FFR AND MICROCIRCULATION:
NEW APPLICATIONS AND FUTURE DEVELOPMENTS

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FFR : NEW APPLICATIONS AND FUTURE DEVELOPMENTS

- *Is hyperemia mandatory?*
- *non-invasive assessment of FFR by CT*
- *“new” hyperemic drugs: rapiscan = regadenoson*

FFR : NEW APPLICATIONS AND FUTURE DEVELOPMENTS

- ***Is hyperemia mandatory?***
- ***Can FFR be calculated without hyperemia***
- ***index "iFR" (~ resting Pd/Pa during part of diastole), claimed to be as accurate as FFR (****Sen et al, JACC 2011)*

→ **VERIFY STUDY** *(Berry et al)*

Basis hypotheses underlying iFR:

- there is a particular period during diastole ("wave-free period") where resistance ***at rest*** would be ***constant and minimal*** and equal to ***average hyperemic*** resistance during the heart cycle

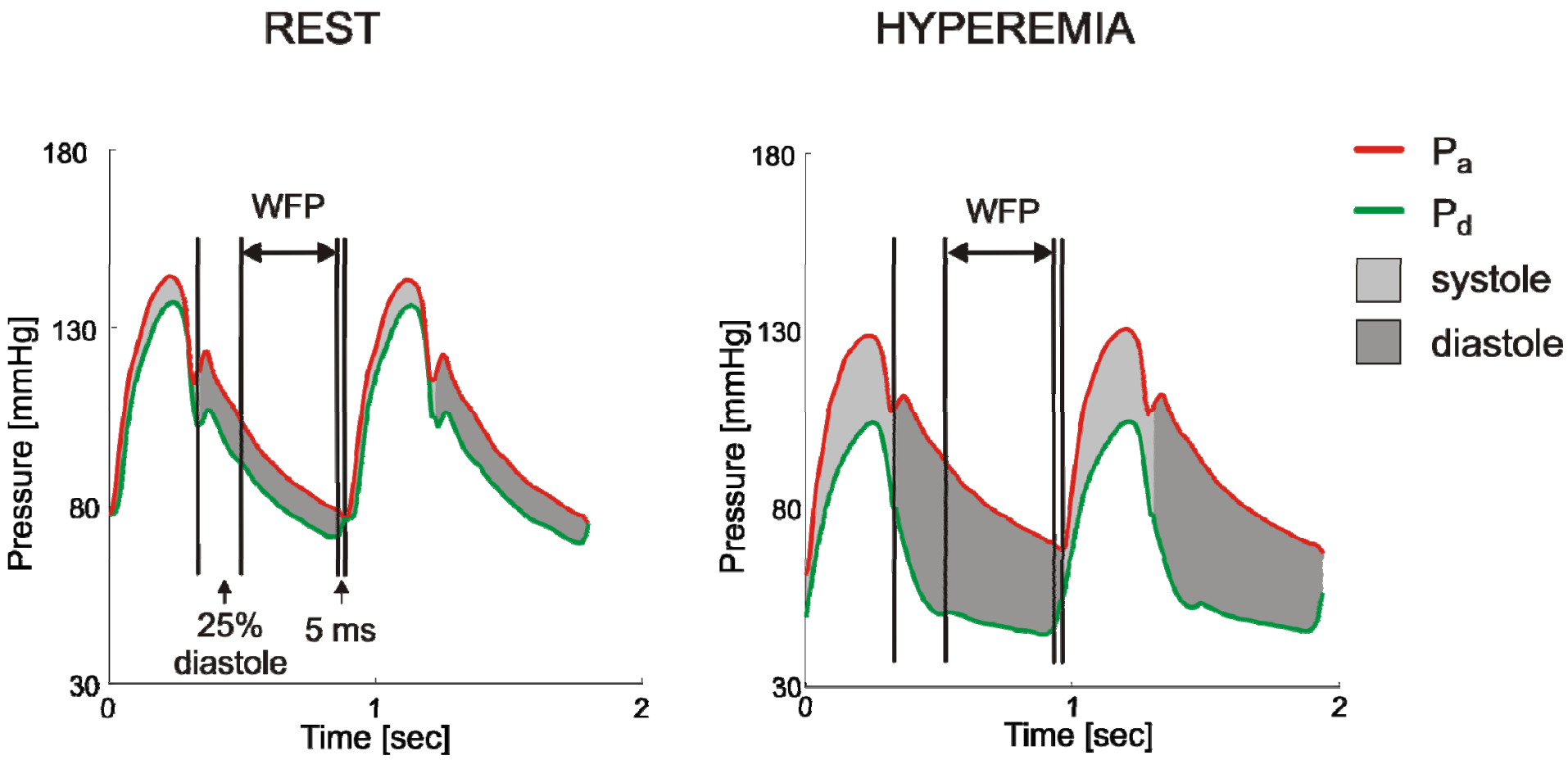
- average (resting) Pd/Pa ratio during that period (approximately 75 % of diastole) is called ***iFR*** *(Sen et al, JACC 2011)*

But at a closer look:

- complex theoretical background without relation to the way iFR is actually calculated *(nothing "instantaneously")*

- no experimental validation

- strongly influenced by hyperemia, *not "hyperemia-free", and poor correlation to FFR* in clinically relevant range (0.6 – 0.9)

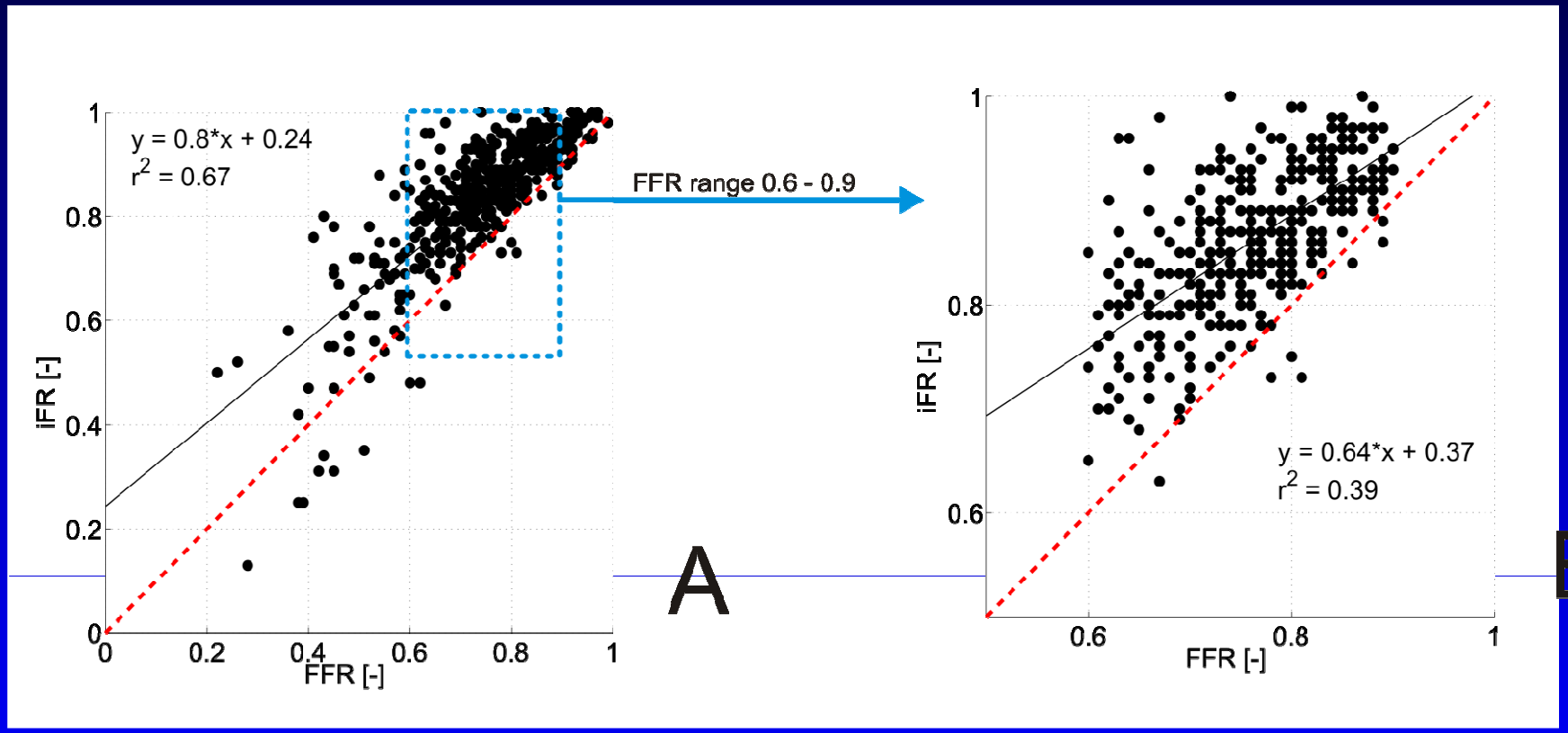


iFR = Pd / Pa at rest during WFP *(Sen et al)*

Claimed to be independent of hyperemia

Retrospective analysis IFR versus FFR

in last 500 patients in Aalst and Eindhoven (per dec 2011)



all data: $R^2 = 0.67$
diagn accuracy = 66 %

FFR range 0.6-0.9: $R^2 = 0.39$
diagn accuracy = 59 %

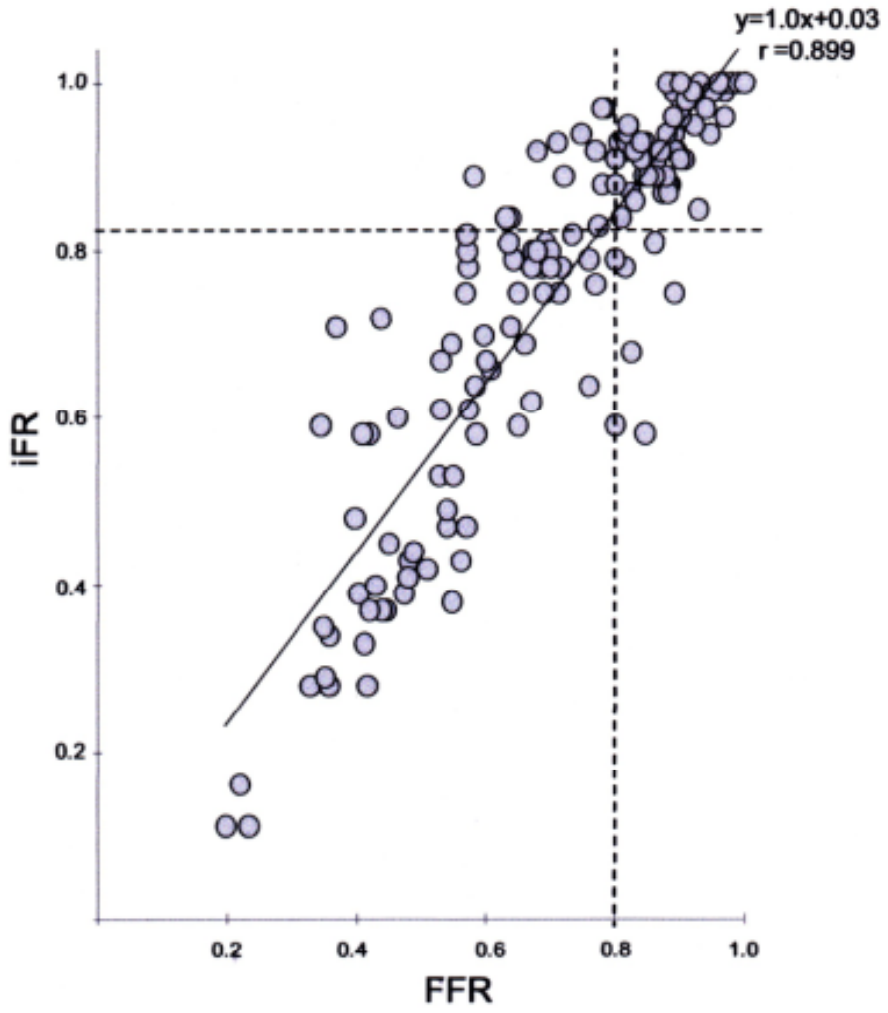
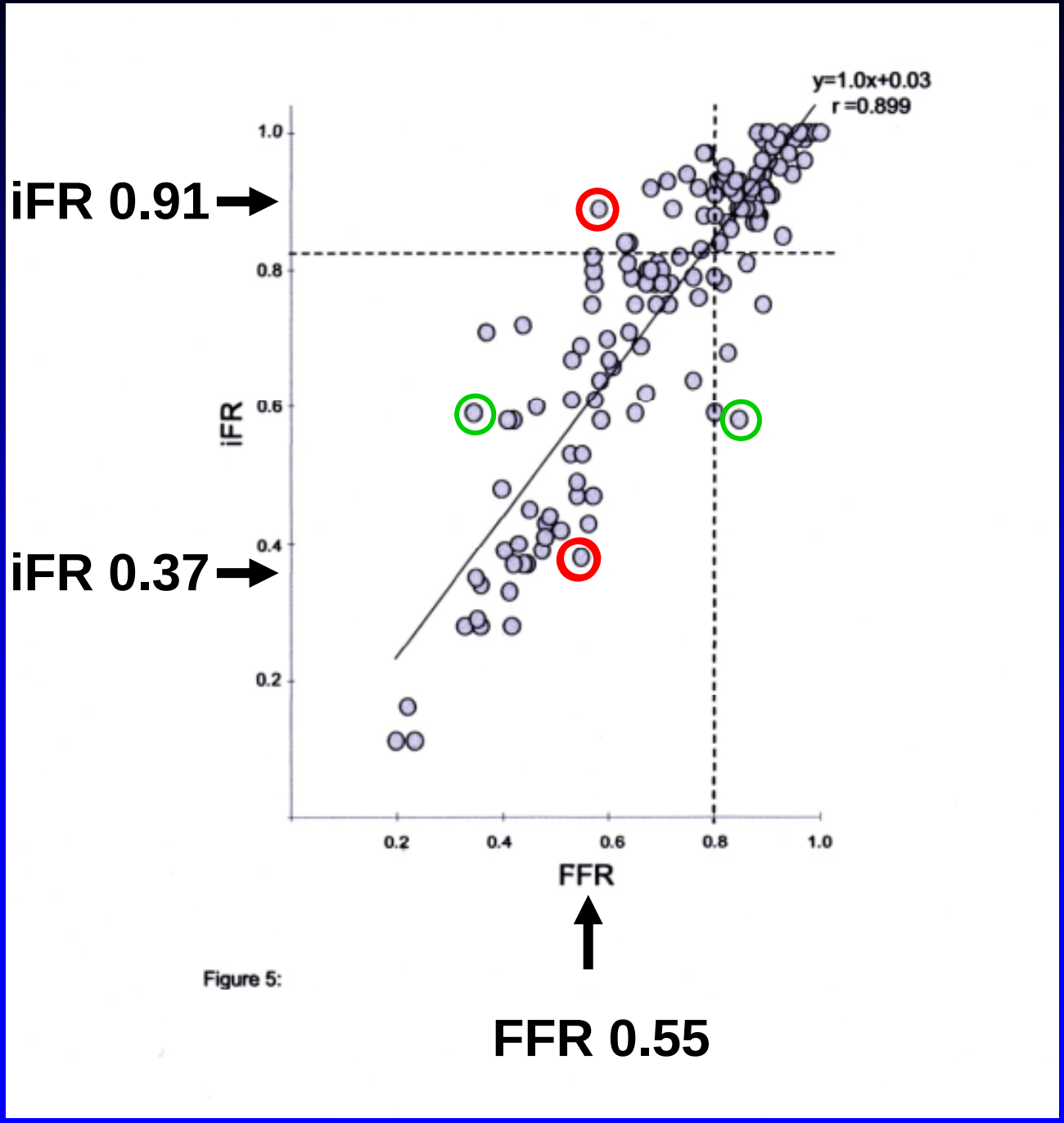


Figure 5:

ADVISE STUDY (N= 131)

From:
Sen, Davies, et al
JACC 2011



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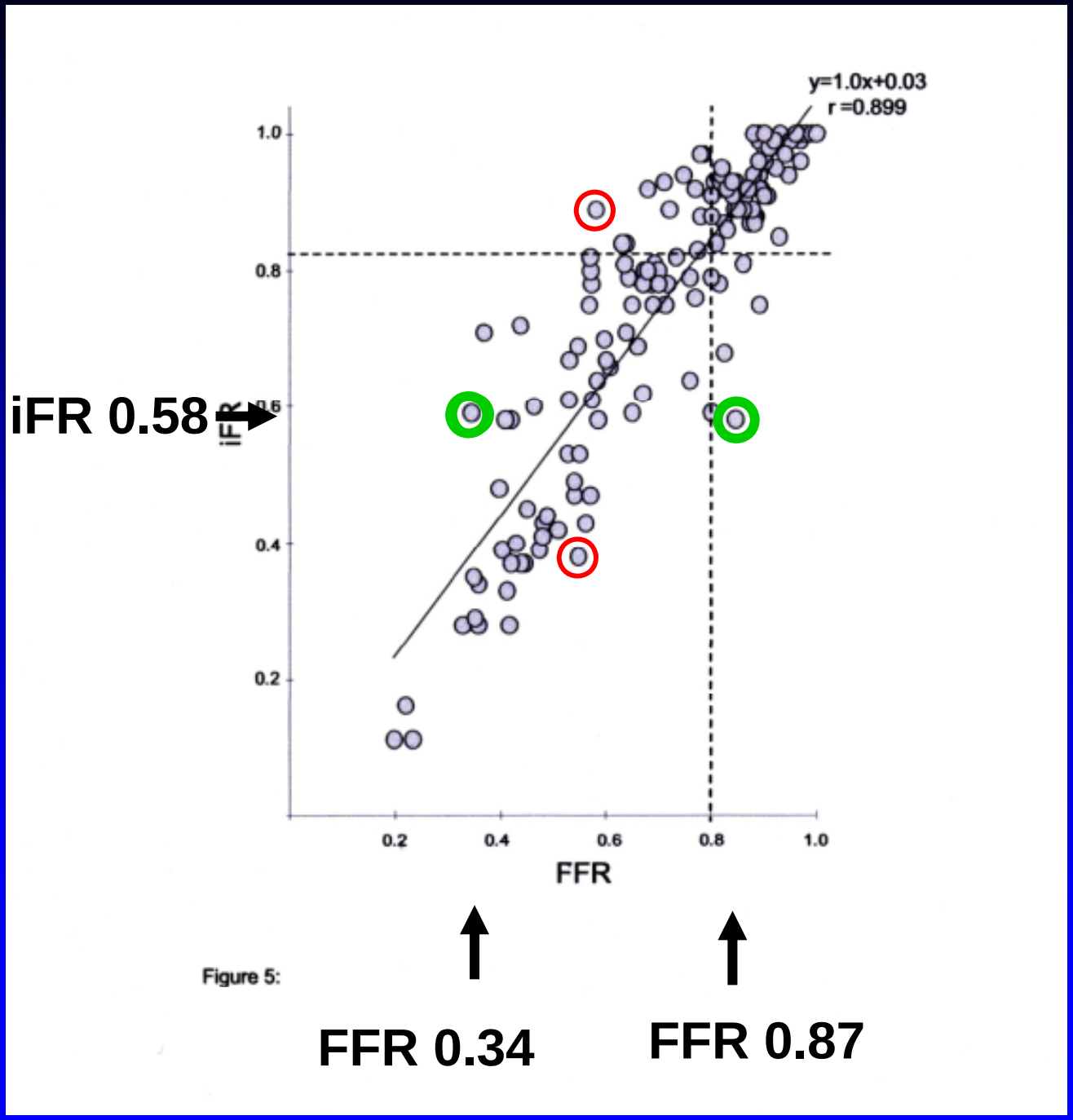

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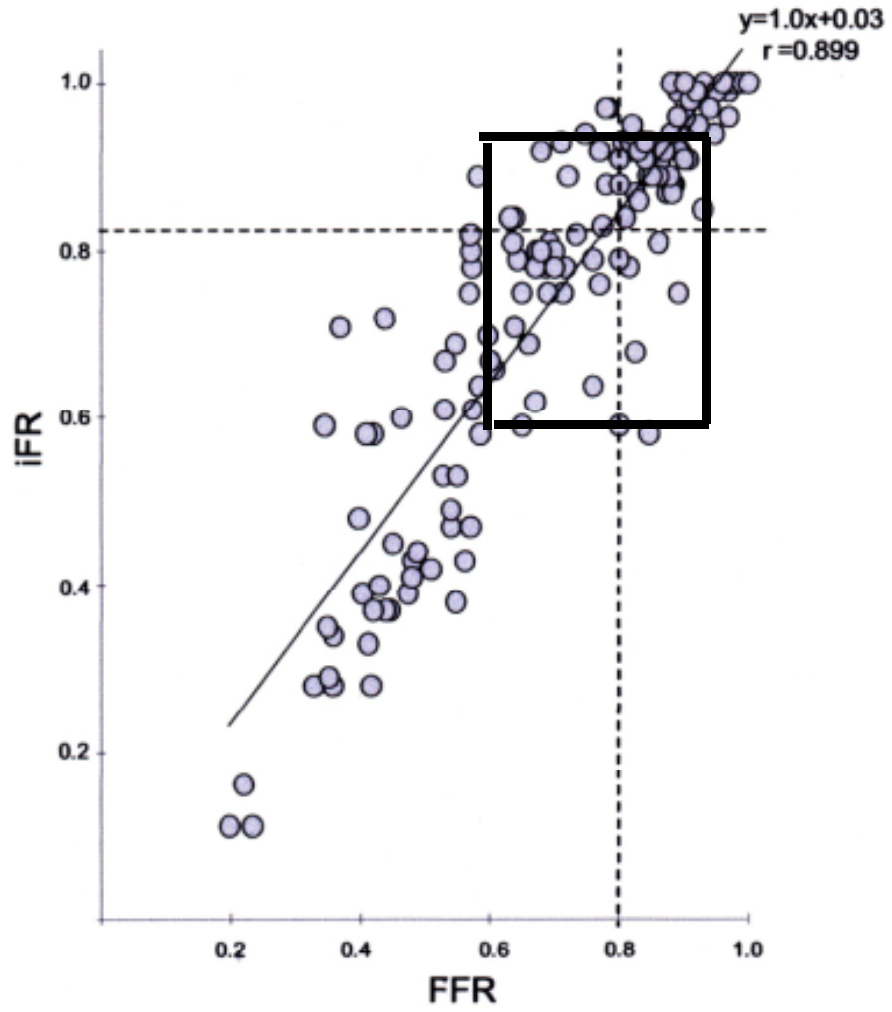


Figure 5:

Clinically relevant range 0.6 – 0.9
almost random distribution

limited accuracy in clinically relevant range

From:
Sen, Davies, et al
JACC 2011

IMPORTANT NOTE:

- in a ***normal*** coronary artery, there is ***no pressure gradient*** and therefore all pressure-derived indexes are equal

- in a ***very tight stenosis***, coronary ***flow reserve is exhausted*** and maximum arteriolar vasodilation (~ maximum hyperemia) is present by itself.
  So, also then all pressure derived indexes are equal by definition

- but in the ***clinically relevant range of stenoses***, where ambiguity is present about the need for revascularization, resting and hyperemic pressures may be greatly different and ***resting indexes are not able to predict true stenosis severity***

VERIFY STUDY

- prospective study of ***FFR and iFR*** in ***ALL 206 consecutive stable patients*** refered for coronary angiography +/- PCI during 5 weeks (jan 4th-feb 10th 2012) in 5 European Centers (Glasgow, Aalst, Eindhoven, Stockholm, Brno)

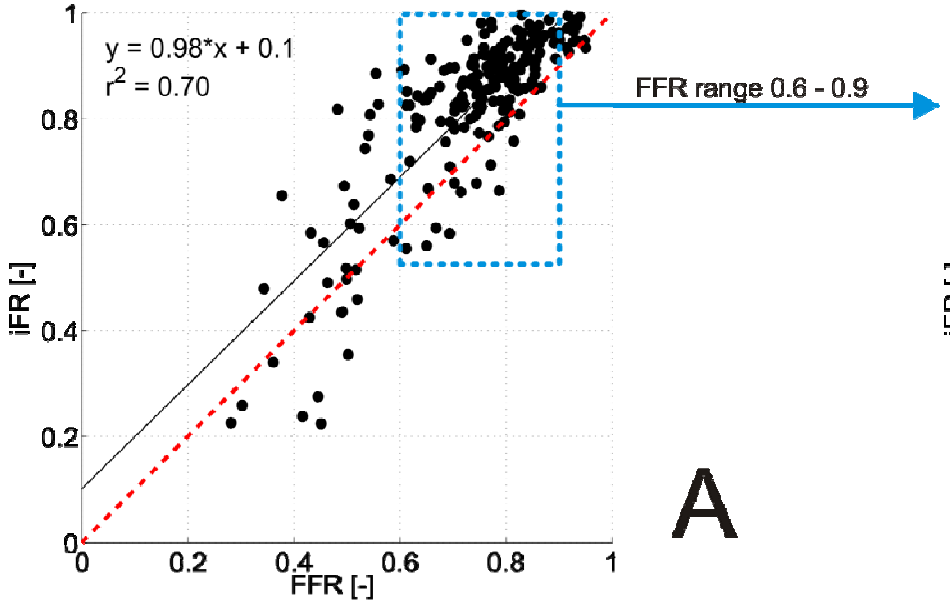
- meticulous measurements at rest and during adenosine-induced hyperemia, ***in –duplo*** : *rest → hyper → rest → hyper*

- ***iFR*** calculated as average Pd / Pa ratio during “wave-free” period *at rest*, according to Sen/Davies, *but also at hyperemia* to test its “freedom of adenosine”

- ***FFR*** calculated as usual by Pd / Pa at maximum hyperemia

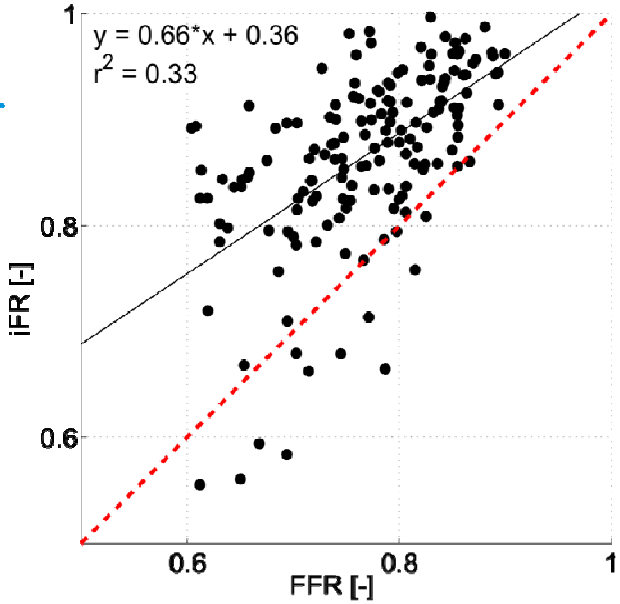
- all analysis in fully automated matter without manual selection in independent core lab and independent statistical analysis

Correlation between iFR and FFR (N=206)



FFR range 0.6 - 0.9

A



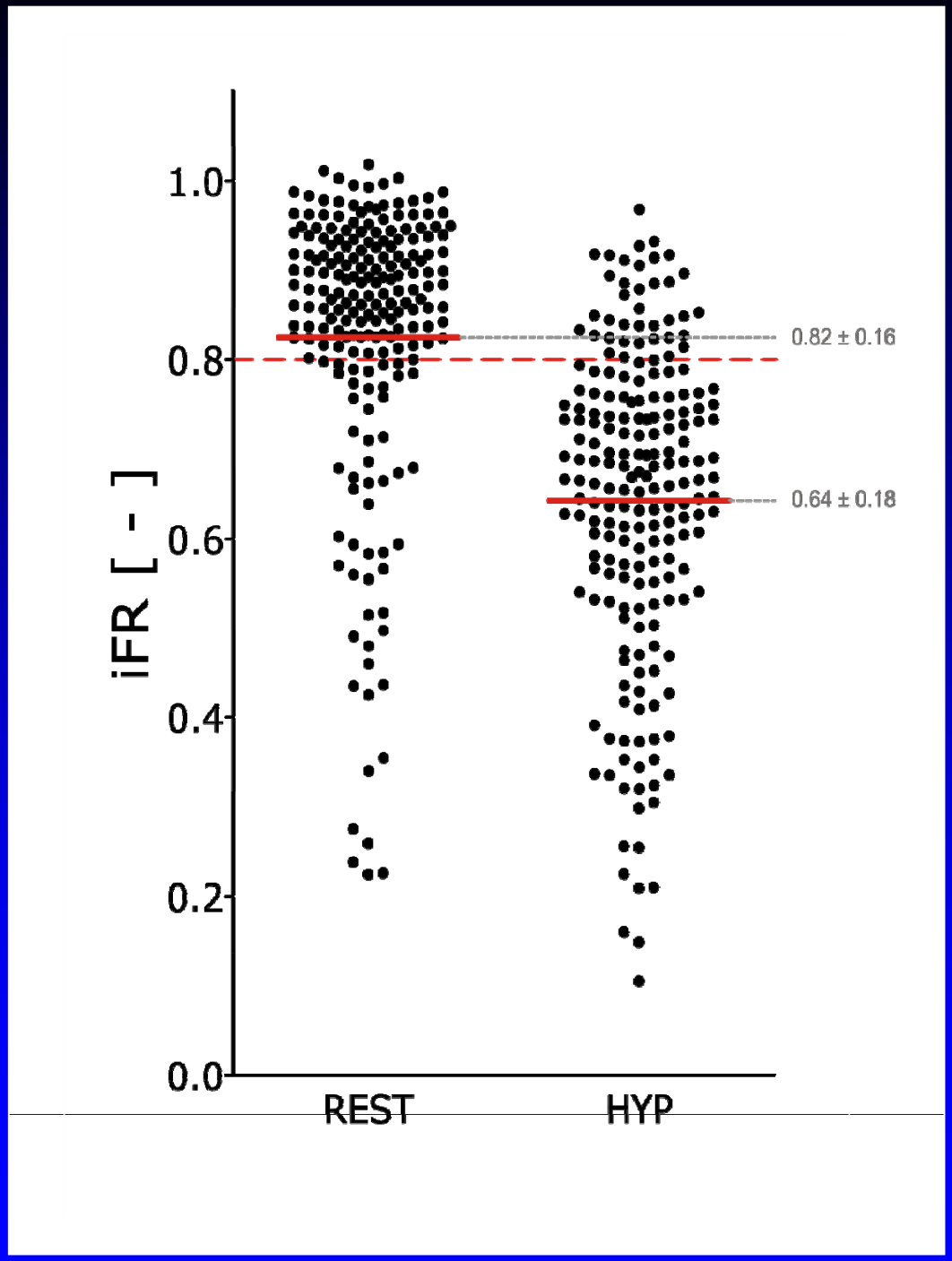
B

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 %)

Is iFR “hyperemia – free”, as claimed ??



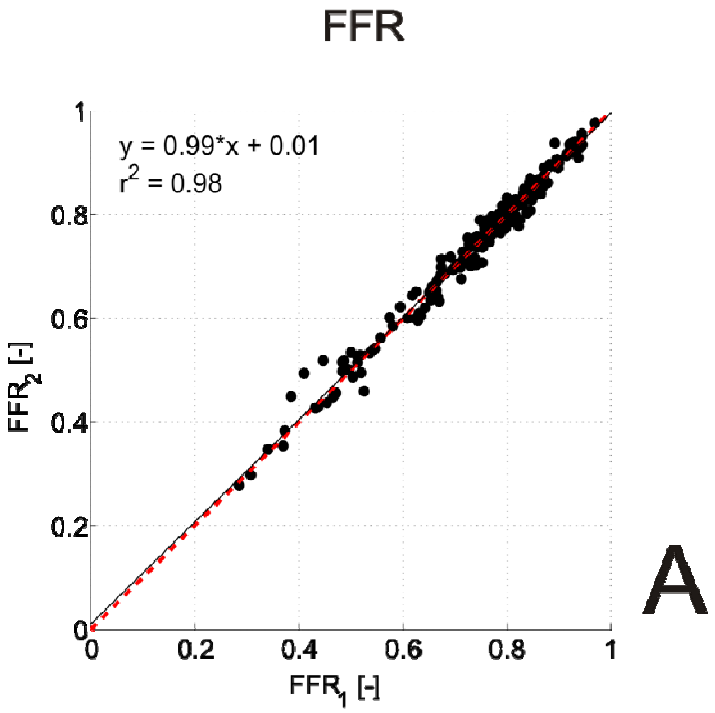
profound influence of hyperemia on iFR:

"iFRhyp" *was already called diastolic FFR by Abe et al in Circulation, 1996)*

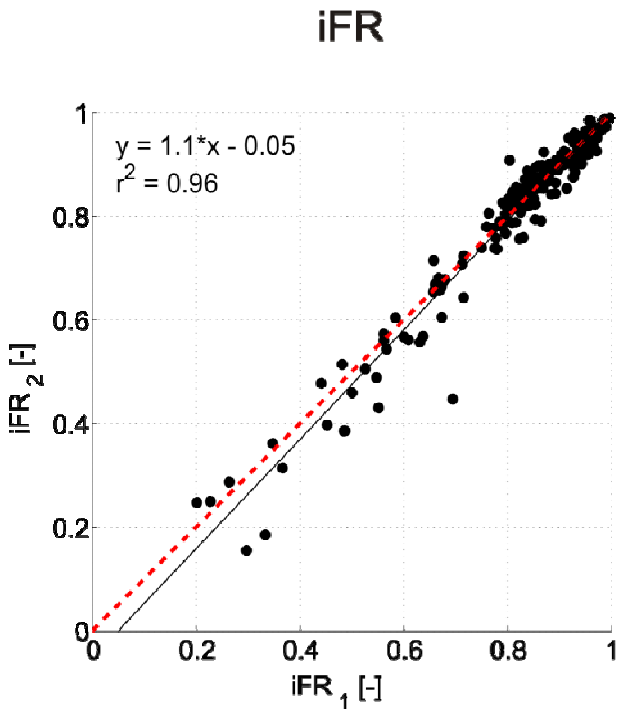
estimated decrease of resistance during "wave-free period"

$$\frac{(1.0 - 0.64)}{(1.0 - 0.82)} = 200\ \%$$

Reproducibilty of FFR and iFR



A



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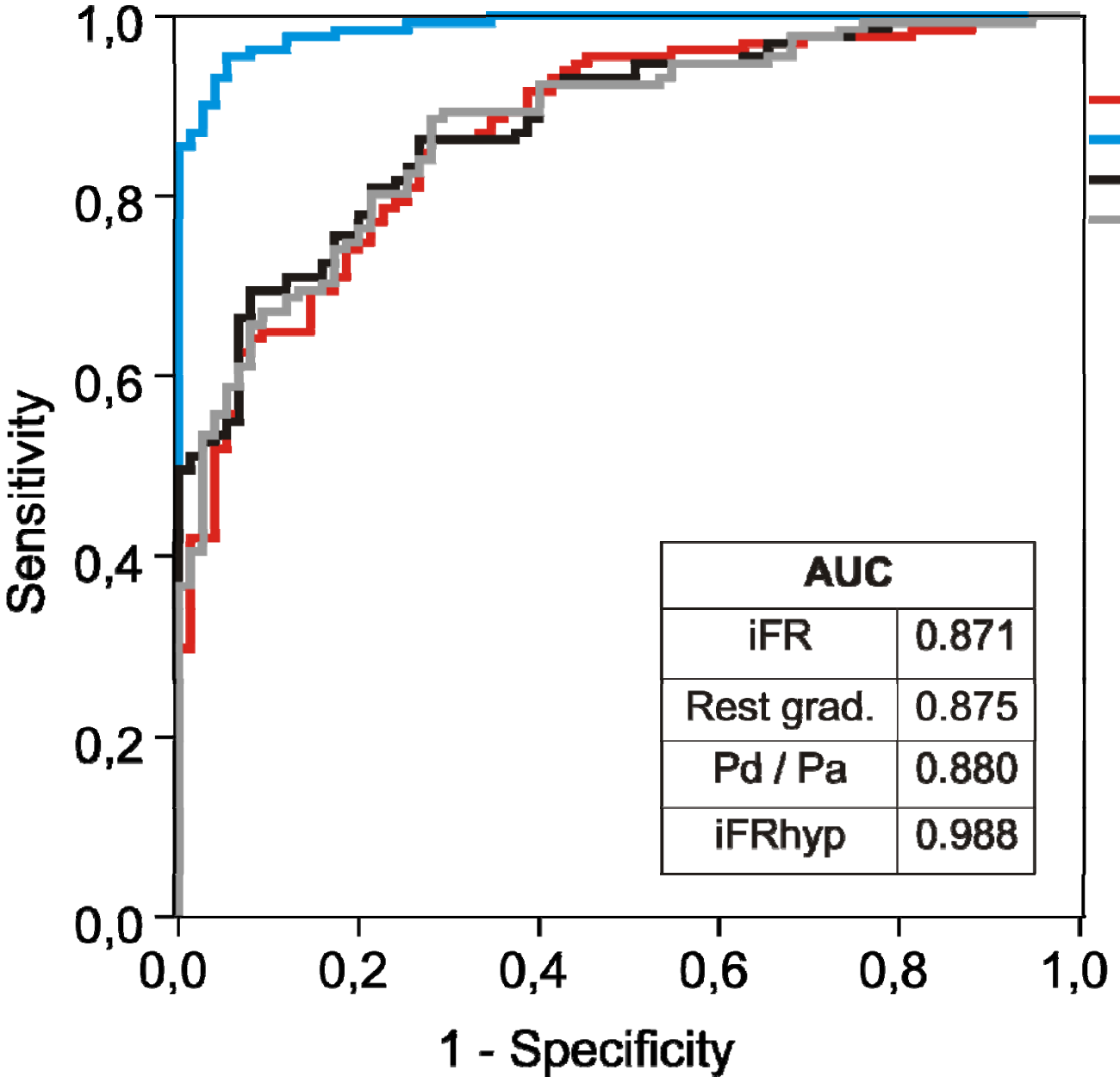
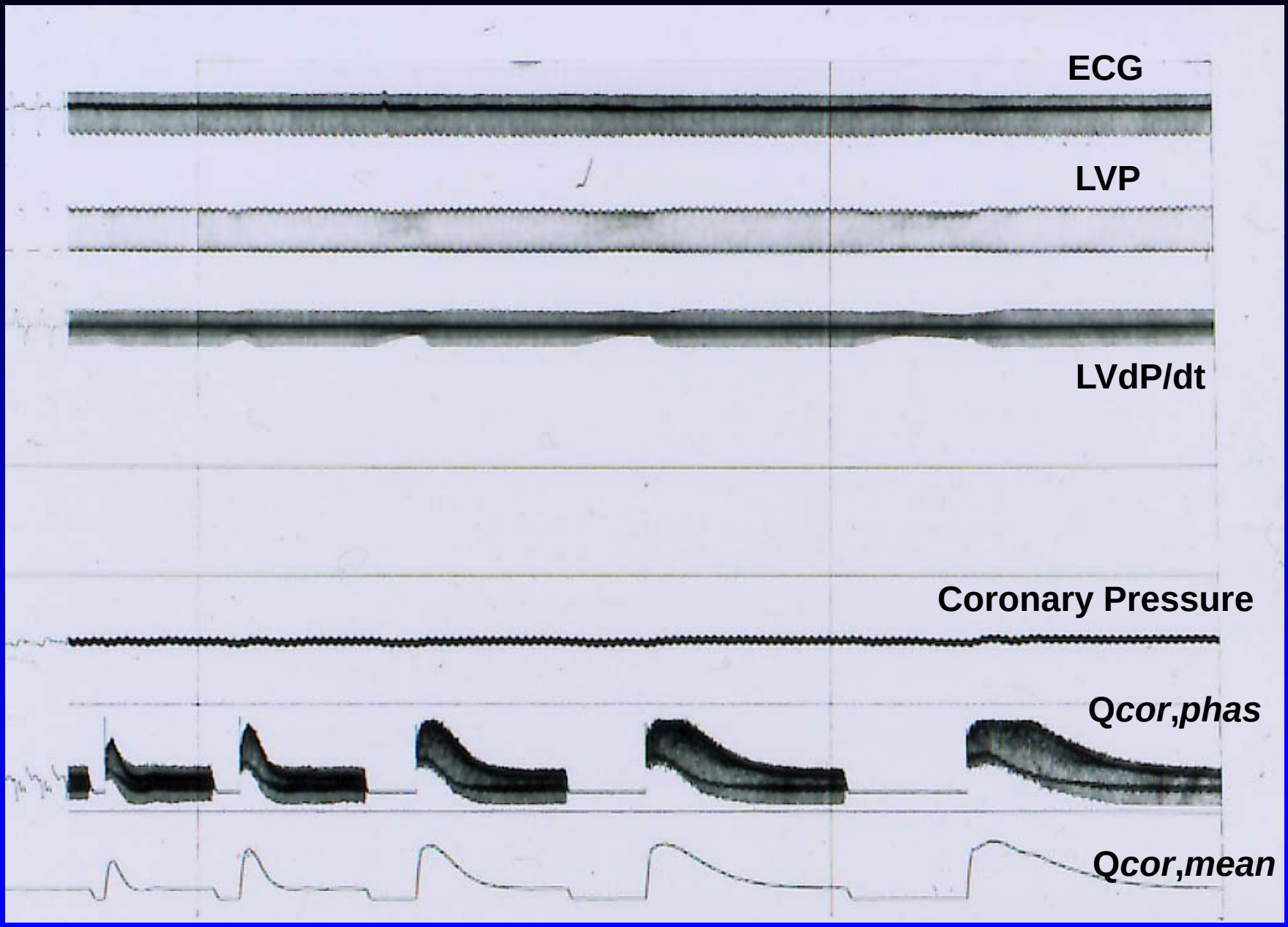


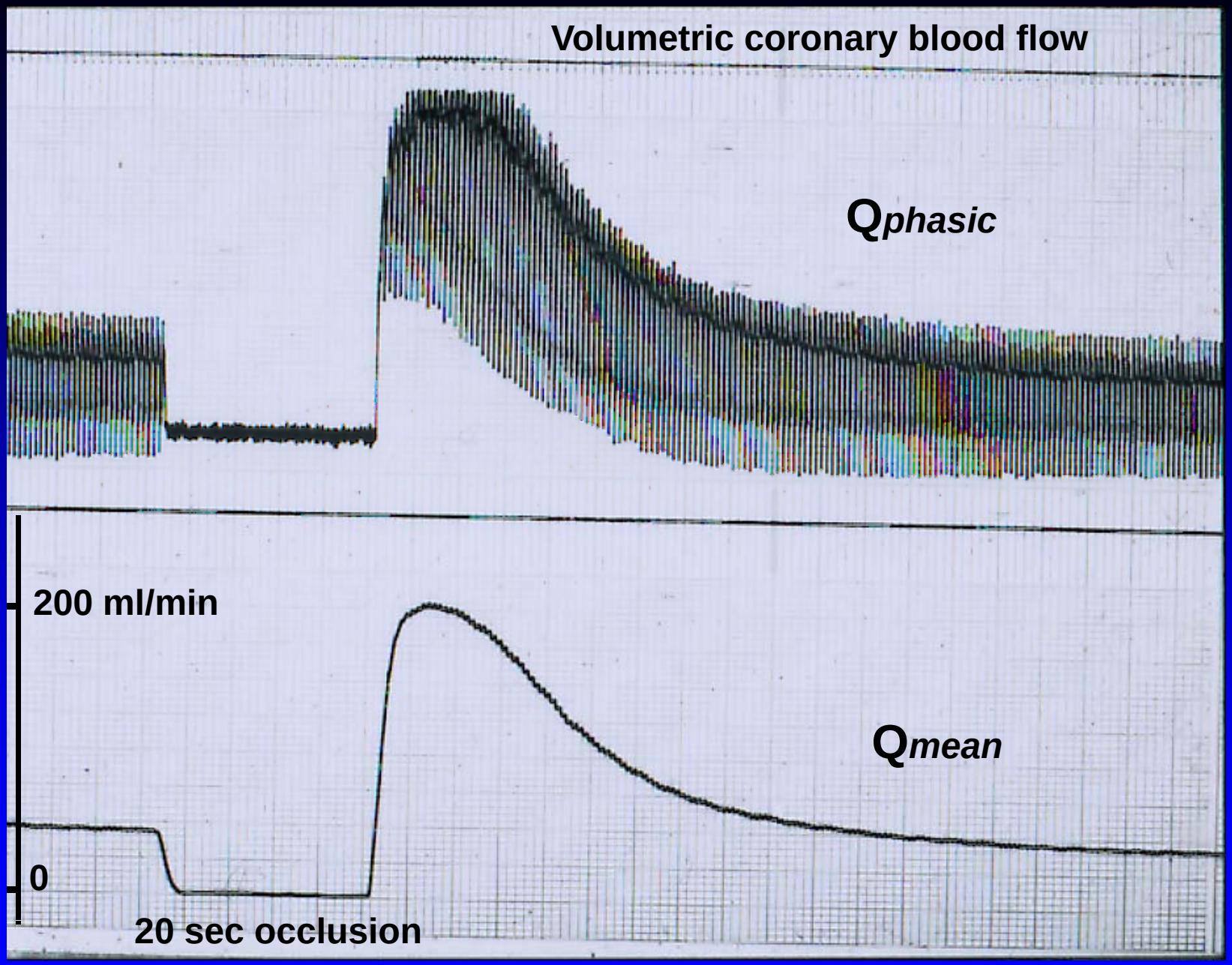
AUC	
iFR	0.871
Rest grad.	0.875
Pd / Pa	0.880
iFRhyp	0.988

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

Are these disappointing results for iFR surprising ?



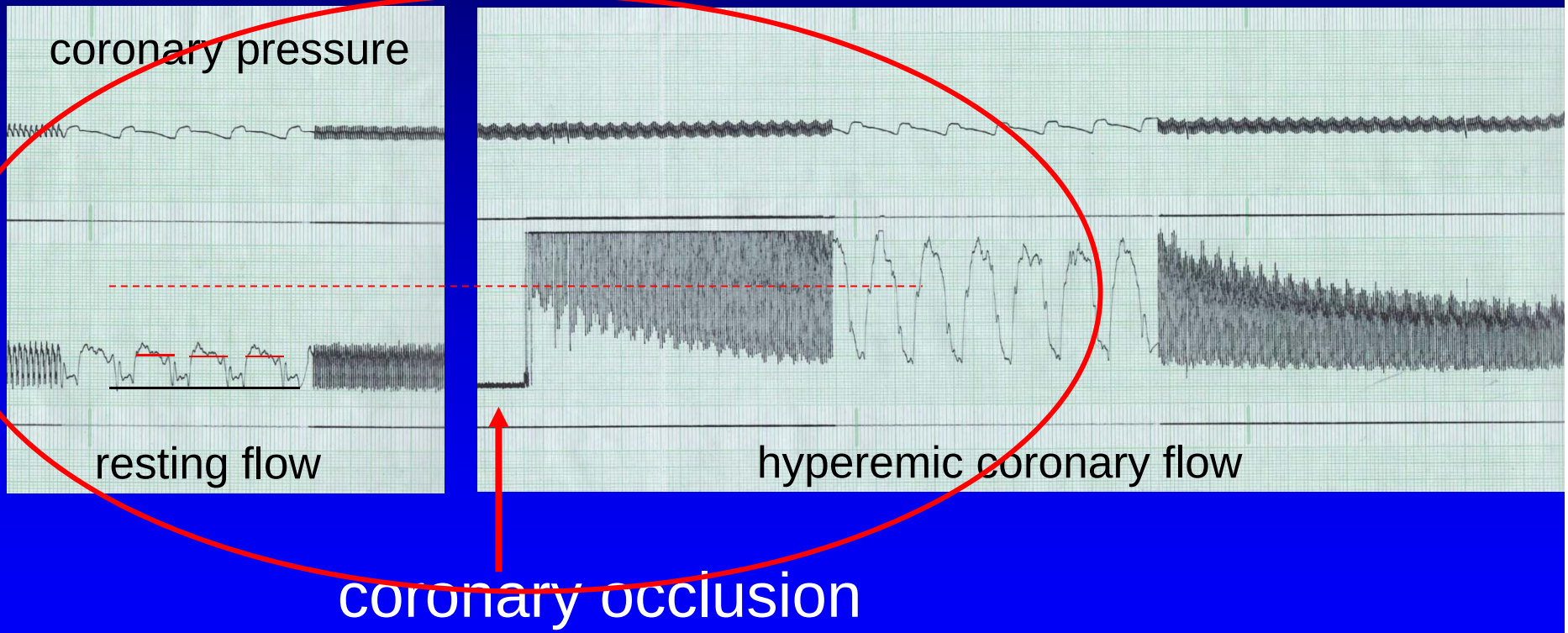
14 cc/hond: 5-10-20-30-60 sec occl



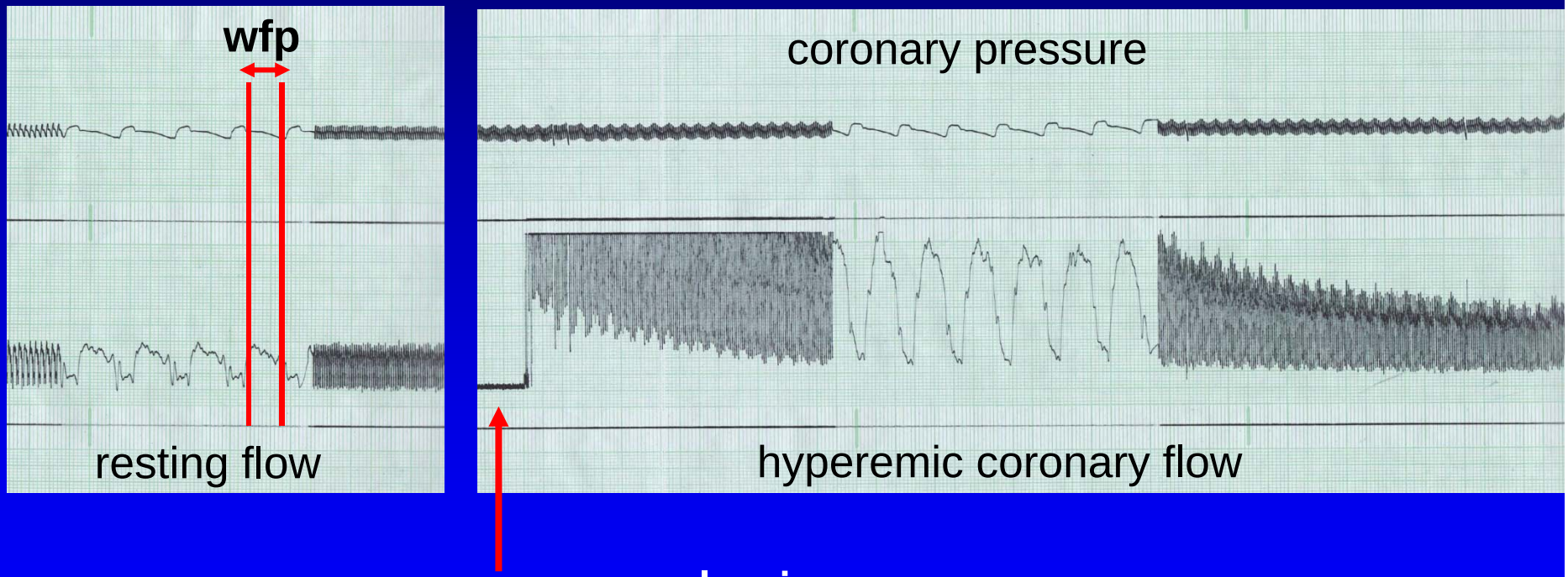
12 cc/hond: 20 sec occl (1)

In the presence of constant coronary pressure

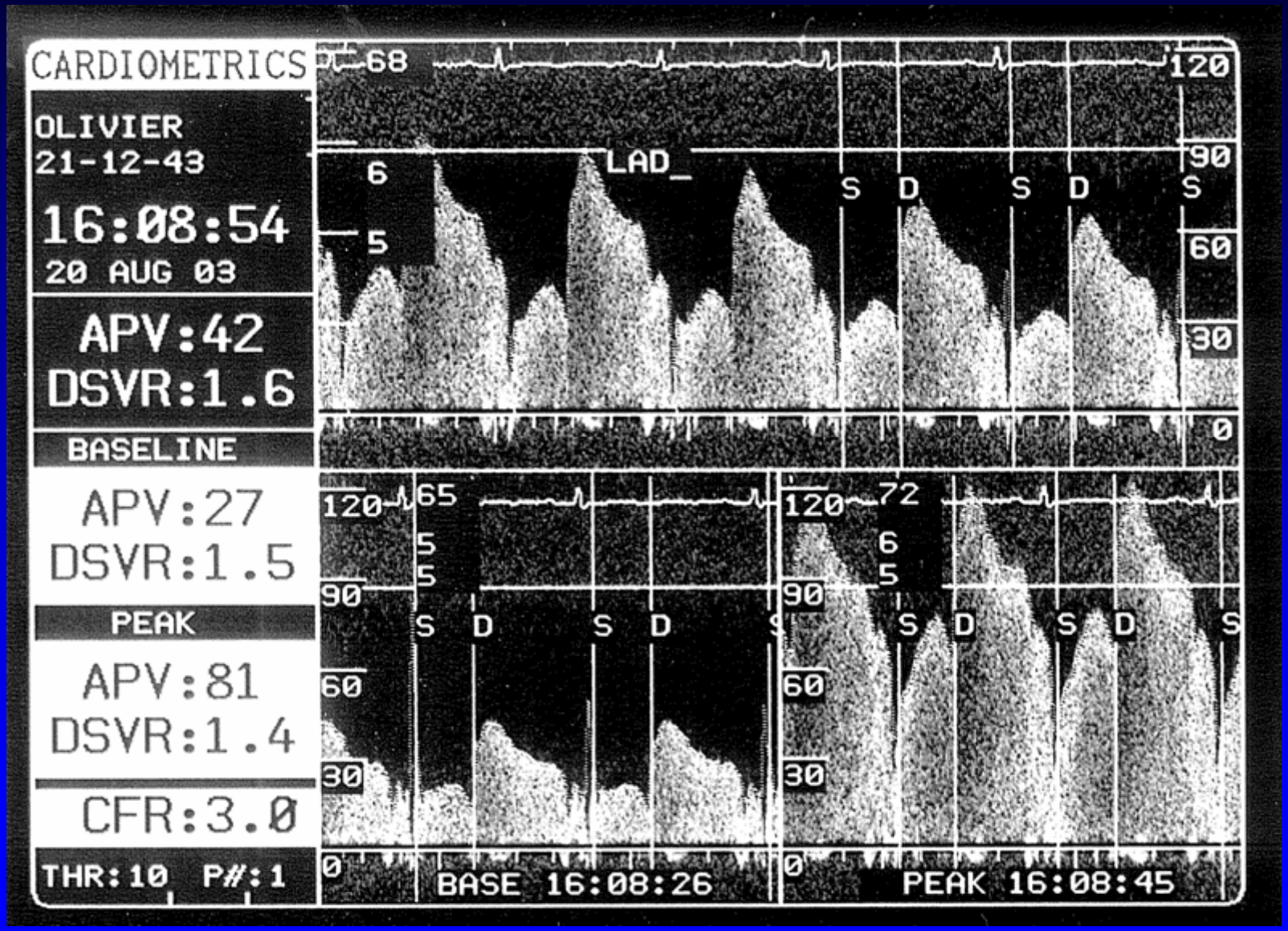
⟶ R ~ 1 / Flow



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



Doppler flow velocity recording in a human coronary artery

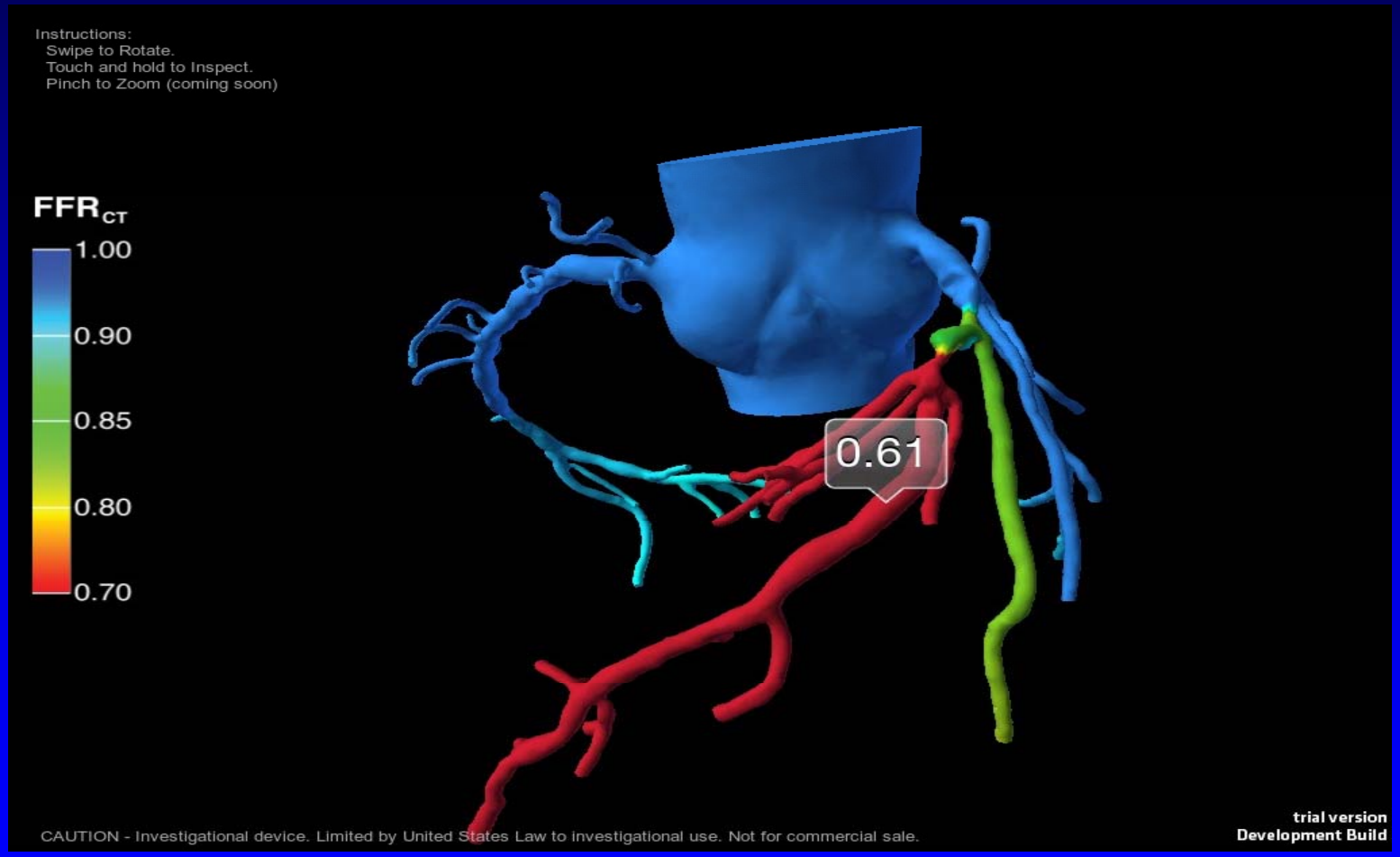


resting **hyperemia (adenosine)**

iFR : Summary from VERIFY study

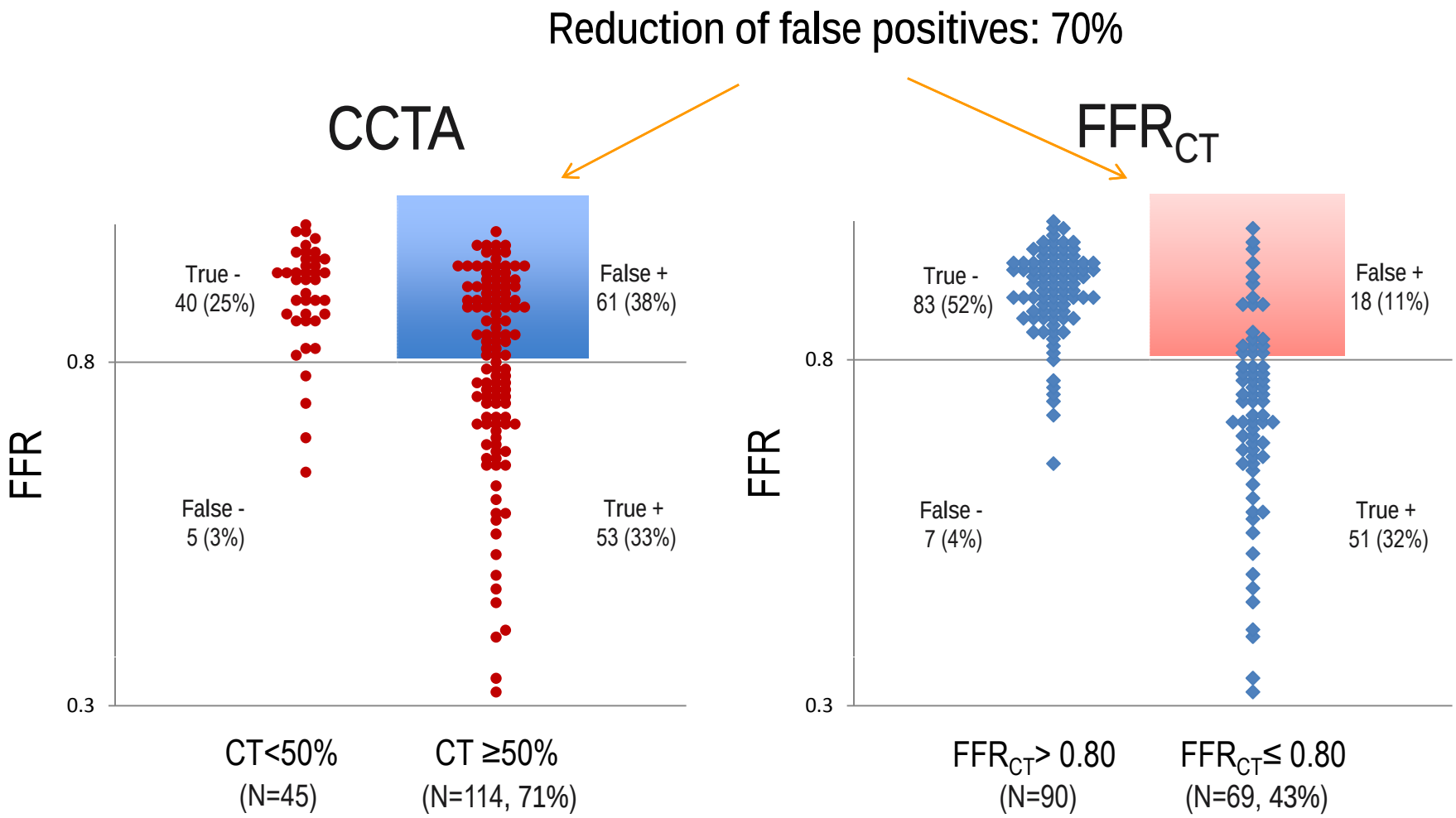
- not instantaneous, not hyperemia-free, just a ratio of mean pressures comparable to resting Pd/Pa
- complex theoretical dogma without relation to the way it is actually calculated in clinical practice
- no experimental validation neither independent clinical validation
- in contrast to what is claimed: strongly influenced by hyperemia
- poor performance and accuracy, not better than resting Pd/Pa and hardly better than flipping a coin
- step back in time: “guessing” instead of “certainty”

FFR_{CT} :


Instructions:
Swipe to Rotate.
Touch and hold to Inspect.
Pinch to Zoom (coming soon)
FFRCT
1.00
0.90
0.85
0.80
0.70
0.61
CAUTION - Investigational device. Limited by United States Law to investigational use. Not for commercial sale.
trial version
Development Build

Regular CCTA has a very high sensitivity (~95%)
but its specificity is too poor (~30-40%) to be advocated
for screening in “normal”populations

DISCOVER-FLOW – Reclassification of CCTA data (Koo et al, N= 159)



Source: Koo et al. J Am Coll Cardiol 2011

FFR_{CT}

IF these data can be confirmed in a large RCT, screening in larger populations might become attractive:

Moderately elevated or high calciumscores with clearly decreased FFR, can get invasive evaluation then anyway (most likely with invasive measurement of FFR for decision with respect to revascularization)

Moderately elevated or high calciumscores but favourable FFR_{CT} (> 0.85 ?? , > 0.90 ???) could be safely treated by medical therapy

Large prospective study mandatory to support this standpoint

REGADENOSON ***(RAPISCAN R)***

- *new hyperemic stimulus*, to be admistered as single bolus of 5cc (400 ug) in either central or peripheral vein

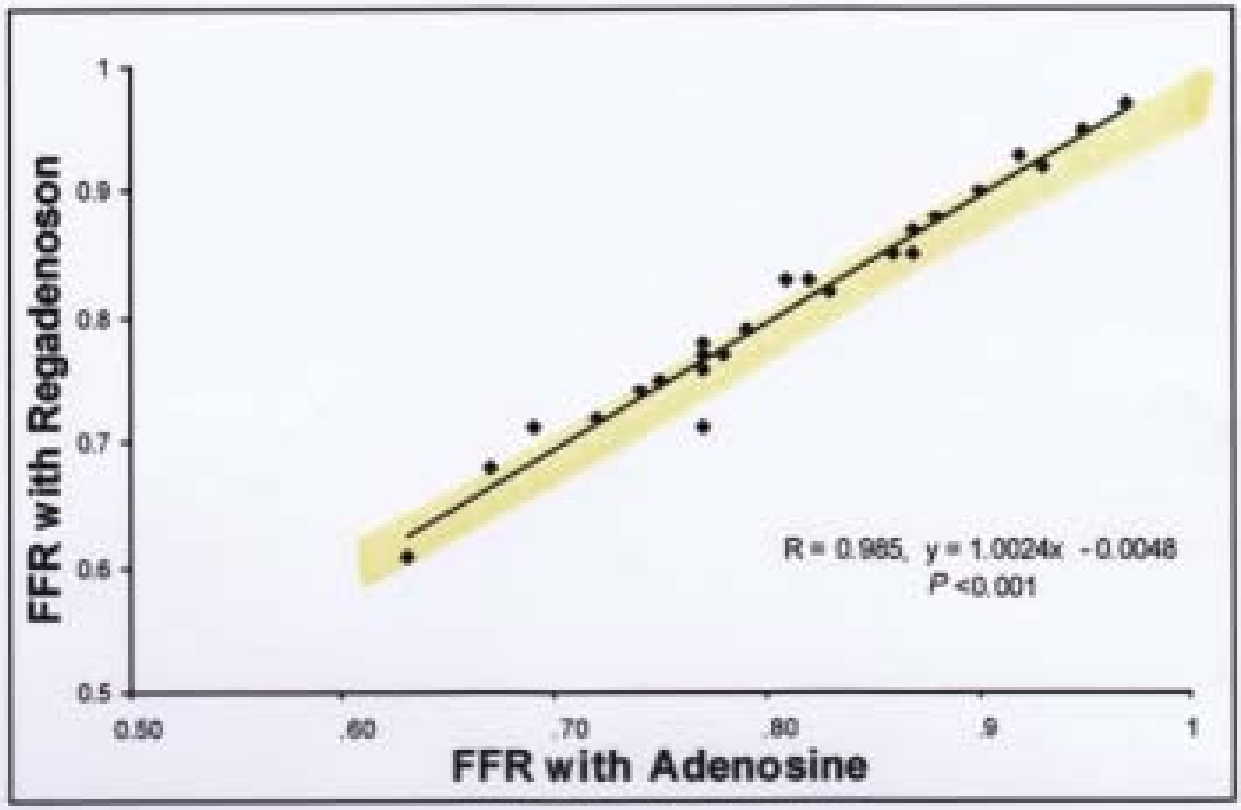
- maximum hyperemia, identical to central venous adenosine, within 1 minute and lasting for 1-7 minutes (*variable*)

- sufficiently long hyperemia for *pressure pullback recording*

- we use it in our lab for simple procedures and in radial access. In complex cases, we do femoral approach with central intravenous adenosine

FIGURES

Figure 1. Linear regression analysis of intra-patient fractional flow reserve (FFR) measured with an intravenous (IV) adenosine infusion and IV regadenoson bolus.



Nair et al, JACC Interv 2011; 4:1085-1092

CONCLUSIONS

- *iFR is like a windtunnel without wind* or a step back in time: making a guess instead of getting certainty.
  patients are too precious to be subjected to that.

- *FFR_{CT} might improve the specificity of CT-angio* and therefore extend the use of CCTA to screening of larger populations. Threshold when to do additional invasive evaluation, needs to be determined

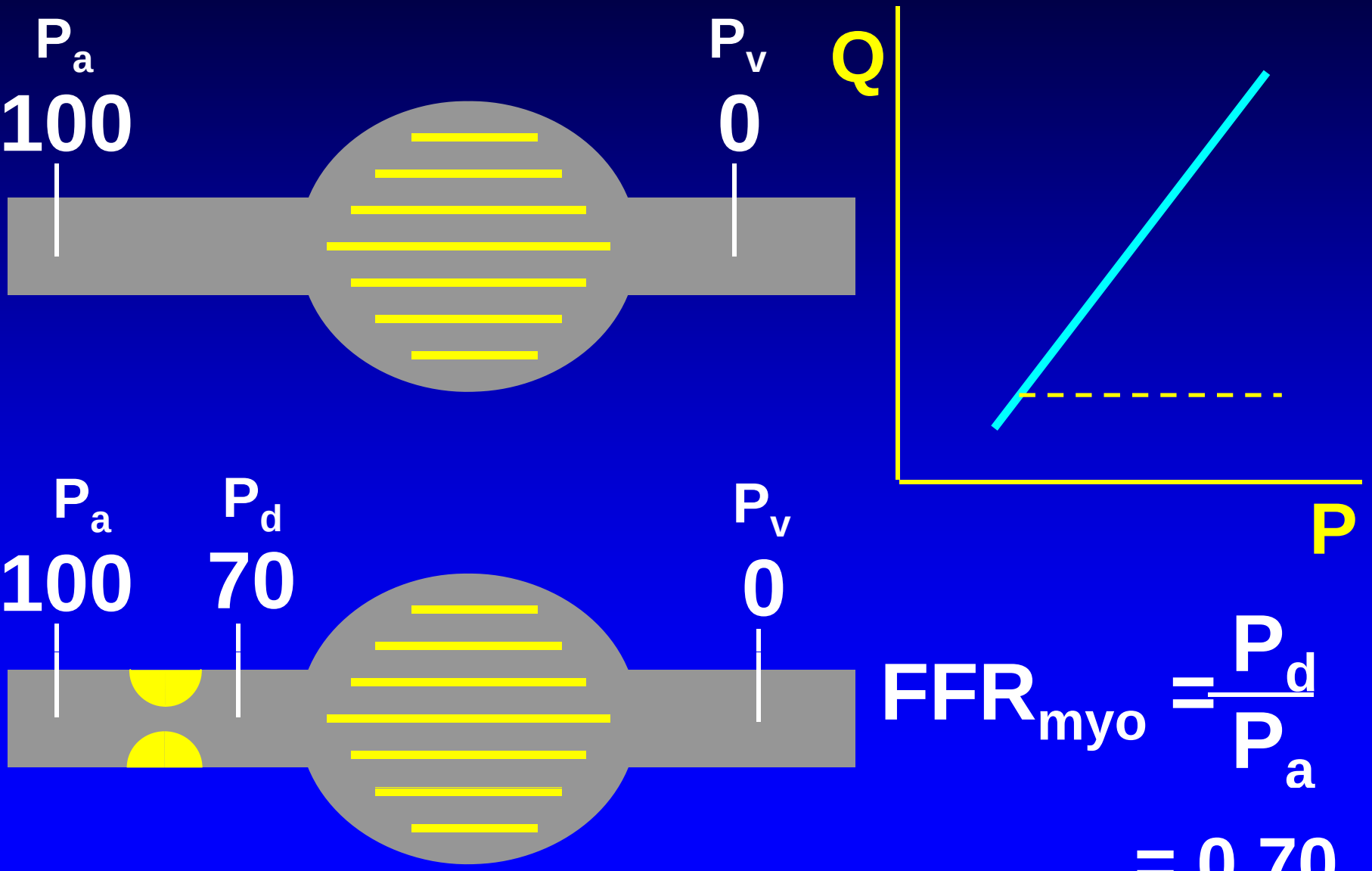
- *Regadenoson is a good alternative for i.v adenosine*, especially in simple cases and radial procedures. Generally it allows pressure pullback recordings but disadvantage is variable lenght of max hyperemia

Einde:

Of nog FFR CT en REG en abs flow

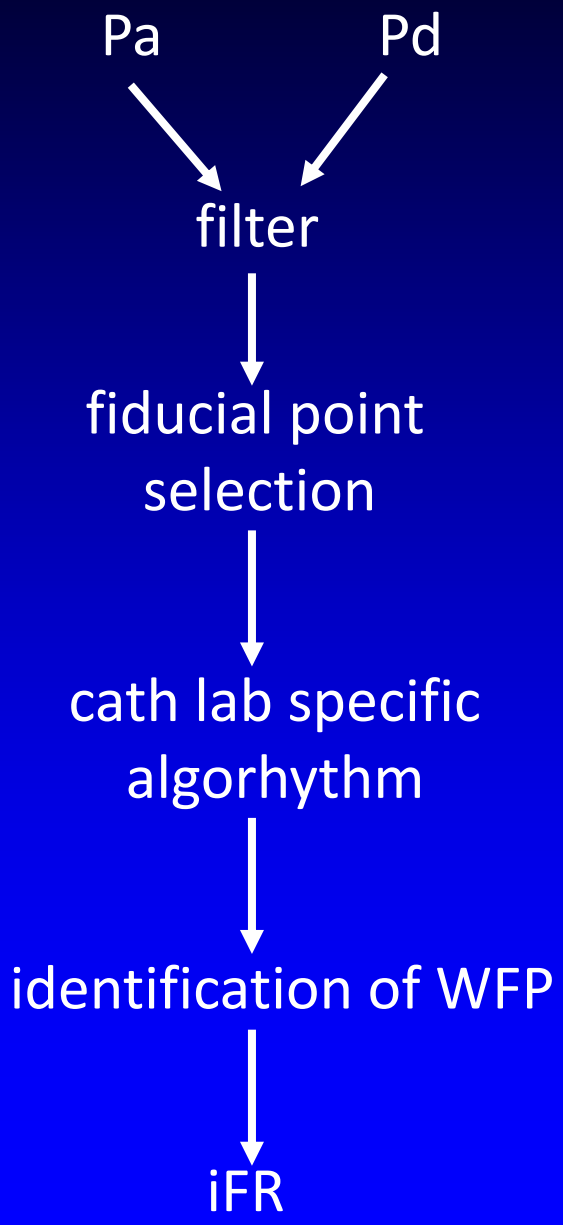
VERIFY STUDY

During Maximal Vasodilatation



$$FFR_{myo} = \frac{P_d}{P_a} = 0.70$$

Dr Davies' IFR Algorhythm:



What does this enigmatic algorhythm mean ???