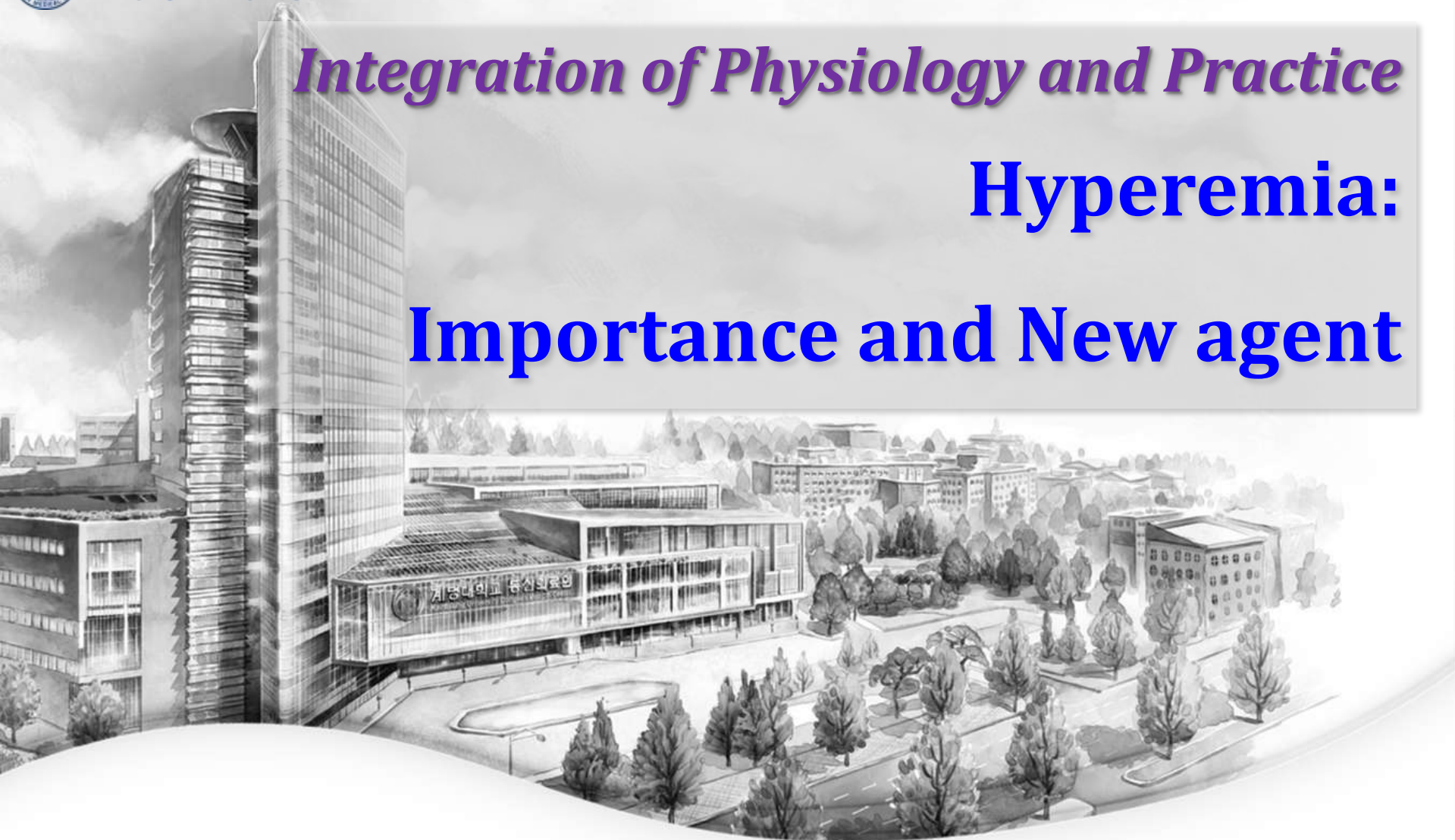




Integration of Physiology and Practice

Hyperemia:

Importance and New agent



Keimyung University Dongsan Medical Center

NAM, Chang-Wook MD, PhD

Disclosure

Research grant

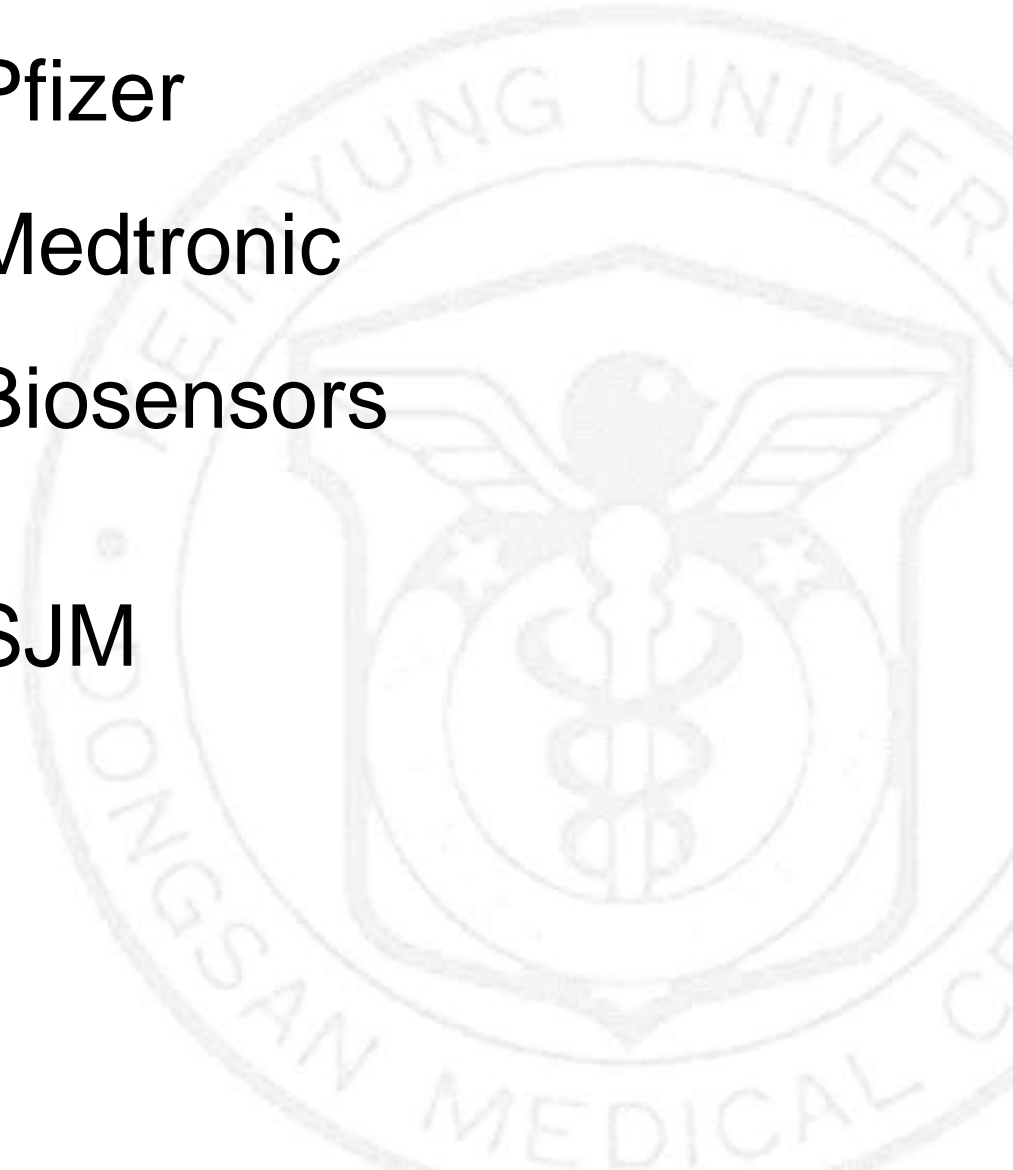
Pfizer

Medtronic

Biosensors

Consultant

SJM



Evidences of FFR-guided PCI

The collage includes several journal covers:

- Journal of the American College of Cardiology**: Vol. 49, No. 21, 2007
- European Heart Journal**: Advance Access published January 23, 2013
- Interventional Cardiology**
- Physiologic Assessment of Jailed Side**
- Journal of the American College of Cardiology**: ORIGINAL ARTICLE
- Fractional Flow Reserve-Guided PCI for Stable Coronary Artery Disease**
- Functional SYNTAX in Multivessel Coro**
- Long-term outcomes of fractional flow**
- Coronary Angiography**
- Prognostic Value of Fractional Flow Reserve**
- angiography in guiding the outcomes in non-ST-elevation myocardial infarction: the FAMOUS-NSTEMI**

The PubMed search results page shows the following details:

- Search term: coronary fractional flow reserve
- Results: 1 to 20 of 1292
- First result: **Variability of fractional flow reserve according to the methods of hyperemia induction.** by Lim WH, Koo BK, Nam CW, Doh JH, Park JJ, Yang HM, Park KW, Kim HS, Takashima H, Waseda K, Armano T, Kato D, Kurita A, Oi M, Toyofuku M, vanNunen L, Pijls NH. *Catheter Cardiovasc Interv.* 2014 Nov 20. doi: 10.1002/ccd.25752. [Epub ahead of print] PMID: 25412690
- Second result: **Long-Term Outcome After Deferral of Revascularization in Patients With Intermediate Coronary Stenosis and Gray-Zone Fractional Flow Reserve.** by Shiono Y, Kubo T, Tanaka A, Ino Y, Yamaguchi T, Tanimoto T, Yamano T, Matsuo Y, Nishiguchi T, Teraguchi I, Ota S, Ozaki Y, Orli M, Shimamura K, Kitabata H, Hirata K, Imanishi T, Akasaka T. *Circ J.* 2014 Nov 19. [Epub ahead of print] PMID: 25410612
- Third result: **Coronary CT angiography-derived fractional flow reserve correlated with invasive fractional flow reserve measurements - initial experience with a novel physician-driven algorithm.** by Baumann S, Wang R, Schoepf UJ, Steinberg DH, Spearman JV, Bayer RR 2nd, Hamm CW, Renker M. *Eur Radiol.* 2014 Nov 18. [Epub ahead of print] PMID: 25403173

To get these results and benefits in your daily practice, you need to have a confidence with your FFR measurement.

10-point Check List for Your Practice

1. General setting for FFR:

Infusion pump, IV connection site,
Level of fluid filled pressure transducer, etc

2. Issues for guiding catheter

Size, Side-holes, Pressure artifact, etc

3. Remove introducer from Y-connector

4. Start with equalization

5. Damping during pullback

6. Drift

7. Whipping

8. Spasm/Accordion effects

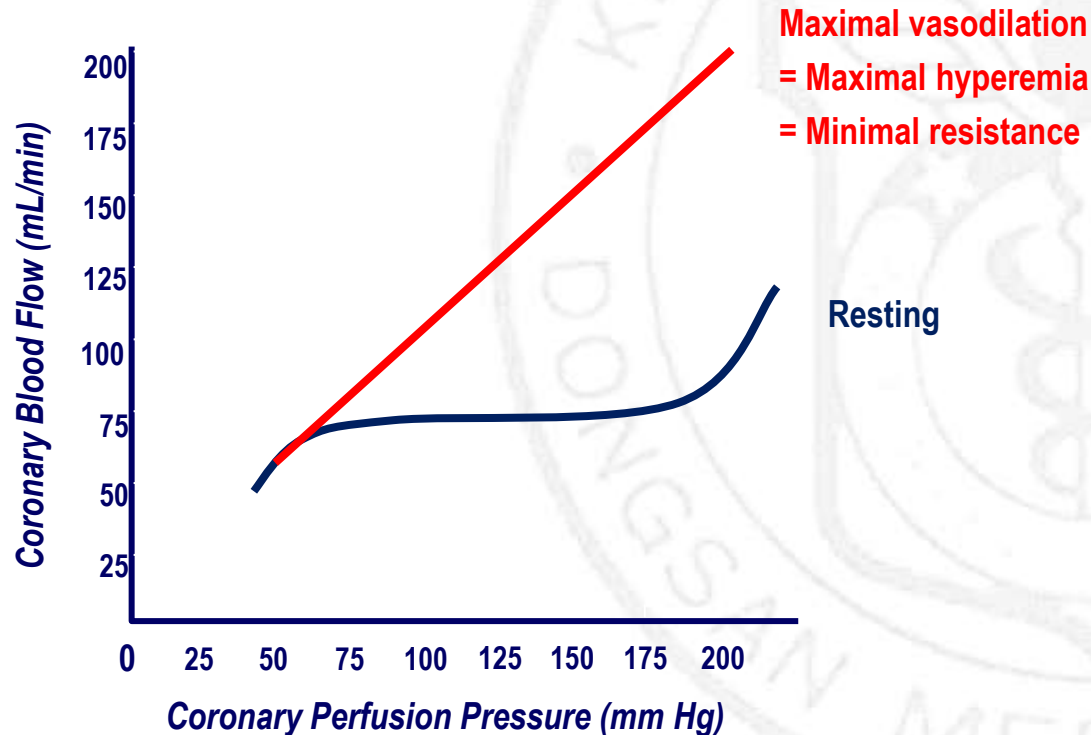
9. Location of pressure sensor

10. Issues for hyperemia

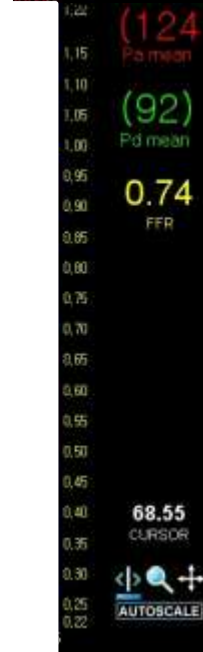
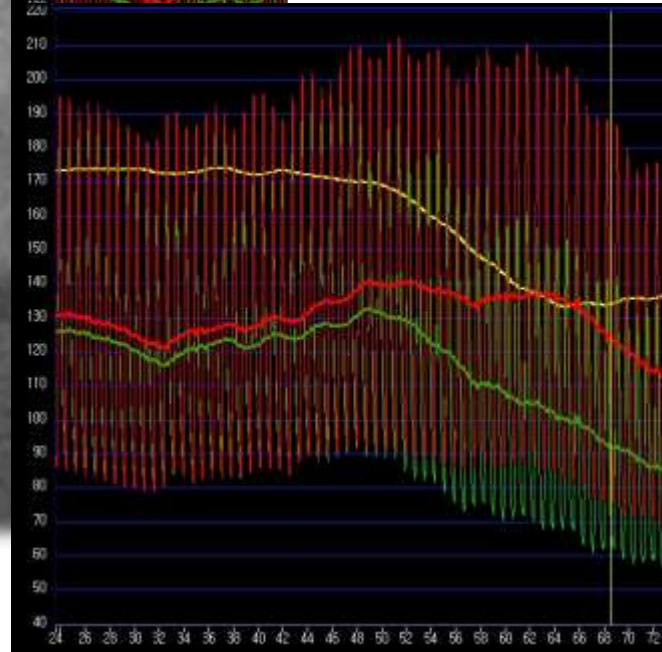
Why Hyperemia?

Major premise in the concept of FFR is
“Measuring pressure under maximal hyperemia”

$$\text{FFR} = \frac{Q_{\max}^S}{Q_{\max}^N} = \frac{(P_d - P_v)/R}{(P_a - P_v)/R} = \frac{P_d}{P_a}$$



Hyperemia: Why important?



Hyperemia: Which and How?

Intravenous continuous infusion

- **Adenosine, ATP** 140 $\mu\text{g}/\text{kg}/\text{min}$
- Dobutamine 20-40 $\mu\text{g}/\text{kg}/\text{min}$

Intracoronary bolus injection

- Papaverine 10 - 20 mg
- **Adenosine, ATP** 20-720 μg
- Nitroprusside 0.3-0.9 $\mu\text{g}/\text{kg}$
- **Nicorandil** 2mg

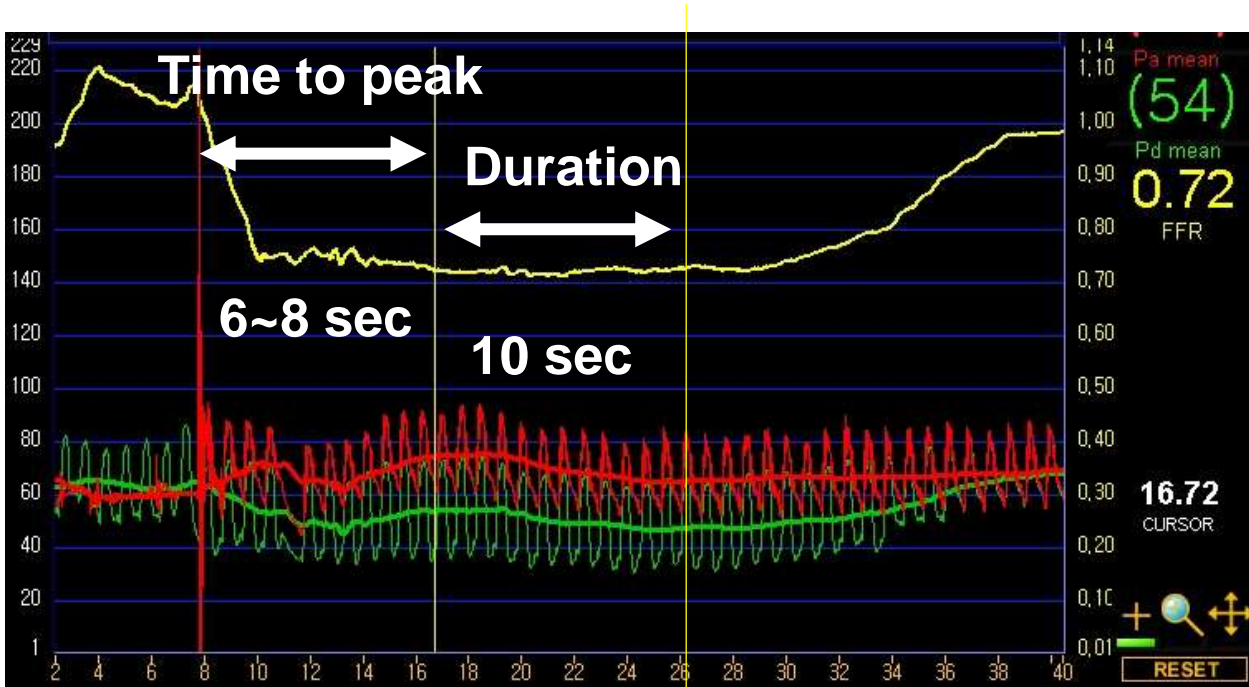
Intracoronary continuous infusion

- Adenosine 240 $\mu\text{g}/\text{min}$

Intravenous bolus injection

- Regadenoson 400 μg

Bolus Intracoronary Adenosine

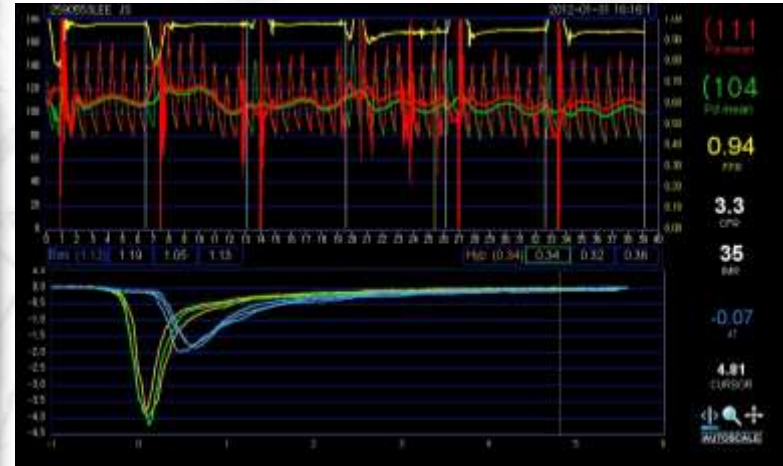
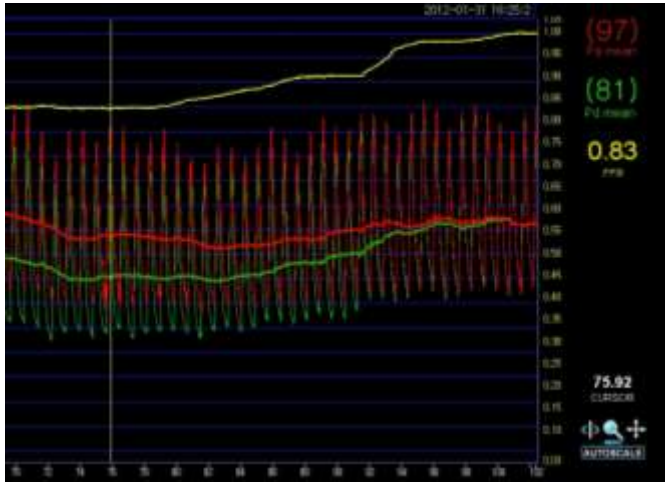


**Quick,
Easy,
Inexpensive.**

BUT.....

- Short action time, not adequate for pressure pullback and IMR/CFR
- Less effective than IV infusion in some patients
- More frequent AV block than with IV infusion
- Difficult to use in patients with ostial disease
- Inaccurate with side hole guiding catheter

Continuous Intravenous Adenosine

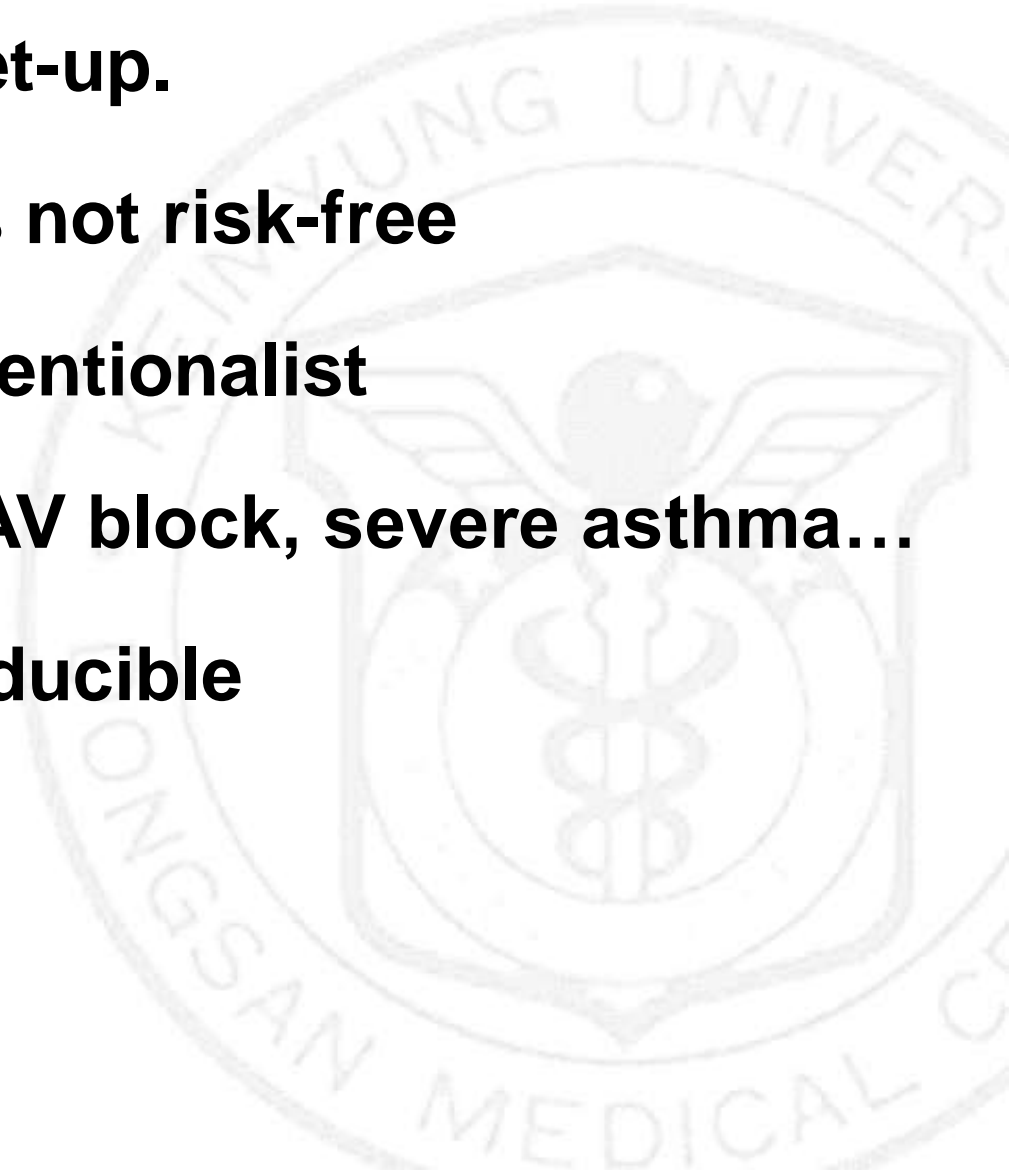


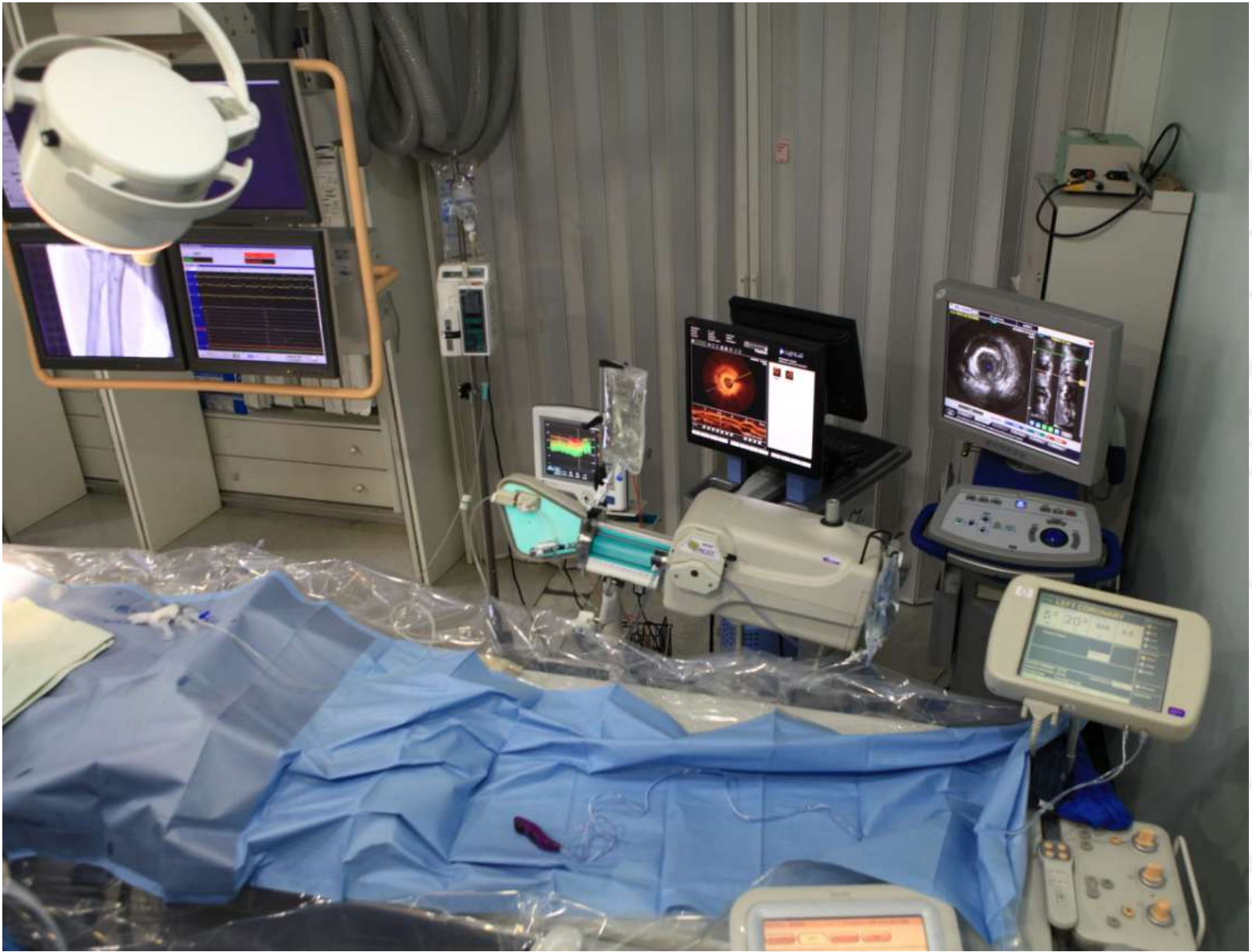
- Very good safety profile
- One dose (140 ug/kg/min) is adequate for almost all patients
- Sustained hyperemia for pressure pullback and for CFR/IMR

Gold Standard!!!

Issues for Adenosine Hyperemia

- **Time consuming to set-up.**
- **Central vein access is not risk-free**
- **For trans-radial interventionalist**
- **Contraindications to AV block, severe asthma...**
- **Not reliable nor reproducible**



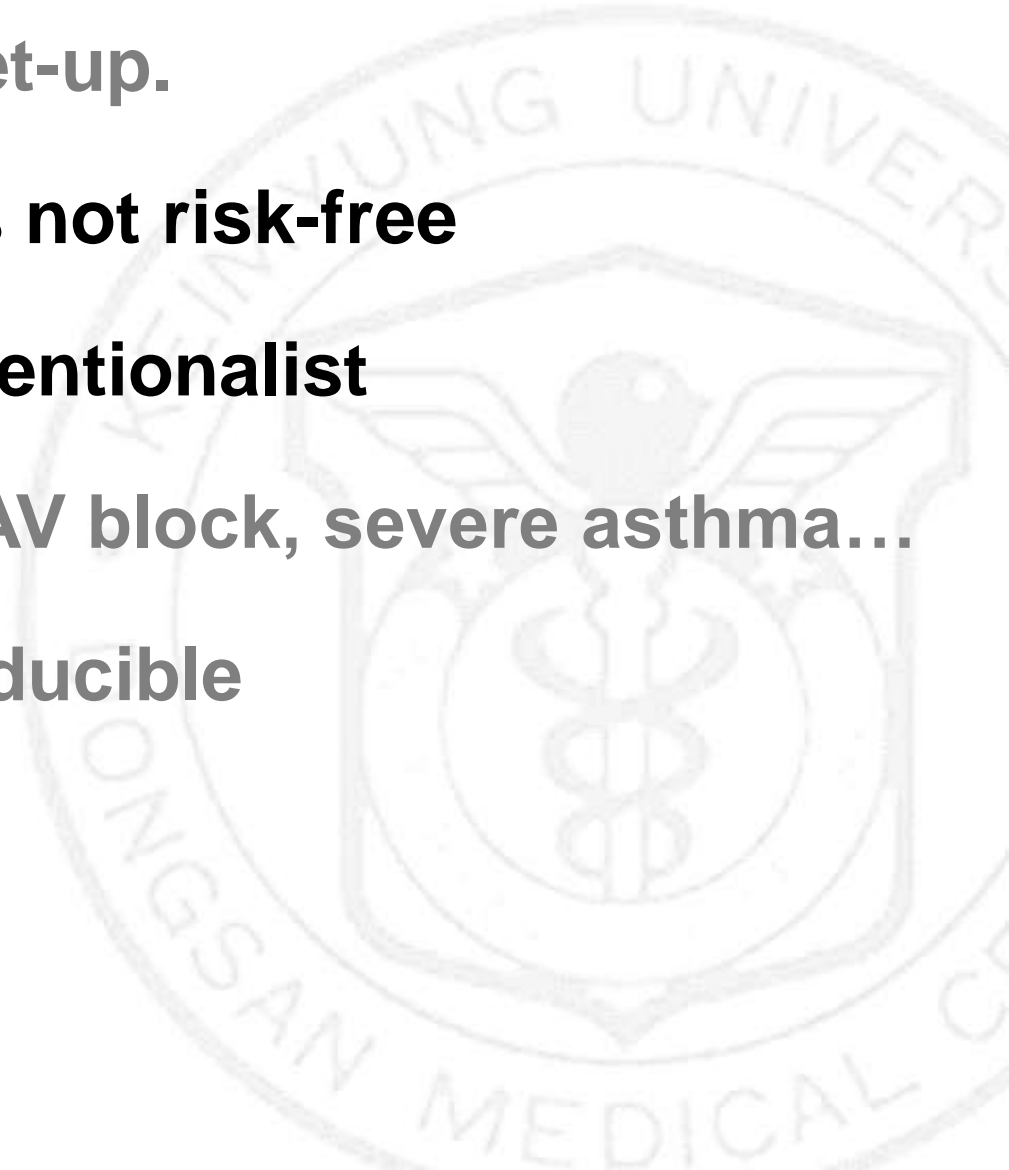


Keimyung University, Korea

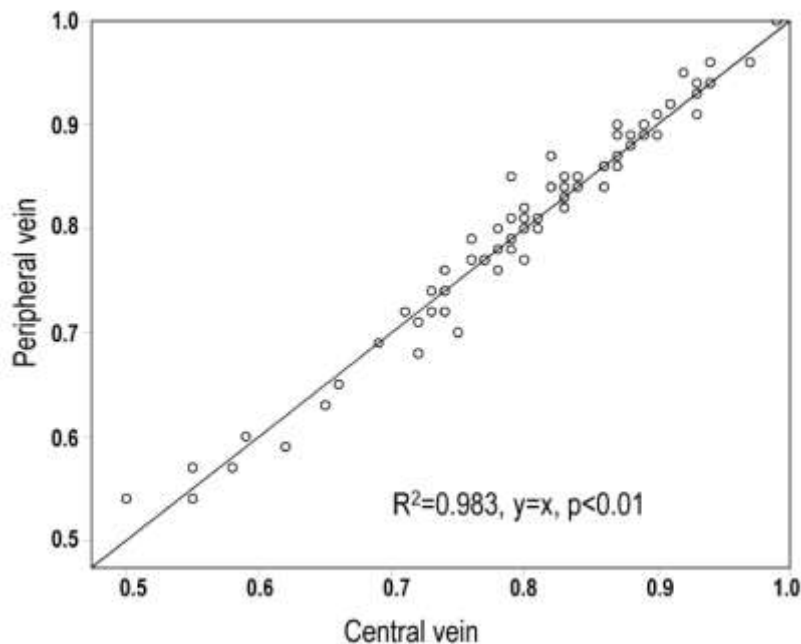
MEDICAL CENTER

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Femoral vein vs. Forearm vein

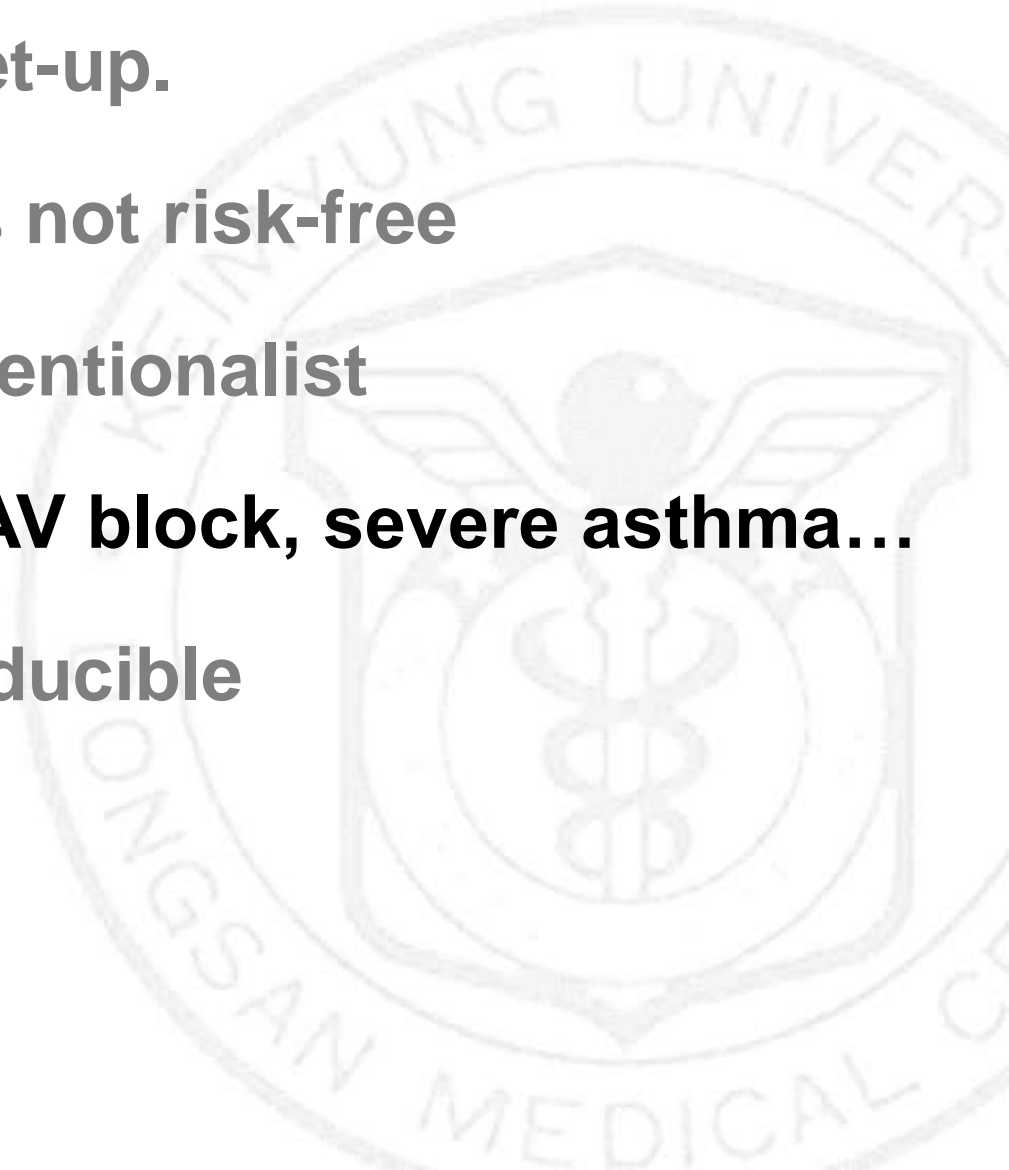


	Bolus	Central Infusion	Peripheral Infusion	P Value
N=68				
FFR	0.81±0.10	0.80±0.10	0.80±0.11	0.22*
Time to maximal hyperemia, s	NA	38.7±17.9	53.7±22.8	<0.01†
Plateau time, s	NA	16.6±13.5	17.4±12.9	0.46†
N=20				
Hyperemic mean transit time, s	NA	0.23±0.14	0.22±0.13	0.55†
IMR	NA	11.8±10.9	11.3±9.2	0.58†

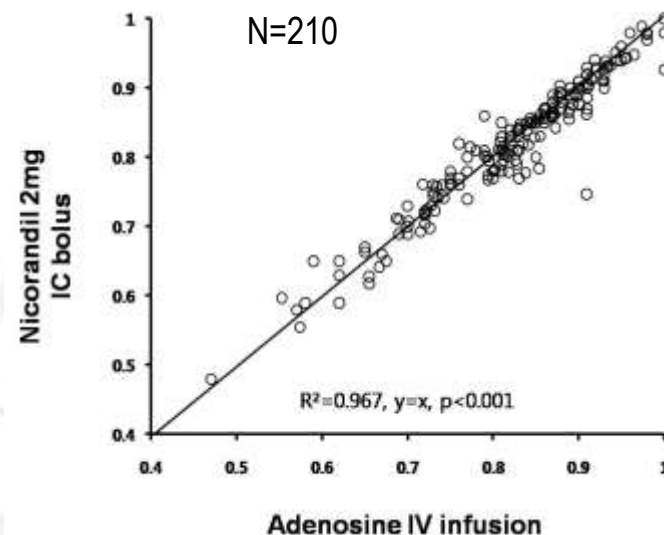
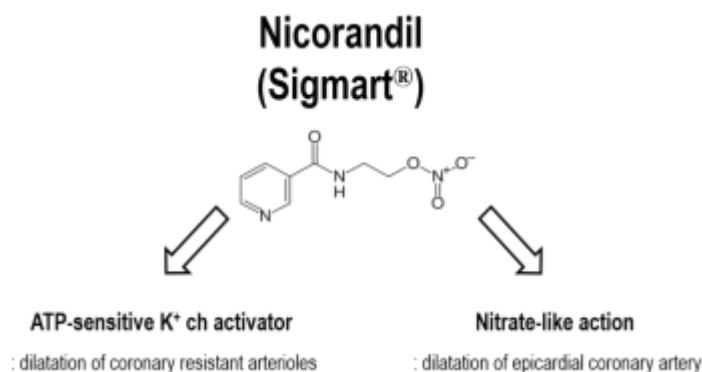
- Peripheral IV infusion can be an alternative to central IV infusion.
- Uninterrupted venous return should be guaranteed and a large needle is used.
- When doubtful, higher dose can be helpful.

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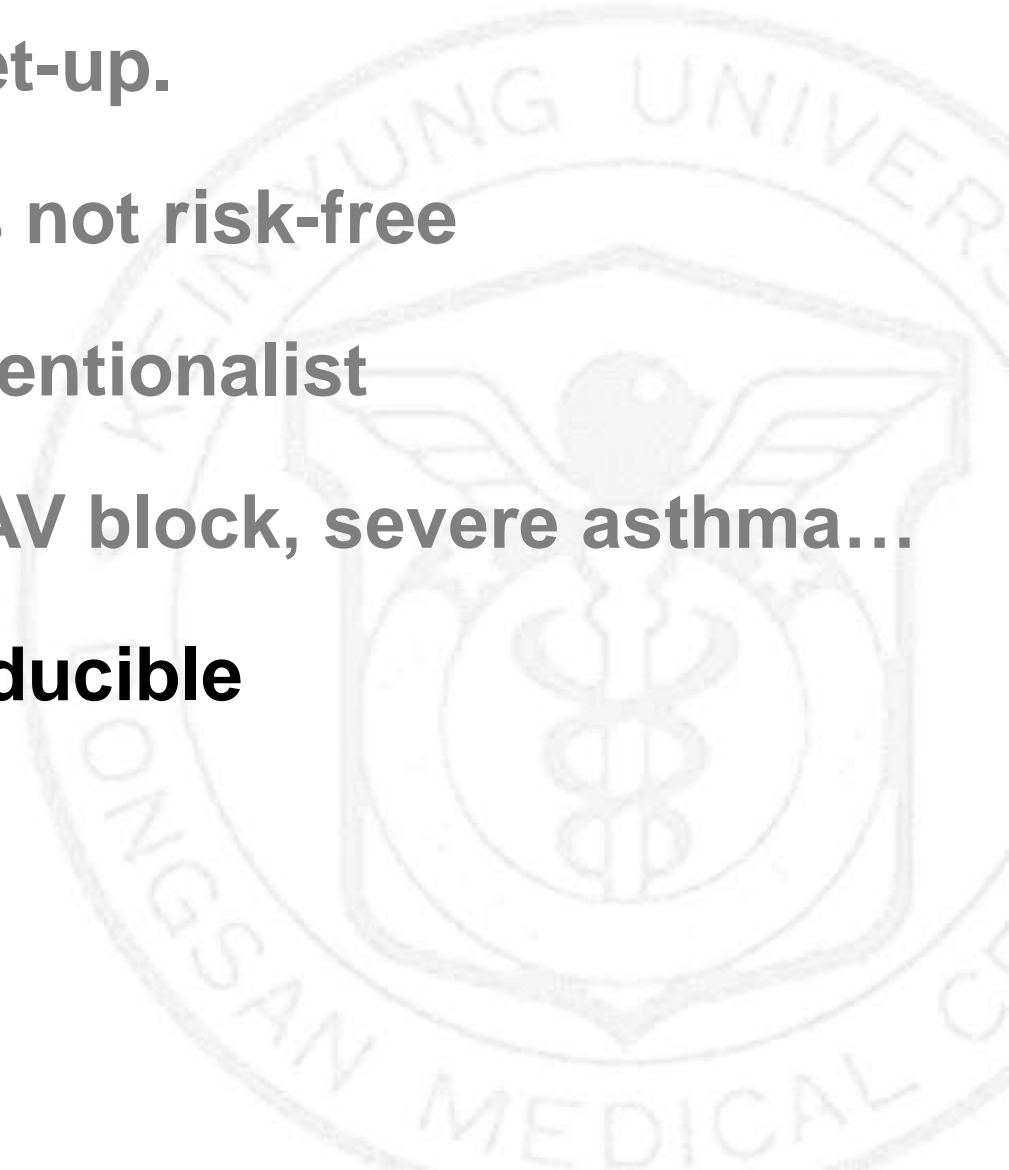
Novel hyperemic agent: intracoronary nicorandil



	Nicorandil bolus 2 mg	Adenosine IV infusion	P value
Fractional Flow Reserve	0.82 ± 0.10	0.82 ± 0.10	0.33
Time to max hyperemia, s	18.3 ± 6.1	43.8 ± 16.0	<0.001
Plateau time, s	27.3 (IQR 17-33)	-	
IMR	17.2 ± 7.6	18.3 ± 8.7	0.29

Issues for Adenosine Hyperemia

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Comparison of vasodilatory stimuli

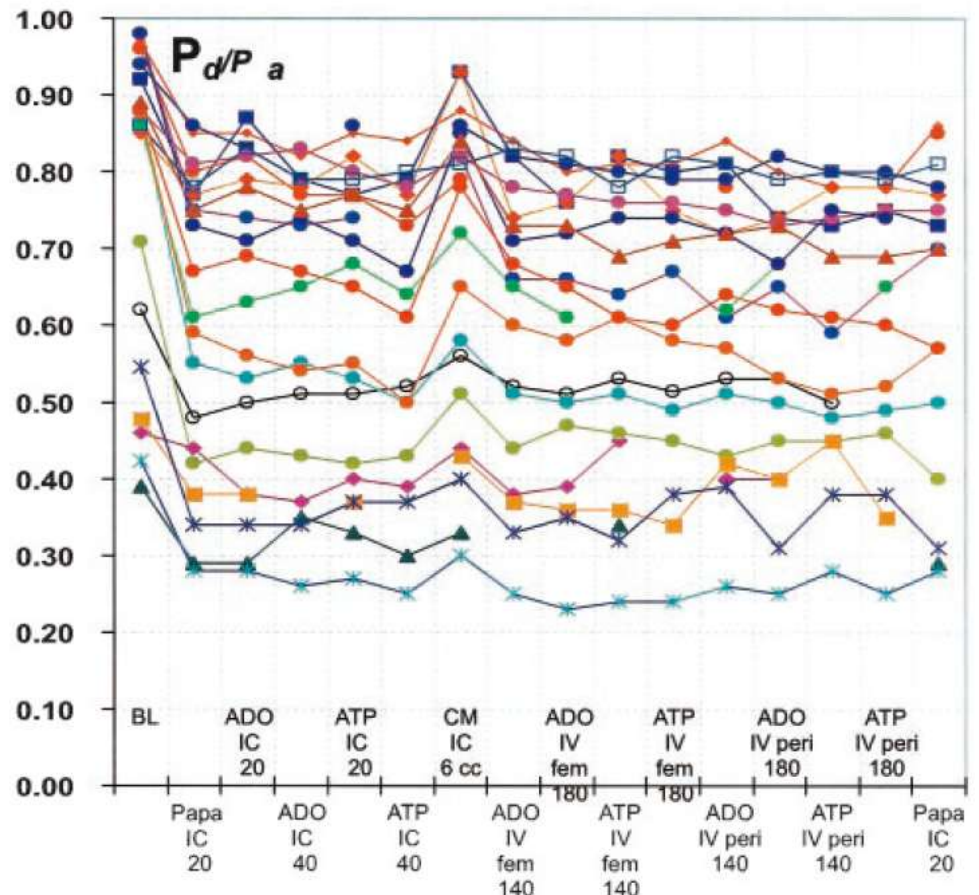
Intracoronary and Intravenous Adenosine 5'-Triphosphate, Adenosine, Papaverine, and Contrast Medium to Assess Fractional Flow Reserve in Humans

Bernard De Bruyne, MD, PhD; Nico H.J. Pijls
 Jozef Bartunek, MD, PhD; Jan
 William Wijns, MD, PhD; Guy R

Background—Inducing both maximal and steady-state coronary hyperemia is essential for accurate measurements of fractional flow reserve. The present study compared the effects of intracoronary adenosine 5'-triphosphate (ATP), adenosine, contrast medium, and papaverine on maximal and steady-state hyperemia.

Methods and Results—In 21 patients with an isolated coronary stenosis, fractional flow reserve was measured by papaverine (20 mg intracoronary), adenosine (20 and 40 μg intracoronary), and contrast medium (6 mL intracoronary), adenosine or ATP through an intracoronary catheter, and adenosine or ATP through a femoral vein (140 and 180 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$). The ratio of distal coronary pressure (P_d) to aortic pressure (P_a) was 0.77 ± 0.21 at rest and decreased to 0.61 ± 0.21 after papaverine. The lowest P_d/P_a ratio was obtained by intracoronary papaverine and by intravenous ATP. Intravenous ATP infusion was varied from 0 to 280 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. At maximal hyperemia, there was no decrease in P_d/P_a ratio nor a further increase in coronary flow.

Conclusion—Provided sufficient dosages are used, ATP, adenosine, and contrast medium induce maximal hyperemia and are therefore suitable to assess fractional flow reserve. Intravenous ATP or adenosine induce steady-state hyperemia and are suitable for assessing diffuse coronary atherosclerosis. (*Circulation*. 2003;

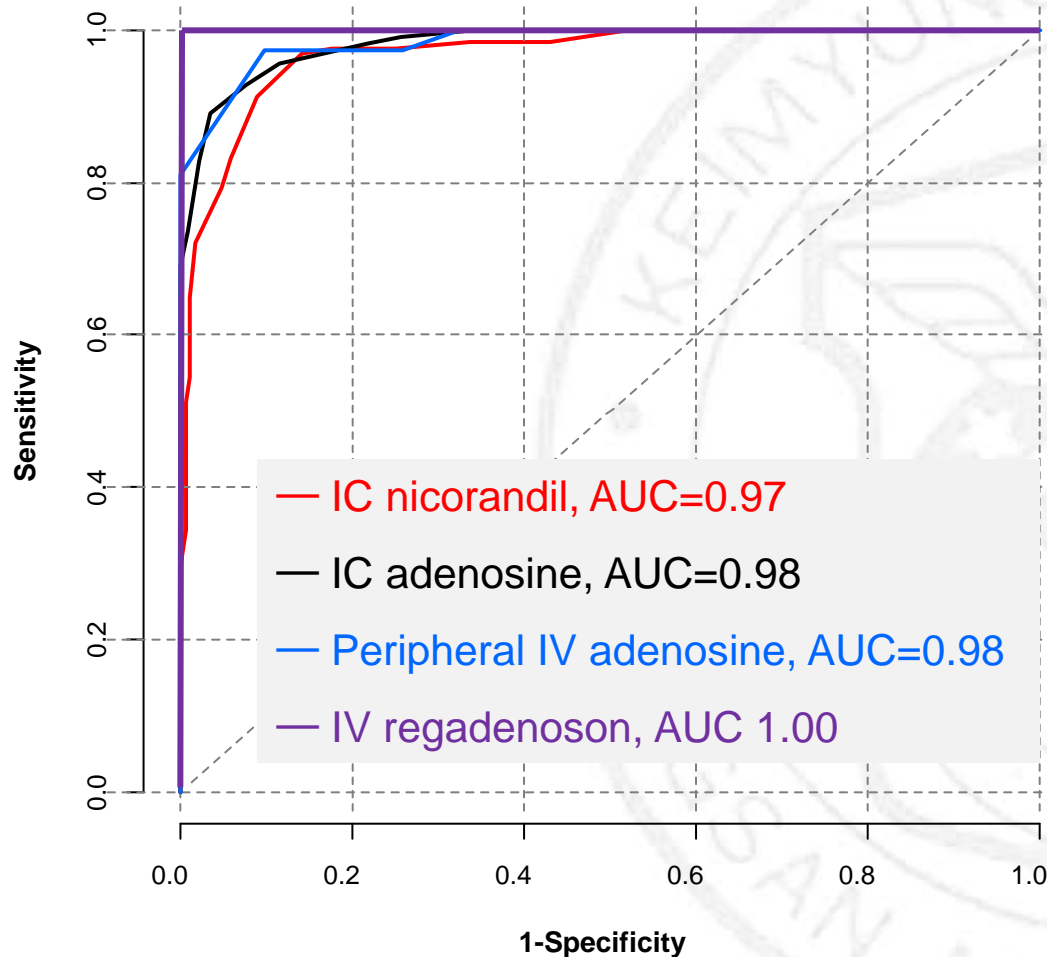


Stability and reproducibility of FFR

with different hyperemic drugs, different routes and different time

Classification agreement

: IV adenosine vs. each alternative methods



Hyperemia for FFR

- **Hyperemia is essential for FFR measurement**
- **IV adenosine infusion is gold standard**
- **But several alternative methods:**
 - IC adenosine, IC nicorandil, IV regadenoson...
- **If the value is out of your expectation,**
 - check the system (line, connection...)
 - dose up of hyperemic agent
 - remeasure with another drug or route

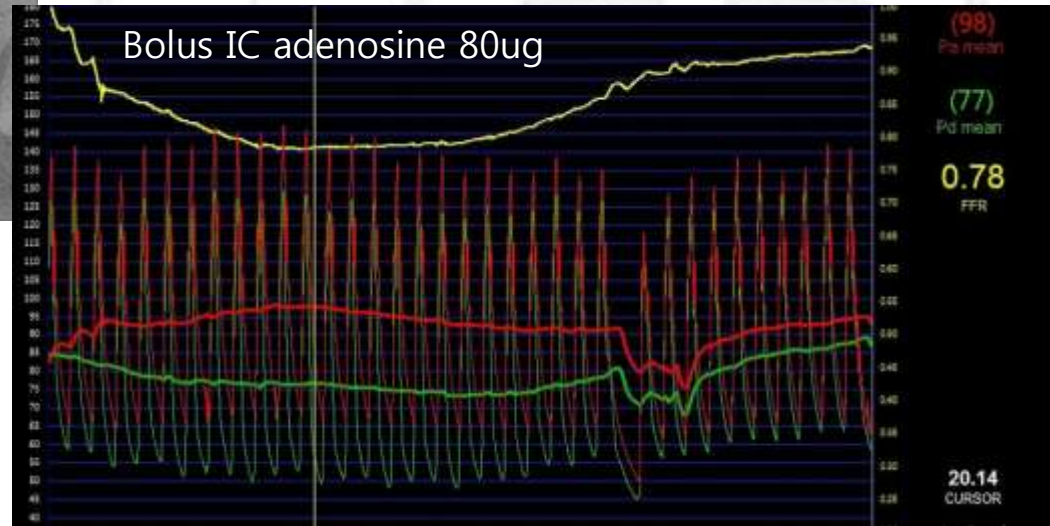
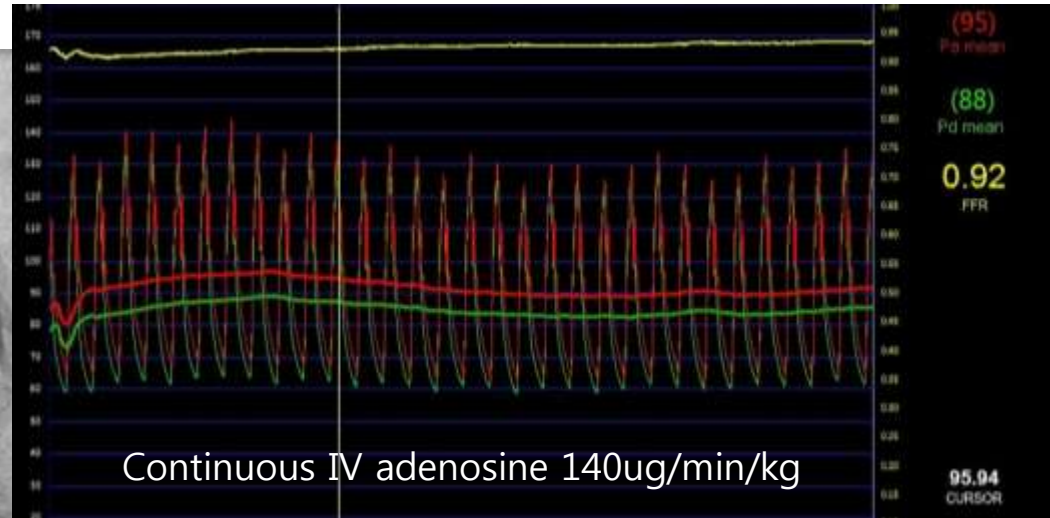
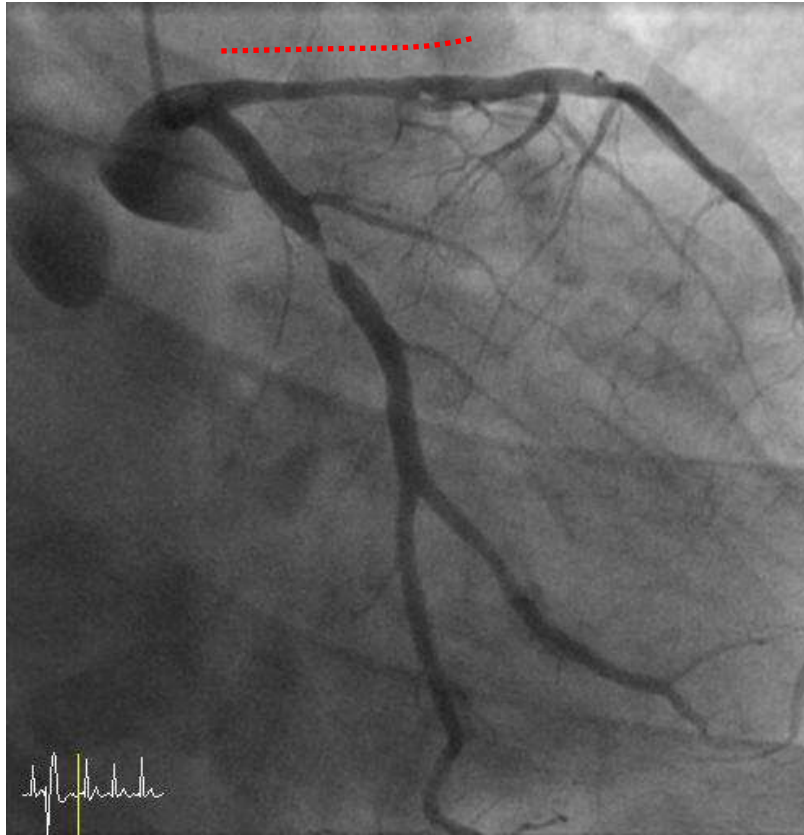


Thank You



Integration of Physiology and Practice

Hyperemia: Importance and New agent



Novel hyperemic agent: intravenous Regadenoson

- Selective A_{2A} – receptor antagonist
- Rapid onset and simple administration: IV bolus 400 μ g

