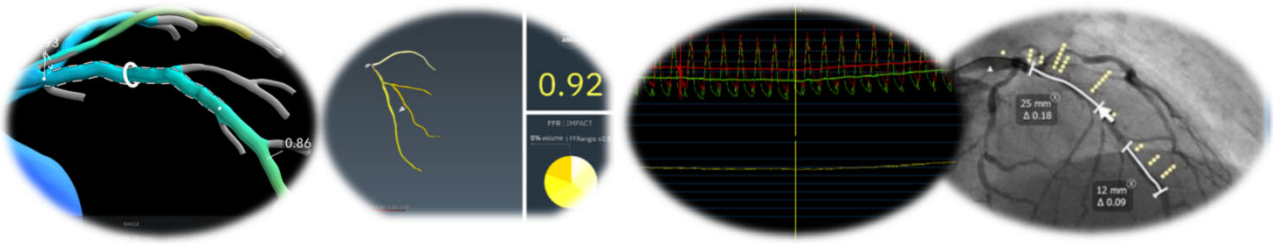
1

Minneapolis Heart Institute Foundation, Cardiovascular Grand Rounds – January 27th, 2025



Modern use of coronary physiology in the CCL

Yader Sandoval, MD, FACC, FSCAI, FESC
Interventional Section, Minneapolis Heart Institute, Abbott Northwestern Hospital
Co-Chairman, Center for Coronary Artery Disease, Minneapolis Heart Institute Foundation.
Adjunct Associate Professor of Medicine, Mayo Clinic College of Medicine and Science

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DISCLOSURES

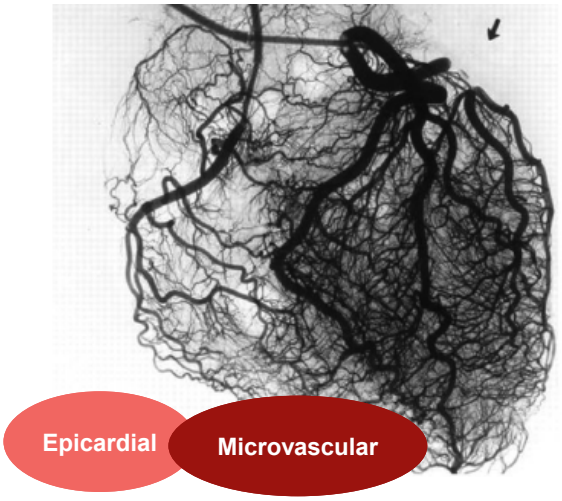
Abbott (consultant, advisory board), CathWorks (consultant, speaker), Cleerly (speaker), GE Healthcare (consultant, advisory board), HeartFlow (consultant, speaker), Medtronic (speaker), Philips (consultant, advisory board, speaker), Roche Diagnostics (consultant, advisory board, speaker), and Zoll (advisory board); owner, Systole LLC. He is an Associate Editor for JACC Advances. He and others hold patent 20210401347.

3

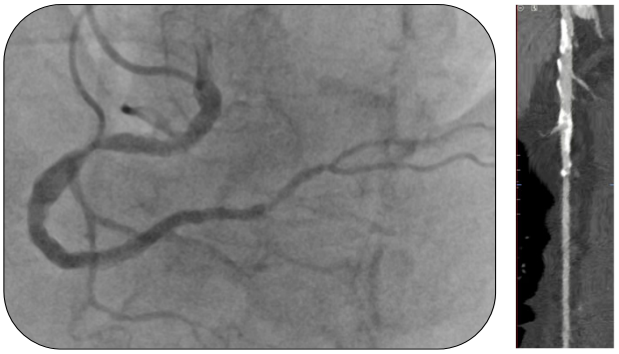
1. Why is coronary physiology relevant?

4

Are the symptoms related to coronary disease ?



Does the lesion warrant revascularization? Defer or treat to improve patient outcomes



2-dimensional representation of a 3-dimensional lumen.
Inter-observer and intra-observer variability, vessel foreshortening, angulations, calcification, eccentricity, vessel overlap, contrast streaming.

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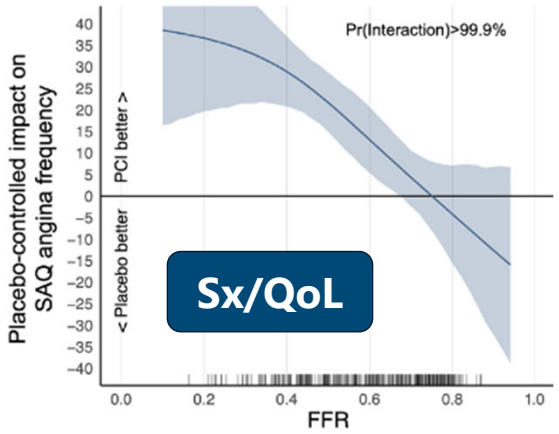
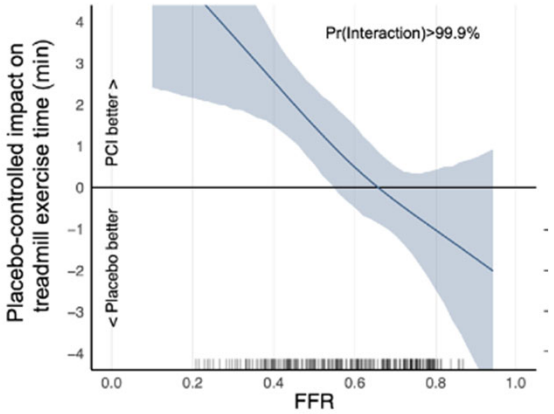
FFR and iFR as Predictors of the Placebo-Controlled Response to PCI in Stable CAD: Lessons from ORBITA-2





Foley MJ, Rajkumar CA, Ahmed-Jushuf F, Simader F, Chotai S, Seligman H, Macierzanka K, Davies JR, Keeble TR, O'Kane P, Haworth P, Routledge H, Kotecha T, Clesham G, Williams R, Din J, Nijjer SS, Curzen N, Sinha M, Petraco R, Spratt J, Sen S, Cole GD, Harrell FE Jr, Howard JP, Francis DP, Shun-Shin MJ, Al-Lamee R; ORBITA-2 Investigators. Fractional Flow Reserve and Instantaneous Wave-Free Ratio as Predictors of the Placebo-Controlled Response to Percutaneous Coronary Intervention in Stable Coronary Artery Disease. Circulation. 2025 Jan 21;151(3):202-214. doi: 10.1161/CIRCULATIONAHA.124.072281. Epub 2024 Oct 27. PMID: 39462291; PMCID: PMC11748910.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Five-Year Outcomes with PCI Guided by Fractional Flow Reserve

P. Xaplanteris, S. Fournier, N.H.J. Pijls, W.F. Fearon, E. Barbato, P.A.L. Tonino, T. Engstrøm, S. Kääb, J.-H. Dambrink, G. Rioufol, G.G. Toth, Z. Piroth, N. Witt, O. Fröbert, P. Kala, A. Linke, N. Jagic, M. Mates, K. Mavromatis, H. Samady, A. Irimpen, K. Oldroyd, G. Campo, M. Rothenbühler, P. Jüni, and B. De Bruyne, for the FAME 2 Investigators*

FAME-2 Five-year outcomes

ABSTRACT

...FR)–guided percutaneous coronary ...al therapy as initial treatment in ...

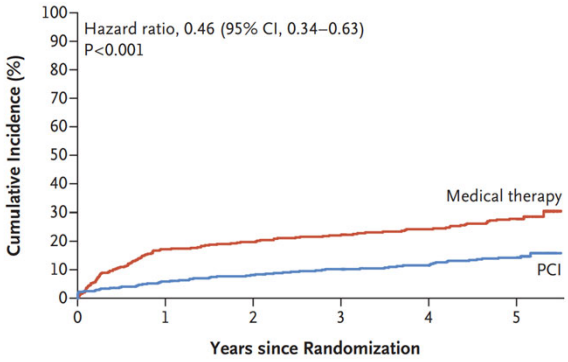
...nificant stenoses, those in whom ...lificant (FFR, ≤0.80) were random- ...erapy or to medical therapy alone. ...more than 0.80 received medical ...rimary end point was a composite ...ecularization.

...tion (447 patients in the PCI group ... 441 in the medical-therapy group). At 5 years, the rate of the primary end point was lower in the PCI group than in the medical-therapy group (13.9% vs. 27.0%; hazard ratio, 0.46; 95% confidence interval [CI], 0.34 to 0.63; P<0.001). The difference was driven by urgent revascularizations, which occurred in 6.3% of the patients in the PCI group as compared with 21.1% of those in the medical-therapy group (hazard ratio, 0.27; 95% CI, 0.18 to 0.41). There were no significant differences between the PCI group and the medical-therapy group in the rates of death (5.1% and 5.2%, respectively; hazard ratio, 0.98; 95% CI, 0.55 to 1.75) or myocardial infarction (8.1% and 12.0%; hazard ratio, 0.66; 95% CI, 0.43 to 1.00). There was no significant difference in the rate of the primary end point between the PCI group and the registry cohort (13.9% and 15.7%, respectively; hazard ratio, 0.88; 95% CI, 0.55 to 1.39). Relief from angina was more pronounced after PCI than after medical therapy.

CONCLUSIONS

In patients with stable coronary artery disease, an initial FFR-guided PCI strategy was associated with a significantly lower rate of the primary composite end point of death, myocardial infarction, or urgent revascularization at 5 years than medical therapy alone. Patients without hemodynamically significant stenoses had a favorable long-term outcome with medical therapy alone. (Funded by St. Jude

DOI: 10.1056/NEJMoa1803538



No. at Risk

Medical therapy	441	360	349	337	271	258
PCI	447	416	403	391	334	321

End Points	PCI Group (N=447)	Medical-Therapy Group (N=441)	Hazard Ratio (95% CI)	Registry Cohort (N=166)
	no. of patients (%)			*no. of patients (%)*
Primary composite end point	62 (13.9)	119 (27.0)	0.46 (0.34–0.63)	26 (15.7)
Components of primary end point				
Death from any cause	23 (5.1)	23 (5.2)	0.98 (0.55–1.75)	7 (4.2)
Myocardial infarction	36 (8.1)	53 (12.0)	0.66 (0.43–1.00)	14 (8.4)
Urgent revascularization	28 (6.3)	93 (21.1)	0.27 (0.18–0.41)	14 (8.4)

N Engl J Med. 2018 Jul 19;379(3):250-259.

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2. What do the guidelines tell us?

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Strong recommendations to use physiology, specially for intermediate stenoses

AHA/ACC Chronic Coronary Disease Guidelines

- In patients with CCD who have angina or anginal equivalent, no previous evaluation for ischemia, and angiographically *intermediate* stenoses, the use of **FFR** or other proven **nonhyperemic pressure ratios** (eg, iFR) is recommended before proceeding with PCI (**Class 1, LOE A**)
- In patients with CCD undergoing coronary angiography without previous stress testing, the use of invasive **FFR** to evaluate angiographically *intermediate* coronary stenoses before proceeding with PCI is a high economically value intervention (Cost Value Statement: **High Value, LOE B-NR**)

AHA/ACC Chest Pain Guidelines

- For patients with obstructive CAD who have stable chest pain despite optimal GDMT, those referred for ICA without prior stress testing benefit from **FFR** or **instantaneous wave free ratio** (**Class 1, LOE A**)
- For intermediate-risk patients with acute chest pain and no known CAD or a coronary artery stenosis *of 40% to 90%* in a proximal or middle segment on CCTA, **FFR-CT** is reasonable for diagnosis of vessel-specific ischemia and to guide decision-making regarding the use of coronary revascularization (Class 2a, LOE B-NR) *adapted

ESC CCS Guidelines (during invasive angiogram, for *intermediate stenoses*)

- **FFR/iFR** (**Class I, LOE A**)
- **QFR** (**Class I, LOE B**)
- **CFR/HSR/CHF** as a complementary investigation (Class IIa, LOE B)
- **Pd/Pa, dPR, RFR, angiography-derived vessel FFR** as alternative (Class IIb, LOE C)
- Systematic & routine wire-based coronary pressure assessment of all coronary vessels is not recommended (Class III, LOE A)

ESC ACS Guidelines

- STEMI: invasive epicardial functional assessment of non-culprit segments of the IRA is not recommended during the index procedure (Class III, LOE C)
- Stable NSTE-ACS: functional invasive evaluation of non-IRA severity during the index procedure may be considered (Class IIb, LOE B)

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3. What are the origins of coronary physiology in the CCL?

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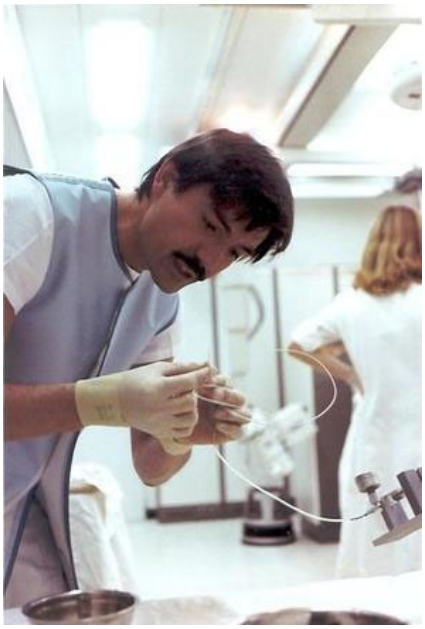

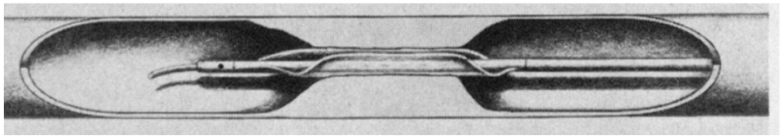

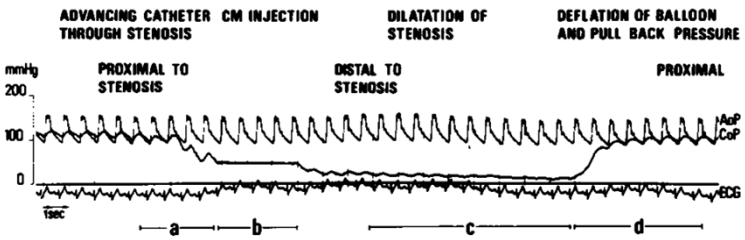

which guides the catheter through the vessel. Proximal to the wire is a side hole connected to the main lumen of the dilating catheter. This lumen is used for pressure recording and contrast-material ejection. The dilating catheter is ad-

N Engl J Med 1979; 301: 61-8.

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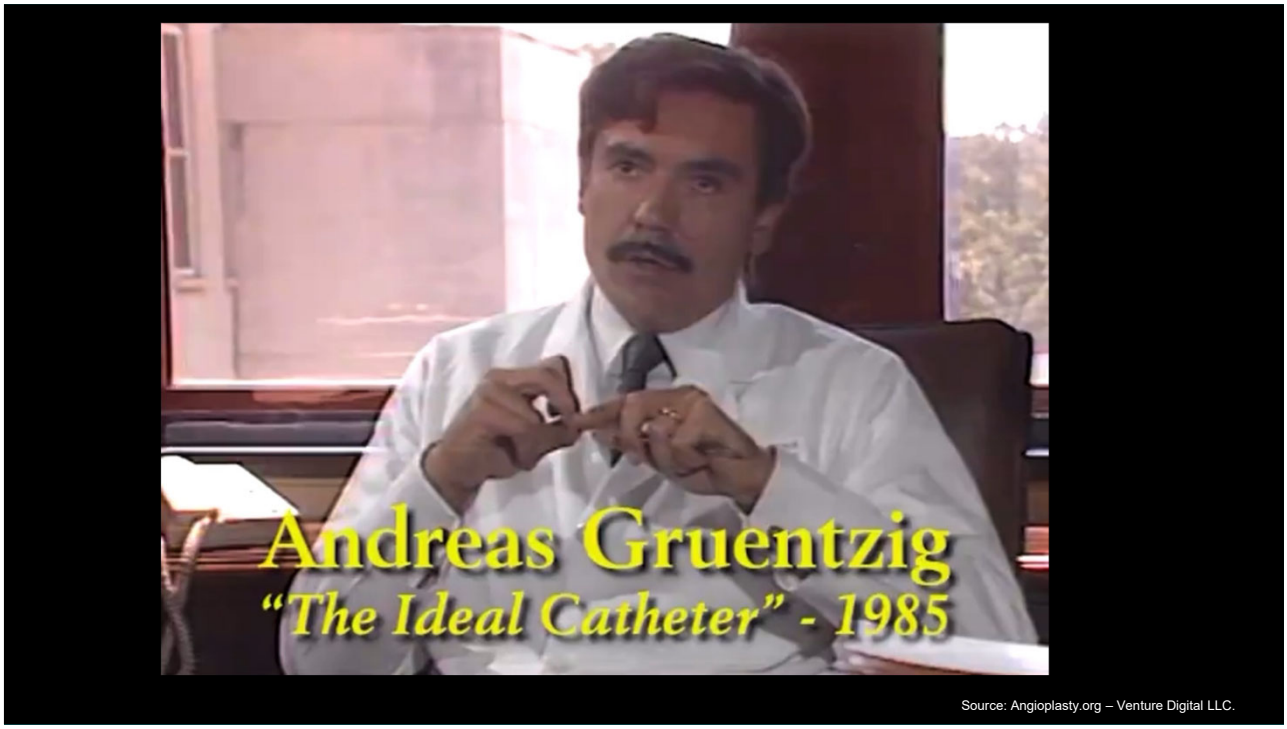

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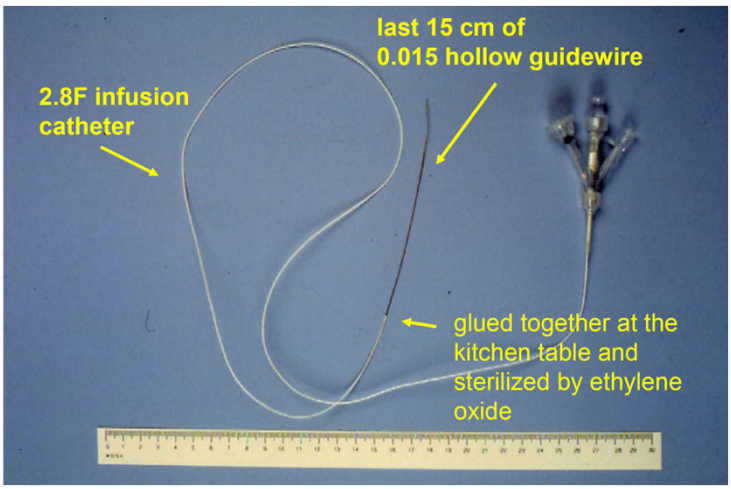
Despite the early, recognized value of measuring coronary pressure, there were barriers that limited clinical use; i.e.: good idea, but not yet at the "*adjacent possible*"



- No reliable device to measure coronary pressure
- Only 3 Fr catheters instead of 0.014 pressure wires
- Concept of maximum hyperemia not yet recognized

Source: Adapted from slides from Coronary Physiology in the Cath Lab. Educational Training Program ESC, European Heart House, Nice, April 24-26, 2014.

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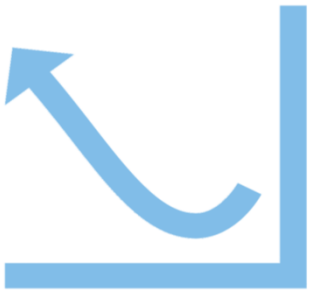
3. The FFR trials:
pressure-wire evidence-base



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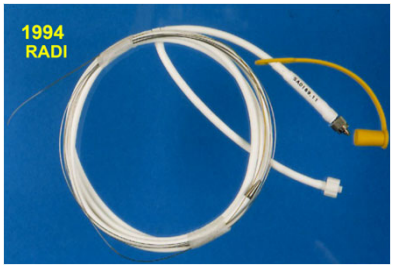
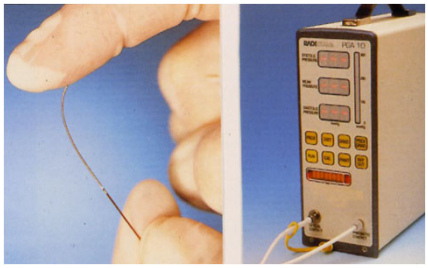
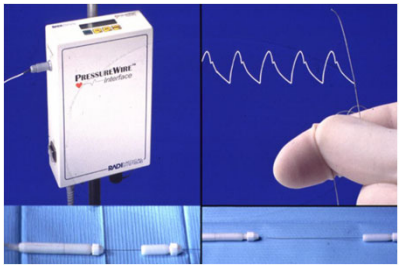
The 1st pressure-wire & the concept of fractional flow reserve

First pressure-wire: *Concept of FFR*	1994-1997 *Validation studies of FFR*	1997-2000 *Clinical trials of FFR*







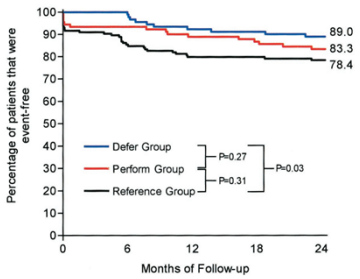
Source: Adapted from slides from Coronary Physiology in the Cath Lab. Educational Training Program ESC, European Heart House, Nice, April 24-26, 2014.

DEFER 2001

Circulation

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; Josef Bartunek, MD, PhD; Jacques J. Koolen, MD, PhD; William Wijns, MD, PhD



Bech GJ et al Fractional flow reserve to determine the appropriateness of angioplasty in moderate coronary stenosis: a randomized trial. Circulation. 2001 Jun 19;103(24):2928-34.

* The primary end point was absence ofadverse cardiac events during 24 months of follow-up. Adverse cardiac events were defined as all-cause mortality, myocardialinfarction, CABG, coronary angioplasty, and any procedure-relatedcomplication necessitating major intervention or prolonged hospitalstay.

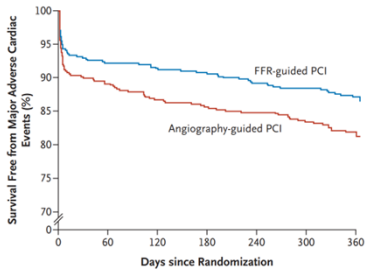
FAME 2009

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*



Tonino PA et al.; FAME Study Investigators. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med. 2009 Jan 15;360(3):213-24.

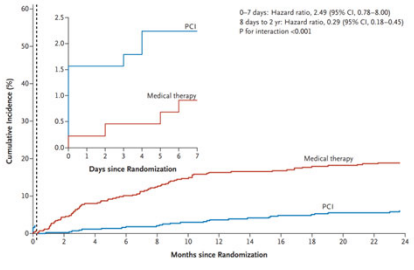
The primary end point was the rate of major adverse cardiac events at 1 year. Major adverse cardiac events were defined as a composite of death, myocardial infarction, and any repeat revascularization.

FAME-2 2012

The NEW ENGLAND JOURNAL of MEDICINE

Fractional Flow Reserve–Guided PCI for Stable Coronary Artery Disease

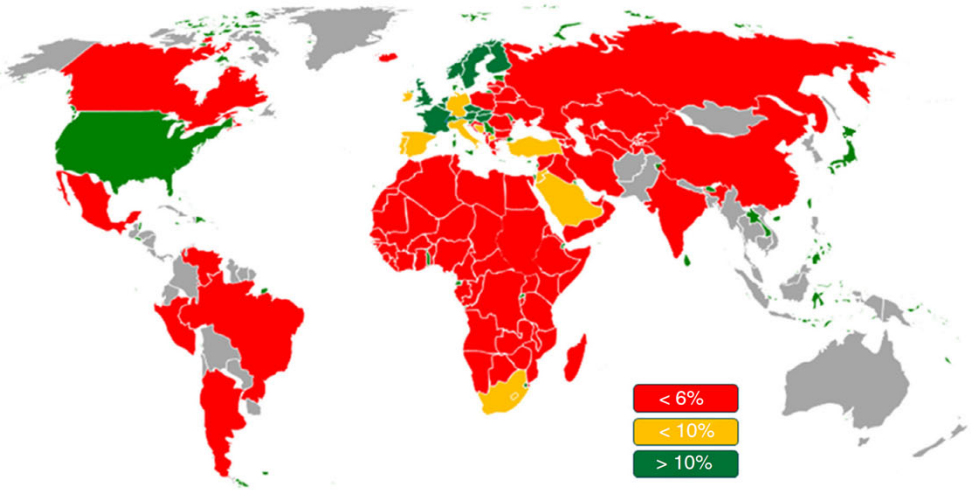
Bernard De Bruyne, M.D., Ph.D., William F. Fearon, M.D., Nico H.J. Pijls, M.D., Ph.D., Emanuele Barbato, M.D., Ph.D., Pim Tonino, M.D., Ph.D., Zsolt Piroth, M.D., Nikola Jagic, M.D., Sven Mobius-Winckler, M.D., Gilles Rioufol, M.D., Ph.D., Nils Witt, M.D., Ph.D., Petr Kala, M.D., Philip MacCarthy, M.D., Thomas Engström, M.D., Keith 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., Andreas Limacher, Ph.D., Eveline Nüesch, Ph.D., and Peter Jüni, M.D., for the FAME 2 Trial Investigators*



De Bruyne B et al.; FAME 2 Trial Investigators. Fractional flow reserve-guided PCI for stable coronary artery disease. N Engl J Med. 2014 Sep 25;371(13):1208-17.

Composite of death from any cause, nonfatal myocardial infarction, or unplanned hospitalization leading to urgent revascularization during the first 2 years

Fractional flow reserve adoption in 2016



Warisawa T, Cook CM, Akashi YJ, Davies JE. Past, Present and Future of Coronary Physiology. Rev Esp Cardiol (Engl Ed). 2018 Aug;71(8):656-667

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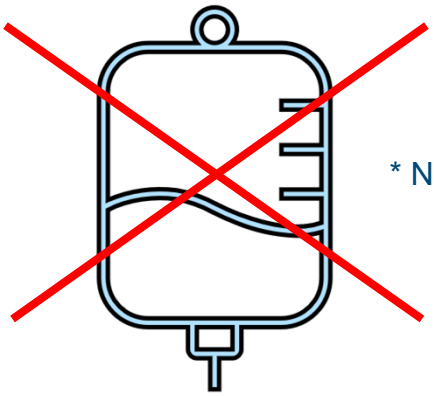
4. The rise of NHPR: ditch hyperemia



* Non-hyperemic pressure ratio

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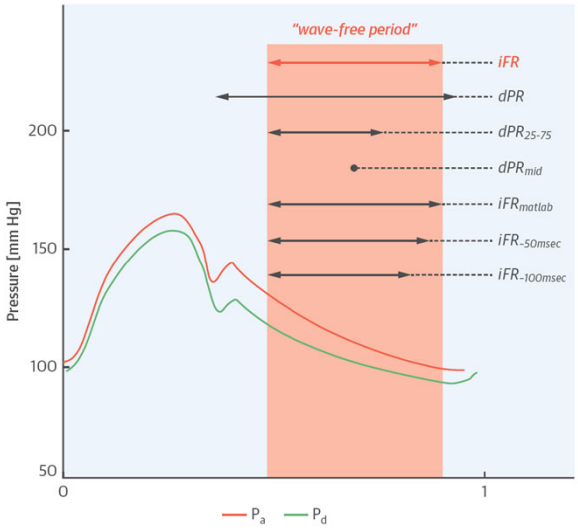
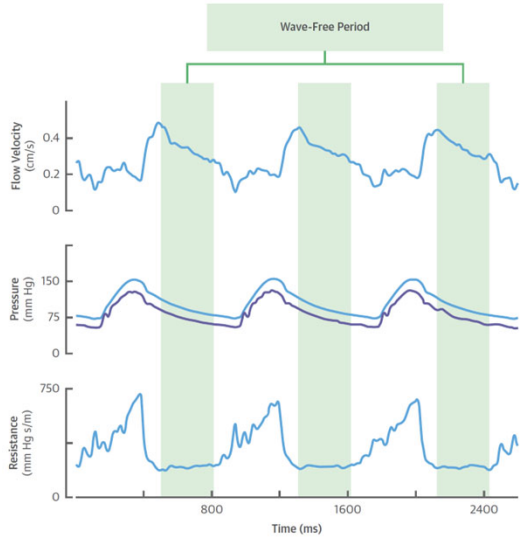
The rise of NHPR: ditch hyperemia





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JACC VOL. 70, NO. 11, 2017

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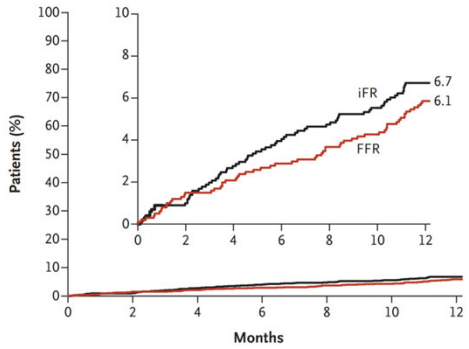
The iFR non-inferiority trials – as good as FFR

iFR-SWEDEHEART

Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI

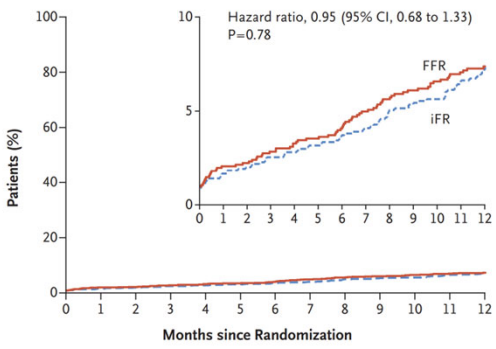
M. Götberg, E.H. Christiansen, I.J. Gudmundsdottir, L. Sandhall, M. Danielewicz, L. Jakobsen, S.-E. Olsson, P. Ohagen, H. Olsson, E. Omerovic, F. Calais, P. Lindroos, M. Maeng, T. Tödt, D. Venetsanos, S.K. James, A. Kåregren, M. Nilsson, J. Carlsson, D. Hauer, J. Jensen, A.-C. Karlsson, G. Panayi, D. Erlinge, and O. Fröbert, for the iFR-SWEDEHEART Investigators*



DEFINE-FLAIR

Use of the Instantaneous Wave-free Ratio or Fractional Flow Reserve in PCI

J.E. Davies, S. Sen, H.-M. Dehbi, R. Al-Lamee, R. Petraco, S.S. Nijjer, R. Bhindi, S.J. Lehman, D. Walters, J. Sapontis, L. Janssens, C.J. Vrints, A. Khashaba, M. Laine, E. Van Belle, F. Krackhardt, W. Bojara, O. Going, T. Härle, C. Indolfi, G. Niccoli, F. Ribichini, N. Tanaka, H. Yokoi, H. Takashima, Y. Kikuta, A. Erglis, H. Vinhas, P. Canas Silva, S.B. Baptista, A. Alghamdi, F. Hellig, B.-K. Koo, C.-W. Nam, E.-S. Shin, J.-H. Doh, S. Brugaletta, E. Alegria-Barrero, M. Meuwissen, J.J. Piek, N. van Royen, M. Sezer, C. Di Mario, R.T. Gerber, I.S. Malik, A.S.P. Sharp, S. Talwar, K. Tang, H. Samady, J. Altman, A.H. Seto, J. Singh, A. Jeremias, H. Matsuo, R.K. Kharbanda, M.R. Patel, P. Serruys, and J. Escaned



AllinaH

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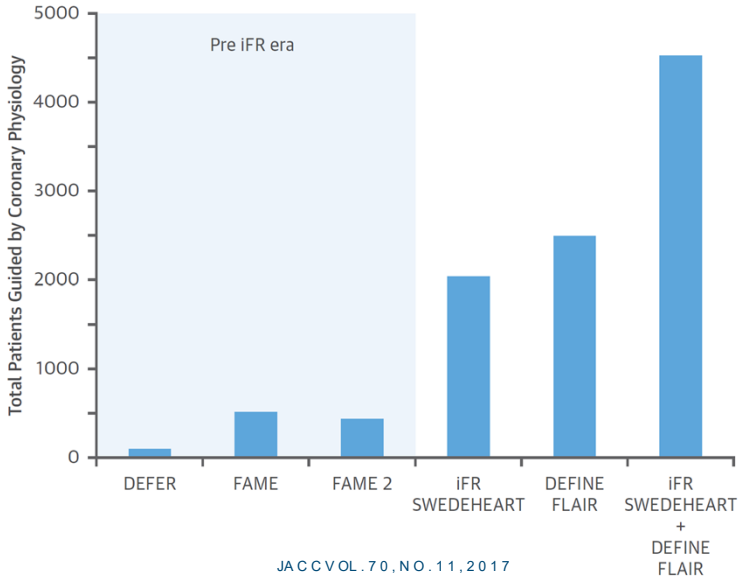
The rise of NHPR: ditch hyperemia



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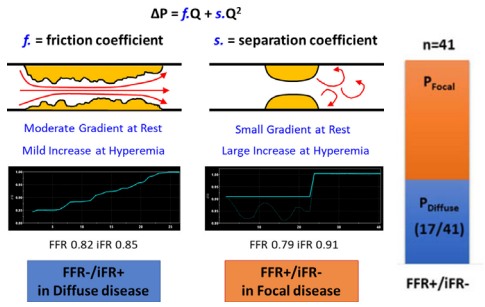
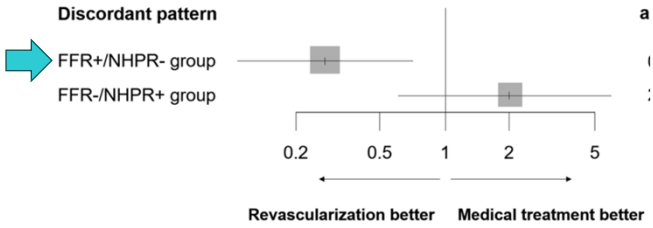
The rise of NHPR: ditch hyperemia….?

Not that simple….. iFR/NHPR discordance in ~20%



Circ Cardiovasc Interv. 2019 May;12(5):e007494



. Circulation. 2025 Jan 9. doi: 10.1161/CIRCULATIONAHA.124.071139. Epub ahead of print.

* Editorial comment - -Apples to apples… FFR_{CT} ~ FFR_{angio} ~ Pressure-wire FFR

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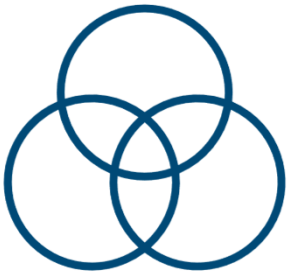
5. Can we do better?
Phenotyping CAD



23

"Negative" results for SIHD PCI: Are we really surprised?

Poor adoption of radial. One-size fits all.

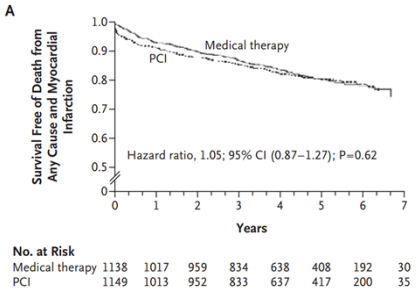
Low use of coronary physiology to identify lesions that benefit from revascularization (patient selection).

Low use of intracoronary imaging for PCI guidance.

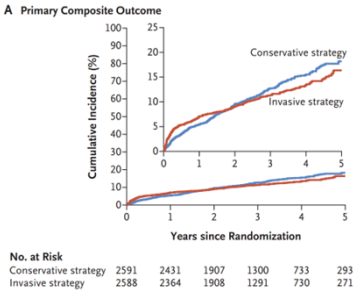
Low use of imaging and/or physiology for assessment post-PCI results.

Downstream effects: under-expanded stents and ISR epidemic, repeat revascularization, poor outcomes.

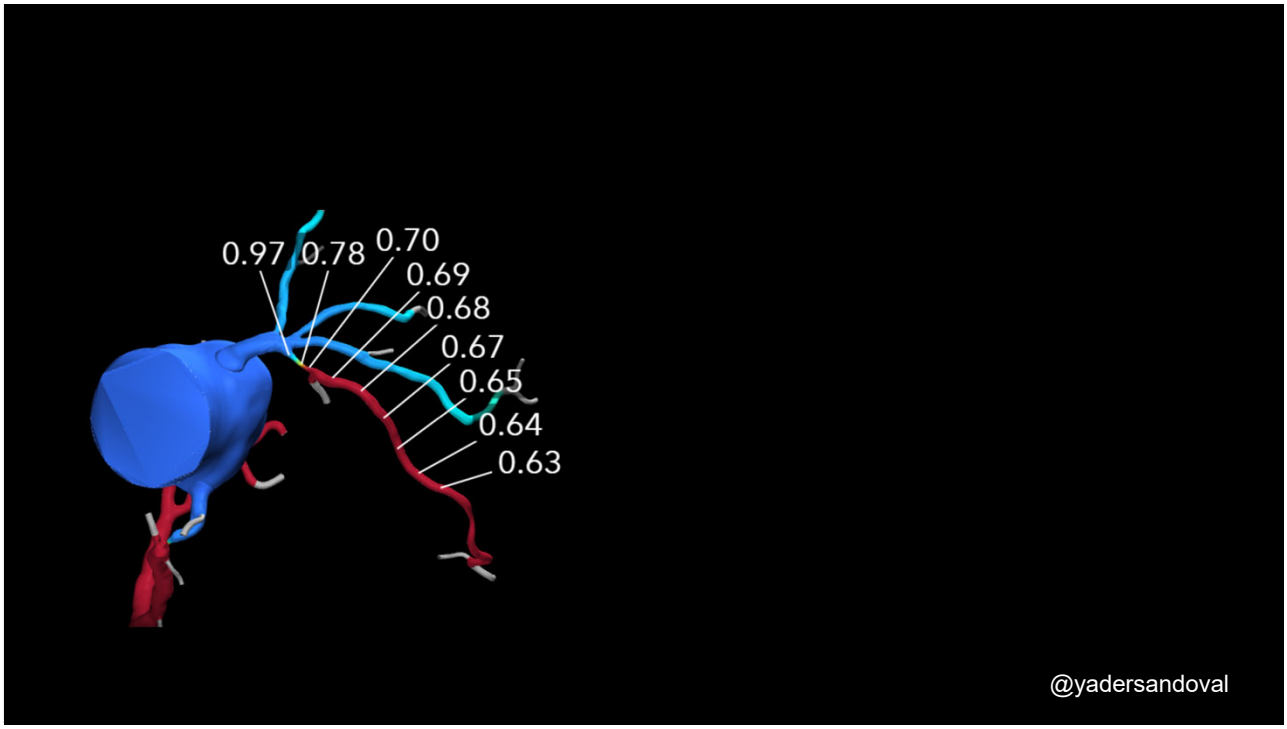
COURAGE trial



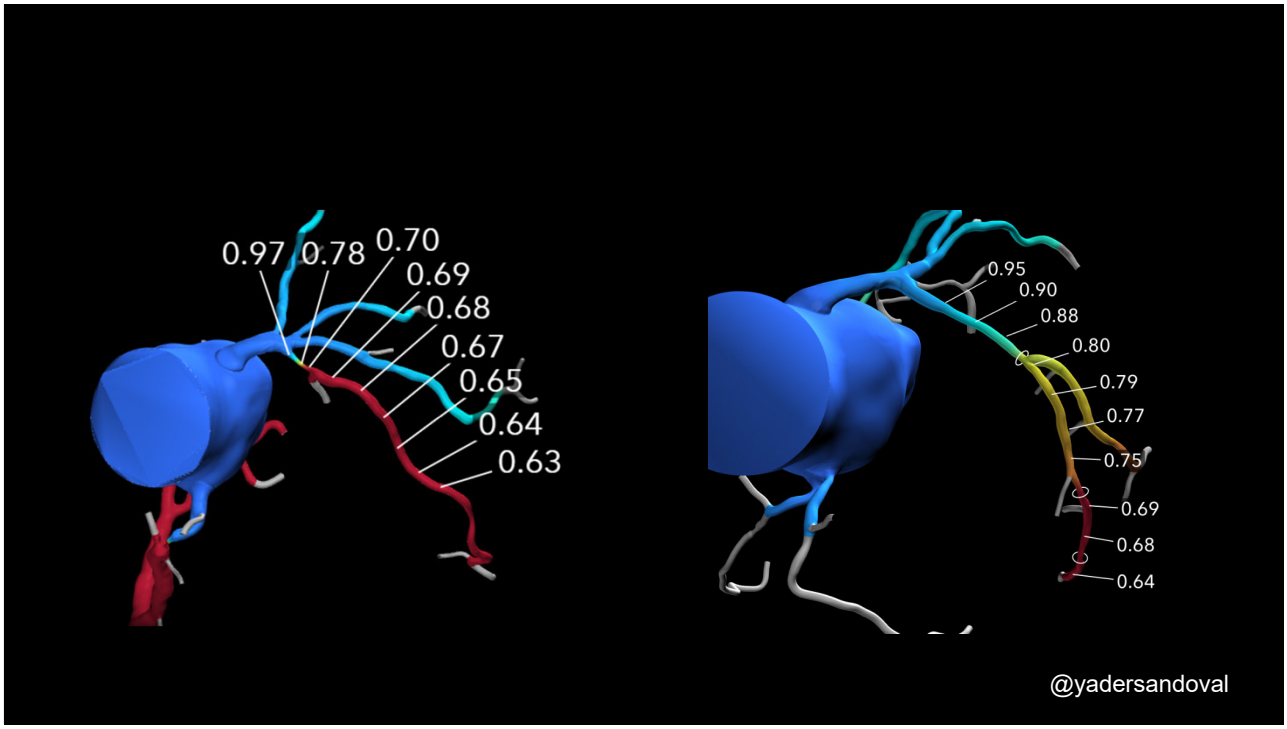
ISCHEMIA trial



24


0.97
0.78
0.70
0.69
0.68
0.67
0.65
0.64
0.63
@yadersandoval

25


0.97
0.78
0.70
0.69
0.68
0.67
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0.77
0.75
0.69
0.68
0.64
@yadersandoval

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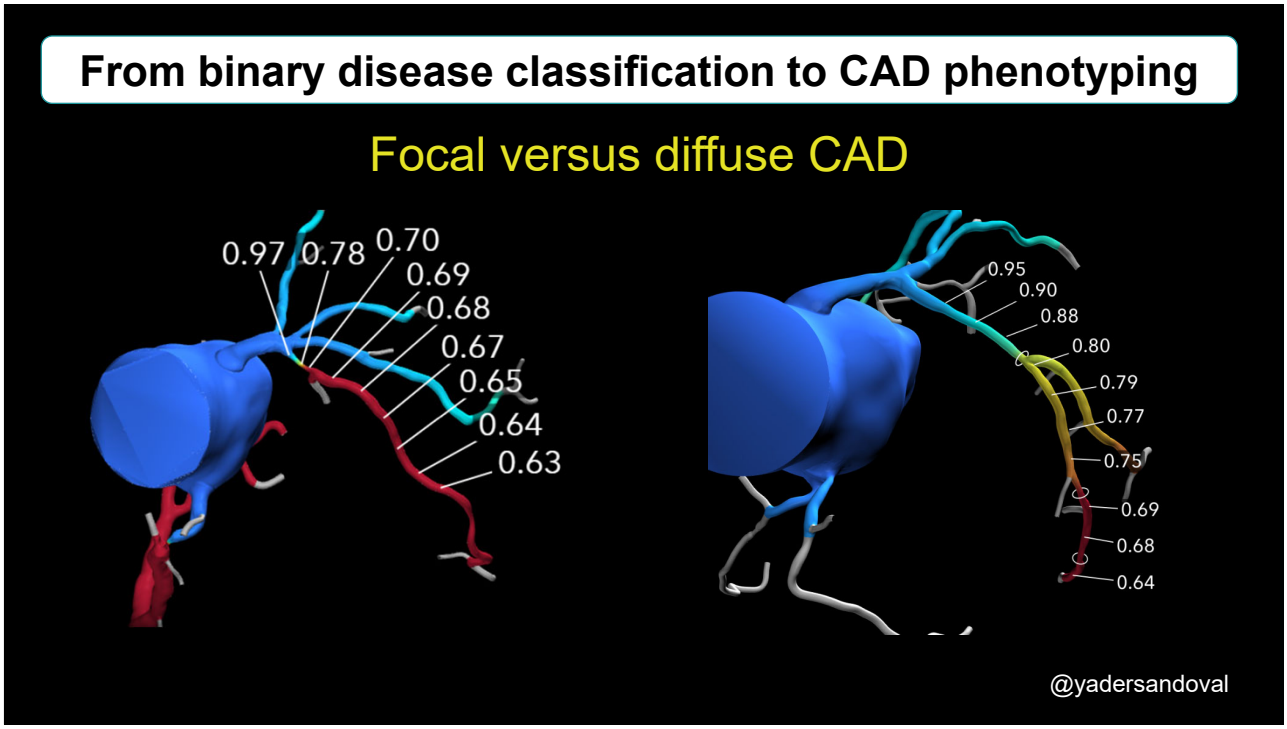
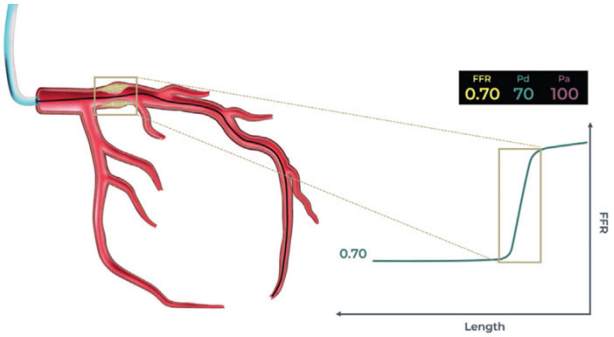


27

Case example #1: What do you do and what is the expected result?



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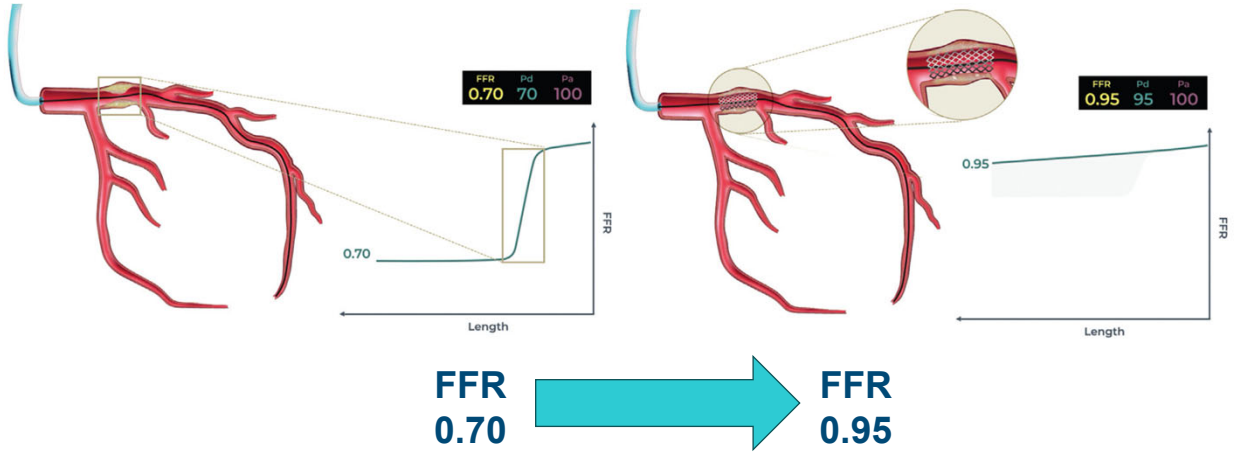
Case example #1: What do you do and what is the expected result?



FFR 0.70 → **FFR 0.95**

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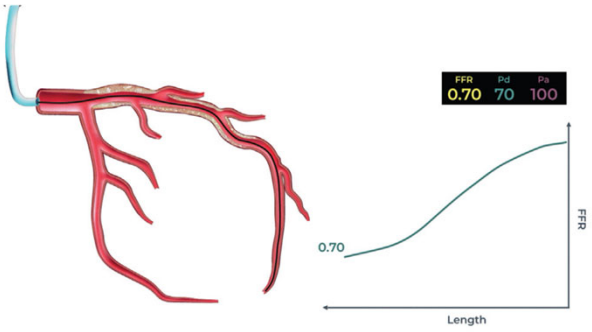
Case example #2: What do you do and what is the expected result?



Curr Opin Cardiol. 2024 Nov 1;39(6):520-528.

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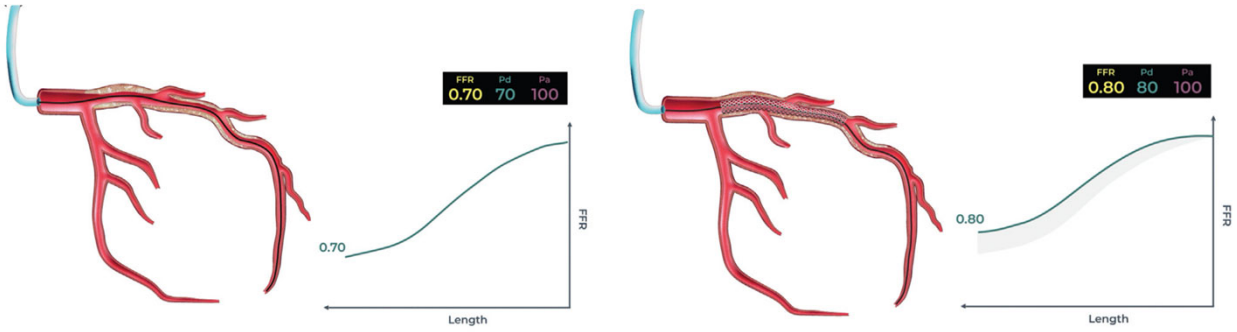
Case example #2: What do you do and what is the expected result?



FFR 0.70 → **FFR 0.80**

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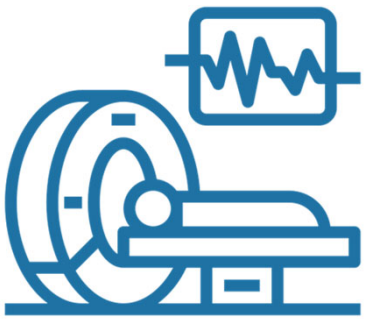
6. Bringing CCTA to the CCL



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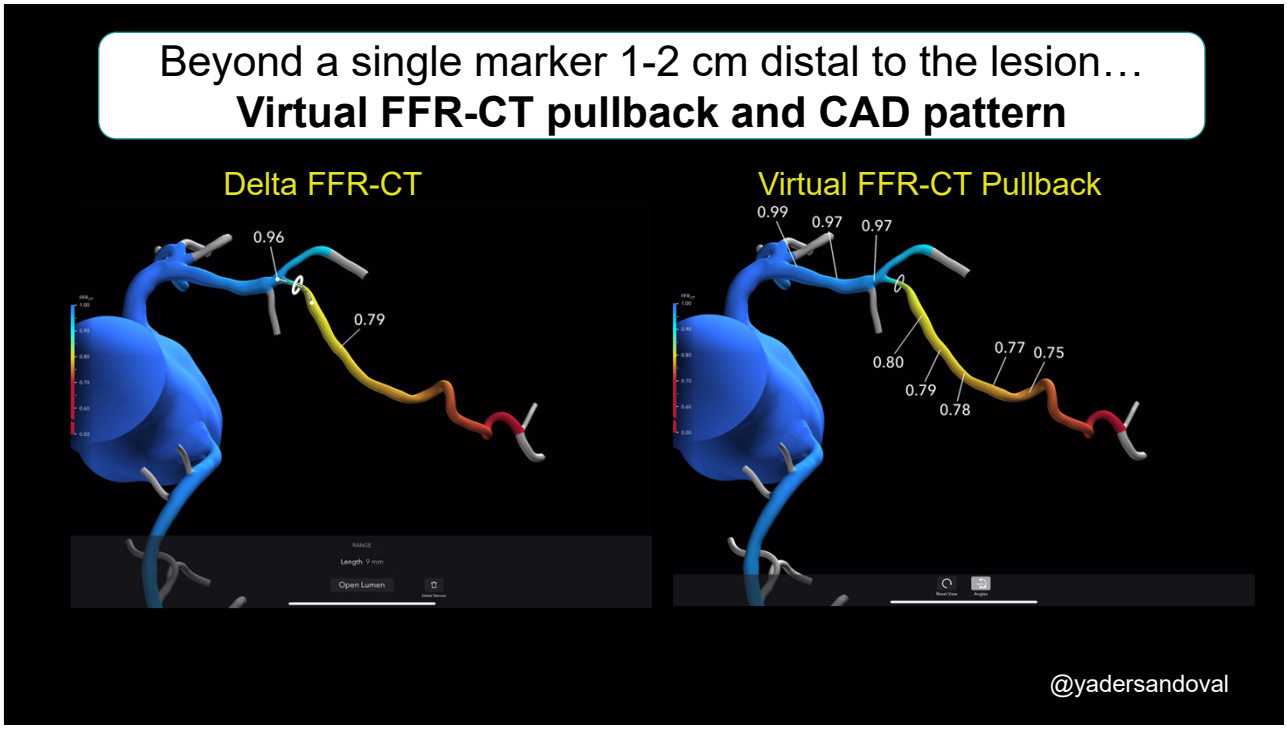
Beyond a single marker 1-2 cm distal to the lesion…
Virtual FFR-CT pullback and CAD pattern
Delta FFR-CT
Virtual FFR-CT Pullback
0.96
0.79
0.99
0.97
0.97
0.80
0.79
0.78
0.77
0.75
@yadersandoval

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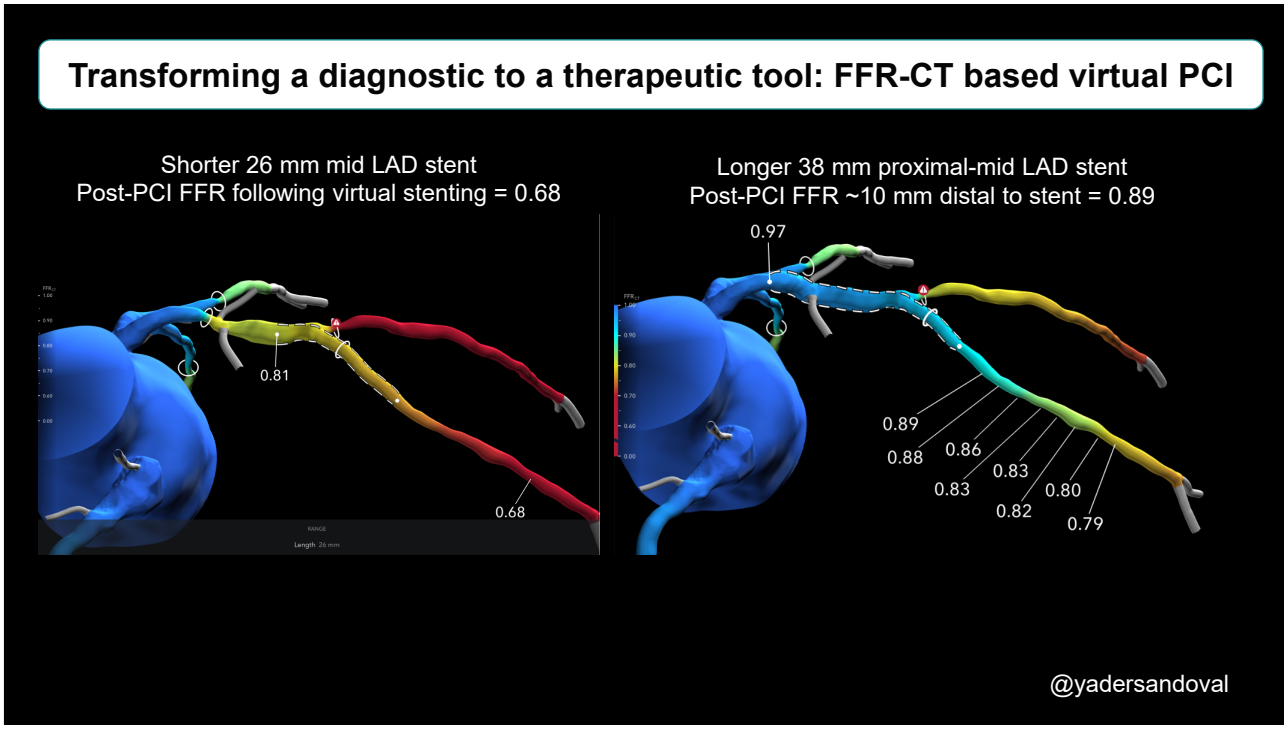
Transforming a diagnostic to a therapeutic tool: FFR-CT based virtual PCI
Shorter 26 mm mid LAD stent
Post-PCI FFR following virtual stenting = 0.68
Longer 38 mm proximal-mid LAD stent
Post-PCI FFR ~10 mm distal to stent = 0.89
0.81
0.68
0.97
0.89
0.88
0.86
0.83
0.83
0.80
0.82
0.79
@yadersandoval

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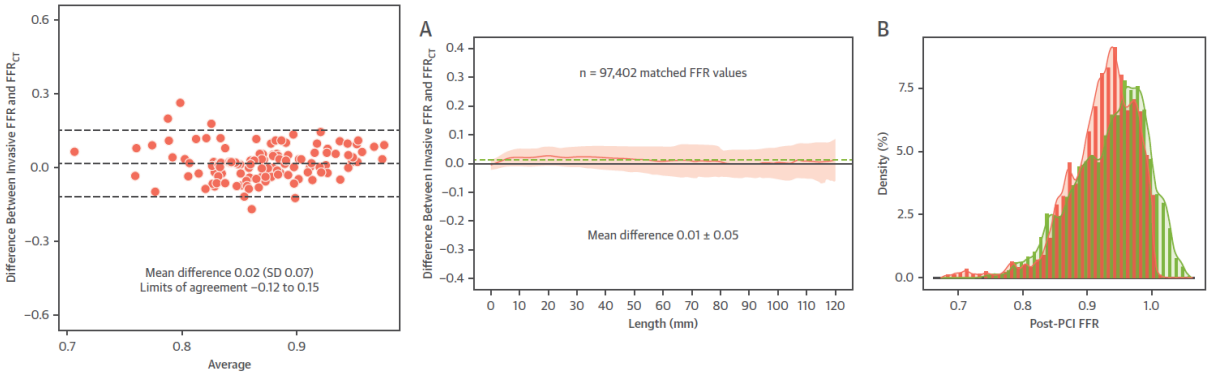
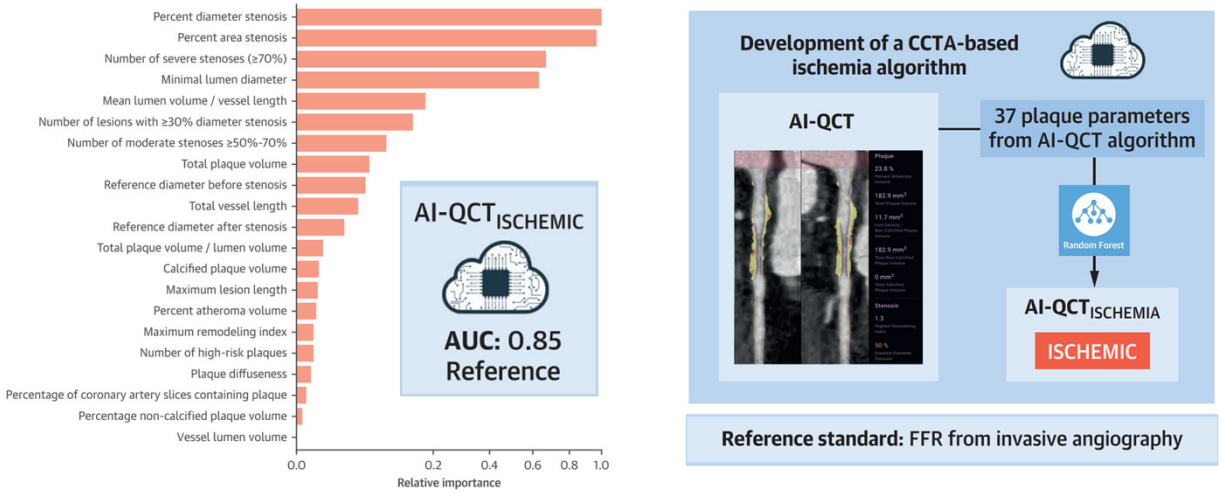
P3: Clinical validation of a virtual planner for coronary interventions based on coronary CT angiography



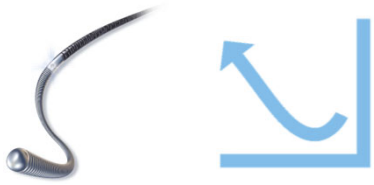
Sonck J, Nagumo S, Norgaard BL, Otake H, Ko B, Zhang J, Mizukami T, Maeng M, Andreini D, Takahashi Y, Jensen JM, Ihdayhid A, Heggermont W, Barbato E, Mileva N, Munhoz D, Bartunek J, Updegrove A, Collinsworth A, Penicka M, Van Hoe L, Leipsic J, Koo BK, De Bruyne B, Collet C. Clinical Validation of a Virtual Planner for Coronary Interventions Based on Coronary CT Angiography. JACC Cardiovasc Imaging. 2022 Jul;15(7):1242-1255.

AI-QCT$_{ISCHEMIA}$ – AI to predict FFR from CCTA anatomical data



Nurmohamed NS, Danad I, Jukema RA, de Winter RW, de Groot RJ, Driessen RS, Bom MJ, van Diemen P, Pontone G, Andreini D, Chang HJ, Katz RJ, Stroes ESG, Wang H, Chan C, Crabtree T, Aquino M, Min JK, Earls JP, Bax JJ, Choi AD, Knaapen P, van Rosendael AR; CREDENCE and PACIFIC-1 Investigators. Development and Validation of a Quantitative Coronary CT Angiography Model for Diagnosis of Vessel-Specific Coronary Ischemia. JACC Cardiovasc Imaging. 2024 Aug;17(8):894-906.

7. Innovations in pressure-wire based assessments



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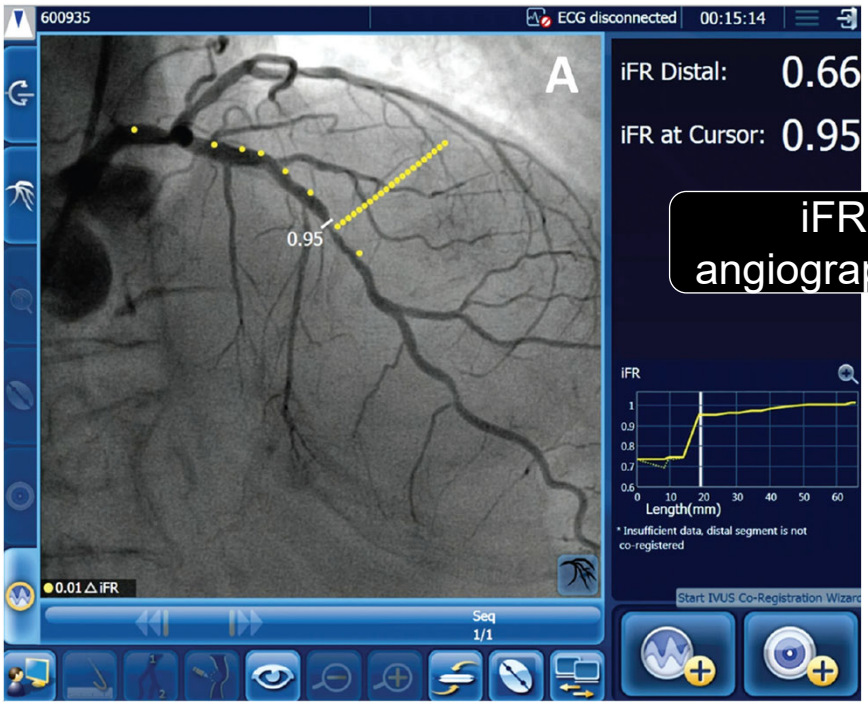

iFR (NHPR) with angiographic co-registration

*SyncVision system

38

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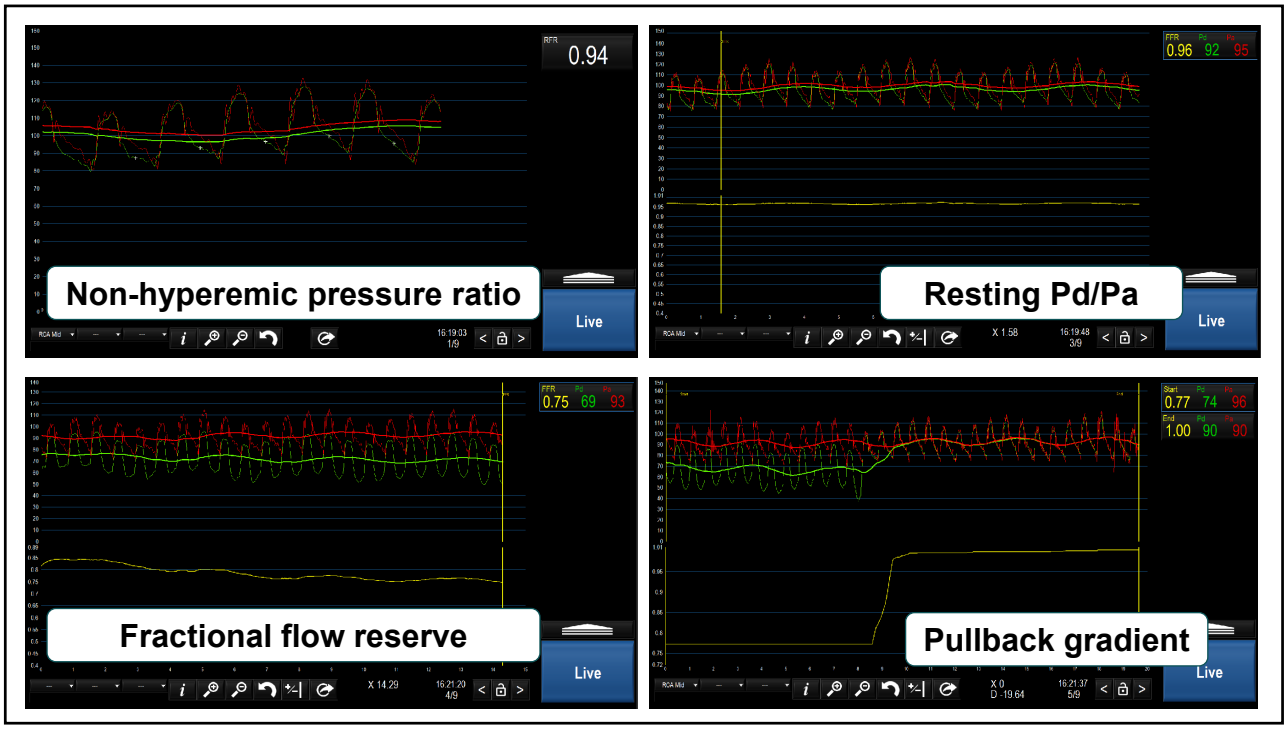
Non-hyperemic pressure ratio
Resting Pd/Pa
Fractional flow reserve
Pullback gradient
Live

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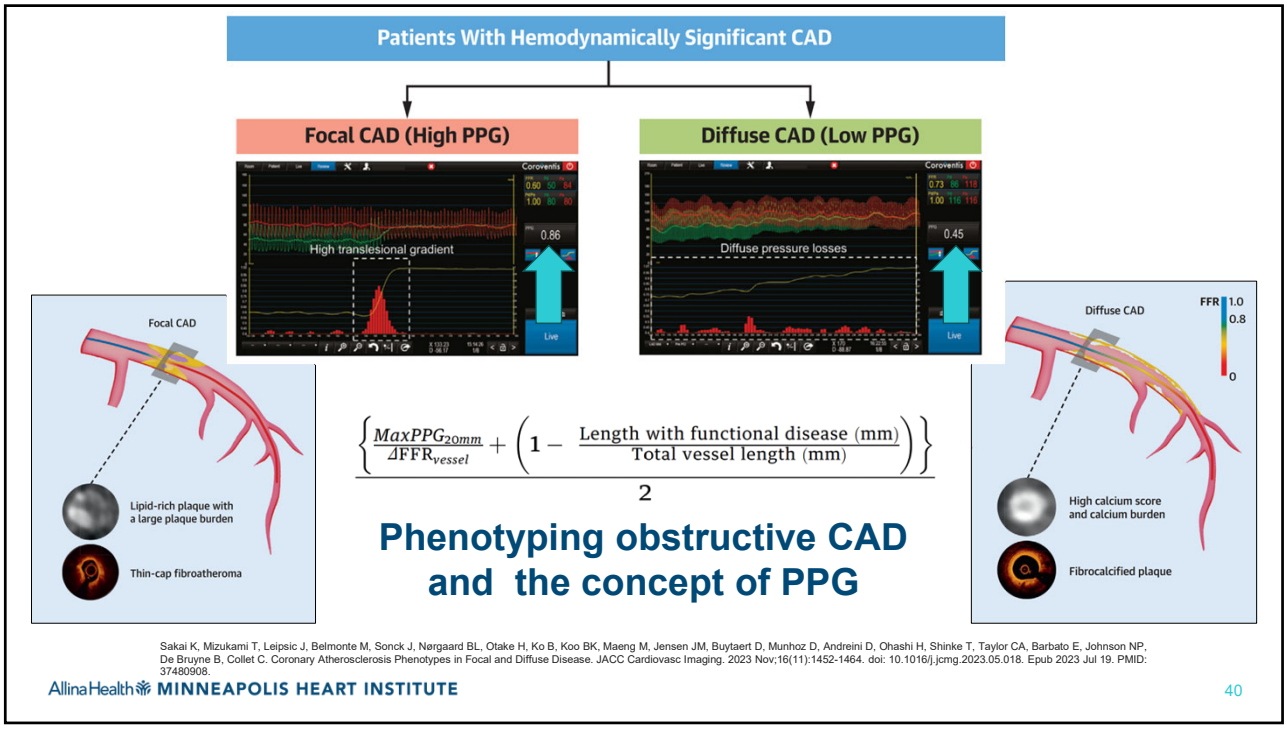
Patients With Hemodynamically Significant CAD
Focal CAD (High PPG)
Diffuse CAD (Low PPG)
High translesional gradient
Diffuse pressure losses
Focal CAD
Lipid-rich plaque with a large plaque burden
Thin-cap fibroatheroma
Diffuse CAD
High calcium score and calcium burden
Fibrocalcified plaque
$\left\{\frac{MaxPPG_{20mm}}{\Delta FFR_{vessel}} + \left(1 - \frac{\text{Length with functional disease (mm)}}{\text{Total vessel length (mm)}}\right)\right\} / 2$
Phenotyping obstructive CAD and the concept of PPG
Sakai K, Mizukami T, Leipsic J, Belmonte M, Sonck J, Nørgaard BL, Otake H, Ko B, Koo BK, Maeng M, Jensen JM, Buytaert D, Munhoz D, Andreini D, Ohashi H, Shinke T, Taylor CA, Barbato E, Johnson NP, De Bruyne B, Collet C. Coronary Atherosclerosis Phenotypes in Focal and Diffuse Disease. JACC Cardiovasc Imaging. 2023 Nov;16(11):1452-1464. doi: 10.1016/j.jcmg.2023.05.018. Epub 2023 Jul 19. PMID: 37480908.
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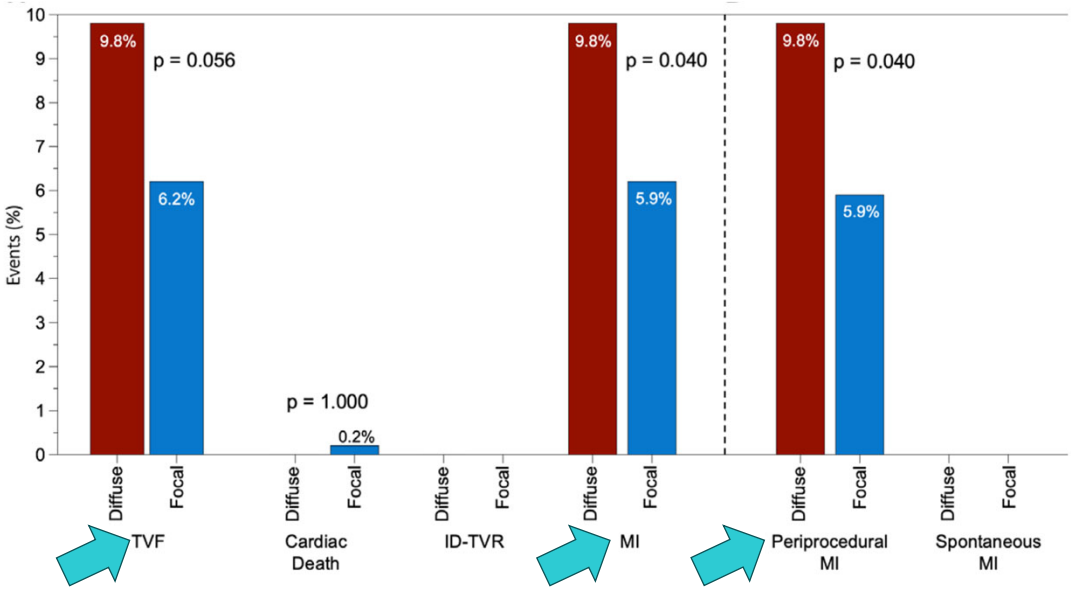
PPG Global Registry: MACE in focal versus diffuse CAD



Circulation. 2024 Aug 20;150(8):586-597.

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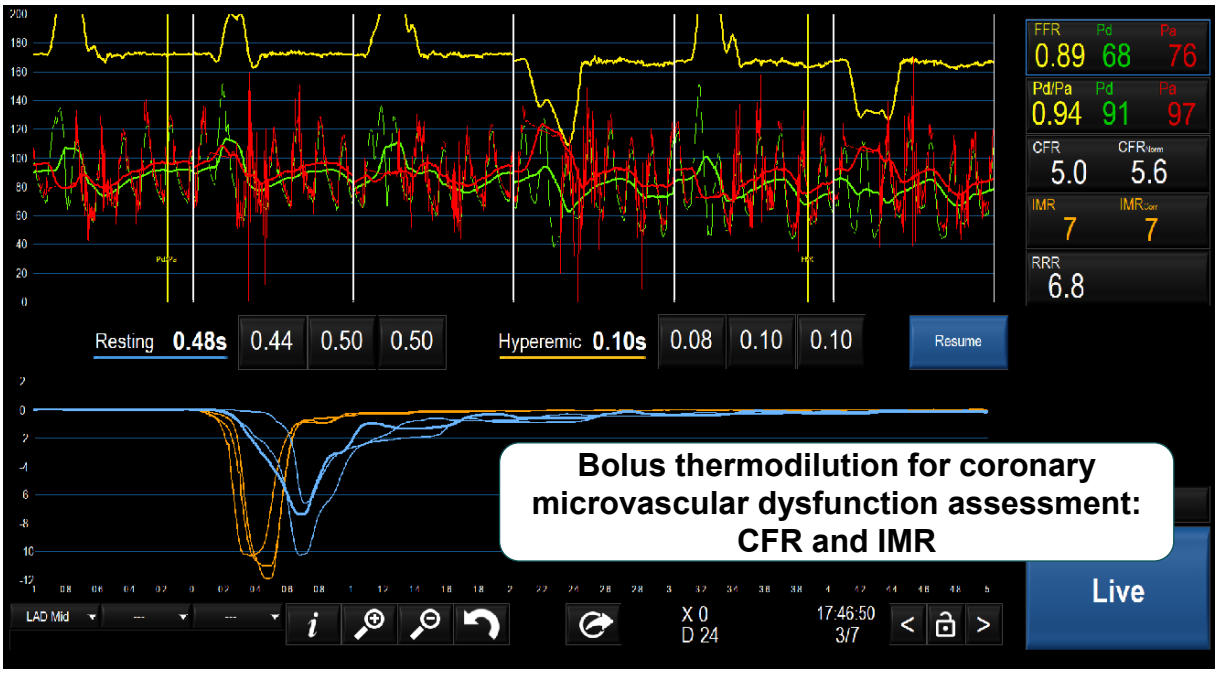

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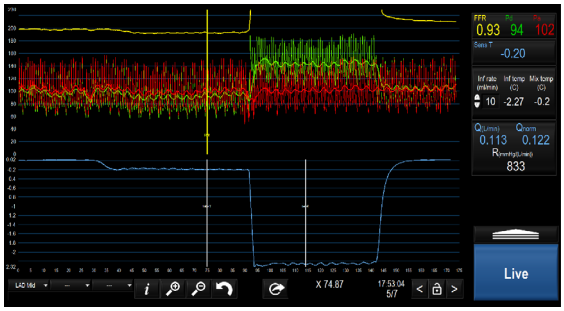
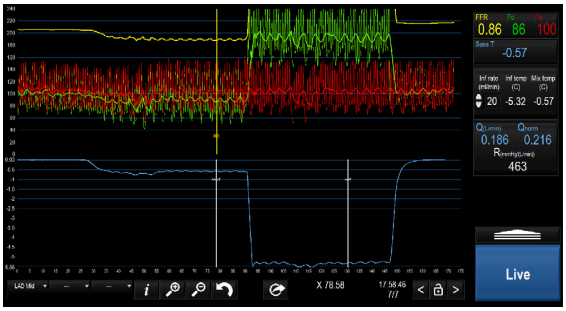
Continuous thermodilution for absolute flow and absolute resistance

Rest
10 ml/min intracoronary saline infusion rate (Rayflow)



Hyperemia
20 ml/min intracoronary saline infusion rate (Rayflow)



Continuous thermodilution: (1) **volumetric flow** (Q), (2) **microvascular resistance at hyperemia** (R_μ), and (3) **microvascular resistance reserve** (MRR)

- **Absolute Q = 1.08 * $T_{I\ (at\ infusion\ microcatheter\ =\ Inf\ temp)}$ / $T_{(distal\ =\ Mix\ temp\ =\ Sens\ T)}$ * $Q_{I\ (saline\ infusion\ rate)}$**
  - **Absolute Q_{rest}** = 1.08 * -2.27 / -0.2 * 10 = 123 mL (**nL 50-100 mL**) / 1000 = 0.0123 L/min
  - **Absolute Q_{hyper}** = 1.08 * -5.32 / -0.57 * 20 = 202 mL (**nL 175-350 mL**) / 1000 = 0.202 L/min
- **CFR_{abs} = Q_{hyper} / Q_{rest}** → 0.186 / 0.113 = 1.6
- **Absolute R_μ = P_d / Q** → **$R_{\mu,\ rest}$** = $P_{d,\ rest}$ / Q_{rest}** → 94 / 0.113 = 832 WU (**nL 1200-1800 WU**); **$R_{\mu,\ hyper}$** = $P_{d,\ hyper}$ / Q_{hyper}** → 86 / 0.186 = 462 WU (**nL 200-470 WU**)
- **MRR=** (Q_{hyper} / Q_{rest}) x ($P_{a,\ rest}$ / $P_{d,\ hyper}$)** → (0.186 / 0.113) * (102 / 86) = 2.0 WU
- **Simplified MRR calculation** → **MRR = CFR / FFR_{abs}** → **MRR** = (0.186 / 0.113) / 0.86 → **MRR** = 1.6 / 0.86 = 1.9 WU (**MRR<3 WU abnormal**)

Summary: **FFR_{abs}** 0.86 (FFR<0.80 abnormal), **CFR_{abs}** 1.6 (CFR<2.0 abnormal), **$R_{\mu,\ hyper}$** 462 (normal 200-470 WU), **Simplified MRR** 1.9 WU (CMD rule-out ≥3, rule-in <2.3)

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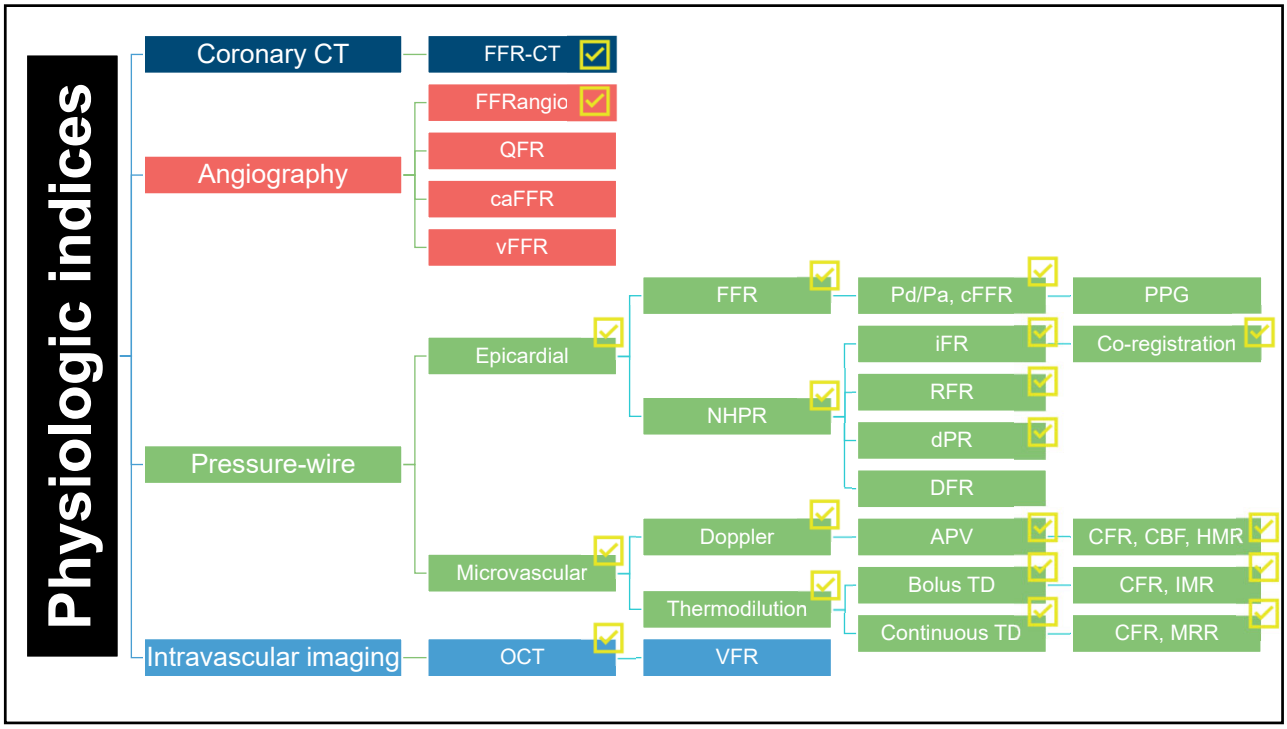

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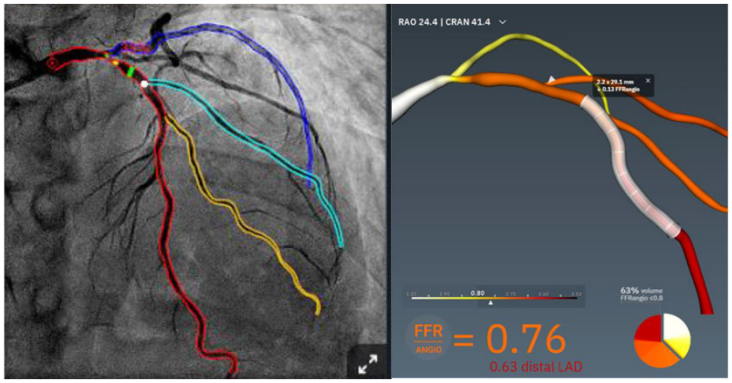
8. Coronary angiography 2.0:
angiography-based physiology



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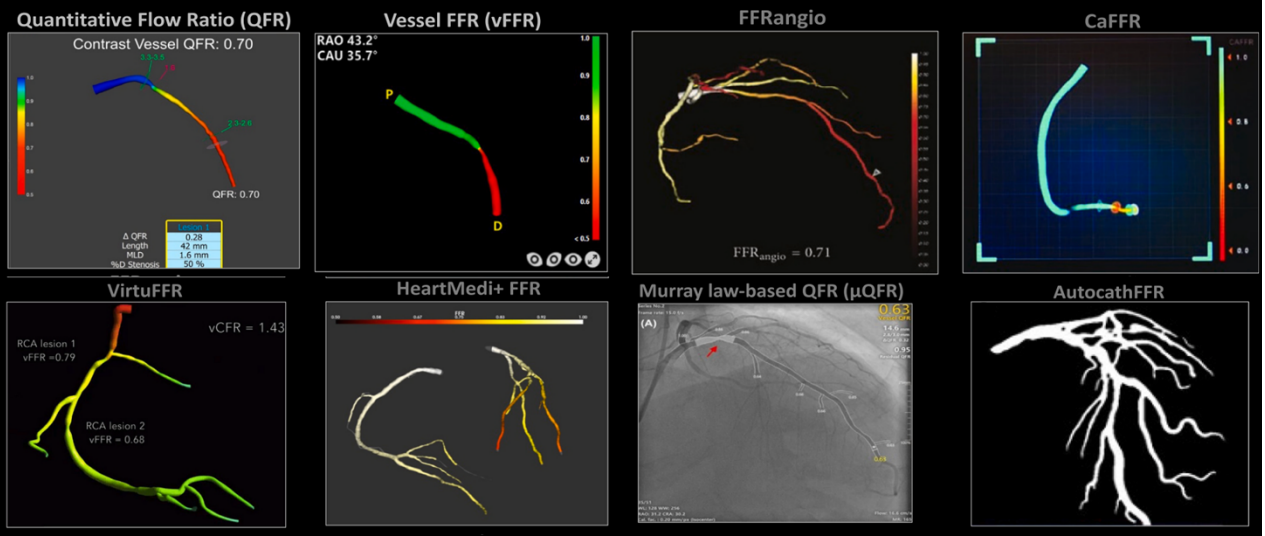
Angiographic-based FFR modalities



Advancements and future perspectives in coronary angiography-derived fractional flow reserve. Prog Cardiovasc Dis. 2024 Aug 8:S0033-0620(24)00111-7. doi: 10.1016/j.pcad.2024.08.002. Epub ahead of print. PMID: 39122203.

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Circulation

ORIGINAL RESEARCH ARTICLE

Accuracy of Fractional Flow Reserve Derived From Coronary Angiography

Editorial, see p 485

William F. Fearon, MD
Stephan Achenbach, MD, PhD
Thomas Engstrom, MD, PhD
Abid Assali, MD
Richard Shlofmitz, MD
Allen Jeremias, MD
Stephane Fournier, MD
Ajay J. Kirtane, MD
Ran Kornowski, MD
Gabriel Greenberg, MD
Rami Jubeh, MD
Daniel M. Kolansky, MD
Thomas McAndrew, PhD
Ovidiu Dressler, MD
Akiko Maehara, MD
Mitsuaki Matsumura, BS
Martin B. Leon, MD
Bernard De Bruyne, MD, PhD
For the FAST-FFR Study Investigators

BACKGROUND: Measuring fractional flow reserve (FFR) with a pressure wire remains underutilized because of the invasiveness of guide wire placement or the need for a hyperemic stimulus. FFR derived from routine coronary angiography (FFR_{angio}) eliminates both of these requirements and displays FFR values of the entire coronary tree. The FFR_{angio} Accuracy versus Standard FFR (FAST-FFR) study is a prospective, multicenter, international trial with the primary goal of determining the accuracy of FFR_{angio}.

METHODS: Coronary angiography was performed in a routine fashion in patients with suspected coronary artery disease. FFR was measured in vessels with coronary lesions of varying severity using a coronary pressure wire and hyperemic stimulus. Based on angiograms of the respective arteries acquired in ≥2 different projections, on-site operators blinded to FFR then calculated FFR_{angio} using proprietary software. Coprimary end points were the sensitivity and specificity of the dichotomously scored FFR_{angio} for predicting pressure wire–derived FFR using a cutoff value of 0.80. The study was powered to meet prespecified performance goals for sensitivity and specificity.

RESULTS: Ten centers in the United States, Europe, and Israel enrolled a total of 301 subjects and 319 vessels meeting inclusion/exclusion criteria which were included in the final analysis. The mean FFR was 0.81 and 43% of vessels had an FFR≤0.80. The per-vessel sensitivity and specificity were 94% (95% CI, 88% to 97%) and 91% (86% to 95%), respectively, both of which exceeded the prespecified performance goals. The diagnostic accuracy of FFR_{angio} was 92% overall and remained high when only considering FFR values between 0.75 to 0.85 (87%). FFR_{angio} values correlated well with FFR measurements (r=0.80, P<0.001) and the Bland–Altman 95% confidence limits were between −0.14 and 0.12. The device success rate for FFR_{angio} was 99%.

CONCLUSIONS: FFR_{angio} measured from the coronary angiogram alone has a high sensitivity, specificity, and accuracy compared with pressure wire–derived FFR. FFR_{angio} has the promise to substantially increase physiological coronary lesion assessment in the catheterization laboratory, thereby potentially leading to improved patient outcomes.

CLINICAL TRIAL REGISTRATION: URL: https://www.clinicaltrials.gov. Unique Identifier: NCT03226262.

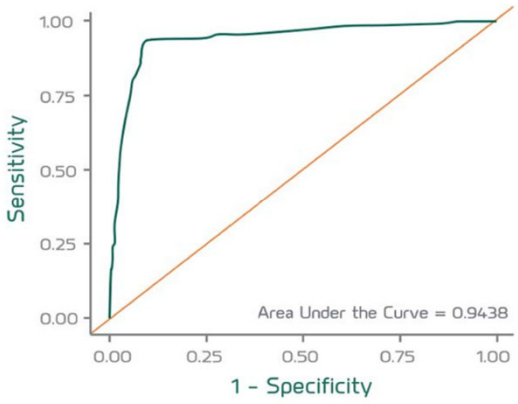
Key Words: coronary artery disease ■ coronary circulation ■ fractional flow reserve, myocardial

Sources of Funding, see page 483

https://www.ahajournals.org/journal/circ

Circulation. 2019;139:477–484. DOI: 10.1161/CIRCULATIONAHA.118.037350

January 22, 2019 477



Diagnostic Characteristic	% (95% CI)
Sensitivity	93.5% (87.8–96.6)
Specificity	91.2% (86.0–94.6)
Diagnostic accuracy	92.2% (88.7–94.8)
Positive predictive value	89.0% (82.6–93.2)
Negative predictive value	94.8% (90.3–97.3)

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Study Design

1924 Patients
Patients presenting w/ coronary lesion(s) with clinical indication for physiology-based assessment

Declare angio-based treatment plan, in detail

1:1 Randomization
Stratified by FFR/NHPR and presentation (ACS/SAP)

962 FFRangio-guided treatment

FFRangio ≤0.80 → PCI

FFRangio >0.80 → Defer

962 Pressure wire-guided Treatment

FFR ≤0.80 NHPR ≤0.89 → PCI

FFR >0.80 NHPR >0.89 → Defer

1-Year Assessment (Clinical & CE, QOL)
Non-inferiority in MACE

1924 patient to be enrolled in up to 60 sites globally, with a limit of up to 200 patients per site.

CATHWORKS

ALLURE

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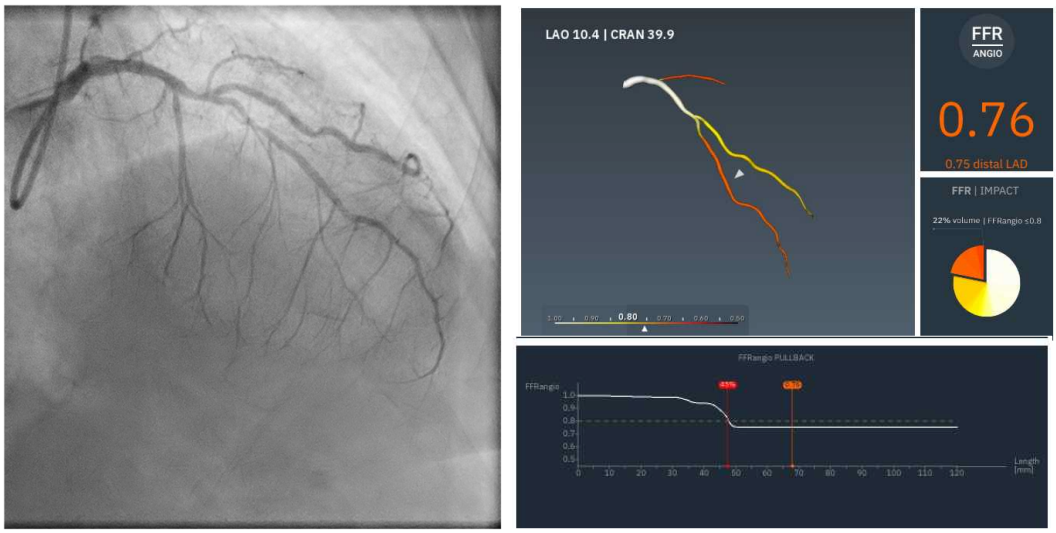
LAD/diagonal assessment with FFRangio: LAD 0.76, Diagonal 0.85



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Coronary angiography 2.0: angiography-based physiology

Software	Study	Trial Design	Study Question/Topic	Estimated Sample Size	Control	Intervention	Endpoint	Estimated completion
caFFR	The Flash FFR II study	Randomized controlled trial	caFFR guided PCI strategy vs FFR guided PCI strategy	2132	FFR	caFFR	MACE and cost data at 2 years	12/2025
vFFR	FAST STEMI II study	Prospective cohort study	Validation of vFFR compared to FFR guided revascularization of non-culprit lesions in STEMI	111	FFR	vFFR	Diagnostic performance of vFFR	06/2023
	LIPSIASTRATEGY	Randomized controlled trial	Comparison of vFFR vs FFR in intermediate coronary stenoses	1926	FFR	vFFR	MACE at 1 year	11/2026
	FAST III	Randomized controlled trial	Comparison of vFFR vs FFR guided PCI strategy	2228	FFR	vFFR	MACE at 1 year	05/2025
QFR	FAVOR III Europe Japan Study	Randomized controlled trial	Is QFR vs FFR in intermediate lesions: Noninferiority	2001	FFR	QFR	MACE at 1 year	12/2025
	CONFIDENT	Randomized controlled trial	Clinical outcomes of CT-FFR vs QFR in stable angina	4648	QFR	CT-FFR	MACE at 1 year	05/2028
FFRangio	All-RISE	Randomized control trial	Clinical outcomes of pressure wire-based assessment vs FFRangio	1924	Pressure Wire-Based Physiology	FFRangio	MACE at 1 year	12/2024

Advancements and future perspectives in coronary angiography-derived fractional flow reserve. Prog Cardiovasc Dis. 2024 Aug 8:S0033-0620(24)00111-7. doi: 10.1016/j.pcad.2024.08.002. Epub ahead of print. PMID: 39122203.

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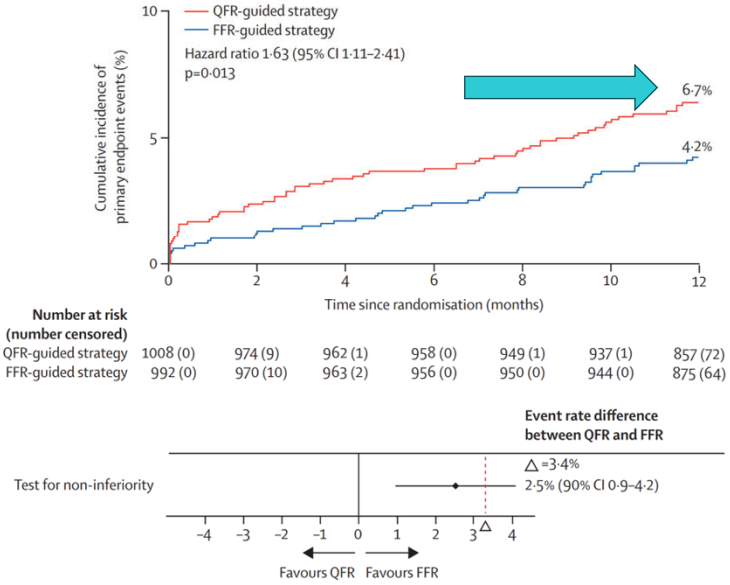
Interpretation The results of the FAVOR III Europe trial do not support the use of QFR if FFR is available to guide revascularisation decisions in patients with intermediate coronary stenosis. This finding could have implications for current clinical guidelines recommending QFR for this purpose.



FAVOR III

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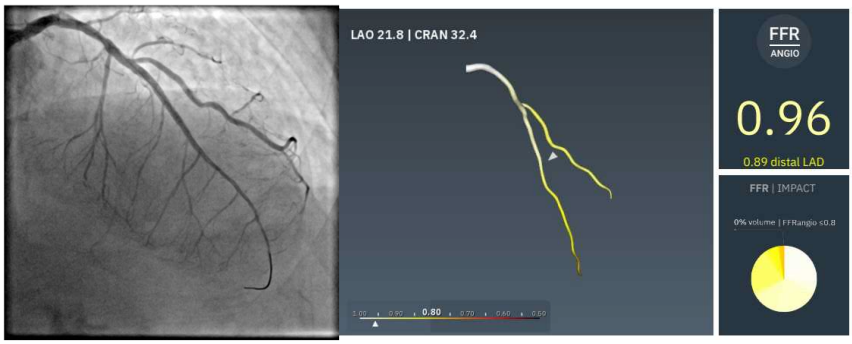
9. Post-PCI physiology:
did we achieve a good result?



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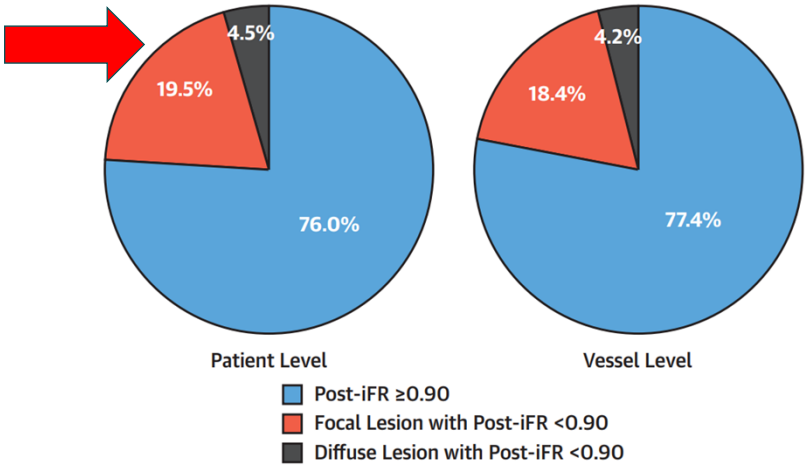
Blinded Physiological Assessment of Residual Ischemia After Successful Angiographic Percutaneous Coronary Intervention

The DEFINE PCI Study



Jeremias, A. et al. J Am Coll Cardiol Intv. 2019;12(20):1991-2001.

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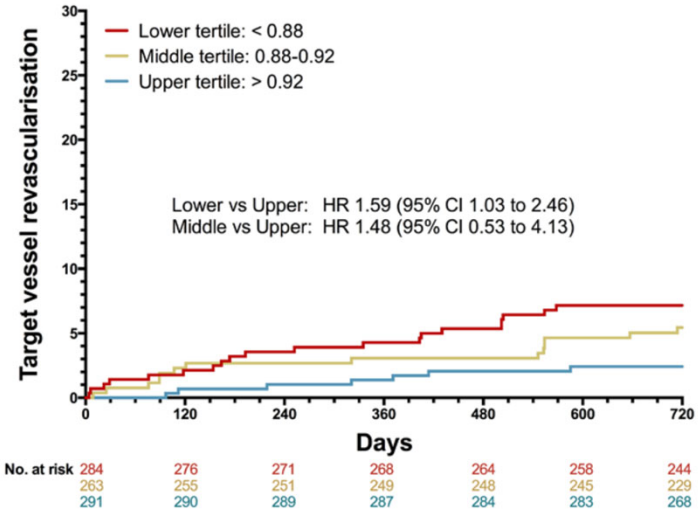
2-years vessel-related event rates across post–PCI FFR tertiles



Piroth Z, Toth GG, Tonino PAL, Barbato E, Aghlmandi S, Curzen N, Rioufol G, Pijls NHJ, Fearon WF, Jüni P, De Bruyne B. Prognostic Value of Fractional Flow Reserve Measured Immediately After Drug-Eluting Stent Implantation. Circ Cardiovasc Interv. 2017 Aug;10(8):e005233. doi: 10.1161/CIRCINTERVENTIONS.116.005233. PMID: 28790165.

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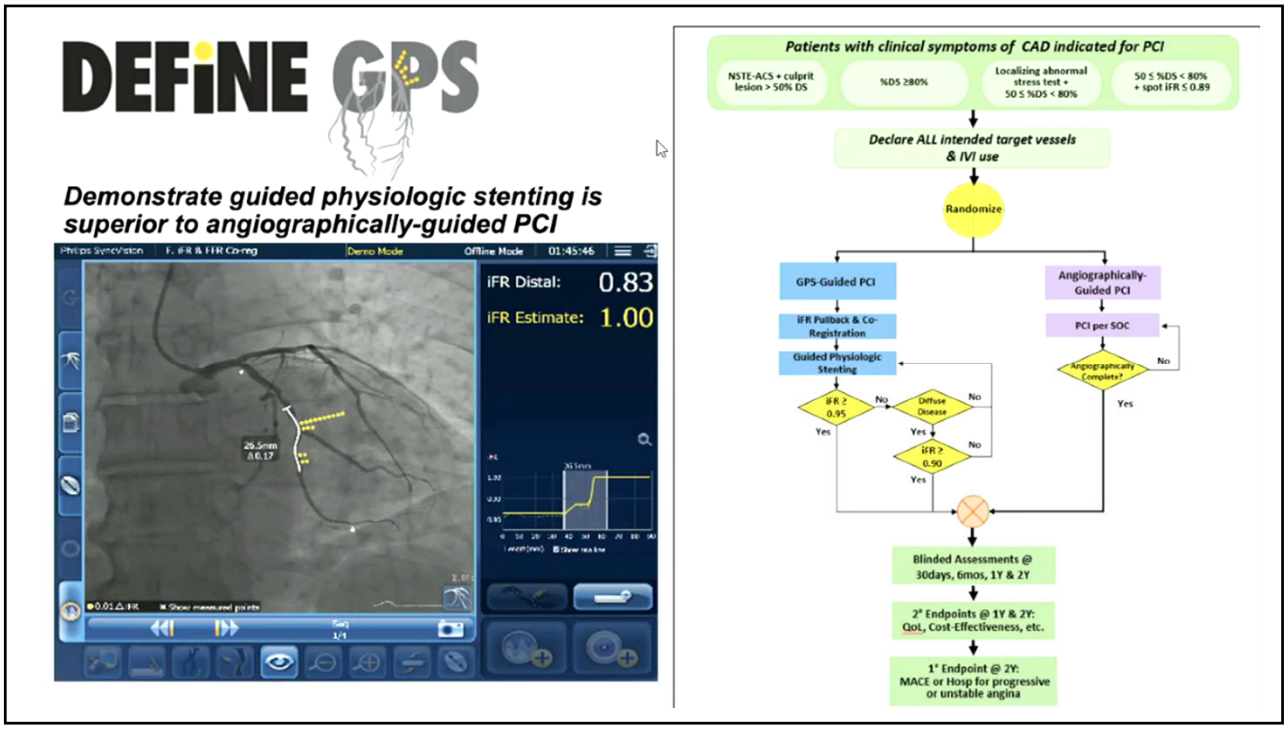
DEFINE GPS
Demonstrate guided physiologic stenting is superior to angiographically-guided PCI
iFR Distal: 0.83
iFR Estimate: 1.00
Patients with clinical symptoms of CAD indicated for PCI
NSTE-ACS + culprit lesion > 50% DS
%DS ≥80%
Localizing abnormal stress test + 50 ≤ %DS < 80%
50 ≤ %DS < 80% + spot iFR ≤ 0.89
Declare ALL intended target vessels & IVI use
Randomize
GPS-Guided PCI
iFR Pullback & Co-Registration
Guided Physiologic Stenting
iFR ≥ 0.95
Diffuse Disease
iFR ≥ 0.90
Angiographically-Guided PCI
PCI per SOC
Angiographically Complete?
Blinded Assessments @ 30days, 6mos, 1Y & 2Y
2° Endpoints @ 1Y & 2Y: QoL, Cost-Effectiveness, etc.
1° Endpoint @ 2Y: MACE or Hosp for progressive or unstable angina

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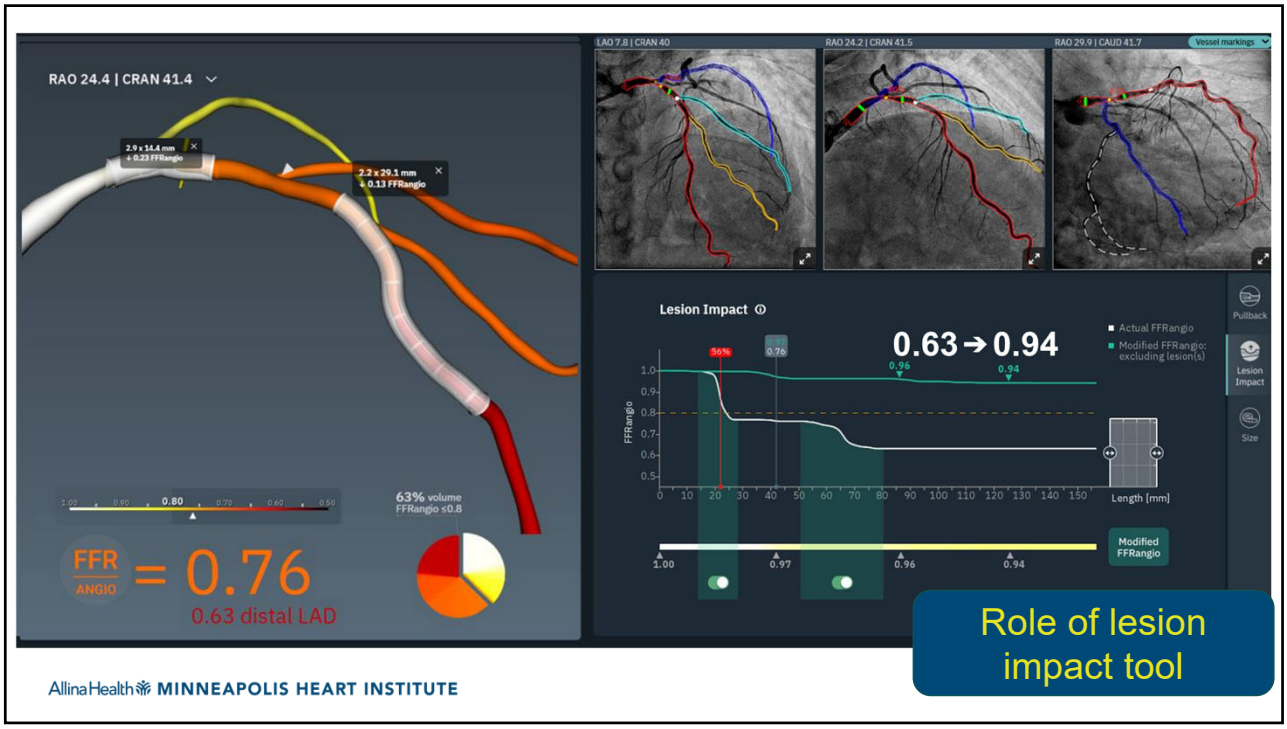
RAO 24.4 | CRAN 41.4
FFR ANGIO = 0.76
0.63 distal LAD
63% volume FFRangio ≤0.8
LAO 7.8 | CRAN 40
RAO 24.2 | CRAN 41.5
RAO 29.9 | CAUD 41.7
Lesion Impact
0.63 → 0.94
Actual FFRangio
Modified FFRangio: excluding lesion(s)
FFRangio
Length [mm]
Modified FFRangio
Role of lesion impact tool
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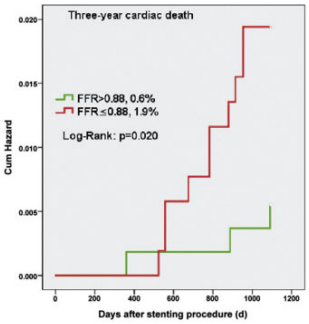
What is the target post-PCI? → Insights from the DKCRUSH VII Registry Study

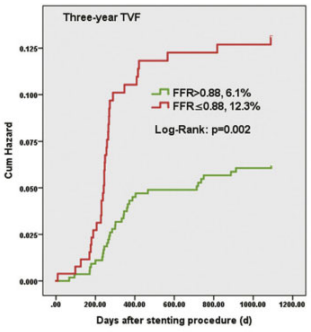
TABLE 4 1- and 3-Year Clinical Outcomes

	Overall (N = 1,476)	FFR >0.88 (n = 998)	FFR ≤0.88 (n = 478)	p Value
1-yr follow-up				
Cardiac death	8 (0.5)	2 (0.2)	6 (1.3)	0.017
Target vessel MI	2 (0.1)	0	2 (0.4)	0.104
CABG	4 (0.3)	4 (0.4)	0	0.311
Target lesion revascularization	67 (4.5)	28 (2.8)	39 (8.1)	0.002
Target vessel revascularization	80 (5.4)	38 (3.8)	42 (8.8)	0.005
Target vessel failure	88 (6.0)	40 (4.0)	48 (10.0)	0.001
Stent thrombosis	2 (0.1)	0	2 (0.4)	0.104
3-yr follow-up				
No. of patients	1,446 (97.9)	973 (97.5)	473 (98.9)	–
Cardiac death	15 (1.0)	6 (0.6)	9 (1.9)	0.018
Target vessel MI	9 (0.6)	4 (0.4)	5 (1.1)	0.086
CABG	7 (0.5)	4 (0.4)	3 (0.6)	0.112
Target lesion revascularization	90 (6.2)	41 (4.2)	49 (10.4)	0.002
Target vessel revascularization	107 (7.4)	51 (5.2)	56 (11.8)	0.001
Target vessel failure	119 (8.2)	60 (6.1)	59 (12.3)	0.002
Stent thrombosis	7 (0.5)	4 (0.4)	3 (0.6)	0.65

Li SJ et al. Cutoff Value and Long-Term Prediction of Clinical Events by FFR Measured Immediately After Implantation of a Drug-Eluting Stent in Patients With Coronary Artery Disease: 1- to 3-Year Results From the DKCRUSH VII Registry Study. JACC Cardiovasc Interv. 2017 May 22;10(10):986-995.

FFR <=0.88 immediately after implantation of a DES had a sensitivity of 83% and specificity of 78% for TVF.





FFR 10 mm distal to the lesion or stent edge measured by the pressure wire.

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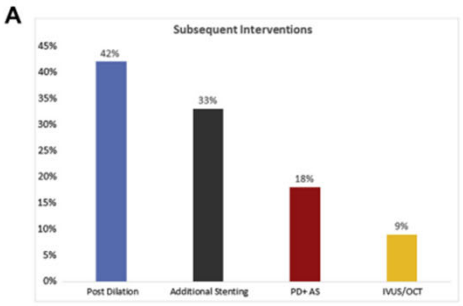

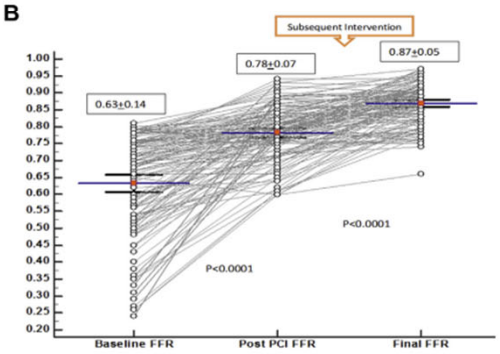

JACC: CARDIOVASCULAR INTERVENTIONS
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http://dx.doi.org/10.1016/j.jcin.2016.01.046

Utilizing Post-Intervention Fractional Flow Reserve to Optimize Acute Results and the Relationship to Long-Term Outcomes

Shiv K. Agarwal, MD,[a] Srikanth Kasula, MD,[a] Yalcin Hacioglu, MD,[a] Zubair Ahmed, MD,[a,b] Barry F. Uretsky, MD,[a,b] Abdul Hakeem, MD[a,b]

CONCLUSIONS Post-PCI FFR reclassified 20% of angiographically satisfactory lesions, which required further intervention thereby providing an opportunity for complete functional optimization at the time of the index procedure. This is particularly important as FFR post-PCI FFR was a powerful independent predictor of long-term outcomes. (J Am Coll Cardiol Intv 2016;9:1022–31) © 2016 by the American College of Cardiology Foundation.

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10. Future directions and opportunities

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JACC: CARDIOVASCULAR IMAGING
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ORIGINAL RESEARCH

Predictors for Vulnerable Plaque in Functionally Significant Lesions

Seokhun Yang, MD,[a] Doyeon Hwang, MD,[a] Koshiro Sakai, MD, PhD,[b,c] Takuya Mizukami, MD, PhD,[b,d,e] Jonathon Leipsic, MD,[f] Marta Belmonte, MD,[b,g] Jeroen Sonck, MD, PhD,[b,h] Bjarne L. Nørgaard, MD, PhD,[i] Hiromasa Otake, MD, PhD,[j] Brian Ko, MD, PhD,[k] Michael Maeng, MD, PhD,[i] Jesper Møller Jensen, MD, PhD,[i] Dimitri Buytaert, MSc,[b] Daniel Munhoz, MD, PhD,[b,h,l] Daniele Andreini, MD, PhD,[m,n] Hirofumi Ohashi, MD, PhD,[b,o] Toshiro Shinke, MD, PhD,[c] Charles A. Taylor, PhD,[p] Emanuele Barbato, MD, PhD,[b,h] Bernard De Bruyne, MD, PhD,[b,q] Carlos Collet, MD, PhD,[b] Bon-Kwon Koo, MD, PhD[a]

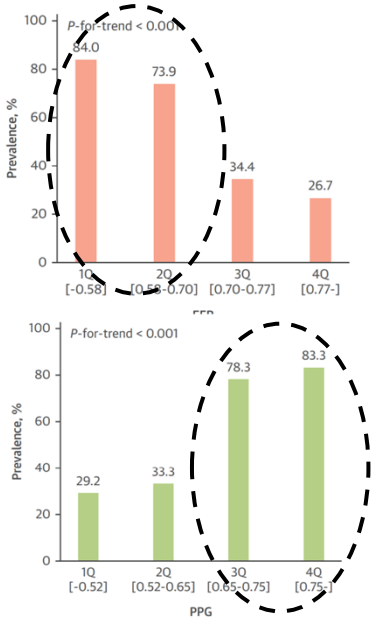
ABSTRACT

BACKGROUND Vulnerable plaque presents prognostic implications in addition to functional significance.

OBJECTIVES The aim of this study was to identify relevant features of vulnerable plaque in functionally significant lesions.

METHODS In this multicenter, prospective study conducted across 5 countries, including patients who had invasive fractional flow reserve (FFR) ≤0.80, a total of 95 patients with available pullback pressure gradient (PPG) and plaque analysis on coronary computed tomographic angiography and optical coherence tomography were analyzed. Vulnerable plaque was defined as the presence of plaque rupture or thin-cap fibroatheroma on optical coherence tomography. Among the 25 clinical characteristics, invasive angiographic findings, physiological indexes, and coronary computed tomographic angiographic findings, significant predictors of vulnerable plaque were identified.

Vulnerable plaque:
Focal lesions (high PPG) with lower FFR values



Yang S et al. Predictors for Vulnerable Plaque in Functionally Significant Lesions. JACC Cardiovasc Imaging. 2024 Sep 11:S1936-878X(24)00311-5.

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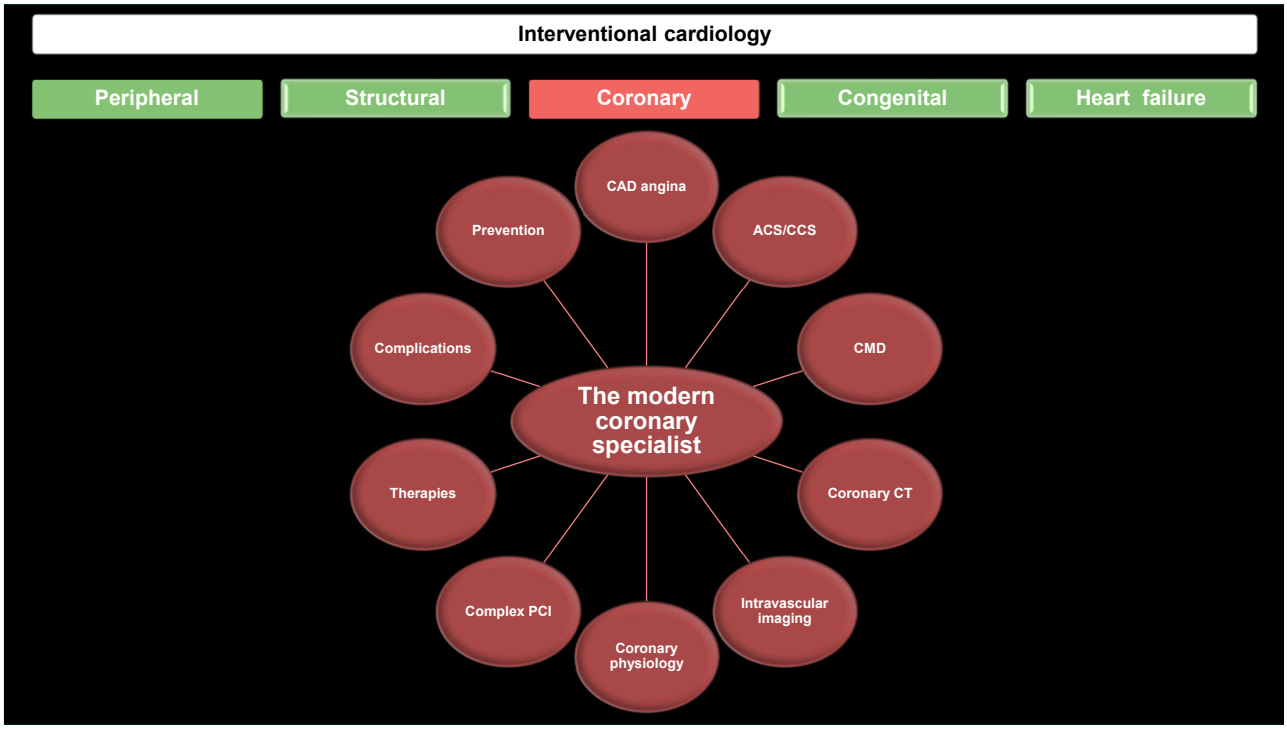
Interventional cardiology
Peripheral
Structural
Coronary
Congenital
Heart failure
The modern coronary specialist
CAD angina
ACS/CCS
CMD
Coronary CT
Intravascular imaging
Coronary physiology
Complex PCI
Therapies
Complications
Prevention

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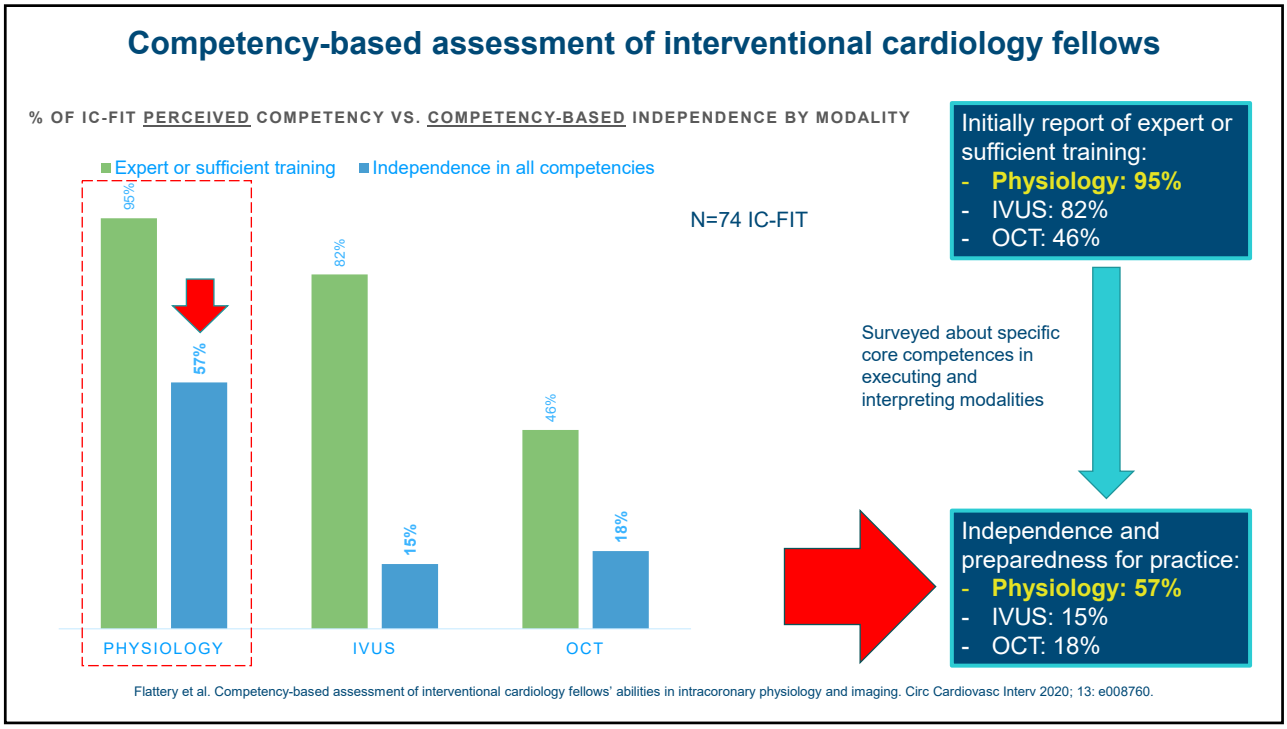
Competency-based assessment of interventional cardiology fellows
% OF IC-FIT PERCEIVED COMPETENCY VS. COMPETENCY-BASED INDEPENDENCE BY MODALITY
Expert or sufficient training
Independence in all competencies
95%
57%
82%
15%
46%
18%
PHYSIOLOGY
IVUS
OCT
N=74 IC-FIT
Initially report of expert or sufficient training:
- Physiology: 95%
- IVUS: 82%
- OCT: 46%
Surveyed about specific core competences in executing and interpreting modalities
Independence and preparedness for practice:
- Physiology: 57%
- IVUS: 15%
- OCT: 18%
Flattery et al. Competency-based assessment of interventional cardiology fellows' abilities in intracoronary physiology and imaging. Circ Cardiovasc Interv 2020; 13: e008760.

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SAVE THE DATE – June 5-6, 2025

Course Directors: Yader Sandoval, Emmanouil S. Brilakis, Carlos Collet, Bernard De Bruyne
Course Faculty: Willian Fearon, Morton Kern, Nils Johnson, Allen Jeremias, Arnold Seto, R. Jay Widmer, Nathaniel Smilowiz, Claire Raphael,

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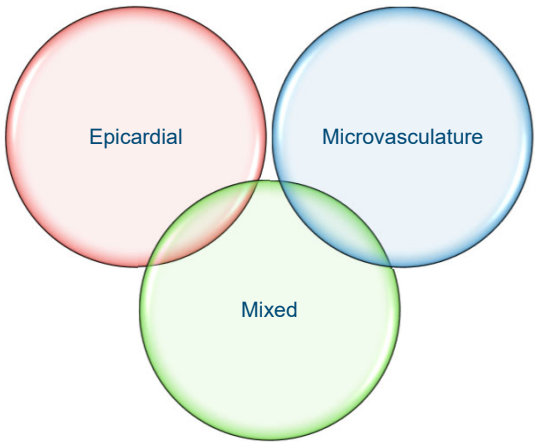
Modern use of coronary physiology in the CCL

- Coronary CT
- Pressure-wire
- Angiography
- Intravascular imaging



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Applications of physiology in planning and guiding PCI procedures

Preprocedural PCI planning and simulation

- Setting of indication for PCI
- Identification of disease pattern: focal, tandem, diffuse
- Simulation of functional results with different PCI strategies

Improving the precision of PCI

- Avoidance of geographic mismatch over PCI by identifying location of target flow-limiting disease
- Intravascular imaging for accurate planning and guidance of stenting

Postprocedural assessment and optimisation

- Longitudinal physiology analysis to rule out flow-limiting disease
- Focal patterns may be amenable to post-PCI optimisation

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