Imaging & Physiology Summit

EXPERIMENTAL BASIS & CLINICAL VALIDATION OF FFR

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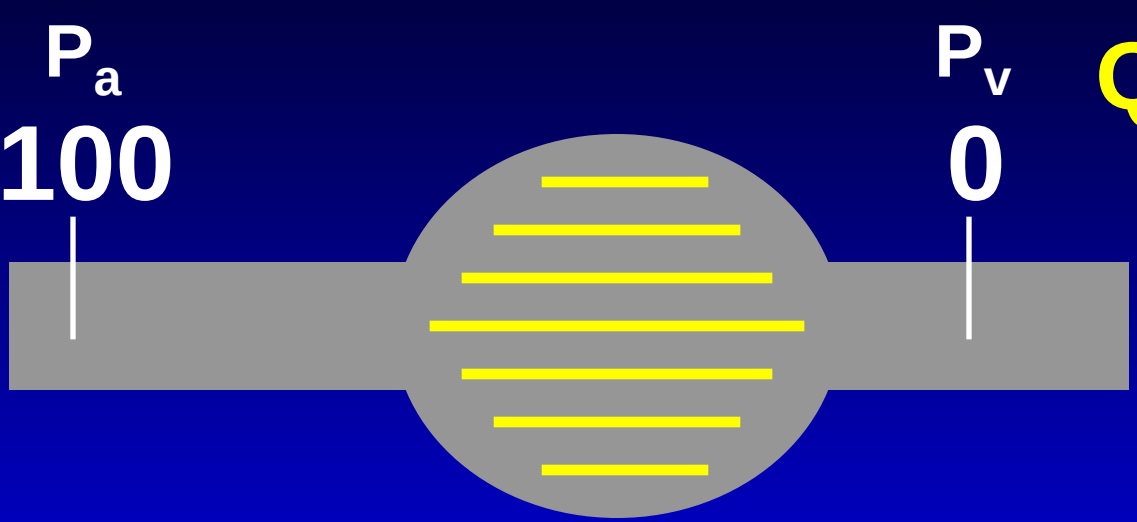
FRACTIONAL FLOW RESERVE:

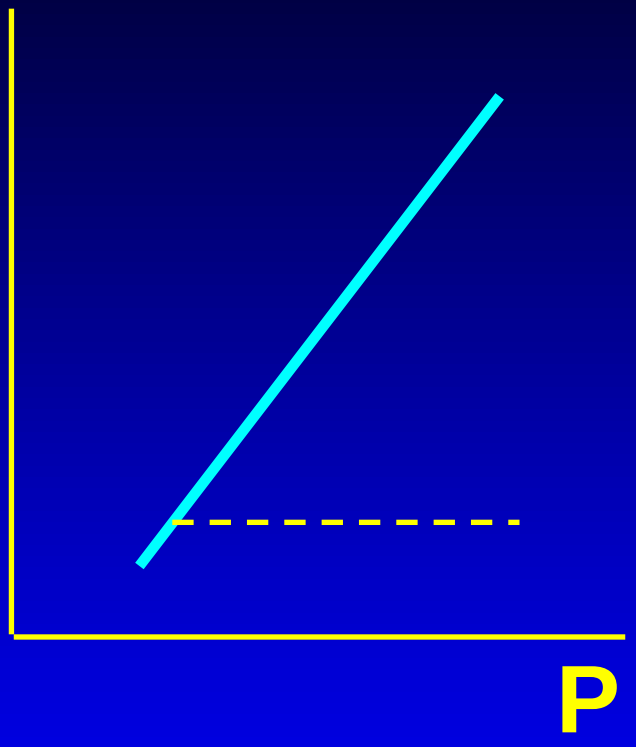
The index FFR (***Fractional Flow Reserve***)
is based upon the two following principles:

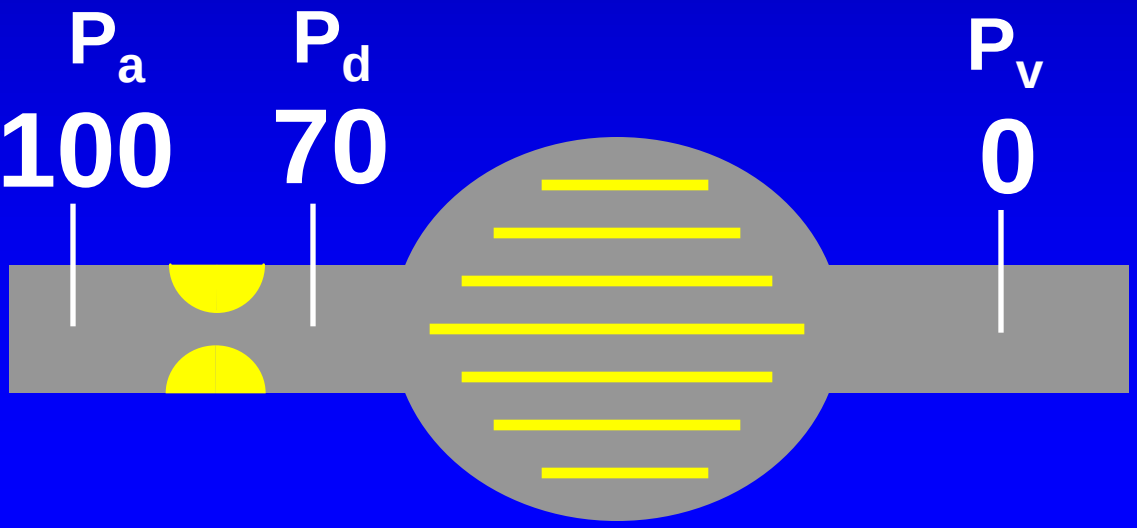
- *It is not resting flow, but **maximum achievable flow** which determines the functional capacity (exercise tolerance) of a patient*

- *At maximum vasodilation (corresponding with maximum hyperemia or with maximum exercise), blood flow to the myocardium is proportional to **myocardial perfusion pressure***
  *(**~hyperemic distal coronary pressure**)*

During Maximal Vasodilatation

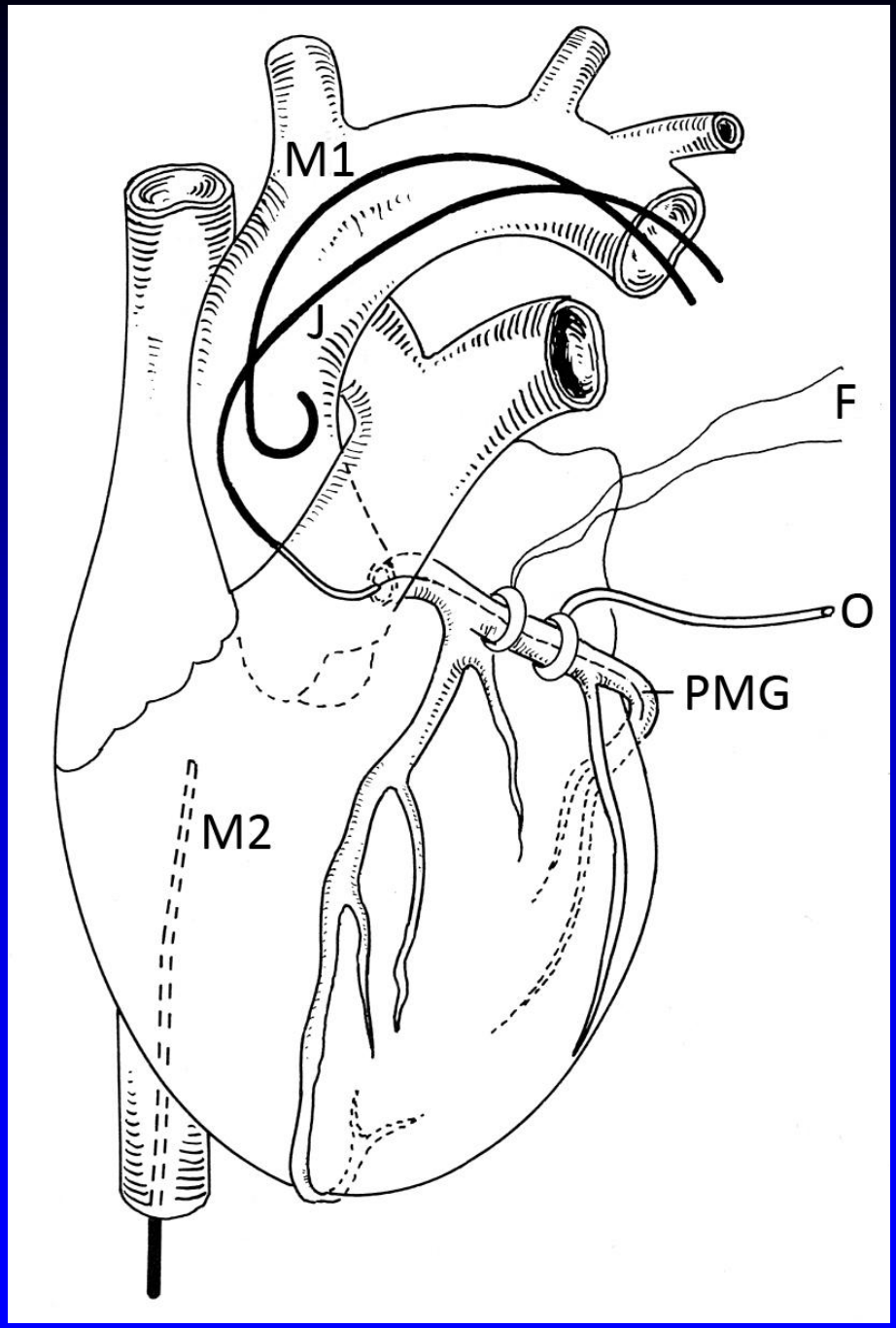




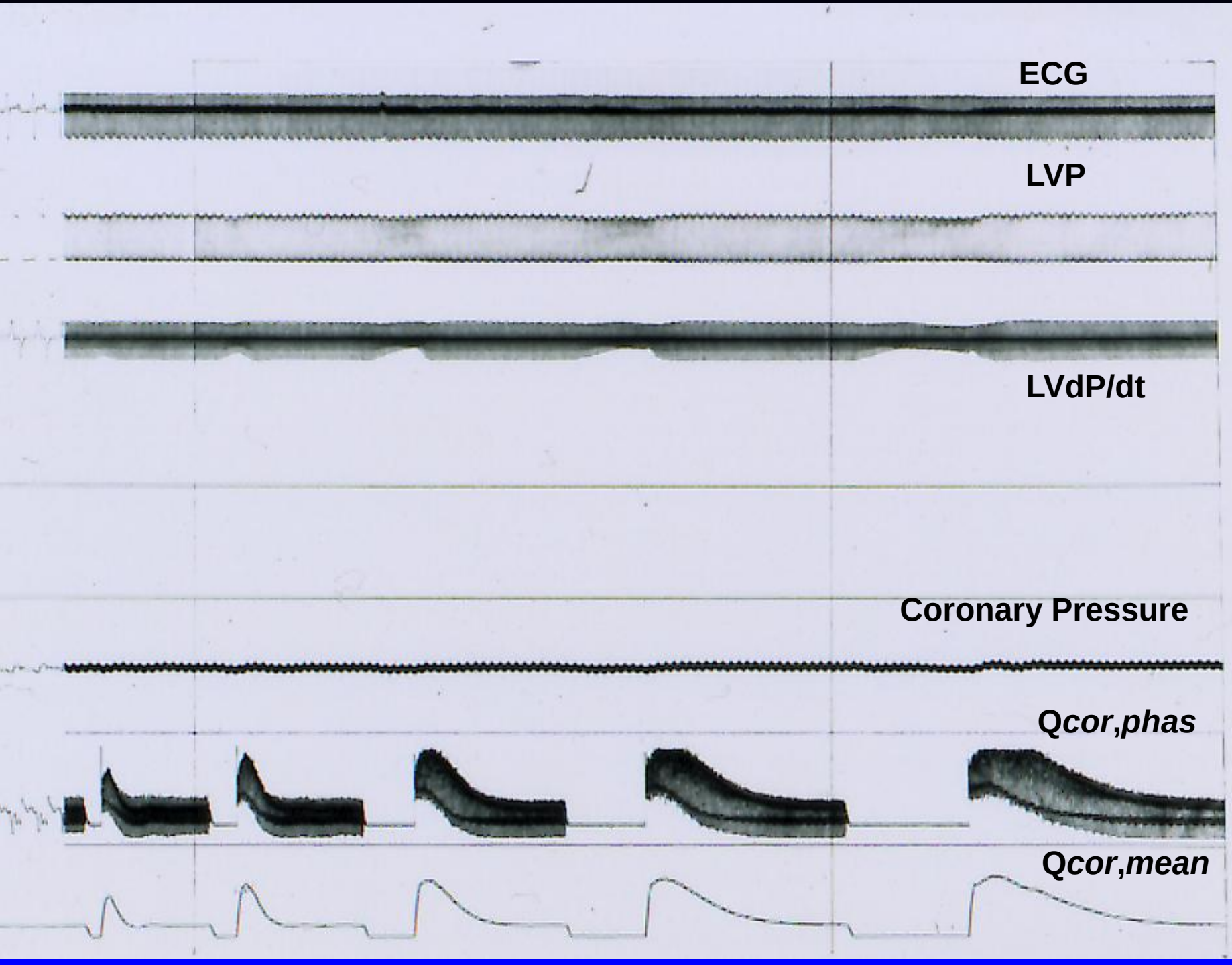


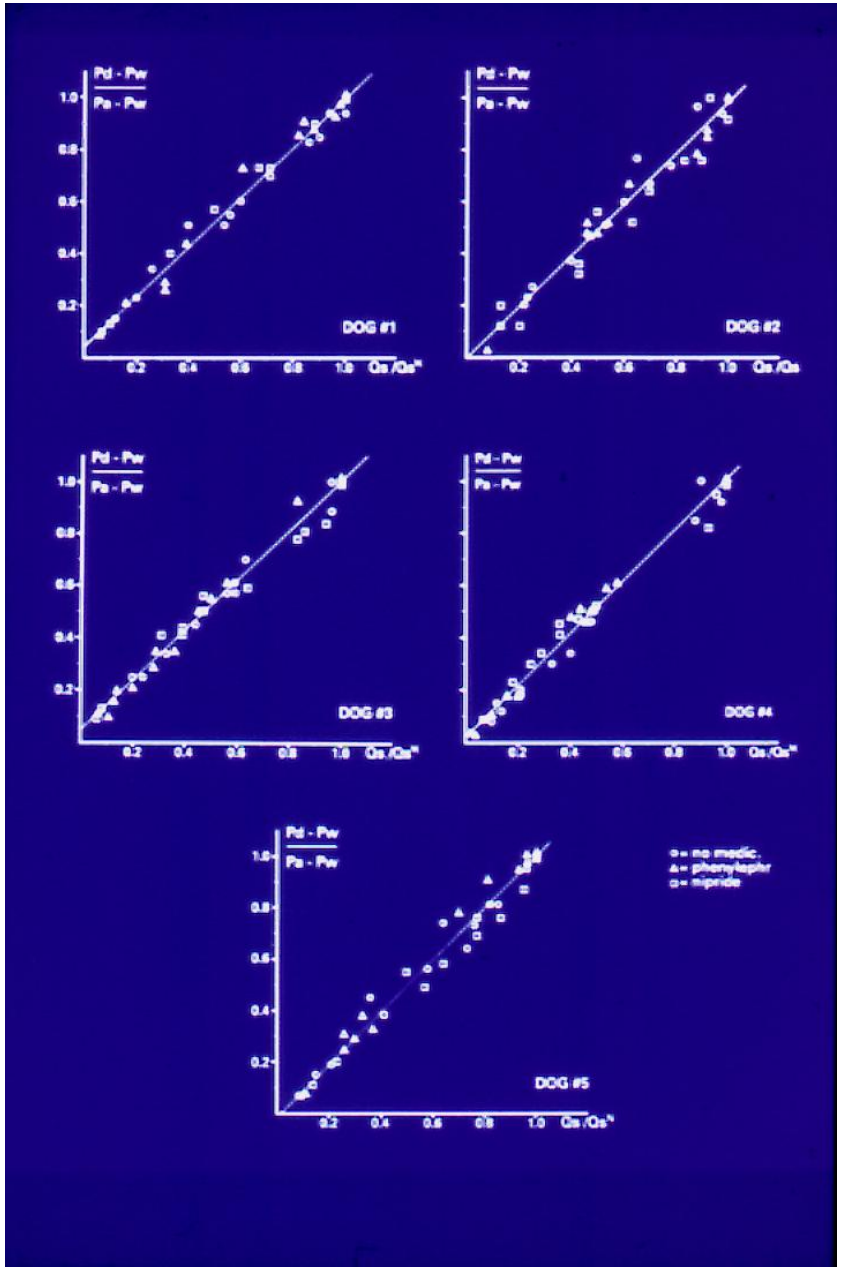
$$FFR_{myo} = \frac{P_d}{P_a}$$

$$= 0.70$$



FFR:
experimental validation in chronic dog studies


ECG
LVP
LVdP/dt
Coronary Pressure
Qcor,phas
Qcor,mean

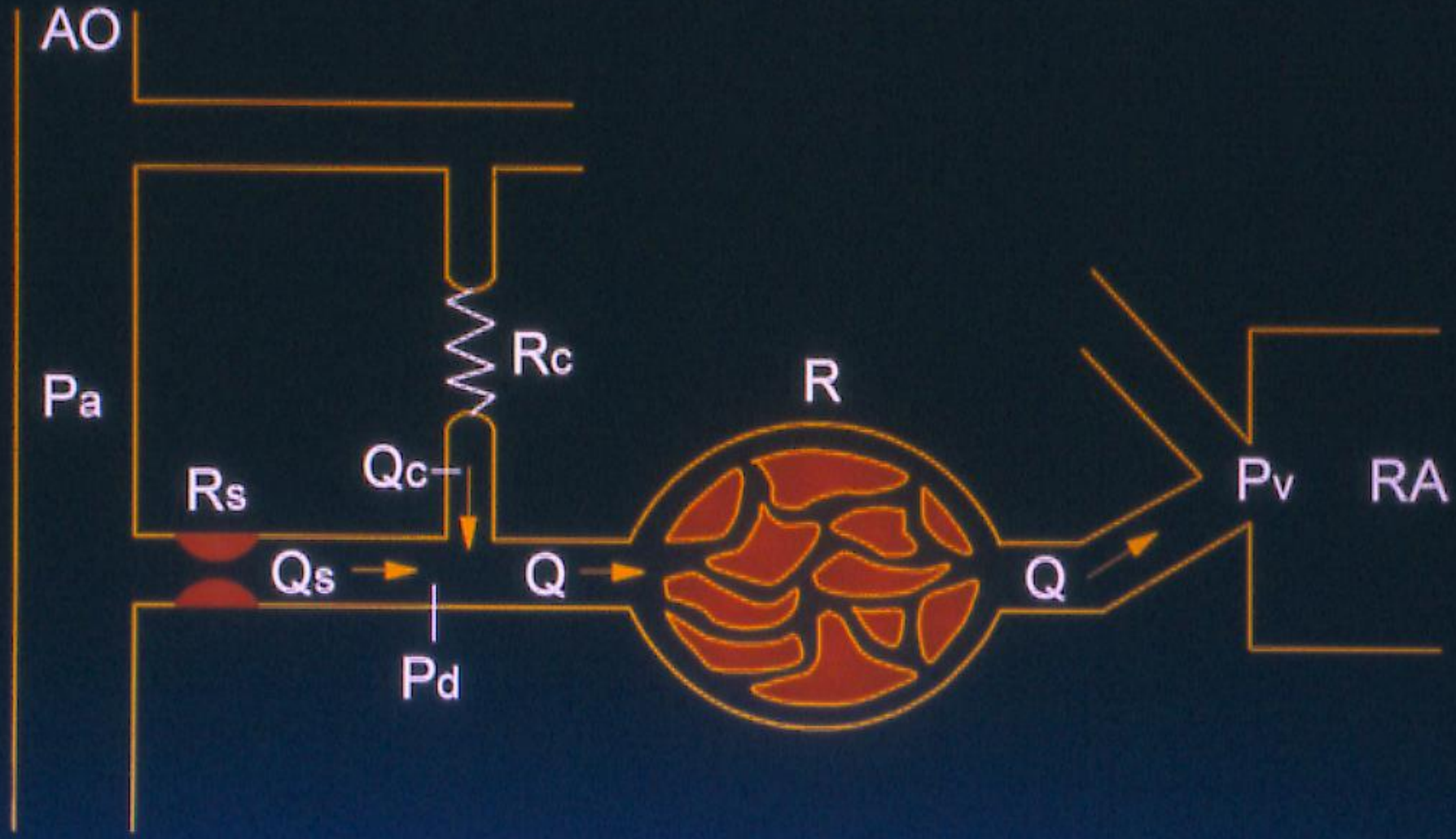


Experimental basis of FFR

Horizontal axis:
FFR measured by true flow

Vertical axis:
FFR measured by
Hyperemic pressure ratio

Pijls et al, Circulation, 1993



Including collaterals in the model…….

I $$\frac{P_a - P_v}{P_w - P_v} = 1 + \frac{R_c}{R} = \text{constant}$$

IIa $$\mathrm{FFR}_{cor} = \frac{P_d - P_w}{P_a - P_w} = 1 - \frac{\Delta P}{P_a - P_w}$$

IIIa $$\mathrm{FFR}_{myo} = \frac{P_d - P_v}{P_a - P_v} = 1 - \frac{\Delta P}{P_a - P_v}$$

IVa $$Q_c = (\mathrm{FFR}_{myo} - \mathrm{FFR}_{cor}) \cdot Q^N$$

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Let's have a closer look to FFR

Prerequisites for a reliable index for decision making

- ***sound scientific basis and experimental validation***
- accurate, i.e. clear cut-off with narrow gray zone
- reproducible
- easy to perform
- predict outcome

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Fractional Flow Reserve in Normal Coronary Arteries

33 truely normal coronary arteries in patients\ without coronary artery disease:

FFR = 0.98 +/- 0.02 (range 0.93 – 1.00)

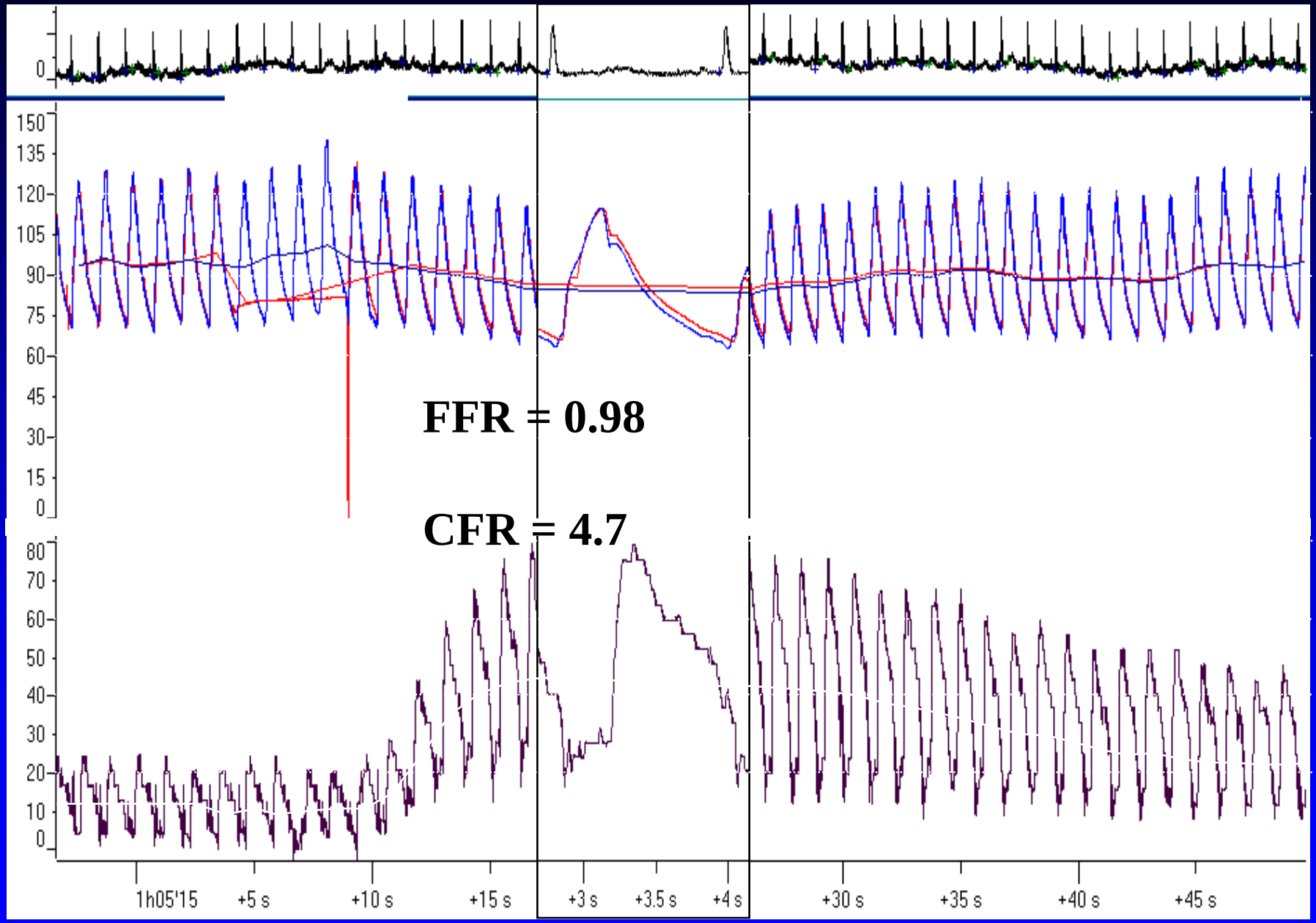
Pijls, Circulation 1995;92: 183-193

86 apparently normal contralateral arteries In patients with coronary disease:

FFR = 0.87 +/- 0.09 (range 0.64 – 0.97)

De Bruyne, Circulation 2001; 104:2401-2406

Normal Coronary Artery



Threshold value of FFR to detect significant stenosis in humans

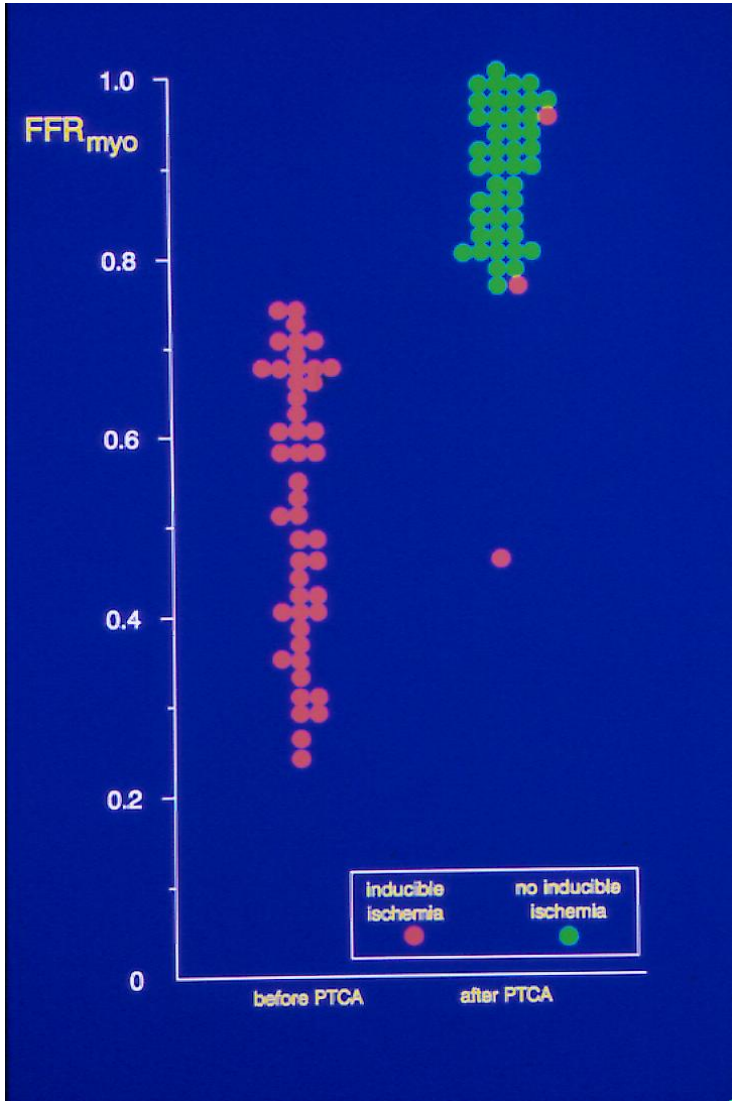
FFR is the ***only*** functional index which has ever been validated versus a **true gold standard**.
(Prospective multi-testing Bayesian methodology)

ALL studies ever performed in a wide variety of clinical & angiographic conditions, found threshold between 0.75 and 0.80

Diagnostic accuracy ≥93%

Pijls et al, N Engl J Med 1996; 334:1703-1708
Oldroyd et al, Circulation 2010

Validation of FFR in humans (step 1)



Proper validation of any index needs ***2 steps:***

1. Searching for the threshold value in a selected population
   (sens, specif, NPV, PPV, ROC analysis)

2. Prospective validation in a population with unknown characteristics

Pijls et al, Circulation 1995
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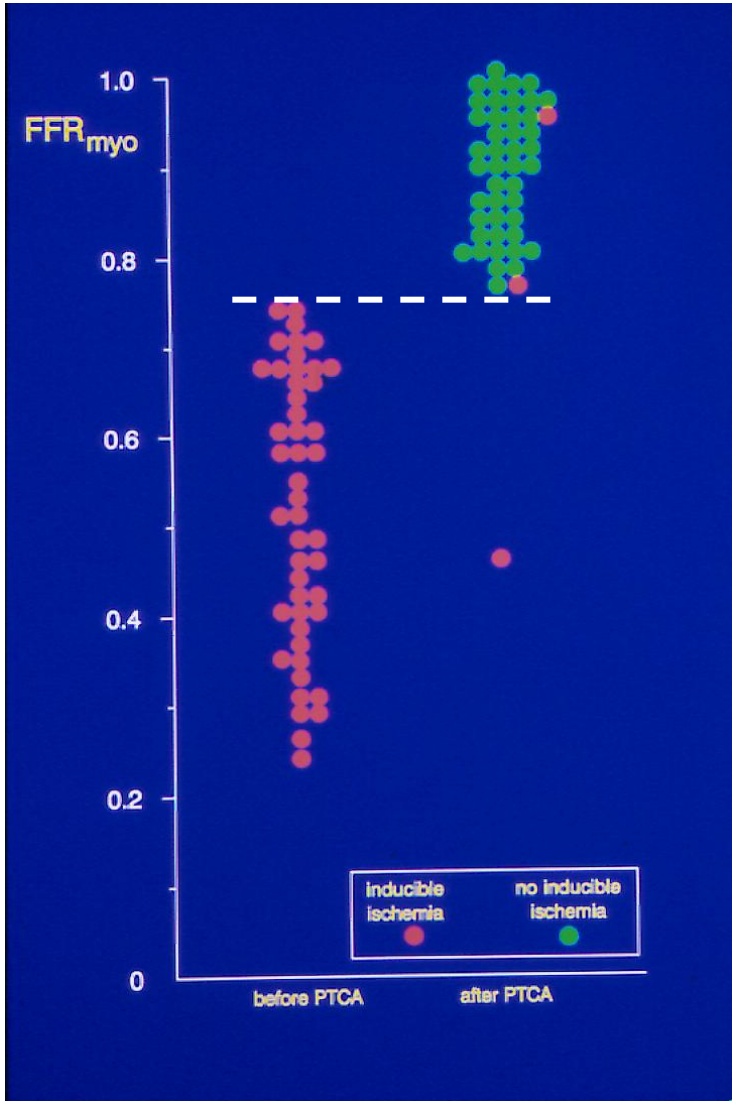

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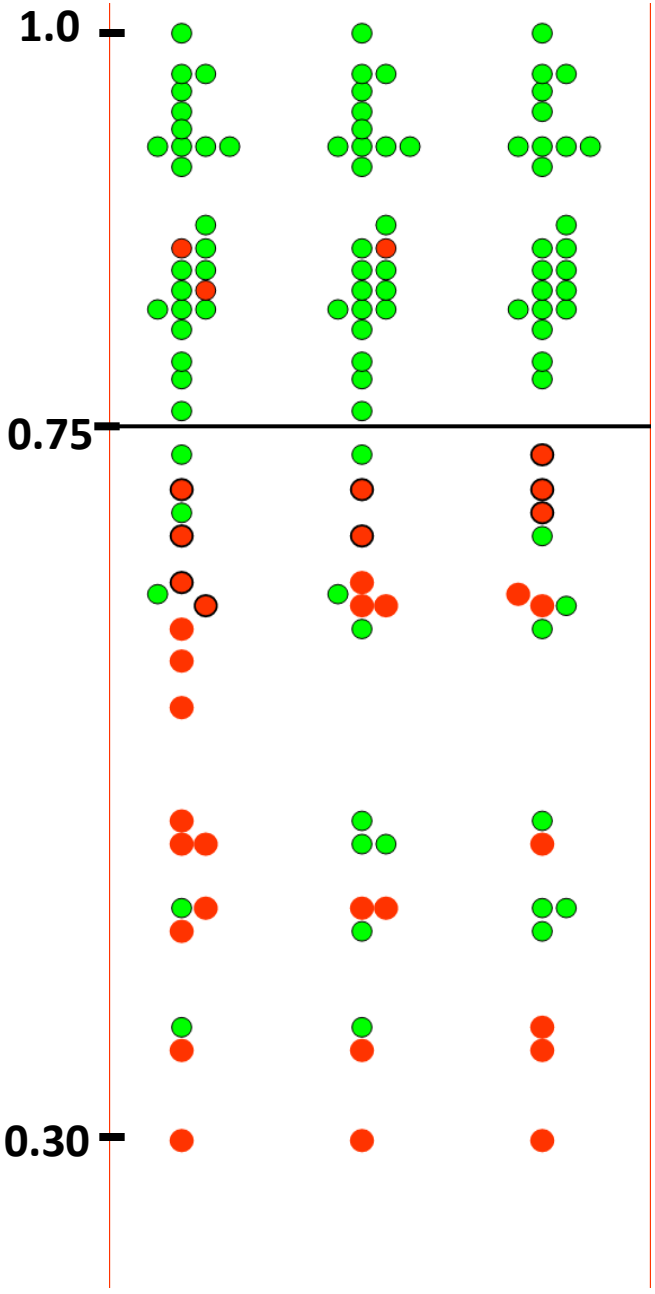

Testing of FFR versus True Gold Standard

Creating a gold standard by ***Prospective Multitesting Sequential Bayesian Approach:***

- Exerc testing = electrical index of ischemia
- MIBISpect = perfusion index of ischemia
- Dobutrex Echo = contractile index of ischemia
- *reversal from positive before to negative after intervention, proves true positivity before and true negativity after test*

Diagnostic accuracy of FFR =

$$\left[(1-0.75) \times (1-0.8) \times (1-0.8)\right]^{-1} = 99\ \%$$

3 unclassifiable patients (no intervention)

→ worst case scenario for FFR → **93 %**

Pijls et al, NEJM 1996

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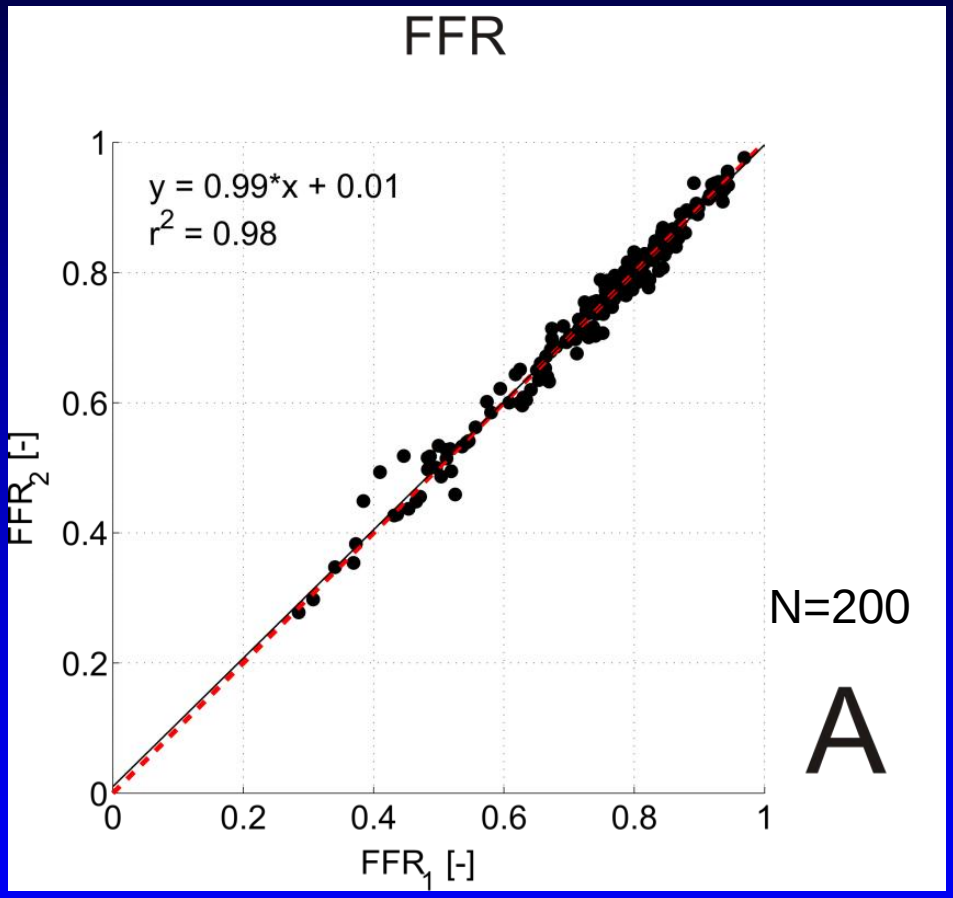
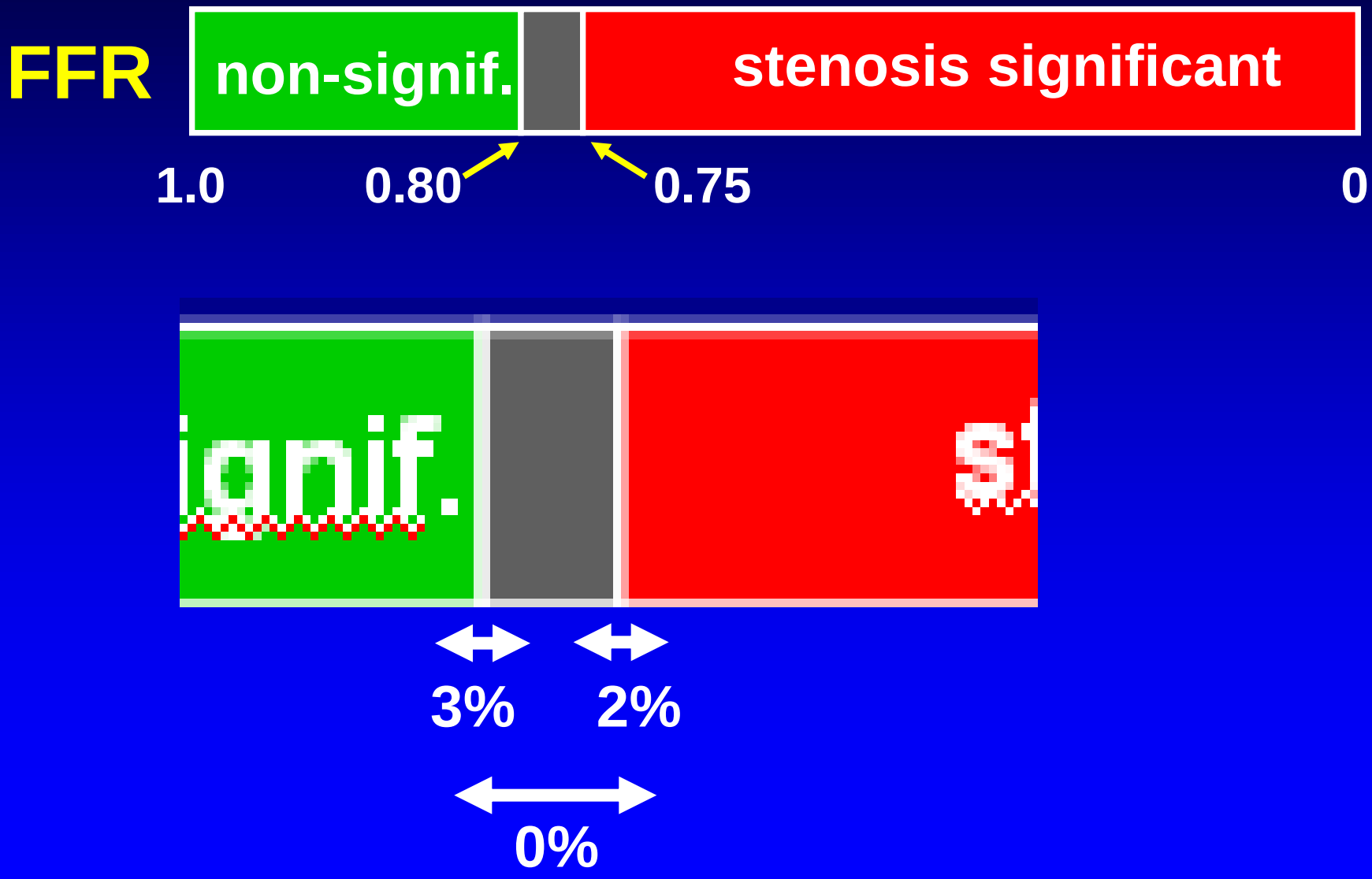
Reproducibility of FFR



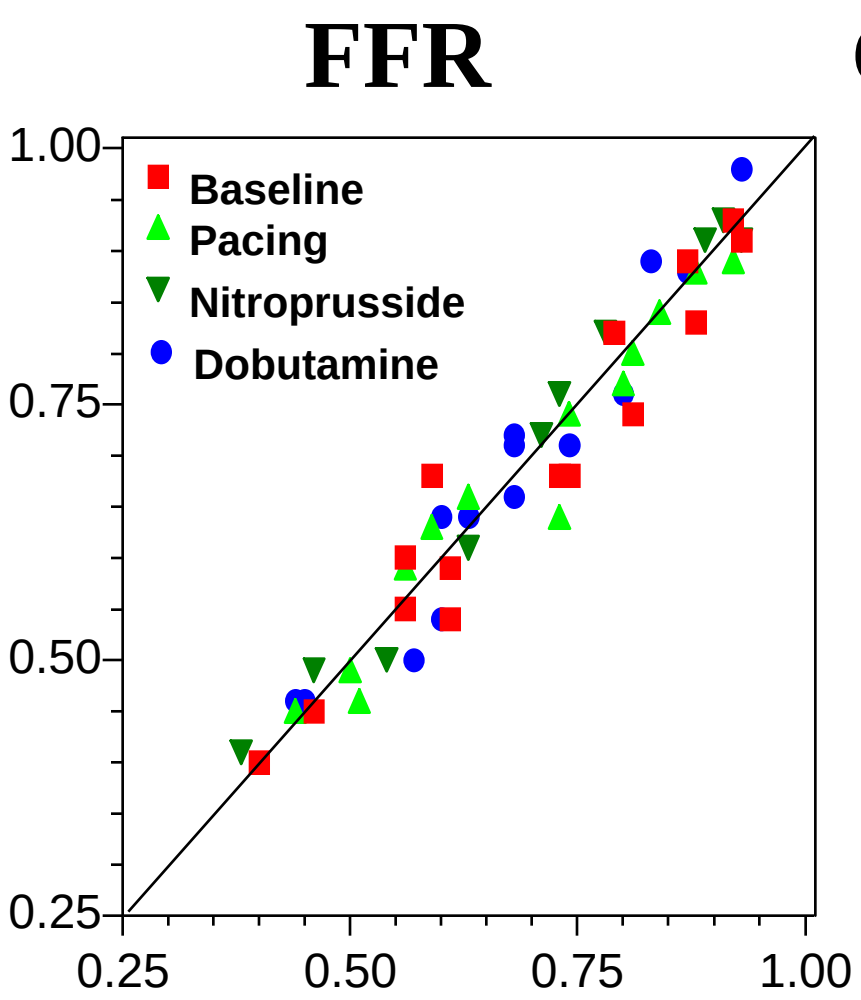
VERIFY study, Berry et al, JACC 2013 (published februari 2013)

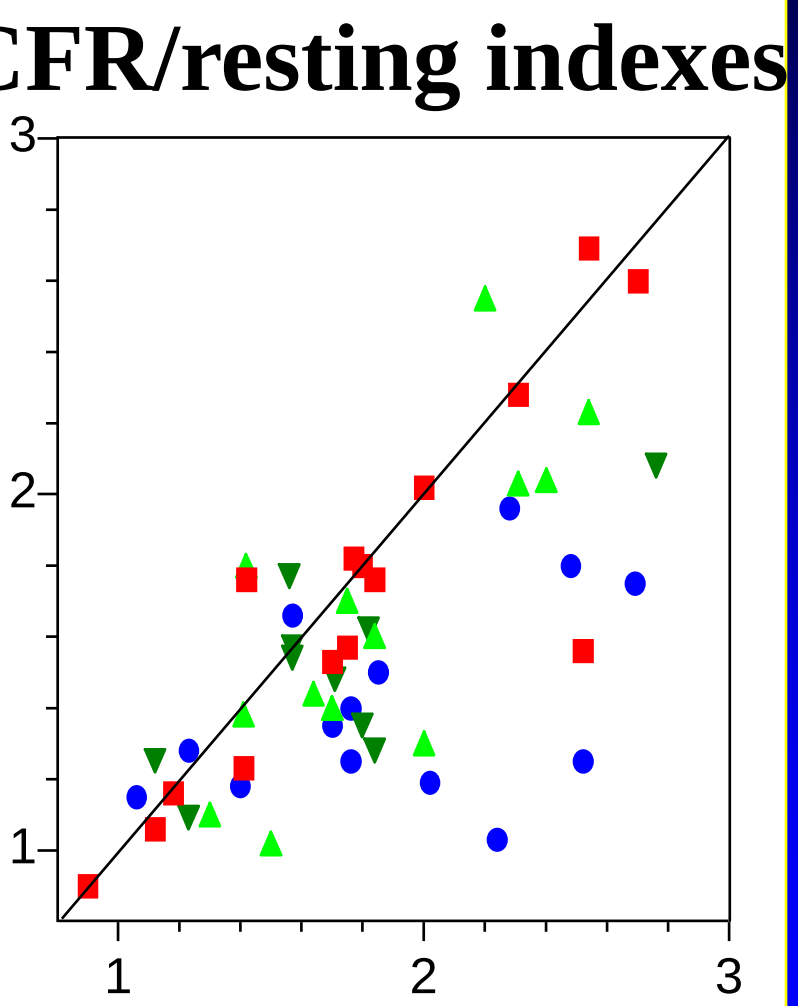
There is not any other index in physiology so reproducible as FFR

At 1200 consecutive in-duplo measurements of FFR, there was NOT ANY cross-over across the gray zone



Hemodynamic Variability of FFR_{myo} and CFR





B. De Bruyne et al Circulation 1996

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

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

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