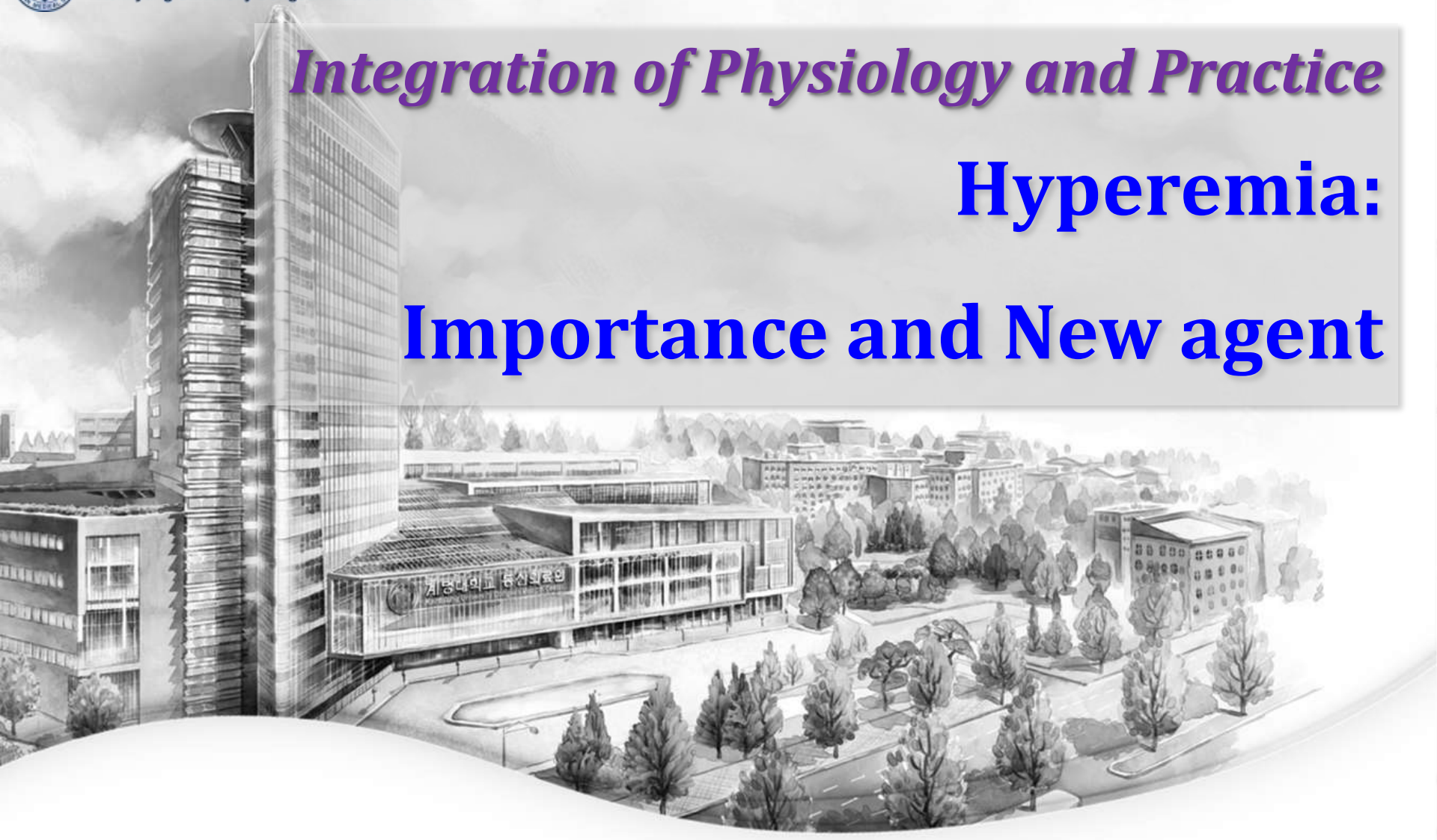
계명대학교 동산의료원
Keimyung University Dongsan Medical Center

Integration of Physiology and Practice

Hyperemia:

Importance and New agent



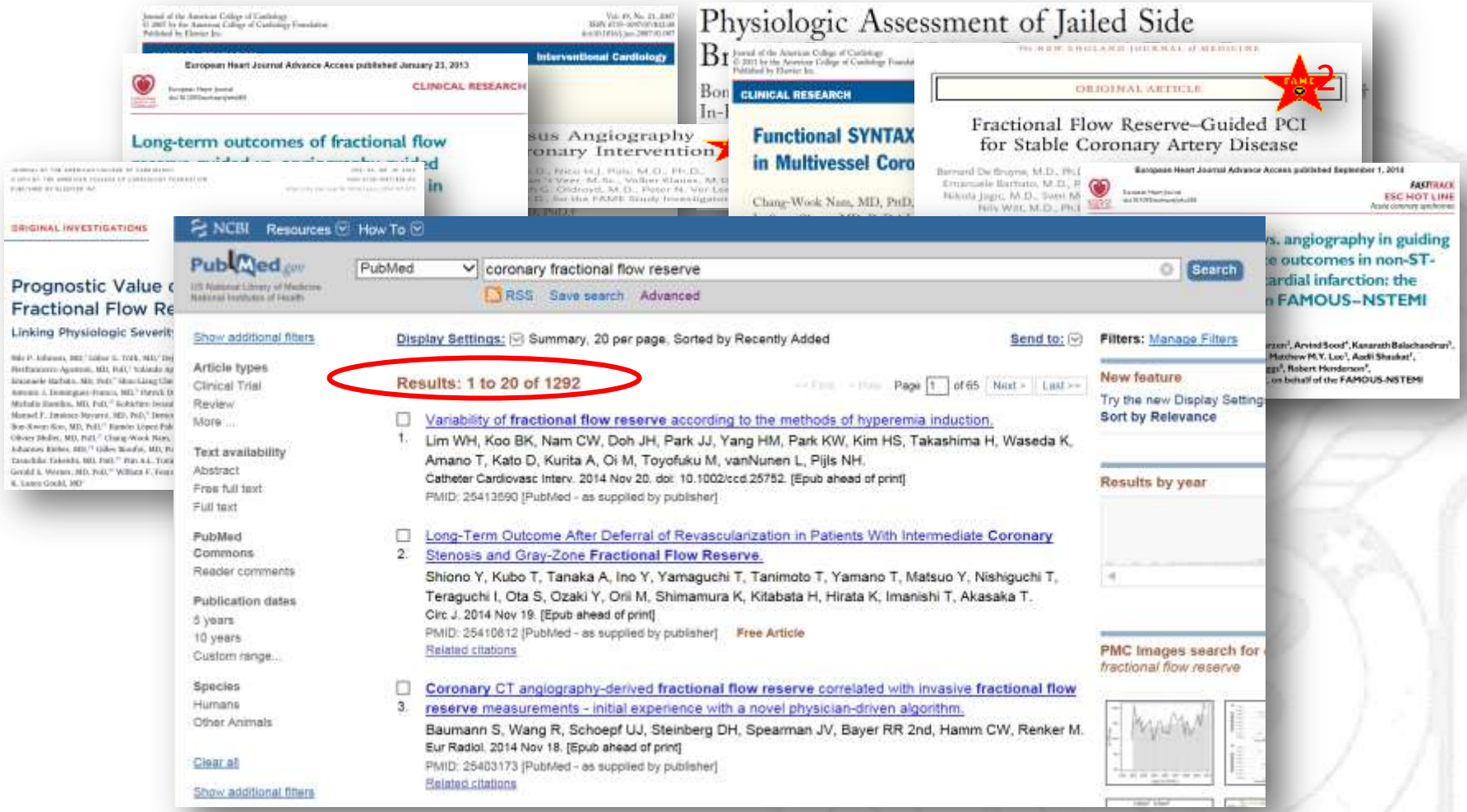
Keimyung University Dongsan Medial Center

NAM, Chang-Wook MD, PhD

Disclosure

Research grant	Pfizer
	Medtronic
	Biosensors
Consultant	SJM

Evidences of FFR-guided PCI



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

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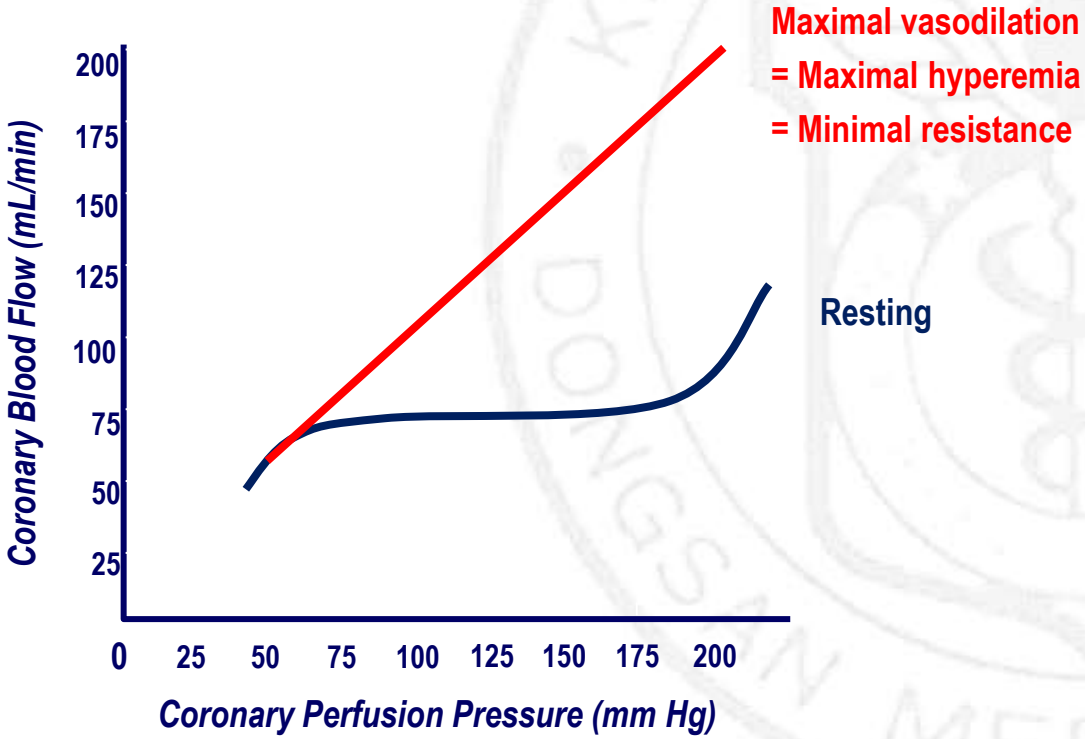
10-point Check List for Your Practice

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?

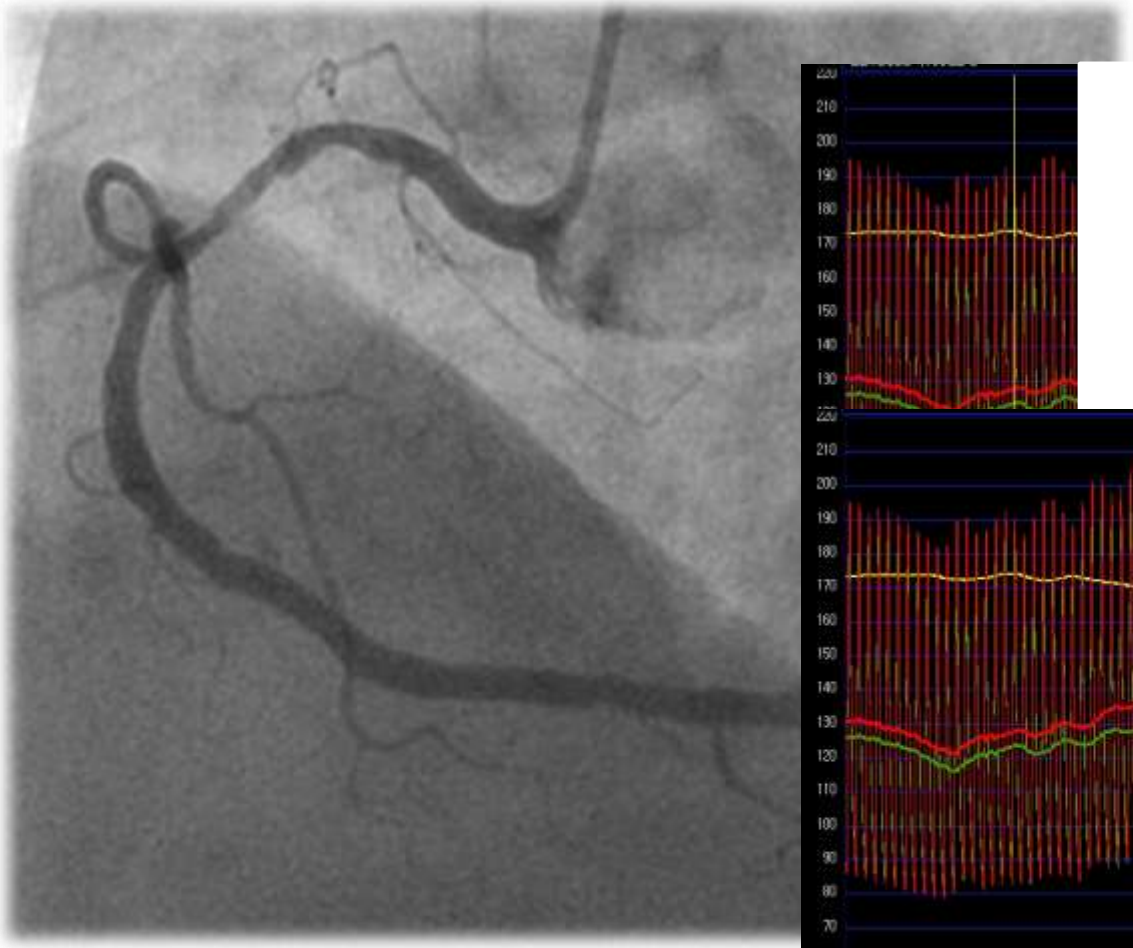
Major premise in the concept of FFR is
"Measuring pressure under maximal hyperemia"

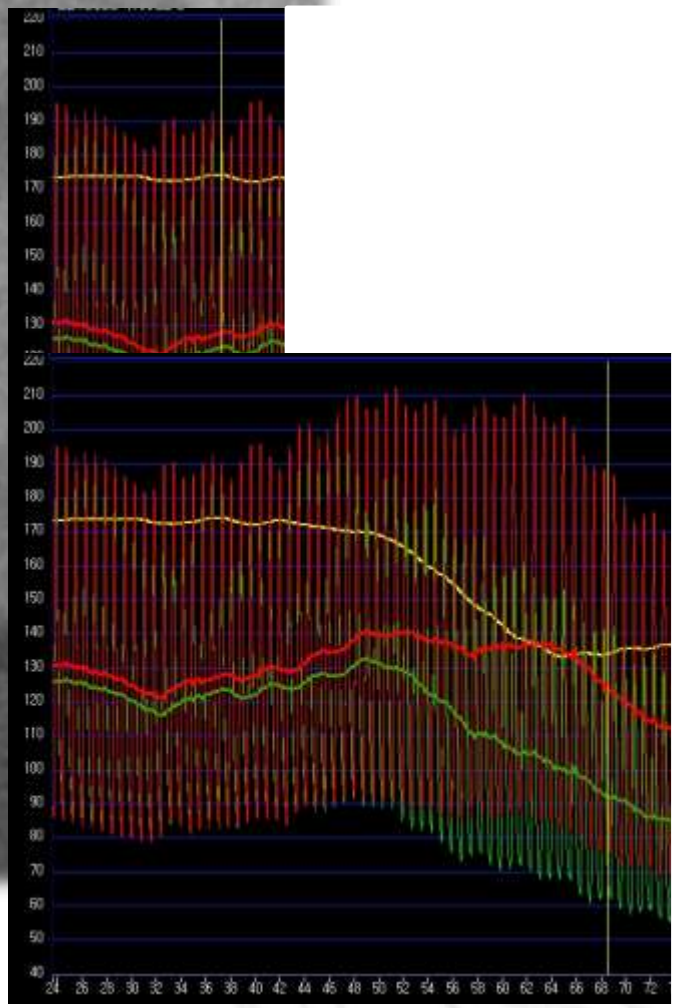
$$FFR = \frac{Q^{S}_{max}}{Q^{N}_{max}} = \frac{(Pd-Pv)/R}{(Pa-Pv)/R} = \frac{P_d}{P_a}$$



Rubio and Berne, Prog CV Disease 1975

Hyperemia: Why important?





Hyperemia: Which and How?

Intravenous continuous infusion

- **Adenosine, ATP**	140 µg/kg/min
- Dobutamine	20-40 µg/kg/min

Intracoronary bolus injection

- Papaverine	10 - 20 mg
- **Adenosine, ATP**	20-720 µg
- Nitroprusside	0.3-0.9 µg/kg
- Nicorandil	2mg

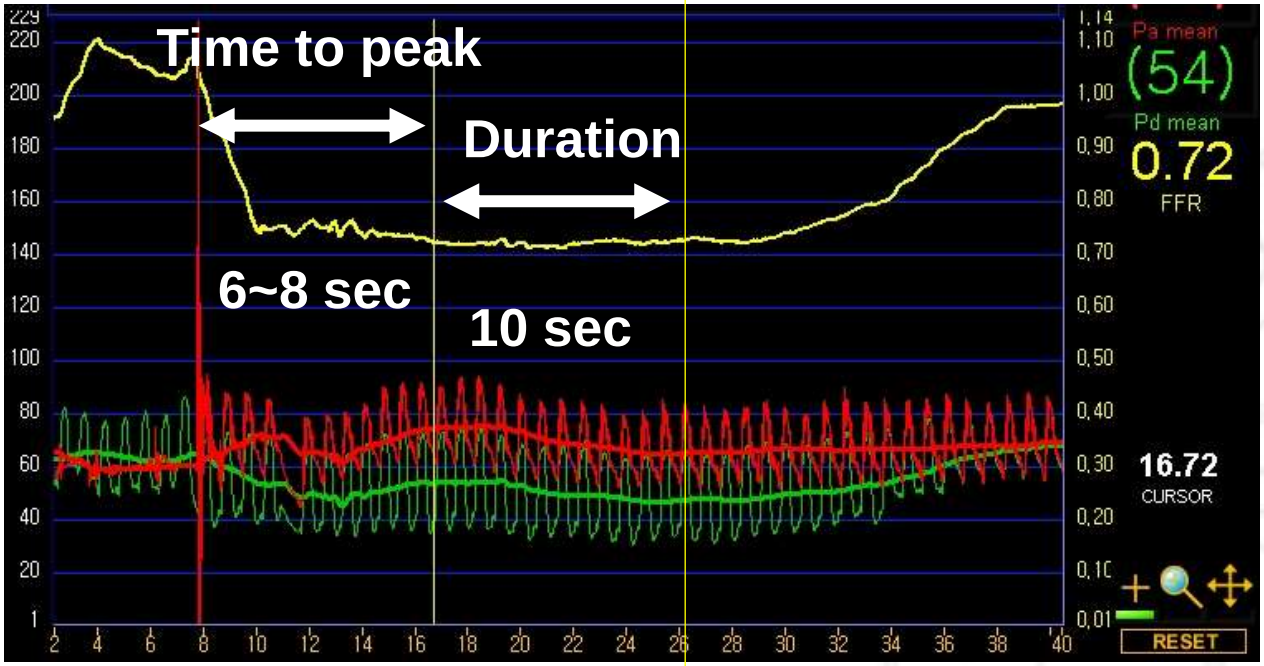
Intracoronary continuous infusion

- Adenosine	240µg/min

Intravenous bolus injection

- **Regadenoson**	400µg

Bolus Intracoronary Adenosine

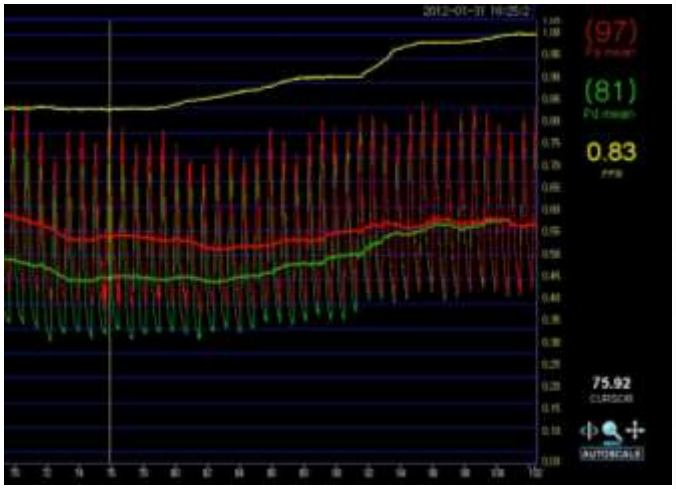


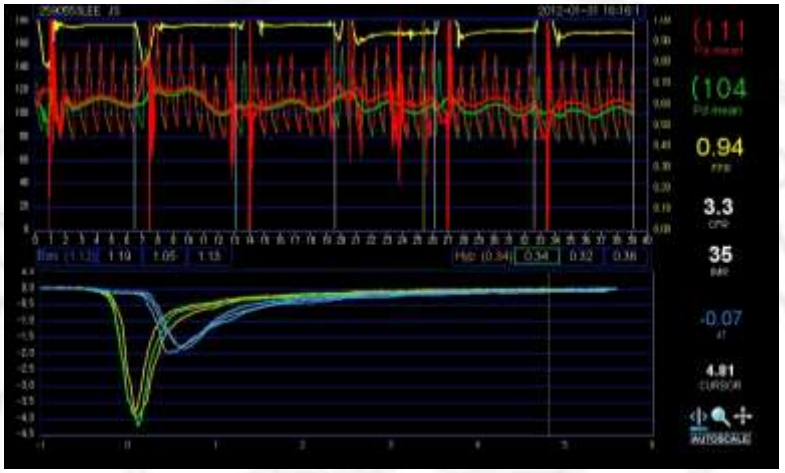
Quick,
Easy,
Inexpensive.

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!!!

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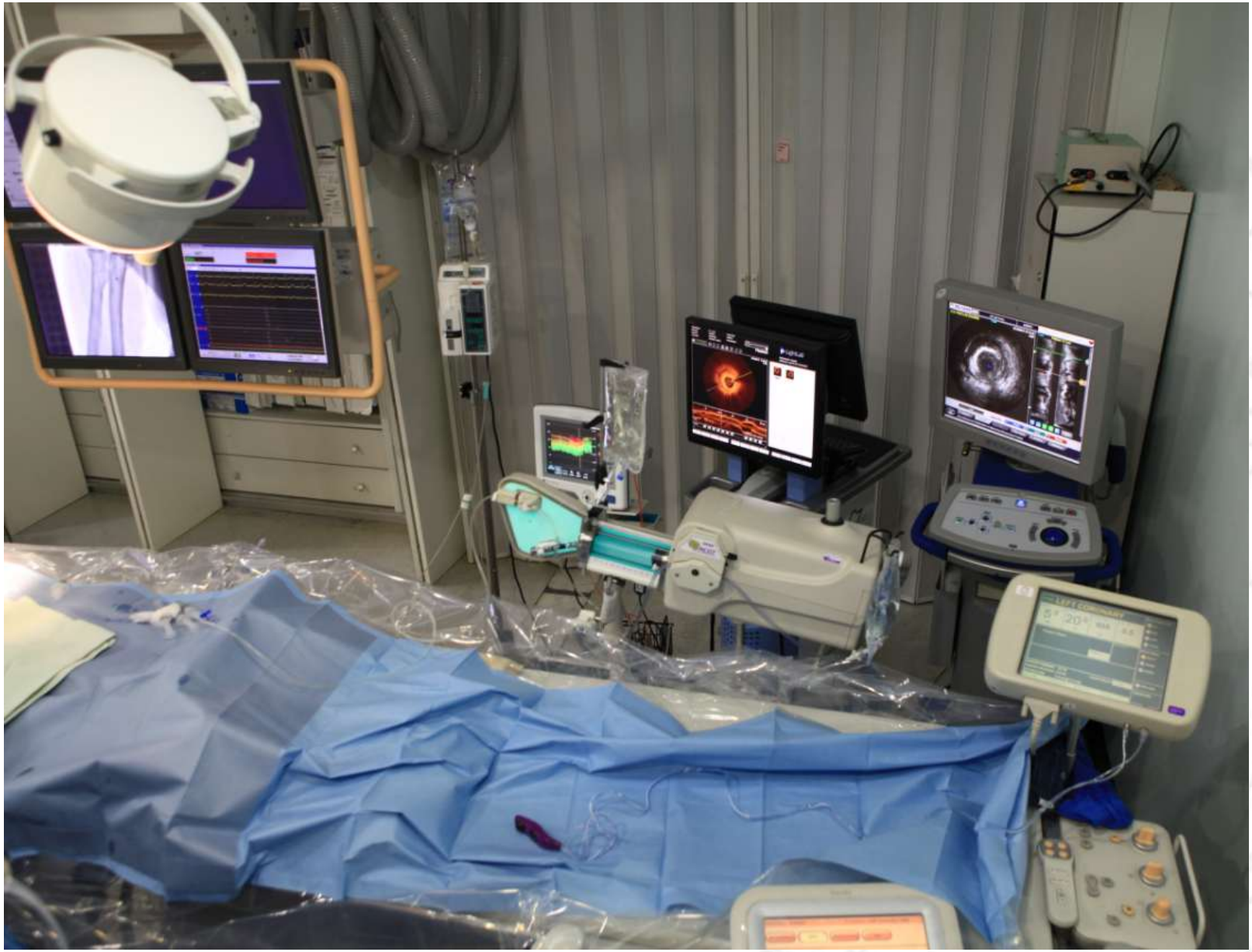
Issues for Adenosine Hyperemia

- **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**



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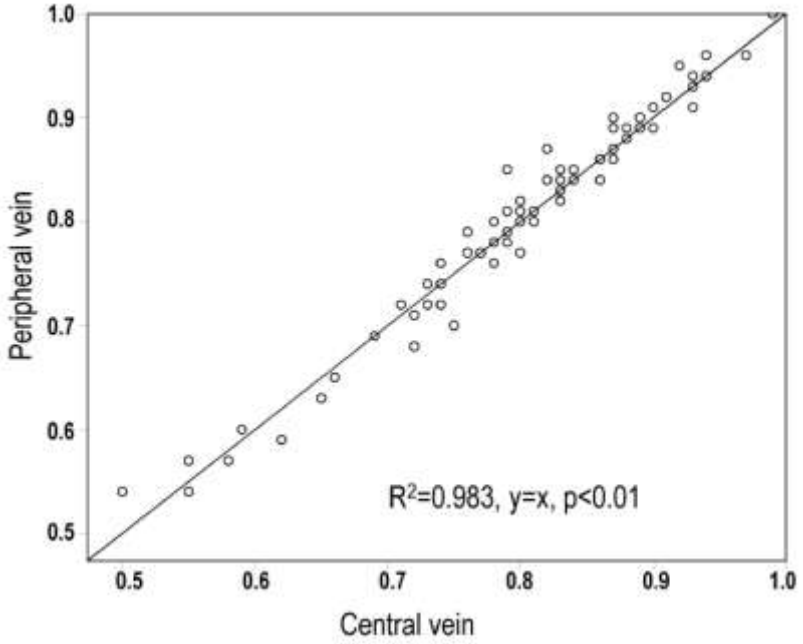
Femoral vein vs. Forearm vein



	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.**

Circ Cardiovasc Interv. 2012 Jun;5(3):401-5

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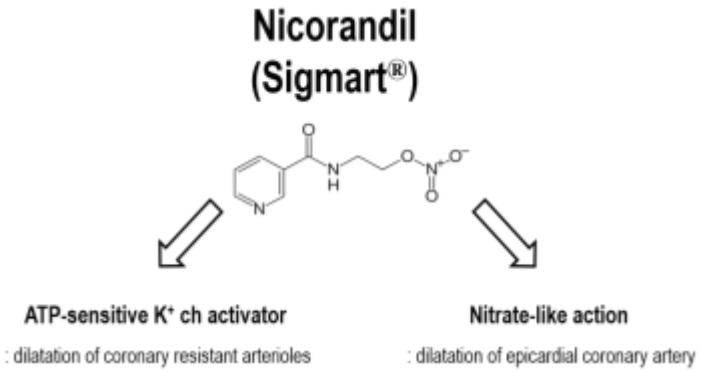
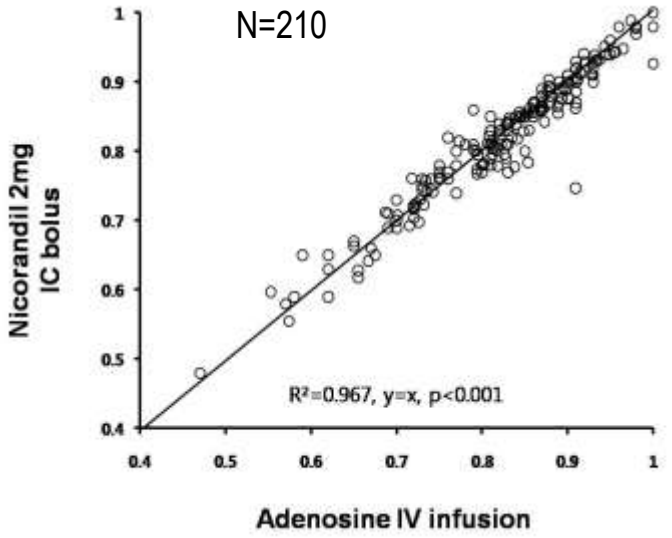
Novel hyperemic agent: intracoronary nicorandil





	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**

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Jang HJ, et al. Eur Heart J. 2013;34(27):2055-62

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Comparison of vasodilatory stimuli

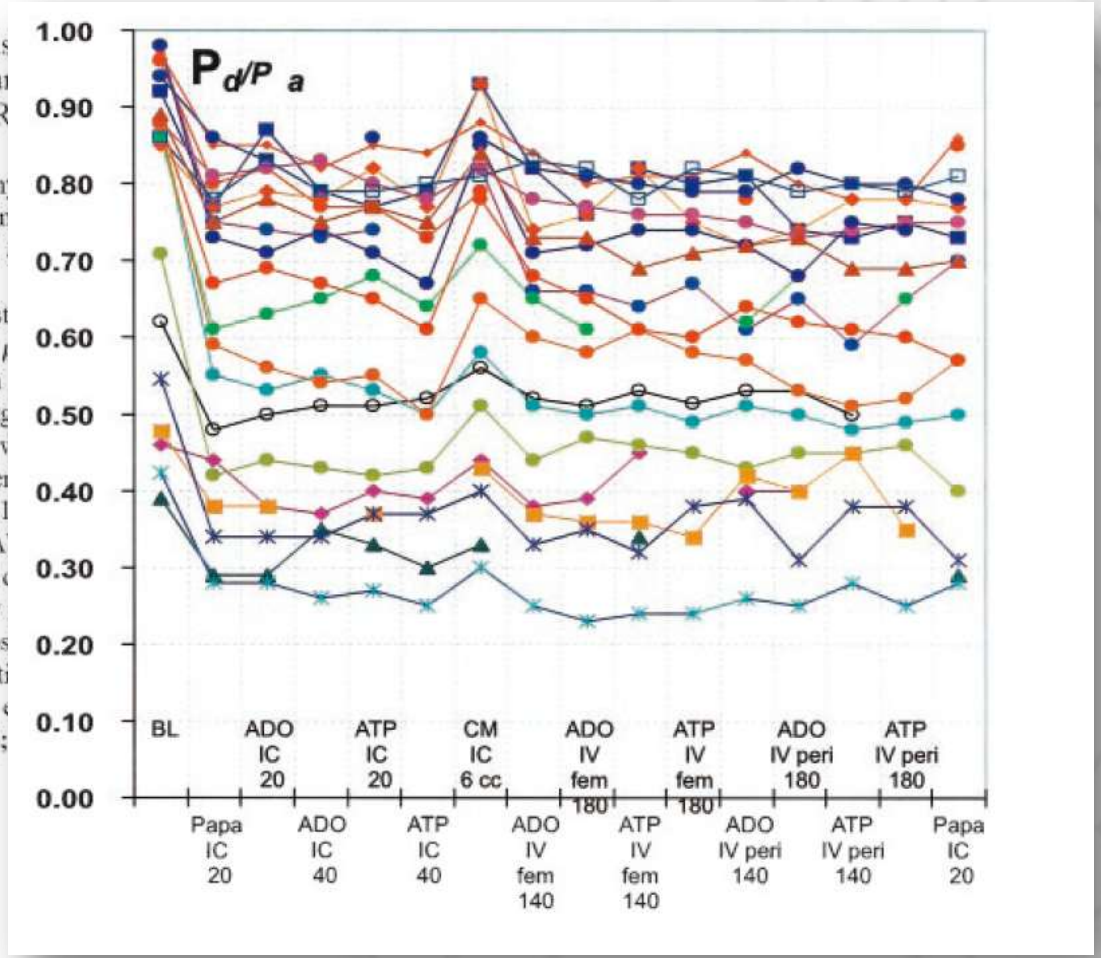
Intracoronary and Intravenous Adenosine 5′-Triphosphate, Adenosine, Papaverine, and Contrast Medium to Assess Fractional Flow Reserve in Humans

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 hy
of fractional flow reserve measurements. The present study cor
adenosine 5′-triphosphate (ATP), adenosine, contrast medium,
maximal and steady-state hyperemia.

Methods and Results—In 21 patients with an isolated coronary st
by papaverine (20 mg intracoronary), adenosine (20 and 40 μ
iohexol (6 mL intracoronary), adenosine or ATP through an
adenosine or ATP through a femoral vein (140 and 180 μg · kg
the ratio of distal coronary pressure (P_d) to aortic pressure (P_a) w
0.77±0.21 at rest and decreased to 0.61±0.21 after papaver
vasodilators, except with contrast medium (0.68±0.21; $P<0.01$
be obtained by intracoronary papaverine and by intravenous A
infusion of ATP was varied from 0 to 280 μg · kg^{-1} · min^{-1}. At
decrease in P_d/P_a ratio nor a further increase in coronary flow

Conclusion—Provided sufficient dosages are used, ATP, adenos
maximal hyperemia and are therefore suitable to assess fracti
intravenous ATP or adenosine induce steady-state hyperemia
assessing diffuse coronary atherosclerosis. (***Circulation***. 2003;



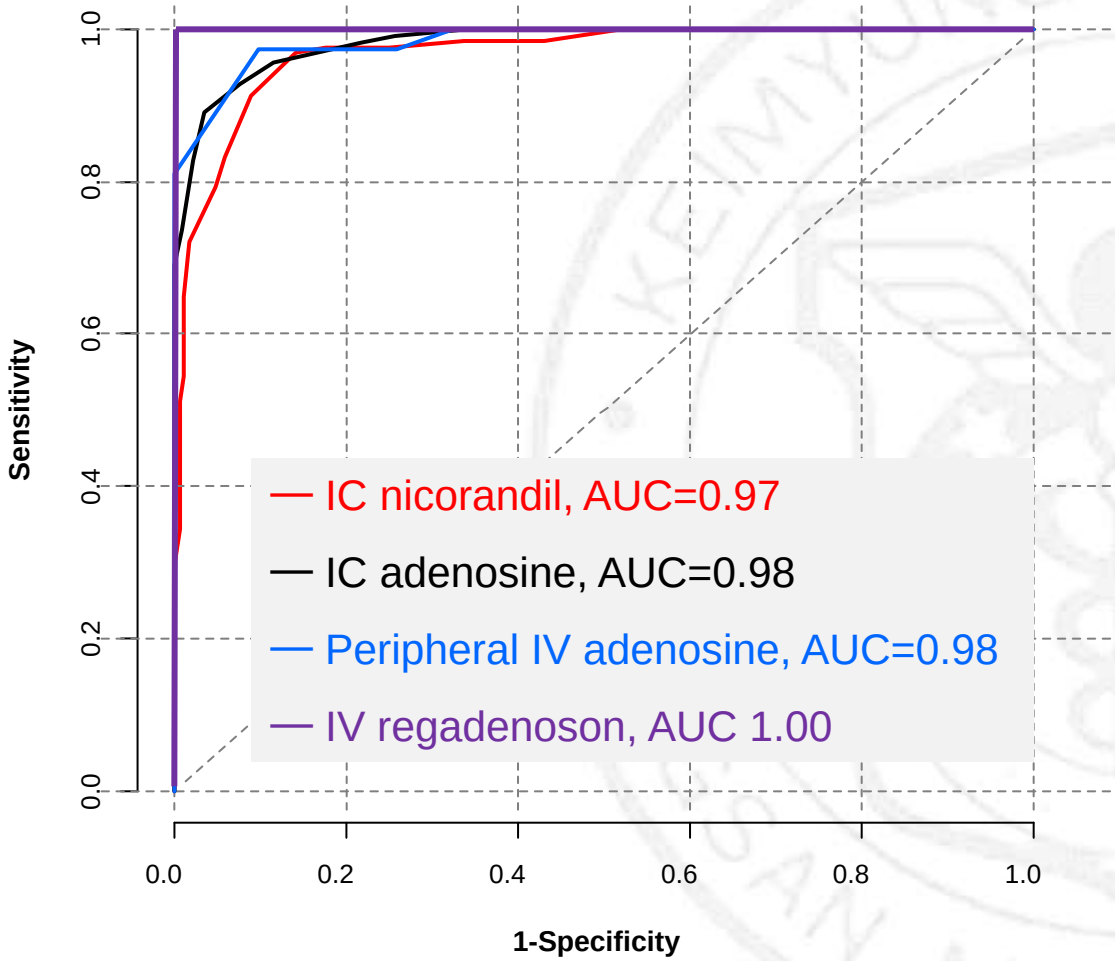
de Bruyne et al. Circulation 2003

Stability and reproducibility of FFR

with different hyperemic drugs, different routes and different time

Classification agreement

: IV adenosine vs. each alternative methods



Lim WH, et al. Catheter Cardiovasc Interv. 2015;85(6):970-6

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

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Thank You

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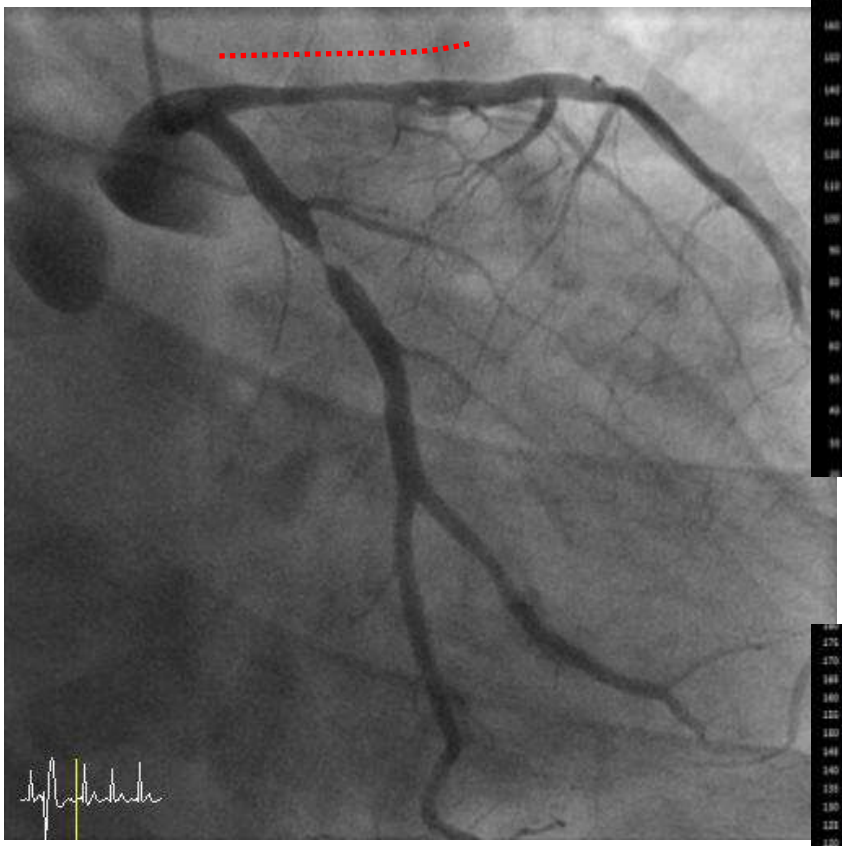
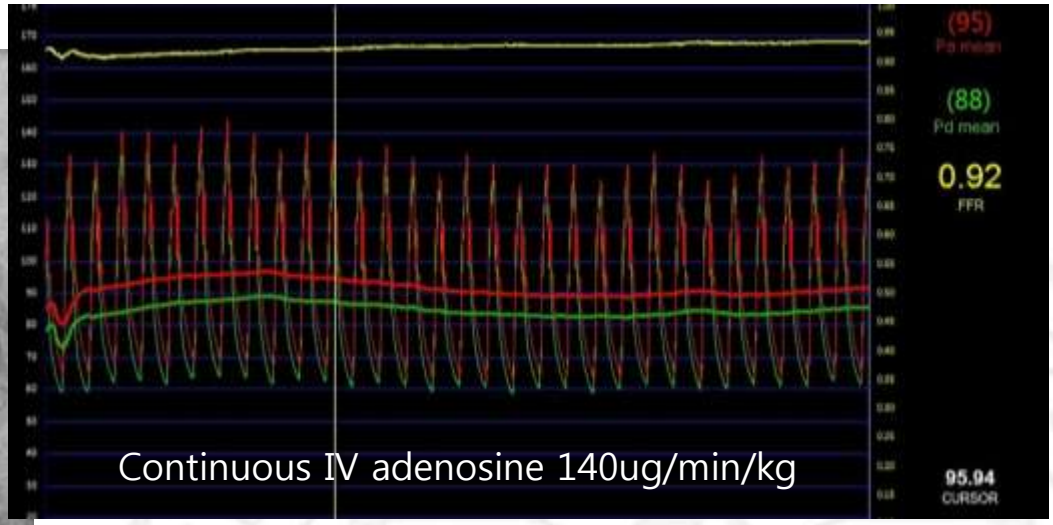
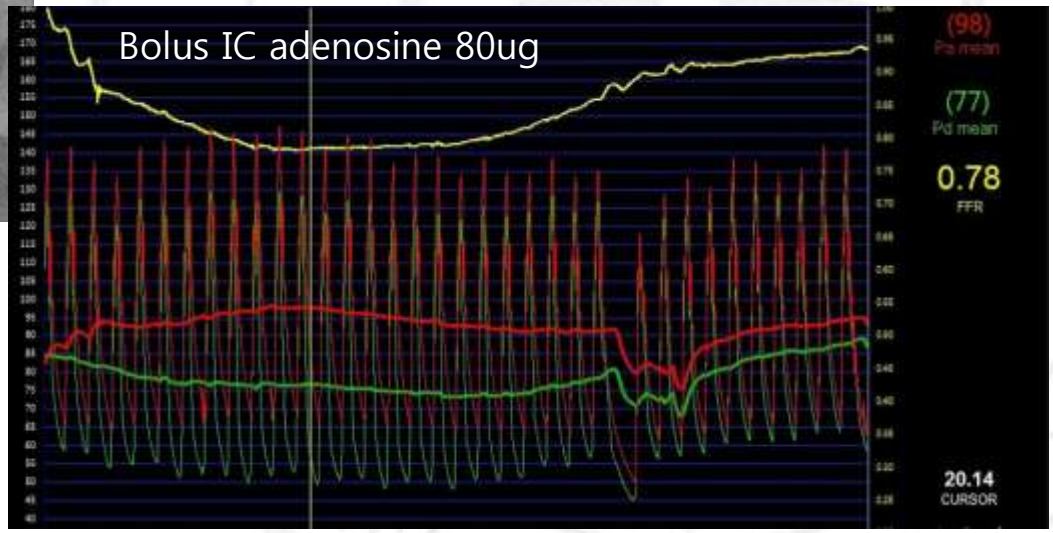




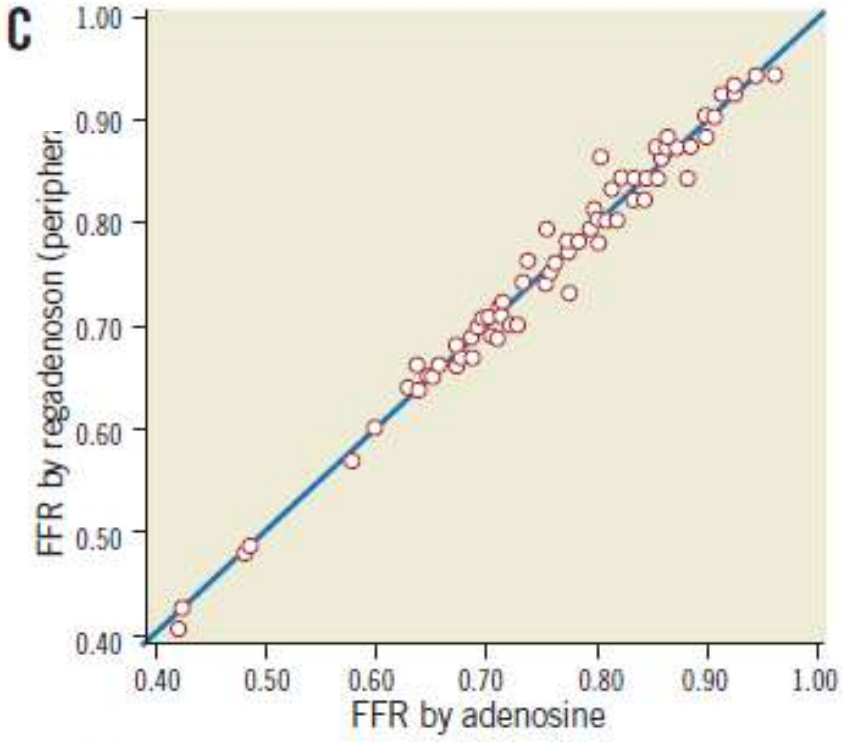
Continuous IV adenosine 140ug/min/kg

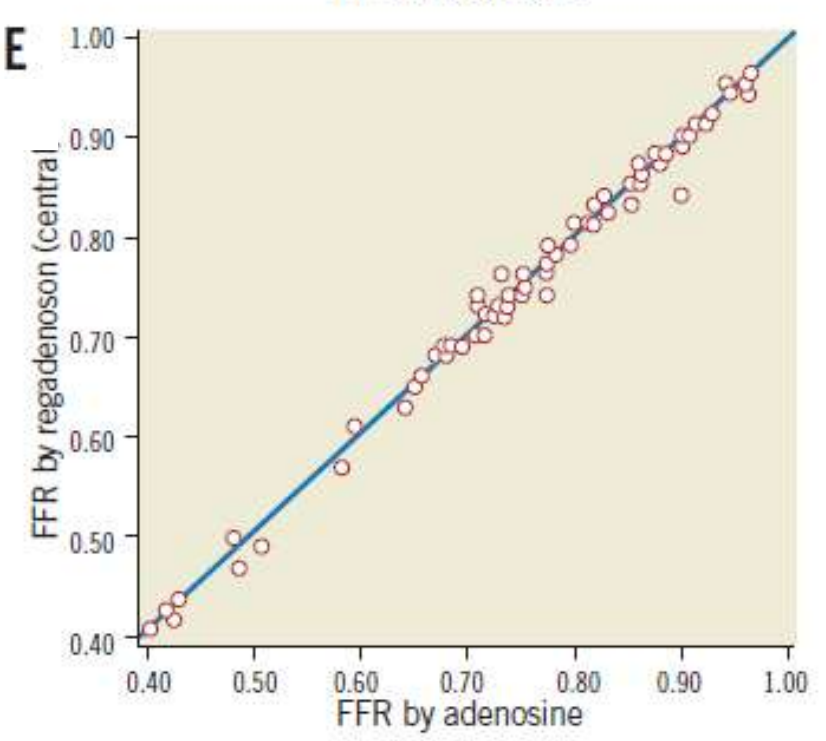


Bolus IC adenosine 80ug

Novel hyperemic agent: intravenous Regadenoson

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





Van Nunen, et al. Eurointervention 2014 in press