

# *TCT Asia Pacific 2017*

**FFR, iFR, Contrast FFR, CFR, IMR, etc  
TOO MANY INDEXES ? PLEASE KEEP IT SIMPLE !**

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Nico H. J. Pijls, MD, PhD  
Catharina Hospital,  
Eindhoven, The Netherlands



# Potential conflicts of interest

Speaker's name: NICO H J PIJLS

I have the following potential conflicts of interest to report:

- Research contracts : St Jude Medical
- Consulting: St Jude Medical, Opsens
- Employment in industry
- Stockholder of a healthcare company: Philips, GE, ASML, Heartflow
- Owner of a healthcare company
- Other(s):

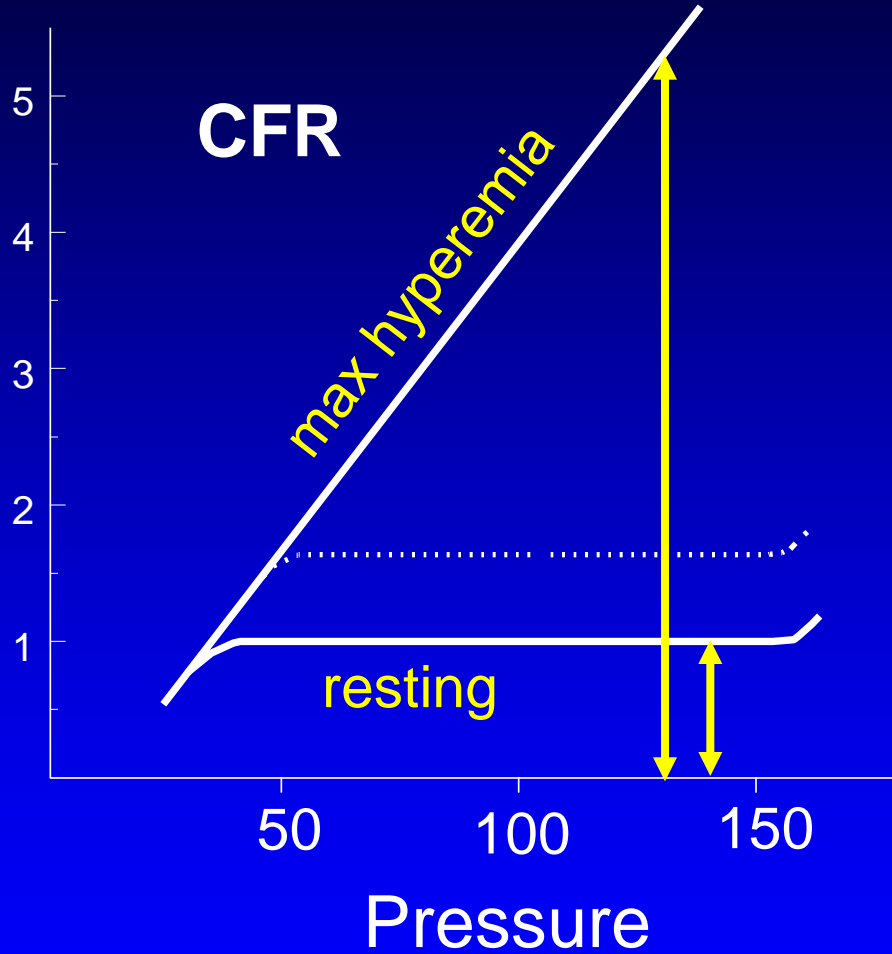
I do not have any potential conflict of interest



## ***Pre-amble:***

- the most important factor with respect to ***symptoms*** (quality of life) and ***outcome*** (longevity) in patients with coronary heart disease, is the ***presence and extent of inducible ischemia***
- coronary angiography (anatomic imaging) is fundamentally limited to establish the functional significance of coronary heart disease
- therefore, the importance of additional ***physiologic methods*** to quantify coronary disease, is undisputable

Flow



$$CFR = a / b$$

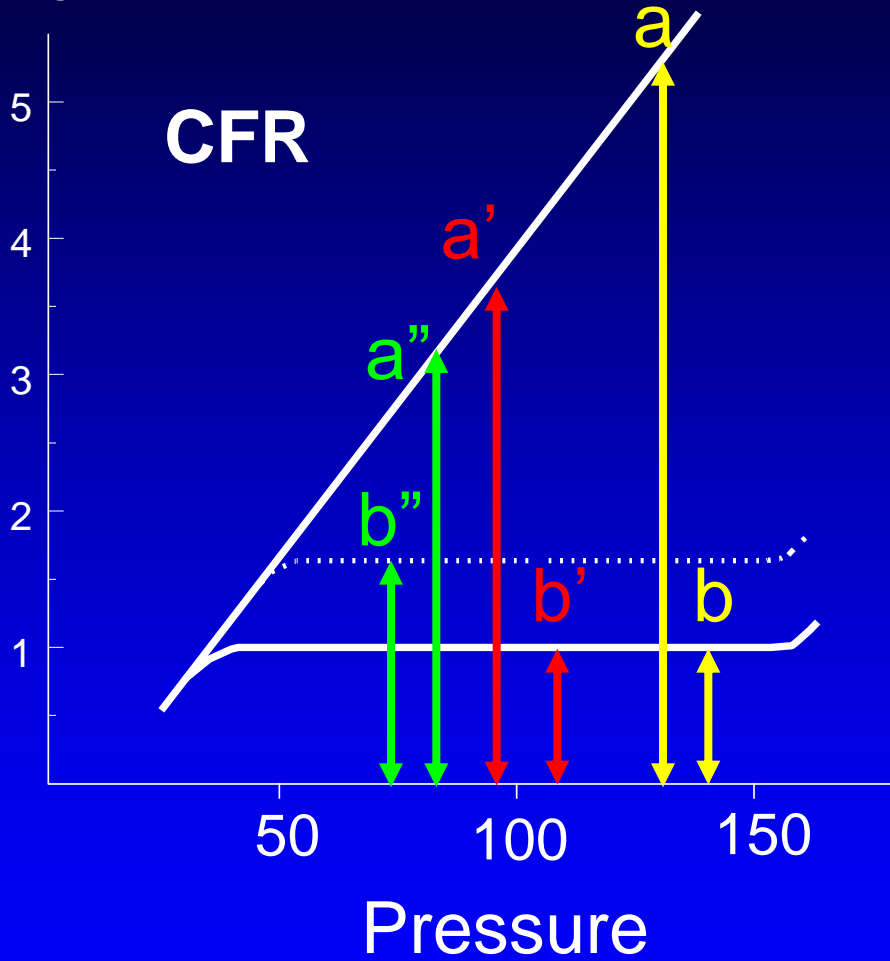
a

b

CFR: hyperemic blood flow / resting blood flow (1974, Gould)

Flow

CFR

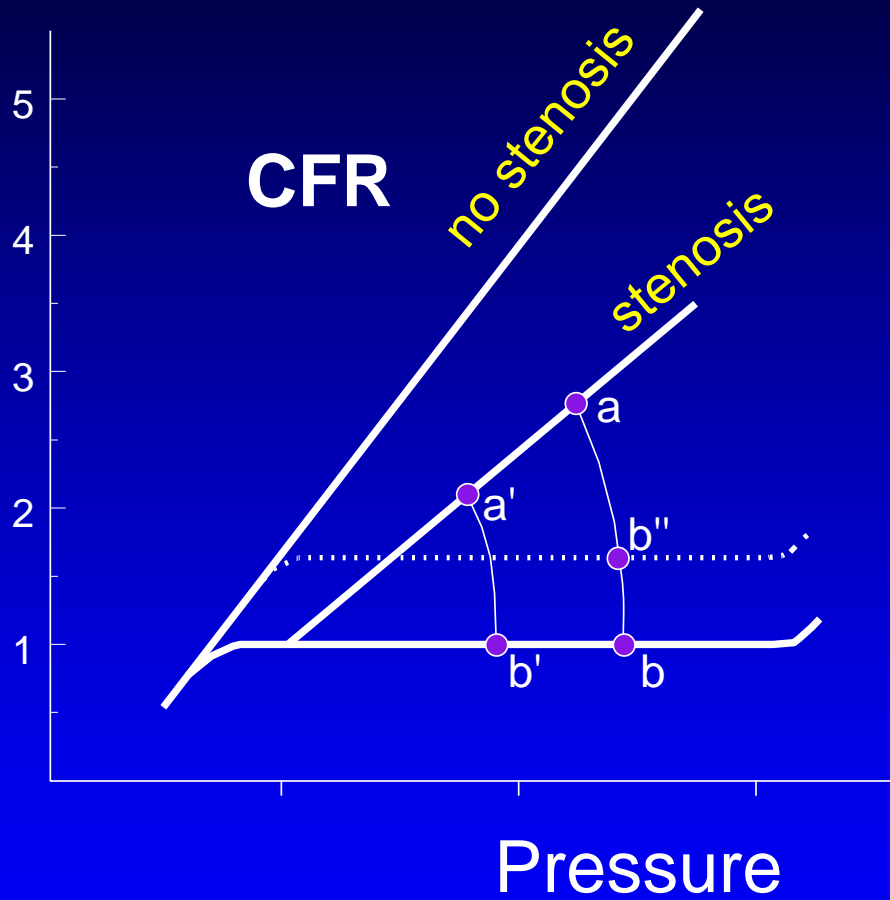


$$\text{CFR} = a / b$$

$$\text{CFR} = a' / b'$$

$$\text{CFR} = a'' / b''$$

Flow



What is CFR ?

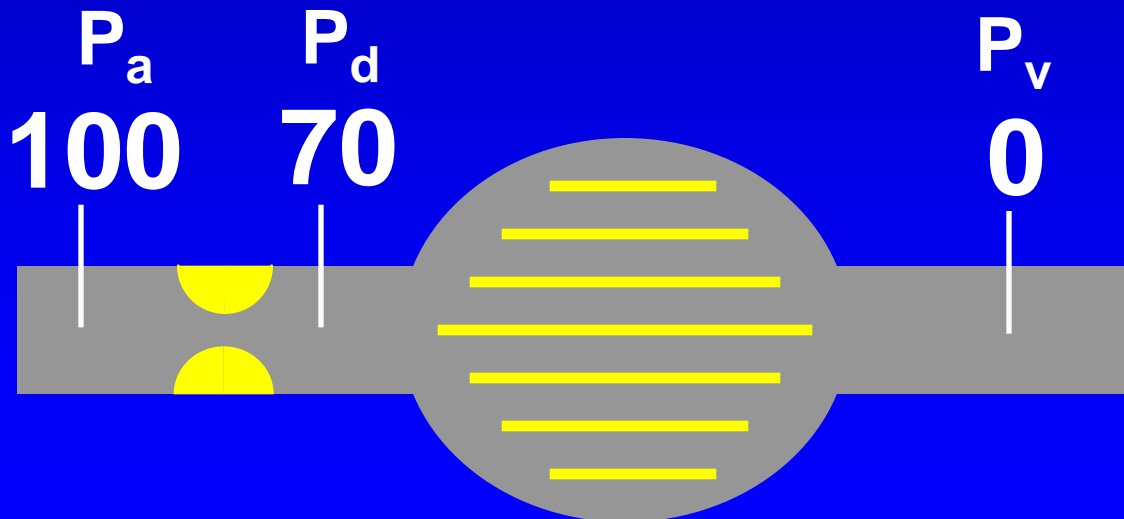
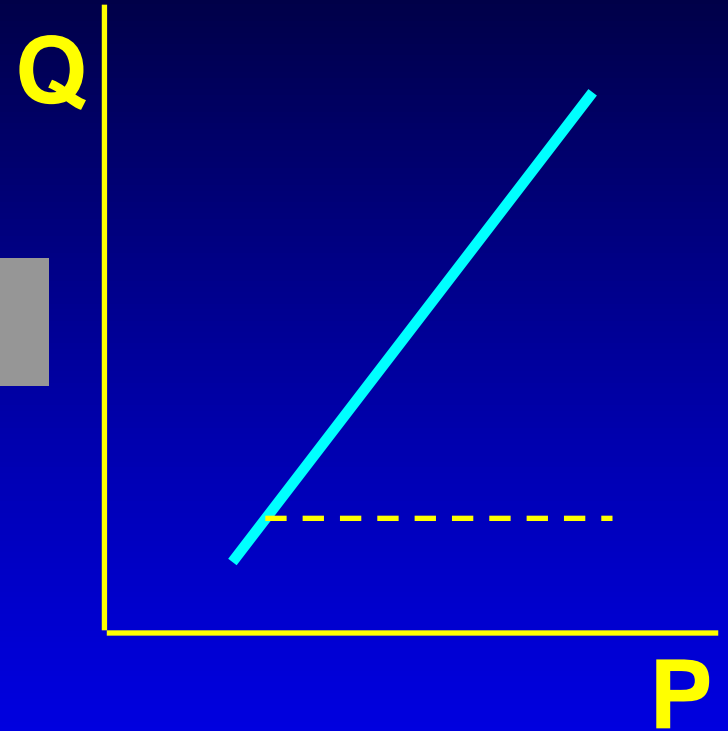
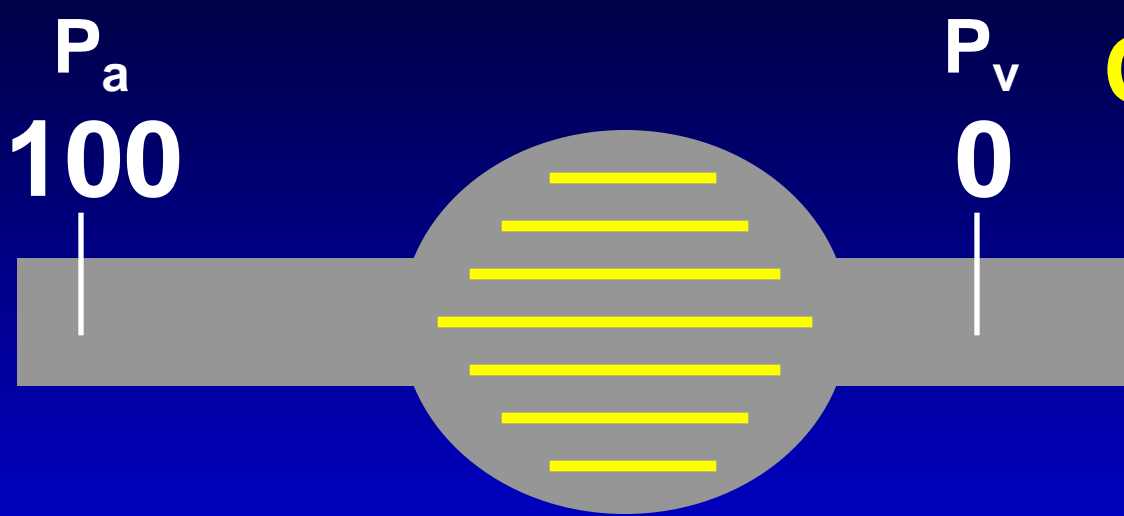
- $a / b$  ??
- $a' / b'$  ??
- $a / b''$  ??

## ***PHYSIOLOGIC PARAMETERS OF STENOSIS SEVERITY:***

- Although CFR is a beautiful physiologic concept, its usefulness for clinical decision making with respect to revascularisation, is limited
- To determine what is an ***abnormal*** value of a particular index, a clear ***normal*** value should be known, valid for ***every patient, every artery***, and independent of the ***location within the artery*** where the measurement is performed !
- clinical measurement of CFR by Doppler is unreliable in > 30% of patients

→ ***Need for a more practical index: FFR*** (Pijls, de Bruyne, 1993)

# During Maximal Vasodilatation

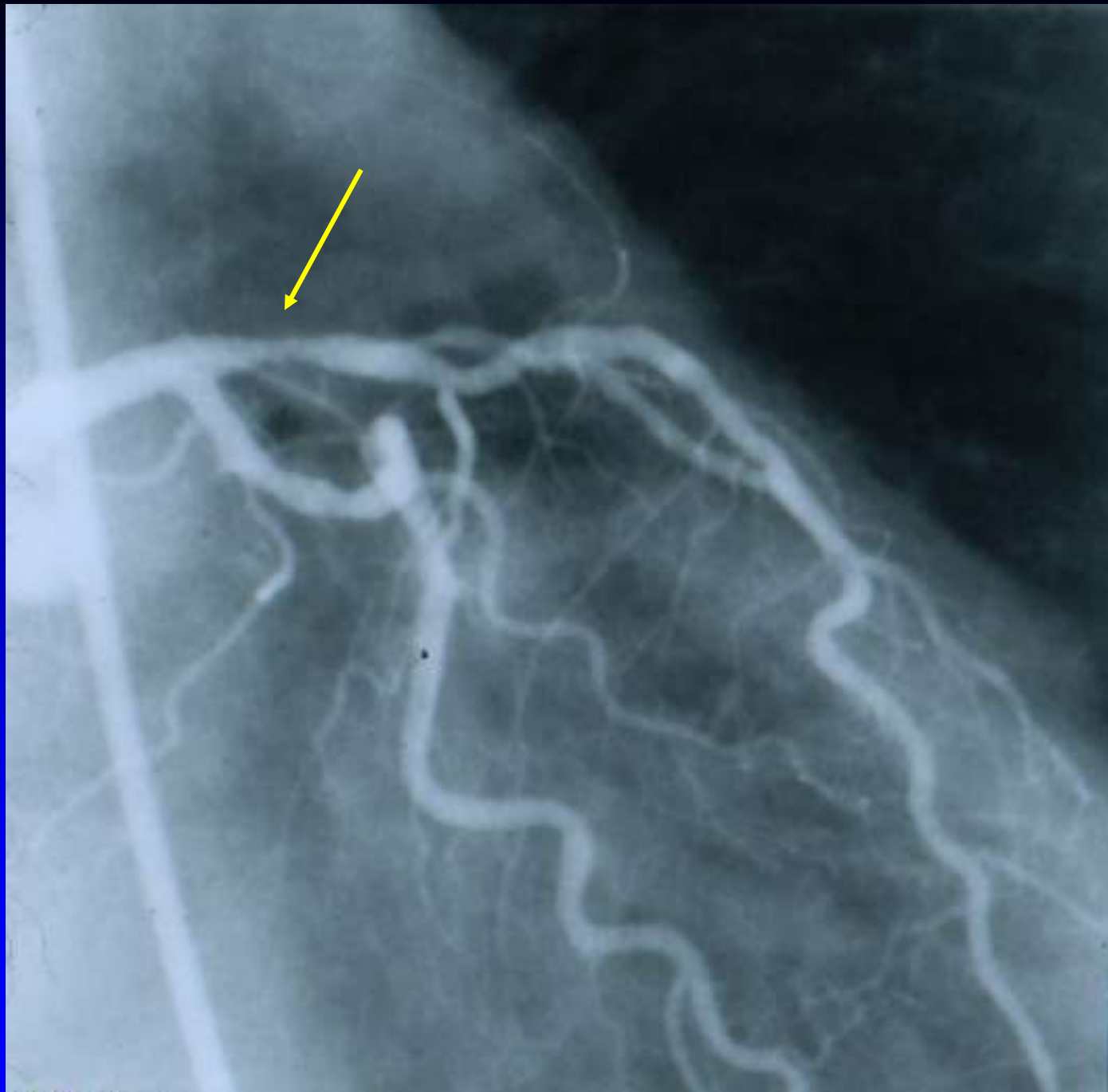


$$\text{FFR}_{\text{myo}} = \frac{P_d}{P_a} = 0.70$$

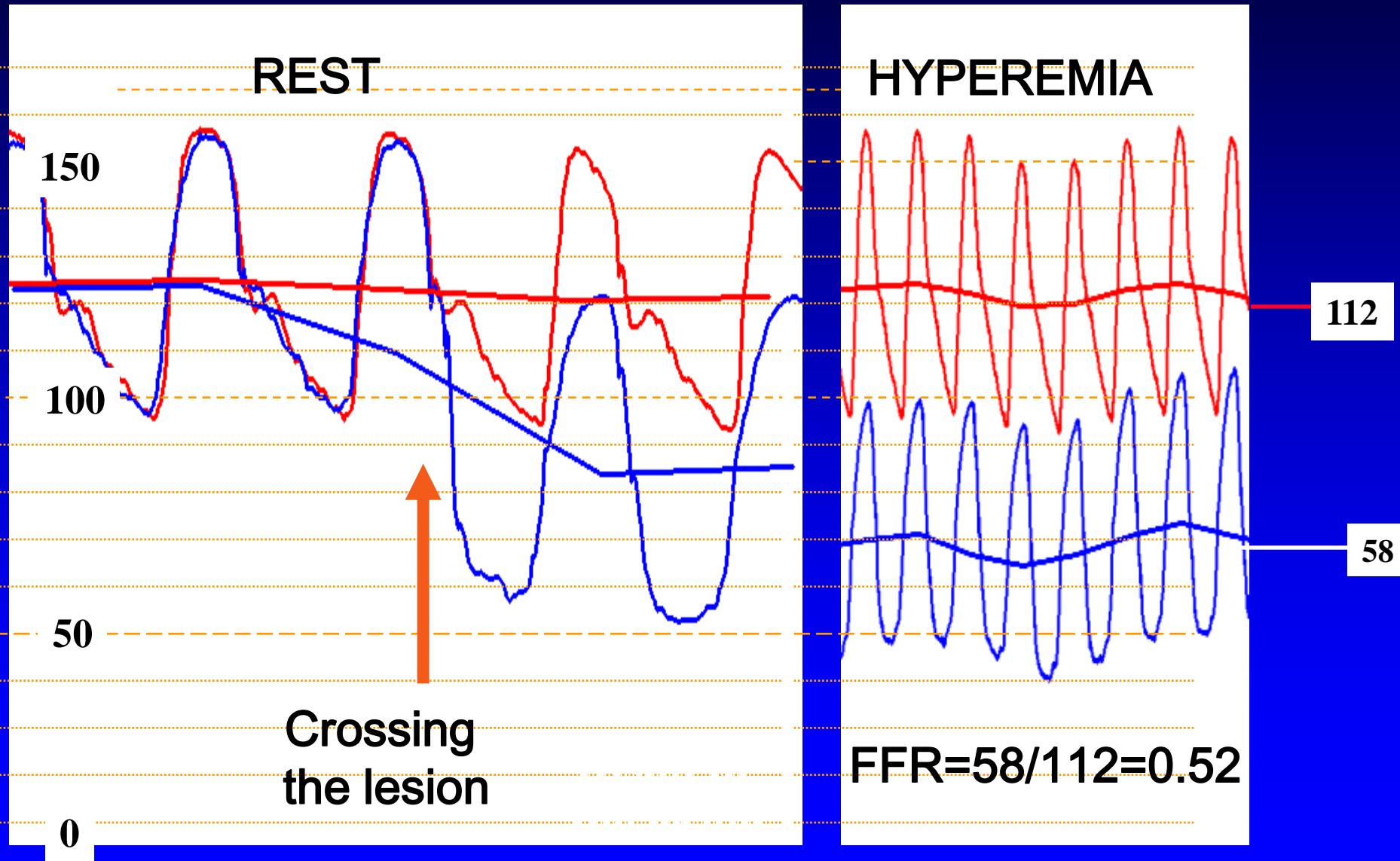


**CLINICAL**  
**PRACTICE:**

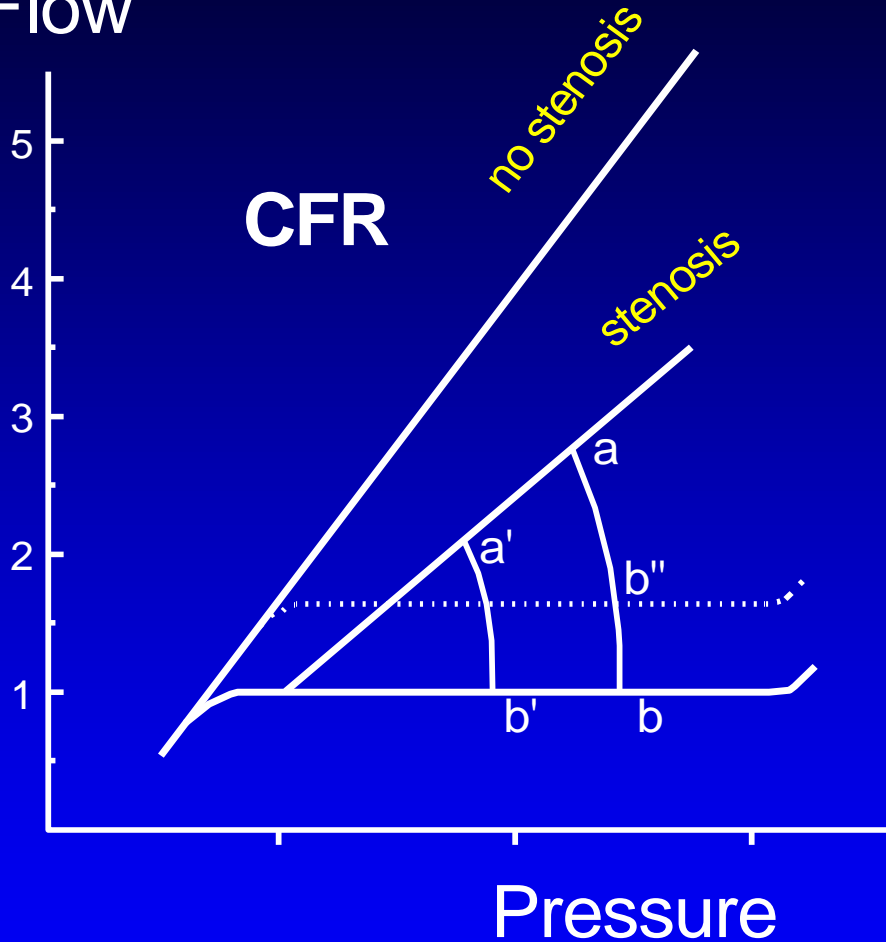
Mr van Z.  
77 years,  
stable ang 2-3  
posit ET



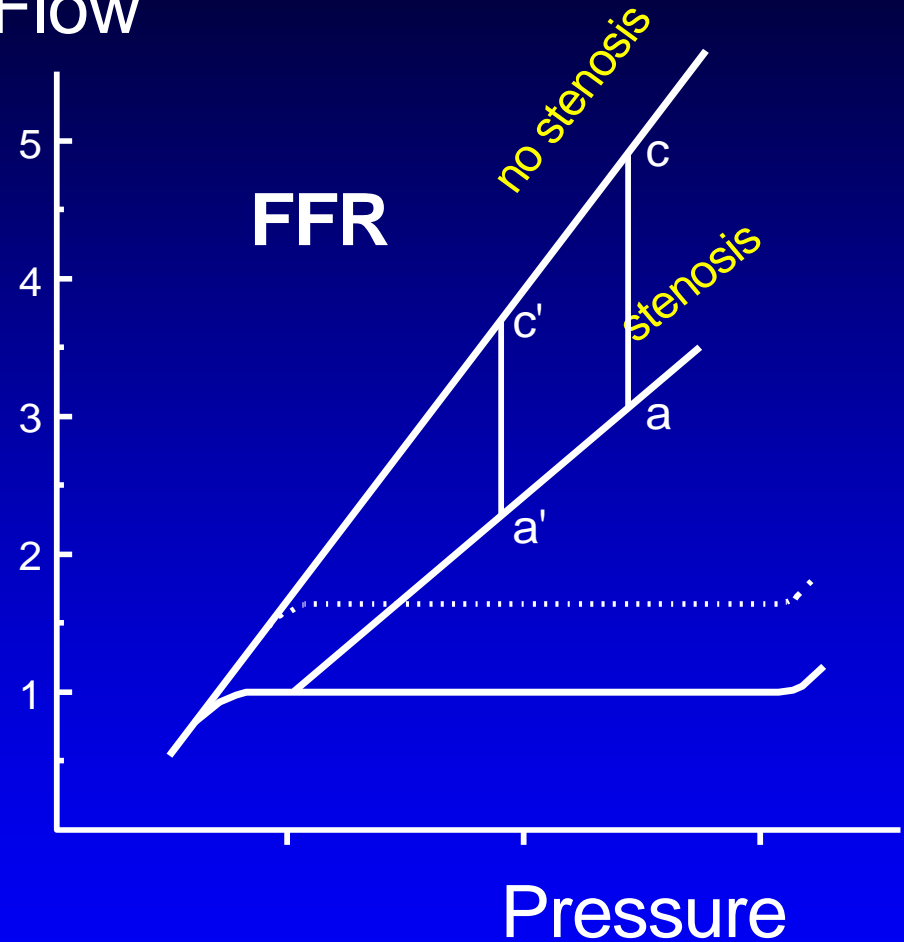
# Fractional Flow Reserve in Clinical Practice



Flow



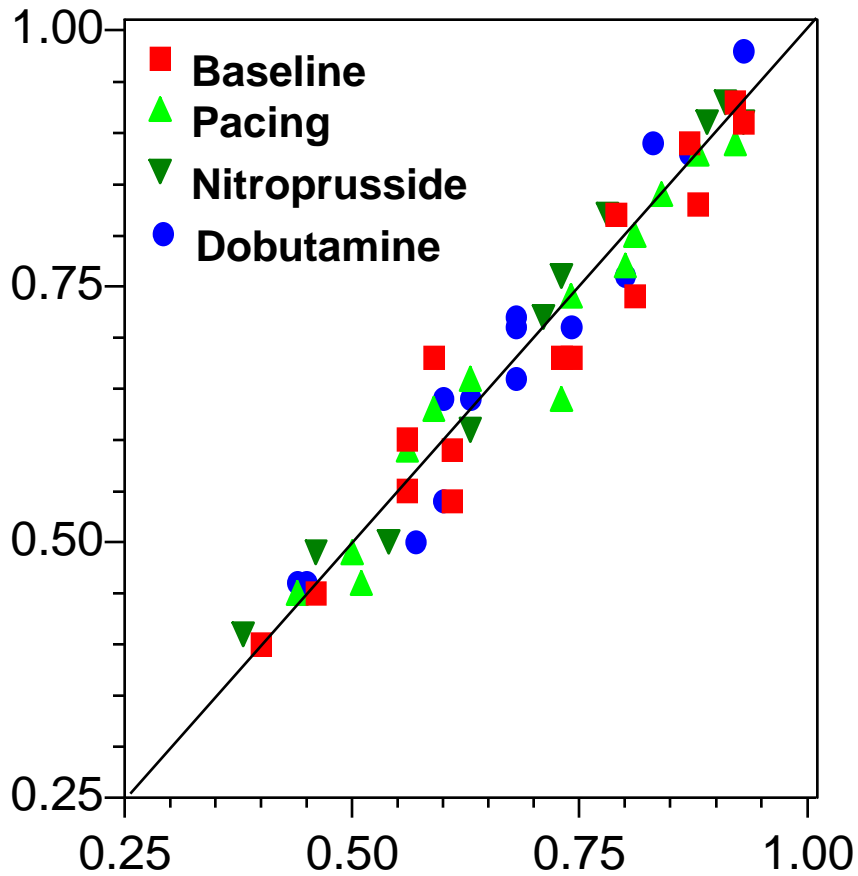
Flow



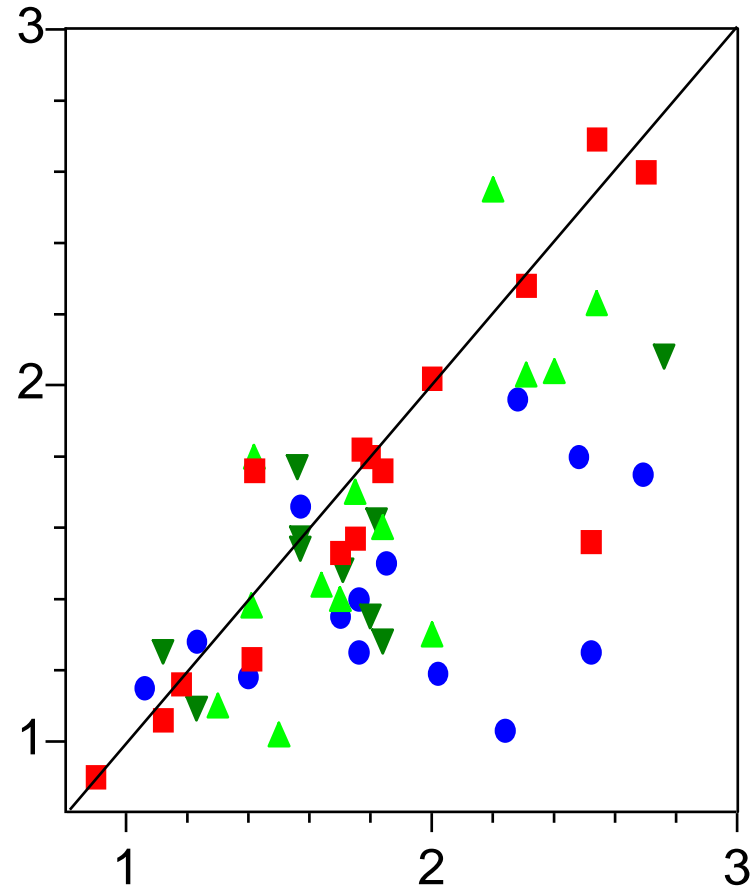
**FFR**: easy to measure, unequivocal normal value, not dependant on heart rate, blood pressure, or contractility

# Hemodynamic Variability of FFR and CFR

## FFR



## CFR



# Threshold value of FFR to detect significant stenosis



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

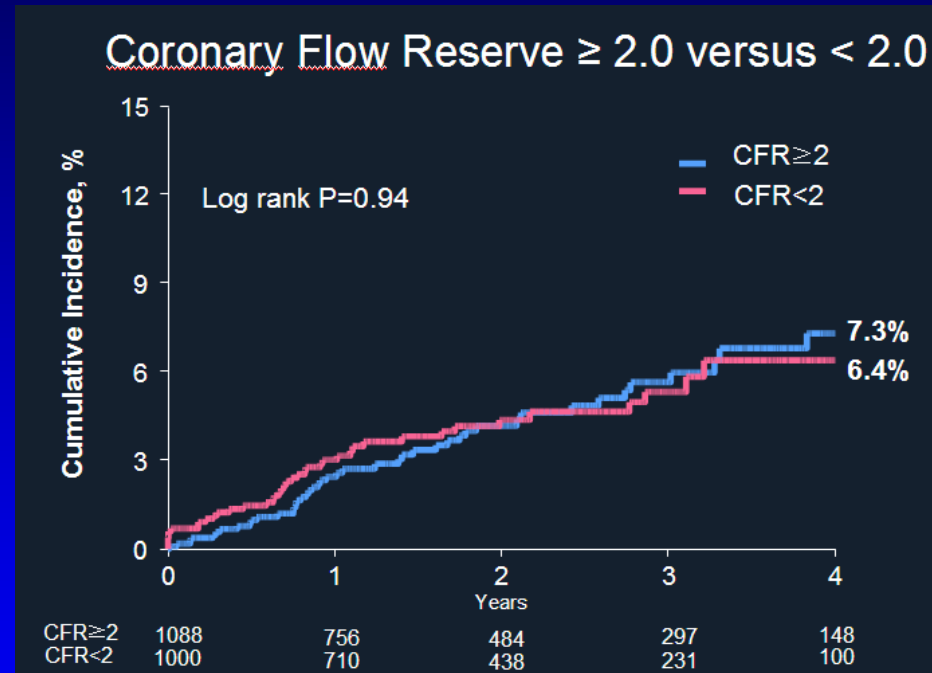
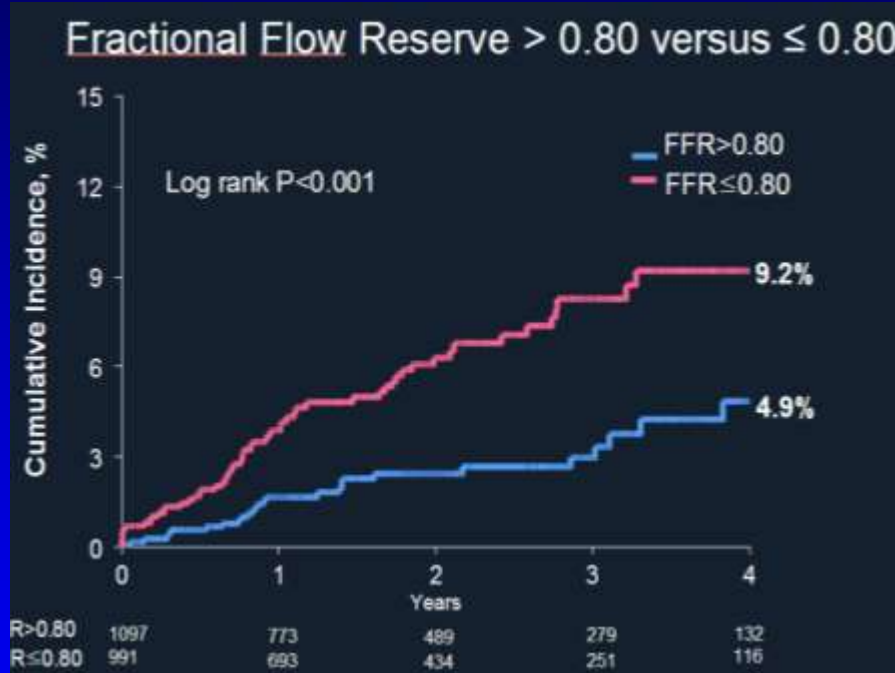
**ALL** studies ever performed in a wide variety of clinical & angiographic conditions, found threshold between 0.75 and 0.80

**Sensitivity : 100 %**

**Specificity : 90 %**

# FFR-guided PCI vs CFR-guided PCI for clinical outcome: N= 2088 patients from IRIS registry

## MACE RATE AFTER 4 YEARS OF FOLLOW-UP



— FFR > 0.80  
— FFR ≤ 0.80

— CFR ≥ 2.0  
— CFR ≤ 2.0

## **FFR and Clinical Outcome: 3 important questions:**

- **Is it safe to defer PCI if FFR is negative ? → YES !**  
*(Defer study 15-y f.u, Lancet 2015)*
- **Is it indicated to perform PCI if FFR is positive ?**  
**→ YES !**  
*(FAME-2 , NEJM 2012 & 2014)*
- **Does systematic use of FFR improve PCI outcome**  
**→ YES !**  
*( FAME, NEJM 2009, EHJ 2015)*

The superiority of FFR-guided PCI to improve outcome has been demonstrated now in many RCT's  
*(comparing FFR-guided strategy directly to standard methods,*  
in almost all clinical and angiographic conditions:

- *From single to complex multivessel disease*
- *For LM disease*
- *Proximal LAD disease*
- *ACS, NSTEMI*
- *STEMI*
- *and many others*



# Non-hyperemic indexes and semi-hyperemic indices

Some older and newer indices derived from pressure measurement at rest:

**iFR,  $P_d / P_a$  at rest, diastolic  $P_d / P_a$  and cFFR (contrast)**

which have in common that they

- all try to avoid hyperemia
- are not independently validated, only vs FFR
- have an accuracy of 80% compared to FFR
- not any single independent outcome study

***advantage:*** no hyperemia needed

***concern:*** in 20% mis-classification, especially in large arteries in young patients

- hybrid approach might be attractive



Recent studies suggest that in some populations resting indices ( $iFR$ ,  $P_d/P_a$ ), may be non-inferior to FFR  
**(*DEFINE-FLAIR & SWEDE-HEART studies*)**

### CAVEAT:

- **both studies were underpowered**  
*(as  $iFR$  and FFR yield similar decision in 80% of all patients, the power is made by the remaining 20% only. This weakens a non-inferior design and would strengthen a superiority design)*
- **had (very) low risk populations**  
*1.4 lesion per patient vs 2.8 in FAME;  
0.7 stent per patient vs 1.9 in FAME;  
45 % of patients no PCI at all vs 11% in FAME*
- **and a large non-inferiority margin** ( $> 50\%$  of event rate)  
*All of which concerns favour showing non-inferiority*

## ***Define-Flair, Swede-Heart studies (NEJM 2017)***

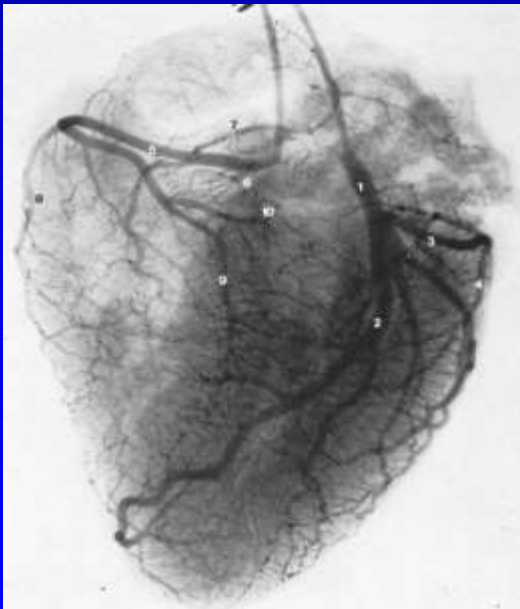
***Worrying finding in meta-analysis of both studies:***

- ***strong trend to increased mortality with iFR ( $p < 0.09$ )***

# ***THE CORONARY MICROCIRCULATION: Still a Black Box ??***

***Presently, we have excellent methods to assess epicardial coronary artery disease (FFR, IVUS, OCT)***

***.... but the coronary microcirculation is still a black box***

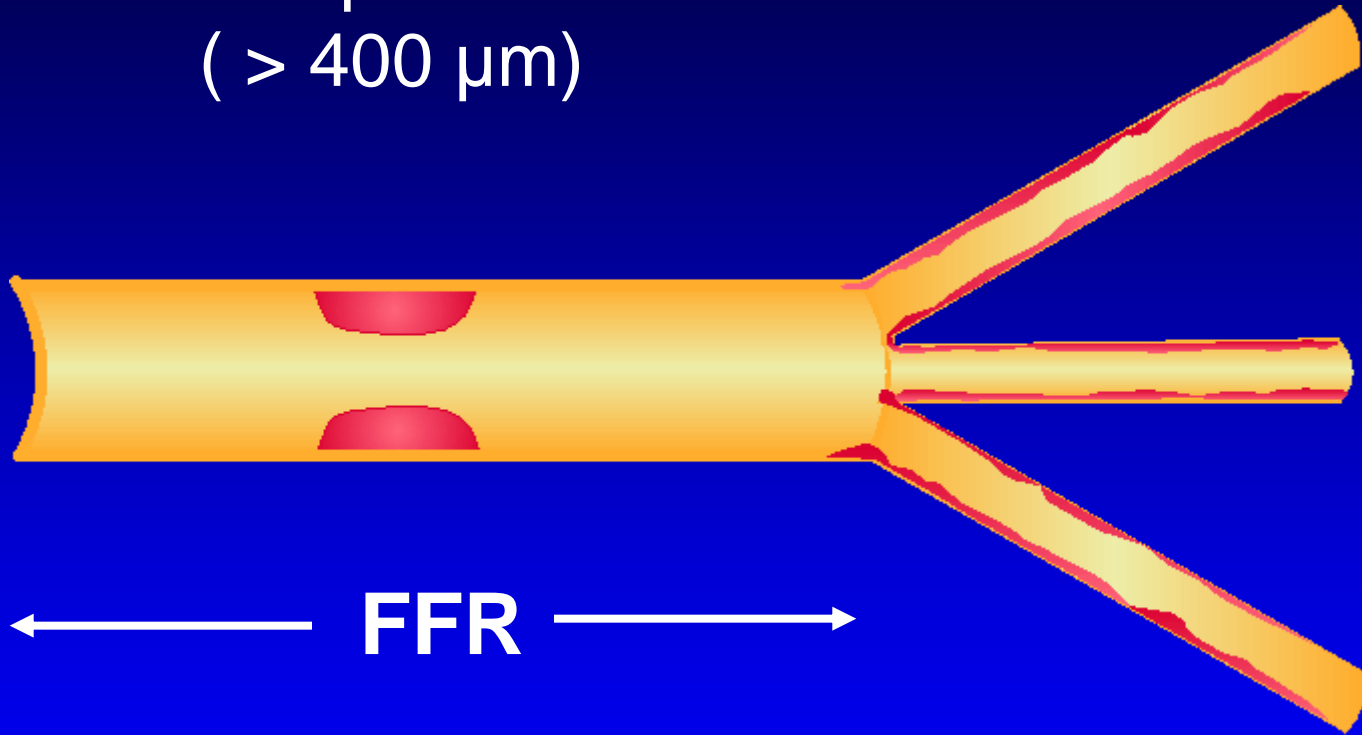


***X 10.5***



epicardial  
compartment  
( > 400  $\mu\text{m}$ )

microvascular  
compartment



← FFR →

IMR  
← →



ARCHIVE CUSTOM

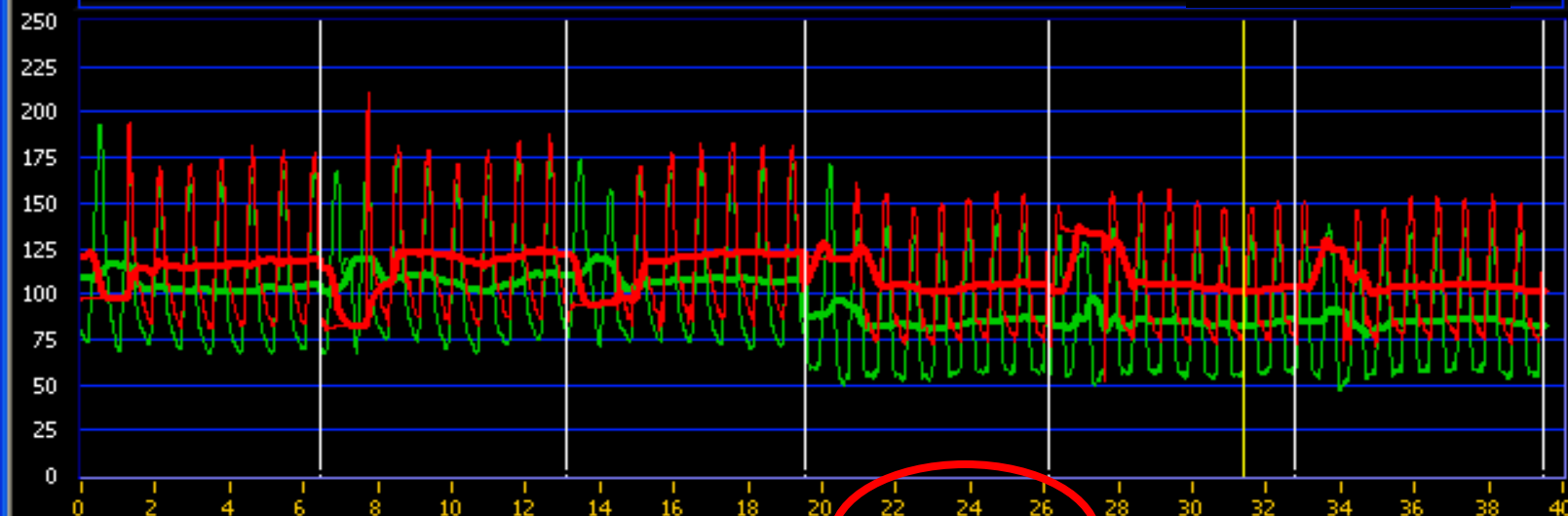
FOLDER

Custom

PATIENT ID DATE TIME VESSEL PROCEDURE ACTION TYPE SIZE

PATIENT ID	DATE	TIME	VESSEL	PROCEDURE	ACTION	TYPE	SIZE
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	CFR	42Kb
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	CFR	42Kb
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	FFR	17Kb
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	CFR	131Kb
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	FFR	26Kb

PRINT EDIT RENAME EXPORT ERASE SETUP



101 Pa mean

82 Pd mean

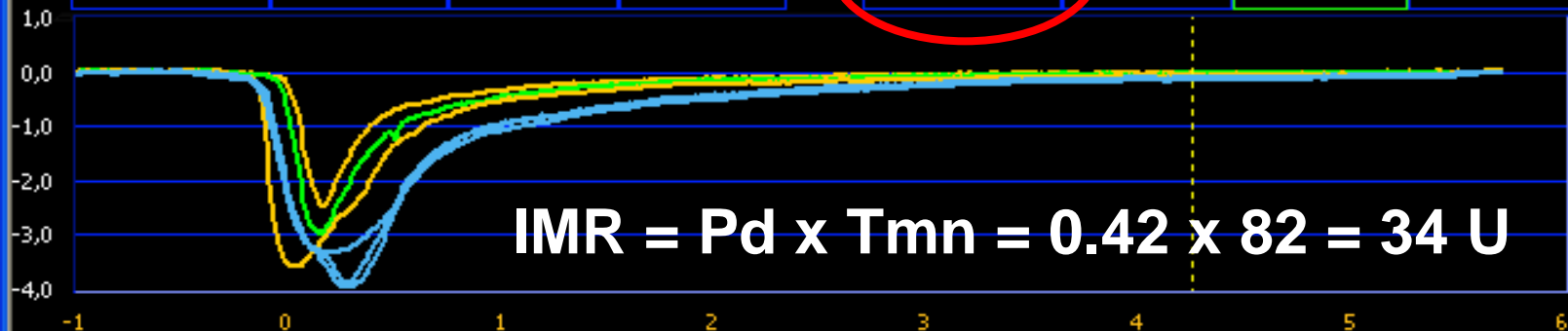
0,82 FFR

1.7 CFR

-0,04 dT

4,2 CURSOR

Bas (0.70)	0.74	0.66	0.72	Hyp (0.42)	0.42	0.43	0.42
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$IMR = Pd \times Tmn = 0.42 \times 82 = 34 U$

RESET

# IMR:

$$\text{IMR} = P_d \times T_{mn}$$

distal coron pressure

mean transit time

- measures **minimal** microvascular resistance
- determined by thermodilution and short coronary injections of saline
- always done 3 x to decrease intrinsic variability
- easy to perform
- hyperemia needed ( relevant clinical parameter is **minimal** resistance; resting value has no clinical meaning)
- variability still rather large (15%) and operator-dependent
- arbitrary units, not absolute units
- value of  $> 25$  U mostly considered as microvascular disease



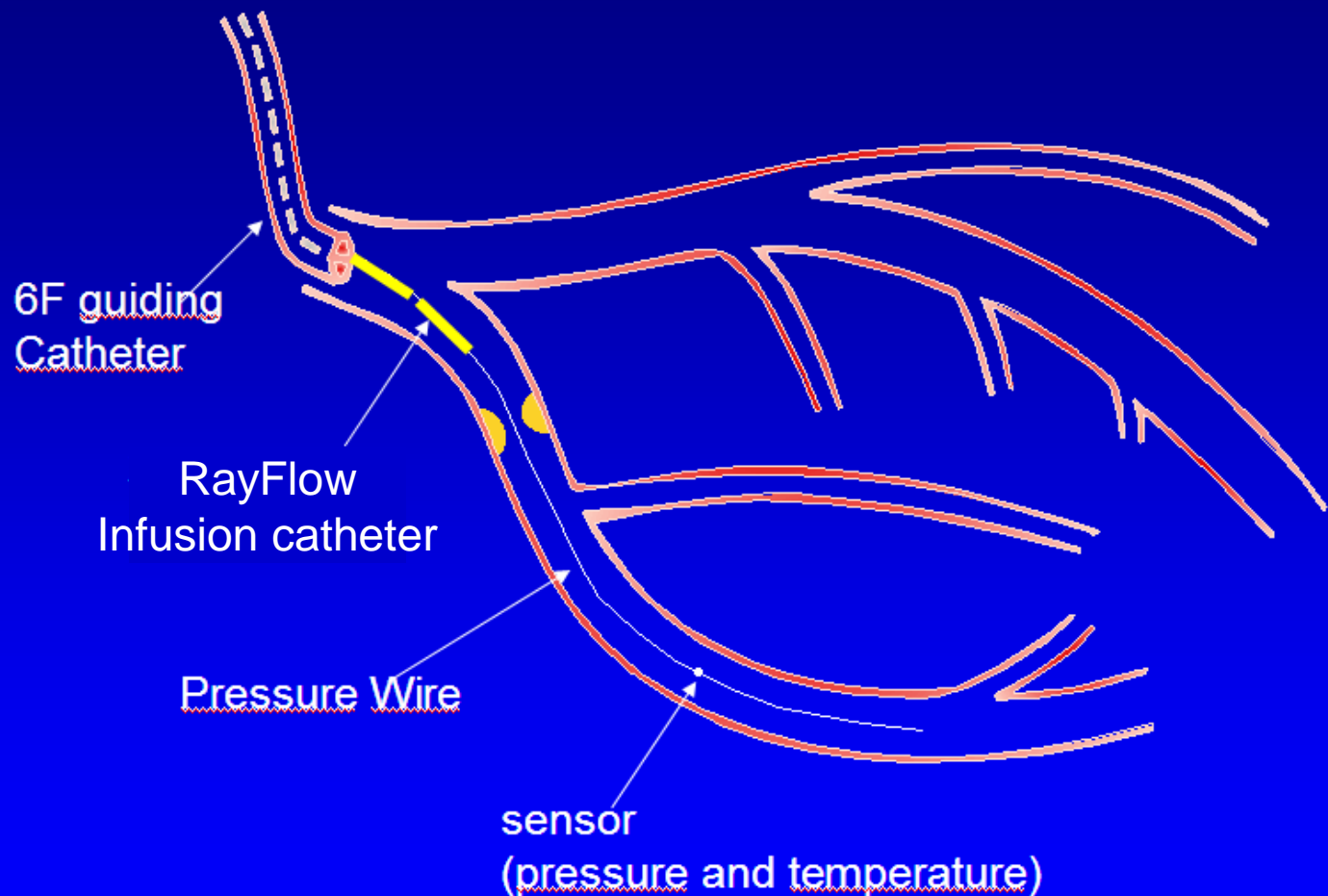
# ***A NEW WINDOW TO THE CORONARY MICROCIRCULATION***

*The ideal technique to assess the microcirculation, should be:*

- understandable from sound physiology view
- easy to perform with standard PCI equipment
- accurate and reproducible
- operator-***independent***

→ *Measurement of absolute flow and resistance by thermodilution and continuous infusion of Saline*

*(RayFlow® catheter, Pressure Wire and Coroventis software)*

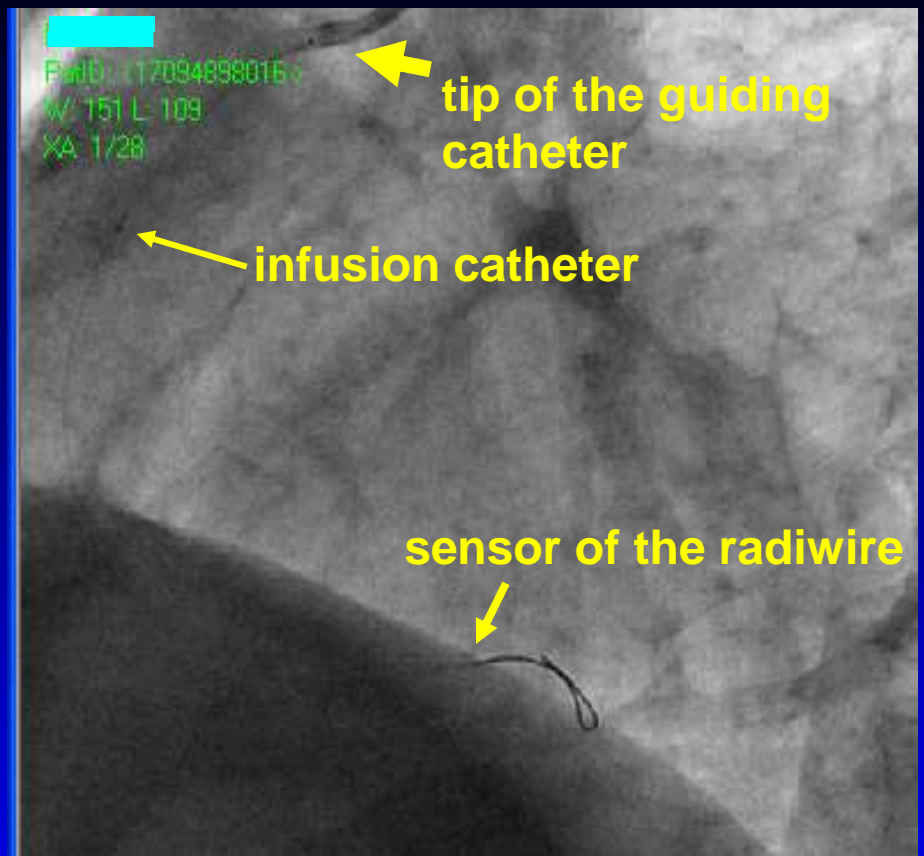


saline infused at 20 ml/min

temperature of saline is 5° below blood temperature

after mixing, temperature of mixtate is 1° below blood temp

→ blood flow must be 5 x infusion flow of saline



PRINT

EDIT

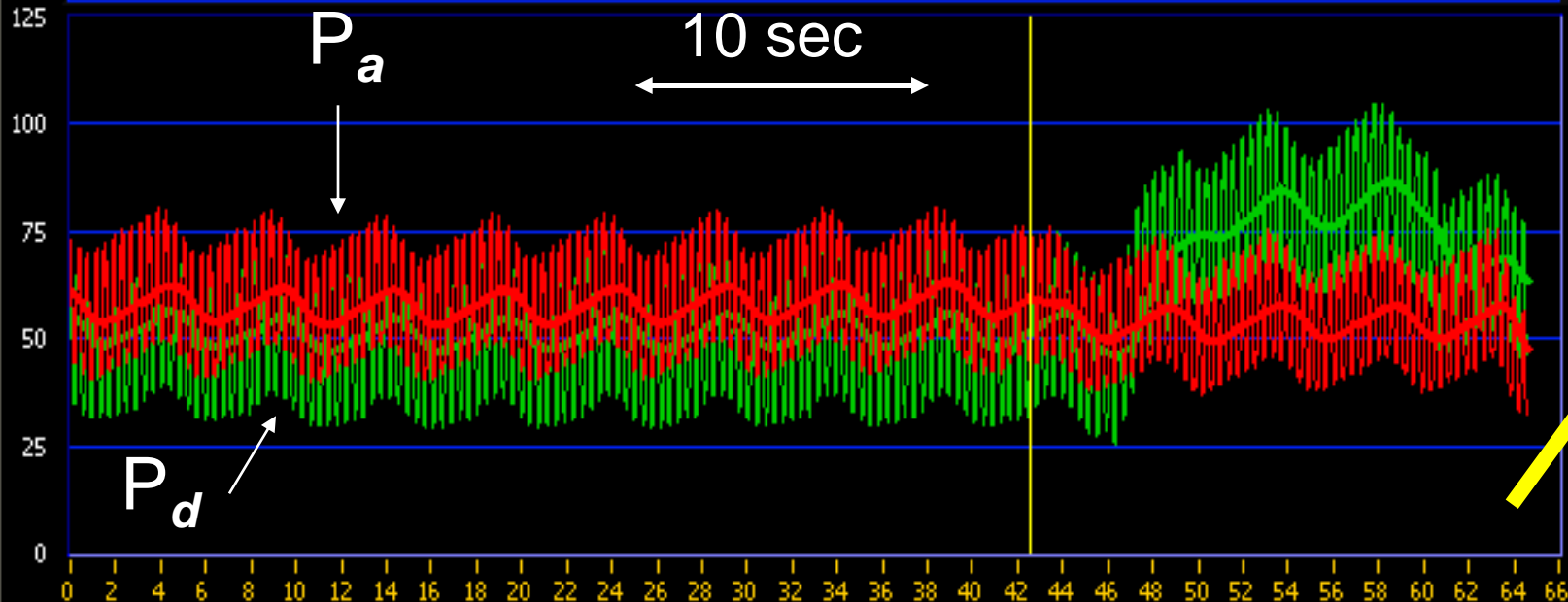
RENAME

EXPORT

ERASE

SETUP

# maximum hyperemia



59 Pa mean

51 Pd mean

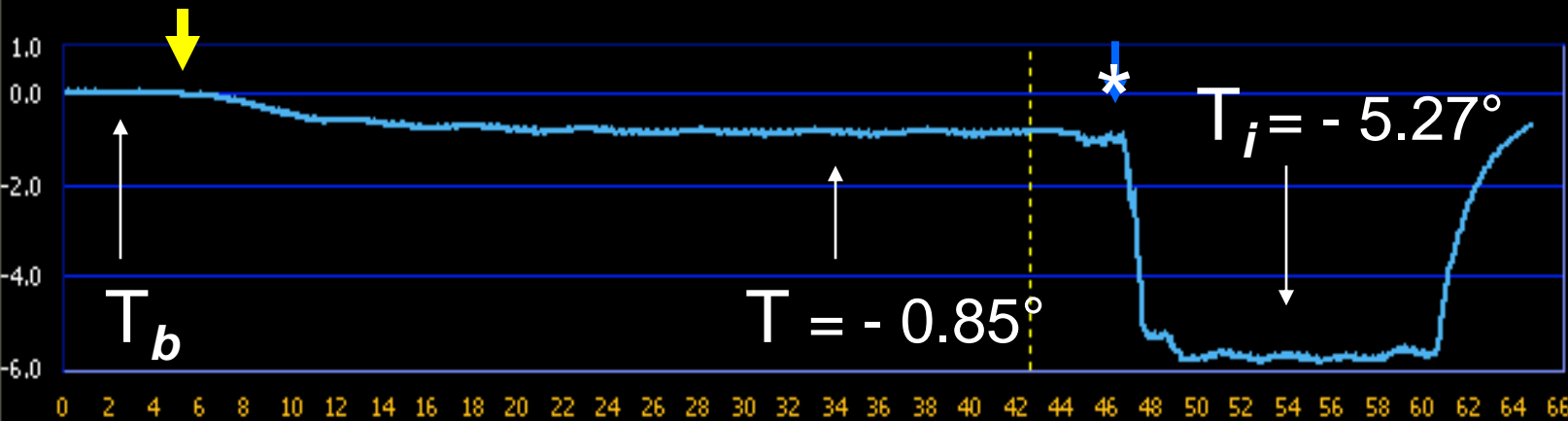
0.86 TTR

-0.85 dT

42.5 CURSOR



RESET



$Q_b = 134 \text{ ml/min} \rightarrow \text{normal max flow} = 100/86 \times 134 = 156 \text{ ml/min}$   
*Absolute microvascular resistance =  $P_d / Q$  (x80.000) = 380 Wood Units*

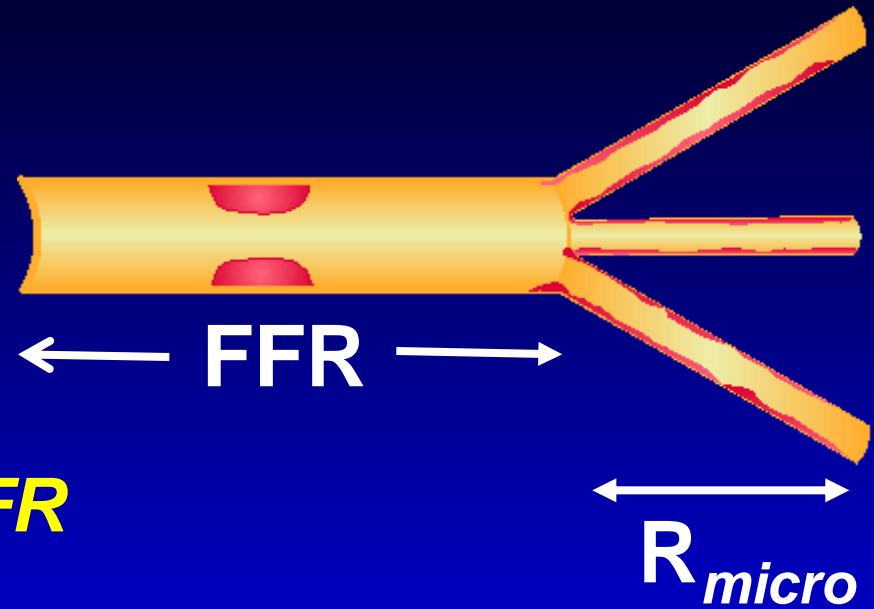
# ***A NEW WINDOW TO THE CORONARY MICROCIRCULATION***

***You like to learn more about this new technique....?***

***→ Wednesday 5 p.m SYMPOSIUM ROOM 2A, level3***

***“A NEW WINDOW TO THE MICROCIRCULATION”***

# SUMMARY: HOW TO KEEP IT SIMPLE..... (1)



## EPICARDIAL DISEASE: FFR

- Workhorse in the CathLab for decision making
- extensively validated in almost all angiographic & clinical conditions (MVD, ACS & STEMI, LM, proxLAD, post-PCI)
- only index which is incontrovertibly related to **better outcome**
- in some conditions: resting indices or hybrid approach (*i*FFR or Pd/Pa, or cFFR), but some caveats

**MICROVASCULAR DISEASE : IMR → Absolute R<sub>micro</sub>**