

FFR

Standardisation and Hyperaemia

Bernard De Bruyne
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Hyperemic Stimuli

Why ?

How ?

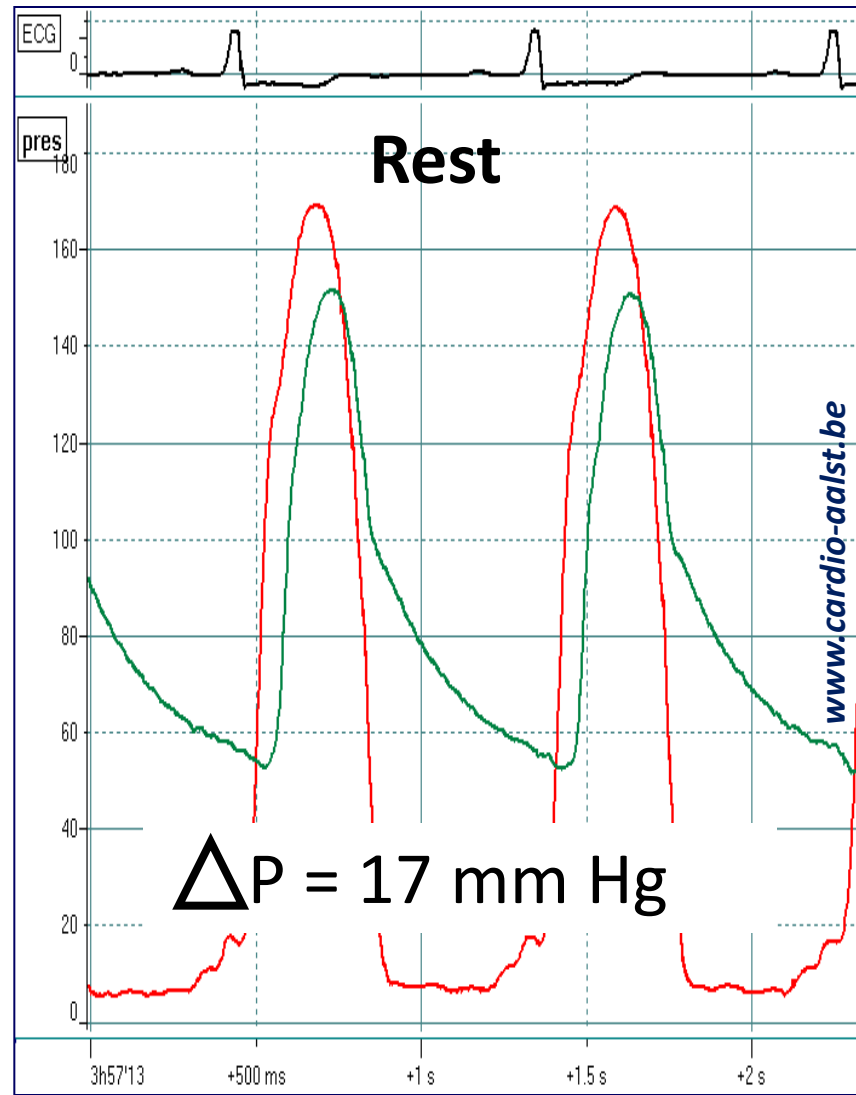
FAQ !

**Bernard De Bruyne, MD, PhD
Cardiovascular Center Aalst
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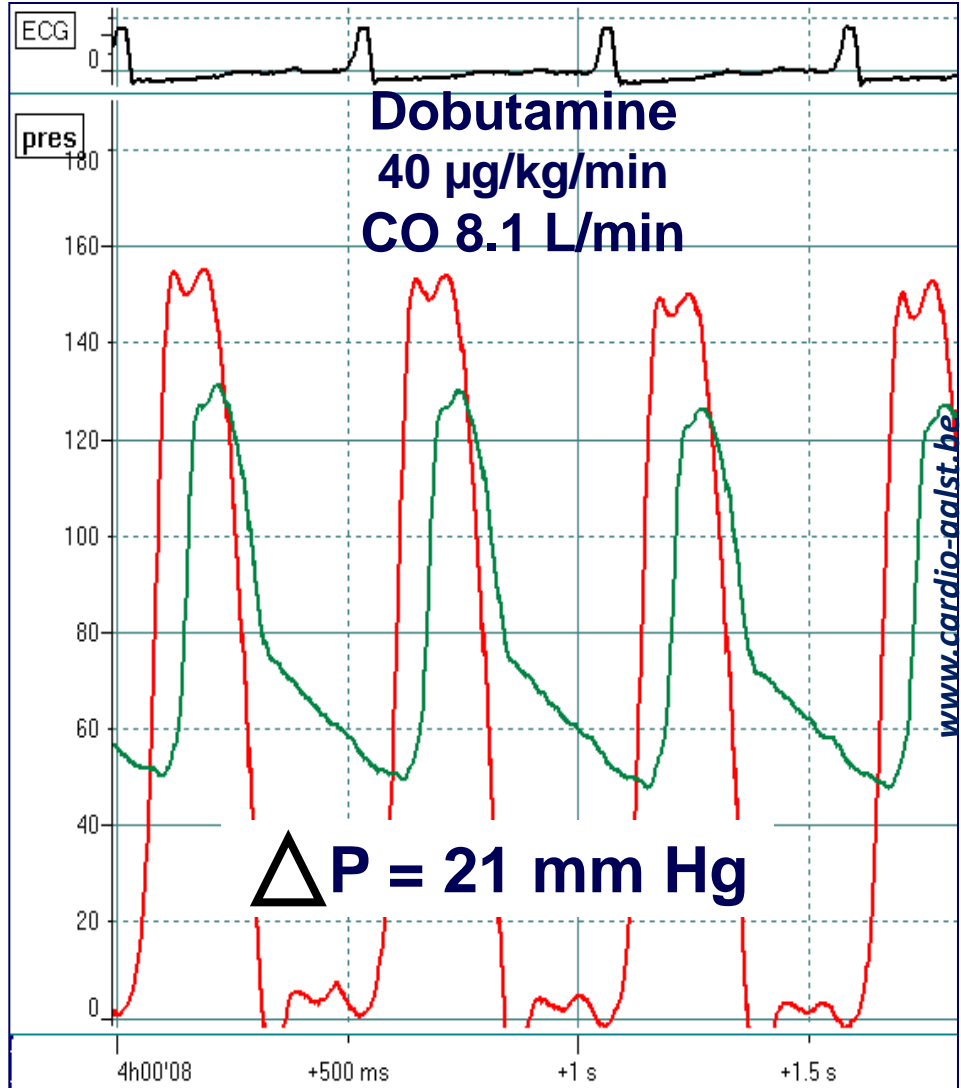
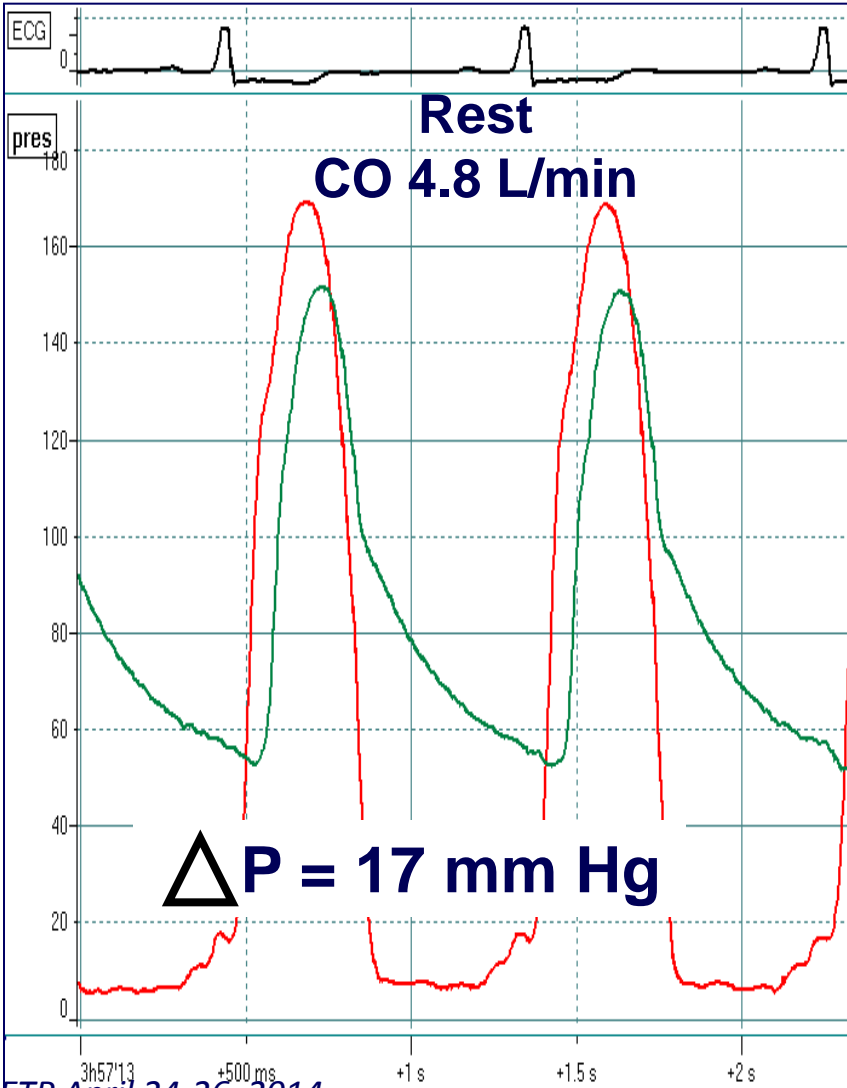
Why?

- 1. General concept of stress test (as opposed to “rest test”)**
- 2. Standardized measurements (as opposed to “moving target”)**
- 3. All clinical outcome data are based on hyperemic data**

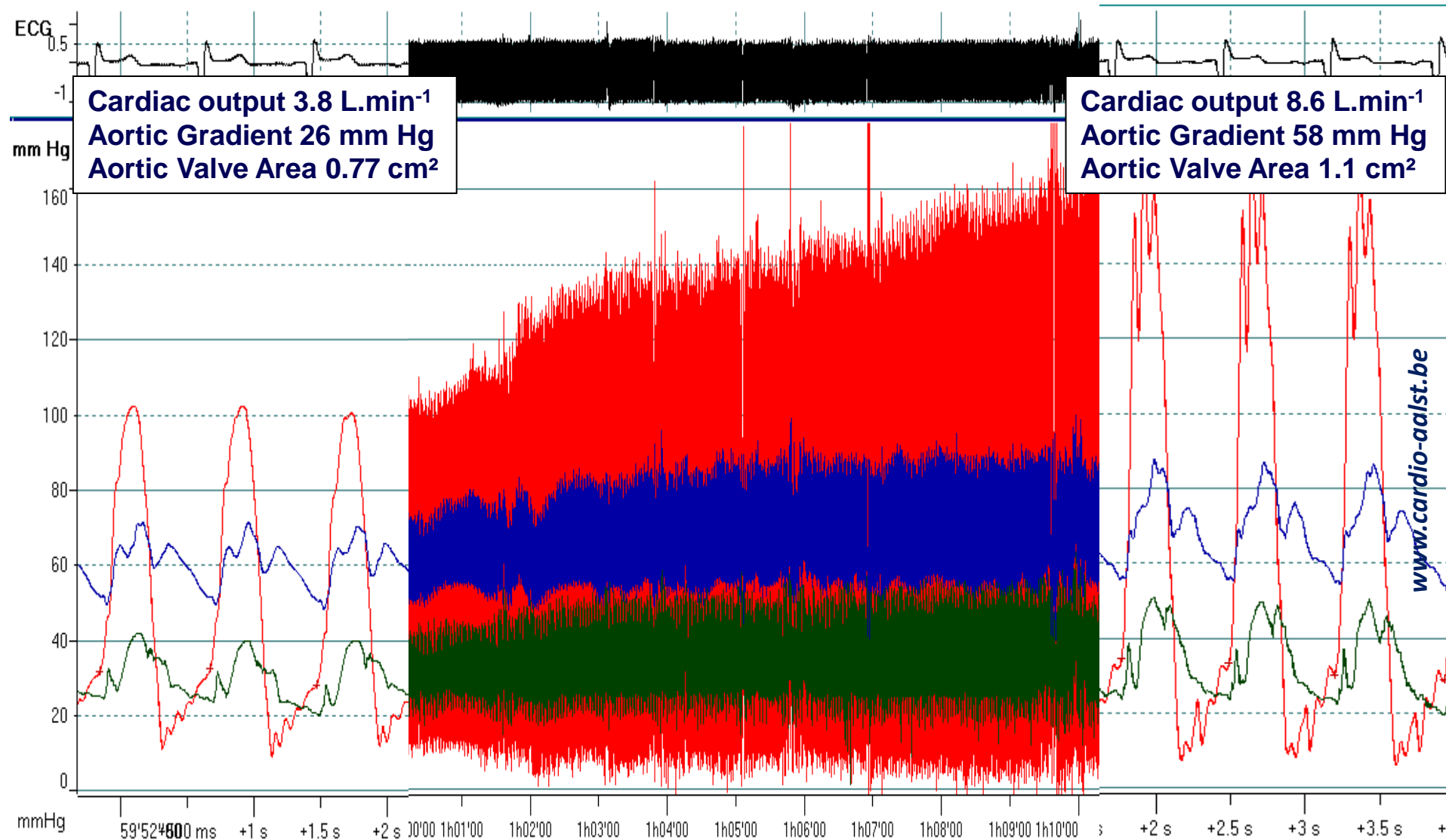
General concept of stress test Mild Aortic Stenosis



General concept of stress test Mild Aortic Stenosis

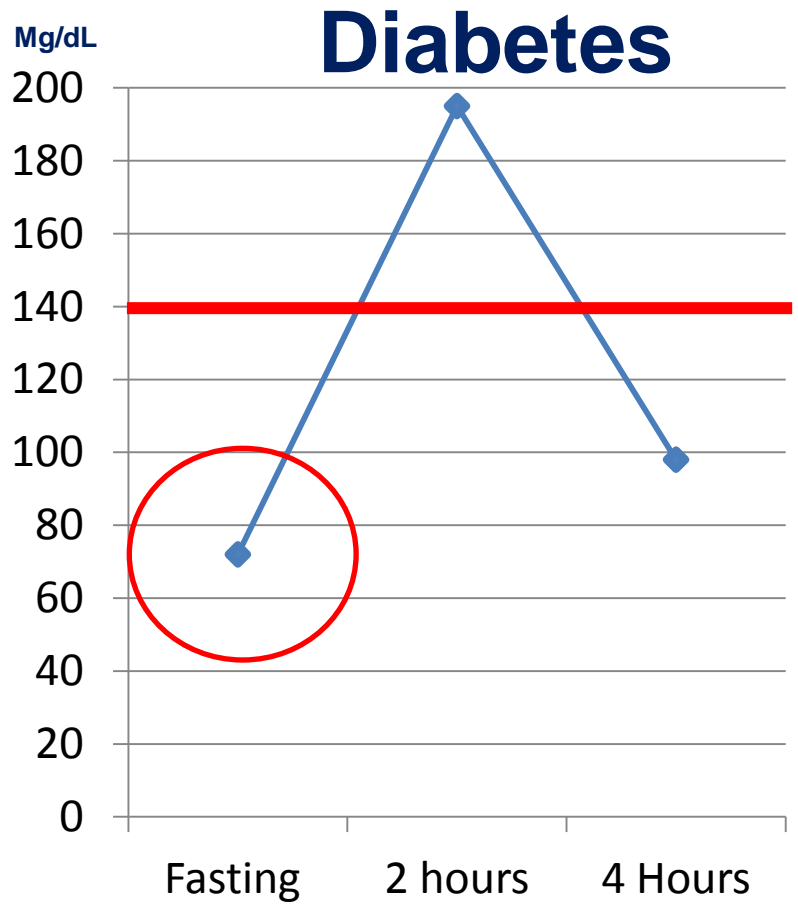
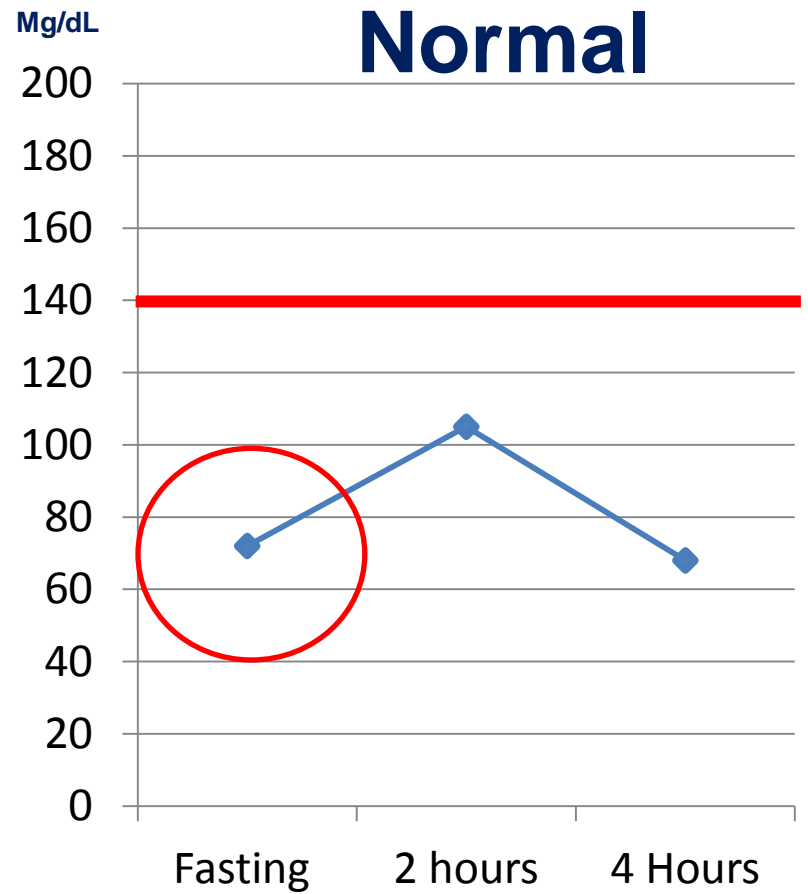


General concept of stress test Aortic Stenosis



General concept of stress test Diabetes

Oral Glucose Tolerance Test:
75 g of sugar to be drunk within 5 minutes



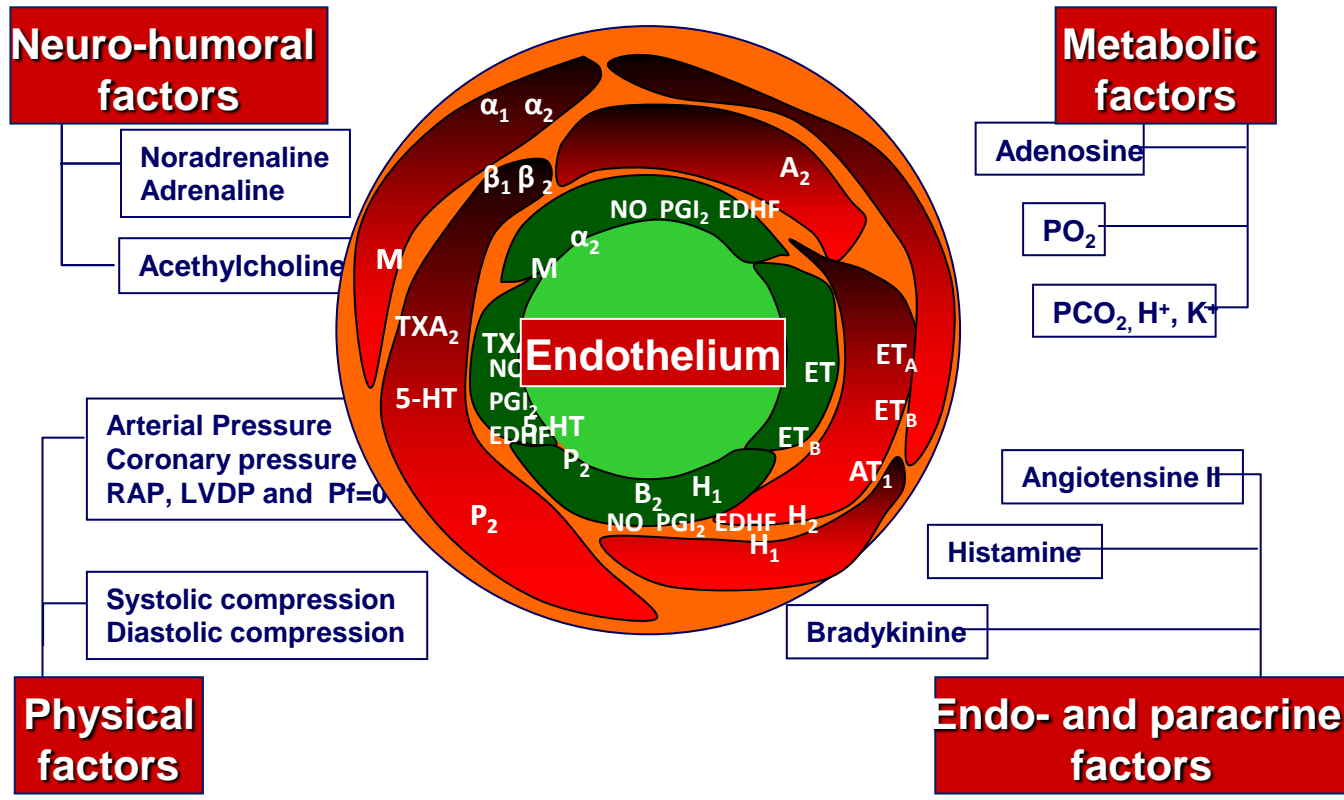
General concept of stress test The Wind Tunnel



Why?

1. **General concept of stress test (as opposed to “rest test”)**
2. **Standardized measurements (as opposed to “moving target”)**
3. **All clinical outcome data are based on hyperemic data (FFR)**

The Control of Resting Myocardial Blood Flow

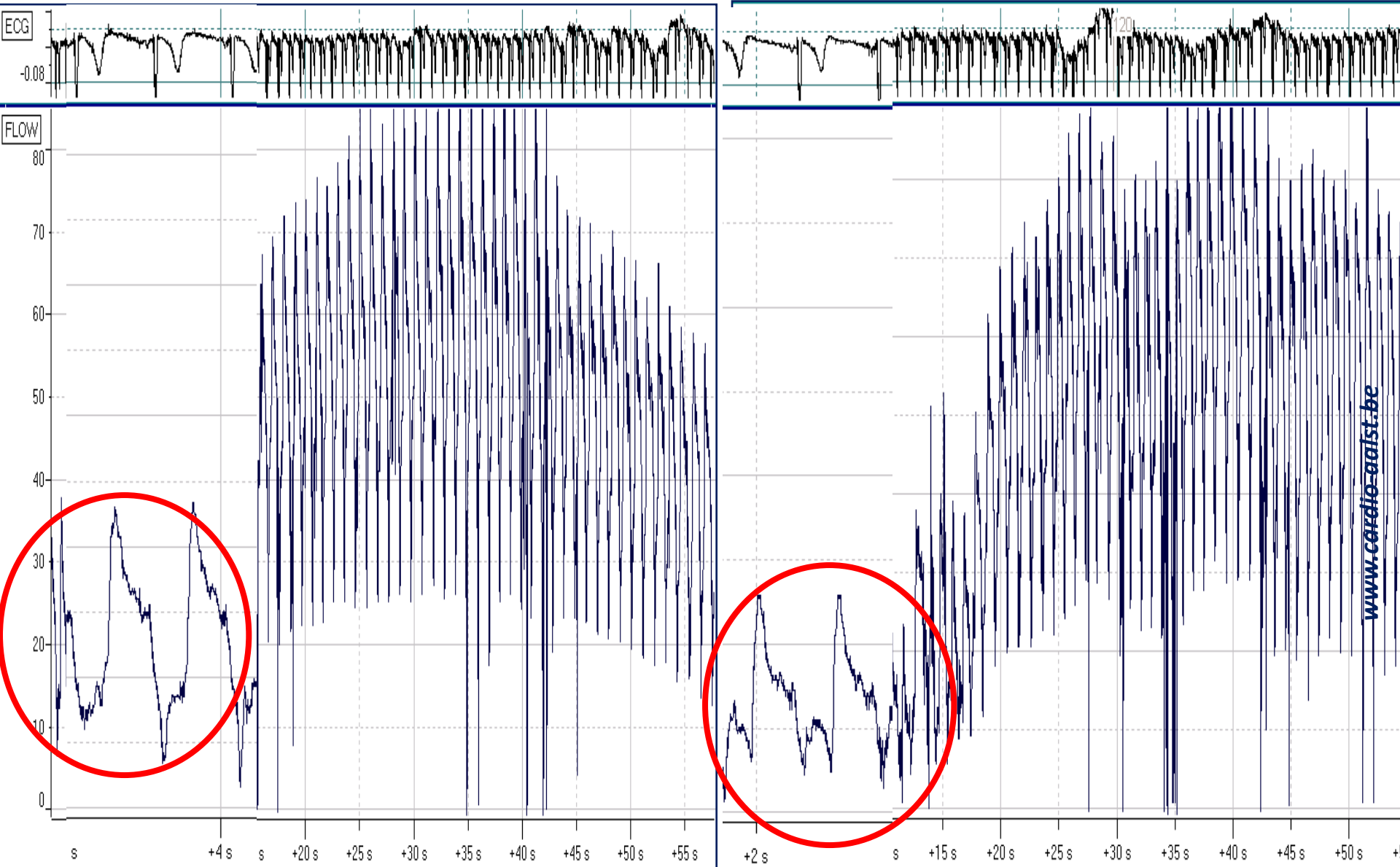


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The “resting state” in biology is wishful thinking of biologists

‘Rest’ is almost never ‘steady state’

The Control of Resting Myocardial Blood Flow



Why?

1. **General concept of stress test (as opposed to “rest test”)**
2. **Standardized measurements (as opposed to “moving target”)**
3. **All clinical outcome data are based on hyperemic data (FFR)**

How?

*“Keep it **Simple and Standardized**”*

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The KISS principle

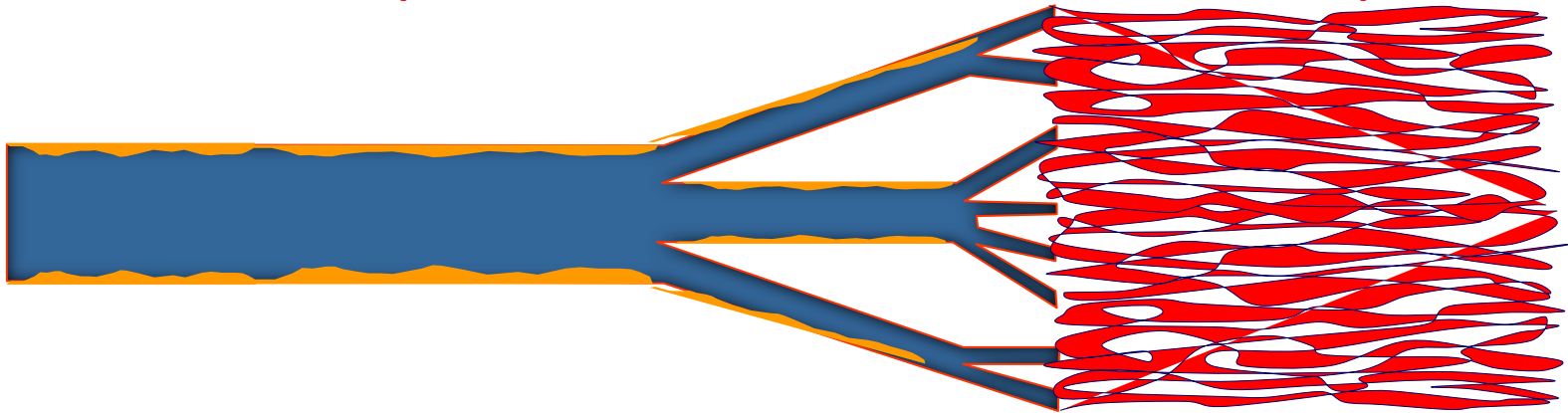
Maximal Vasodilation

Epicardial

= Conductance
Arteries $> 550 \mu$

Microvasculature

= Resistance
Arteries $< 550 \mu$



~~Vasospasm~~

~~Autoregulation~~

Maximal Vasodilation

1. Nitrates → Epicardial arteries

2. Adenosine → Microvasculature

➤ **IV: 140 $\mu\text{g}/\text{kg}/\text{min}$**

➤ **IC: 100 – 200 μg in bolus**

Maximal Vasodilation

1. Nitrates → Epicardial arteries

2. Adenosine → Microvasculature

3. Papaverine
4. Regadenoson
5. Apadenoson
6. Binodenoson
7. Nitroprusside
8. Nicorandil
9. Dopamine
10. Exercise
11. Coronary occlusion

inhibition of phosphodiesterase → cyclic **adenosine** MP ↑
precursor of **adenosine**
precursor of **adenosine**
precursor of **adenosine**
NO pathways direct non-selective vasodilator
↑ guanylate cyclase to increase formation of cyclic GMP
 β_1 -agonist → ↑ O₂ consumption → **adenosine** ↑
Adren stimulation → ↑ O₂ consumption → **Adenosine** ↑
Ischemia → release of **adenosine**

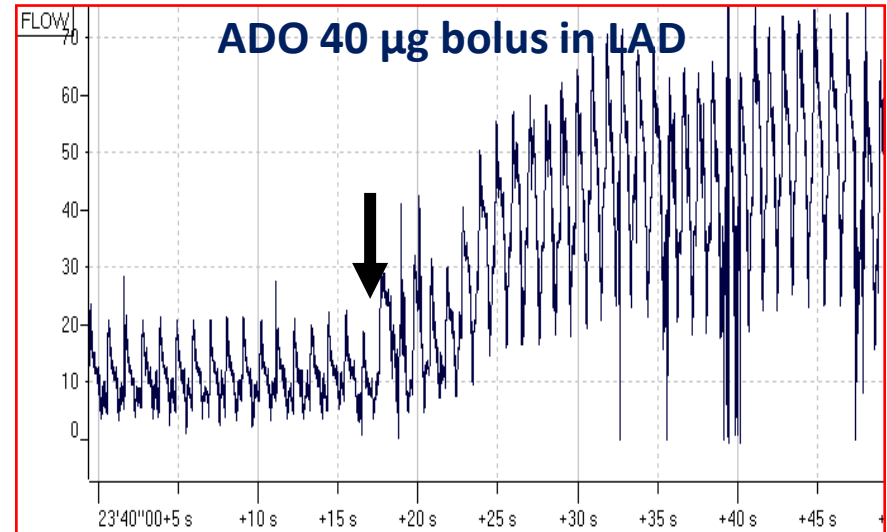
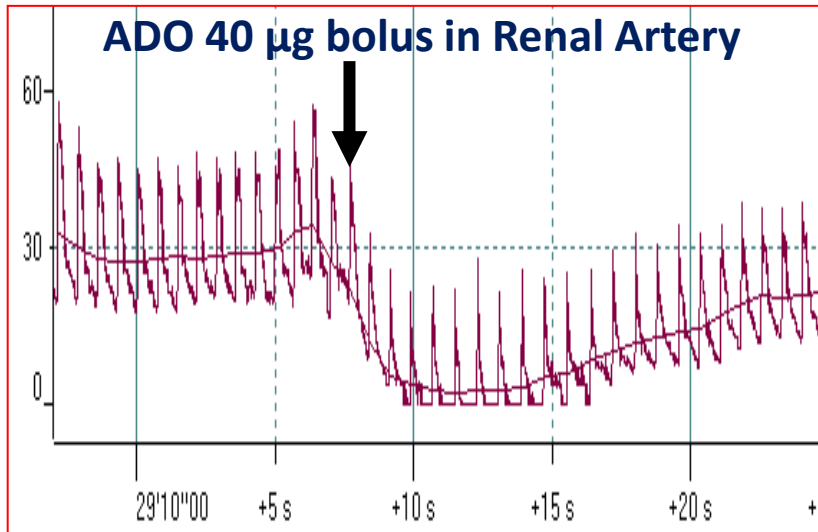
Adenosine: Mechanisms of Action

Target organs

- Coronary arteriolar smooth muscle cells
- Renal arteries (organ level)
- Peripheral and central nervous system
- Myocardium
- Cardiac Conduction system
- Respiratory tract
- Fibroblast, Adipocytes, Immune System

Receptors (A_1 , A_{2A} , A_{2B} , A_3)

A_{2A}
 A_1
 $A_1 A_{2A}$
 A_3
 A_1
 A_1
 A_{2B}



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Half Life = 4 to 10 s

Maximal Vasodilation

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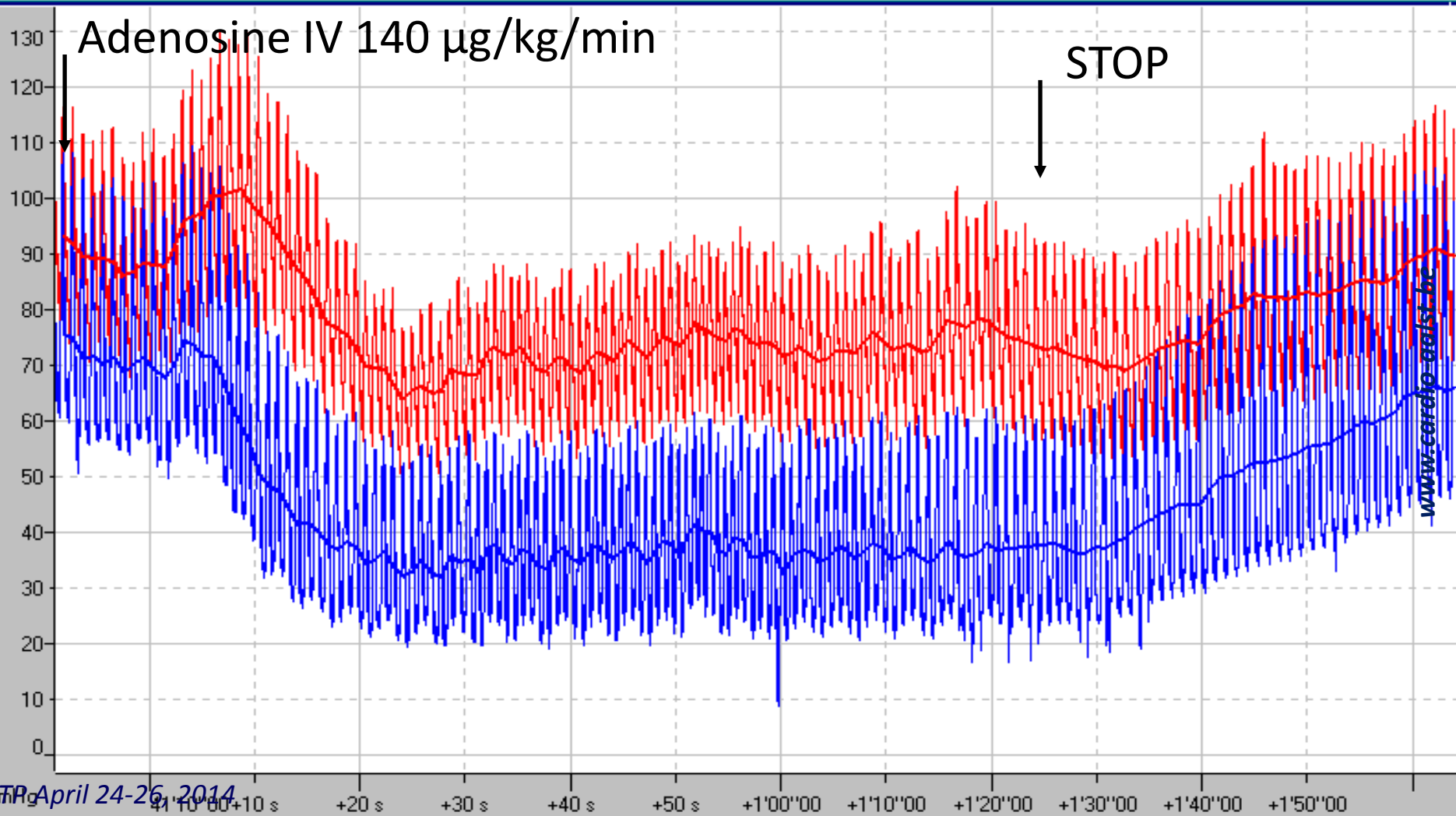
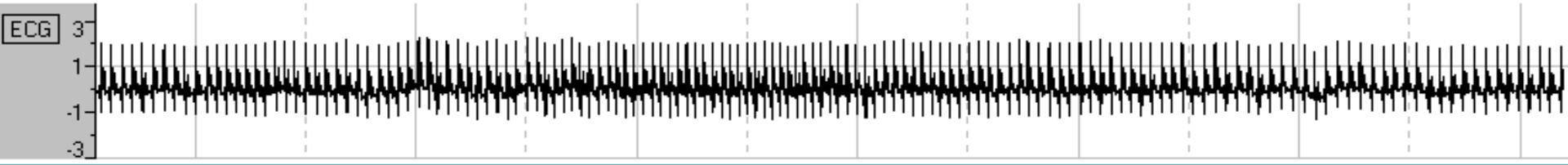
➤ **IV: 140 $\mu\text{g}/\text{kg}/\text{min}$**

➤ **IC: 100 – 200 μg in bolus**

Adenosine IV

Specificities of **IV Adenosine** (140 µg/kg/min)

1. Preferred route when a pressure pull back is needed
2. Induces a brief increase in systemic pressure followed by a decrease in systemic pressure by 10-20%
3. Is almost uniformly accompanied by a burning sensation
4. Fluctuation of the P_d/P_a ratio are observed in some cases
5. A-V blocks are relatively frequent, always transient

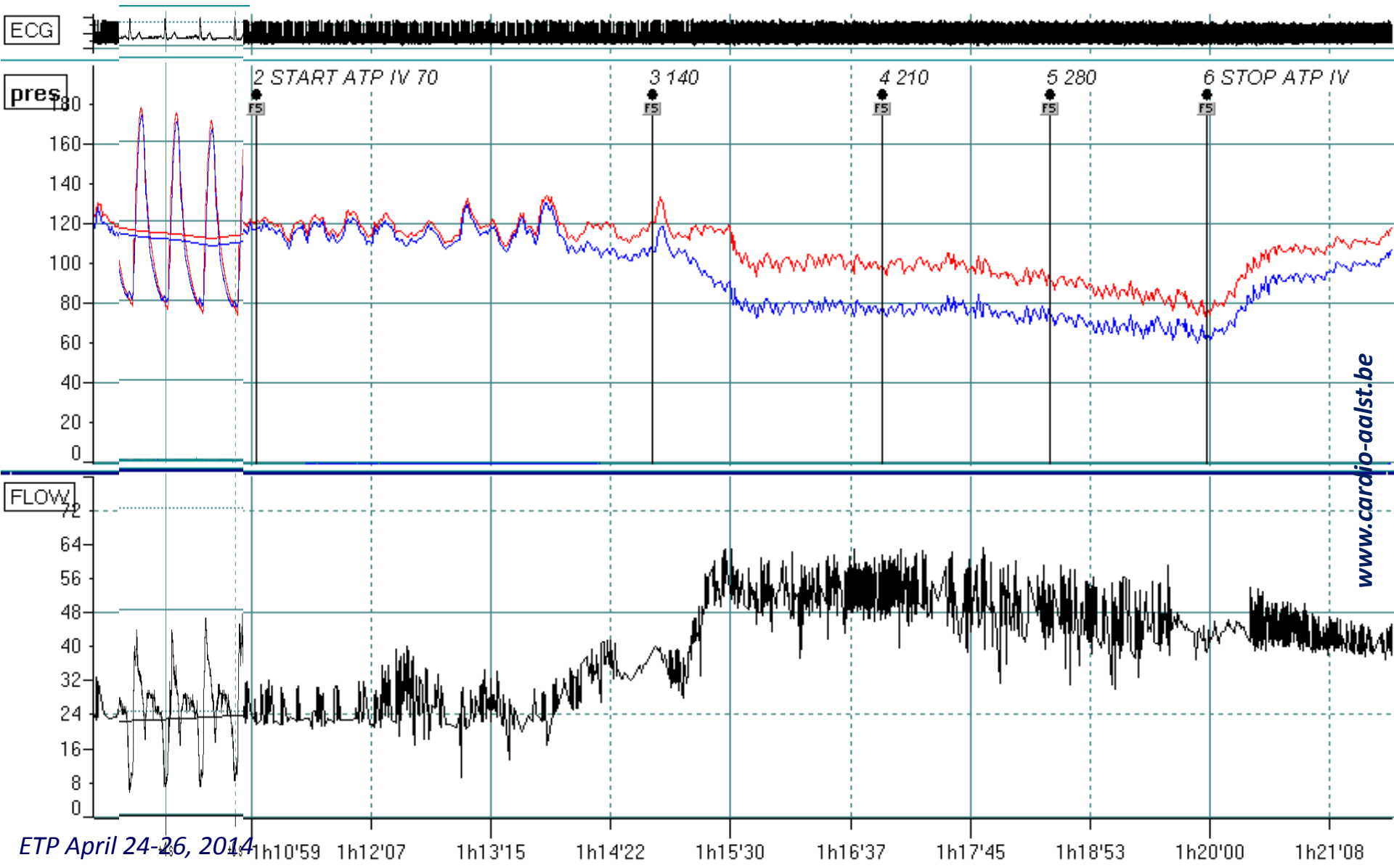


FAQ

Useful to increase the dose of IV ado > 140 µg/kg/min ?

NO

Increasing the dose above 140 $\mu\text{g}/\text{kg}/\text{min}$ decreases systematic BP and increases the thoracic pain

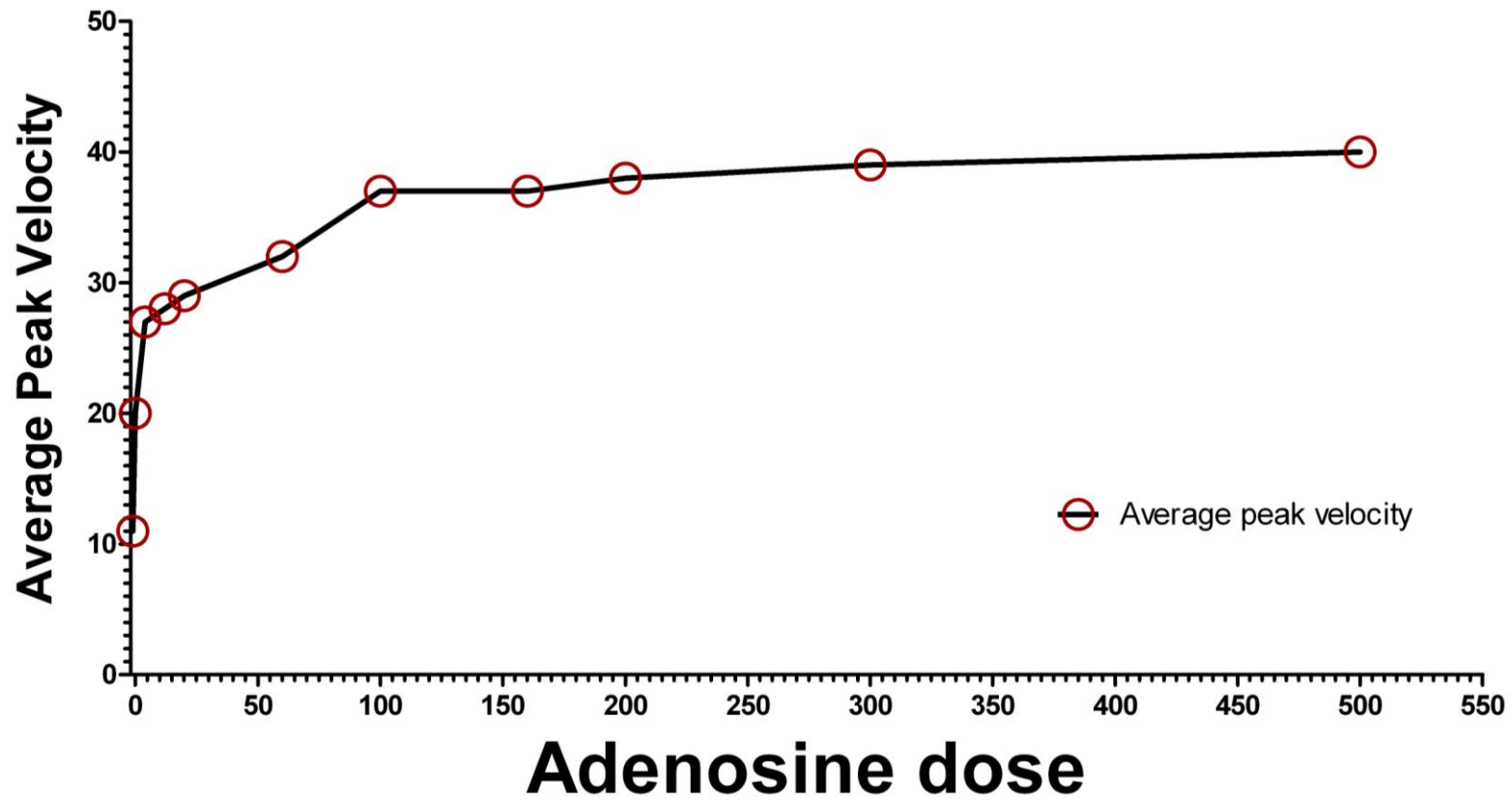


Adenosine IC

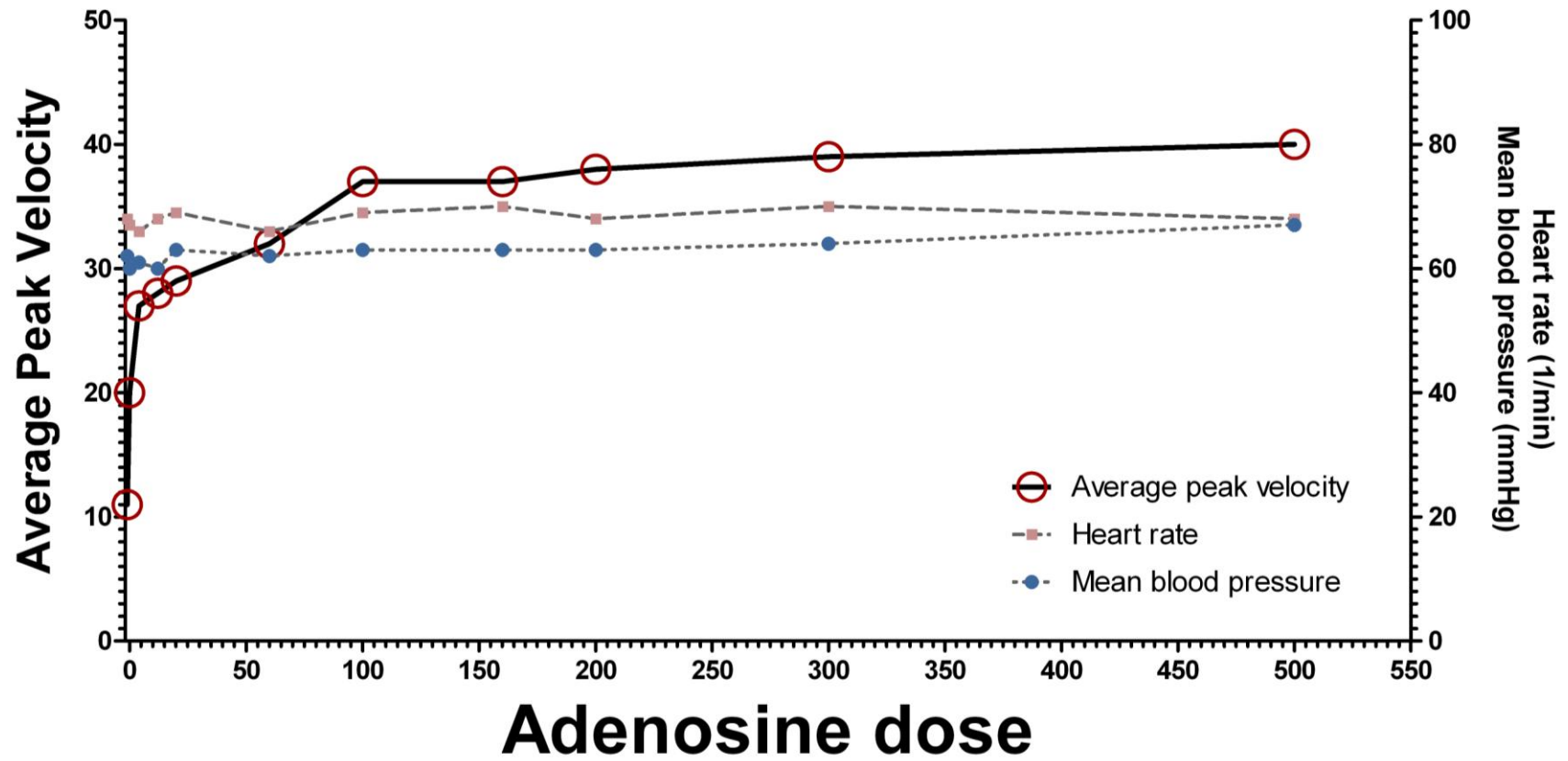
Specificities of IC Adenosine (100-200 µg)

1. Can be used in the vast majority of lesions
2. Short half live
3. Rare AV blocks, always transient
4. Extremely reproducible: do it twice or more!

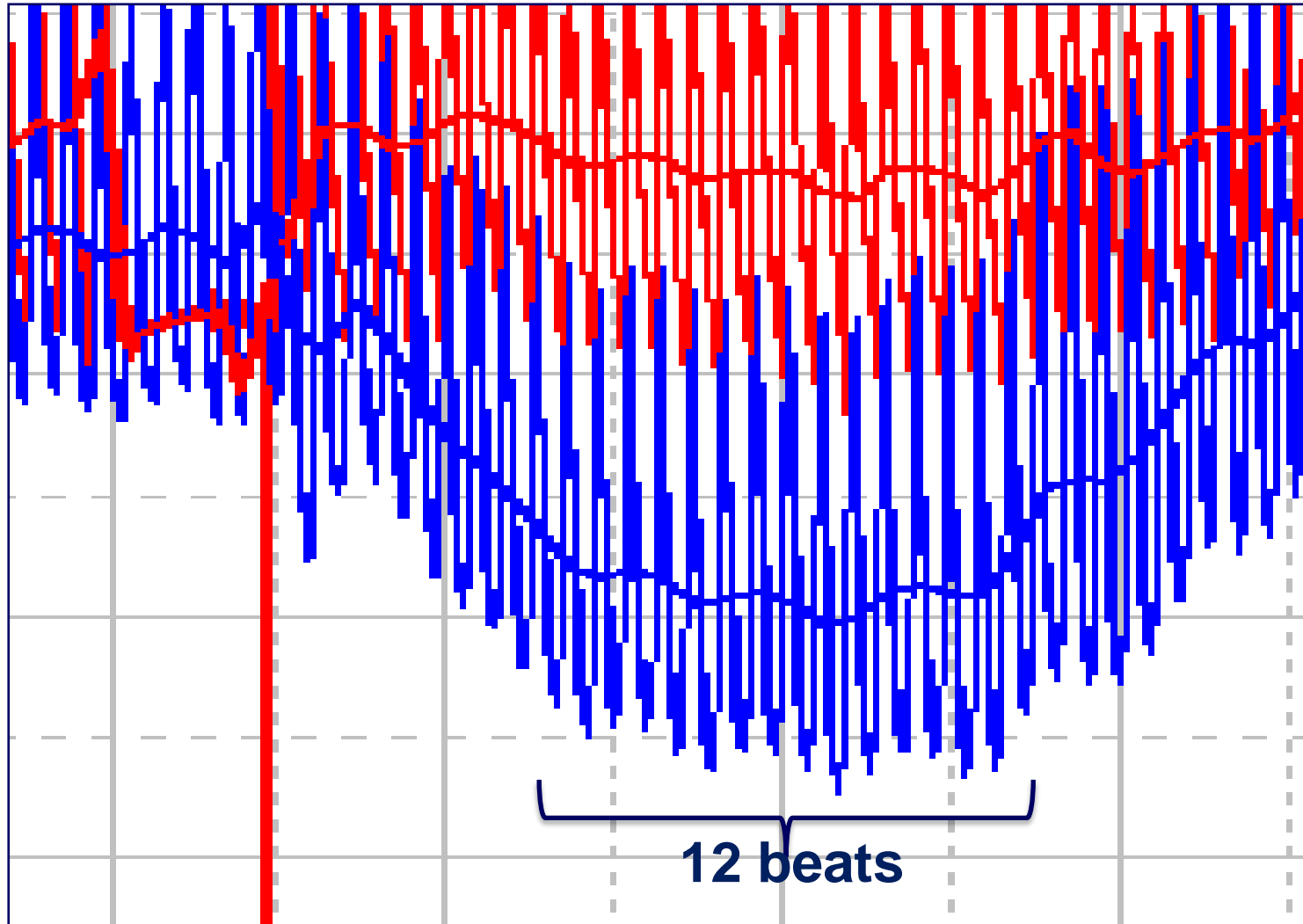
Adenosine ic dose-response curve

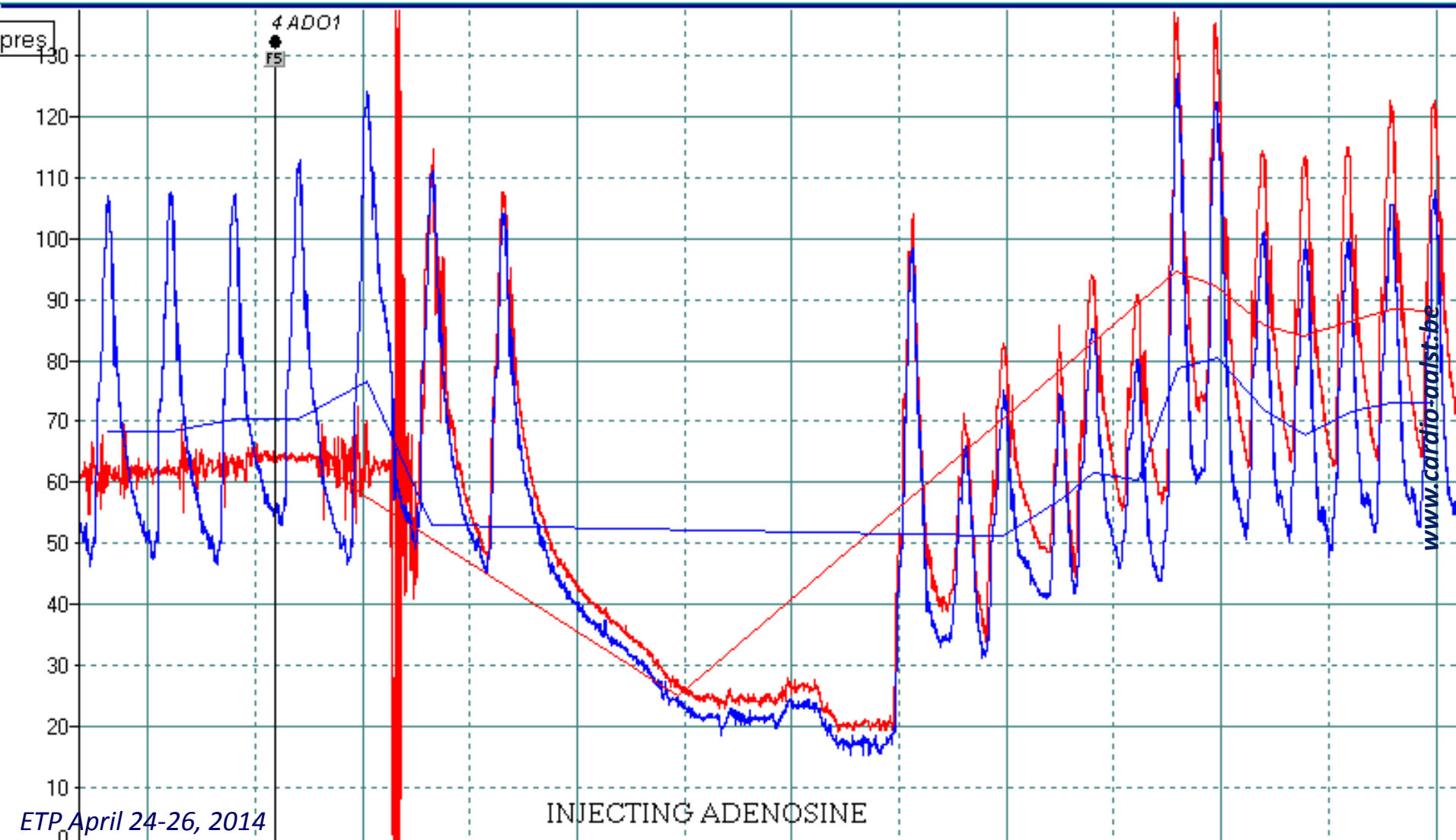
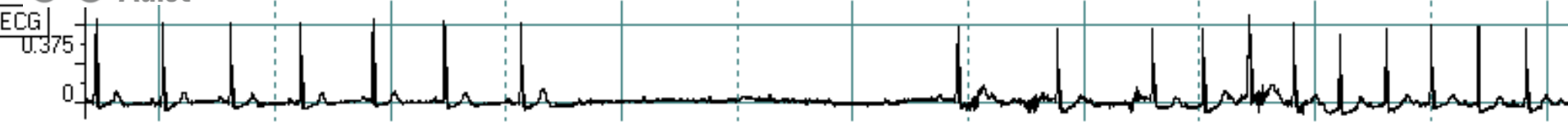


Adenosine ic dose-response curve



IC Adenosine ... Not that shortlasting

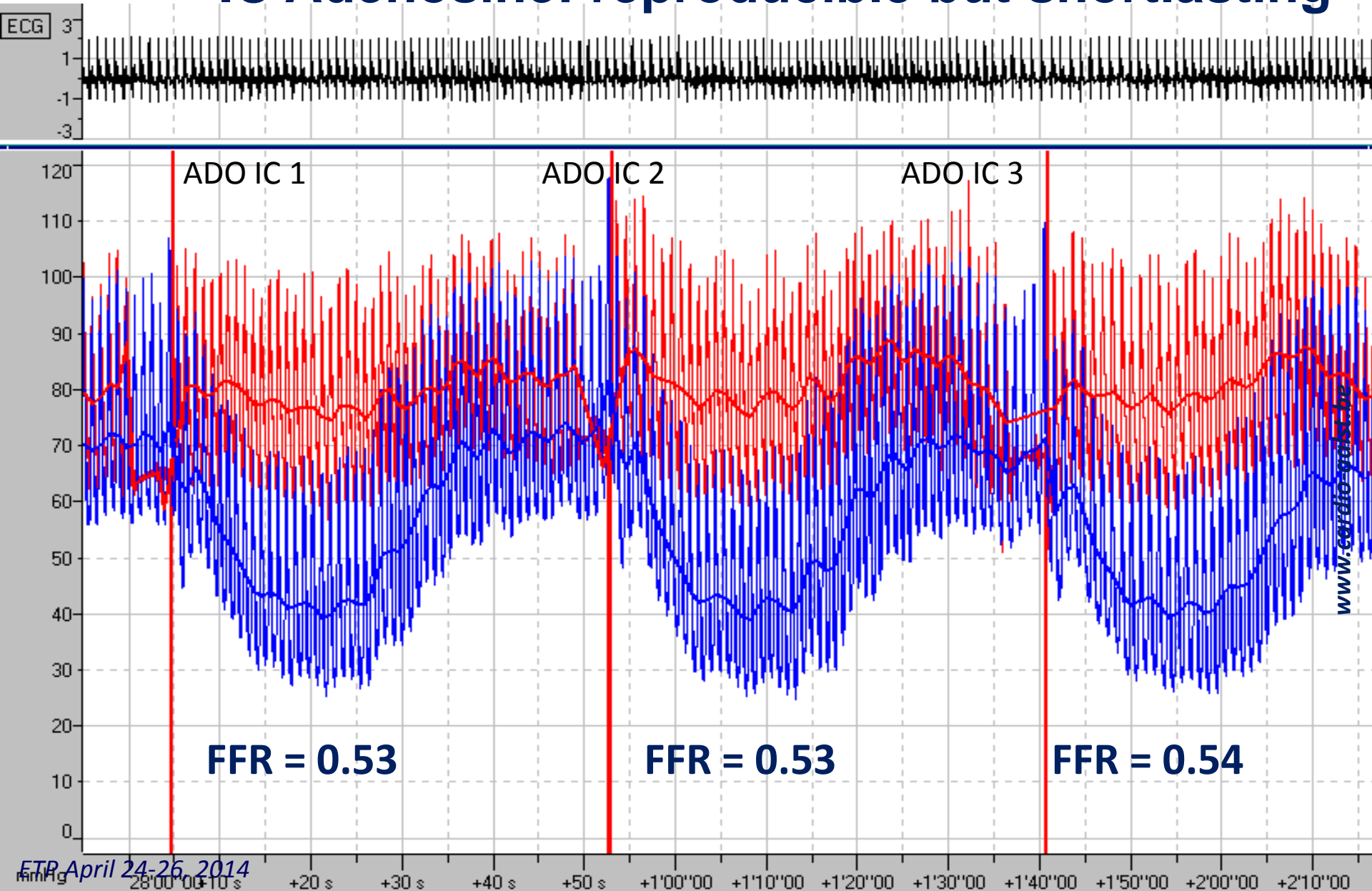




Specificities of IC Adenosine (100-200 µg)

1. Can be used in the vast majority of lesions
2. Short half live
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4. Extremely reproducible: do it twice (or more!)

IC Adenosine: reproducible but shortlasting



Regadenosone IV peripheral



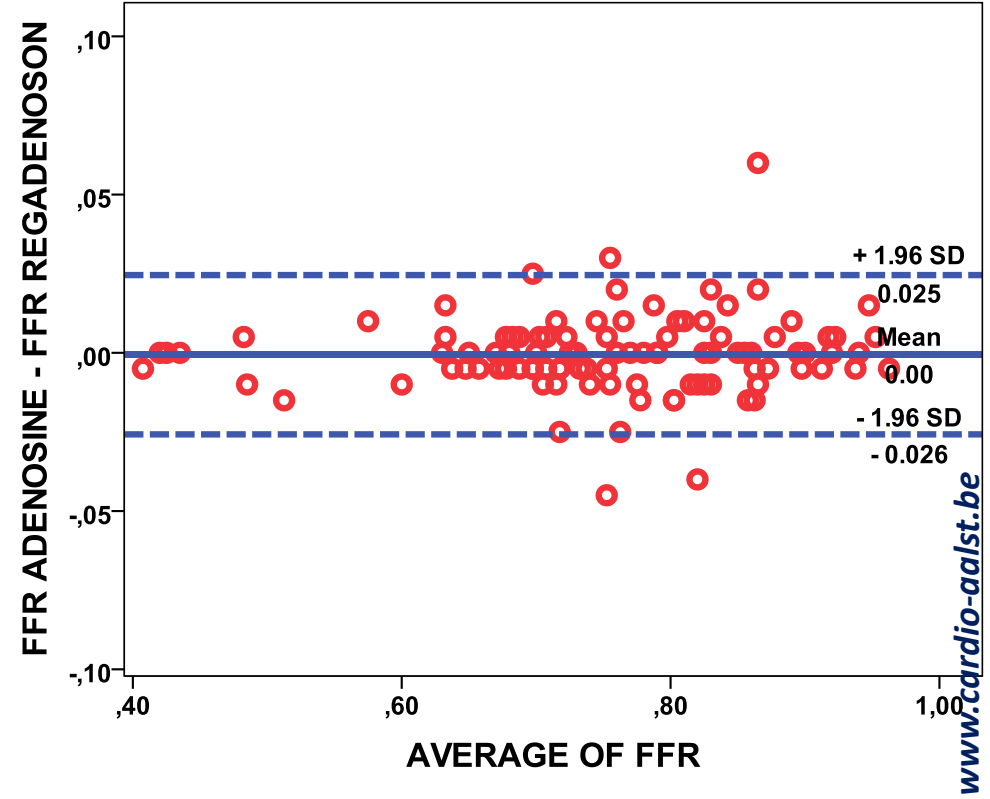
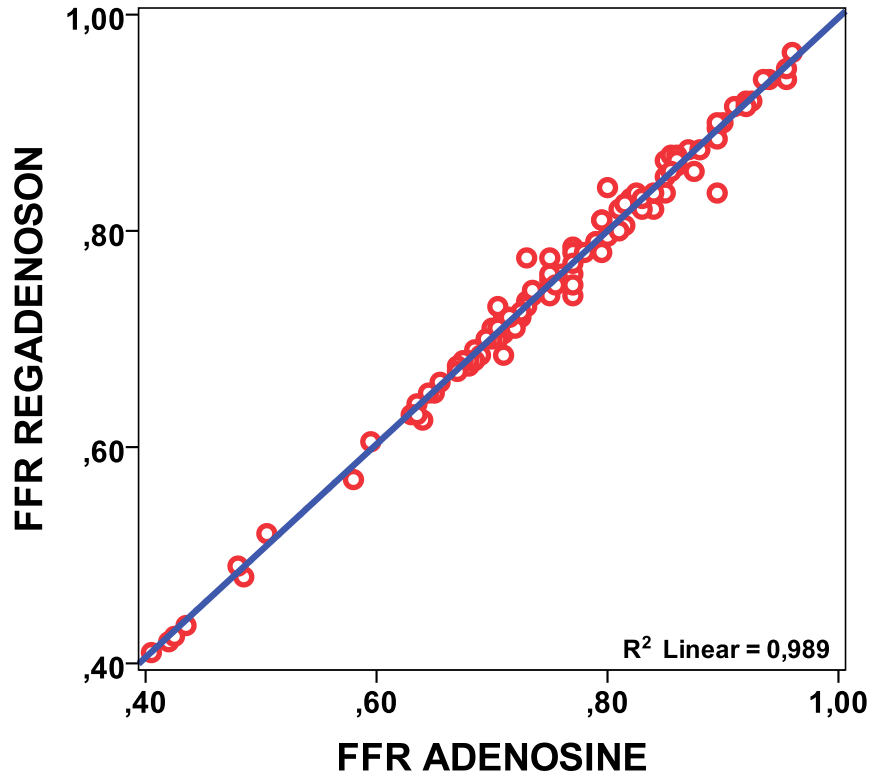
Regadenoson (= Rapiscan®)

Regadenoson as single peripheral i.v. bolus 400 µg

- maximum hyperemia within 60 sec and lasting for at least 30 seconds (sufficient for pull-back recording)
- can be safely repeated after 10 min
- hyperemia completely comparable to i.v. adenosine

➔ *ideal in radial procedures or ad-hoc FFR*

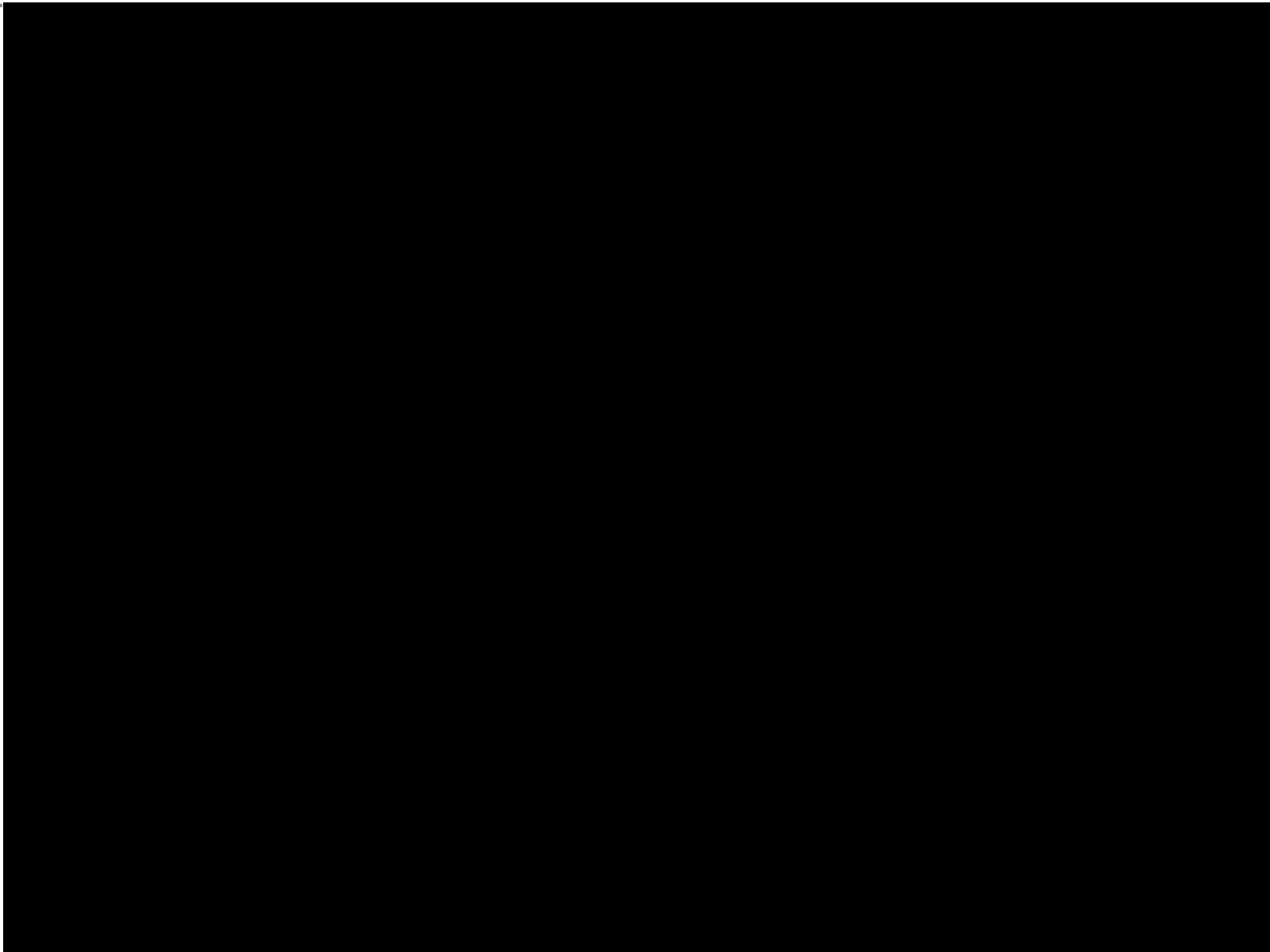
Regadenoson vs Adenosine (N=100)



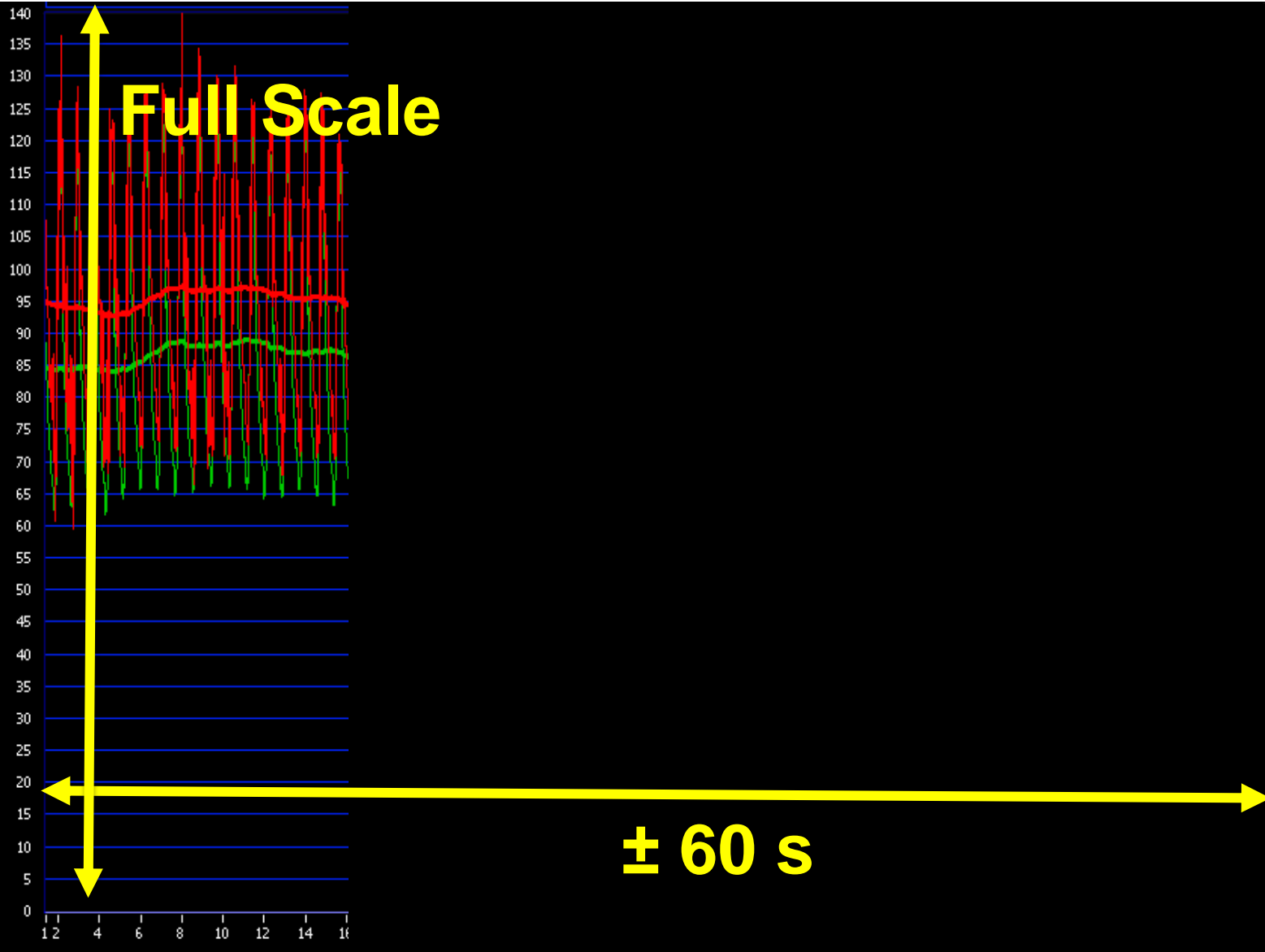
- Mean Difference 0.00 ± 0.01

Quality of the Pressure Recordings

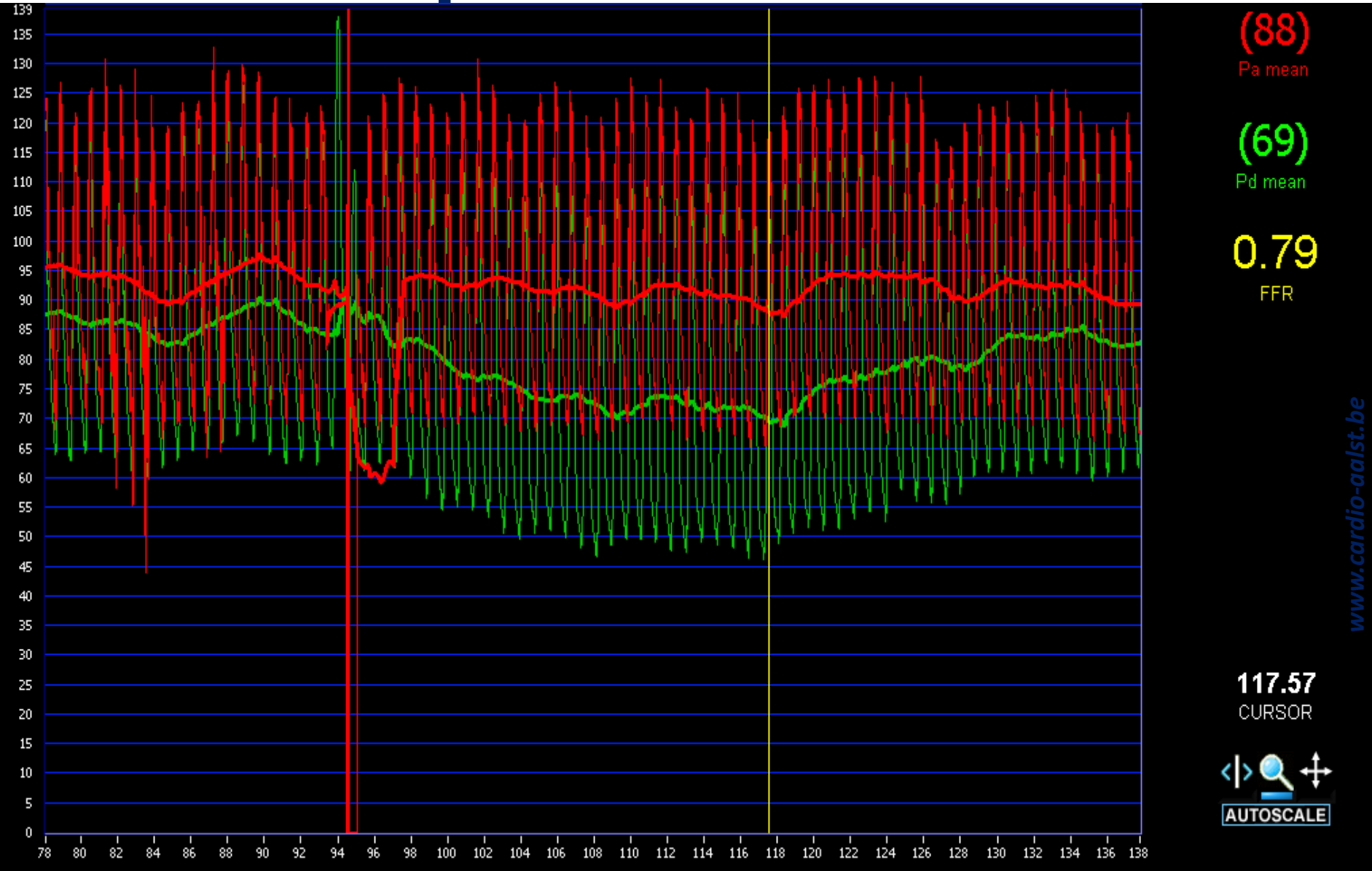
- *Recording of 12 beats steady state at rest*
- *Very short (1-2 s) injections of ado*
- *Total recording of 45-60 s*

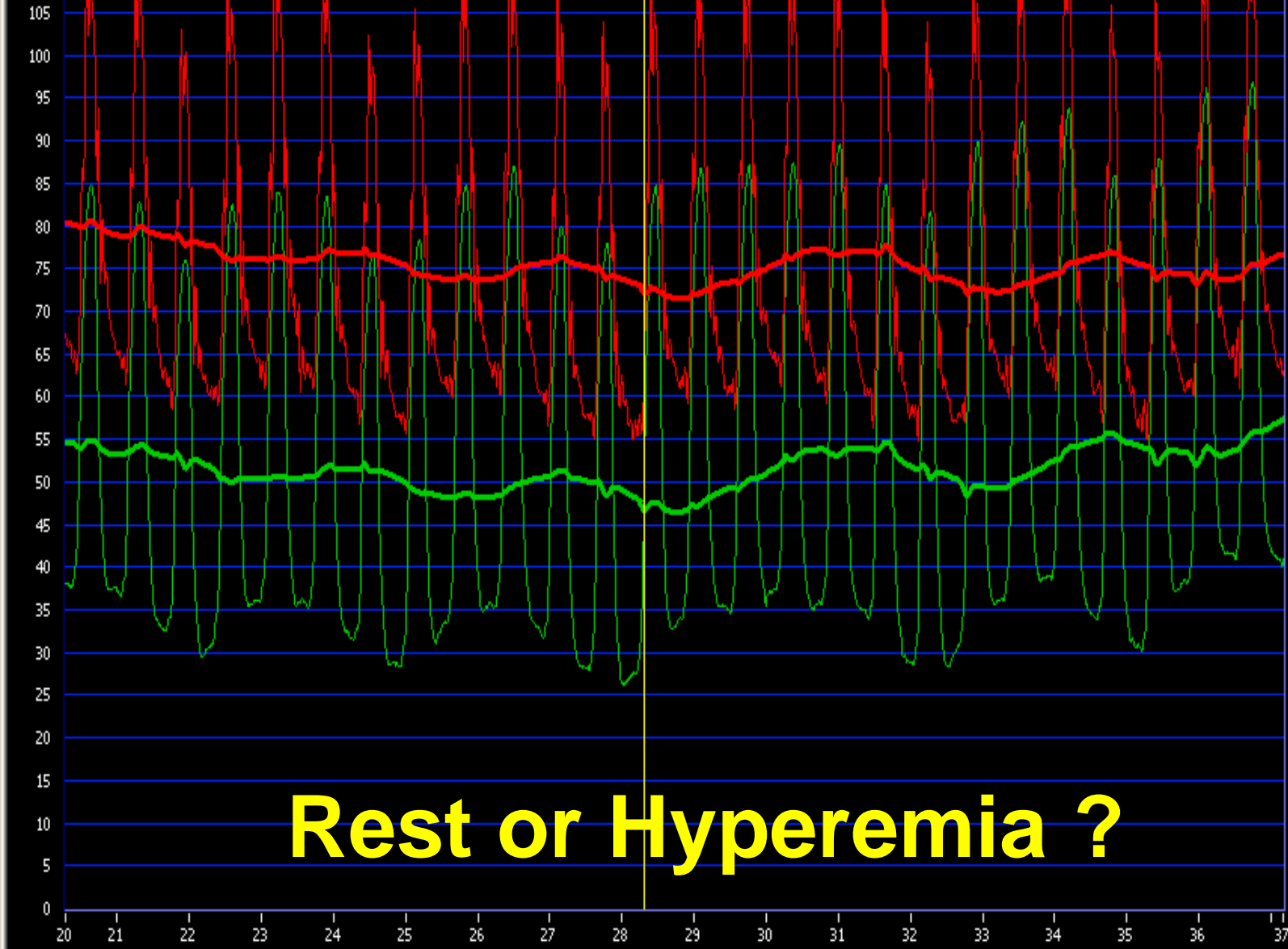


Tips and Tricks



Tips and Tricks





(72)
Pa mean
(47)
Pd mean
0.65
FFR

28.31
CURSOR

Rest or Hyperemia ?

Navigation icons: left arrow, magnifying glass, right arrow, and crosshair.
AUTOSCALE

(82)

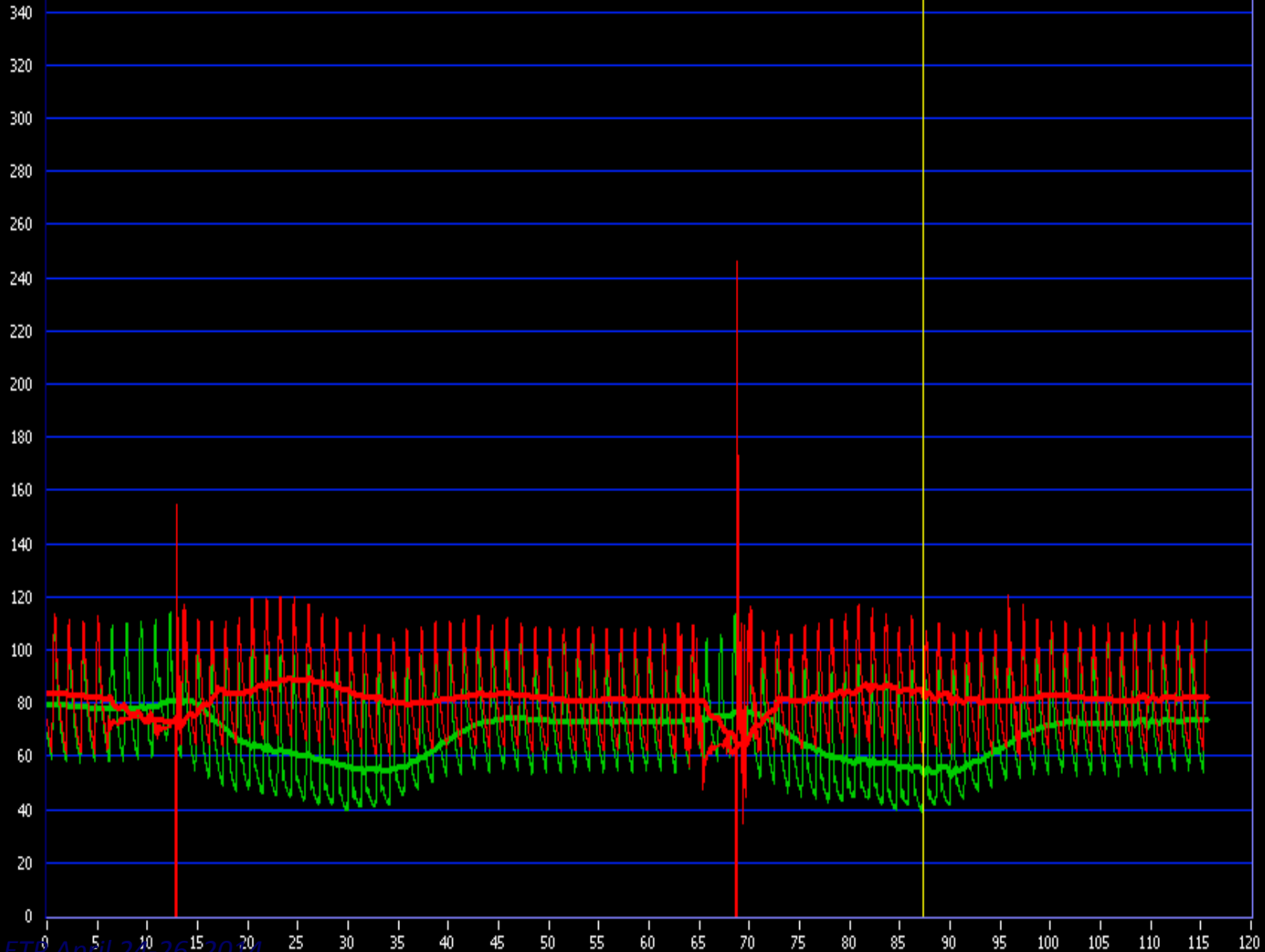
Pa mean

(53)

Pd mean

0.64

FFR



87.35

CURSOR



AUTOSCALE



(82)
Pa mean

(53)
Pd mean

0.64
FFR

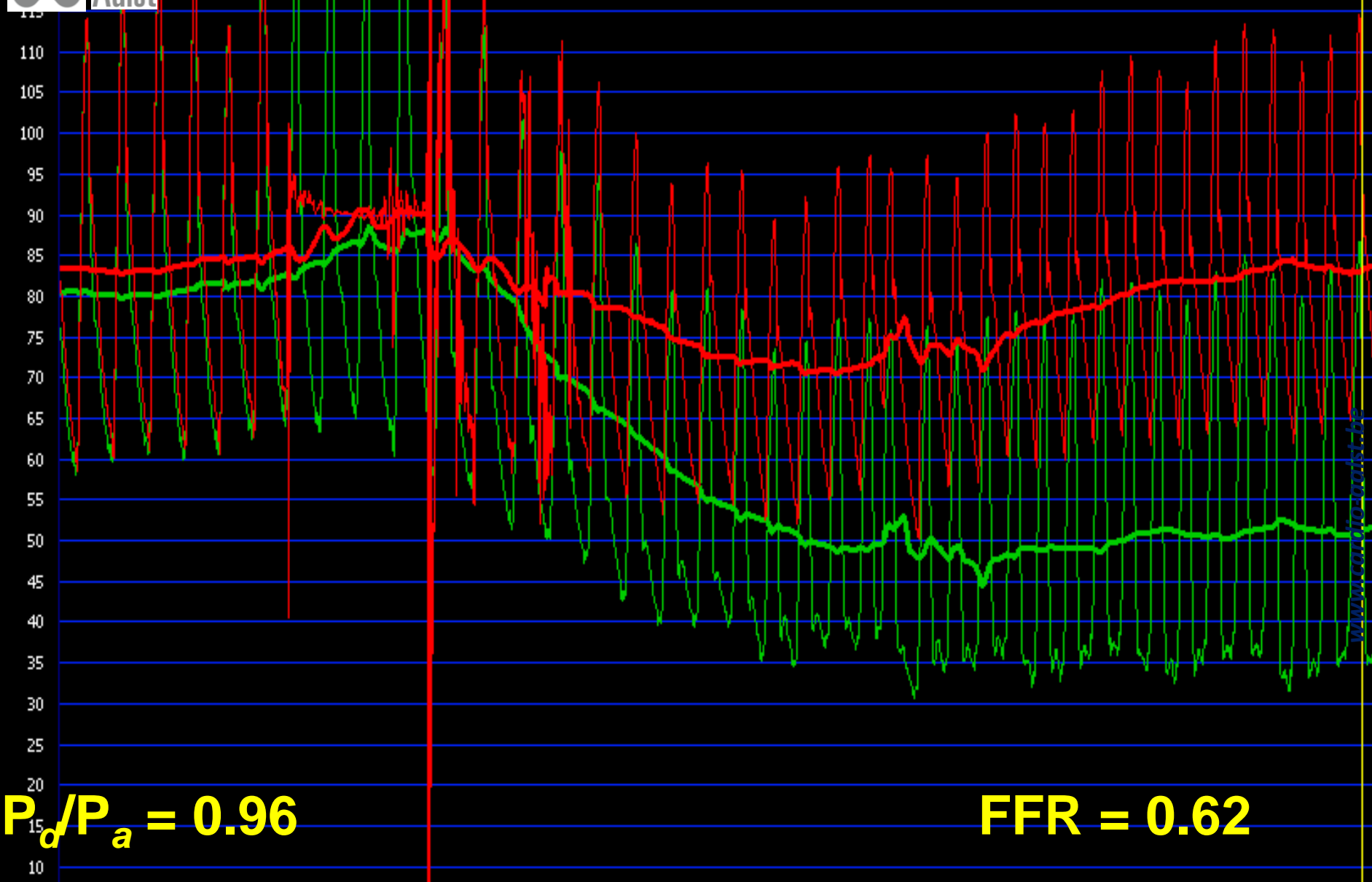
0.65

0.64

87.35
CURSOR

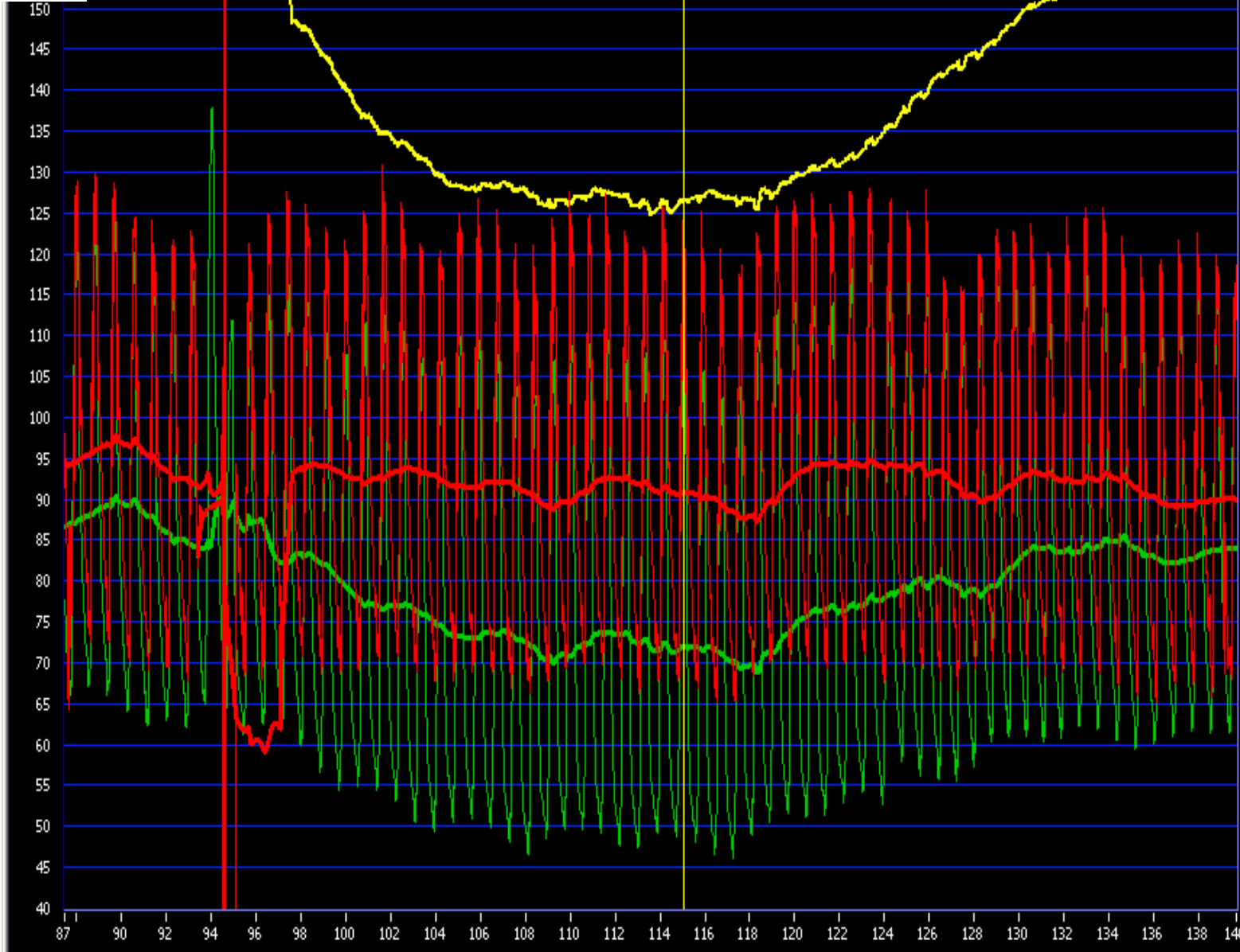
Navigation icons: left arrow, right arrow, magnifying glass, and crosshair. Below them is a button labeled "AUTOSCALE".

When P_d/P_a at rest > 0.90 , hyperemia ?



$P_d/P_a = 0.96$

$FFR = 0.62$




(91)
Pa mean

(72)
Pd mean

0.79
FFR

115.06
CURSOR


AUTOSCALE

Conclusive Remarks

- 1. Hyperemia is mandatory to “interrogate” a lesion properly**
- 2. Can be obtained very easily, safely, cheaply, ...**
- 3. Provided it is standardized in each laboratory**

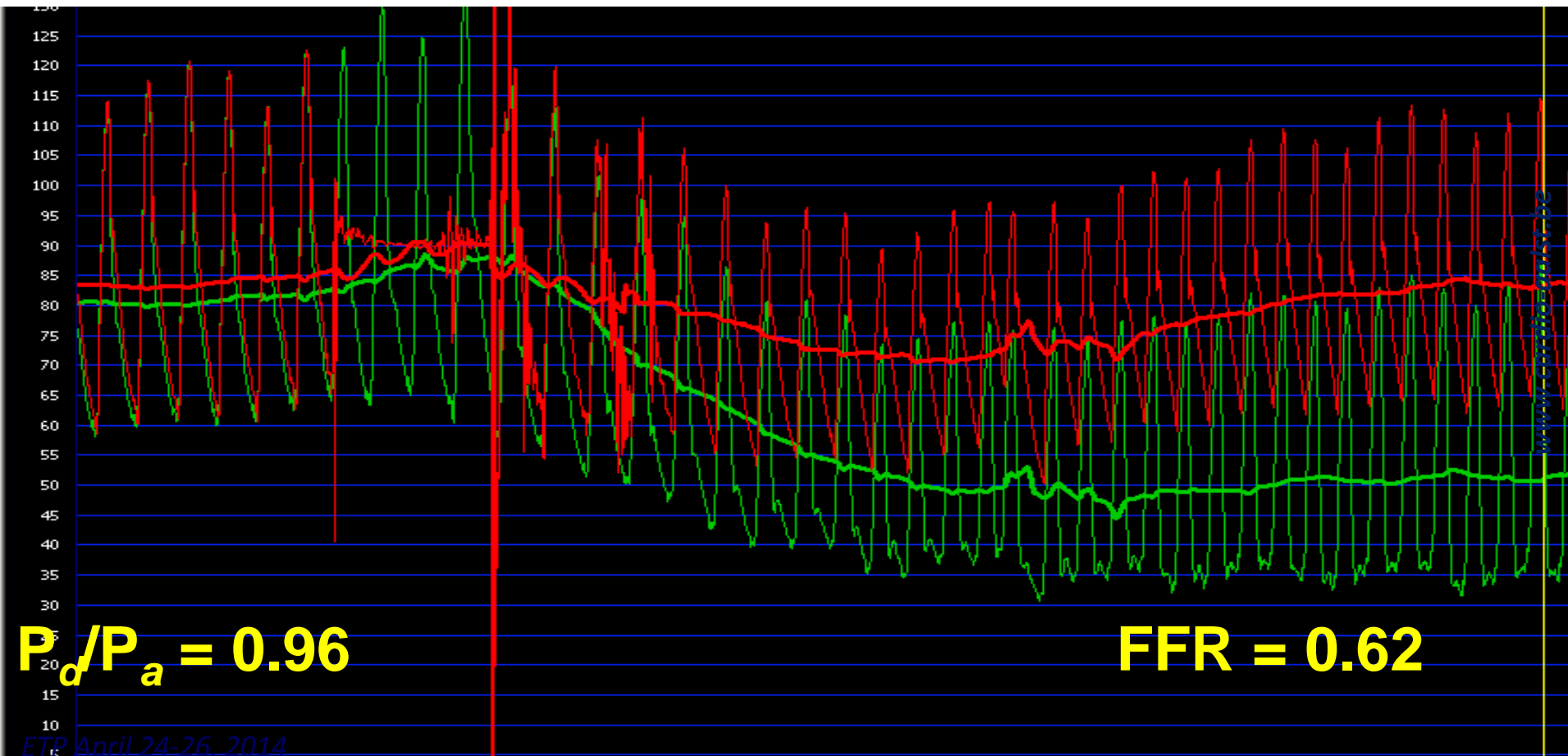
FAQ

- ✓ When P_d/P_a at rest > 0.90 , do we have to induce hyperemia ?
- ✓ When P_d/P_a at rest < 0.80 , do we have to induce hyperemia ?
- ✓ Useful to increase the dose of IV ado $> 140 \mu\text{g}/\text{kg}/\text{min}$?
- ✓ Useful to increase the dose of IC ado $> 200 \mu\text{g}$ (bolus) ?
- ✓ Is the burning sensation related to ischemia ?
- ✓ Are some patients resistant to Adenosine ?
- ✓ Can Papaverine be used instead of Adenosine ?
- ✓ Is hyperemia expensive ?
- ✓ What to do with radial procedures ?
- ✓ Interference with some medications ?
- ✓ Is adenosine contraindicated in patients with lung disease?

FAQ

When P_d/P_a at rest > 0.90 , do we have to induce hyperemia ?

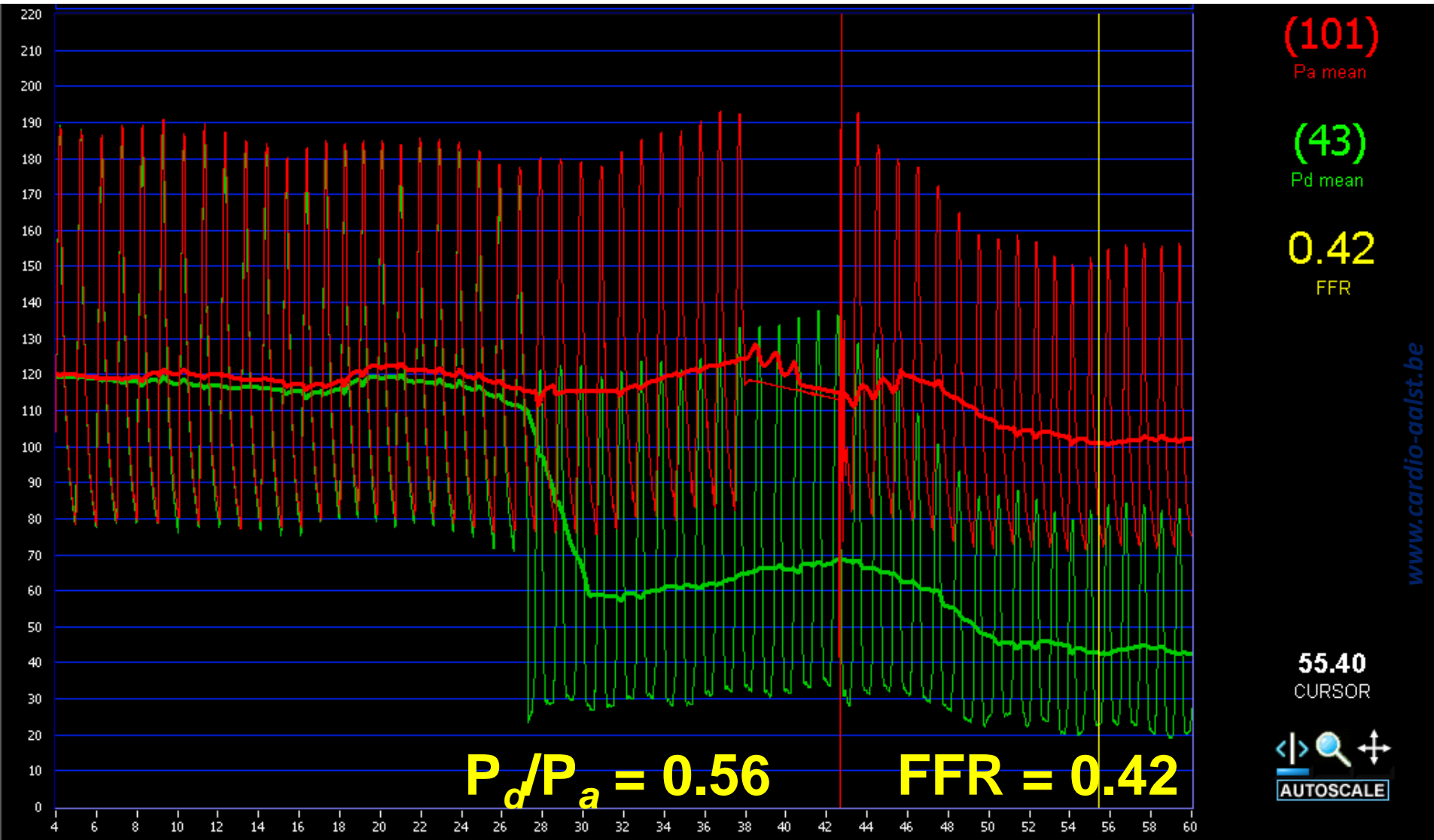
YES



FAQ

When Pd/Pa at rest < 0.80, do we have to induce hyperemia ?

When Pd/Pa at rest < 0.80, do we have to induce hyperemia ?

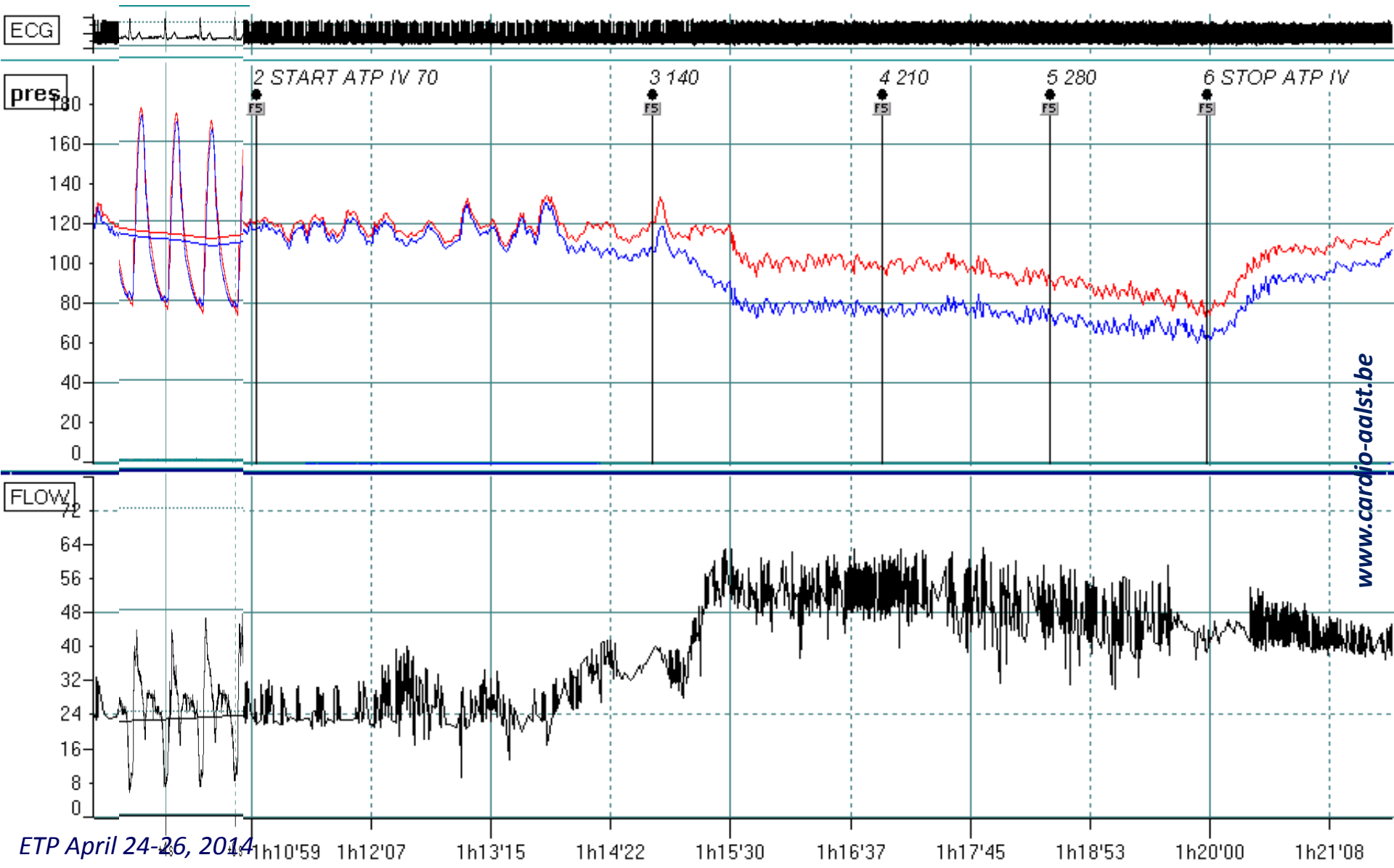


FAQ

Useful to increase the dose of IV ado > 140 µg/kg/min ?

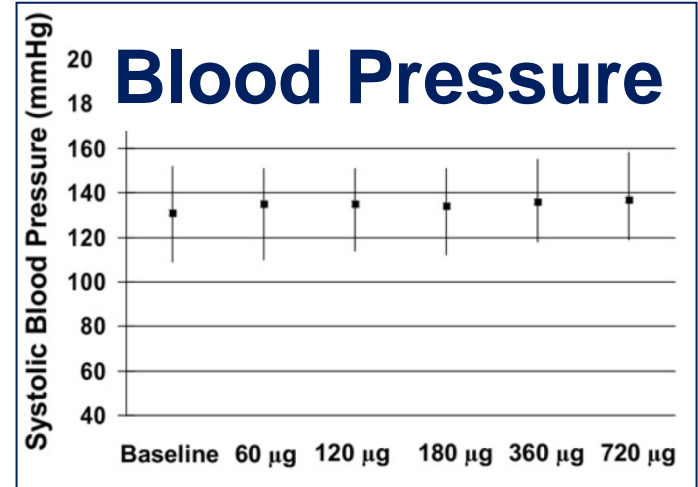
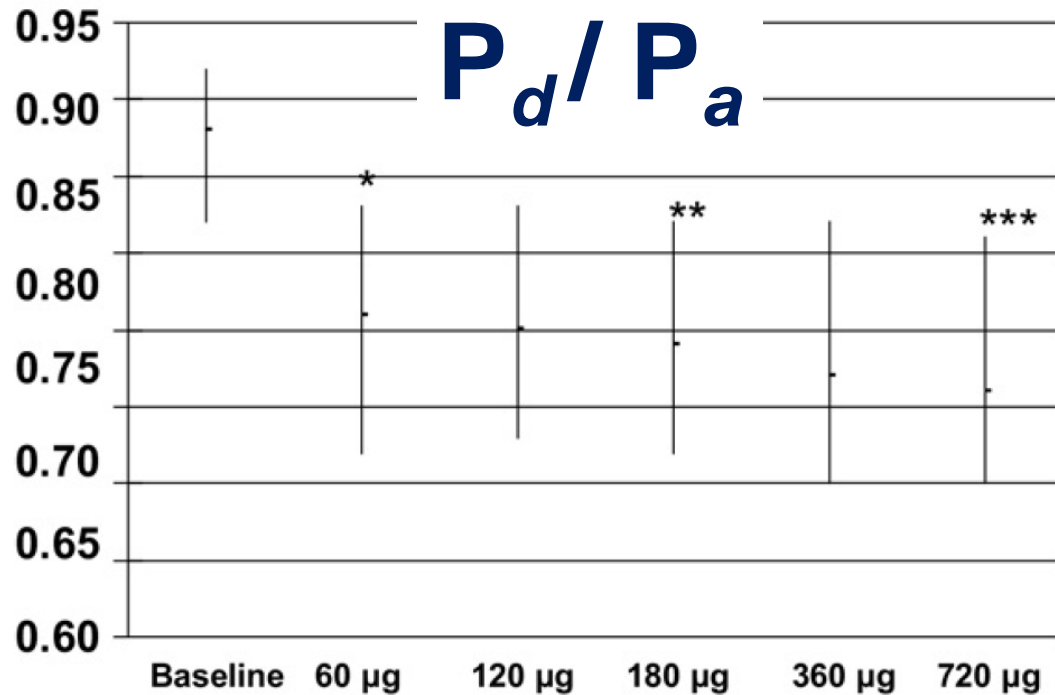
NO

Increasing the dose above 140 $\mu\text{g}/\text{kg}/\text{min}$ decreases systematic BP and increases the thoracic pain



FAQ

Useful to increase the dose of IC ado > 200 µg (bolus) ?



N=46

720 µg decreases P_d/P_a a bit further w/o any decrease in BP, any increase in HR and no heart blocks ????

FAQ

Is the burning sensation related to ischemia ?

NO

Adenosine is an algescic substance which stimulates the same nerves than those resposnsible for angina ... which is also due to the local release of adenosine during ischemia

FAQ

Are some patients resistant to Adenosine ?

NO,

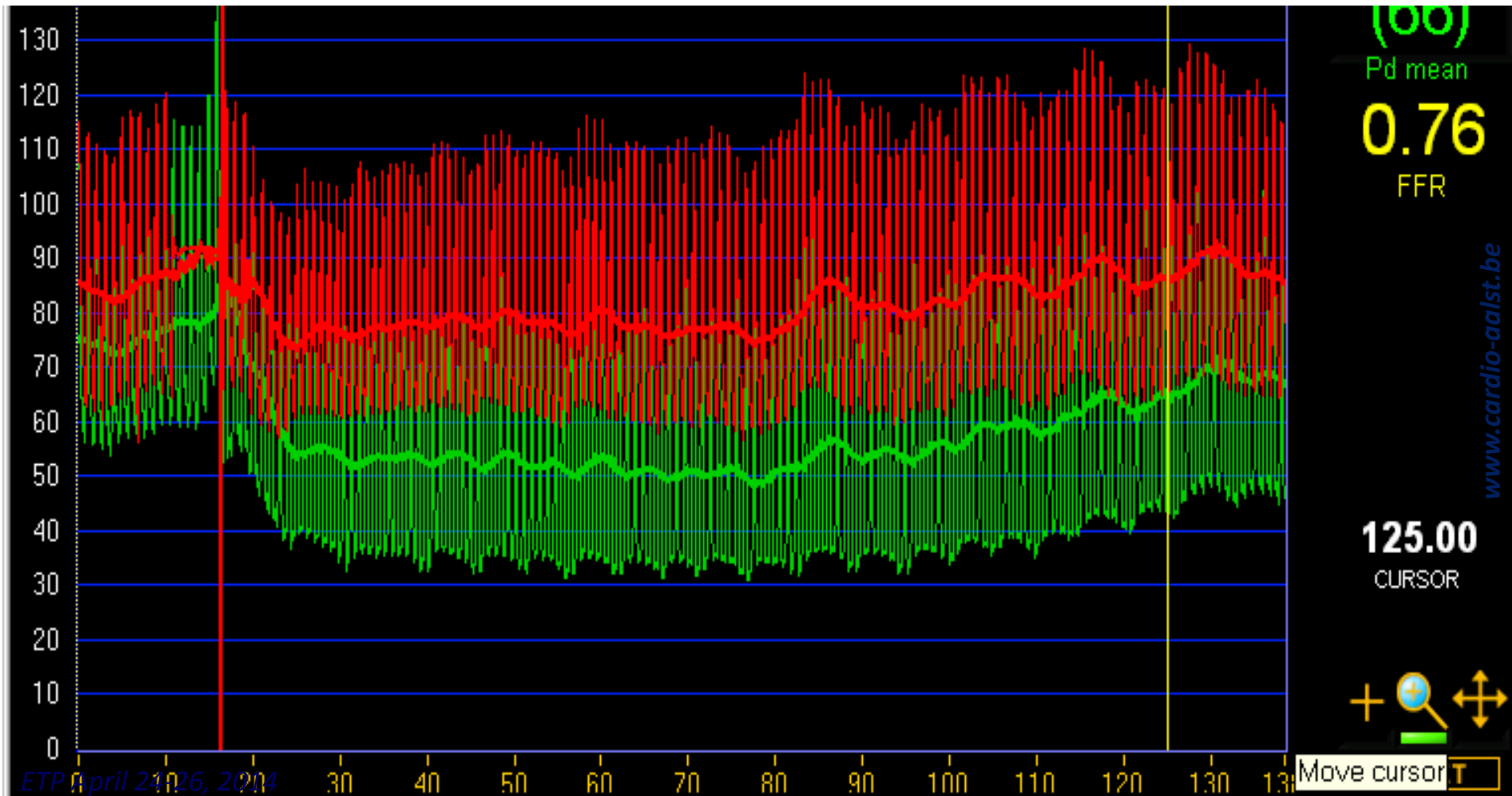
Resistance to exogenous Adenosine does not exist

FAQ

Can Papaverine be used instead of Adenosine ?

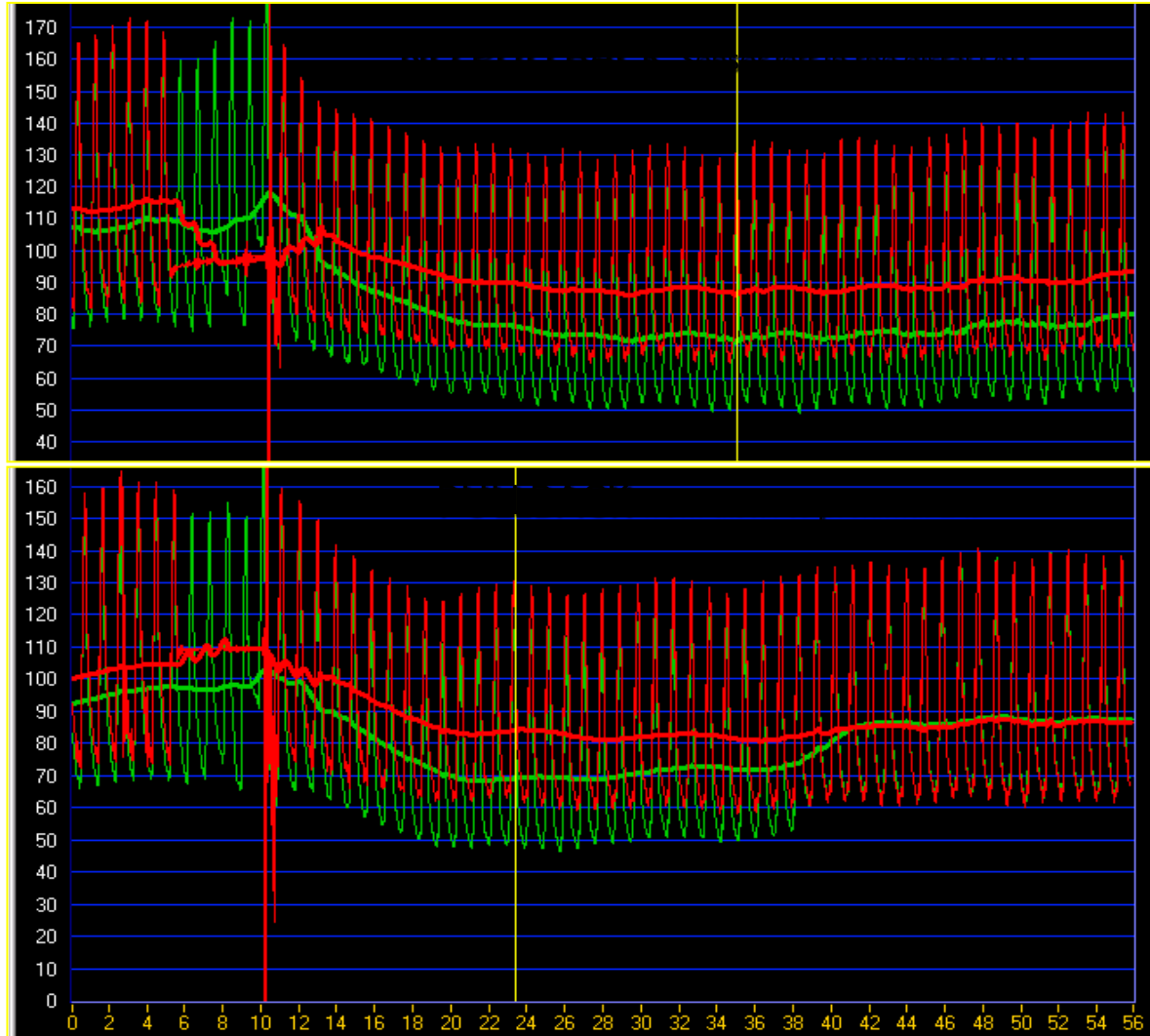
Papaverine IC

16 mg IC in LCA 12 mg IC in RCA



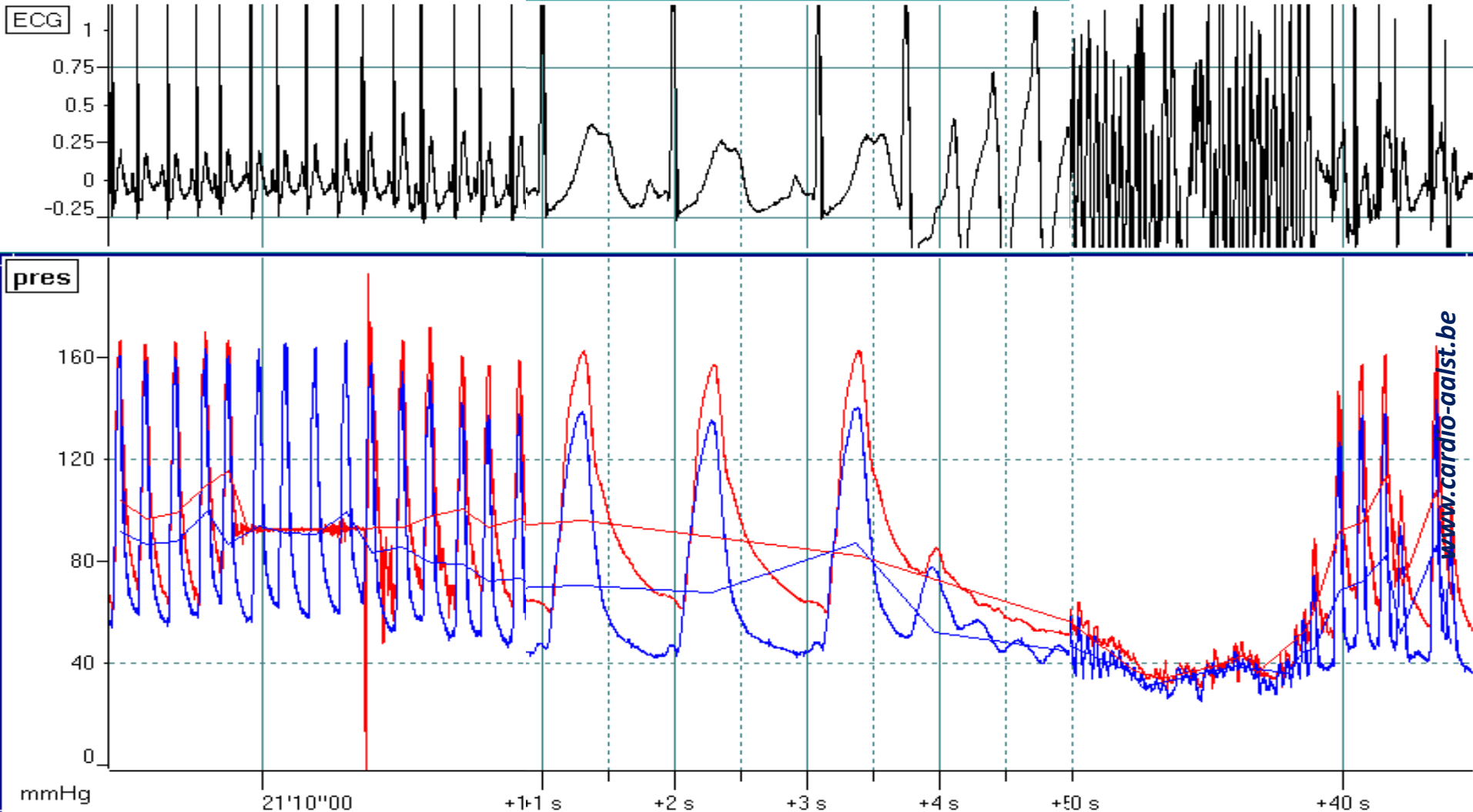
Papaverine IC

16 mg IC in LCA 12 mg IC in RCA



Papaverine IC

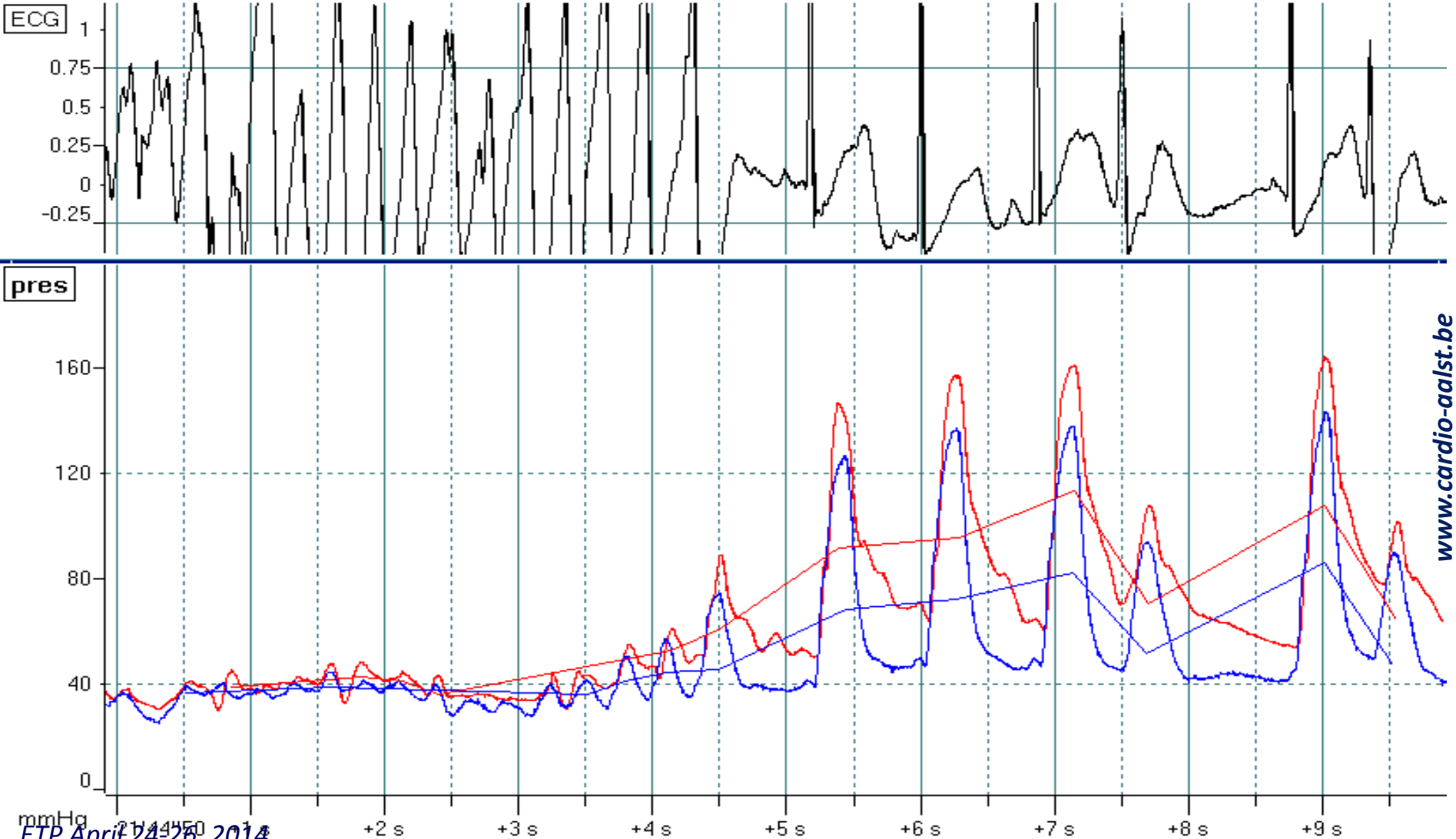
16 mg IC in LCA 12 mg IC in RCA



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Papaverine IC

16 mg IC in LCA 12 mg IC in RCA



FAQ

Is hyperemia expensive ?

... NOT REALLY:

0.12 € / bolus of 100 µg IC; 0.24 € / bolus of 200 µg

1.34 € / syringe needed for approx 15 minutes of IV administration

FAQ

What to do with radial procedures ?

IC BOLUS

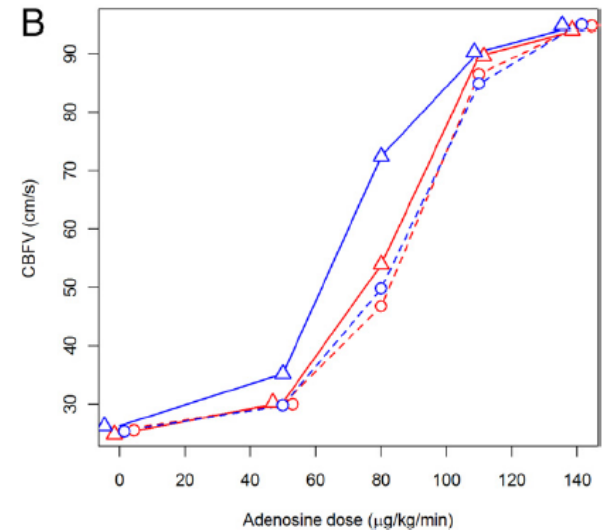
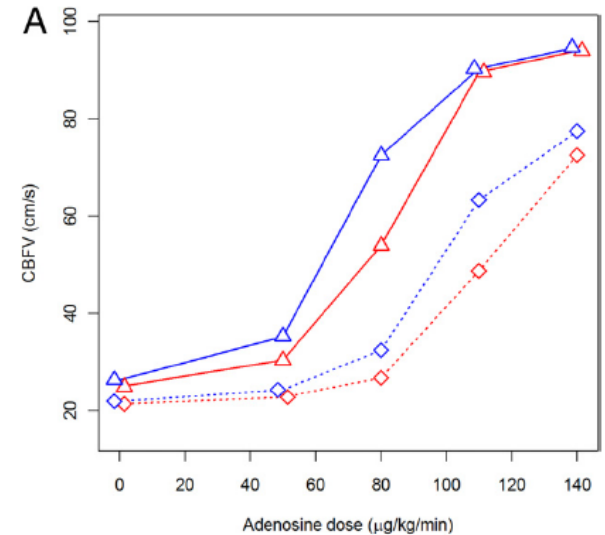
IV adenosine INFUSION

IV Regadenosone BOLUS

FAQ

Some medications interfere with Adenosine

Beta-blockers
Alpha-blockers
Caffeine
Ticagrelor
ACE-inhibitors

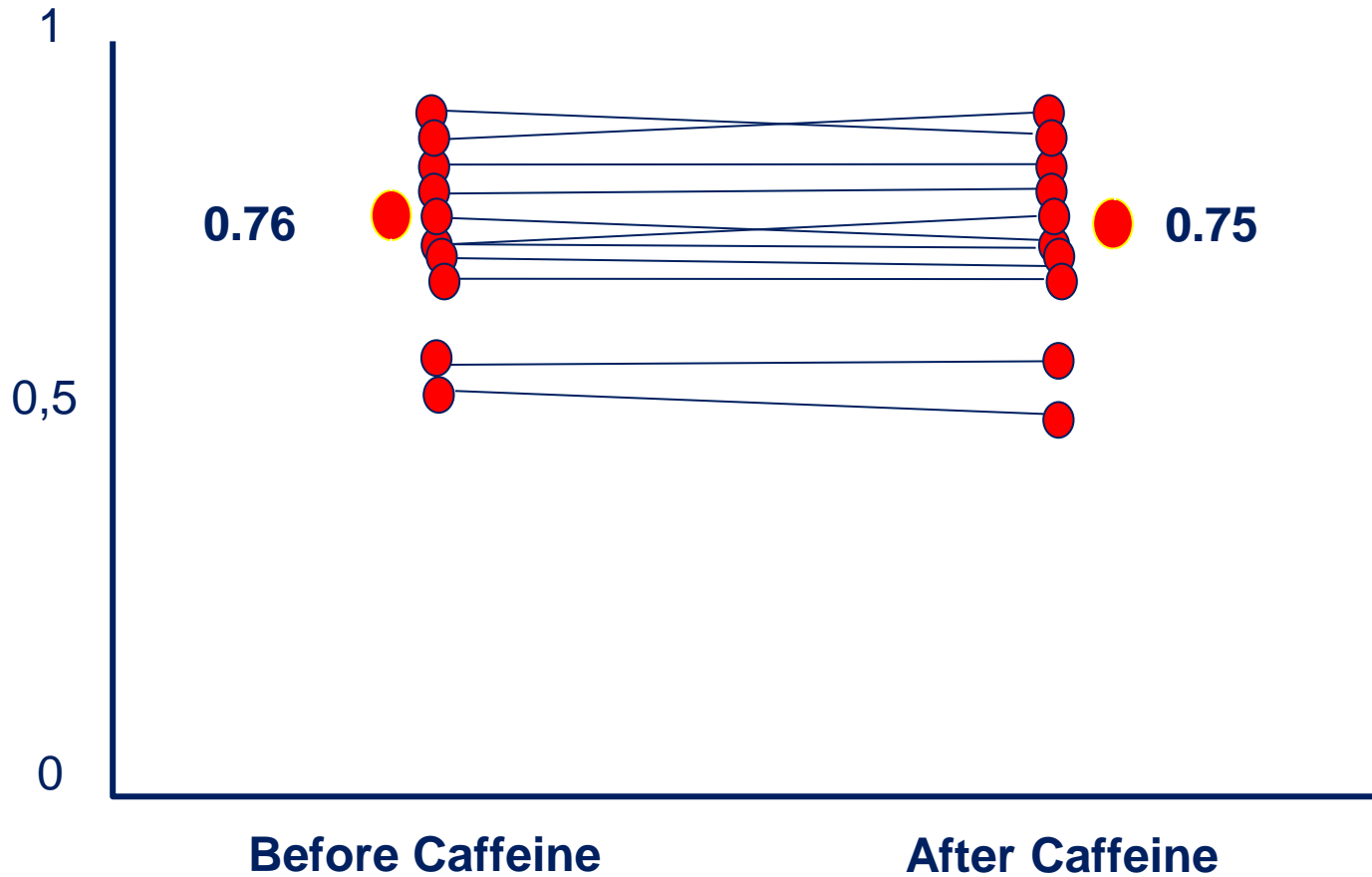


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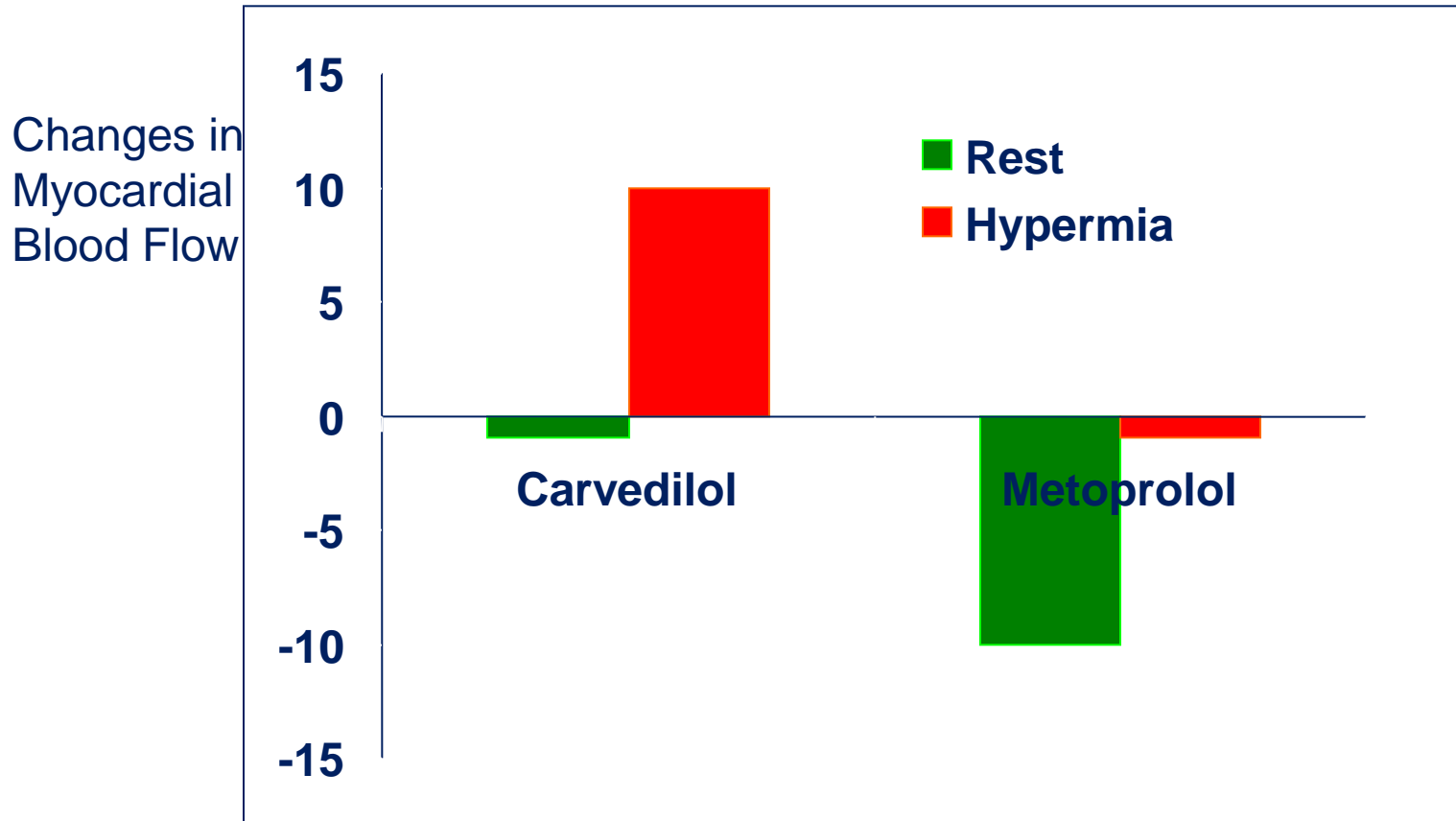
Figure 3 Treatment Effect on Adenosine-Induced CBFV

(A) Adenosine-induced mean coronary blood flow velocity (CBFV) and (B) mean CBFV after theophylline. Symbols are given by pre-placebo (red dashed line, ○), post-placebo (red solid line, Δ), pre-ticagrelor (blue dashed line, ○), post-ticagrelor (blue solid line, Δ), post-theophylline-placebo (red dotted line, ◇), and post-theophylline-ticagrelor (blue dotted line, ◇). Overlapping symbols have been slightly separated for visibility.

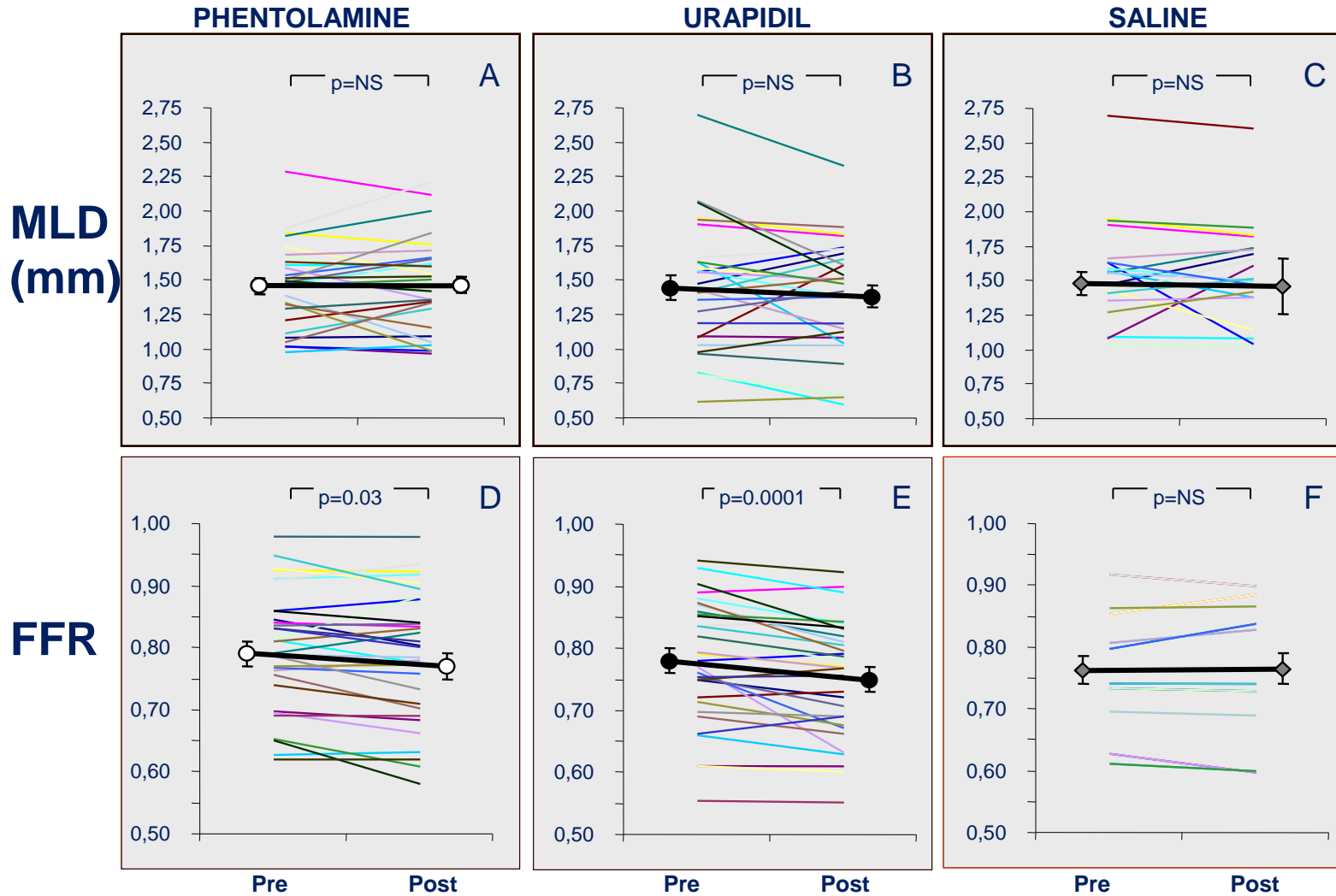
Effect of Caffeine on FFR



Beta-Adrenergic Blockade and Myocardial Flow



Effect of α -Blockers on Diameter and FFR



FAQ

Is adenosine contraindicated in all patients with lung disease ?

NO

- 1. Adenosine is strictly contra indicated in asthma**
- 2. Adenosine is NOT contra indicated in COPD**

