“Top 10” issues in FFR

Hard endpoints. Angiographic FFR.

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Disclosure Statement of Financial Interest

Within the past 12+ months, Nils Johnson has had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Organizations (alphabetical)
• Grant/research support (to *institution*)	• St Jude Medical (for CONTRAST study) • Volcano/Philips (for DEFINE-FLOW study)
• Licensing and associated consulting (to *institution*)	• Boston Scientific (for smart-minimum FFR algorithm)
• Support for educational meetings/training (honoraria/fees donated to *institution*)	• Various, including academic and industry
• PET software 510(k) from FDA (application by Lance Gould, to *institution*)	• K113754 (cfrQuant, 2011) • K143664 (HeartSee, 2014) • K171303 (HeartSee update, 2017)
• Patent pending (USPTO serial number 62/597,134)	• SAVI and ΔP/Q methods

24th CARDIOVASCULAR SUMMIT
TCTAP 2019
April 27-30, 2019
Coex, Seoul, Korea

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TCTAP Workshops

Saturday, April 27

Coronary Physiology

11:34 AM	Top 10 Issues(or more) in FFR Measurement *Lecturer: Nils Johnson*
11:42 AM	How to Make Optimal Hyperemia: From Adenosine to Contrast *Lecturer: Bon-Kwon Koo*
11:50 AM	Many Pressure Wires in Cath Lab: Advantages and Disadvantages *Lecturer: William F. Fearon*
11:58 AM	Synergetic Approach for Discordant Lesions Between FFR and Hyperemia Free Indexes *Lecturer: Jung-Min Ahn*
12:06 PM	Understanding of Post Stent FFR *Lecturer: Joo Myung Lee*
12:14 PM	Interactive Discussion with Audience Q&A

1. Hyperemia
2. Hardware
3. NHPR
4. Post-PCI

Hard endpoints

Why does PCI work?

Stable PCI: skeptical guidelines

ESC 2013 (stable CAD)

9.10 Gaps in evidence (see web addenda)

These guidelines suffer from limitations inherent in the evidence available, uncertainties on the best imaging modalities, on what is the best modern pharmacologic approach and on what is the real benefit from myocardial revascularization.

ESC 2018 (revascularization)

5.4 Gaps in the evidence

It remains to be determined whether revascularization by PCI improves prognosis in patients with SCAD.

ACC/AHA 2012 (stable CAD)

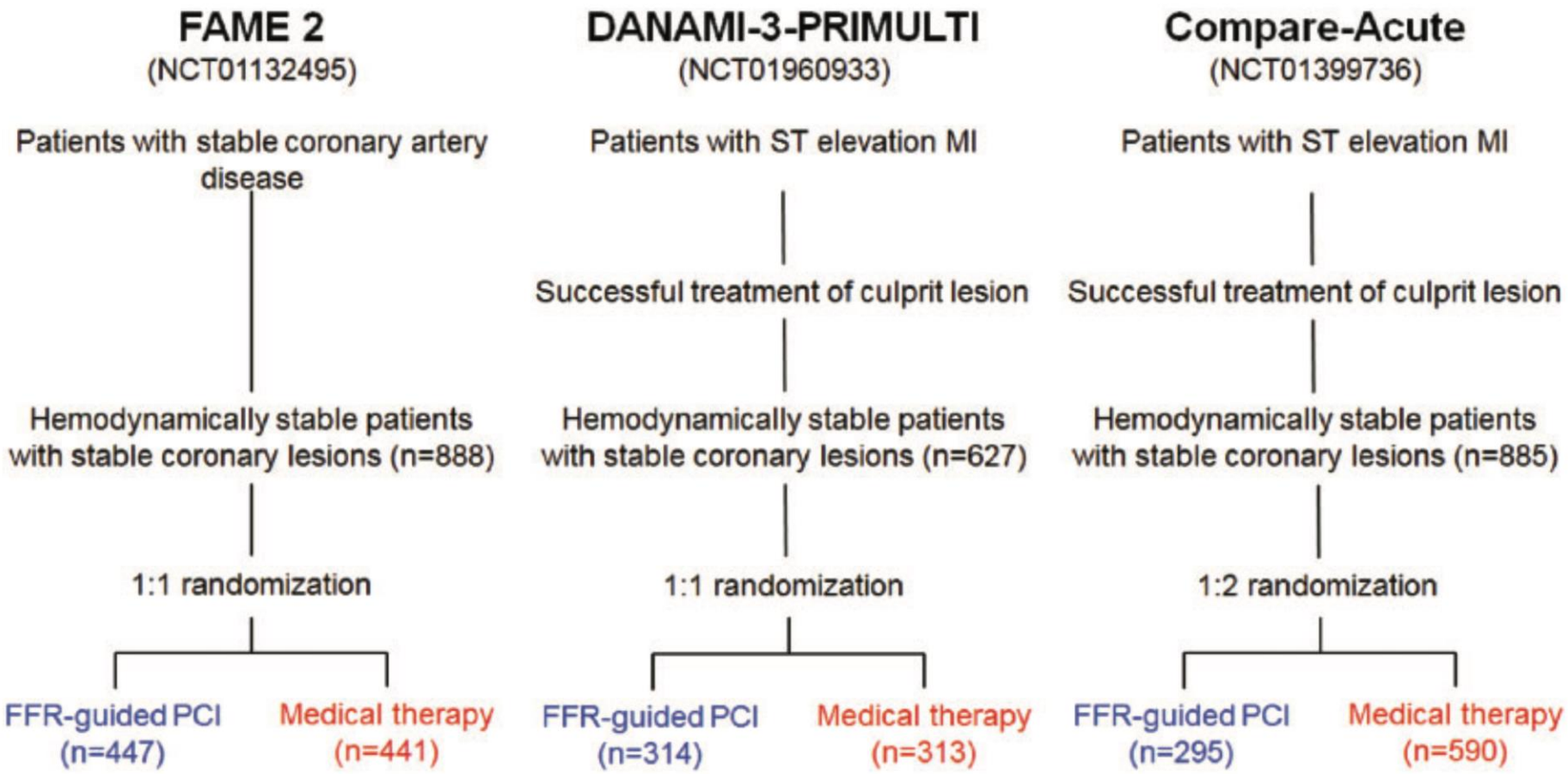
5.5. PCI Versus Medical Therapy

The findings from individual studies and systematic reviews of PCI versus medical therapy can be summarized as follows:

- PCI reduces the incidence of angina (366,407,1016, 1020,1033,1045).
- PCI has not been demonstrated to improve survival in stable patients (138,1041,1042).
- PCI may increase the short-term risk of MI (366, 397,1041,1045).
- PCI does not lower the long-term risk of MI (138,366,397,408,1041,1042).

ACC 2012 = Fihn SD, *JACC*. 2012 Dec 18;60(24):e44-e164. (Section 5.5 excerpt with *emphasis*)
ESC 2013 = Montalescot G, *EHJ*. 2013 Oct;34(38):2949-3003. (Section 9.10 text with *emphasis*)
ESC 2018 = Neumann FJ, *EHJ*. 2019 Jan 7;40(2):87-165. (Section 5.4 excerpt with *emphasis*)

Pool RCT's of PCI for stable lesions



combined N = 2400 subjects

mean follow-up 35 months

Zimmermann FM, *EHJ*. 2019 Jan 7;40(2):180-186. (Figure 1)

FFR stable = pooling valid

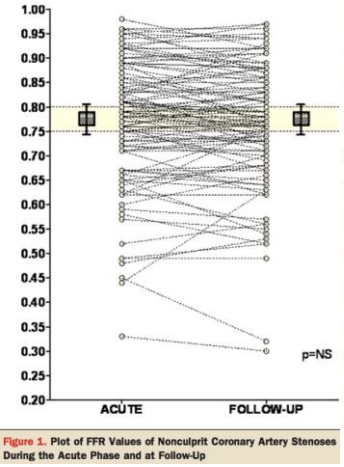
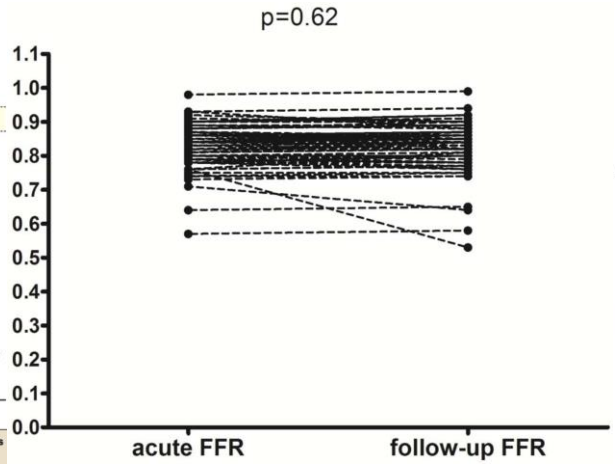
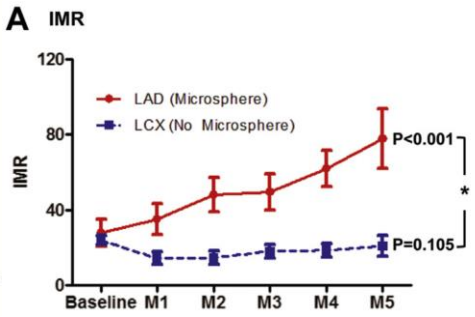
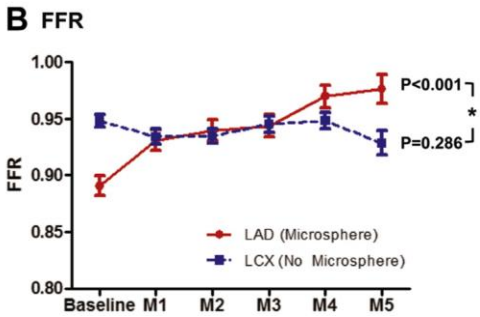


Figure 1. Plot of FFR Values of Nonculprit Coronary Artery Stenoses During the Acute Phase and at Follow-Up







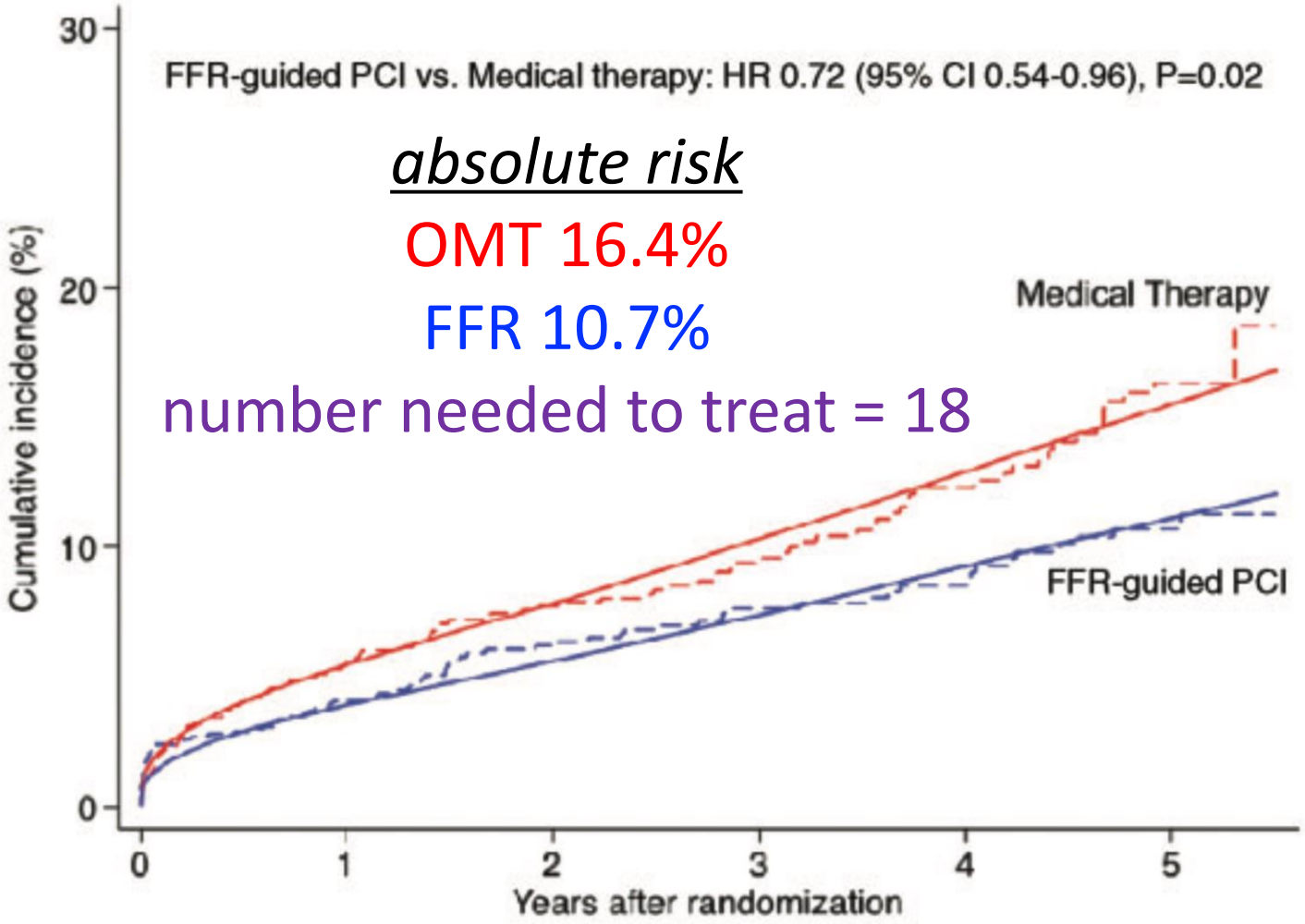
101 patients with ACS
STEMI in 75%
FFR acute = 0.77 ± 0.13
FFR late = 0.77 ± 0.13
(measured 35 days later)
Only 2 changed >0.8 to <0.75

50 patients with STEMI
66 non-culprit lesions
FFR acute = 0.82 ± 0.07
FFR late = 0.82 ± 0.08
(measured 5-8 days later)

Animal model
microsphere emboli
FFR/IMR stable in LCx (non-culprit)
FFR/IMR unstable in LAD (culprit)

left = Ntalianis A, *JACC Cardiovasc Interv*. 2010 Dec;3(12):1274-81. (Figure 1 with annotations)
middle = Musto C, *Am Heart J*. 2017 Nov;193:63-69. (Figure 1B and results from Table 2)
right = Lee JM, *JACC Cardiovasc Interv*. 2018 Apr 23;11(8):717-24. (Figure 2)

Reduction in CV death + MI



absolute risk

OMT 16.4%

FFR 10.7%

number needed to treat = 18

Zimmermann FM, *EHJ*. 2019 Jan 7;40(2):180-186. (Figure 2 plus results)

Benefit driven by MI and not death

Table I Clinical events: primary and secondary endpoints

	Estimated cumulative incidence at 5 years		Hazard ratio (95% CI)	*P*-value
	FFR-guided PCI	Medical therapy		
Cardiac death or MI[a]	10.7% (8.4–13.6%)	16.4% (13.3–20.1%)	0.72 (0.54–0.96)	0.02
Death or MI	13.9% (11.2–17.2%)	19.4% (16.0–23.4%)	0.76 (0.59–0.99)	0.04
MI	8.5% (6.5–11.1%)	13.4% (10.7–16.8%)	0.70 (0.51–0.97)	0.03
Cardiac death	3.2% (2.1–5.1%)	3.0% (1.9–4.8%)	1.04 (0.58–1.78)	0.89
All-cause mortality	7.0% (5.2–9.6%)	6.5% (4.7–8.9%)	1.03 (0.69–1.54)	0.89

[a]Pre-specified primary outcome. FFR-guided PCI (*N* = 1056) and medical therapy (*N* = 1344).
CI, confidence interval; FFR, fractional flow reserve; MI, myocardial infarction; PCI, percutaneous coronary intervention.

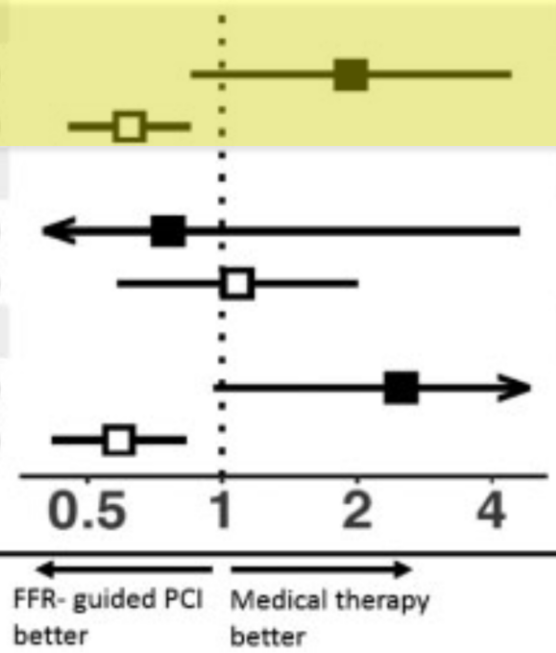
Myocardial infarction

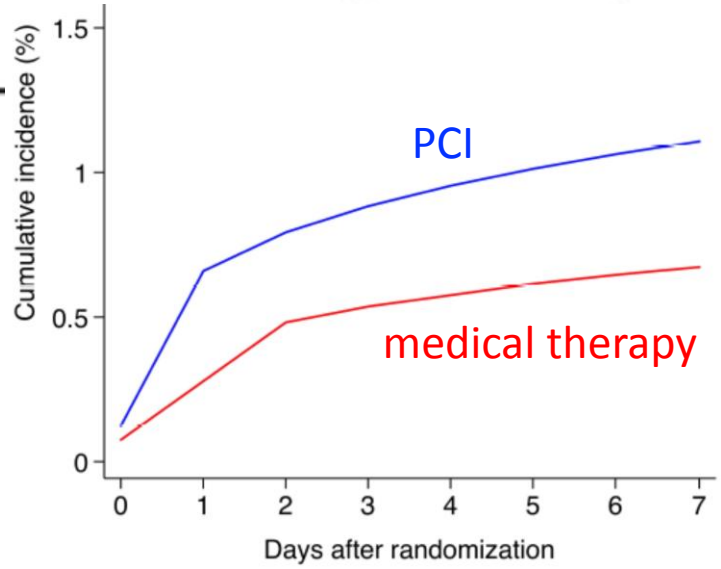
- 8.5% FFR
- 13.4% OMT

Zimmermann FM, *EHJ*. 2019 Jan 7;40(2):180-186. (Table 1)

Early hazard in first week from PCI

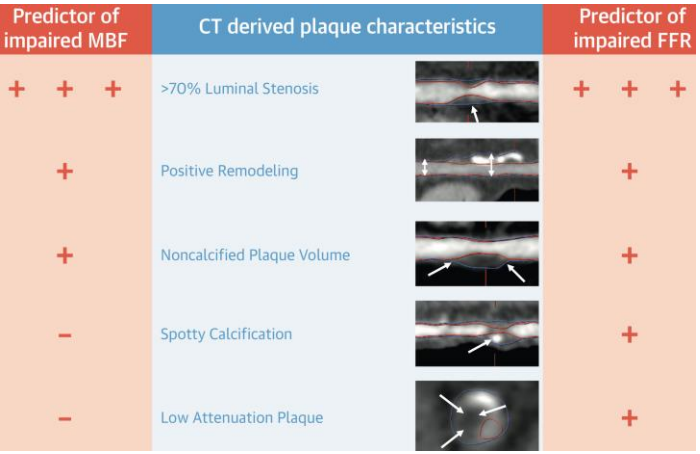
	HR (95% CI)	P-value	P-value for interaction
Cardiac death or myocardial infarction			0.003
Day 0 to 7	1.94 (0.85 to 4.42)	0.12	
Day 8 to maximum follow-up	0.62 (0.46 to 0.85)	0.003	
Cardiac death			0.83
Day 0 to 7	0.76 (0.12 to 4.60)	0.76	
Day 8 to maximum follow-up	1.08 (0.58 to 2.01)	0.81	
Myocardial infarction			0.001
Day 0 to 7	2.51 (0.96 to 6.57)	0.06	
Day 8 to maximum follow-up	0.59 (0.42 to 0.83)	0.002	



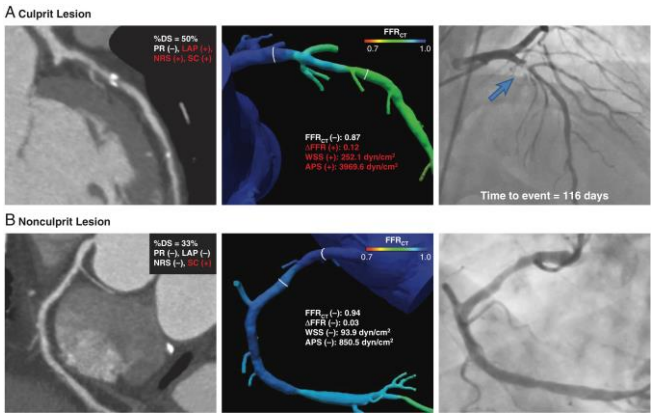


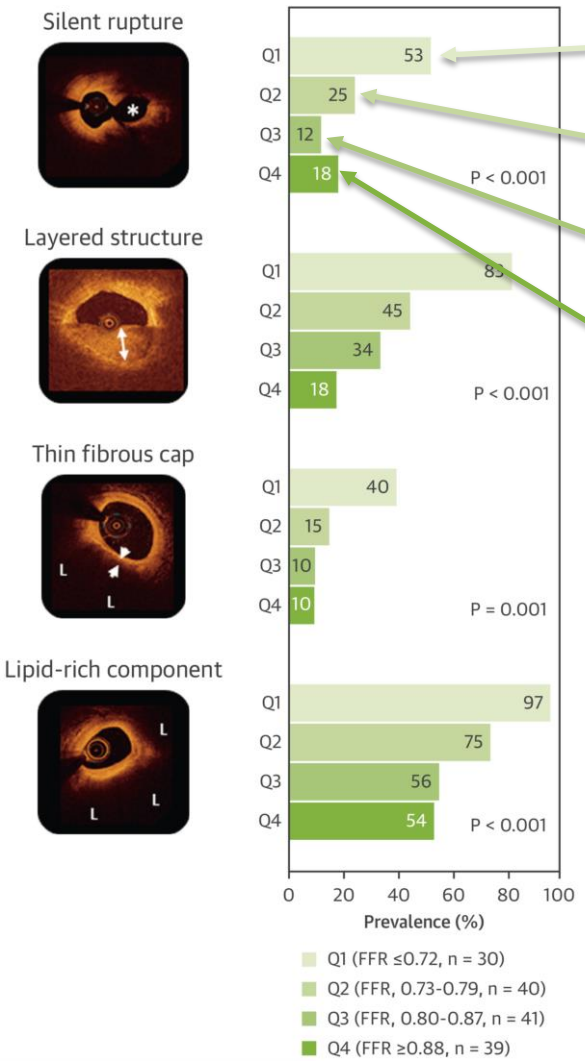
Zimmermann FM, *EHJ*. 2019 Jan 7;40(2):180-186. (Figure 4 and S2 inset)

Low FFR plaque = vulnerable plauqe



Low FFR lesion
Vulnerable features
Exposed to mechanical stress





FFR≤0.72

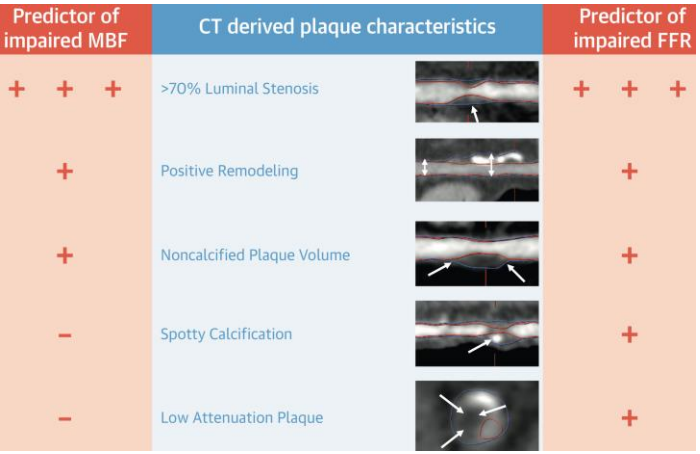
FFR=0.73-0.79

FFR=0.80-0.87

FFR≥0.88

left, top = Driessen RS, *JACC*. 2018 Feb 6;71(5):499-509. (Central Illustration)
left, bottom = Lee JM, *JACC Cardiovasc Imaging*. 2018 Mar 14. [Epub ahead of print] (Figure 2)
right = Matsuo Y, *JACC Cardiovasc Imaging*. 2019 Jan 9. [Epub ahead of print] (Figure 1 portion with custom legend)

Unifying hypothesis



Low FFR lesion
Vulnerable features
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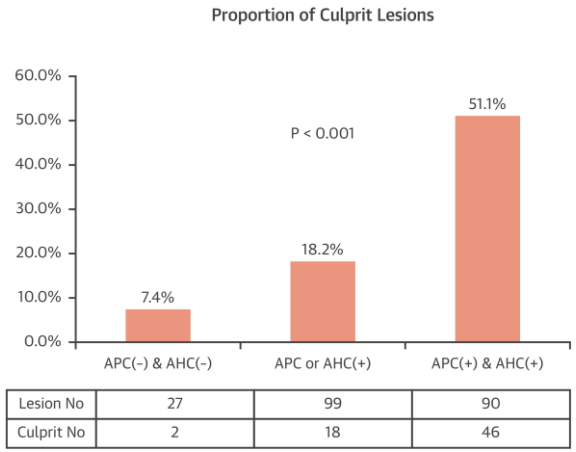
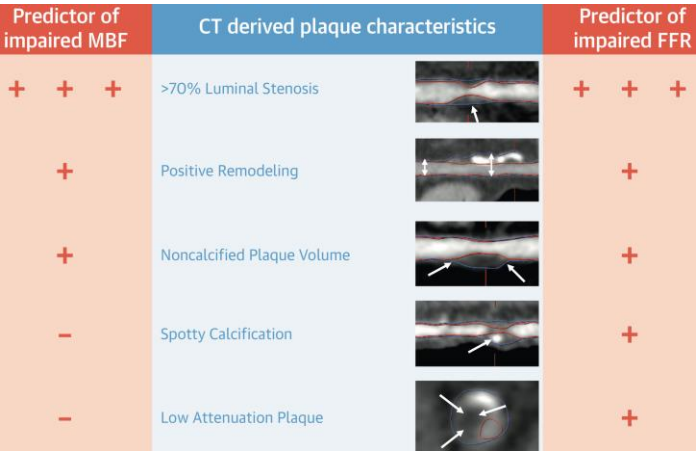


Lesion No	27	99	90
Culprit No	2	18	46

Natural history leads
to plaque rupture

left = Driessen RS, *JACC*. 2018 Feb 6;71(5):499-509. (Central Illustration)
middle = Lee JM, *JACC Cardiovasc Imaging*. 2018 Mar 14. [Epub ahead of print] (Figure 4A)

Unifying hypothesis



Low FFR lesion
Vulnerable features
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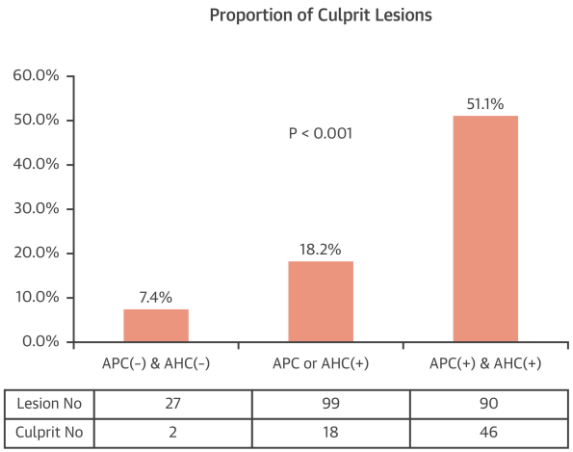

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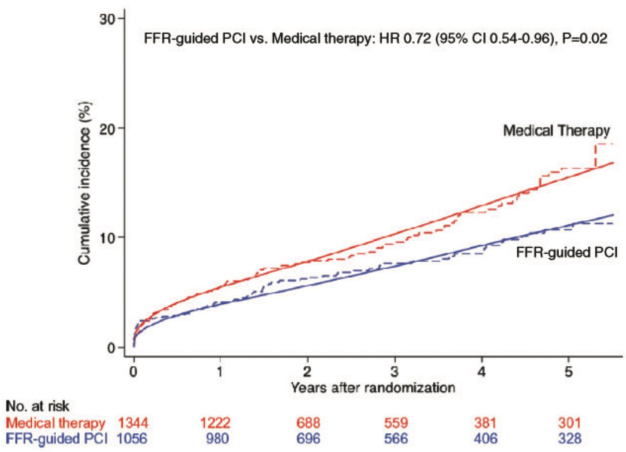


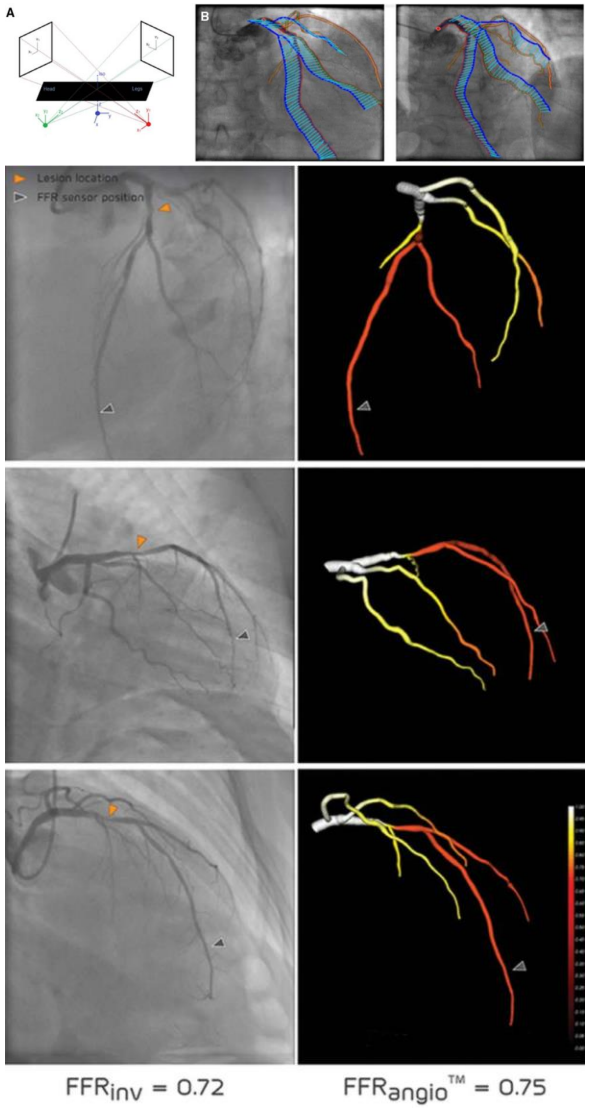
PCI stabilizes lesion
At short-term cost
But long-term benefit

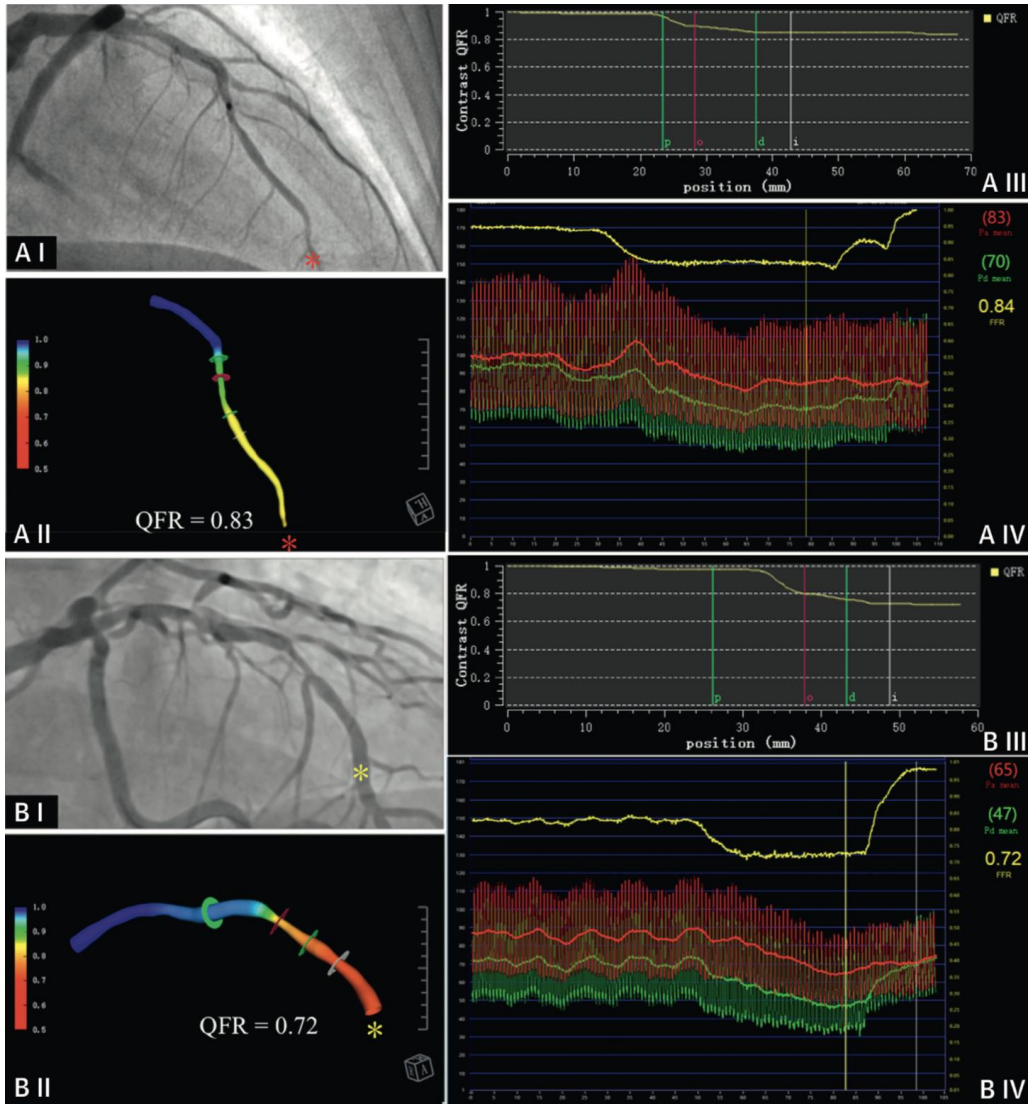
left = Driessen RS, *JACC*. 2018 Feb 6;71(5):499-509. (Central Illustration)
middle = Lee JM, *JACC Cardiovasc Imaging*. 2018 Mar 14. [Epub ahead of print] (Figure 4A)
right = Zimmermann FM, *EHJ*. 2019 Jan 7;40(2):180-186. (Figure 2)

Angiography

Simulating physiology

Predict FFR using biplane QCA

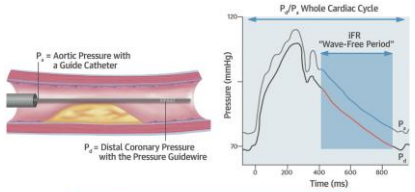


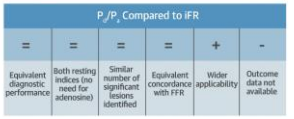


left (FFR$_{angio}$) = Pellicano M, *Circ Cardiovasc Interv*. 2017;10:e005259. (Figures 1 and 2)
right (QFR) = Xu B, *JACC*. 2017 Dec 26;70(25):3077-87. (Figure 2)

Non-hyperemic pressure ratios (NHPR)

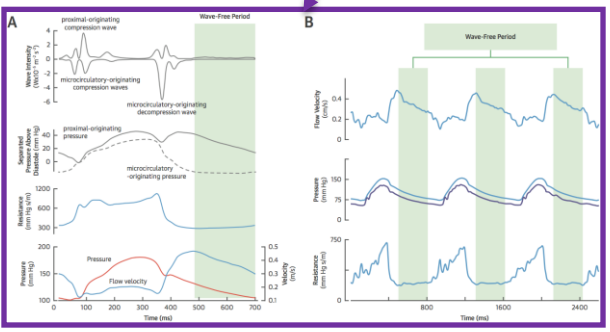
Whole-cycle



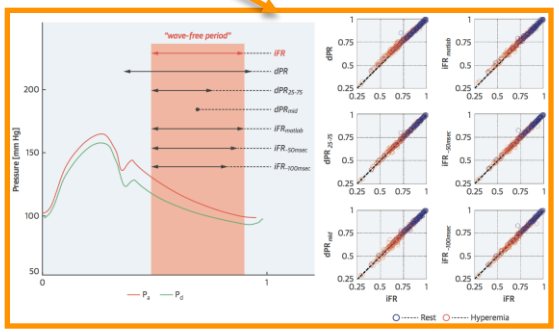


Pd/Pa (all devices)

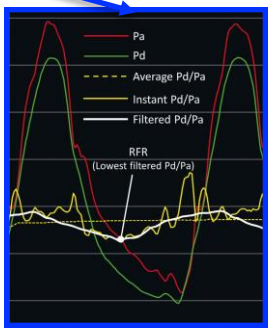
Sub-cycle
(mainly diastole)



iFR (Philips/Volcano)



dPR (Opsens)

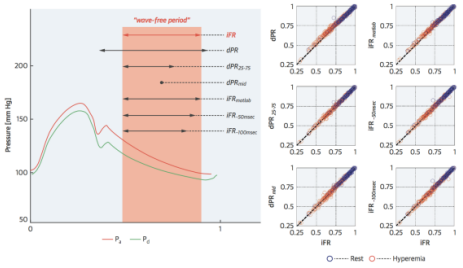


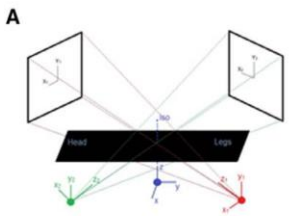
RFR (Abbott)

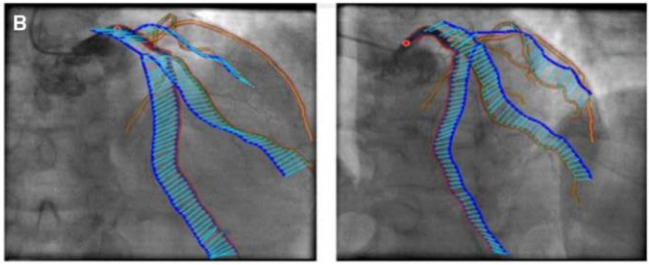
DFR (Boston Scientific)

iFR = Götberg M, *JACC*. 2017 Sep 12;70(11):1379-1402. (Figure 6)
dPR = van 't Veer M, *JACC*. 2017 Dec 26;70(25):3088-3096. (Central Illustration)
RFR = Svanerud J, *EuroIntervention*. 2018 Sep 20;14(7):806-814. (Figure 1)
Pd/Pa = Kobayashi Y, *JACC*. 2017 Oct 24;70(17):2105-2113. (Central Illustration)

NHPR vs Angiographic FFR







NHPR

Advantages

- Measures Pa, Pd directly
- Avoids hyperemia drug

Disadvantages

- Fixed Δ between Pd/Pa and FFR
- Requires pressure wire

Angiographic FFR

Advantages

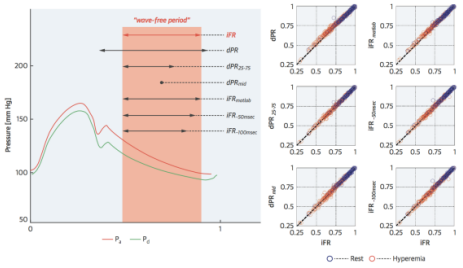
- Simulates hyperemia
- Avoids pressure wire

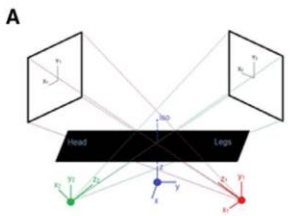
Disadvantages

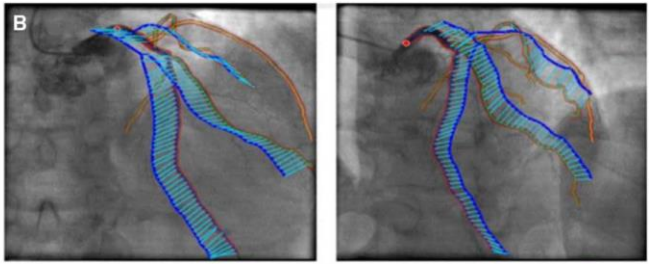
- Computes Pd indirectly
- Requires special software

left = van 't Veer M, *JACC*. 2017 Dec 26;70(25):3088-3096. (Central Illustration)
right = Pellicano M, *Circ Cardiovasc Interv*. 2017;10:e005259. (Figure 1)

NHPR vs Angiographic FFR







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NHPR vs FFR_{angio} to predict FFR

left = van 't Veer M, *JACC*. 2017 Dec 26;70(25):3088-3096. (Central Illustration)
right = Pellicano M, *Circ Cardiovasc Interv*. 2017;10:e005259. (Figure 1)

8 groups and 4 patterns of cases

FFR_{angio}	Pd/Pa	FFR≤0.80	FFR_{angio}≤0.80	NHPR≤limit
correct	correct	Y	Y	Y
correct	correct	N	N	N
incorrect	*incorrect*	*Y*	*N*	*N*
incorrect	*incorrect*	*N*	*Y*	*Y*
correct	incorrect	Y	Y	N
correct	incorrect	N	N	Y
incorrect	**correct**	**Y**	**N**	**Y**
incorrect	**correct**	**N**	**Y**	**N**

FFR_{angio} agreed with iFR in 80%

iFR		FFR_{angio} correct	FFR_{angio} incorrect
	correct	215	
	incorrect		6

Circulation

substudy of FAST-FFR
clinicaltrials.gov
NCT03226262

ORIGINAL RESEARCH ARTICLE

Accuracy of Fractional Flow Reserve Derived From Coronary Angiography

Fearon WF, *Circulation*. 2019 Jan 22;139(4):477-484.

FFR_{angio} outperformed iFR!

		FFR_{angio} correct	FFR_{angio} incorrect
iFR	correct	215	**15**
	incorrect	**42**	6

FFR_{angio} almost 3-fold more likely to win disagreements

42/15 = 2.8 with McNemar p<0.001

Johnson NP, *JACC* (accepted, in press).

FFR_{angio} beats wire without hyperemia!

FFR_{angio}	NHPR	iFR	dPR	Pd/Pa
correct	correct	215	215	223
incorrect	incorrect	6	6	7
correct	incorrect	**42**	**42**	**34**
incorrect	correct	**15**	**15**	**14**
	McNemar ratio	2.8	2.8	2.4
	p-value	<0.001	<0.001	0.006

Key message: simulated hyperemia *better* than invasive resting physiology

Johnson NP, *JACC* (accepted, in press).

FFR_{angio} vs invasive NHPR