Quantitative Flow Ratio (QFR®)

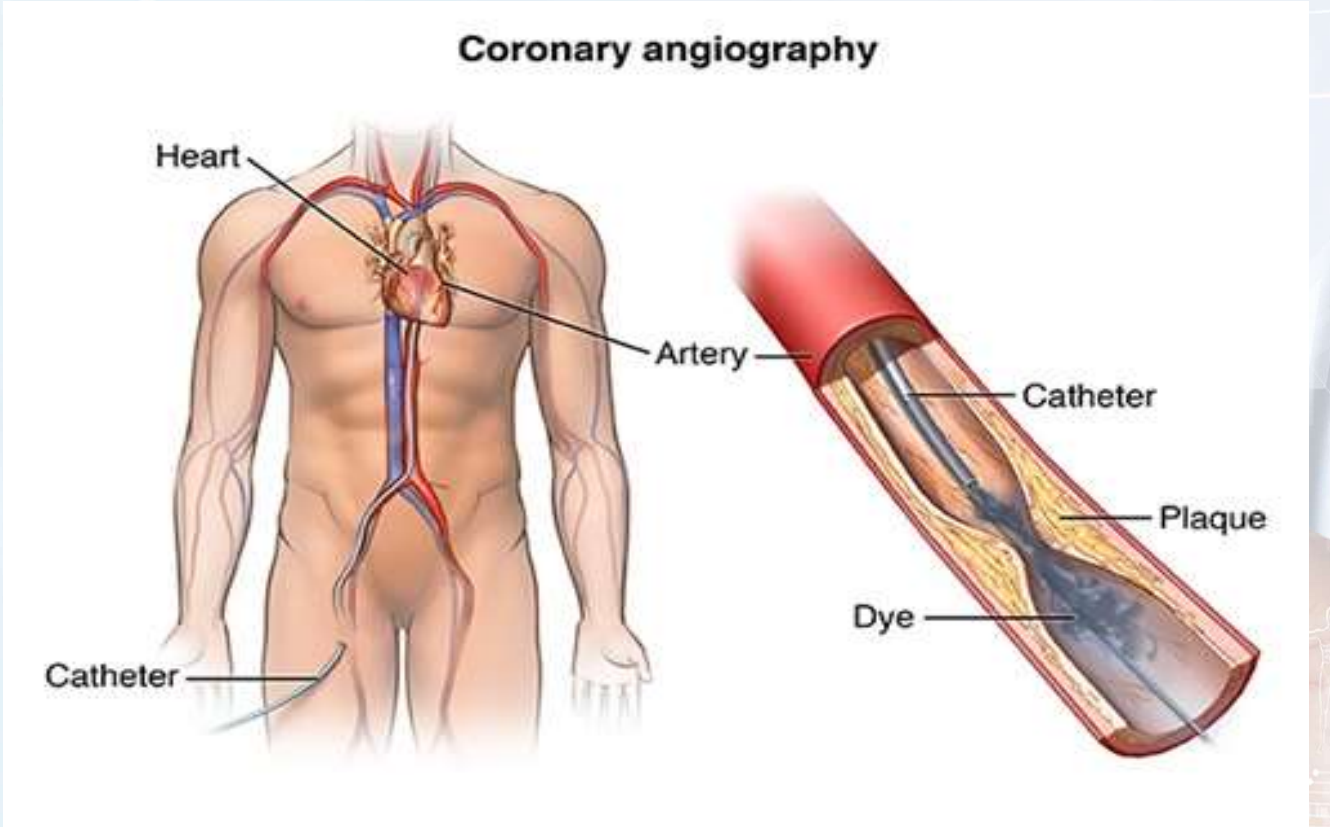
An image-based assessment of coronary physiology

Johan HC Reiber, PhD
CSO
Medis medical imaging systems bv
Leiden, The Netherlands

Ischemic heart disease

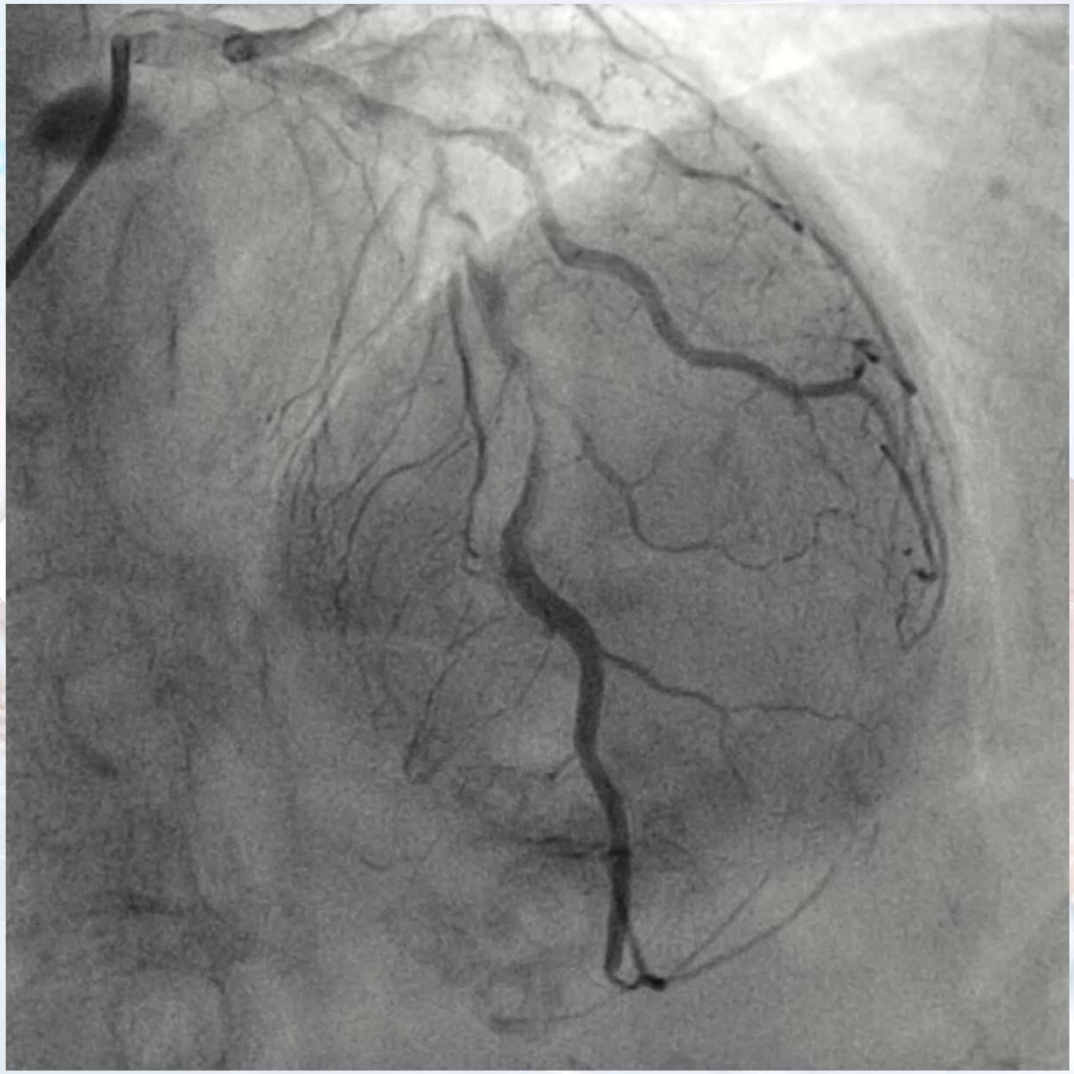
- Ischaemic Heart Disease (IHD) is the world's leading cause of mortality, and responsible for the death of 1.8 million Europeans each year.
- In IHD, plaque formation narrows the blood vessels of the heart, reducing the functional capacity of a coronary artery to perfuse the heart muscle.
- Current clinical guidelines demand physiologic assessment of coronary plaques (i.e. effect of narrowings on the perfusion of the heart muscle) during a cardiac catheterization to guide treatment decisions (medical treatment vs. stent placement).

Cardiac catheterization

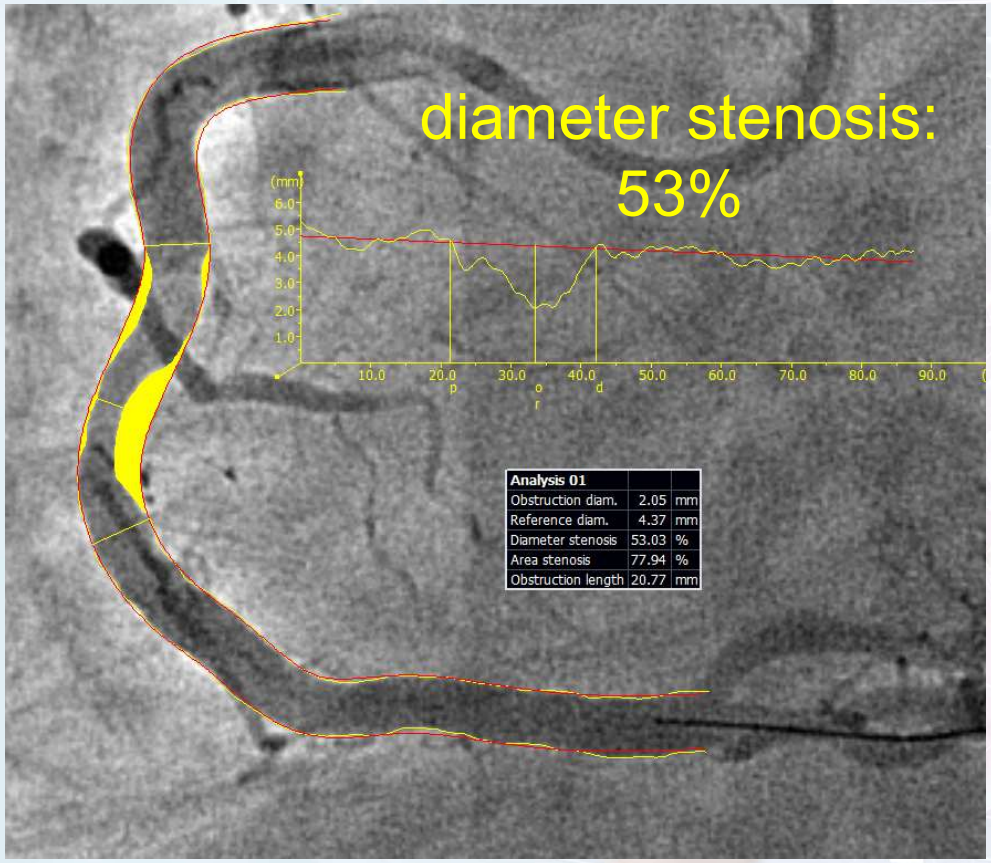


Cardiac catheterization is a procedure used to diagnose and treat certain **cardiovascular** conditions. During **cardiac catheterization**, a long thin tube called a **catheter** is inserted in an artery or vein in your groin, neck or arm and threaded through your blood vessels to your **heart**.

Movie catheterization



To treat or not to treat?



Anatomy: diameter stenosis = 53%

vs.

Physiology: FFR = 0.85

Quantitative Coronary Angiography (QCA)

Our first QCA was developed in 1979

Fractional Flow Reserve (FFR)

- **FFR** is a quantitative measurement of the functional severity of the coronary stenosis

$$\mathbf{FFR} = \frac{Distal\ Coronary\ Pressure\ (Pd)}{Proximal\ Coronary\ Pressure\ (Pa)}$$

During maximum hyperemic

Intervention Yes/No is typically based on FFR ≤ or > 0.80

FFR was developed by Prof Nico Pijls et. al. in the 1995's

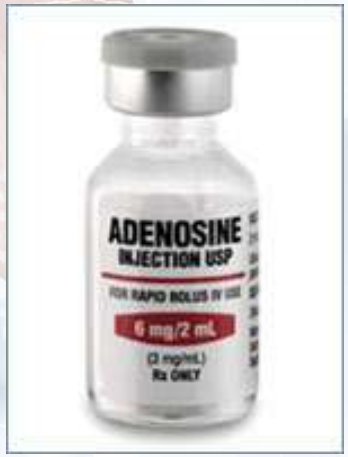
2018 ESC/EACTS Guidelines on myocardial revascularization

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

European Heart Journal, September 2018

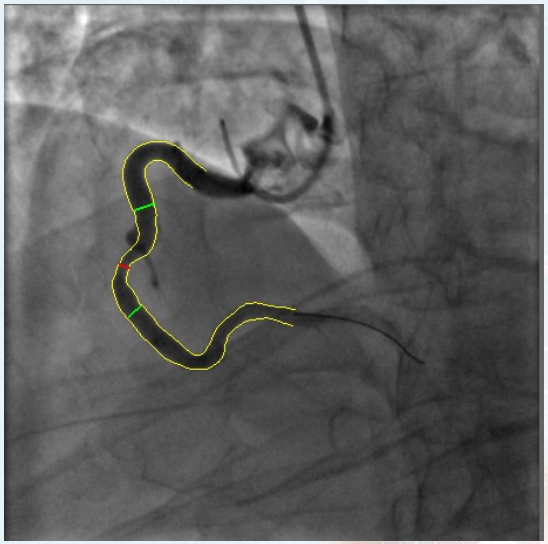
Limitations pressure wire

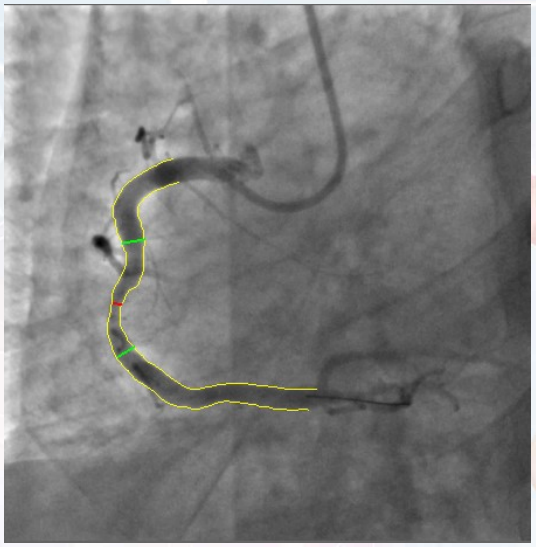
- Invasive
- Need for adenosine:
  - Discomfort; Arrythmia
- Time consuming
- Pullback device not available
- Suboptimal FFR measurements occur in about 1/3 of tracings; JACC Interv 2017; 10:1392;
  FFR is not reproducible
- For bifurcations, wire in both main vessel and sidebranch
- Expensive for operator or hospital
- Worldwide acceptance 7-10% max

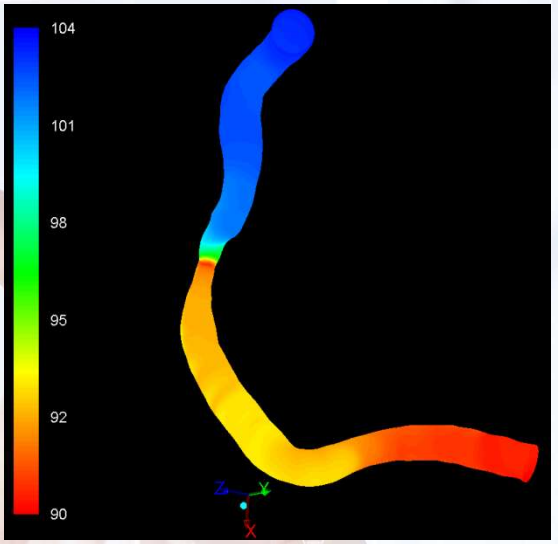


QFR

(Quantitative Flow Ratio = Medis' QCA derived FFR)







3D model reconstructed from 2 angiographic projections with angles ≥ 25º apart, acquired by monoplane or biplane systems.

QFR = 0.87

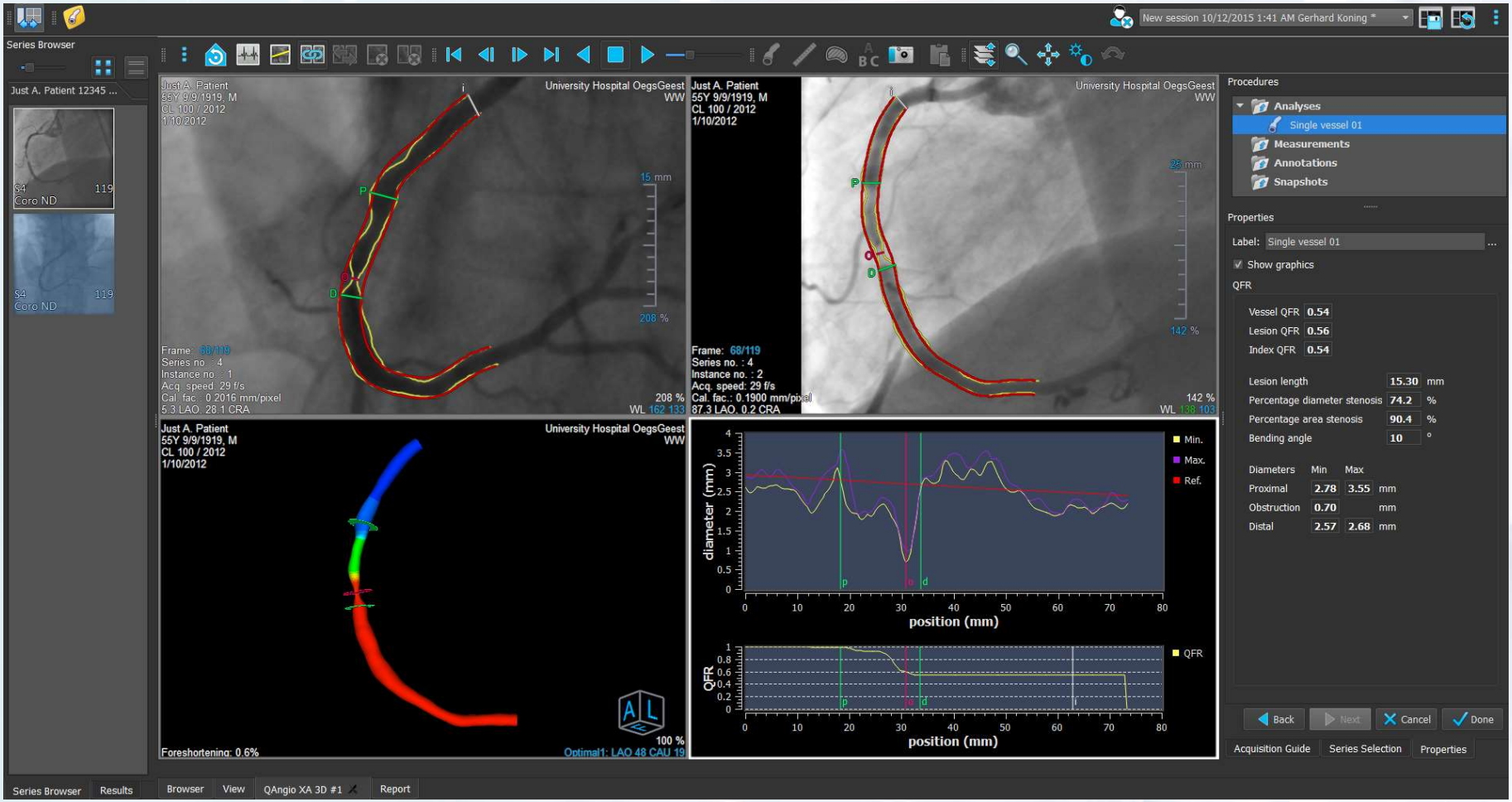
FFR = 0.85

Patient-specific **volumetric flow rate** (at hyperaemia) calculated using the combination of contrast bolus front **frame count** and **3D QCA**;

In-procedure time: < 5 min

Based on EuroPCR presentation by Niels Holm, MD
Aarhus University Hospital, Skejby ● Denmark

QFR: One-stop shop? V 1



Medis First Clinical Trial Publications

JACC: CARDIOVASCULAR INTERVENTIONS
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VOL. 7, NO. 7, 2
ISSN 1936-8798/$3
http://dx.doi.org/10.1016/j.jcin.2014.03.

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*

Leiden, the Netherlands; Aalst, Belgium; Nyiregyyhaza, Hungary; Guangzhou and Tianjin, China; and Skejby, Denmark

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EDITORIAL COMMENT

Fractional Flow Reserve From 3-Dimensional Quantitative Coronary Angiography

Fresh Light Through an Old Window*

Alexandra J. Lansky, MD, Cody Pietras, BSc

New Haven, Connecticut

In this issue of *JACC: Cardiovascular Interventions*, Tu et al. (1) report on an initial validation study for a less-invasive approach to derive fractional flow reserve (FFR) based on the coronary angiogram. The investigators should be congratulated on developing an innovative means to expand the diagnostic value of angiography by including physiological ischemic assessment, potentially broadening access FFR data to every patient undergoing cardiac catheterization.

FAVOR II Pilot Trial

- Finalized recruitment and analyses of 73 patients in multi-center setting for optimizing algorithms;
- Tested 3 different scenarios:
  - 1) with adenosine;
  - 2) without adenosine; and
  - 3) fixed flow velocity;
- FAVOR II confirmed results of FAVOR I;
- **Major result: Image-based physiology feasible: no wire, no adenosine**
- Manuscript published JACC Interv;2016;9: 2024-35
- Available as imaging vendor independent commercial product July 1, 2016;

FAVOR II Pilot Trial

JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 9, NO. 19, 2016

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http://dx.doi.org/10.1016/j.jcin.2016.07.013

Diagnostic Accuracy of Fast Computational Approaches to Derive Fractional Flow Reserve From Diagnostic Coronary Angiography

The International Multicenter FAVOR Pilot Study

Shengxian Tu, PhD,[a] Jelmer Westra, MS,[b] Junqing Yang, MD,[c] Clemens von Birgelen, MD, PhD,[d] Angela Ferrara, MD,[e] Mariano Pellicano, MD,[e,f] Holger Nef, MD,[g] Matteo Tebaldi, MD,[h] Yoshinobu Murasato, MD, PhD,[i] Alexandra Lansky, MD, PhD,[j] Emanuele Barbato, MD, PhD,[e,f] Liefke C. van der Heijden, MD,[d] Johan H.C. Reiber, PhD,[k] Niels R. Holm, MD,[b] William Wijns, MD, PhD,[e,l] on behalf of the FAVOR Pilot Trial Study Group

FAVOR II EU/JP

Diagnostic Accuracy of On-line Quantitative Flow Ratio Functional Assessment by Virtual Online Reconstruction

An academic international multicenter trial by Aarhus University Hospital, Denmark

Purpose

- To evaluate the feasibility and diagnostic precision of QFR during CAG with FFR as gold standard.

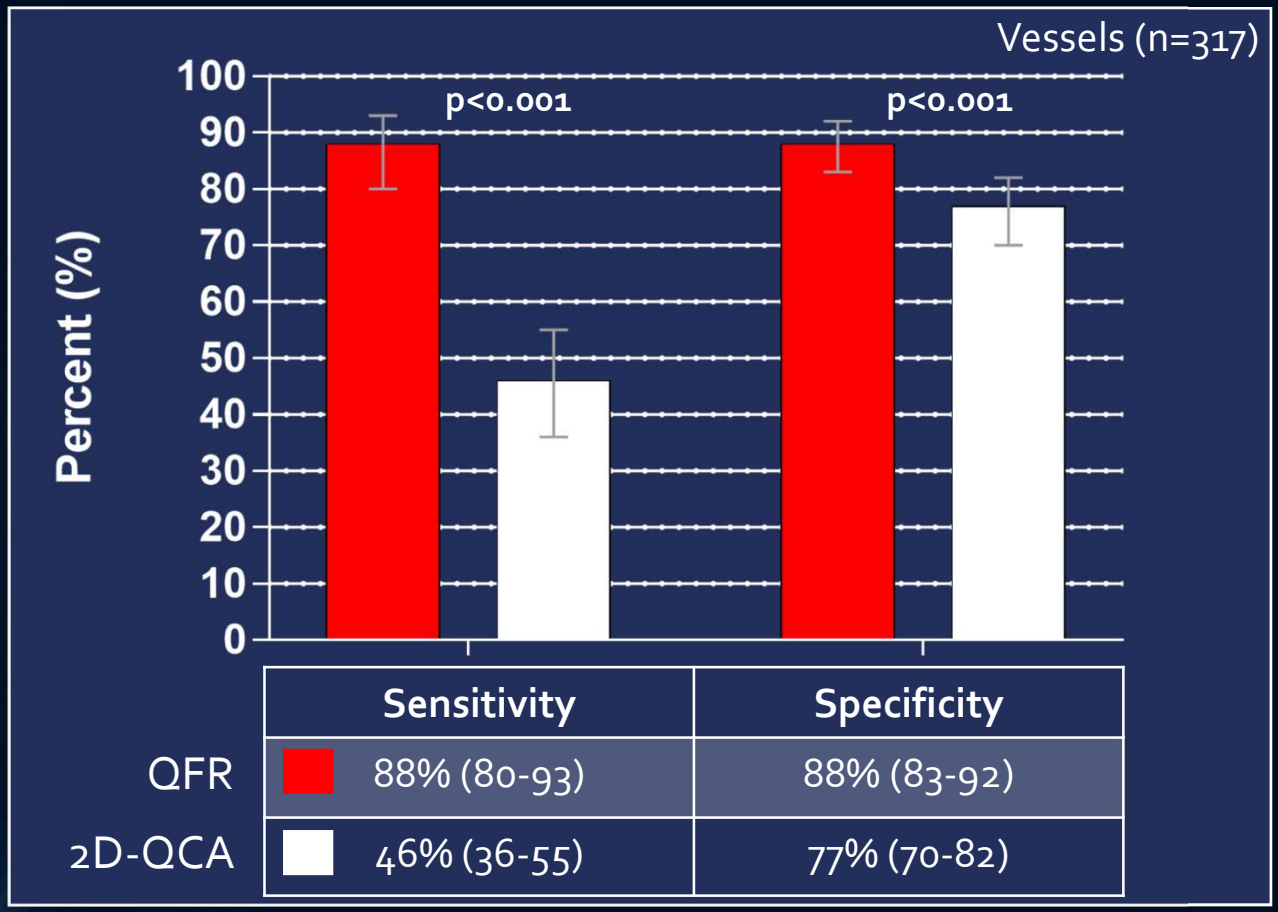
Hypothesis

- 1) QFR can be assessed during the cardiac catheterization procedure for stenosis interrogated by FFR
- 2) QFR is accurate with FFR as gold standard

Design

- Prospective, observational, multicenter study with inclusion of 300 patients.

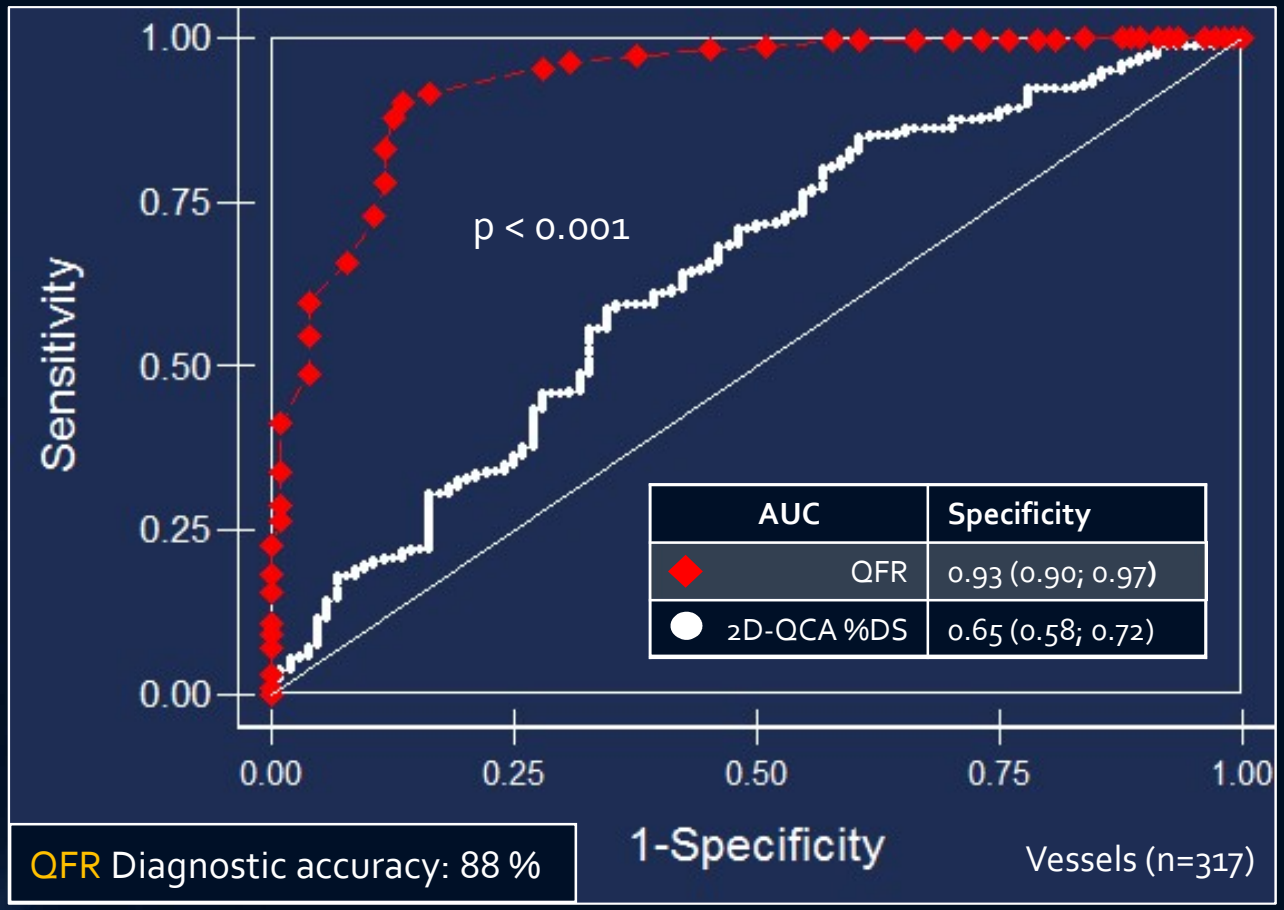
Primary endpoint



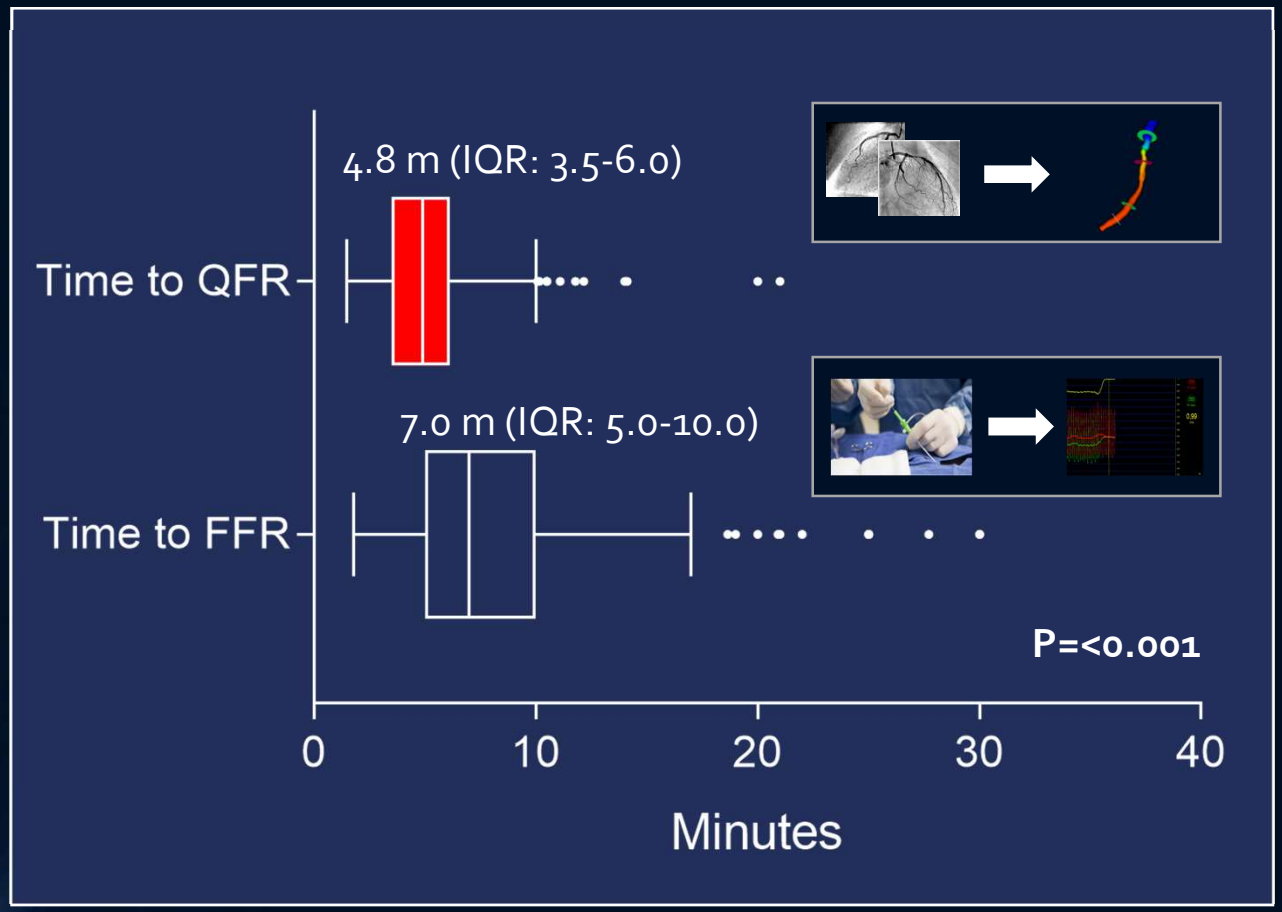
	Sensitivity	Specificity
QFR	88% (80-93)	88% (83-92)
2D-QCA	46% (36-55)	77% (70-82)

Comparisons by McNemar's test

Results – QFR vs. 2D-QCA with FFR as reference



Results – Time to QFR and FFR



FAVOR II China

Diagnostic Accuracy of the Angiographic Quantitative Flow Ratio in Patients With Coronary Artery Disease

Bo Xu, MBBS

On behalf of the FAVOR II China Investigators

Quantitative Flow Ratio (QFR)

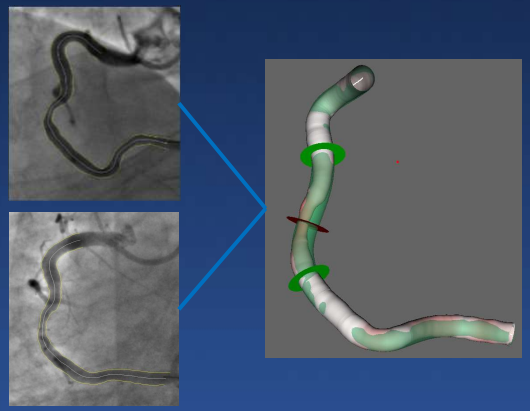
Standard Angiogram

Data Transmission System

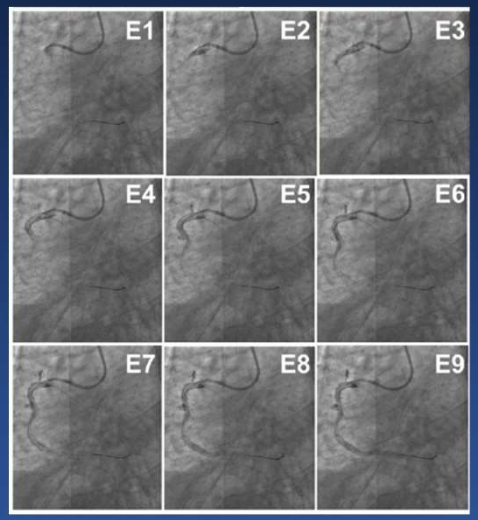
Two image runs with angle difference ≥25°

AngioPlus System

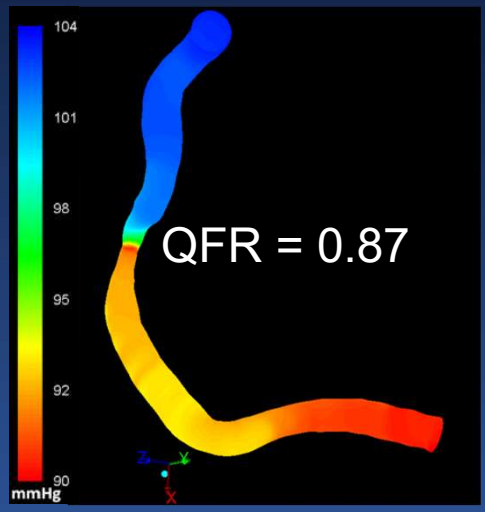
3D Reconstruction



Modified Frame Count



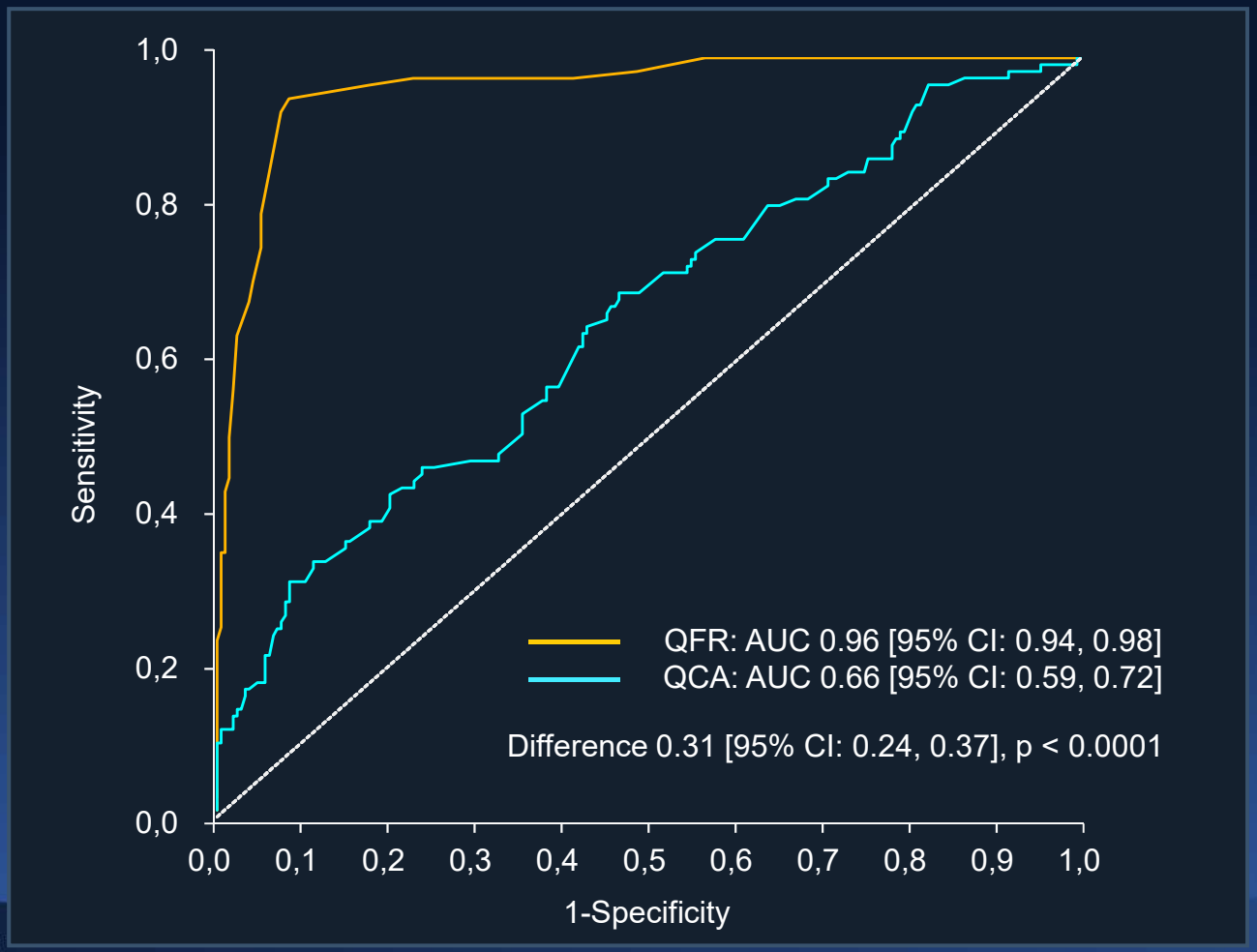
QFR



Without Inducing Hyperemia

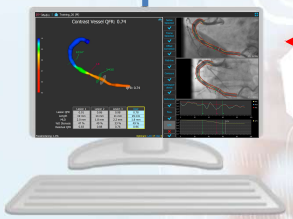
Tu S et al. *JACC Cardiovasc Interv*. 2014;7:768-77; Tu S et al. *JACC Cardiovasc Interv*. 2016;9:2024-35

Receiver Operating Curves for the Discrimination of Functionally Significant Stenosis (Online Analysis)



Cath lab setup and workflow

Display is replicated to the Large Display Monitor



Medis Suite with QAngio XA 3D / QFR in control room

Image data
Dicom files can be sent to Medis Suite, either manually or automatically

X-ray system in cath lab

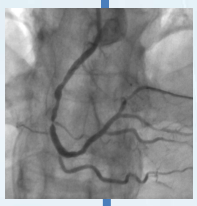
QFR can be assessed with most modern Philips, Siemens, GE and Canon X-ray systems

DGM21

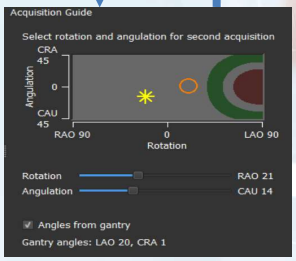
QFR fits very well in the clinical workflow

Start

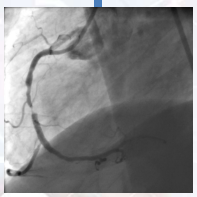
Give Nitroglycerin



1st angio to QFR workstation

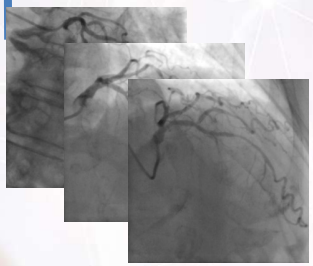


Determine 2nd viewing angle



2nd angio to QFR workstation

Perform all other diagnostic angios



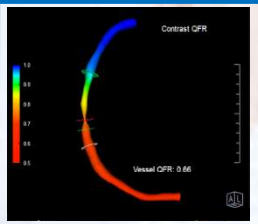
First QFR analysis is performed during the acquisition of the other diagnostic angios.
Hardly any waiting time in the cathlab.

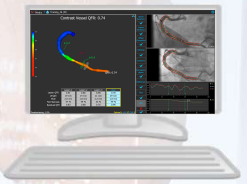
QFR analysis (< 5 min)

Decide how to prodeed

PCI ?...

Show QFR result AND lesion dimensions on LDM





Slide 22

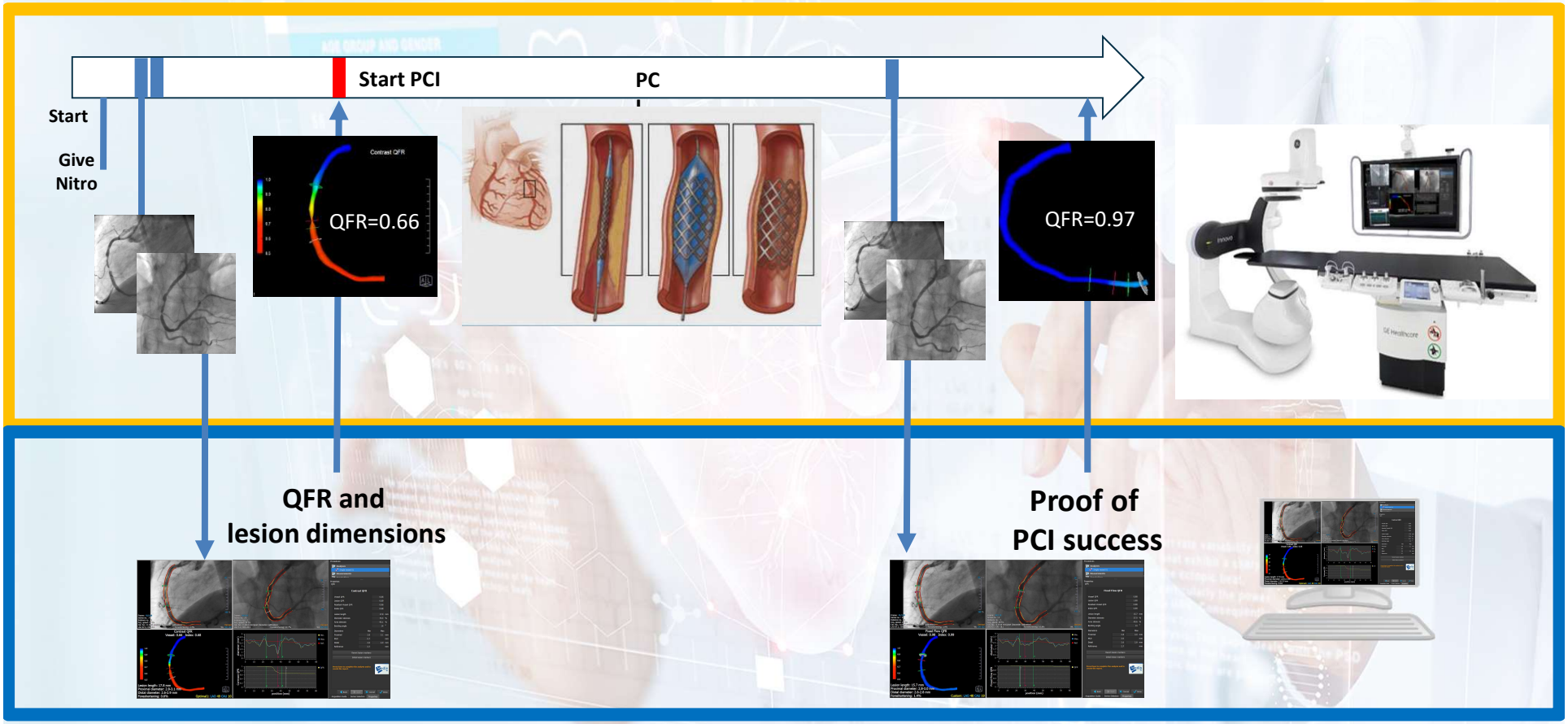
DGM21 Slide is good but requires simplifications. GE syggestions: 1) Ask Dr Maillard for testimonial about time saved due to QFR. Set up small study to show the time for patient study without phisiology; the time for patient study with FFR vs the QFR analysis needed where teh QFR analysis is performed while the other diagnostic agios are being cquired

Daniel Garcia Miranda; 28-04-19

DGM22

QFR fits very well in the clinical workflow

QFR pre- (, during) and post-PCI



Slide 23

DGM22 GE feedback: More emphasis on the proof of success, second QFR is actually a test of success which failed.
For GE sepecific: in the middle it should become PCI assist.

If you use no FFR or QFR you take some risk
If use FFR it takes longer

Too many things on the slide: does not give the impression that QFR will reduce the work flow
Daniel Garcia Miranda; 29-04-19

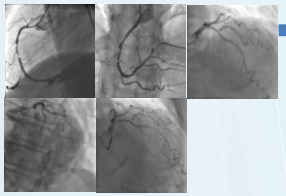
QFR reduces unnecessary referrals

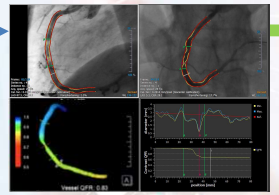
Peripheral Hospitals can perform QFR at the point of care

Peripheral Hospital

Diagnostic Cath Lab

Scenario 1:

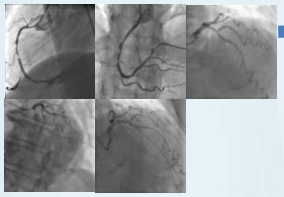


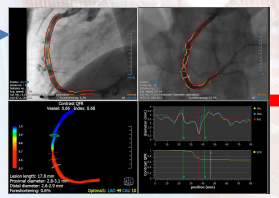


QFR > 0.80

Patient goes home
(with medication)

Scenario 2:

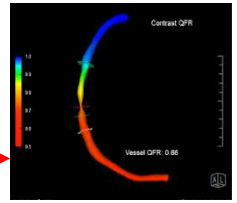




QFR < 0.80

Transfer of QFR results to other hospital

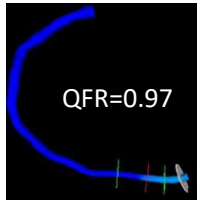
PCI Center



\+
Lesion
Dimensions

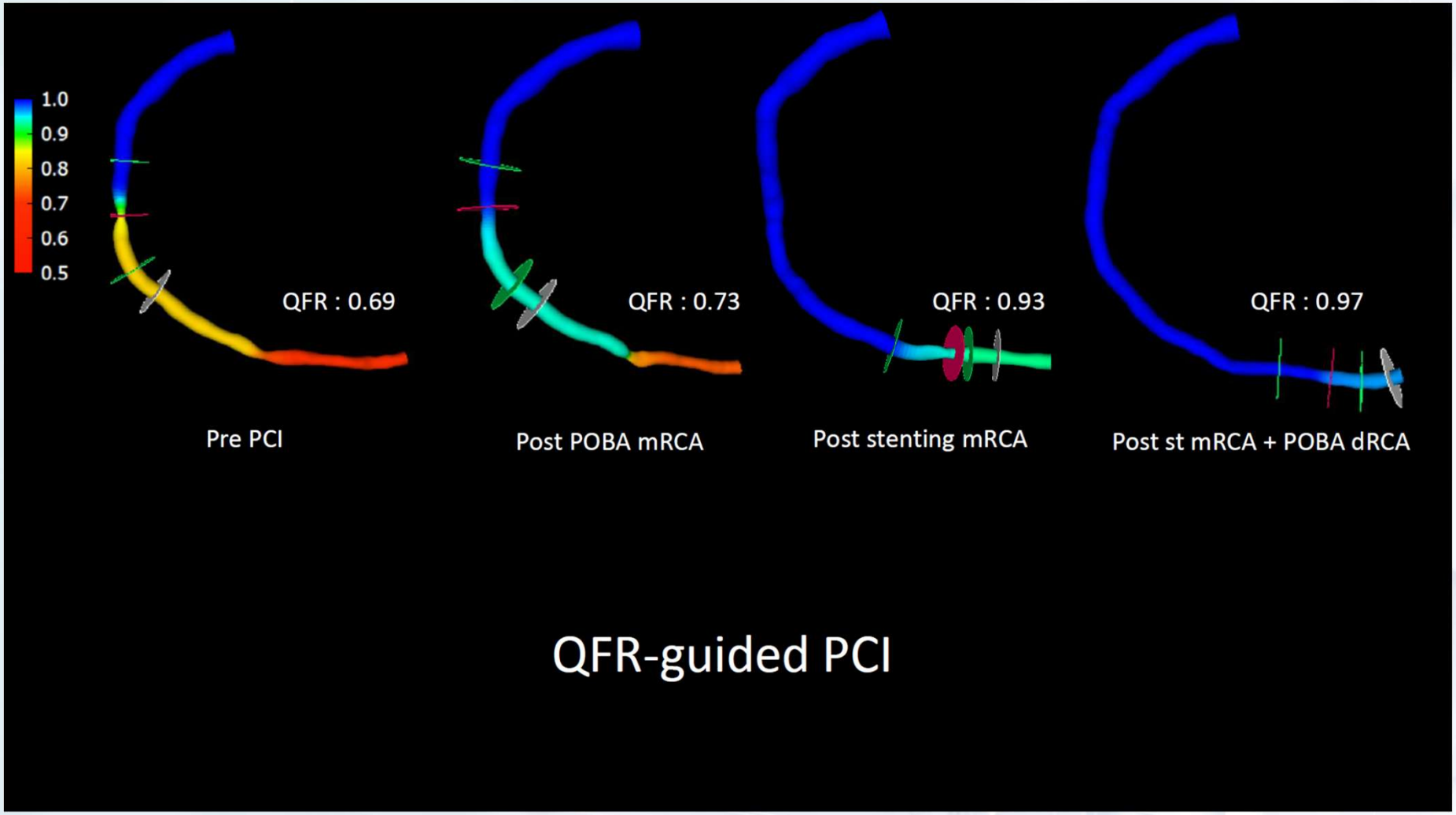
PCI Cath Lab

PCI procedure



Proof of PCI success

Example QFR-guided PCI



Courtesy Dr Liew – Queen Elizabeth Hospital – Kota Kinabalu

Scientific evidence supporting QFR®

QFR has an excellent correlation with FFR and good clinical accuracy

Scientific evidence since 2014:

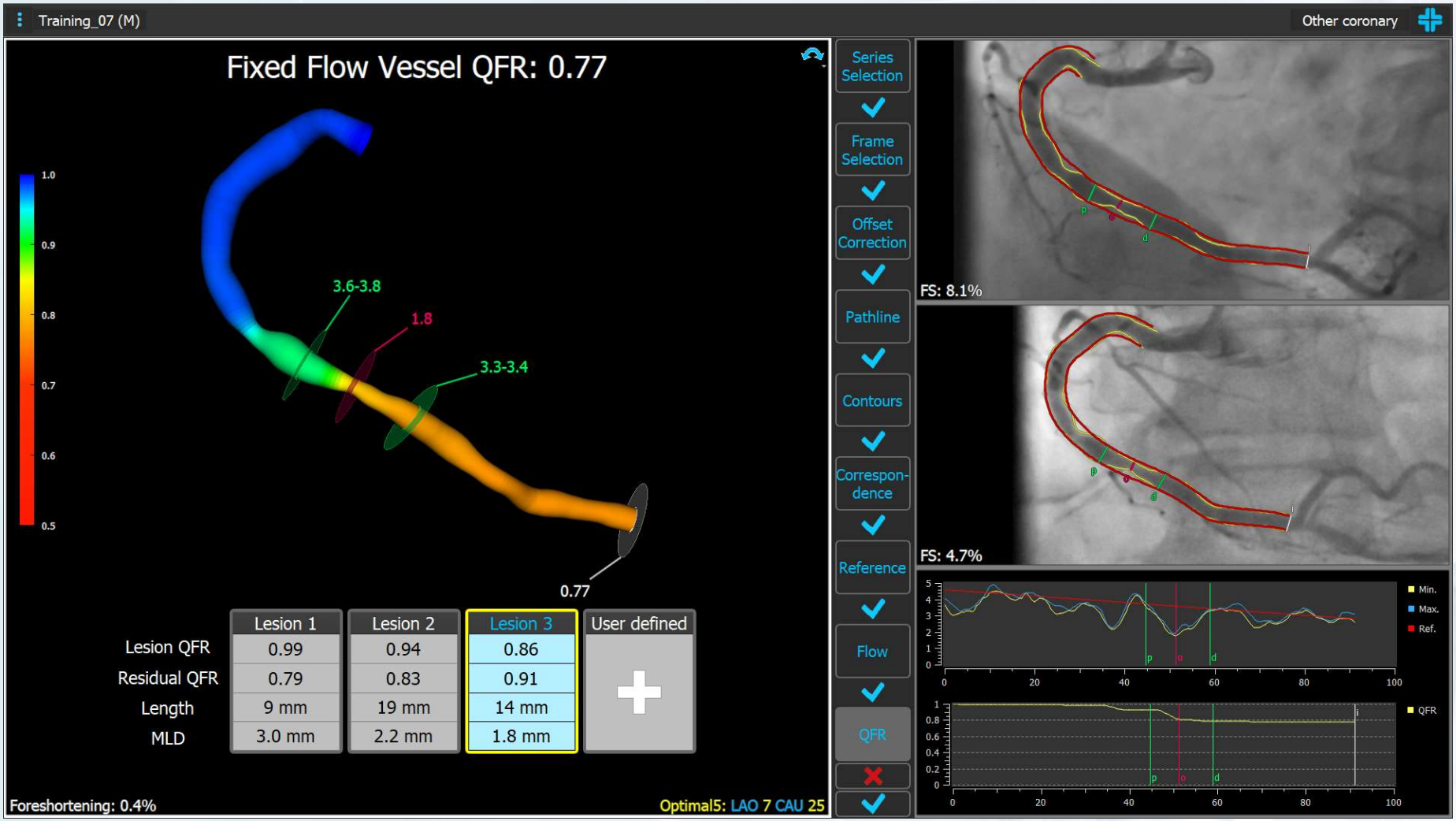
- 50+ peer reviewed papers in international literature, incl. > 10.000 patients
- 70+ congress abstracts
- 15+ live case demonstrations worldwide
- All data very consistent and robust

QFR meta-analysis of four major multi-center QFR clinical trials [1-4], conducted by Aarhus University, Denmark, shows:

- Good correlation to FFR, no systemic differences
- Good clinical diagnostic accuracy

1. Westra J et al. Circ Cardiovasc Imaging 2018; 11.
2. Tu S et al. J Am Coll Cardiol Interv 2016; 9: 2024-35.
3. Westra J et al. J Am Heart Assoc 2018; 7.
4. Xu B et al. J Am Coll Cardiol 2017; 70: 3077-87.

QFR Version 2.0



QFR

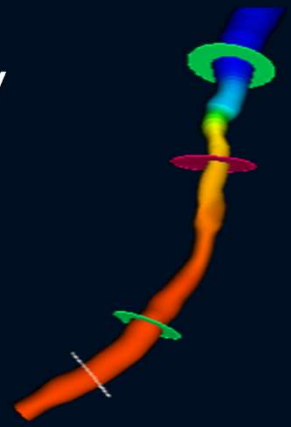
QFR Next steps: RCTs

FAVOR III Europe - Japan

- QFR vs FFR
- Non-inferiority study

FAVOR III China

- QFR vs present practice
- Superiority study



PCI Research
Aarhus University Hospital, Skejby ● Denmark
niels.holm@clin.au.dk
Aarhus University Hospital
SKEJBY

Design overview

- Stable angina pectoris or evaluation of secondary stenosis
- Coronary stenosis of 40-90% by visual estimate

1:1 randomization of 2000 patients

QFR guiding

FFR guiding

Primary endpoint: One year PoCE for non-inferiority

Two-year follow-up Only clinical follow-up

PCI Research
Aarhus University Hospital, Skejby ● Denmark
favor@clin.au.dk
Aarhus University Hospital
SKEJBY

QFR regulatory status

- **QFR is market cleared in the following countries:**

Country	Clerance	Description
European Union	YES	(CE)
Iceland	YES	(CE)
Liechtenstein	YES	(CE)
Norway	YES	(CE)
Switzerland	YES	(CE)
Turkey	YES	(CE)
Canada	YES	(CMDR)
Australia	YES	(TGA)
Brazil	YES	(ANVISA)
China*	YES	(CFDA)
Singapore	YES	(HAS)
Indonesia	YES	(KKRI)
South Africa	YES	(SAHPRA)
South Korea	Pending	(MFDS)
Japan	Pending	(PMDA)
USA	YES	(FDA)

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) .
- The use of QFR is not without a stiff learning curve, which requires that users be certified by Medis before being able to start.
- Current indications: Patients with stable angina;
- Under investigations: MI, bifurcation lesions, lengthy diffuse disease, etc.
- CE certification April 2017
- FDA 510(k) approval May 2019

Benefits

- **For patients:**
  - No adenosine with side-effects
  - No extra radiation
  - Less chances on complications due to wire insertion
- **For (interventional) cardiologist:**
  - Applicable in diagnostic cases;
  - Applicable pre-, during-, and post-PCI
  - Applicable in all coronary vessels without repeat insertions of wire
- **For hospitals:**
  - Cost-effective

Hurdles

- **Outcome study**
  - Despite all the extensive clinical global evidence, the technology will not appear in a Guideline until an Outcome Study with non-inferiority relative to the standard pressure wire has been performed (> 2000 ptns); Ongoing FAVOR III
- **Reimbursement by insurance companies**
  - In many countries very complex, lengthy, expensive and unpredictable process
  - Even if there is no reimbursement, to change the healthcare system to go from one established technique to a newer one is difficult
  - In the Netherlands " van kastje naar de muur"
  - UK has a very clear and professional approach with the NICE Guidelines
- **Significant investment to roll out the new technology worldwide**
  - The use of QFR is not without a learning curve, which requires that users be certified by Medis before they are allowed to use clinically;
  - This is not scalable: AI needed to further simplify and automate the process.

Thank you for your attention