THURSDAY 4 JULY 2019
10:23-10:33 MAIN ARENA / LEVEL 4

asia AiCT PCR
The Official Course of APSIC

The Impact of Coronary Physiology on Clinical Decision Making
Where Do We Stand in 2019?

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Erasmus university
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The University of Melbourne

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Potential conflicts of interest

Speaker's name : Patrick W. Serruys

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship

- Grant/Research Support
- Consulting Fees/Honoraria

Company

- Abbott
- Boston Scientific
- Biosensors
- Medtronic
- Philips/Volcano
- Sinomedical Sciences Technology
- SMT
- Xeltis

Coronary physiology on clinical decision making

1. Before procedure outside the cathlab

- FFR_{CT}

2. Before procedure in the cathlab

- FFR (gold standard)
- iFR and other non-hyperemic indices (DFR, RFR, etc)
- Angiography derived FFR (QFR, FFR_{angio}, vFFR)
- Intracoronary imaging derived FFR (OFR)

3. During or after procedure in the cathlab

- FFR: several studies
- iFR: DEFINE PCI
- QFR: HAWKEYE

Coronary physiology on clinical decision making

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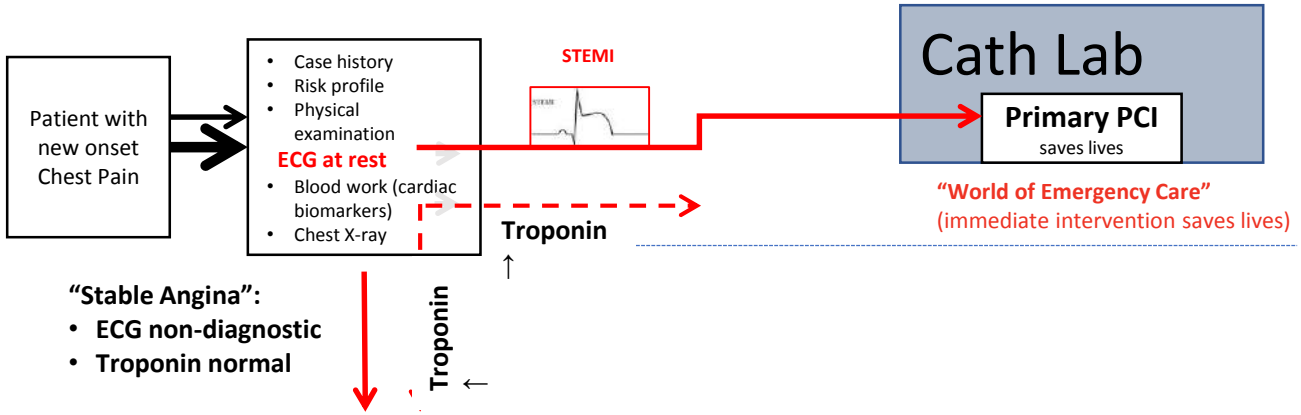
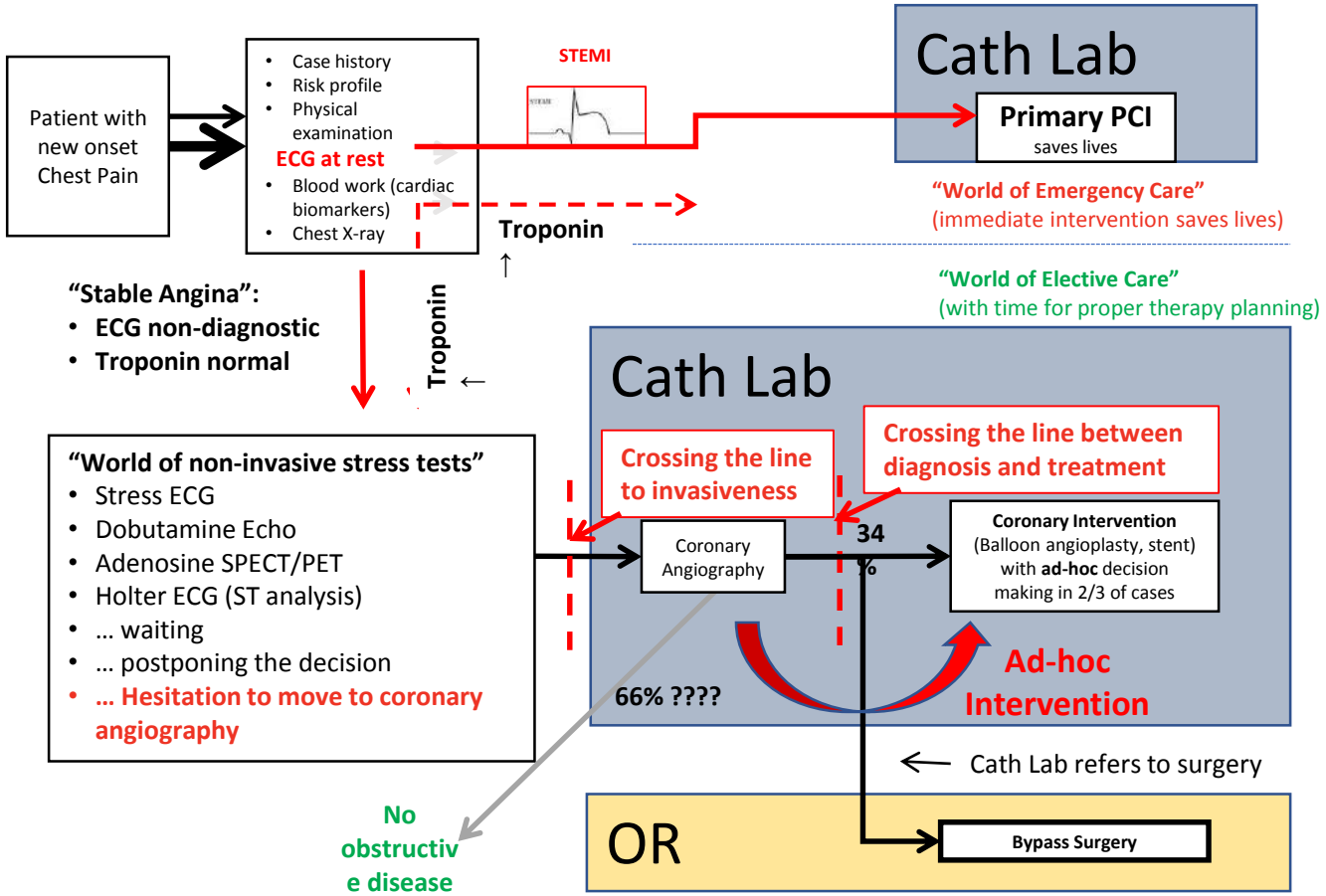
Chest Pain Pathway Today: Coronary Angiography and Ad-hoc Intervention



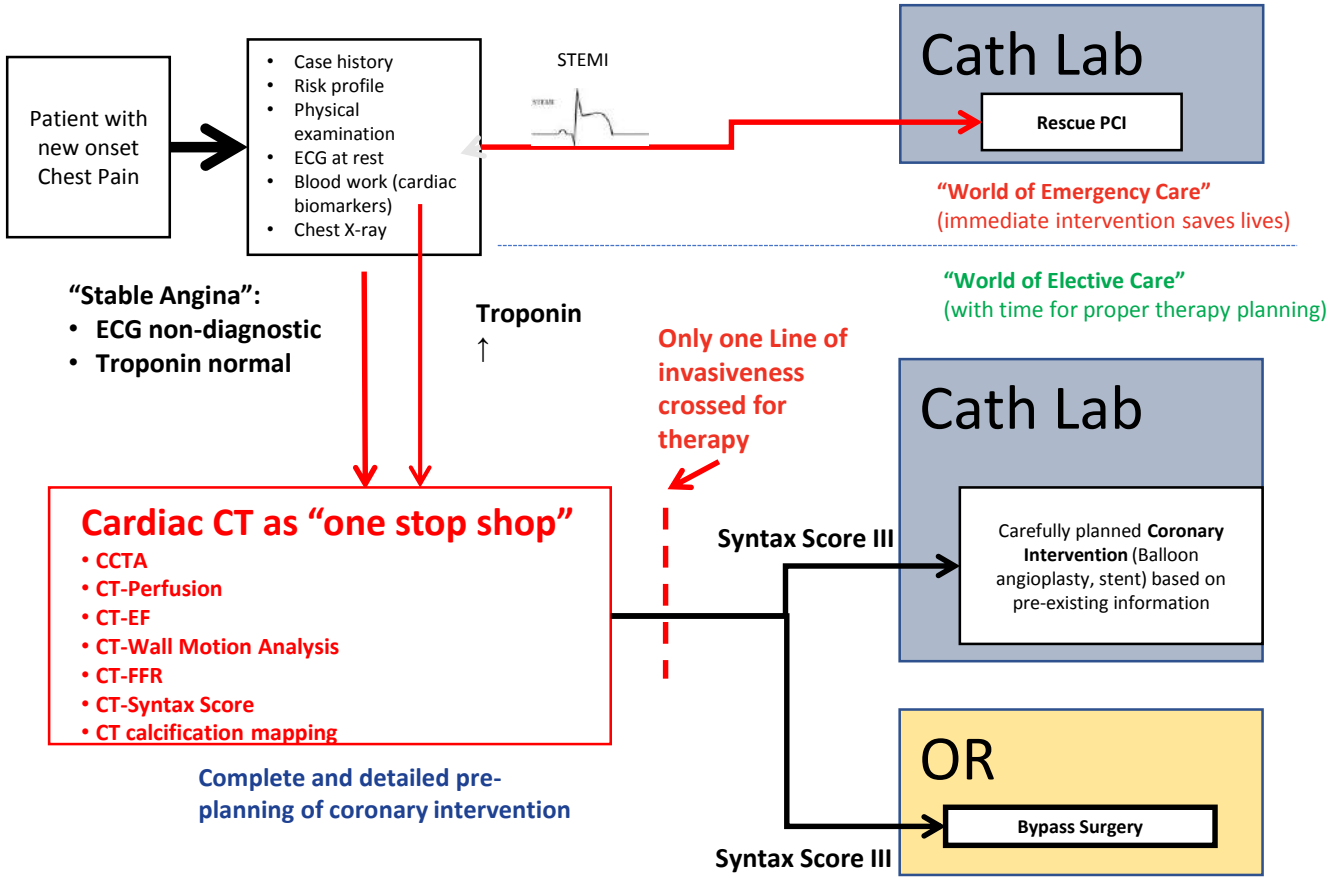
"World of non-invasive stress tests"

- Stress ECG
- Dobutamine Echo
- Adenosine SPECT/PET
- Holter ECG (ST analysis)
- … waiting
- … postponing the decision
- **… Hesitation to move to coronary angiography**

Chest Pain Pathway Today: Coronary Angiography and Ad-hoc Intervention



Future Vision: Cardiac CT as One-Stop-Shop Increases Quality and Effectiveness

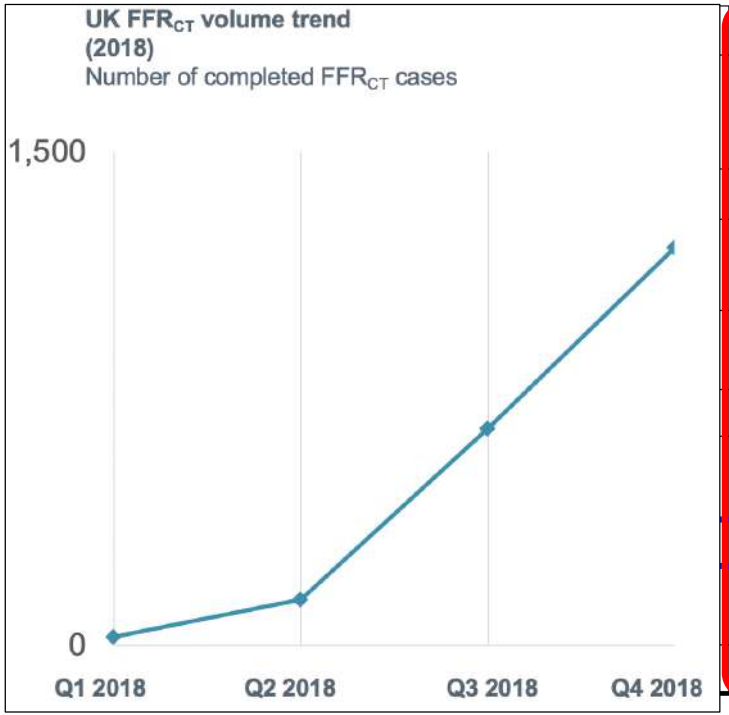


NICE UK Guidance (Nov 2017)

Based on the current evidence and assuming there is access to appropriate coronary **CT angiography facilities, using HeartFlow FFR_{CT} may lead to cost savings of £214 per patient.** By adopting this technology, the NHS in England may save a minimum of £9.1 million by 2022 through **avoiding invasive investigation and treatment.**

Putting NICE guidance into practice

Table 4 Estimated annual savings from year 5 onwards



	Proposed	
	Numbers of tests	Cost (£000s)
0	0 ↓100%	0
16,866	8,433 ↓50%	2,336
16,866	8,433 ↓50%	3,095
5,952	2,976 ↓50%	1,548
0	0 ↓100%	0
39,684	116.892 ↑400%	18,352
24,804	9,921 ↓60%	11,638
104,172	**146,656** ↑11%	**36,968**

Coronary physiology on clinical decision making

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3. During or after procedure in the cathlab

- FFR: several studies
- iFR: DEFINE PCI
- QFR: HAWKEYE

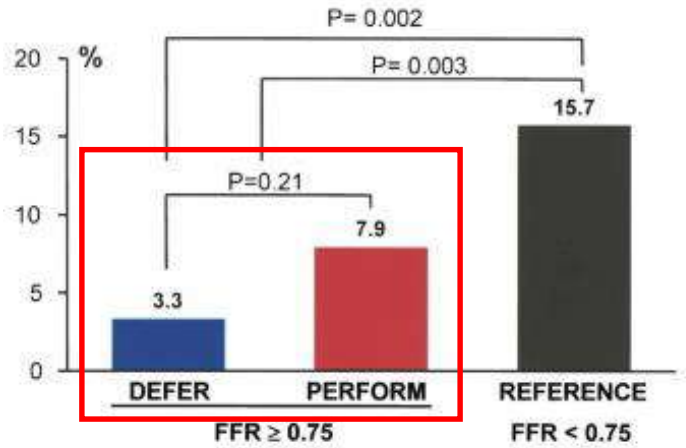
No Benefit of Stenting a Non-ischemic Stenosis (FFR ≥ 0.75)

CLINICAL RESEARCH

Percutaneous Coronary Intervention of Functionally Nonsignificant Stenosis

5-Year Follow-Up of the DEFER Study

Cardiac death or MI at 5 years



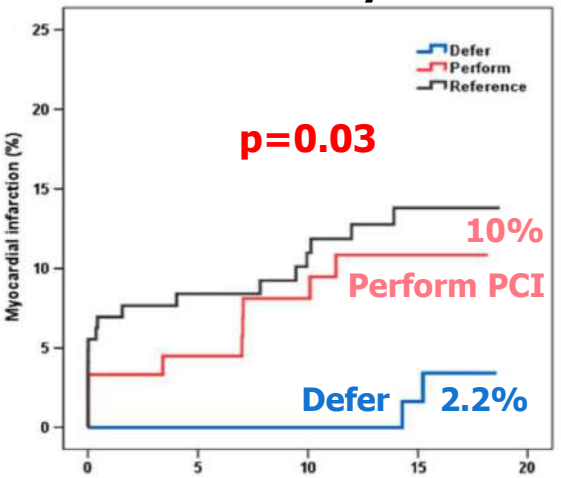
Pijls NHJ et al. *JACC* 2007;49(21):2105.

European Heart Journal (2015) 36, 3182–3188
doi:10.1093/eurheartj/ehv452

CLINICAL RESEARCH
Coronary artery disease

Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial

MI at 15 years



Zimmerman et al. EHJ 2015;36:3182-3188

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FFR-guided PCI for patients with MVD

Superior to Angio-guided PCI

FAME I

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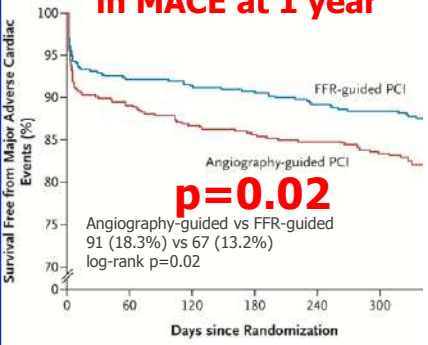
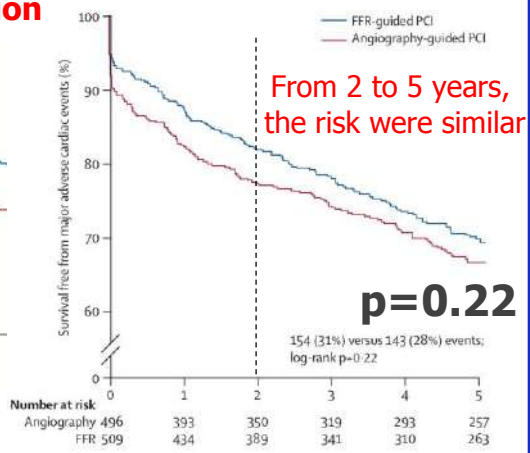
Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial

Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention

28% relative risk reduction in MACE at 1 year





Tonino PAL et al. *NEJM* 2009;360:213.

Van Nunen, LX et al. Lancet 2015;386(3):1853-60

Superior to OMT Alone

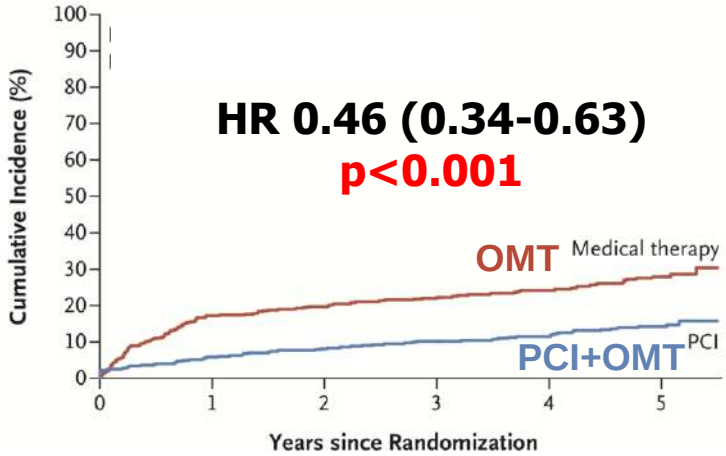
FAME II

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Five-Year Outcomes with PCI Guided by Fractional Flow Reserve

death, MI, or urgent revascularization at 5 years



Xaplanteris et al. *NEJM* 2018;379:250.

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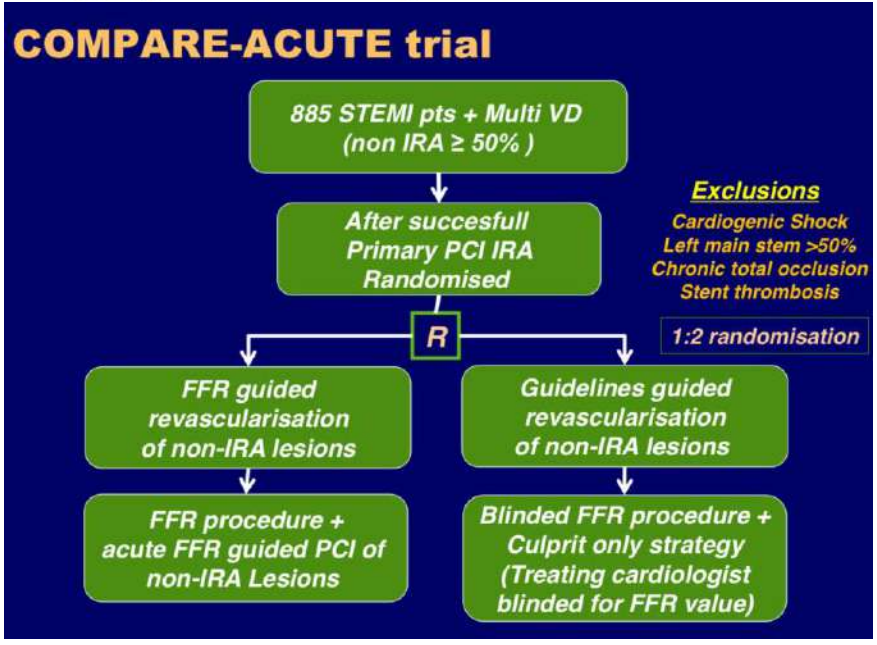
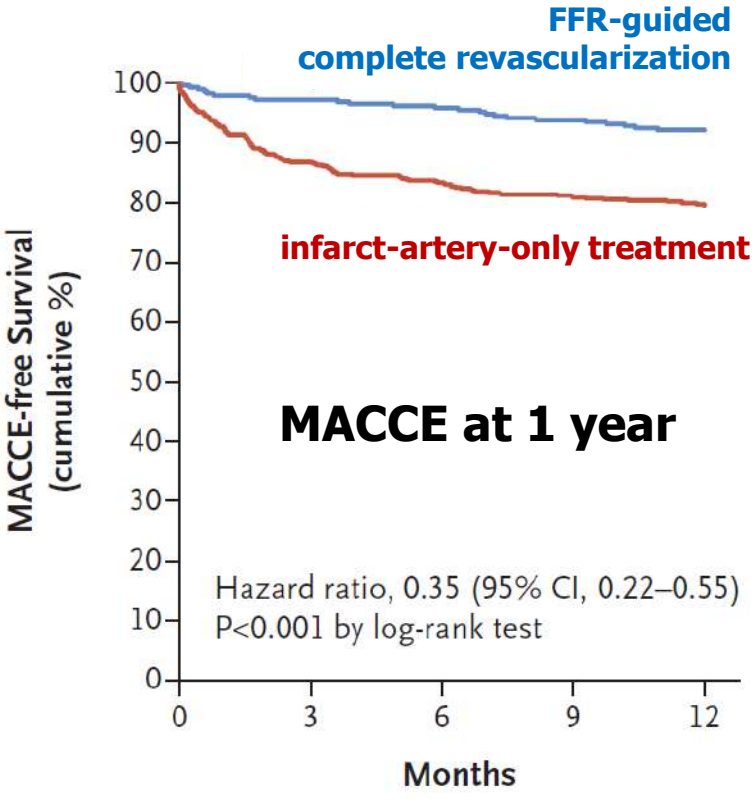
In patients with **STEMI and MVD**, FFR-guided complete revascularization is superior to infarct-artery-only treatment

ORIGINAL ARTICLE

Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction





Smits PC, et al. *N Engl J Med* 2017; 376(13):1234-1244

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FFR measurement to guide revascularization is a class I level A indication (ESC GL 2018)

Recommendations on functional testing and intravascular imaging for lesion assessment

Recommendations	Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.[15,17,18,39]	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI.[29,31]	IIa	B
IVUS should be considered to assess the severity of unprotected left main lesions.[35–37]	IIa	B

FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; IVUS = intravascular ultrasound; PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.

Neumann et al. Eur Heart J 2018 Aug 25

However, FFR is not yet widely adopted due to following limitations

- **Prolonged procedure time**
- **additional cost**
- **Discomfort or side effect from drugs**
- **Heterogeneous effect of hyperemic agent**
- **Erroneous coronary pressure measurement** (occur in up to 1/3 of cases; Pressure drift, Aortic pressure ventricularization, Aortic waveform distortion)
- **Not an optimal guidewire to negotiate vessel with complex anatomy**

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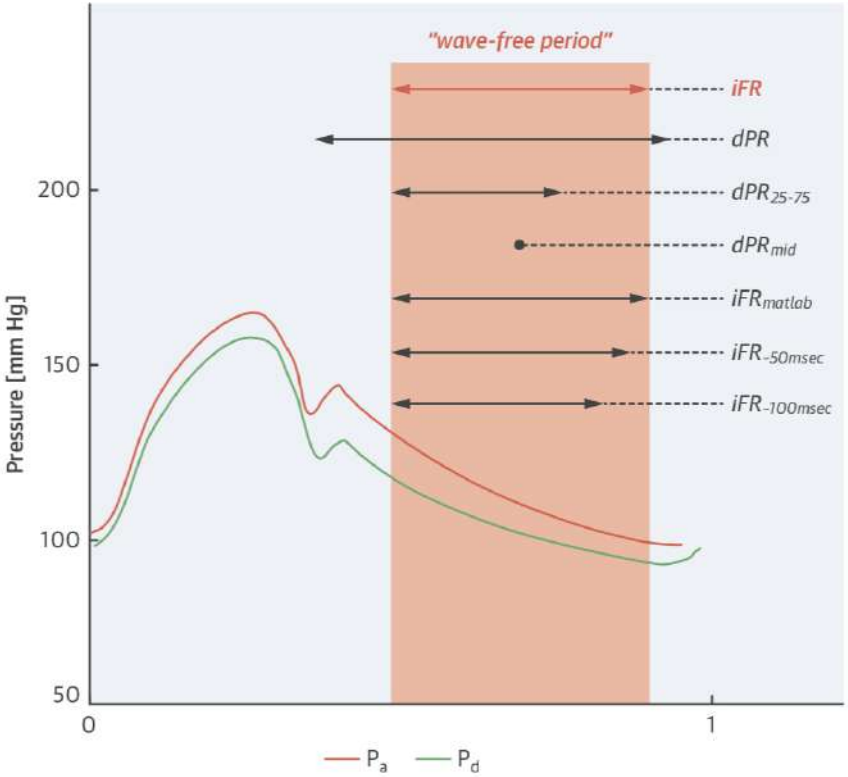
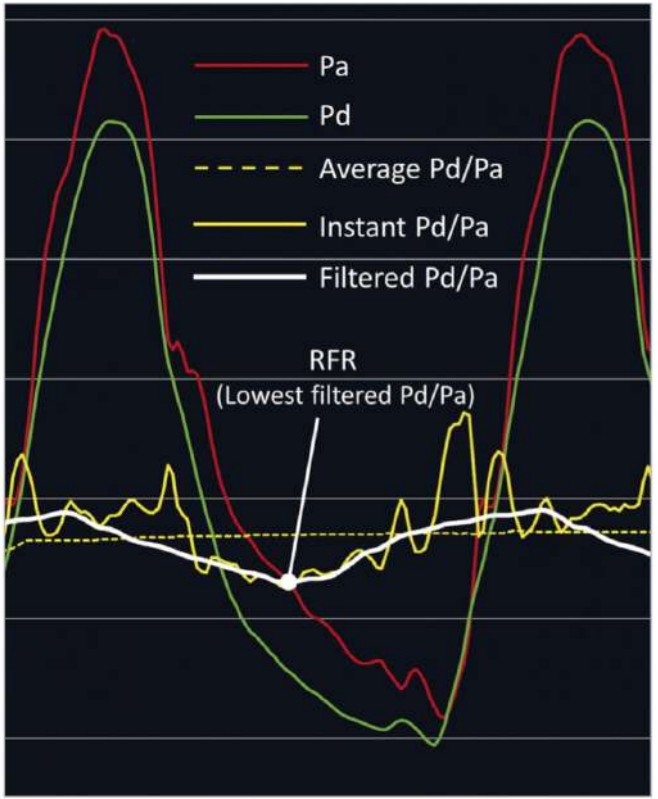
iFR and other resting indices does not need hyperemic agent



van't Veer, M. et al. J Am Coll Cardiol. 2017;70(25):3088-96.



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iFR is noninferior to FFR regarding MACE at 1 year

without hyperemic agent

SWEDEHEART

iFR® SWEDEHEART

The NEW ENGLAND JOURNAL of MEDICINE
MAY 11, 2017

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

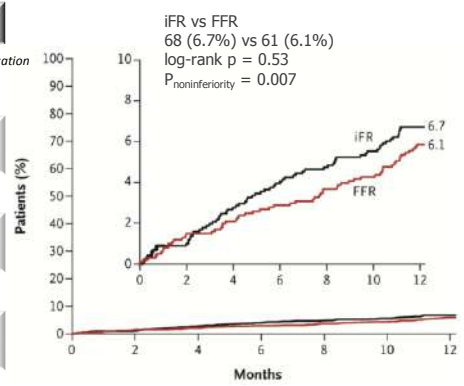
10,052 Patients were Included in the SCAAR Registry

Patients Enrolled in the iFR SWEDEHEART Trial (n=2042)

2037 Patients Underwent 1:1 Randomization

Assigned to the FFR Group (n = 1018)	Assigned to the iFR Group (n = 1019)
Underwent FFR-guided Revascularization (n = 1007)	Underwent iFR-guided Revascularization (n = 1012)
Follow-Up (n = 1018)	Follow-Up (n = 1019)

Primary Endpoint: MACE* within 1 year after the procedure



Davies, J.E. et al., N Engl J Med 2017;376:1824-34.

DEFINE-FLAIR

DEFINE FLAIR

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

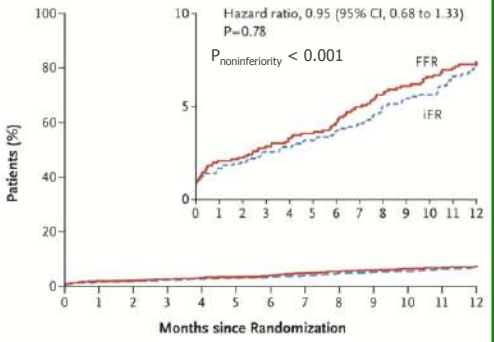
Use of the Instantaneous Wave-free Ratio or Fractional Flow Reserve in PCI

Coronary stenosis in which physiological severity was in question (n=2492)

1:1 Randomization

FFR-guided Revascularization (1250)		iFR-guided Revascularization (1242)	
FFR>0.8 Defer PCI	FFR≤0.8 Perform PCI	iFR>0.89 Defer PCI	iFR≤0.89 Perform PCI

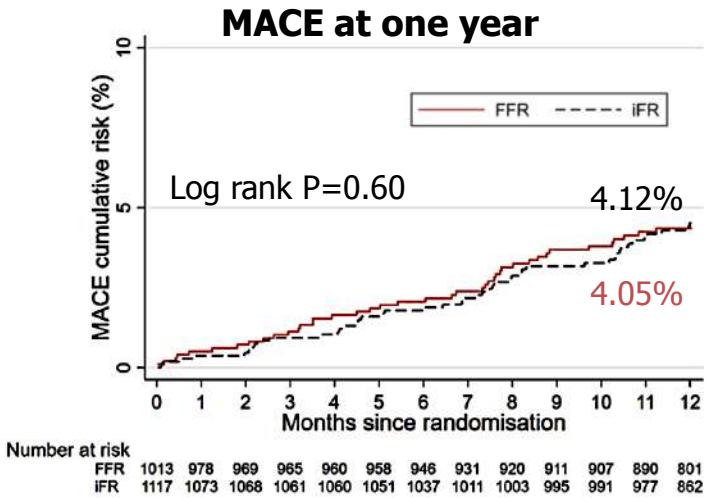
30 day, 1-, 2-, and 5-year Follow-Up



Götberg, M. et al., N Engl J Med 2017;376(19):1813-23.

Deferral of revascularization is equally safe with iFR and FFR.

Escaned J et al. JACC Cardiovasc Interv. 2018 Aug 13;11(15):1437-1449.



	SAP (n = 1,675)	ACS (n = 440)	SAP vs. ACS Unadjusted HR (95% CI)	SAP vs. ACS Fully Adjusted HR (95% CI)	p Value
MACE	3.64 (61)	5.91 (26)	0.62 (0.39-0.99)	0.61 (0.38-0.99)	**0.04**
All-cause death	0.66 (11)	1.36 (6)	0.50 (0.19-1.36)	0.44 (0.16-1.23)	0.12
Cardiovascular death	0.18 (3)	0.45 (2)	0.41 (0.07-2.45)	0.21 (0.02-1.71)	0.14
Noncardiovascular death	0.48 (8)	0.91 (4)	0.55 (0.16-1.82)	0.46 (0.13-1.59)	0.22
Myocardial infarction	0.90 (15)	2.50 (11)	0.34 (0.16-0.76)	0.36 (0.16-0.79)	**0.01**
Unplanned revascularization	2.87 (48)	3.64 (16)	0.81 (0.46-1.43)	0.83 (0.46-1.49)	0.53

- 2130 patients was deferred PCI based on iFR ≥0.90 or FFR >0.80 in **DEFINE-FLAIR and iFR-SWEDEHEART.**

❖ **In deferred patients, ACS was associated with higher incidence of MACE compared with SAP.**

FFR and iFR to guide revascularization is a class I level A indication (ESC GL 2018)

Recommendations on functional testing and intravascular imaging for lesion assessment

Recommendations	Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.[15,17,18,39]	I	A
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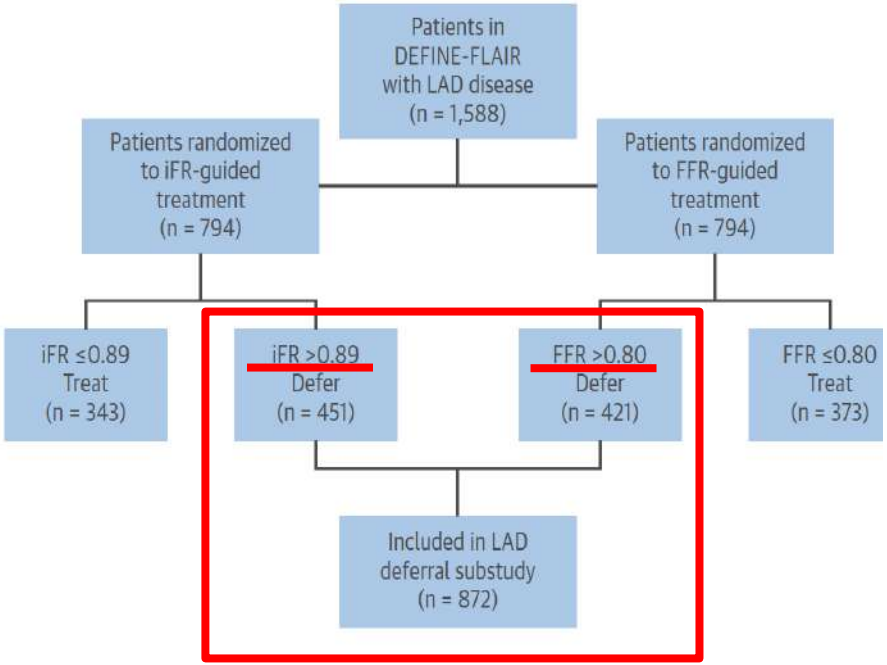
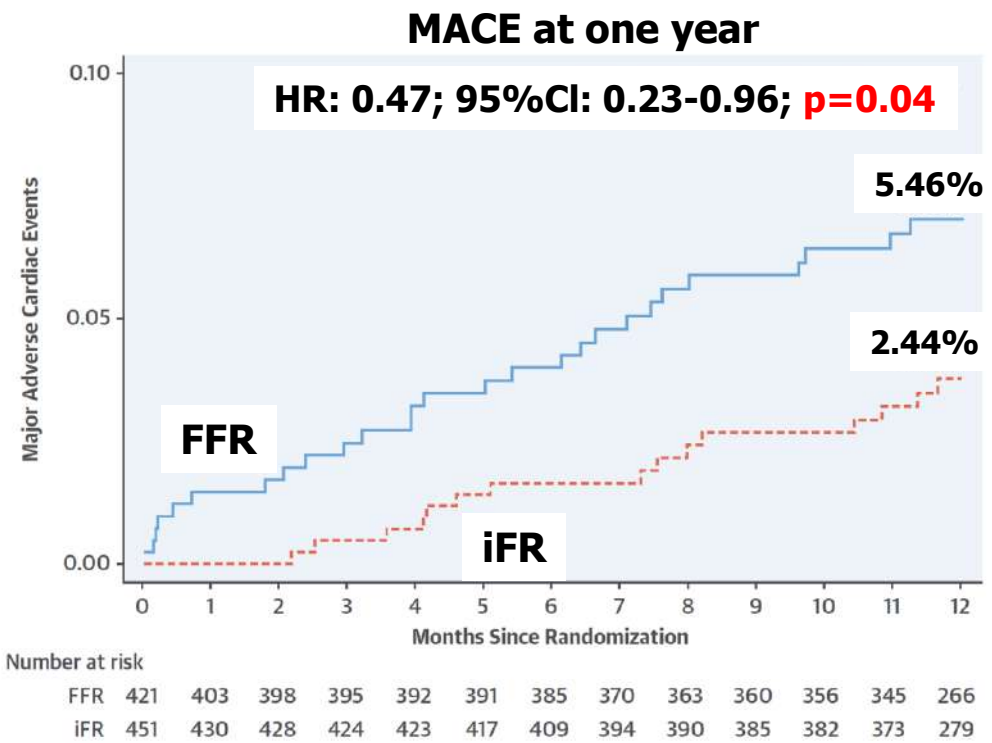
FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; IVUS = intravascular ultrasound; PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.

- Advantage
  - Shorter procedure time
  - Less patient discomfort
  - Easiness of iFR pullback
- Controversy
  - Discordance with FFR in up to 30% of LM or proximal LAD lesions
  - However, for LAD lesion, iFR-guided deferral had lower event rates than FFR-guided deferral.

Neumann et al. Eur Heart J 2018 Aug 25

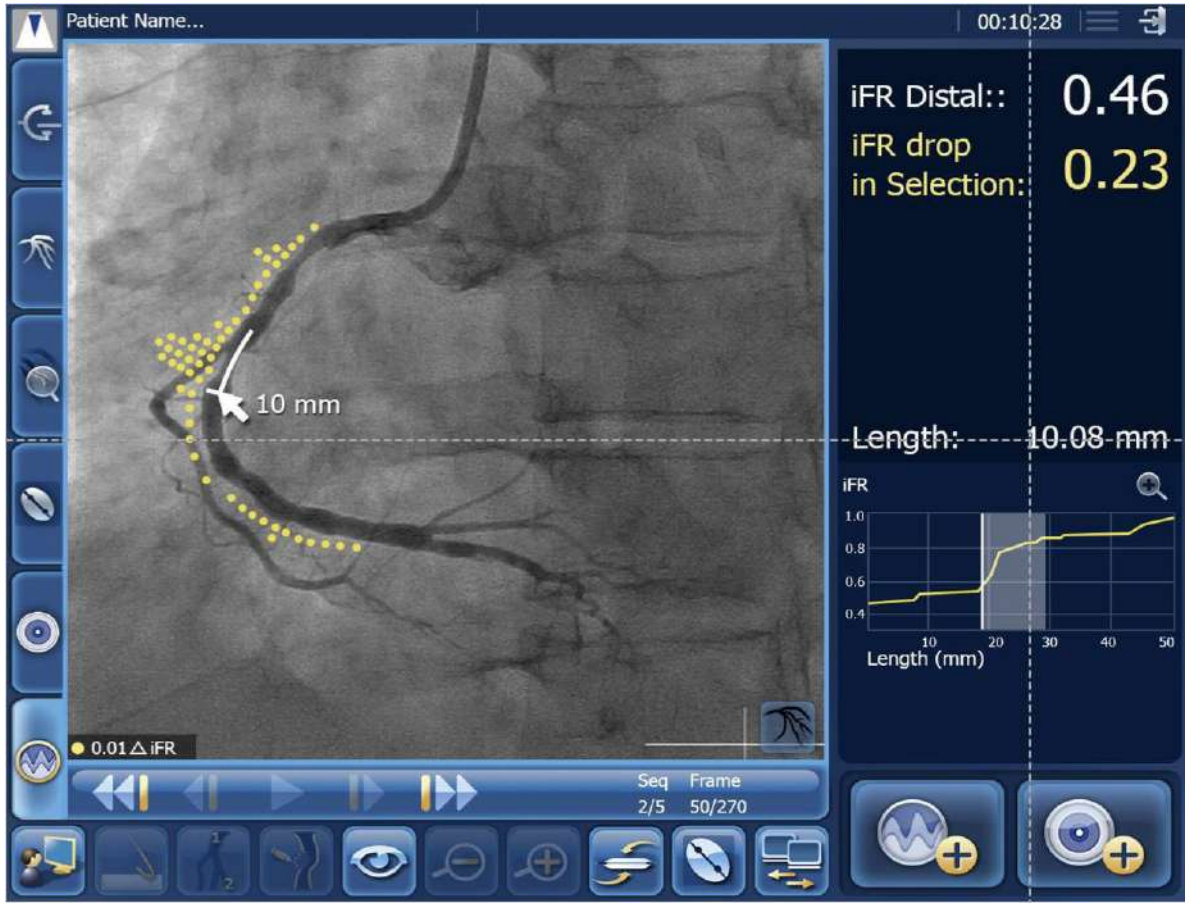
For LAD lesion, iFR-guided deferral had lower event rates than FFR-guided deferral





Sen S et al. JACC 2019.

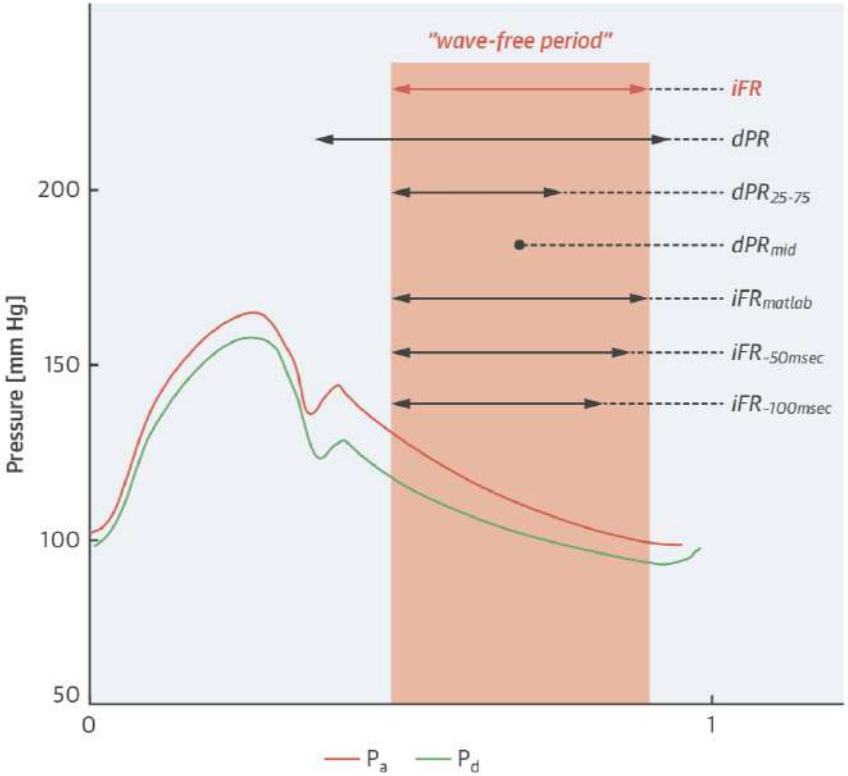
Co-registration is indispensable to guide treatment



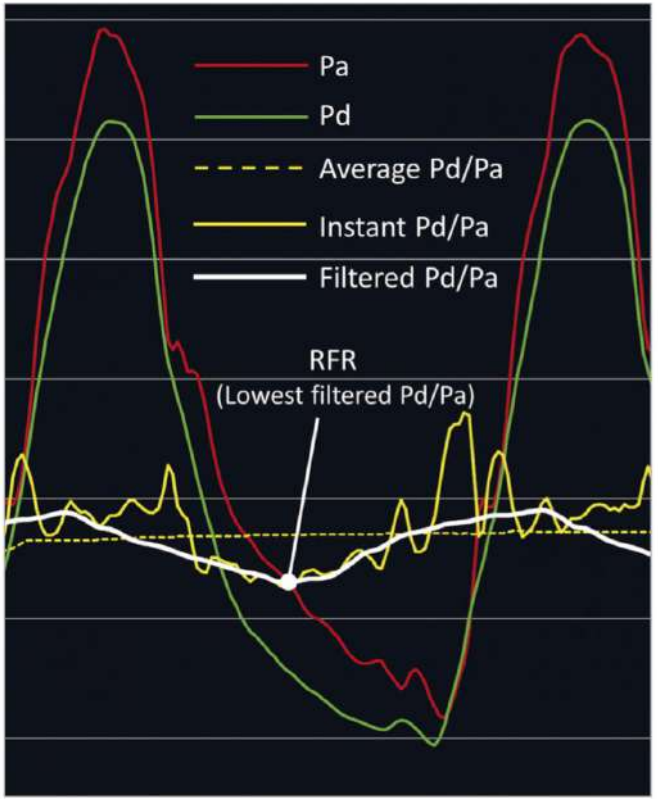
- **Pullback of wire under live fluoro screening**
- **Automatic 3D tracking of wire tip to co-register pressure drop**
- **Plot locations of pressure loss onto angiogram in an interactive manner**

Slides courtesy of Sukhjinder S Nijjer

Battle of "Resting Indices"

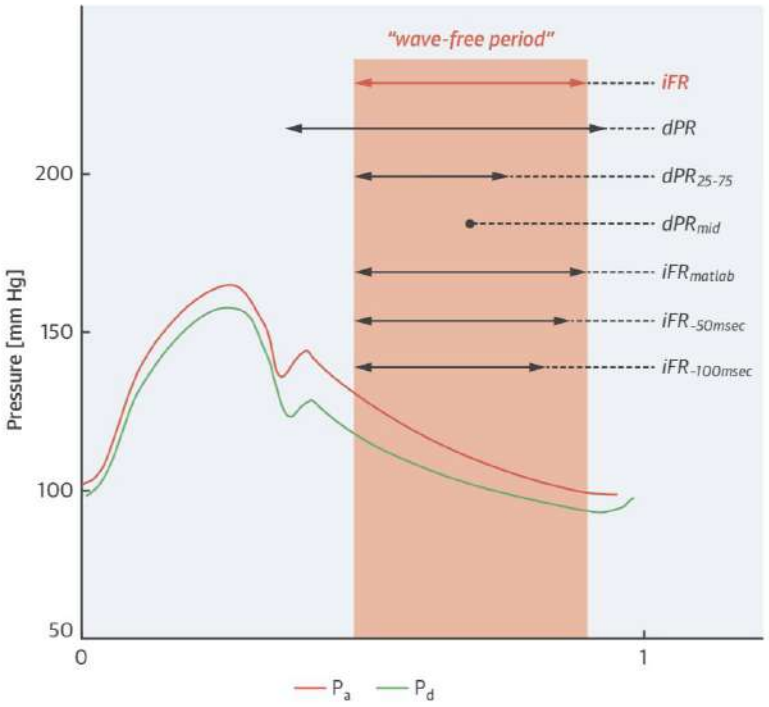


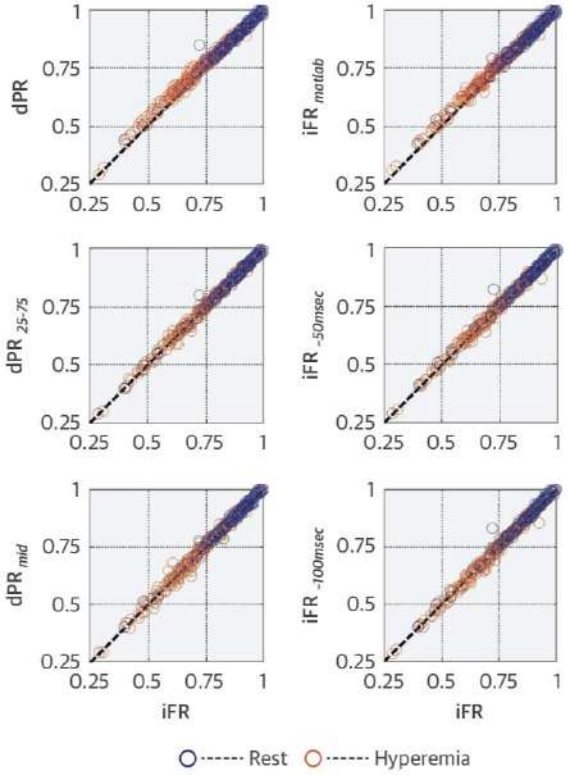
van't Veer, M. et al. J Am Coll Cardiol. 2017;70(25):3088-96.



iFR: Philips, DFR: Boston Scientific, dPR: OPSENS, RFR: Abbott

All diastolic resting indices are **identical to iFR**, both numerically and with respect to their agreement with FFR.



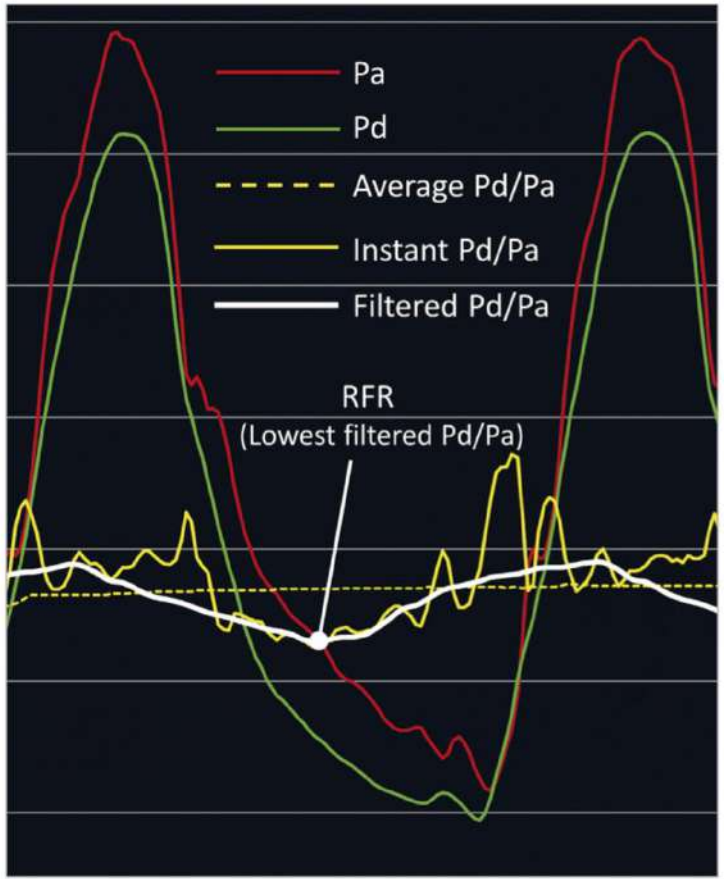


However, RCT comparing clinical outcomes by these indices based diagnostic strategies and standard diagnostic strategies are warranted.

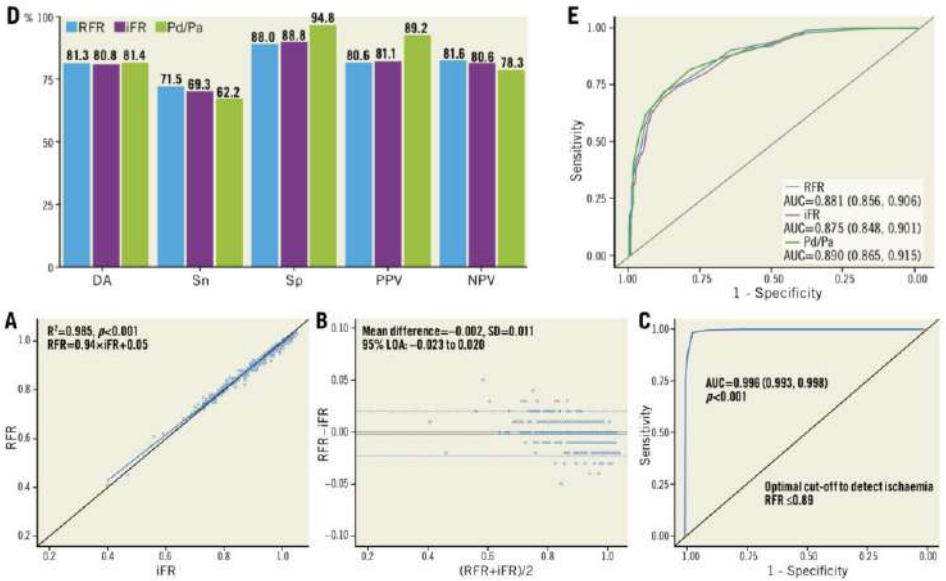
"I guess they (RCT) will be all equivalent"

van't Veer, M. et al. J Am Coll Cardiol. 2017;70(25):3088-96.

RFR is diagnostically equivalent to iFR

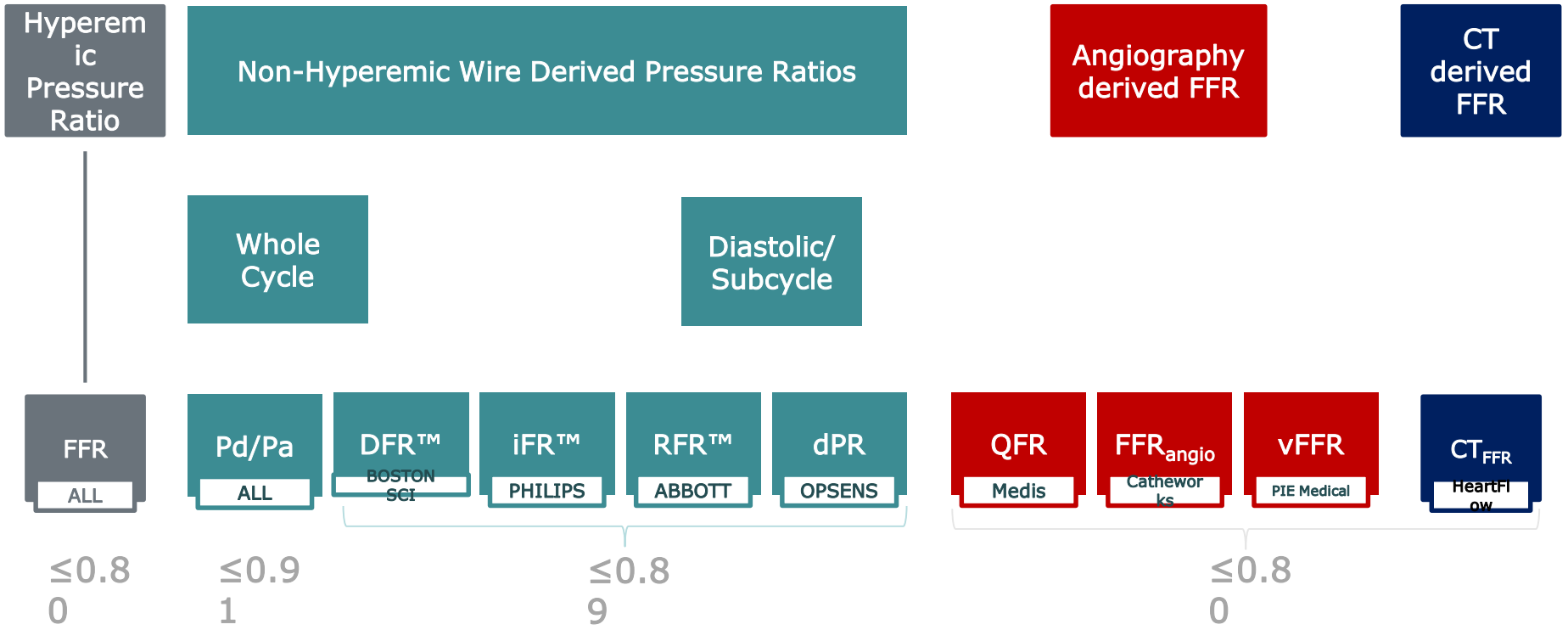


- **Resting full-cycle ratio (RFR) is an independent of the ECG, landmark identification, and timing within the cardiac cycle.**
- **There is excellent agreement between RFR and iFR.**

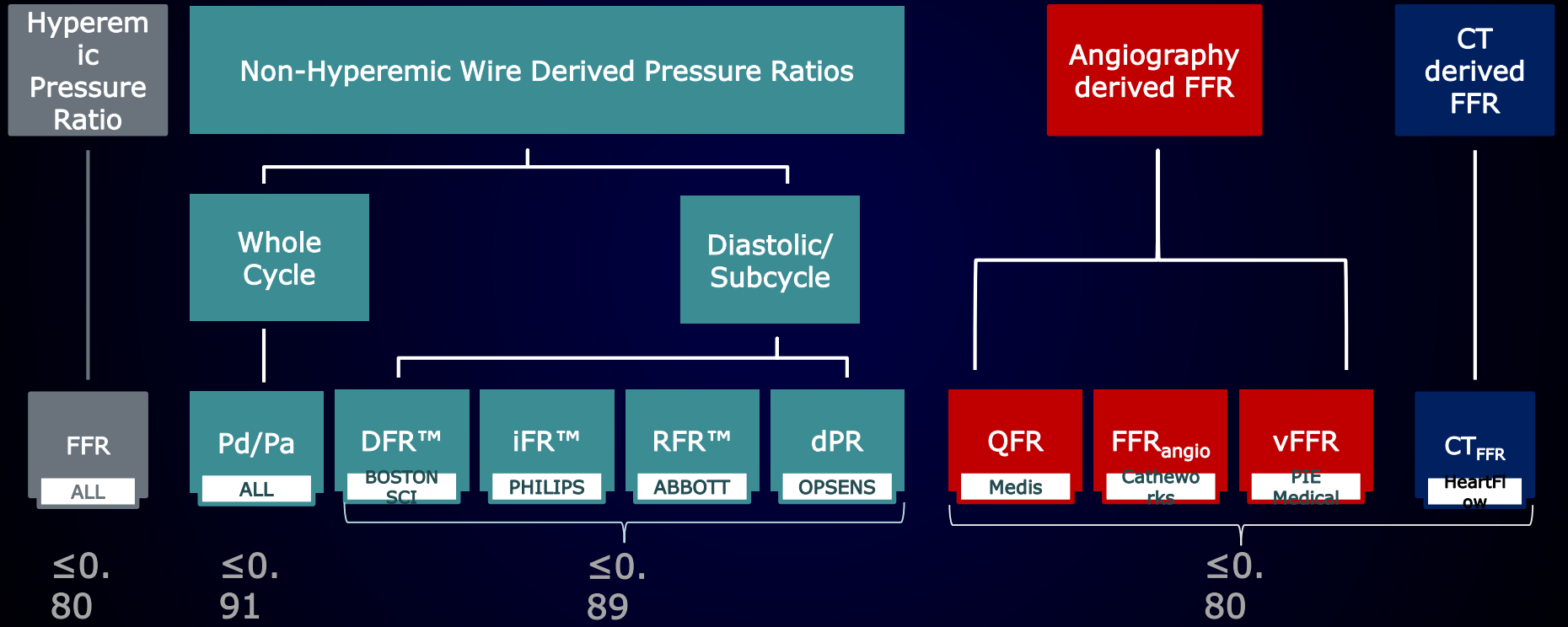


Svanerud, Ahn, et.al. EuroIntervention. 2018 Sep 20;14(7):806-814.

Angiography derived physiology is diagnostically equivalent to pressure derived physiology

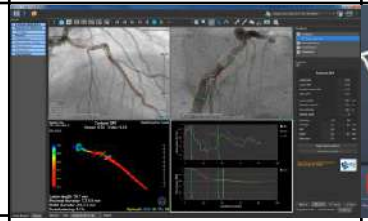
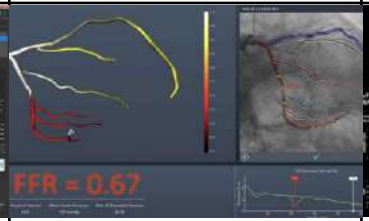
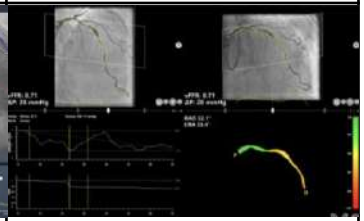


Physiological Assessment of Coronary Stenosis



Caution: DFR is an investigational product and restricted by Federal law to investigational use only. Not available for sale in the US. CE Marked.

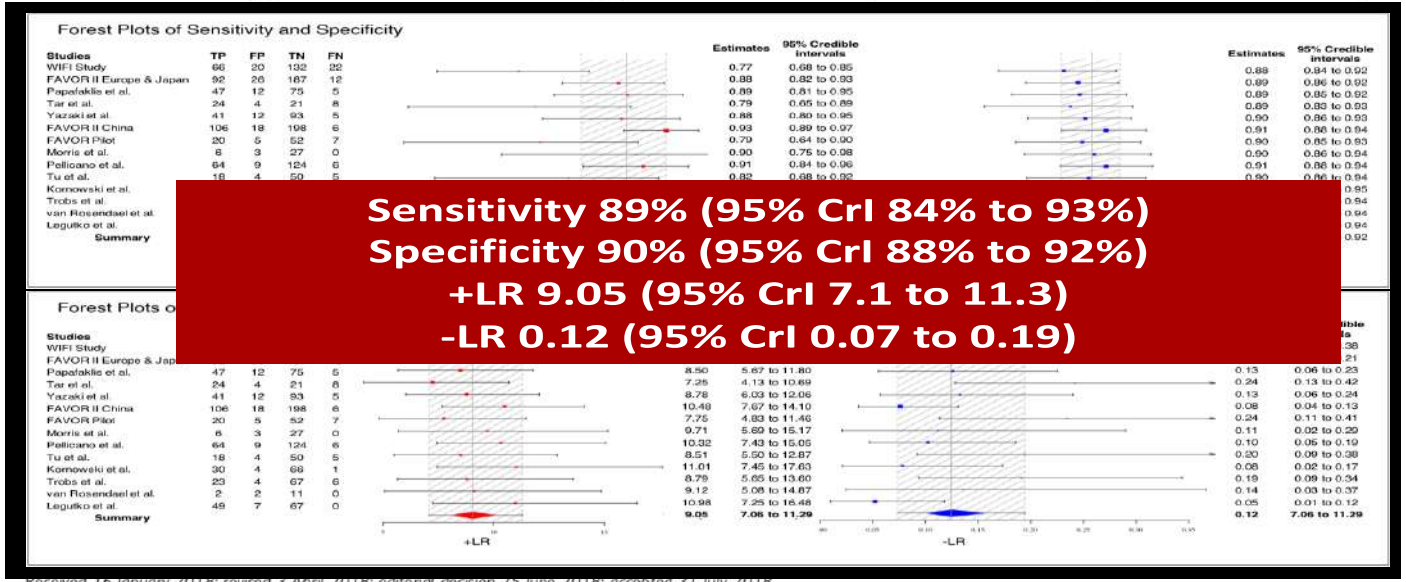
Angio-derived FFR does not need wire and hyperemic agent

	QFR (Medis)	FFR_{angio} (CATHWORKS)	vFFR (PIE MEDICAL)
			
On-line	Available	Available	Available
Required angio	2 projections 25 degrees apart	≥2 projections	2 projections 30 degrees apart
Process	Mathematical formula (Lance Gould)	Rapid flow analysis	Mathematical formula (Lance Gould)
Published Clinical data	FAVOR pilot, II China, Europe/Japan, WiFi II Xu B, et al. JACC. 2017 Dec 26;70(25):3077-3087 Westra J, et al. J Am Heart Assoc. 2018 Jul 6;7(14)	FAST-FFR Fearon, et al. Circulation. 2019;139:477–484.	FAST Masdjedi K, et al. EuroIntervention 2019; Jaa-580 2019, doi: 10.4244/EIJ-D-19-00466
AUC for predicting FFR≤0.8	**0.92-0.96**	**0.94**	**0.93**
Time to computation	**5 min** **(vs 7 min in FFR, p<0.001)**	(2.7 min: without manual correction and lesion identification)	NA

ESC European Society of Cardiology
European Heart Journal (2018) **00**, 1–9
doi:10.1093/eurheartj/ehy445

CLINICAL RESEARCH

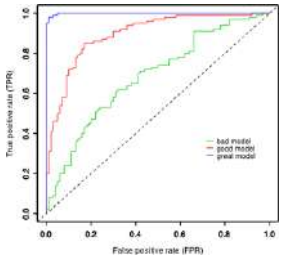
Diagnostic performance of angiography-derived fractional flow reserve: a systematic review and Bayesian meta-analysis

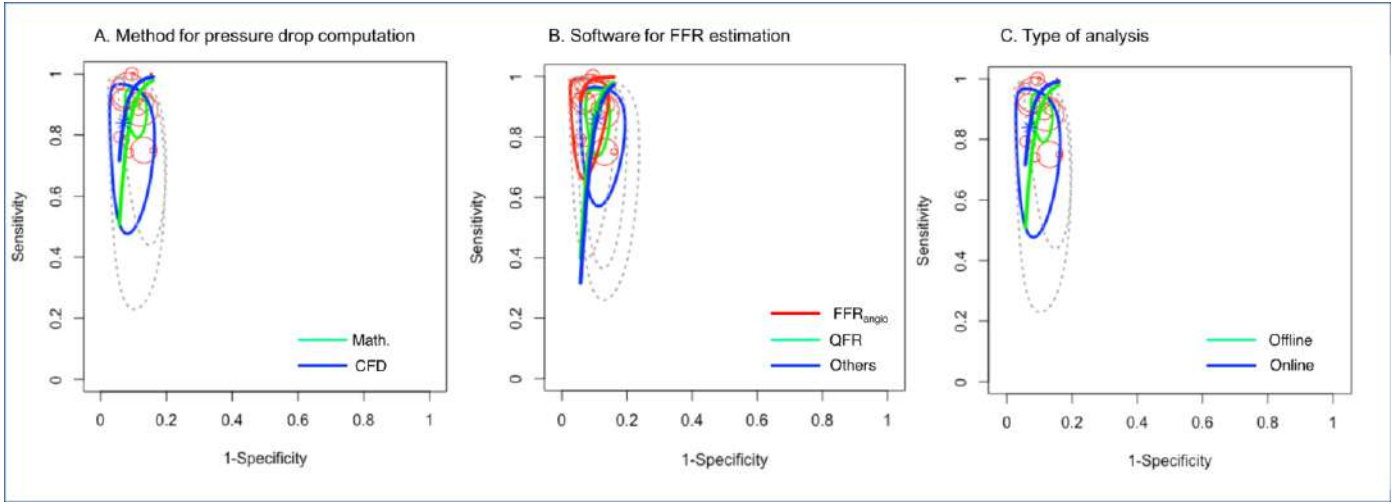


Received 16 January 2018; revised 3 April 2018; editorial decision 25 June 2018; accepted 31 July 2018

No difference in Diagnostic Performance (AUC) between type of method for pressure drop computation, Software or online/offline analysis.

Bayesian Meta-regression





Collet et al. Eur Heart J. 2018 Sep 14;39(35):3314-3321

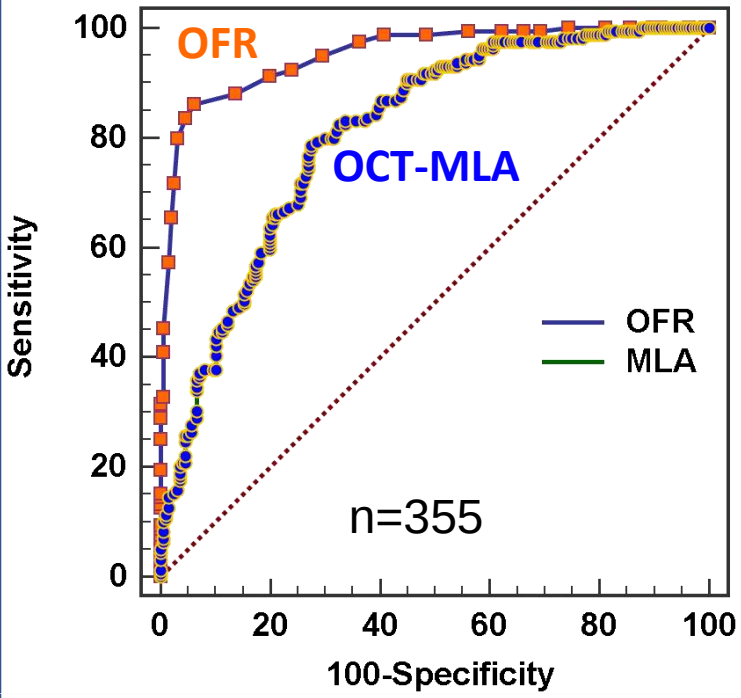
Advantage and limitation of QFR against FFR

- Advantage (No need for wire and hyperemic agent)
  - Shorter procedure time
  - Less patient discomfort
  - Eliminate erroneous coronary pressure measurement (occur in up to 1/3 of cases; Pressure drift, Aortic pressure ventricularization, Aortic waveform distortion)

- Limitation
  - The benefit on clinical outcomes has not yet been fully investigated (FAVORIII China n=3800 (NCT03729739), Europe/Japan n= 2000 (NCT03656848))
  - Analysis for specific lesion subsets are not reliable (i.e. LM, bifurcation, ostium lesion)
  - Results depend on the quality of angiography.

OCT-based FFR (OFR)

Excellent AUC of 0.95 for predicting FFR≤0.80

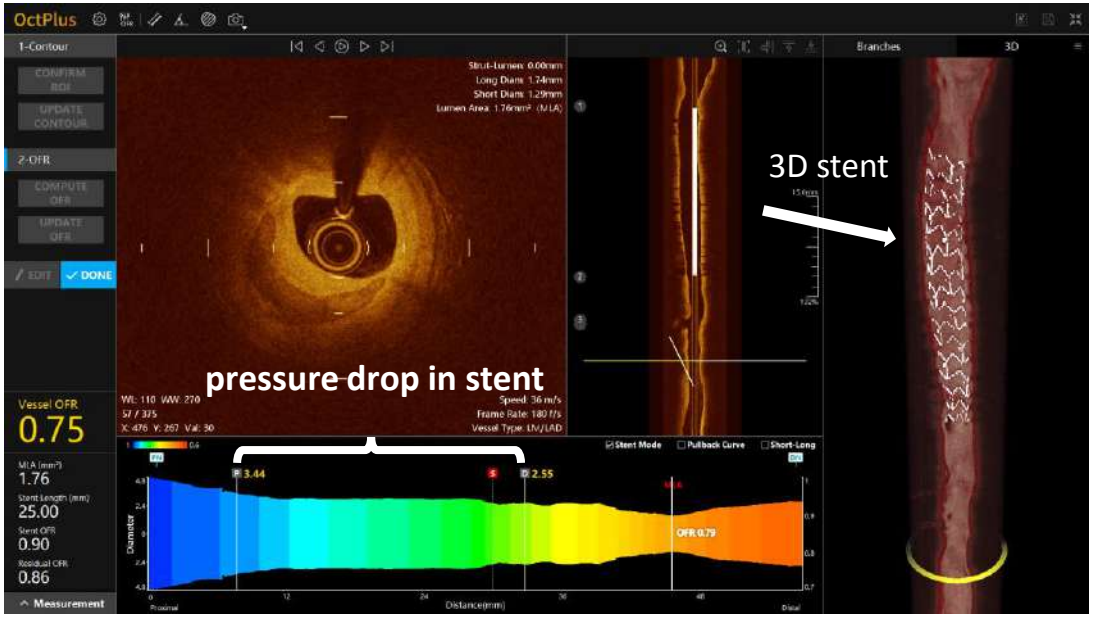


Presented at euroPCR2019 by Tu S

morphology and coronary physiology

1 procedure and instrumentation

OCT + computed FFR



OCT co-registered OFR

Coronary physiology on clinical decision making

1. **Before procedure outside the cathlab**
   - FFR_{CT}

2. **Before procedure in the cathlab**
   - FFR (gold standard)
   - iFR and other non-hyperemic indices (DFR, RFR, etc)
   - Angiography derived FFR (QFR, FFR_{angio}, vFFR)
   - Intracoronary imaging derived FFR (OFR)

3. **During or after procedure in the cathlab**
   - FFR: several studies
   - iFR: DEFINE PCI
   - QFR: HAWKEYE

A higher post-PCI FFR value is associated with a better clinical outcome.

	Primary end point	Cutoff value of FFR(AUC)	Comparison of low vs. high post PCI FFR on primary end point	
Piroth et al (FAME 1,2) (2017) n=838 vessels	2-Y VOCE (Vessel-oriented composite end point)	**0.92 (NA)**	9.2% vs. 3.8% (lower(<0.88) vs. upper(>0.92) tertiles)	**p=0.037**
DKCRUSH VII (2017) n=1476pts	1-Y TVF (cardiac death, TV-MI, CD-TVR)	**0.88 (0.831)**	8.0% vs. 4.0%	**p=0.001**
Agarwal et al (2016) N=574pts	MACE (death, MI, TVR) Follow-up 31±16M	**0.86 (NA)**	23% vs. 17%	**p=0.02**

However, in real world practice **adoption rate of post PCI FFR** is **quite low (less than 10%).**

Tebaldi M, et al. JACC Cardiovasc Interv 2018;11:1482-1491.

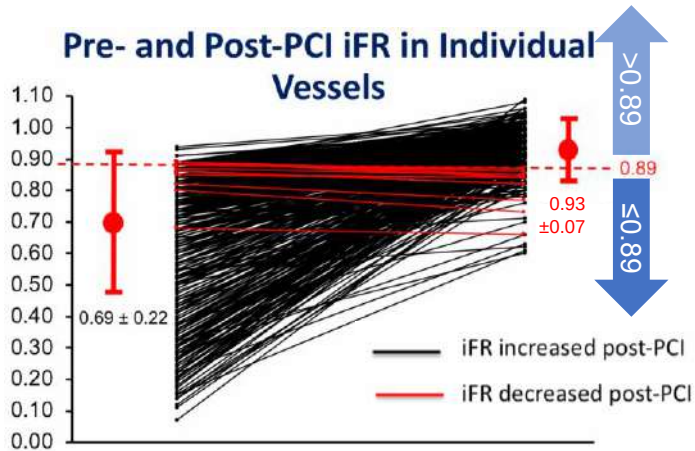
Post-PCI iFR measurement detected 24% of residual ischemia defined with iFR≤0.89

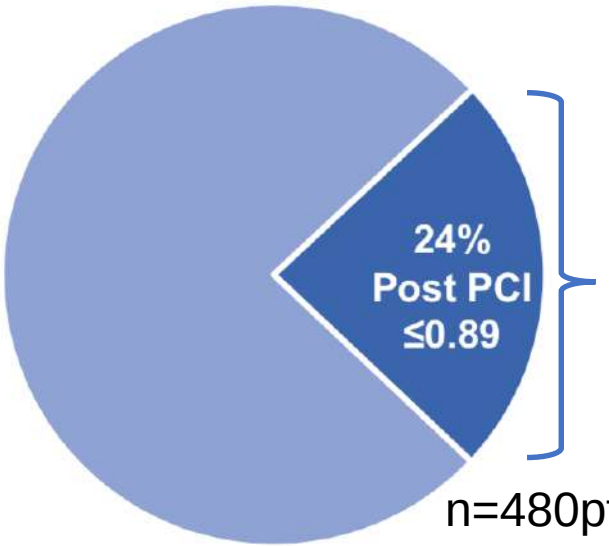
DEFINE PCI

Angiographic confirmation of PCI result

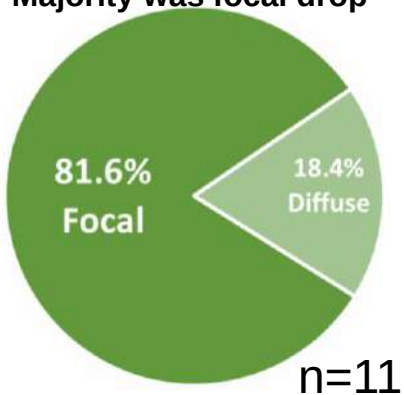
↓

Blinded iFR with pullback at end of procedure



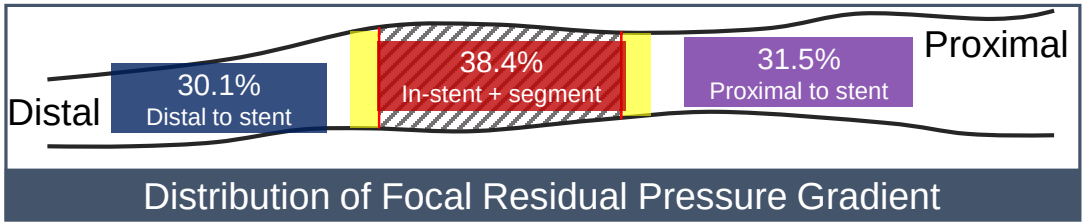


Majority was focal drop



n=112pts

■ Post iFR≤0.89 ■ Post iFR>0.89

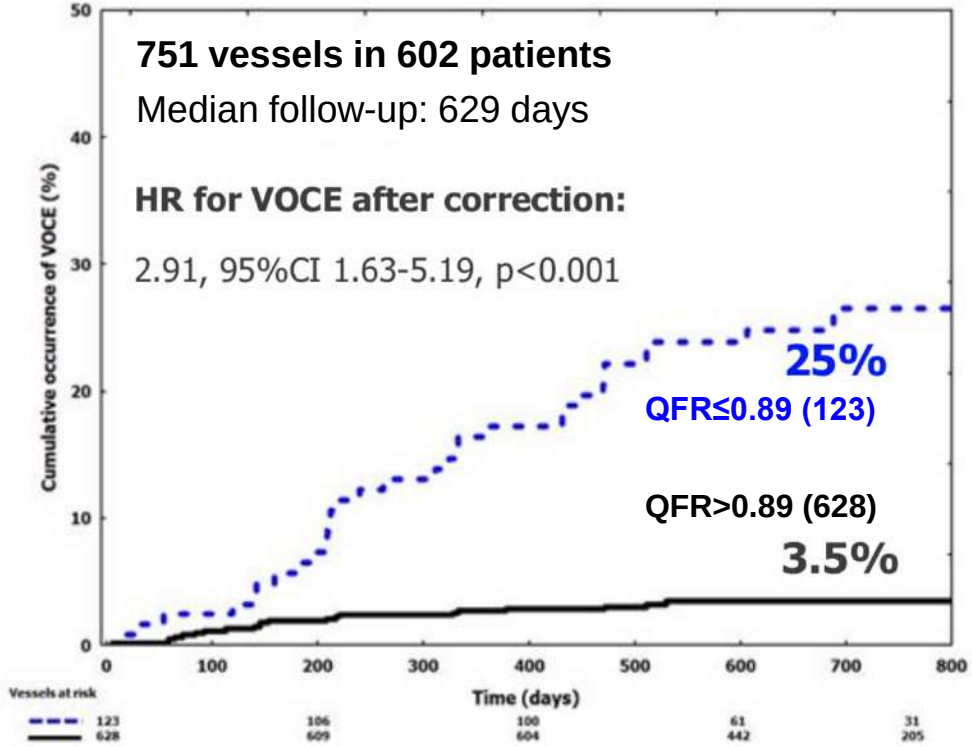


Distribution of Focal Residual Pressure Gradient

Jeremias A et al. presented at ACC 2019.

Post-PCI QFR highly correlates with prognosis and is applicable in most of the cases.

HAWKEYE NCT02811796



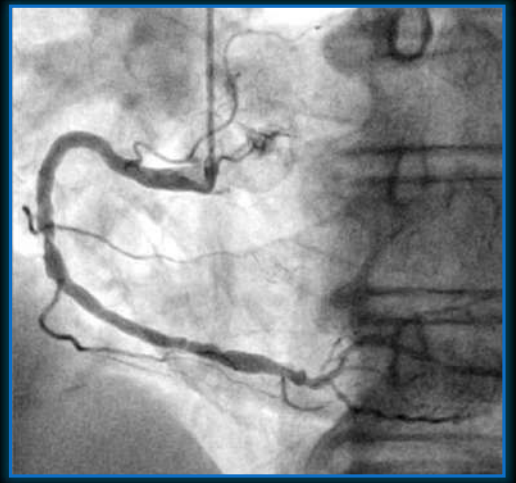
Post-PCI **QFR** cut-off of ≤0.89 as having the best predictive accuracy for VOCE
AUC 0.77 (0.74-0.80)
p<0.001
sensitivity 60%
specificity 87%

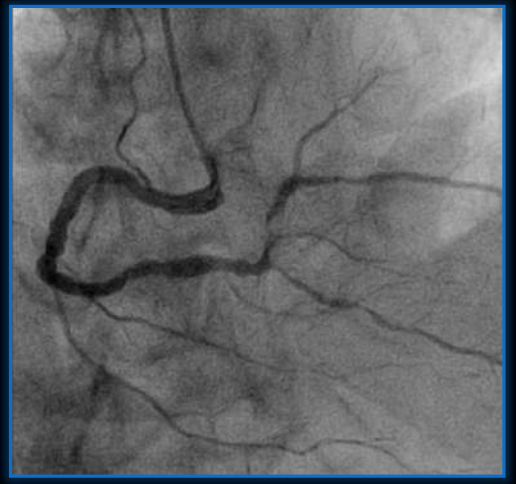
Presented by Simone Biscaglia at euroPCR2019

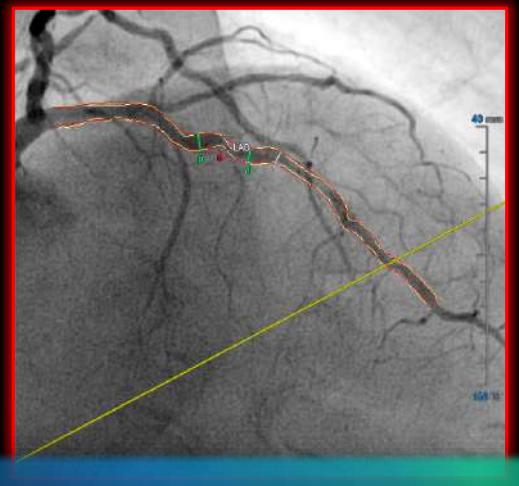
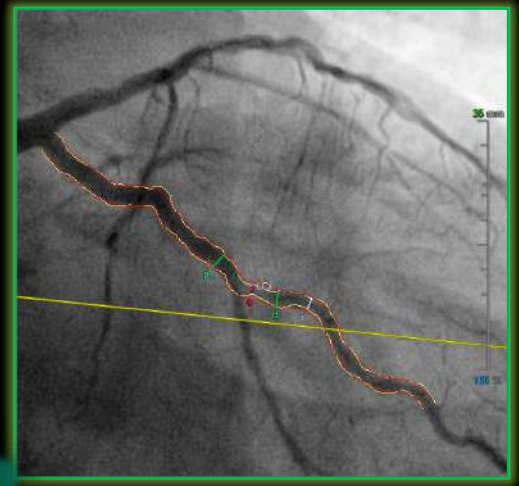
Was the ball inside or outside the court, Ask the HAWKEYE system…

Serruys PW et al. Editorial in JACC Interv (in press)

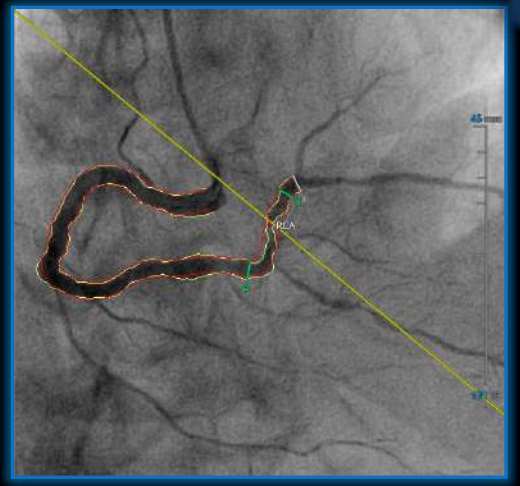
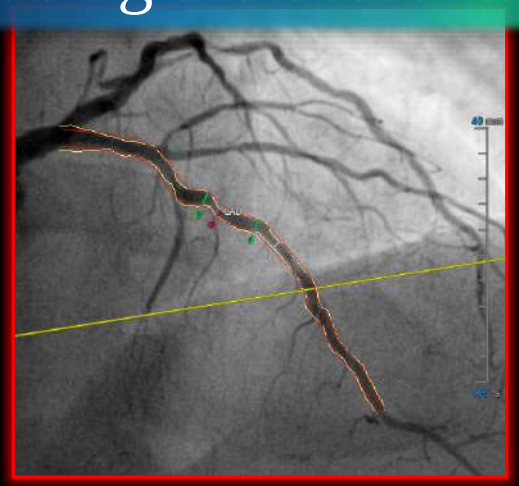
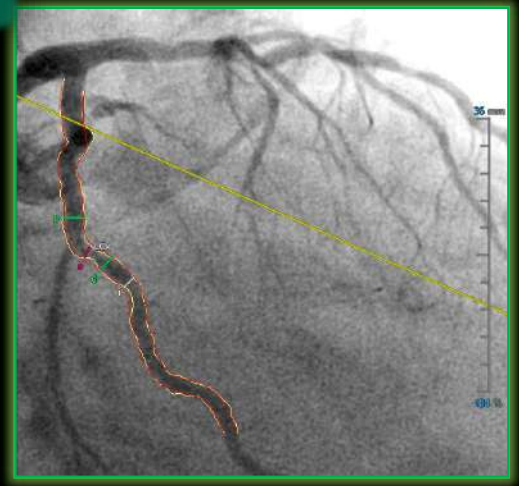
HAWKEYE NCT02811796



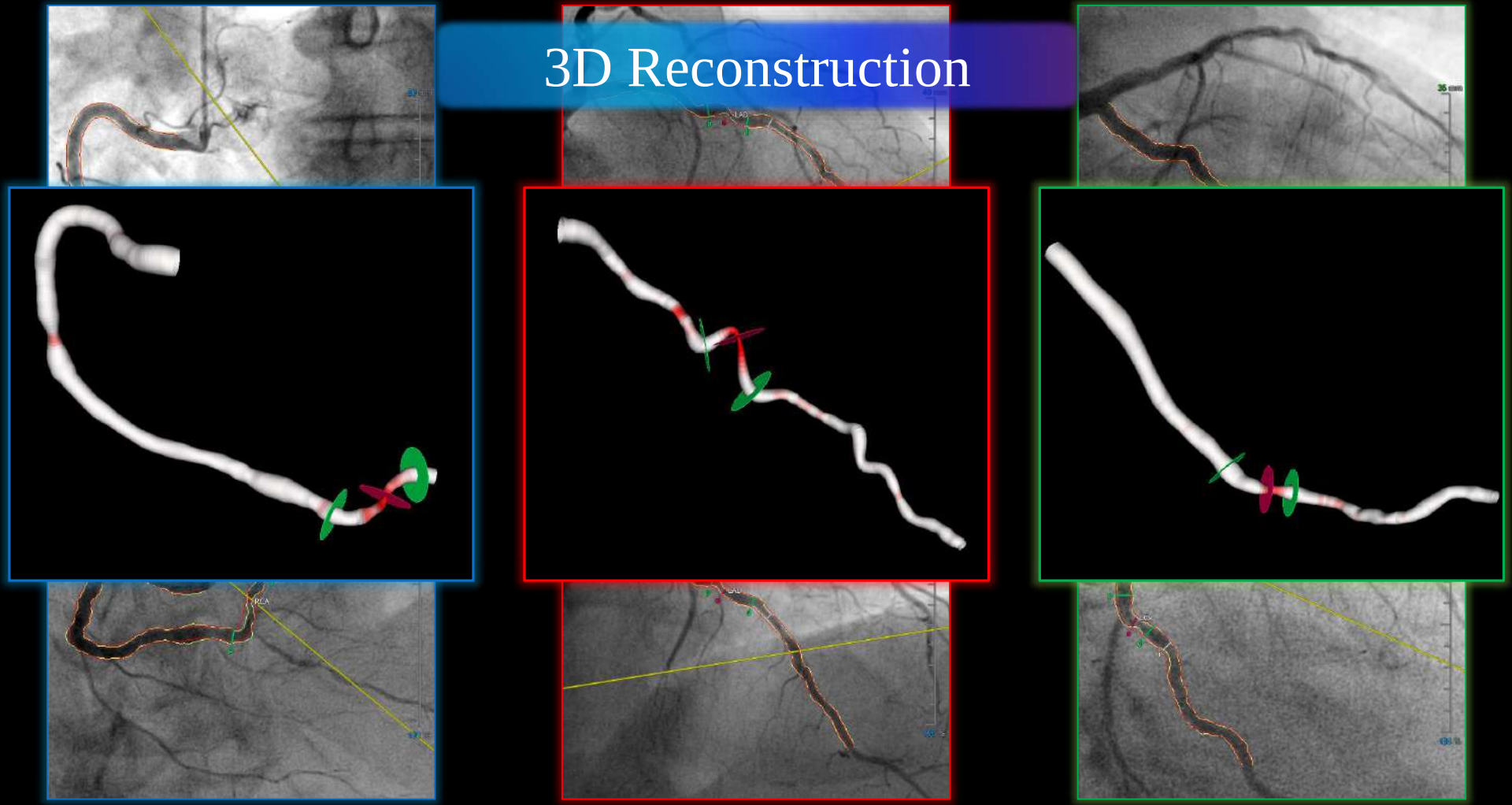



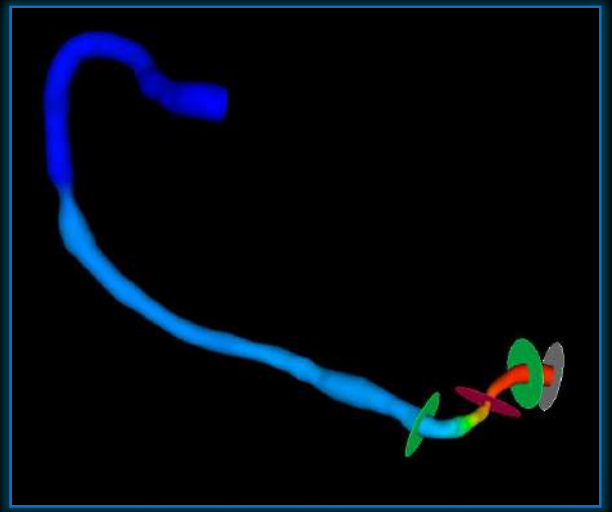
Tracing the vessel wall

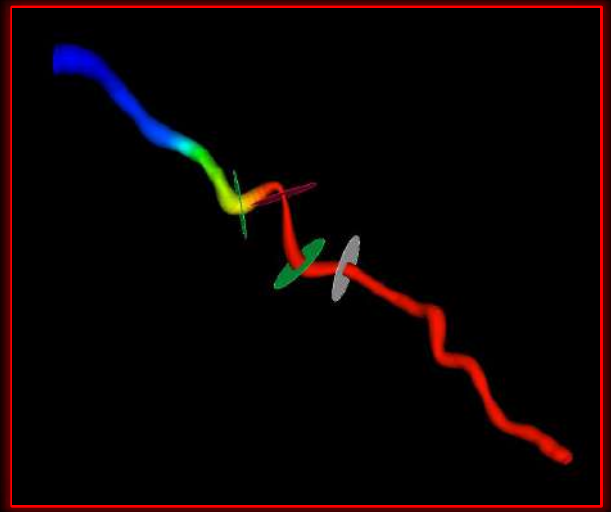




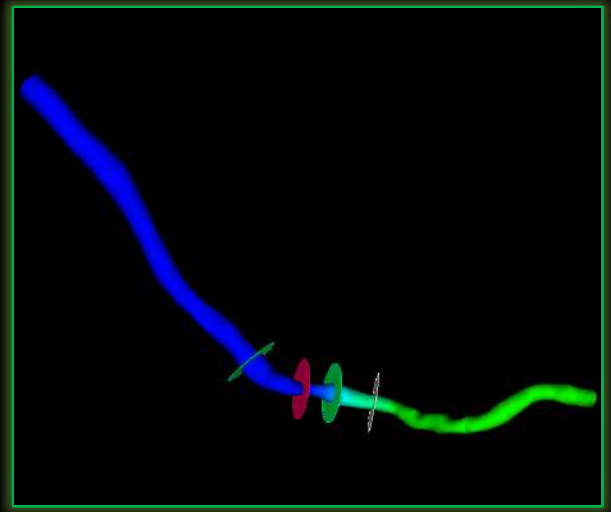
3D Reconstruction

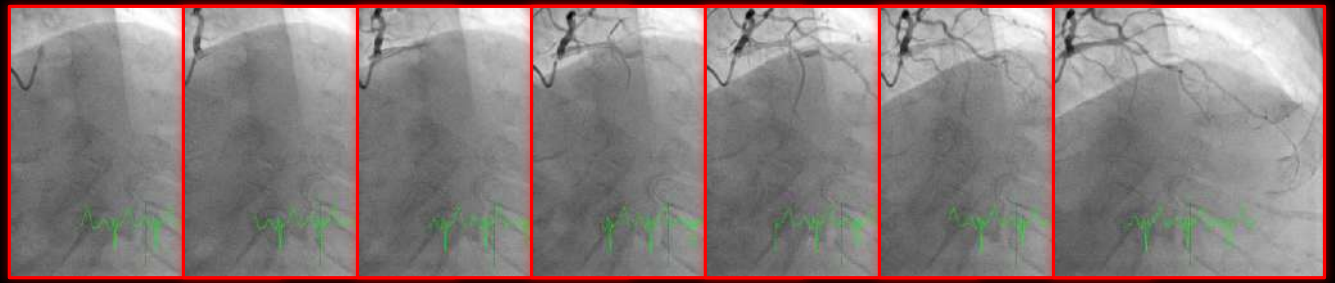


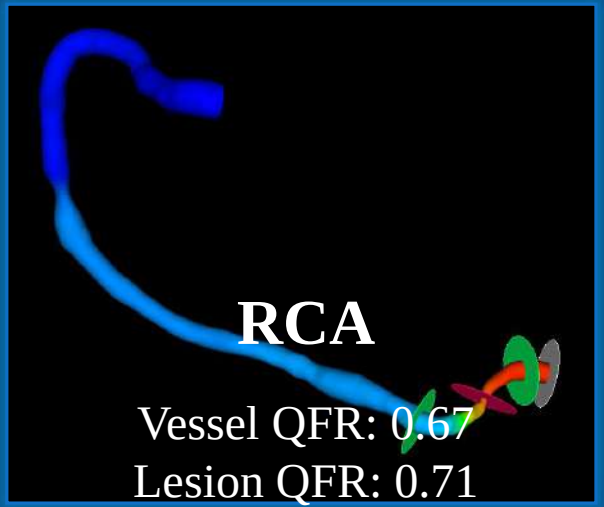
Frame Counting







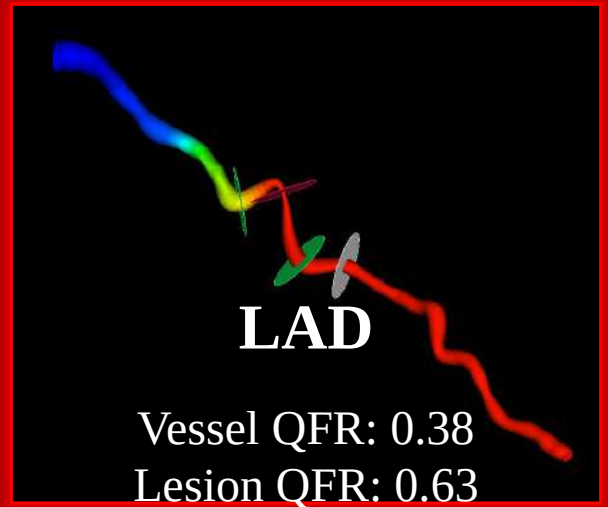




RCA

Vessel QFR: 0.67
Lesion QFR: 0.71
Residual Vessel QFR: 0.96

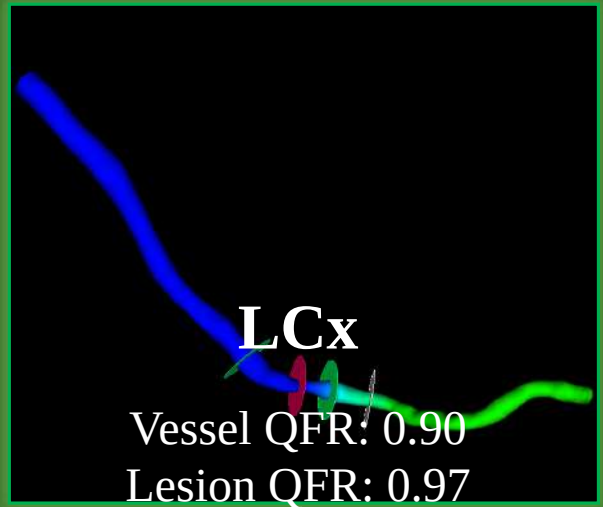
PCI Eligible



LAD

Vessel QFR: 0.38
Lesion QFR: 0.63
Residual Vessel QFR: 0.75

PCI Eligible

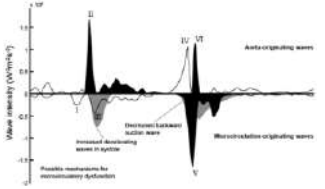


LCx

Vessel QFR: 0.90
Lesion QFR: 0.97
Residual Vessel QFR: 0.93

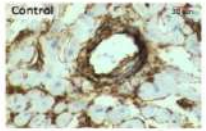
Defer

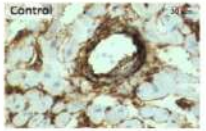
Physiological indices and interrogated coronary domain

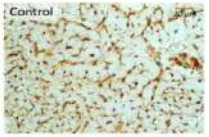


Wave intensity analysis

FFR, iFR,
d-FFR, RFR

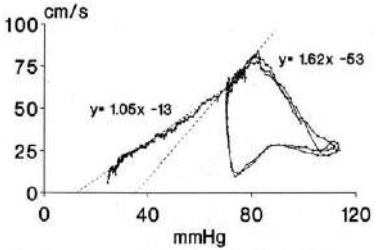






Epicardial -------- Arteriolar -------- Capillary

Instantaneous hyperemic diastolic pressure velocity slope



Slides courtesy of Escaned J

Conclusion

- **FFR is the gold standard for clinical decision making before procedure. iFR can be considered as equivalent to FFR.**
- **Other non-hyperemic indices, angio-derived FFR, OFR, showed comparable diagnostic performance for the diagnosis of hemodynamically significant stenosis defined by FFR ≤0.80.**
- **However, RCT comparing clinical outcomes by these indices based diagnostic strategies and standard diagnostic strategies are warranted.**
- **In terms of decision making during procedure, several studies demonstrated that a higher post-PCI FFR value is associated with a better clinical outcome. However, adoption rate is still quite low. At this point, iFR and QFR can be good alternatives.**


asia
AiCT
PCR
The Official Course of APSIC

MONDAY 1 JULY 2019
09:00- EUROMAST

QFR in MultiTALENT trial

Patrick W. Serruys, MD, PhD

Yoshinobu Onuma, MD, PhD
Masafumi Ono, MD
Norihiro Kogame, MD
Hideyuki Kawashima, MD
Hironori Hara, MD

CARDIALYSIS
Clinical Trial Management - Core Laboratories

Amsterdam UMC
Universitair Medische Centra

Dr. Honoris Causa
in Biomedical Engineering
The University of Melbourne

THE UNIVERSITY OF MELBOURNE

Erasmus university
Emeritus Professor of Cardiology

Erasmus MC
Universitair Medisch Centrum Rotterdam

Professor of
Cardiology of
Imperial College

SCIENTIA
SCIENTIA IMPERII DECUS ET TUTAMEN

Quantitative Flow Ratio in MultiTALENT trial

1. *State of the art and best practice PCI*
2. *Physiological assessment in multi-vessel disease*
3. *What's QFR?*
4. *The methodology of QFR*

Clinical outcomes of state-of-the-art percutaneous coronary revascularisation in patients with three-vessel disease: two-year follow-up of the SYNTAX II study

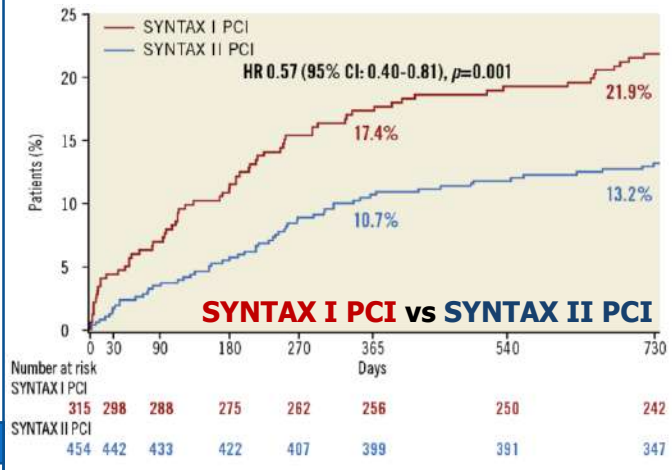
Patrick W. Serruys[1,2]*, MD, PhD; Norihiro Kogame[3], MD; Yuki Katagiri[3], MD; Rodrigo Modolo[3], MD; Pawel E. Buszman[4,5], MD, PhD; Andres Iniguez[6], MD, PhD; Javier Goicolea[7], MD, PhD; David Hildick-Smith[8], MD; Andrzej Ochala[5], MD, PhD; Dariusz Dudek[9], MD, PhD; Jan J. Piek[3], MD, PhD; Joanna J. Wykrzykowska[3], MD, PhD; Javier Escaned[10], MD, PhD; Adrian P. Banning[11], MBBS, MD; Vasim Farooq[12], MBChB, PhD; Yoshinobu Onuma[2], MD, PhD

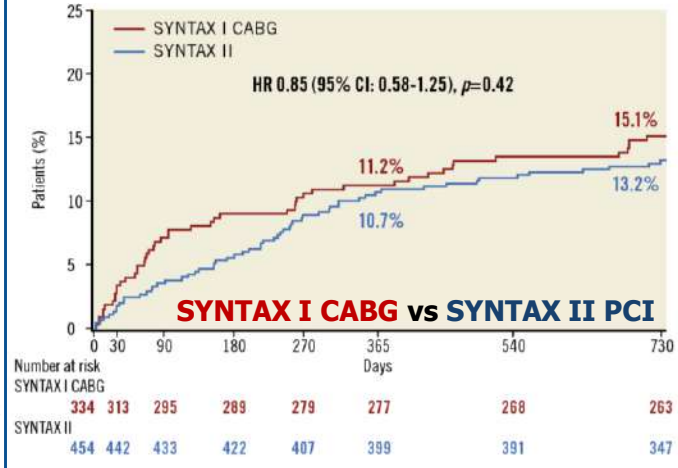
Achievement of SYNTAX II strategy

		SYNTAX II		SYNTAX-I PCI	*p*-value
SYNTAX score II calculated		100% (454/454)		100% (315/315)	1.000
iFR/FFR per patient	Excellent!!	96.4% (431/447)		NA	NA
iFR/FFR per lesion	Good!	75.5% (1,177/1,559)		NA	NA
Post-stenting IVUS per patient	Good!	84.1% (384/454)	Poor...	4.8% (15/311)	<0.001
Post-stenting IVUS per lesion	Good!	76.4% (872/1,142)		NA	NA
Success rate of CTO PCI per lesion	Good!	87.0% (94/108)	Poor...	57.4% (54/94)	<0.001
Current-generation DES used	Excellent!!	98.4% (440/447)	Poor...	0% (0/315)	<0.001
		SYNERGY EES (strut thickness: 74 µm)		TAXUS PES (strut thickness: 132 µm)	
Statin at discharge	Excellent!!	97.3% (437/449)	Good!	85.4% (268/314)	<0.001

CTO: chronic total occlusion; DES: drug-eluting stent; FFR: fractional flow reserve; iFR: instantaneous wave-free ratio; IVUS: intravascular ultrasound; PCI: percutaneous coronary intervention

Major Adverse Cardiac or Cerebrovascular Events





The 2010-2014-2018 trilogy of ESC–EACTS Guidelines on myocardial revascularisation: we cannot jump three steps this way and then return to where we began

David Glineur[1], MD, PhD; William Wijns[2]*, MD, PhD

1. Division of Cardiac Surgery, University of Ottawa Heart Institute, Ottawa, Canada; 2. The Lambe Institute for Translational Medicine and Curam, Saolta University Healthcare Group, Galway, Ireland

Components of "best practice" PCI in patients with three-vessel disease

1.	***Calculation of SYNTAX II score for inclusion based on calculated equipoise between PCI and CABG.***
2.	***Targeted PCI based on physiology and anatomy using combined resting and hyperemic indices of stenosis significance.***
3.	***Use of intracoronary imaging for complex procedures (intravascular ultrasound [IVUS]).***
4.	***PCI of chronic total coronary occlusion for complete revascularization.***
5.	***Use of current-generation DES.***
6.	***Optimal medical care including statin treatment at discharge.***

Quantitative Flow Ratio in MultiTALENT trial

1. *State of the art and best practice PCI*
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The importance of physiological assessment of coronary artery stenosis

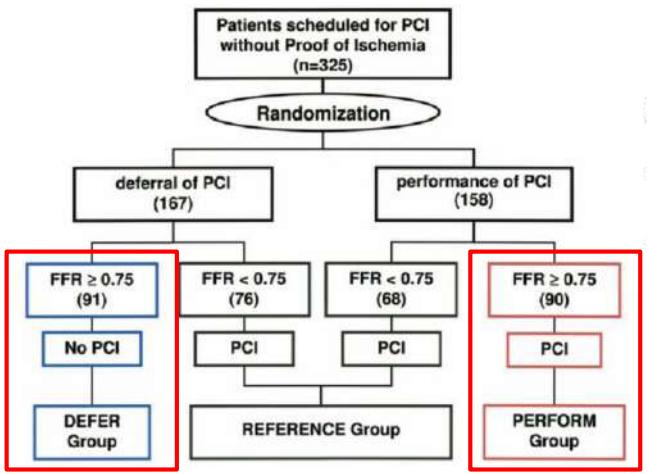
DEFER

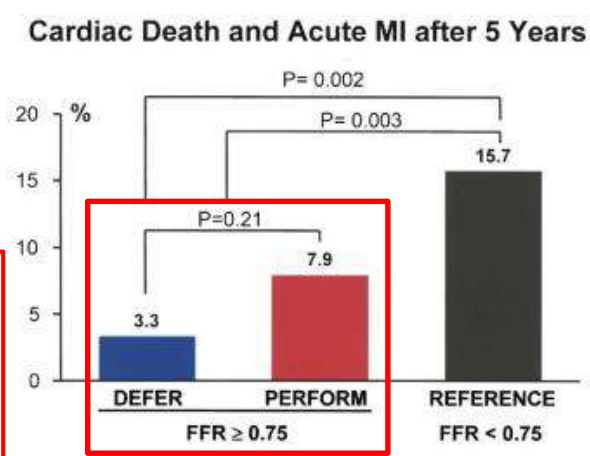
No Demonstrated Benefit of Stenting a Non-ischemic Stenosis (FFR ≥ 0.75)

CLINICAL RESEARCH Interventional Cardiology

Percutaneous Coronary Intervention of Functionally Nonsignificant Stenosis

5-Year Follow-Up of the DEFER Study

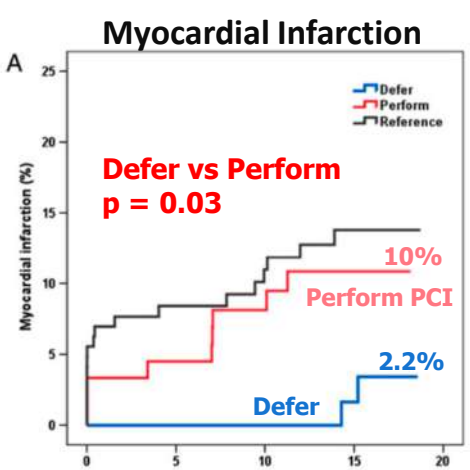




European Heart Journal (2015) 36, 3182–3188 doi:10.1093/eurheartj/ehv452

CLINICAL RESEARCH Coronary artery disease

Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial



Pijls NHJ et al. *JACC* 2007;49(21):2105.

The importance of physiological assessment of coronary artery stenosis

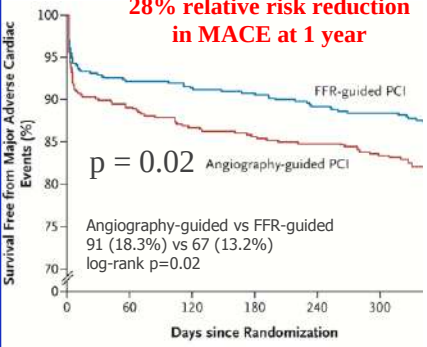
FAME I

FFR-guided PCI Results in Fewer Stents and Fewer Events Compared to Angio-guided PCI

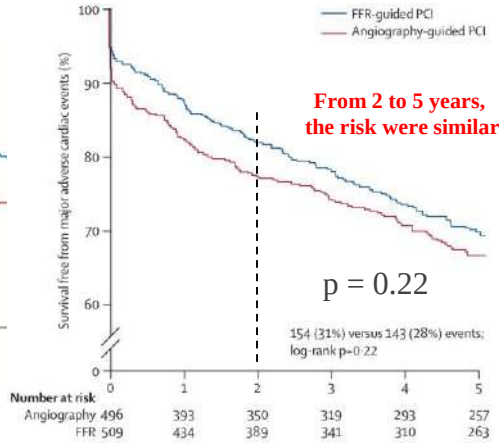
The NEW ENGLAND JOURNAL of MEDICINE
JANUARY 15, 2009

Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial

Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention



MACE



Tonino PAL et al. *NEJM* 2009;360:213.

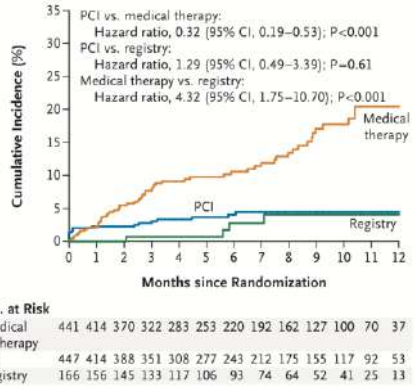
Van Nunen, LX et al. Lancet 2015;386(3):1853-60

FAME II

FFR-Guided PCI with Medical Therapy (MT) Improves Outcomes versus MT Alone

The NEW ENGLAND JOURNAL of MEDICINE
SEPTEMBER 13, 2012

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

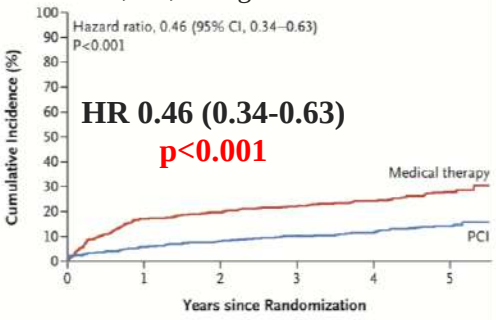


Bruyne BD et al. *NEJM* 2012;367:991.

The NEW ENGLAND JOURNAL of MEDICINE
ORIGINAL ARTICLE

Five-Year Outcomes with PCI Guided by Fractional Flow Reserve

death, MI, or urgent revascularization



Xaplanteris et al. *NEJM* 2018;379:250.

All scenarios require proof of ischemia according to 2018 ESC/EACTS Guideline

Indications for revascularization in patients with stable angina or silent ischaemia

Extent of CAD (anatomical and/or functional)		Class[a]	Level[b]
For prognosis	Left main disease with stenosis >50%.[c 68–71]	I	A
	Proximal LAD stenosis >50%.[c 62,69,70,72]	I	A
	Two- or three-vessel disease with stenosis >50% with impaired LV function (LVEF ≤35%).[c 61,62,69,70,73–83]	I	A
	Large area of ischaemia detected by functional testing (≥10% LV) or abnormal invasive FFR.[d 24,69,84–90]	I	B
	Single remaining patent coronary artery with stenosis >50%.[c]	I	C
For symptoms	Haemodynamically significant coronary stenosis[c] in the presence of limiting angina or angina equivalent, with insufficient response to optimized medical therapy.[e 24,63,91–97]	I	A

© ESC 2018

CAD = coronary artery disease; FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; LAD = left anterior descending coronary artery; LV = left ventricular; LVEF = left ventricular ejection fraction.

[a]Class of recommendation.

[b]Level of evidence.

[c]With documented ischaemia or a haemodynamically relevant lesion defined by FFR ≤0.80 or iwFR ≤0.89 (see section 3.2.1.1), or >90% stenosis in a major coronary vessel.

[d]Based on FFR ≤0.75 indicating a prognostically relevant lesion (see section 3.2.1.1).

[e]In consideration of patient compliance and wishes in relation to the intensity of anti-anginal therapy.

C: With **documented ischemia** or hemodynamically relevant lesion defined by **FFR≤0.80 or iFR≤0.89**, or **>90% stenosis** in a major coronary vessel.

Recommendation on functional testing

2018 ESC/EACTS Guideline

Recommendations on functional testing and intravascular imaging for lesion assessment

Recommendations	Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.[15,17,18,39]	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI.[29,31]	IIa	B
IVUS should be considered to assess the severity of unprotected left main lesions.[35–37]	IIa	B

FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; IVUS = intravascular ultrasound; PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.

Is recommended/is indicated

Multiple RCTs (DEFER, DEFINE-FLAIR, SWEDEHEART,)

Should be considered

Single RCT (FAME)

Quantitative Flow Ratio in MultiTALENT trial

1. *State of the art and best practice PCI*
2. *Physiological assessment in multi-vessel disease*
3. *What's QFR?*
4. *The methodology of QFR*

Quantitative Flow Ratio (QFR)

Medis
Medical Imaging Systems

Standard Angiogram

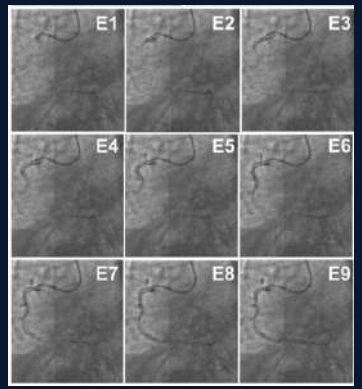
Data Transmission System

Two image runs with angle difference ≥25°

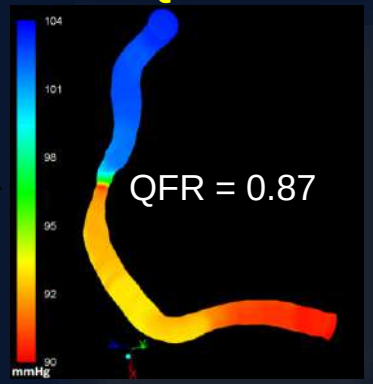
AngioPlus System

3D Reconstruction

Modified Frame Count



QFR



Without Inducing Hyperemia

Tu S et al. *JACC Cardiovasc Interv*. 2014;7:768-77; Tu S et al. *JACC Cardiovasc Interv*. 2016;9:2024-35

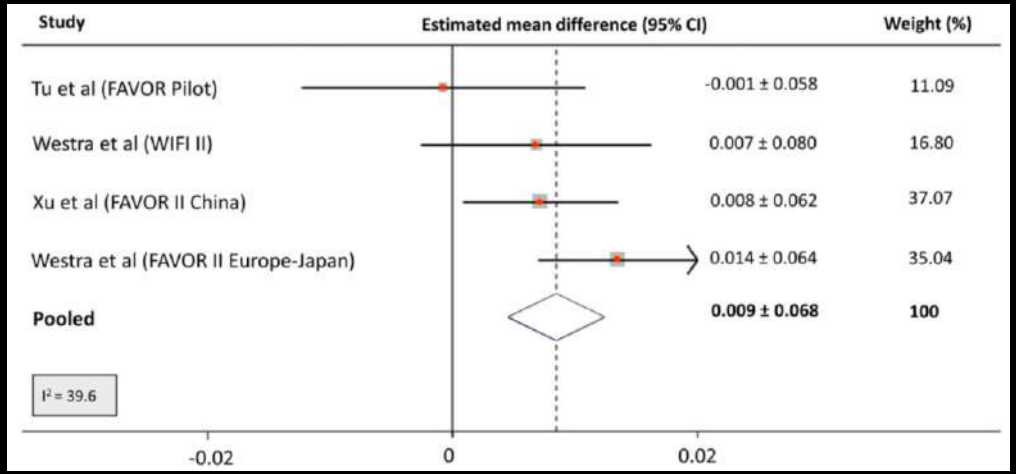
ORIGINAL STUDIES

WILEY

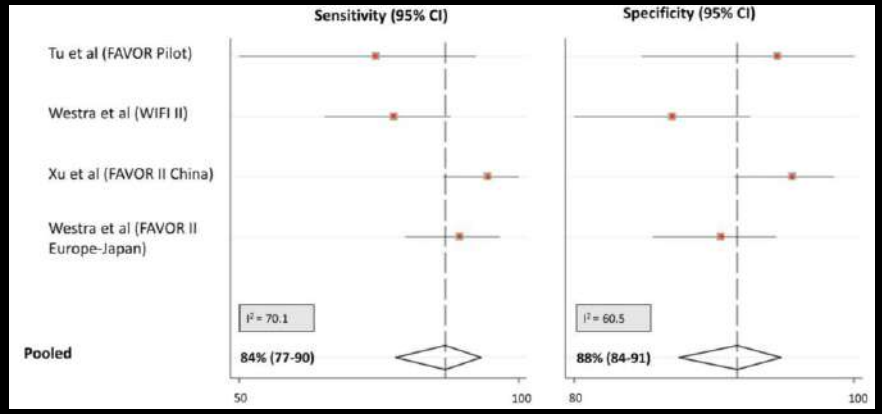
Diagnostic performance of quantitative flow ratio in prospectively enrolled patients: An individual patient-data meta-analysis

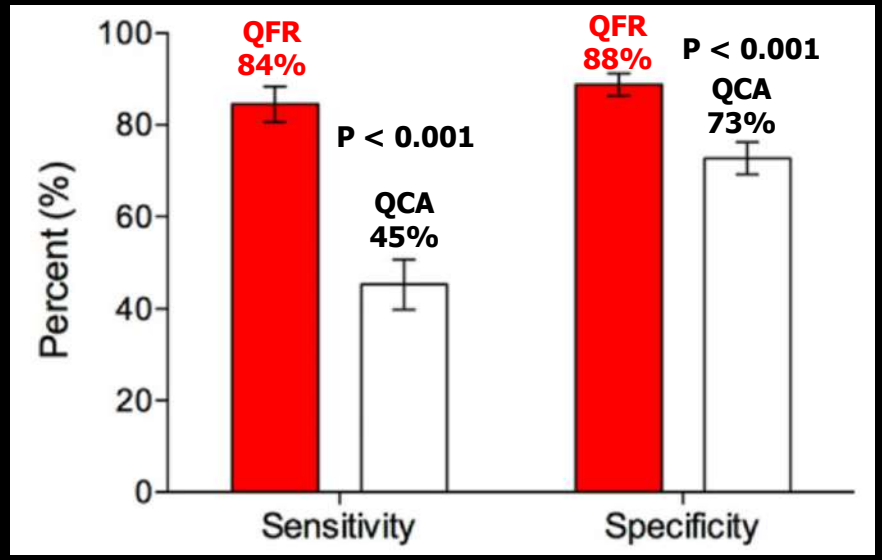
Jelmer Westra MD[1] | Shengxian Tu PhD[2] | Gianluca Campo MD[3,4] | Shubin Qiao MD[5] | Hitoshi Matsuo MD, PhD[6] | Xinkai Qu MD[7] | Lukasz Koltowski MD, PhD[8] | Yunxiao Chang MSc[2] | Tommy Liu MD[9] | Junqing Yang MD[10] | Birgitte Krogsgaard Andersen BSc[1] | Ashkan Eftekhari MD[1] | Evald Høj Christiansen MD, PhD[1] | Javier Escaned MD, PhD[11] | William Wijns MD, PhD[12] | Bo Xu MBBS[5] | Niels Ramsing Holm MD[1]

A individual patient-data meta-analysis from 4 studies
A total of 819 patients and 969 vessels



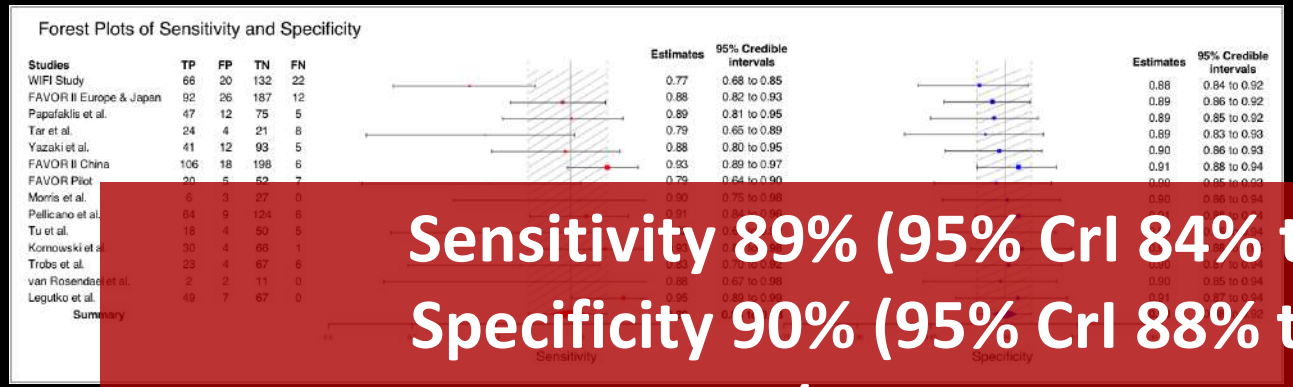
Mean agreement of QFR and FFR.

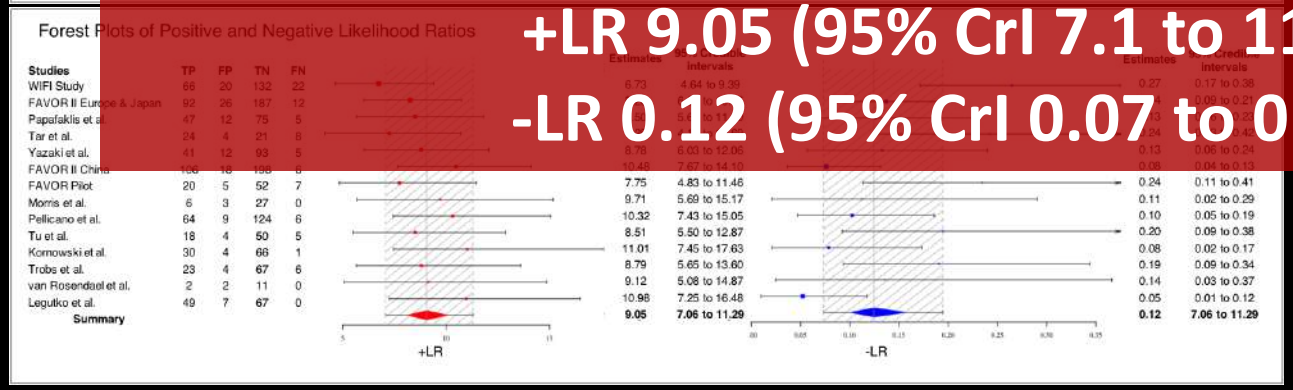




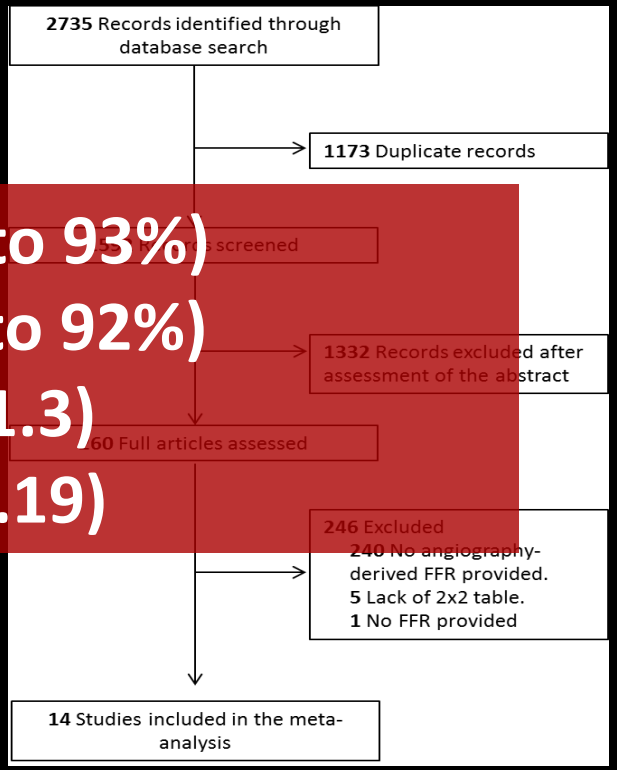
Sensitivity and specificity of QFR with FFR as a refer

Diagnostic performance of angiography-derived FFR
a systematic review and Bayesian meta-analysis



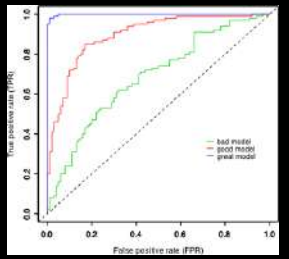


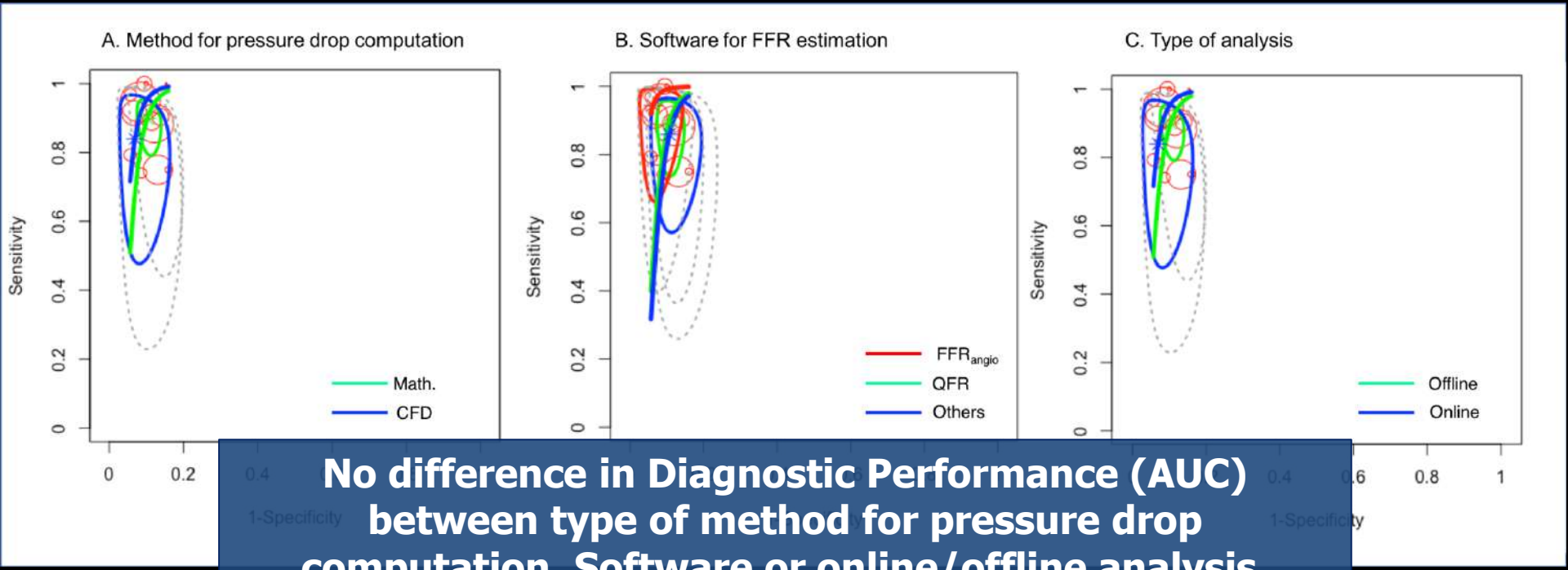
Sensitivity 89% (95% CrI 84% to 93%)
Specificity 90% (95% CrI 88% to 92%)
+LR 9.05 (95% CrI 7.1 to 11.3)
-LR 0.12 (95% CrI 0.07 to 0.19)



Collet et al. Eur Heart J. 2018 Sep 14;39(35):3314-3321

Bayesian Meta-regression



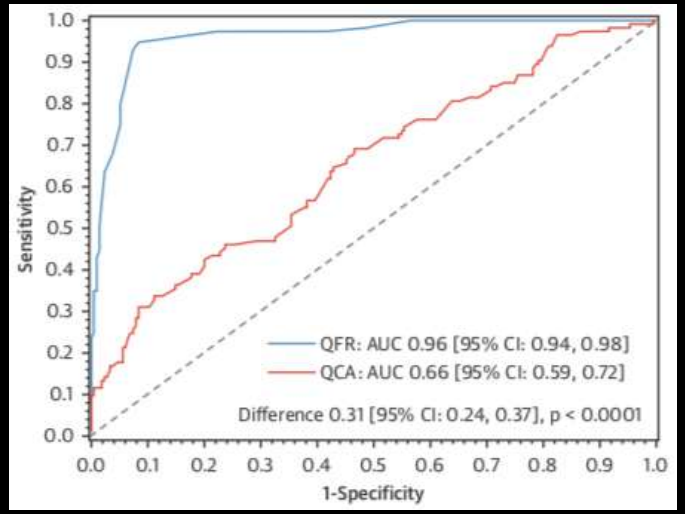


No difference in Diagnostic Performance (AUC) between type of method for pressure drop computation, Software or online/offline analysis.

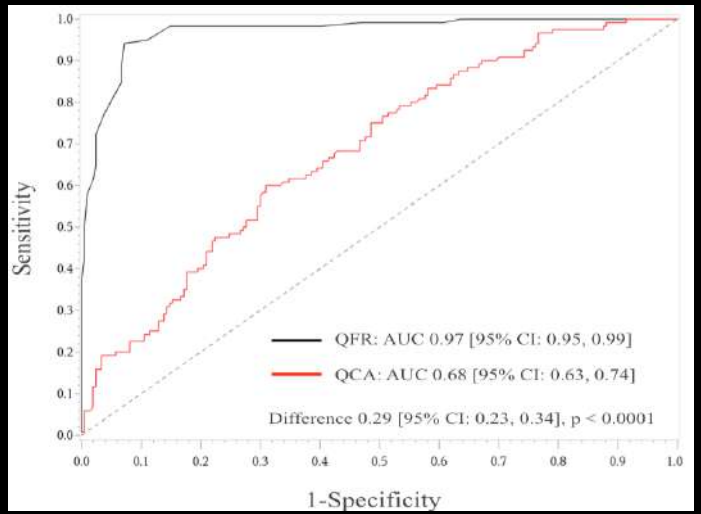
Collet et al. Eur Heart J. 2018 Sep 14;39(35):3314-3321

On-line vs Off-line QFR: Insight from FAVOR II China

ROC for the discrimination of functionally significant stenosis



On-line
AUC 0.96
Accuracy 92.7



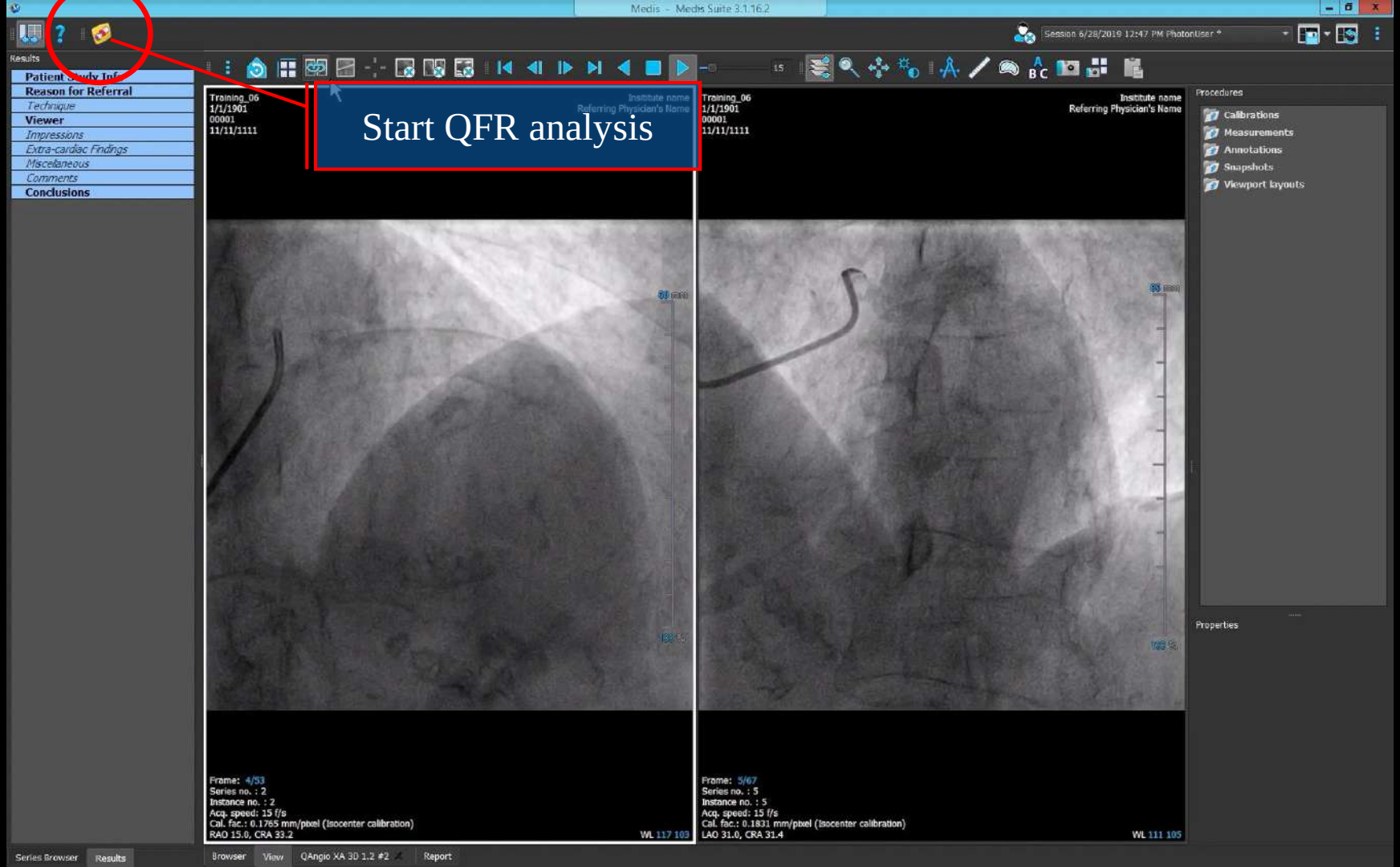
Off-line
AUC 0.97
Accuracy 93.3

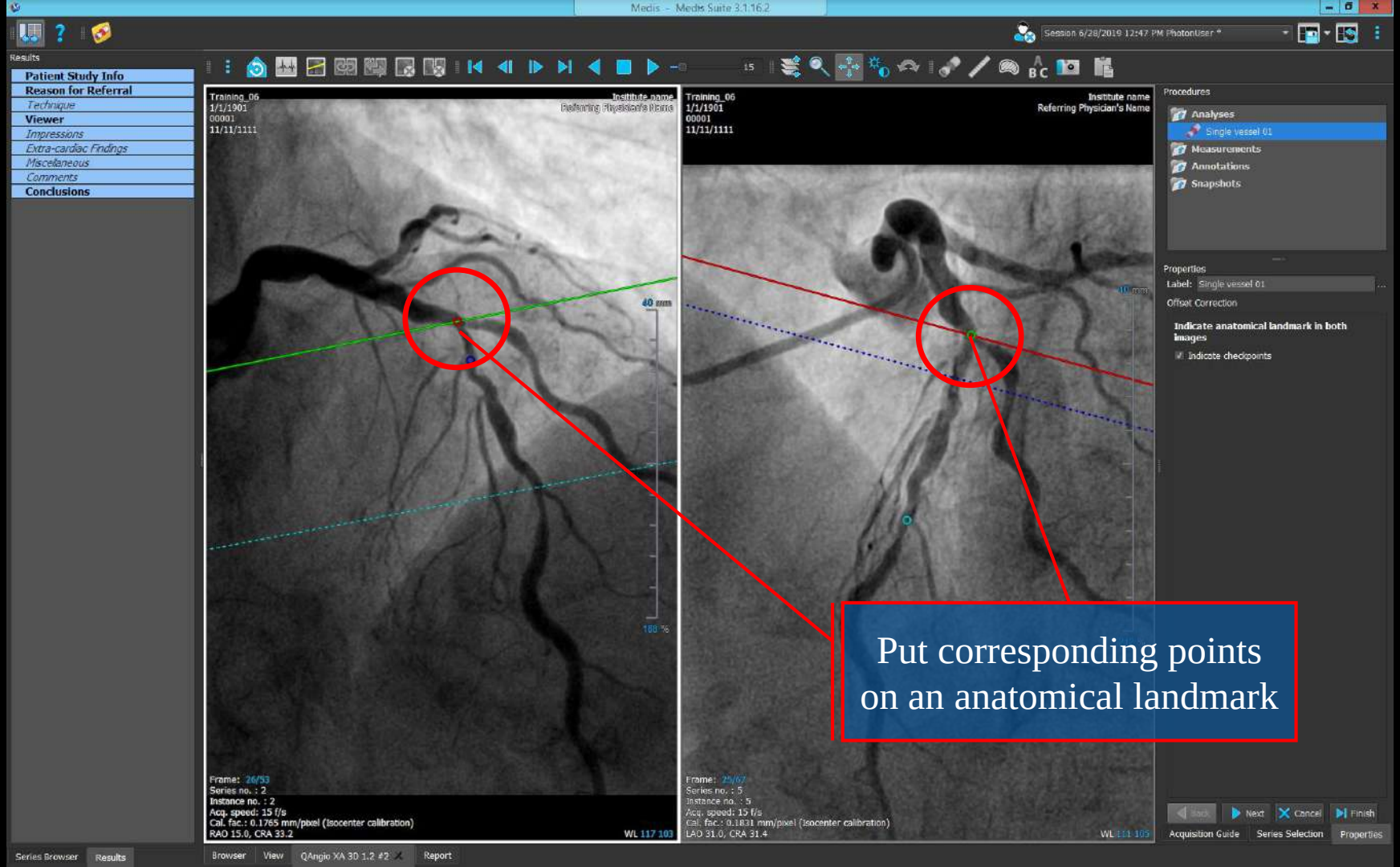
On-line QFR showed excellent predictive value and comparable accuracy to Off-line.

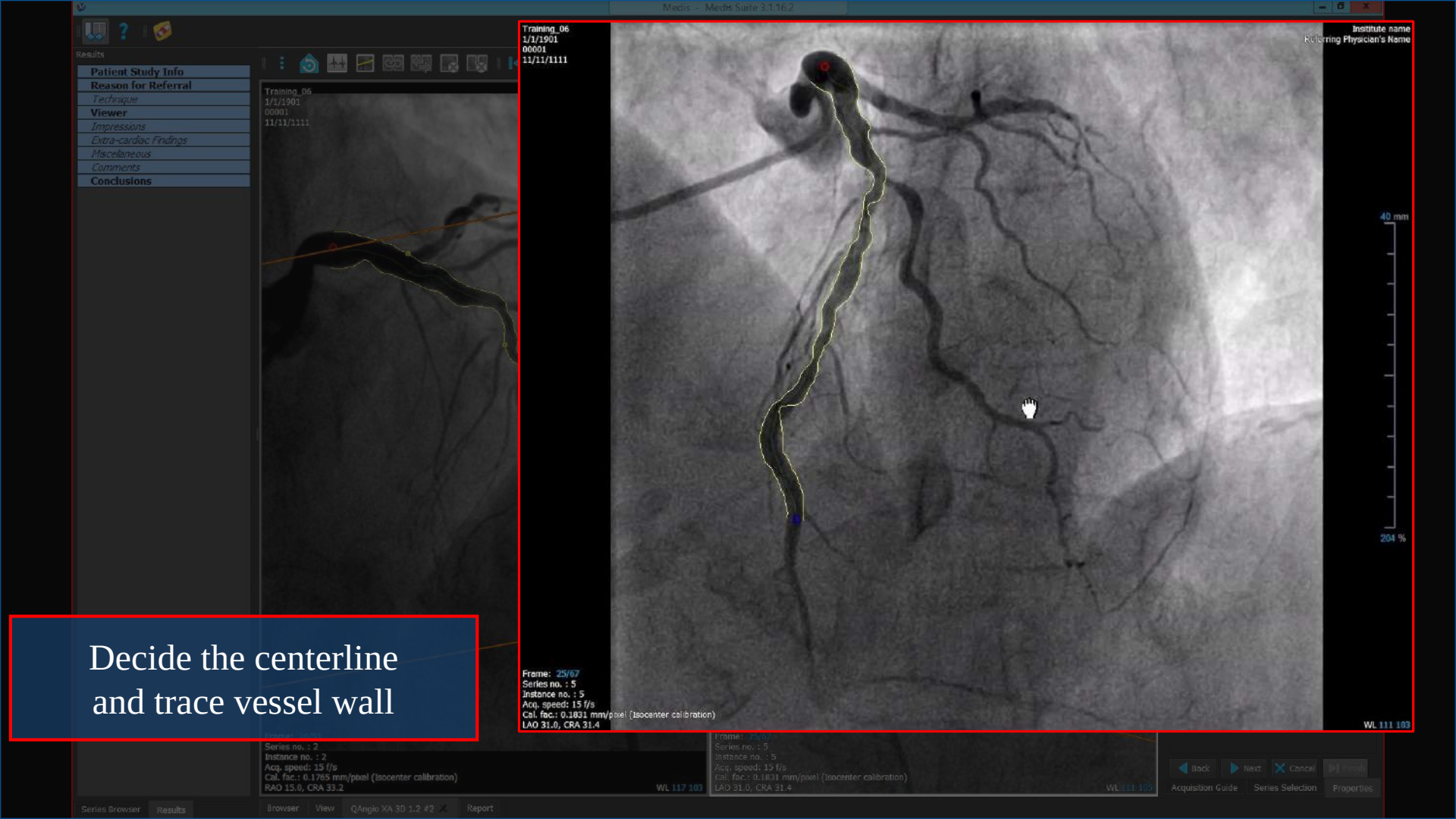
Xu B, et al. J Am Coll Cardiol. 2017 Dec 26;70(25):3077-3087

Quantitative Flow Ratio in MultiTALENT trial

1. *State of the art and best practice PCI*
2. *Physiological assessment in multi-vessel disease*
3. *What's QFR?*
4. *The methodology of QFR*


Medis - Medis Suite 3.1.16.2
Start QFR analysis
Results
Patient Study Info
Reason for Referral
Technique
Viewer
Impressions
Extra-cardiac Findings
Miscelaneous
Comments
Conclusions
Training_06
1/1/1901
00001
11/11/1111
Institute name
Referring Physician's Name
Frame: 4/53
Series no. : 2
Instance no. : 2
Acq. speed: 15 f/s
Cal. fac.: 0.1765 mm/pixel (Isocenter calibration)
RAO 15.0, CRA 33.2
WL 117 103
Frame: 5/67
Series no. : 5
Instance no. : 5
Acq. speed: 15 f/s
Cal. fac.: 0.1831 mm/pixel (Isocenter calibration)
LAO 31.0, CRA 31.4
WL 111 105
Procedures
Calibrations
Measurements
Annotations
Snapshots
Viewport layouts
Properties
Series Browser
Results
Browser
View
QAngio XA 3D 1.2 #2
Report

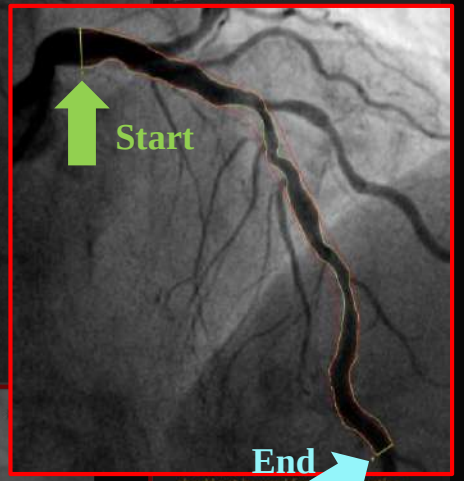

Medis - Medis Suite 3.1.16.2
Results
Patient Study Info
Reason for Referral
Technique
Viewer
Impressions
Extra-cardiac Findings
Miscelaneous
Comments
Conclusions
Training_06
1/1/1901
00001
11/11/1111
Institute name
Referring Physician's Name
Frame: 26/53
Series no. : 2
Instance no. : 2
Acq. speed: 15 f/s
Cal. fac.: 0.1765 mm/pixel (isocenter calibration)
RAO 15.0, CRA 33.2
WL 117 103
Frame: 25/67
Series no. : 5
Instance no. : 5
Acq. speed: 15 f/s
cal. fac.: 0.1831 mm/pixel (isocenter calibration)
LAO 31.0, CRA 31.4
WL 111 105
Procedures
Analyses
Single vessel 01
Measurements
Annotations
Snapshots
Properties
Label: Single vessel 01
Offset Correction
Indicate anatomical landmark in both images
Indicate checkpoints
Put corresponding points on an anatomical landmark
Back
Next
Cancel
Finish
Acquisition Guide
Series Selection
Properties
Series Browser
Results
Browser
View
QAngio XA 3D 1.2 #2
Report



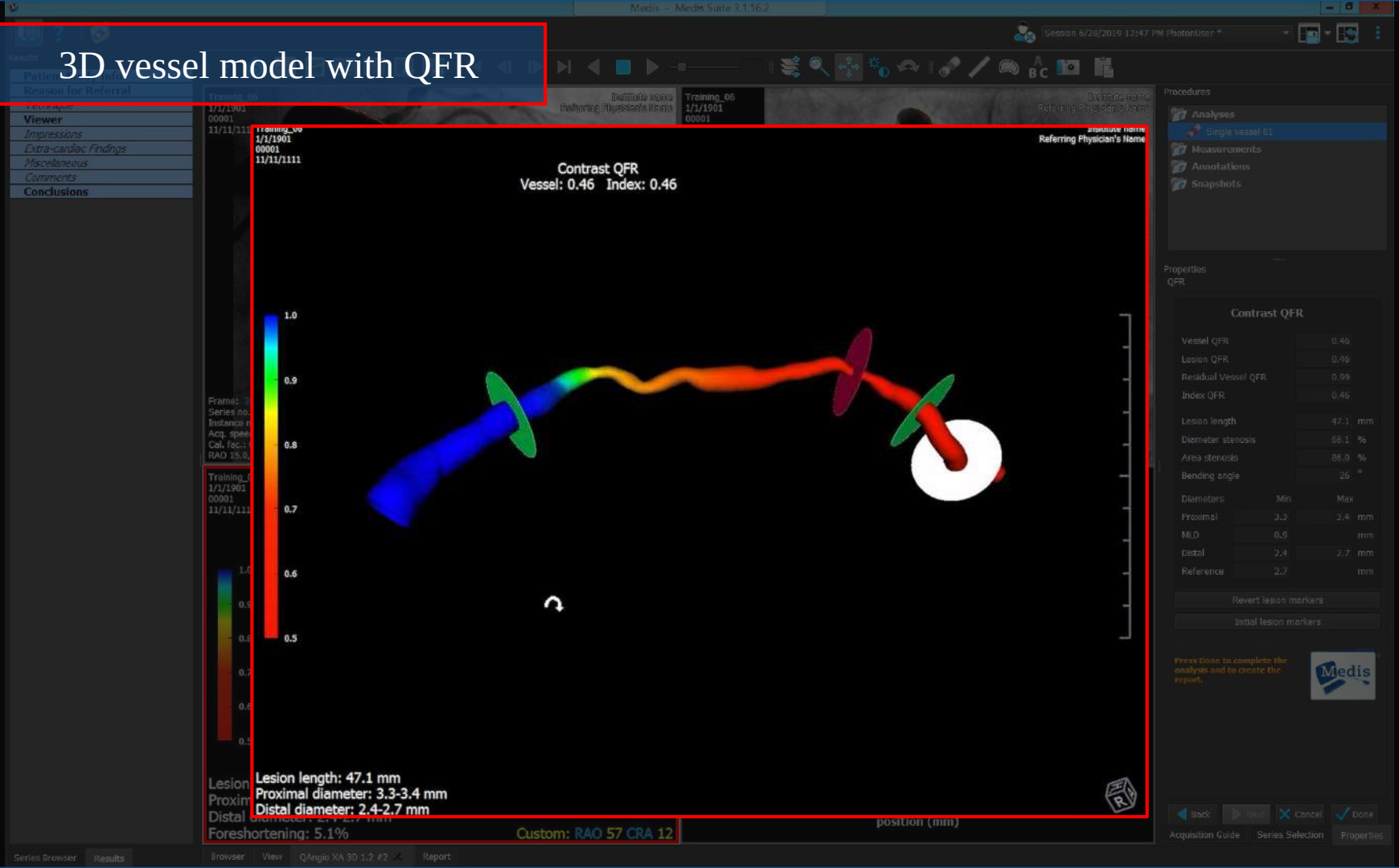
Decide the centerline
and trace vessel wall

3D vessel model

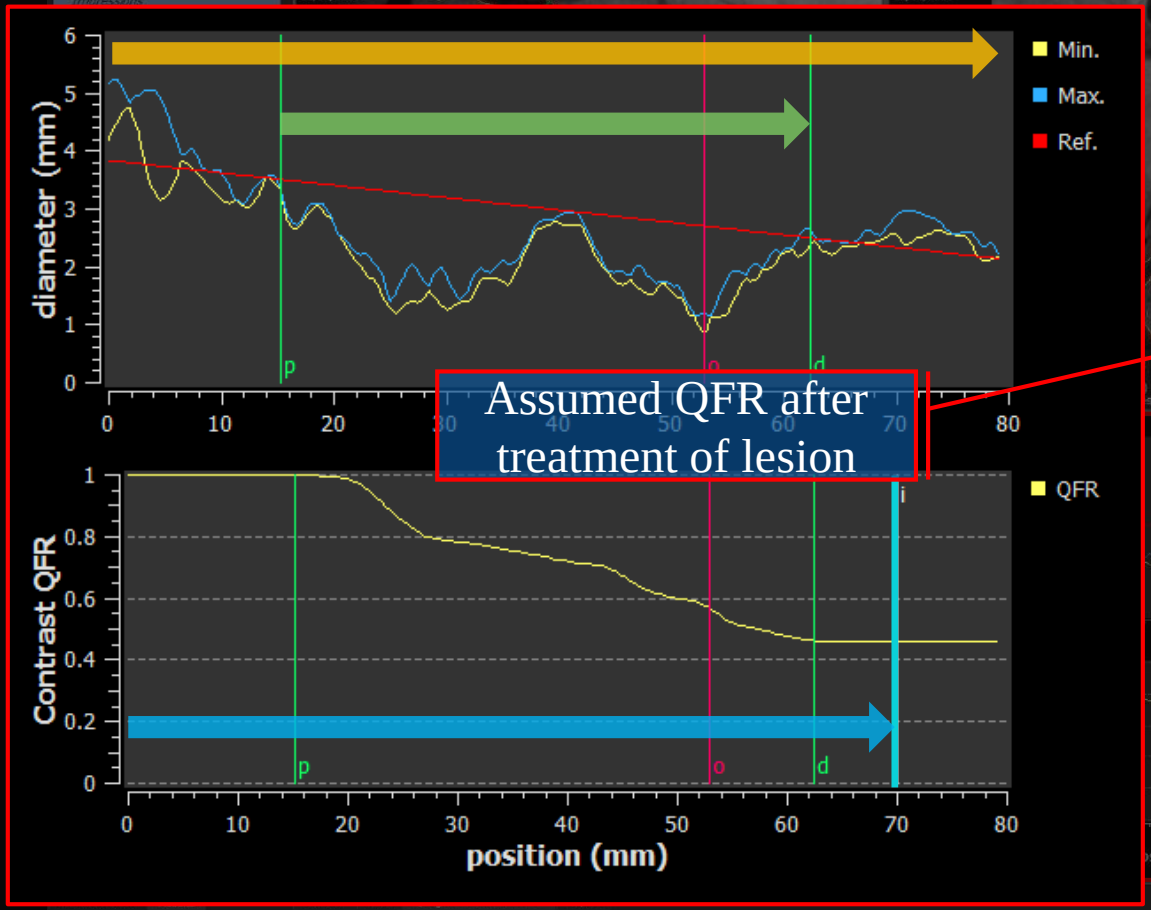
Frame count for blood flow speed



3D vessel model with QFR



Properties of QFR



Assumed QFR after treatment of lesion

Properties
QFR

Contrast QFR

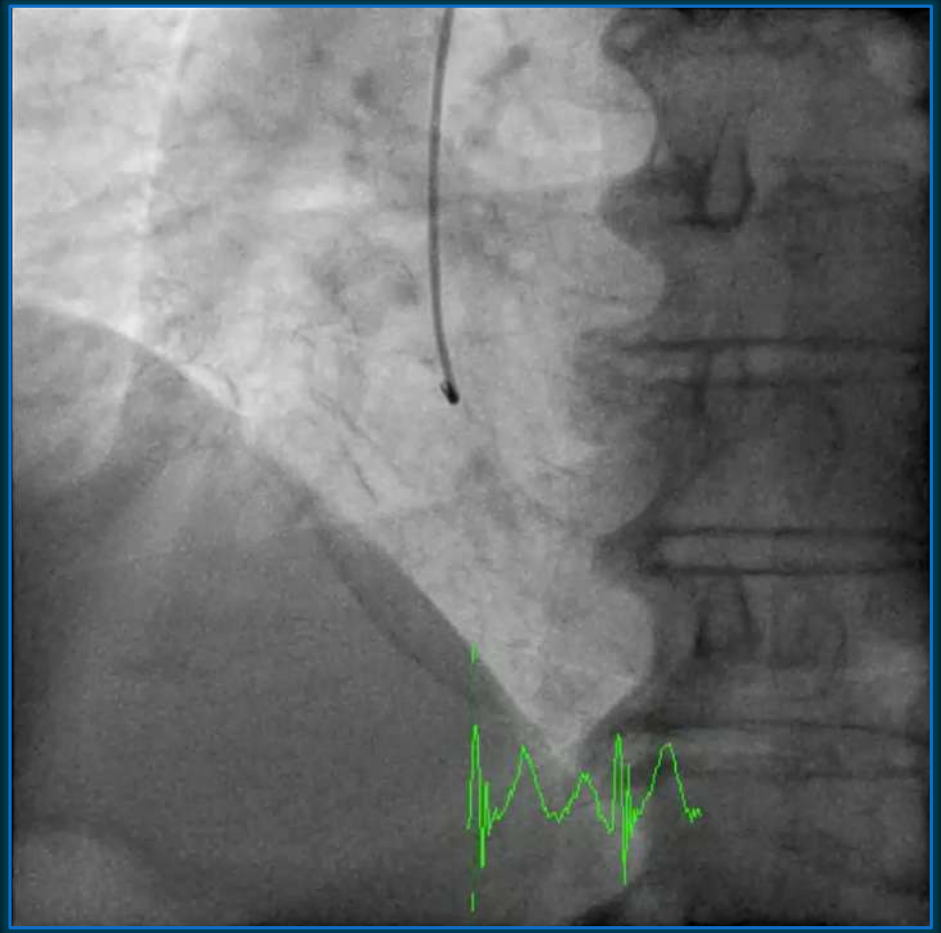
Vessel QFR	0.46
Lesion QFR	0.46
Residual Vessel QFR	0.99
Index QFR	0.46

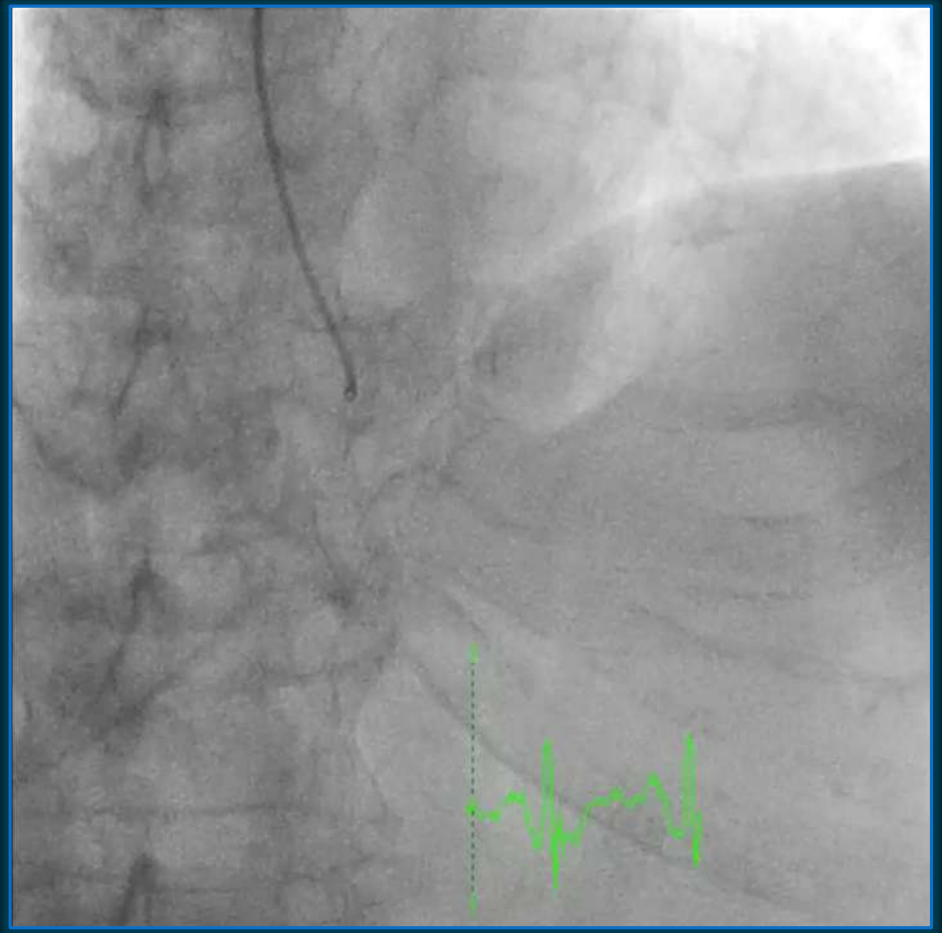
QFR of any selected point

Lesion length	47.1	mm
Diameter stenosis	68.1	%
Area stenosis	86.0	%
Bending angle	26	°

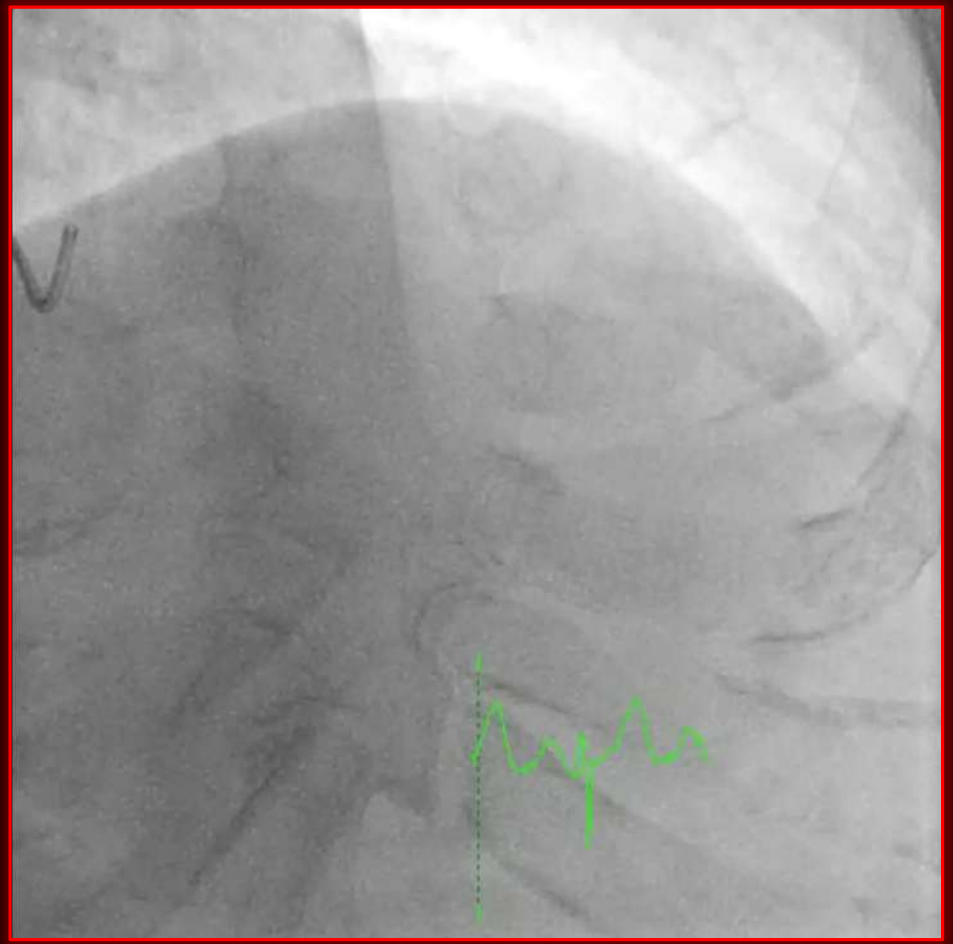
Diameters	Min	Max	
Proximal	3.3	3.4	mm
MLD	0.9		mm
Distal	2.4	2.7	mm
Reference	2.7		mm

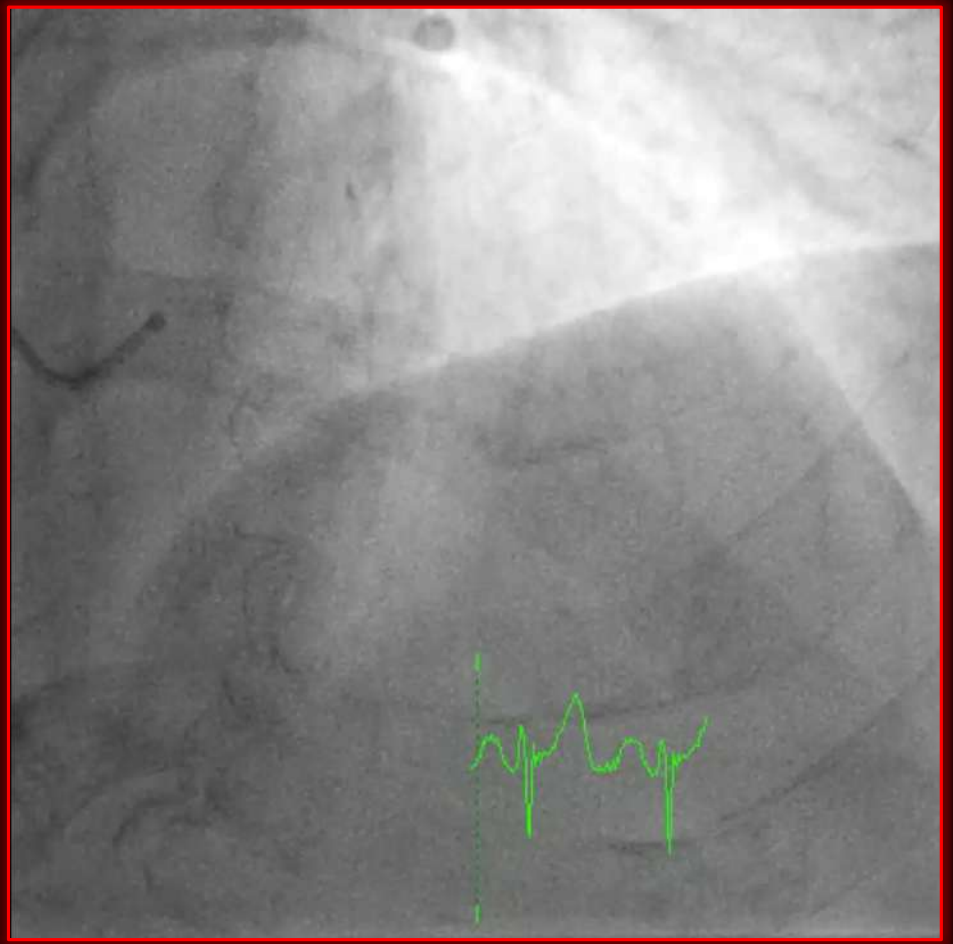
A Case from SYNTAX II trial





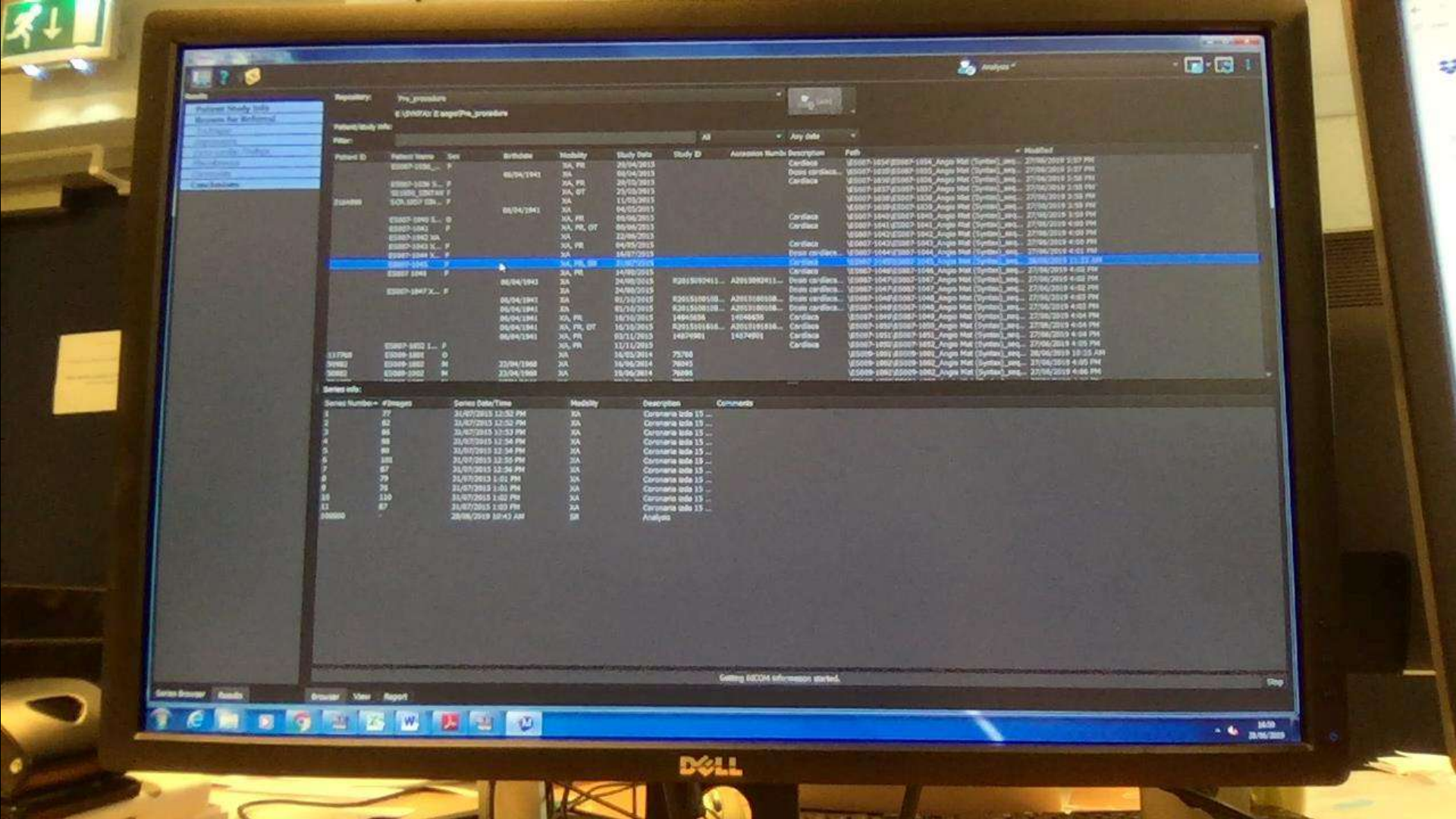
RCA





LAD

LCx

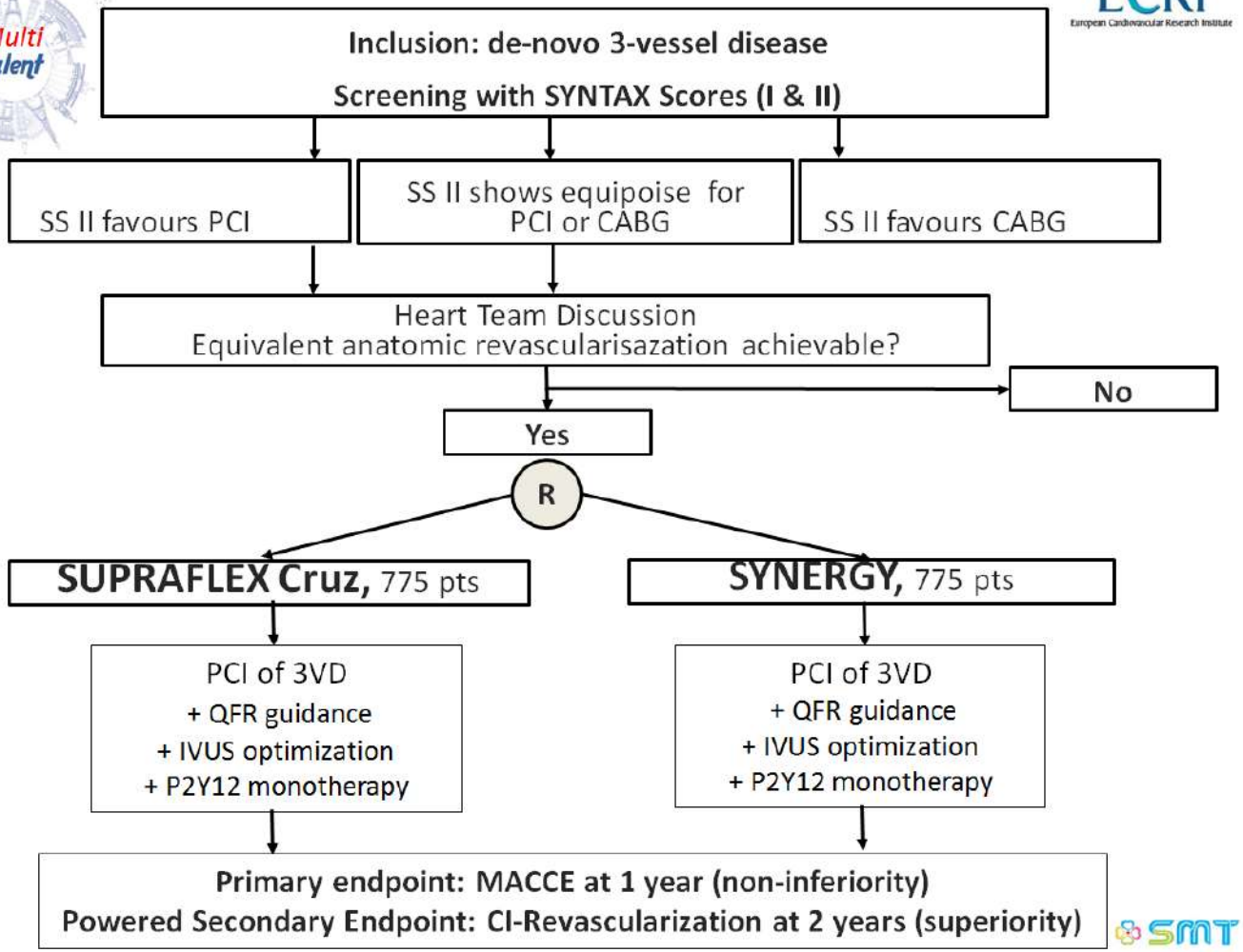

DELL

Application of QFR for clinical practice

Application of QFR for clinical practice

Conclusion

- In the contemporary era, physiological assessment of stenotic lesion is mandatory as one of the components of “best practice” PCI in patients with multi-vessel disease.
- Among several methods for coronary physiological assessment, QFR has shown the high sensitivity and specificity with pressure-wire measured FFR as a reference.
- The time for analysis of QFR takes approximately 5 min per lesion, which would be quite acceptable for clinical practice.
- In the MultiTALENT trial, QFR will be expected as a reliable decision guidance tool.


Inclusion: de-novo 3-vessel disease
Screening with SYNTAX Scores (I & II)
SS II favours PCI
SS II shows equipoise for PCI or CABG
SS II favours CABG
Heart Team Discussion
Equivalent anatomic revascularisazation achievable?
No
Yes
R
SUPRAFLEX Cruz, 775 pts
SYNERGY, 775 pts
PCI of 3VD
+ QFR guidance
+ IVUS optimization
+ P2Y12 monotherapy
PCI of 3VD
+ QFR guidance
+ IVUS optimization
+ P2Y12 monotherapy
Primary endpoint: MACCE at 1 year (non-inferiority)
Powered Secondary Endpoint: CI-Revascularization at 2 years (superiority)