Hyperemia

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Maximal Hyperemia

- Maximal Vasodilation
- Maximal Possible Blood-Flow to the Myocardium

Jeremias A, TCT 2009

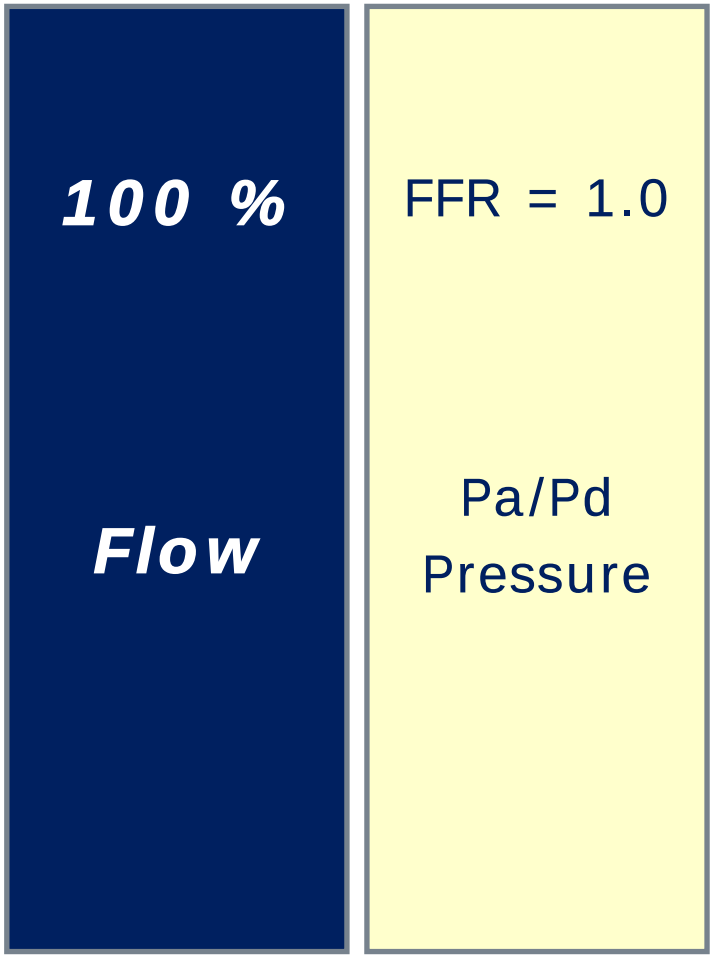
Importance of maximal hyperemia

- Pressure and Flow are proportional only at the point of *maximal hyperemia*

- To detect the presence and extent of myocardial ischemia, maximal hyperemia is mandatory

Jeremias A, TCT 2009

Flow-Pressure Relationship



- We are measuring coronary ***pressure*** to measure coronary ***flow***
- It is at the point of ***maximal hyperemia*** that FFR is proportional to blood flow
- At this point further blood flow is impossible, thus

100% flow = FFR 1.0

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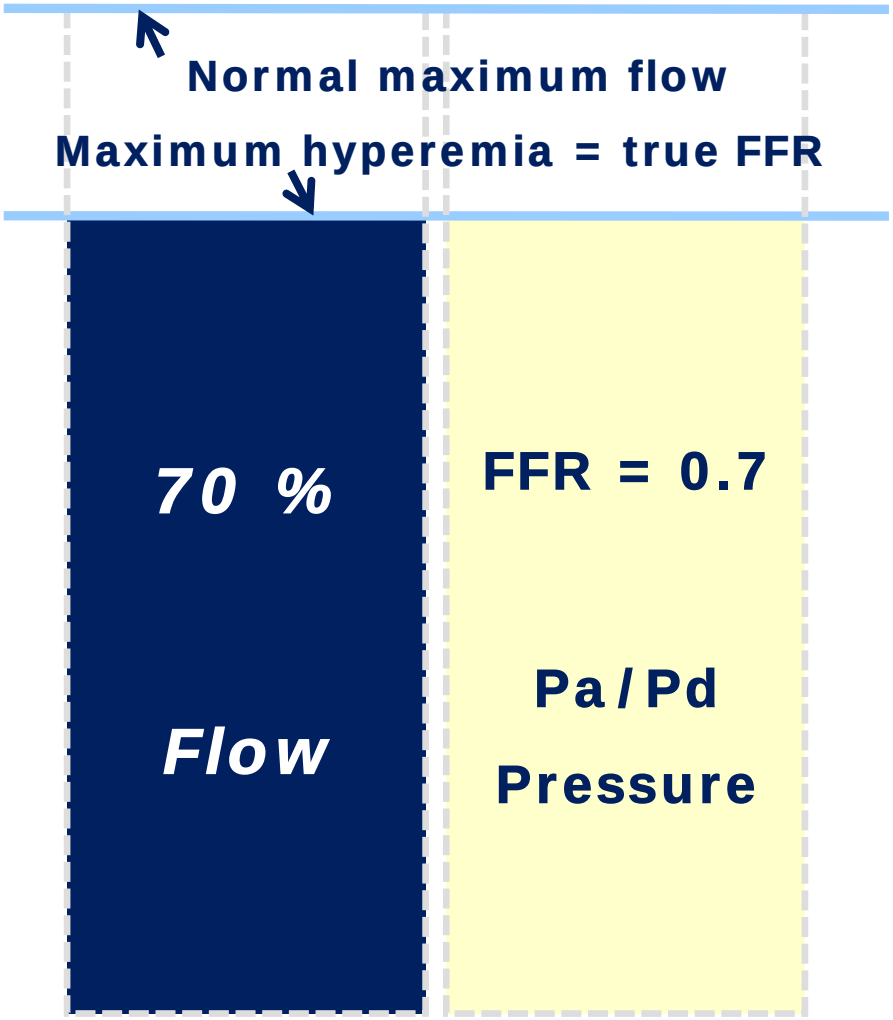
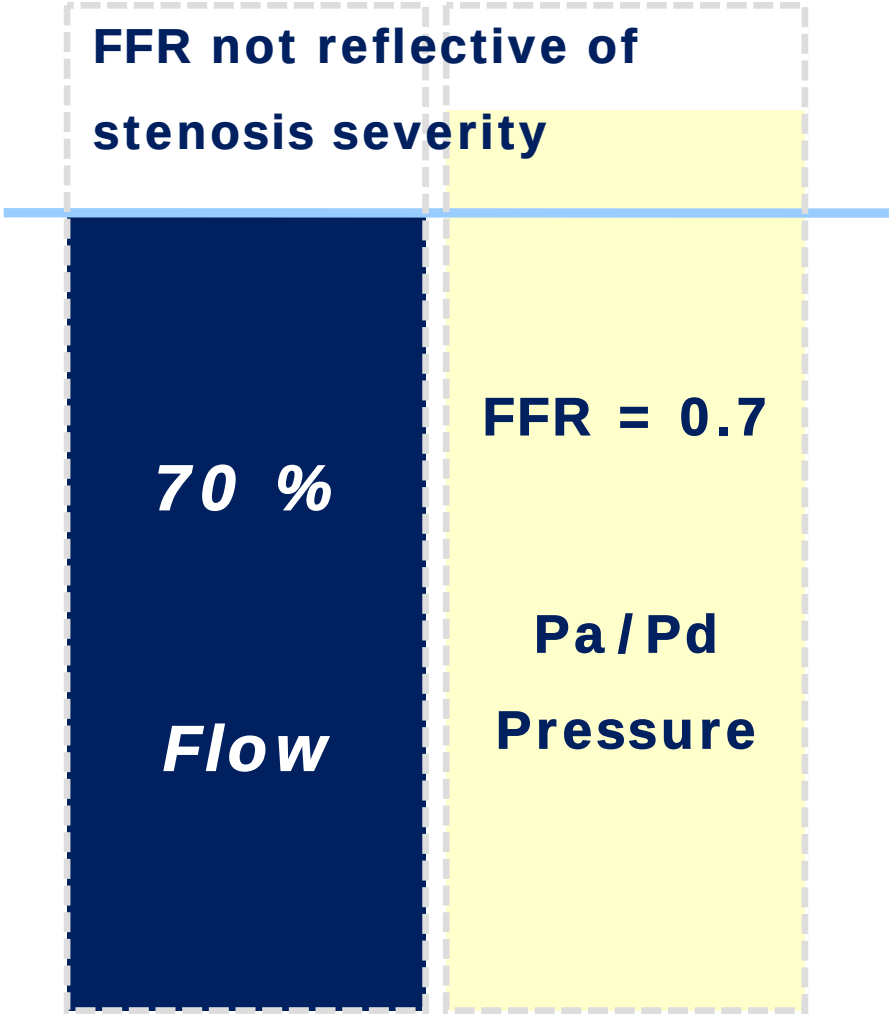
Flow-Pressure Relationship
Significant Coronary Stenosis



- With a stenosis, maximal blood flow is lower despite maximal stimulation of the microvasculature- in this case only reaching 70% compared to normal
- The corresponding Pd/Pa pressure will therefore be proportional to the flow at this new point
- 70% blood flow is proportional to FFR 0.70

Jeremias A, TCT 2009

Flow-Pressure Relationship
Sub-maximal Hyperemia



- With sub-maximal hyperemia, ***flow ≠ pressure***
- FFR is higher, thus ***underestimating*** stenosis severity
- Only at point of maximal hyperemia = true FFR

Jeremias A, TCT 2009

Pharmacologic Hyperemic Stimuli

Intravenous Adenosine Infusion

- Current gold standard for FFR measurement
- Hyperemia mediated via A2 receptor on cell membrane on resistance vessels
- Exogenously administered adenosine causes profound microvascular dilation
- Hyperemia is independent of metabolic demand

Jeremias A, TCT 2009

Pharmacologic Hyperemic Stimuli

Intravenous Adenosine Infusion

- 140mcg/kg/min
- Administered through a central (femoral) vein
- Intracoronary nitrate
- Peak effect in 30~45secs with effect wearing off in same time frame after the infusion is stopped
- Produces “Steady state hyperemia”

Jeremias A, TCT 2009

Pharmacologic Hyperemic Stimuli

Intravenous Adenosine Infusion

- AV block is much less common than with ic adenosine
- Brochoconstriction
  - Main contraindication is significant asthma (or COPD)
- Often accompanied by an angina like sensation in the chest and throat which can be associated with dyspnea
  - Harmless and does not indicate myocardial ischemia
  - Warn and reassure patients
  - Encourage patients to breathe normally (avoid valsalva)

Pharmacologic Hyperemic Stimuli

Intravenous Adenosine Infusion

- Advantages
  - Steady state hyperemia : Pull back curve & CFR
- Limitations
  - Infusion in femoral vein
  - High cost d/t large dose of adenosine
  - Setup cumbersome and time consuming

Pharmacologic Hyperemic Stimuli

Intravenous Adenosine Infusion

** SNUH protocol

Dextrose 5% 80 mL

+

Adenosine 60mg/20 mL

Mixed solution : 600ug/mL

** Infusion rate :

140ug * Bwt (kg) /min

= 140ug*Bwt (kg) *60 / hr

= 14* Bwt (kg) * 600ug/hr

= 14×Bwt (ml/hr) with infusion pump

Pharmacologic Hyperemic Stimuli

Intracoronary bolus adenosine

- Peak effect <10sec after administration
- Short duration of action of <20secs
- Recent studies
  - 40ug in the RCA
  - 60ug in the LCA
- If FFR remains >0.80 → incremental dose escalation
  - 20~30ug increments
  - Maximum of 150ug if FFR remains 0.75~0.80
- Main side effect is transient AV block
  - RCA or dominant LCx

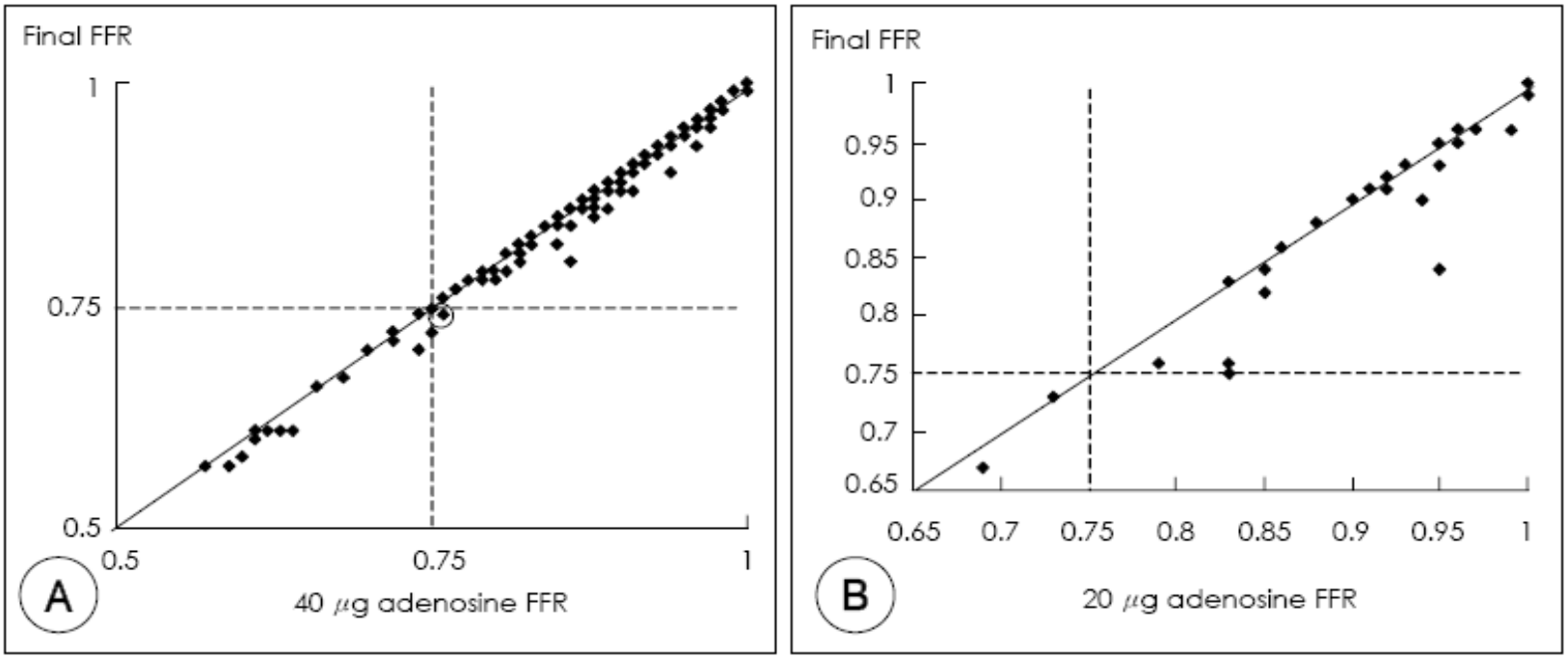
Pharmacologic Hyperemic Stimuli

Intracoronary bolus adenosine

- Advantages
  - Easy administration : no IV setup, no central vein
  - Rapid testing : no wait for max hyperemia

- Limitations
  - Too transient hyperemia : Pull back, CFR impossible
  - Dose escalation frequently necessary to achieve maximal hyperemia

IC bolus injection of adenosine in Korean



LCA

RCA

*46% of LCA lesions and 42% of RCA lesions showed additional decrease of FFR after IC bolus injection of high dose adenosine (LCA 80ug, RCA 40ug).

Suh JW, et al. Korean Cir J 2006

Practical considerations when using intracoronary bolus adenosine

- Administer a standard dose of **IC nitrate** to decrease the possibility of arterial spasm influencing the FFR
- Use a guide catheter without side holes and ensure coaxial engagement
- Ensure the anlayzer is set to display beat to beat mean
- Ensure the interruption in recorded aortic pressure (Pa) is as short as possible after the IC injection

Intracoronary Continuous Adenosine Infusion

—— A Novel and Effective Way of Inducing Maximal Hyperemia for Fractional Flow Reserve Measurement ——

Bon-Kwon Koo, MD, PhD; Cheol-Ho Kim, MD, PhD*; Sang-Hun Na, MD; Tae-Jin Youn, MD, PhD*; In-Ho Chae, MD, PhD*; Dong-Ju Choi, MD, PhD*; Hyo-Soo Kim, MD, PhD; Myoung-Mook Lee, MD, PhD; Byung-Hee Oh, MD, PhD; Young-Bae Park, MD, PhD; Yun-Shik Choi, MD, PhD; Seung-Jae Tahk, MD, PhD**

Background Various methods are used to induce maximal hyperemia for physiologic studies, but the feasibility and efficacy of continuous intracoronary (IC) infusion of adenosine for measurement of fractional flow reserve (FFR) has not been well-defined.

Methods and Results Patients with intermediate coronary artery stenosis were consecutively enrolled. In the phase I study, FFR was measured after 3 dosages of IC adenosine infusion (180, 240 and 300• g/min) in 30 patients. The phase II study was performed to compare the hyperemic efficacy of IC infusion (240• g/min) with IC bolus injection (40, 80• g) and intravenous (IV) infusion (140• $g \cdot kg^{-1} \cdot min^{-1}$) of adenosine in 20 patients. In the phase I study, no significant differences in FFR were observed with the 3 different doses of IC infusion (p=0.06). In the phase II study, FFR after an IC bolus injection (0.83±0.06) was significantly higher than with IV (0.79±0.07) or IC (0.78±0.09) infusion (p<0.01). However, no difference in FFR was observed for IC and IV infusions.

Conclusion IC infusion of adenosine seems to be a safe and effective method of inducing maximal hyperemia for FFR measurement. (*Circ J* 2005; **69:** 908–912)

Key Words: Adenosine; Fractional flow reserve; Hyperemia

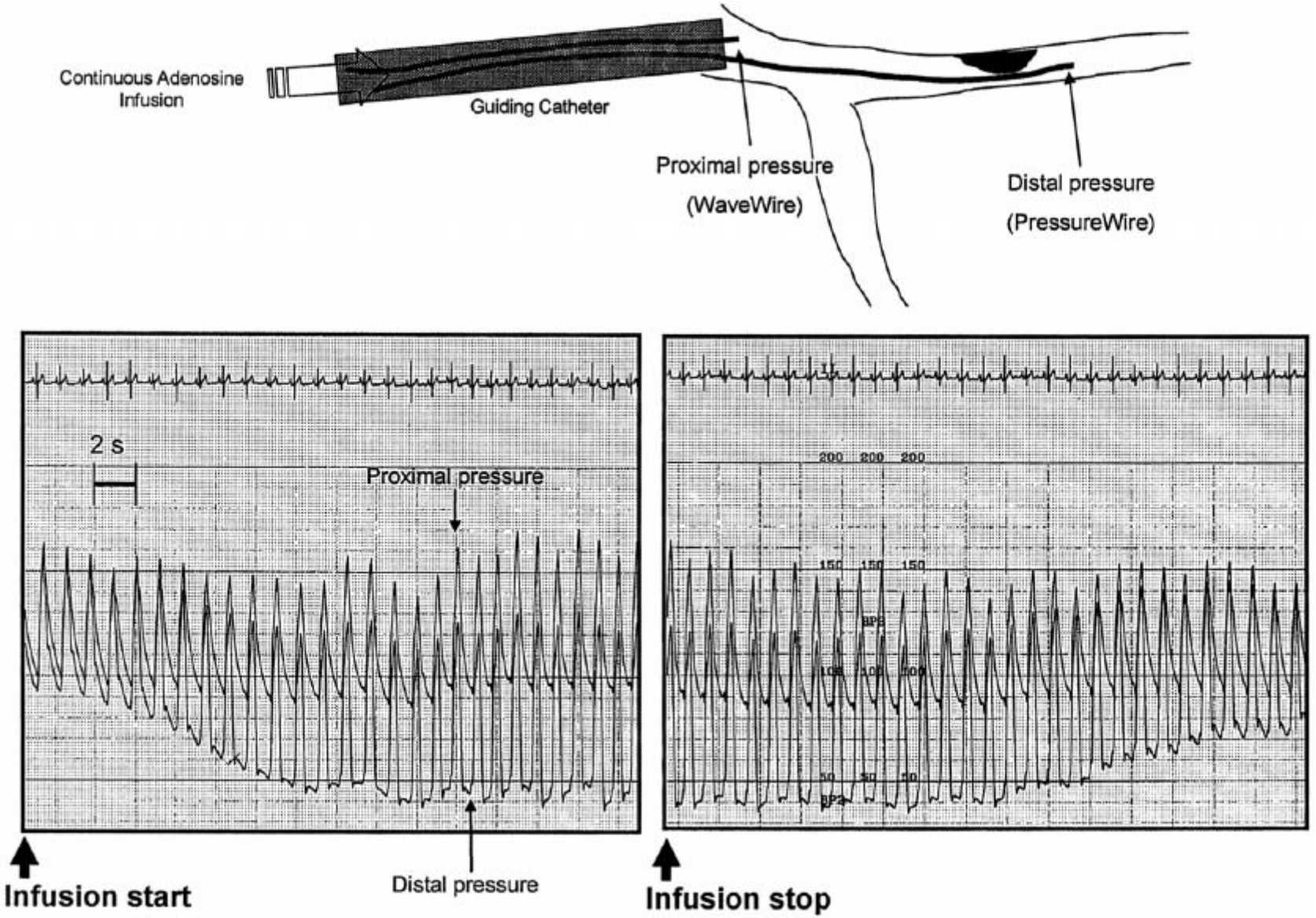
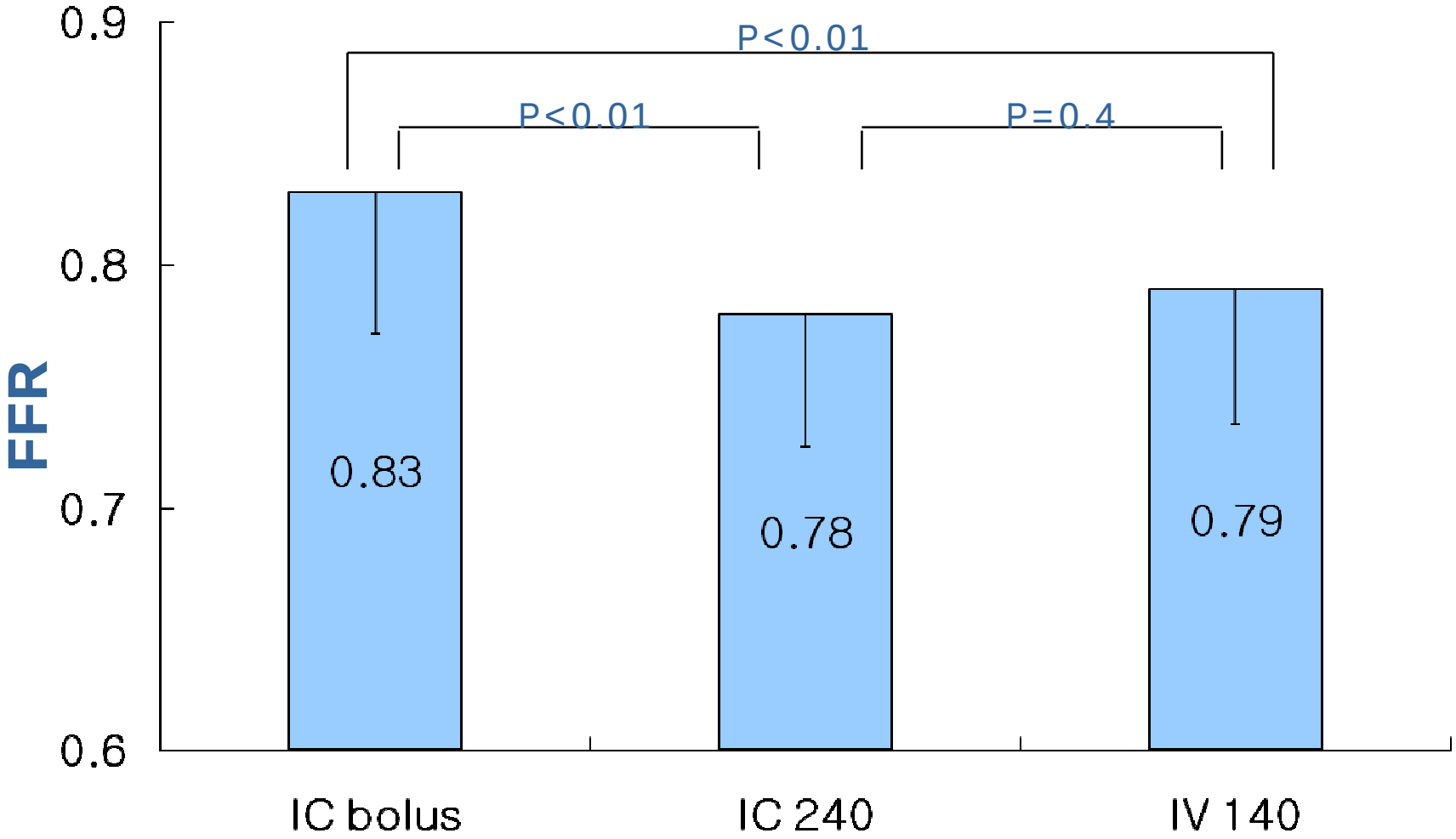


Fig 1. Continuous recording of proximal and distal pressures during the intracoronary continuous infusion of adenosine using 2 pressure wires. Fractional flow reserve was calculated by the ratio of the mean distal pressure to the mean proximal pressure in each beat.

FFR according to the different methods of adenosine administration



Comparison with IC bolus

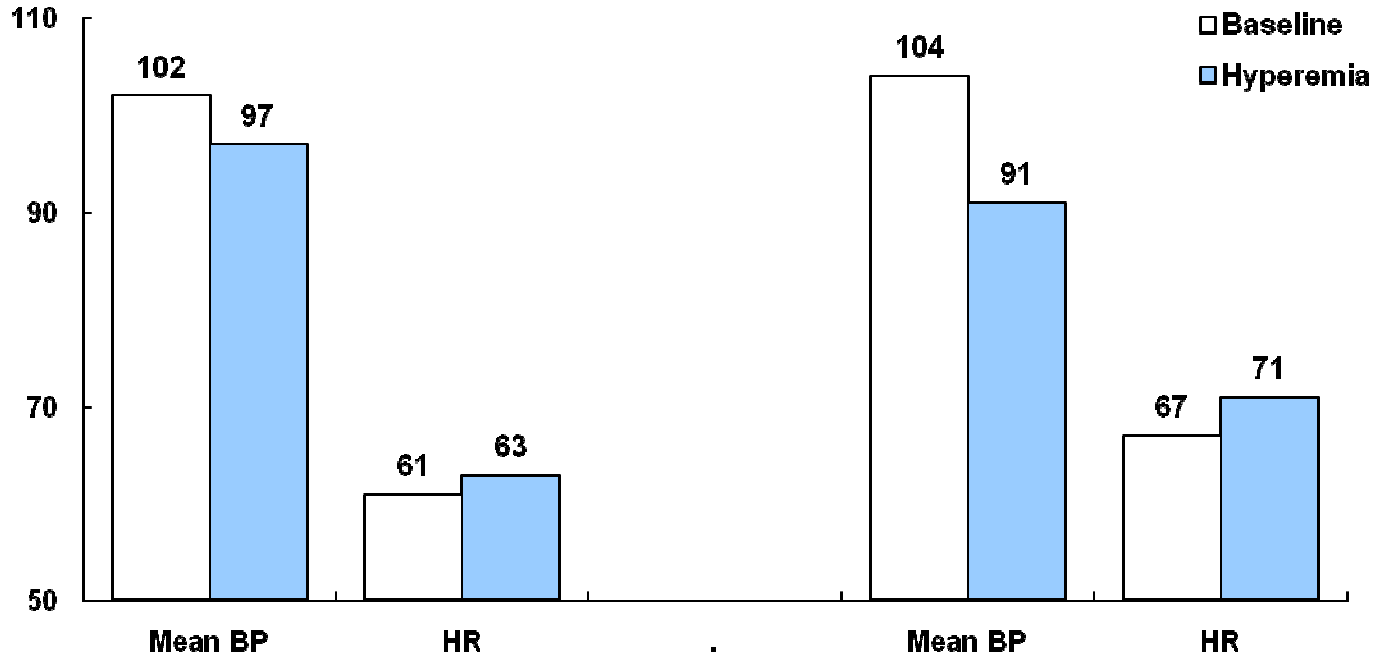
* **IC bolus vs. Infusion** (n=48)

	FFR	P value
IC bolus	0.85 ± 0.07	< 0.001
IC infusion	0.81 ± 0.08	

* Borderline FFR (0.75 – 0.8) at IC bolus
  - N = 9
  - All < 0.75 during IC infusion

Comparison with IV infusion

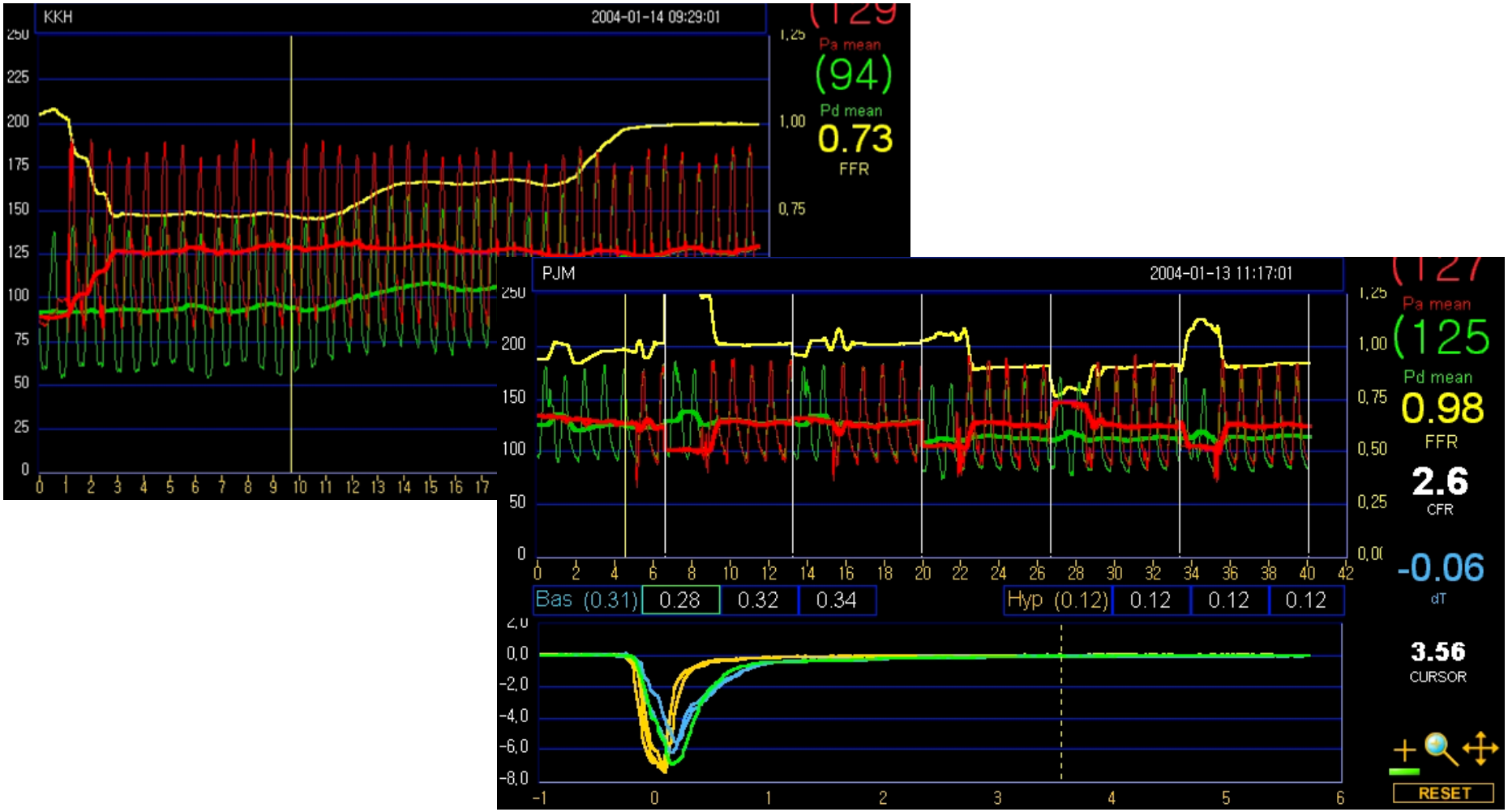
* Hemodynamic changes (Pa) during IC & IV infusion



	IC infusion	IV infusion	P value
Δ BP (%)	- 4.1 ± 6.1	- 11.4 ± 12.5	0.03
ΔHeart rate (%)	4.1 ± 9.1	6.3 ± 10.7	0.5

Possible “steady state hyperemia”

Pressure pullback & CFR measurement possible?



Adenosine Triphosphate (ATP)

- ATP has a short half-life in plasma and is rapidly degraded into ADP, AMP and adenosine (pro-drug)
- Yamada et al / Sondoa et al
  - 50ug of IC ATP = 10ug of IC papaverine without any significant hemodynamic or ECG changes
- De Bruyne et al.
  - ATP and adenosine equipotent with no difference in their times of onset or duration of effect
  - Increasing the IV infusion of ATP to greater than 140ug/kg/min induced a marked decline in BP in some pts.

Intracoronary papaverine

- IC papaverine induces maximal coronary vasodilation
- Longer duration of action than IC adenosine
  - Peak effect is at 10~30sec
  - Duration of plateau is around 45~60sec
- Recommended dosages
  - 12~16ug in RCA
  - 16~20ug in LCA
- IC papaverine should not be used in combination with Hexabrix as crystalization can occur

Intracoronary papaverine

- Transient QT prolongation and T-wave abnormalities
- Polymorphic VT/ VF
  - Rare & Fatal complication
  - Associated with hypokalemia
  - Avoid use with QT-prolonging drugs

Intracoronary papaverine

Advantages

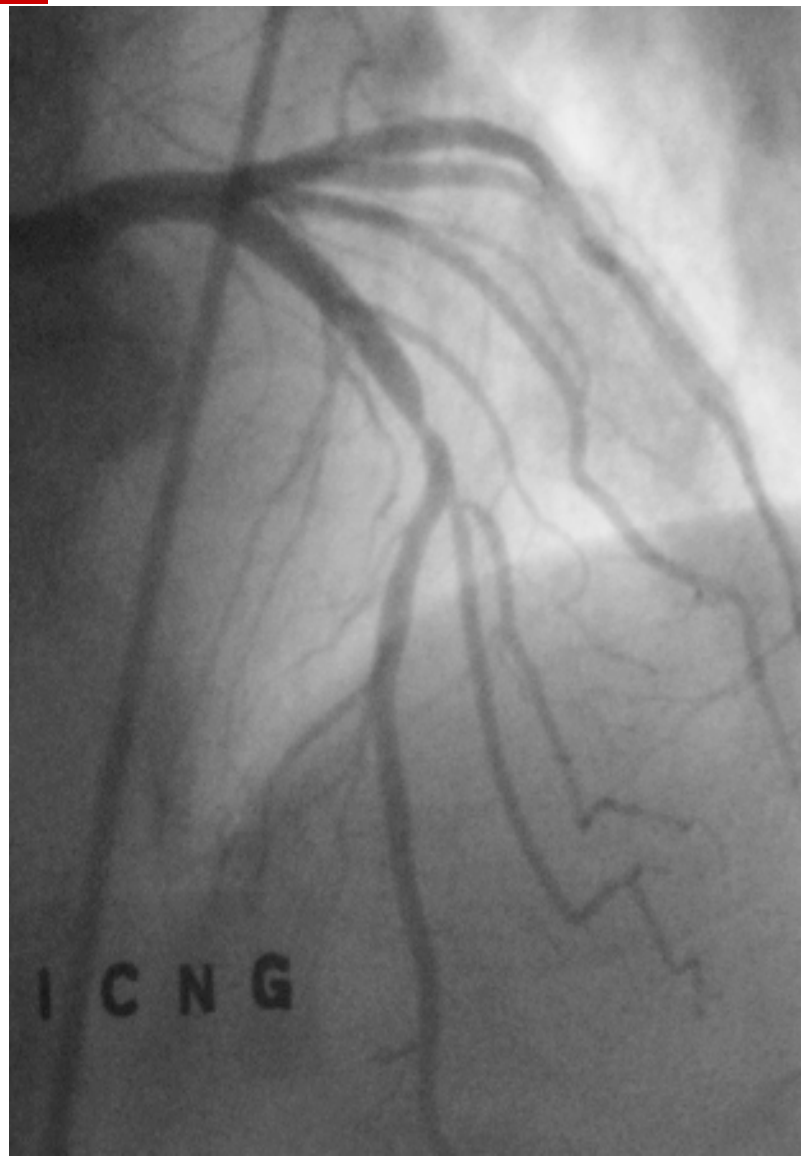
- Easy administration : no IV setup required, no central vein access
- Rapid testing : no wait for maximal hyperemia
- Steady state hyperemia : Pull back curve & CFR

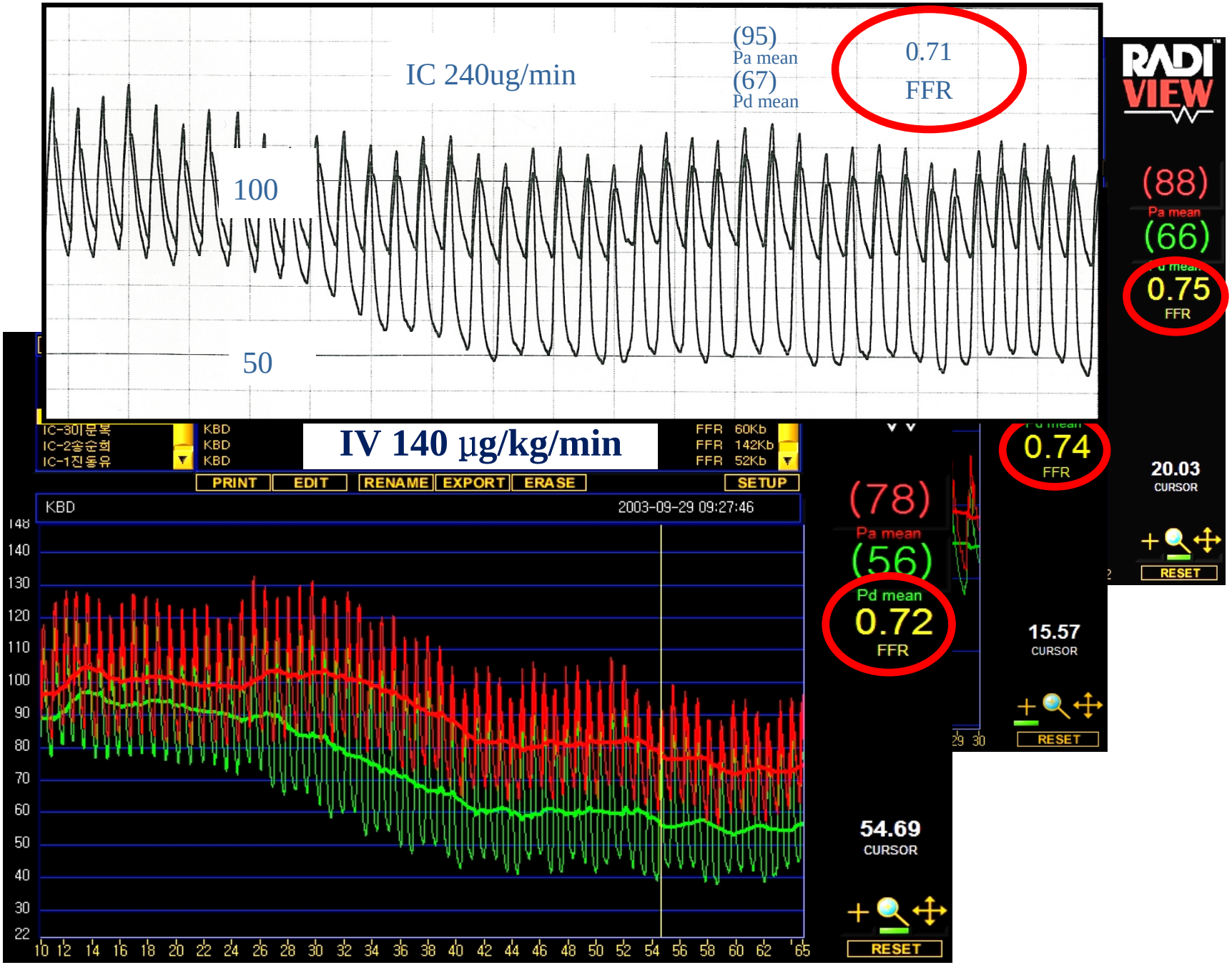
Limitations

- Wait 5min b/w measurements : Hyperemia resolves in that time
- No more than 3 doses : limit risk for side effects

Case

- M/56
- Intermittent resting chest pain for 1mo
- Risk factor : smoking
- Lab
    - * ECG : NSR
    - * Outside TMT : inadequate study
    - * Gated myocardial SPECT : negative
    - * Echocardiography
        - - EF 60%, relaxation abnormality




IC 240ug/min
(95)
Pa mean
(67)
Pd mean
0.71
FFR
100
50
RADI VIEW
(88)
Pa mean
(66)
0.75
FFR
IV 140 µg/kg/min
IC-30|문복
IC-2송순희
IC-1진동유
KBD
KBD
KBD
FFR 60Kb
FFR 142Kb
FFR 52Kb
PRINT
EDIT
RENAME
EXPORT
ERASE
SETUP
KBD
2003-09-29 09:27:46
(78)
Pa mean
(56)
Pd mean
0.72
FFR
0.74
FFR
20.03
CURSOR
15.57
CURSOR
54.69
CURSOR
RESET
RESET
RESET

Patients with borderline FFR
with IC bolus adenosine
(0.75~0.85)

Incremental dose of IC bolus
or
IV infusion *(IC infusion?)* of adenosine

Conclusions

- IV adenosine infusion is a safe, reliable and well tolerated method for the induction of maximal coronary hyperemia
- IC adenosine is an acceptable alternative but does not produce steady state maximal hyperemia
- IC papaverine is a good alternative in pts with a contraindication to adenosine

Thank you !!