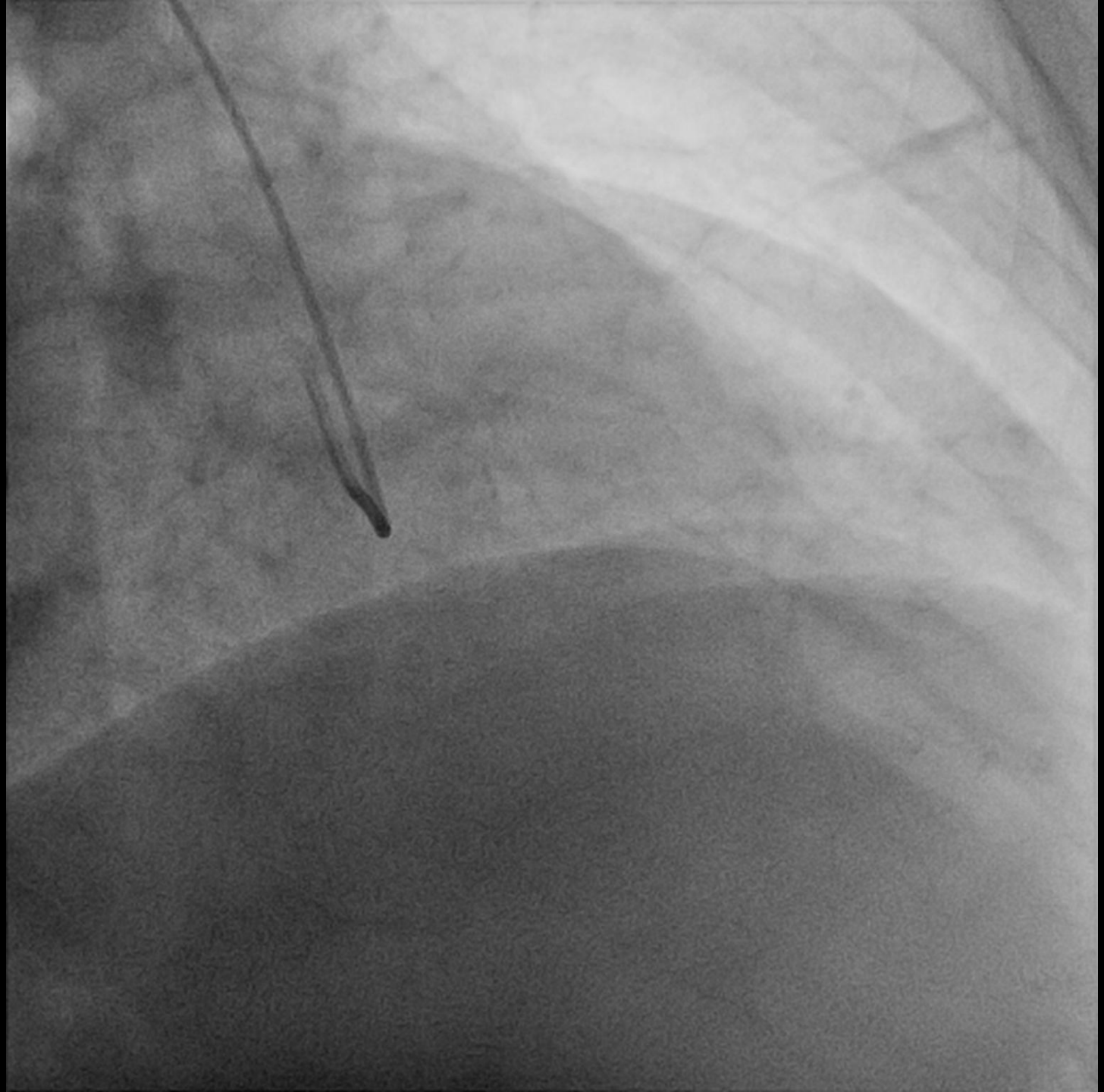
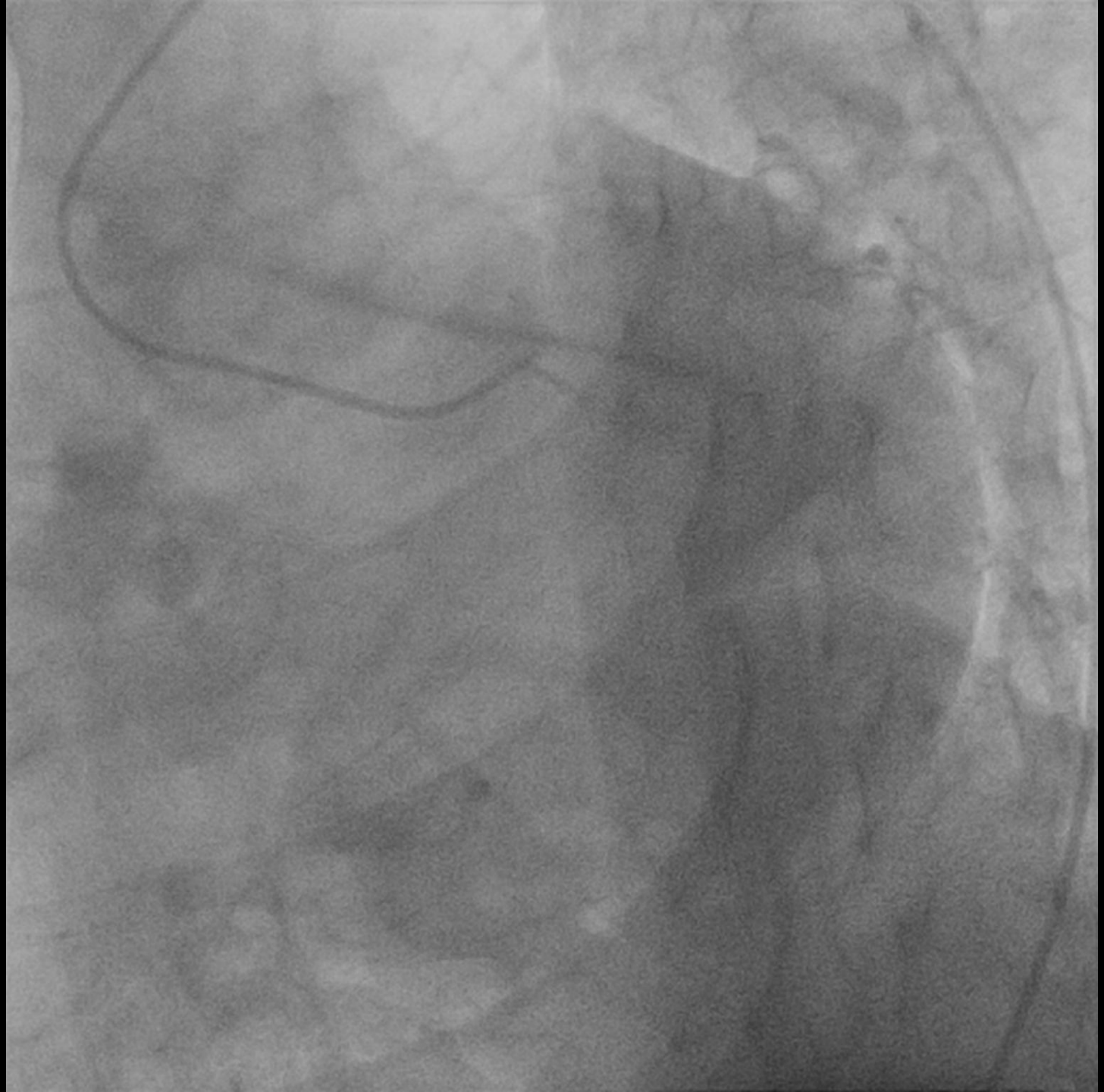
Dave Kettles, St Dominics Hospital East London.

FFR, the why and the how






0:04
iFR™
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List of Runs
iFR
FFR
05:16:34 PM 0.92
05:16:42 PM 0.94
05:16:49 PM 0.95
05:16:56 PM 0.95
05:19:20 PM 0.87
05:19:49 PM 0.85
05:21:53 PM 0.82
05:22:07 PM 0.91
05:22:17 PM 0.91
05:22:24 PM 0.91
05:23:24 PM 0.84
05:24:11 PM 0.83
05:26:26 PM 0.84
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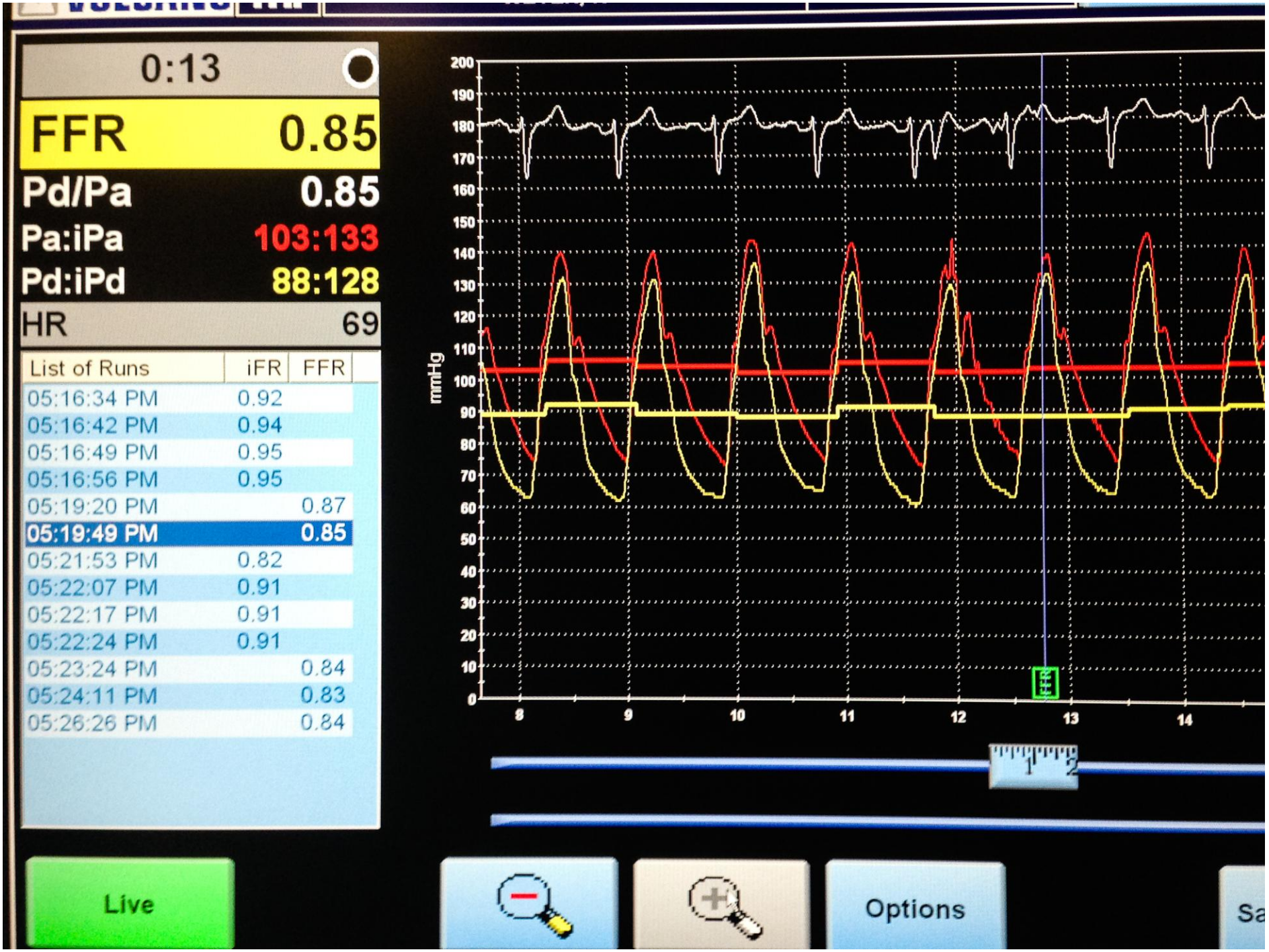
0:13
FFR 0.85
Pd/Pa 0.85
Pa:iPa 103:133
Pd:iPd 88:128
HR 69
List of Runs iFR FFR
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05:16:42 PM 0.94
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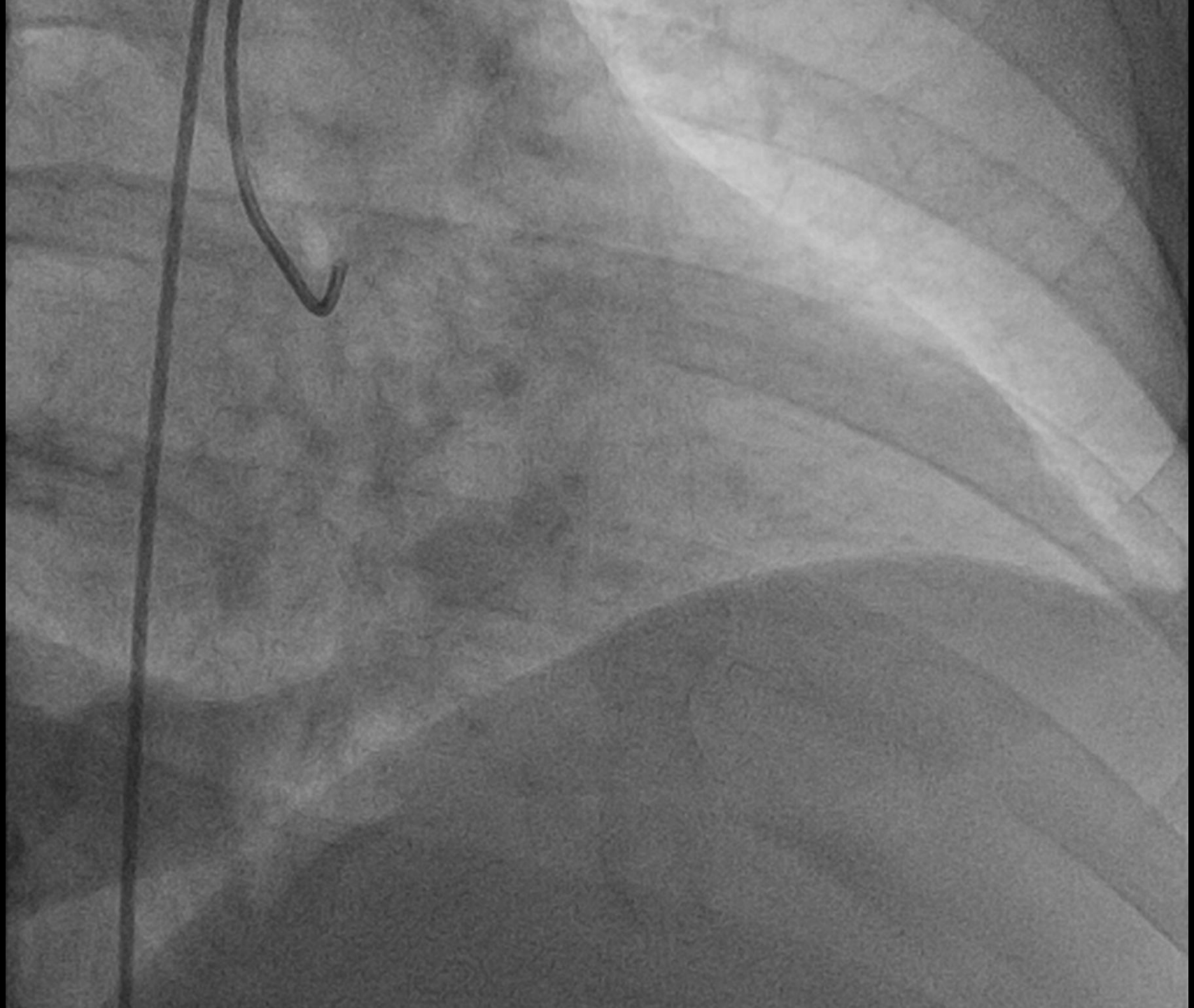
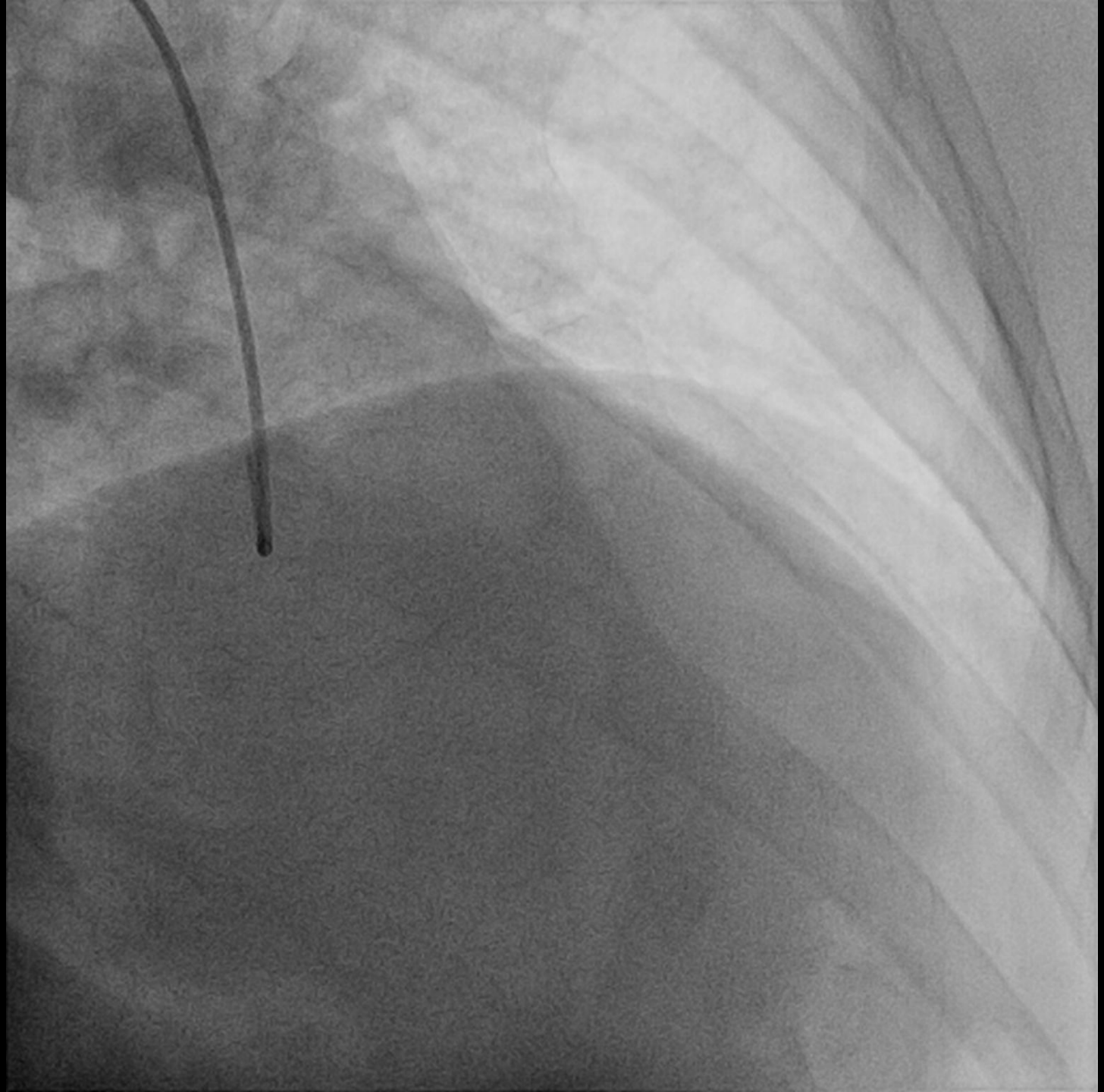
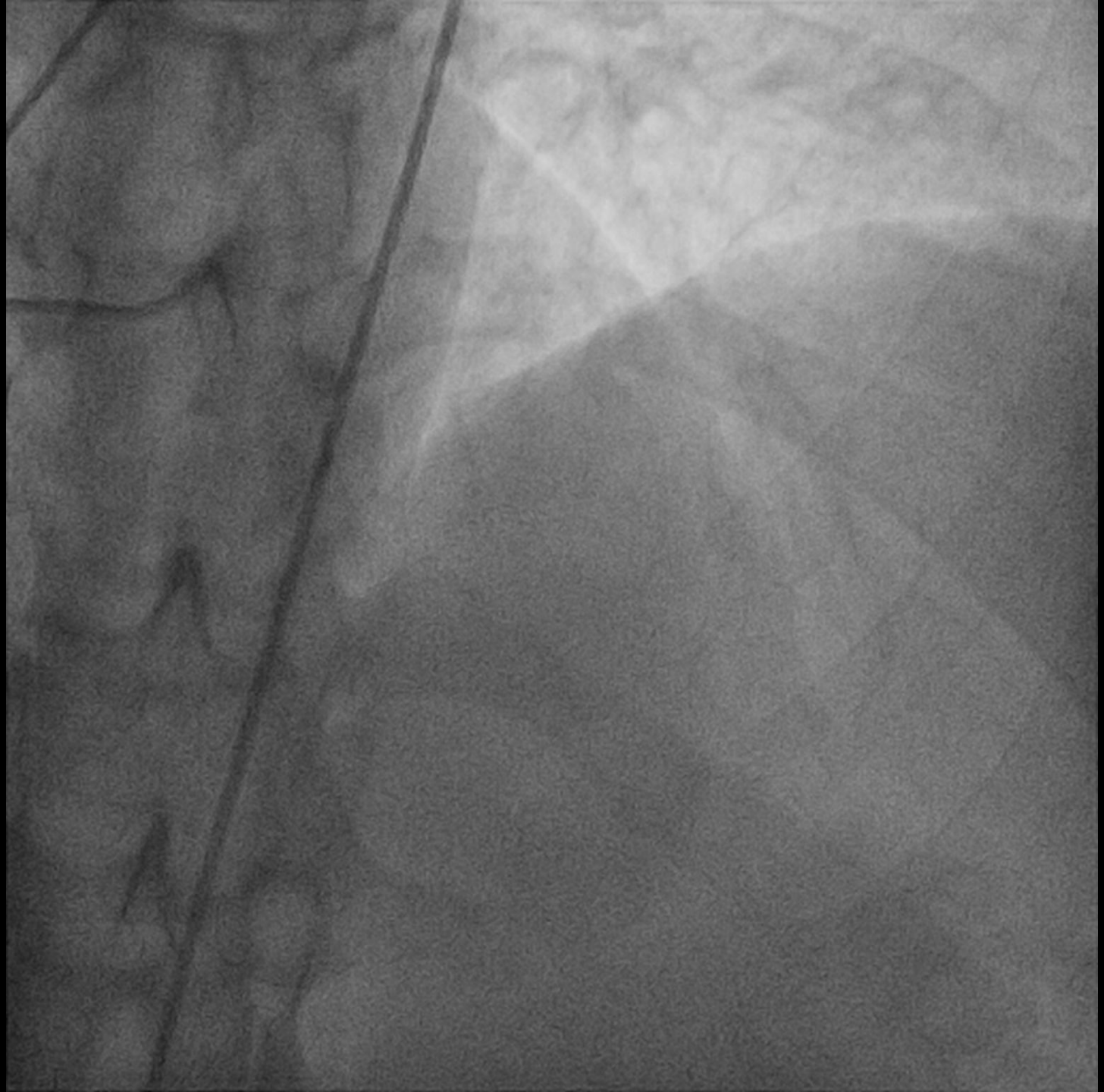
FFR
Live
Options

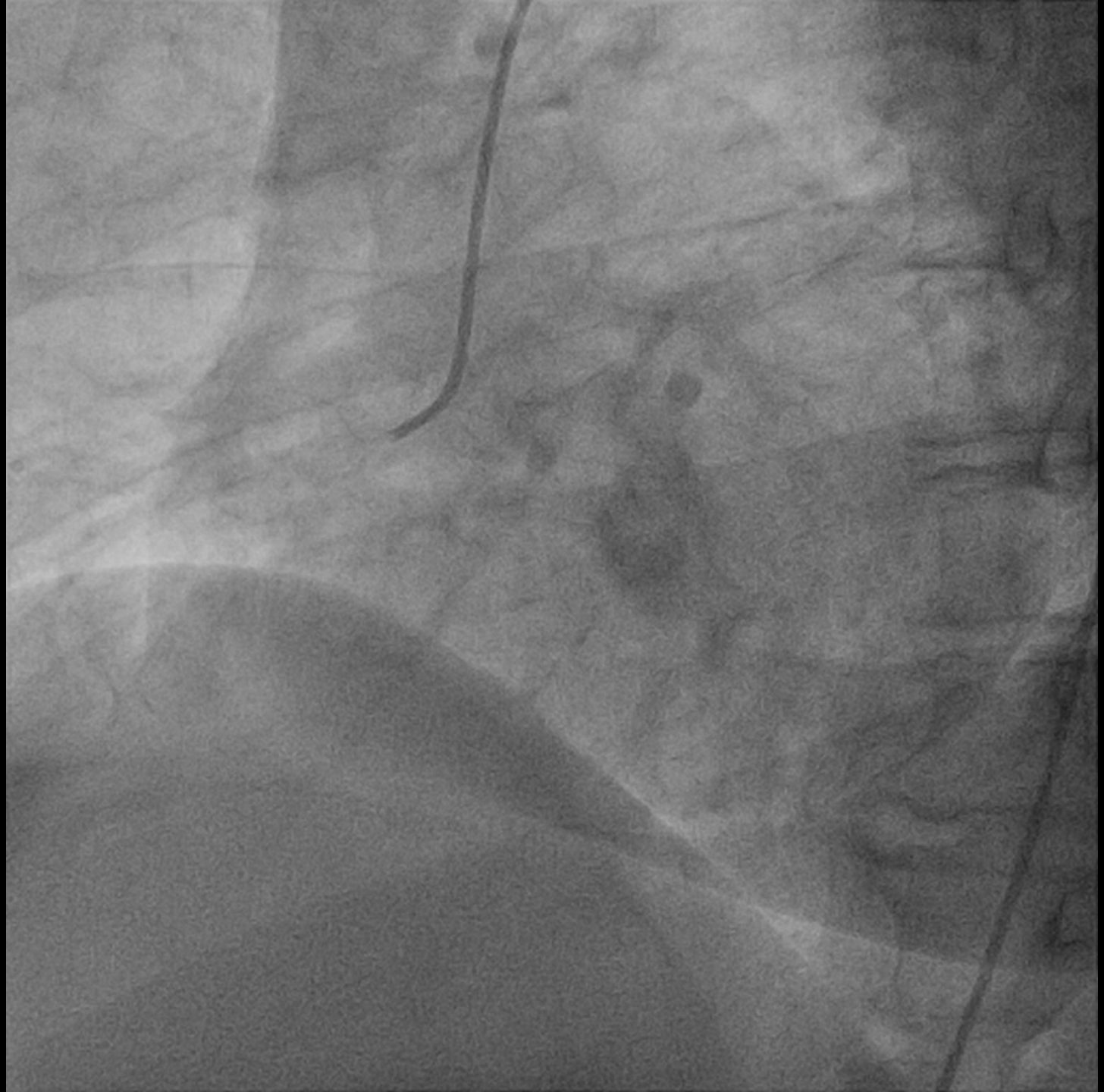
Case 2

- 110 x 150
- Angina for a couple of months
- Trop T negative
- T wave inversion across the chest leads
- Not wanting to risk radial…
  - Huge struggle with femoral access
  - Vascular ultrasound is very useful
  - But….

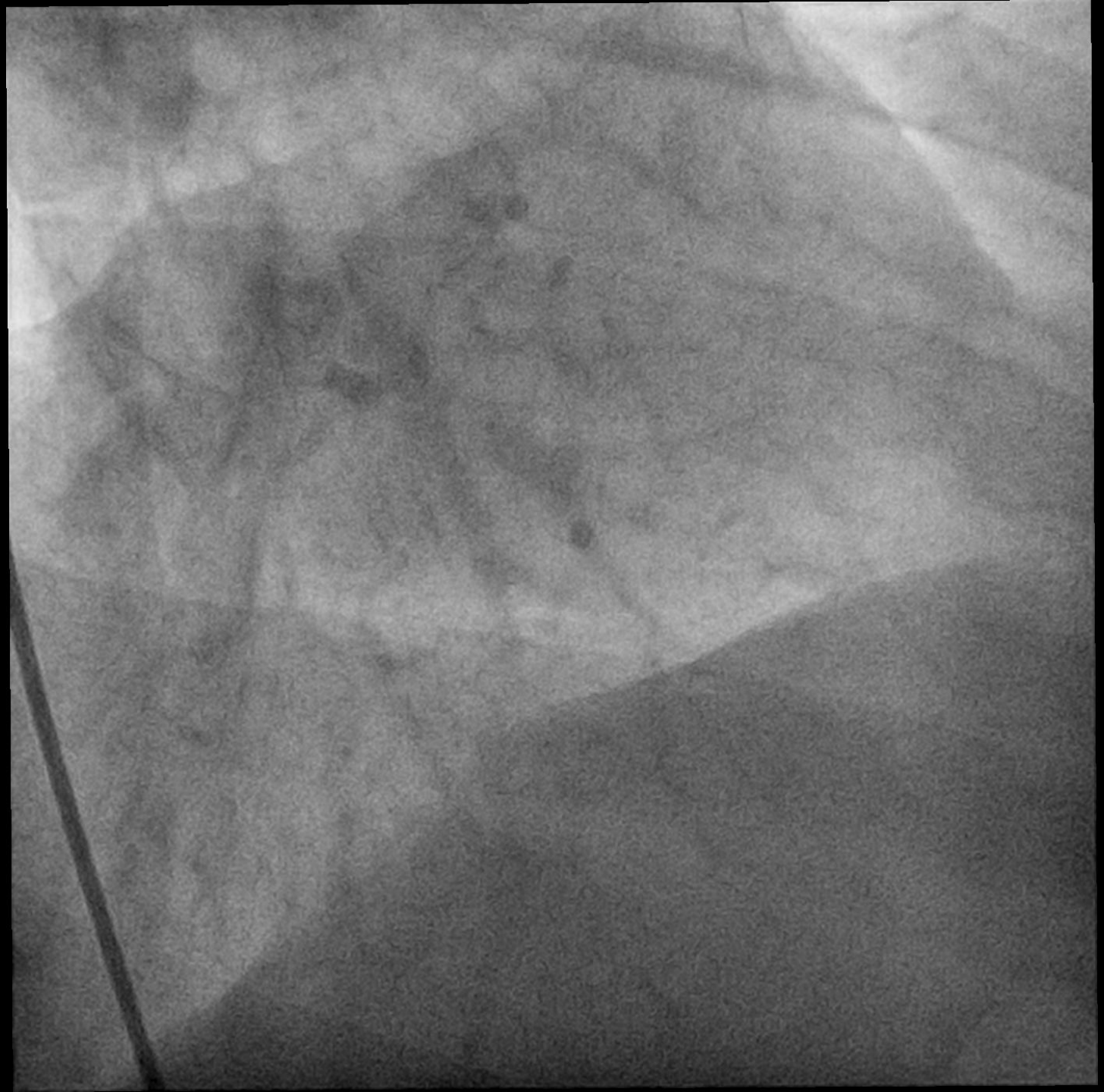


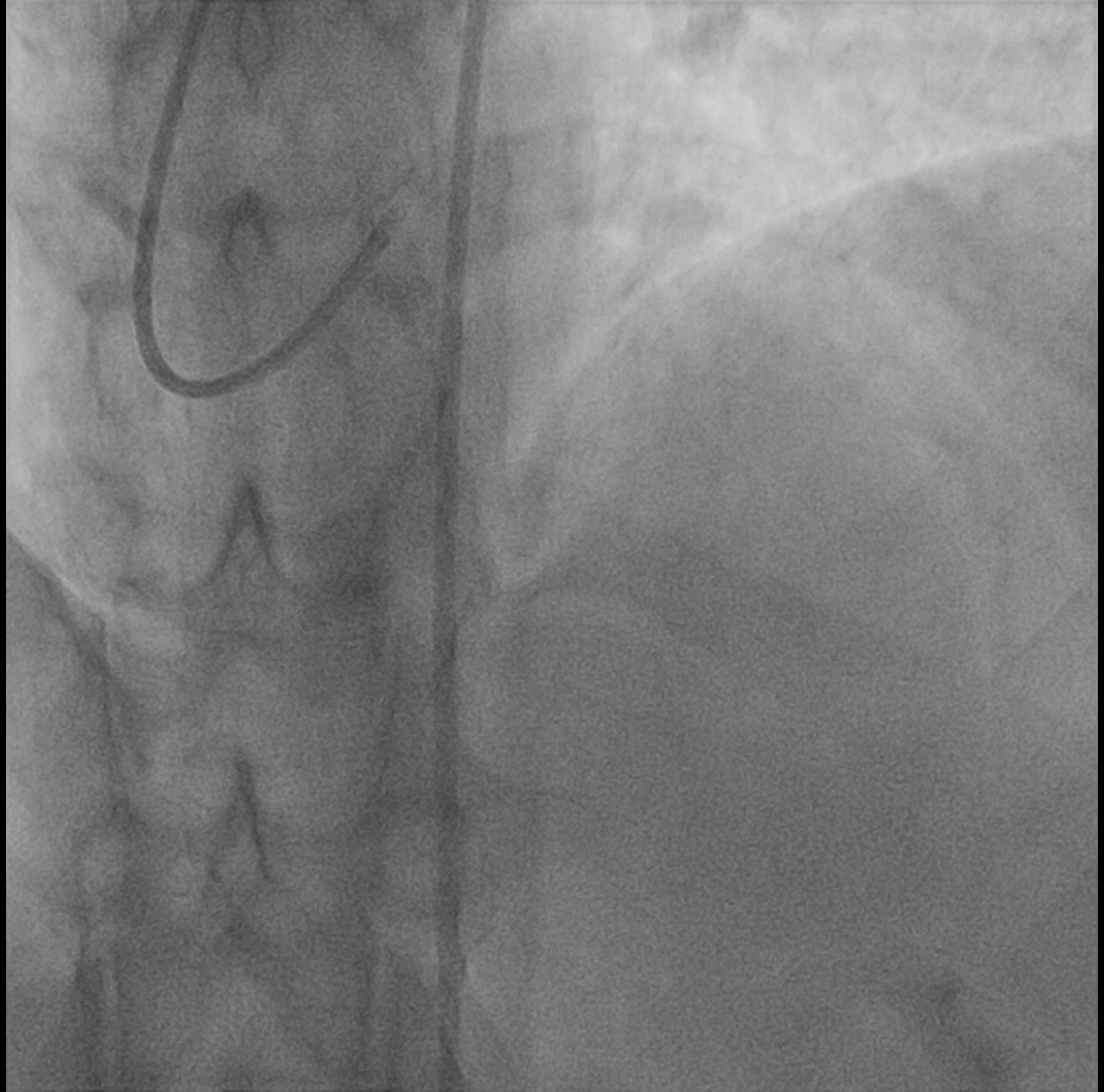


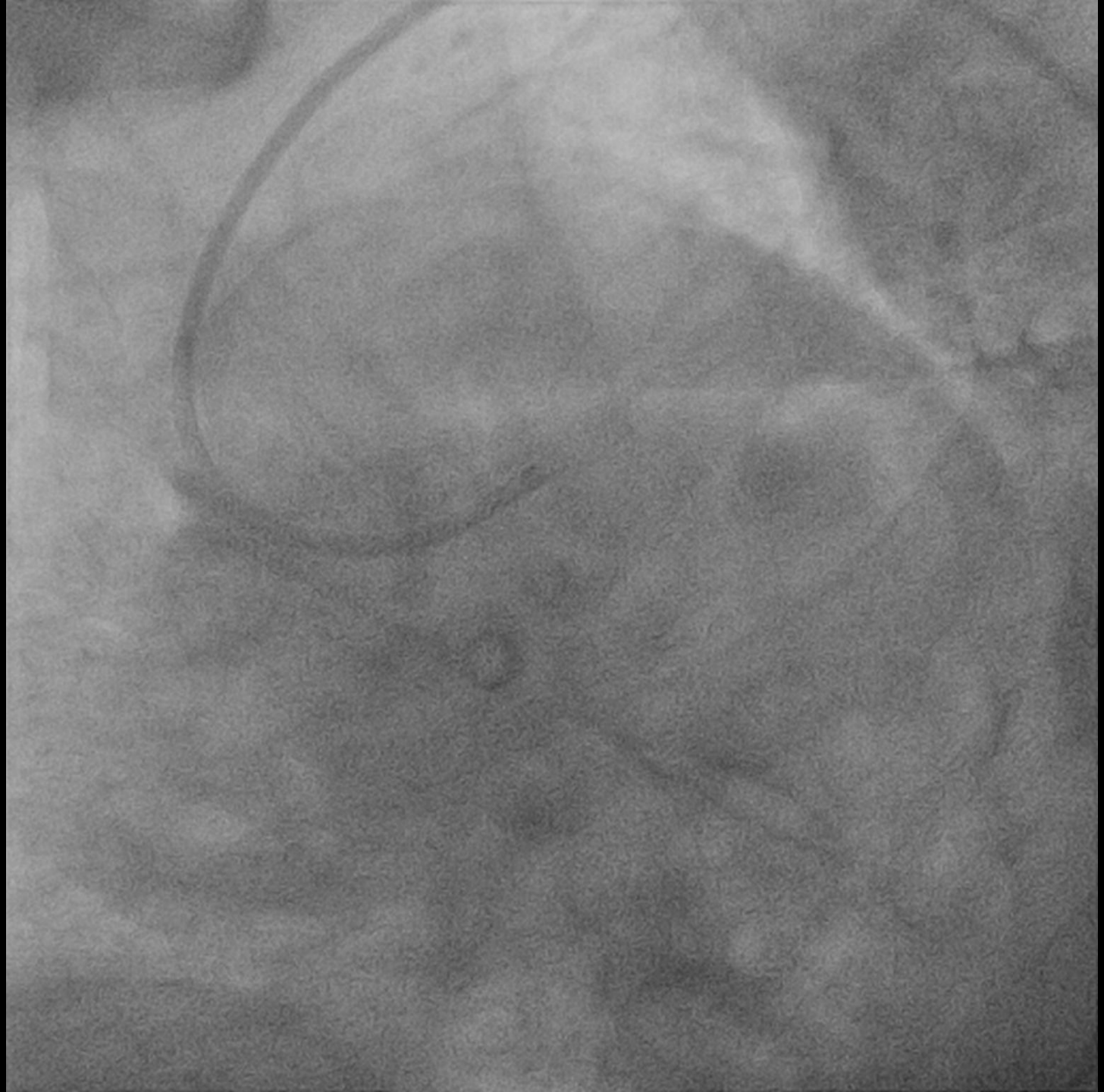


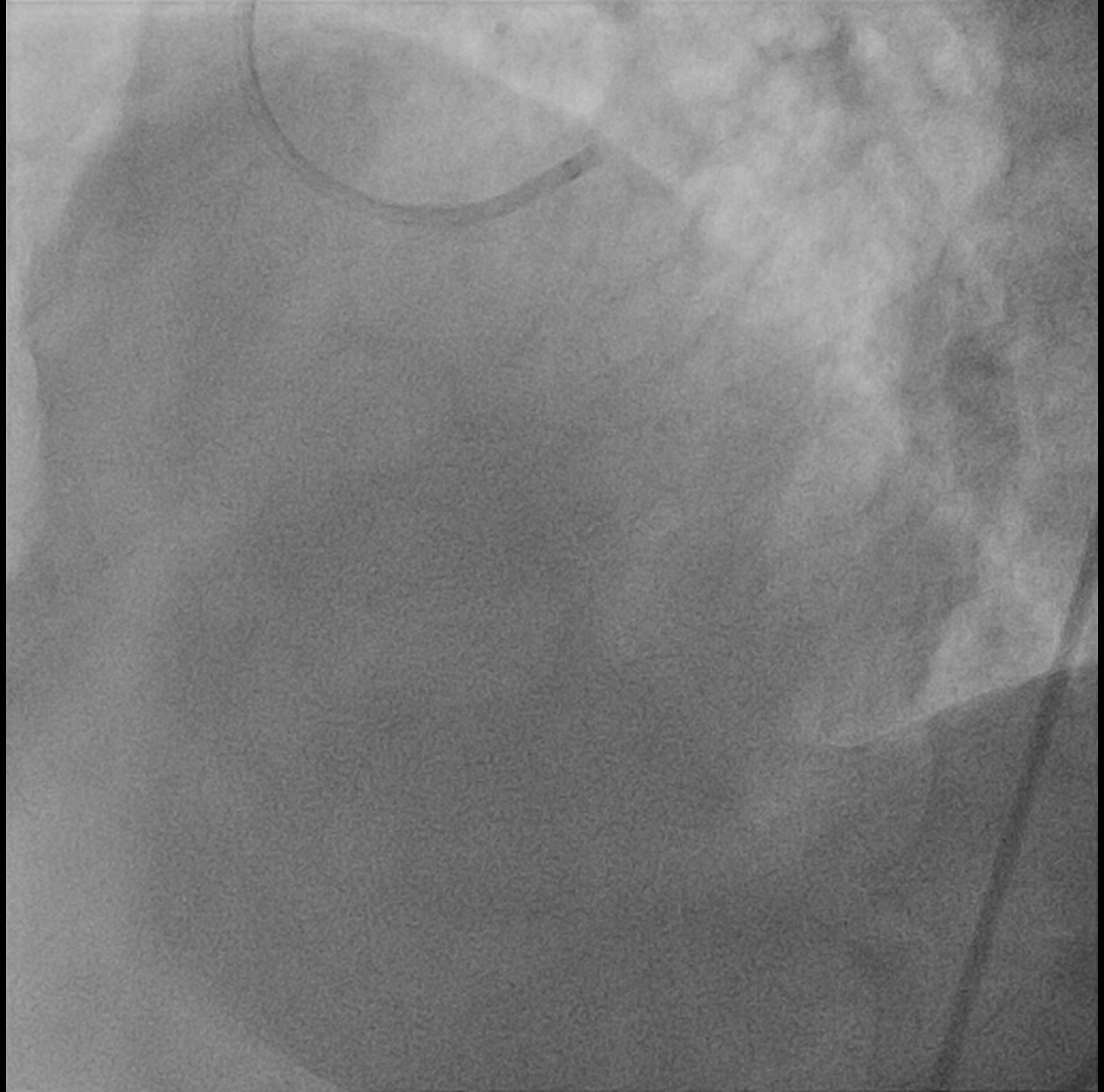


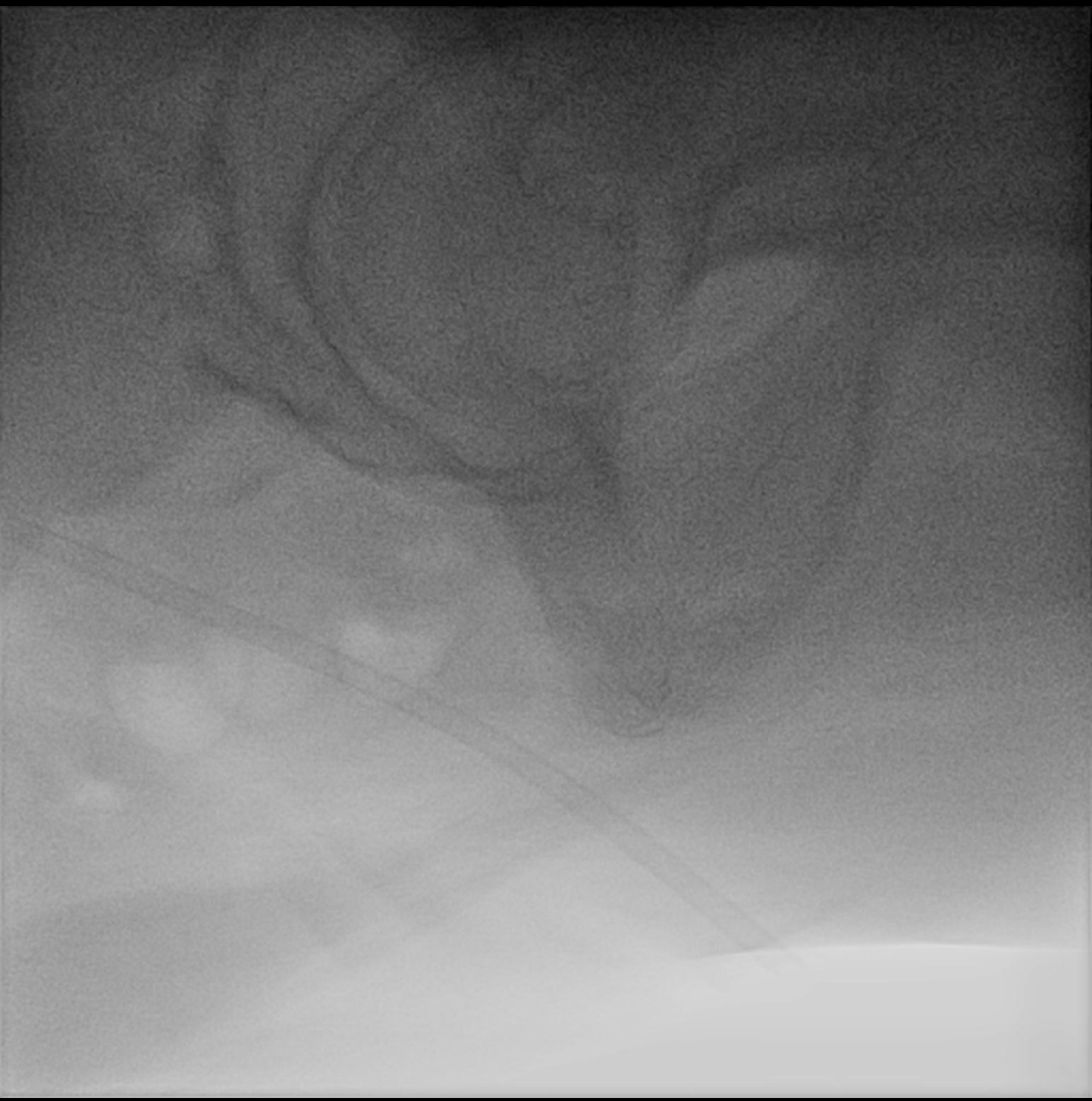
What now?



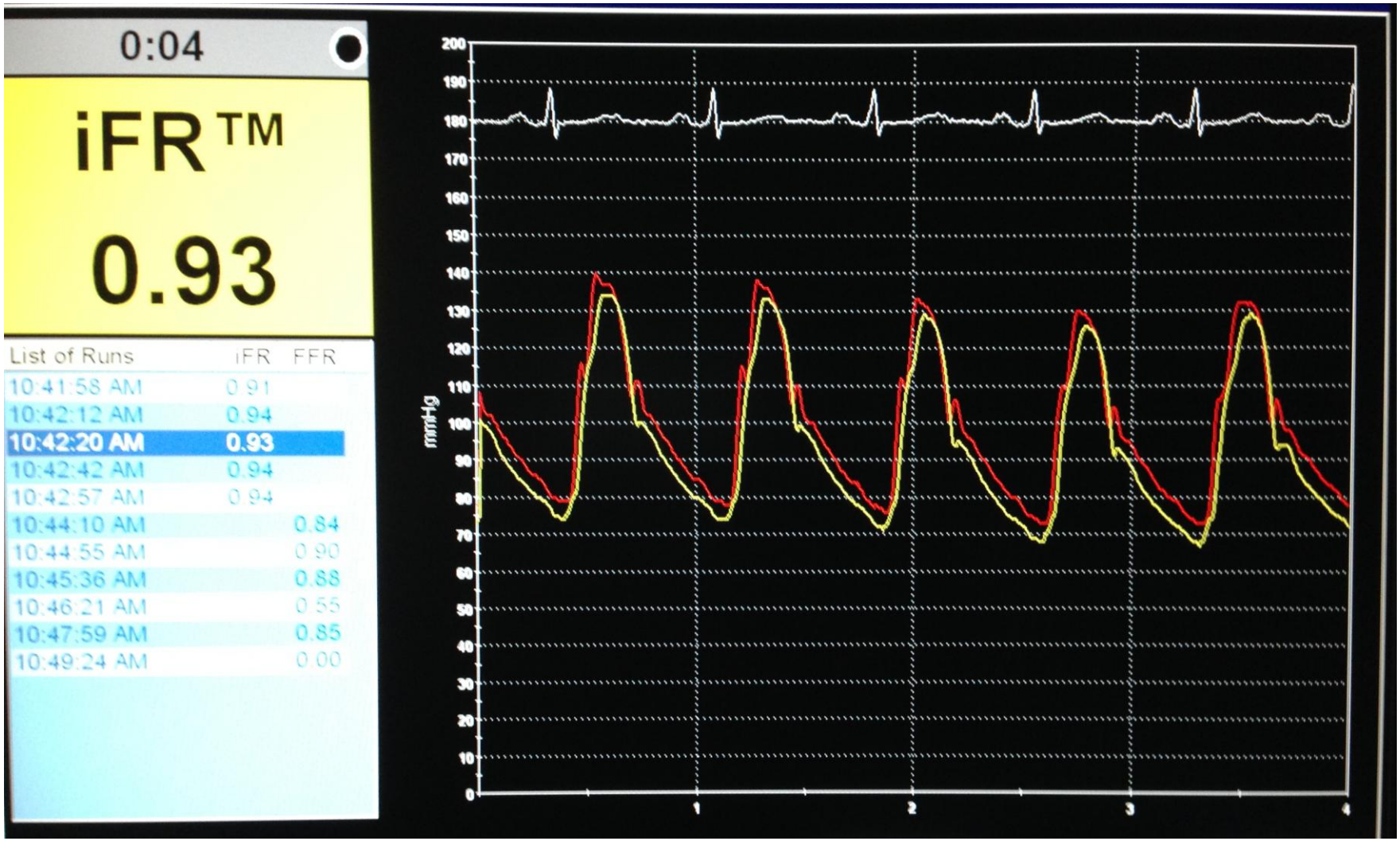








Of course?


0:04
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List of Runs iFR FFR
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10:42:20 AM 0.93
10:42:42 AM 0.94
10:42:57 AM 0.94
10:44:10 AM 0.84
10:44:55 AM 0.90
10:45:36 AM 0.88
10:46:21 AM 0.55
10:47:59 AM 0.85
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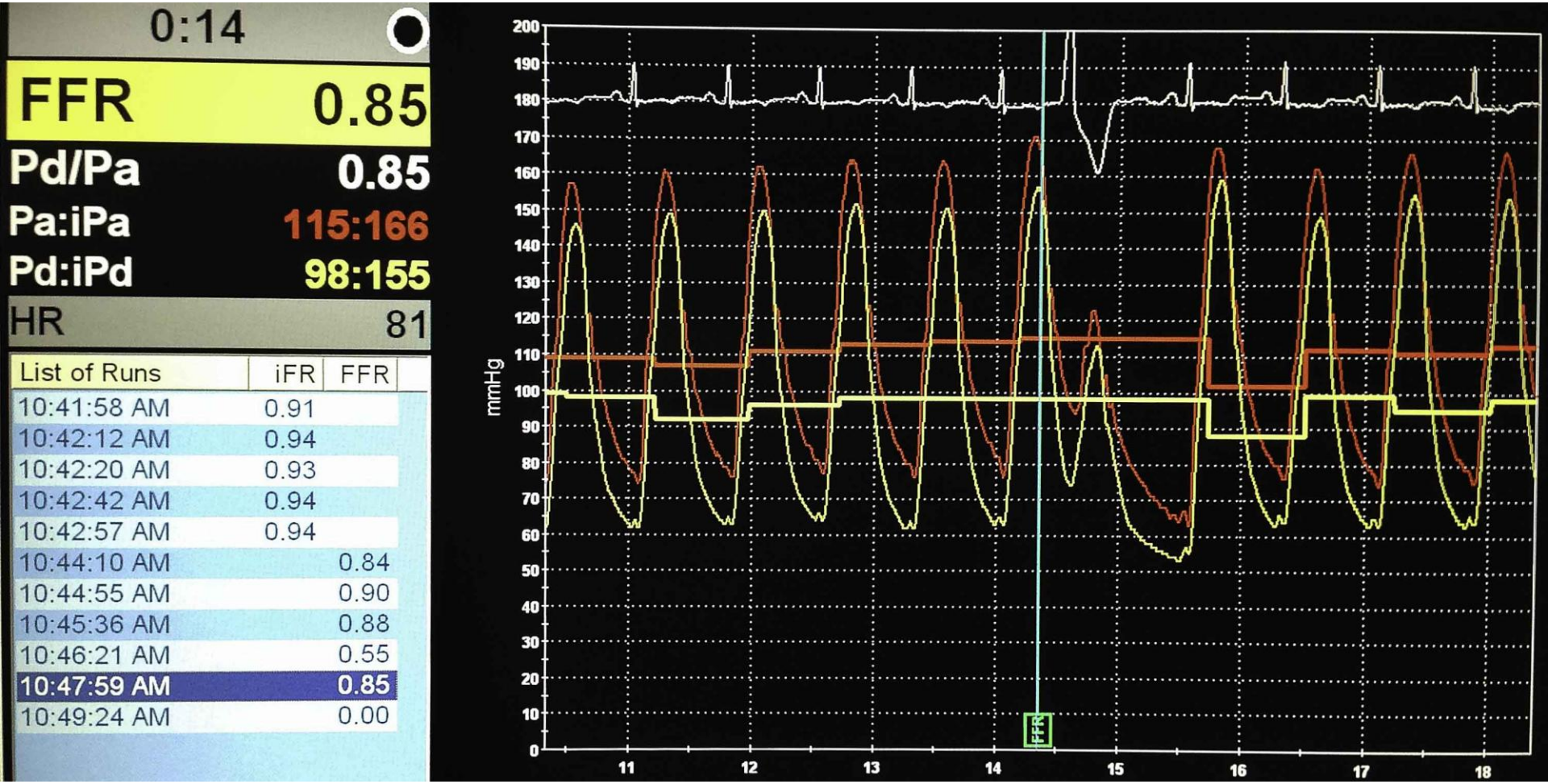
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FFR 0.85
Pd/Pa 0.85
Pa:iPa 115:166
Pd:iPd 98:155
HR 81
List of Runs iFR FFR
10:41:58 AM 0.91
10:42:12 AM 0.94
10:42:20 AM 0.93
10:42:42 AM 0.94
10:42:57 AM 0.94
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FFR

Why?

- Revascularisation, PTCA, stent, or CABG is only useful for significant lesions:
- 'Significant' coronary lesion: one which is physiologically, functionally, or haemodynamically significant, ie: associated with 'inducible myocardial ischaemia'
- How do you know what is significant?

Non invasive tests

- In SA: exercise test
  - Low sensivity, low specificity
  - Not possible in many patients, result often confounded
  - Abnormal ECG at rest: results even less reliable
- Radionuclide scans:
  - Expensive, not widely available locally
  - Very unreliable eg in multivessel disease

Non invasive tests:

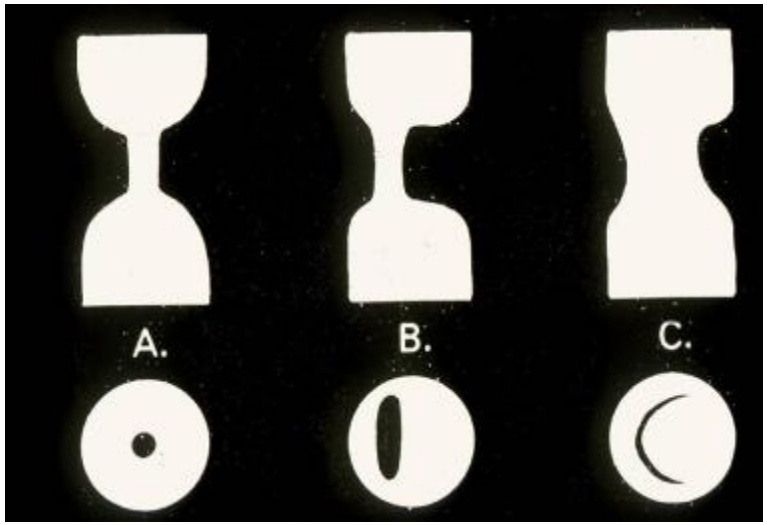
- Many patients arrive in the cath lab with no non invasive tests available
  - Acute coronary syndromes
  - LBBB
  - Cannot walk etc….
- What about looking at the angiogram
  - ‘that is what we have always done….’

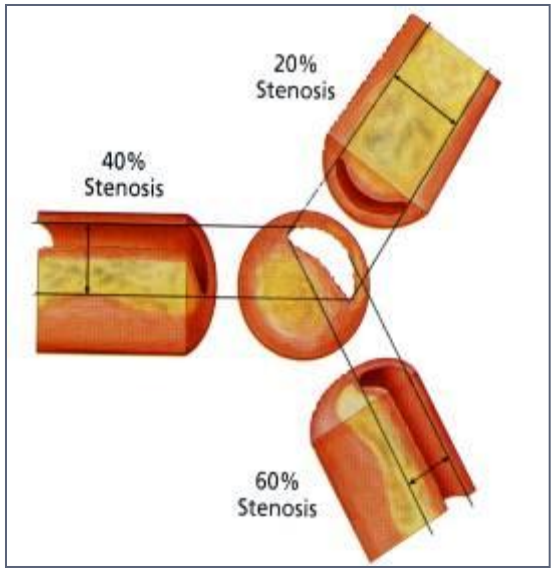
SO, how good is looking at the angiogram?

- Huge potential for observer error: 35%
- Error in interpreting angiograms: the more modest lesions underestimated, the more severe lesions overestimated
- 2D representation of a complex, eccentric lesion with length and angulation!
- What is the real reference vessel?
- These errors: mostly in lesions between around 30-80%!

Why do we need physiology?

- 2-D angiograms fail to provide enough information.





- In a study of patients with LMCA stenoses (n=51), 4 experienced cardiologists achieved correct lesion classification **no more than 50% of the time** using angio when comparing to FFR as the gold standard.

Lindstaedt et al, Int J Cardiol 2007; 120(21): 254-261


What proportion of patients in your lab benefit from the stents that they receive?

Coronary angiography

- Remains the road map
  - But not the gold standard!
  - Has limited value to determine which lesions are associated with ischaemia
  - Has unacceptable inter and intra observer variability in assessing lesion significance.
  - Despite this: Many trials have used angio as the gold standard when testing the benefits of revascularisation!

FFR

- Developed to investigate the functional significance of a coronary artery stenosis
- The gold standard for the detection of myocardial ischemia related to a particular stenosis
- It should be a routinely available diagnostic tool
  - Relatively cheap
  - Quick, safe, easy to perform
  - Immediate results for decision making
  - Saves much unnecessary revascularisation
  - Allows better patient outcomes

FFR

- ‘maximal achievable blood flow to a myocardial territory in the presence of an epicardial coronary stenosis expressed as a ratio to the normal maximal achievable blood flow to that same myocardial territory in the hypothetical situation that the supplying artery were completely normal’
- FFR expresses maximal blood flow in the presence of a stenosis as a fraction of normal maximum blood flow

Background

- Exercise tolerance in stable coronary artery disease determined by the maximal amount of myocardial blood flow during exercise
  - Maximal flow the most important parameter to quantify severity of CAD
  - Expressing ml/min meaningless: varies according to territory size
  - So flow in disease should be expressed as a proportion of normal flow

FFR

- FFR wires measure pressure
- During maximal hyperaemia, myocardial perfusion pressure is directly proportional to myocardial flow so the ratio of maximum stenotic flow to normal maximum flow can be expressed as the ratio of distal coronary pressure to aortic pressure at hyperaemia (full vasodilation)

Background

- FFR normal value is 1.0 for every artery
- Takes into account extent of perfusion area, presence of collaterals
- Clear threshold value and a narrow grey zone of 0.75-0.8
- Very suitable tool for making decisions

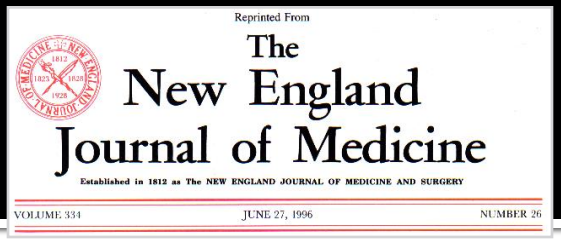
Practical consideration

- Sensor 30mm back from the tip of 0.014 wire
- Connector to measuring system
  - On demand, plug and play
  - Wireless
- Need to ensure epicardial vessels and microvasculature fully dilated
  - IC nitro
  - Adenosine – bolus (or infusion)
    - 40-80 mics

Summary: special features

- Unequivocal normal value
- Well defined cut off
- Independent of heart rate, BP, myocardial contractility
- Takes into account collateral flow and viability
- Don’t need a normal coronary to compare with
- Highly reproducible and easily obtainable.

1996 NEJM Article



MEASUREMENT OF FRACTIONAL FLOW RESERVE TO ASSESS THE FUNCTIONAL SEVERITY OF CORONARY-ARTERY STENOSES

NICO H.J. PIJLS, M.D., PH.D., BERNARD DE BRUYNE, M.D., KATHINKA PEELS, M.D., PEPIJN H. VAN DER VOORT, M.D., HANS J.R.M. BONNIER, M.D., PH.D., JOZEF BARTUNEK, M.D., AND JACQUES J. KOOLEN, M.D., PH.D.

Abstract *Background.* The clinical significance of coronary-artery stenoses of moderate severity can be difficult to determine. Myocardial fractional flow reserve (FFR) is a new index of the functional severity of coronary stenoses that is calculated from pressure measurements made during coronary arteriography. We compared this index with the results of noninvasive tests commonly used to detect myocardial ischemia, to determine the usefulness of the index.

Methods. In 45 consecutive patients with moderate coronary stenosis and chest pain of uncertain origin, we performed bicycle exercise testing, thallium scintigraphy, stress echocardiography with dobutamine, and quantitative coronary arteriography and compared the results with measurements of FFR.

Results. In all 21 patients with an FFR of less than 0.75, reversible myocardial ischemia was demonstrated unequivocally on at least one noninvasive test. After coronary angioplasty or bypass surgery was performed, all the positive test results reverted to normal. In contrast, 21 of the 24 patients with an FFR of 0.75 or higher tested negative for reversible myocardial ischemia on all the noninvasive tests. No revascularization procedures were performed in these patients, and none were required during 14 months of follow-up. The sensitivity of FFR in the identification of reversible ischemia was 88 percent, the specificity 100 percent, the positive predictive value 100 percent, the negative predictive value 88 percent, and the accuracy 93 percent.

Conclusions. In patients with coronary stenosis of moderate severity, FFR appears to be a useful index of the functional severity of the stenoses and the need for coronary revascularization. (N Engl J Med 1996;334:1703-8.)

$FFR = P_{dist} / P_{aorta} < 0.75$ significant

$FFR = P_{dist} / P_{aorta} \geq 0.75$ non-significant

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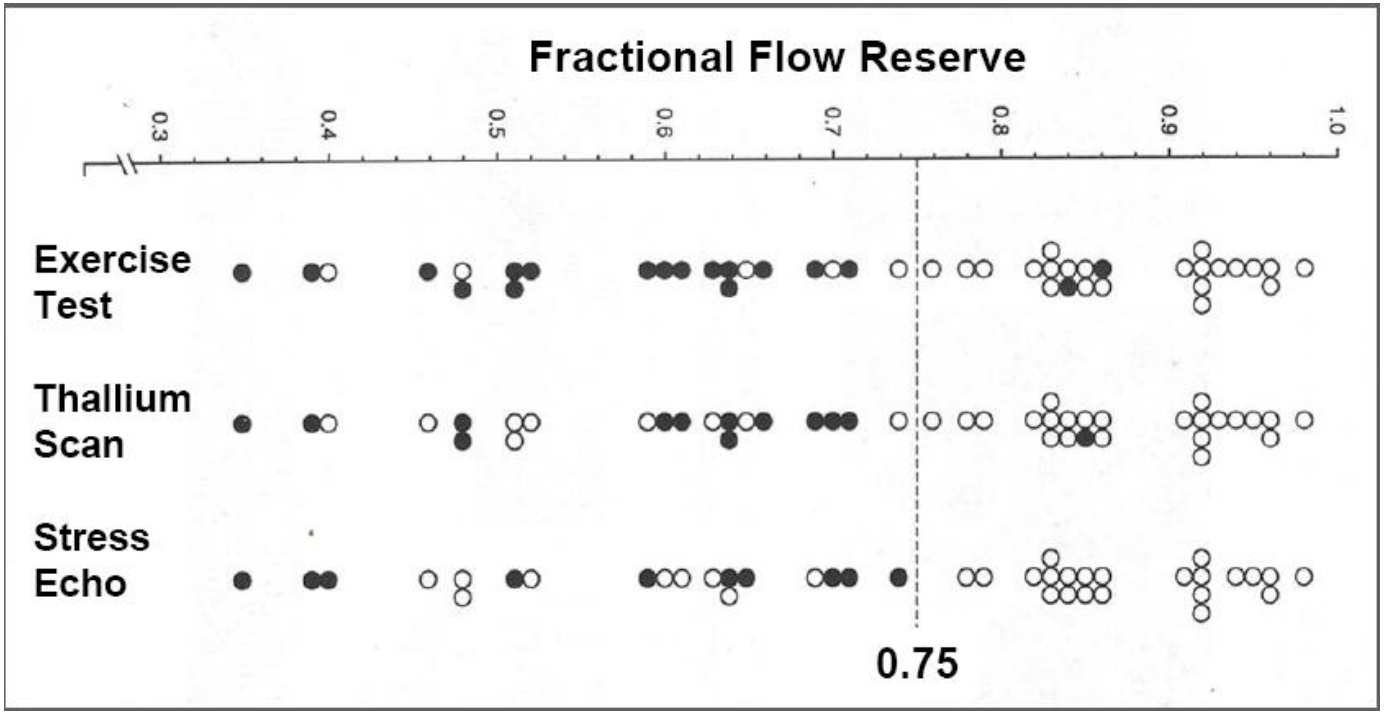
VOLUME 334 JUNE 27, 1996 NUMBER 26



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

Pijls, et al. New England Journal of Medicine 1996; 334:1703

Circulation (2001)

DEFER Trial

Prospective, randomized, multi-center trial (14 centers) in 325 patients with stable chest pain and an intermediate stenosis without objective evidence of ischemia…

Objective:

- *test safety of deferring PCI of stenoses not responsible for inducible ischemia as indicated by FFR > 0.75* ("outcome")
- *to compare* quality of life *in such patients, whether or not treated by PCI (CCS-class need for anti anginal drugs)* ("symptoms")

Bech GJW, De Bruyne B, Pijls NHJ, Muinck E, Hoorntje JCA, Escaned J, Stella P, Boersma E, Bartunek J, Koolen JJ, Wijns W. (2001). Fractional Flow Reserve to Determine the Appropriateness of Angioplasty in Moderate Cornonary Stenosis, A Randomized Trial. *Ciruclation* 103:2928-2934.

Fractional Flow Reserve to Determine the Appropriateness of Angioplasty in Moderate Coronary Stenosis

A Randomized Trial

G. Jan Willem Bech, MD; Bernard De Bruyne, MD, PhD; Nico H.J. Pijls, MD, PhD; Ebo D. de Muinck, MD, PhD; Jan C.A. Hoorntje, MD, PhD; Javier Escaned, MD, PhD; Pieter R. Stella, MD; Eric Boersma, MSc, PhD; Jozef Bartunek, MD, PhD; Jacques J. Koolen, MD, PhD; William Wijns, MD, PhD

Background—PTCA of a coronary stenosis without documented ischemia at noninvasive stress testing is often performed, but its benefit is unproven. Coronary pressure–derived fractional flow reserve (FFR) is an invasive index of stenosis severity that is a reliable substitute for noninvasive stress testing. A value of 0.75 identifies stenoses with hemodynamic significance.

Methods and Results—In 325 patients for whom PTCA was planned and who did not have documented ischemia, FFR of the stenosis was measured. If FFR was >0.75, patients were randomly assigned to deferral (deferral group; n=91) or performance (performance group; n=90) of PTCA. If FFR was <0.75, PTCA was performed as planned (reference group; n=144). Clinical follow-up was obtained at 1, 3, 6, 12, and 24 months. Event-free survival was similar between the deferral and performance groups (92% versus 89% at 12 months and 89% versus 83% at 24 months) but was significantly lower in the reference group (80% at 12 months and 78% at 24 months). In addition, the percentage of patients free from angina was similar between the deferral and performance groups (49% versus 50% at 12 months and 70% versus 51% at 24 months) but was significantly higher in the reference group (67% at 12 and 80% at 24 months).

Conclusions—In patients with a coronary stenosis without evidence of ischemia, coronary pressure–derived FFR identifies those who will benefit from PTCA. (***Circulation***. **2001;103:2928-2934.**)

Key Words: coronary disease ■ angioplasty ■ pressure ■ blood flow

In patients with chest pain and a coronary stenosis at angiography, revascularization is warranted if objective evidence of reversible ischemia is present and medical therapy fails.[1] Yet, PTCA is often recommended solely on the basis of the angiogram, although noninvasive testing for reversible ischemia is either negative, equivocal, or not performed at all.[2] In such patients, it is unclear whether the chest pain must be attributed to the coronary stenosis and whether PTCA improves event-free survival or functional class.[3] Fractional flow reserve (FFR) is an invasive index of the functional severity of a stenosis determined from coronary pressure measurement during cardiac catheterization. FFR expresses maximum achievable blood flow to the myocardium supplied by a stenotic artery as a fraction of normal maximum flow. Its normal value is 1.0, and a value of 0.75 reliably identifies stenoses associated with inducible ischemia. The diagnostic accuracy of FFR for that purpose is >90%, which is higher than for any other invasive or noninvasive test.[3–7]

See p 2873

Retrospective studies suggest that deferral of angioplasty in patients with FFR >0.75 is safe and results in an excellent clinical outcome.[6,8] This has never been investigated, however, in a prospective study. Therefore, the present randomized study was undertaken in patients referred for PTCA without documented ischemia to investigate whether FFR discriminates patients in whom PTCA is appropriate from those in whom it is not.

Methods

Selection of Patients

Patients were eligible if they were referred for elective PTCA of an angiographically significant de novo stenosis (>50% diameter stenosis by visual assessment) in a native coronary artery with a reference diameter >2.5 mm and if no evidence of reversible ischemia had been documented by noninvasive testing within the previous 2 months. Noninvasive tests were either negative, incon-

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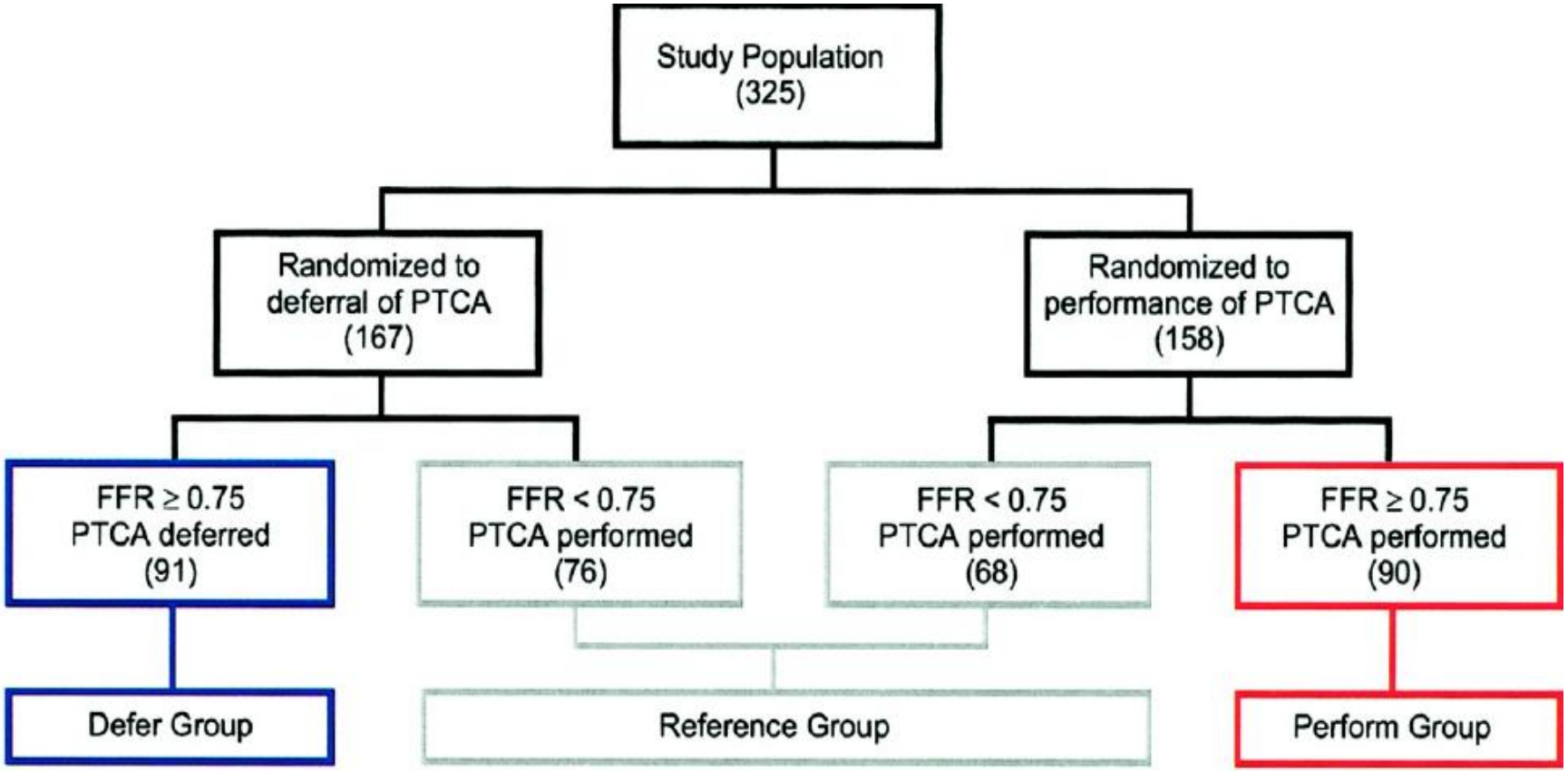
From the Catharina Hospital, Eindhoven, the Netherlands (G.J.W.B., N.H.J.P., E.B., J.J.K.); Cardiovascular Center, Aalst, Belgium (B.D.B, J.B., W.W.); Academic Hospital, Maastricht, the Netherlands (E.D.d.M.); Isala Clinics, Zwolle, the Netherlands (J.C.A.H.); Academic Hospital, Utrecht, the Netherlands (P.R.S.); and Hospital Universitario San Carlos, Madrid, Spain (J.E.).
Correspondence to Nico H.J. Pijls, MD, PhD, Catharina Hospital, Department of Cardiology, PO Box 1350, 5602 ZA Eindhoven, The Netherlands. E-mail Nico.Pijls@inter nl.net

Circulation is available at http://www.circulationaha.org

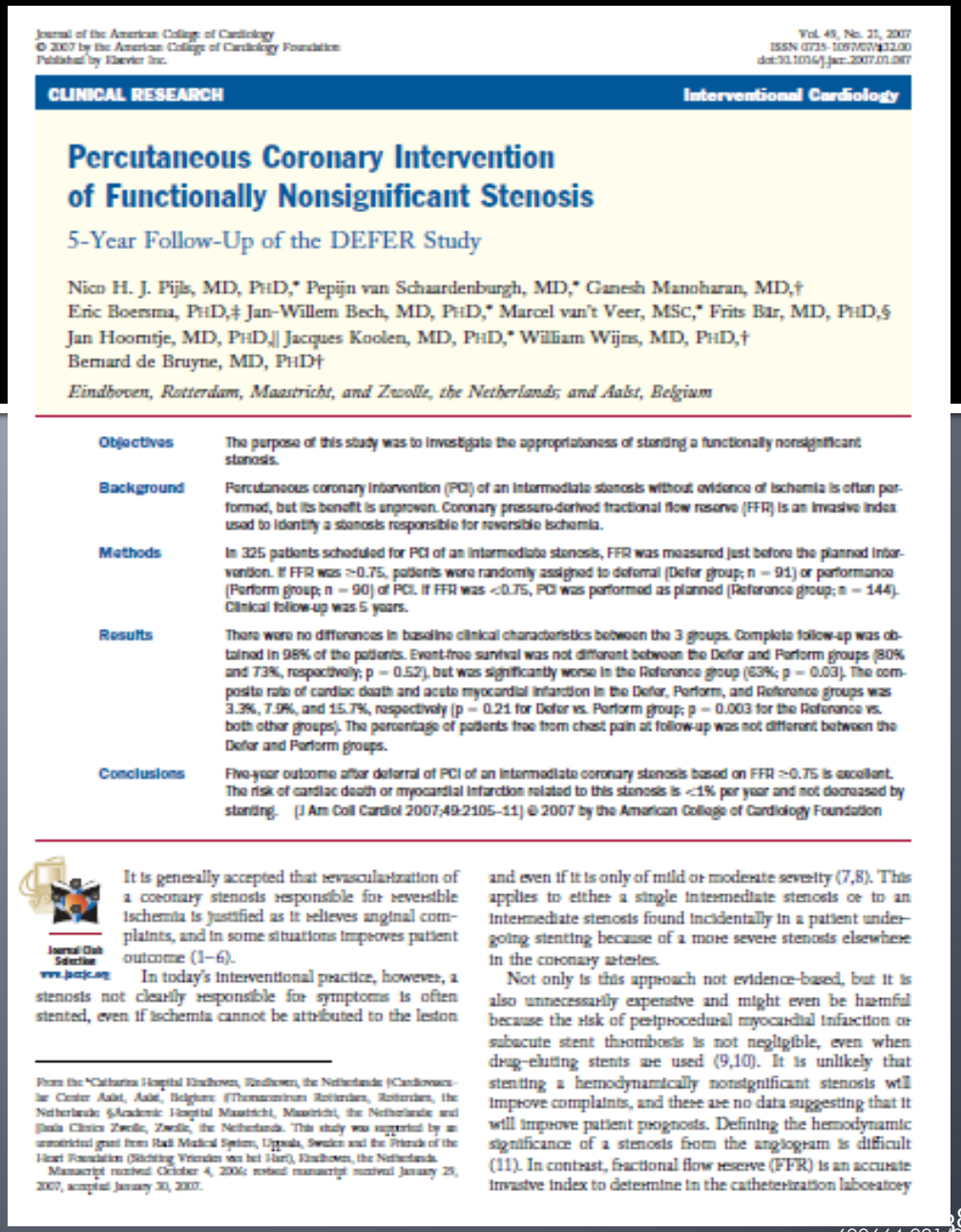
Defer Trial Design



Bech, et al. Circulation 2001; 103:2928-2934

JACC (2007)

5-Year DEFER Data



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Percutaneous Coronary Intervention of Functionally Nonsignificant Stenosis

5-Year Follow-Up of the DEFER Study

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Eindhoven, Rotterdam, Maastricht, and Zwolle, the Netherlands; and Aalst, Belgium

Objectives The purpose of this study was to investigate the appropriateness of stenting a functionally nonsignificant stenosis.

Background Percutaneous coronary intervention (PCI) of an intermediate stenosis without evidence of ischemia is often performed, but its benefit is unproven. Coronary pressure-derived fractional flow reserve (FFR) is an invasive index used to identify a stenosis responsible for reversible ischemia.

Methods In 325 patients scheduled for PCI of an intermediate stenosis, FFR was measured just before the planned intervention. If FFR was ≥0.75, patients were randomly assigned to deferral (Defer group; n = 91) or performance (Perform group; n = 90) of PCI. If FFR was <0.75, PCI was performed as planned (Reference group; n = 144). Clinical follow-up was 5 years.

Results There were no differences in baseline clinical characteristics between the 3 groups. Complete follow-up was obtained in 98% of the patients. Event-free survival was not different between the Defer and Perform groups (80% and 73%, respectively; p = 0.52), but was significantly worse in the Reference group (63%; p = 0.03). The composite rate of cardiac death and acute myocardial infarction in the Defer, Perform, and Reference groups was 3.3%, 7.9%, and 15.7%, respectively (p = 0.21 for Defer vs. Perform group; p = 0.003 for the Reference vs. both other groups). The percentage of patients free from chest pain at follow-up was not different between the Defer and Perform groups.

Conclusions Five-year outcome after deferral of PCI of an intermediate coronary stenosis based on FFR ≥0.75 is excellent. The risk of cardiac death or myocardial infarction related to this stenosis is <1% per year and not decreased by stenting. (J Am Coll Cardiol 2007;49:2105–11) © 2007 by the American College of Cardiology Foundation

Journal Club Selection
www.jacjc.org

It is generally accepted that revascularization of a coronary stenosis responsible for reversible ischemia is justified as it relieves anginal complaints, and in some situations improves patient outcome (1–6).

In today's interventional practice, however, a stenosis not clearly responsible for symptoms is often stented, even if ischemia cannot be attributed to the lesion and even if it is only of mild or moderate severity (7,8). This applies to either a single intermediate stenosis or to an intermediate stenosis found incidentally in a patient undergoing stenting because of a more severe stenosis elsewhere in the coronary arteries.

Not only is this approach not evidence-based, but it is also unnecessarily expensive and might even be harmful because the risk of periprocedural myocardial infarction or subacute stent thrombosis is not negligible, even when drug-eluting stents are used (9,10). It is unlikely that stenting a hemodynamically nonsignificant stenosis will improve complaints, and there are no data suggesting that it will improve patient prognosis. Defining the hemodynamic significance of a stenosis from the angiogram is difficult (11). In contrast, fractional flow reserve (FFR) is an accurate invasive index to determine in the catheterization laboratory

From the *Catharina Hospital Eindhoven, Eindhoven, the Netherlands; †Cardiovascular Center Aalst, Aalst, Belgium; ‡Thoraxcentrum Rotterdam, Rotterdam, the Netherlands; §Academic Hospital Maastricht, Maastricht, the Netherlands; and ‖Isala Clinics Zwolle, Zwolle, the Netherlands. This study was supported by an unrestricted grant from Radi Medical System, Uppsala, Sweden and the Friends of the Heart Foundation (Stichting Vrienden van het Hart), Eindhoven, the Netherlands.

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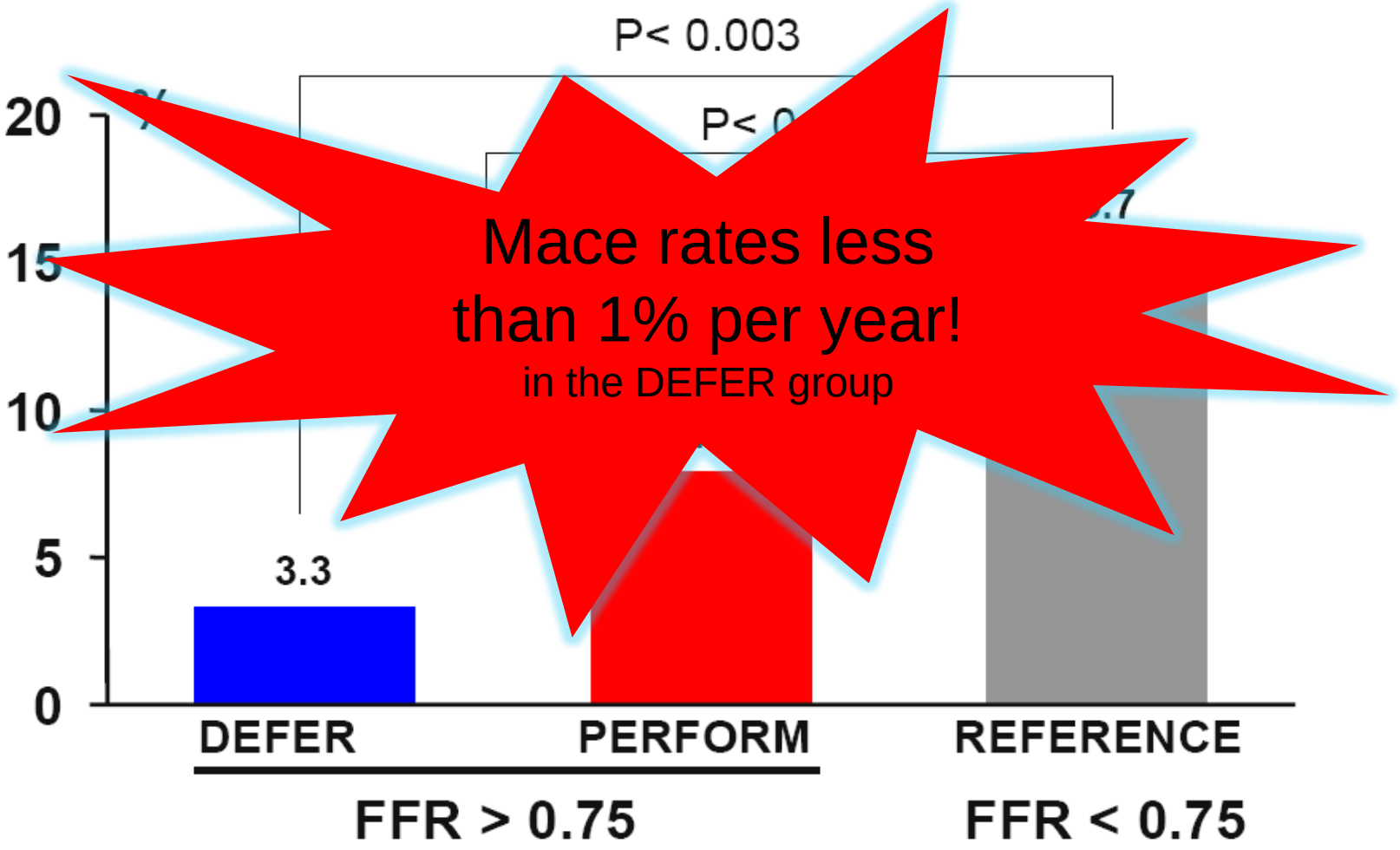
Pijls NHJ, Schaardenburgh P, Manoharan G, Boersma E, Bech JW, Veer M, Bar F, Hoorntje J, Koolen J, Wijns W, De Bruyne B. (2007). Percutaneous Coronary Intervention of Functionally Nonsignificant Stenosis: 5-Year Follow-Up of the DEFER Study. *Journal of the American College of Cardiology*. Volume 49, Number 21:2105-2111.

Defer: 5 Year Cardiac Death and MI



Pijls, et al. JACC 2007

FAME – one year results

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Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention

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FAME Study Design

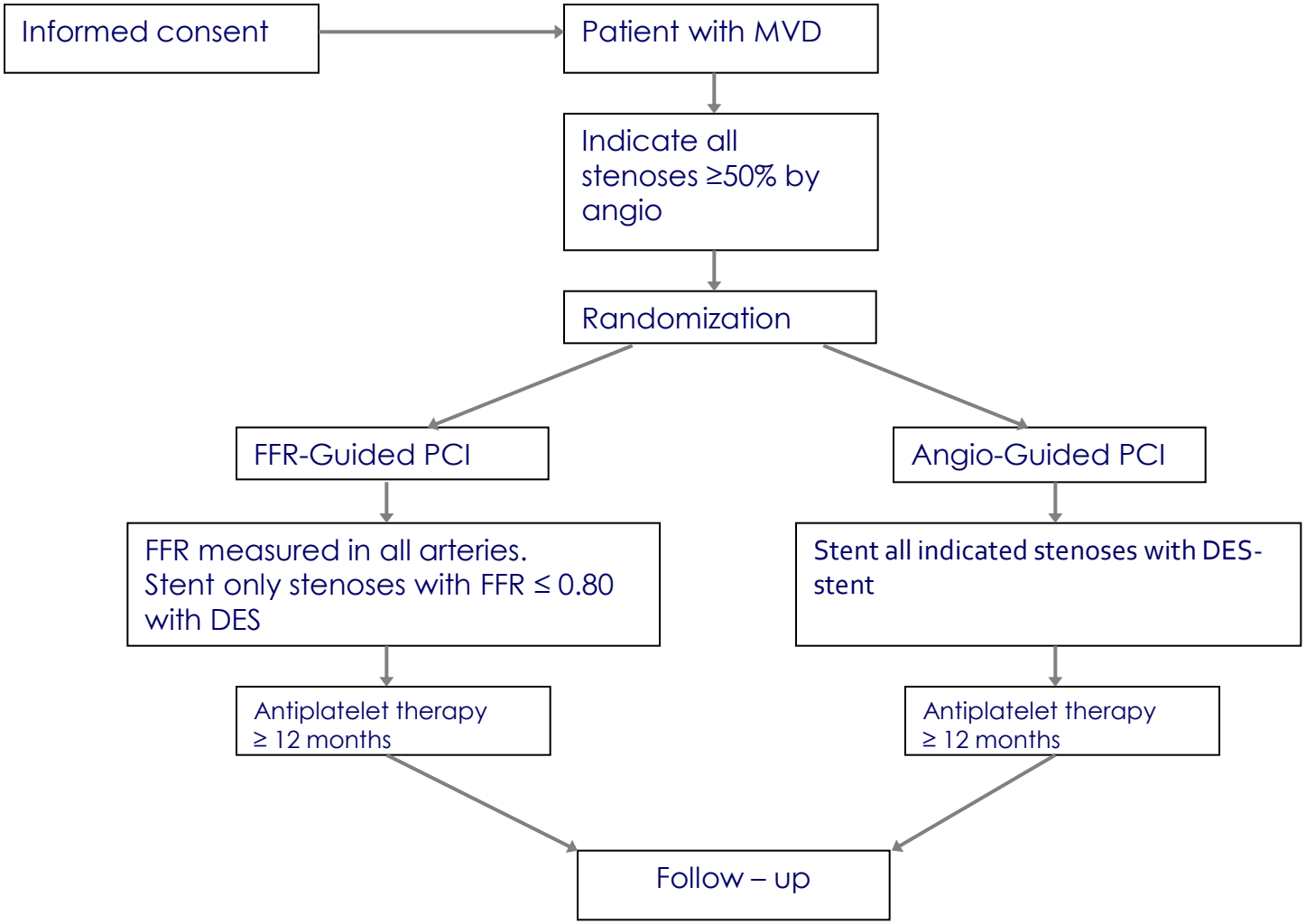


Chart courtesy Dr. Pijls and FAME investigators as presented at TCT 2008

FAME Study Population

- 1005 patients – randomized into 2 groups
  - Angio-guided PCI: Stent all lesions with >50% stenosis (n = 496)
  - FFR-guided PCI: Stent all lesions with FFR <0.80 (n = 509)

Key Inclusion Criteria

- At least two ≥50% diameter stenoses in at least two major epicardial vessels

Key Exclusion Criteria

- LM disease
- Previous CABG
- Recent (<5 days) MI patient if peak CK >1000 units per liter
- Extremely tortuous or calcified vessels

Fearon et al. (2009). Fractional Flow Reserve Versus Angiography for Guiding Percutaneous Coronary Intervention. *New England Journal of Medicine*. Volume 360, Number 3:213-224.

Procedural Results

	ANGIO-Group n = 496	FFR-Group n = 509	P-value
Mean # of Indicated Lesions per Patient	2.7 ± 0.9	2.8 ± 1.0	0.34
FFR results			
Lesions successfully measured (%)	-	1329 (98%)	-
Lesions with FFR ≤ 0.80 (%)	-	874 (63%)	-
Lesions with FFR > 0.80 (%)	-	513 (37%)	-
Stents per patient	2.7 ± 1.2	1.9 ± 1.3	<0.001
Lesions successfully stented (%)	92%	94%	-
Total DES	1359	980	-

★ **FFR-guided group used 0.8 less stents per patient!**

Fearon et al. (2009). Fractional Flow Reserve Versus Angiography for Guiding Percutaneous Coronary Intervention. *New England Journal of Medicine*. Volume 360, Number 3:213-224.

Procedural Results

	ANGIO-Group n = 496	FFR-Group n = 509	P-value
Procedure time, min	70 ± 44	71 ± 43	0.51
Contrast agent used, mL	302 ± 127	272 ± 133	<0.001
Material cost during procedure, USD	$6007	$5332	<0.001
Length of hospital stay, days	3.7 ± 3.5	3.4 ± 3.3	0.05

- ★ FFR-guided group used less contrast while reducing material costs by $675 per patient!
- ★ Using FFR does not increase procedure time.
- ★ Hospital stay per patient was reduced by 0.3 days.

Fearon et al. (2009). Fractional Flow Reserve Versus Angiography for Guiding Percutaneous Coronary Intervention. *New England Journal of Medicine*. Volume 360, Number 3:213-224.

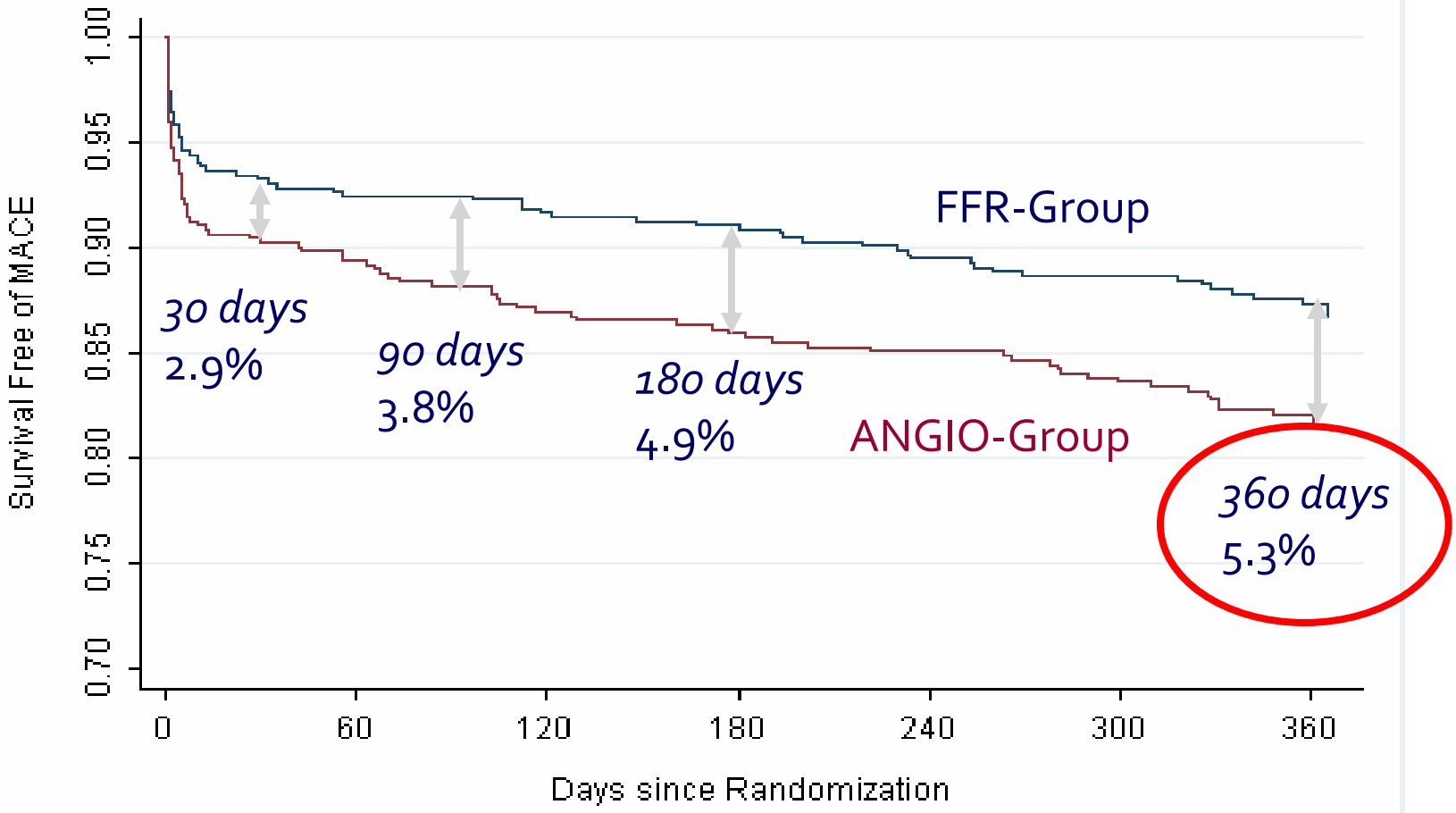
Patient Outcomes

	ANGIO-Group n = 496	FFR-Group n = 509	P-value
Events at 1 year, # (%)			
Death, MI, CABG, or repeat-PCI	91 (18.4)	67 (13.2)	0.02
Death	15 (3.0)	9 (1.8)	0.19
Death or MI	55 (11.1)	37 (7.3)	0.04
CABG or repeat PCI	47 (9.5)	33 (6.5)	0.08
Total # of MACE	113	76	0.02

- ★ MACE rates in the FFR-guided group are 28% lower than the Angio-guided group!
- ★ Death or MI in the FFR-guided group is 34% lower than in the Angio-guided group!

Fearon et al. (2009). Fractional Flow Reserve Versus Angiography for Guiding Percutaneous Coronary Intervention. *New England Journal of Medicine*. Volume 360, Number 3:213-224.

MACE-Free Survival Rates



Fearon et al. (2009). Fractional Flow Reserve Versus Angiography for Guiding Percutaneous Coronary Intervention. *New England Journal of Medicine*. Volume 360, Number 3:213-224.

Recap of Key Points from FAME

1. FFR-guided PCI in MVD provides outcomes equal to or better than Angio-guided PCI
   - ★ **MACE rates in the FFR-guided group are 28% lower!**
   - ★ **Death & MI in the FFR-guided group is 34% lower!**

2. FFR-guided PCI results in a functional class (symptoms) equal to or better than angio-guided PCI
   - ★ **Functional class between the two study groups are similar. FFR lowers adverse events while delivering functionally complete revascularization.**

3. FFR-guided PCI is more cost effective for the hospital than is angio-guided PCI
   - ★ **FFR-guided group used 0.8 less stents per patient!**
   - ★ **FFR-guided group used less contrast per procedure**
   - ★ **FFR-guided procedures' direct costs were $675 less per patient!**
   - ★ **Using FFR in MVD does not increase procedure time.**
   - ★ **Hospital stay per patient was reduced by 0.3 days.**

Fearon et al. (2009). Fractional Flow Reserve Versus Angiography for Guiding Percutaneous Coronary Intervention. *New England Journal of Medicine*. Volume 360, Number 3:213-224.

FAME 2

- To compare outcomes in ischemia-guided PCI with medical therapy
- Single or multivessel stable IHD
- Stopped early: highly significant difference, favouring PCI, in patients randomized to PCI
  - Primary endpoint: death/MI/urgent revasc
  - Greater need for urgent revasc: 11% vs 1.6%

FFR

- FFR is one of those rare instances in medicine where a new technology not only improves outcome, but saves resources

One other thing…

- In Fame:
  - QCA 50-70% stenosis: only 35% significant
  - QCA 71-90% stenosis: 20% NOT significant
- 'Functional syntax score' may change '3VCAD' for CABG to '2V disease for PCI'
- FFR is the preferred technique for evaluating intermediate LMS lesions.
- Valid for culprit and non culprits in NSTEMI, and most non culprits in STEMI
- NOT for culprit, acute, in STEMI

Any problems?

- The accuracy depends exquisitely on the ability to induce maximal hyperaemia
- FFR is overestimated in the presence of high LVEDP
  - Thus not appropriate in decompensated STEMI to assess other vessels!
- Where to stent in serial focal lesions/diffuse disease?
- Not yet enough data regarding the effect of revascularisation/medical therapy on post treatment FFR!

Wijns and Pixaras, JACC Intervention, vol 6 no 3 2013

Take home?

- Understand it
- Use it, routinely
- Trust your results, and act accordingly

- Your patients will benefit
- And you will save money

But there is more!!!

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EDITORIAL COMMENT

An Adenosine-Independent Index of Stenosis Severity From Coronary Wave–Intensity Analysis

A New Paradigm in Coronary Physiology for the Cath Lab?*

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Long Beach, California

More than 15 years ago, Nico Pijls, from Eindhoven, the Netherlands, conceived, and, along with Bernard De Bruyne from Aalst, Belgium and others, developed and tested the fractional flow reserve (FFR) concept (1–3). They are to be credited for one of the most important advances in the diagnosis and treatment of coronary artery disease in the percutaneous coronary intervention (PCI) era. The current paradigm of FFR revolutionized coronary physiology and translated directly to the practical in-lab functional assessment of coronary stenosis in patients before and during PCI.

the lower cost of achieving such outcomes (8), the use of FFR in the interventional community at large is <10% of PCI procedures performed in the absence of appropriate clinical evidence and at times in contravention to guideline recommendations (9,10). Why is the use of FFR less than what one would expect for such a strongly supported in-lab measure of ischemia, a measurement that is particularly helpful, if not critical, when uncertainty exists regarding the "treat/not treat" decision? The barriers to FFR adoption, as discussed previously (11), involve concerns regarding the perceived increased procedure time and cost, physician reimbursement, uncertainty about the technique or data, and the cumbersome requirement of adenosine with complaints about dose, route of administration, femoral venous access, and achievement of maximal hyperemia.

Motivated by both science and practicality, Sen et al. (12) now present a novel concept, the instantaneous wave-free pressure ratio (iFR), using and expanding on the tenets of FFR. iFR, an index of stenosis severity, is based on the instantaneous ratio of translesional pressures acquired during a specific period of diastole in which the coronary microcirculatory resistance is constant and minimal, fulfilling the FFR resistance criteria without the need for adenosine hyperemia.

In their most recent and perhaps the most clinically relevant work, Sen et al. (12) identified through their earlier studies of coronary wave–intensity analysis (13) a period of diastole in which an equilibrium or balance between pressure waves from the aorta and distal microcirculatory wave reflections is established; that is, a wave-free period beginning just after the onset of diastole. Importantly, during the wave-free period, the calculated coronary microcirculatory

Physiologic Assessment

- Pressure only indices for lesion assessment

iFR

- 5 beats Resting Physiological

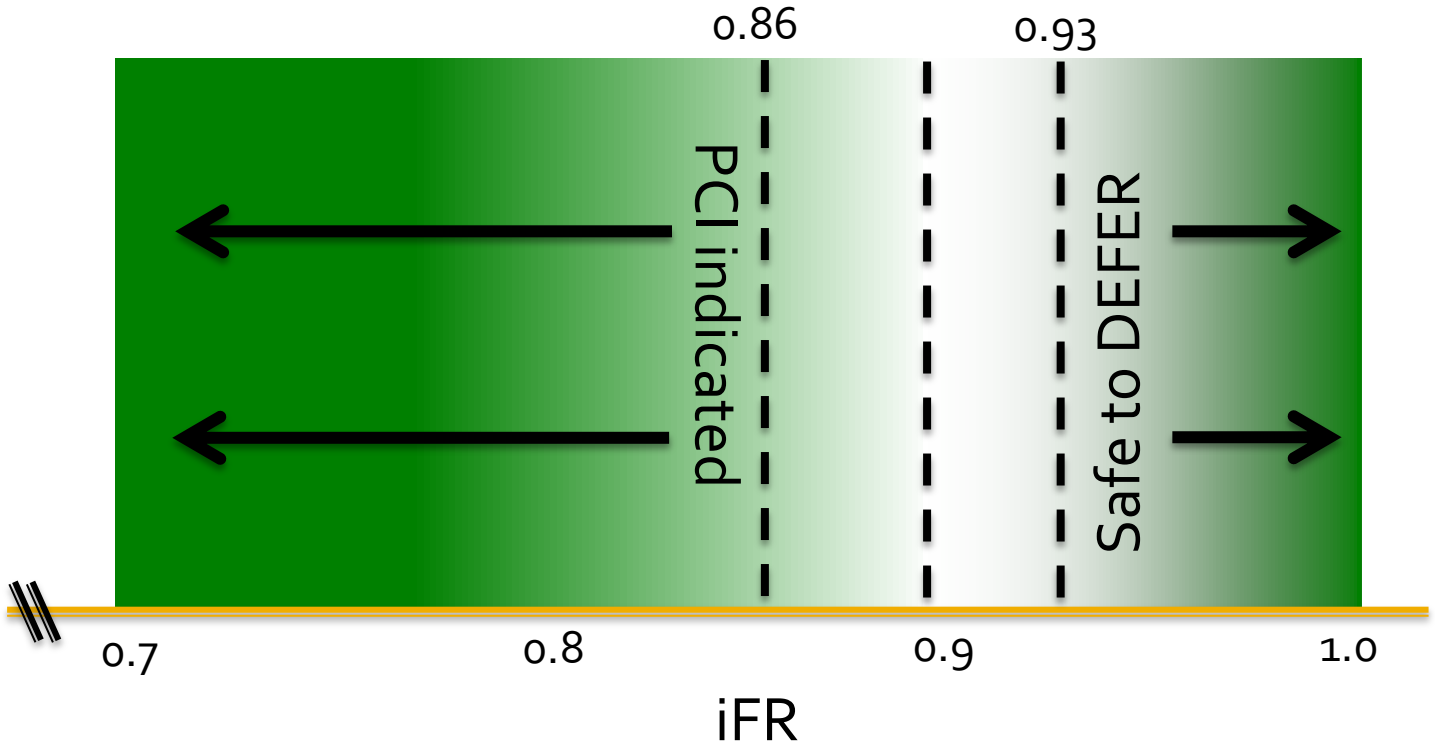
FFR

- At least 1 minute Requires hyperaemia Pharmacological

Physiologic Assessment

95% classification match with FFR

- IFR and FFR: Hybrid Approach



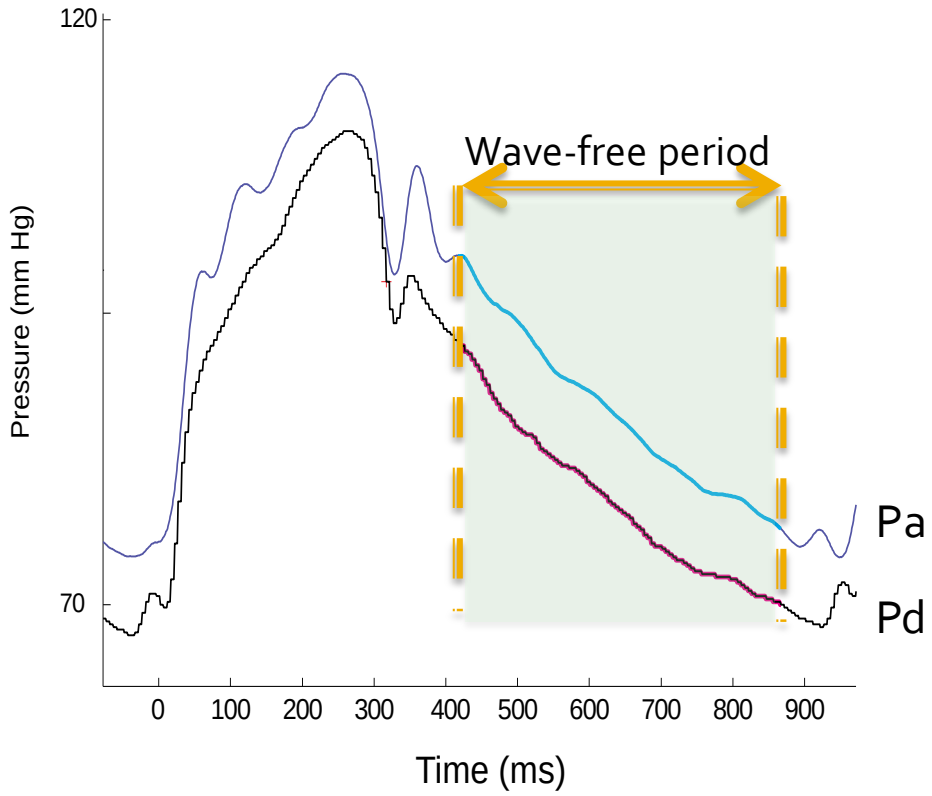
iFR Physiologic Assessment

- Rapid multi-vessel assessment
- Assess multiple points within vessel without requiring long vasodilator infusions
- Assess hemodynamic improvement after coronary intervention

Introduction of the iFR® Modality

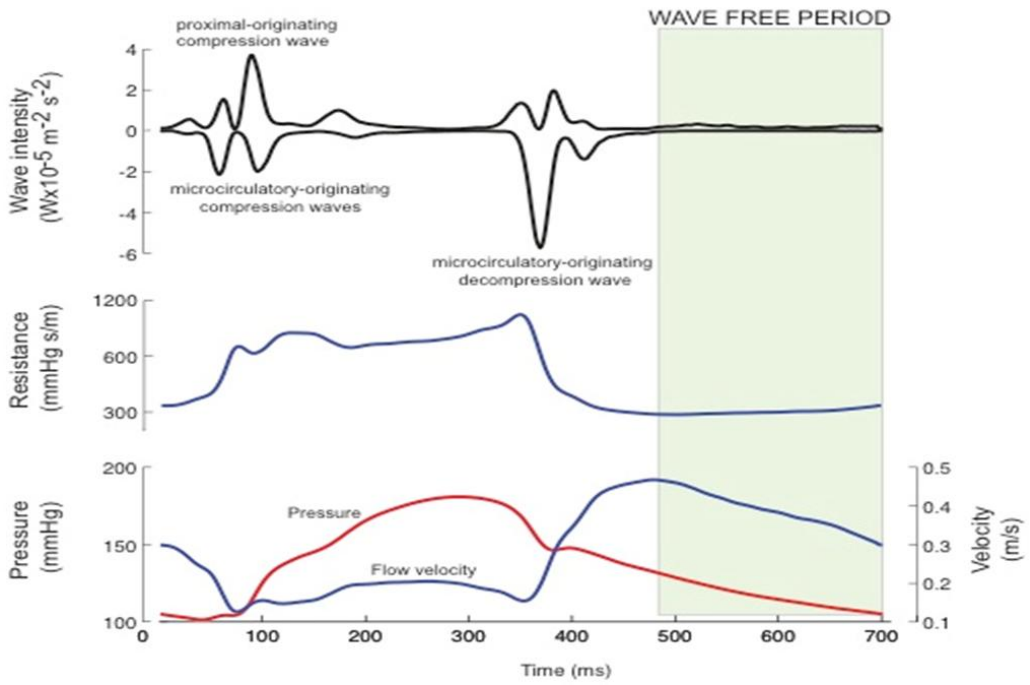
Definition:

Instantaneous pressure ratio, across a stenosis during the wave-free period, when ***resistance is naturally constant*** and minimised in the cardiac cycle



Sen S, *et al.* 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. *J Am Coll Cardiol*. 2012 Apr 10;59(15):1392-402.

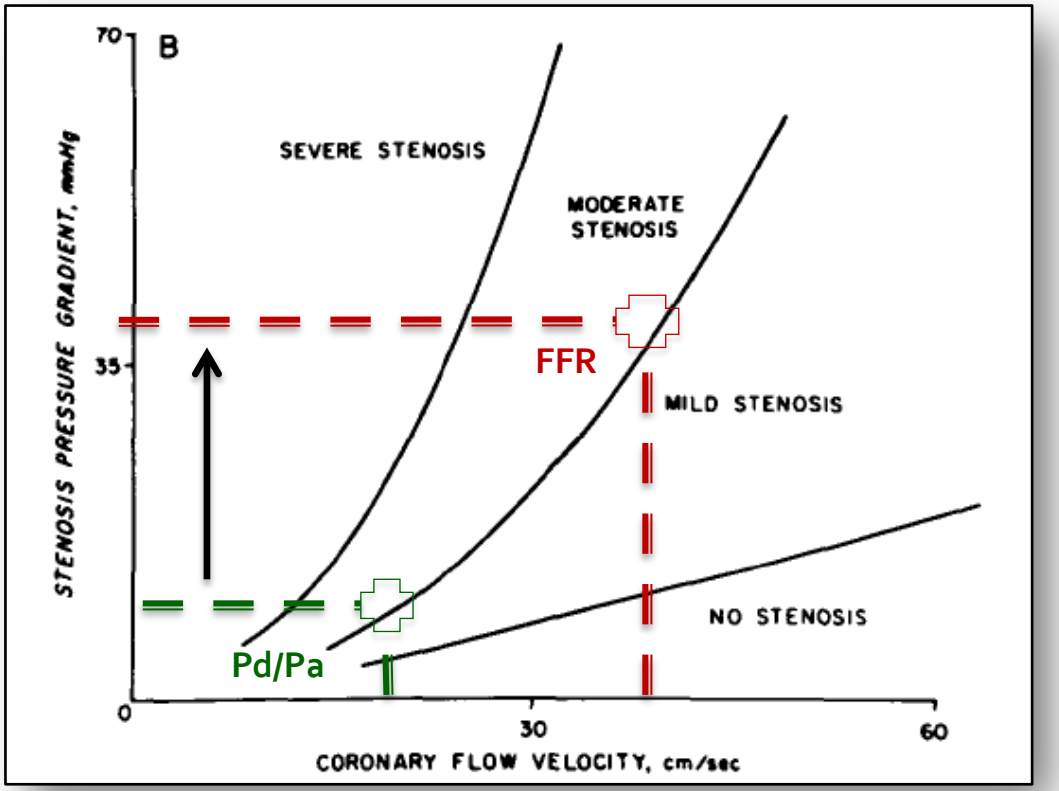
Three Benefits to the iFR® Window



1. Noise from compression and suction waves is minimized
2. Resistance is constant so ΔP is proportional to ΔQ (flow)
3. Velocity is higher so better power to discriminate

Sen S, *et al.* 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. *J Am Coll Cardiol*. 2012 Apr 10;59(15):1392-402.

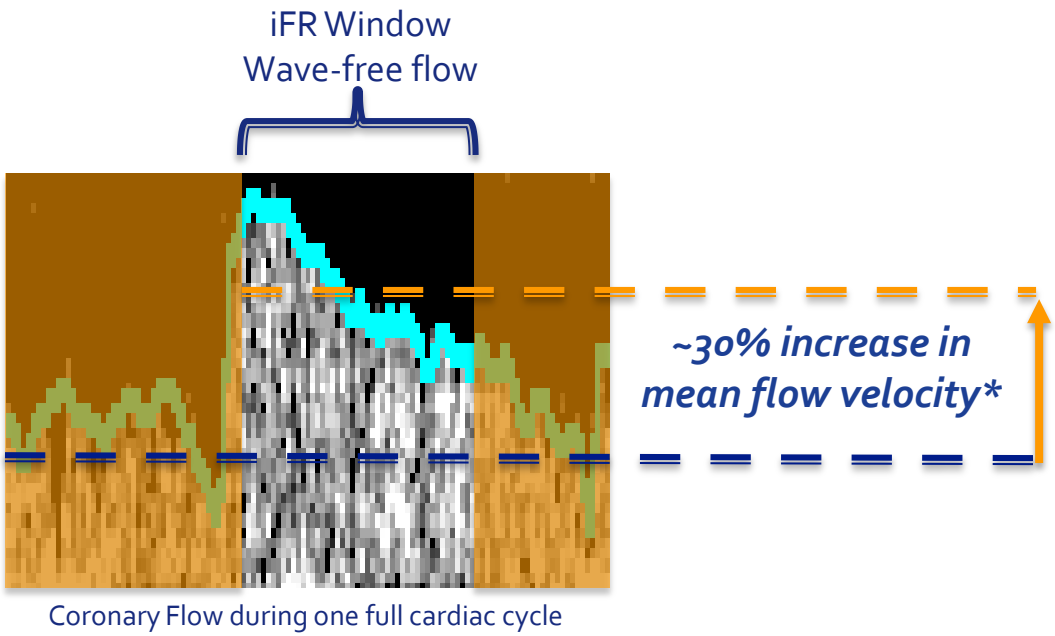
Higher Velocity = Better Classification

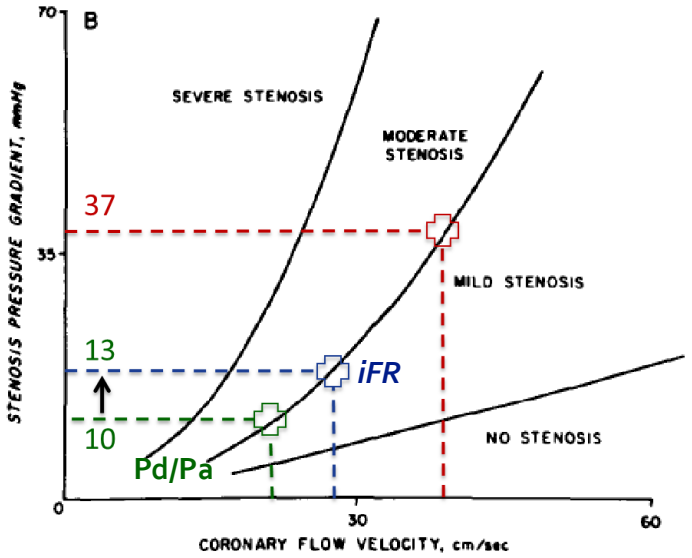


- Increasing Flow Velocity exaggerates the pressure drop across a stenosis
- Bigger pressure drop allows for better classification of stenosis severity

Gould, K. Pressure-flow characteristics of coronary stenoses in unsedated dogs at rest and during coronary vasodilation Circulation research 1978;43:242-253

- iFR Flow is 30% higher which ***amplifies the signal*** vs. Pd/Pa alone





- ***Bigger pressure drop = better classification of stenosis severity***

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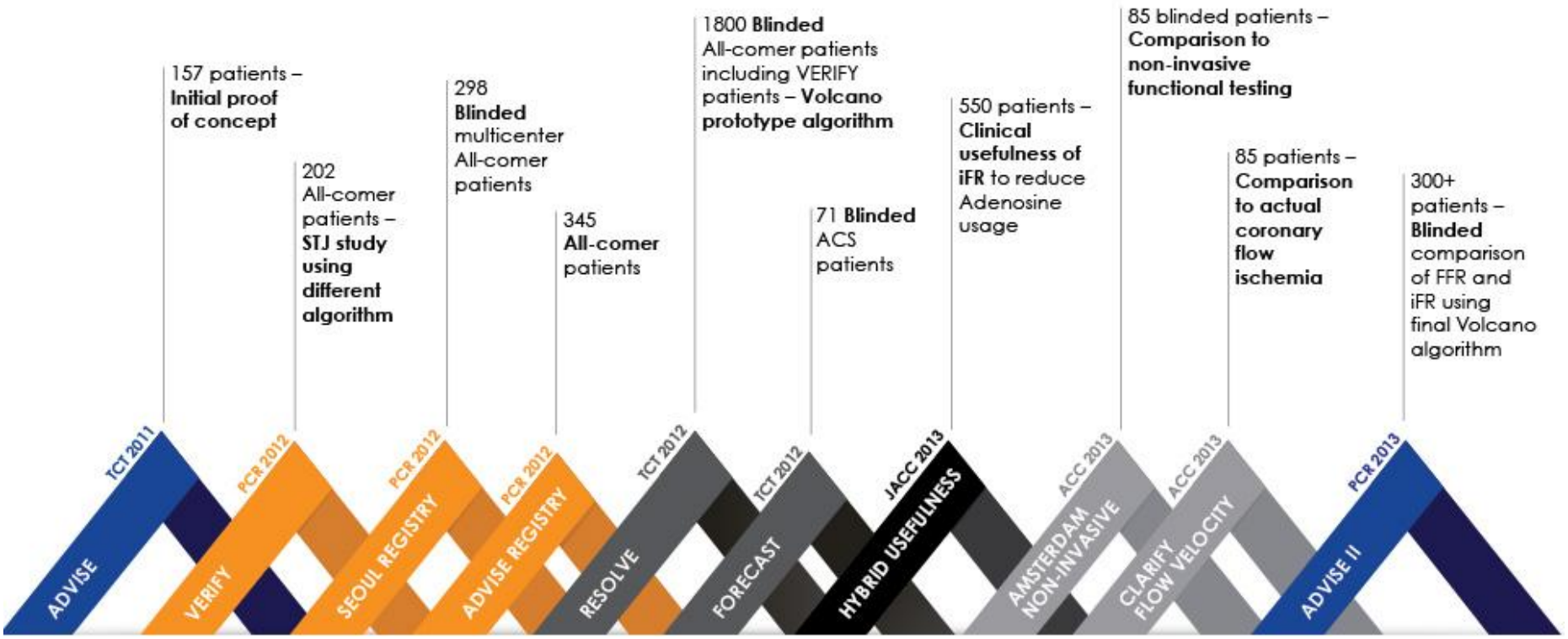
Validated in the Past, Selected for the Future

iFR® (instant wave-Free Ratio™) Clinical Progress



Take home message

- I think it's a severe lesion and so will stent it?
  - This thinking can no longer be justified
- When you are in the lab think physiology:
  - Will this patient benefit from the procedure we are offering?
- Practice makes perfect: with regular routine use physiology assessments become simpler, quicker and no fuss at all!