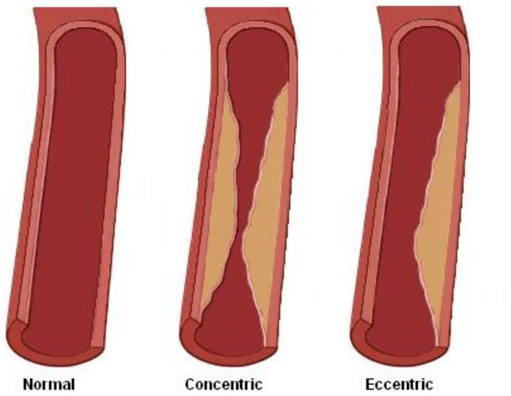
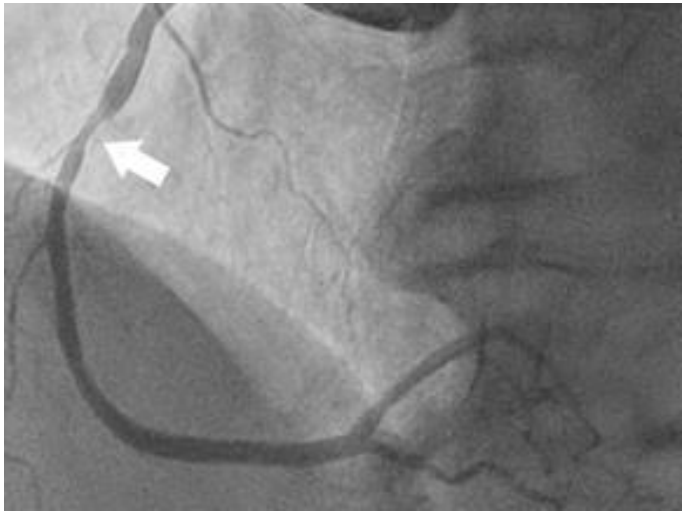
ΛΕΙΤΟΥΡΓΙΚΕΣ ΔΟΚΙΜΑΣΙΕΣ ΣΤΟ ΑΙΜΟΔΥΝΑΜΙΚΟ ΕΡΓΑΣΤΗΡΙΟ

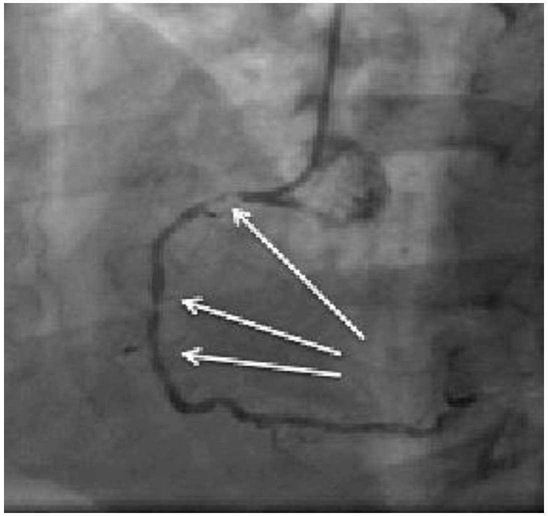
ΡΑΜΜΟΣ ΑΗΔΟΝΗΣ
ΚΑΡΔΙΟΛΟΓΟΣ
Β' ΚΑΡΔΙΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ
Π.Γ.Ν.Ι.

- Στεφανιογραφία (coronary angiography) => ***gold standard*** στην εκτίμηση Στεφανιαίας Νόσου

- Διαγνωστικό Πρόβλημα:
  - Ενδιάμεσες βλάβες (40-70%)
  - Έκκεντρες βλάβες
  - Διάχυτες στενώσεις



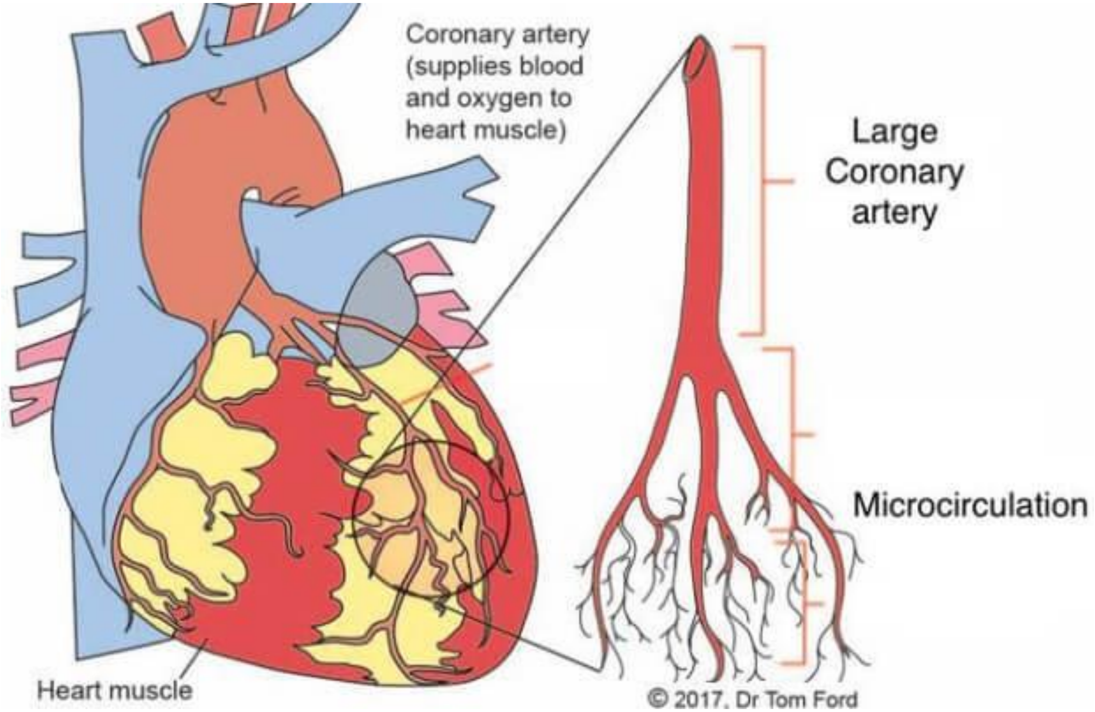




- Πολύ συχνά

  - Σύμπτωμα (στηθάγχη) => Χωρίς αγγειογραφικά κριτική στένωση

  - Μικροαγγειακή
    ή
  - Ενδοθηλιακή Δυσλειτουργία



Δομή και Φυσιολογία Στεφανιαίων Αγγείων

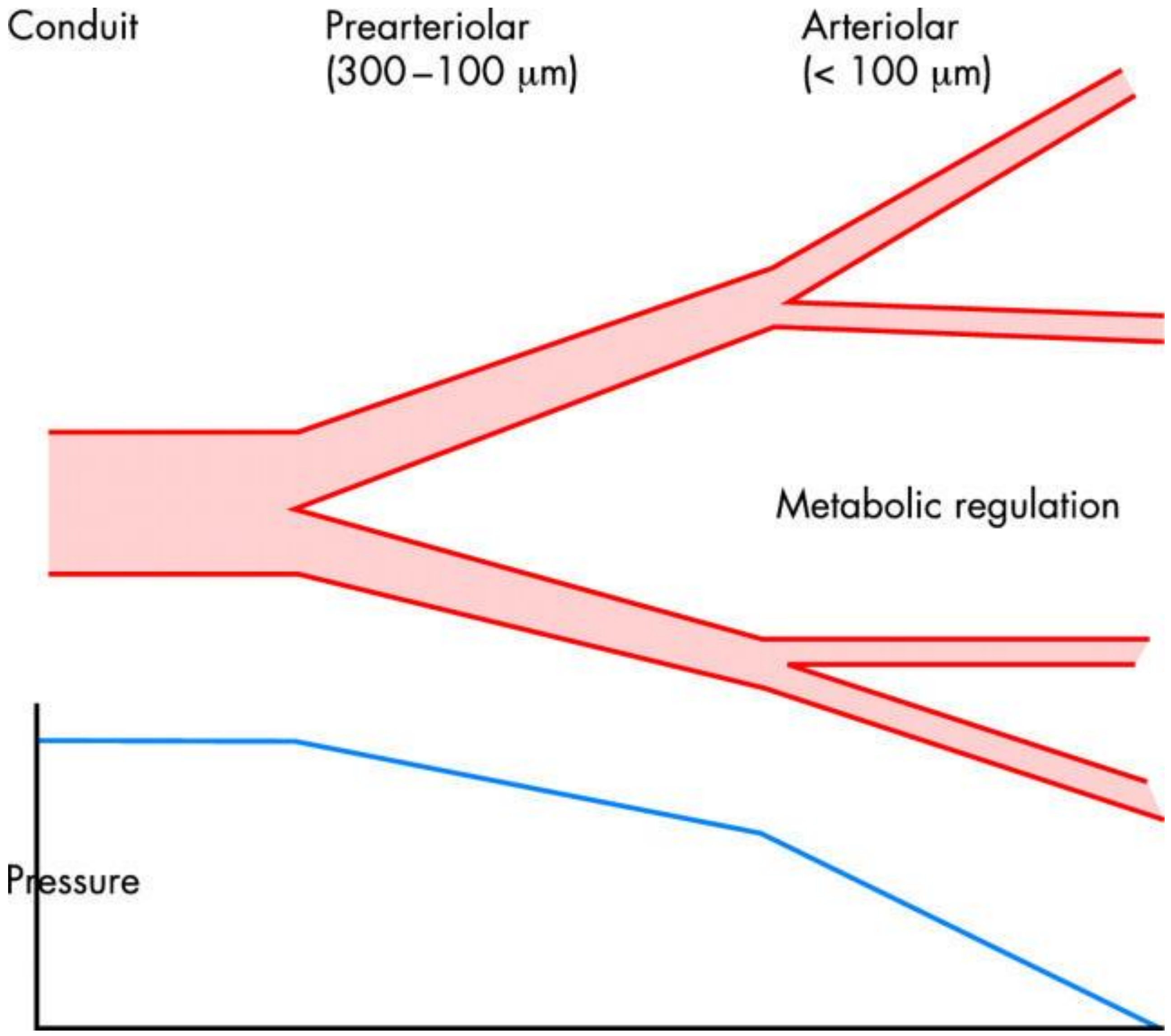
Στεφανιαία Κυκλοφορία:3 τμήματα

- Μεγάλες επικαρδιακές στεφανιαίες αρτηρίες
  - Μέγεθος > 500μm
  - <10% της συνολικής αντίστασης
  - Η ΑΠ παραμένει σταθερή στα αγγεία αυτά

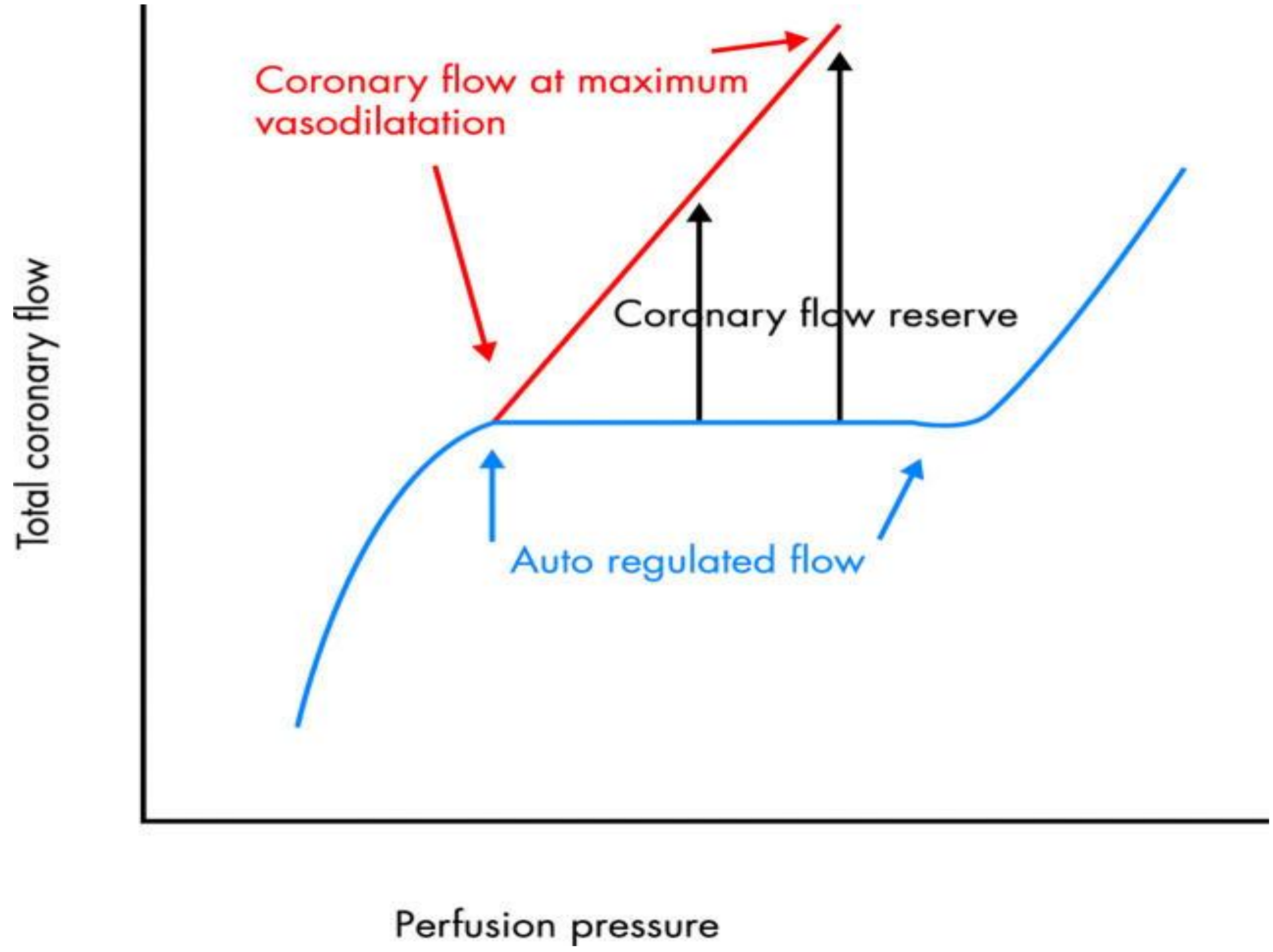
- Εξωκαρδιακά Περιαρτηρίδια
  - 100-500μm

- Τριχοειδή αγγεία

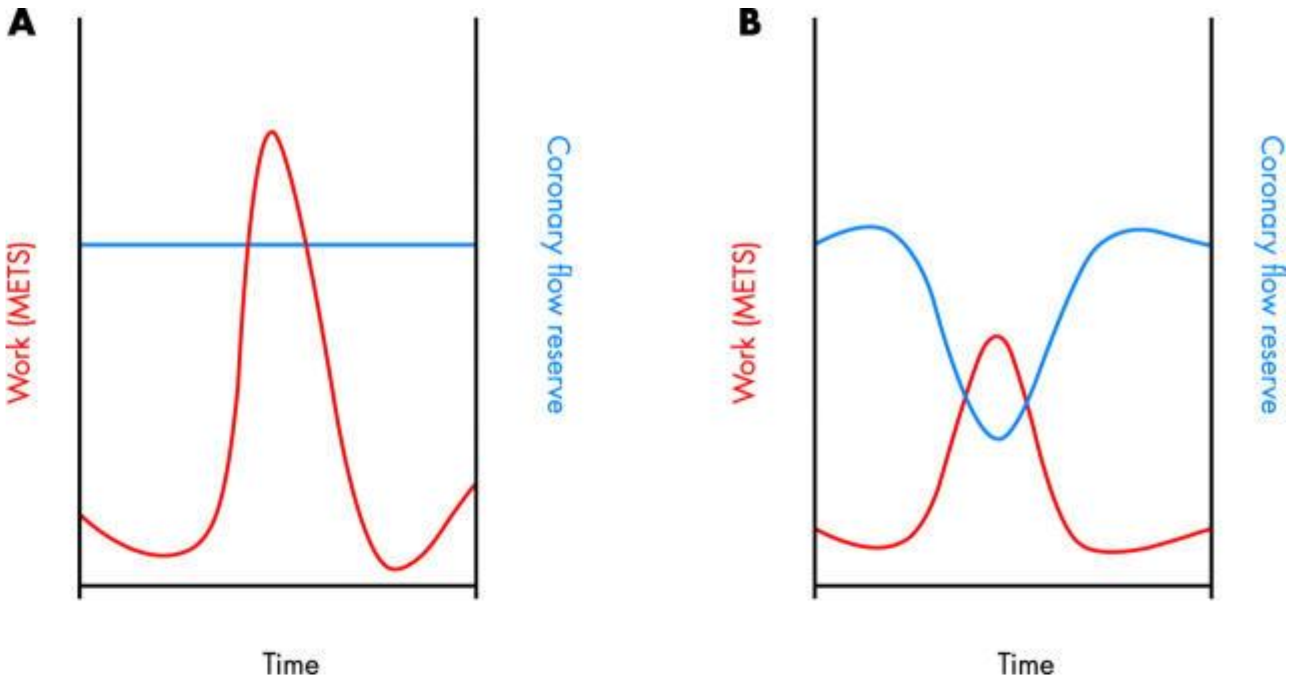
90% των αντιστάσεων (μικροκυκλοφορία)



Conduit
Prearteriolar
(300–100 μm)
Arteriolar
(< 100 μm)
Metabolic regulation
Pressure



The sigmoid line shows resting coronary blood flow which has an autoregulated range at physiological pressure. Following metabolic demands the coronary circulation undergoes vasodilatation which when maximal becomes a pressure driven system (the oblique straight line). The difference between the two lines is the coronary flow reserve which is a variable parameter depending on the perfusion pressure.



(A) Coronary flow reserve is fixed and an increase in metabolic demand causes ischaemia when not accommodated by the coronary flow reserve.

(B) Coronary flow reserve is variable because of microvascular influences and now a lesser amount of myocardial demand also produces ischaemia.

- Μέγιστη διάθεση O_2 στα στεφανιαία αγγεία: **Ηρεμία**
- Αύξηση αναγκών O_2 => Αύξηση ροής
- Τμήμα 1 & 2 σε φυσιολογικές συνθήκες επιτυγχάνουν διάταση μέσω ρύθμισης ροής
- Όταν υπάρχει στένωση σε στεφανιαίο αγγείο => πτώση πίεσης στο άπω τμήμα
- Τμήμα 2 => αγγειοδιαστολή

Φάρμακα για ΥΠΕΡΑΙΜΙΑ

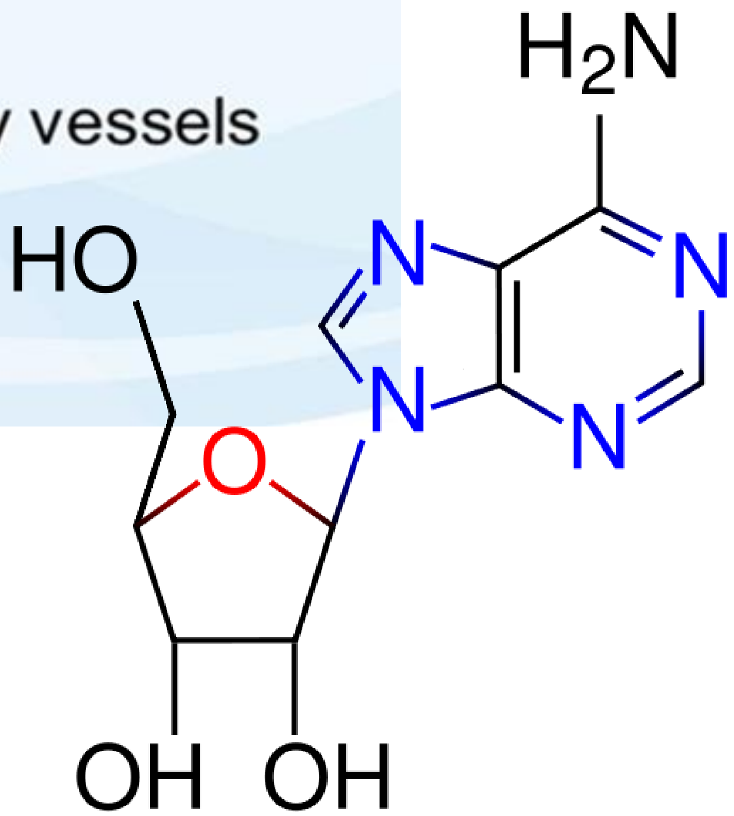
Table 1 Substances used in the catheterization laboratory for coronary vascular function assessment

Substance	Doses	Site of action	Endothelium response	Effect
Adenosine	Iv: 140 μg/kg per minute Ic: 20-150 μg bolus	Microvascular	Independent	Direct vasodilation
Acetylcholine	Ic: 10^{-6} M/10^{-5} M/ 10^{-4} M	Micro and macrovascular	Dependent	Vasodilation if normal endothelial function; vasoconstriction if endothelial dysfunction
Nitroglycerin	Ic: 200 μg bolus	Macrovascular	Independent	Vasodilation
Nitroprusside	Ic 0.3-0.9 μg/kg bolus	Micro and macrovascular	Independent	Vasodilation
Papaverine	Ic: 8-20 mg bolus	Micro and macrovascular	Independent	Enzyme Phosphodiesterase inhibition Vasodilation
Regadenoson	Iv: 400 μg bolus	Microvascular	Independent	Adenosine receptor agonist vasodilation

World J Cardiol 2015; 7(9): 525-538

Four Types of Adenosine Receptors

- A1 – AV Block
- A2A – Vasodilate small coronary vessels
- A2B – Mast cell degranulation
- A3 - Bronchoconstriction



ΑΔΕΝΟΣΙΝΗ

- Παράγεται από αγγειακούς λείους μύες και ενδοθηλιακά κύτταρα
- Αγγειοδιαστολή: Σύνδεση με A2a
- A1, A3 και A2β υποδοχείς
  - Βρογχόσπασμος
  - AV Nodal Blockade
- Πλεονέκτημα: Πολύ μικρός χρόνος ημίσειας ζωής (2-10 sec)
- Ενδοστεφανιαία χορήγηση
- Χρειάζεται μετά αμινοφυλλίνη

Intracoronary adenosine

- Intracoronary adenosine is an extremely safe agent to induce maximal hyperaemia due to short half time – repeated doses.
- Peak effect occurs less than 10 sec after administration but has a duration of action of less than 20 sec

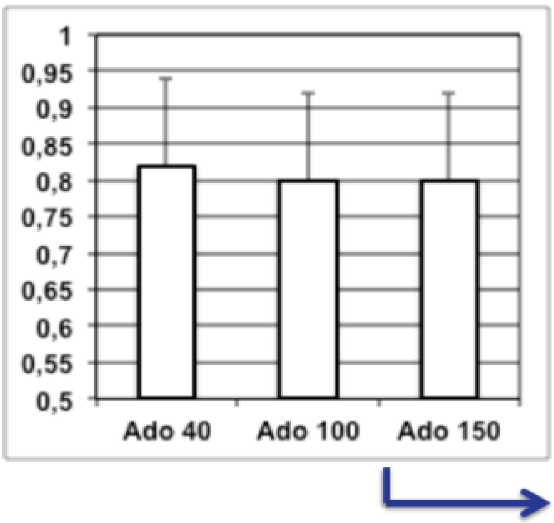
  RCA: 40 µg

  LCA: 60 µg
- This should be increased in 20–30 mcg increments to a maximum of 150 µg if FFR between 0.75 and 0.80
- Main side effect is short lasting, transient AV-block, most frequently noted after administration of the drug into the right coronary artery

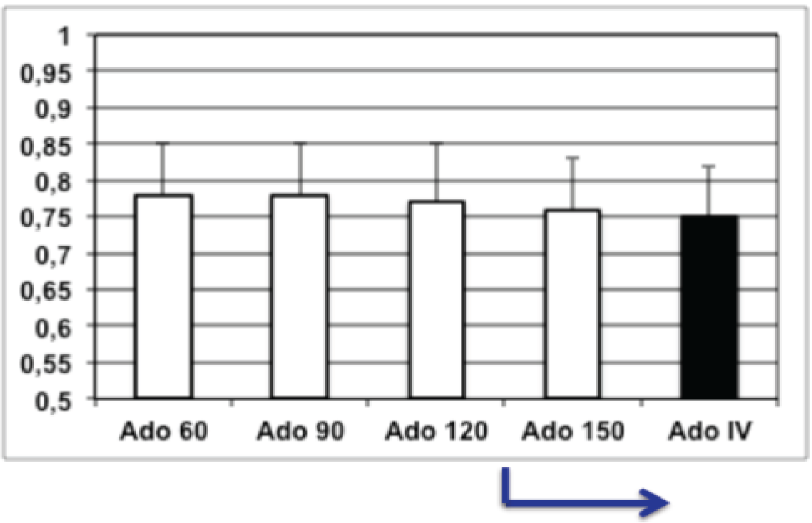
IC adenosine >100µg (up to 150µg to 200µg)

IC Adenosine 150 µg

82 pts/108 stenoses



50 pts/50 stenoses



4% Stenoses > 0.80
➔ < 0.75

6% Stenoses > 0.80
➔ < 0.75

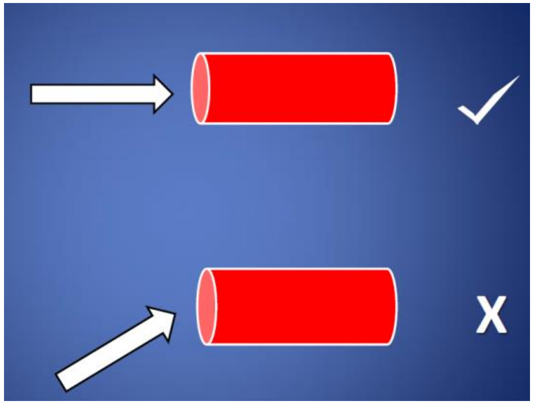
www.cardio-aalst.be

Mod. By Casella G Am Heart J 2004

Mod. By Rioufol Eurointervention 2005

Intracoronary Adenosine preparation

- **Nitrates** prior to measurement – to avoid spasm.



- Guide catheter
  - **Without side-holes**
  - **Coaxial engagement**

- Setup of the machine. **Beat-to-beat basis** rather than from a mean. Mean readings are likely to result in an underestimation of the maximum gradient

- Make sure **to interrupt the AO pressure** for as short as possible

IC Preparation

1 amp = 1 ml = 5 mg (Item)

Add: 5 mg adenosine (1 ml)
To: 250 ml NaCl

20 µg/ml

5 milligrams of adenosine can be added to 250ml NaCl to produce 20µg/ml

RCA: (40 µg/ml) = 2 ml (20 µg/ml)
LCA: (60 µg/ml) = 3 ml (20 µg/ml)

OR

1 amp = 2 ml = 6 mg (Sanofi)

Add: 5 mg adenosine (1.7 ml)
To: 500 ml NaCl

10 µg/ml

5 milligrams of adenosine can be added to 500ml NaCl to produce 10µg/ml

RCA: (40 µg/ml) = 4 ml (10 µg/ml).
LCA: (60 µg/ml) = 6 ml (10 µg/ml).

1) Gilles Rioufol, et al.
150 microgram intracoronary adenosine bolus for accurate fractional flow reserve assessment of
angiographically intermediate coronary stenosis.
EuroIntervention. 2005;2:204-207.

2) R Lopez Palop
Adequate Intracoronary Adenosine Doses to Achieve Maxmimum Hyperaemia in Coronary Functional
Studies by Pressure Derived Fractional Flow Reserve: A Dose Response Study
Heart. 2004;90:95-96.

3) Gianni Casella
Are high doses of intracoronary adenosine an alternative to standard intravenous adenosine for the
assessment of fractional flow reserve?
Am Heart J 2004;148:590-5.

4) N Pijls and B De Bruyne
Coronary Pressure 2nd Edition
Kluwer Academic Publishers

5) Clinical practice at the Coronary Intervention Department, Stockholm South Hospital, Stockholm, Sweden.

6) From the protocols of Nico Pijls, MD, Catharina Hospital, The Eindhoven, NL and Istvan Herzfeld, MD, Stockholm South Hospital, Sweden.

7) R Wilson et al.
Effects of Adenosine on Human Coronary Arterial Circulation
Circulation. 1990;82:1595-1606.

8) N Pijls et al.
Practice and potential pitfalls of coronary pressure measurement
Catheter Cardiovasc Interv. 2000;49:17-18.

Intravenous Adenosine

- Administered through the **femoral vein** or a large **cubital vein** the usual dose in clinical practice is 140 μg/kg/min
- Peak effect in around 1 min. Effect wears off 1 min after the infusion is stopped.
- FFR measurement of 0.75–0.80 the dose of the IV infusion can be safely increased to 180 μg/kg/min

Intravenous Adenosine

- AV block less common - Can provoke bronchoconstriction – not for asthma or COPD

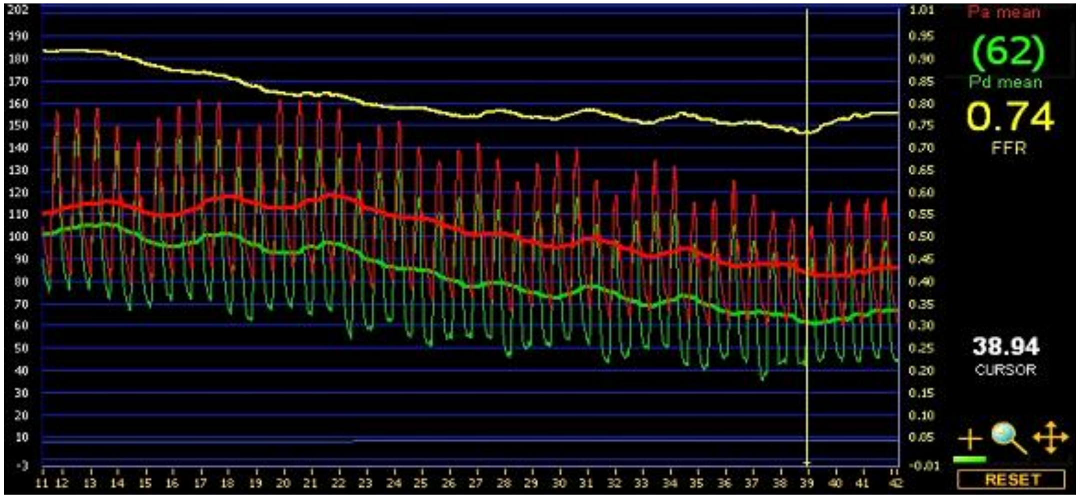
- **Unpleasant angina like sensation** – NOT harmful – informed patient prevents undue alarm

- Sensation passes quickly after ending the infusion If asymptomatic patient – drug administered correctly?

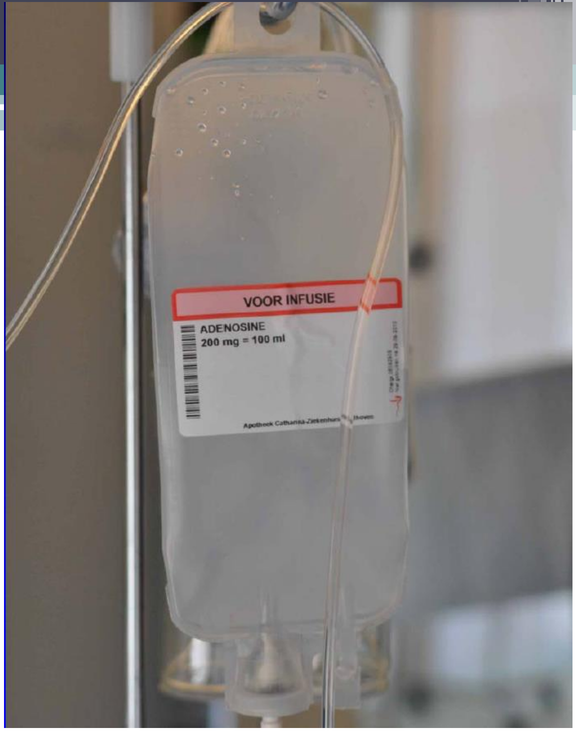
- Decrease of BP (10 – 20 %) similar increase of the Heart Rate

Intravenous Adenosine

- High infusion rate pump
- If brachial vein – arm extended
- Nitrates
- Steady state hyperemia, allows pullback curve to be recorded (for serial stenosis)
- Short half life – avoid valsalva maneuver (no interruption of venous return) – fluctuation of Pd/Pa curve
- Breath normally



Preparation



Preparation of Intravenous Adenosine

1. Remove 40 ml from a 100 ml bag of iv saline and discard.
2. Draw up 30 ml (90 mg) of adenosine (3 mg/ml; either 15 × 2ml vials or 3 × 10 ml vials).
3. Add adenosine to the 60 ml iv saline giving a concentration of 1 mg/ml.

Ex: 90 mg (30 ml) = 90mg/30 + 60 ml = 1mg/ml

Patient 75kg → 630 mg/h → 10,5 mg/min = 10,5 ml/min →
Procedure: 2,5 min/ vessel (incl inf - peak) = 7,5 min → ~ 80 ml

Dosage Chart

TABLE I. Dosage Table for IV Adenosine at 140 µg/kg/min

Weight (lb)	Weight (kg)	Infusion (ml/hr)
99	45	378
110	50	420
121	55	462
132	60	504
143	65	546
154	70	588
165	75	630
176	80	672
187	85	714
198	90	756
209	95	798
220	100	840
231	105	882
243	110	924
254	115	966
265	120	1008

When IV Adenosine?

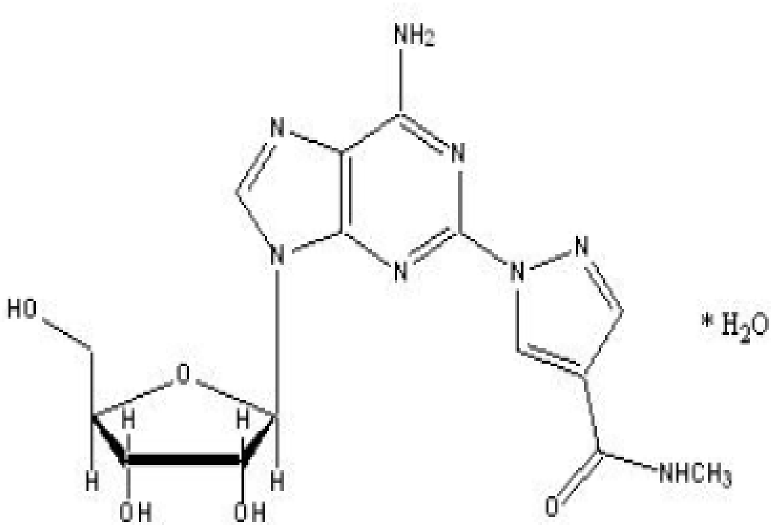
- Serial lesions
- Diffuse disease
- Stent assessment

When IC Adenosine?

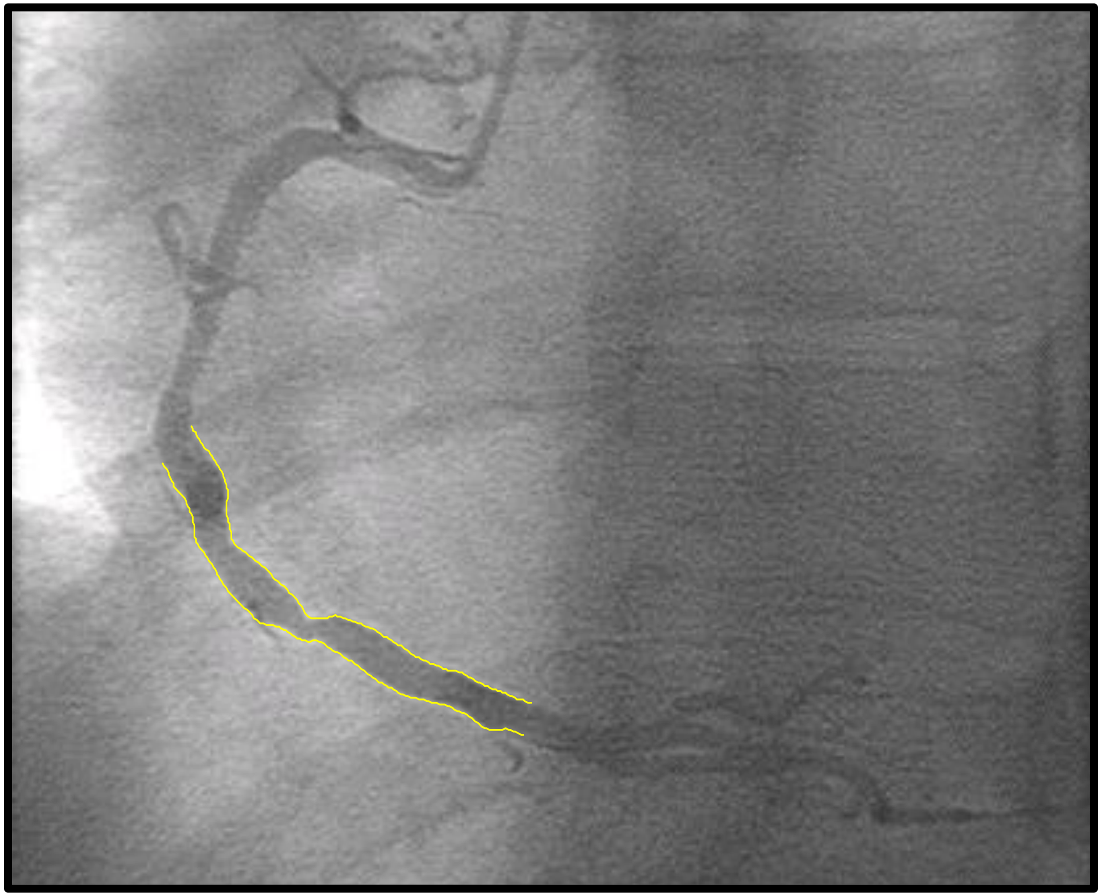
- Single lesions
- Patients with asthma

Regadenoson

- Εκλεκτικός Α2α Αγωνιστής
- Υπεραιμία ~2-5 λεπτά
- Χορήγησε σε μια δόση



Quantitative Coronary Angiography (QCA)
Edge detection



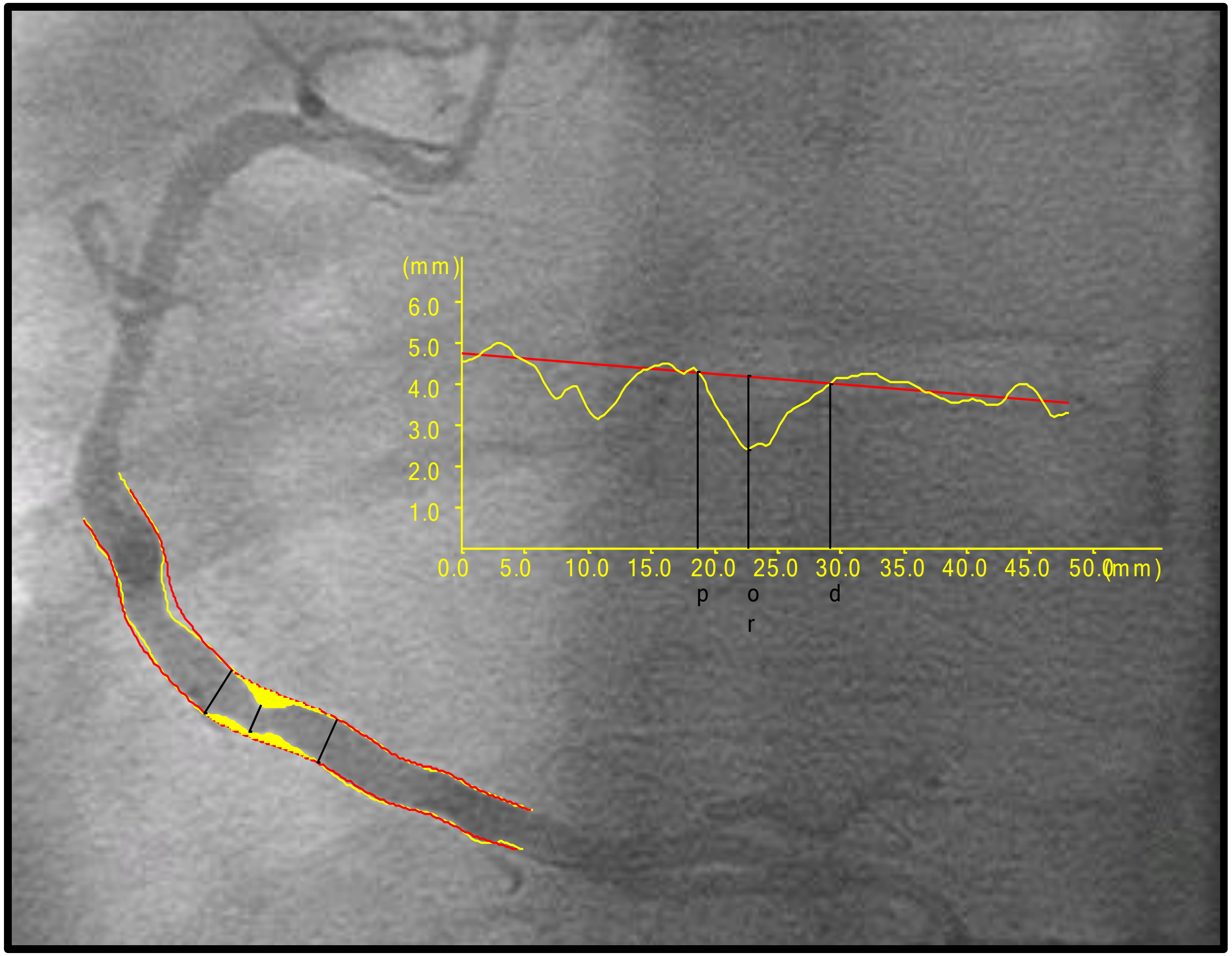
Δεν είναι ακριβώς λειτουργική δοκιμασία

Δε χρησιμοποιούμε υπεραιμία

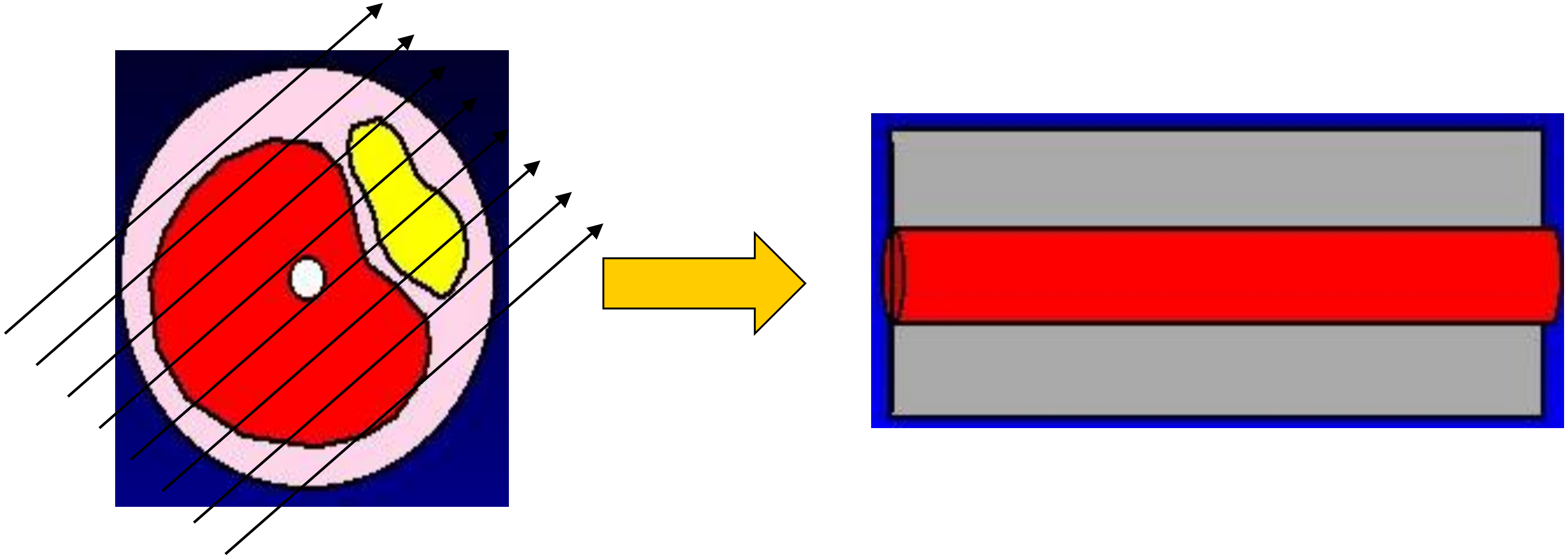
Οπτική επιθεώρηση του διαγράμματος του αυλού από το σκιαγραφικό

Πλεονέκτημα: Ελευθερία από σφάλμα παρατηρητή (intraobserver and interobserver variability)

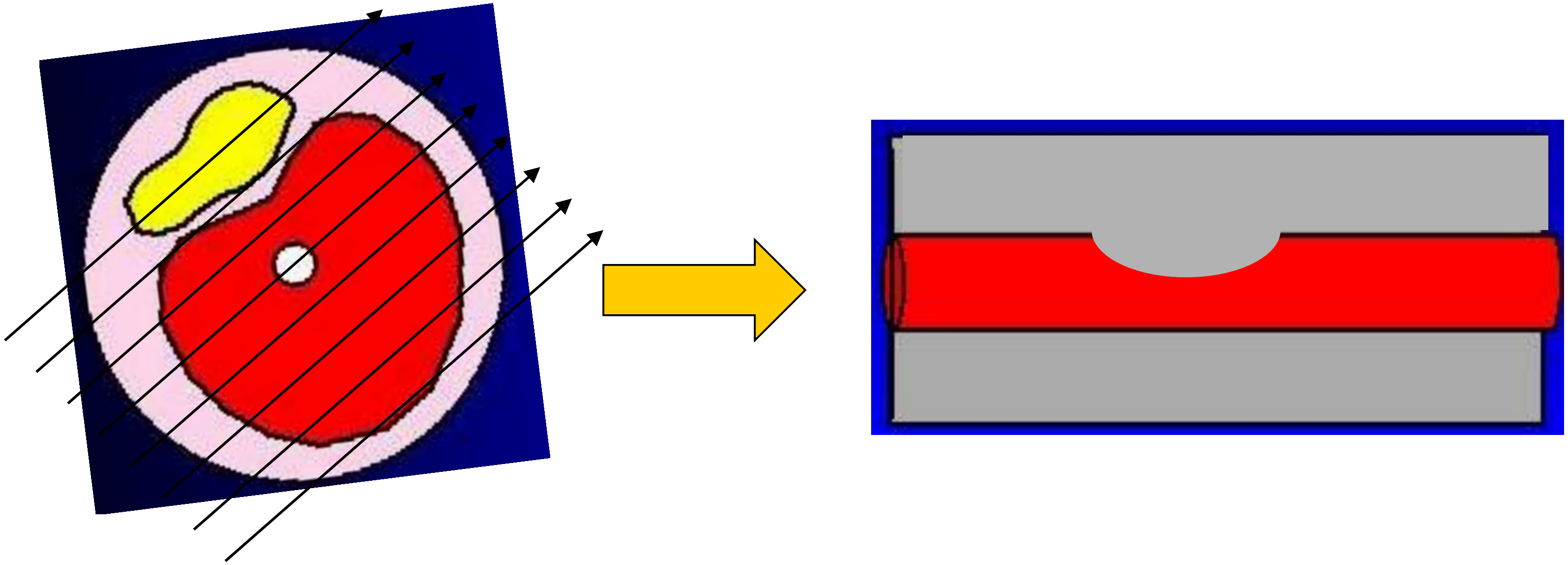
Quantitative Coronary Angiography



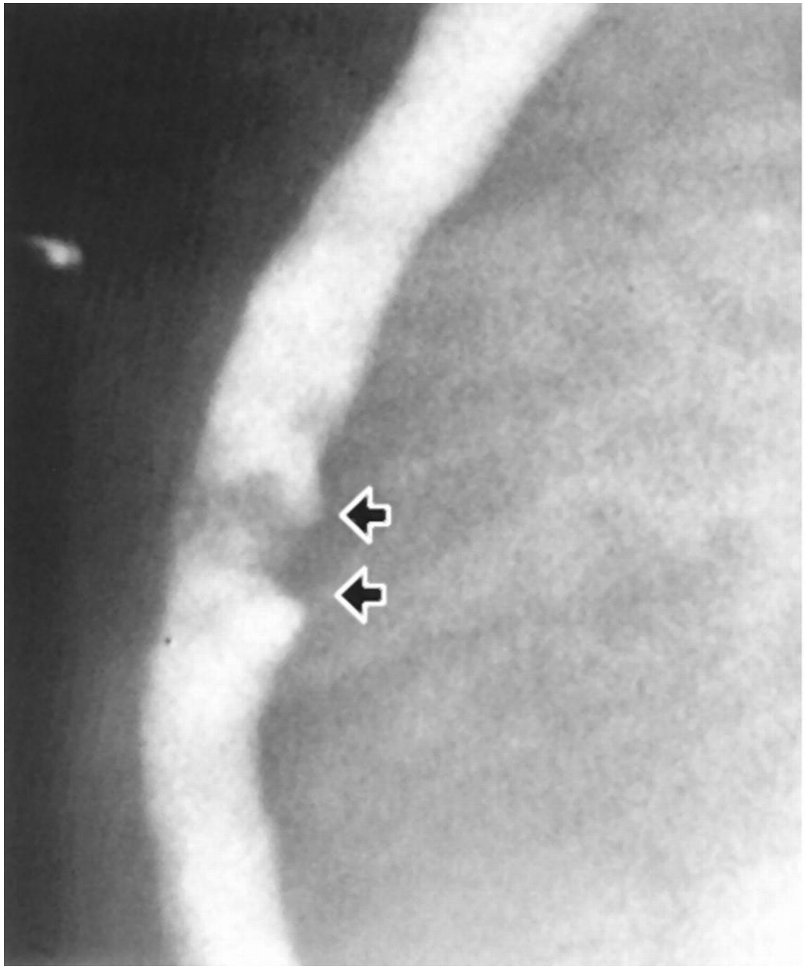
PITFALL : LESION ECCENTRICITY

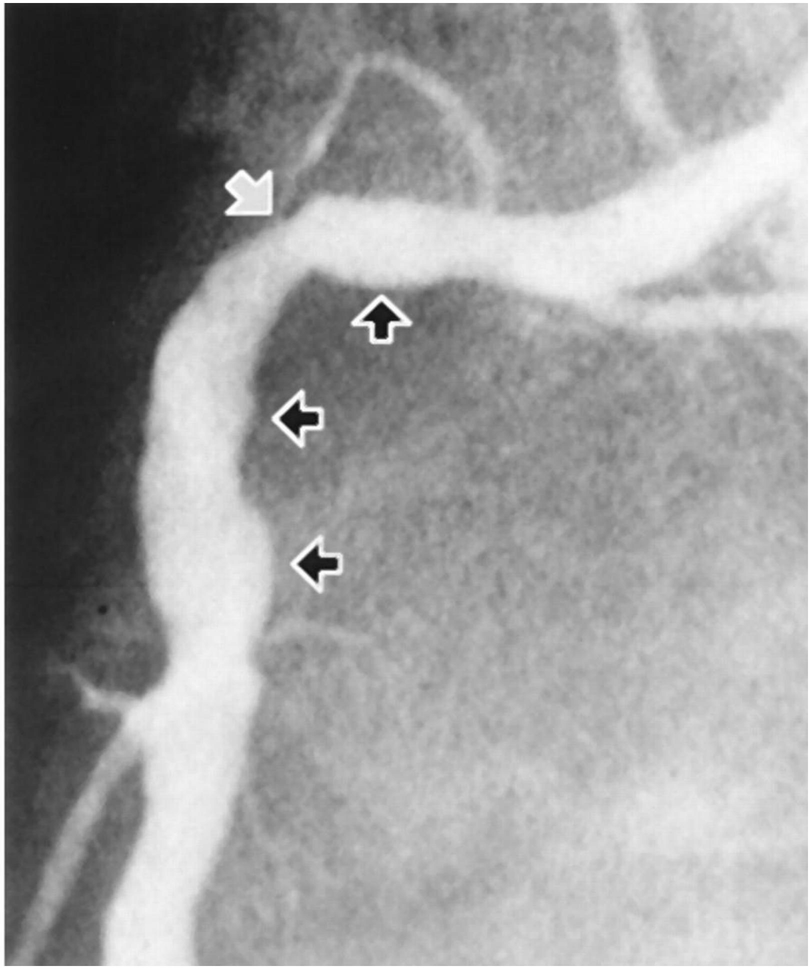


PITFALL : LESION ECCENTRICITY

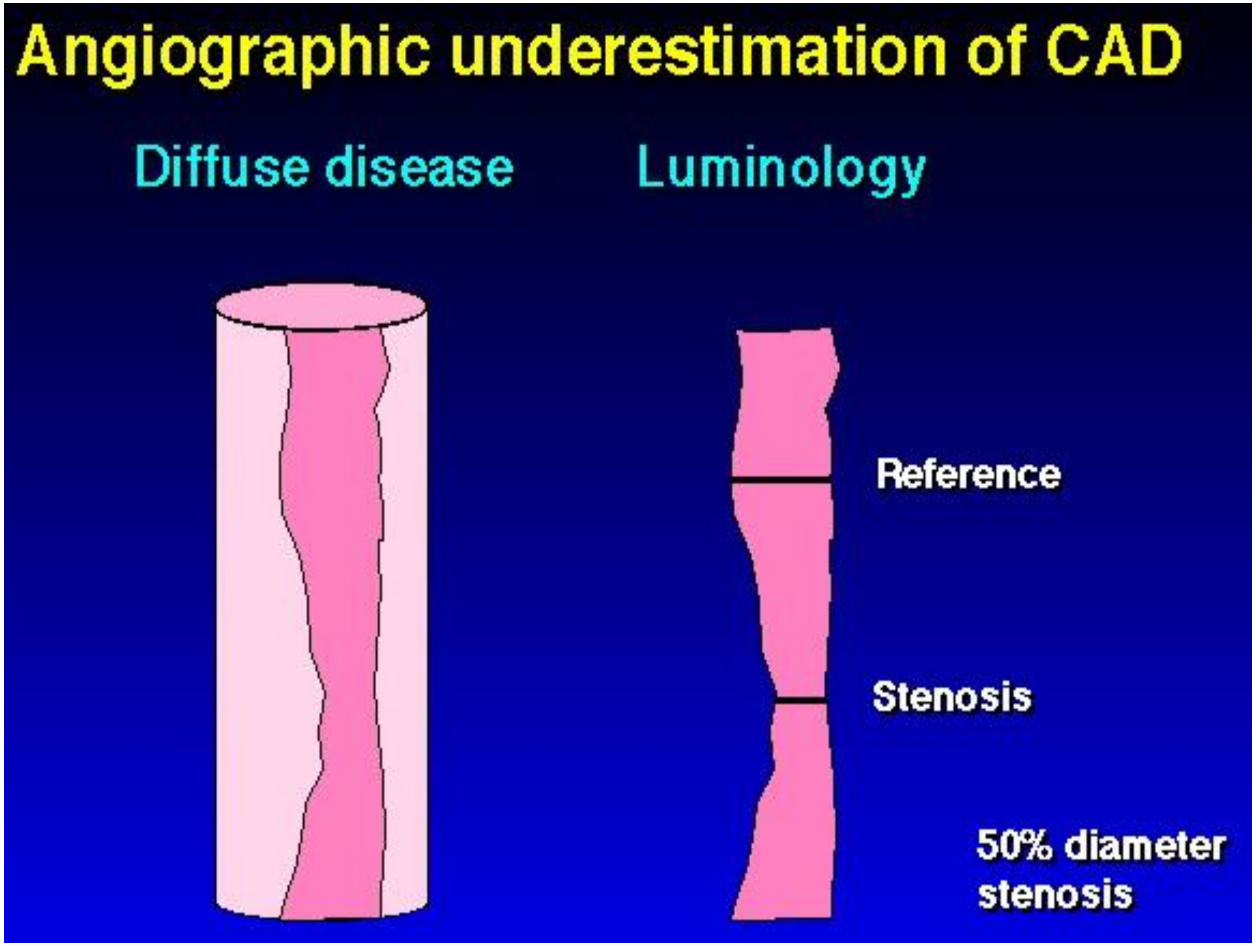


Two examples of angiograms difficult to evaluate by quantitative angiography.

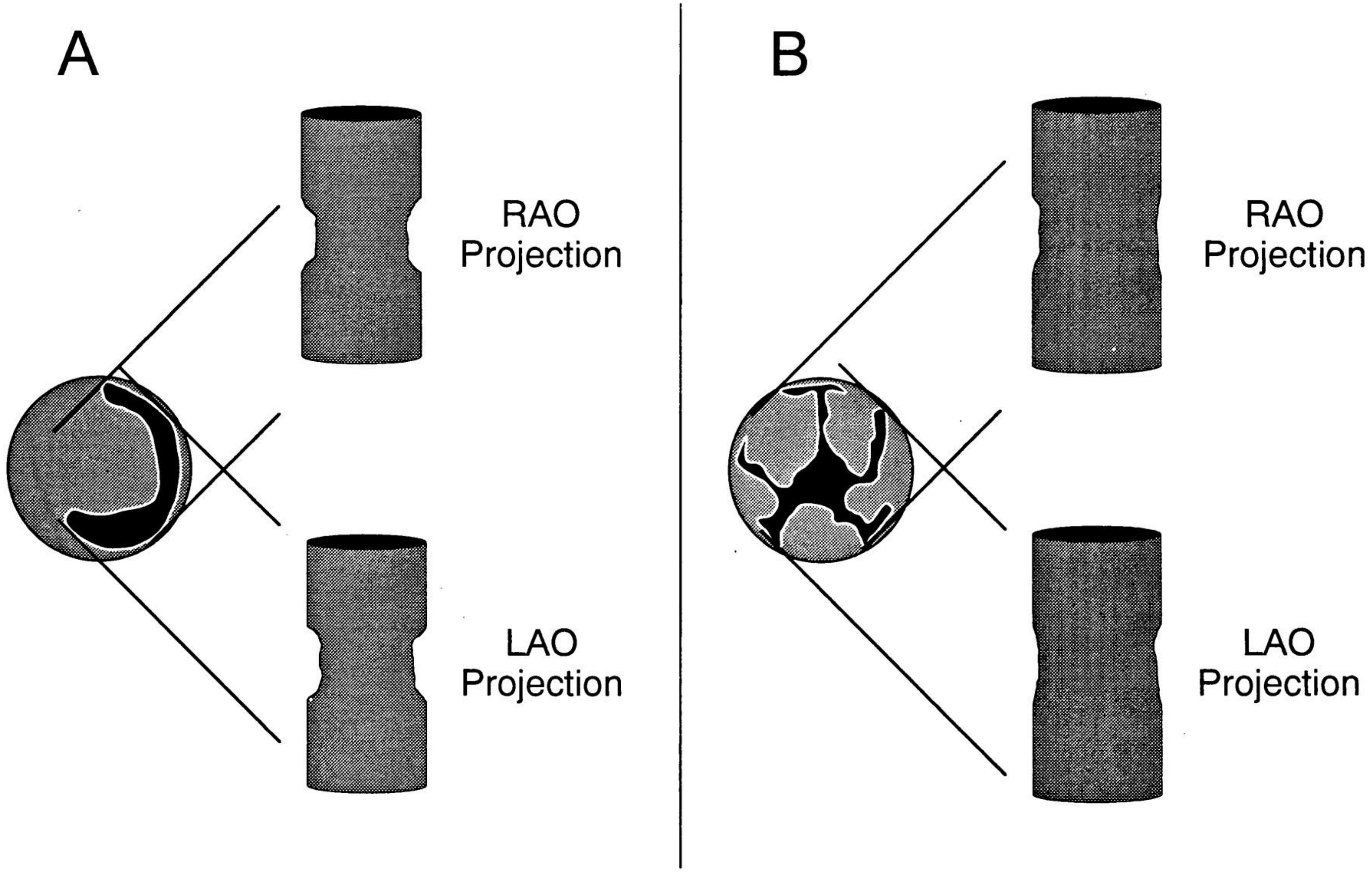




Topol E J , and Nissen S E *Circulation*. 1995;92:2333-2342


Angiographic underestimation of CAD
Diffuse disease
Luminology
Reference
Stenosis
50% diameter
stenosis

Schematic representation of an important limitation of projection imaging.



Topol E J , and Nissen S E *Circulation*. 1995;92:2333-2342

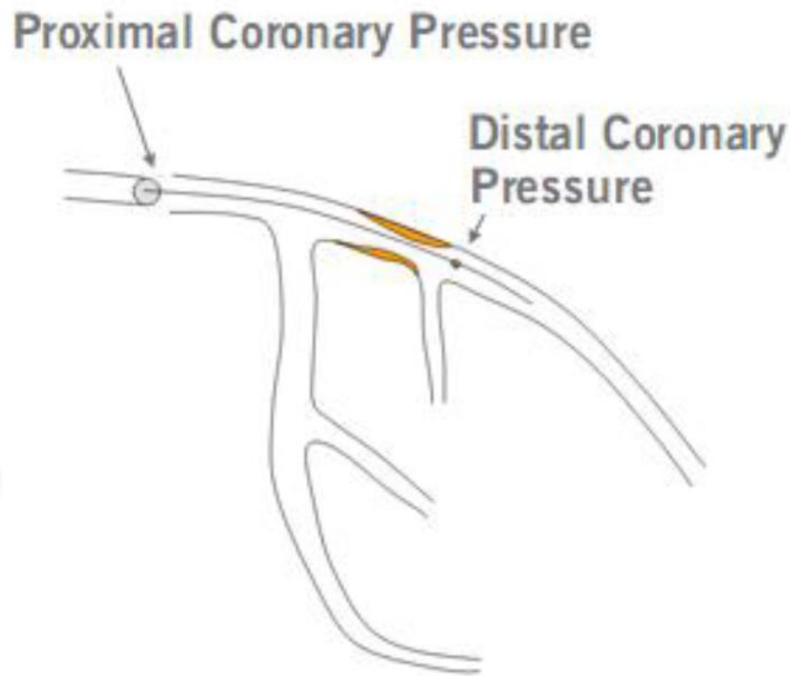
Fractional Flow Reserve (FFR)

$$FFR = \frac{\text{Distal Coronary Pressure}}{\text{Proximal Coronary Pressure}}$$

(During Maximum Hyperemia)

Measure post intra -coronary Adenosine

No flow obstruction FFR > 0.8
Flow obstruction FFR < 0.75



FFR

Fractional flow reserve (FFR) is the ratio of hyperemic myocardial flow in the stenotic territory (Q_s^{max}) to normal hyperemic myocardial flow (Q_N^{max})

$$FFR = \frac{Q_s^{max}}{Q_N^{max}}$$

FFR

Since the flow (Q) is the ratio of the pressure (P) difference across the coronary system divided by its resistance (R), Q can be substituted as follows:

$$FFR = \frac{(P_d - P_v)/R_s^{max}}{(P_a - P_v)/R_N^{max}}$$

FFR

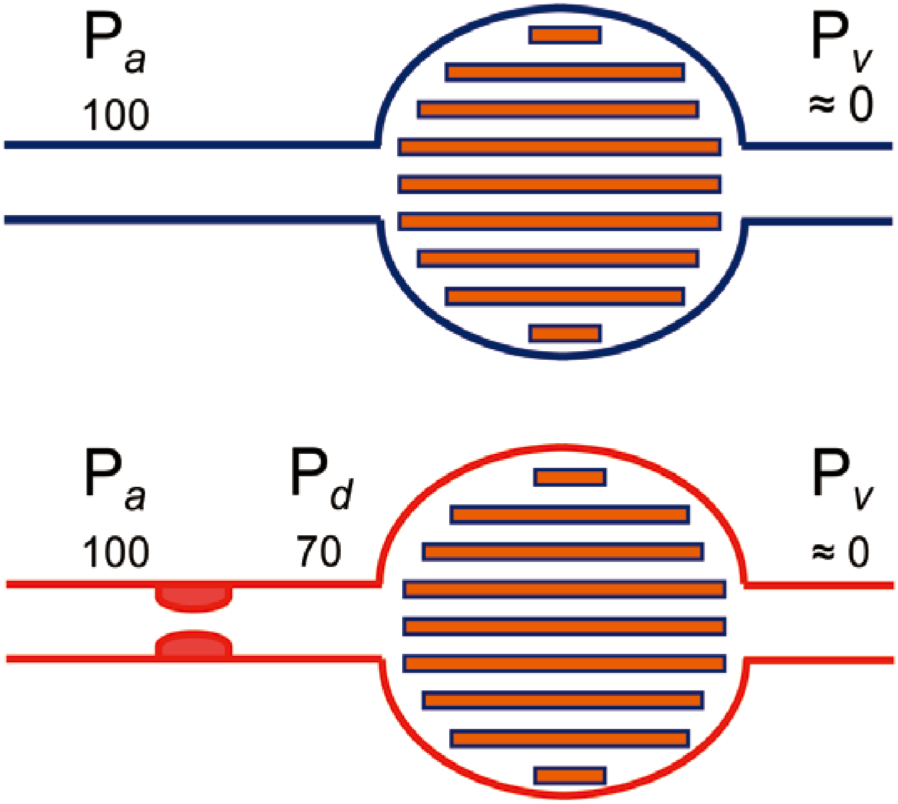
Since the measurements are obtained under maximal hyperemia, resistances are minimal and therefore equal, and thus they cancel out:

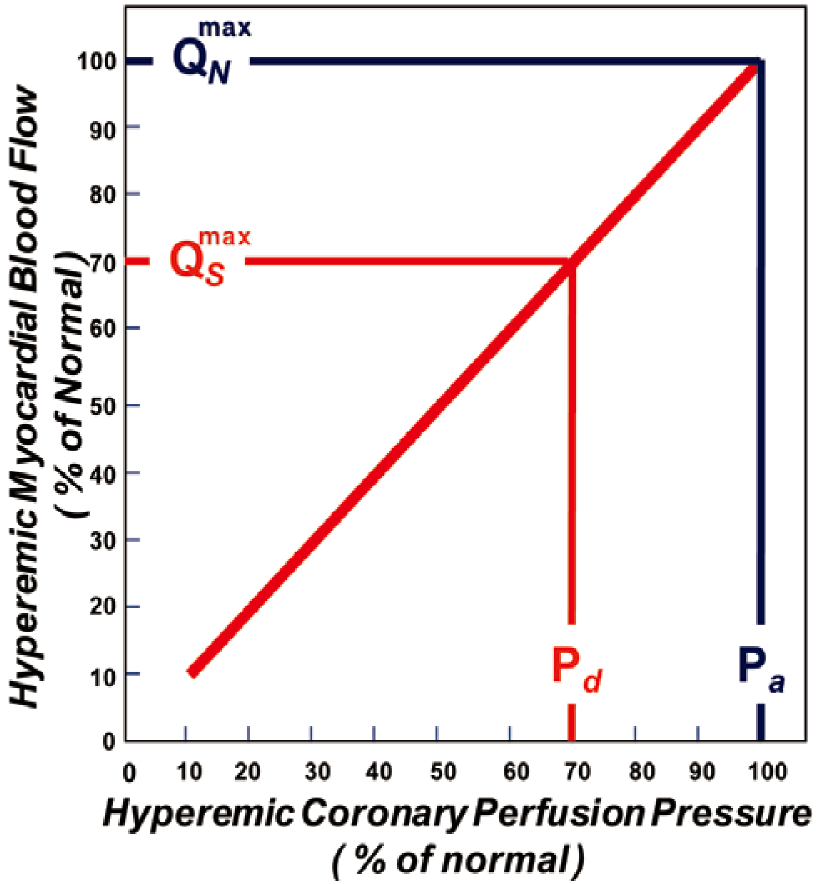
$$FFR = \frac{(P_d - P_v)}{(P_a - P_v)}$$

FFR

In addition Pv is negligible as compared to Pa or Pd, therefore:

$$FFR = \frac{P_d}{P_a}$$

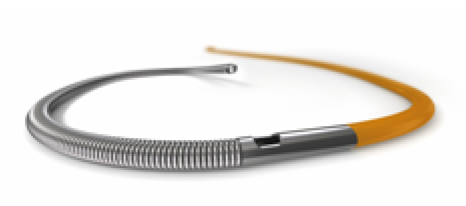


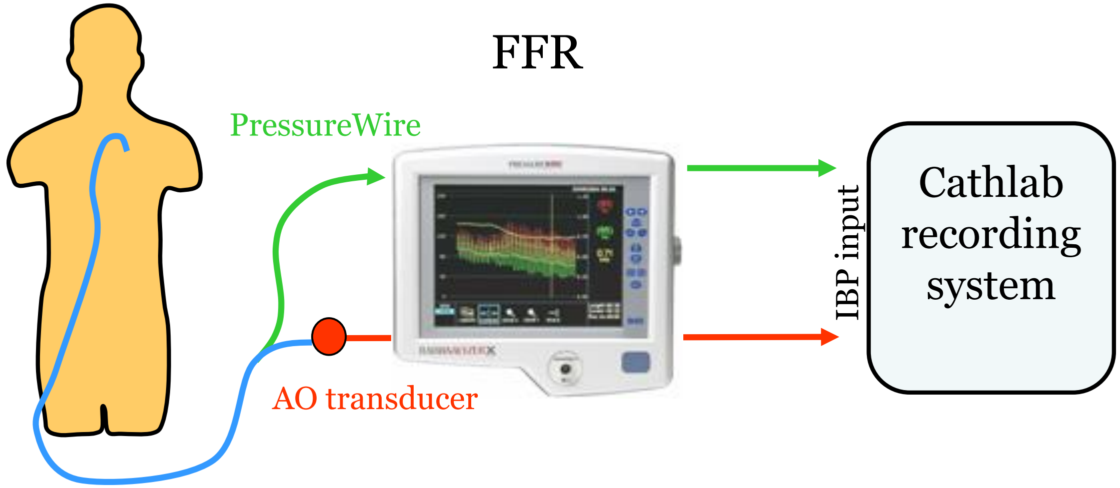


$$FFR = \frac{P_d - P_v}{P_a - P_v} \approx \frac{P_d}{P_a}$$

Analyzer for FFR?

PressureWire® is attached to an Analyzer (console), an interface which makes the FFR calculations automatically during the procedure.
It displays both aortic and distal pressure wave forms.



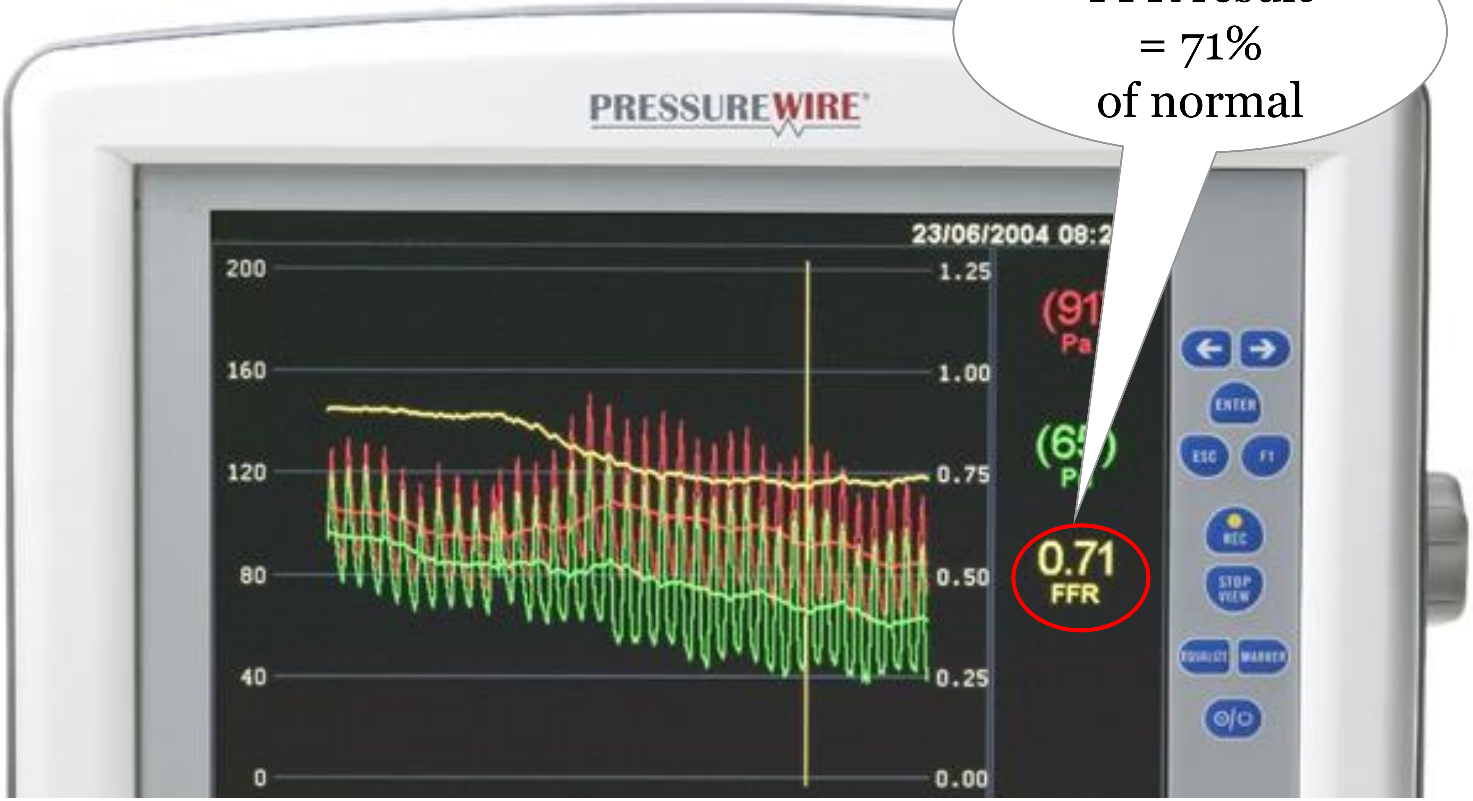


FFR

Pressure Wire – 0.014 hollow wire

Shape tip and use like a normal work horse wire for ptca/stent

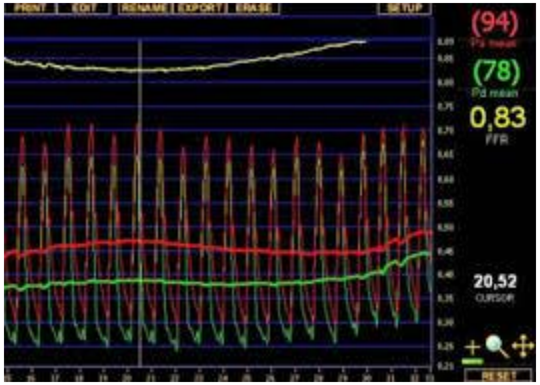
The Meaning of an FFR Value



FFR result
= 71%
of normal

ΦΥΣΙΟΛΟΓΙΚΗ ΤΙΜΗ FFR 1

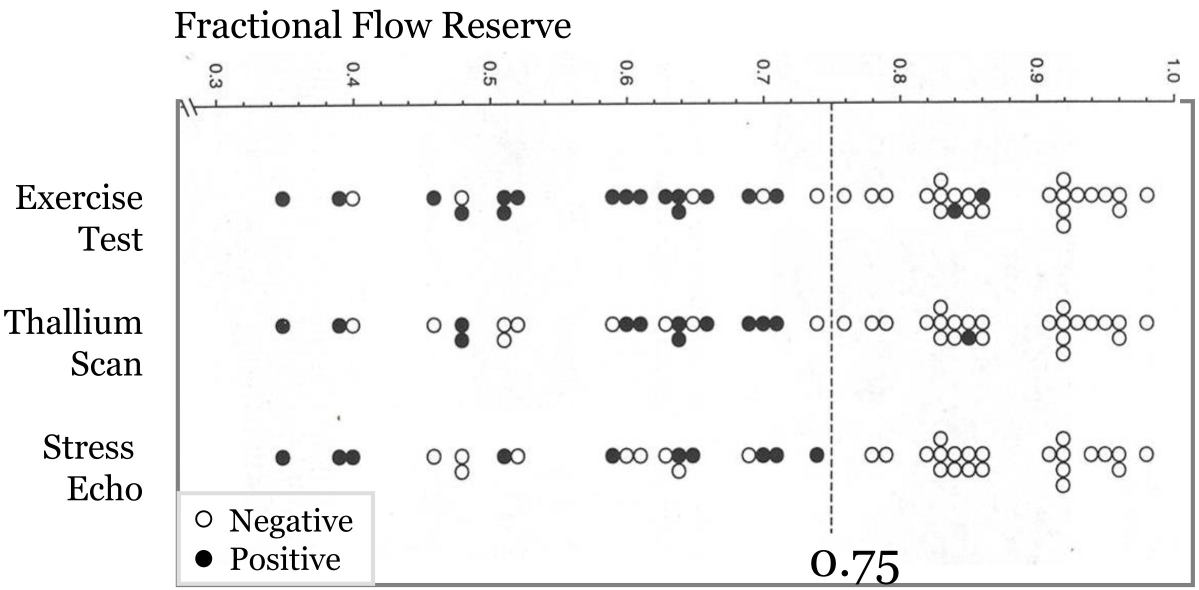
Όσο χαμηλότερη είναι η τιμή του FFR τόσο χαμηλότερη η ροή στο μυοκάρδιο (γραμμική συσχέτιση)



FFR >0.8 Φυσιολογικό
FFR <0.75 Παθολογικό
0.75<FFR<0.8 Γκρίζα ζώνη
(χρειάζεται περισσότερη υπεραιμία)

How Accurate is the Value?

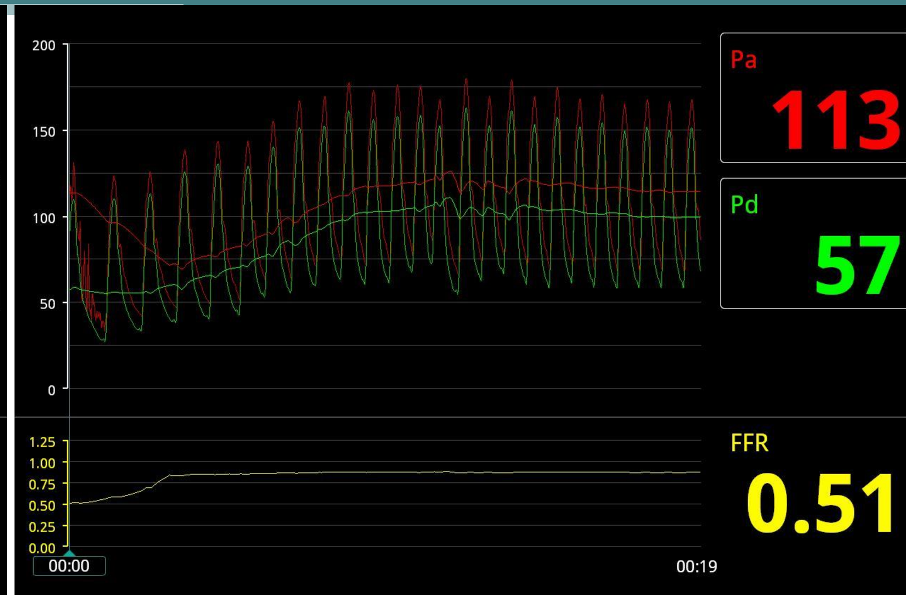
FFR < 0.75 : Sensitivity = 88%
Specificity = 100%

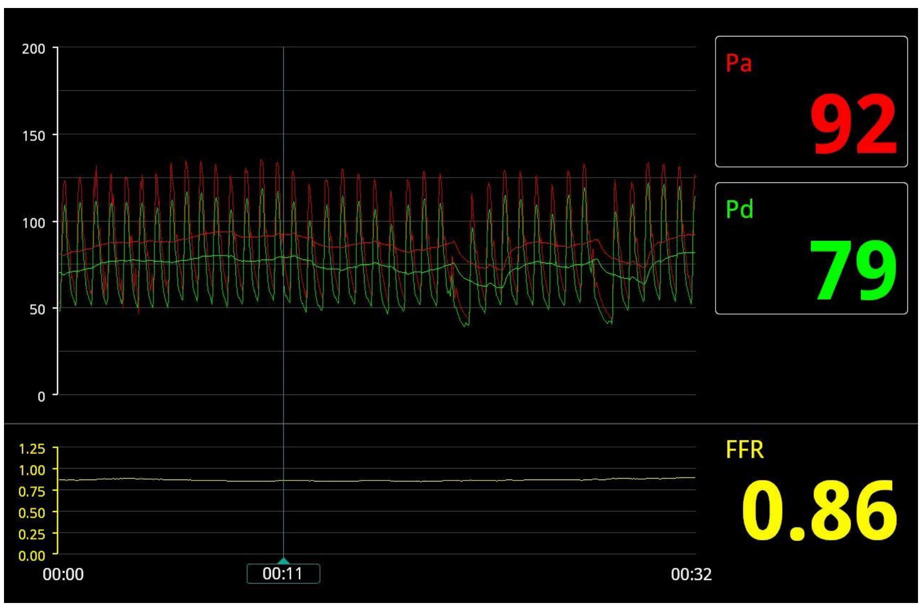


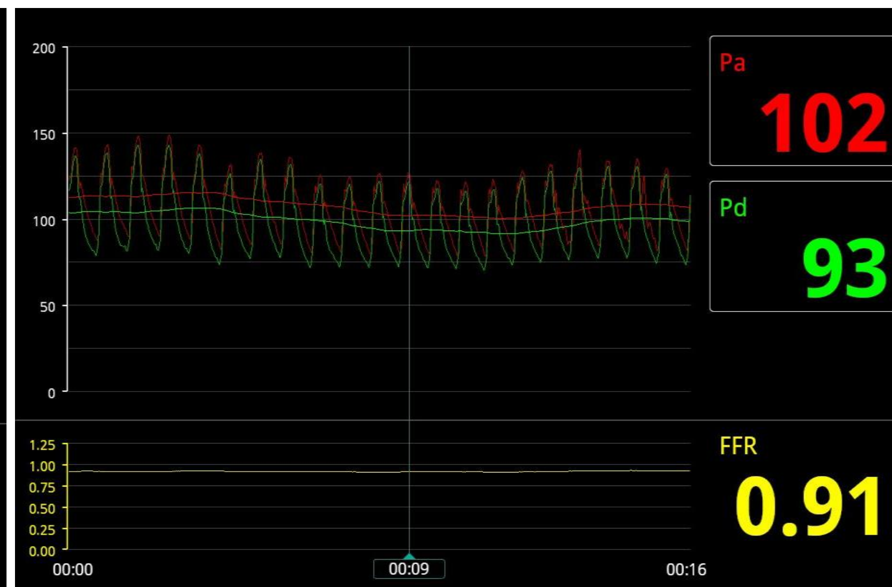
FFR has been validated against a "gold standard" of reversible ischemia, composed of all non-invasive tests.

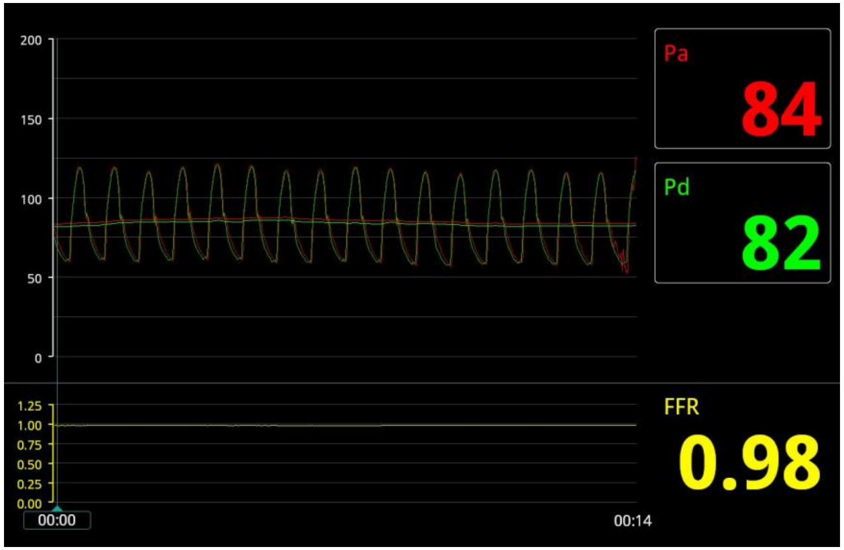
Pijls NHJ et al.
N Eng J Med. 1996;334(no26): 1703-08.

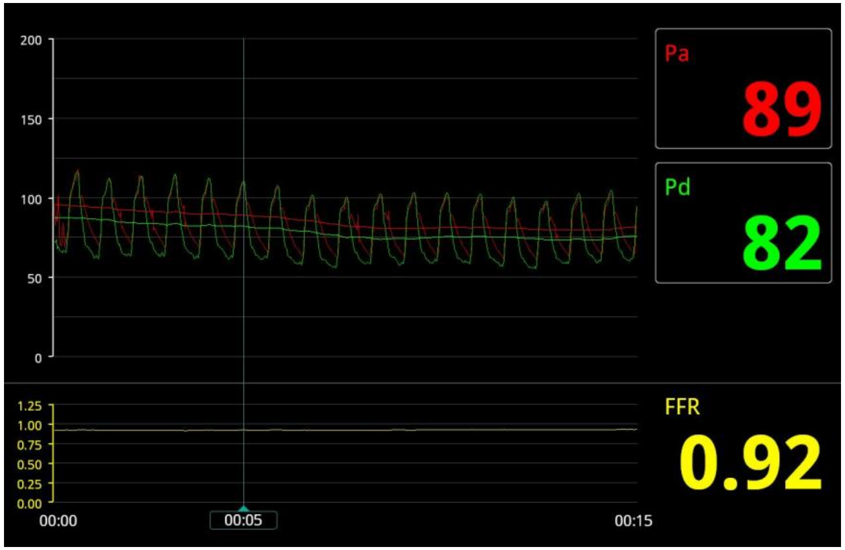

200
150
100
50
0
Pa
97
Pd
83
1.25
1.00
0.75
0.50
0.25
0.00
FFR
0.85
00:00
00:07
00:17

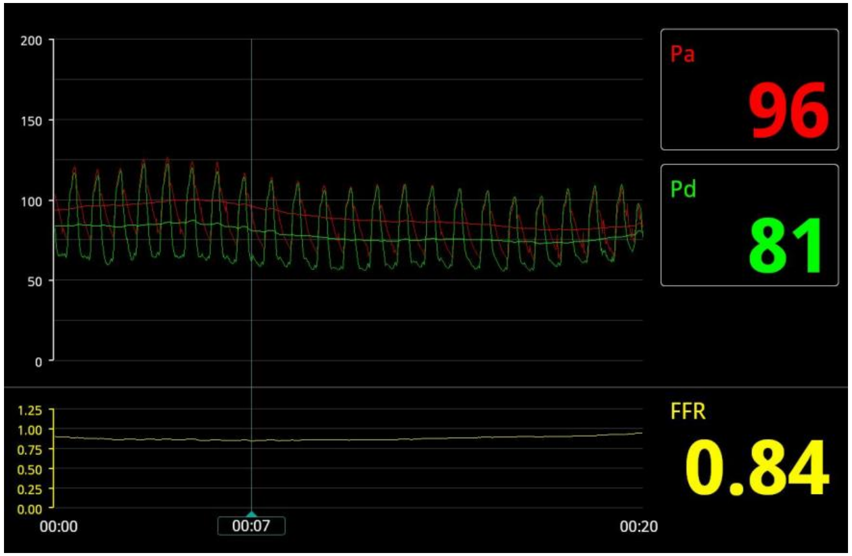

200
150
100
50
0
Pa
113
Pd
57
1.25
1.00
0.75
0.50
0.25
0.00
FFR
0.51
00:00
00:19


200
150
100
50
0
Pa
92
Pd
79
1.25
1.00
0.75
0.50
0.25
0.00
FFR
0.86
00:00
00:11
00:32


200
150
100
50
0
Pa
102
Pd
93
1.25
1.00
0.75
0.50
0.25
0.00
FFR
0.91
00:00
00:09
00:16


200
150
100
50
0
1.25
1.00
0.75
0.50
0.25
0.00
00:00
00:14
Pa
84
Pd
82
FFR
0.98


200
150
100
50
0
1.25
1.00
0.75
0.50
0.25
0.00
00:00
00:05
00:15
Pa
89
Pd
82
FFR
0.92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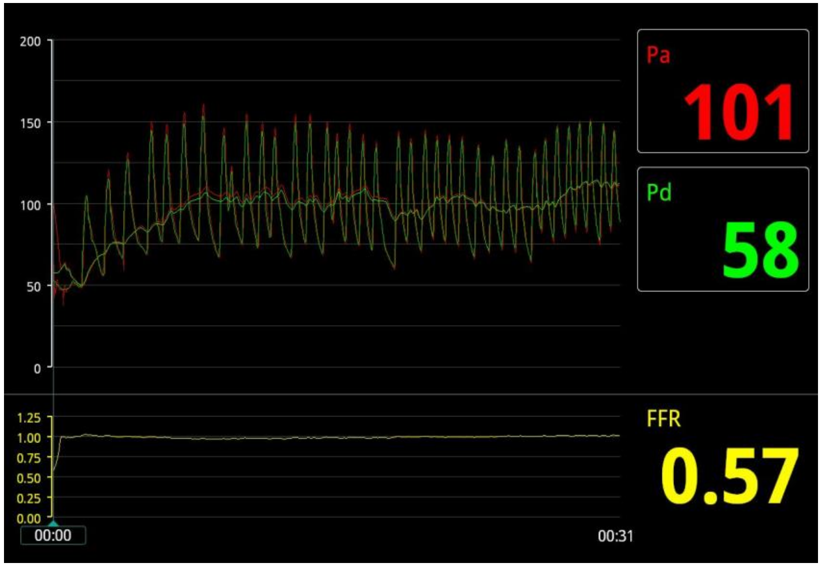
150
100
50
0
1.25
1.00
0.75
0.50
0.25
0.00
00:00
00:07
00:20
Pa
96
Pd
81
FFR
0.84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1.00
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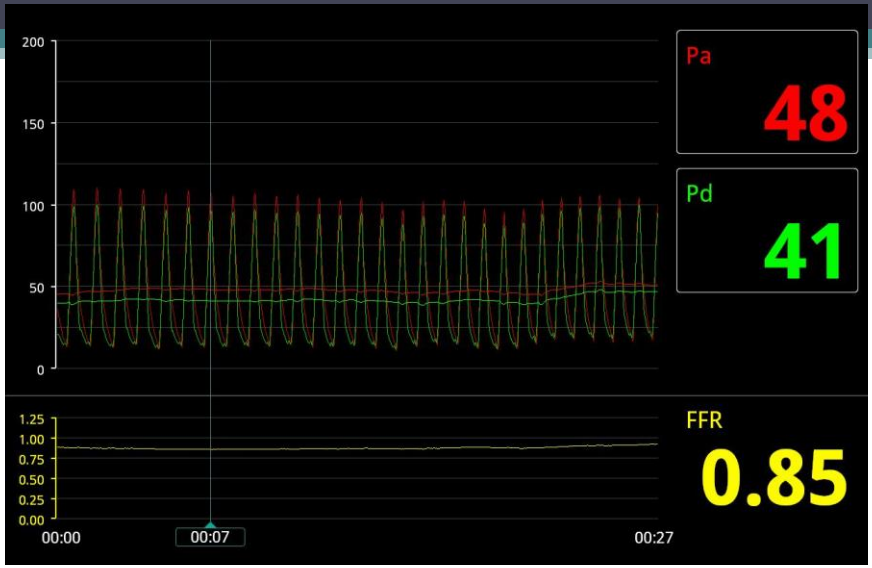
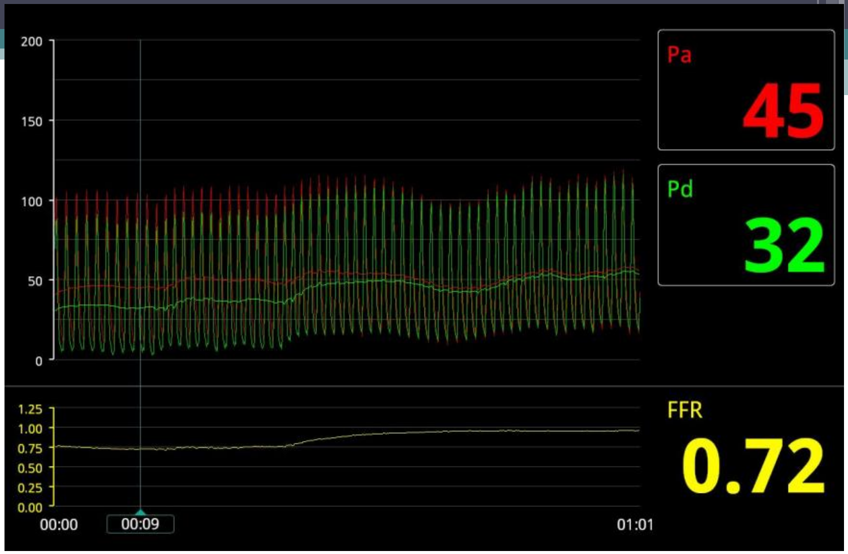
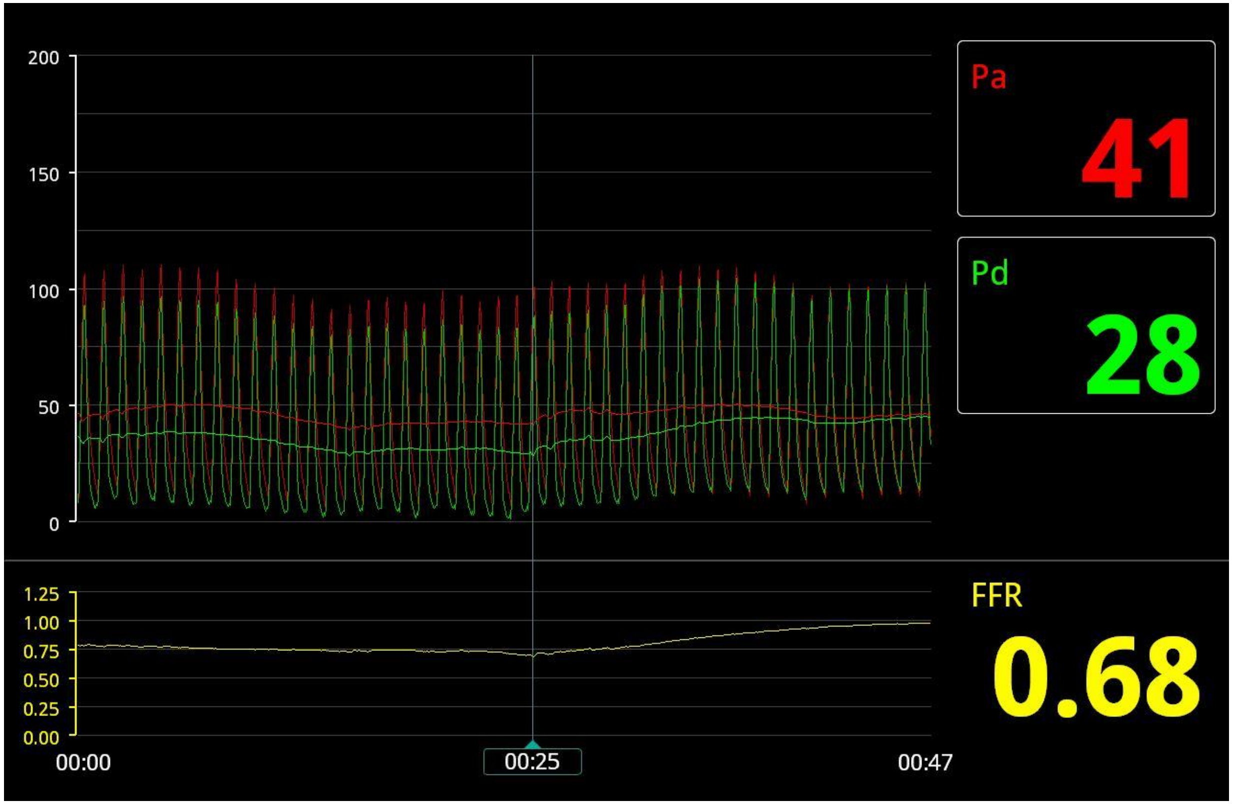
0.50
0.25
0.00
00:00
00:31
Pa
101
Pd
58
FFR
0.57


200
150
100
50
0
Pa
48
Pd
41
1.25
1.00
0.75
0.50
0.25
0.00
FFR
0.85
00:00
00:07
00:27


200
150
100
50
0
Pa
45
Pd
32
1.25
1.00
0.75
0.50
0.25
0.00
FFR
0.72
00:00
00:09
01:01


200
150
100
50
0
Pa
41
Pd
28
1.25
1.00
0.75
0.50
0.25
0.00
FFR
0.68
00:00
00:25
00:47

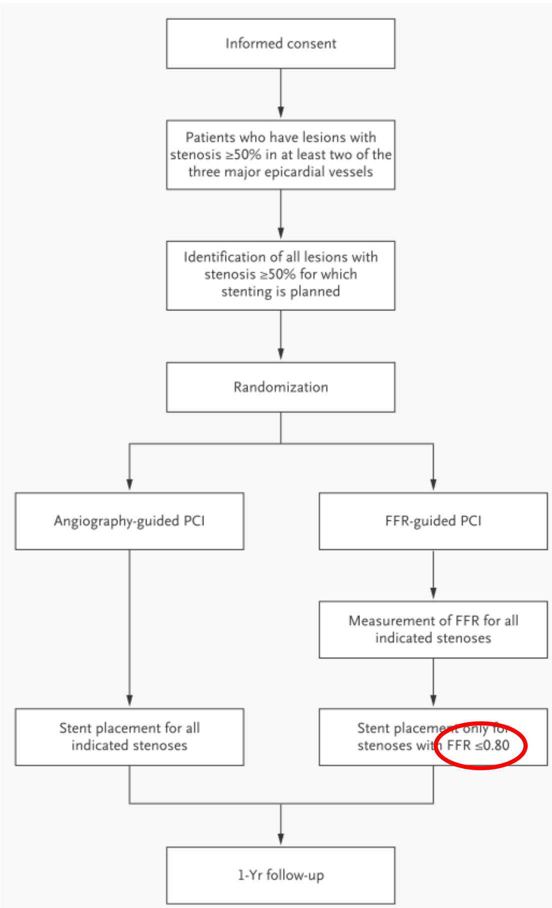
FFR STUDIES

1. DEFER
2. FAME
3. FAME 2

DEFER STUDY (2007)

- RCT
- 325 PATIENTS with functionally not significant stenosis (i.e. without ischemia)
- According to the study protocol:
  - If FFR < 0.75: PCI performed
  - If FFR > 0.75: randomization DEFER or PCI
- 50% of patients with intemediate lesions do not need intervention and will not benefit from it

FAME 1 Trial (2009)



The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812 JANUARY 15, 2009 VOL. 360 NO. 3

Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention

Pim A.L. Tonino, M.D., Bernard De Bruyne, M.D., Ph.D., Nico H.J. Pijls, M.D., Ph.D., Uwe Siebert, M.D., M.P.H., Sc.D., Fumiaki Ikeno, M.D., Marcel van 't Veer, M.Sc., Volker Klauss, M.D., Ph.D., Ganesh Manoharan, M.D., Thomas Engstrøm, M.D., Ph.D., Keith G. Oldroyd, M.D., Peter N. Ver Lee, M.D., Philip A. MacCarthy, M.D., Ph.D., and William F. Fearon, M.D., for the FAME Study Investigators*

CONCLUSIONS

Routine measurement of FFR in patients with multivessel coronary artery disease who are undergoing PCI with drug-eluting stents significantly reduces the rate of the composite end point of death, nonfatal myocardial infarction, and repeat revascularization at 1 year. (ClinicalTrials.gov number, NCT00267774.)

FAME 1 Trial

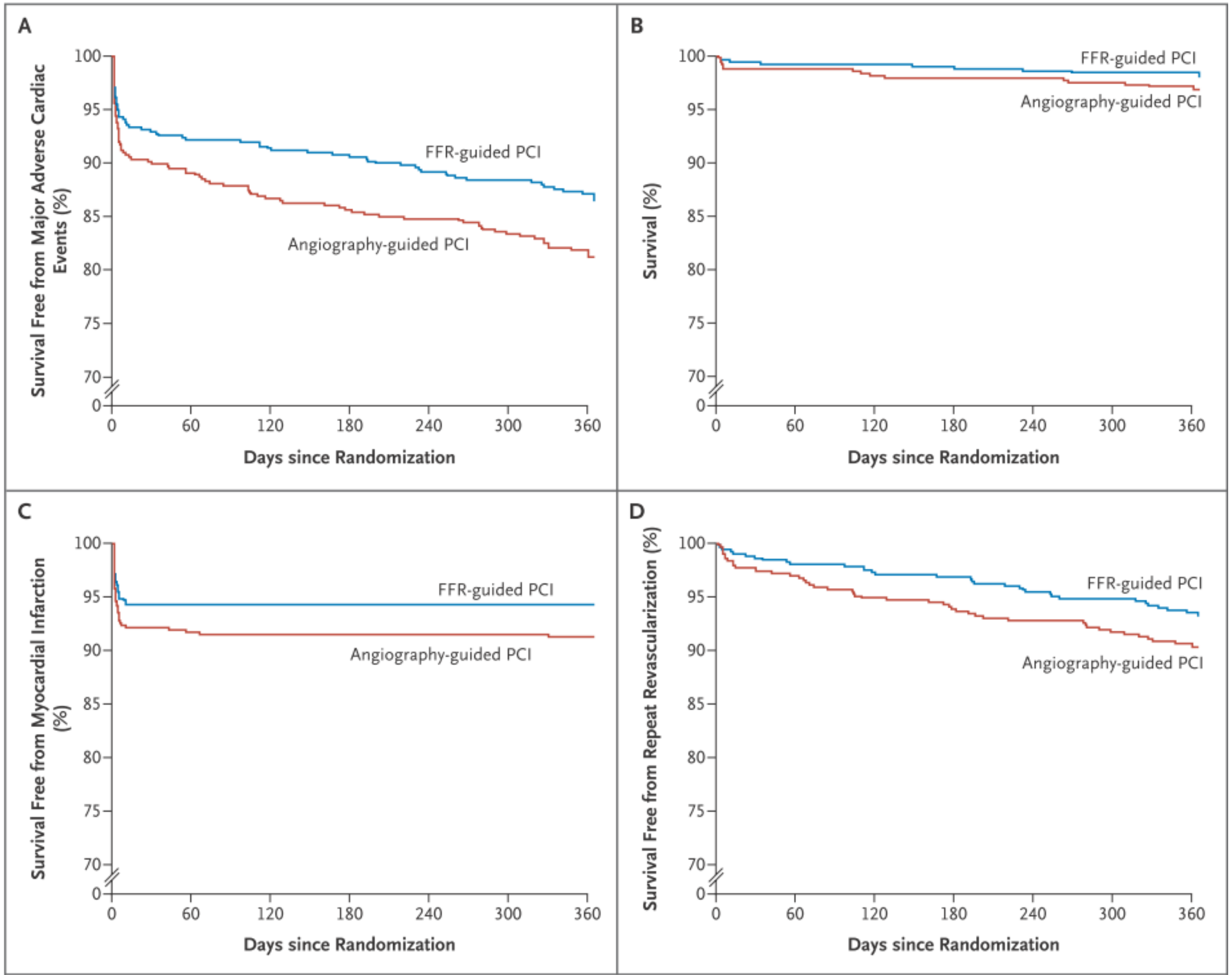


Figure 3. **Kaplan–Meier Survival Curves According to Study Group.**
FFR denotes fractional flow reserve, and PCI percutaneous coronary intervention.

Βελτιώνει MACE
Όχι επιβίωση!

FAME 2 Trial (2012)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 13, 2012 VOL. 367 NO. 11

Fractional Flow Reserve–Guided PCI versus Medical Therapy in Stable Coronary Disease

Bernard De Bruyne, M.D., Ph.D., Nico H.J. Pijls, M.D., Ph.D., Bindu Kalesan, M.P.H., Emanuele Barbato, M.D., Ph.D., Pim A.L. Tonino, M.D., Ph.D., Zsolt Piroth, M.D., Nikola Jagic, M.D., Sven Möbius-Winkler, M.D., Gilles Rioufol, M.D., Ph.D., Nils Witt, M.D., Ph.D., Petr Kala, M.D., Philip MacCarthy, M.D., Thomas Engström, M.D., Keith G. Oldroyd, M.D., Kreton Mavromatis, M.D., Ganesh Manoharan, M.D., Peter Verlee, M.D., Ole Frobert, M.D., Nick Curzen, B.M., Ph.D., Jane B. Johnson, R.N., B.S.N., Peter Jüni, M.D., and William F. Fearon, M.D., for the FAME 2 Trial Investigators*

CONCLUSIONS

In patients with stable coronary artery disease and functionally significant stenoses, FFR-guided PCI plus the best available medical therapy, as compared with the best available medical therapy alone, decreased the need for urgent revascularization. In patients without ischemia, the outcome appeared to be favorable with the best available medical therapy alone. (Funded by St. Jude Medical; ClinicalTrials.gov number, NCT01132495.)

FAME 2 Trial

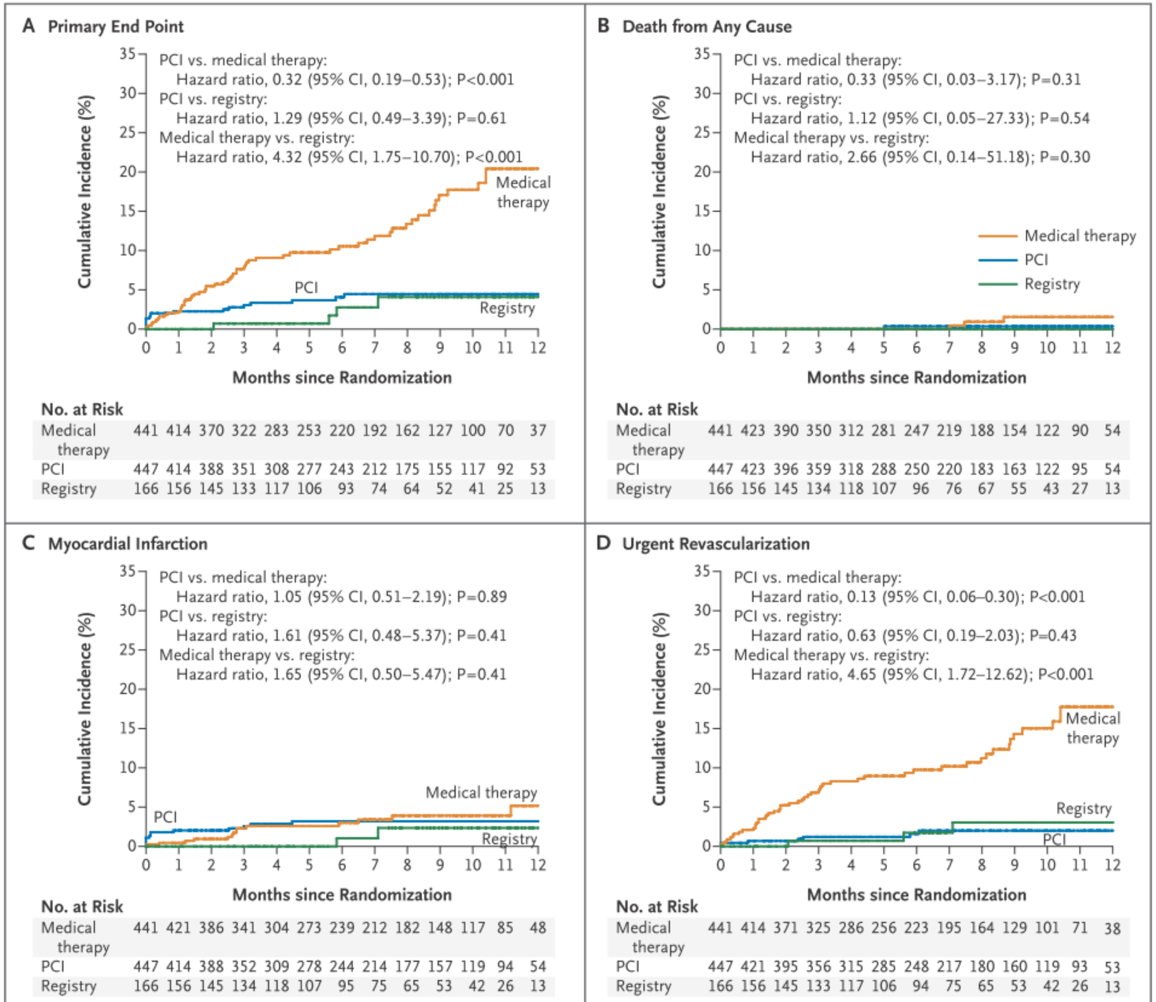


Figure 1. Cumulative Incidence of the Primary End Point and Its Components.

FFR doesn’t just improve health outcomes, it decreases costs

- FAME 1 showed that FFR both improves patient outcome and lowers procedural costs – FFR is cost-saving when used to guide PCI in MVD.

- FAME 2 demonstrated that angina and quality of life are significantly improved by FFR-guided PCI as compared to OMT and that FFR-guided PCI is cost-effective with ICER $32,000/QALY.

STUDY	COMPARATORS	COST-EFFECTIVENESS RATIO	RESULT
COURAGE	Angio-guided PCI vs Medical Therapy	>$168,000 / QALY	>$150,000 / QALY
FAME	Angio-guided PCI vs FFR-guided PCI	FFR-guided PCI is Dominant (↓$ / ↑QALY)	<$50,000 / QALY
FAME 2	FFR-guided PCI vs Medical Therapy	$32,000 / QALY	<$50,000 / QALY

Very Cost-Effective
<$50,000 / QALY

Cost-Effective
$50,000-150,000 / QALY

Not Cost-Effective
>$150,000 / QALY

* A utility is a numeric way of expressing of a patient’s preference for a particular state of health; a higher value equals improved health (typically, 0.0=dead; 1.0=complete health).

Fearon WF. FAME 2 Cost-effectiveness: A Prospective, Randomized Trial Evaluating the Cost-effectiveness of FFR-Guided PCI in Patients with Stable Coronary Artery Disease. Presented at Late Breaking Clinical Trials 1 at TCT 2012, Miami, Florida, October 24, 2012.

FFR doesn't just improve health outcomes, it decreases costs

Methods and results

- Initial costs of the index hospitalization were $6,026 higher for PCI, but over the course of 1 year, follow-up costs were higher for medical therapy, narrowing the gap to $2,883.

	PCI (n=447)	Medical Therapy (n=441)	P Value
Index Procedure	$9,927	$3,900	< 0.001
Follow-up	$2,719	$5,863	< 0.001
Total at 12 months	$12,646	$9,763	< 0.001

Recommendations for the clinical value of intracoronary diagnostic techniques

Recommendations	Class[a]	Level[b]	Ref.[c]
FFR to identify haemodynamically relevant coronary lesion(s) in stable patients when evidence of ischaemia is not available.	I	A	50,51,713
FFR-guided PCI in patients with multivessel disease.	IIa	B	54
IVUS in selected patients to optimize stent implantation.	IIa	B	702,703,706
IVUS to assess severity and optimize treatment of unprotected left main lesions.	IIa	B	705
IVUS or OCT to assess mechanisms of stent failure.	IIa	C	
OCT in selected patients to optimize stent implantation.	IIb	C	

ESC Guidelines 2014
(Stable CAD)

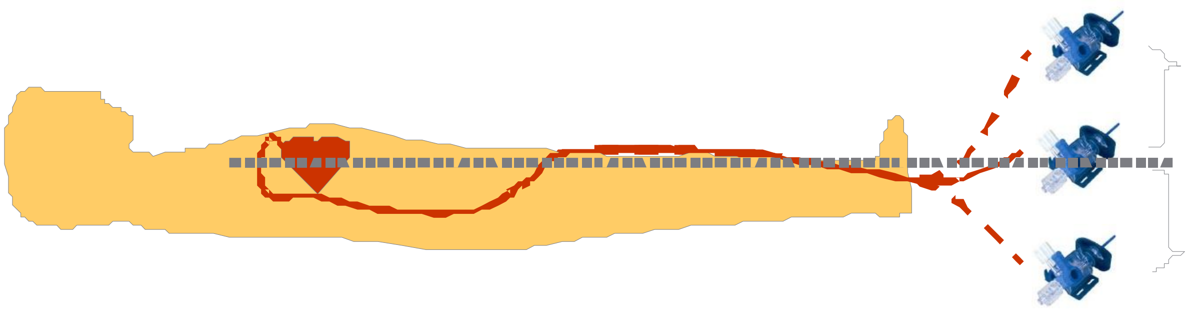
Initial studies suggested that the cut-off figure of 0.75 was reliable for identifying ischaemia-producing lesions, but subsequently the 0.80 criterion has gained widespread acceptance and its clinical role has been validated in outcome studies.

Pitfalls & Practical Tips

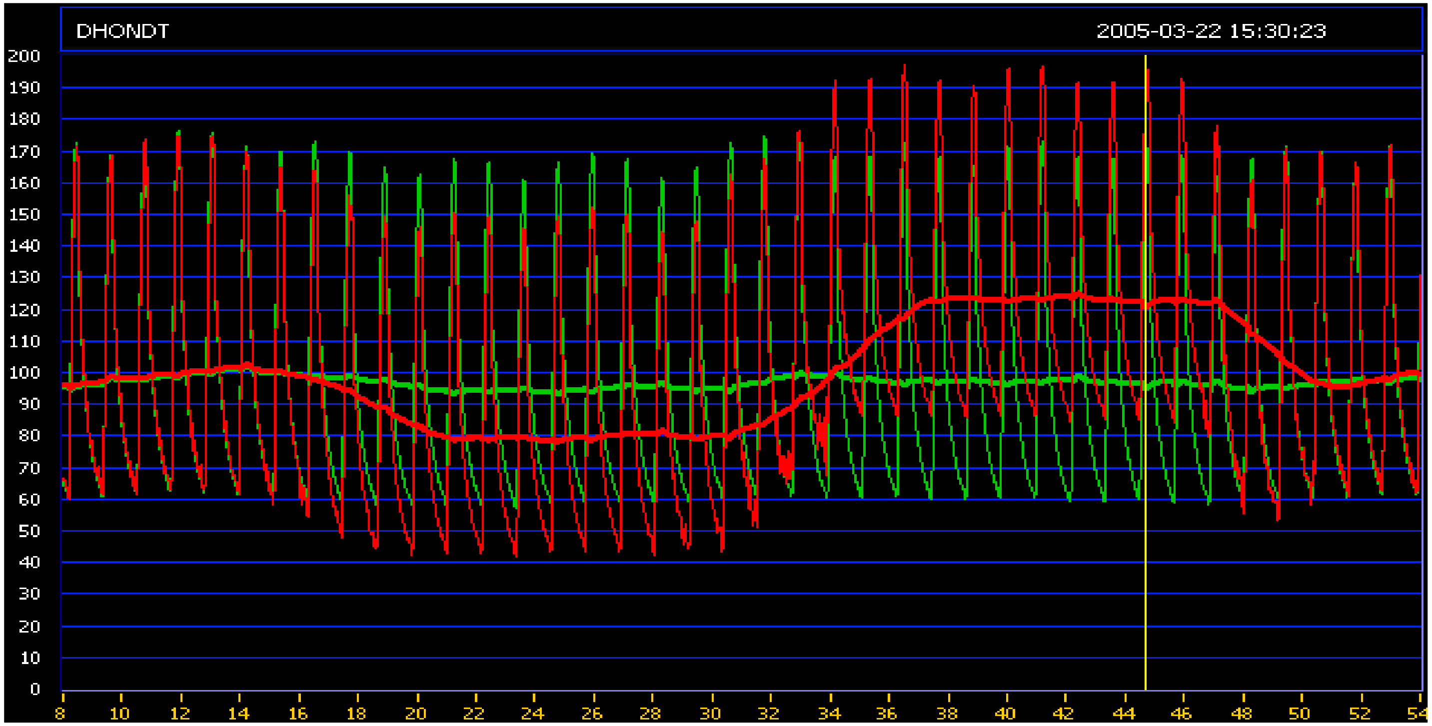
- **Transducer Height and AO Pressure**
- Equalization
- Guide wire Introducer Needles
- Guide Catheter (wedging, damping & side holes)
- Pressure Wire™ Drift
- Artifacts
- Mean-beat Setting
- Sensor Element Against Vessel Wall
- **Suboptimal Hyperaemia**

Importance of Transducer Height and AO Pressure

Position the AO transducer at patient’s heart level (midaxillary line)



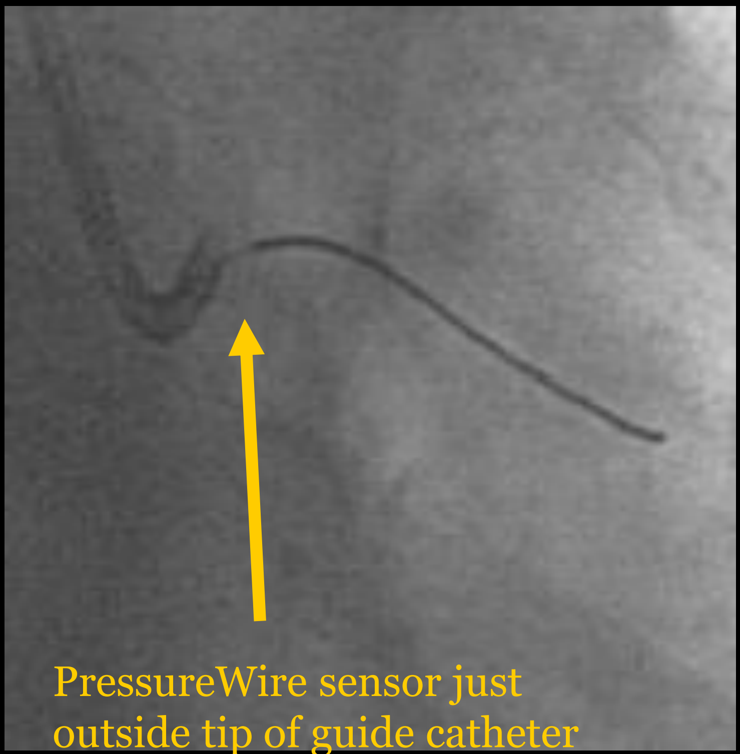
Effect of Moving the Aortic Transducer

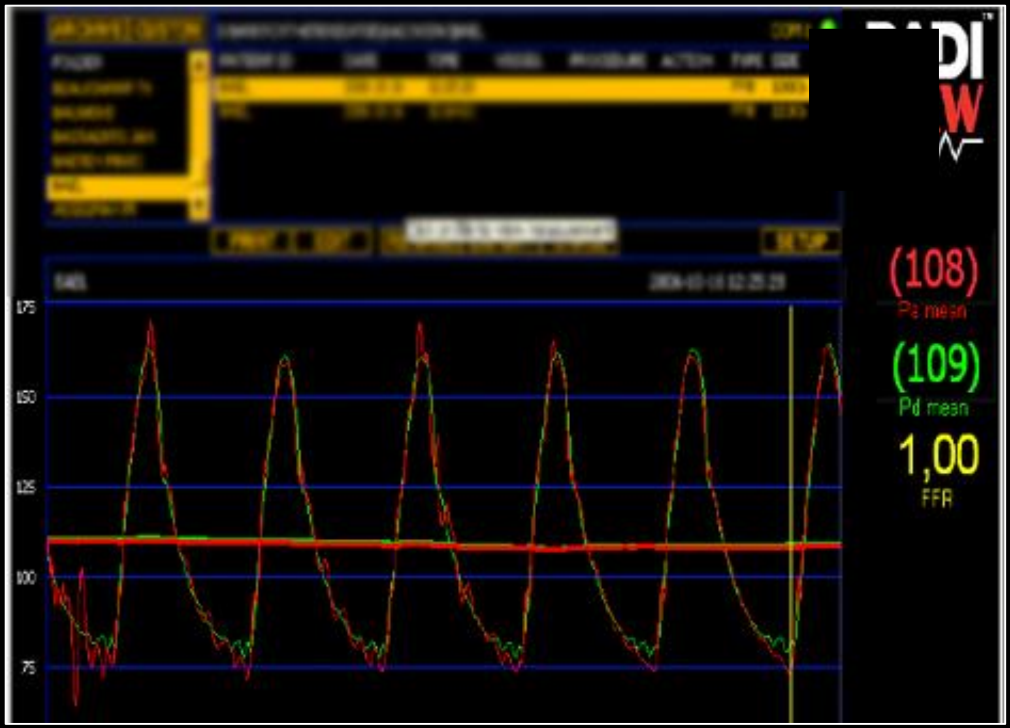


Pitfalls & Practical Tips

- Transducer Height and AO Pressure
- **Equalization**
- Guide Wire Introducer Needles
- Guide Catheter (wedging, damping & side holes)
- Pressure Wire Drift
- Artifacts
- Mean-beat Setting
- Sensor Element Against Vessel Wall
- Suboptimal Hyperaemia

Equalization



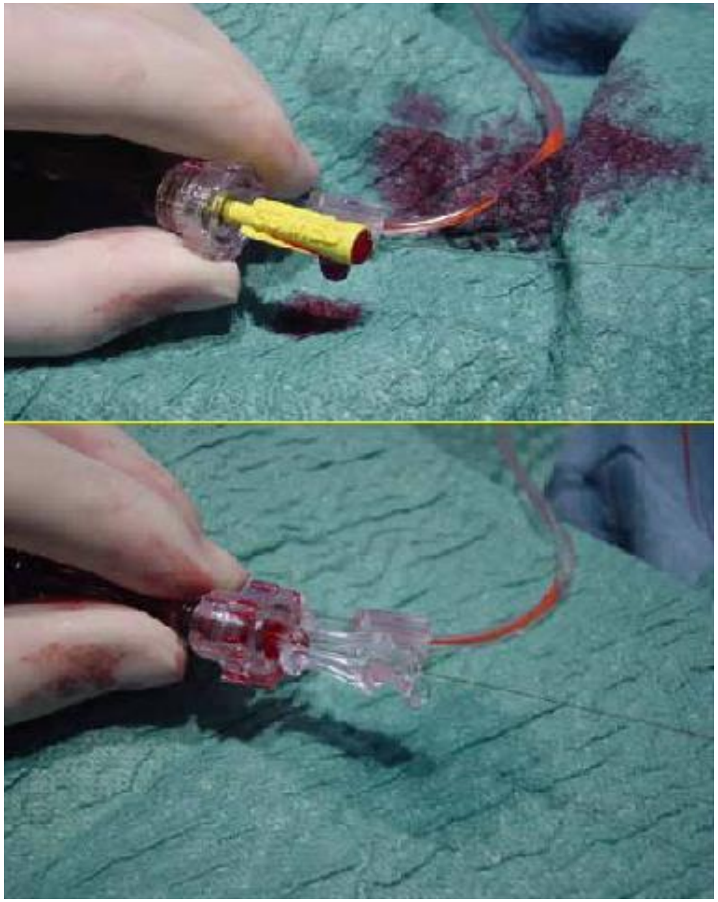


Equalization between the aortic pressure transducer and Pressure Wire sensor must always take place with PressureWire sensor just outside the tip of the guide catheter.

Pitfalls & Practical Tips

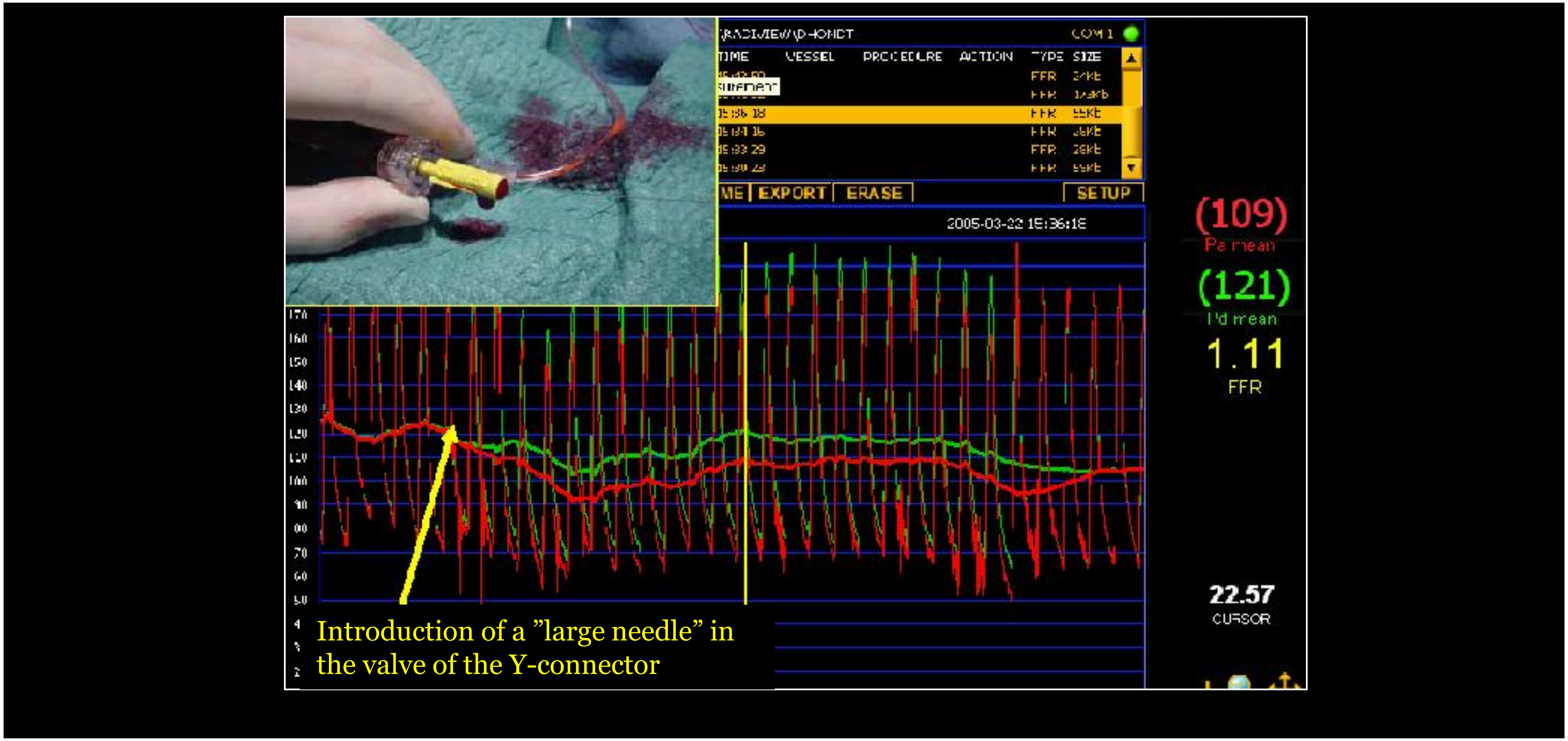
- Transducer Height and AO Pressure
- Equalization
- **Guidewire Introducer Needles**
- Guide Catheter (wedging, damping & side holes)
- PressureWire Drift
- Artifacts
- Mean-beat Setting
- Sensor Element Against Vessel Wall
- Suboptimal Hyperemia

Guidewire Introducer Needles



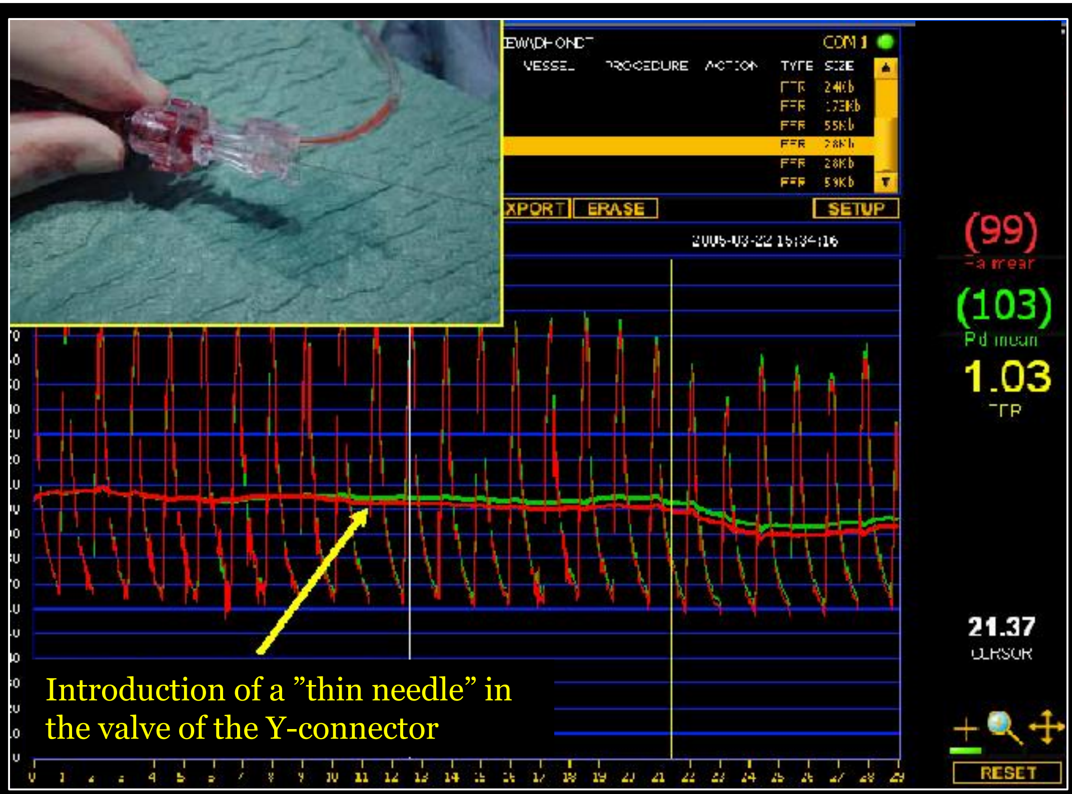
The introducer needle may leak blood and decrease aortic pressure (Pa) by 0–10 mmHg and result in a falsely high FFR.
More leakage from larger bore needles (shown in yellow) than small ones (clear).

Effect of Large Needle



In this example, using a large bore, the yellow needle causes a drop in aortic pressure of approximately 10 mmHg.

Effect of Thin Needle

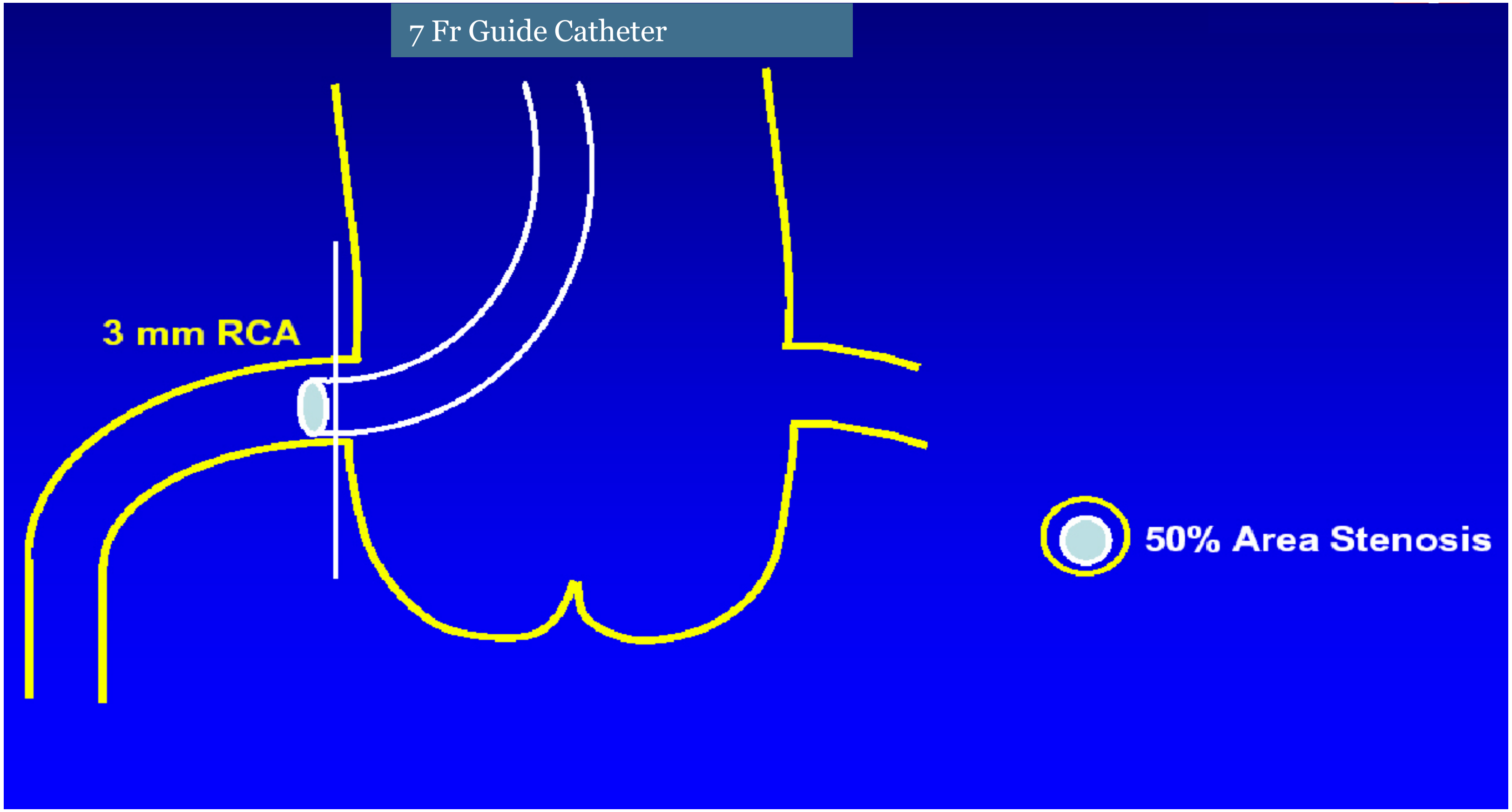


In this case, the introducer needle has a small lumen, which creates minimal pressure leakage.

Pitfalls & Practical Tips

- Transducer Height and AO Pressure
- Equalization
- Guide Wire Introducer Needles
- **Guide Catheter (wedging, damping & side holes)**
- Pressure Wire Drift
- Artifacts
- Mean-beat Setting
- Sensor Element Against Vessel Wall
- Suboptimal Hyperaemia

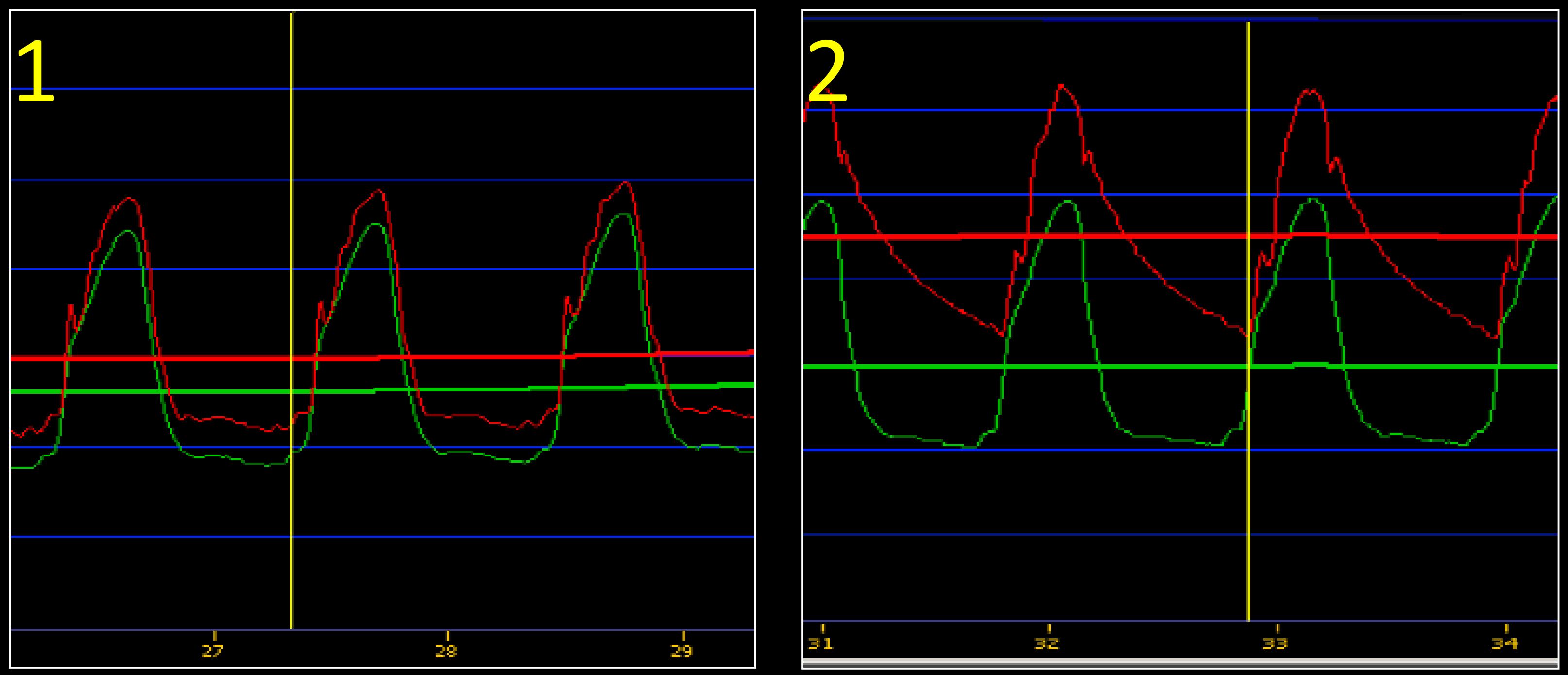
Wedging of Guide Catheter



The presence of a guide catheter in the coronary ostium induces some degree of "stenosis" depending on the relative size of the guide and the coronary ostium.

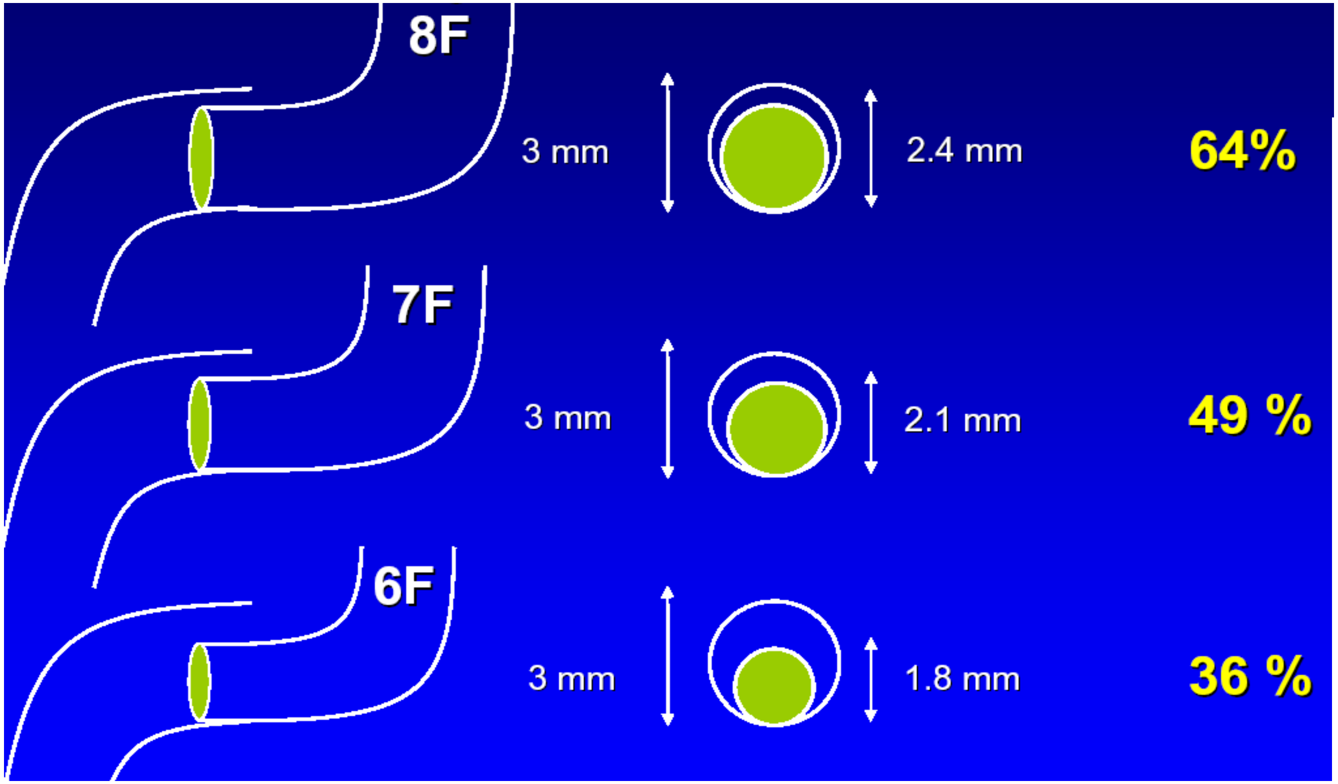
Pa value falsely low and FFR falsely high.

Deep-Seated (Wedged) Guide Catheter



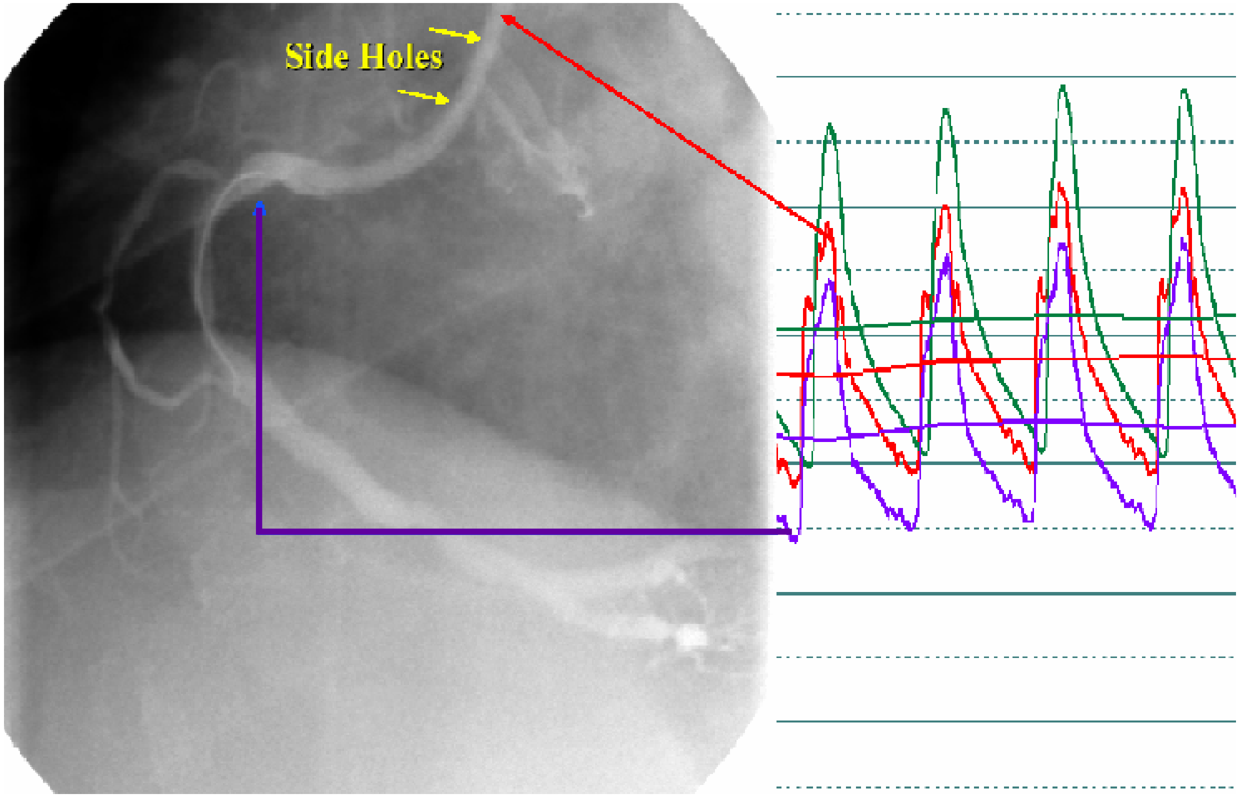
A deep-seated (wedged) guide catheter in the ostium of the right or left main vessels can cause damping of the aortic waveform. Waveform 1 shows the effect with the catheter inserted and waveform 2 shows the effect when the catheter is withdrawn into the aorta, revealing an immediate pressure gradient.

Guide Catheter in Ostium = Stenosis



This is a schematic representation of the space occupied by different sizes of guide catheters in an ostium 3 mm in diameter (radius = 1.5 mm).

Effect of Guide Catheter with Side Holes



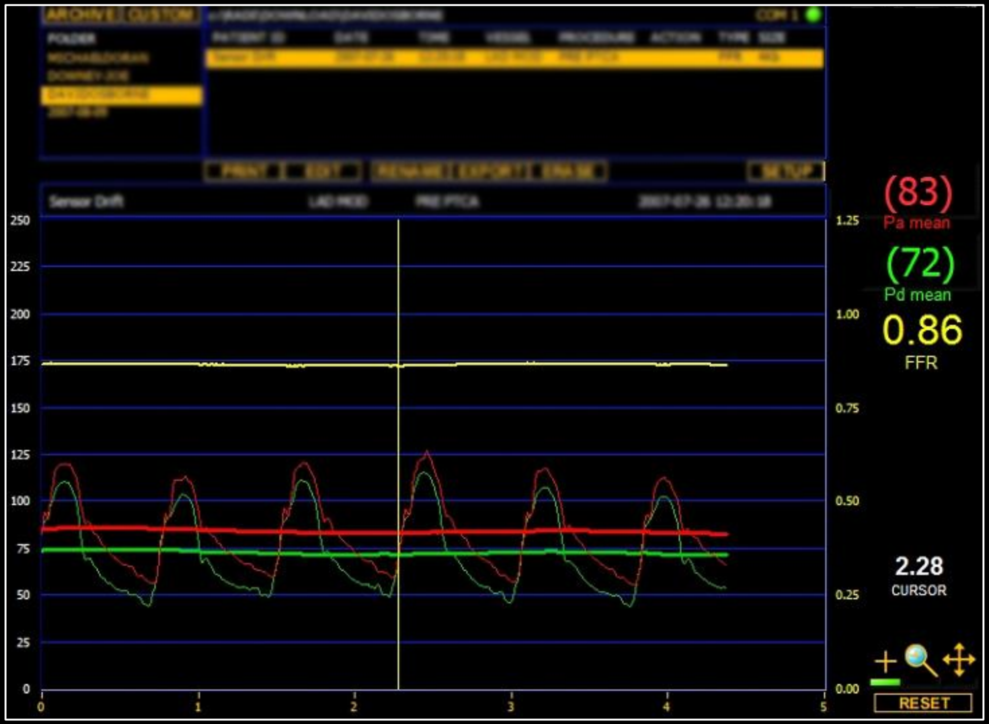
If a guide catheter with side holes is used, the pressure signal recorded through the catheter does not necessarily correspond to the pressure in the proximal segment of the coronary artery since it is influenced by both coronary pressure (through the distal end of the catheter) and by aortic pressure (through the side holes).

Pitfalls & Practical Tips

- Transducer Height and AO Pressure
- Equalization
- Guidewire Introducer Needles
- Guide Catheter (wedging, damping & side holes)
- **PressureWire Drift**
- Artifacts
- Mean-beat Setting
- Sensor Element Against Vessel Wall
- Suboptimal Hyperemia

Drift Waveform

Drift



After a long procedure, differences may sometimes occur between aortic and distal pressures even if this difference does not correspond to a true pressure gradient.

Pitfalls & Practical Tips

- Transducer Height and AO Pressure
- Equalization
- Guidewire Introducer Needles
- Guide Catheter (wedging, damping & side holes)
- PressureWire Drift
- **Artifacts**
- Mean-beat Setting
- Sensor Element Against Vessel Wall
- Suboptimal Hyperemia

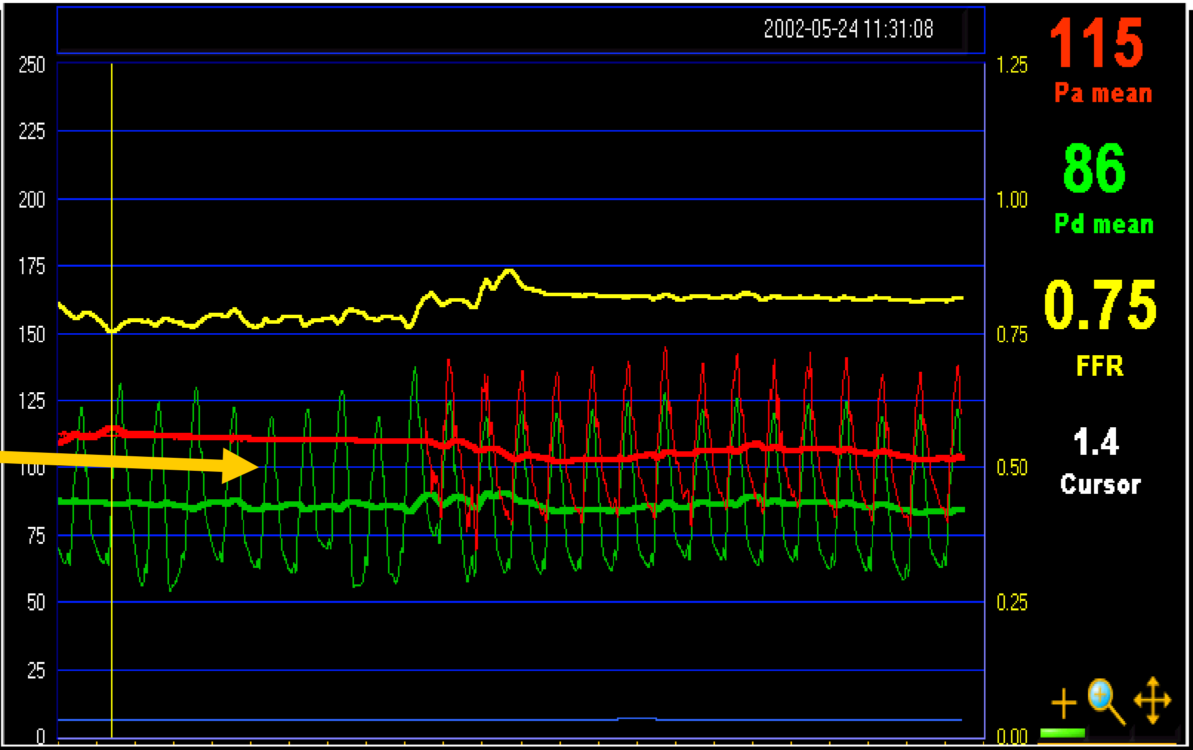
Flush Artifact

RadiAnalyzer Xpress selects artifact

Actual FFR is 0.83

Blunted Flush Artifact

No red phasic signal but mean signal remains



One-Beat Artifact

Pitfalls & Practical Tips

- Transducer Height and AO Pressure
- Equalization
- Guidewire Introducer Needles
- Guide Catheter (wedging, damping & side holes)
- PressureWire Drift
- Artifacts
- Mean-beat Setting
- Sensor Element Against Vessel Wall
- **Suboptimal Hyperemia**

Suboptimal Maximal Hyperaemia

Fluctuating Pd/Pa line = steady state NOT achieved and likely sub-optimal maximal hyperaemia

Steady-State Maximal Hyperaemia

steady state

Practical Aspects of LM FFR:

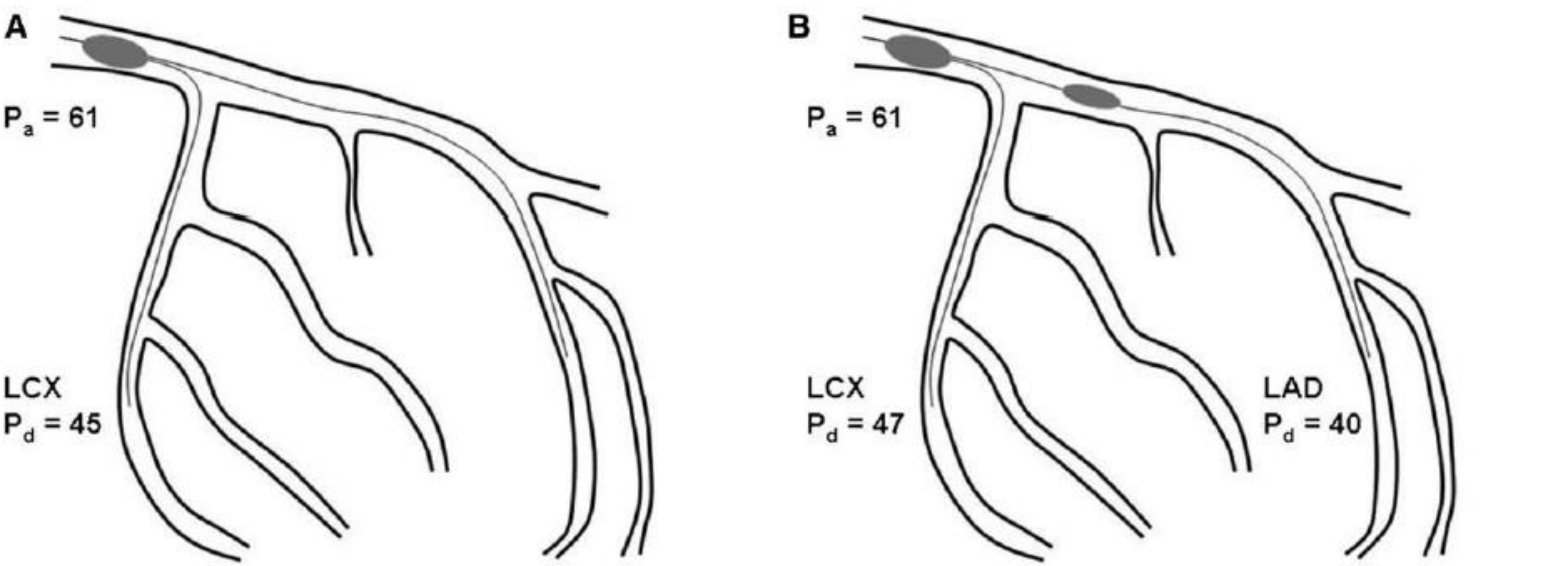
- First measure FFR in the least diseased vessel, preferably the LAD, with a pullback
  - If FFR < 0.80, then revascularize
  - If FFR >0.85, then treat medically
  - If FFR between 0.80 and 0.85 and there is significant downstream epicardial disease in the other epicardial vessel, then can consider IVUS

Practical Aspects of LM FFR:

- Intravenous adenosine is the ideal hyperemic agent because it allows time to pull the guide catheter out of the ostium.
- A physiologic evaluation of left main disease, compared to an anatomic evaluation alone, is safe and appropriate, just as it is in non-left main CAD.
- Never forget the patient and the clinical scenario.

Effect of Epicardial Lesions on FFR Assessment of Intermediate LM Disease

Animal Model



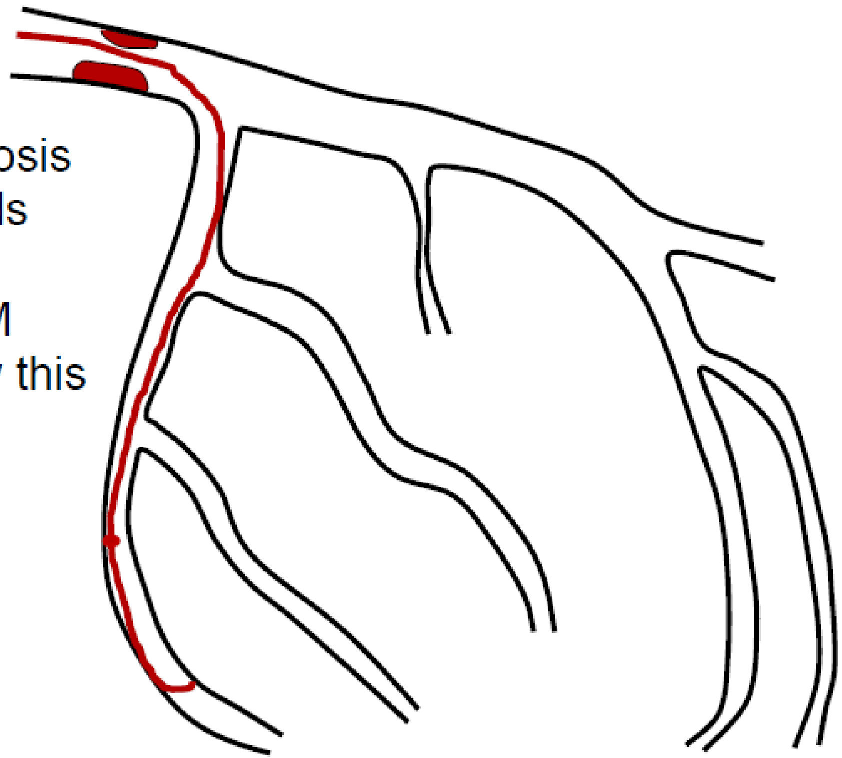
FFR_{true} = 45/61 = 0.74

FFR_{app} = 47/61 = 0.77 $FFR_{epicardial}$ = 40/61 = 0.66

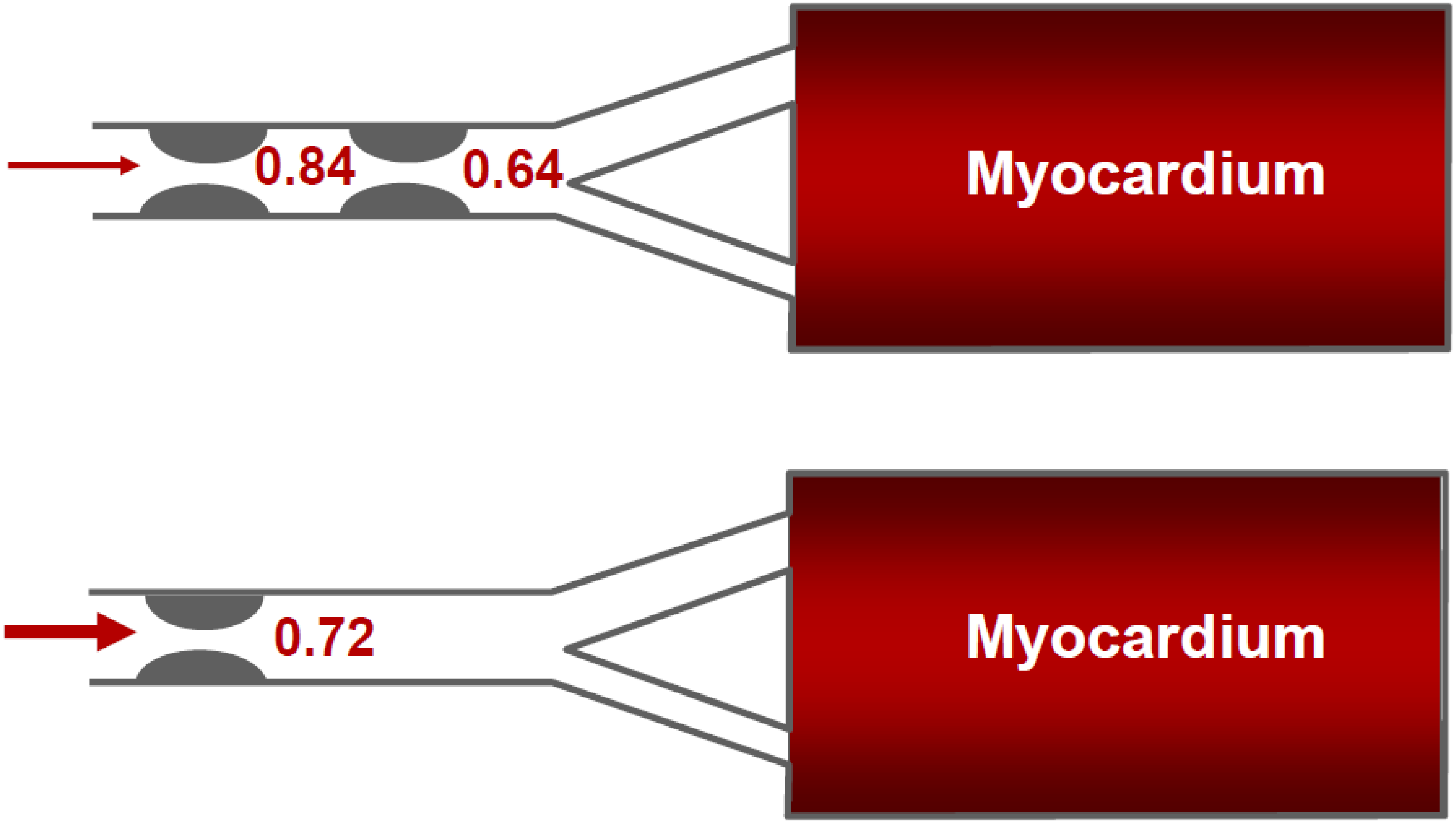
Left Main Stem Stenoses are Rarely Isolated

The influence of a distal stenosis on the FFR of the LM depends on the extent to which hyperemic flow across the LM stenosis will be decreased by this distal lesion

- Severity
- Myocardial mass



Effect of Tandem Lesions



FFR KAI PCI

FFR CUT-OFF μετά από αγγειοπλαστική είναι το **0.9,** όχι 0.8

- **ΜΟΝΟ ΜΙΑ ΜΙΚΡΗ ΜΕΛΕΤΗ**

Korean Circ J 2011;41:304-307

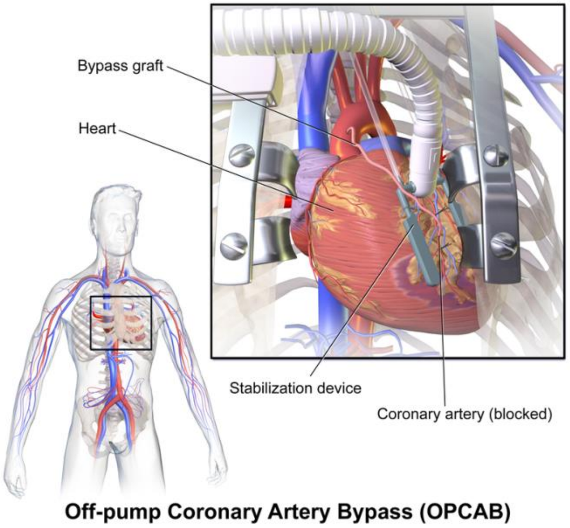
FFR KAI CABG

Ασθενείς με ενδιάμεσες στενώσεις (όχι LM)

- GROUP 1 (Σ/Φ => CABG)
- GROUP 2 (FFR => CABG)
- **FFR CUT-OFF => 0.8**

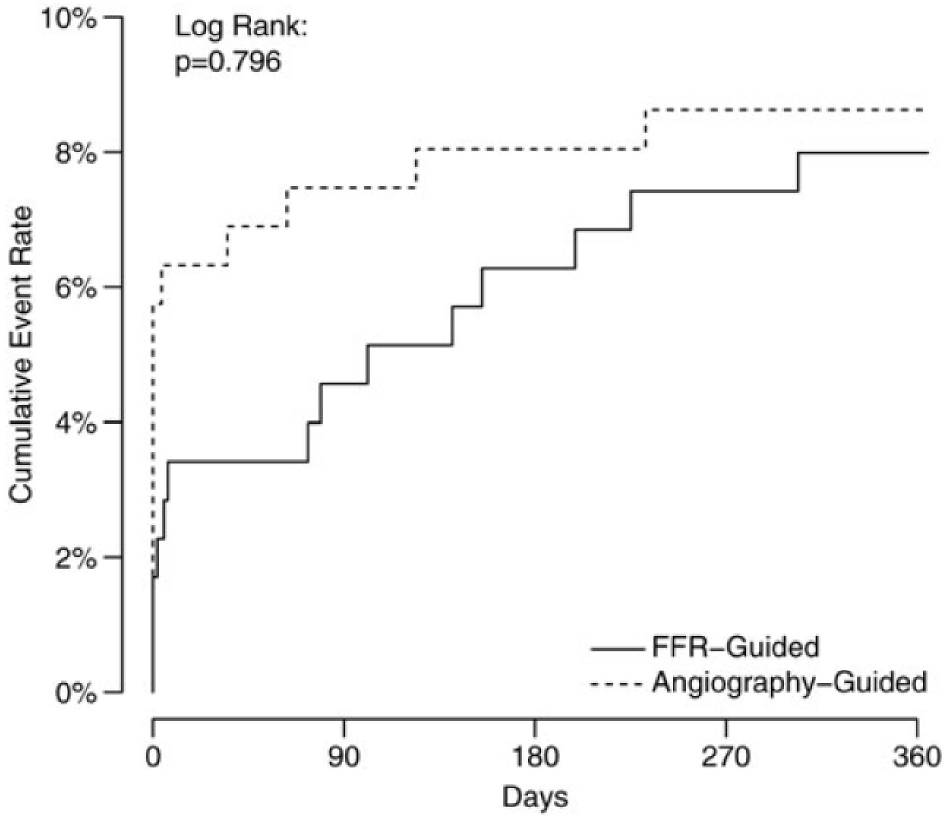
GROUP 2 =>

- ↓ αριθμός μοσχευμάτων
- ↓ on-pump χειρουργείο
- ↓ μετεγχειρητική στηθάγχη



Circulation. 2013;128:1405-1411

FFR KAI nSTEMI



ΥΠΑΡΧΕΙ ΜΟΝΟ ΜΙΑ ΜΕΛΕΤΗ (FAMOUS – NSTEMI)

CONCLUSION:
In NSTEMI patients, angiography-guided management was associated with higher rates of coronary revascularization compared with FFR-guided management. A larger trial is necessary to assess health outcomes and cost-effectiveness.

European Heart Journal (2015) **36**, 100–111

Instantaneous wave free ratio (iFR)

- iFR isolates a **specific period in diastole**, called the wave-free period, and uses the ratio of distal coronary pressure (Pd) to the pressure observed in the aorta (Pa) over this period.
- When stenoses are flow limiting, Pd and Pa pressures over the wave-free period diverge; a normal ratio is 1.0 and iFR values of below 0.90 suggest flow limitation.
- iFR can be calculated using dedicated consoles available for medical use and typically uses an average over 5 heart beats but can be performed **using a single heart beat**.
- iFR is measured at rest, without the need for pharmacological vasodilators or stressors and compares well to other invasive and non-invasive markers of ischemia or flow limitation.

Instantaneous wave free ratio (iFR)

- iFR vs FFR
- Δε χρειάζεται υπεραιμία!

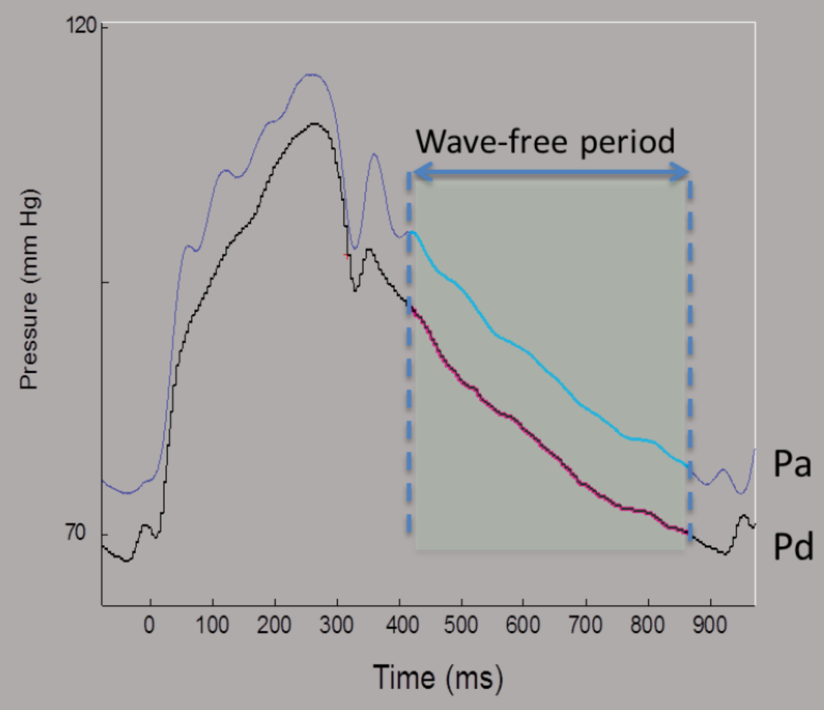
  - FFR => Μέση πίεση άπω της στένωσης => Σε όλη τη διάρκεια του κύκλου => Μέγιστη υπεραιμία

  - iFR => Μέτρηση πίεσης εγγύς και άπω της βλάβης από το 25% της διαστολικής φάσης => έως την τελοδιαστολή

iFR

IFR = Pd/Pa

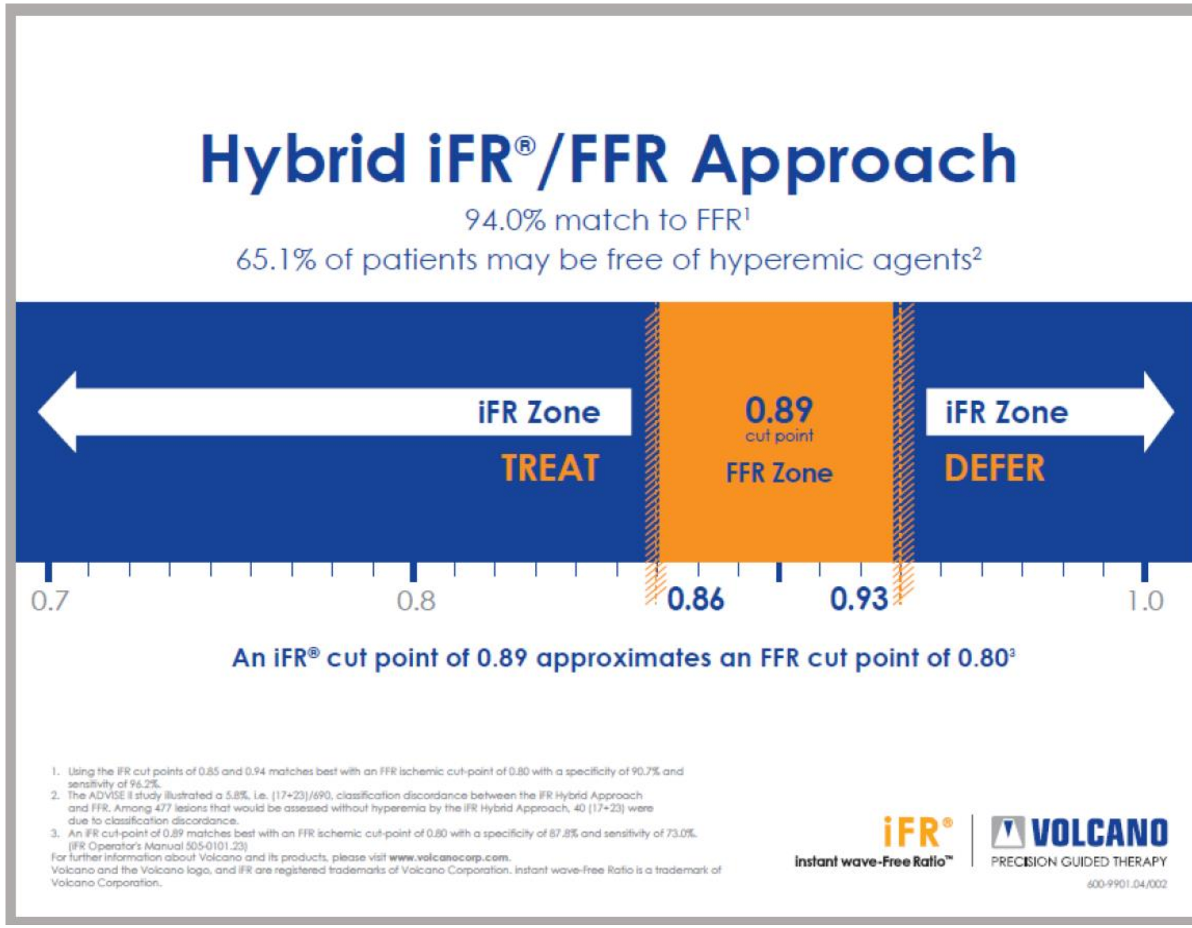
No adenosine



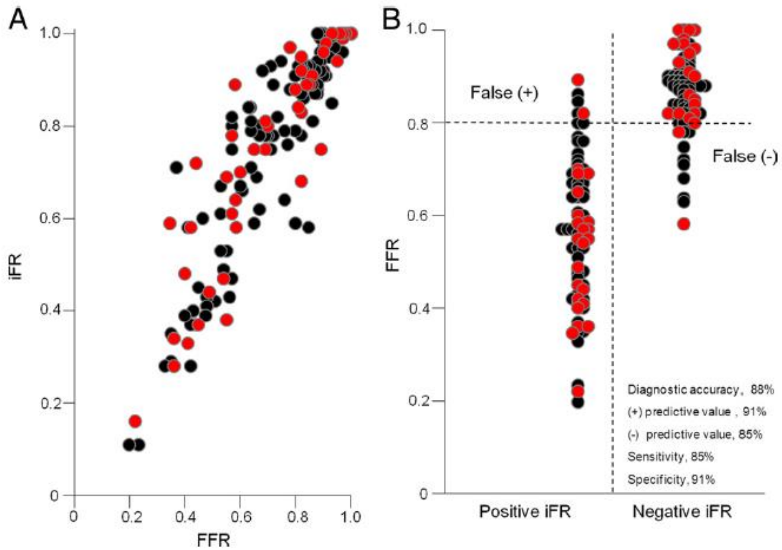
Period of maximal coronary
Blood flow during diastole

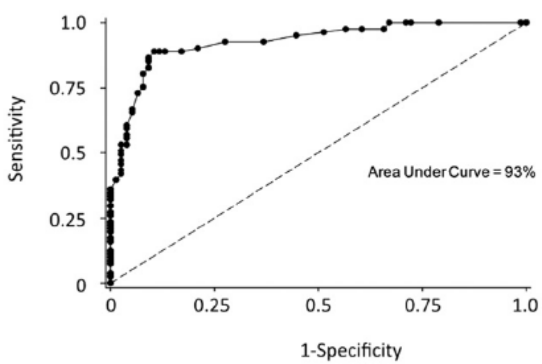
ΜΕΛΕΤΕΣ iFR

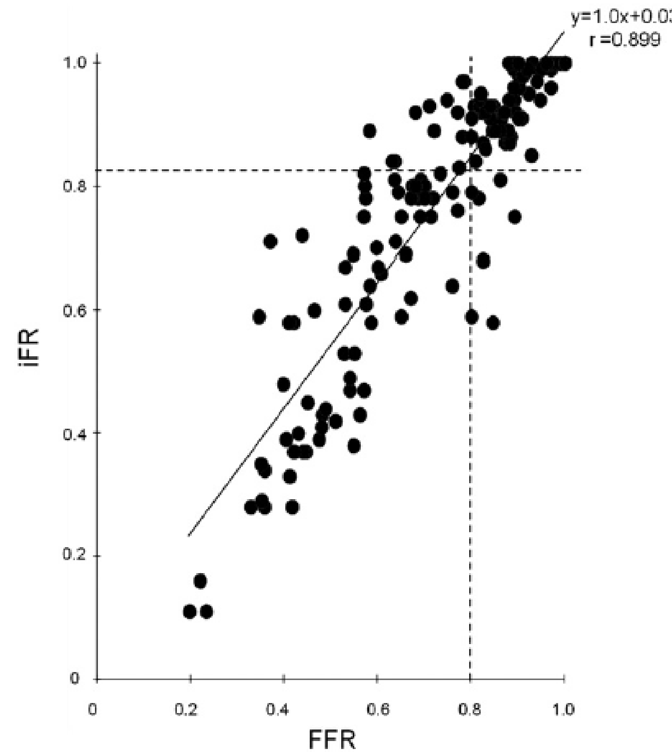
- ADVISE
- CLARIFY
- VERIFY



ADVISE STUDY=establishment







ELSEVIER

Journal of the American College of Cardiology

Volume 59, Issue 15, 10 April 2012, Pages 1392-1402

Focus Issue: Transcatheter Cardiovascular Therapeutics

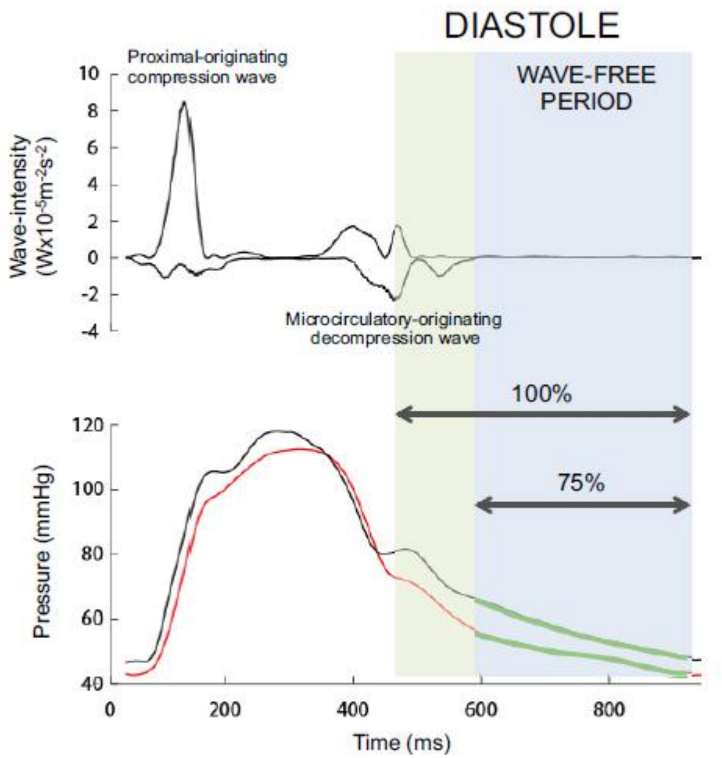
Coronary Disease

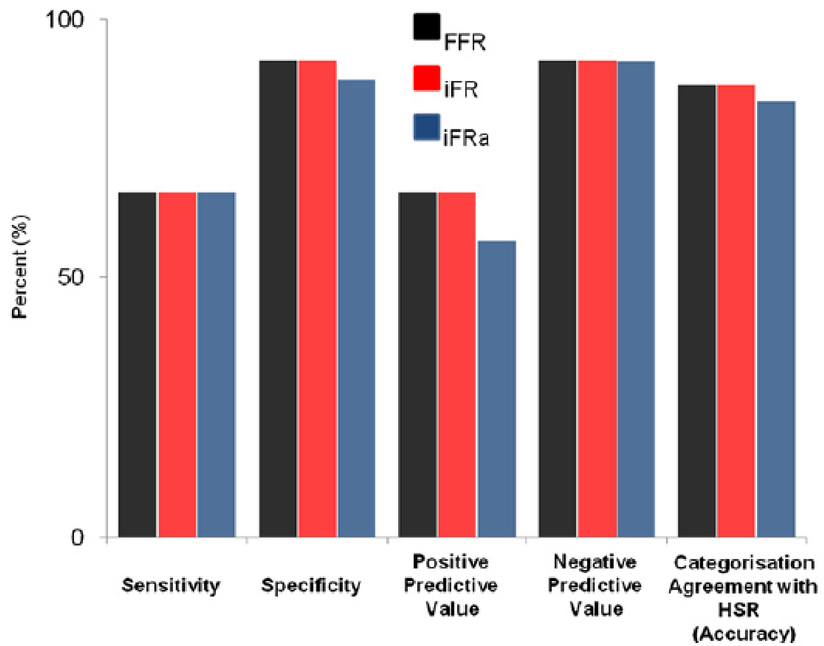
Development and Validation of a New Adenosine-Independent Index of Stenosis Severity From Coronary Wave–Intensity Analysis: Results of the ADVISE (ADenosine Vasodilator Independent Stenosis Evaluation) Study

Sayan Sen MBBS [*], Javier Escaned MD, PhD [†], Iqbal S. Malik MBBS, PhD [‡], Ghada W. Mikhail MBBS, MD [‡], Rodney A. Foale MD [*], Rafael Mila MD [†], Jason Tarkin MBBS [*], Ricardo Petraco MD [*], Christopher Broyd MBBS [*], Richard Jabbour MBBS [*], Amarjit Sethi MBBS, PhD [‡, †], Christopher S. Baker MBBS, PhD [‡], Micheal Bellamy MBBS, MD [‡], Mahmud Al-Bustami MD [‡], David Hackett MD [‡], Masood Khan MB, BChir, MA [‡], David Lefroy MB, BChir, MA [‡], Kim H. Parker PhD [§] … Justin E. Davies MBBS, PhD [*]

J Am Coll Cardiol 2012;59: 1392–402

CLARIFY STUDY

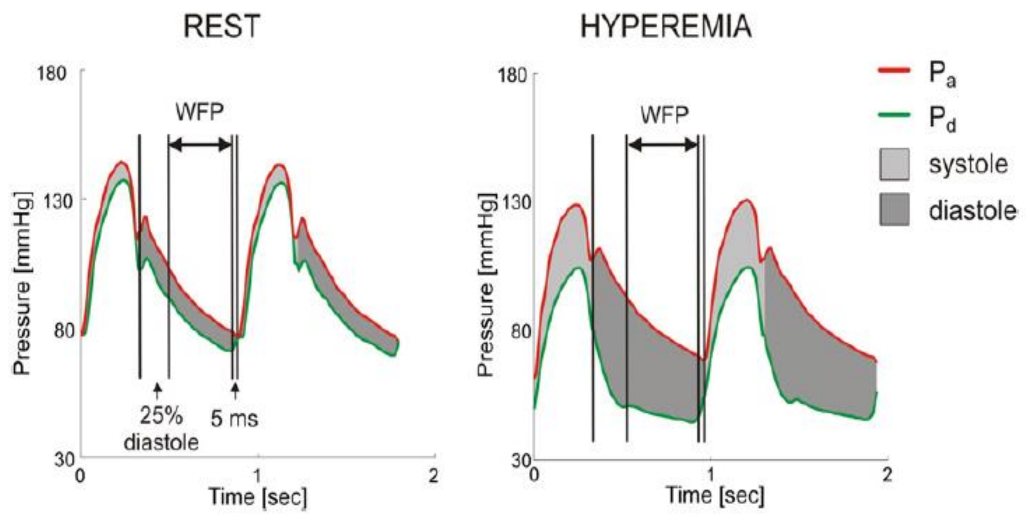


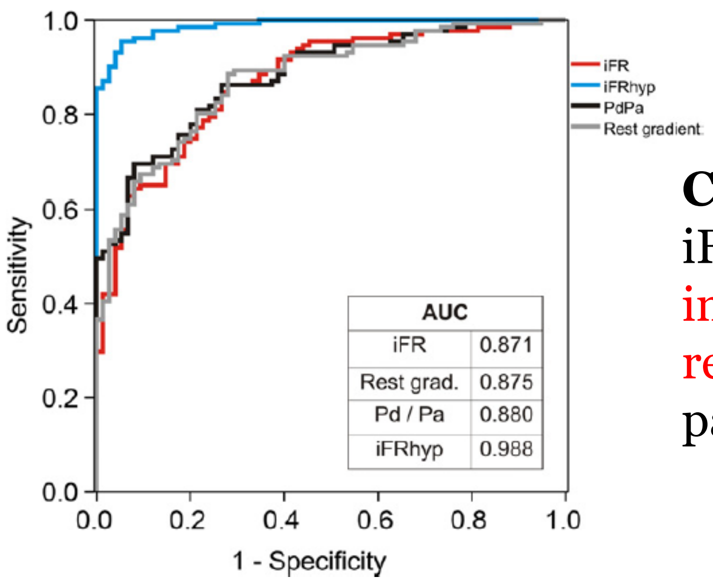


CONCLUSIONS:
iFR and FFR had equivalent agreement with classification of coronary stenosis severity by HSR. Further reduction in resistance by the administration of adenosine did not improve diagnostic categorization, indicating that iFR can be used as an adenosine-free alternative to FFR.

J Am Coll Cardiol 2013;61:1409–20

VERIFY STUDY





CONCLUSIONS:
iFR correlates weakly with FFR and is not independent of hyperemia. iFR cannot be recommended for clinical decision making in patients with coronary artery disease.

J Am Coll Cardiol 2013;61:1421–7

VIRTUAL FFR

- Επεξεργασία και
- 3D απεικόνιση δεδομένων από Σ/Φ
- Computational fluid dynamics remodelling

- ΜΕΛΕΤΗ VIRTU -1

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VIEWPOINT

INTERVENTIONAL ISSUES

"Virtual" (Computed) Fractional Flow Reserve

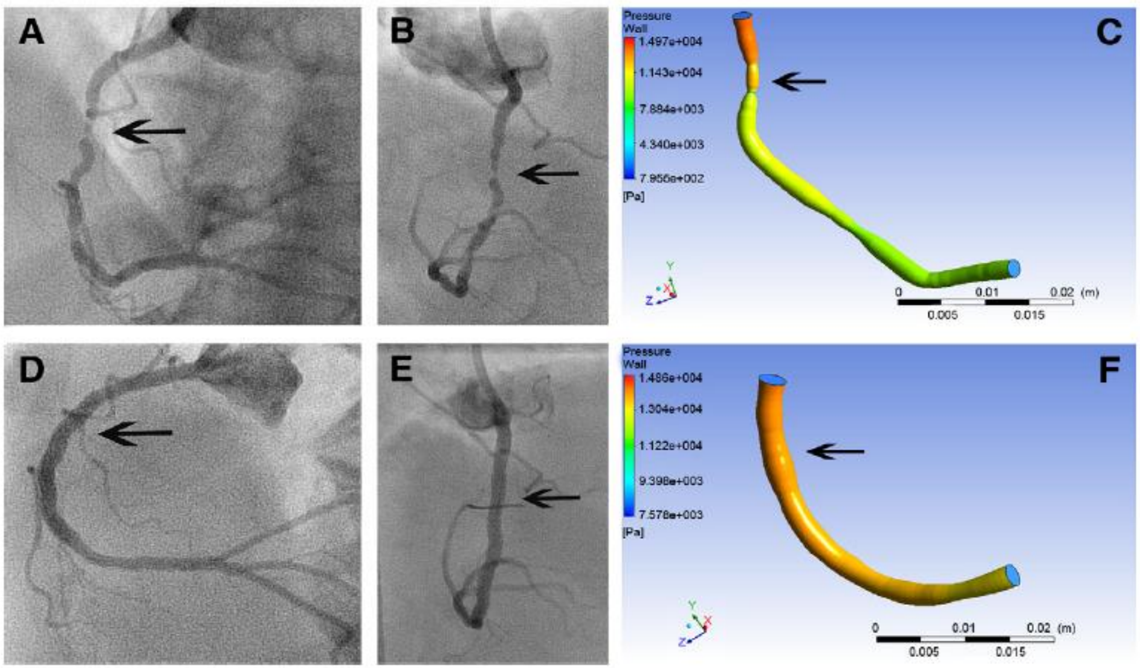
Current Challenges and Limitations

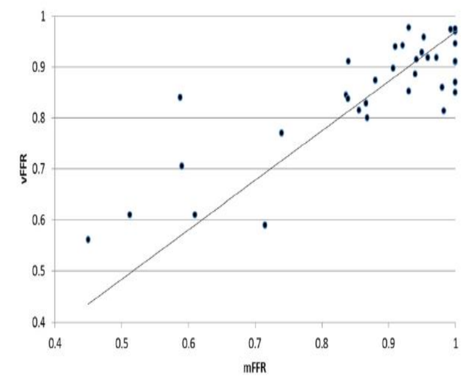
Paul D. Morris, MBChB,*† Frans N. van de Vosse, PhD,‡ Patricia V. Lawford, PhD,* D. Rodney Hose, PhD,* Julian P. Gunn, MD*†

ΜΕΛΕΤΗ VIRTU -1

- 35 Στεφανιαίες στενώσεις – 22 αγγεία
- Κάθετες λήψεις (τουλάχιστον 35° μεταξύ τους)
- Μέγιστη υπεραιμία με αδενοσίνη
- vFFR => FFR ± 0.06
- Ειδικό Software => 24h Ανάλυση Δεδομένων

ΜΕΛΕΤΗ VIRTU -1





J Am Coll Cardiol Intv 2013;6:149–57