Diagnostic Accuracy of A Fast Computational Approach to Derive Fractional Flow Reserve from Coronary X-Ray Angiography: Results from the International Multicenter FAVOR (Functional Assessment by Various FlOw Reconstructions) Pilot Study

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Speaker's name:

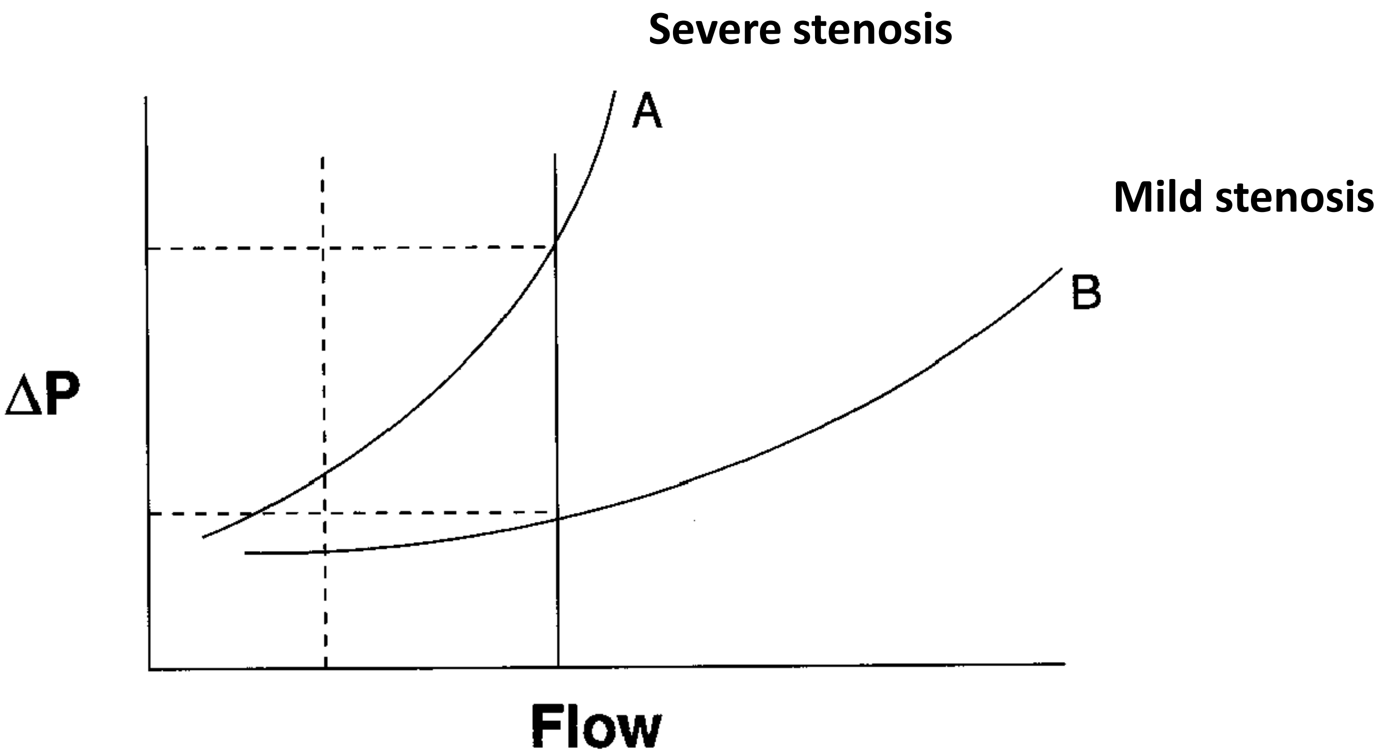
- ❑ **I have the following potential conflicts of interest to report:**

  Institutional grant/research support: Medis medical imaging systems bv

Background

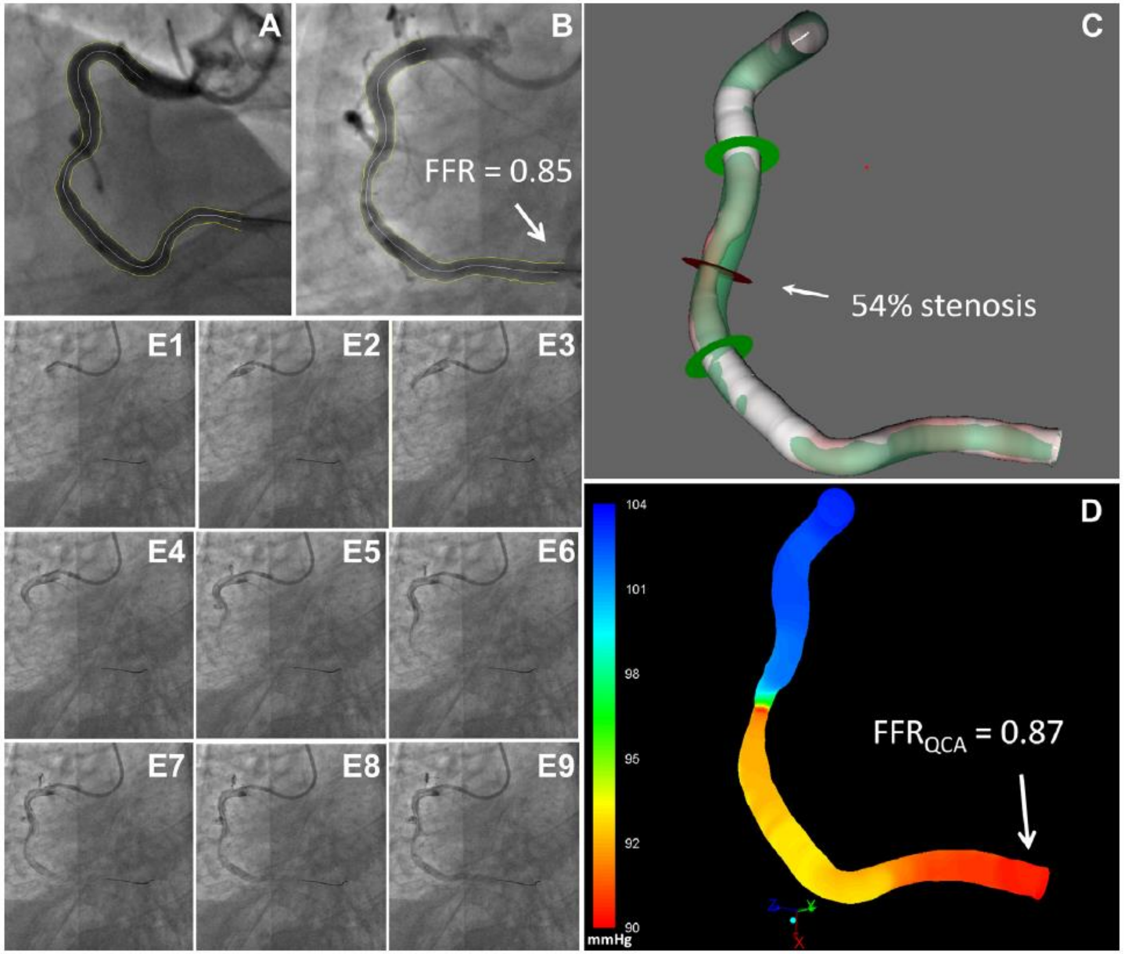
The pressure gradient across a stenosis is related to the flow

Pressure-based FFR is determined by both the stenosis geometry and the flow modulated by the downstream perfusion!



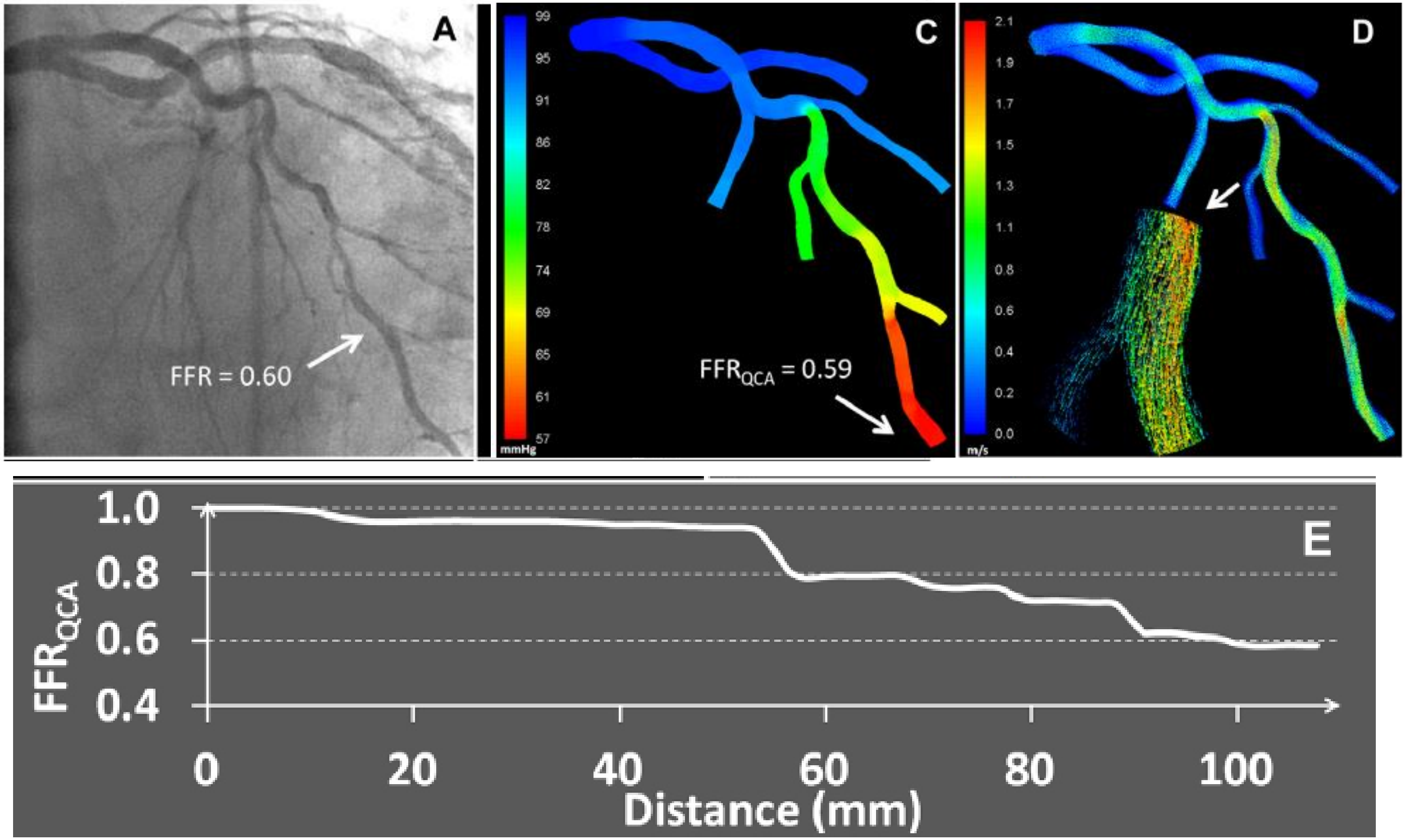
Kern MJ. Circulation 2000; 101:1344-51

Background



Tu et al. JACC Cardiovasc Interv 2014, 7:768-777

Background



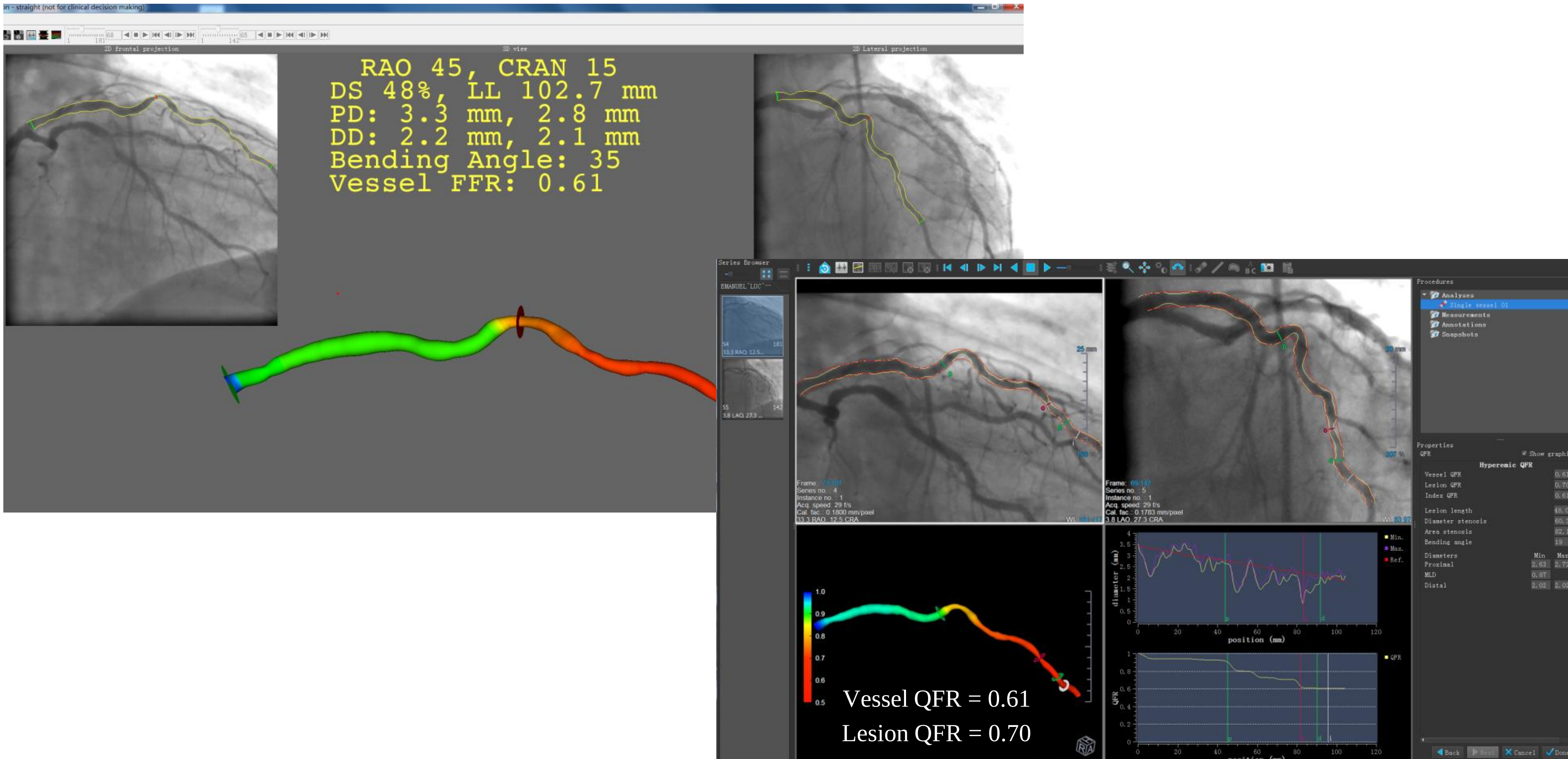
Pressure drop in the main vessel will be substantially overestimated if the side branches are not reconstructed, especially in hyperemic condition!

Tu et al. JACC Cardiovasc Interv 2014, 7:768-777.

Li et al. JACC 2015;66:125-35.

Background

Quantitative flow ratio (QFR) is a novel method for rapid computation of FFR from X-ray coronary angiography.



The validated QFR algorithms transferred from prototype to alpha version of QAngio XA 3D (February 2016)

Background

Quantitative flow ratio (QFR) is a novel method for rapid computation of FFR from X-ray coronary angiography.

QFR can be derived from 3 flow models with:

- fixed-flow QFR (fQFR) → empiric hyperemic flow
- contrast-flow QFR (cQFR) → modeled hyperemic flow
- adenosine-flow QFR (aQFR) → measured hyperemic flow

The aim of this study was to identify the optimal approach for simple and fast QFR computation.

cQFR ≠ rest Pd/Pa

cQFR ≠ contrast Pd/Pa

Study Design

- Observational multicenter study;
- Feasibility and accuracy of 3 different QFR computational methods;
- Pressure wire FFR measured at maximal stable hyperemia as the standard reference;
- Blinded QFR core laboratory;
- Separated and blinded FFR core laboratory.

Study Organization

Principle investigators

- William Wijns, MD, PhD, FESC, Principal investigator
- Shengxian Tu, PhD, FESC, Principal investigator

Co-principal Investigator: Johan H.C. Reiber, PhD, FESC, FACC

Participating centers

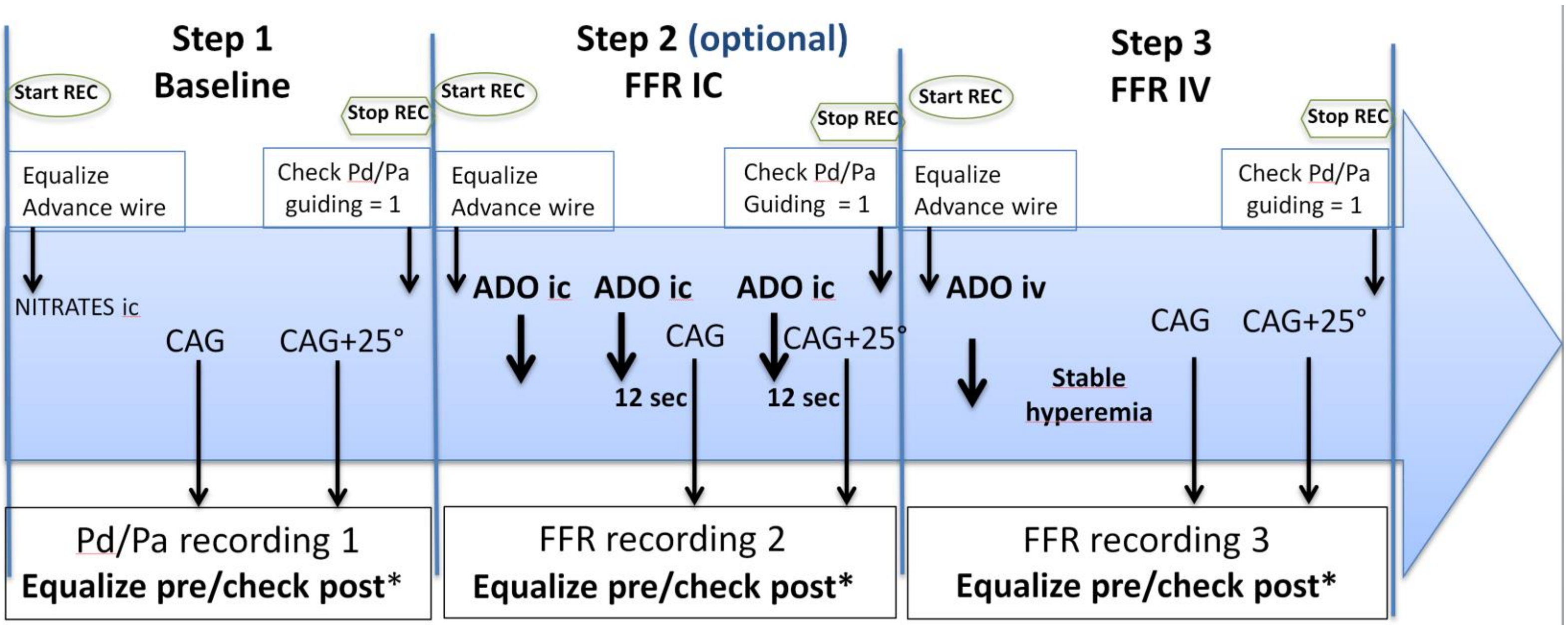
1. Cardiovascular Research Center Aalst, OLV Hospital, Belgium; William Wijns, MD, PhD
2. Department of Cardiology, Guangdong General Hospital, Guangzhou, China; Junqing Yang, MD
3. Department of Cardiology, Yale Medical School, New Haven, Connecticut, USA; Alexandra Lansky, MD
4. Division of Cardiology, Federico II University, Naples, Italy; Emanuele Barbato, MD, PhD
5. Cardiovascular Institute, Azienda Ospedaliero-Universitaria di Ferrara, Ferrara, Italy; Gianluca Campo, MD
6. Department of Cardiology, MST, Enschede, the Netherlands; Clemens von Birgelen, MD, PhD
7. Department of Cardiology, Univ Clinic Giessen & Marburg, Giessen, Germany; Holger Nef, MD
8. Department of Cardiology, Kyushu Medical Center, Fukuoka, Japan; Yoshinobu Murasato, MD, PhD

Core laboratories

- FFR: Interventional Coronary Imaging Core Laboratories, Aarhus University Hospital, Skejby, Denmark
- QCA and QFR: ClinFact, Leiden, the Netherlands

Funding: This was a non-funded investigator-initiated study. Expenses associated with study enrolment and procedures were covered by the participating centers.

Study Protocol

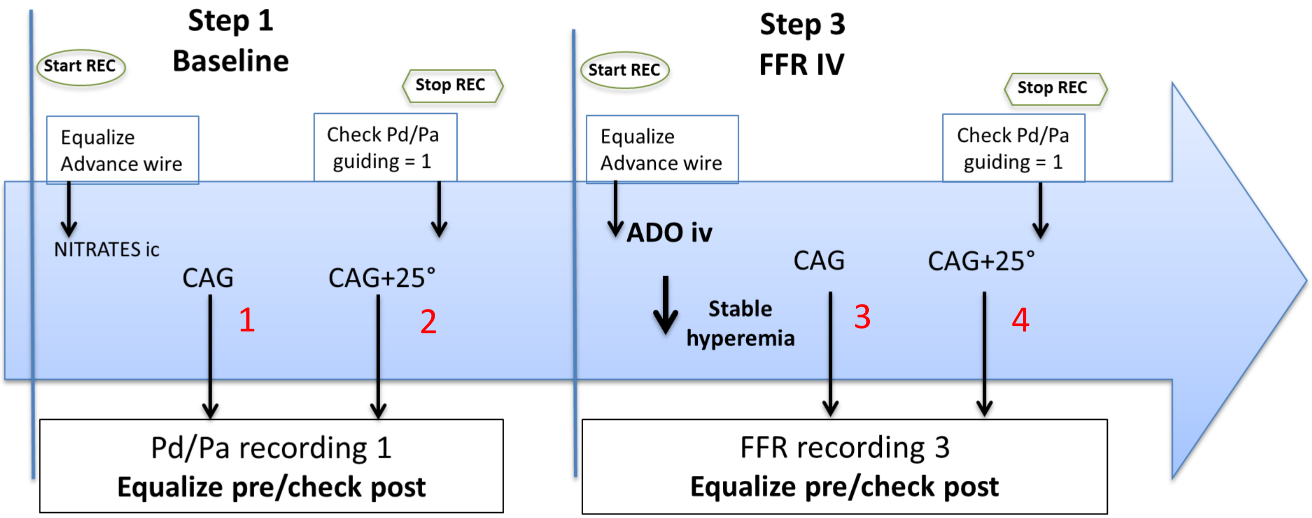


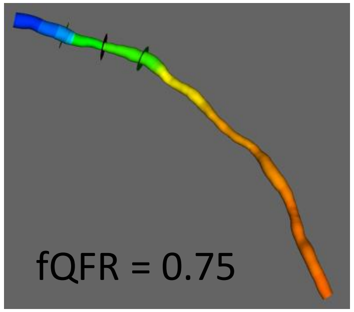
Pressure drift check

***Check Pd/Pa guiding = 1**

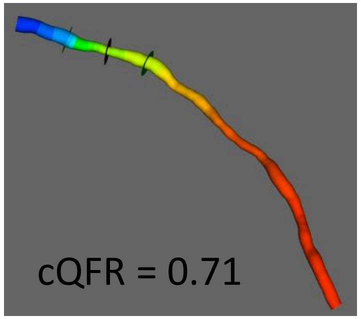
- When FFR <0.75 or > 0.85
  If Pd/Pa <0.95 or >1.05: **equalize and repeat step**
- When FFR between 0.75-0.85
  If Pd/Pa <0.98 or >1.02 : **equalize and repeat step**

QFR Analysis (core lab)

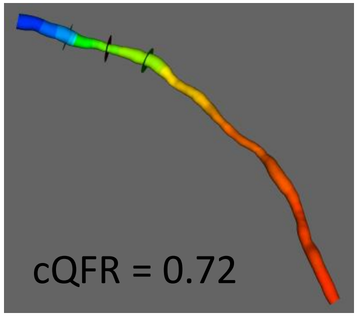




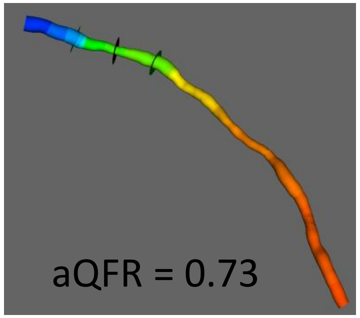
flow 0.35 m/s



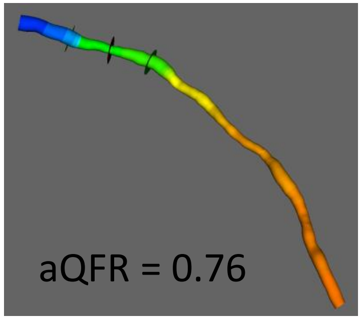
based on CAG 1



based on CAG 2



based on CAG 3



based on CAG 4

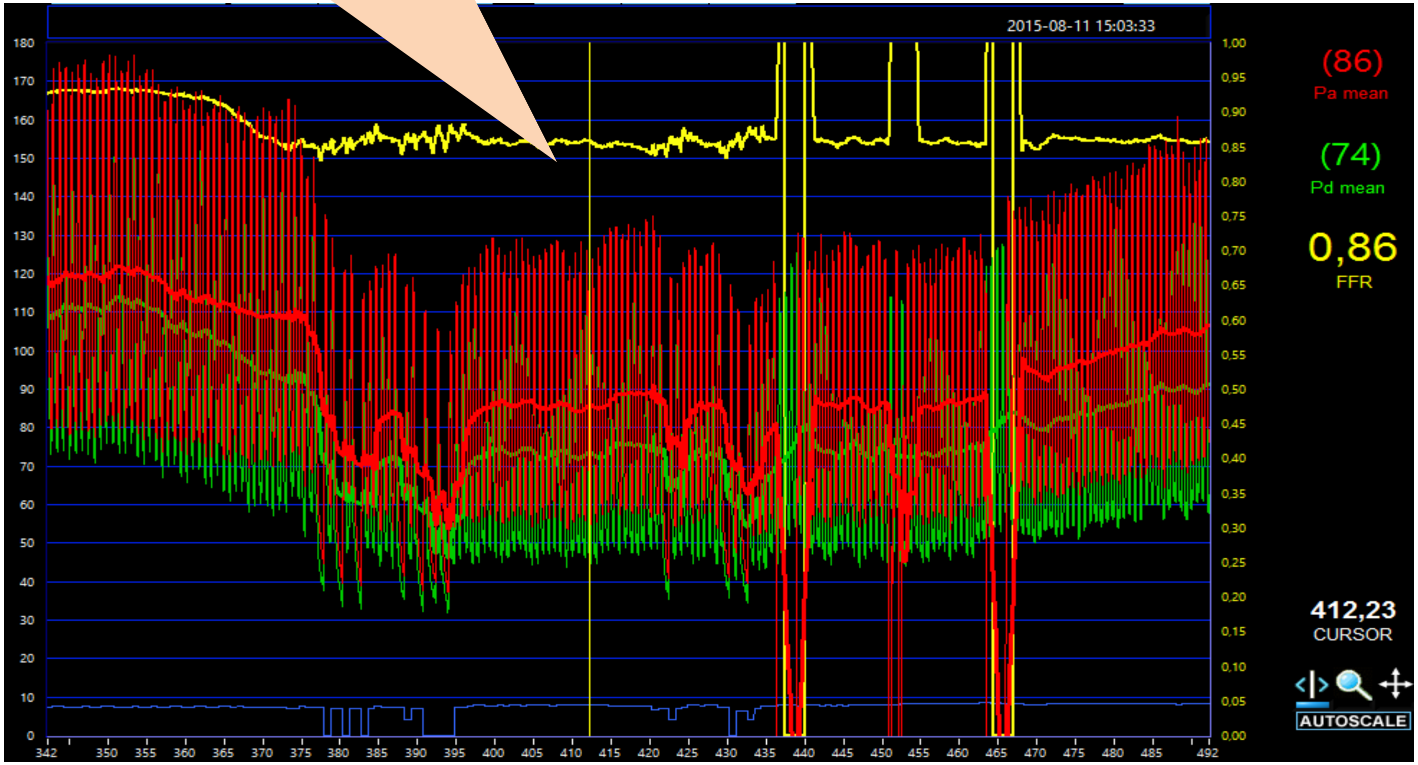
fQFR = 0.75

cQFR = 0.72

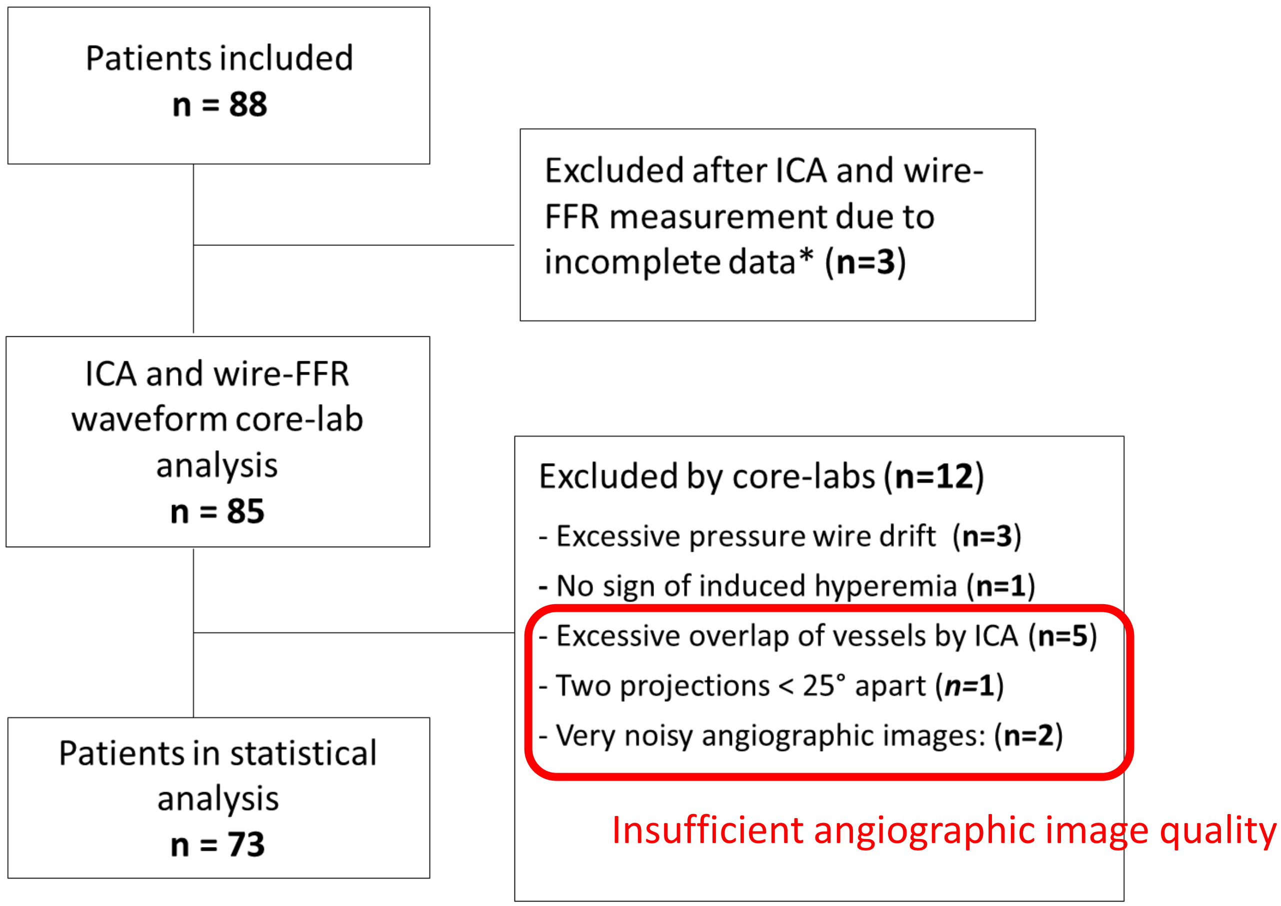
aQFR = 0.73

FFR Analysis (core lab)

maximal stable hyperemia



Study Flow Chart



*Pressure wire-based FFR traces were missing for the cases that were not analyzed by the ICA/FFR core-labs.

Baseline Characteristics

Patient characteristics

	n = 73
Age, yrs	65.8±8.9
Male	61 (83.5)
Body mass index	26.3±6.3
Hypertension	32 (43.8)
Diabetes mellitus	17 (27.4)
Cardiovascular history	
Prior MI	23 (31.5)
Prior PCI	28 (38.4)
Prior CABG	2 (2.7)

Vessel and procedural related

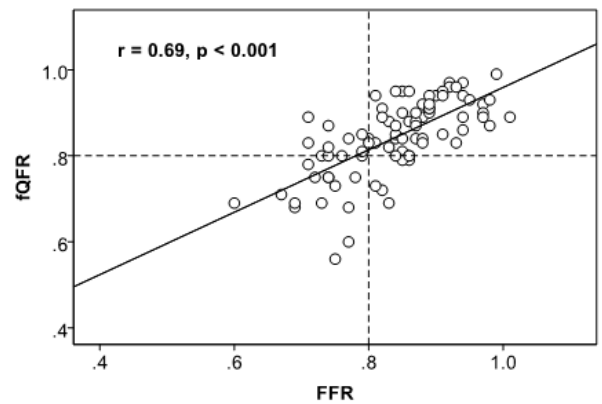
	n = 84
Lesion location	
Left main stem	1 (1.2)
Left anterior descending artery	46 (54.8)
Diagonal branch	1 (1.2)
Left circumflex artery	12 (14.3)
Obtuse marginal branch	5 (6.0)
Right coronary artery	19 (22.6)
Fractional flow reserve	
Mean ± SD	0.84±0.08
Median [IQR]	0.85 [0.77, 0.89]
Minimum lumen area, mm^2	1.94 [1.41, 2.62]
Percent area stenosis, %	64.5±4.5
Reference diameter, mm	2.84 [2.57, 3.06]

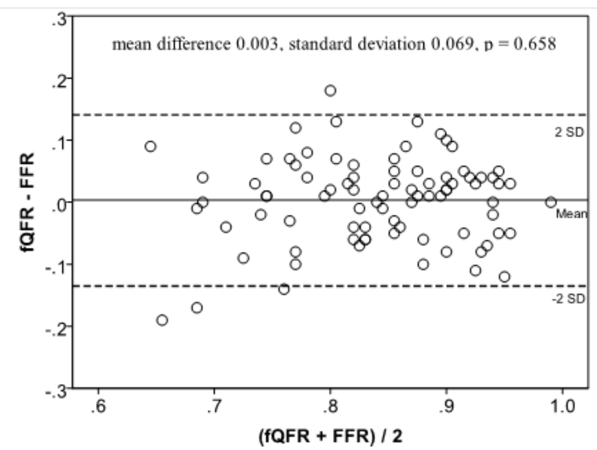
Homogeneity of intermediate lesions

Values are n (%), mean±SD, or median [IQR].

Correlation and Agreement

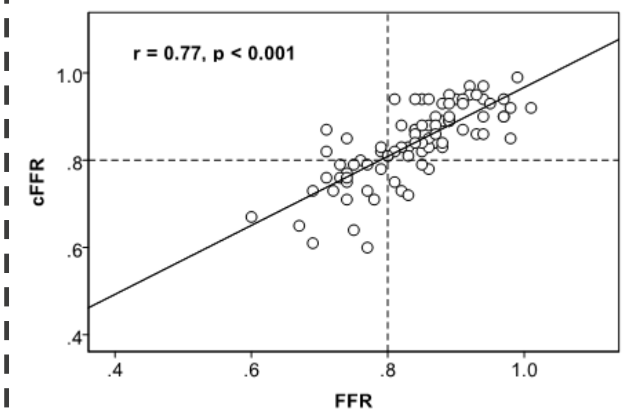
Fixed-flow

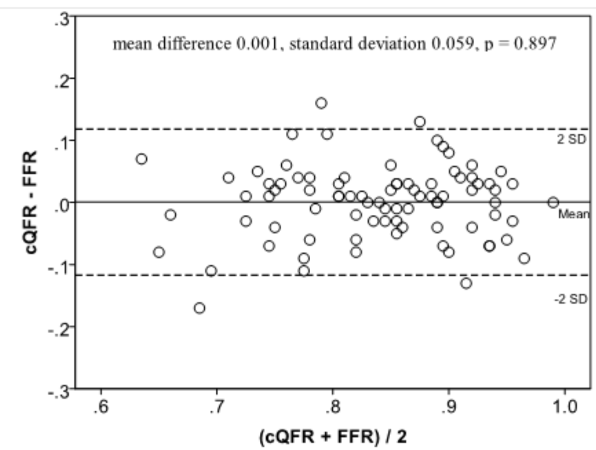




Difference: 0.003 ± 0.069

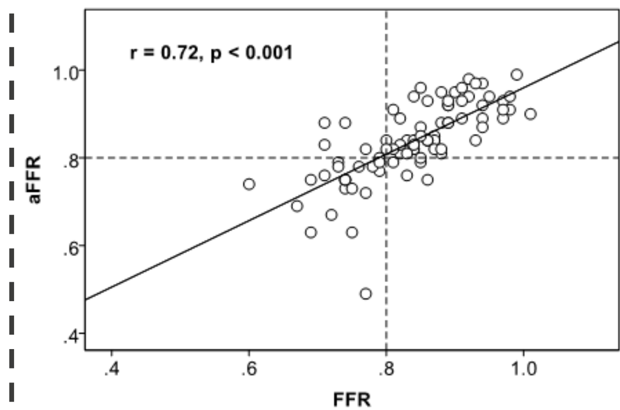
Contrast-flow

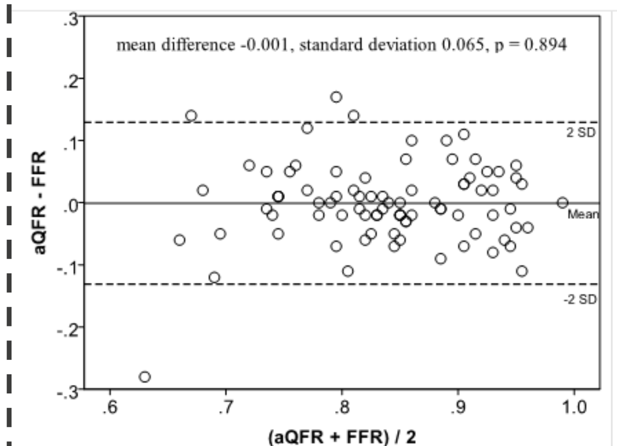




0.001 ± 0.059

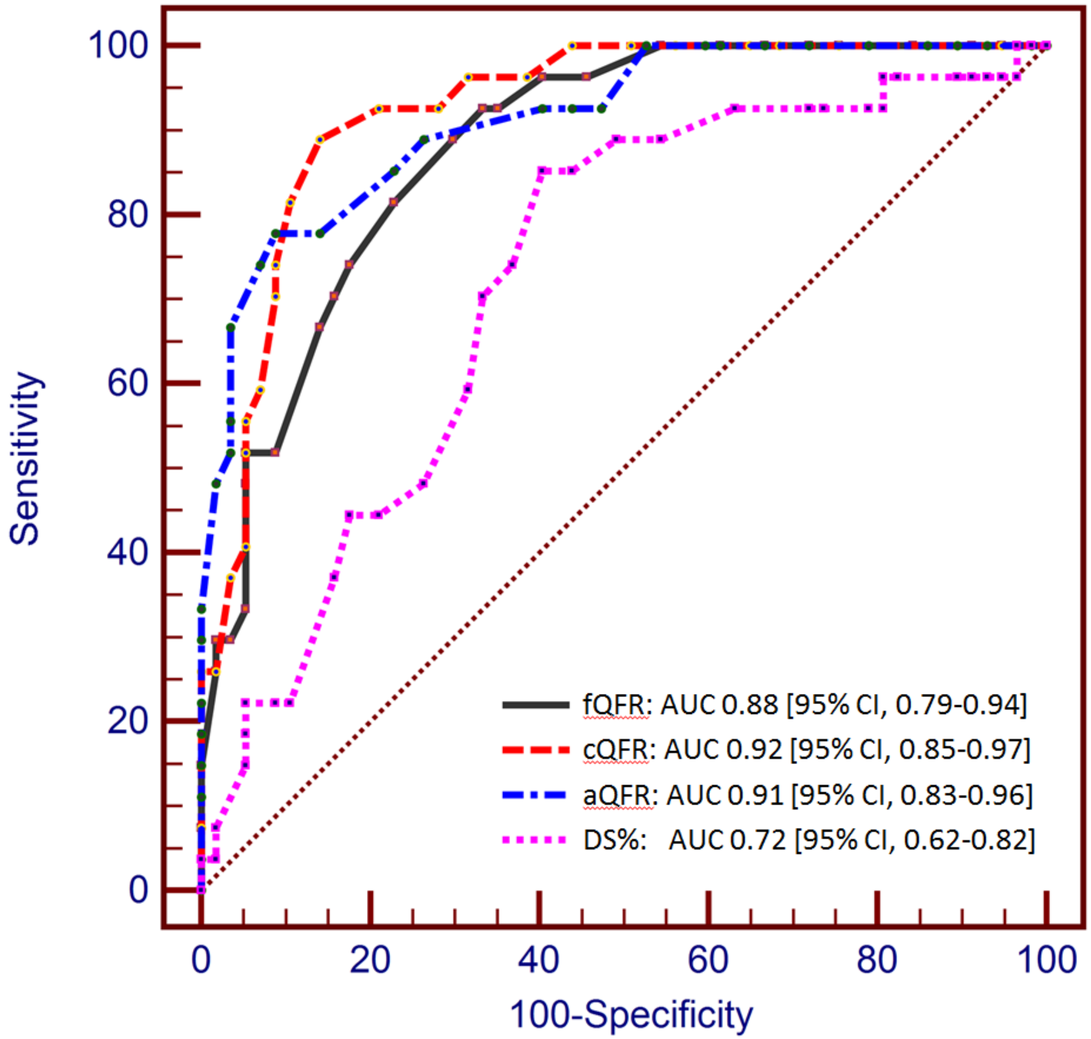
Adenosine-flow





-0.001 ± 0.065

Diagnostic Performance



Increase in AUC

fQFR – DS%: 0.16 ($p = 0.003$)

cQFR – DS%: 0.20 ($p < 0.001$)

aQFR – DS%: 0.19 ($p < 0.001$)

cQFR – fQFR: 0.04 ($p = 0.006$)

cQFR – aQFR: 0.01 ($p = 0.646$)

Diagnostic Performance

Clinical population requiring FFR.
Consistent with previous studies[1,2,3]

	fQFR ≤ 0.8	cQFR ≤ 0.8	aQFR ≤ 0.8	S% ≥ 50%
Accuracy	80 (71-89)	86 (78-93)	87 (80-94)	65 (55-76)
Sensitivity	67 (46-84)	74 (54-89)	78 (58-91)	44 (26-65)
Specificity	86 (74-94)	91 (81-97)	91 (81-97)	79 (66-89)
PPV	69 (48-86)	80 (59-93)	81 (61-93)	50 (29-71)
NPV	85 (73-93)	88 (77-95)	90 (79-96)	75 (62-85)
LR+	4.8 (2.4-9.5)	8.4 (3.6-20.1)	8.9 (3.7-21.0)	2.1(1.1-4.1)
LR-	0.4 (0.2-0.7)	0.3 (0.1-0.5)	0.2 (0.1-0.5)	0.7 (0.5-1.0)
AUC	0.88 (0.79-0.94)	0.92 (0.85-0.97)	0.91 (0.83-0.96)	0.72 (0.62-0.82)

Good diagnostic accuracy

1. Toth et al. Eur Heart J 2014; 35:2831-8.
2. Tu et al. JACC Cardiovasc Interv 2014, 7:768-77.
3. Tu et al. JACC Cardiovasc Interv 2015, 8:564-74.

Projection-related Variation

Contrast-flow QFR

- In 5 (6%) vessels, frame count analysis was performed in 1 projection only, due to poor visualization of dye flow in the other projection.
- Difference of two cQFR computations: 0.003 ± 0.030 ($p=0.31$).

Adenosine-flow QFR

- In 11 (13%) vessels, frame count analysis was performed in 1 projection only, due to poor visualization of dye flow in the other projection.
- Difference of two aQFR computations: 0.005 ± 0.026 ($p=0.12$).

Conclusions

- Fast computation of FFR from coronary angiography (QFR), acquired with or without pharmacological hyperemia-induction, is feasible.
- Contrast-flow QFR (cQFR) based on conventional diagnostic coronary angiography provides results similar to QFR based on hyperemic conditions, and is superior to fixed-flow QFR.
- The favorable results of cQFR bears the potential of a wider adoption of FFR-based lesion assessment, as cQFR might reduce procedure time, risk, and costs (no need to use pressure wire, and no need to induce maximal hyperemia) .