Oxford University Hospitals
NHS Foundation Trust

AMIIC
Acute Multidisciplinary Imaging & Interventional Centre

University of Oxford

"Imaging-derived physiology"
una soluzione per integrare i due approcci?

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CUORE È NON SOLO

CeNS, Genova 14.04.2023

Conflicts of Interest

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

Affiliation/Financial Relationship	Company
Grant/Research Support	Miracor Medical SA, Abbott, Philips, Medtronic, Terumo, Medis Medical Imaging, Opsens
Consulting Fees/Honoraria	Miracor Medical SA, Abbott

Agenda

- *Why Imaging-derived Physiology*
- *Basic Principles of Imaging-derived Physiology*
- *Overview of main indices: Modalities of Imaging Derived Physiology*
- *Clinical Applications & Supporting Evidence*

Why Imaging-derived Physiology?

ESC European Society of Cardiology
European Heart Journal (2019) **40**, 87–165
doi:10.1093/eurheartj/ehy394

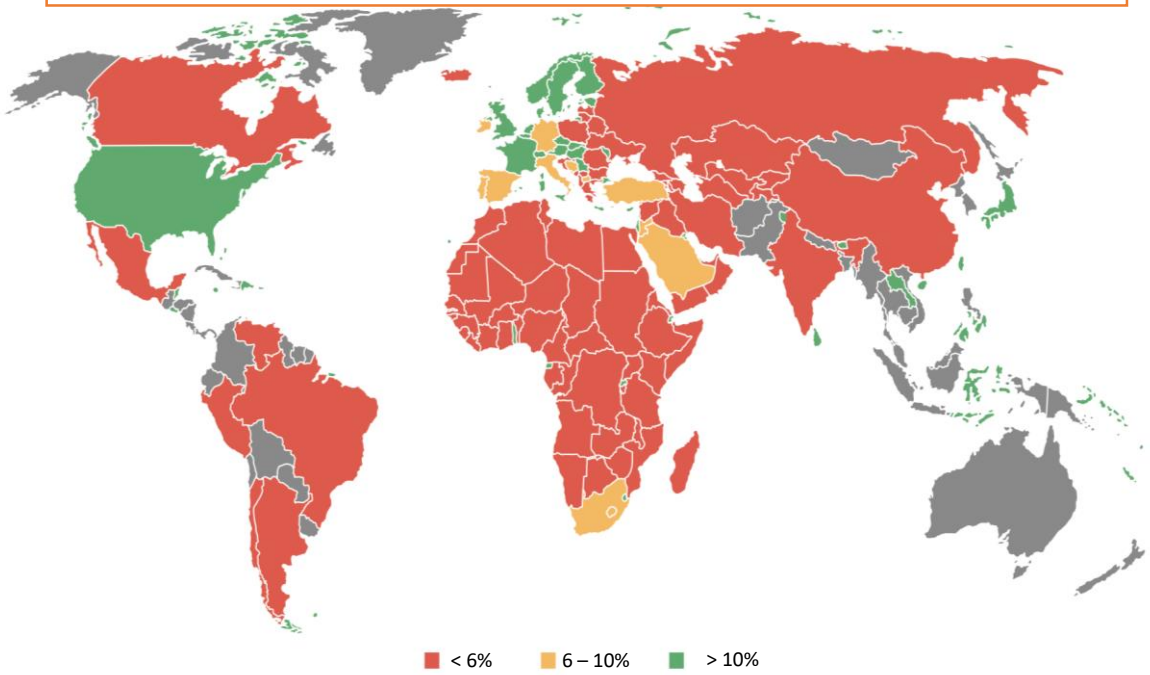
ESC/EACTS GUIDELINES

2018 ESC/EACTS Guidelines on myocardial revascularization

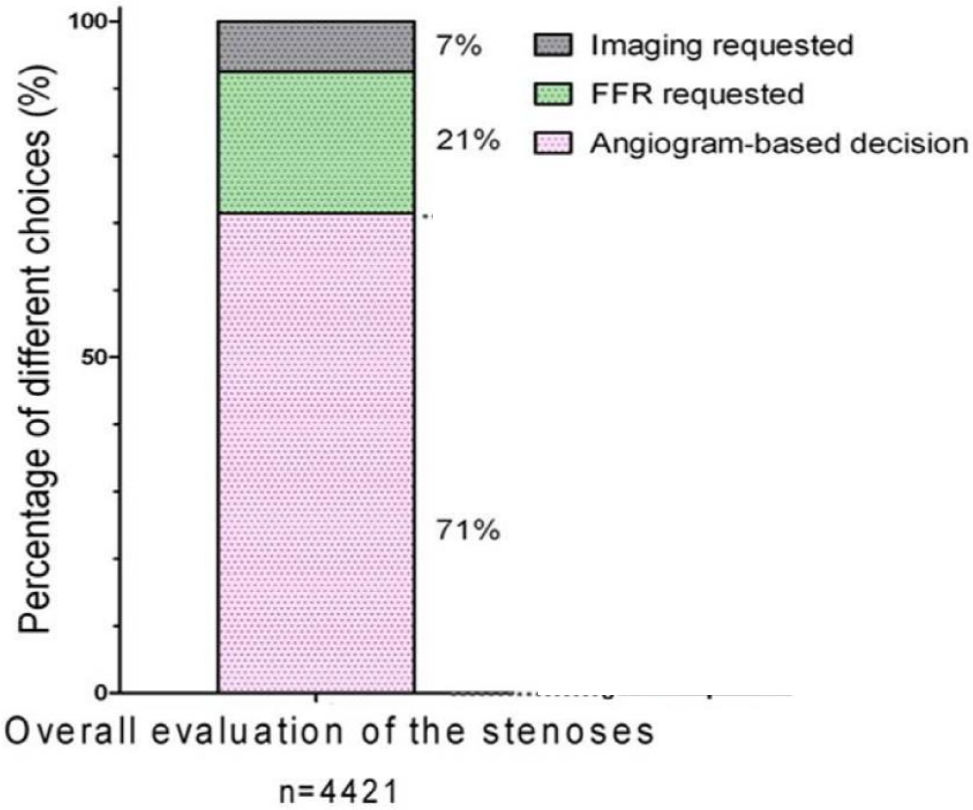
Recommendations	Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.[15,17,18,39]	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI.[29,31]	IIa	B

BUT

FFR adoption world-wide



Gottberg M et al JACC 2017

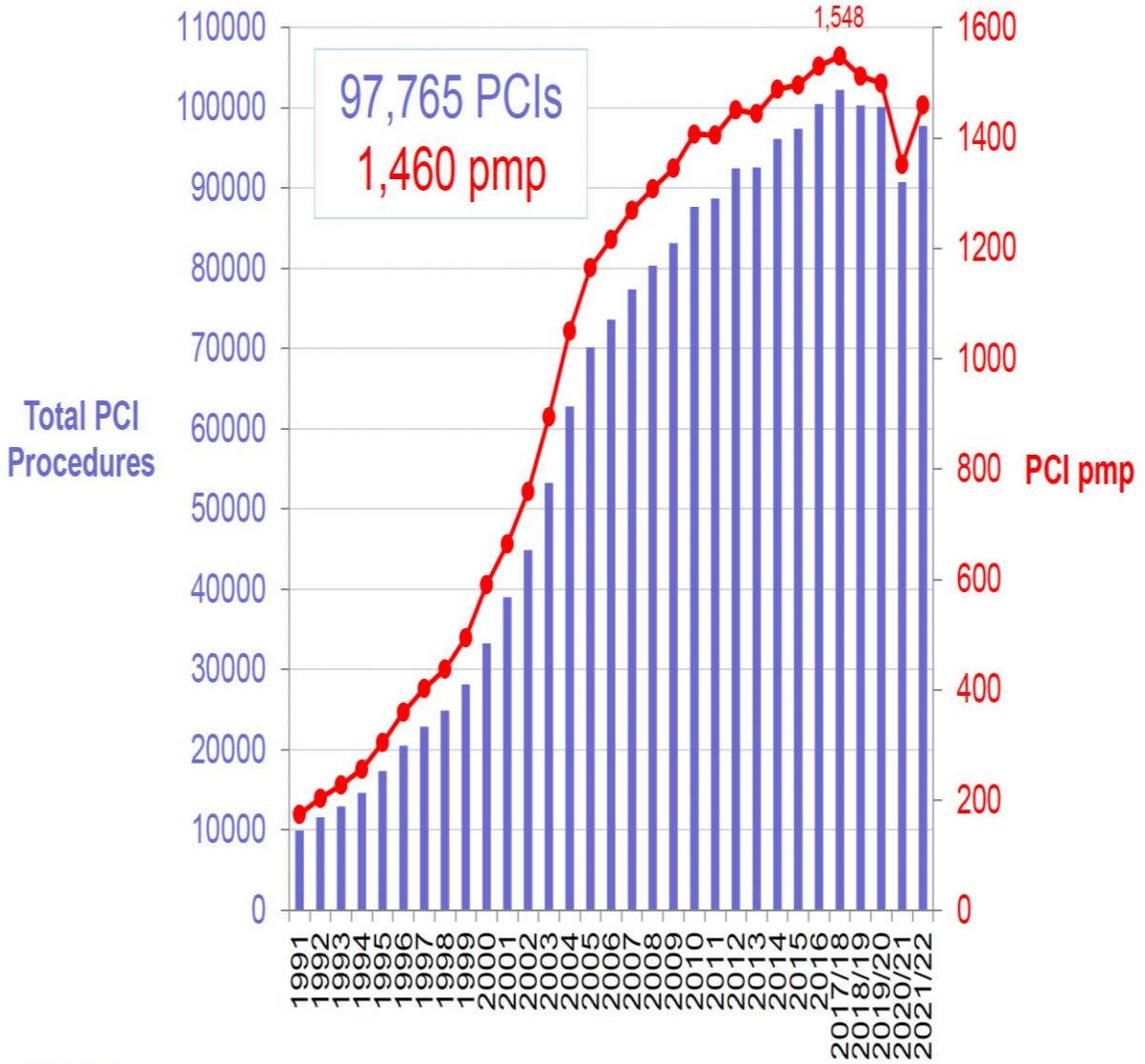


ISIS Survey- Toth G et al Circ Intv 2014

NICOR
Survey

BCIS
2021-22 data
Ludman

Total PCI activity all UK



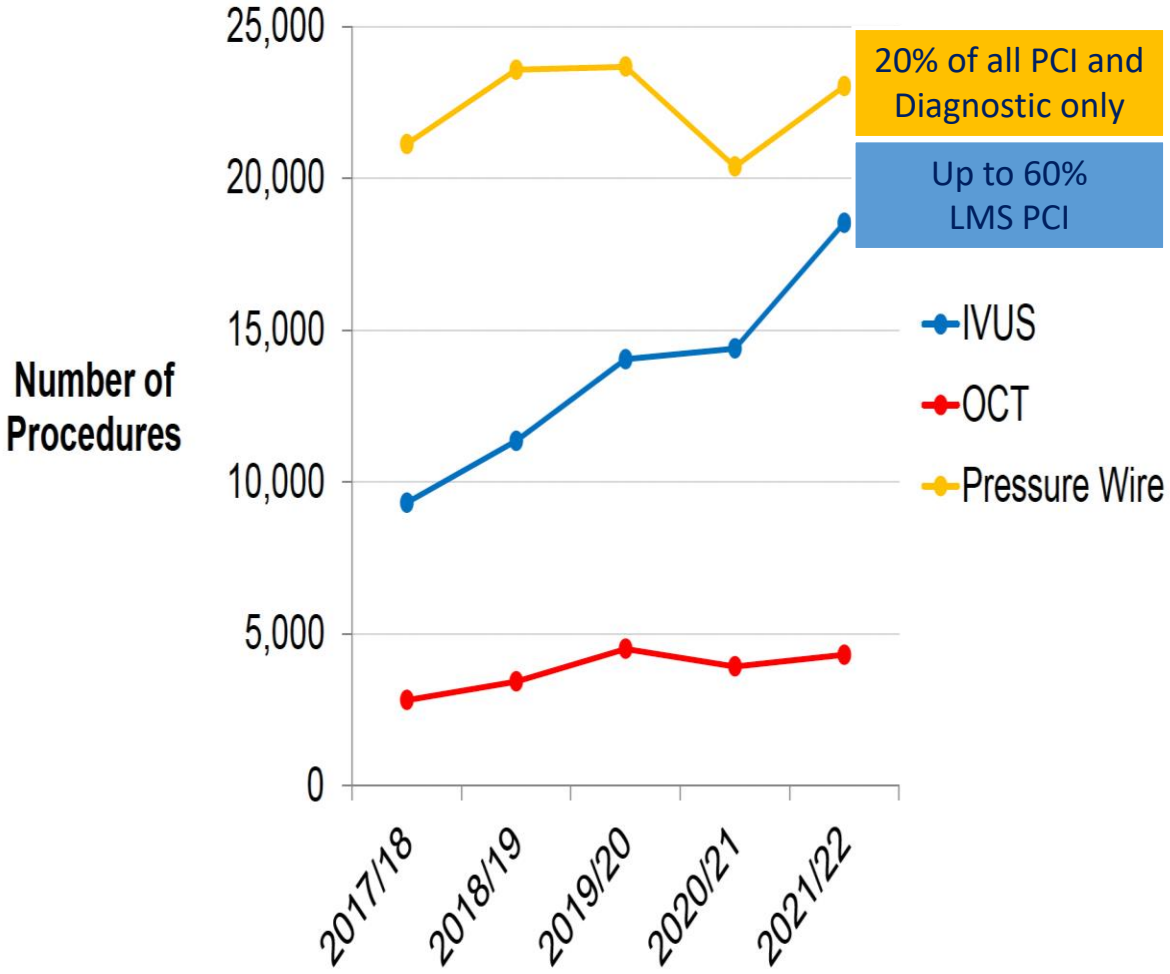
To Contents

NICOR
Data extract
22-11-2022

BCIS
2021-22 data
Ludman

Additional Interventional Coronary Techniques

All cases: Diagnostic only + when part of a PCI procedure



To Contents

Diagnostic only data from Survey Monkey, PCI data from NICOR

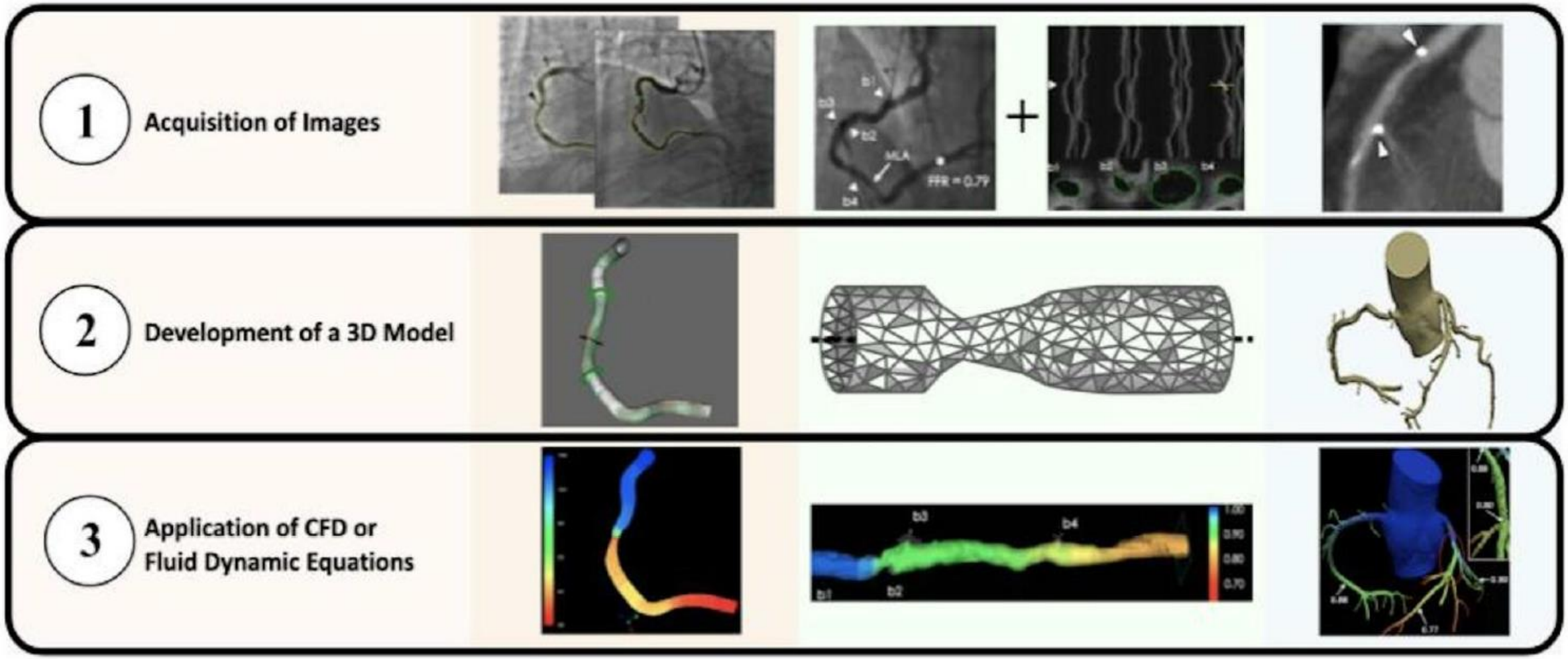
Why still sub-optimal diffusion of FFR

Technique-related *(the way FFR is measured)*

- Additional procedural time
- Additional vessel instrumentation & manipulation
- Additional cost (no reimbursement in some countries)
- Patient's discomfort (adenosine-related)

Imaging-derived Physiology: Basic Principles

Imaging Based Indices
(Anatomy-derived physiology)



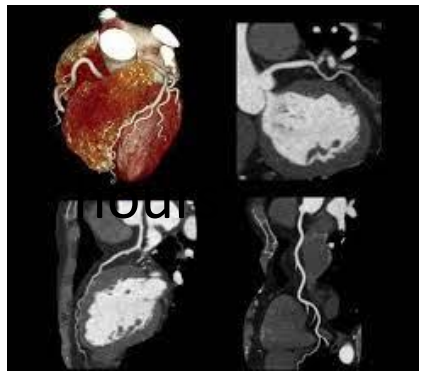
De Maria GL et al Minerva Cardiology & Angiology 2021

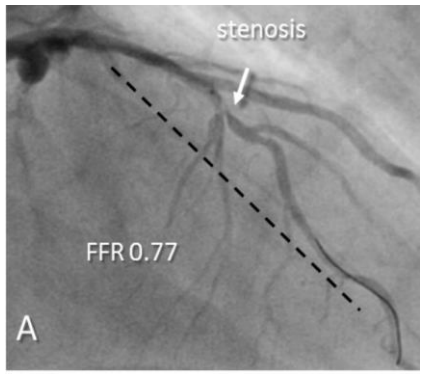
Imaging Based Indices

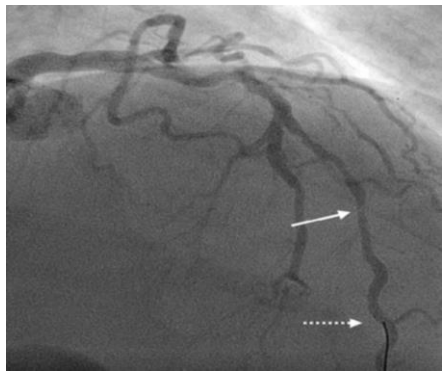
(Anatomy-derived physiology)

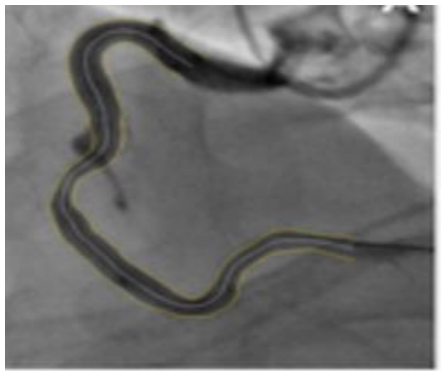
Computational Flow Dynamics (CFD)

Several hours → < 10 minutes

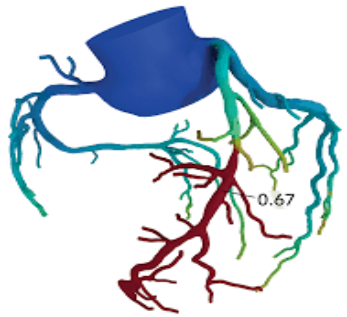








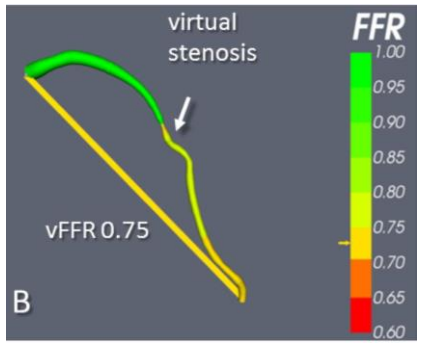
- **High computational power**
- **Long calculation times**



FFR_{CT}

Koo B et al

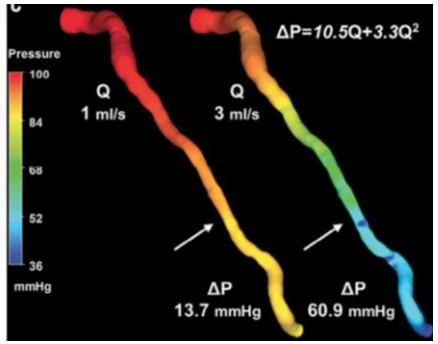
JACC 2011



vFFR *(virtual FFR)*

Morris P et al

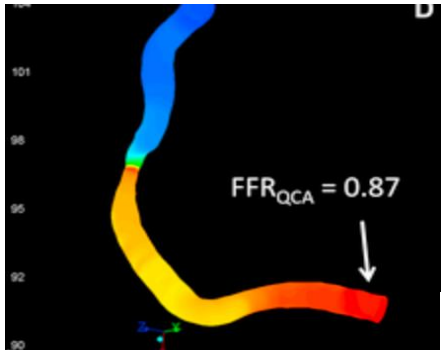
JACC Intv 2013



vFAI

Papafaklis M et al

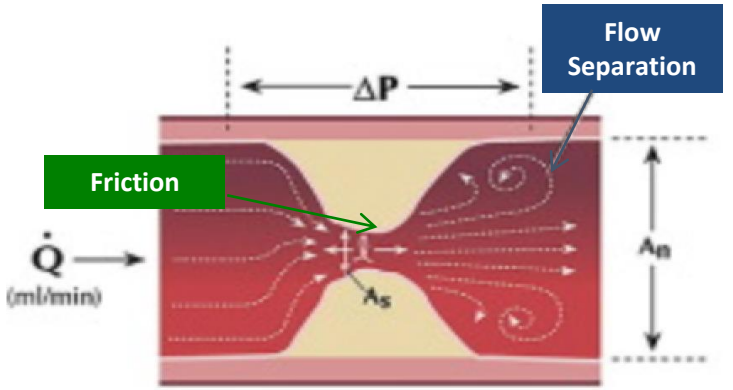
EuroIntervention 2013



FFR_{QCA}

Tu S et al

JACC Intv 2014



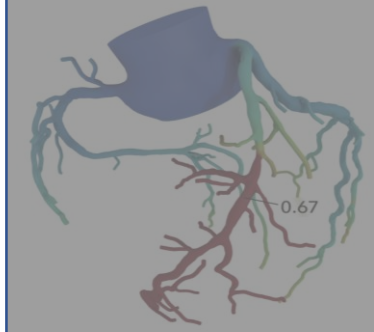
$$\Delta P = (f_1 L Q \rho 1/A^2_{stenosis}) + (f_2 Q^2 1/A^2_{stenosis} 1/A^2_{normref})$$

Friction **Separation**

Imaging Derived Physiology: Overview of main indices & Validation Studies

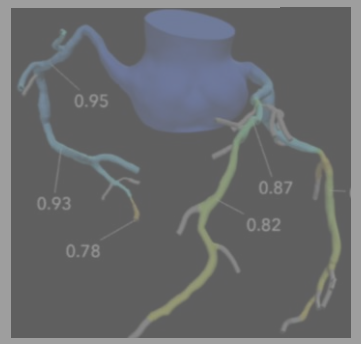
CTCA Derived Physiology

HeartFlow



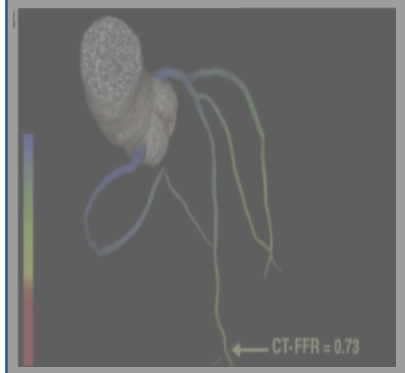
FFR_{CT}

SIEMENS Healthineers



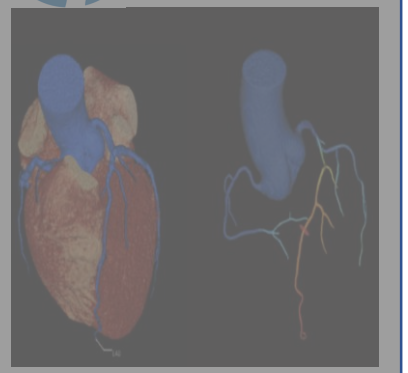
C- FFR

TOSHIBA



CT FFR

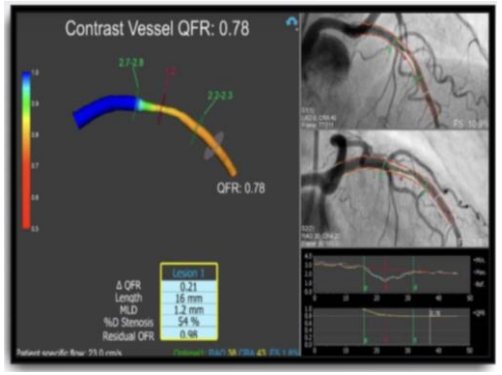
PULSE



CT μFR

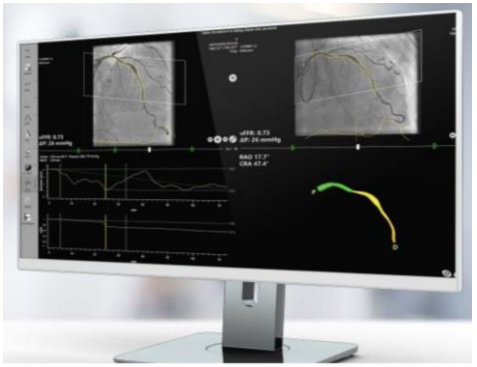
Angiography Derived Physiology

Medis Imaging Solutions in a Heartbeat
MEDICAL IMAGING



QFR

Caas
vFFR



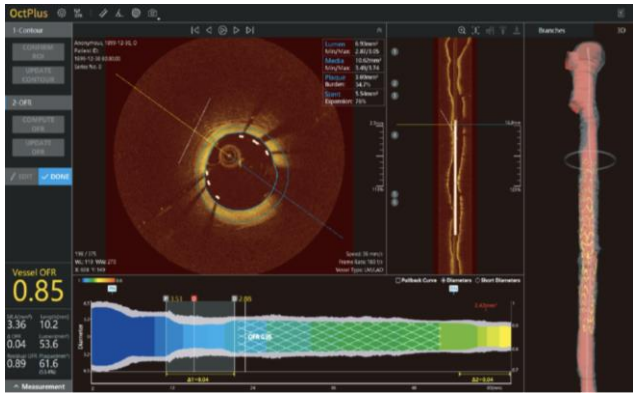
vFFR

CATHWORKS

FFRangio

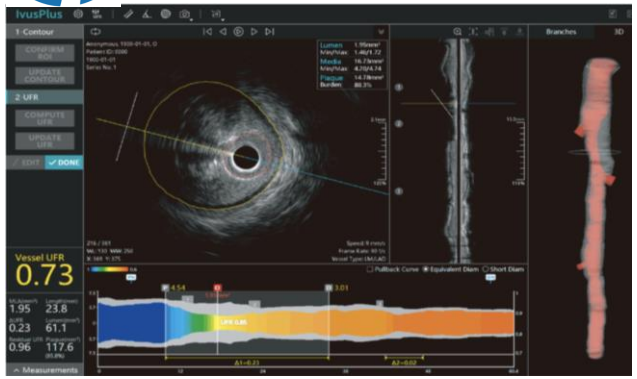
Intravascular Imaging Derived Physiology

PULSE



OCT derived - OFR

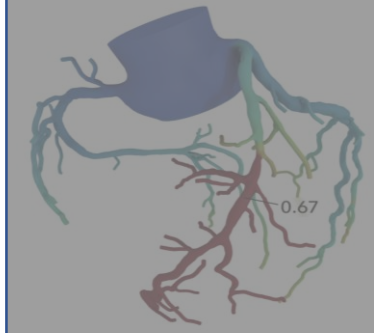
PULSE



IVUS derived - UFR

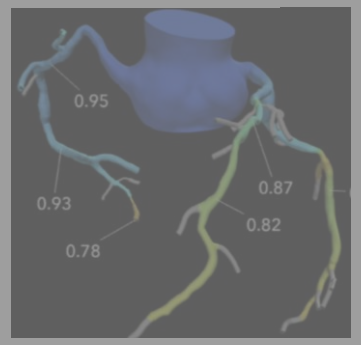
CTCA Derived Physiology

HeartFlow



FFR_{CT}

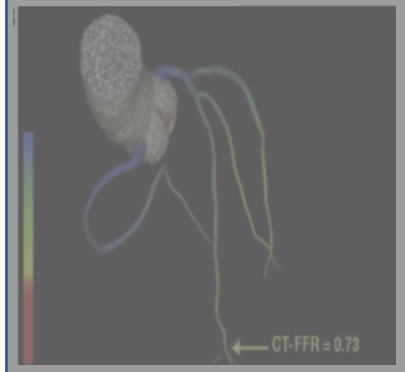
SIEMENS Healthineers



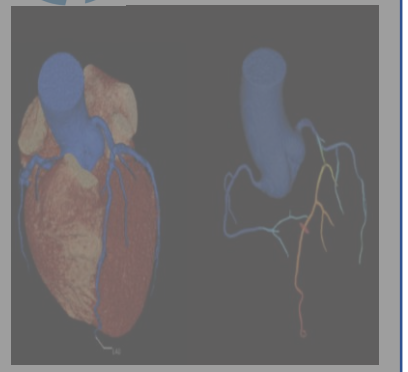
C- FFR

TOSHIBA

PULSE



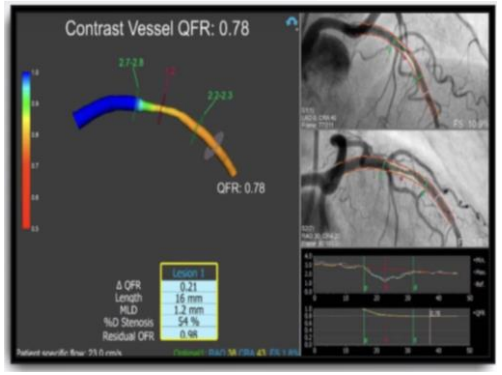
CT FFR



CT μFR

Angiography Derived Physiology

Medis Imaging Solutions in a Heartbeat
MEDICAL IMAGING



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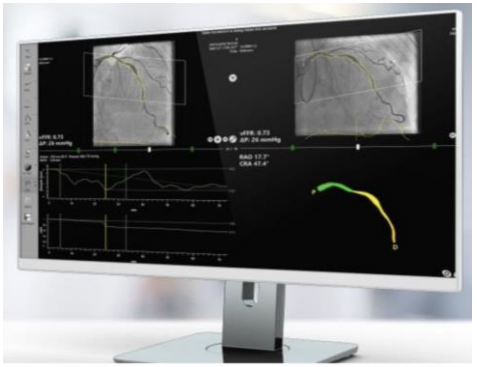
vFFR



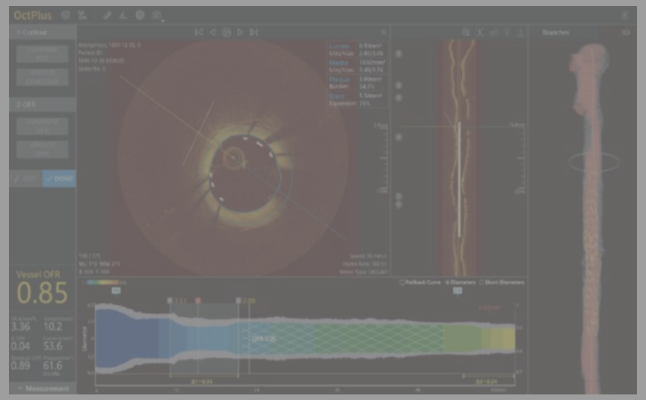
vFFR

CATHWORKS

FFRangio

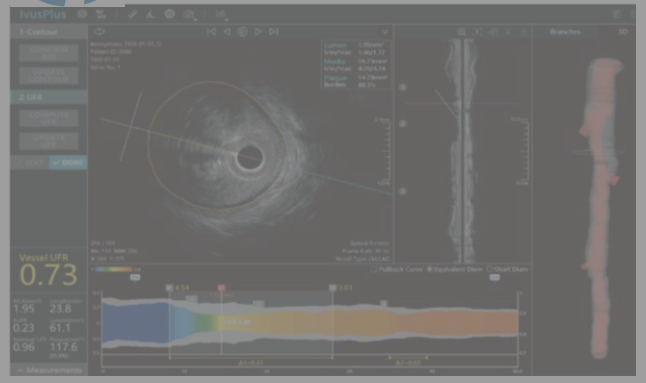
Intravascular Imaging Derived Physiology

PULSE



OCT derived - OFR

PULSE

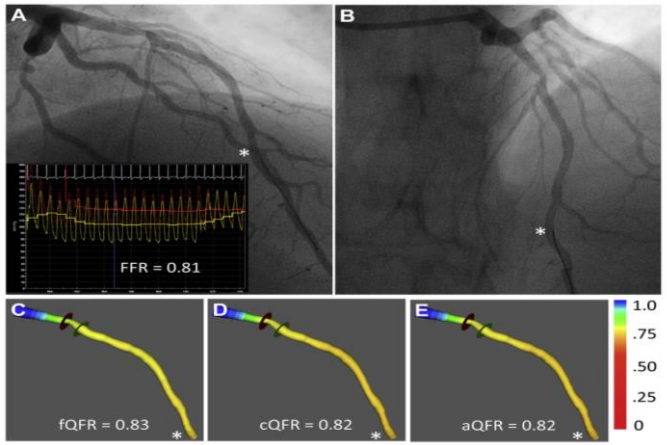


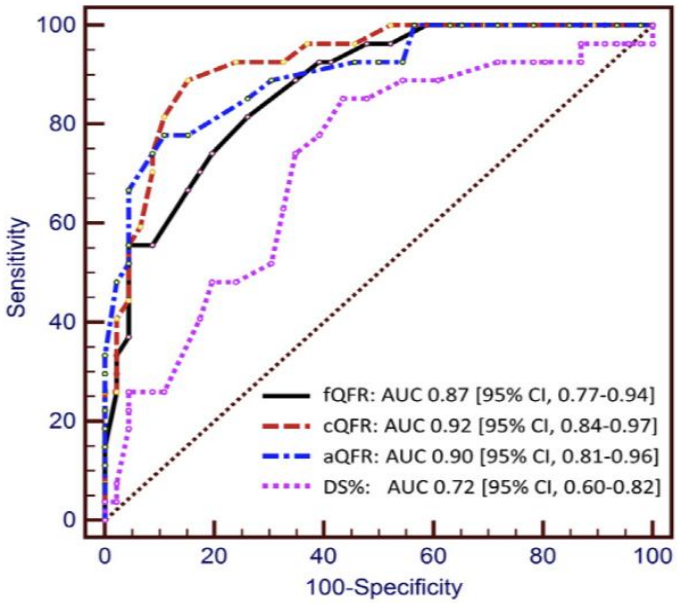
IVUS derived - UFR

Angiography Derived Physiology

QFR Medis MEDICAL IMAGING PULSE

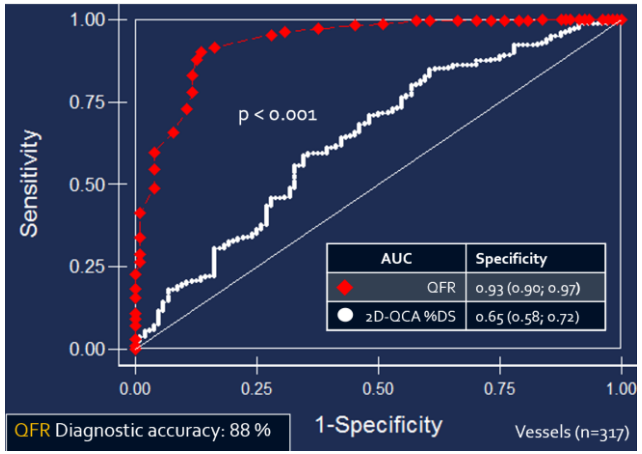
FAVOR I (n= 73)

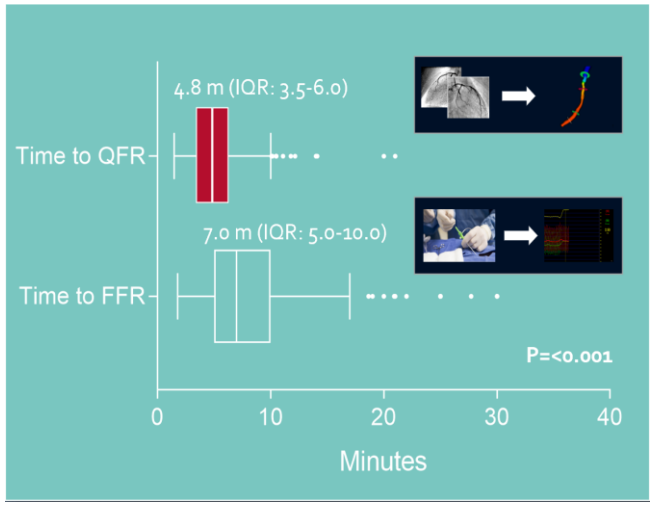




Tu S et al JACC Cardiovasc Intv 2016

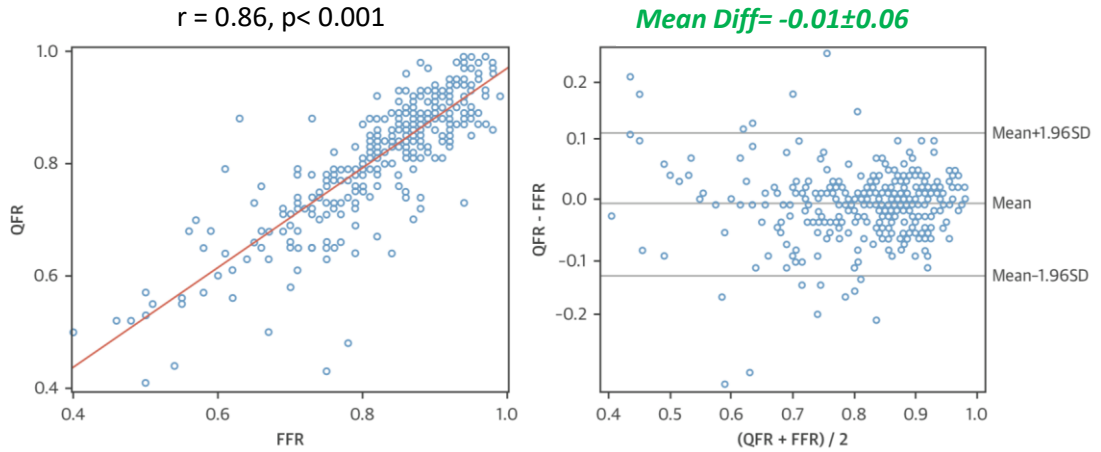
FAVOR II Europe-Japan (n= 272)

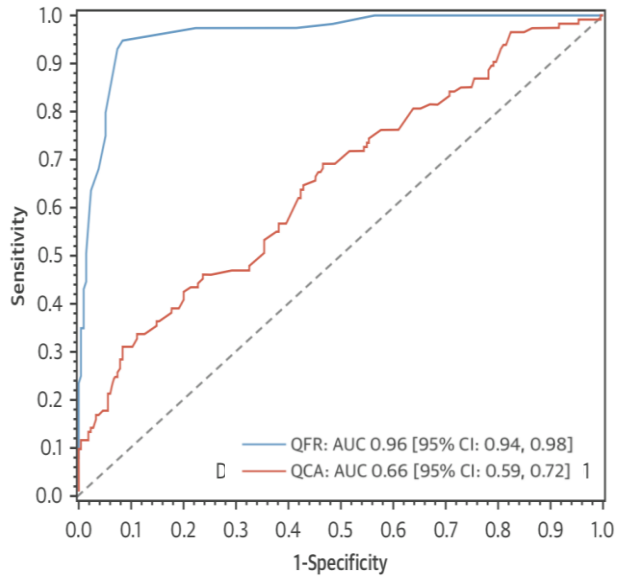




Westra J et al JAHA 2018

FAVOR II China (n= 304)





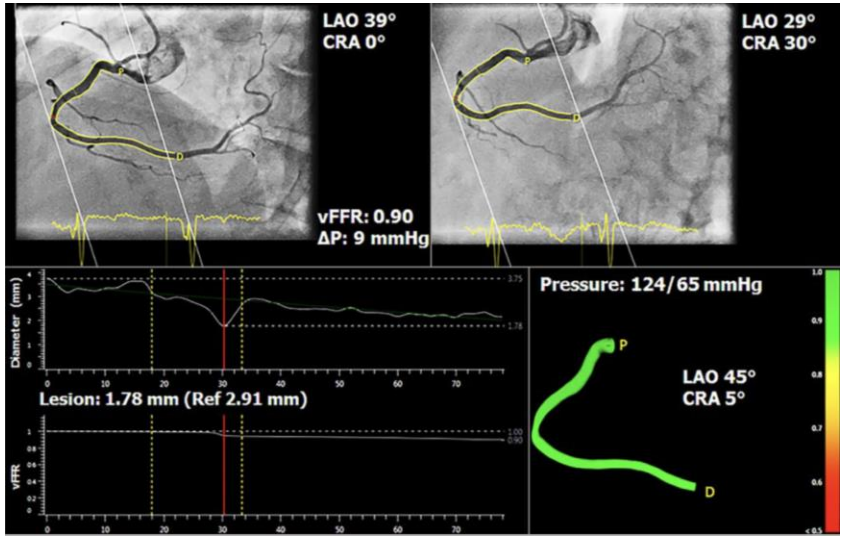
	Estimate, % (95% CI)
Accuracy	92.7 (89.3-95.3)
Sensitivity	94.6 (88.7-98.0)
Specificity	91.7 (87.1-95.0)
PPV	85.5 (78.0-91.2)
NPV	97.1 (93.7-98.9)

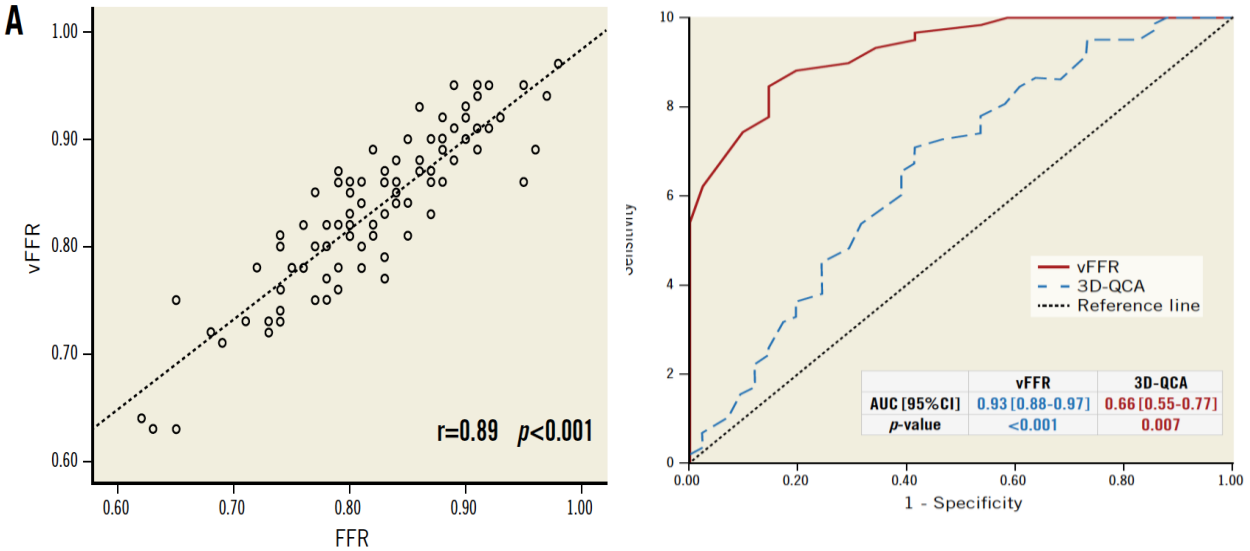
Xu B et al J Am Coll Cardiol 2017

Angiography Derived Physiology

vFFR PIE MEDICAL IMAGING

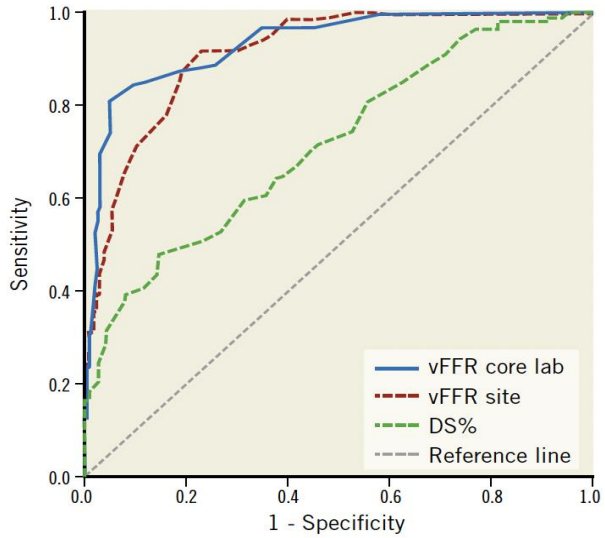
FAST study – 100 pts



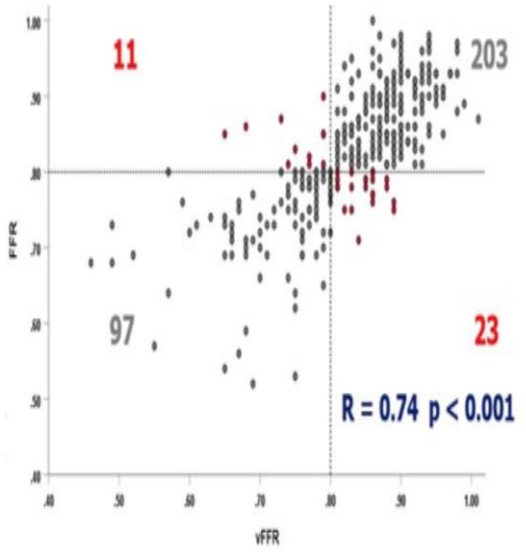


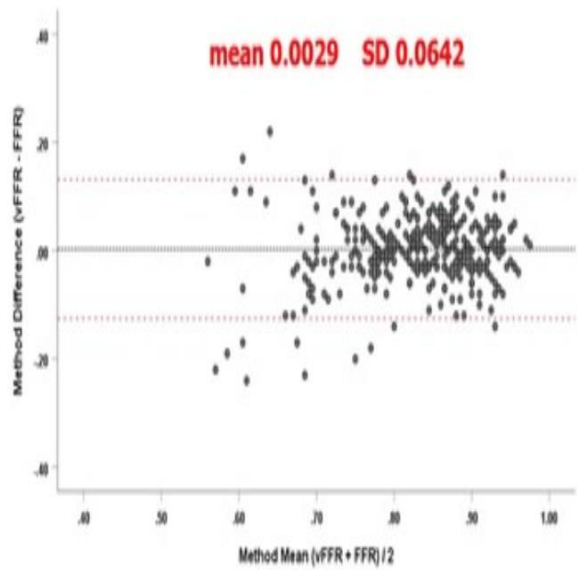
Masdjedi K et al EuroIntervention 2020

FAST II study [Multicenter]– 344 pts



	AUC [95% CI]	p-value
vFFR core lab	0.93 [0.90-0.96]	<0.001
vFFR site	0.91 [0.88-0.94]	<0.001
3D-QCA DS (core lab)	0.71 [0.66-0.77]	<0.001

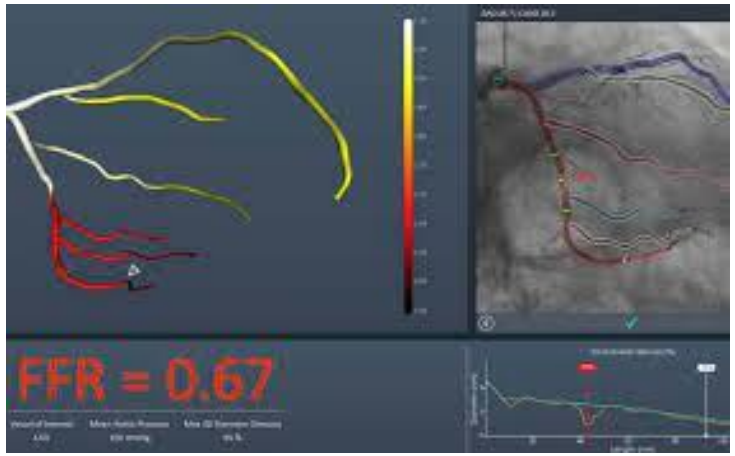




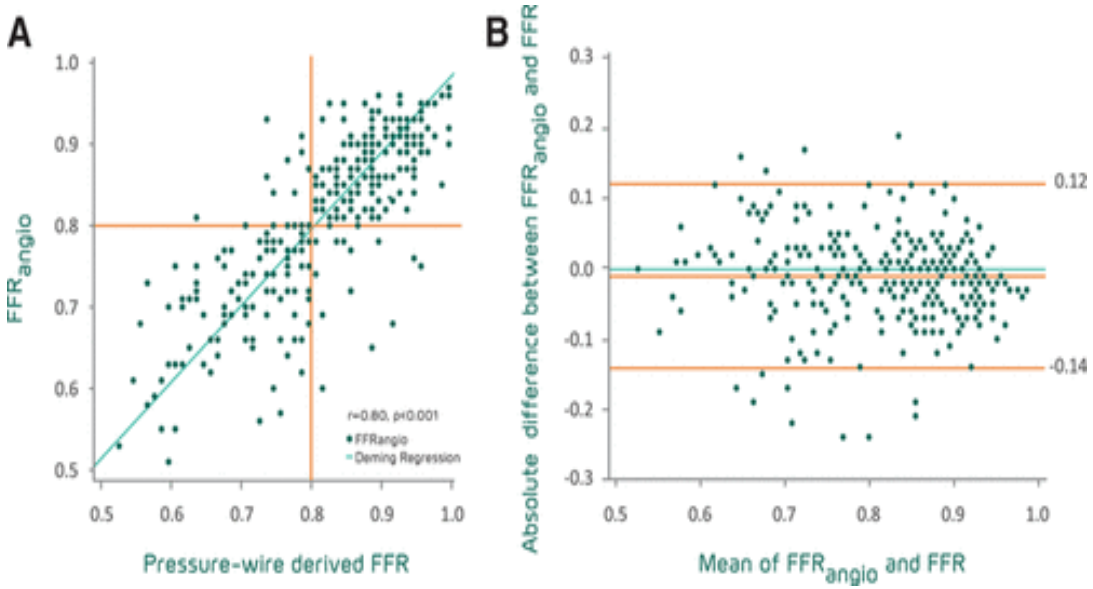
Masdjedi K et al EuroIntervention 2022

Angiography Derived Physiology

FFRangio CATHWORKS

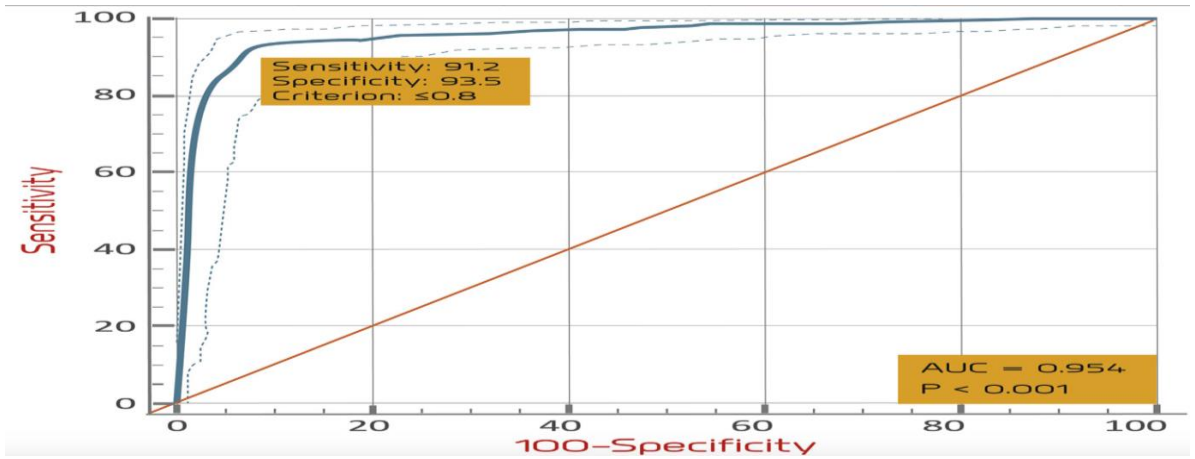


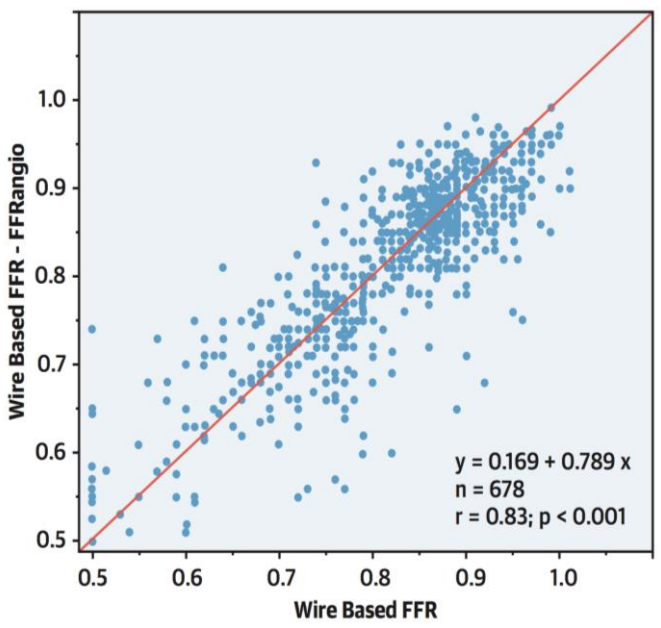
FAST-FFR study – (multicentre) 301 pts, 319 vessels

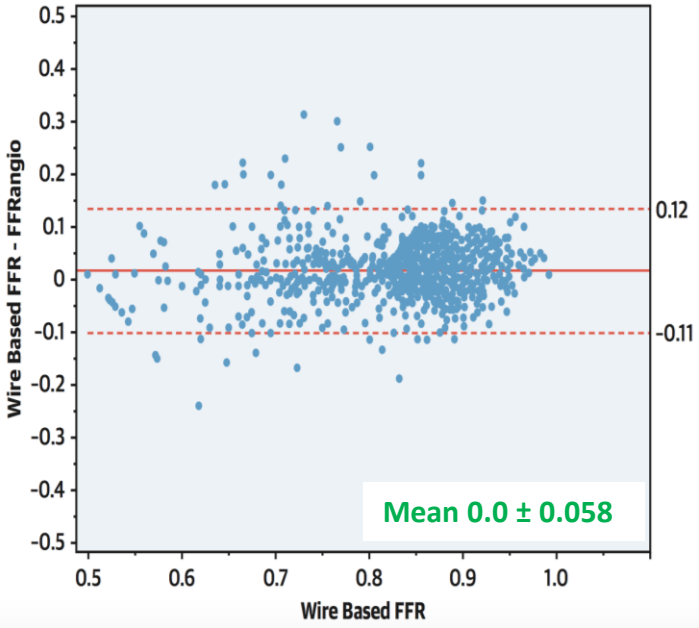


Fearon W et al Circulation 2019

Witberg et al – (multicentre retrospective) 500 pts, 700 vessels



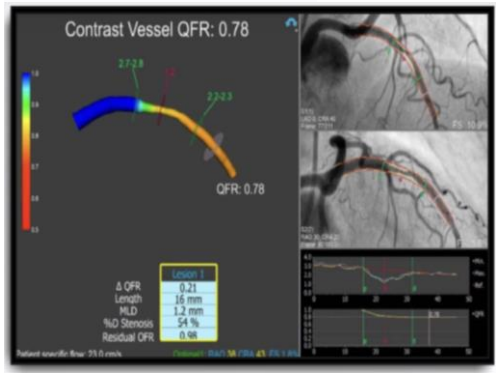




Witberg G et al JACC Cardiovasc Intv 2020

Angiography Derived Physiology

Medis Imaging Solutions in a Heartbeat
MEDICAL IMAGING



QFR

3D Model from 2 views

BP conditions fixed

Flow "measured" as derived from TIMI frame count

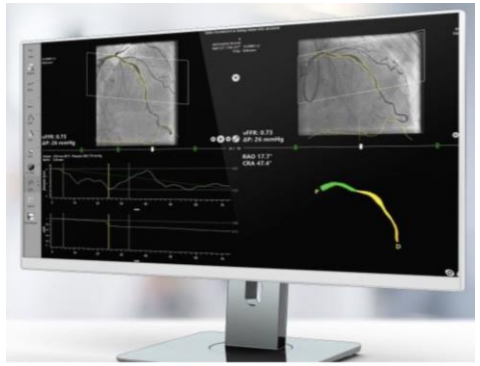
Single vessel

No Bifurcation

No Co-Registration

Manual

Caas
vFFR



vFFR

3D Model from 2 views

Input aortic BP

Flow not "measured" proprietary algorithm

Single vessel

No Bifurcation

No Co-Registration

Manual

CATHWORKS

FFRangio

3D Model from *3 views*

Input aortic BP

Drop Pressure from "lump model" Electrical resistance

Multiple vessels

Bifurcation

No Co-Registration

Manual

RainMed

FlashAngio caFFR

3D Model from 2 views

"Beat by Beat" aortic BP

Flow not "measured" proprietary algorithm

Single vessel

No Bifurcation

No Co-Registration

Manual

PULSE

μFR

3D Model from 1 view

BP conditions fixed

Flow "measured" as derived from TIMI frame count

Single vessel

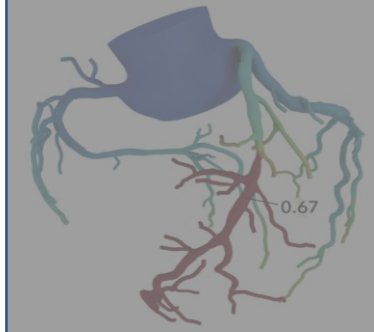
Bifurcation

Co-Registration

AI-Based

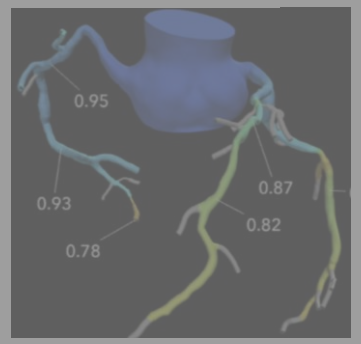
CTCA Derived Physiology

HeartFlow



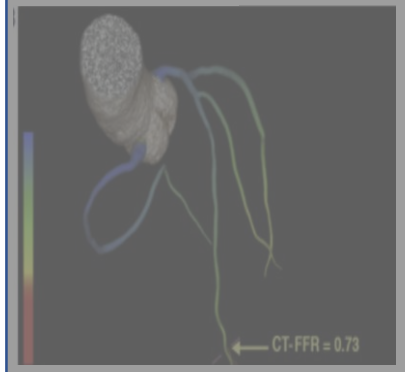
FFR_{CT}

SIEMENS Healthineers



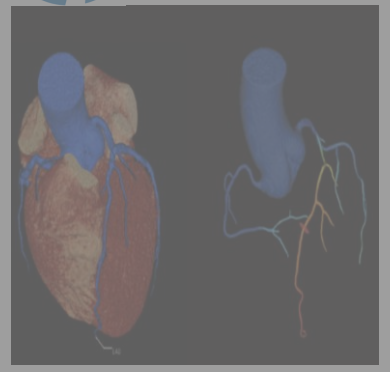
C- FFR

TOSHIBA



CT FFR

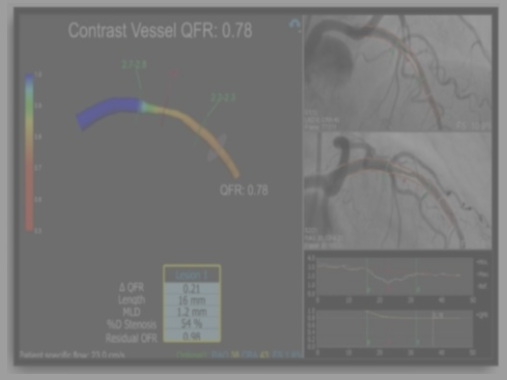
PULSE



CT μFR

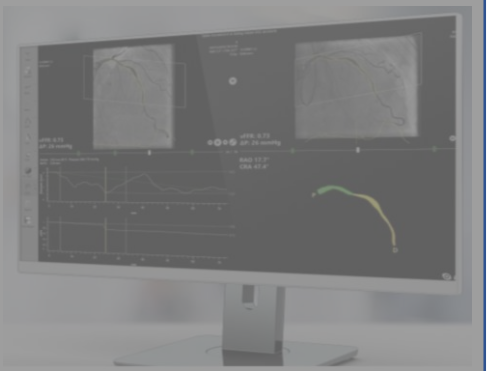
Angiography Derived Physiology

Medis Imaging Solutions in a Heartbeat
MEDICAL IMAGING



QFR

Caas
vFFR



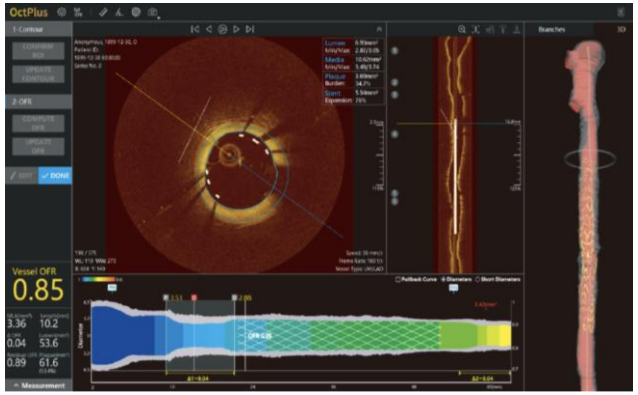
vFFR

CATHWORKS

FFRangio

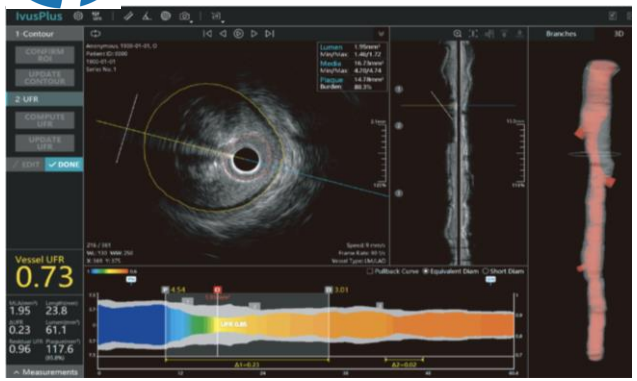
Intravascular Imaging Derived Physiology

PULSE



OCT derived - OFR

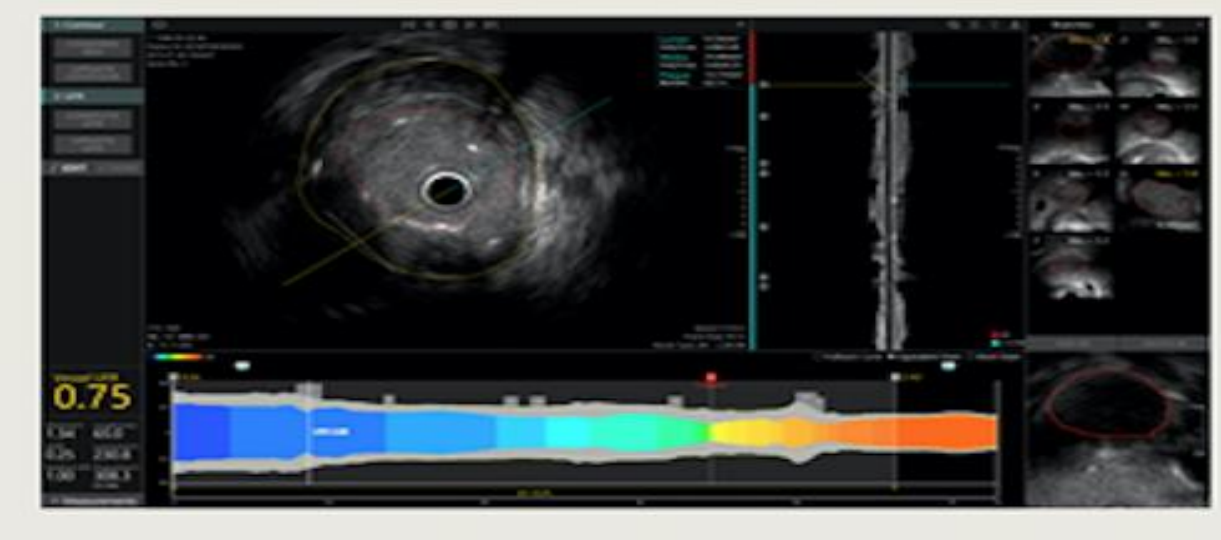
PULSE



IVUS derived - UFR

Intravascular Imaging Derived Physiology

UFR



N = 94 pts, 97 vessels

A B

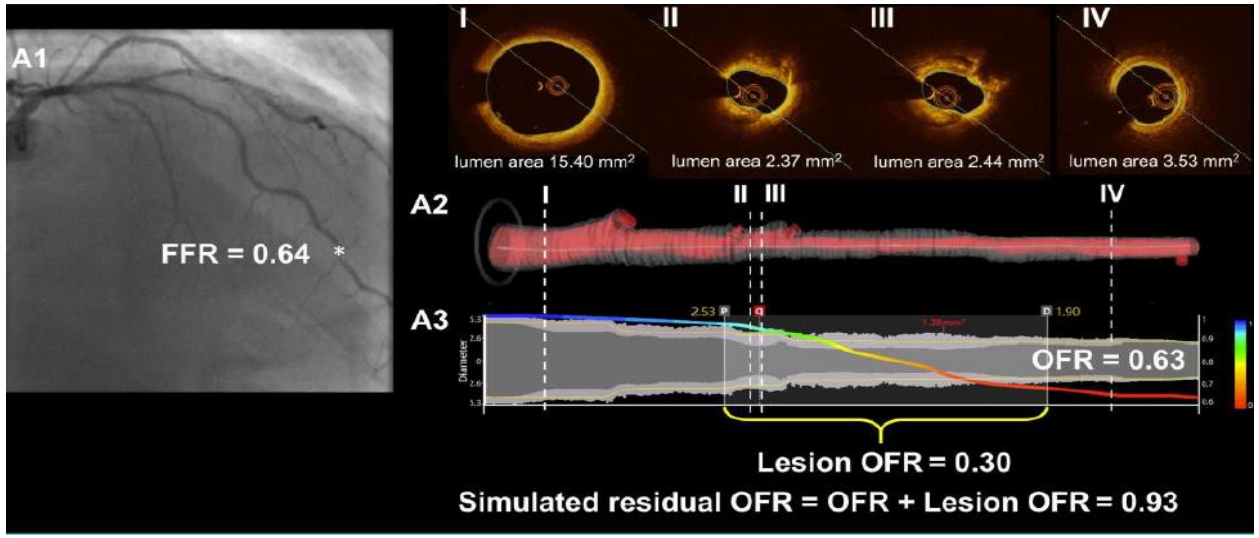
Table 3. Diagnostic Performance of UFR- and IVUS-Derived MLA to Identify FFR≤0.80

	UFR≤0.80	MLA≤2.01 mm²
Accuracy, % (95% CI)	92 (87–96)	83 (78–89)
Sensitivity, % (95% CI)	91 (82–96)	89 (81–95)
Specificity, % (95% CI)	96 (90–99)	78 (68–87)
PPV, % (95% CI)	96 (89–99)	81 (71–88)
NPV, % (95% CI)	91 (93–96)	88 (78–94)

FFR

Yu W et al Circ Intv 2021

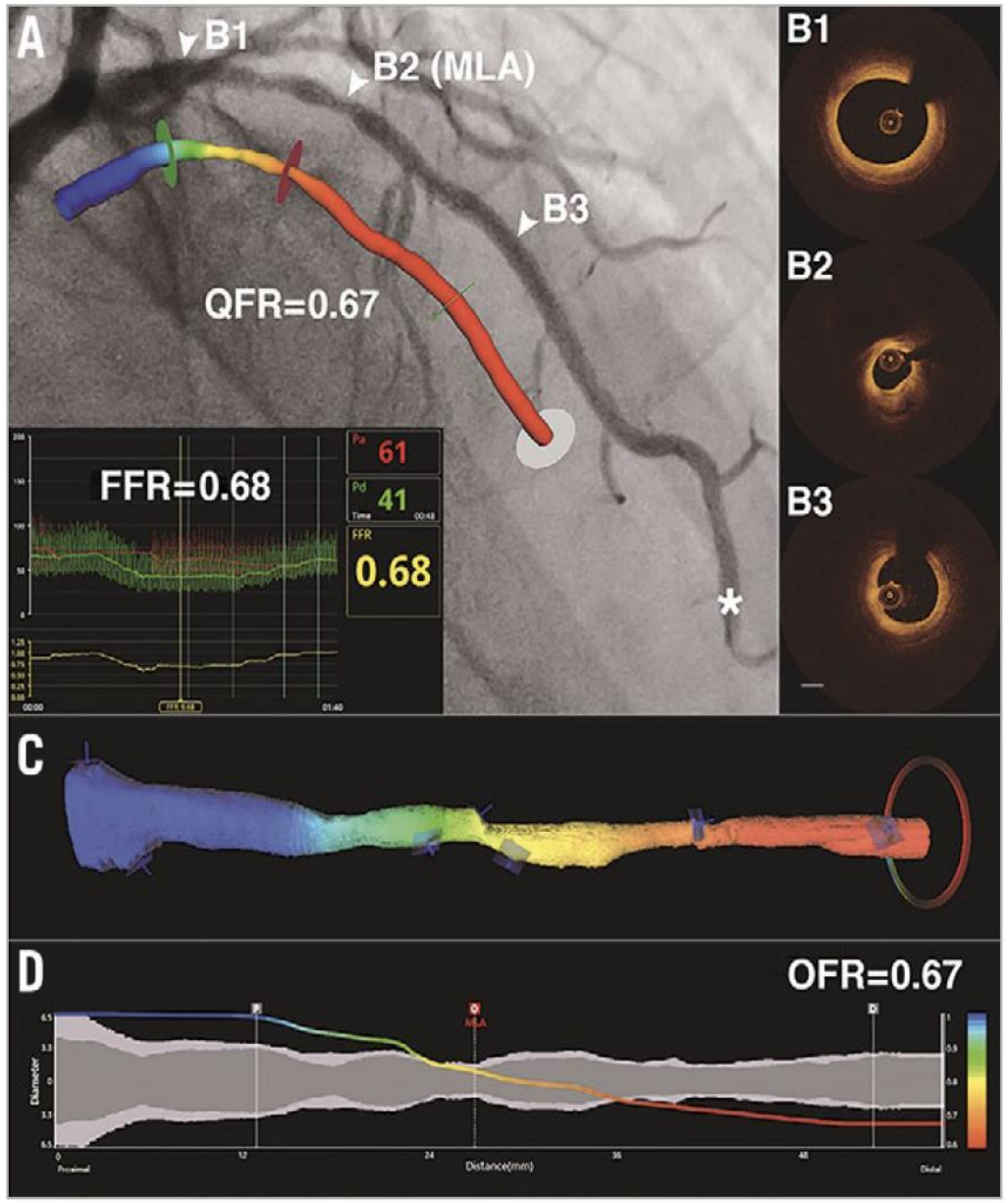
OFR

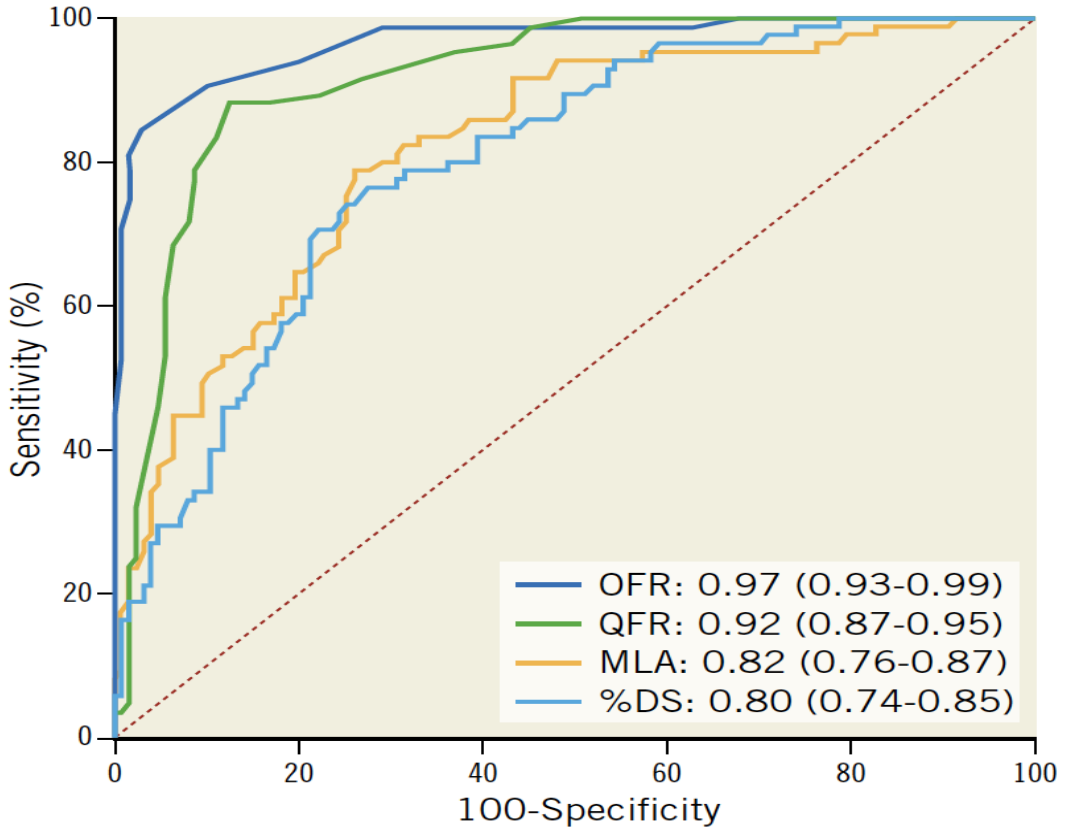


N = 118 pts, 125 vessels

	OFR ≤0.80	MLA ≤1.89
Accuracy, % (95% CI)	90 (84-95)	74 (67-82)
Sensitivity, % (95% CI)	87 (77-94)	78 (66-87)
Specificity, % (95% CI)	92 (82-97)	71 (58-82)
PPV, % (95% CI)	92 (82-97)	73 (61-83)
NPV, % (95% CI)	88 (77-95)	76 (63-86)
LR+ (95% CI)	10.8 (4.6-25.2)	2.7 (1.8-4.0)
LR– (95% CI)	0.1 (0.1-0.3)	0.3 (0.2-0.5)

N = 181 pts; 212 vessels





	OFR ≤0.80	OCT-derived MLA ≤1.88	QFR ≤0.80	3D QCA-derived %DS >50.7%
Accuracy	92 (88-95)	76 (70-82)	87 (83-92)	75 (69-80)
Sensitivity	86 (77-93)	79 (69-87)	88 (79-94)	74 (64-83)
Specificity	95 (90-98)	74 (66-81)	87 (80-93)	75 (66-82)
PPV	92 (84-97)	67 (57-76)	82 (73-90)	66 (56-76)
NPV	91 (85-95)	84 (76-90)	92 (85-96)	81 (73-88)

Huang J et al EuroIntervention 2020

Applications

#1 : Defining Indication for Stenting

#2 : Assessing final PCI results

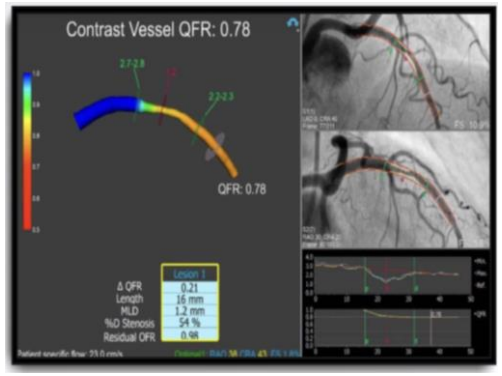
#3 : Define Pattern & Distribution of Atherosclerosis

#4 : Planning PCI strategy

#5 : Optimising PCI result

#1 : Defining Indication for Stenting

CathLab vs No Cathlab



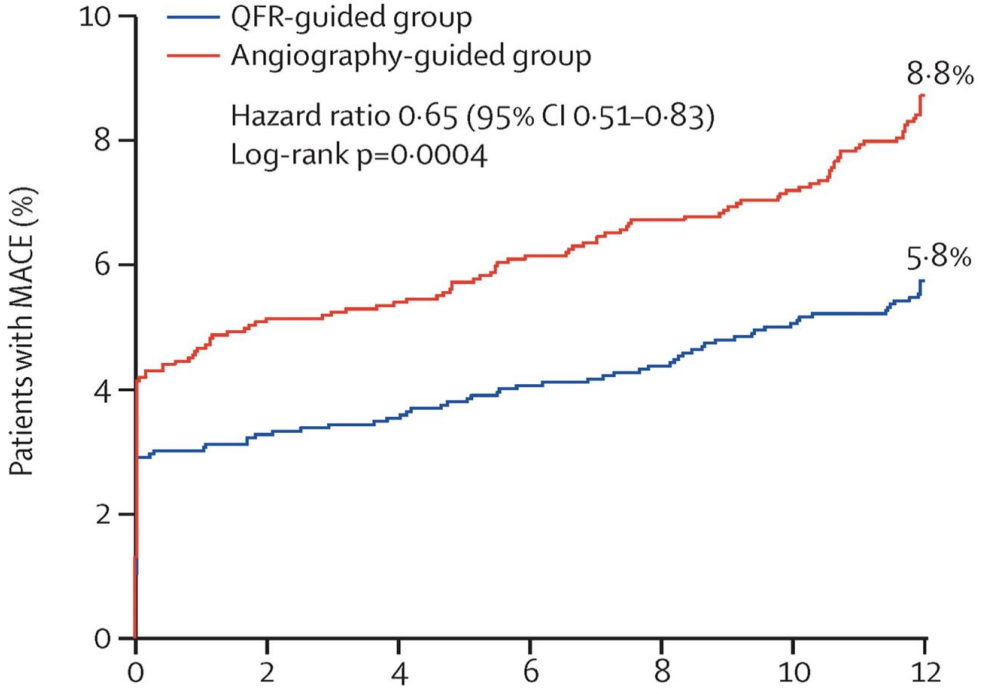
Stenting vs Medical Therapy

FAVOR III CHINA

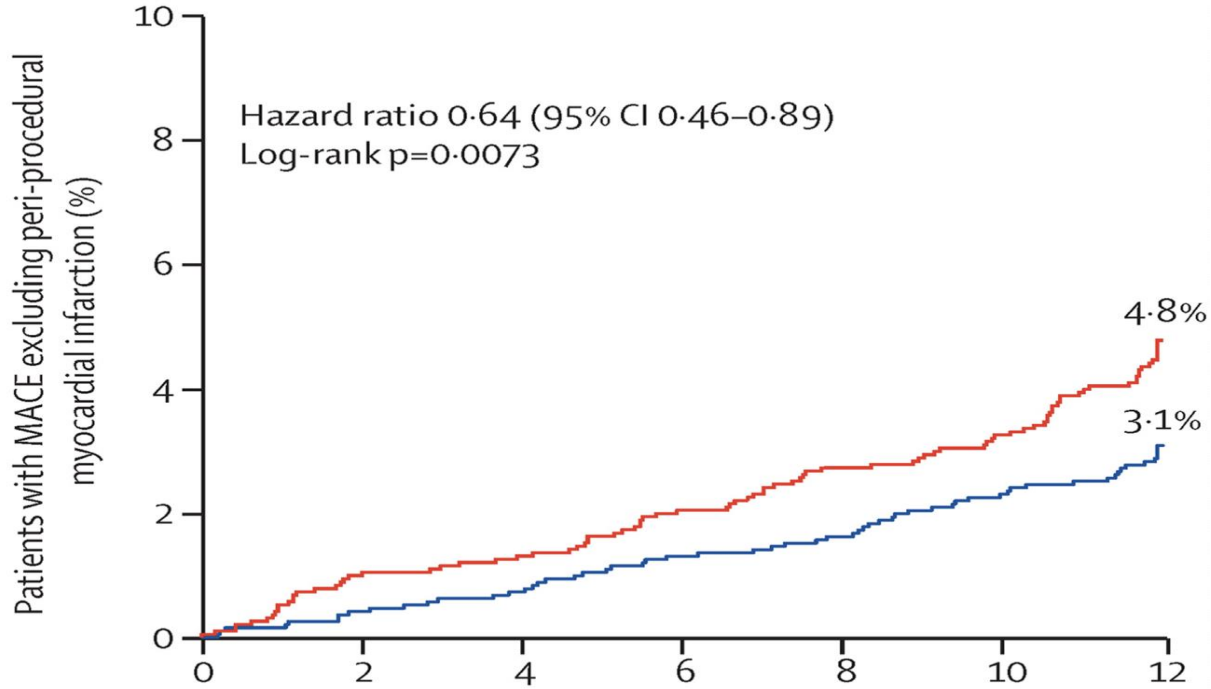
- 3825 Patients referred for PCI (stable CAD or > 72h NSTE-ACS)
- Stenosis Diameter 50-90%

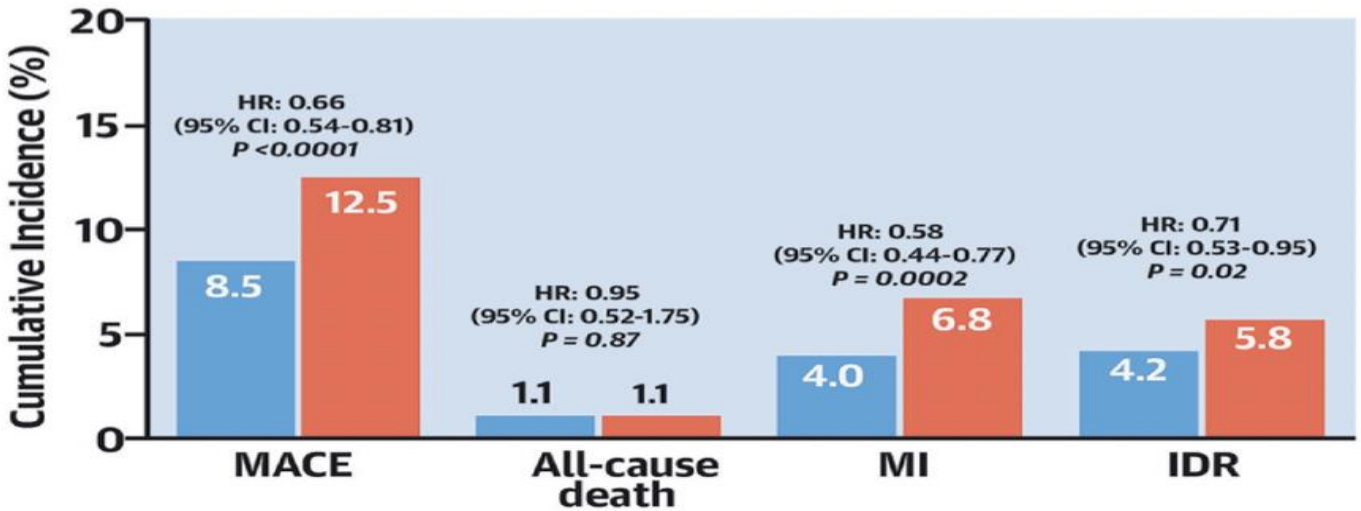
	QFR-guided group (n=1913)	Angiography-guided group (n=1912)	p value
Radial artery approach	1885 (98·5%)	1869 (97·8%)	0·071
PCI performed	1731 (90·5%)	1895 (99·1%)	<0·0001
Drug-eluting stents placed	1667 (87·1%)	1812 (94·8%)	<0·0001
Drug-coated balloon angioplasty	55 (2·9%)	58 (3·0%)	0·77
Non-drug-coated balloon angioplasty	9 (0·5%)	25 (1·3%)	0·0049
Number of stents placed per patient	1·45 (1·02)	1·58 (0·97)	<0·0001
Stent length, mm	42·7 (26·3)	41·9 (26·3)	0·36
Stent diameter, mm	3·03 (0·41)	3·01 (0·41)	0·34
Patients with intended vessel deferral or unintended vessel treatment	445 (23·3%)	119 (6·2%)	<0·0001

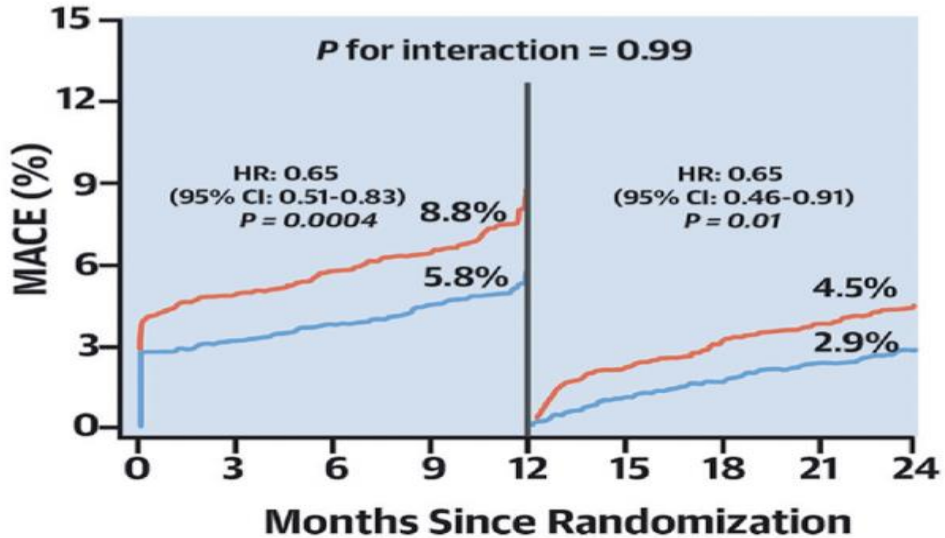
MACE = Death, All MI, Ischaemia Driven Revasc



MACE = Death, MI (no periprocedural), Ischaemia Driven Revasc







Song L, et al. J Am Coll Cardiol. 2022;80(22):2089–2101.

Superior to Angiogram …. But Equivalent to wire-based FFR?

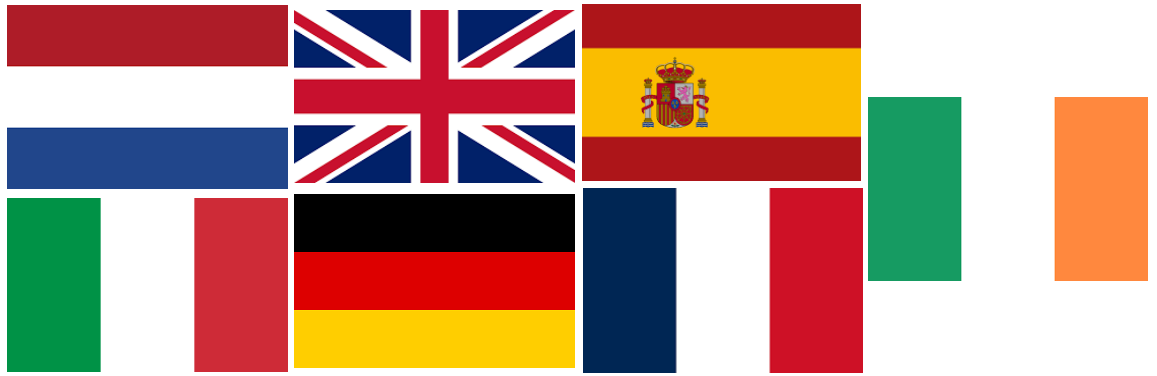
FAVOR III Europe Japan

Functional Assessment by Virtual Online Reconstruction

2000 patients randomized to QFR guidance
vs
wb-FFR guidance

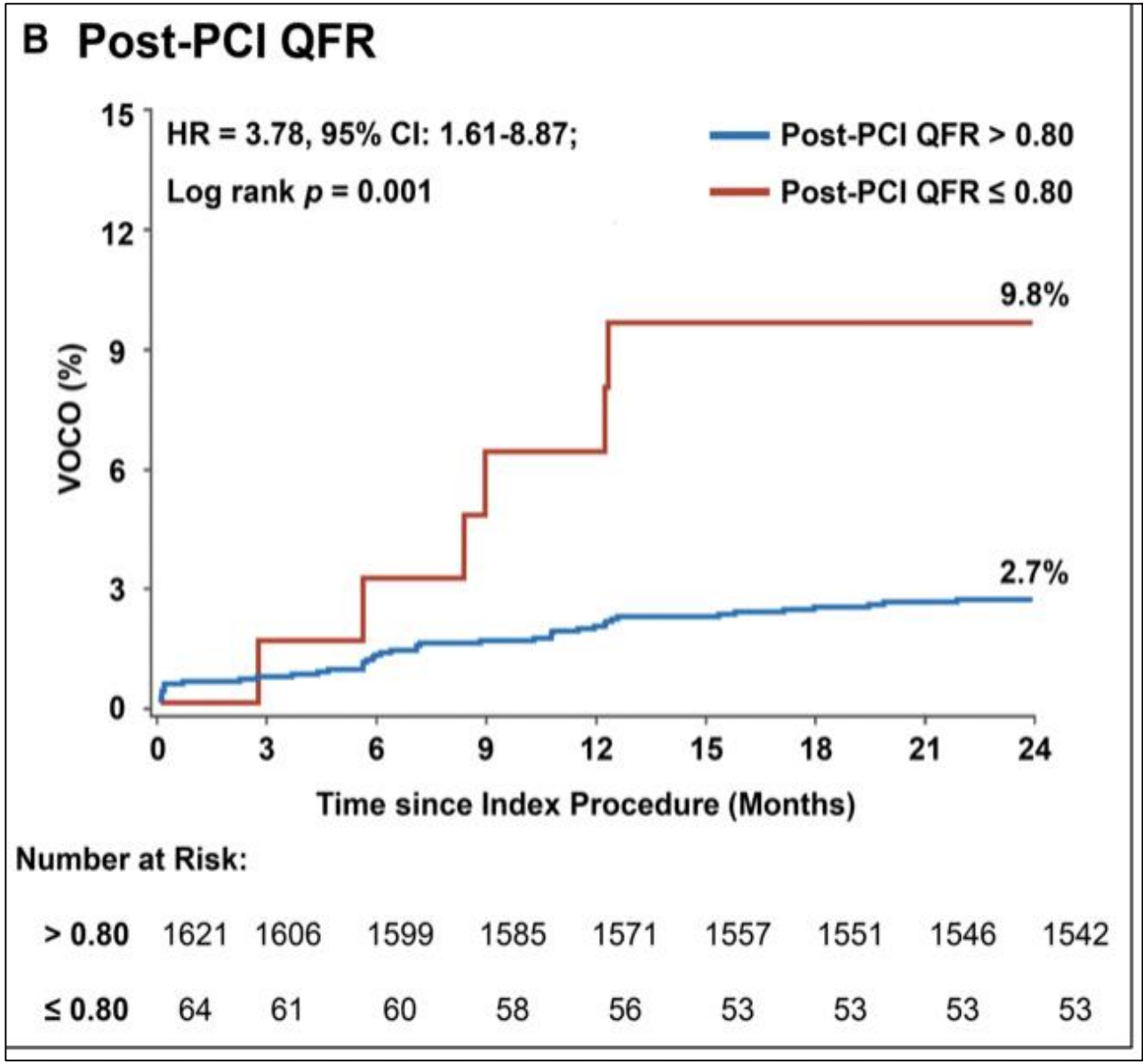
FAST3

2228 patients randomized to vFFR guidance
vs
wb-FFR guidance



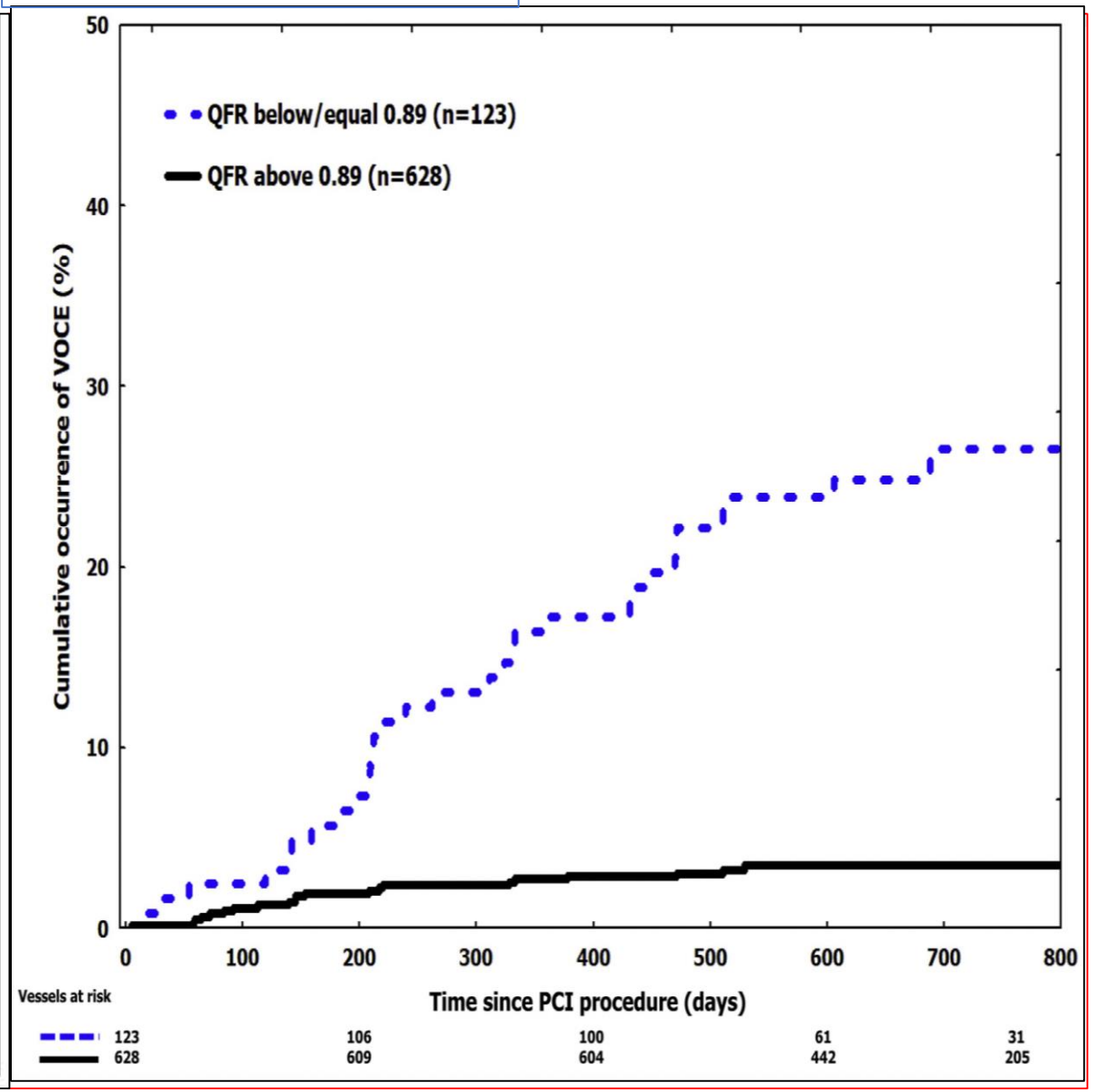
Application #2: Assessing Final PCI result

N = 1395 pts, 1685 vessels



Dan N et al JAHA 2022 – PANDA III study

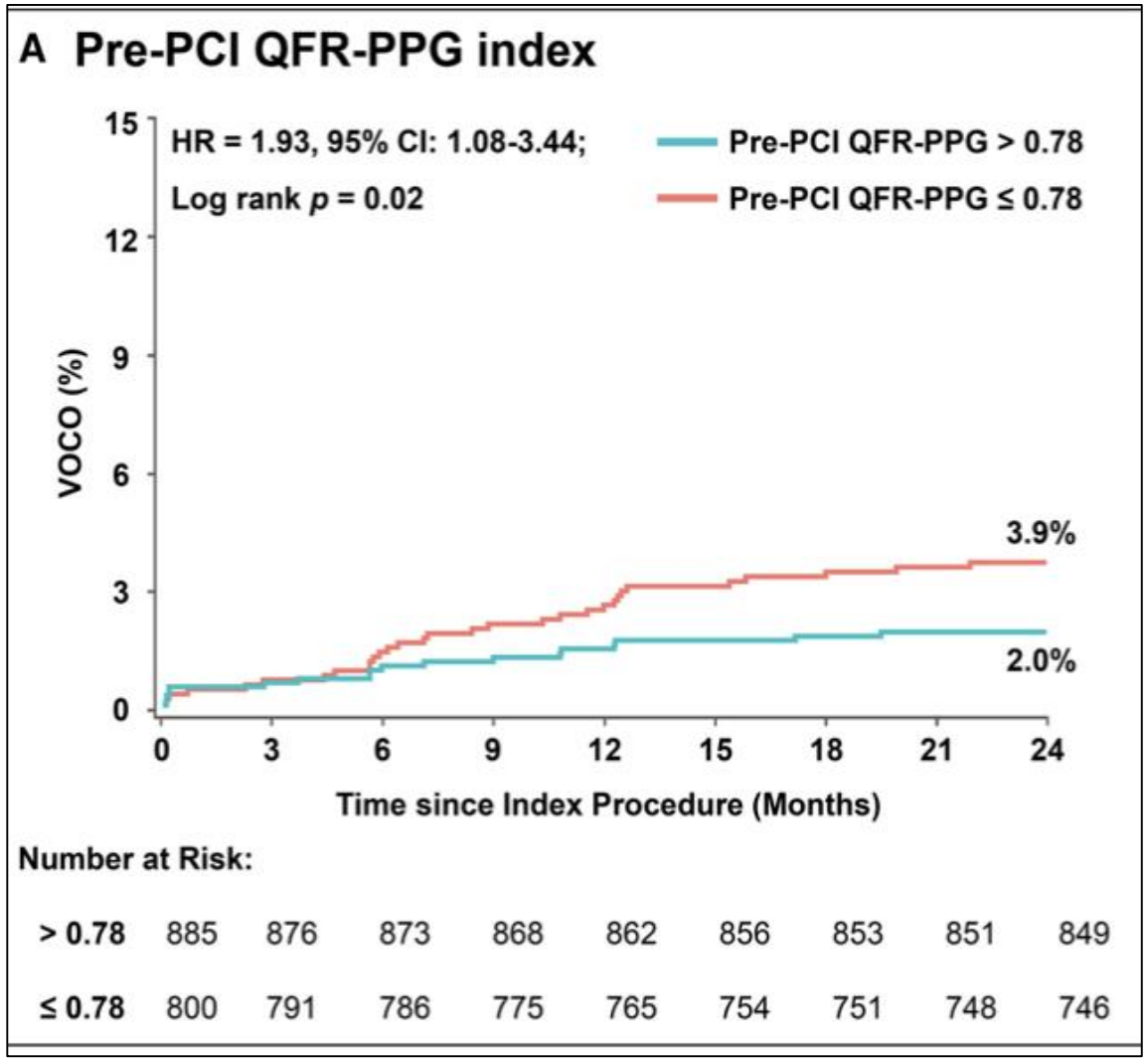
N = 602 pts, 751 vessels

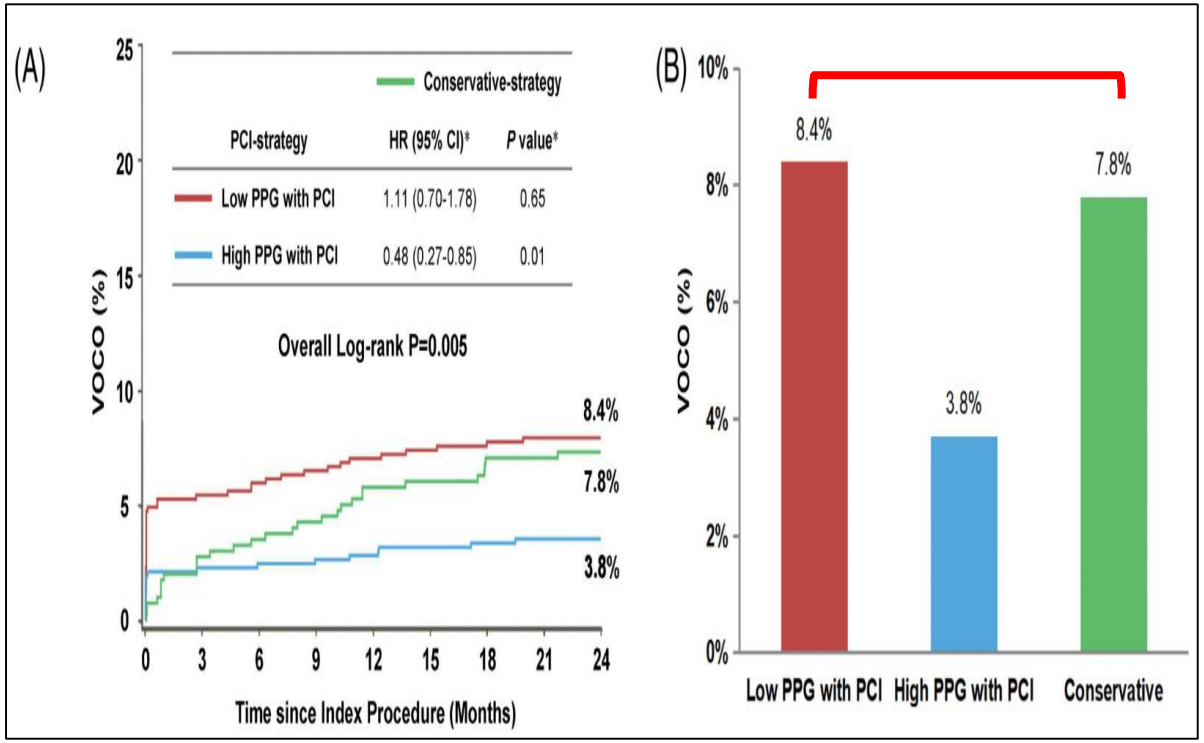


Biscaglia S et al JACC Intv 2019 – HAWKEYE study

Application #3: Defining pattern of atherosclerosis

N = 1003 pts, 1444 vessels ***ALL with QFR < 0.80***





Dan N et al JAHA 2022 – PANDA III study
Dan N et al CCI 2022

Revascularization with successful stent implantation

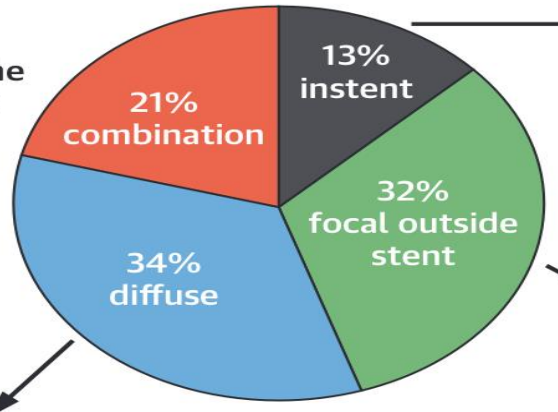
Post-PCI measurement of QFR → QFR value >0.89

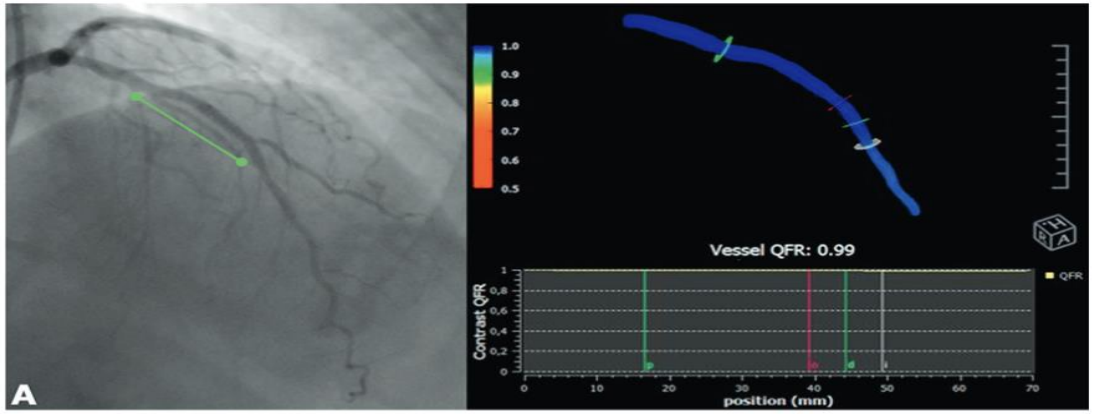
Low rate of adverse events and need of repeat revascularization

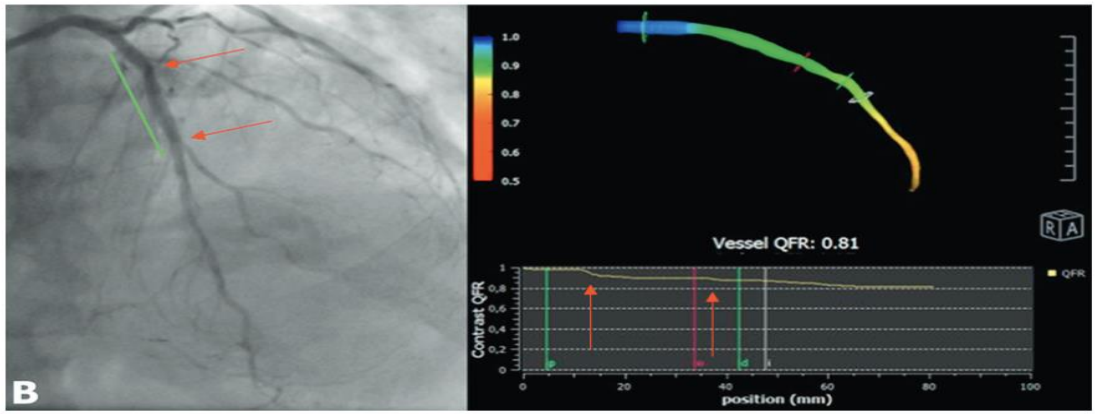
QFR value ≤0.89

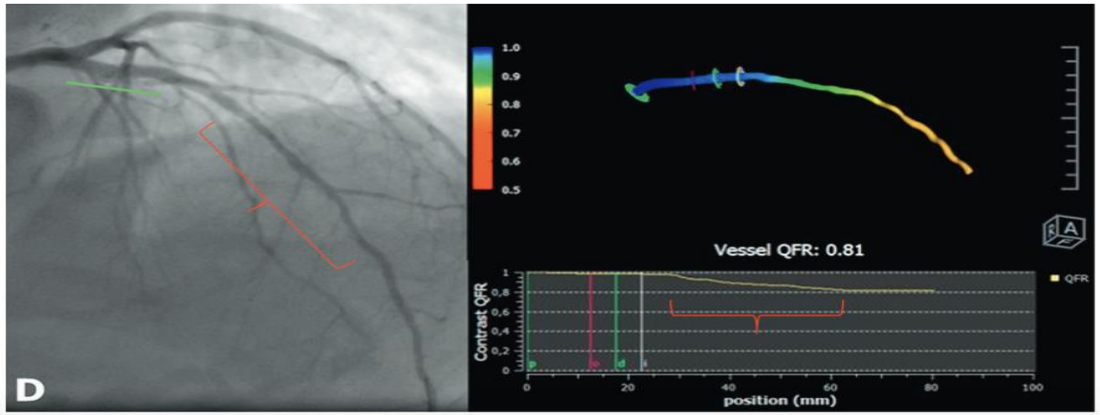
3-time increase in the risk of VOCE
Adjusted HR 2.91, 95% CI 1.63-5.19

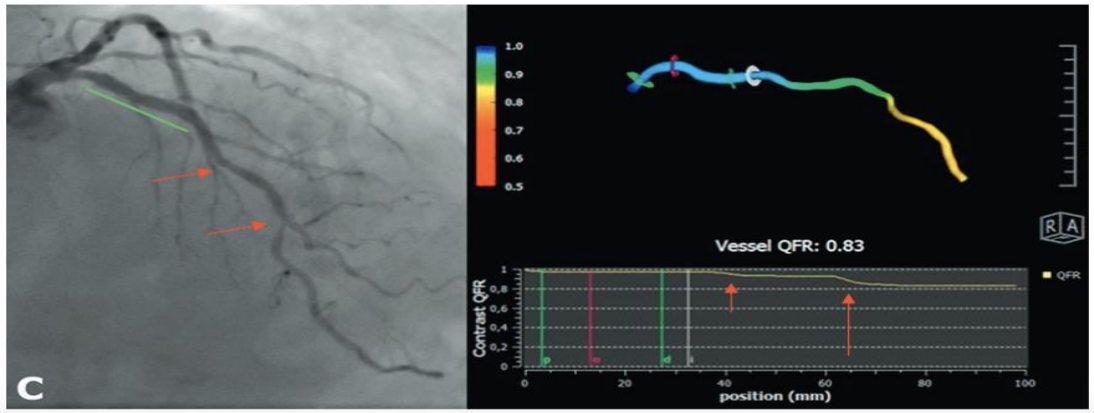
Identification of the site of QFR drop







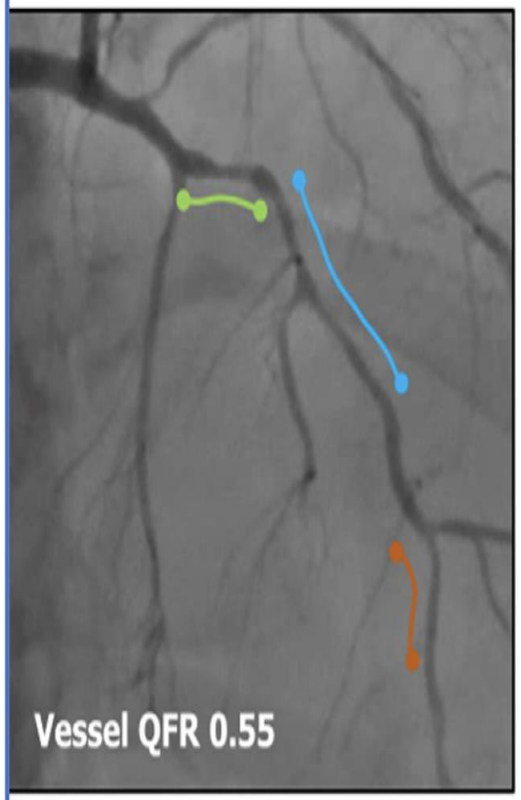




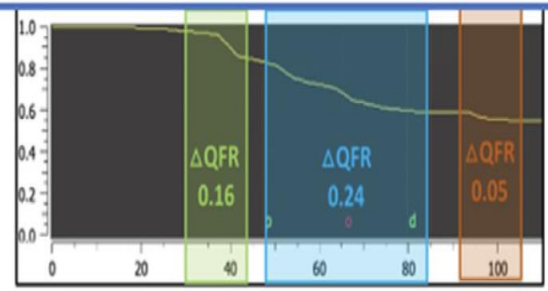
Biscaglia S et al JACC Intv 2019 – HAWKEYE study

Application #4: Planning PCI

LEAVE FOCAL LESION

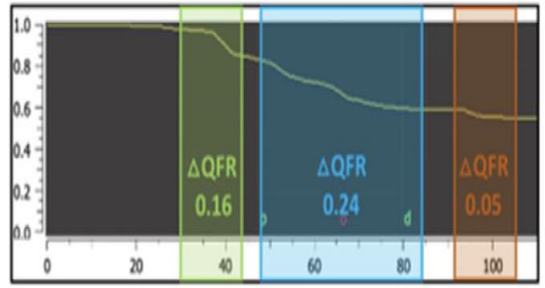


OPTION 1



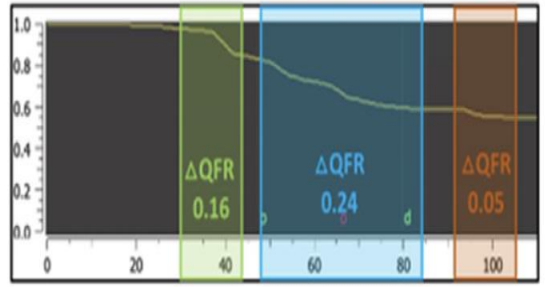
RESIDUAL QFR 0.76

OPTION 2



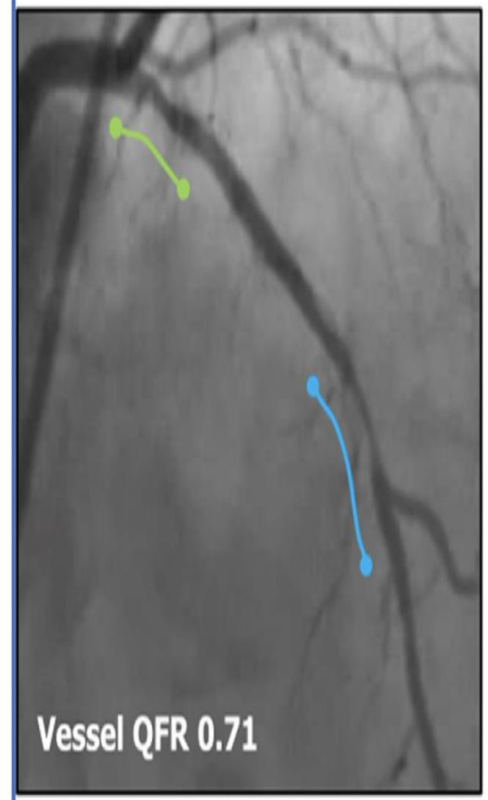
RESIDUAL QFR 1.00

OPTION 3

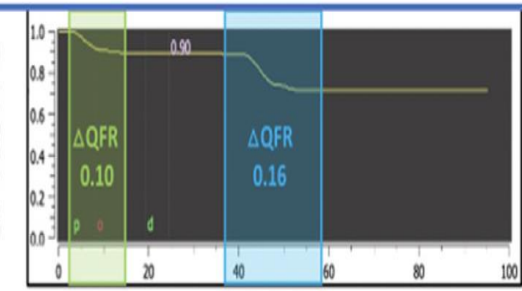


RESIDUAL QFR 0.95

TREAT SERIAL LESIONS

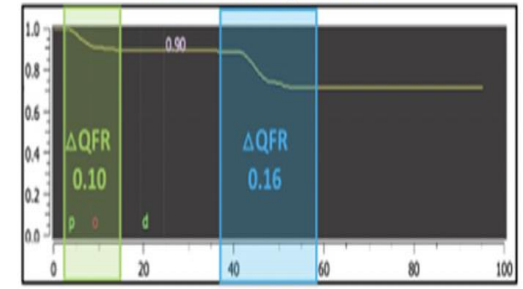


OPTION 1



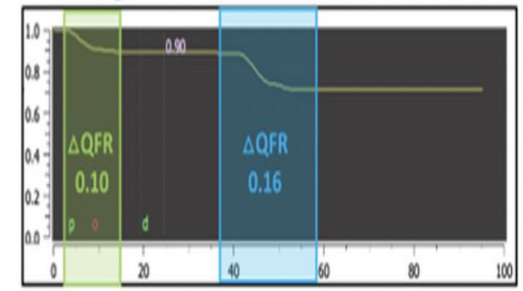
RESIDUAL QFR 0.87

OPTION 2



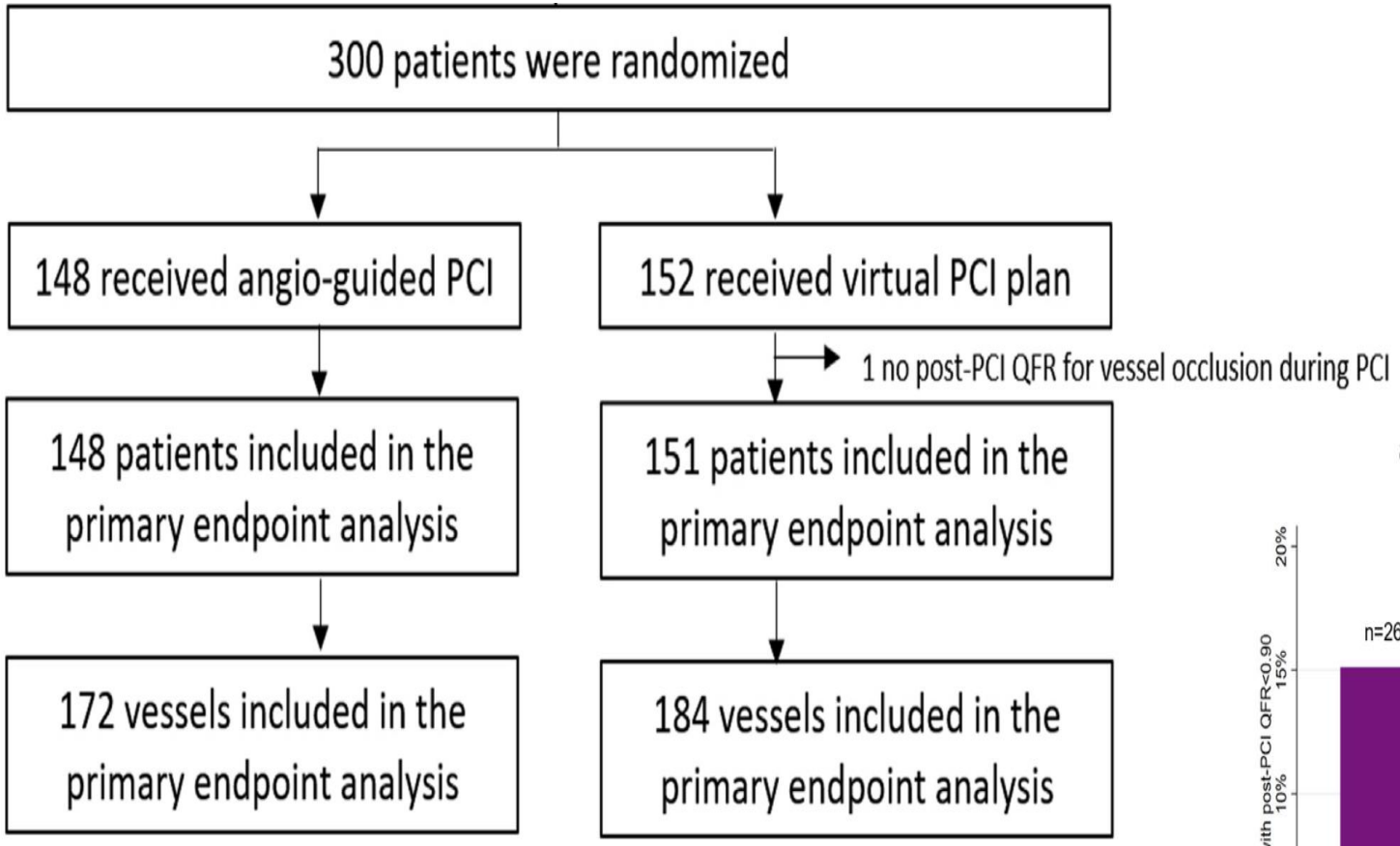
RESIDUAL QFR 0.81

OPTION 3



RESIDUAL QFR 0.97

AQVA study



Primary Endpoint: rate of vessels with post-PCI QFR < 0.90

ARTICLE IN PRESS

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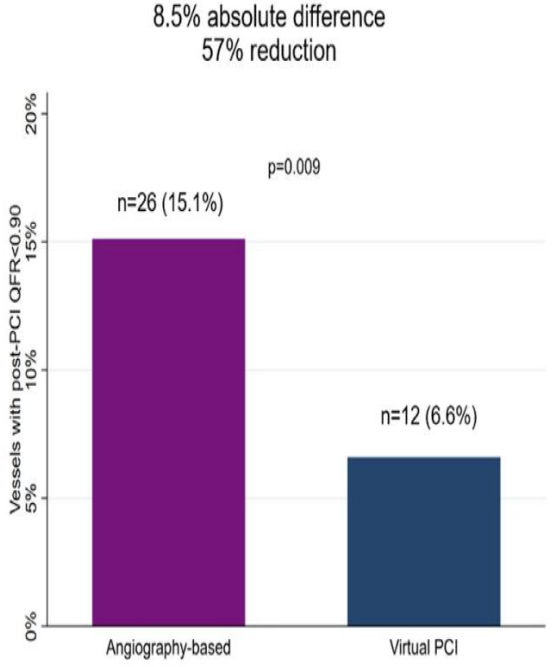
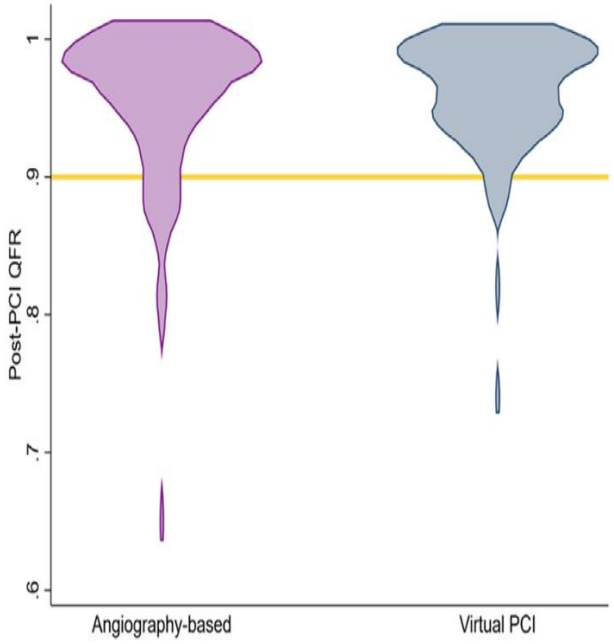
QFR-Based Virtual PCI or Conventional Angiography to Guide PCI

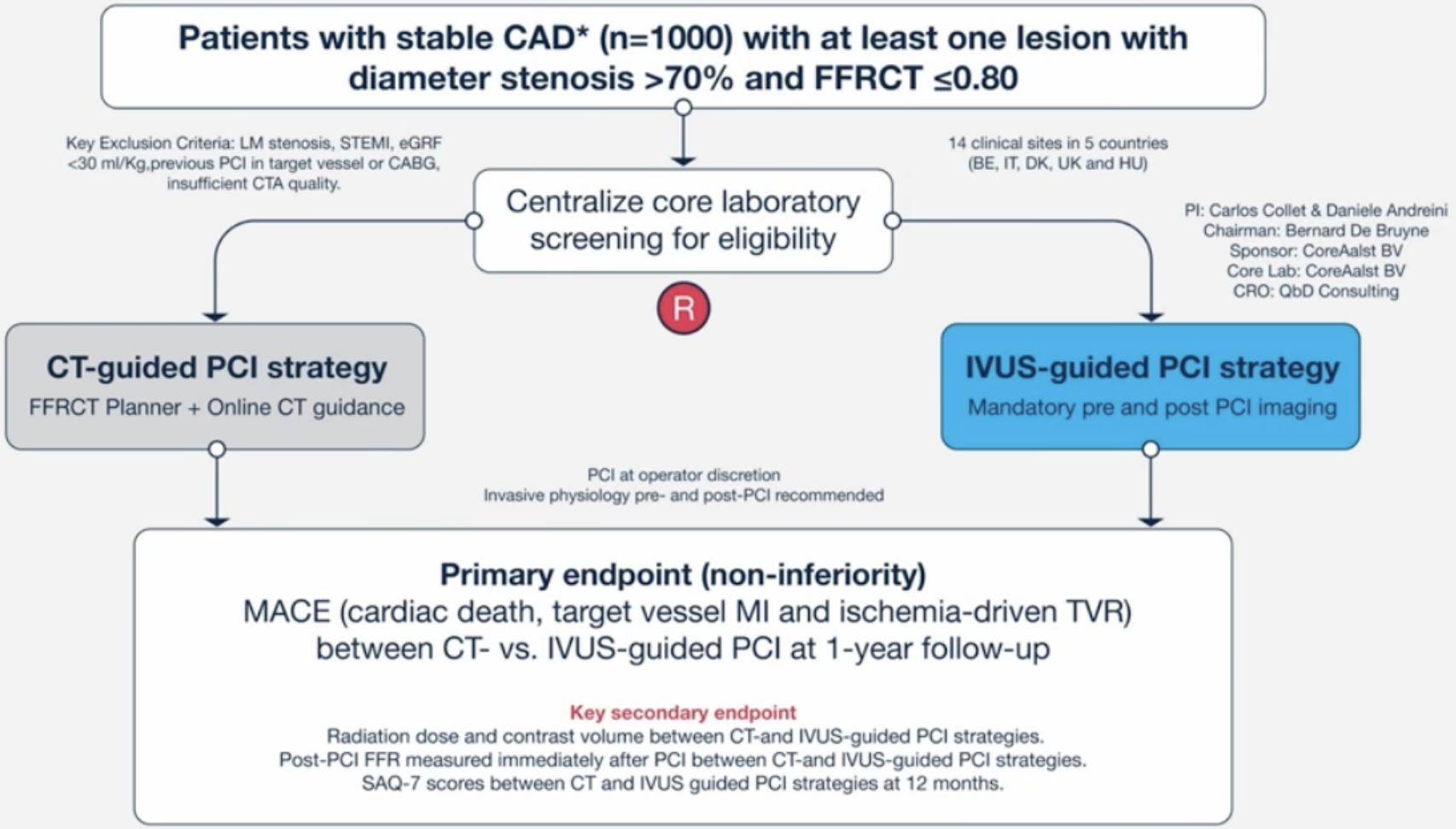
The AQVA Trial

Simone Biscaglia, MD,[a] Filippo Maria Verardi, MD,[a] Matteo Tebaldi, MD,[a] Vincenzo Guiducci, MD,[b] Serena Caglioni, MD,[a] Roberta Campana, MD,[a] Antonella Scala, MD,[a] Andrea Marrone, MD,[a] Graziella Pompei, MD,[a] Federico Marchini, MD,[a] Davide Scancarello, MD,[a] Gianluca Pignatelli, MD,[b] Sergio Musto D'Amore, MD,[b] Iginio Colaiori, MD,[b] Pierluigi Demola, MD,[b] Luigi Di Serafino, MD,[c] Carlo Tumscitz, MD,[a] Carlo Penzo, MD,[a] Andrea Erriquez, MD,[a] Marco Manfrini, BSc,[d] Gianluca Campo, MD[a]





P4 RCT



Hypothesis: A CT-guided PCI strategy is **non-inferior** to IVUS guided PCI with respect to **MACE**

Application #5: Optimizing PCI results

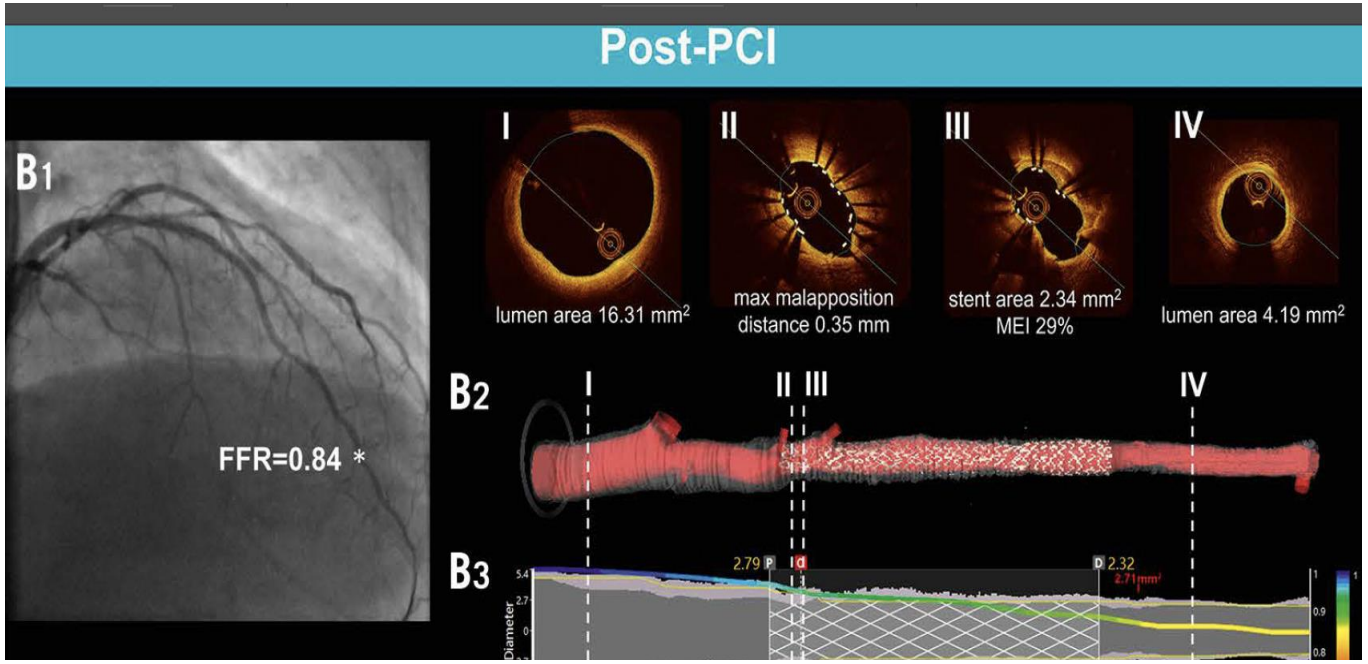
Optical flow ratio for assessing stenting result and physiological significance of residual disease

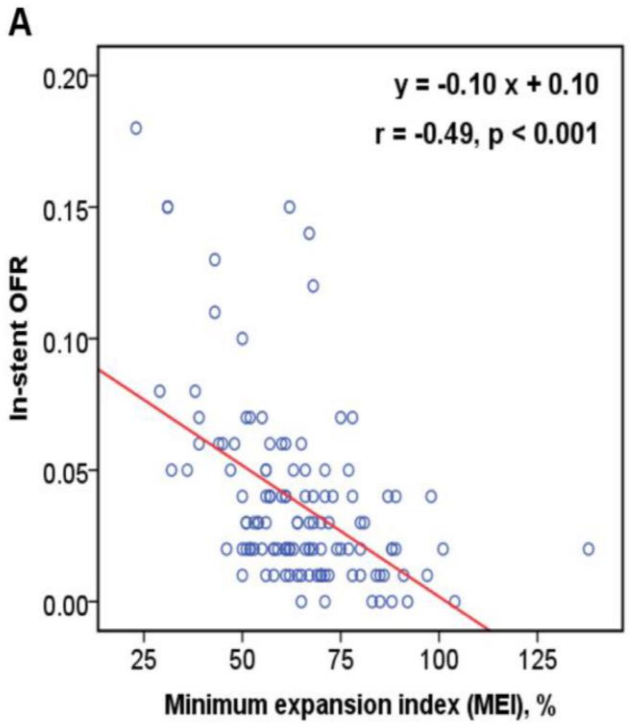
Daixin Ding[1,2], MSc; Wei Yu[1], BSc; Hélène Tauzin[3], PhD; Giovanni Luigi De Maria[4], MD, PhD; Peng Wu[1], BSc; Fan Yang[1], BSc; Rafail A. Kotronias[4], MBChB, MSc; Dimitrios Terentes-Printzios[4], MD, PhD; Mathias Wolfrum[4], MD; Adrian P. Banning[4], MBBS, MD; Nicolas Meneveau[3], MD, PhD; William Wijns[2], MD, PhD; Shengxian Tu[1,5]*, PhD

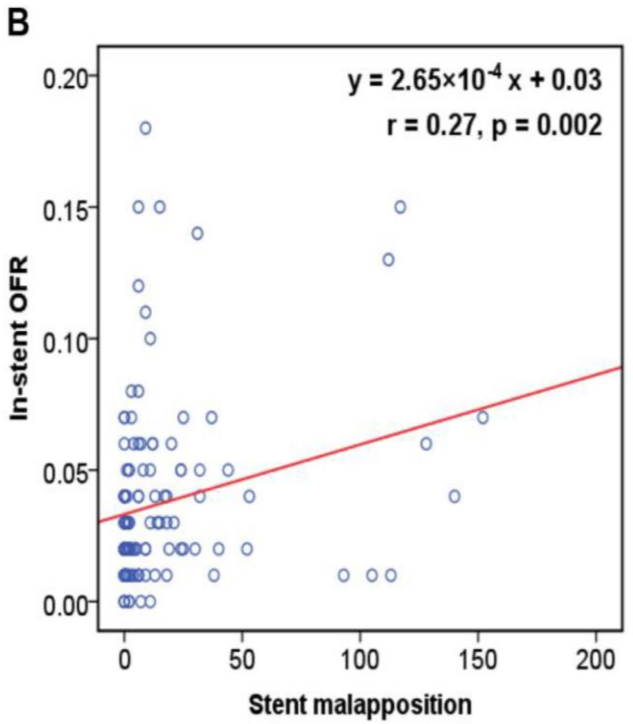
1. Biomedical Instrument Institute, School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, China; 2. The Lambe Institute for Translational Medicine and CÚRAM, National University of Ireland Galway, Galway, Ireland; 3. Department of Cardiology, University Hospital Jean Minjoz, Besançon, France; 4. Oxford Heart Centre, John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom; 5. Department of Cardiology, Fujian

N = 155 pts (DOCTORS & OxOPT studies)

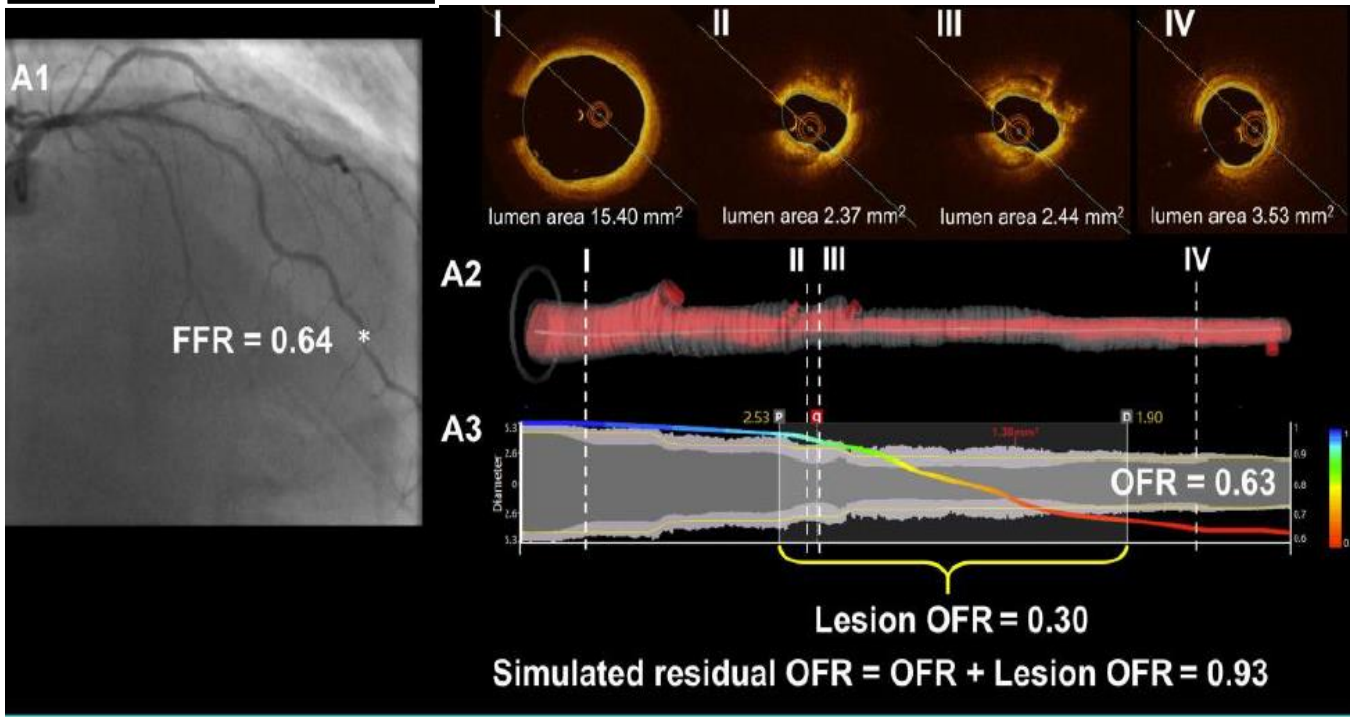
	Post-PCI OFR ≤0.90
Accuracy, % (95% CI)	84 (77-91)
Sensitivity, % (95% CI)	61 (44-77)
Specificity, % (95% CI)	93 (86-98)
PPV, % (95% CI)	79 (59-92)
NPV, % (95% CI)	86 (77-92)

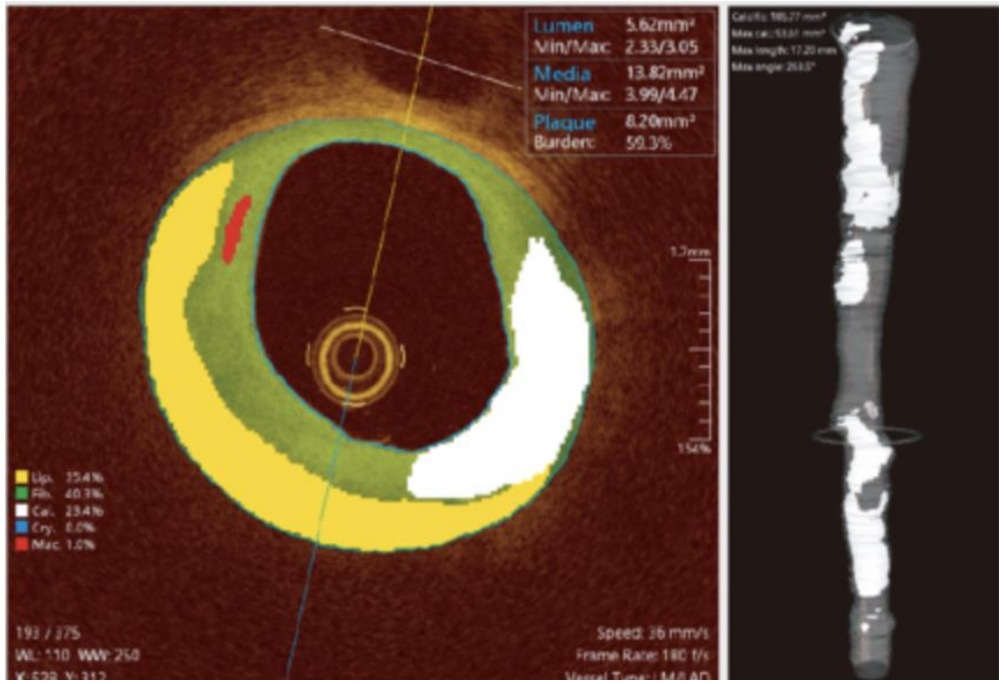


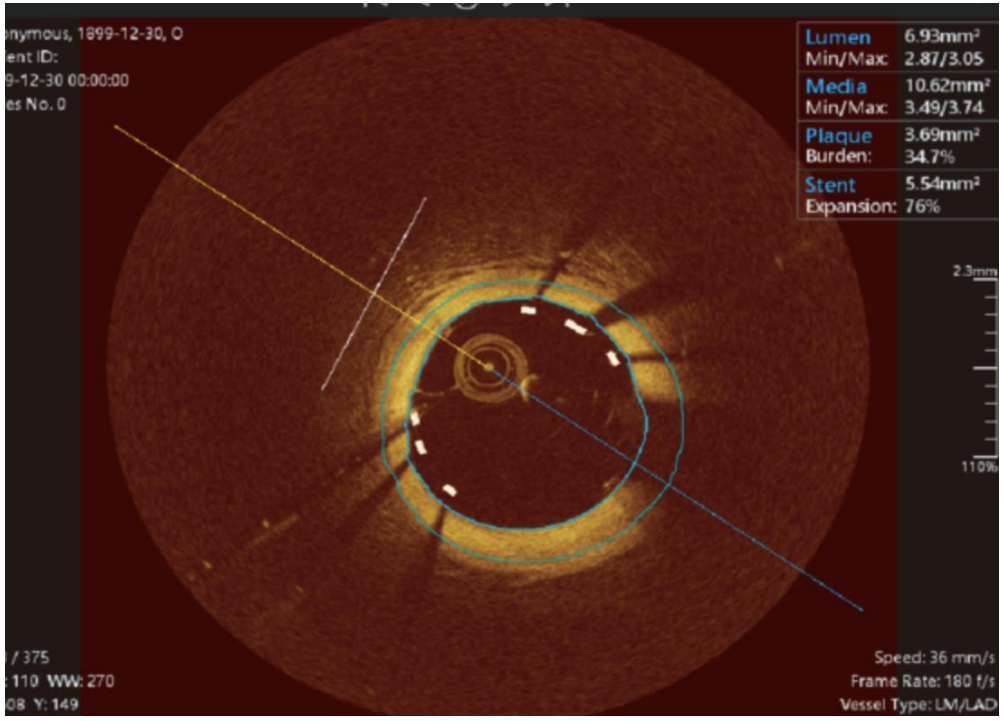


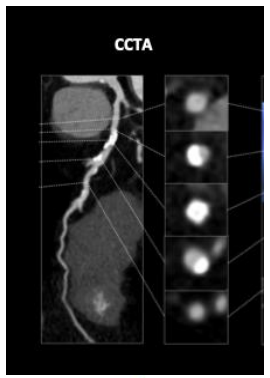


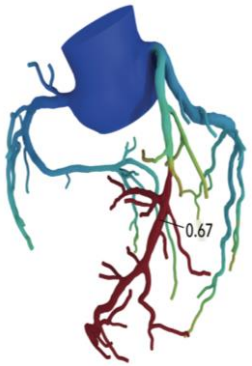
OFR


A1
FFR = 0.64 *
I
II
III
IV
lumen area 15.40 mm²
lumen area 2.37 mm²
lumen area 2.44 mm²
lumen area 3.53 mm²
A2
A3
OFR = 0.63
Lesion OFR = 0.30
Simulated residual OFR = OFR + Lesion OFR = 0.93

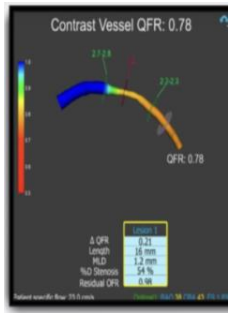

Lumen 5.62mm²
Min/Max 2.33/3.05
Media 13.82mm²
Min/Max 3.99/4.47
Plaque 8.20mm²
Burden: 59.3%


Lumen 6.93mm²
Min/Max 2.87/3.05
Media 10.62mm²
Min/Max 3.49/3.74
Plaque 3.69mm²
Burden: 34.7%
Stent 5.54mm²
Expansion: 76%
Speed: 36 mm/s
Frame Rate: 180 f/s
Vessel Type: LM/LAD





CathLab



< 0.74

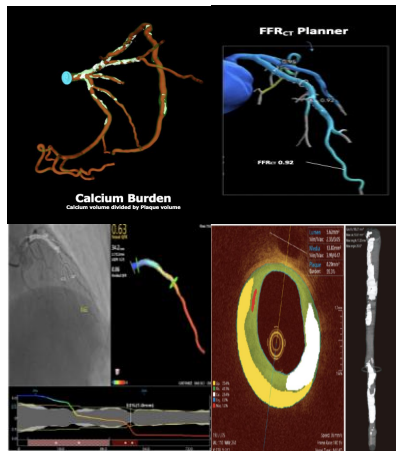
0.74 – 0.85*

> 0.85

< 0.80

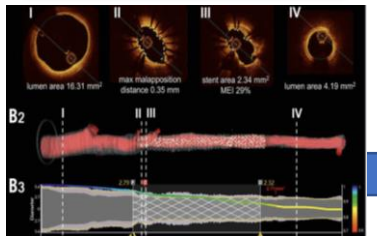
> 0.80

PLANNING

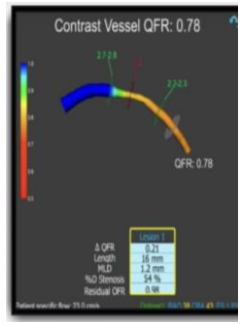


Diffuse pattern virtual PPG

OPTIMISING



< 0.90



> 0.90

*Lauri FM et al EHJ Suppl 2018