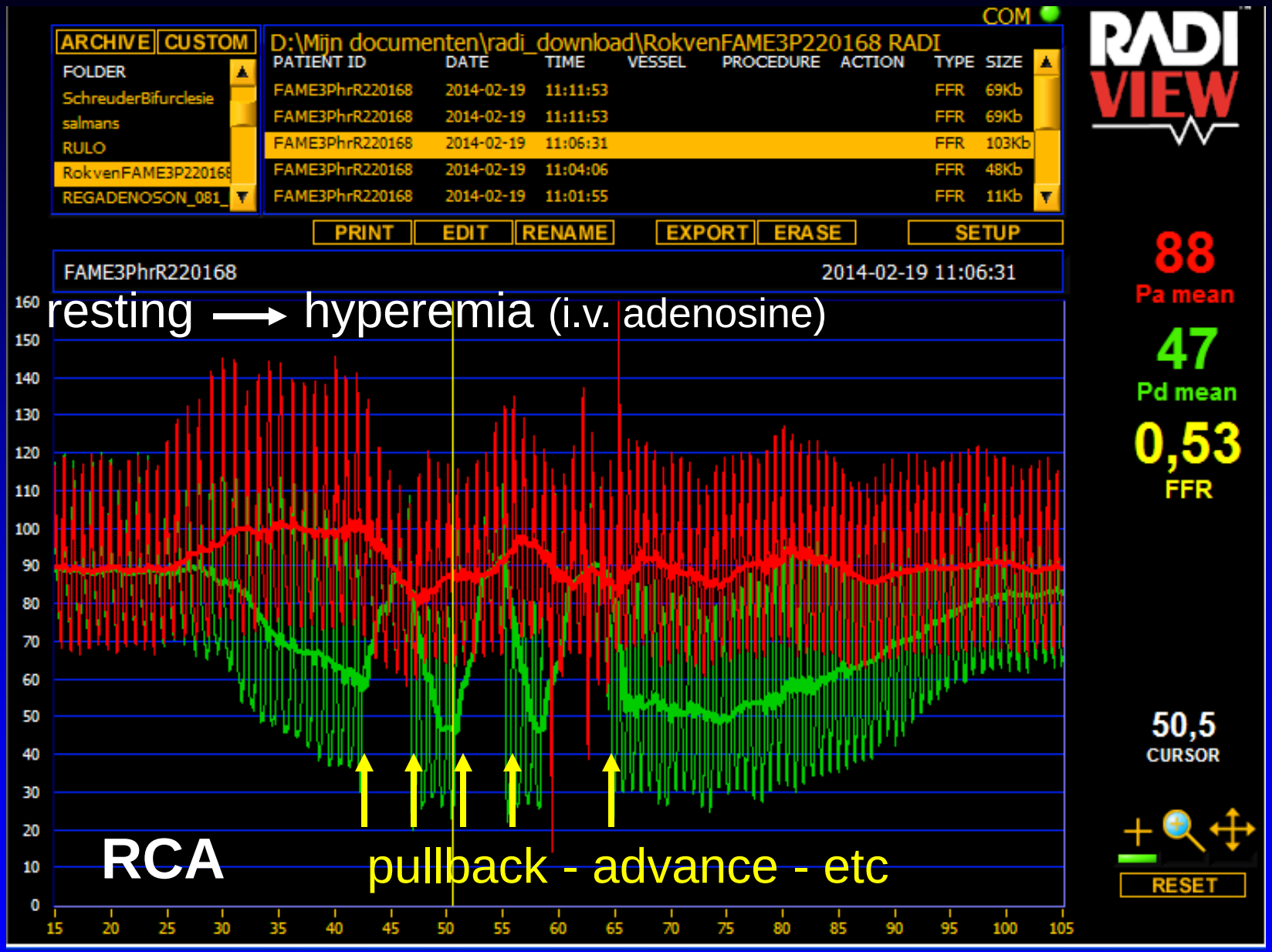
- large perfusion territory, proximal stenosis, young patient, short lesion, large artery, good microvasculature:

  → *often minimal gradient at rest with large increase at hyperemia*

Especially these lesions are missed by resting indexes



Male 46 years old, PressureWire in RCA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FAME3PhrR220168 2014-02-19 11:11:53 FFR 69Kb
FAME3PhrR220168 2014-02-19 11:06:31 FFR 103Kb
FAME3PhrR220168 2014-02-19 11:04:06 FFR 48Kb
FAME3PhrR220168 2014-02-19 11:01:55 FFR 11Kb
PRINT
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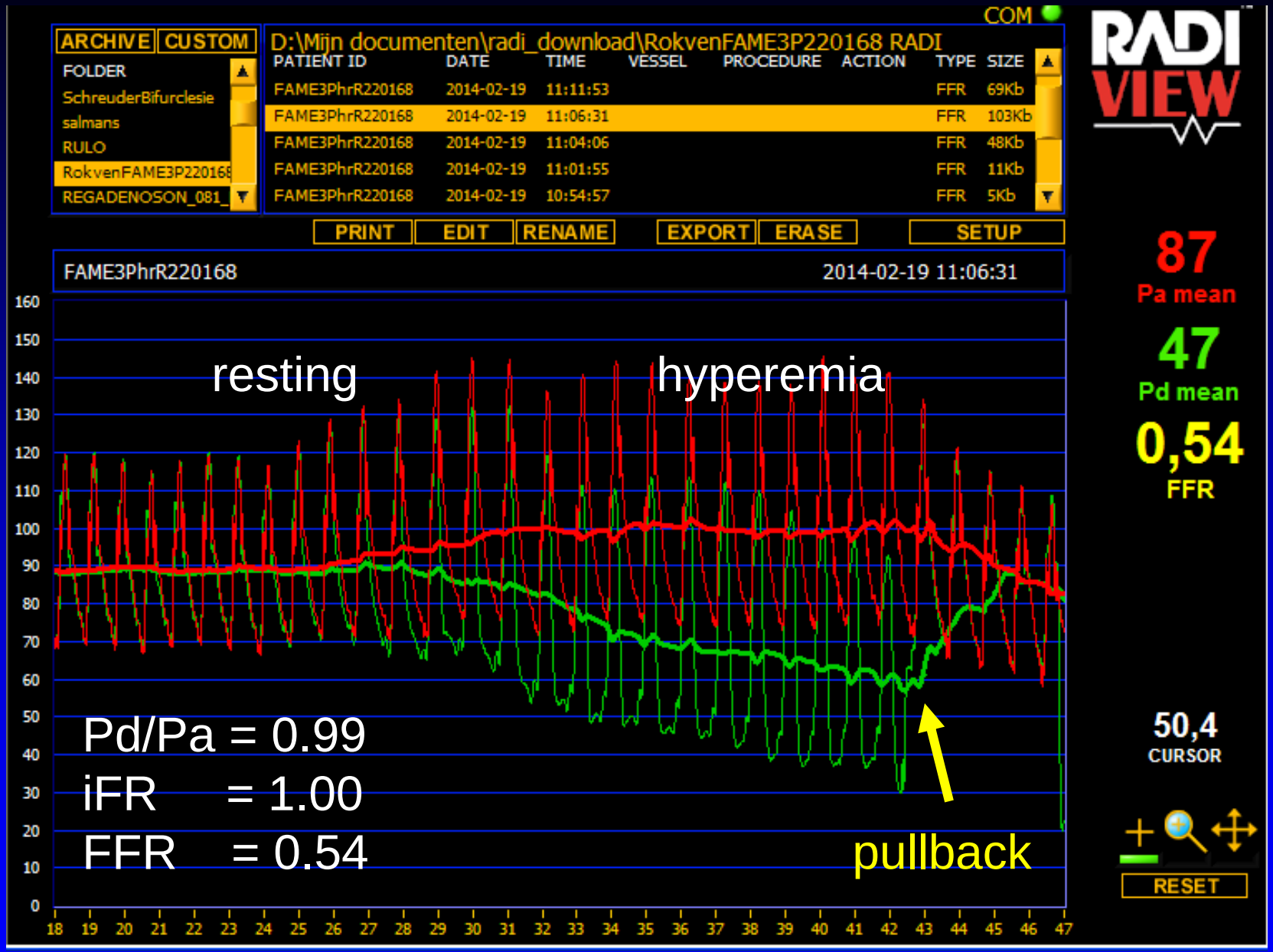
SETUP
FAME3PhrR220168
2014-02-19 11:06:31
resting ⟶ hyperemia (i.v. adenosine)
88
Pa mean
47
Pd mean
0,53
FFR
50,5
CURSOR
RESET
RCA
pullback - advance - etc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RADI VIEW
FAME3PhrR220168
2014-02-19 11:06:31
87
Pa mean
47
Pd mean
0,54
FFR
resting
hyperemia
Pd/Pa = 0.99
iFR = 1.00
FFR = 0.54
pullback
50,4
CURSOR
RESET
160
150
140
130
120
110
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90
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70
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18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47

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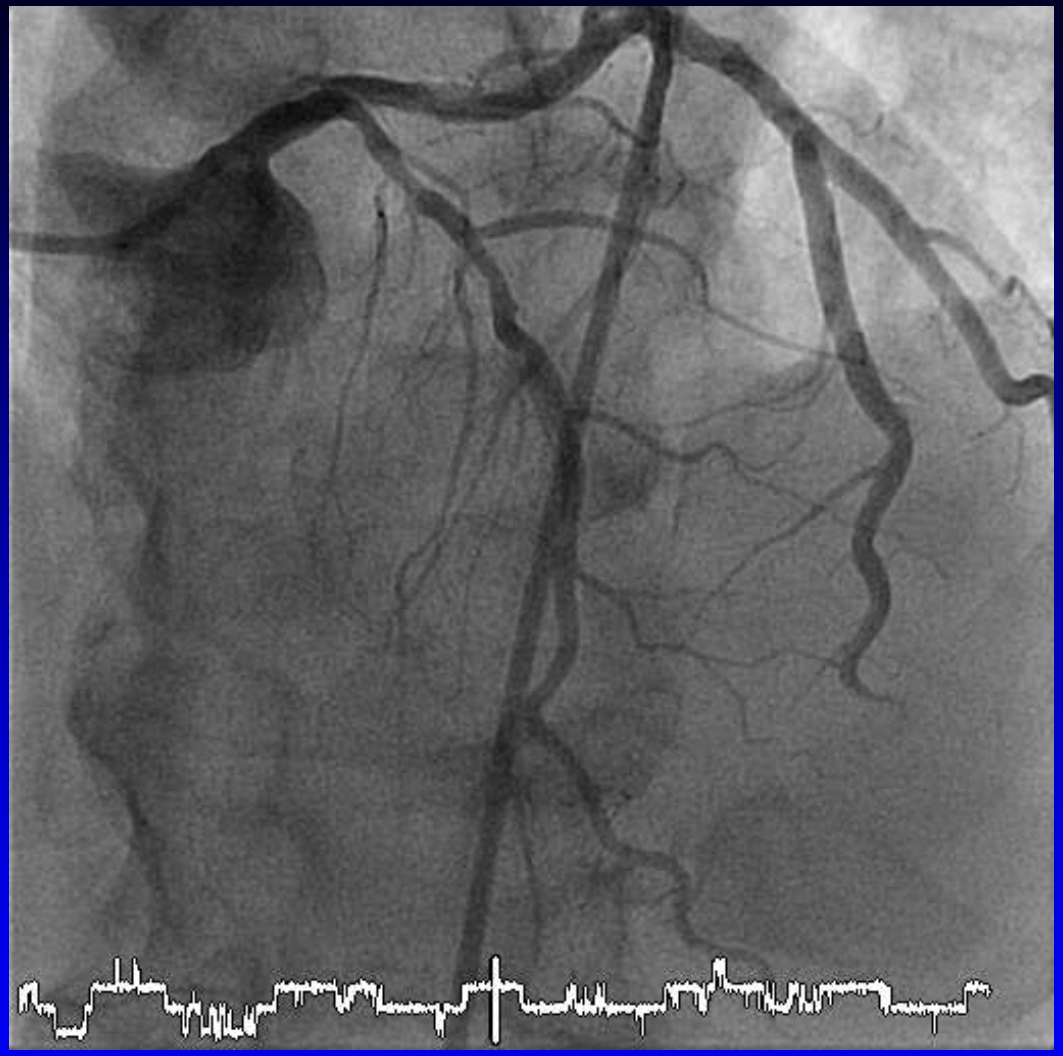
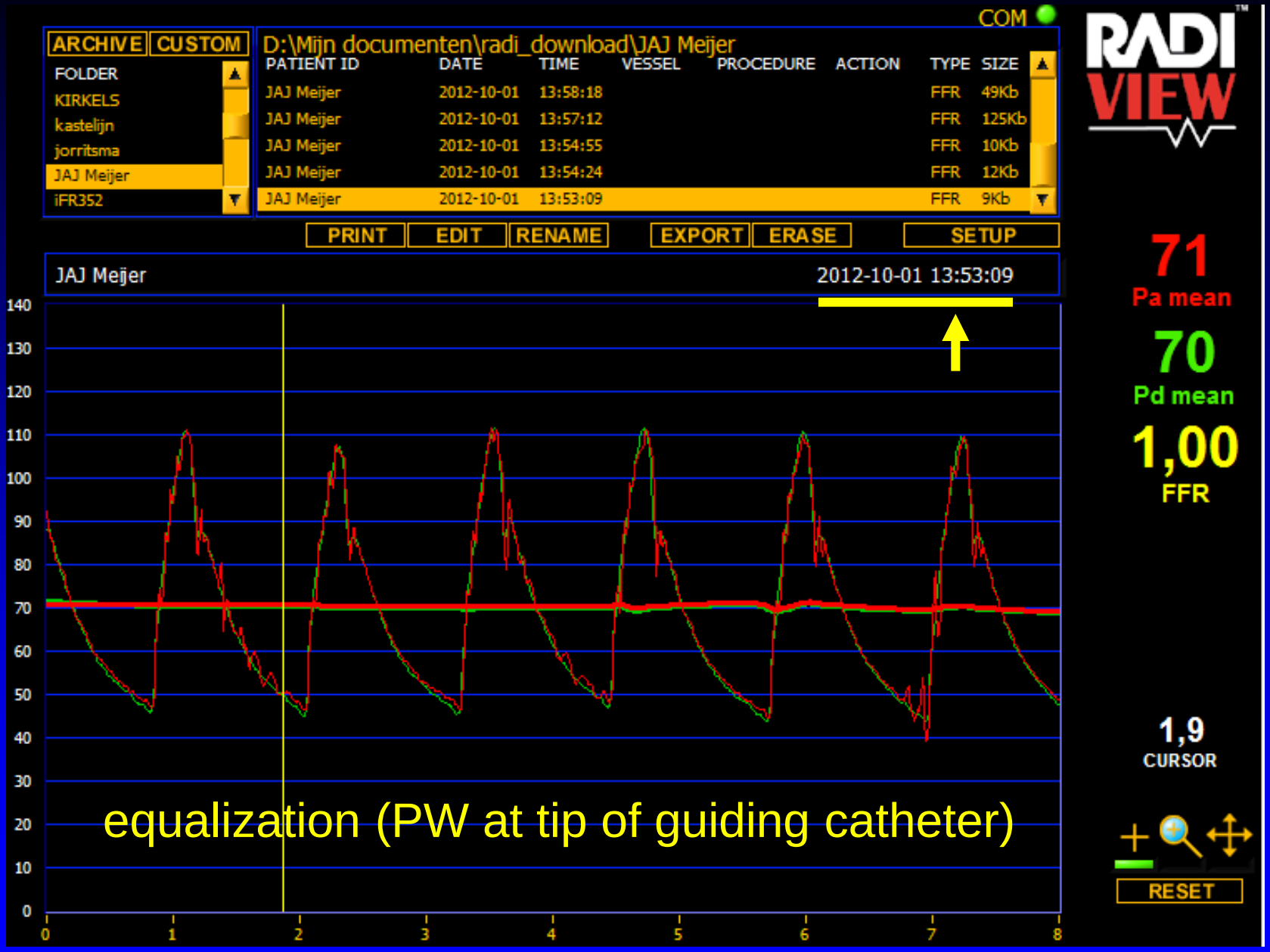
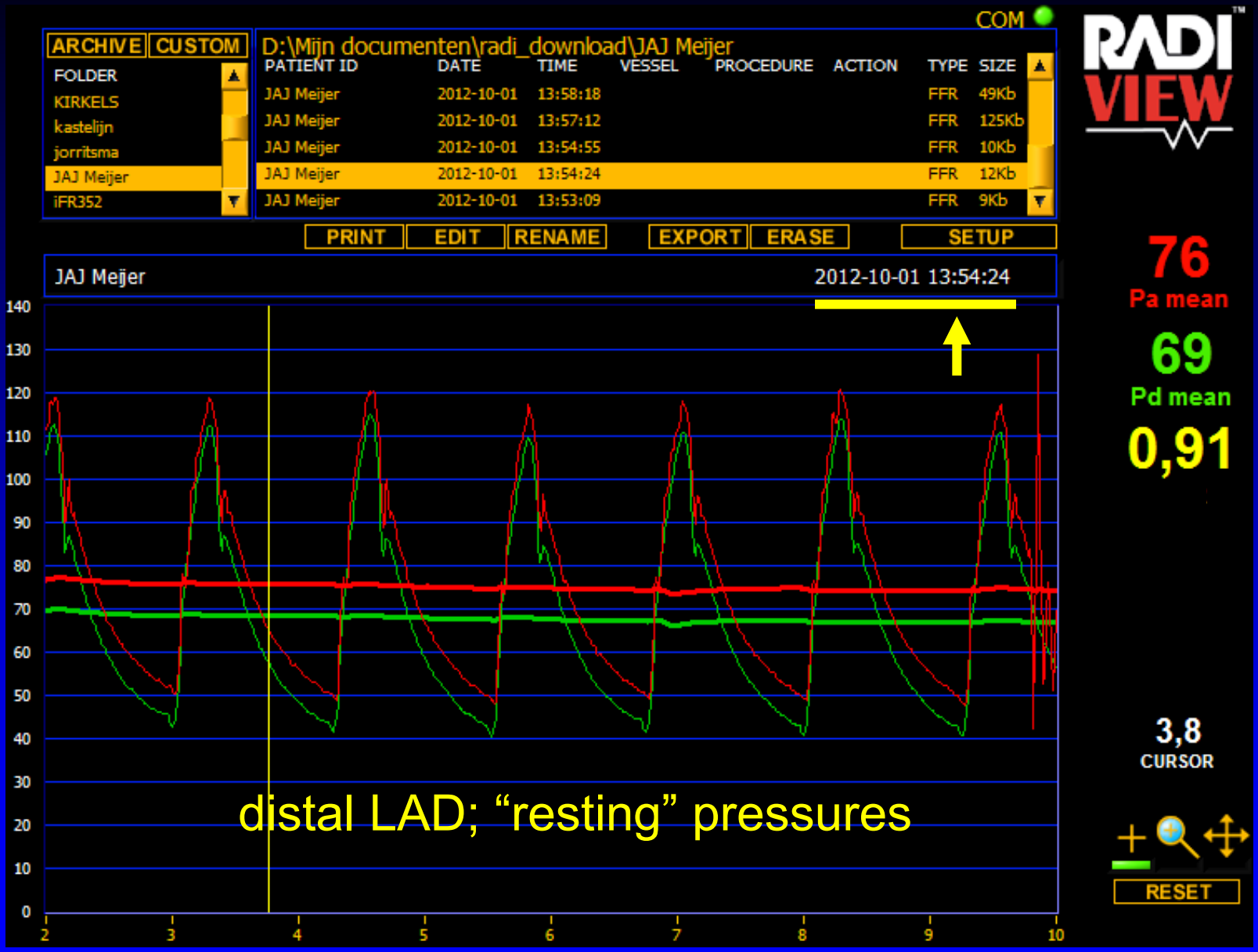


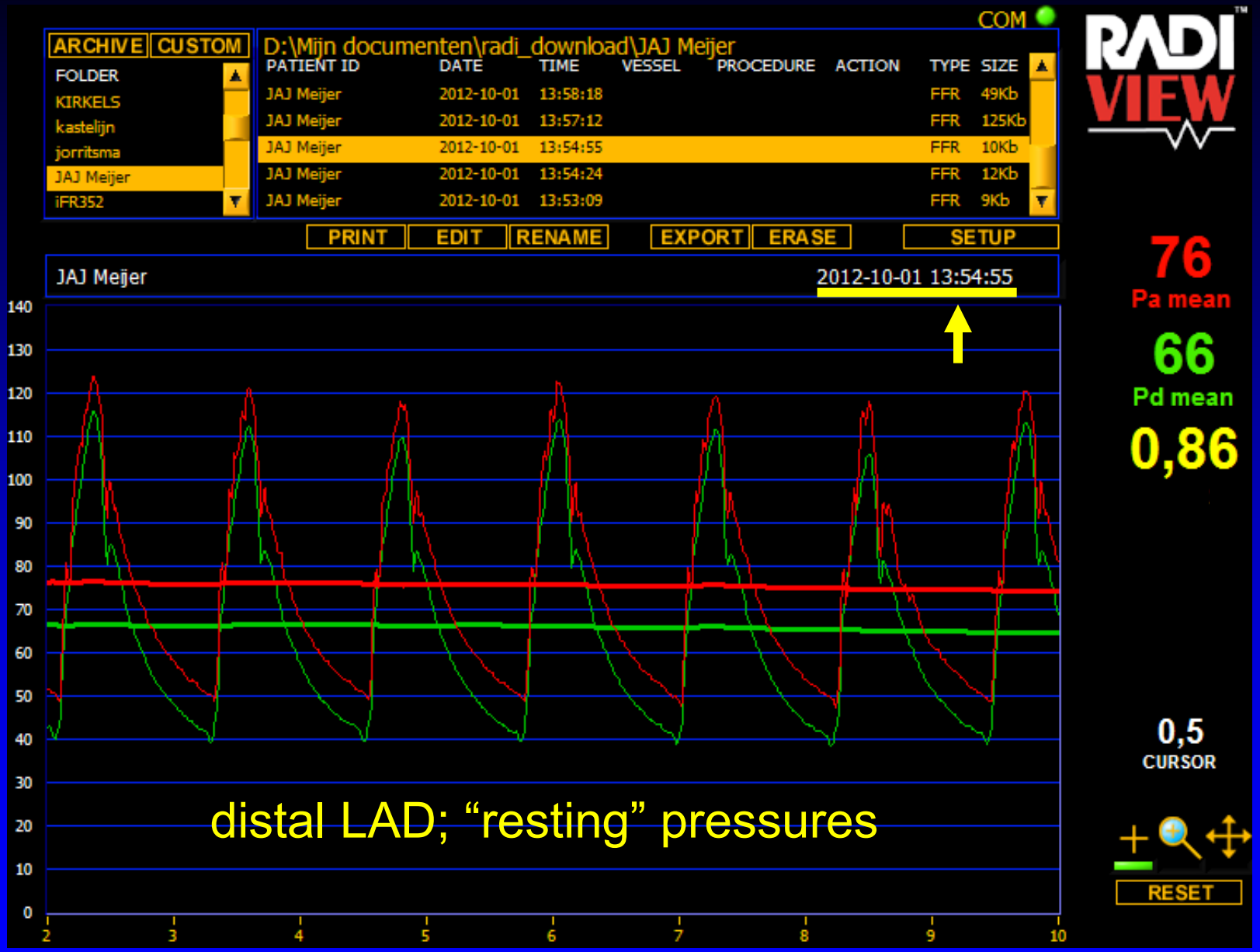
Mr M, born 26-03-1937,
long mild/moderate proximal LAD lesion



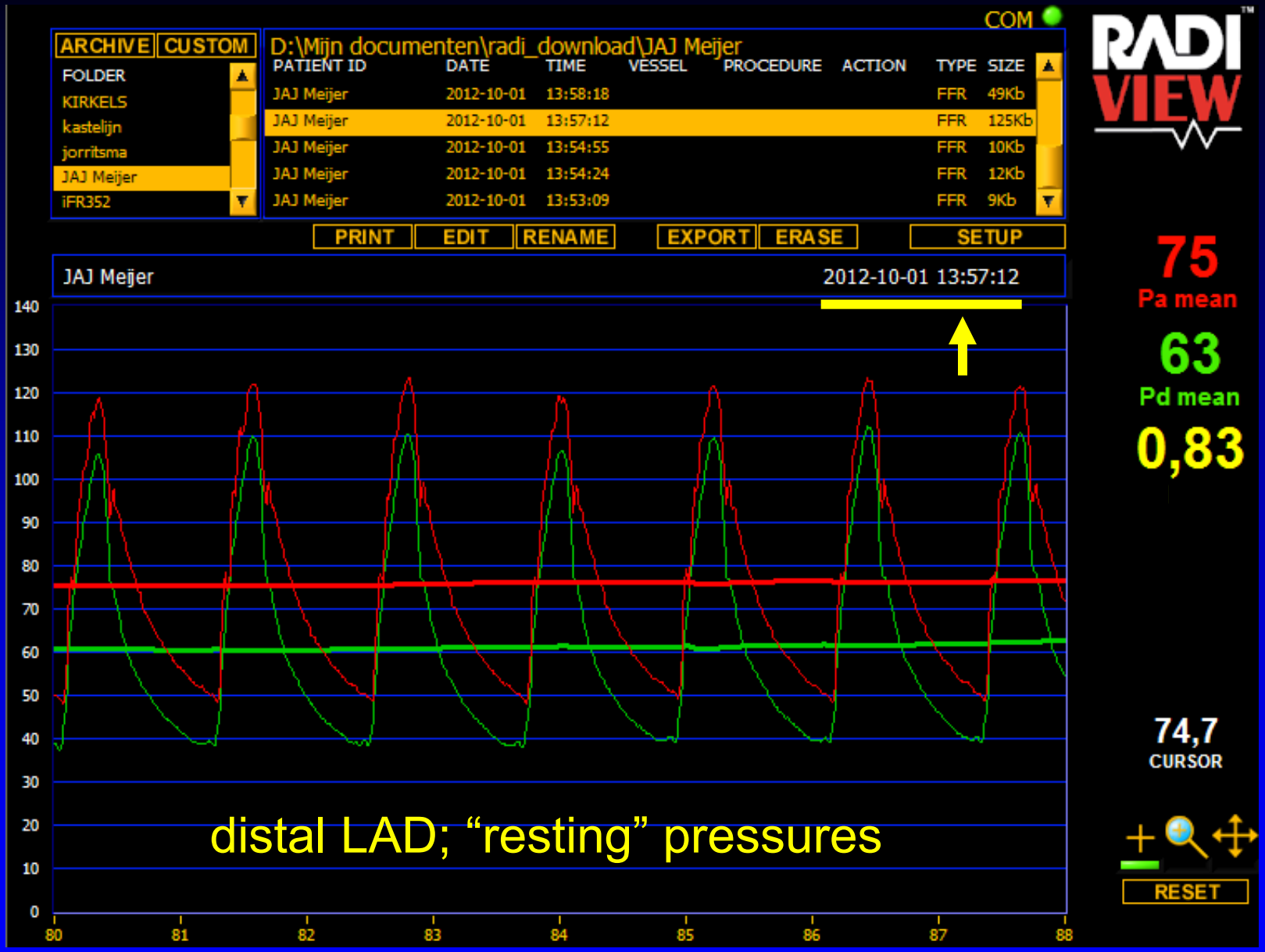
long moderate proximal LAD lesion; equalization



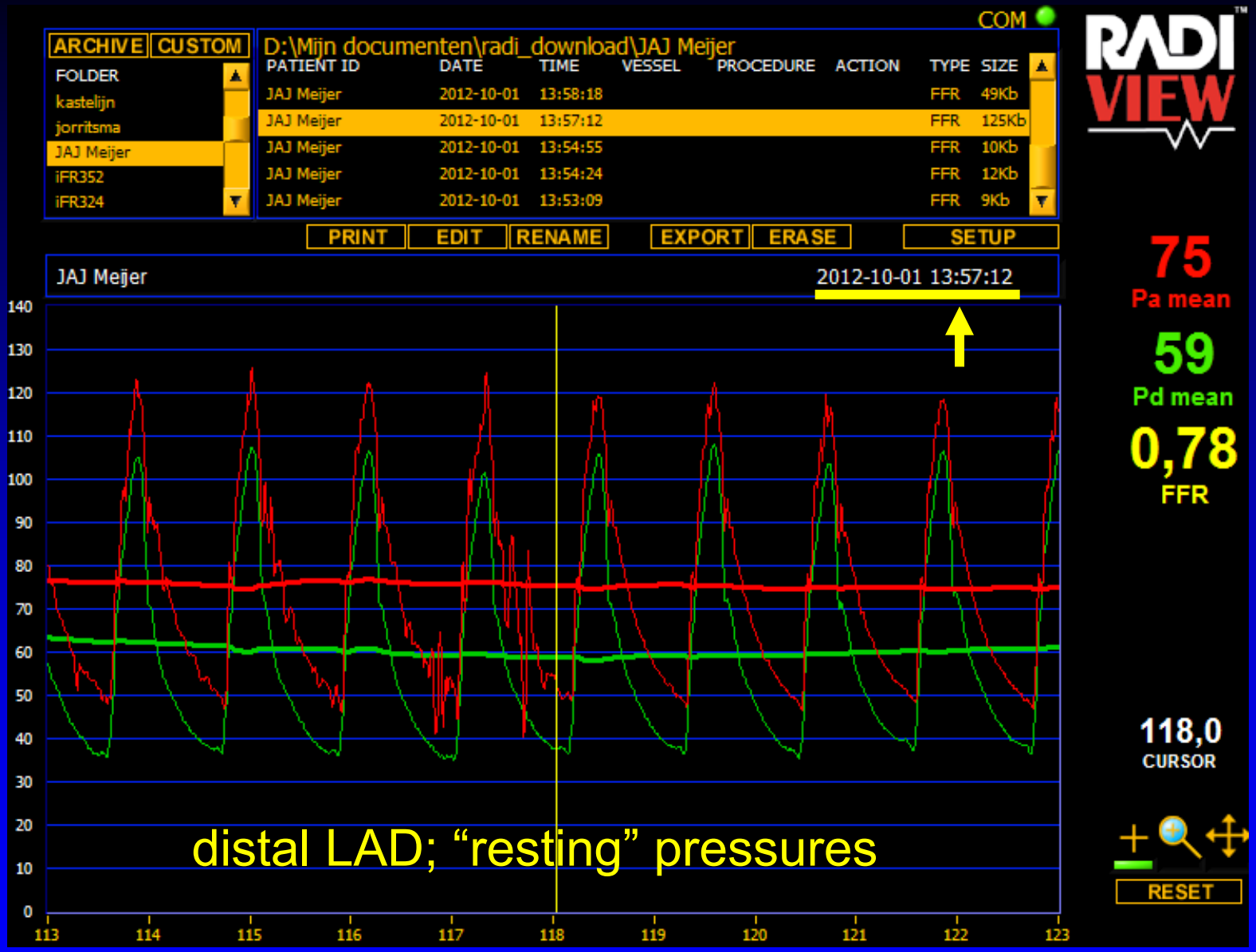
PW in distal LAD; patient “asleep” (relaxed)



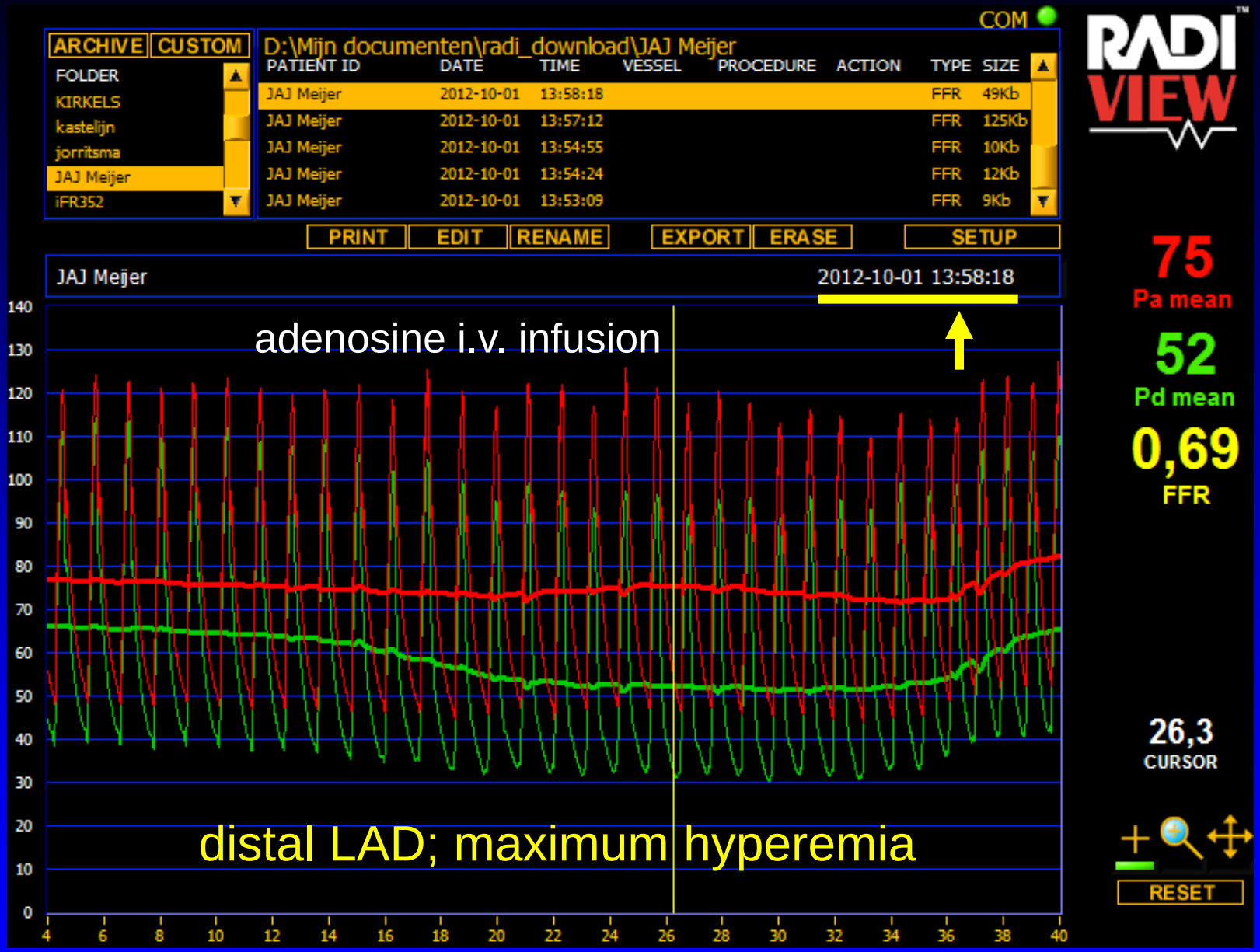
PW in distal LAD; patient “awake”



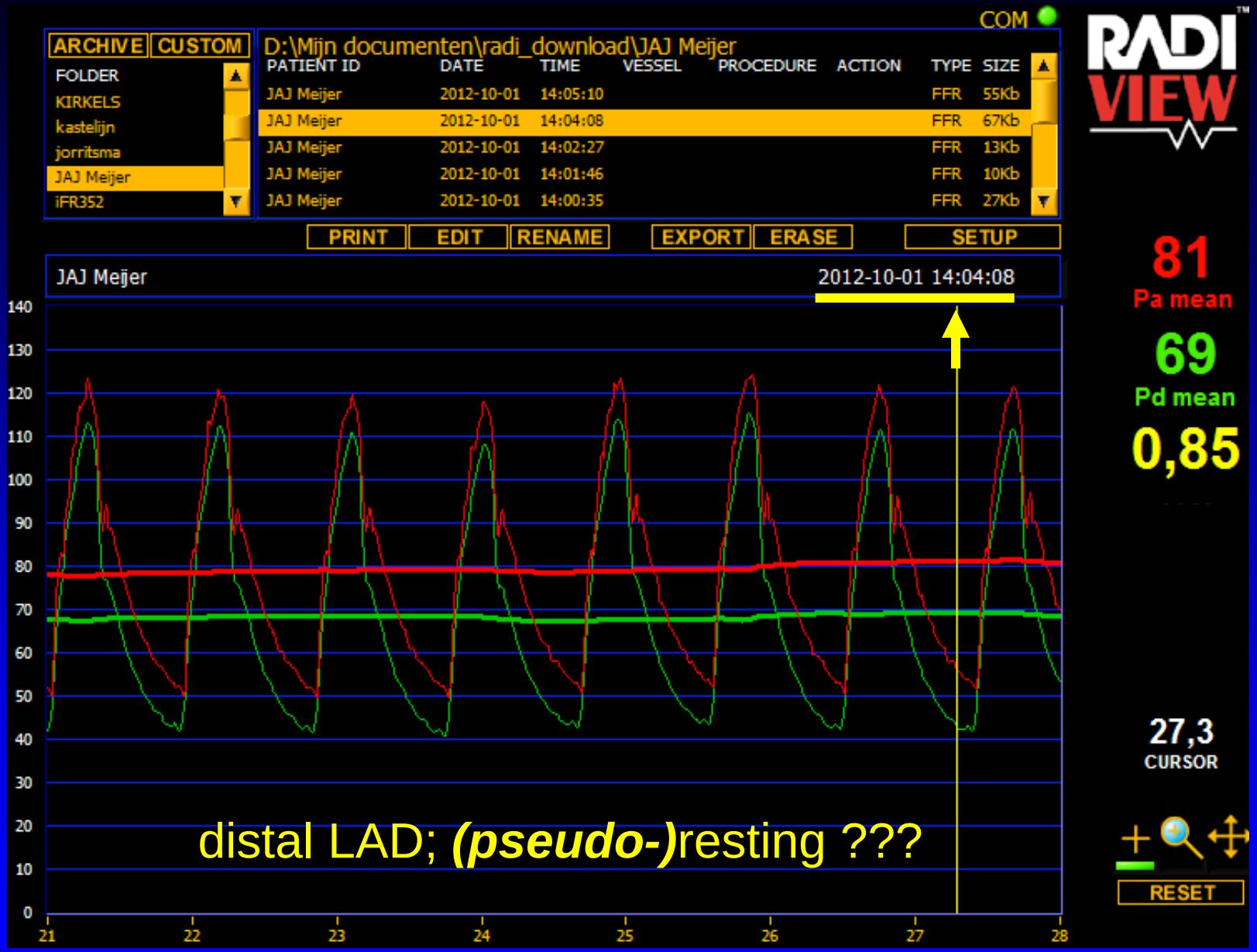
prior to adenosine: explanation to patient what is going to happen



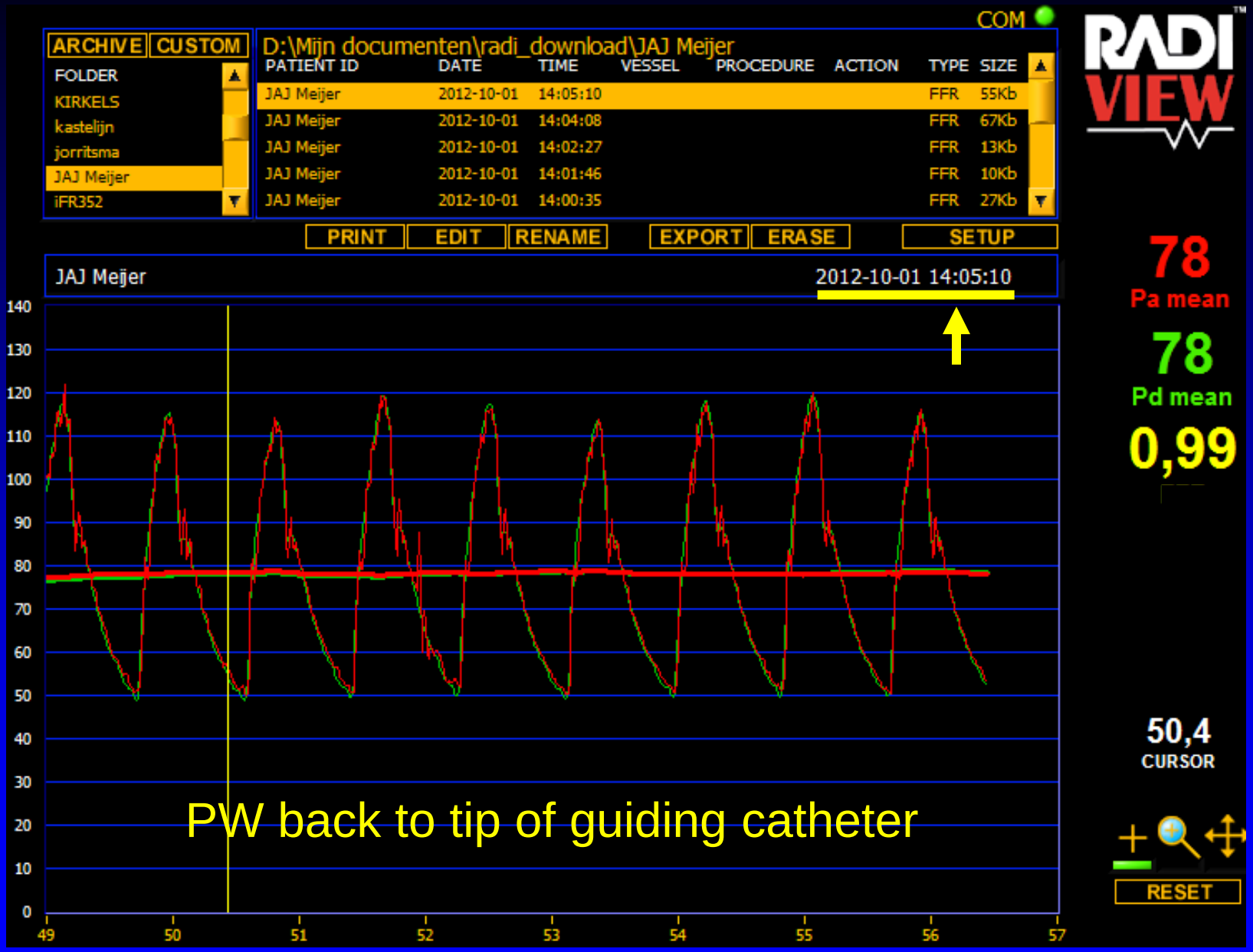
advancing the wire 2 cm and pulling it back again



Measurement of FFR



After waiting for 5 minutes, not touching anything



verification of equal pressures and absence of drift

iFR = 0.89

P_d/P_a=0.90

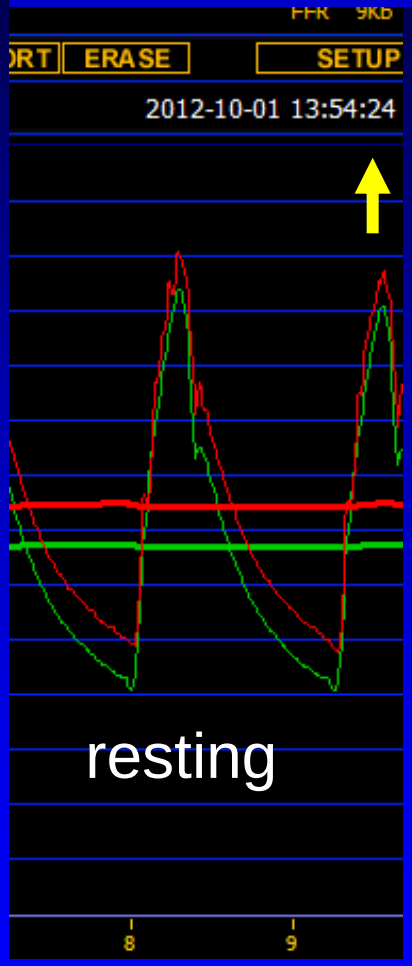
iFR = 0.84

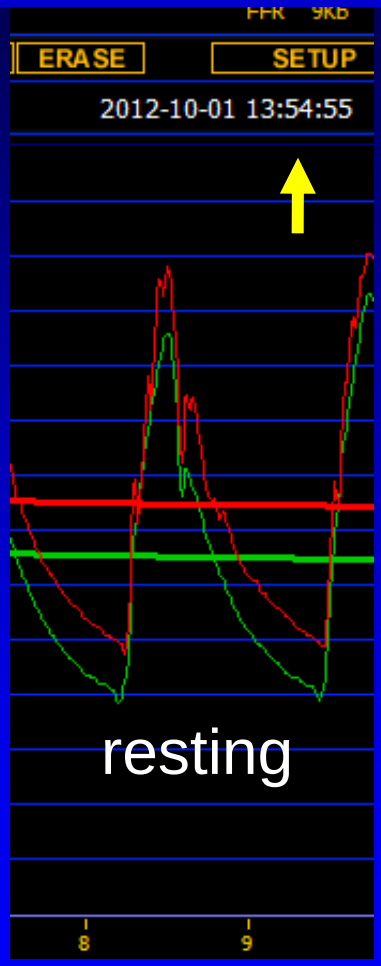
P_d/P_a=0.87

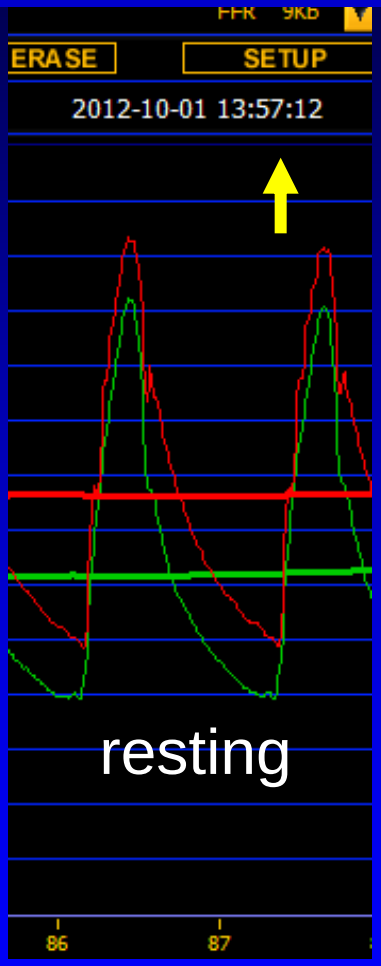
iFR = 0.76

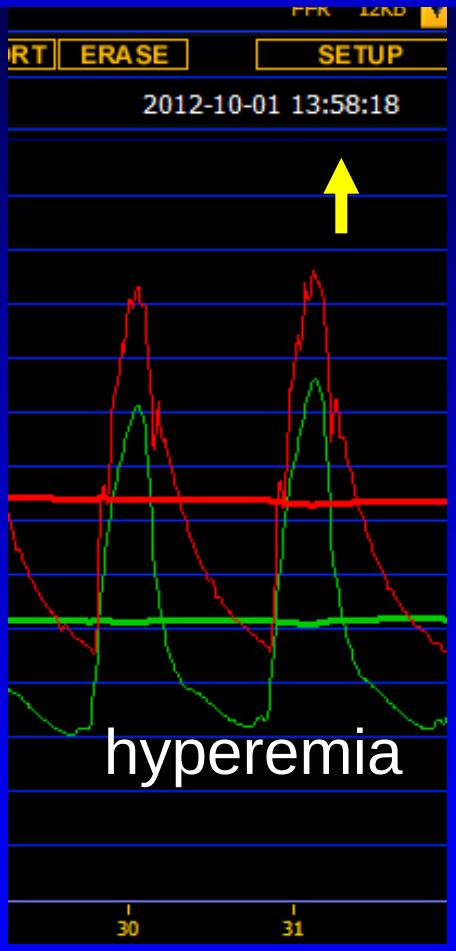
P_d/P_a=0.80

FFR = 0.69









what is "resting"?

nothing is so variable in the cathlab as "resting"

- obtaining true resting conditions in a conscious patient in the catheterization laboratory, is illusionary…….

…..and as a consequence, large variation in cut-off values to detect ischemia are found for resting indices:

Traditional CFR: ischemic threshold varies from 1.6 to 3.5

iFR: 0.83 (Advise study, Sen et al)
0.88 (Koo et al)
0.92 (Jeremias et al)

Similar for all indexes which rely upon resting value of flow

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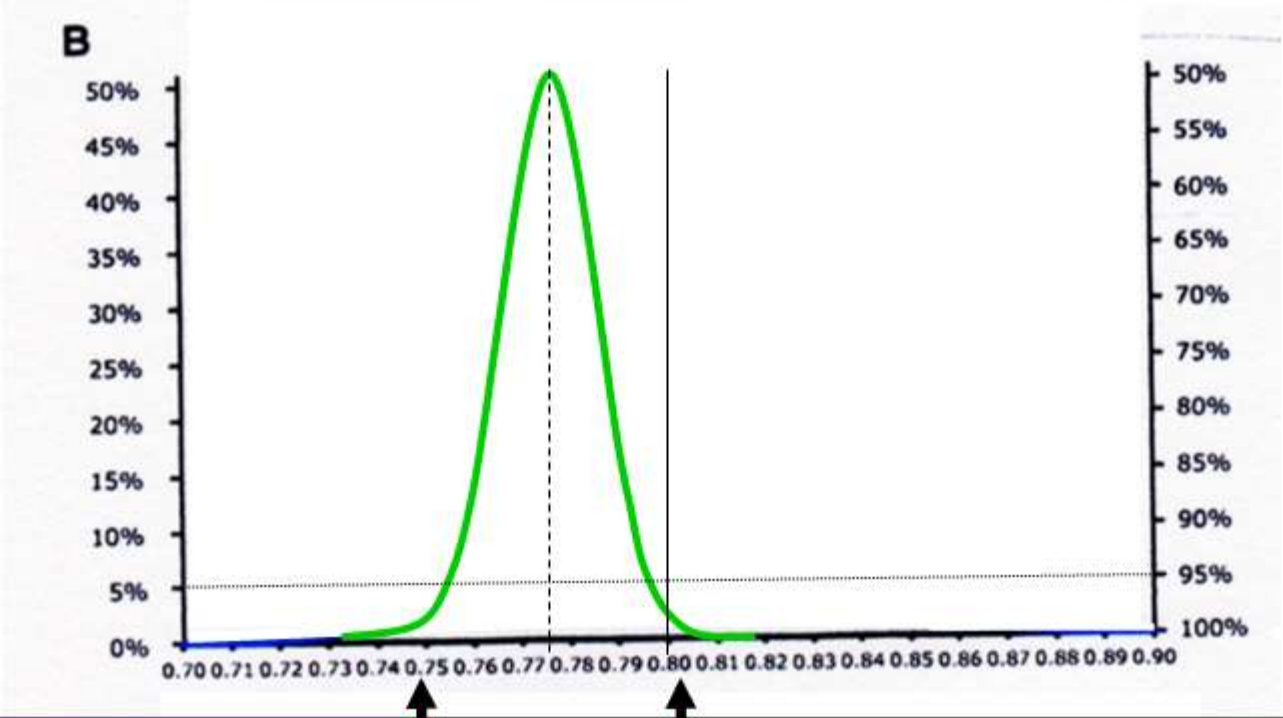
- *no independent outcome data for iFR or cFFR*
- *decreased signal to noise ratio without hyperemia*

Probability that treatment decision will change if the respective index measurement is repeated

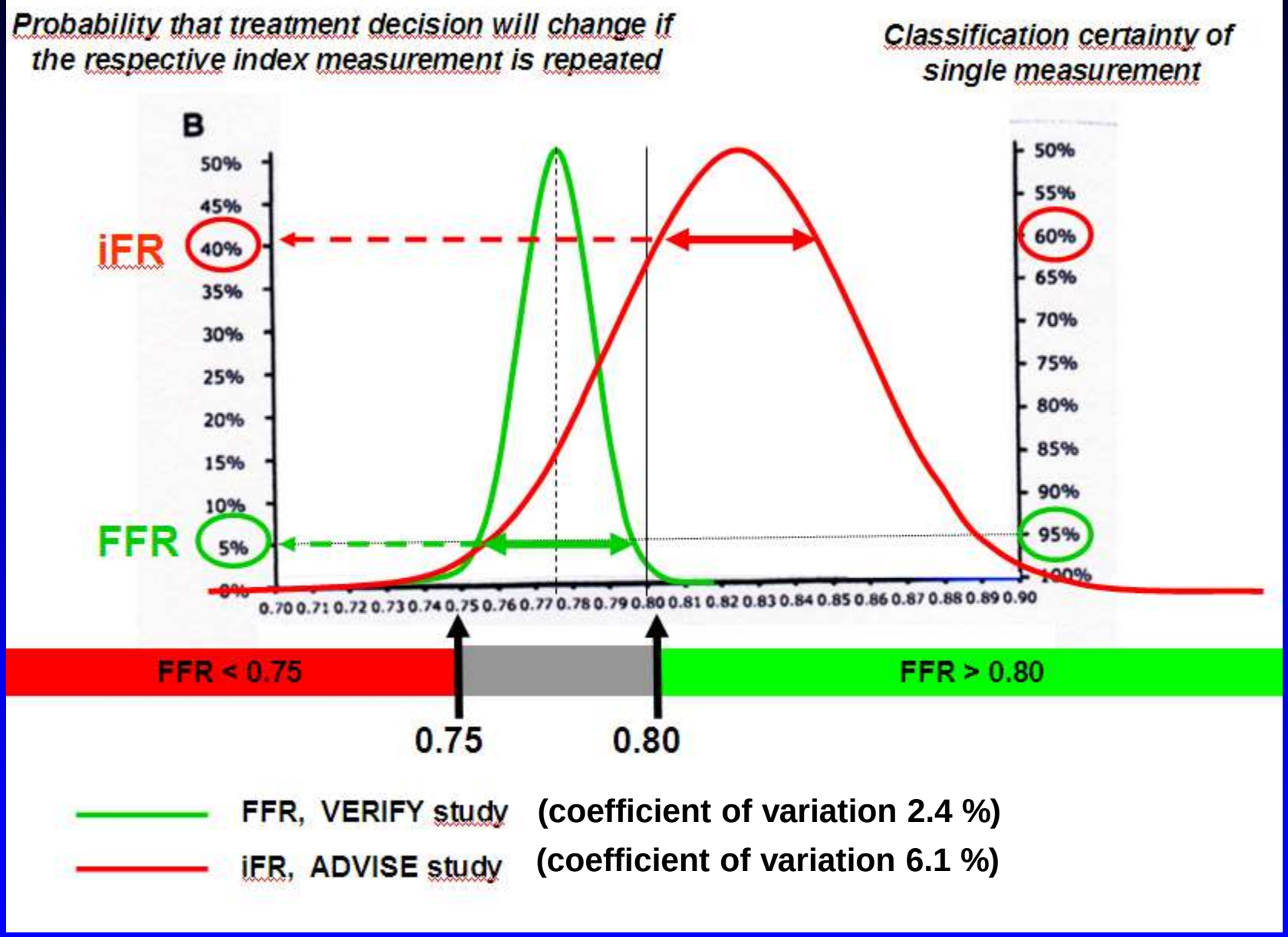
Classification certainty of single measurement

FFR



2.4 % of patients go from green to gray or v.v. and 2.4 % from red to gray
Almost nobody ever crosses from red to green or v.v.

FFR (Fractional Flow Reserve)



Modified from Petraco et al; EuroIntervention 2013

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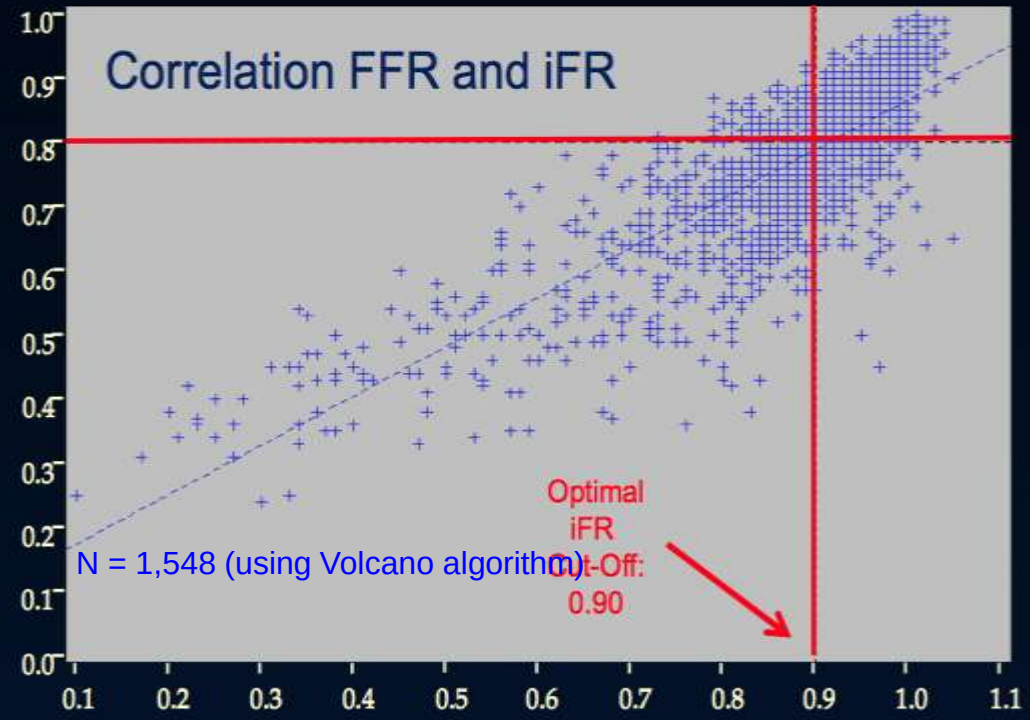
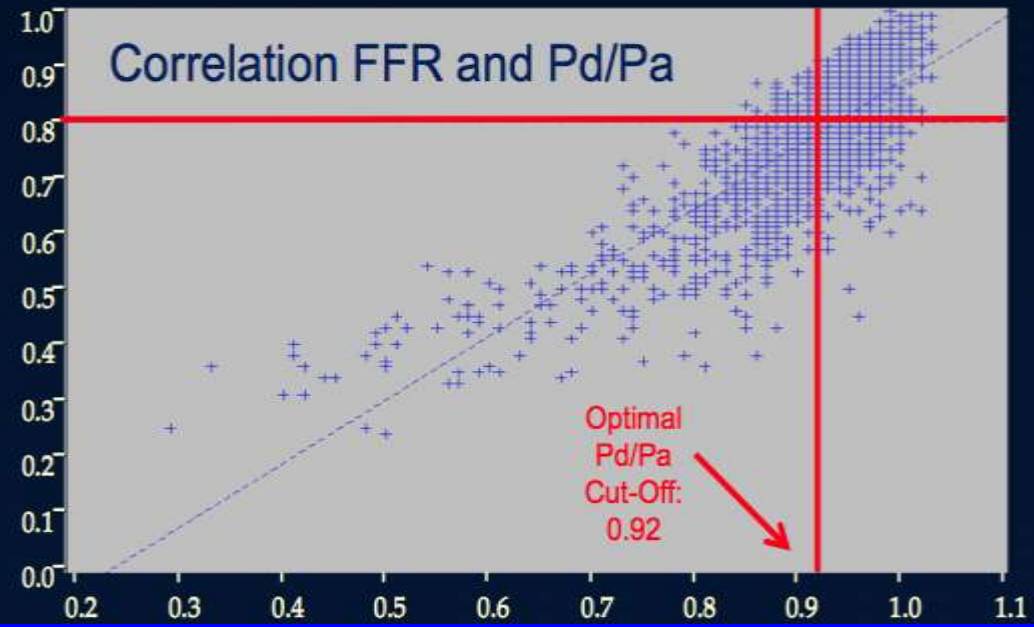
- *Resting Conditions Are Hard to Obtain*
- *Large gray zone without hyperemia*
- *limited reliabilty (80% at most) and no independent outcome data for iFR or cFFR*
- *decreased signal to noise ratio without hyperemia*

RESOLVE study (N=1768)





iFR

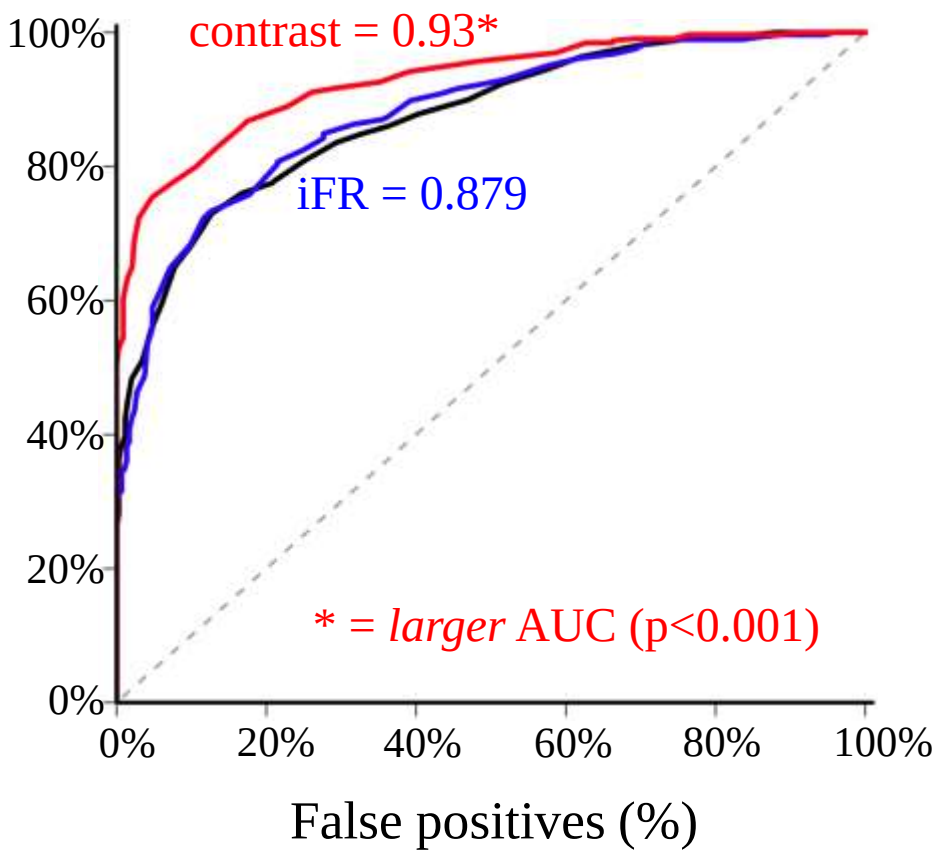
C-Statistic	0.80
Sensitivity	78.5%
Specificity	82.3%
PPV	86.0%
NPV	73.5%
Accuracy	80.1%

Pd/Pa

C-Statistic	0.82
Sensitivity	75.9%
Specificity	87.4%
PPV	89.3%
NPV	72.6%
Accuracy	80.7%

Jeremias, CRF, 2013

Submaximal Hyperemia with a single routine Contrast injection: CONTRAST study (LBT at PCR)



Diagnostic accuracy of different indices compared to FFR:

iFR:	***79%***	***P < 0.001***
Pd/Pa at rest:	***80%***	
Contrast FFR (cFFR):	***85 %***	

Optimum binary cut-off for contrast P*d*/P*a* : 0.83

Johnson et al, LBT at PCR, in press

Outcome data in RCT only available for FFR

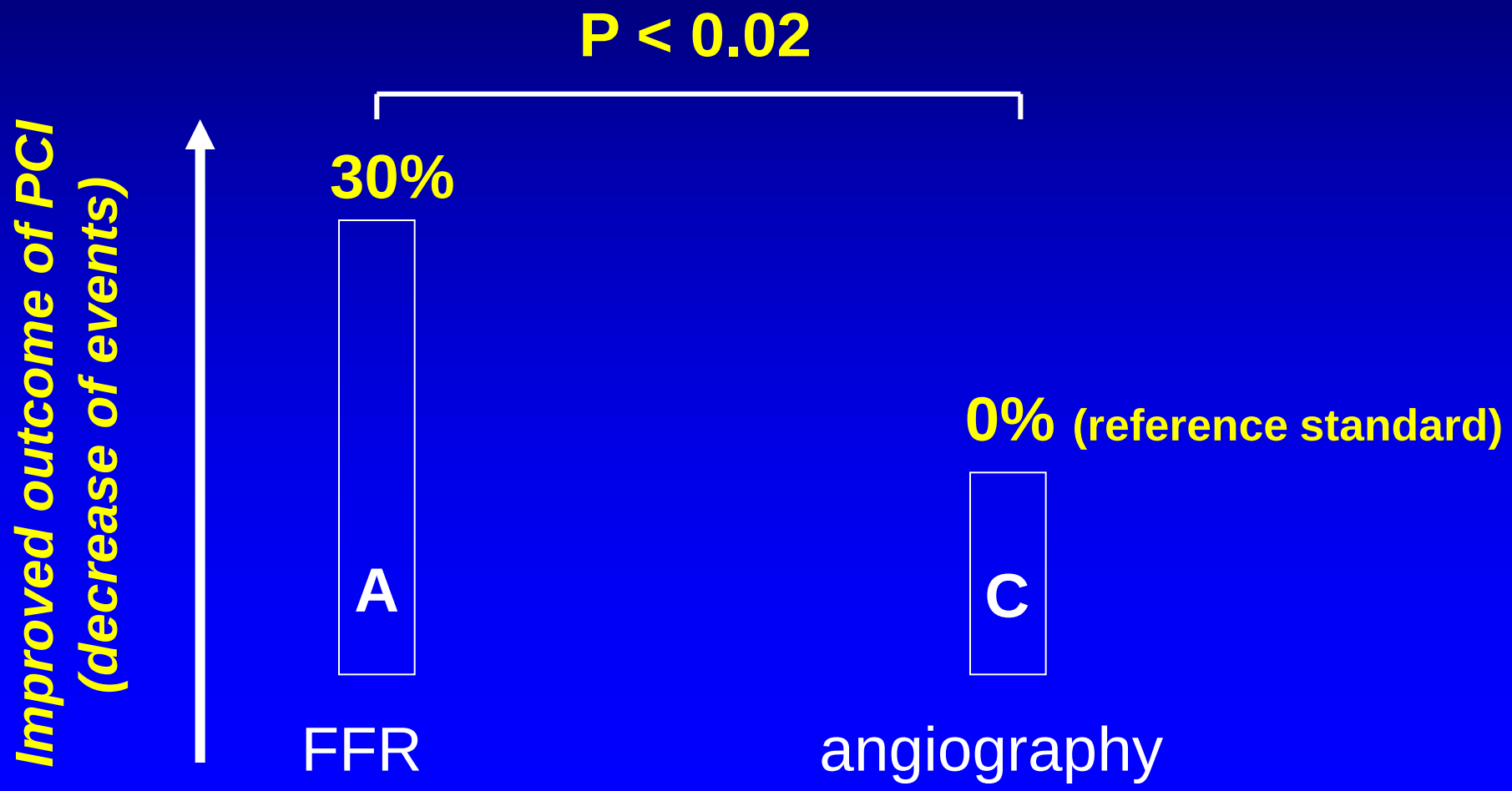
- there are no independent outcome data for iFR

- diagnostic accuracy is decreased to 80% in all studies
  (whether performed by proponents or opponents)
  Verify study, N=200, prospective and consecutive
  Resolve study, N=1600, retrospective
  Advise-2 study, N = 650, prospective
  Contrast study, N= 750, prospective
  and in none of these studies, there was any difference between iFR and Pd/Pa at rest

- ongoing studies *(Define-Flair, Swedish Heart….)*
  do not independently investigate outcome for iFR
  (non-inferiority design in low-risk patients)

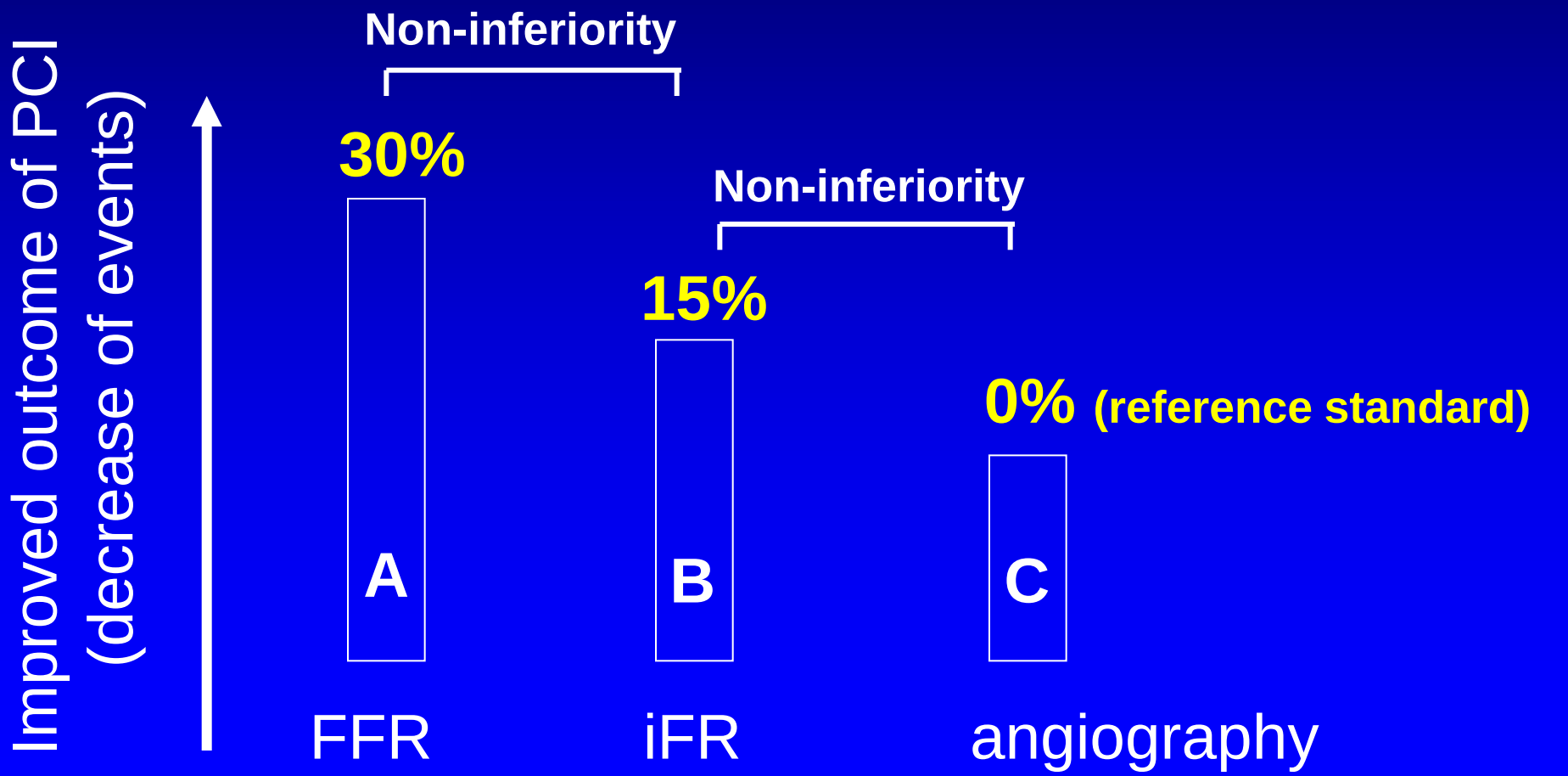
Outcome data in RCT only available for FFR

In the ***FAME study***, FFR guided PCI in MVD was ***superior*** to angiograpy guided PCI and reduced all types of events by approximately 30%



Outcome data in RCT only available for FFR

Take a low-risk population, a non-inferiority design with a liberal margin, make people believe that RC registry is the same as a RCT……*and you can prove anything !*



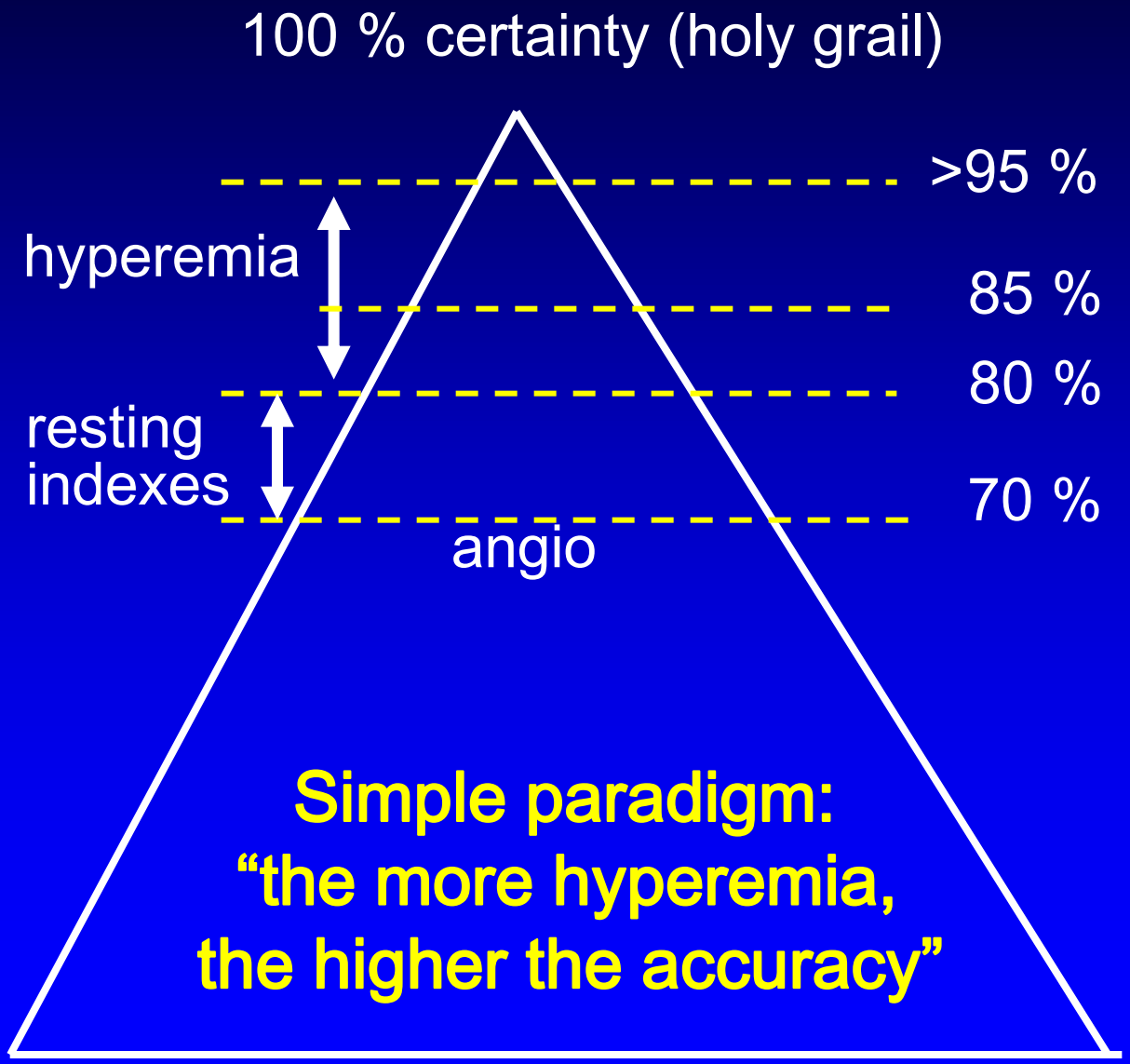
Correct Classification of Ischemic Stenosis

FFR

Contrast cFFR

resting Pd/Pa, iFR,

angiography



HYPEREMIA MANDATORY ? ⟶ YES !

- Leaving away (full) hyperemia, means decrease of accuracy and false decision making in 20% of patients. With so-called “hybrid” approaches (i.e. hyperemia in part of the patients) 10% false decisions

- *Does a few minutes of extra work and a very moderate saving of money for a hyperemic drug justify a wrong decision in 1 out of every 5-10 patients?*

For us, PCI might be routine….

…..for the patient, it is a big deal!

Therefore, we should do it in the best possible way !