Imaging and Physiology
Coronary Physiology
Presentation Theater 1, Level 1

Can Angio-FFR Change Our Cath Lab Practice?

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CARDIOVASCULAR SUMMIT TCTAP 2019

Monday, Apr 29, 2019
5:32 PM – 5:40 PM

CVRF

Angio-derived FFR in cath lab

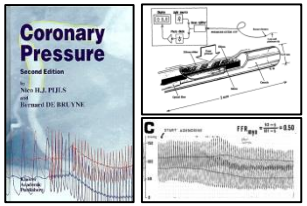
- What is the basic principle of angio-derived FFR?
- What is the diagnostic performance of angio-derived FFR?
- Can we use it in complex lesions?
- Can we use angio-derived FFR to PCI planning (Simulation of post procedural FFR, tandem lesion, number of stent, and stent length)?
- What is the potential clinical impact of post procedural QFR?
- From late loss to QFR: new parameter of device efficiency and QFR for event adjudication in the context of clinical trial

History of physiology

1975 D. Young $\frac{\Delta p}{\rho U^2} = \frac{K_v}{Re} + \frac{K_t}{2}\left(\frac{A_0}{A_1} - 1\right)^2$

1978 K. Lance Gould $\Delta P = FV + SV^2 + D\,(V/V_r\text{-}1)V^2$

1983 R. Kirkeeide



1988 PW. Serruys — Velocity wire, Flow-velocity validation

1991 Pressure wire

1993 P.W. Serruys (Double-wire Pressure-velocity)

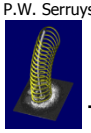
1993 Håkan Emanuelsson, P.W. Serruys (SFR)

1993 Carlo Di Mario, P.W. Serruys (Hyperemic Index)

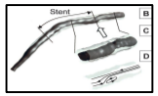
1994 FFR — Nico Pijls, Bernard De Bruyne → **2001** DEFER → **2009** FAME → 2012 FAME 2

1997 CFR era — DEBATE 1,2, DESTINY, FROST

2001 ANGUS — Slager C, P.W. Serruys



2002 Shear stress — Thury A, Wentzel J, P.W. Serruys



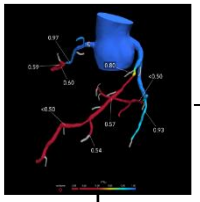
Non-Newtonian Pulsatile
Shear-stress microenvironment (fusion OCT/IVUS and angiography).
Navier-Stokes + Quemada equation

2011 iFR® — J. Davies, J. Escaned — *Hybrid algorithm* — ADVISE, ADVISE II, SYNTAX II

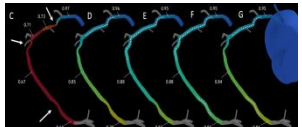
iFR® — DEFINE-FLAIR, SWEDEHEART

2010 FFR_{CT} — Charles A. Taylor — **Navier-Stokes**

DISCOVER FLOW, DE FACTO, NXT TRIAL, PLATFORM, SYNTAX III



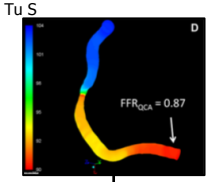
FFR_{CT} PLANNER

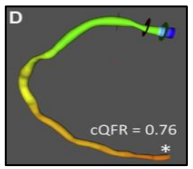


3D Angiography + "CFD" Navier-Stokes + TIMI Frame Count — Papafaklis, P.W. Serruys

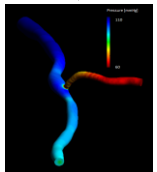
→ **3D Angiography, or 2D Angiography + Lance Gould "≠ CFD"**

Tu S





QFR



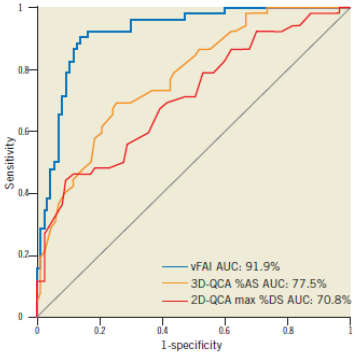
3D Bifurcation QCA
CFD
Finite Elements
Navier-Stokes

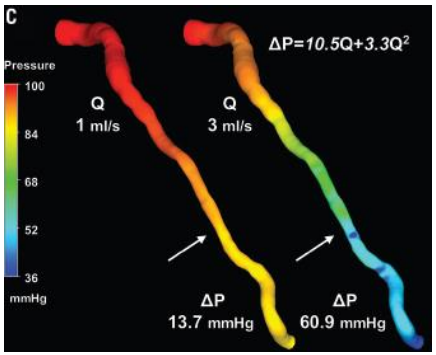
3

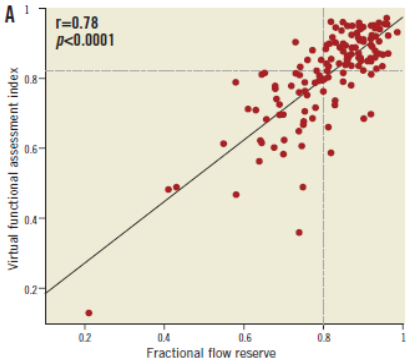
Fast virtual functional assessment of intermediate coronary lesions using routine angiographic data and blood flow simulation in humans: comparison with pressure wire – fractional flow reserve

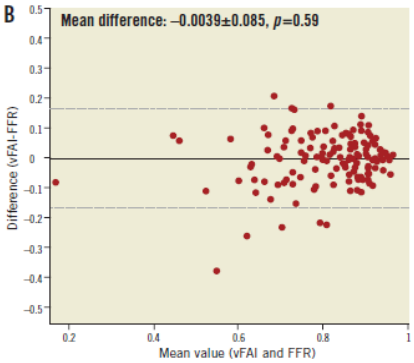
Michail I. Papafaklis[1,2], MD, PhD, FESC; Takashi Muramatsu[3], MD; Yuki Ishibashi[3], MD; Lampros S. Lakkas[1], MD; Shimpei Nakatani[3], MD; Christos V. Bourantas[3], MD, PhD; Jurgen Ligthart[3], BSc; Yoshinobu Onuma[3], MD, PhD; Mauro Echavarria-Pinto[4], MD; Georgia Tsirka[1], MD; Anna Kotsia[5], MD; Dimitrios N. Nikas[1], MD, PhD, FESC; Owen Mogabgab[5], MD; Robert-Jan van Geuns[3], MD, PhD; Katerina K. Naka[1], MD, PhD, FESC; Dimitrios I. Fotiadis[6], PhD; Emmanouil S. Brilakis[5], MD, PhD; Héctor M. Garcia-Garcia[3], MD, PhD; Javier Escaned[4], MD, PhD, FESC; Felix Zijlstra[3], MD, PhD; Lampros K. Michalis[1], MD, MRCP, FESC; Patrick W. Serruys[3,7]*, MD, PhD, FESC

- Virtual functional assessment index (vFAI) was derived from 3D-QCA.
- A Comparison with wire-FFR was studied in 139 lesions with intermediate stenosis.









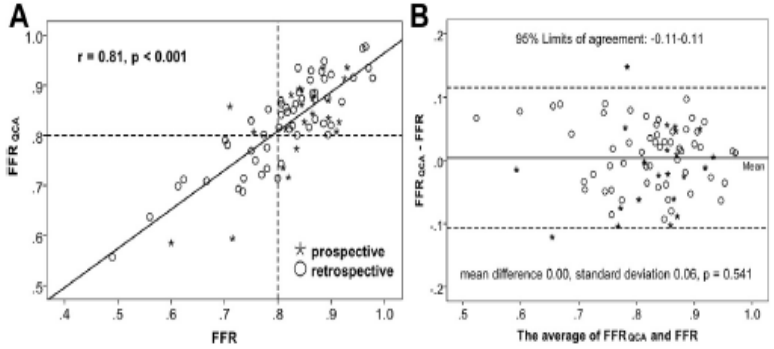
Eurointervention 2014

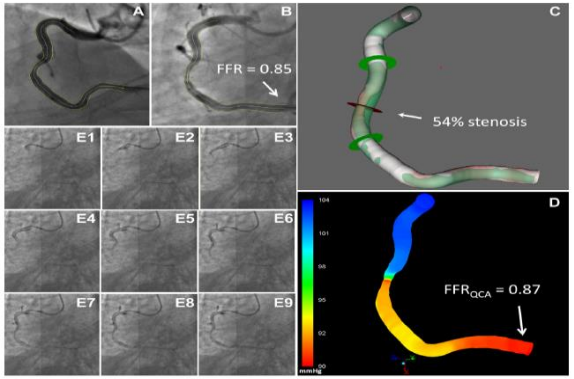
Fractional Flow Reserve Calculation From 3-Dimensional Quantitative Coronary Angiography and TIMI Frame Count

A Fast Computer Model to Quantify the Functional Significance of Moderately Obstructed Coronary Arteries

Shengxian Tu, PhD,* Emanuele Barbato, MD, PhD,† Zsolt Köszegi, MD, PhD,‡ Junqing Yang, MD,§ Zhonghua Sun, MD,‖ Niels R. Holm, MD,¶ Balázs Tar, MD,‡ Yingguang Li, MSc,* Dan Rusinaru, MD,† William Wijns, MD, PhD,† Johan H.C. Reiber, PhD*

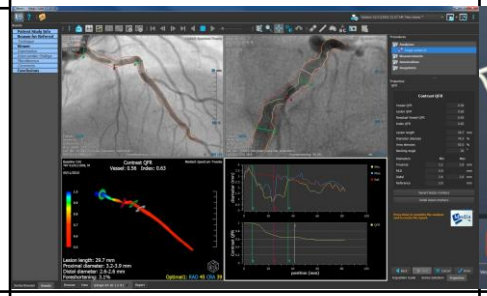
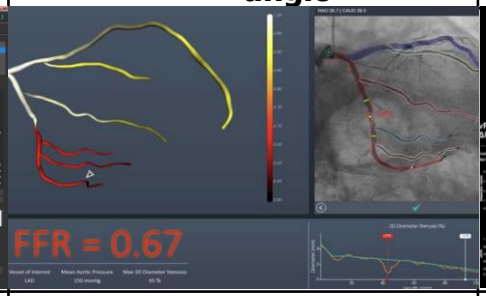
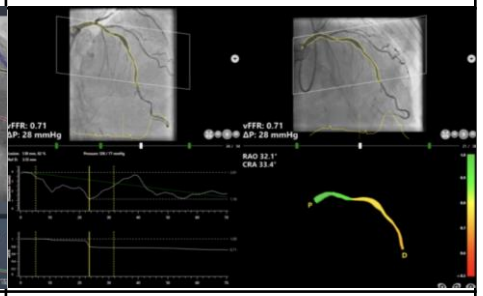
- FFR_{QCA} was derived from 3D QCA and TIMI (Thrombolysis In Myocardial Infarction) frame count.
- FFR_{QCA} was retrospectively compared with wire-based FFR in 77 intermediate lesions.





JACC Cardiovasc Interv 2014

Available software in cath lab

	QFR	FFR_{angio}	vFFR
			
On-line	Available	Available	Available
Required angio	2 projections 25 degrees apart	≥2 projections	2 projections 30 degrees apart
Process	Mathematical formula	Rapid flow analysis	NA
Published Clinical data	FAVOR pilot, II China and 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* *presented at euroPCR2018
AUC for predicting FFR≤0.8	**0.92-0.96**	**0.94**	**0.93**
Time to computation	5 min	(2.7 min: without manual correction and lesion identification)	NA

Quantitative Flow Ratio (QFR)

Medis

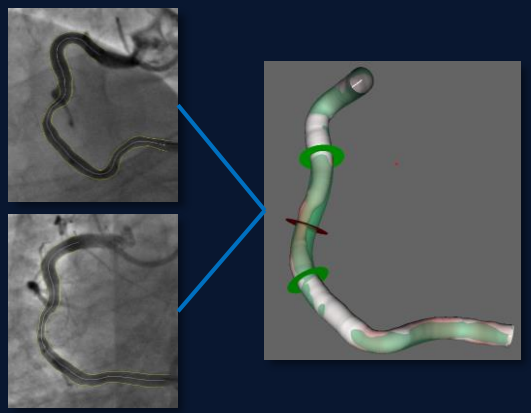
Standard Angiogram

Data Transmission System

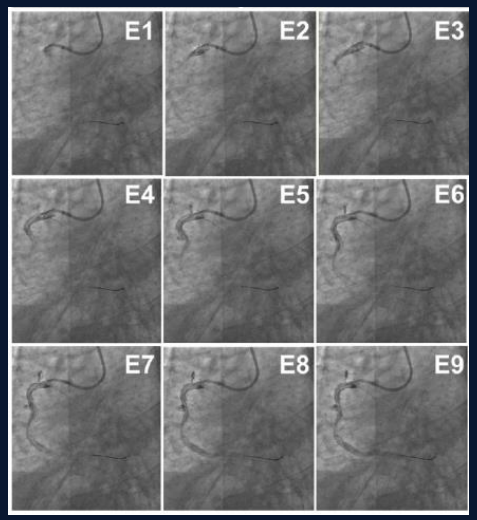
Two image runs with angle difference ≥25°

AngioPlus System

3D Reconstruction



Modified Frame Count

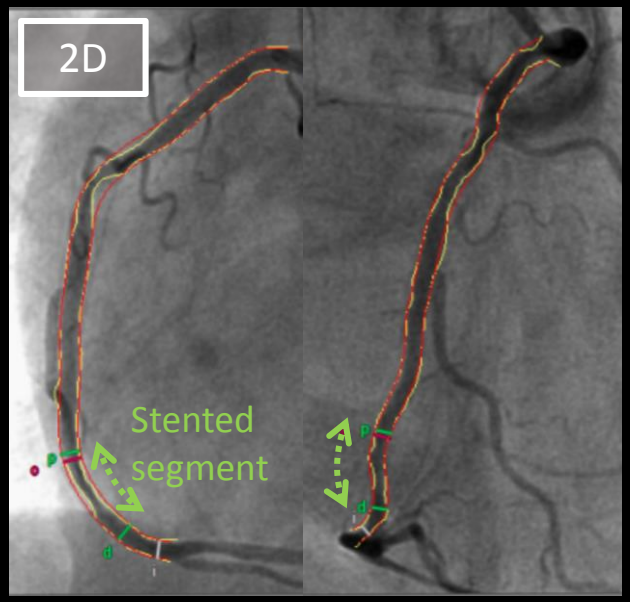


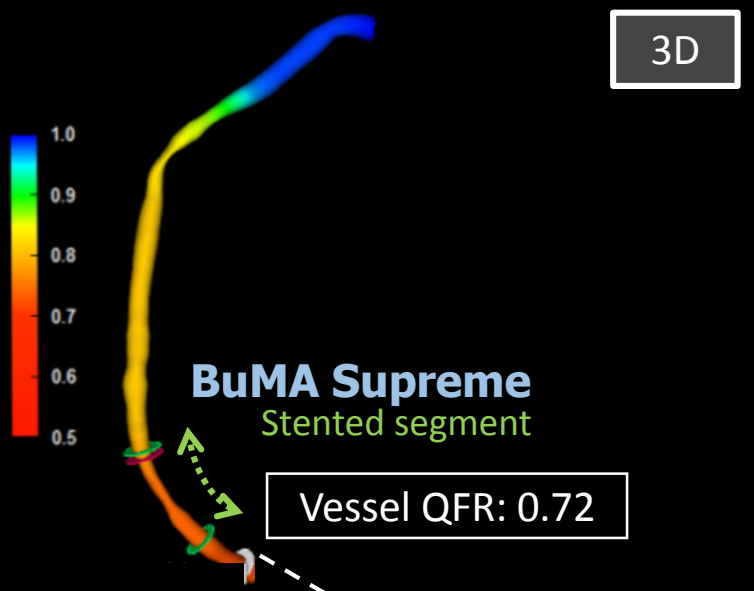
QFR

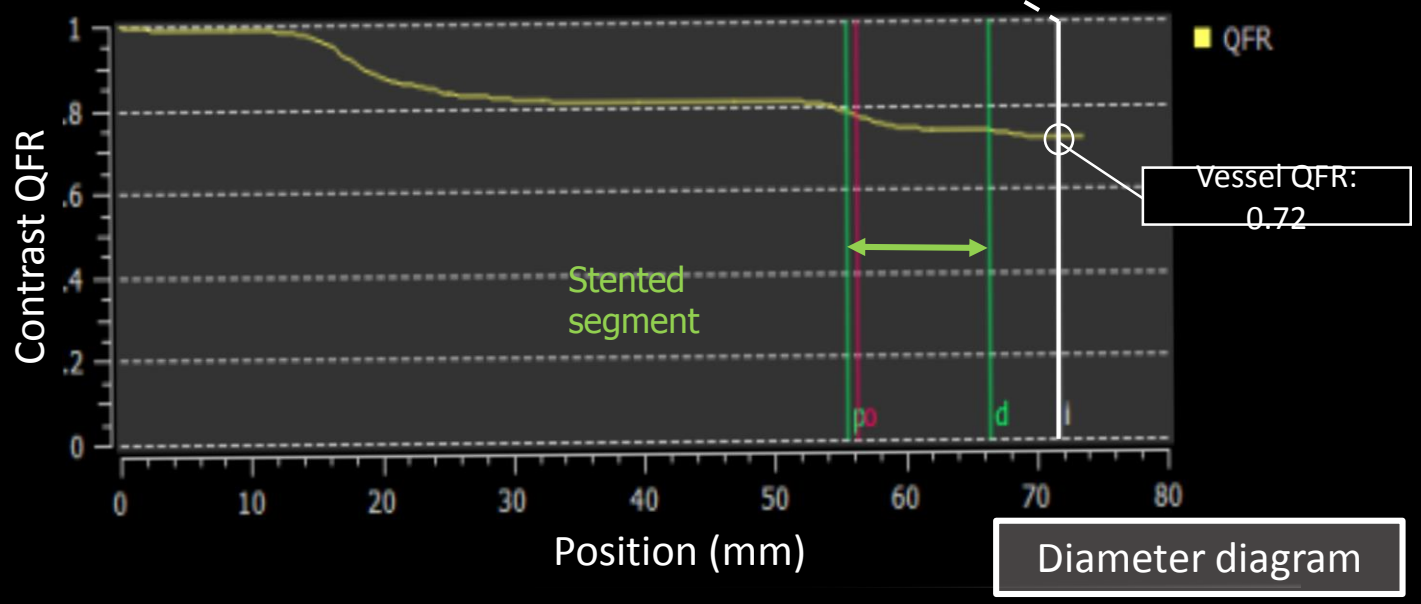
Without Inducing Hyperemia

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

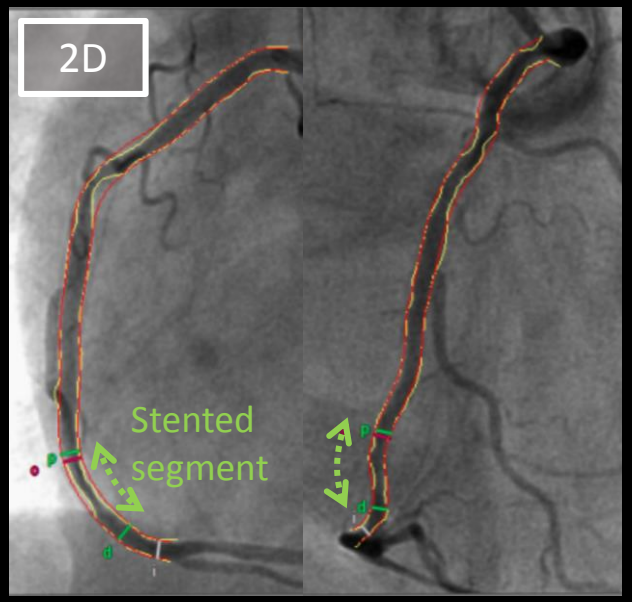
The Quantitative Flow Ratio (QFR)

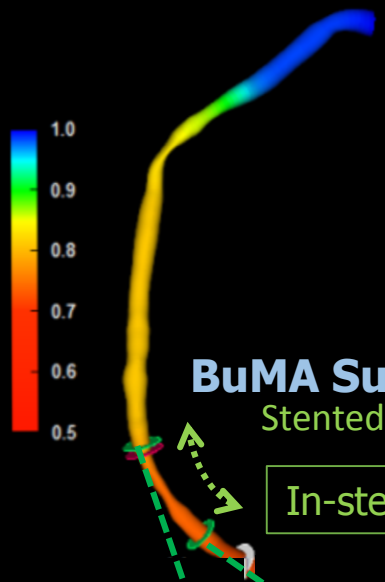






The Quantitative Flow Ratio (QFR)

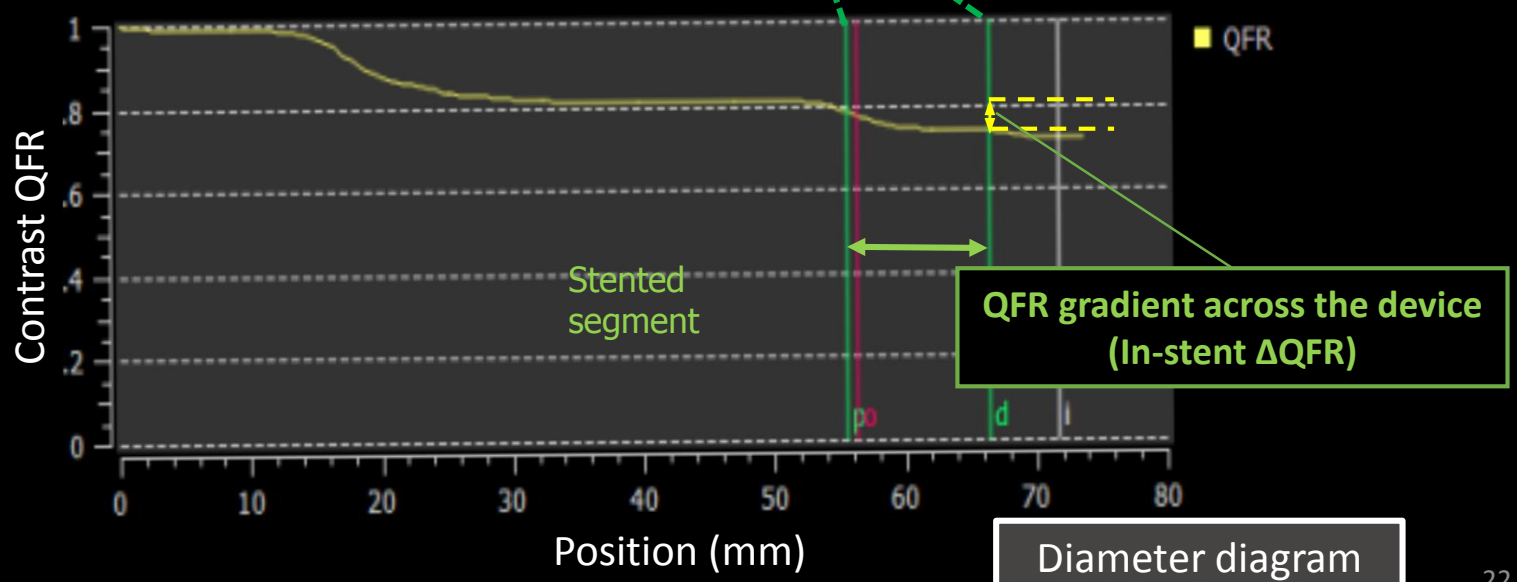




3D

BuMA Supreme
Stented segment

In-stent ΔQFR: 0.05



QFR gradient across the device (In-stent ΔQFR)

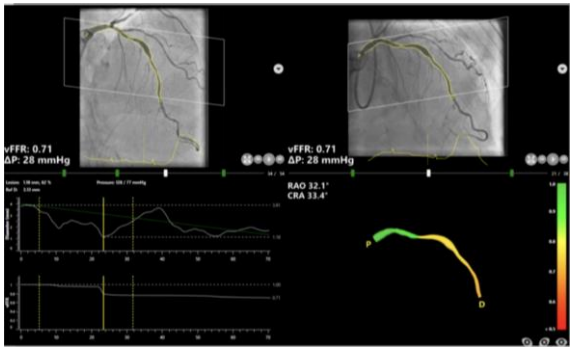
Diameter diagram

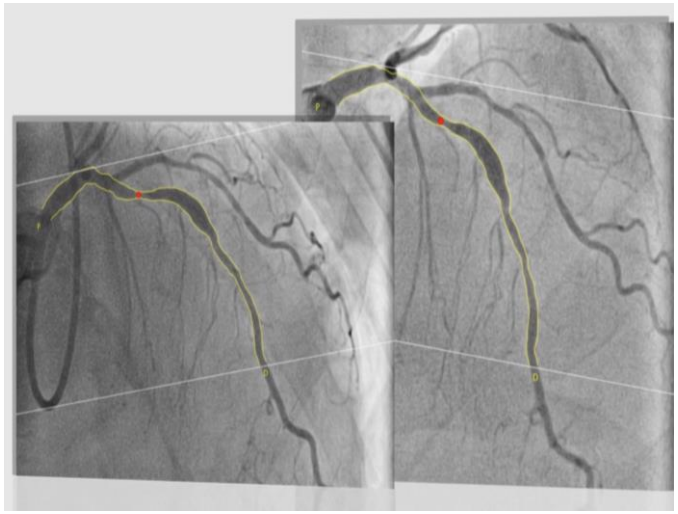
FFR angio (Cathworks)

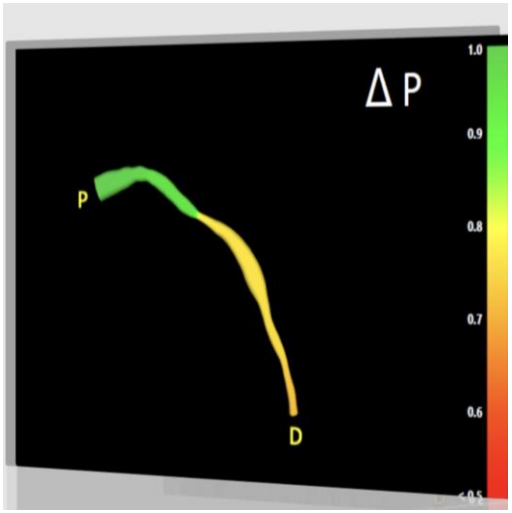
The FFR_{angio} is calculated as the ratio between the flow rate in the stenosed artery, and the flow rate in the same artery in the absence of the stenosis

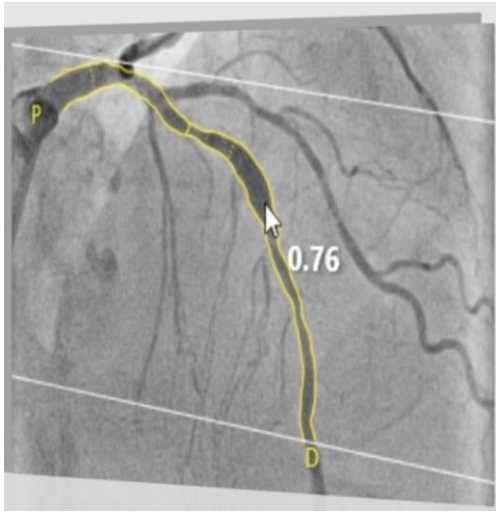
CATHWORKS™

vFFR: flow of computation









2 angiograms 30 degrees apart for 3D reconstruction

A pressure drop is calculated based on 3D reconstruction

vFFR without induced hyperemia

Angio-derived FFR in cath lab

- What is the basic principle of angio-derived FFR?
- What is the diagnostic performance of angio-derived FFR vs. wire-based FFR?
- Can we use QFR in complex lesions?
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- What is the potential clinical impact of post procedural QFR?
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ESC European Society of Cardiology

European Heart Journal (2018) **00**, 1–9
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CLINICAL RESEARCH

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

**Carlos Collet[1,2], Yoshinobu Onuma[3,4], Jeroen Sonck[2], Taku Asano[1], Bert Vandeloo[2], Ran Kornowski[5], Shengxian Tu[6], Jelmer Westra[7], Niels R. Holm[7], Xu Bo[8], Robbert J. de Winter[1], Jan G. Tijssen[1], Yosuke Miyazaki[4], Yuki Katagiri[1], Erhan Tenekecioglu[4], Rodrigo Modolo[1], Ply Chichareon[1], Bernard Cosyns[2], Daniel Schoors[2], Bram Roosens[2], Stijn Lochy[2], Jean-Francois Argacha[2], Alexandre van Rosendael[9], Jeroen Bax[9], Johan H.C. Reiber[10,11], Javier Escaned[12], Bernard De Bruyne[13], William Wijns[14], and Patrick W. Serruys[15]*

[1]Department of Cardiology, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; [2]Department of Cardiology, Universitair Ziekenhuis Brussel, Brussel, Belgium; [3]Cardialysis BV, Rotterdam, The Netherlands; [4]Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands; [5]Cardiology Department, Rabin Medical Center, Belinson Hospital Affiliated to the "Sackler" Faculty of Medicine, Tel Aviv University, Petah Tikva, Israel; [6]Biomedical Instrument Institute, School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, China; [7]Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark; [8]Fu Wai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences, Beijing, China; [9]Department of Cardiology, Leiden University Medical Center, The Netherlands; [10]Division of Image Processing (LKEB), Department of Radiology, Leiden University Medical Center (LUMC), Leiden, The Netherlands; [11]Medis Medical Imaging Systems, Leiden, The Netherlands; [12]Hospital Clinico San Carlos IDISSC and Universidad Complutense de Madrid, Madrid, Spain; [13]Cardiovascular Center Aalst, OLV Clinic, Aalst, Belgium; [14]The Lambe Institute for Translational Medicine and Curam, National University of Ireland, Galway, Saolta University Healthcare Group, Galway, Ireland; and [15]Department of Cardiology, Imperial College London, London, UK

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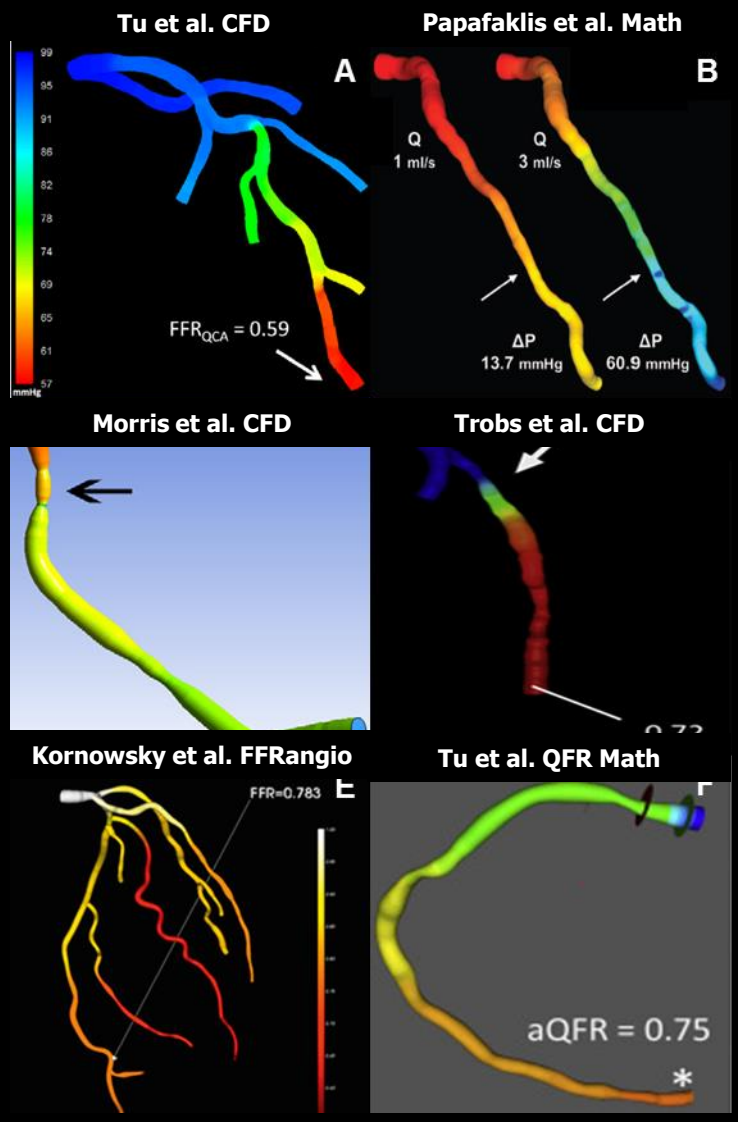
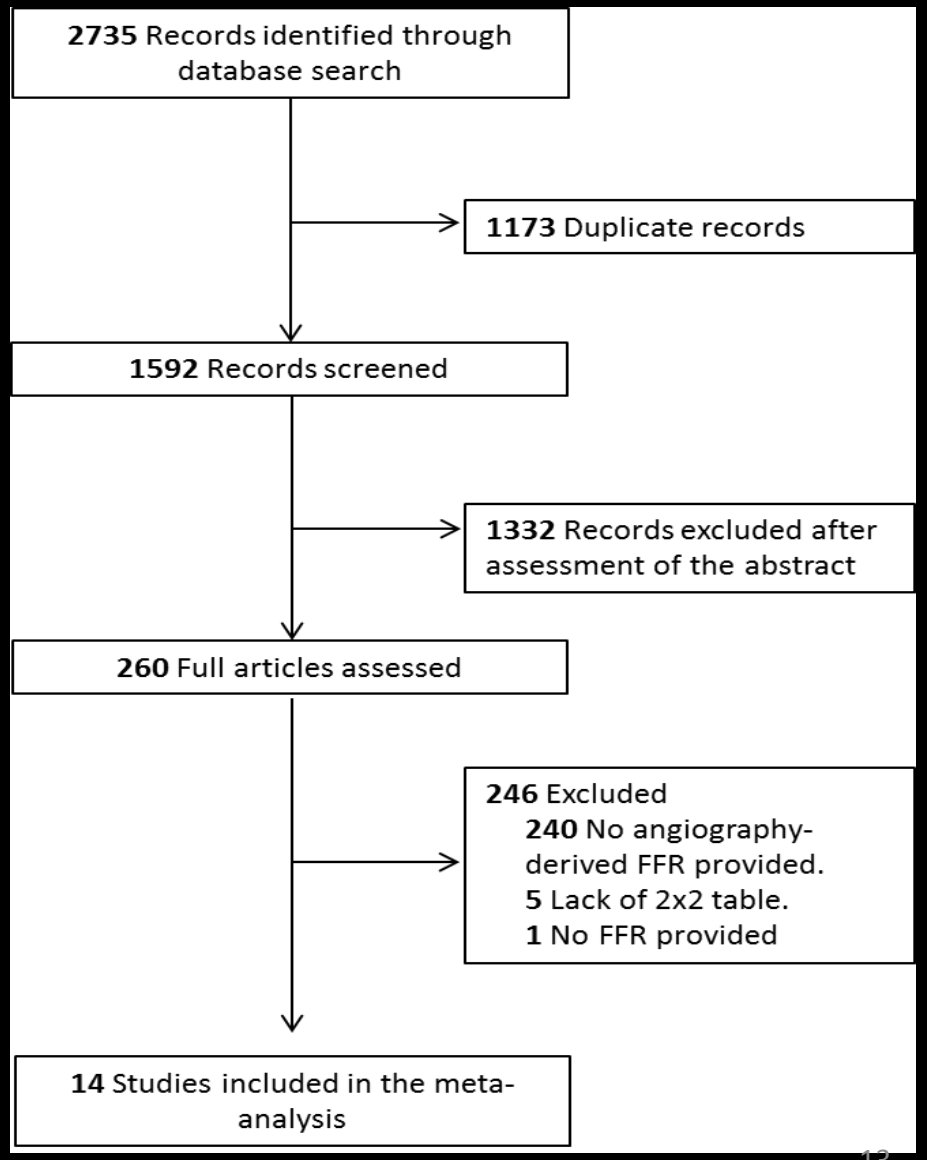
Diagnostic performance of angiography-derived FFR
a systematic review and Bayesian meta-analysis





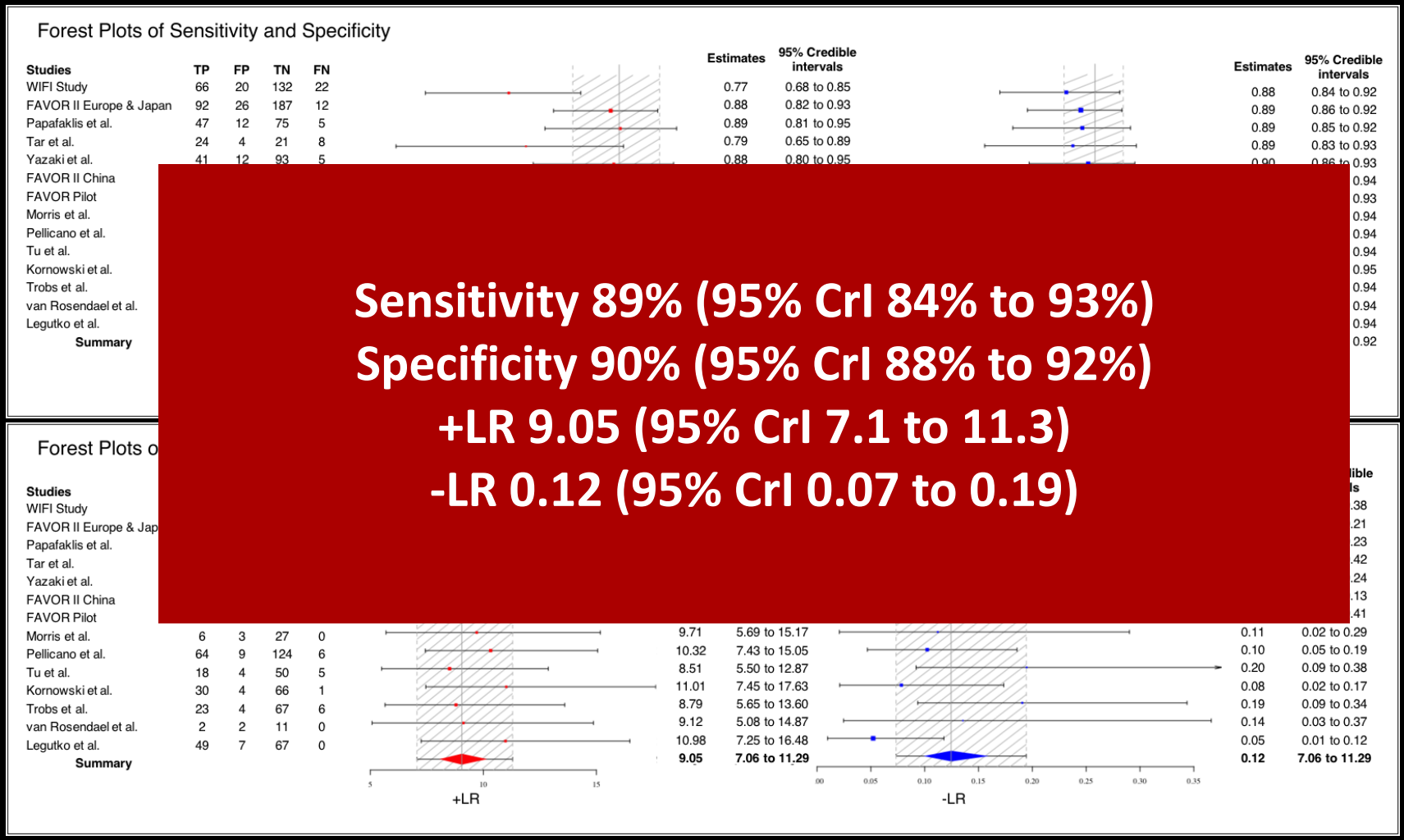
Collet et al. Eur Heart J. 2018 Sep 14;39(35):3314-3321

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

Study	Number of lesions	Technology	Process	Reference Standard	Threshold	Prevalence of ischaemia (%)
WIFI II, 2017	240	QFR	Mathematical formula	IV FFR	≤0.8	28
FAVOR II Europe and Japan, 2017	317	QFR	Mathematical formula	IV FFR	≤0.8	29
Tar *et al.*, 2017	68	MEDIS 3D-QCA	Mathematical formula	IV FFR	≤0.8	42
Yazaki *et al.*, 2017	151	QFR	Mathematical formula	IV FFR	≤0.8	27
FAVOR II China, 2017	328	QFR	Mathematical formula	IV FFR	≤0.8	32
FAVOR Pilot, 2016	84	QFR	Mathematical formula	IV FFR	≤0.8	24
Morris *et al.*, 2013	35	Virtual fractional flow reserve derived	CFD	IV FFR	≤0.8	17
Pellicano *et al.*, 2017	203	FFR_{angio}	Rapid flow analysis	IV or IC FFR	≤0.8	32
Tu *et al.*, 2014	77	FFR_{QCA}	CFD	IV FFR	≤0.8	23
Kornowski *et al.*, 2016	101	FFR_{angio}	Rapid flow analysis	IV or IC FFR	≤0.8	30
Trobs *et al.*, 2015	100	Syngo IZ3D for anatomic reconstruction	CFD	IV or IC FFR	≤0.8	23
van Rosendael *et al.*, 2017	15	QFR	Mathematical formula	IV FFR	≤0.8	13
Legutko *et al.*, 2017	123	QFR	Mathematical formula	NA	≤0.8	40

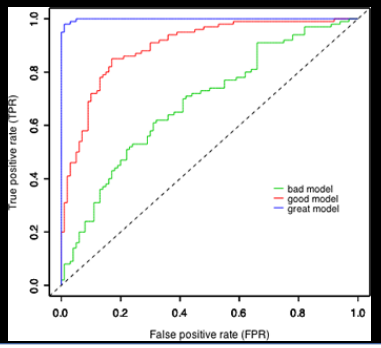
Collet et al. Eur Heart J. 2018 Sep 14;39(35):3314-3321

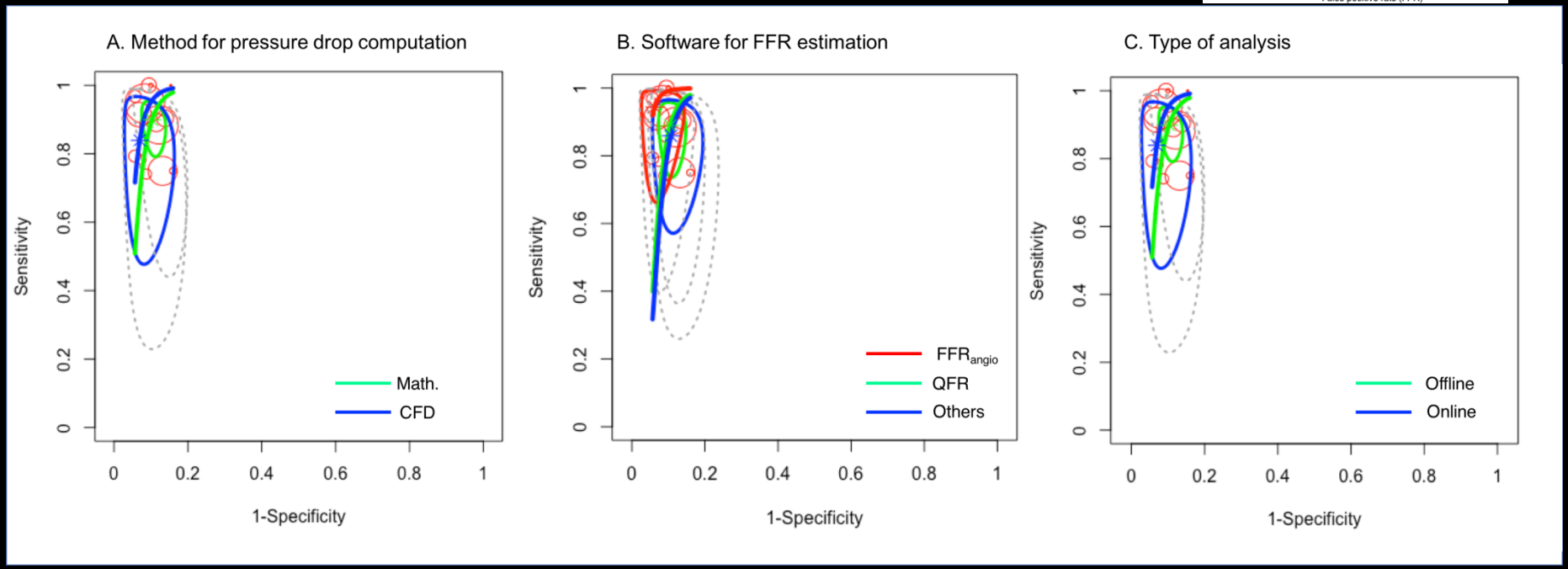
Diagnostic performance of angiography-derived FFR
a systematic review and Bayesian meta-analysis



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

Bayesian Meta-regression



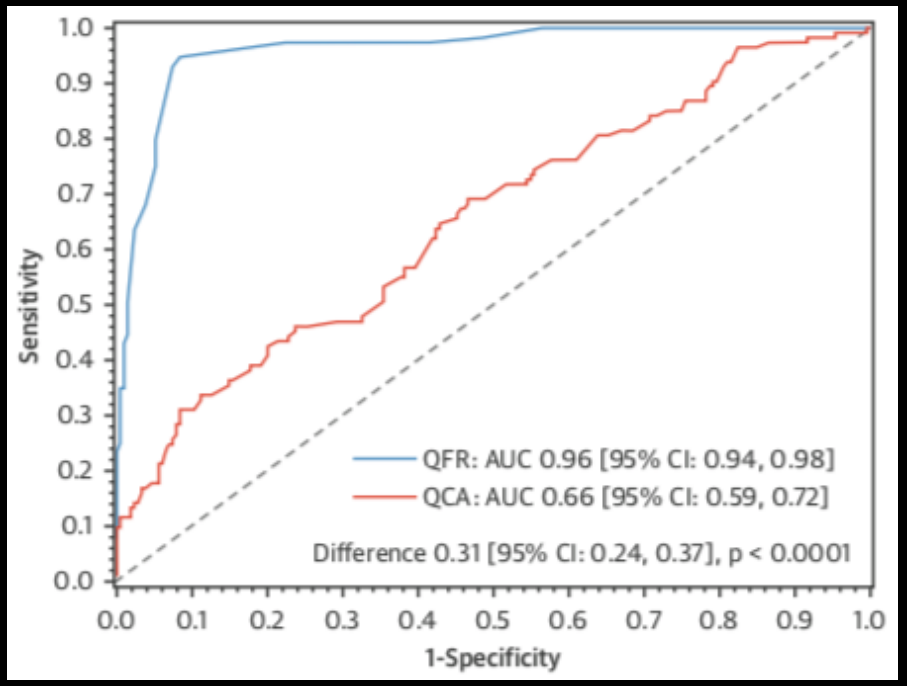


No difference in Diagnostic Performance (AUC) between type of method for pressure drop computation, Software or online/offline analysis.

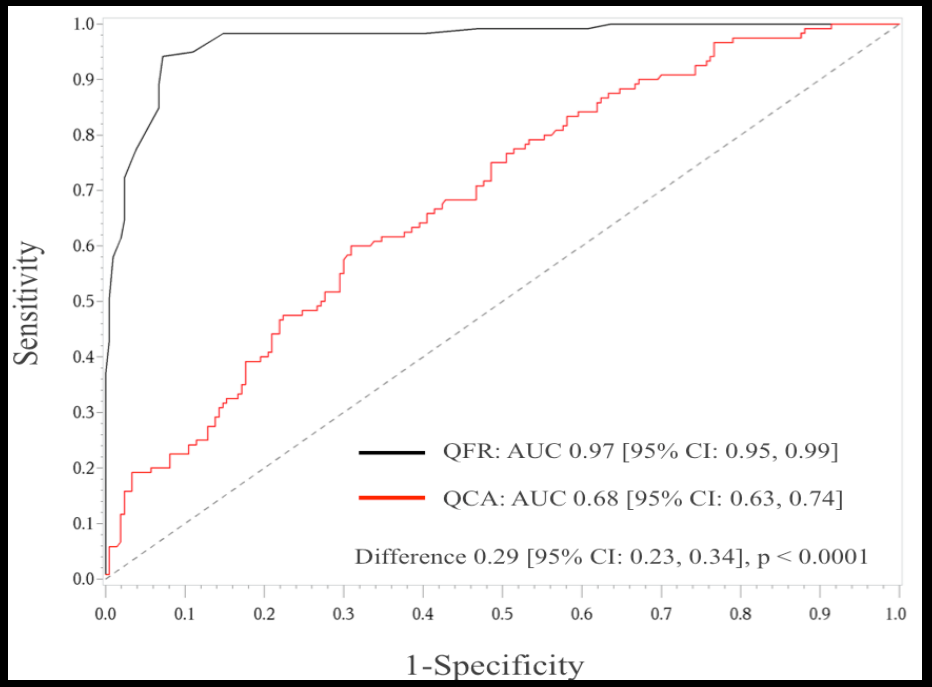
Collet et al. Eur Heart J. 2018 Sep 14;39(35):3314-3321

On-line vs Off-line QFR: Insight from FAVOR III 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

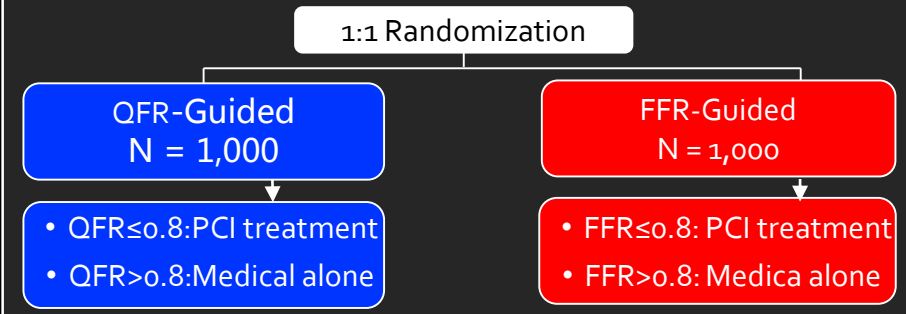
Impact of QFR on clinical outcomes is under-investigation

Pre-procedural QFR

FAVOR III –RCT-

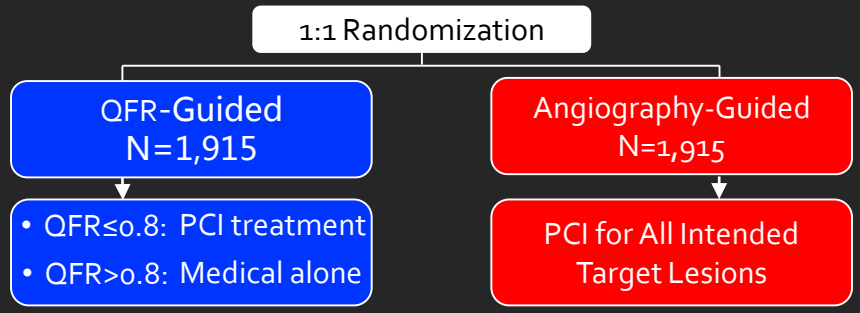
Europe-Japan

- QFR vs FFR
- Non-inferiority study



China

- QFR vs present practice
- Superiority study



- Primary endpoint: MACE at 1Y: all-cause death, MI, any ID revascularization

Secondary Endpoints: Procedure time, contrast volume, fluoroscopy time etc.

NCT03729739

Secondary Endpoints: Cost-effectiveness at 1Y etc.

NCT03656848

Angio-derived FFR in cath lab

- What is the basic principle of angio-derived FFR?
- What is the diagnostic performance of angio-derived FFR vs. wire-based FFR?
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- Can we use angio-derived FFR to PCI planning (Simulation of post procedural FFR, tandem lesion, number of stent, and stent length)?
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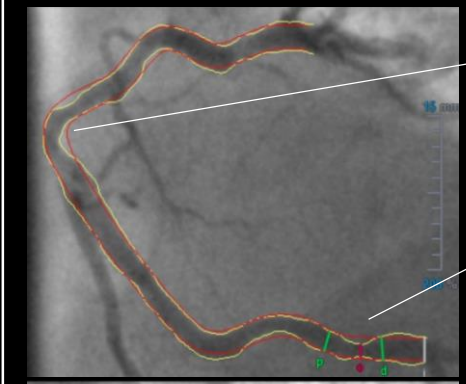
Case example of functional SYNTAX score calculation by QFR

SYNTAX II

Anatomic SYNTAX Score 27

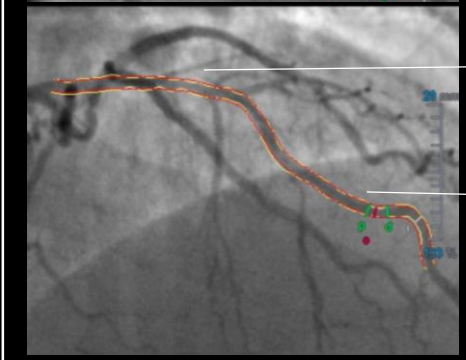
RCA



2.0 points

2.0 points

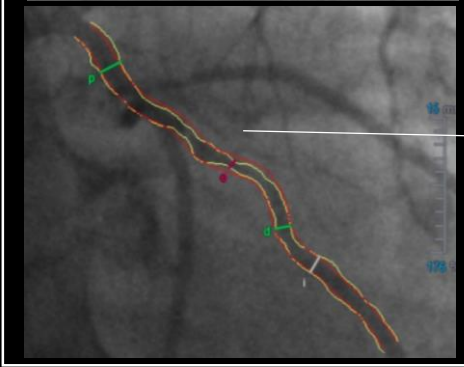
LAD



12.0 points

2.0 points

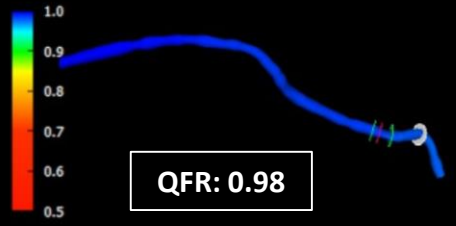
LCX



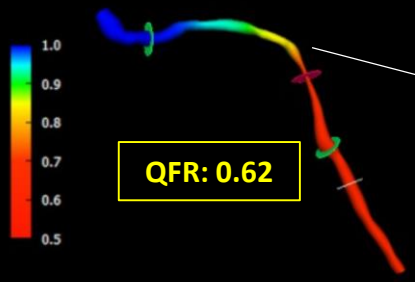
9.0 points

Functional SYNTAX Score 9

0 points



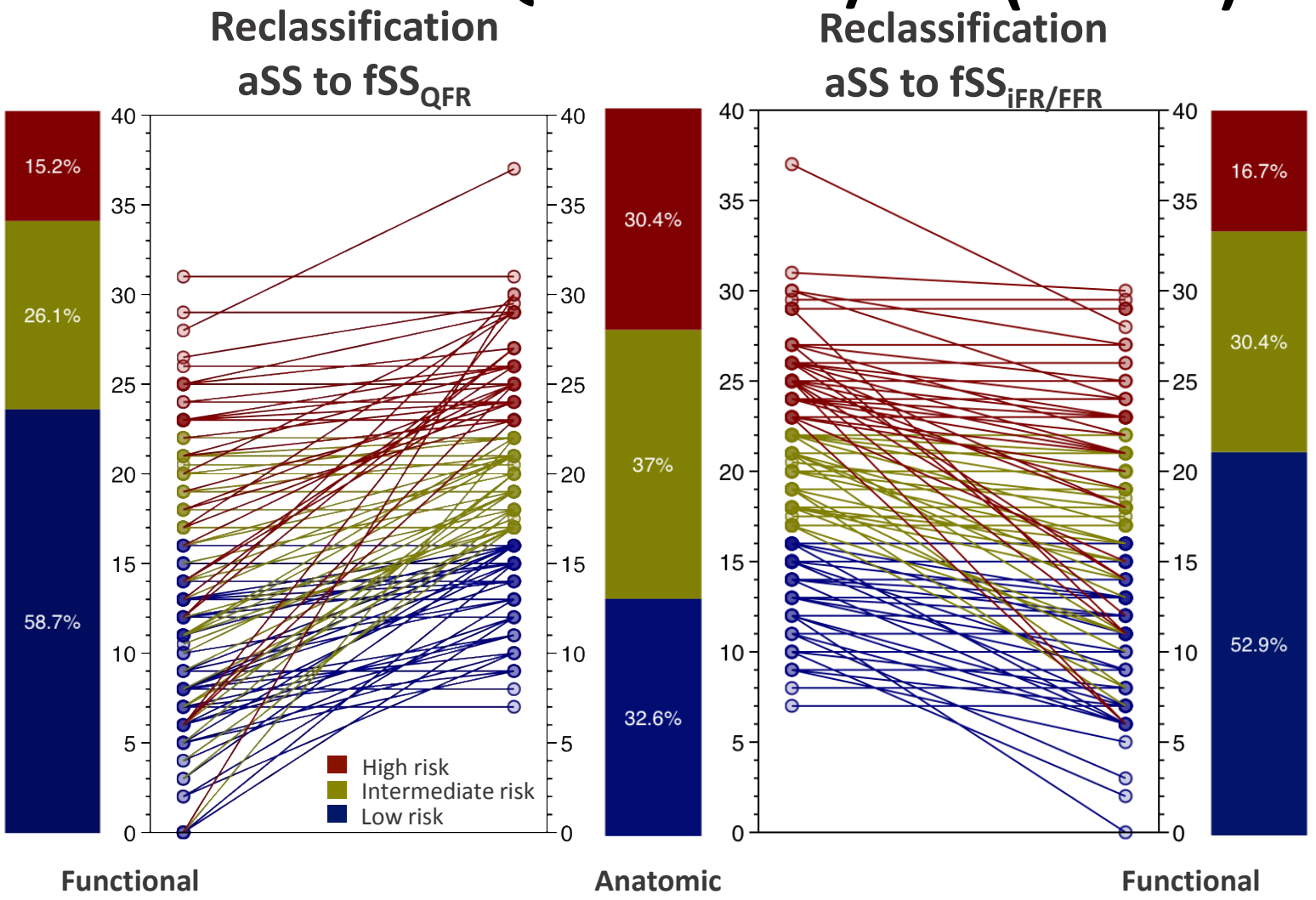
0 points



9.0 points

Asano T, OnumaY, Serruys PW et al. JACC Cardiovasc Interv. 2019 Feb 11;12(3):259-270.

Reclassification of functional SYNTAX score derived from QFR and iFR/FFR (N=138)



Functional SYNTAX score derived from QFR yielded significantly improved risk classification compared to anatomic SYNTAX Score.

Asano T, OnumaY, Serruys PW et al. JACC Cardiovasc Interv. 2019 Feb 11;12(3):259-270.

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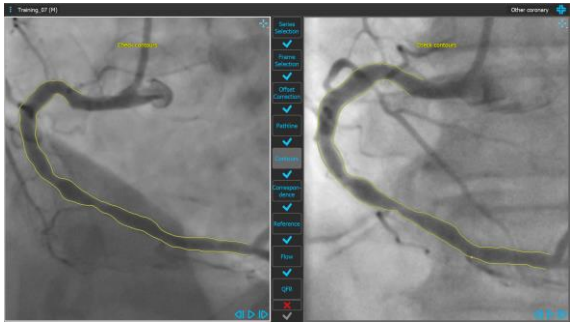
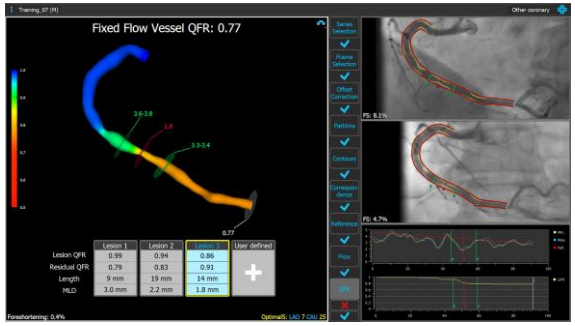
QFR version 2.0 (work in progress)

- Full screen user interface
- Easy and visible workflow
- Automatic end-diastolic detection from ECG
- Reduction of all redundant information on and around the images
- Reduction of mouse miles





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Impact of QFR on clinical outcomes is under-investigation

Post-procedural QFR

HAWKEYE NCT02811796

-prospective observational study-

Aim: To assess the relationship between post-QFR and adverse events

600 patients

Successful PCI with post procedural QFR assessment (off-line)

Primary endpoint: DOCE at 1Y: cardiac death, TV-MI, TLR

Primary result will be presented at euroPCR2019

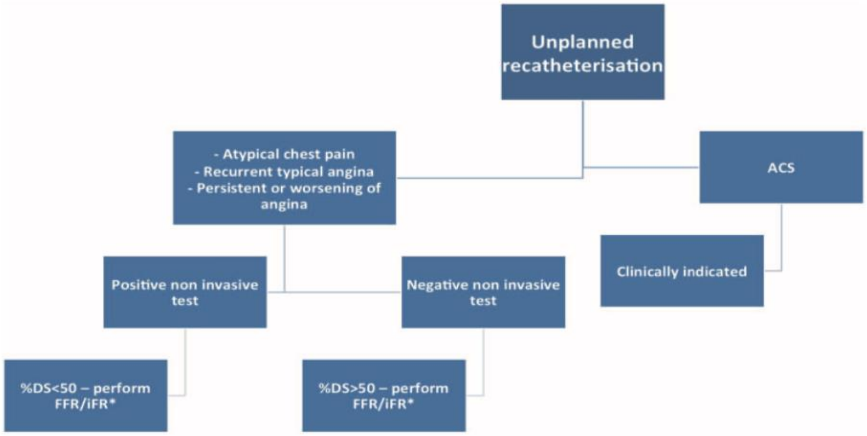
QFR for Event Adjudication of Clinically Indicated Repeat Revascularization

The Academic Research Consortium-2 Consensus Document (ARC-2)

Table 7 Fractional Flow Reserve and Quantitative Coronary Analysis for Event Adjudication of Clinically Indicated Repeat Revascularizations

Hierarchically

1. Core laboratory–reported fractional flow reserve ≤0.80 or instant wave-free ratio ≤0.89
2. Site-reported fractional flow reserve ≤0.80 or instant wave-free ratio ≤0.89
3. Quantitative coronary analysis* diameter stenosis >50% (based on the average of multiple views) with either recurrent symptoms or positive noninvasive functional test
4. Quantitative coronary analysis* diameter stenosis >70% (based on the average of multiple views) regardless of other criteria
5. Quantitative coronary analysis diameter stenosis >70% (based on the worst view) regardless of other criteria



*If FFR/iFR result is lower than the proposed threshold, revascularization will be adjudicated as clinically indicated

ARC-2 gives priority to functional assessment with <u>FFR or equivalent technique.</u>

ARC-2 recommends that resting dp/da, contrast/saline FFR, **<u>QFR</u>**, and FFR_{CT}, although not yet widely available, can be used for adjudication purposes if specified in the protocol.

Garcia-Garcia HM, Onuma Y, Serruys PW et al. Eur Heart J 2018 Jun 14;39(23):2192-2207.

Conclusion

- ✓ Commercially available online-QFR and on-site-FFR_{angio} demonstrated feasibility and similar diagnostic accuracy compared to wire-based FFR in the prospective observational trials. Meta-analysis demonstrated that angio-derived FFR is reliable surrogate for invasive wire-based FFR irrespective of computational approaches and software packages.

- ✓ Assessment of functional SYNTAX score by QFR was feasible in selected 3VD cases. With a new version of software, simulation of post-stenting QFR is feasible, which could further guide planning of PCI (stent length, number of stent etc).

- ✓ In context of clinical trial, angio-derived FFR could be used to evaluate efficacy of coronary device. According to ARC-2, in the context of clinical trial, QFR could be utilized to adjudicate ischemia driven revascularization.

- ✓ Impact of both pre- and post-procedural QFR on clinical outcomes is under-investigation in prospective randomized trials. If clinical noninferiority to wire based FFR and/or superiority to angio-guided approach is established, angio-derived FFR could become standard approach.

- ✓ Angio-derived FFR will change our practice in cath lab.