Coronary Physiology: New Insights

Coronary Microvascular Dysfunction: *Invasive Evaluation*

TCT Asia Pacific
Incheon, April 26th, 2024

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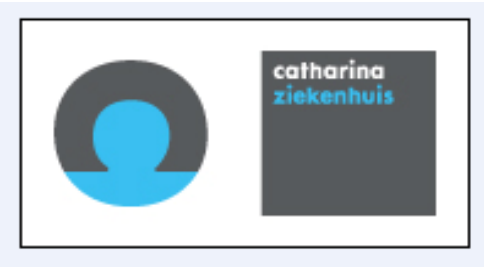


Disclosure

- Institutional Research Grants from Abbott
- Consulting relations and fees from Abbott and Coroventis
- Minor equity in Philips, ASML, Heartflow, and General Electric
- Member of the Scientific Advisory Board of Heartflow
- Patents pending in the field of the Coronary Microcirculation and Aortic Valve Stenosis.

The coronary microcirculation:

- In the last 20 years, awareness arose that - *in particular in women* – angina pectoris and coronary ischemia are not the exclusive domain of the epicardial arteries, but that also disease of the coronary microcirculation may play an important role

- This can be mainly restricted to the microcirculation itself (***ANOCA, MINOCA***) or in combination with frank epicardial disease (*persisting complaints after successful PCI*)

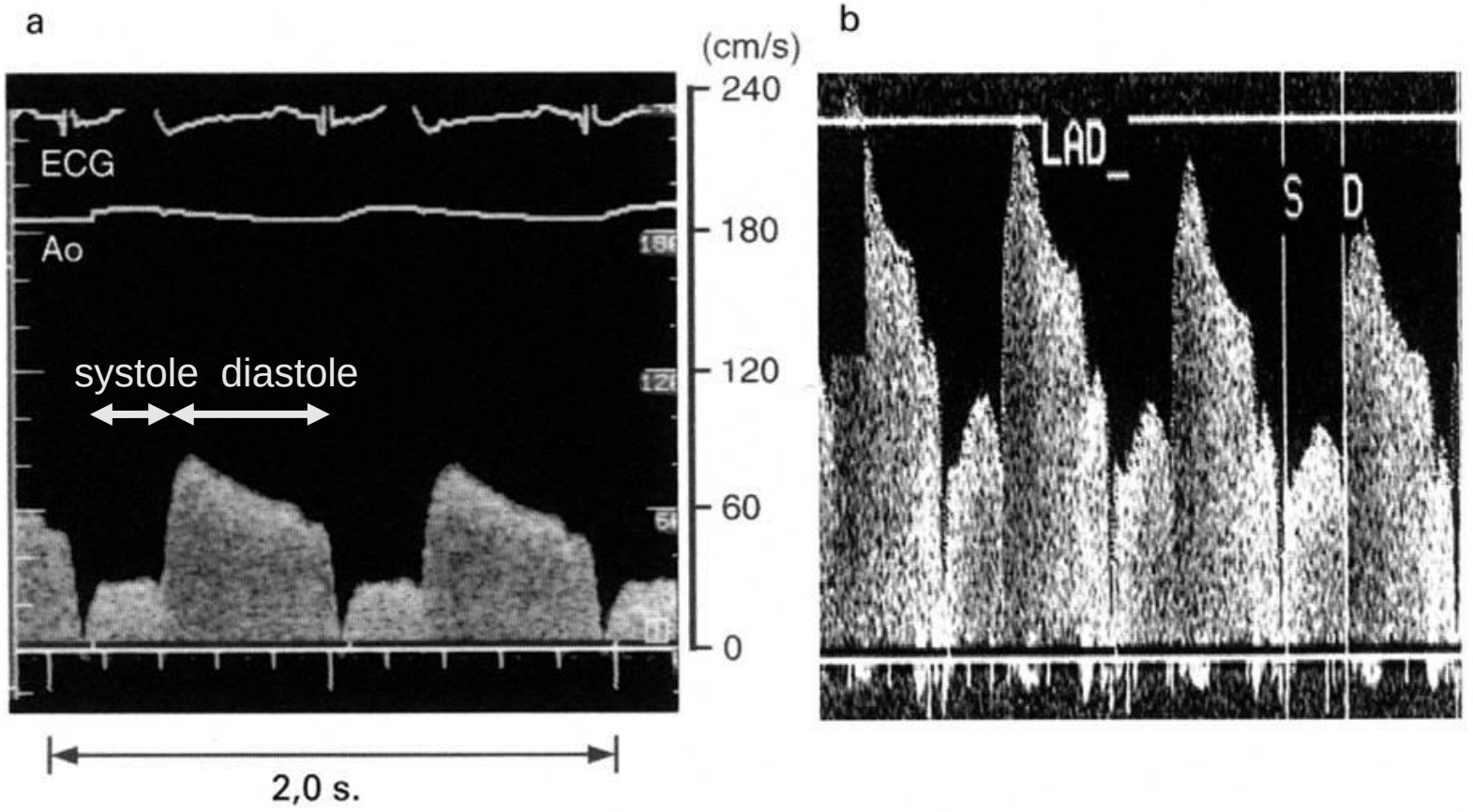
- Presently, it is believed that this may be the case in at least 25% - 40 % of all patients.

- Microcirculatory disease can be ***structural*** (generalized atherosclerosis, post-MI, micro-emboli, LVH, etc), or ***functional*** (microcirculatory spasm or blunted dilatation in response to physiologic intrinsic transmitters) or a combination of both

How to assess microvascular disease invasively ??

- ***Doppler*** ⟶ ***CFR***
- ***Bolus thermodilution*** ⟶ ***IMR***
- ***Continuous Thermodilution*** ⟶ ***absolute blood flow & resistance; MRR***

Doppler guidewire (1989, ***Morton Kern)*** measures intracoronary blood flow velocity and investigates ***CF(V)R*** in humans as a measure of functional stenosis severity.



Flow velocity signals in a coronary artery at resting conditions and at maximum hyperemia

The Doppler wire was a great step forward and enabled the first time acquisition of CF(V)R

However …….

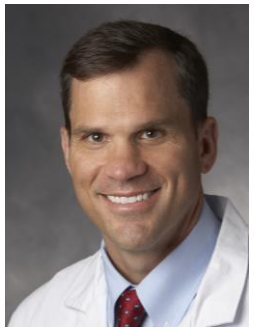
- ***CFR is not a specific index*** for the microcirculation but also influenced by (hidden or overt) epicardial disease

- *CFR can vary considerably within one patient* due to changes in "resting flow" and blood pressure, making interpretation of CFR rather difficult.

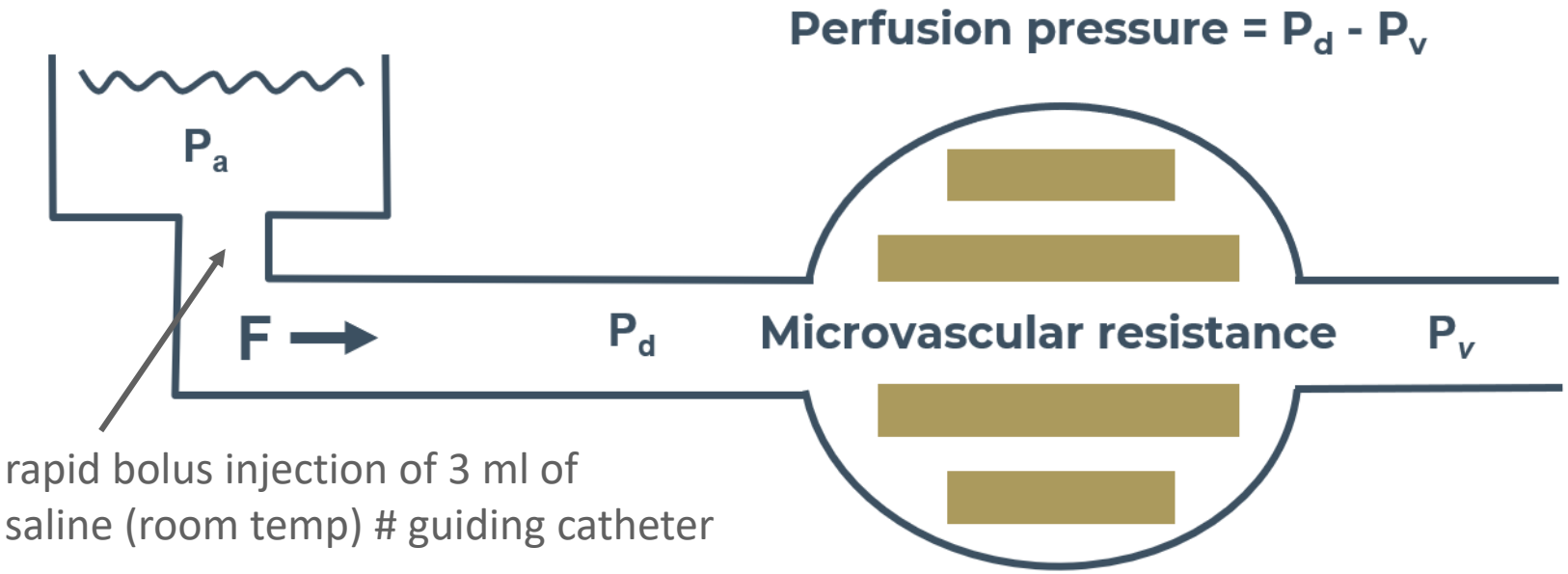
- CFR by Doppler is *often difficult to measure* reliably: in at least 30% of patients no reliable tracing could be obtained *("week 22 study")*

……...and the necessity was felt to have an index which is more specific for the microcirculation and easier to measure

⟶ ***Index of Microvascular Resistance*** *by bolus thermodilution (Fearon 2001)*



Concept of index of microcirculatory resistance (IMR)



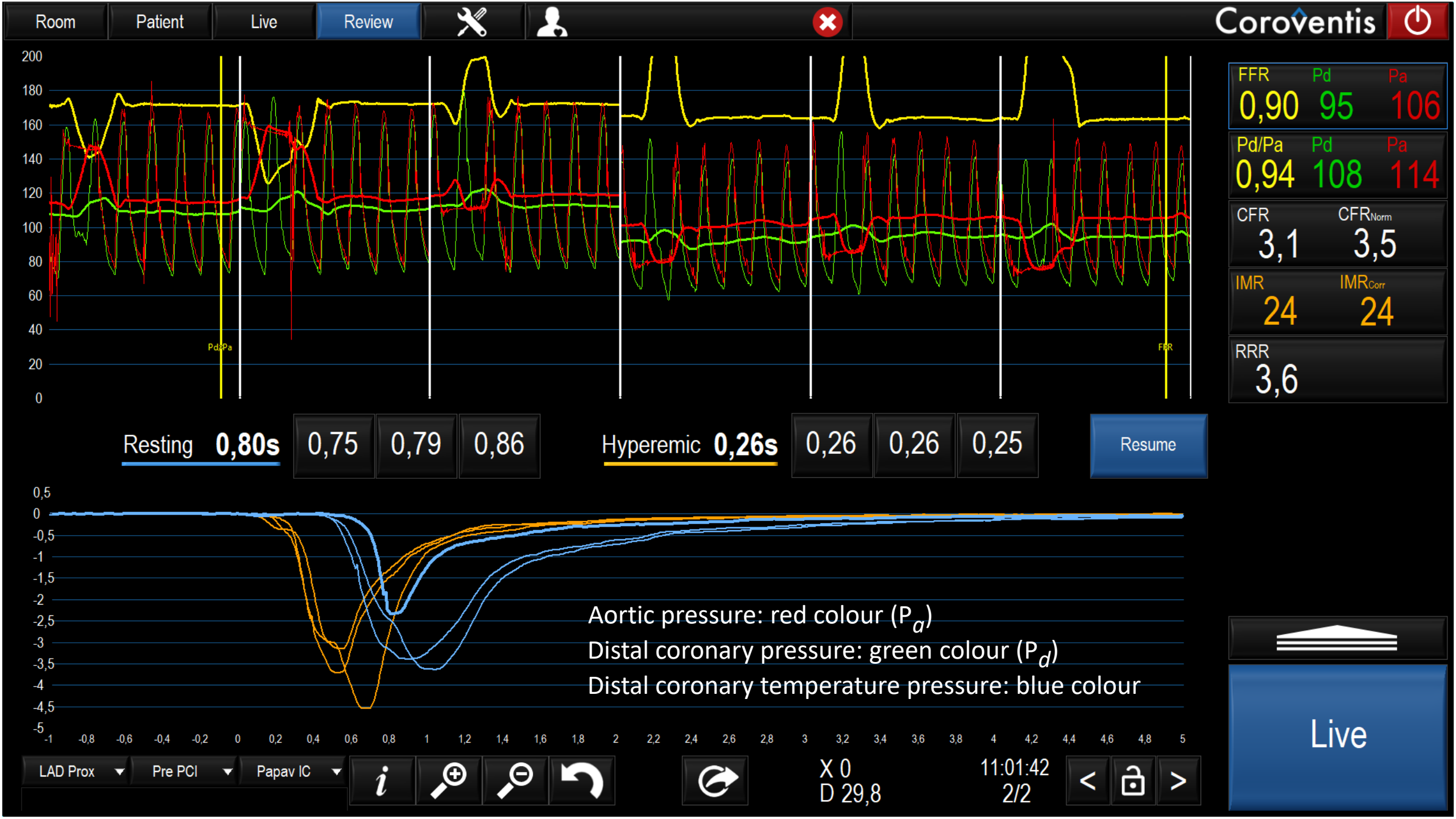
IMR

Microvascular resistance = distal pressure / flow

at maximum hyperemia: ≈ hyperemic distal pressure x hyperemic T*mn*

→ **IMR ≈ P*d* x T*mn***

Fearon WF et al. Circulation. 2003;107:3129–3132


Room
Patient
Live
Review
Coroventis
200
180
160
140
120
100
80
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40
20
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Pd/Pa
FFR
FFR
0,90
Pd
95
Pa
106
Pd/Pa
0,94
Pd
108
Pa
114
CFR
3,1
CFRNorm
3,5
IMR
24
IMRCorr
24
RRR
3,6
Resting 0,80s
0,75
0,79
0,86
Hyperemic 0,26s
0,26
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0,25
Resume
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Aortic pressure: red colour (Pa)
Distal coronary pressure: green colour (Pd)
Distal coronary temperature pressure: blue colour
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2/2
Live

Index of Microcirculatory resistance (IMR):

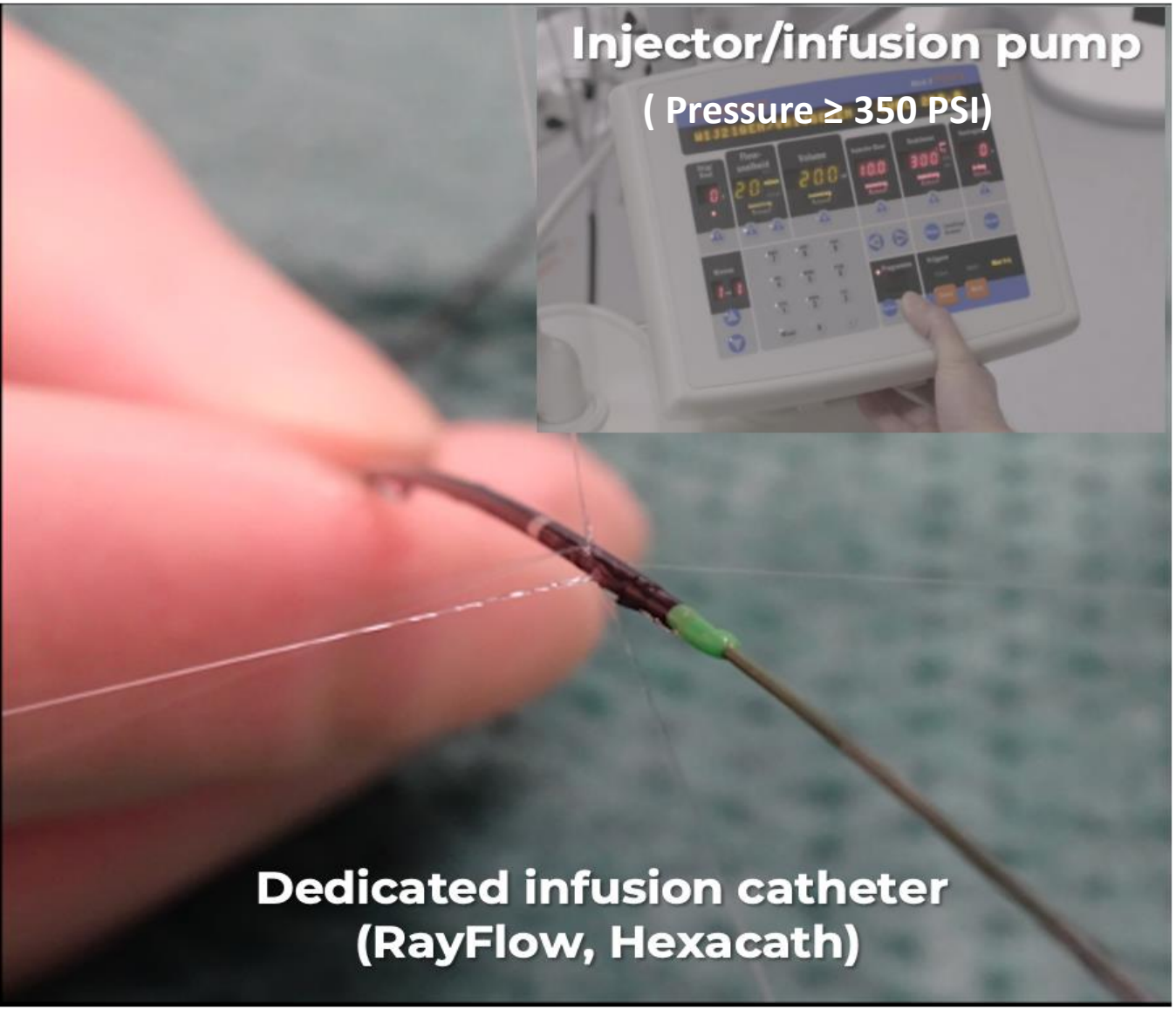
- Is rather specific for the microcirculation
- but needs correction at higher degree of coronary stenosis *(Aarnoudse, Yong)*
- has been shown to have *prognostic significance, both in stable angina and post- STEMI*
- and was the best we had during almost 20 years, but….

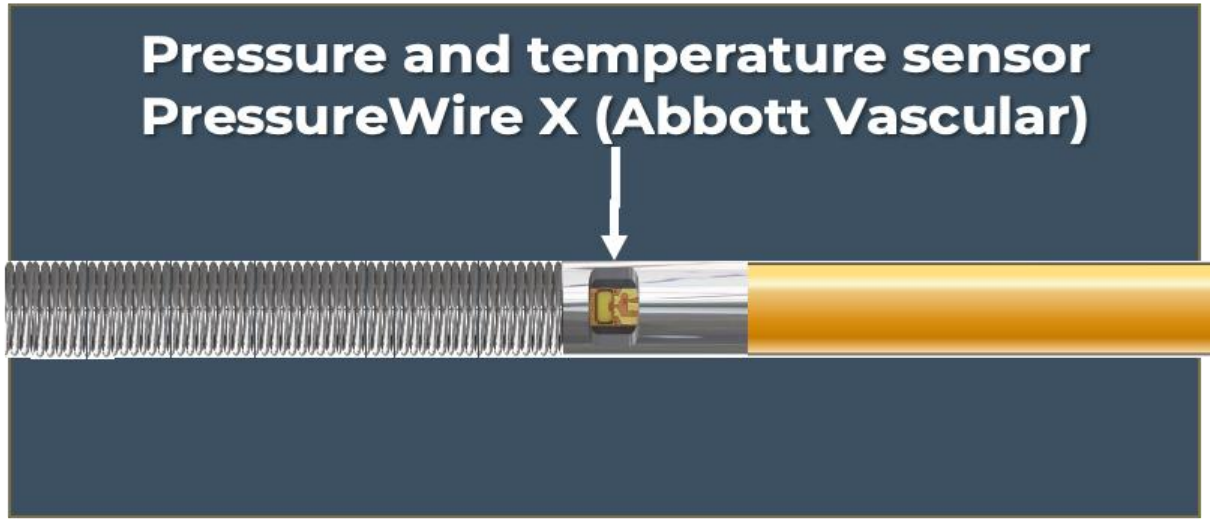
- *its reproducibility is far from optimal*
- *not always easy to determine (multiple repeated injections of saline)*
- *no direct measurement of microvascular resistance (R_μ)*

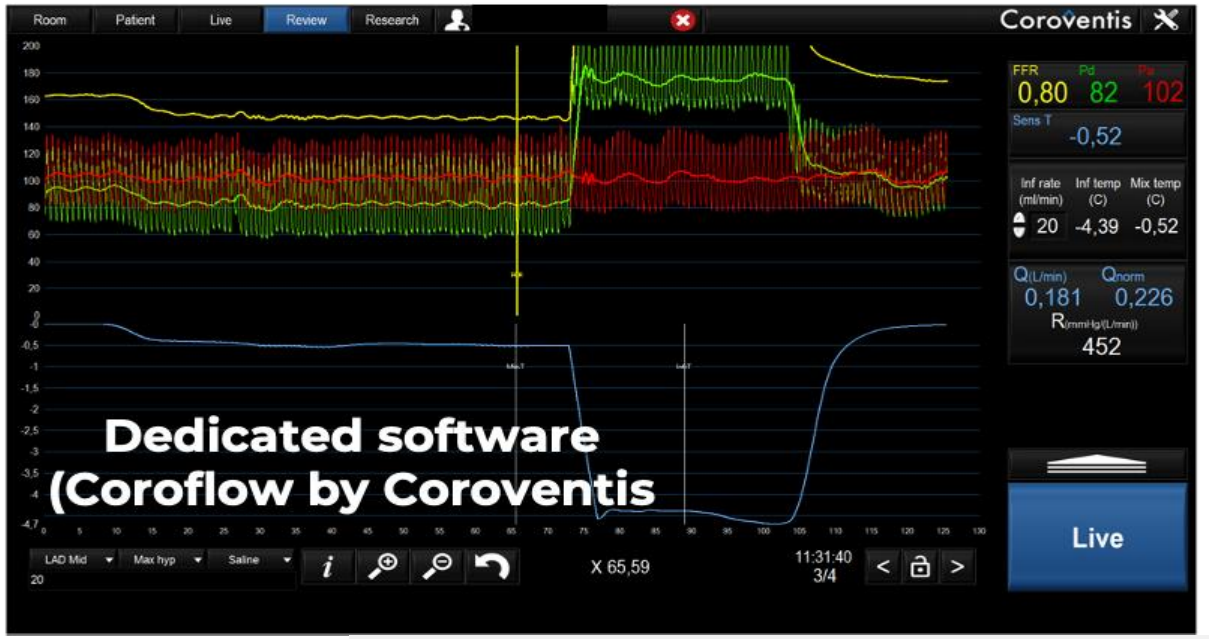
→ ***Volumetric measurent of absolute flow (Q) and microvascular resistance (R_μ)***

and Microvascular Resistance Reserve (MRR)

Continuous thermodilution for absolute Q & R measurements: *equipment*

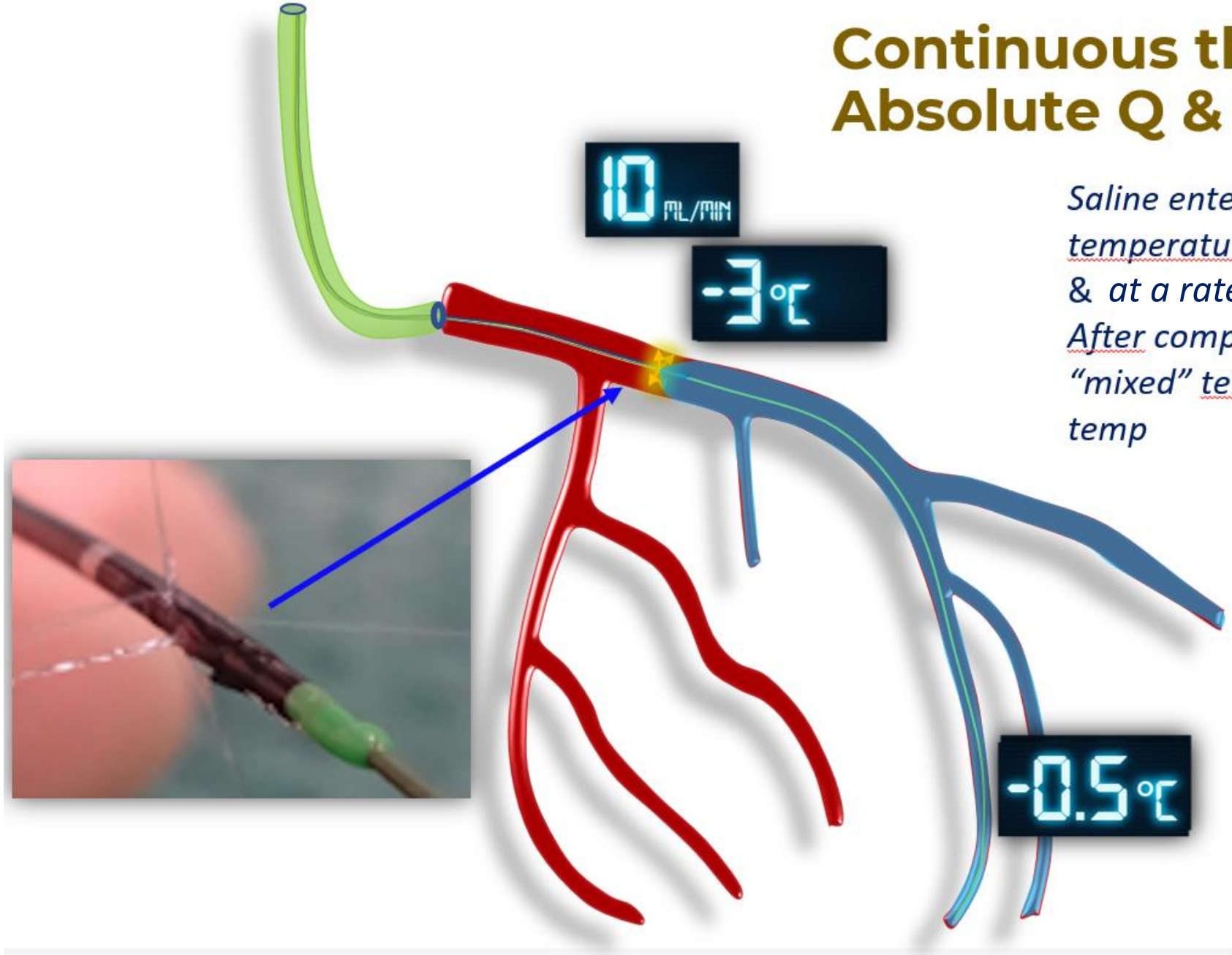






PressureWire (Abbott); Coroventis Sofware; Rayflow catheter (Hexacath); high-pressure infusion power pump (≥ 350 PSI)

Continuous thermodilution for Absolute Q & R measurements



Saline enters the proximal coronary artery at a temperature of 3°C below blood temperature & at a rate of 10 ml/min

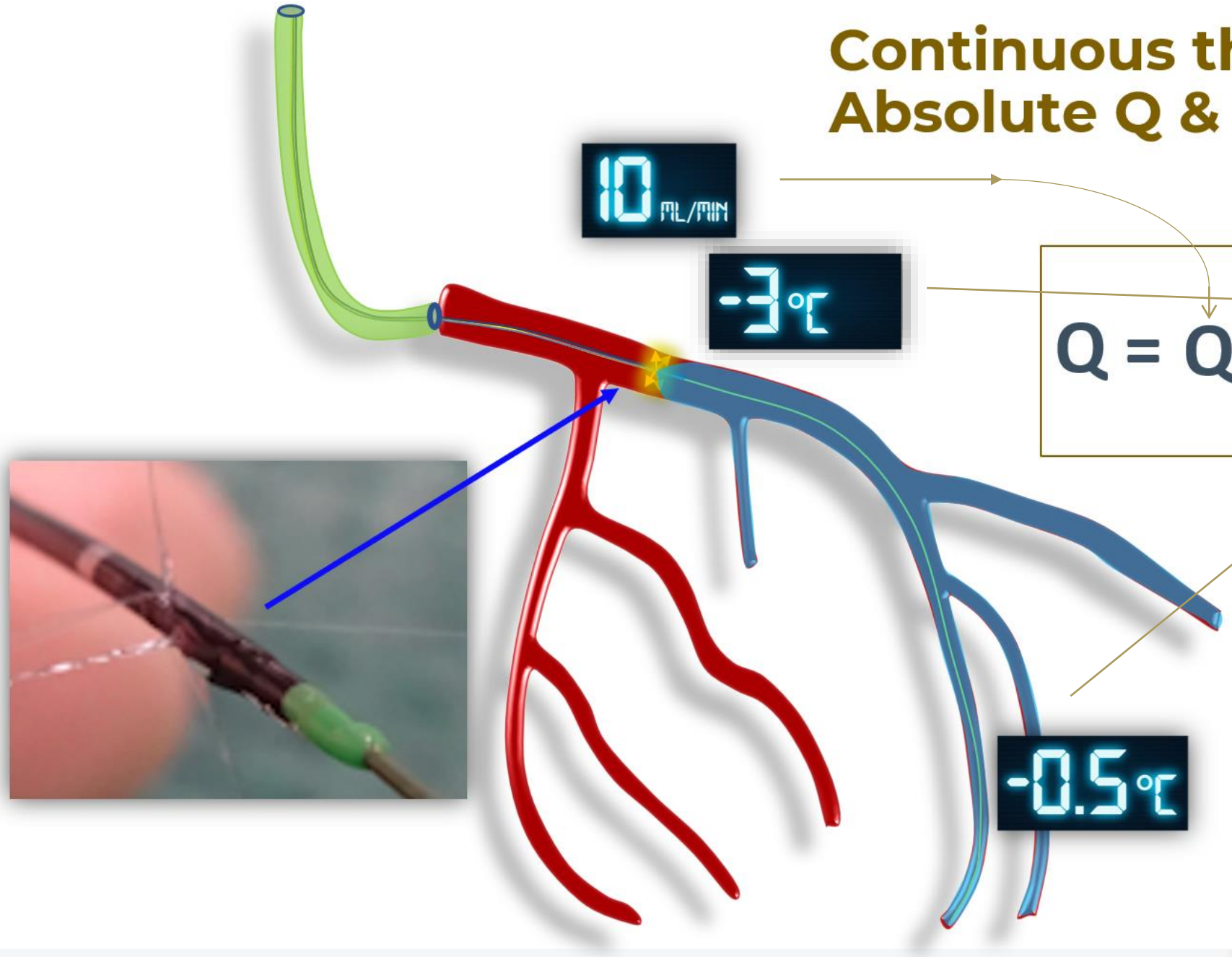
After complete mixing of blood and saline, the "mixed" temperature equals 0.5 °C below blood temp

Blood flow must be 6 x infusion flow of saline

60 ml/min

Suppose you are interesting in the flow and resistance of the complete LAD perfusion territory (anterior wall)…….

Continuous thermodilution for Absolute Q & R measurements



$$Q = Q_{saline} \times \frac{T_{saline}}{T_{mixture}} \quad X\ 1.08$$

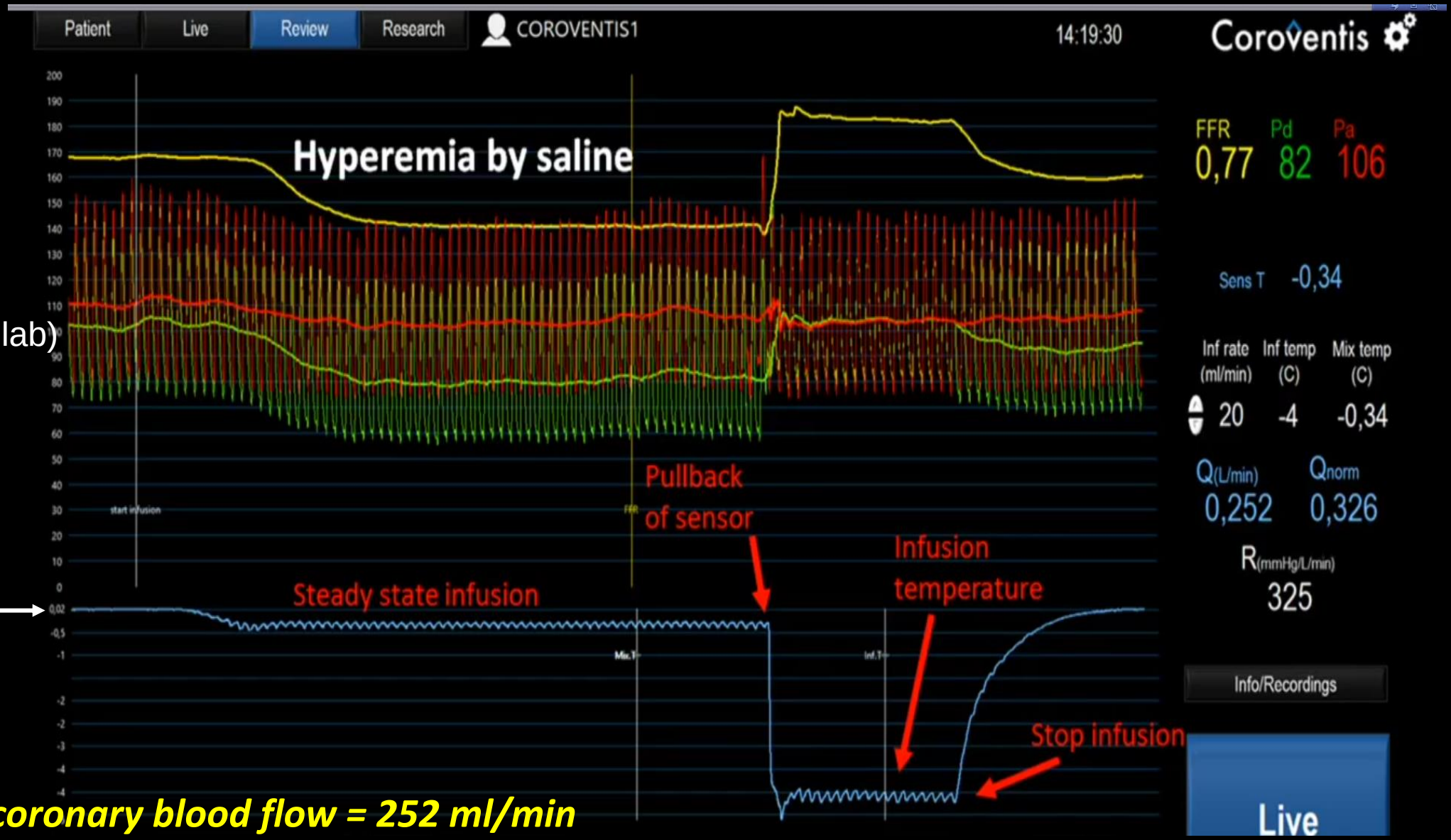
Q_{saline} is known infusion rate of saline (mL/min)

T_{saline} , T_{mix} are the **difference** vs body temperature (°C)

1.08 accounts for difference in **specific heats** of saline and blood

Example of one hyperemic run (20ml/min)

Coroventis software
(fully integrated in cath lab)



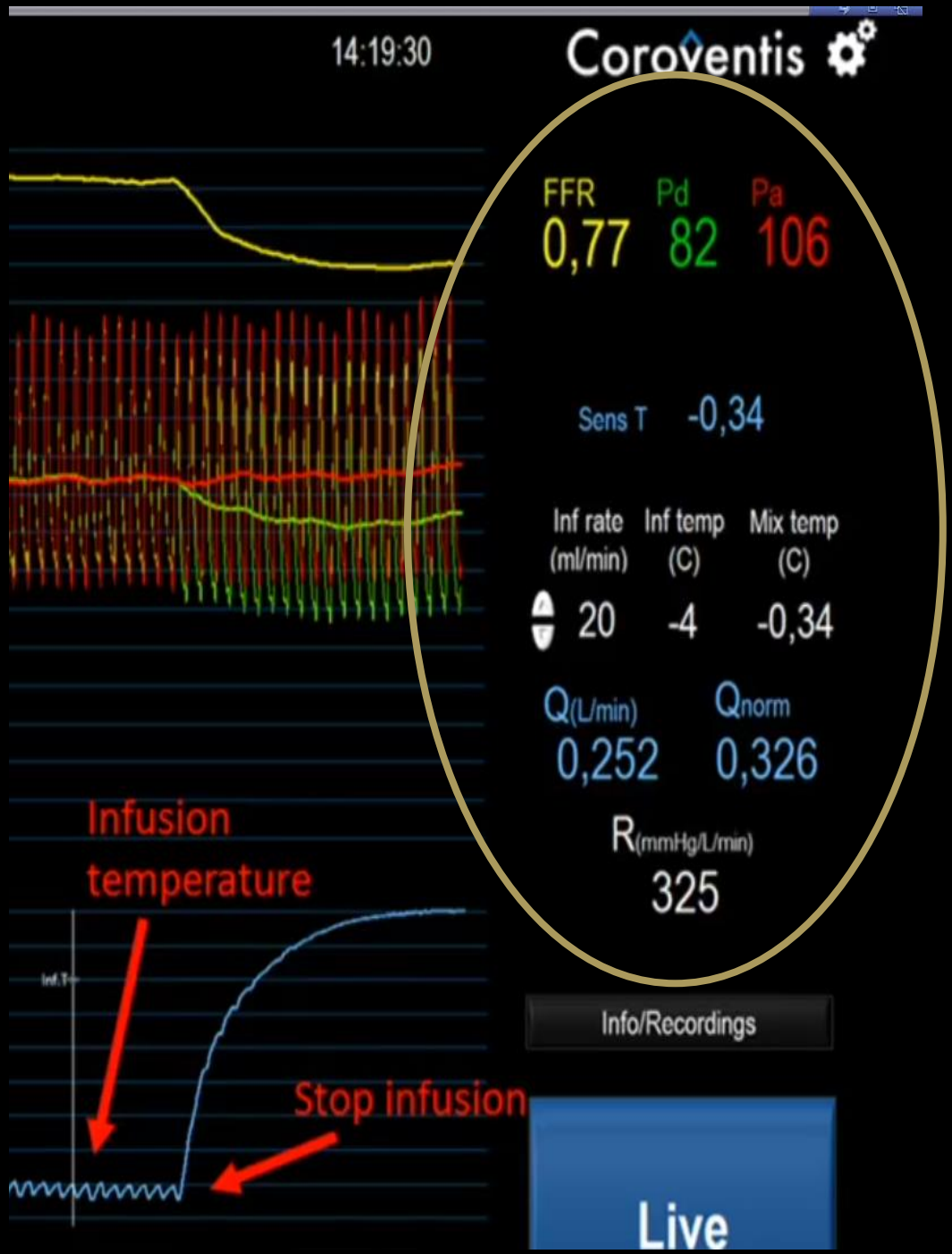
FFR = 0.77

maximum coronary blood flow = 252 ml/min

minimal microvascular resistance = 325 WU

All relevant parameters for epicardial artery and microcirculation are obtained within 5 minutes and clearly displayed in one nice simple screen, together with the normal values.

Can be done ***at rest (saline 10ml/min)*** *and at*
Full hyperemia (saline 20 ml/min)



Measurement of absolute microvascular resistance *

In conjunction with FFR, all flow and resistance measurements can be performed *within 5-10 minutes*:

- position the pressure/temp wire in the coronary artery
- advance the RayFlow® monorail multi-side holes infusion catheter (ultrathin profile)
- connect infusion catheter to saline pump and measure temperature in the distal coronary artery during steady state.
- Pull back pressure/temp sensor into tip of the RayFlow catheter for infusion temperature
- *10 ml/min = **resting** and 20 ml/min = **full hyperemia**)*

* ***Complete description of the technology: Belmonte et al, JACC 2024 (Februari 13th) 83; 699-709***

Absolute coronary Flow Measurement and Microvascular Resistance Reserve:

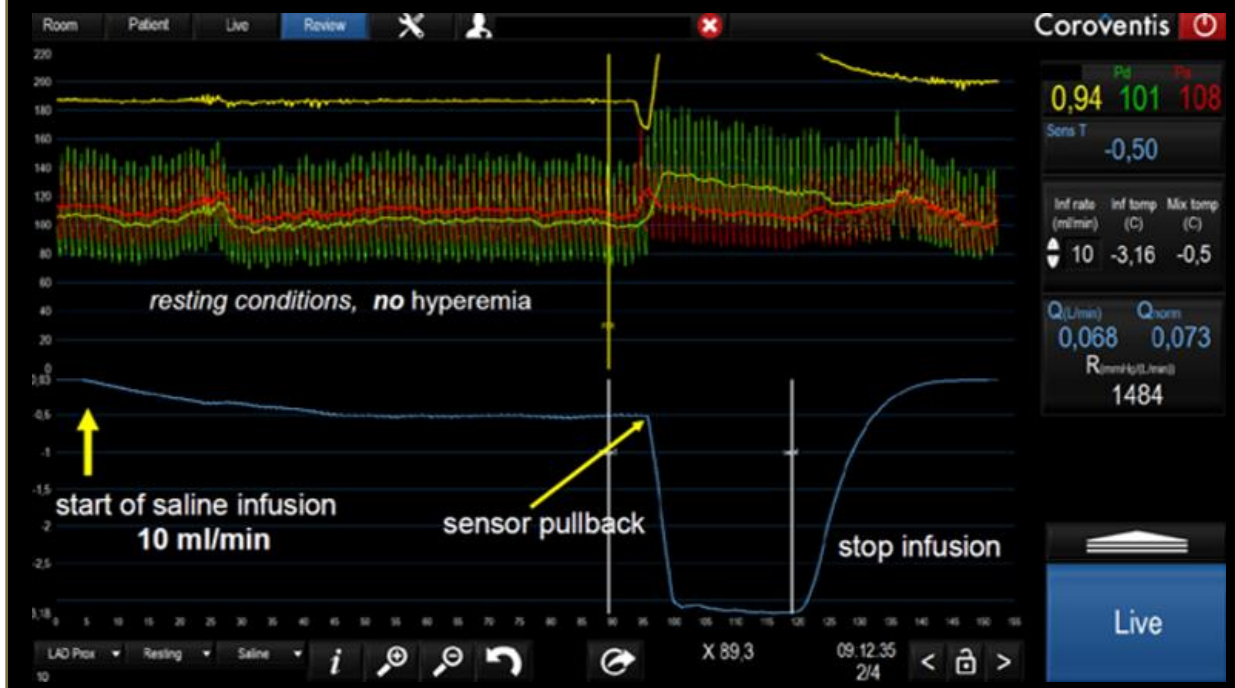
The Holy Grail of Coronary Physiology ?

- Can be measured at rest (Q_{rest}, $R_{\mu,rest}$) and at hyperemia (Q_{max} , $R_{\mu,hyper}$)
- No hyperemic drug needed because 20 ml/min of saline in itself creates maximum hyperemia
- ***FFR*** is automatically measured at the same time
- And therefore, also *normal reference values for Q and R* are known
- For the first time in history, direct invasive measurement of ***absolute CFR*** is possible
- And finally, also ***Microvascular Resistance Reserve (MRR)*** can be calculated, which is the most accurate, reproducible, and super-specific index of the coronary microcirculation.
- ***MRR*** is not affected by mass, epicardial disease, or hemodynamic variations and is *operator-independent and calculated from the measured data above automatically in 5 seconds*

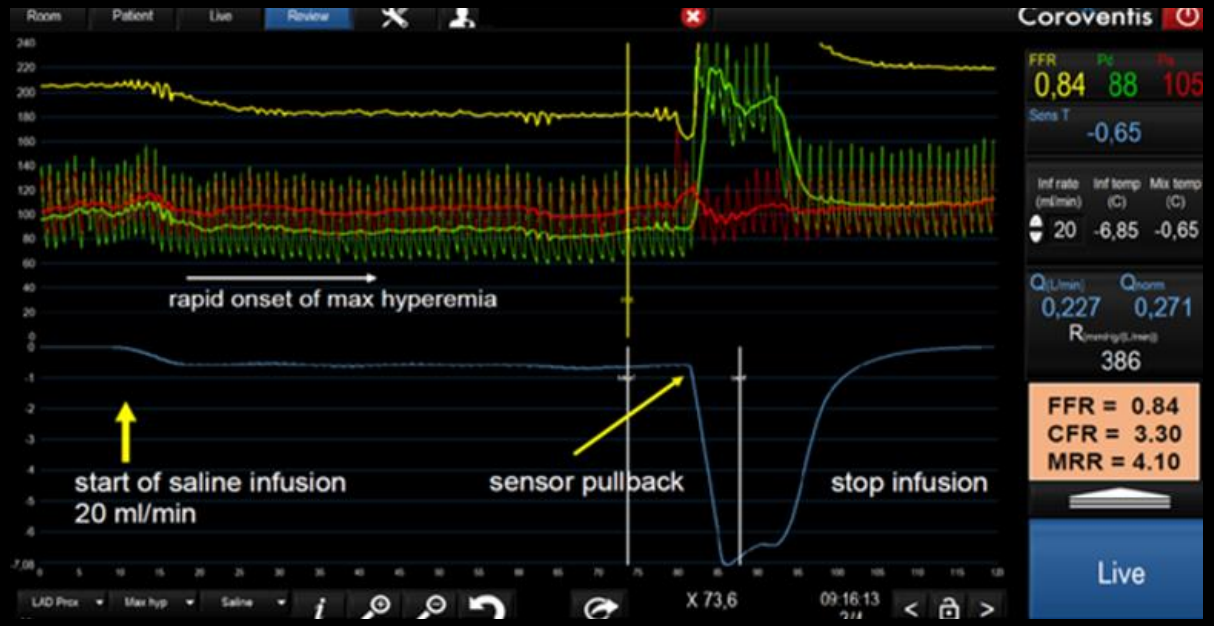
$$MRR = CFR / FFR \times P_{a,rest} / P_{a,hyp}$$

(unifying equation of coronary physiology)

De Bruyne, Pijls et al, JACC 2021; 78: 1541-1549



Resting flow measurement
(10 ml/min saline infusion)



hyperemic flow measurement
(20 ml/min saline infusion)

FFR = 0.84

(Absolute) **CFR = 227 / 68 = 3.30**

MRR = 3.30 / 0.84 x 108 / 105 = 4.1

Detailed description of the technology ("cookery book"): Belmonte et al, JACC 2024 (Februari 13th); 83: 699-709

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J Am Coll Cardiol. 2024 Feb, 83 (6) 699–709

Measuring Coronary Blood Flow And Microvascular Resistance By Thermodilution: JACC Review Topic of the Week

Valentin Fuster

February 5, 2024

-16:15

"… continuous thermodilution should be substituting Doppler flow velocity and bolus thermodilution-derived T_{mn} for the assessment of the microvasculature" ***(Valentin Fuster, 2024)***