

# Hyperemic Stimuli

**Why ?  
How ?  
FAQ !**

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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**

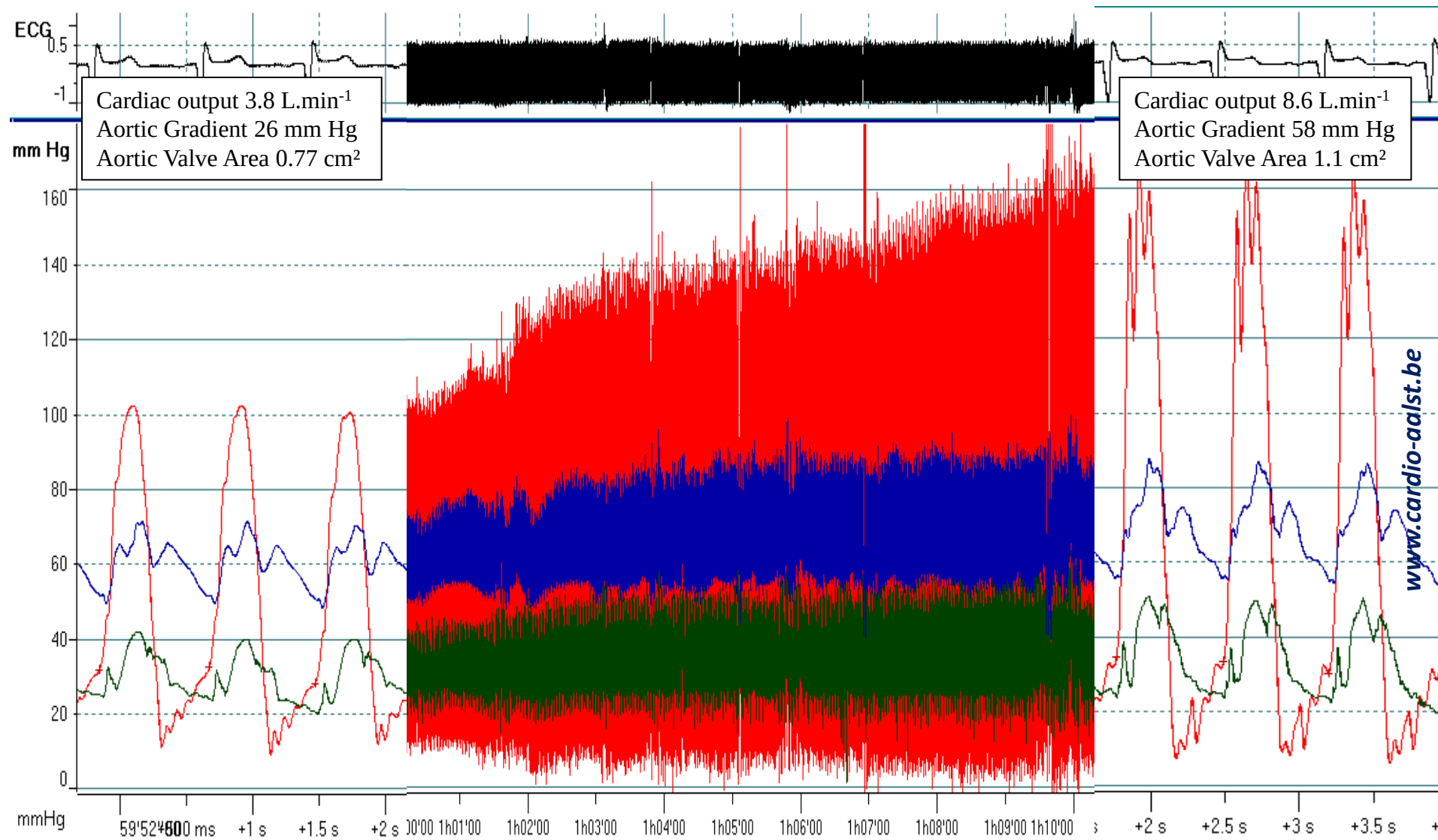
# Aortic Stenosis: Severe ???



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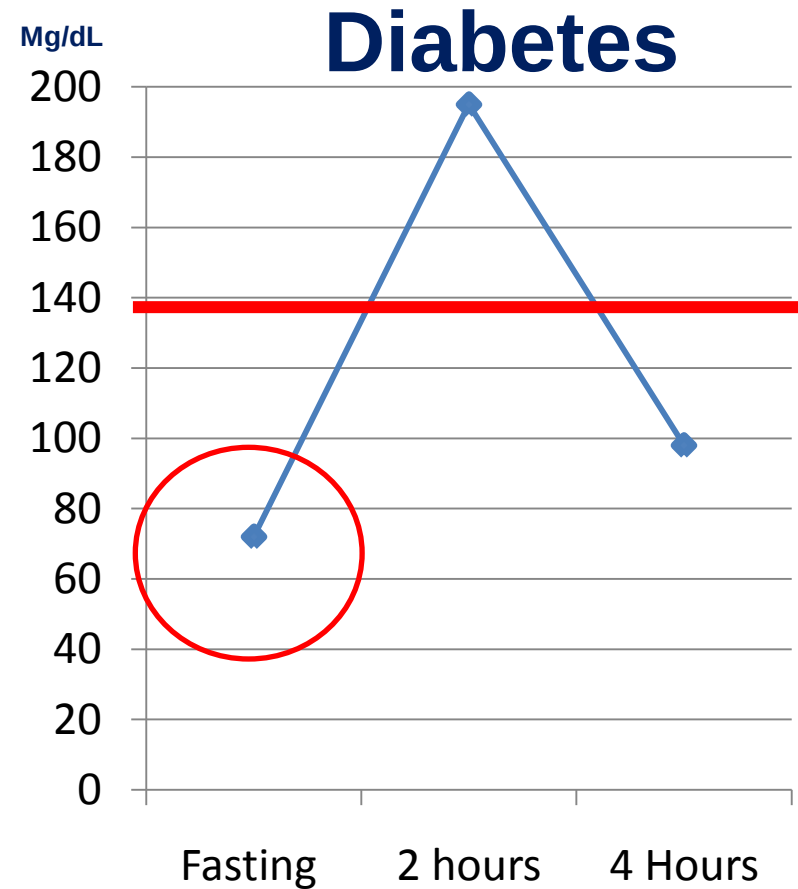
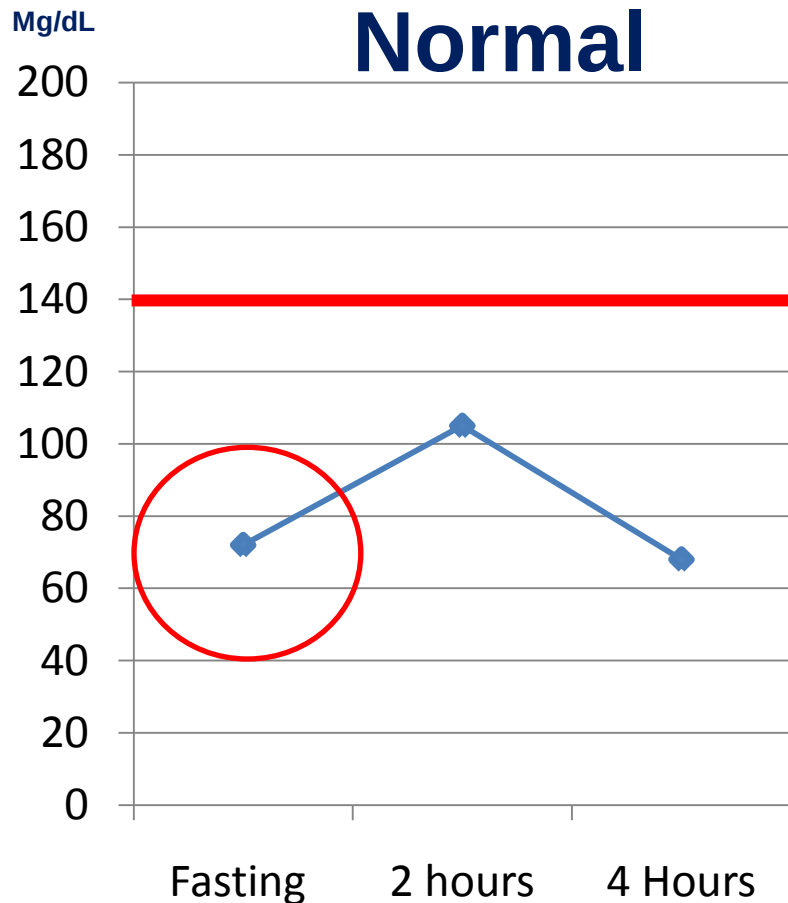


# Aortic Stenosis: Severe ???

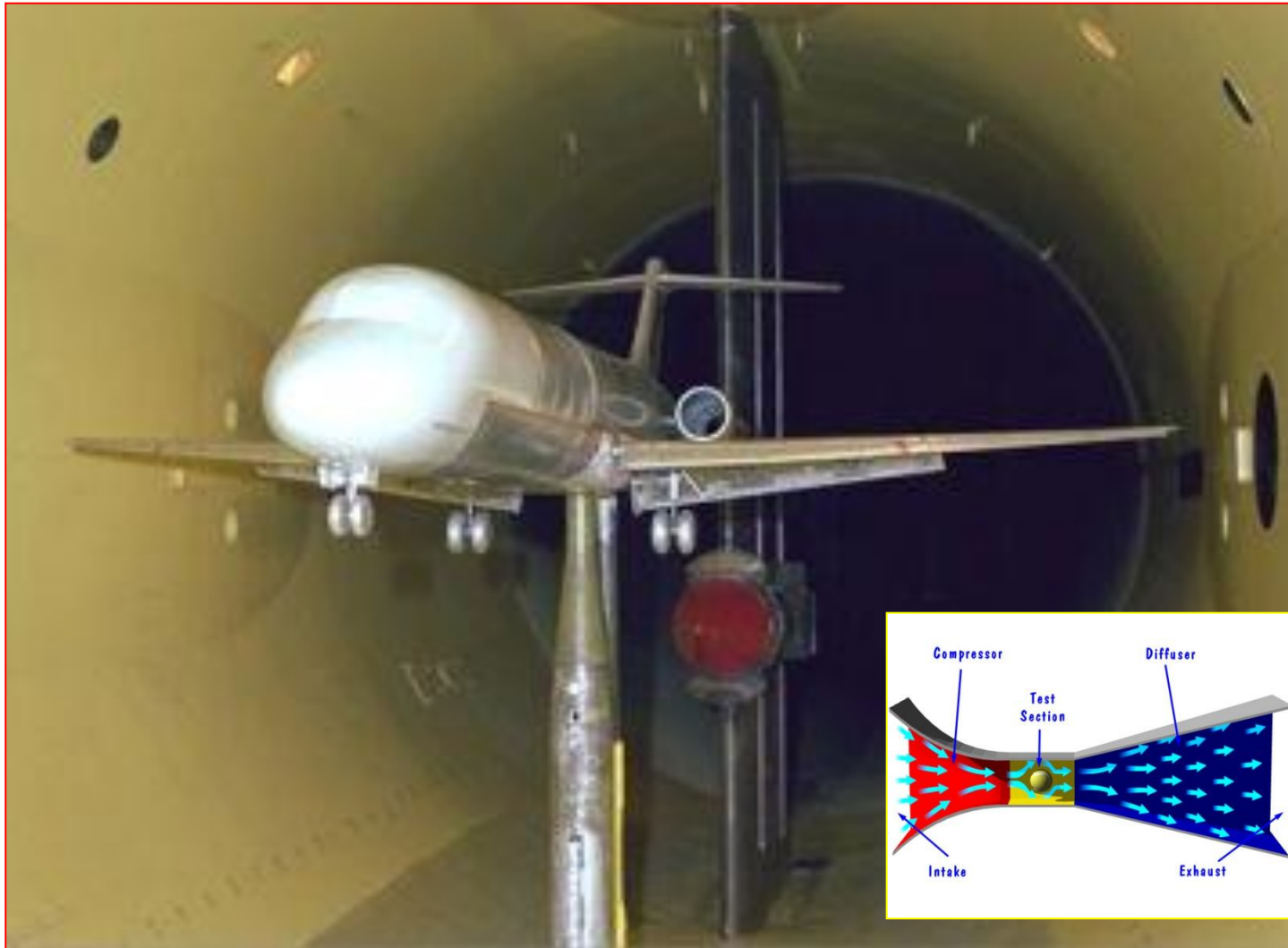


# Oral Glucose Tolerance Test (OGTT)

75 g of sugar to be drunk within 5 minutes



## Hyperemia puts the stenosis in a windtunnel

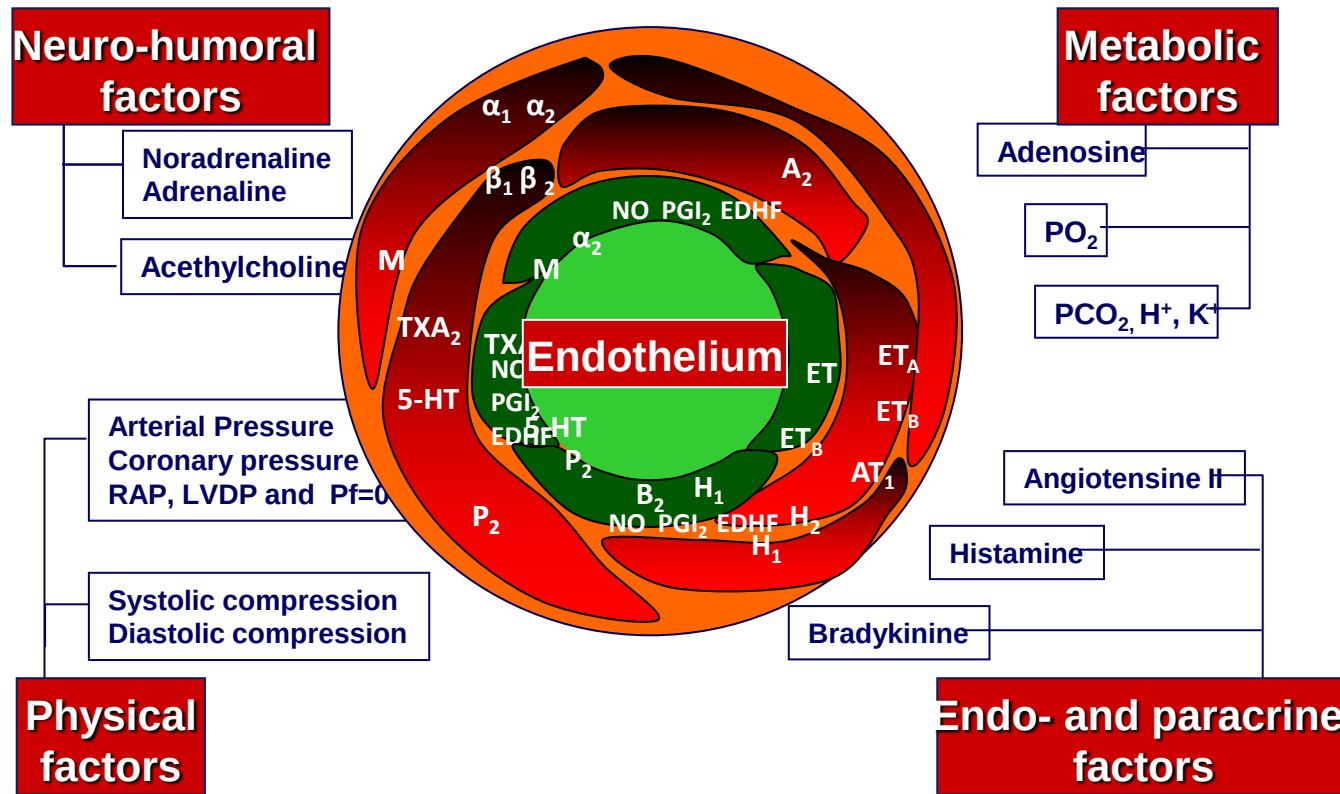


# Why?

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



The balance between supply and demand depends on mechanisms which are multiple, interacting, cumulative, nonlinear



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

# Why?

1. General concept of stress test (as opposed to “rest test”)
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# How?

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

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## The KISS principle

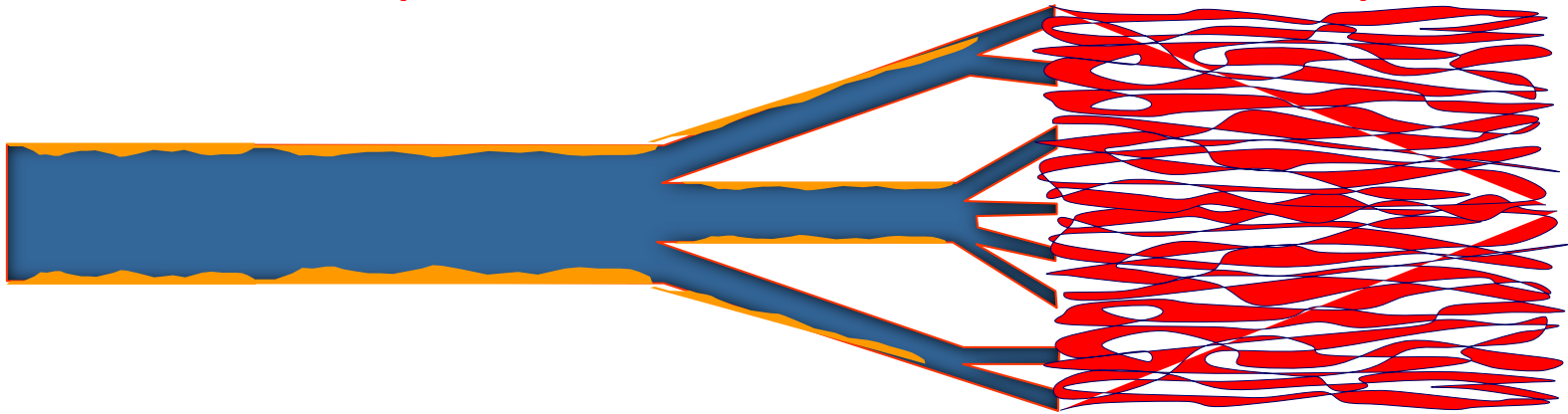
# Maximal Vasodilation

## Epicardial

= Conductance  
Arteries  $> 550 \mu$

## Microvasculature

= Resistance  
Arteries  $< 550 \mu$



~~Vasospasm~~

~~Autoregulation~~

# Maximal Vasodilation

- 1. Nitrates** → **Epicardial arteries**
- 2. Adenosine** → **Microvasculature**
  - **IV: 140  $\mu\text{g/kg/min}$**
  - **IC: 100 – 200  $\mu\text{g}$  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  
 $\beta_1$ -agonist → ↑  $O_2$  consumption → **adenosine** ↑  
 Adren stimulation → ↑  $O_2$  consumption → **Adenosine** ↑  
 Ischemia → release of **adenosine**

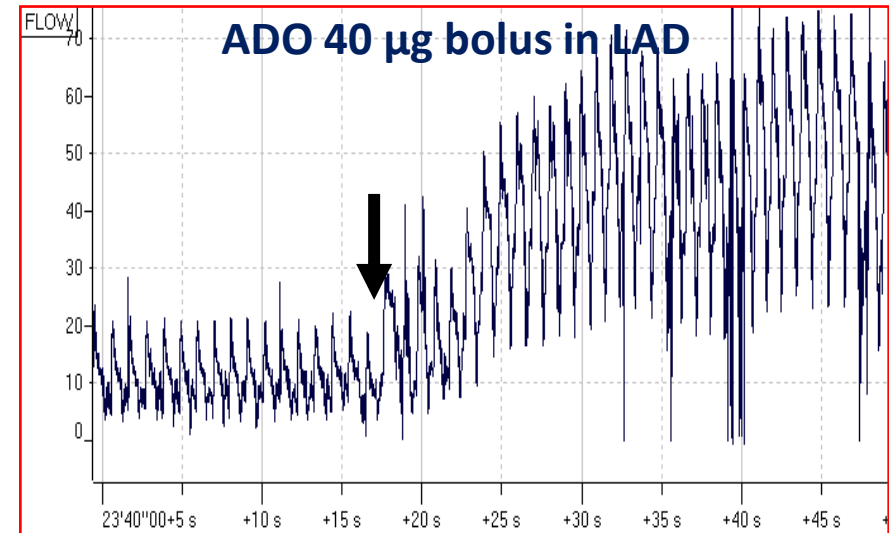
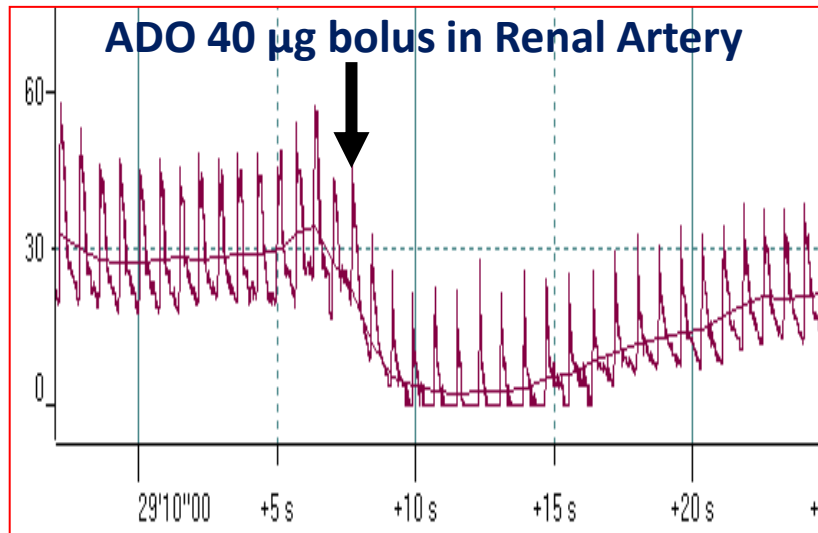
# Adenosine: Mechanisms of Action

## Target organs

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

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

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



**Half Life = 4 to 10 s**



# Maximal Vasodilation

**1. Nitrates → Epicardial arteries**

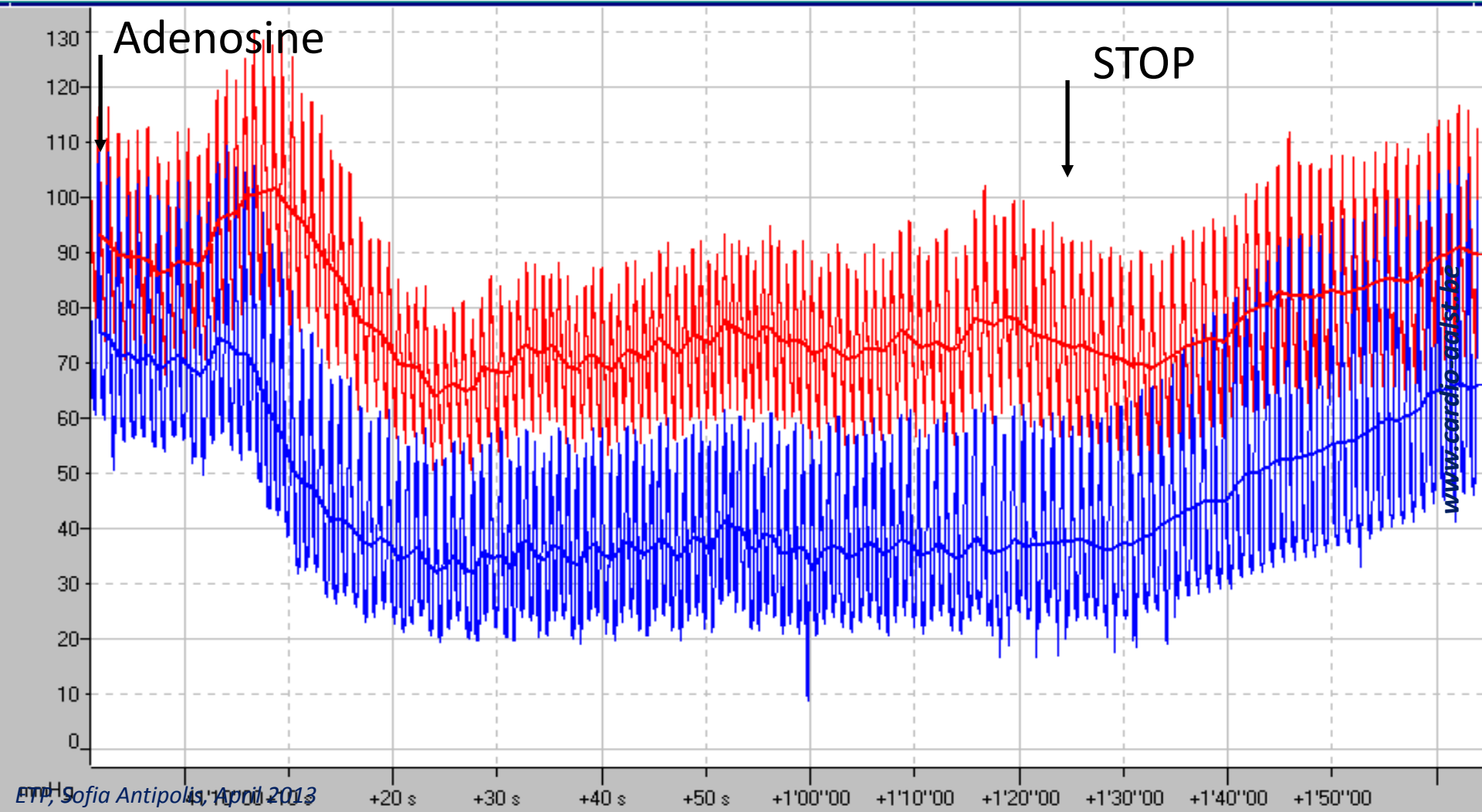
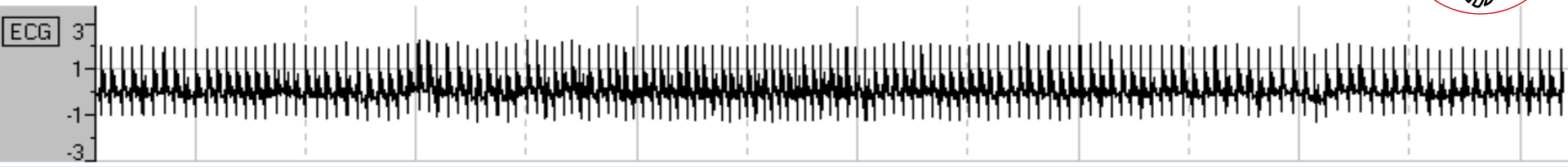
**2. Adenosine → Microvasculature**

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

➤ **IC: 100 – 200  $\mu\text{g}$  in bolus**

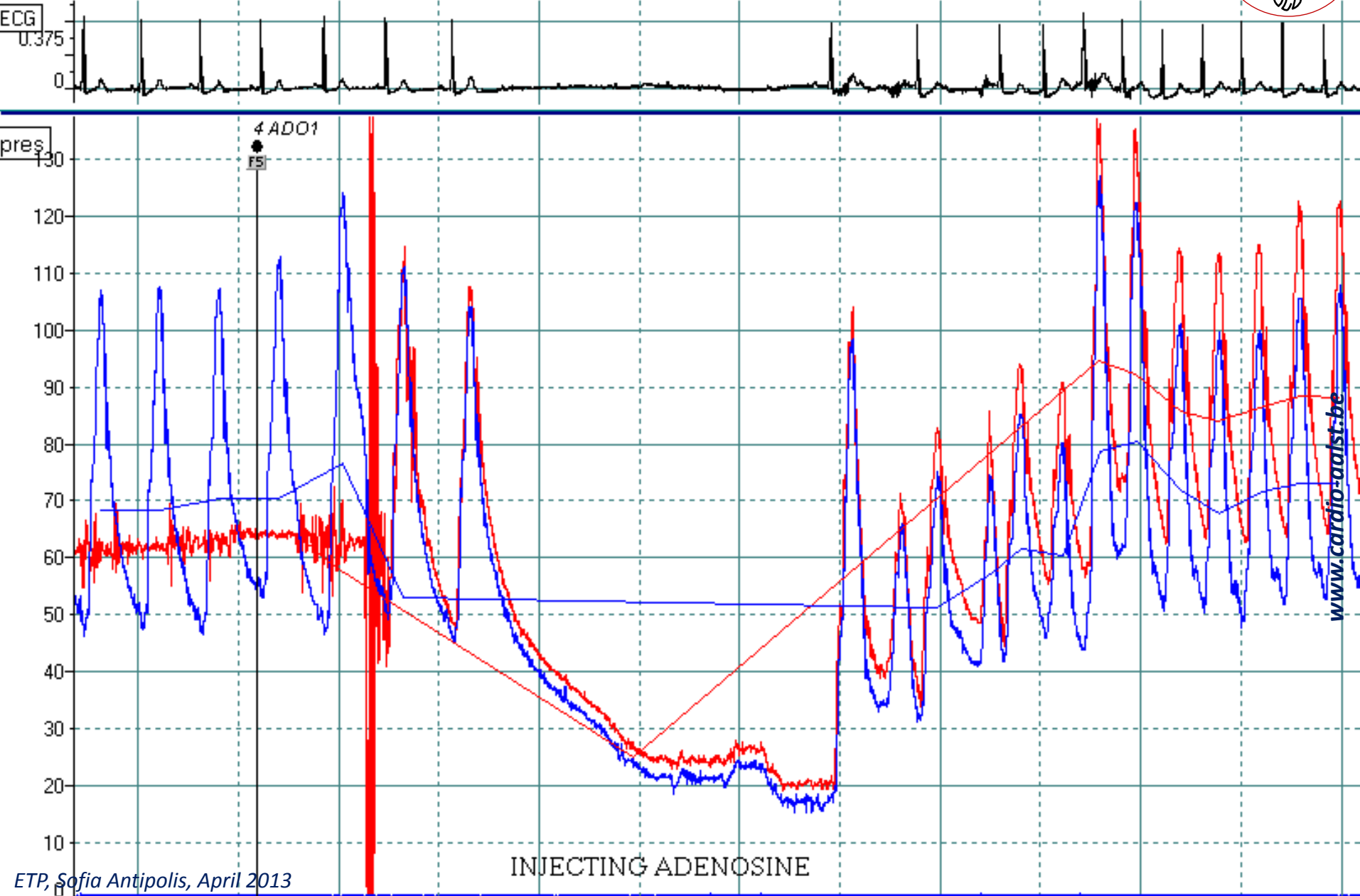
## Specificities of IV Adenosine (140 µg/kg/min)

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



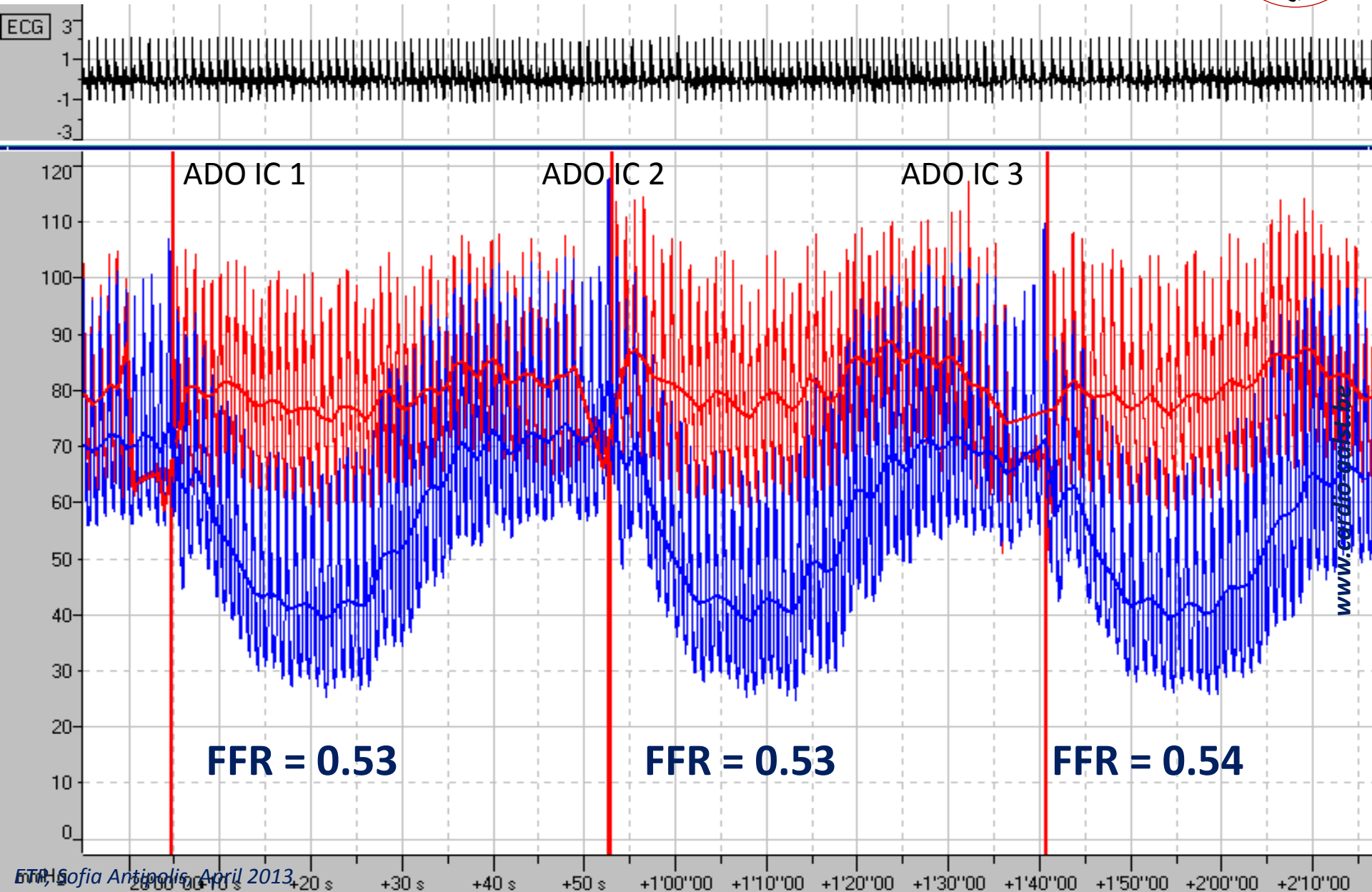
## Specificities of IC Adenosine (100-200 µg)

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!



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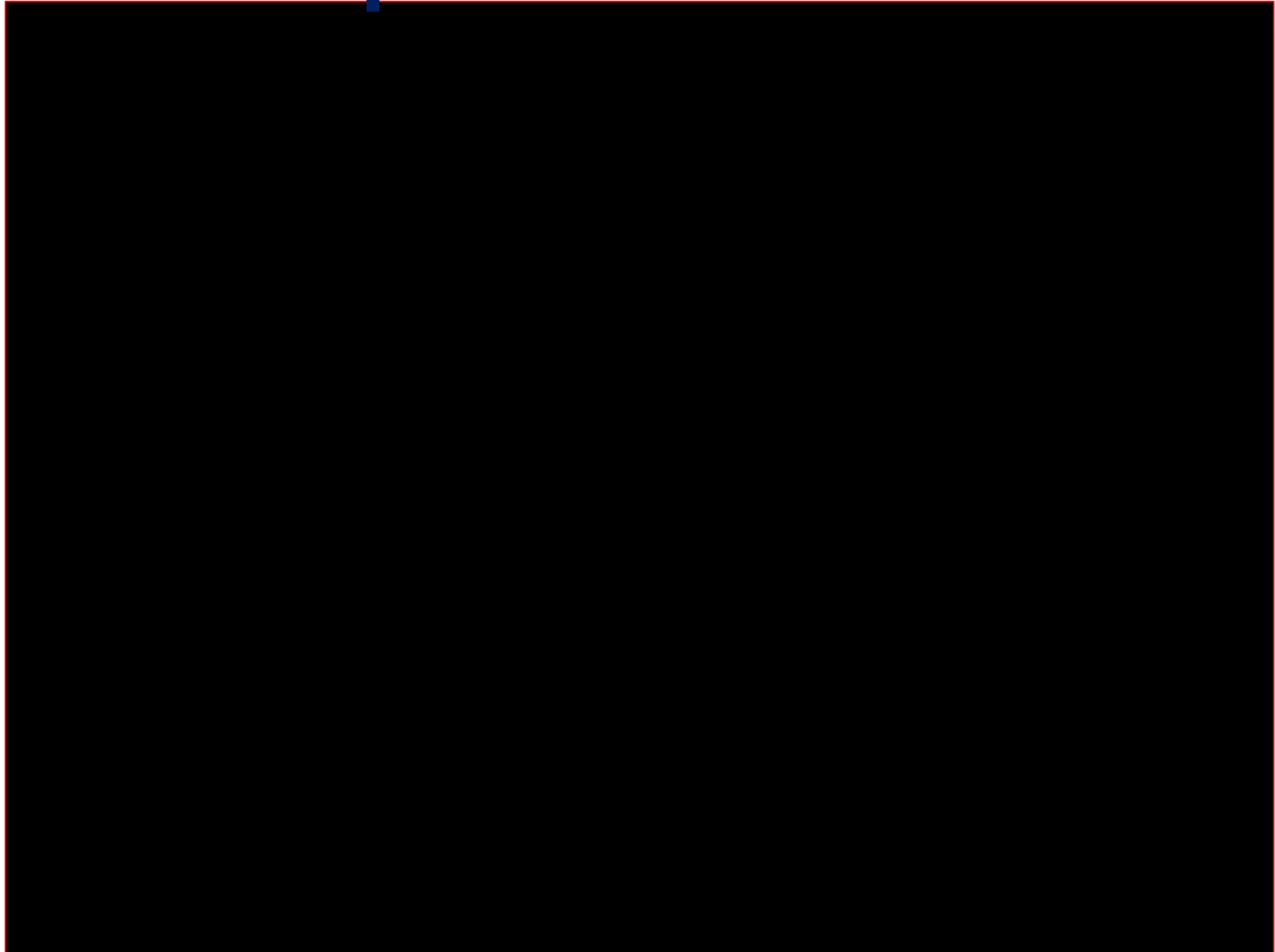


# Tips and Tricks

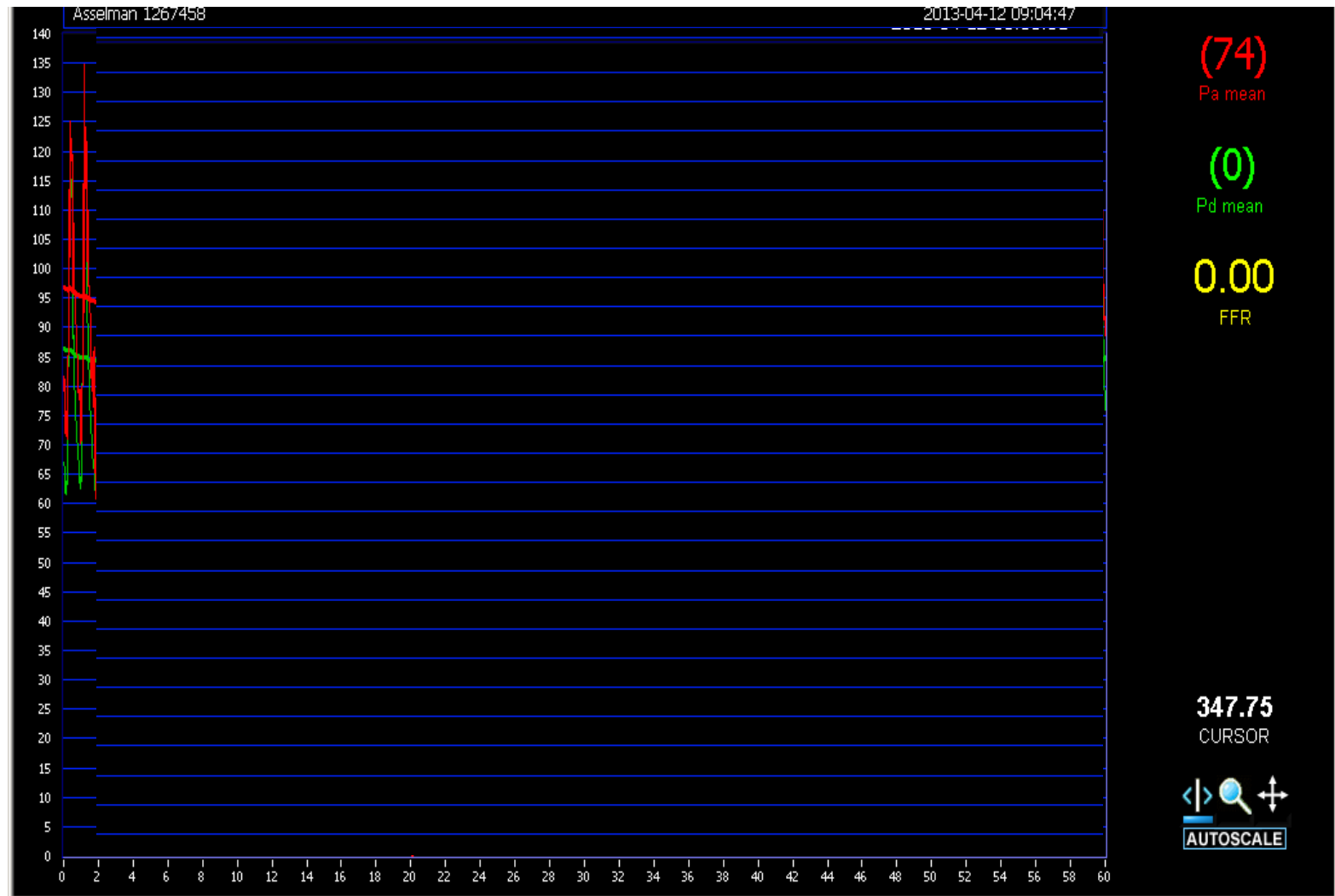
1. IV: either central or large venous access
2. IC: keep the injection as short as possible
3. Be consistent, teach the nursing staff, the techs, ...
4. Pay attention to the quality of the recording of the tracings:  
*“record every tracing as if you have to present this case at the opening session of the AHA”*



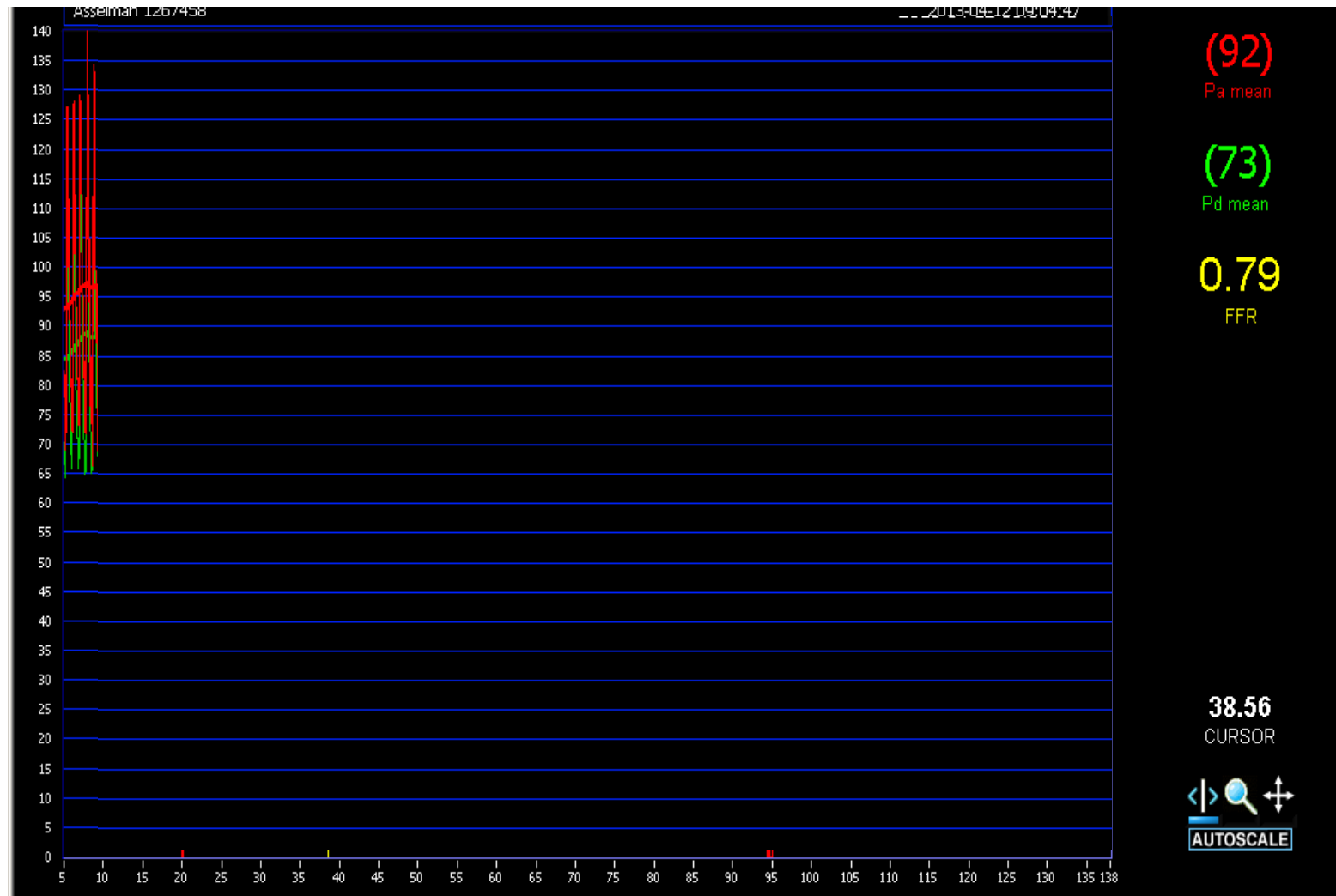
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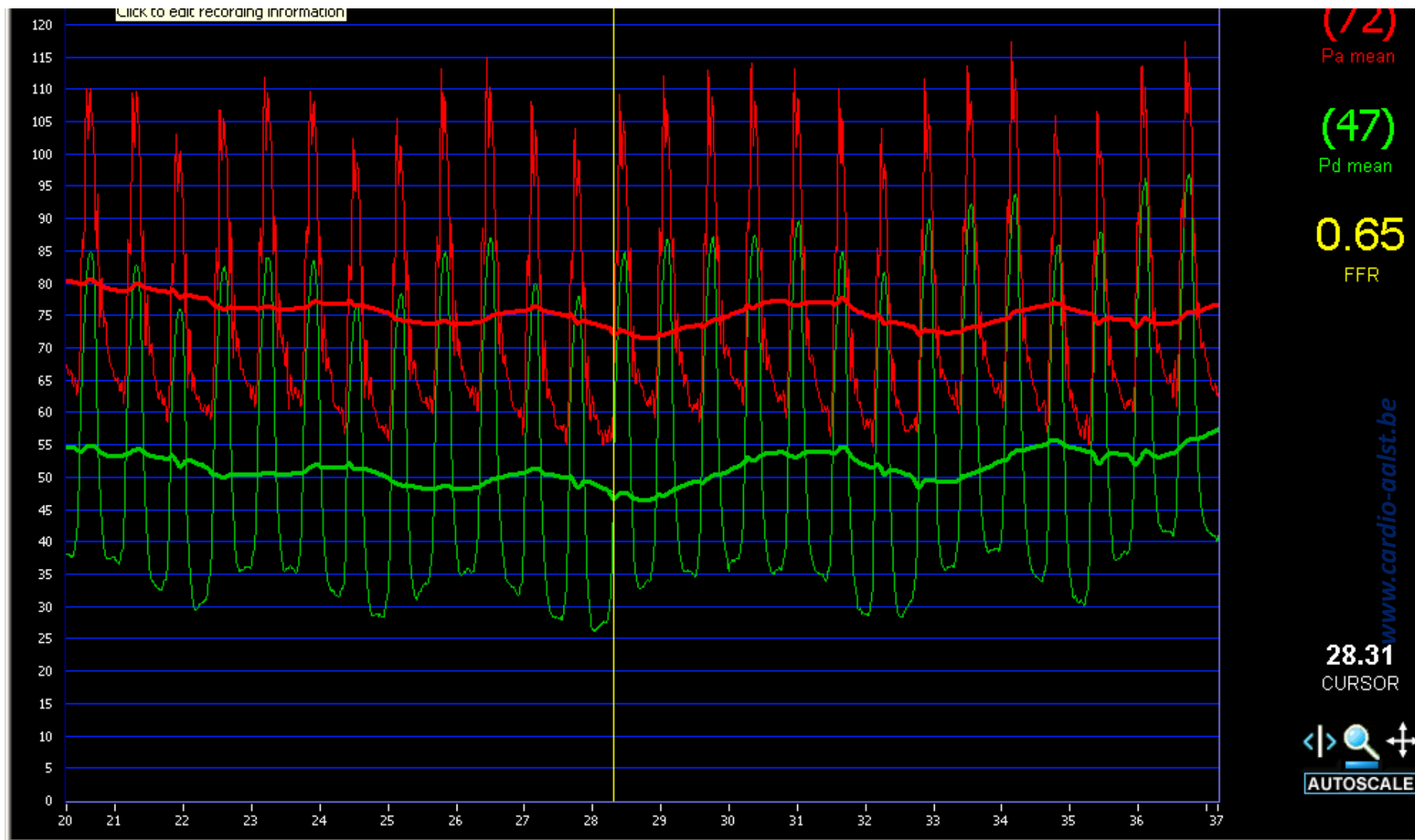


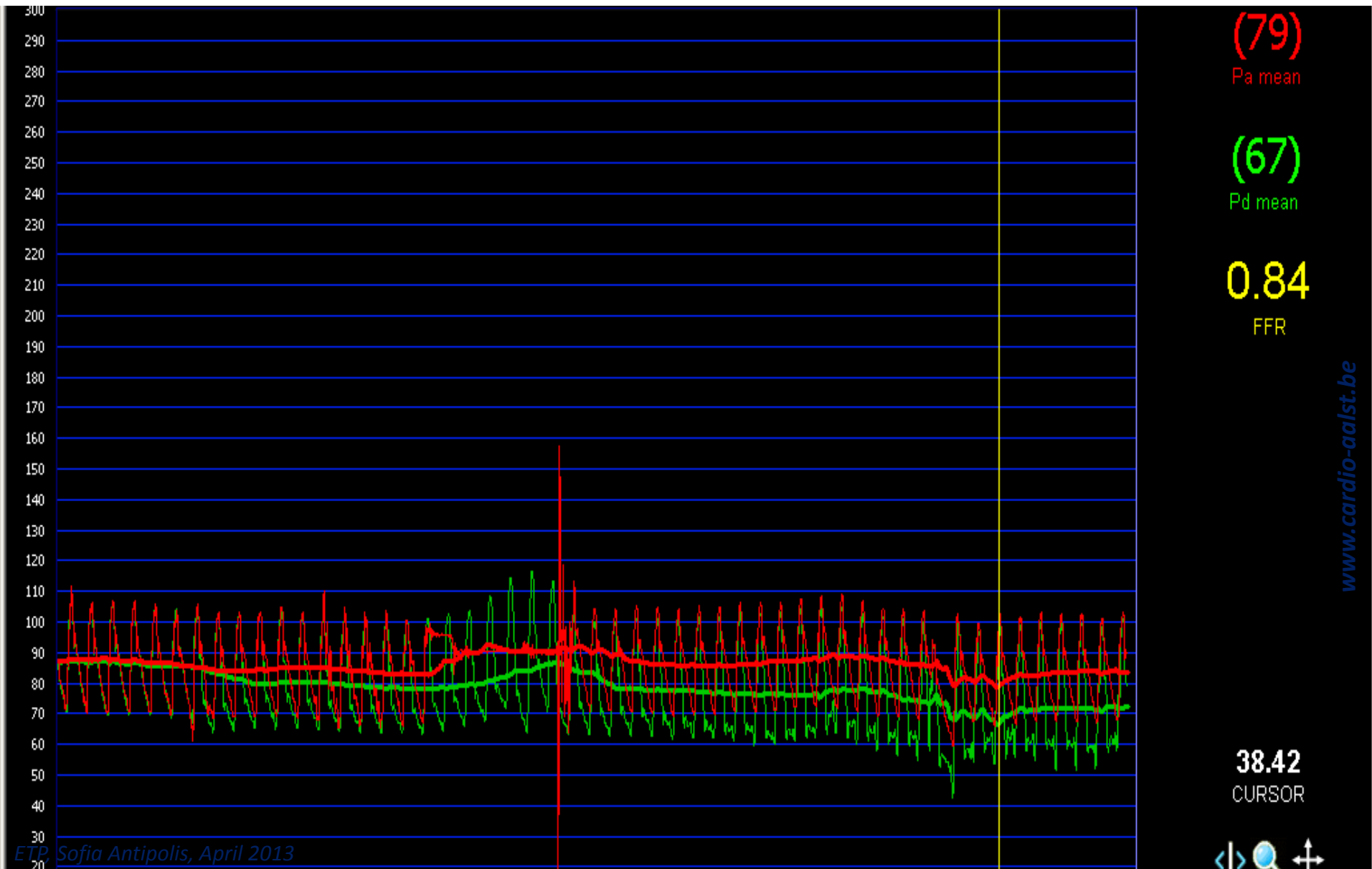
## Tips and Tricks



# Tips and Tricks







# Hyperemia



(53)

Pd mean

0.64

FFR

87.35

CURSOR

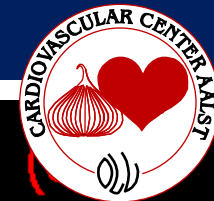


AUTOSCALE

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# Hyperemia



Pa mean

(53)

Pd mean

0.64

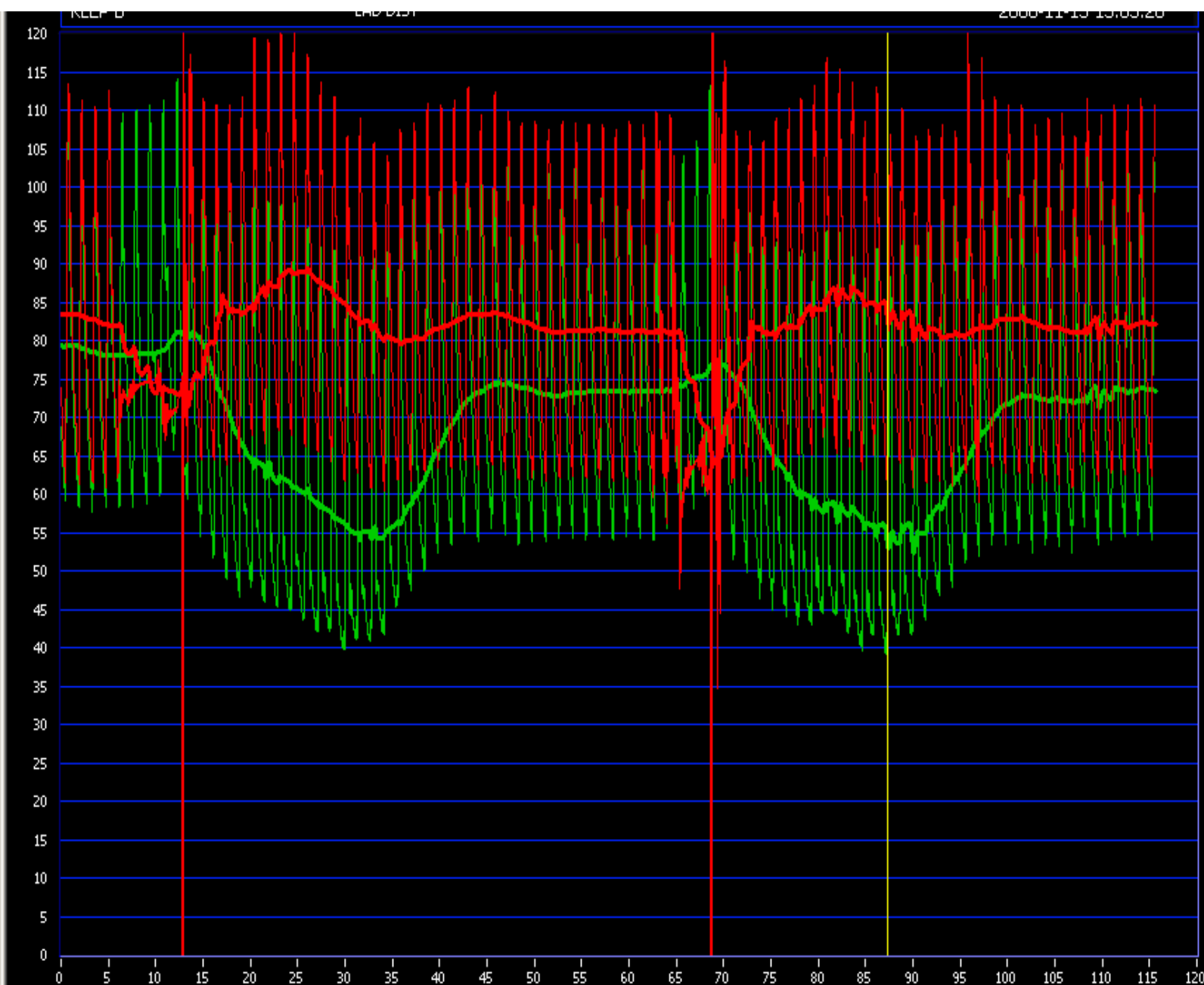
FFR

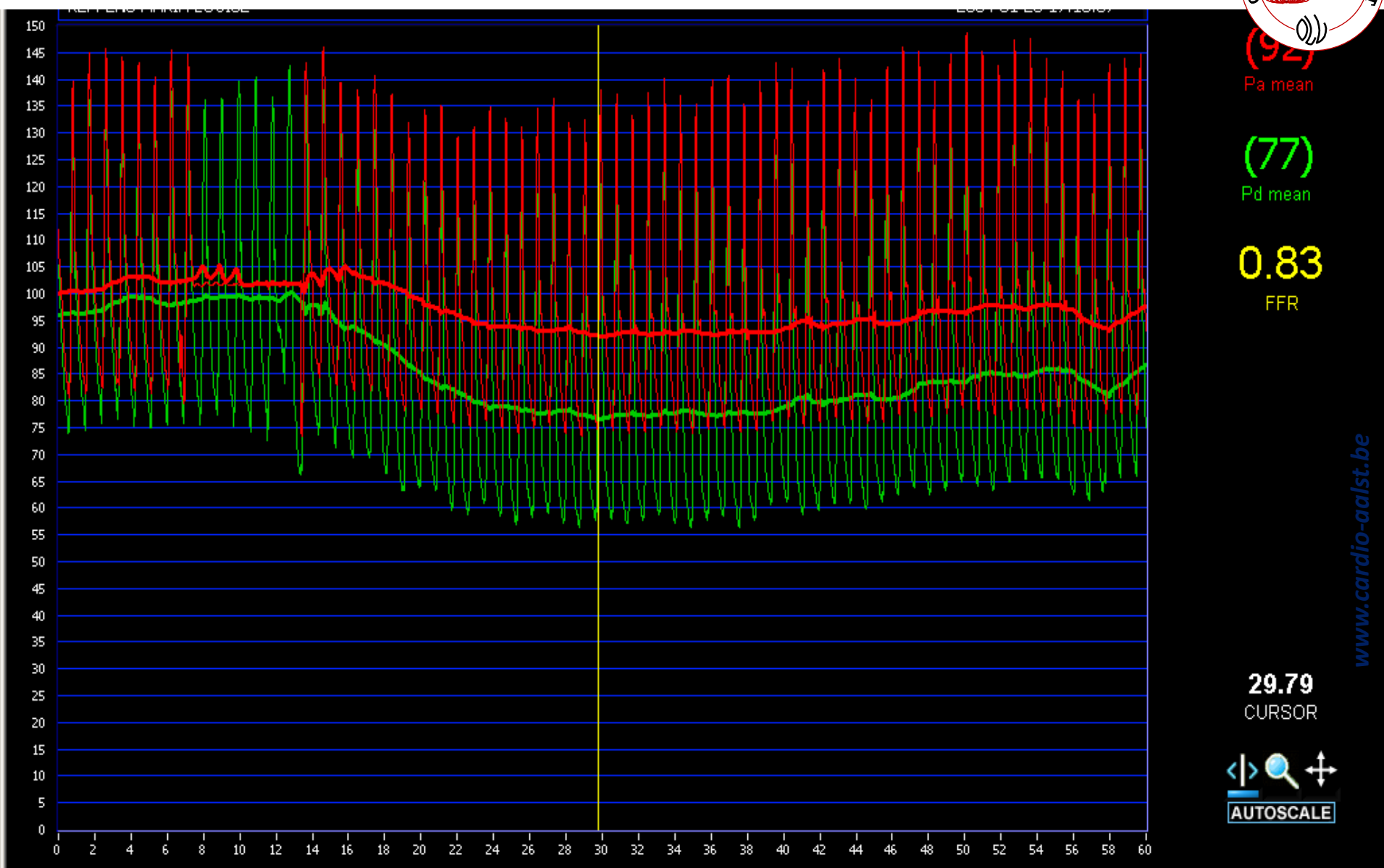
87.35

CURSOR



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# Conclusive Remarks

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

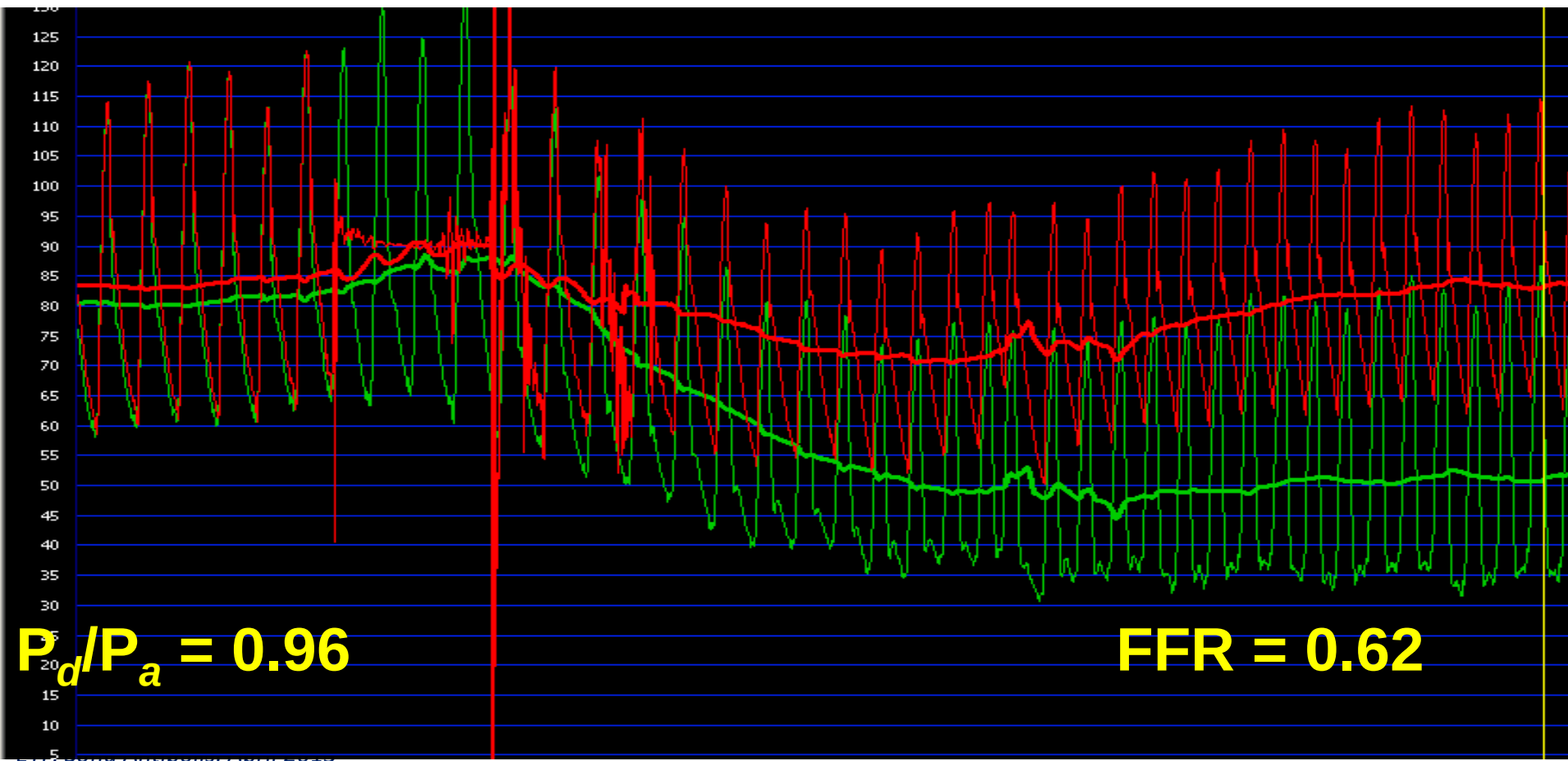
## FAQ

- ✓ 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  $> 140 \mu\text{g/kg/min}$  ?
- ✓ 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 ?

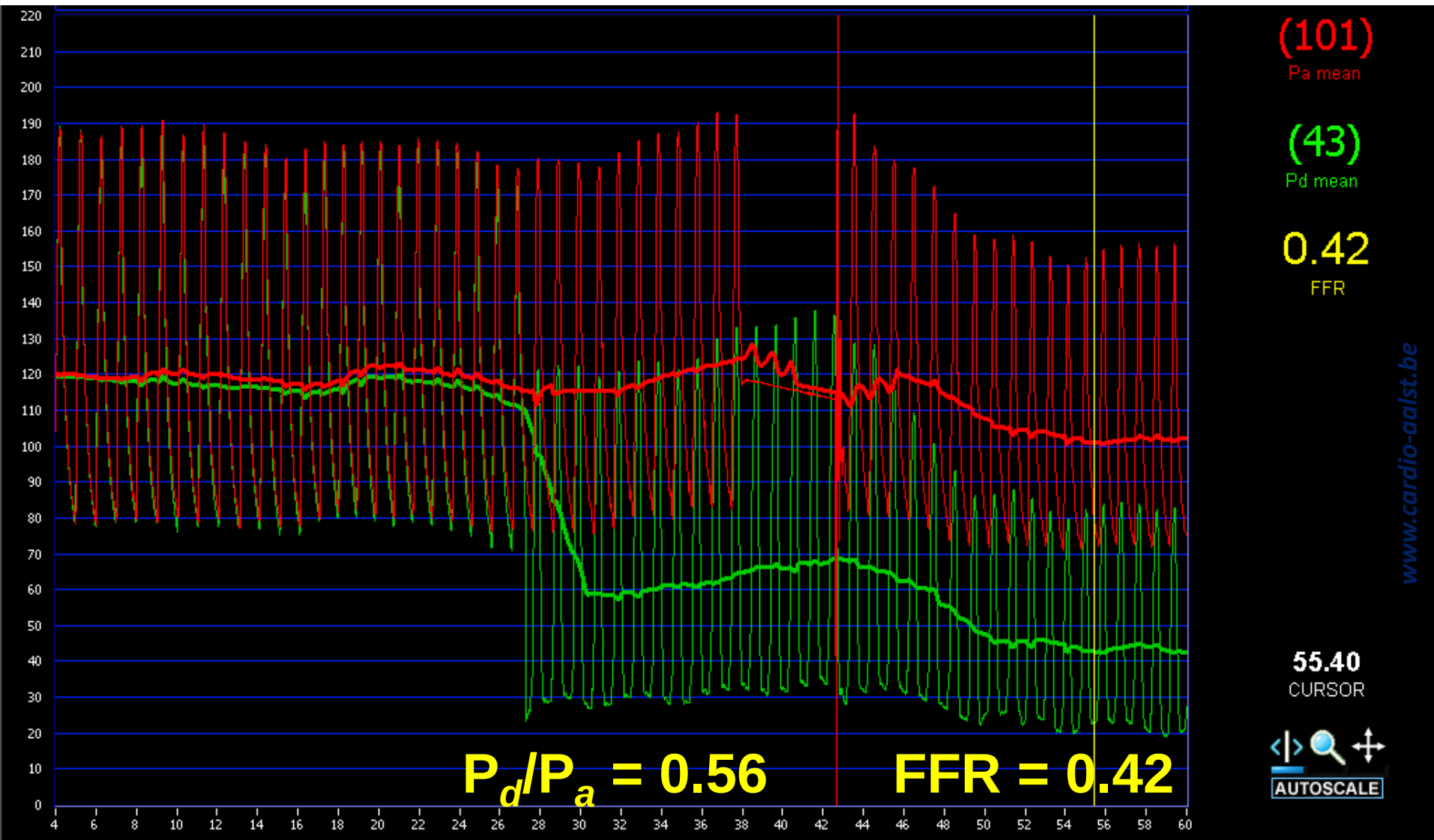
## YES



## FAQ

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

When  $P_d/P_a$  at rest  $< 0.80$ , do we have to induce hyperemia ?

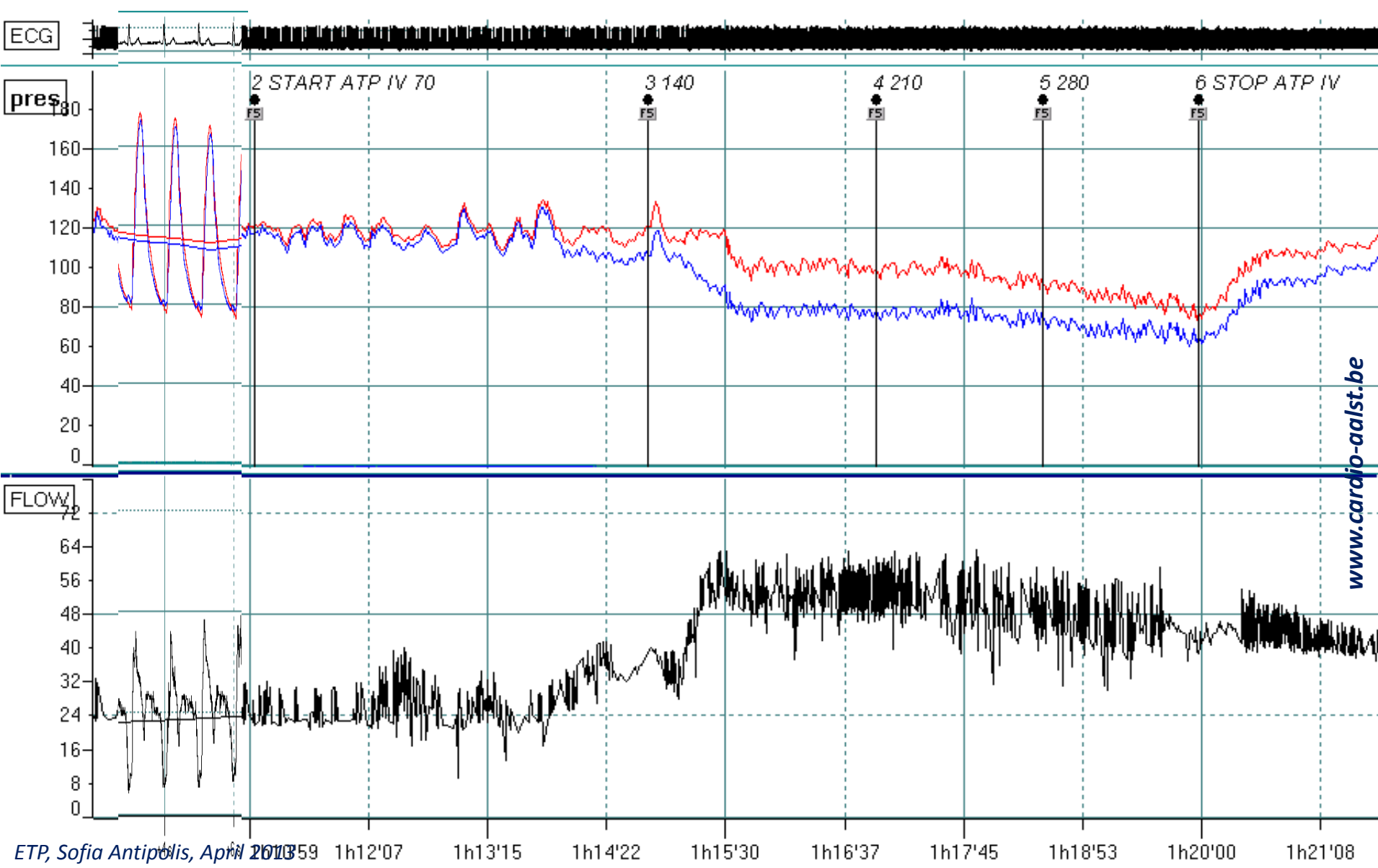


## FAQ

Useful to increase the dose of IV ado  $> 140 \mu\text{g/kg/min}$  ?

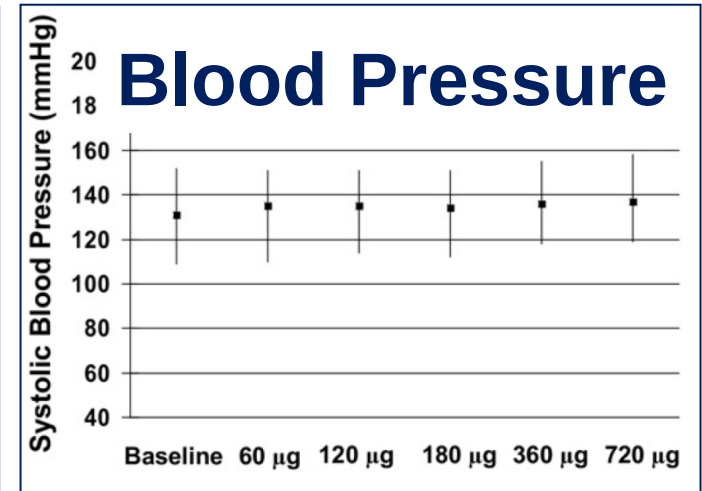
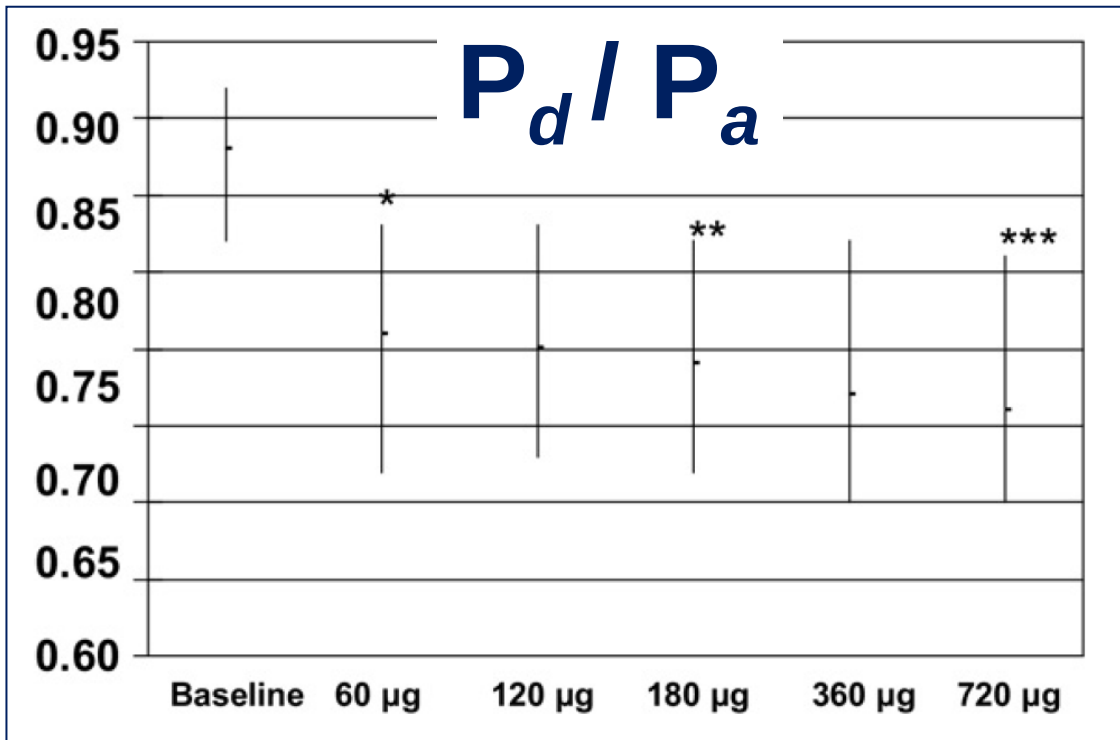
**NO**

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



# FAQ

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



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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 algesic substance which stimulates the same nerves than those responsible 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**

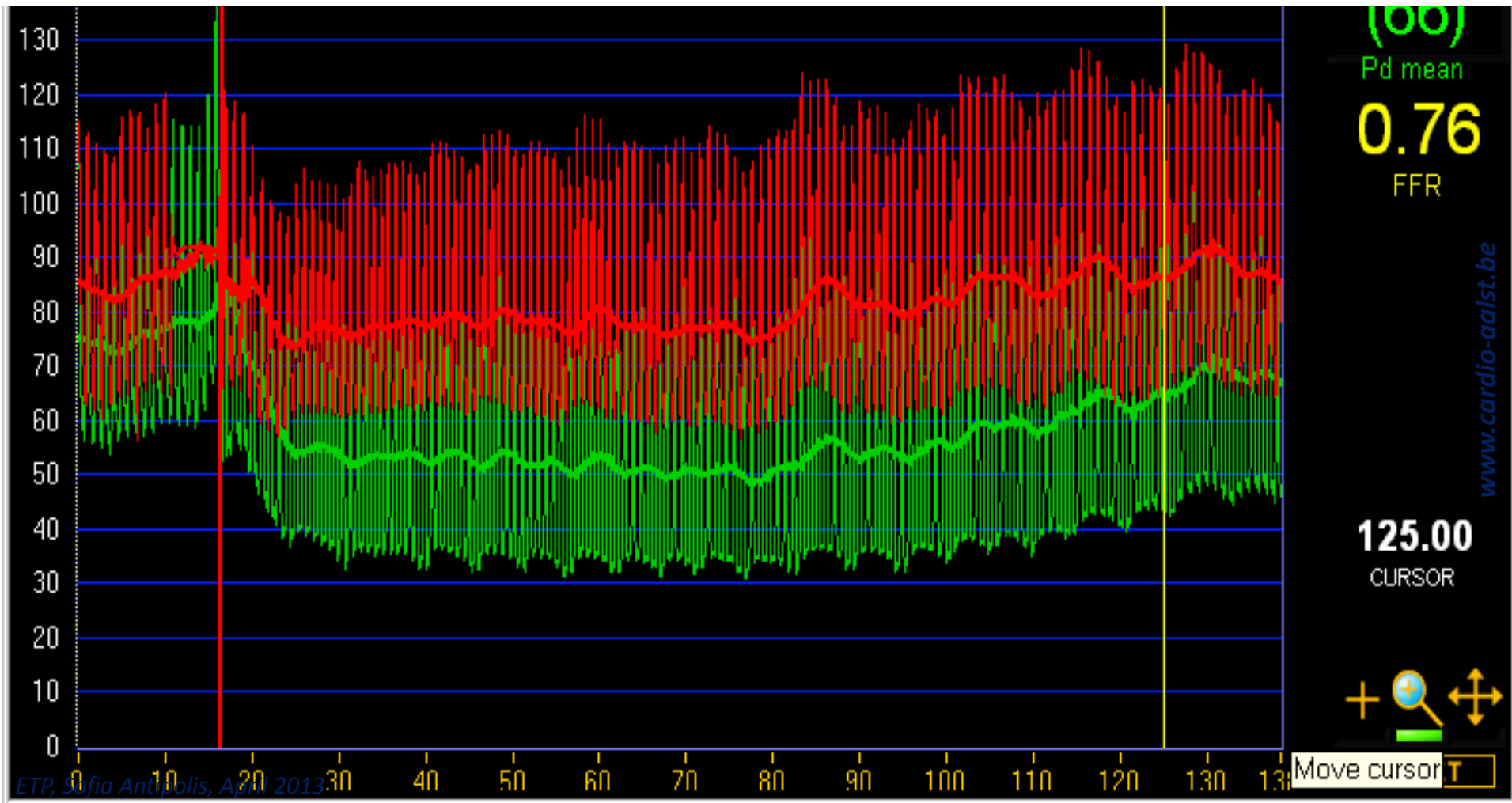
# FAQ

**Can Papaverine be used instead of Adenosine ?**

# Papaverine IC

16 mg IC in LCA

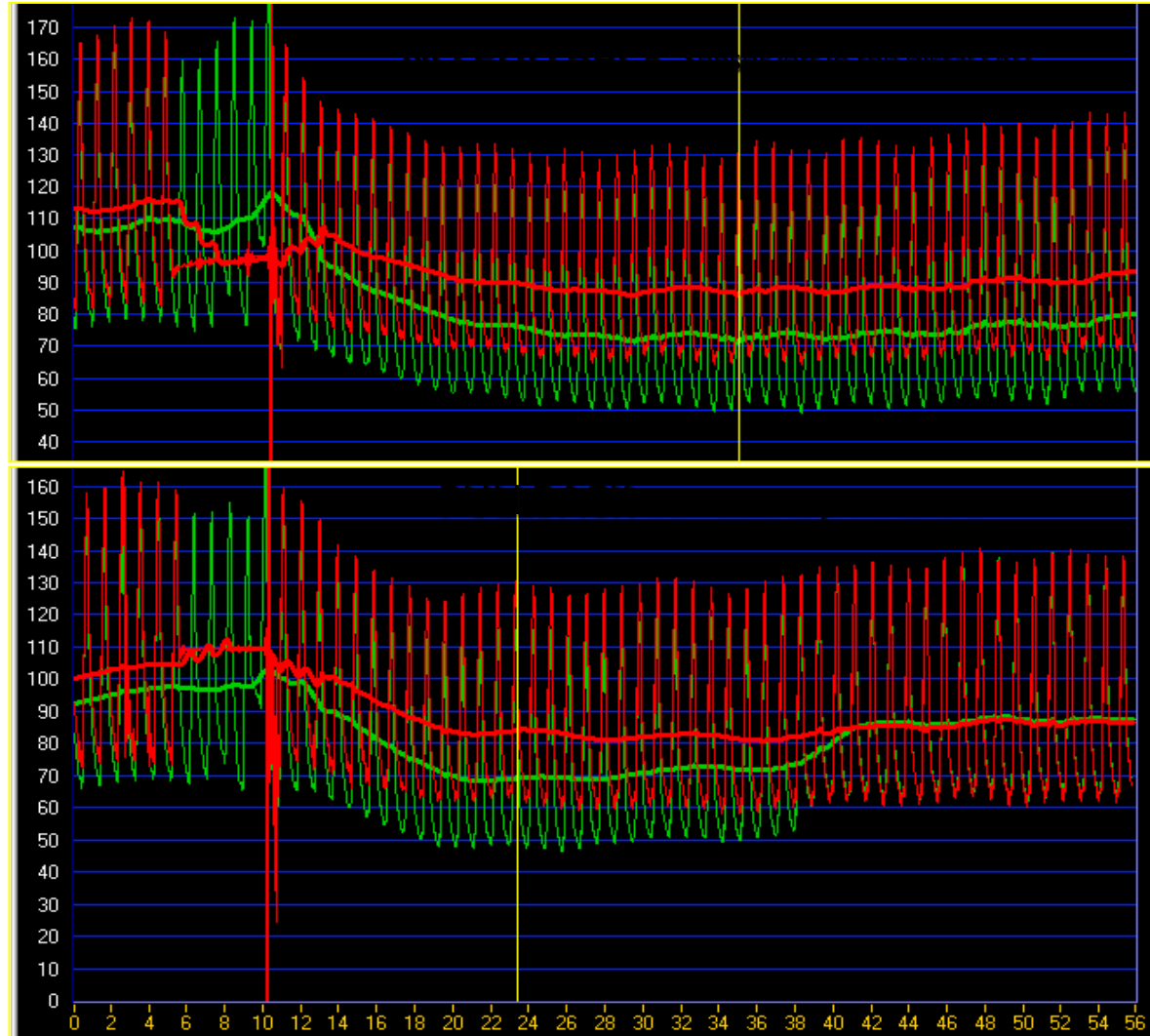
12 mg IC in RCA



# Papaverine IC

16 mg IC in LCA

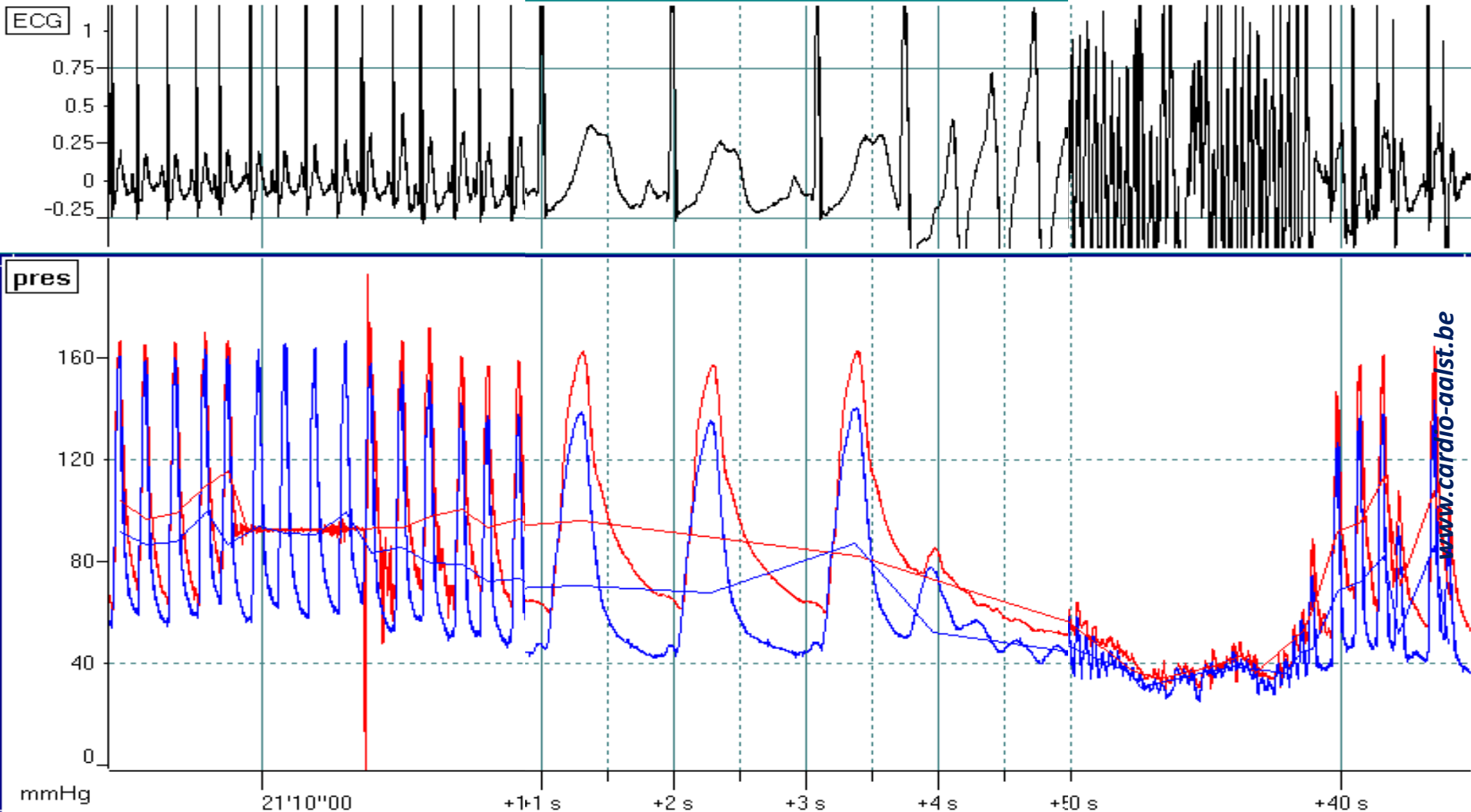
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## Papaverine IC

16 mg IC in LCA

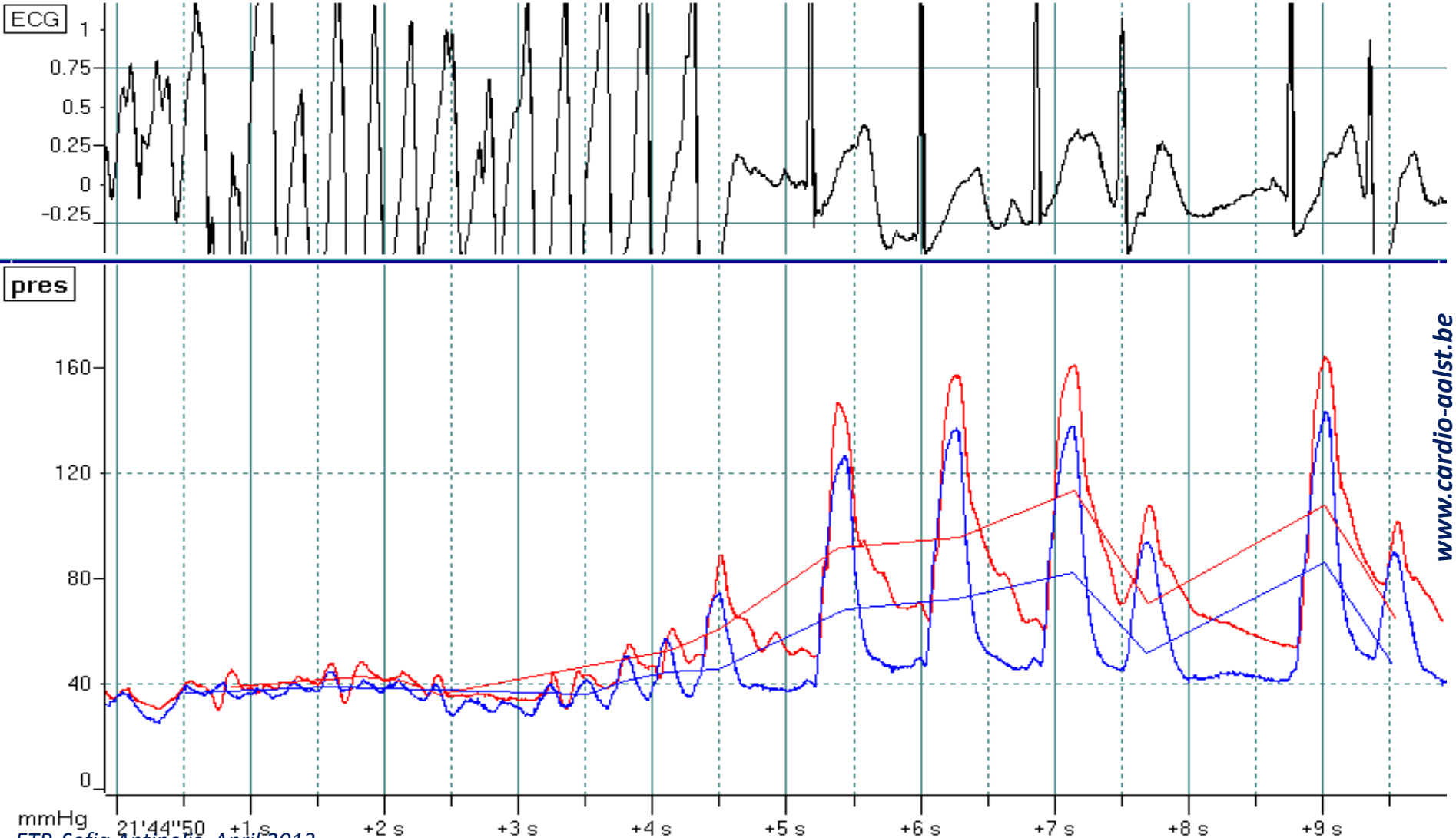
12 mg IC in RCA



## 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

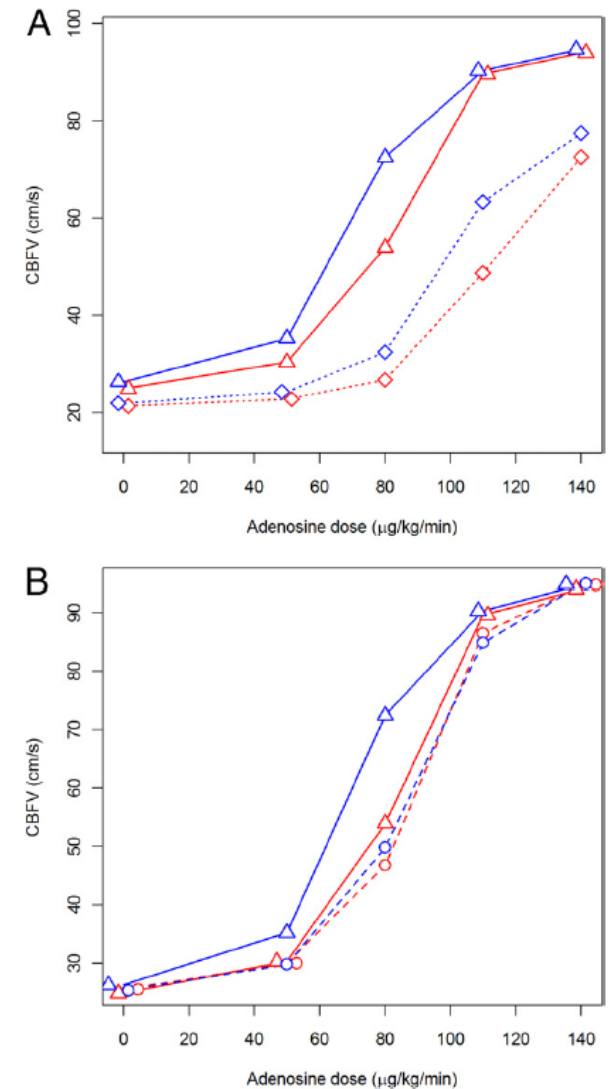
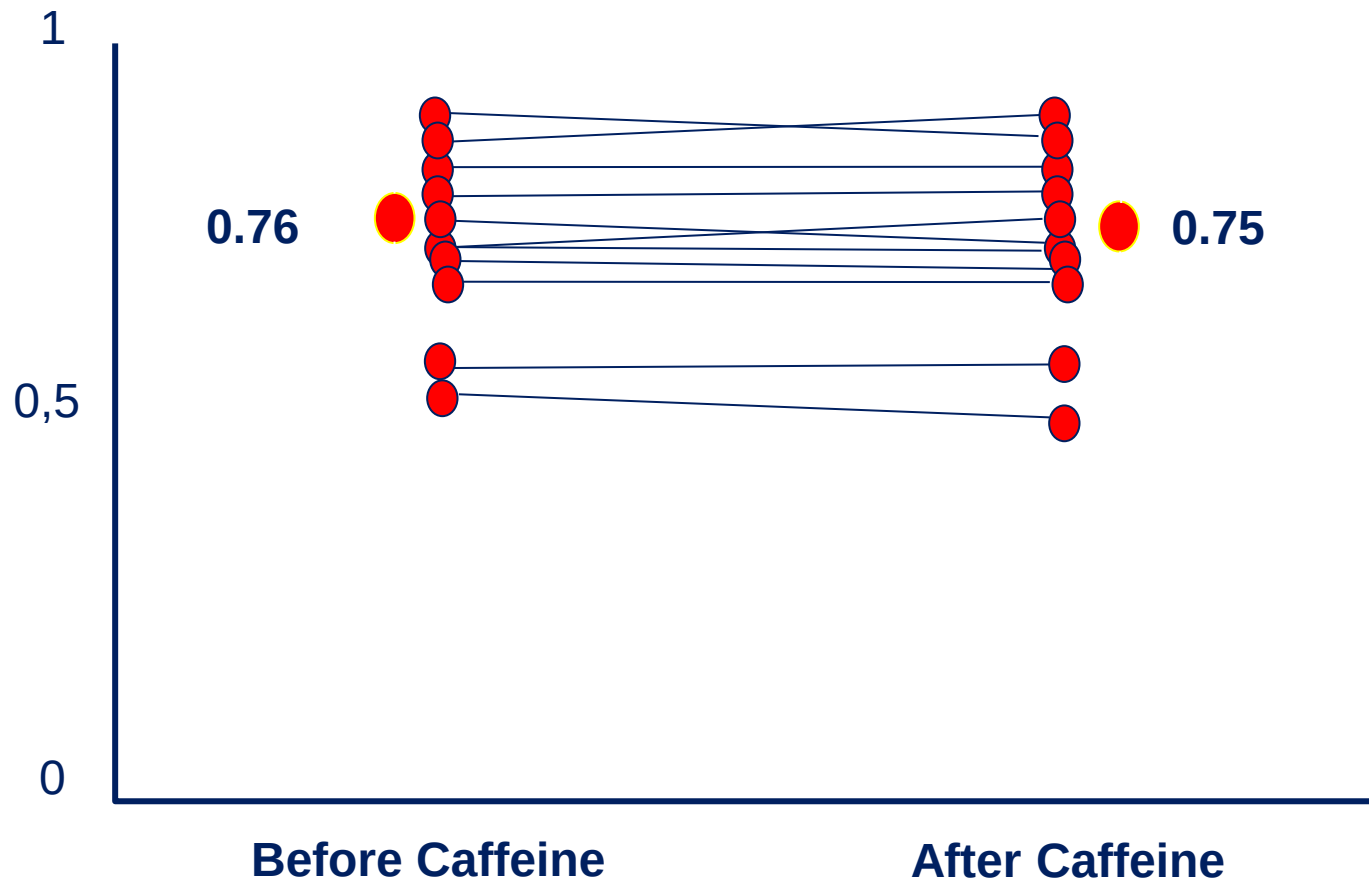


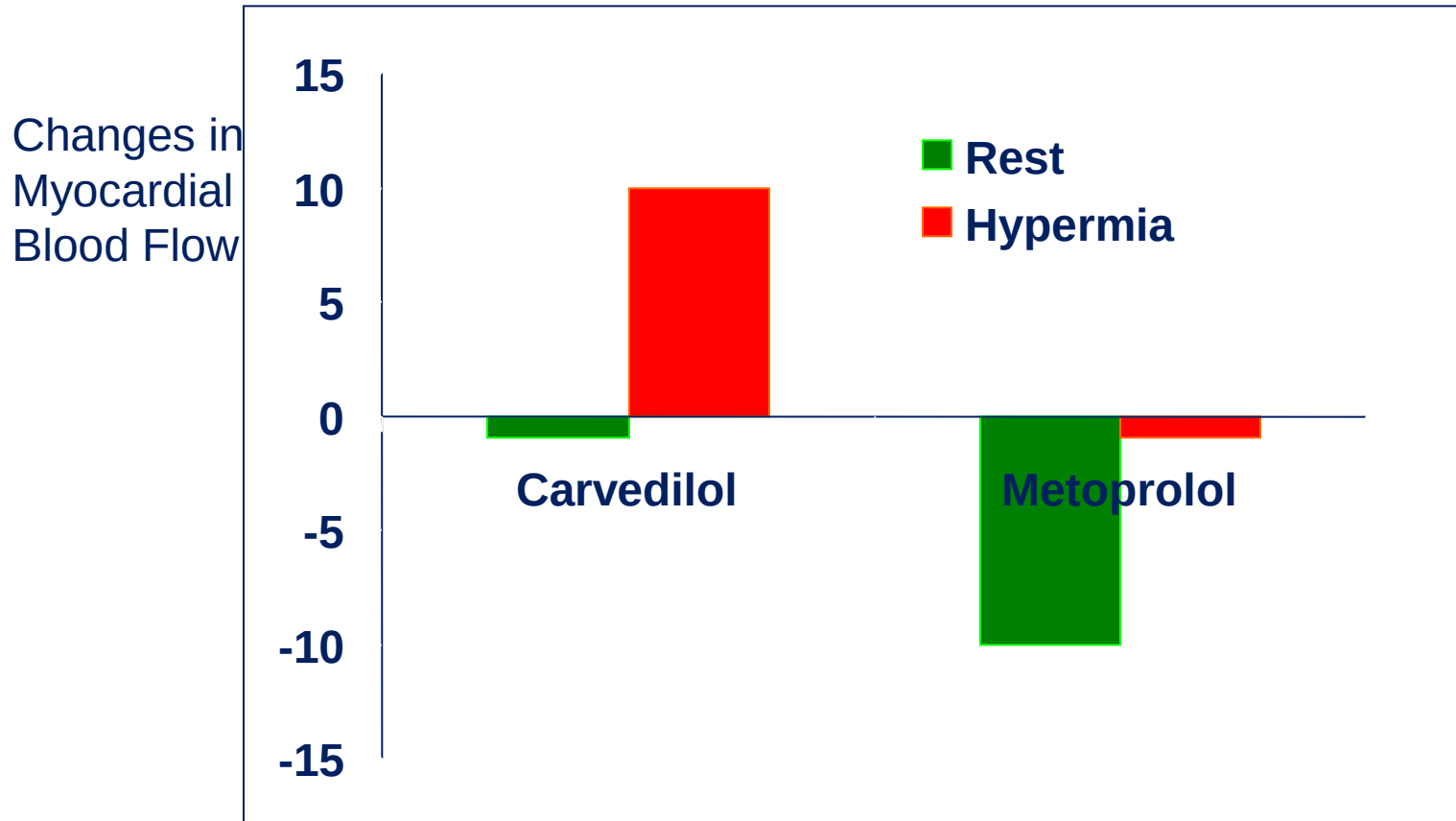
**Figure 3** Treatment Effect on Adenosine-Induced CBFV

(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.

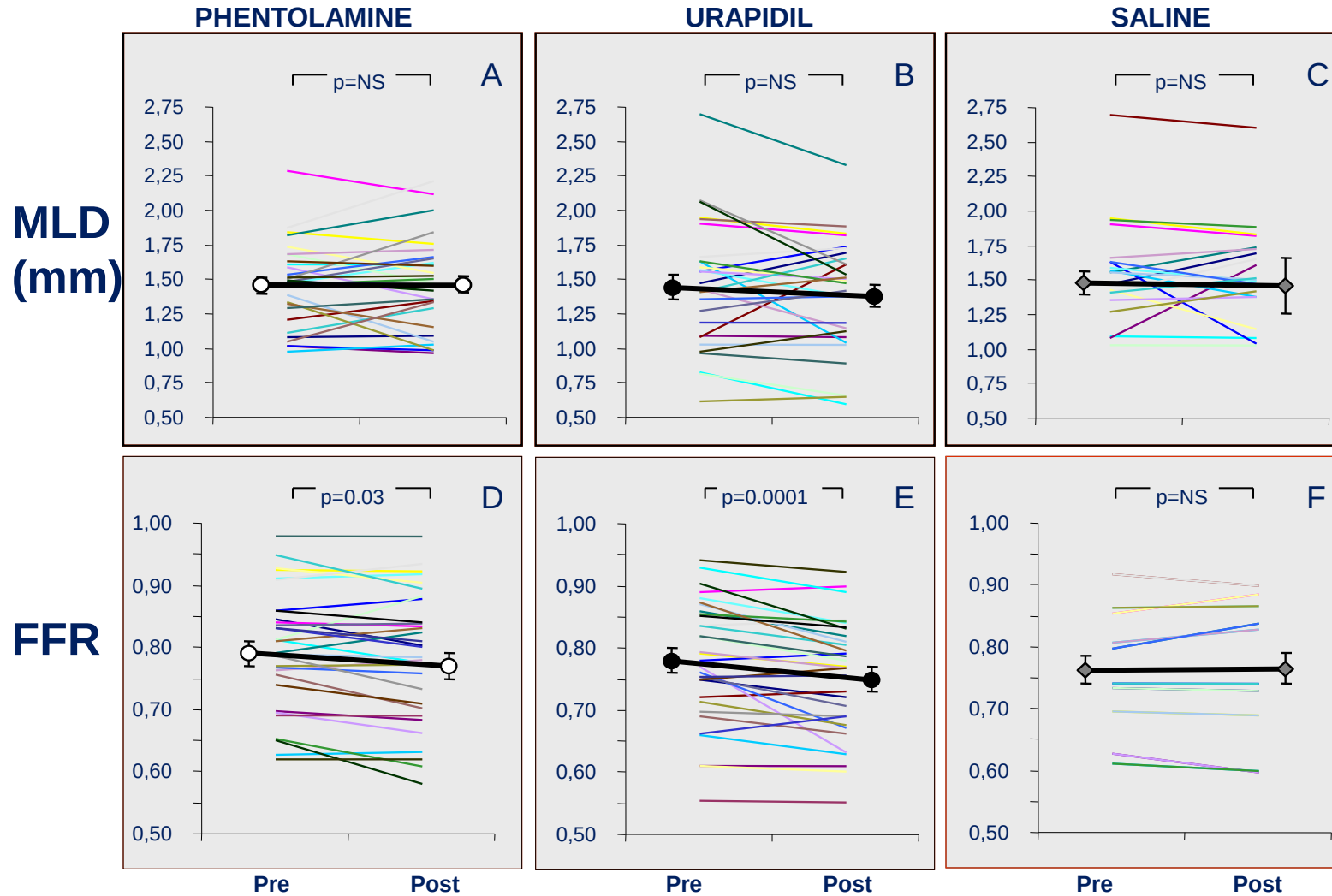
# Effect of Caffeine on FFR



## Beta-Adrenergic Blockade and Myocardial Flow



## Effect of $\alpha$ -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**

