Disclosures

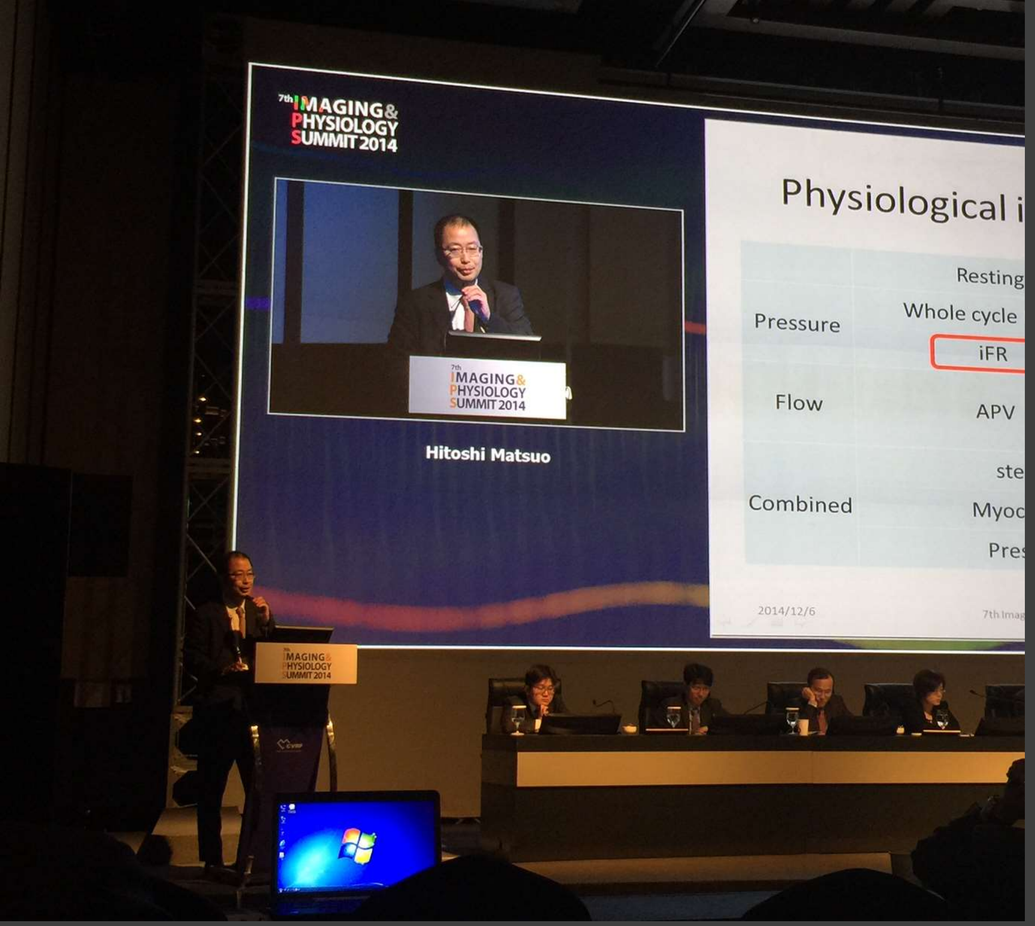
- Speaker's name: Hitoshi Matsuo M.D.,

✓ I have the following potential conflicts of interest to report in the field of this presentation:

Speaker at educational events and consultancies:

PHILLIPS-VOLCANO, BOSTON SCIENTIFIC, Abbott Vascular, Zeon

Nippon Mediphysics, Fuji Film RI pharmaceuticals,



Hyperemia is not mandatory
7th IPS 2014

My standpoint in 2014

- Maximum hyperemia is mandatory to measure FFR .
- Diagnostic power of resting index iFR is almost equal to FFR, if both indexes are compared with another physiological golden standard.
- From above reason, maximum hyperemia is not mandatory for the discrimination of ischemia causing stenosis.
- The linkage to clinical event is also mandatory to regard iFR as the easy efficacious physiological index for decision making of revascularization in cath labo.

iFR Outcome Trials

DEFINE FLAIR

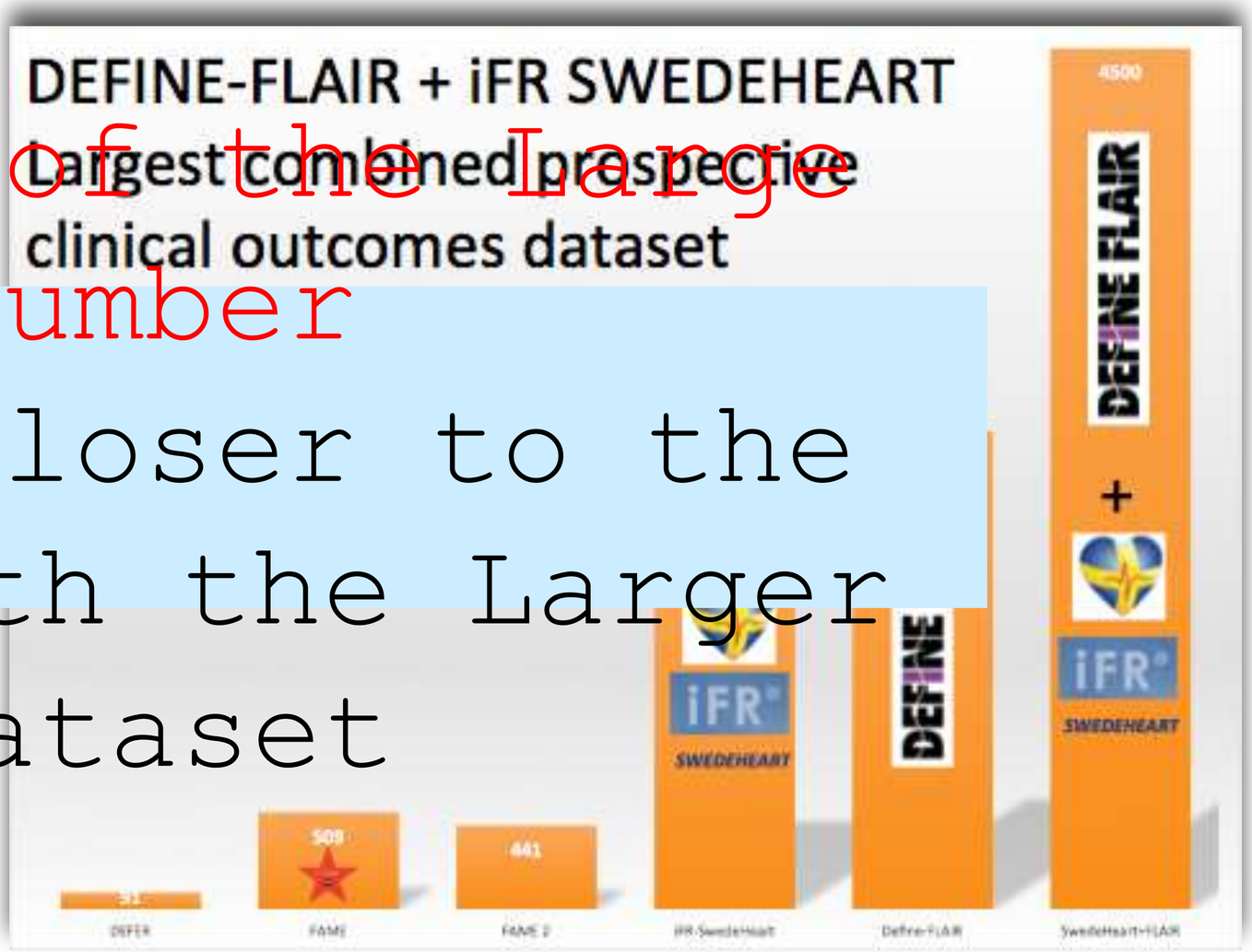
n=2,492
Doubl

SWEDEHEART

n=2,037
Randomized registry
blinded events adjudication

The Law of the Large Number

We are Closer to the Truth with the Larger Dataset



Davies JE *et al. N Engl J Med* 2017; Götberg M, *et al. N Engl J Med* 2017

DEFINE FLAIR

iFR®
SWEDEHEART

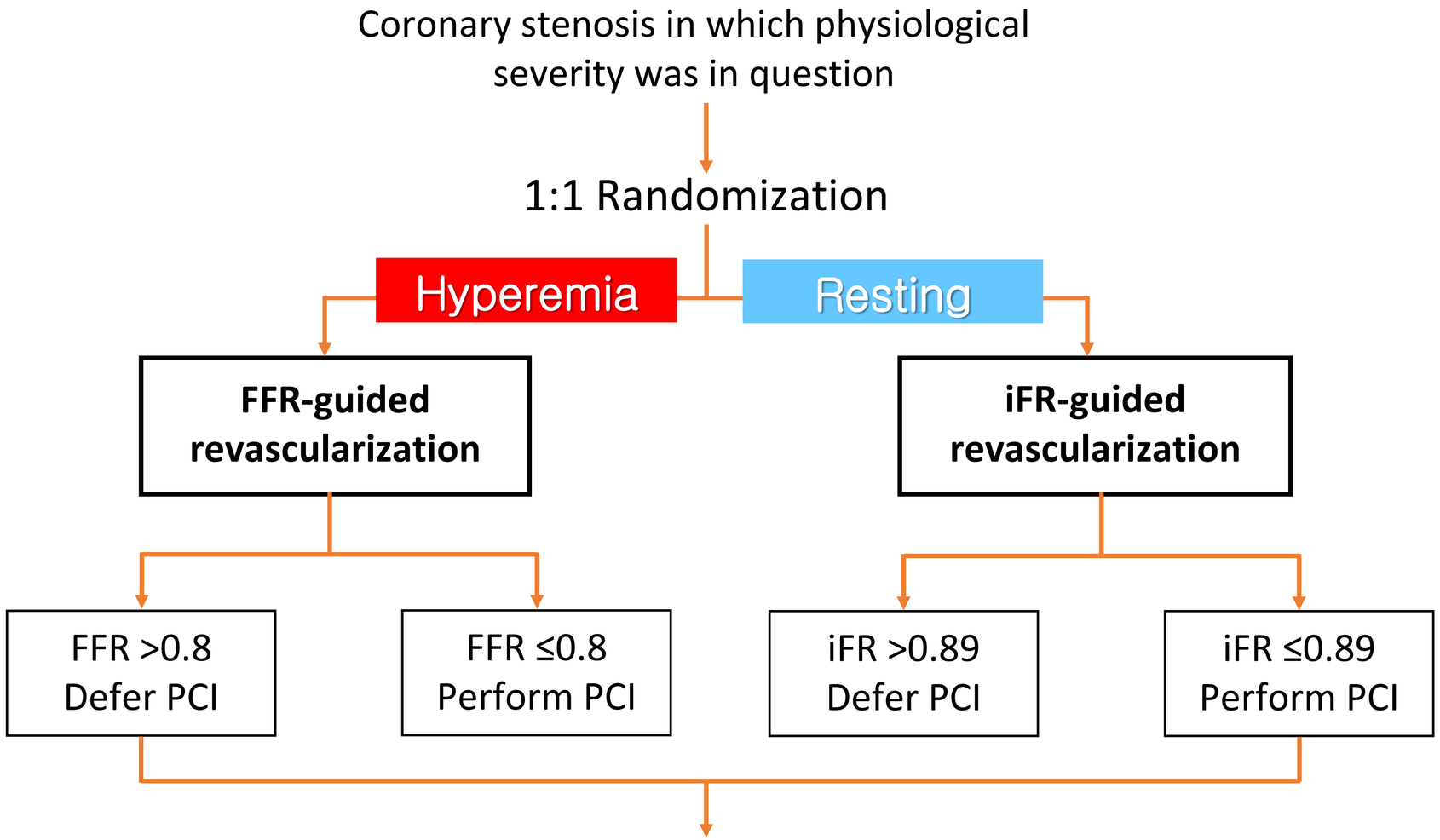
Principal hypothesis of DEFINE FLAIR and IFR SWEDEHEART

iFR is non-inferior to FFR for major adverse cardiac events (MACE) at 1 year in patients undergoing physiological-guided revascularization.

MACE : composite endpoint of:

- Death
- Non-fatal myocardial Infarction
- Unplanned revascularization

Study Design



MACE composite endpoint of:

- Death
- Non-fatal myocardial infarction
- Unplanned revascularization

Non-inferiority margin for risk difference: 3.4%

Davies JE *et al. N Engl J Med* 2017; Götberg M, *et al. N Engl J Med* 2017

DEFINE FLAIR. https://clinicaltrials.gov/ct2/show/NCT02053038.

DEFINE FLAIR

iFR®
SWEDEHEART

RESULTS

Baseline Characteristics

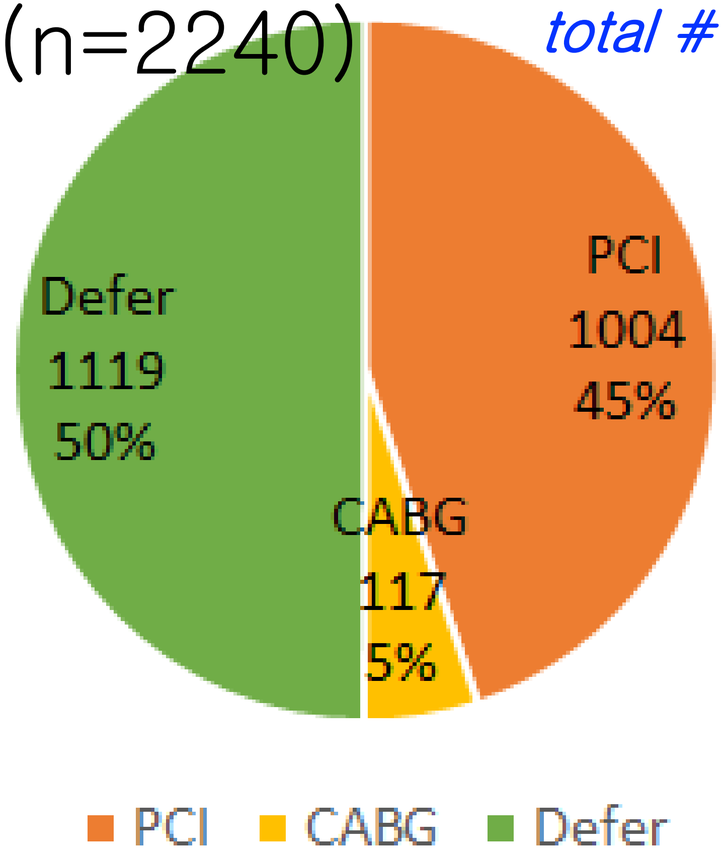
	DEFINE FLAIR		iFR-Swedeheart	
	iFR N=1242	FFR N=1250	iFR N=1019	FFR N=1018
Age	65.5±10.8	65.2±10.6	67.6±9.6	67.4±9.2
ACS (%)	235 (18.9%)	226 (18.1%)	387 (38.0%)	386 (37.9%)
MVD (%)	505 (40.7%)	519 (41.5%)	364 (35.7%)	368 (37.1%)
DM	382 (30.8%)	376 (30.1%)	232 (22.8%)	213 (20.9%)
HT	873 (70.3%)	884 (70.7%)	730 (71.6%)	710 (69.7%)
DL	794 (63.9%)	792 (63.6%)	733 (71.9%)	704 (69.2%)
C/Ex-Smoker	704 (56.7%)	705 (56.4%)	660 (64.8%)	634 (62.2%)
Previous MI	358 (28.8%)	376 (30.1%)	337 (33.1%)	335 (36.1%)
Previous PCI	489 (39.4%)	527 (42.2%)	429 (42.1%)	425 (41.7%)

Davies JE *et al. N Engl J Med* 2017; Götberg M, *et al. N Engl J Med* 2017

pooled analysis of Define FLAIR and iFR Sweedeheart

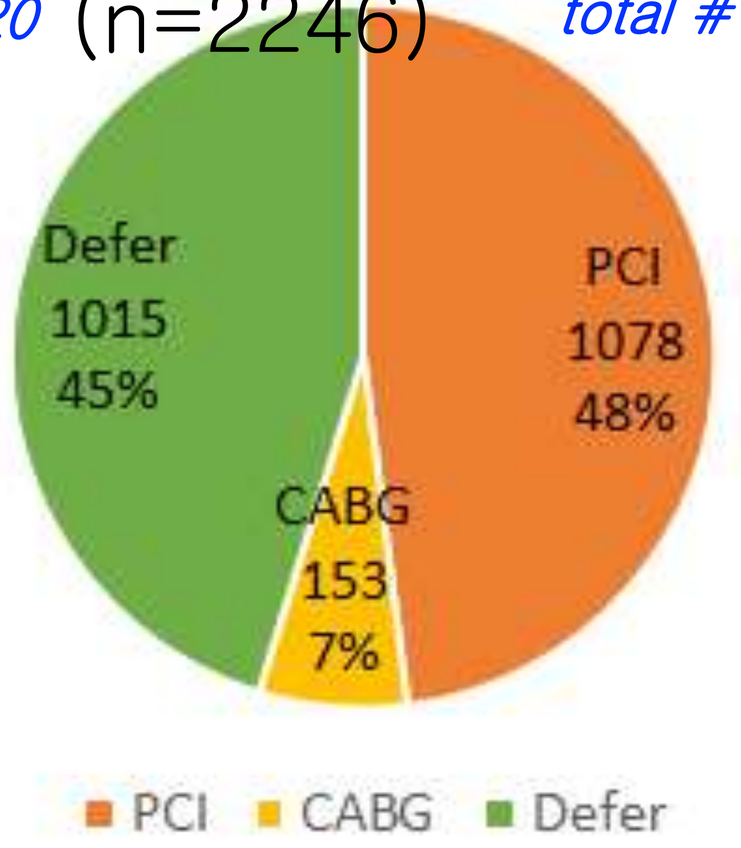
iFR guide
(n=2240)

total # of stents 1520



FFR guide
(n=2246)

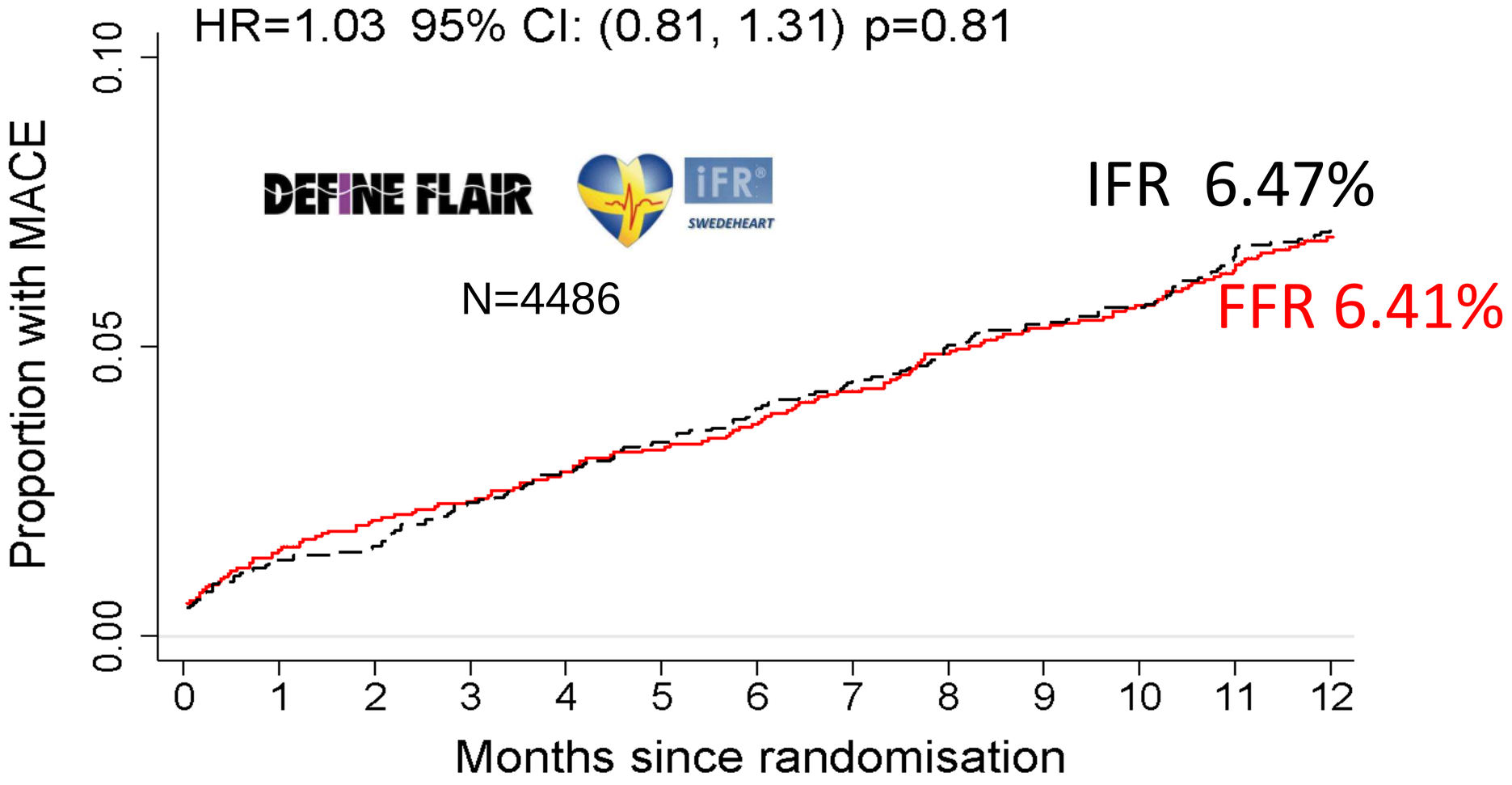
total # of stents 1693



Significantly less revascularisation based on iFR interrogation (P < 0.01)

Escaned, et al EUROPCR 2017

MACE in iFR and FFR guided decision-making: **pooled data**

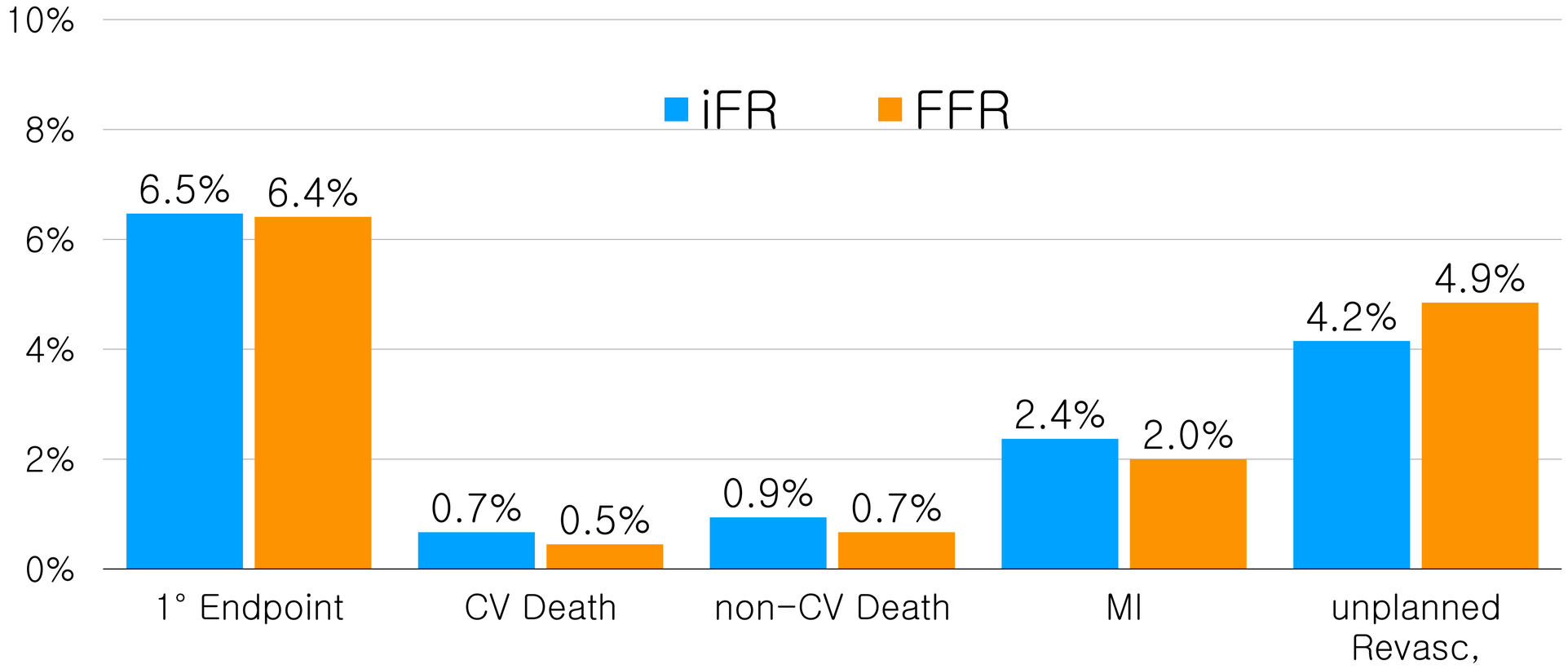


MACE similar and low at 1 year after iFR- and FFR-based decision-making

Escaned, et al EUROPCR 2017

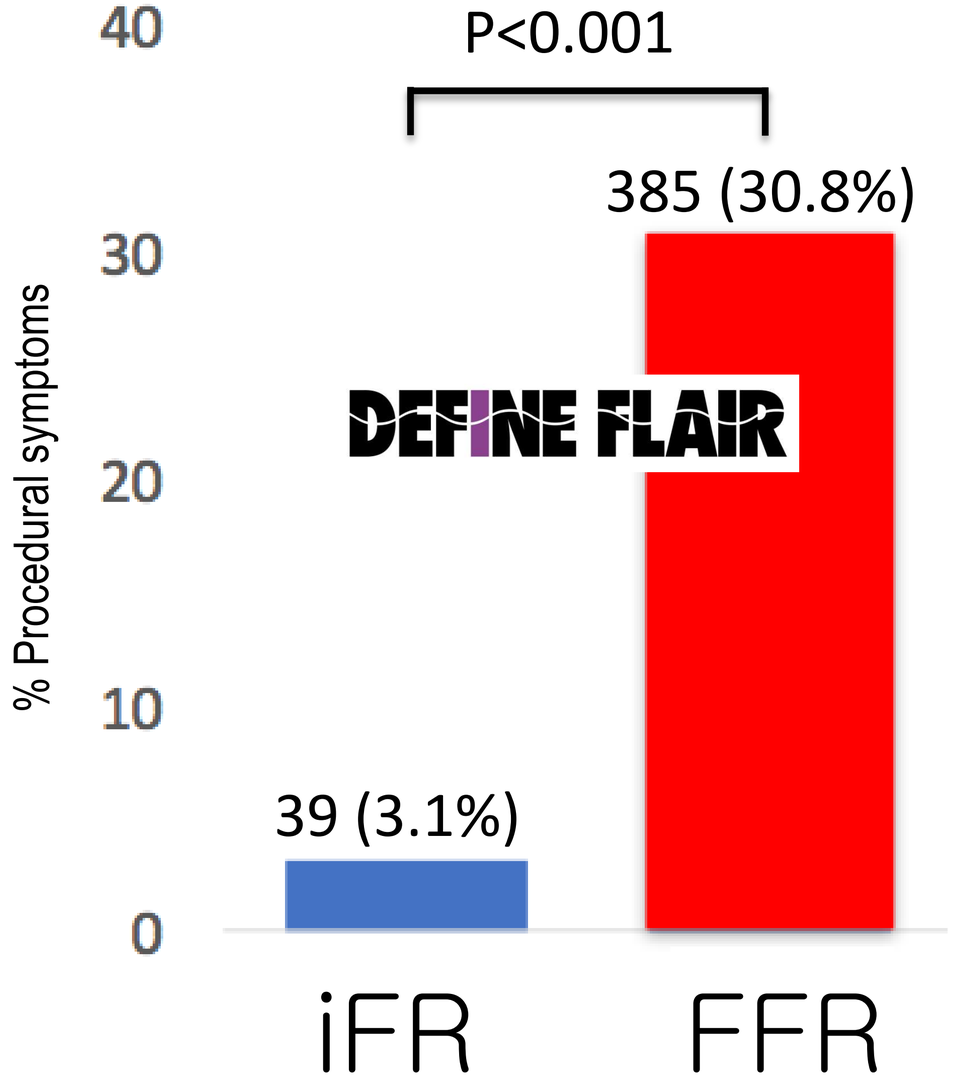
MACE component @ 1 year. pooled data

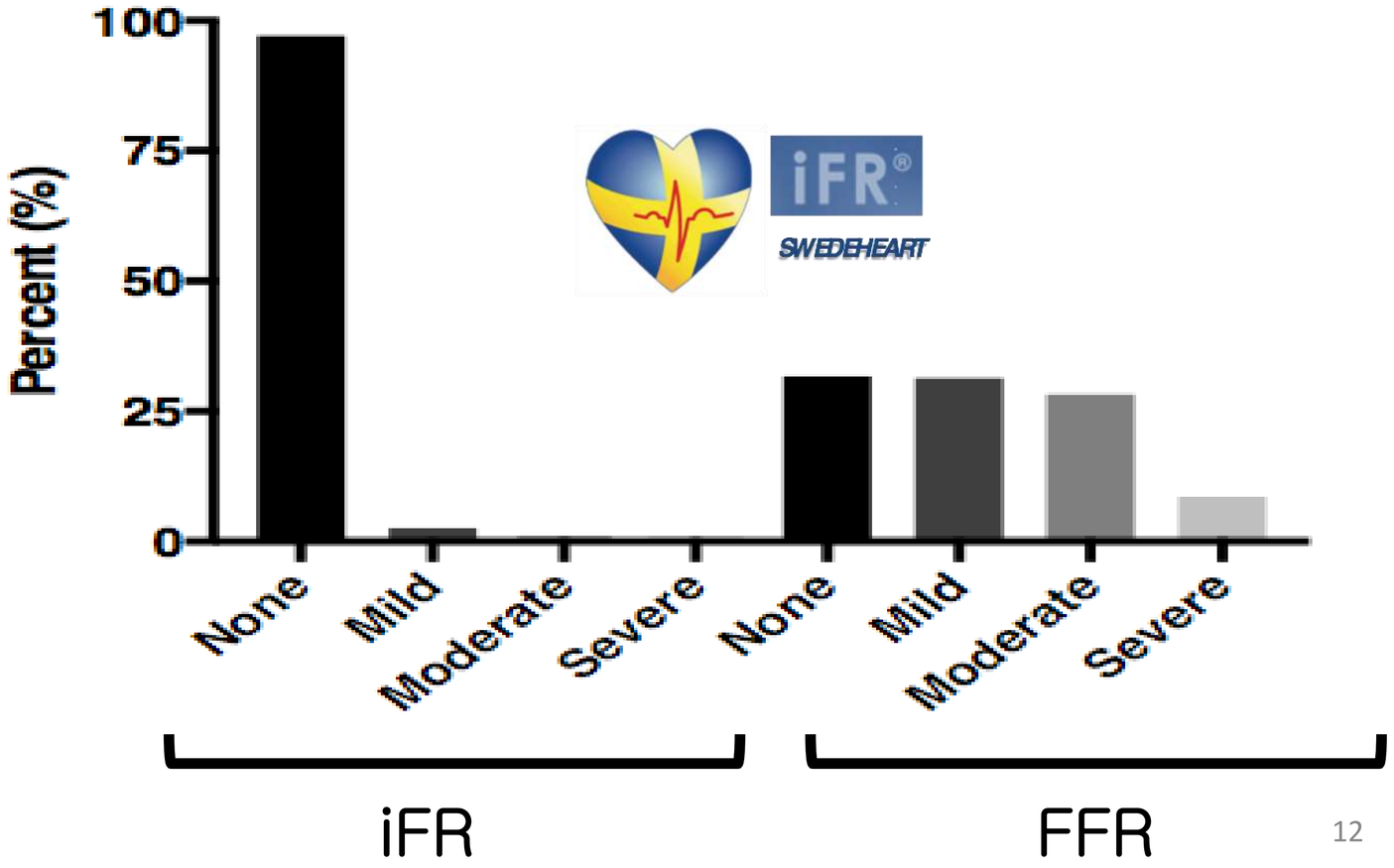
p = n.s. for all components



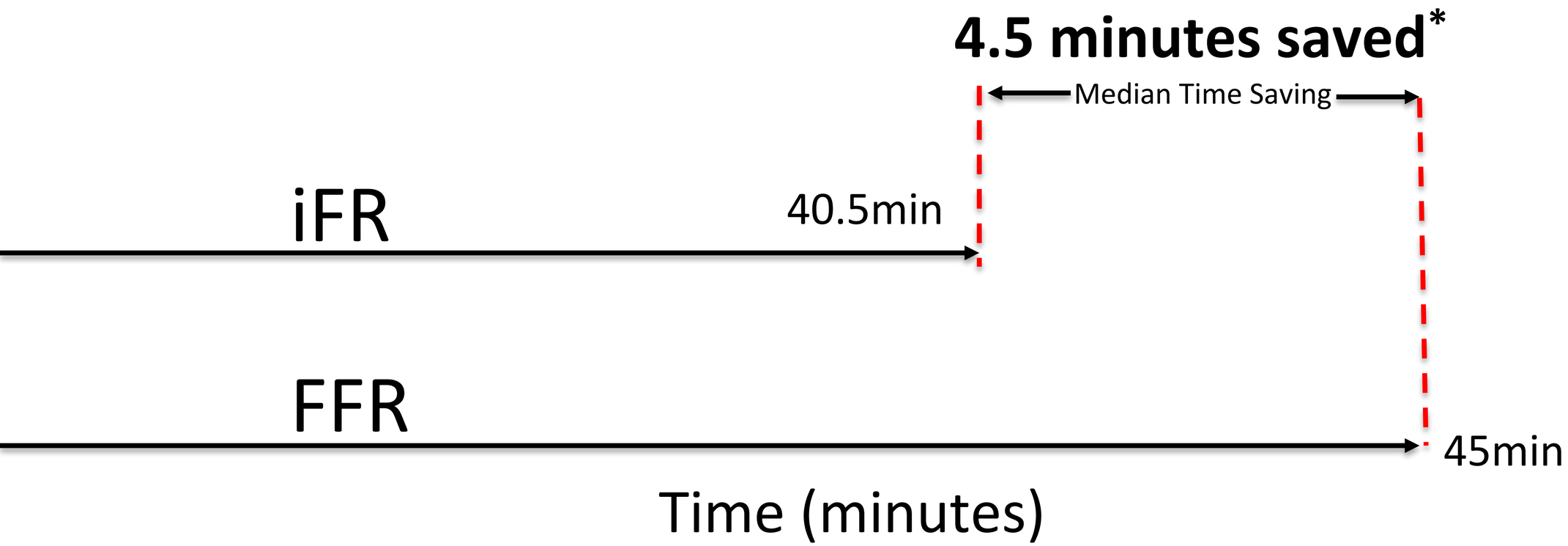
Escaned, et al EUROPCR 2017

iFR: fewer side effect



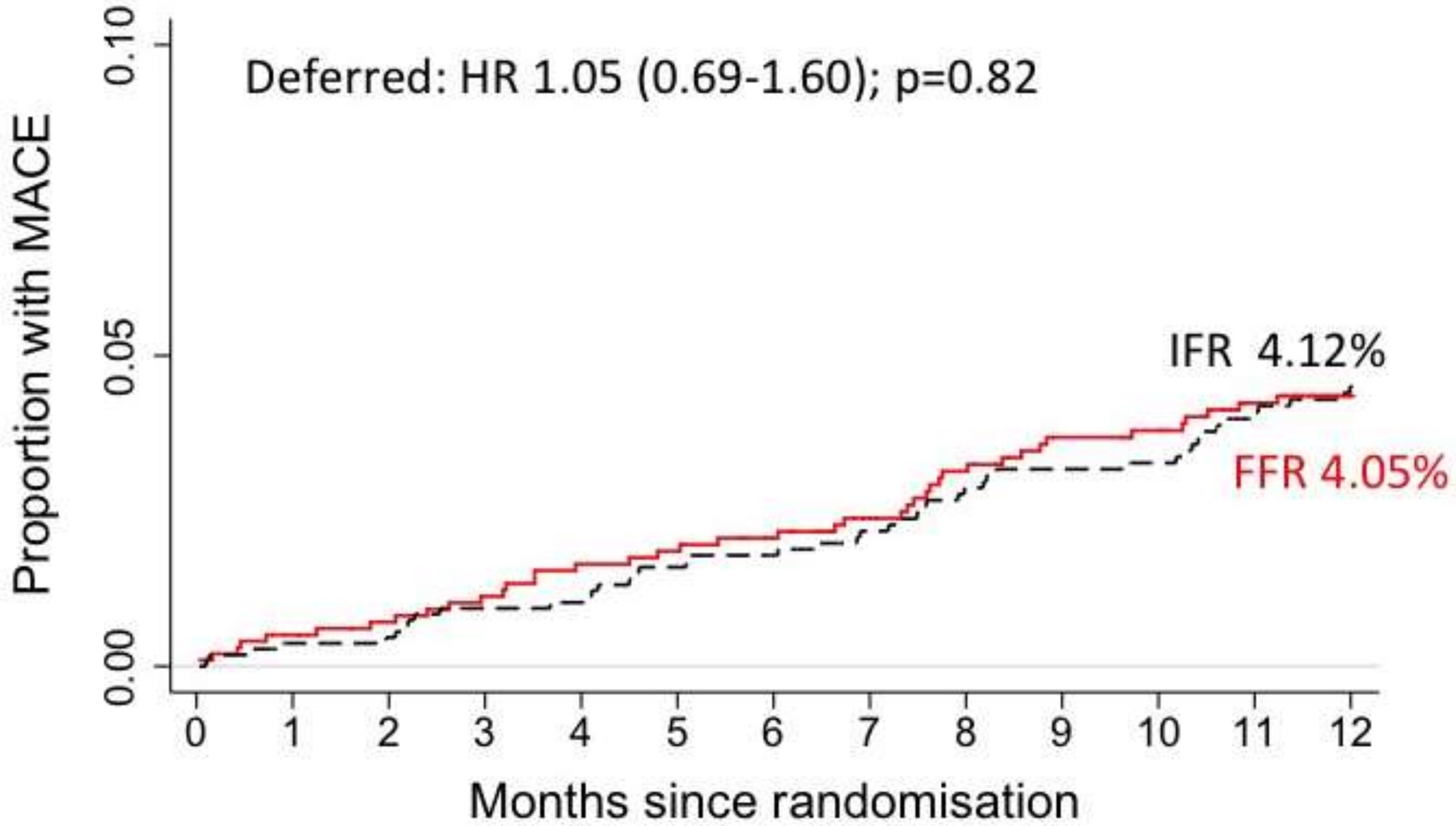


DEFINE FLAIR: iFR guided revascularization reduces procedure time



* Threshold for reduction in median time (p=0.001)

Pooled data: analysis of deferred revascularisation patients



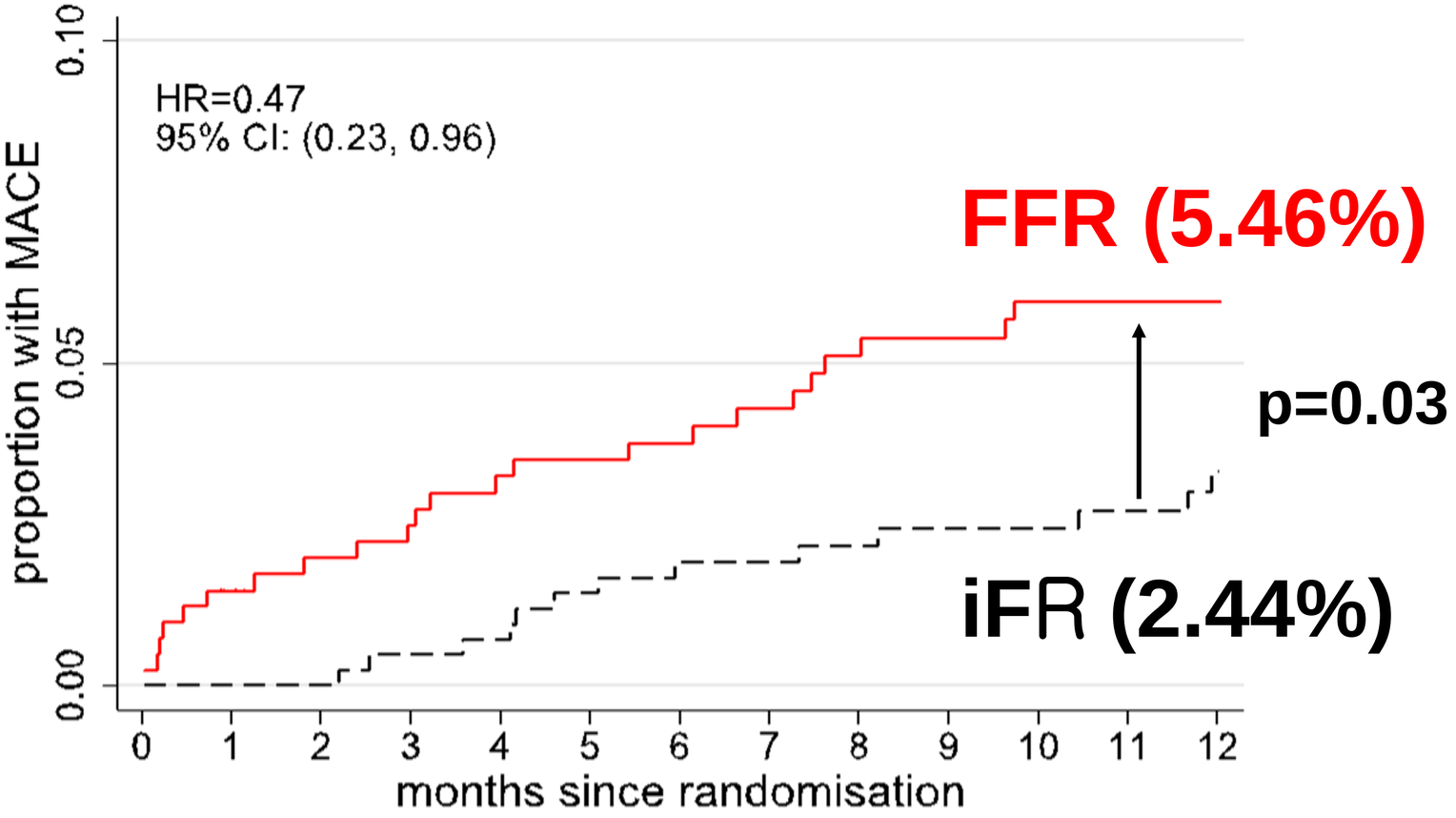
Similar and low MACE rates at 1 year after iFR- and FFR- based deferral

Escaned, et al EUROPCR 2017

In LAD – Deferral with iFR is considerably safer than FFR

DEFINE FLAIR

Functional Lesion Assessment of Intermediate stenosis to guide Revascularisation



Take home:

FFR is associated with >100% increase in events compared to iFR when used to defer revasc in LAD

Under review

ACS

Management of *non-culprit* lesions?

Culprit Lesions → PCI

Non-culprit 40-70% →

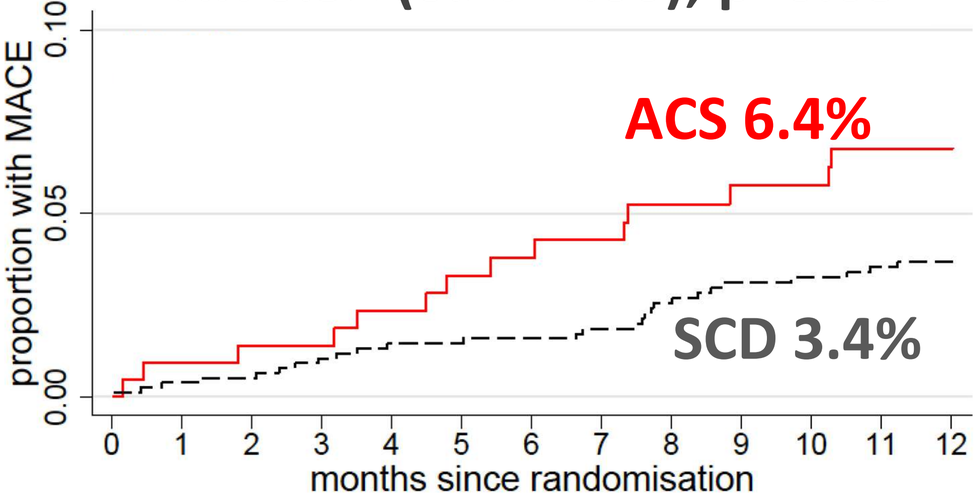
- FFR — *Safe?*
- iFR — *Safe?*

Unadjusted outcomes after deferral by clinical presentation and iFR or FFR

DEFINE FLAIR
Functional Lesion Assessment of Intermediate stenosis to guide Revascularisation

FFR

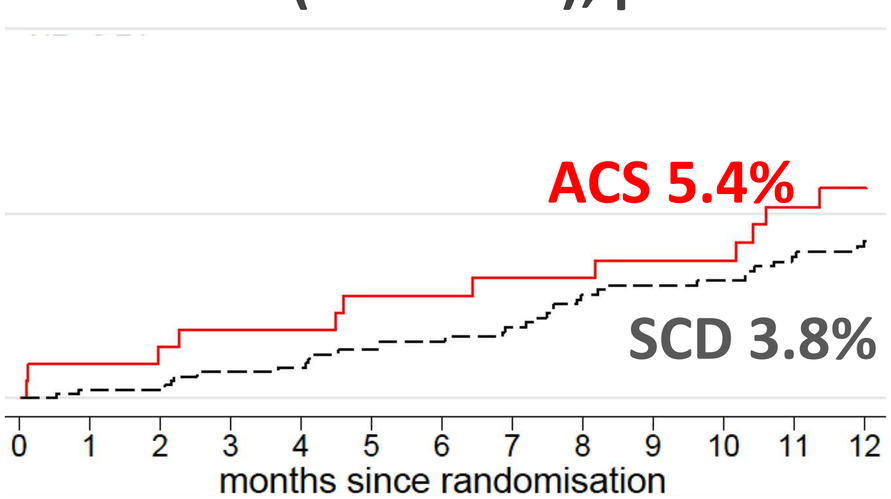
HR 0.52 (0.27-1.00); p<0.05



In FFR-deferred patients, MACE is significantly higher in ACS than SCD

iFR

HR 0.74 (0.38-1.43); p=0.37



In iFR-deferred patients, MACE is similar in ACS and SCD

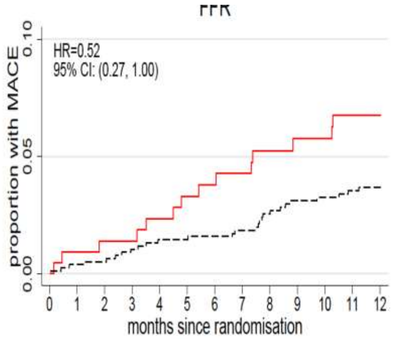
Take home:
Deferral using FFR is associated with increased event rate when compared to iFR in ACS

Escaned J, Tanaka N, Yokoi H, Takashima H, Kikuta Y, Matsuo H, Koo BK, Nam CW, SerruysPW, Götberg M, Davies JE *et al.* Submitted.

Improved Safety with iFR in ACS

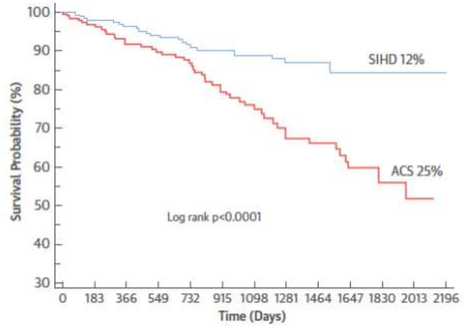
FFR

p<0.05



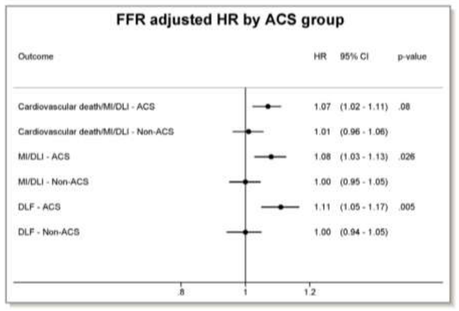
N=4529

p<0.0001



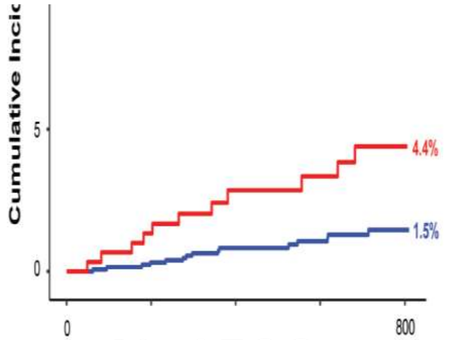
N=576

p=0.026



N=674

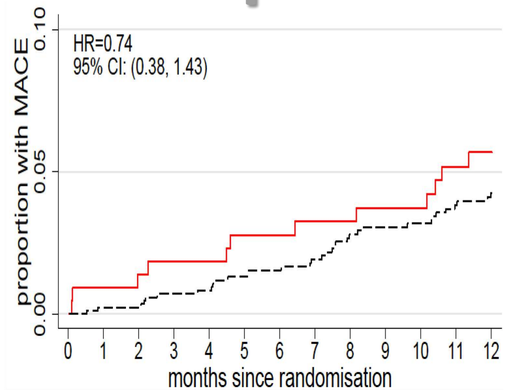
p=0.002



N=1596

iFR

p=0.37



Hakeem A, *et al. J Am Coll Cardiol* 2016;68:1181–91.

Masrani Mehta *et al. J Am Heart Assoc* 2015;4:e002172.

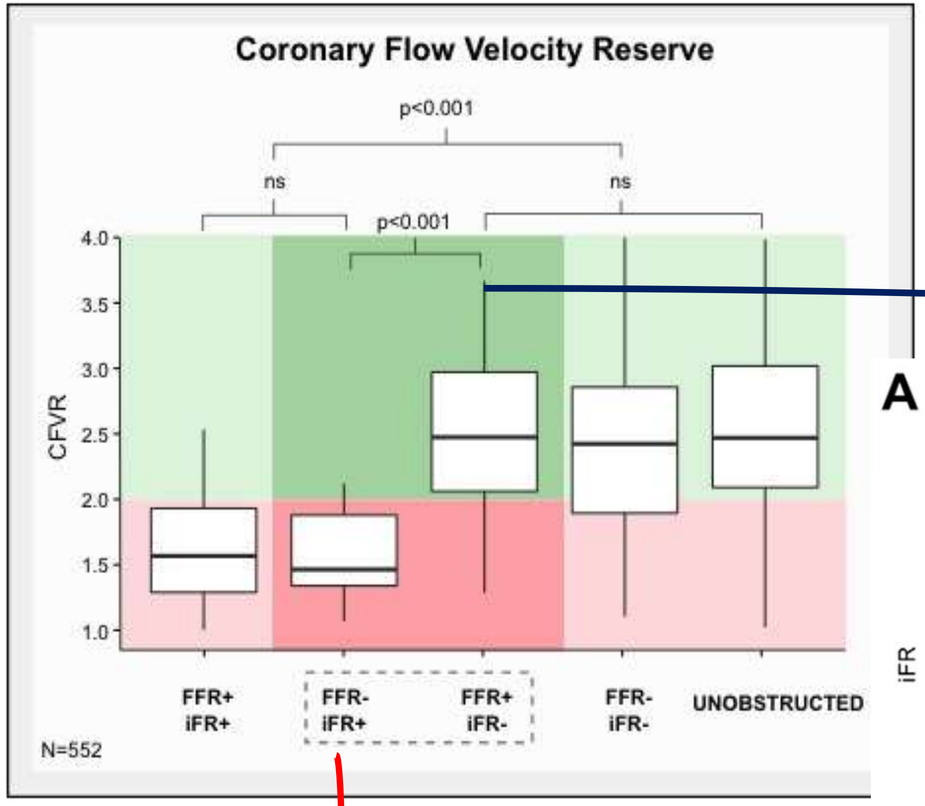
Lee JM, Koo BK, *et al. Eurointervention* 2017;10:4244.

Escaned J, Tanaka N, Yokoi H, Takashima H, Kikuta Y, Matsuo H, Koo BK, Nam CW, SerruysPW, Götberg M, Davies JE *et al.* Submitted.

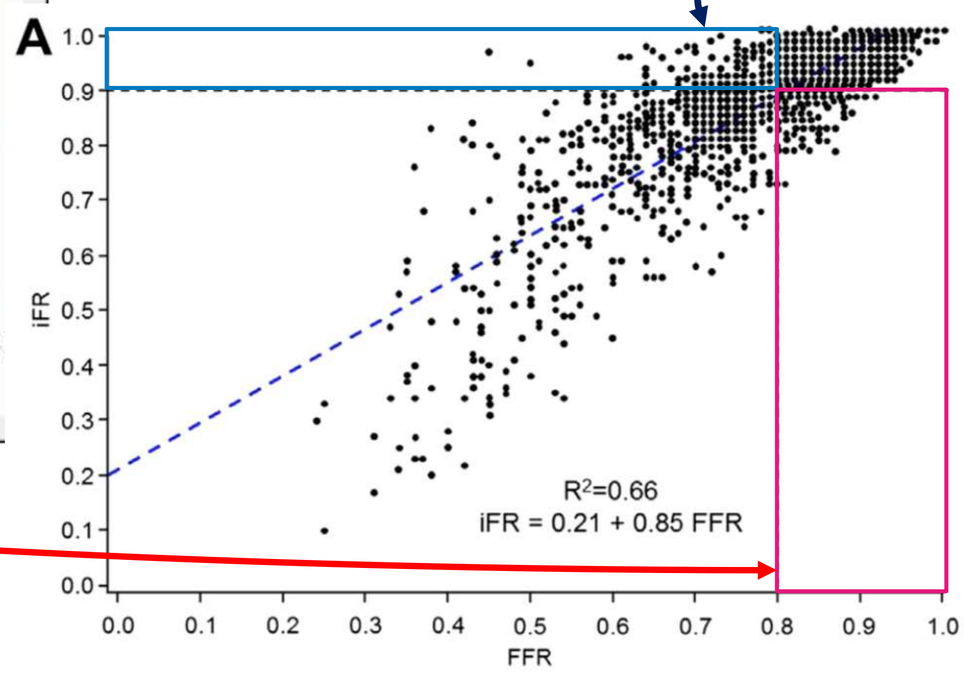
DEFINE FLAIR

iFR® SWEDEHEART

iFR is more Accurate for assessing Hyperemic Flow indexes even when Hyperemic Pressure FFR Disagrees with Hyperemic Flow



iFR (0.99)
FFR (0.74)



iFR (0.83)
FFR (0.83)

Cook, Jeremias, Kikuta, Shiono, Stone, Davies et al. J Am Coll Cardiol Cardiovasc Interv 2017.

Jeremias A, Fearon WF, Pijls NHJ *et al.* RESOLVE. J Am Coll Cardiol 2014;63:1253–61.

Health Economics of FFR vs. iFR

March 10, 2018, 12:15 PM

Late-Breaking Clinical Trials. 402. Featured Clinical Research I

Room 311 E

ACC.18

67th Annual Scientific Session & Expo

402-08 - Comparative Cost Effectiveness of the Instantaneous Wave-free Ratio versus Fractional Flow Reserve in Coronary Revascularization Decision-making

March 10, 2018, 12:15 - 12:25 PM | Room 311 E

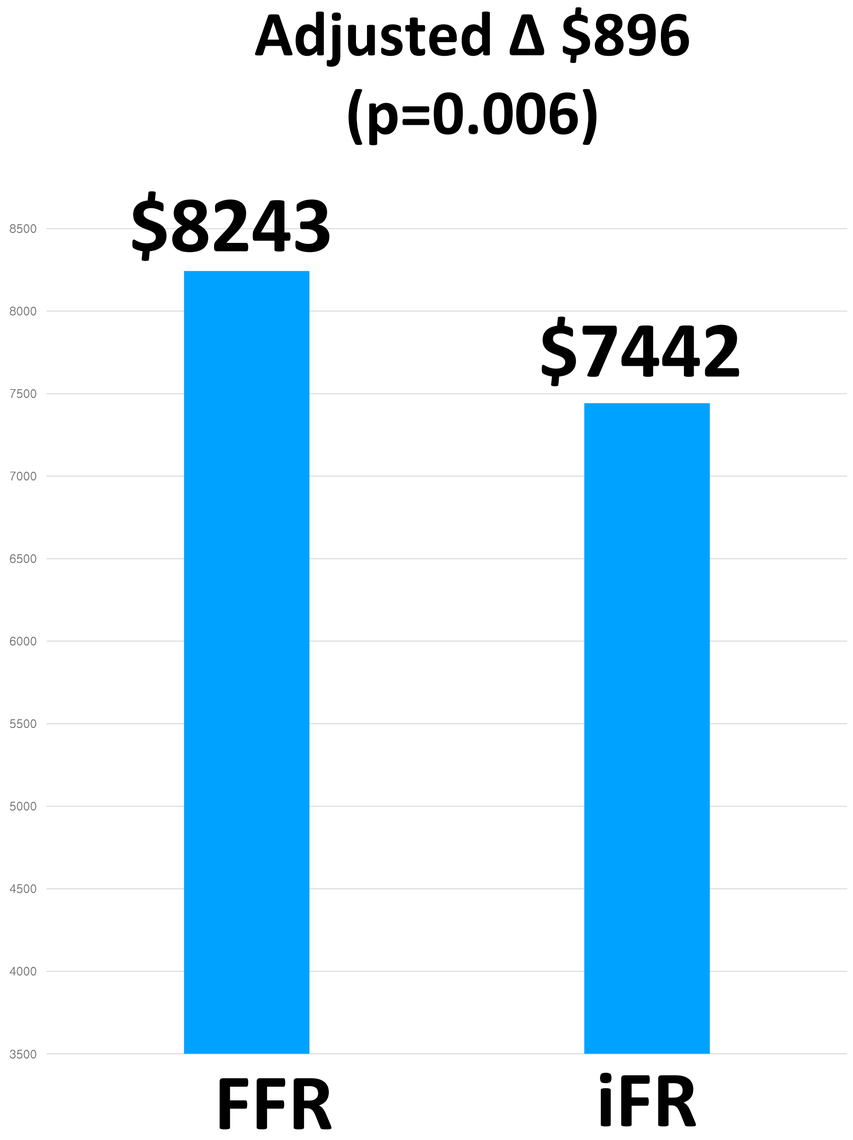
Authors

Manesh Patel, Rasha Al-Lamee, Jo Lord, Keith Cooper, Sayan Sen, Patrick Serruys, Javier Escaned, Justin Davies, Imperial College London, London, United Kingdom

Abstract

Abstract embargoed at this time.

Significantly Lower Cost with iFR



Shorter procedural duration

No hyperaemic medication

Lower PCI rates

Fewer CABG procedures

Fewer Unplanned PCI (LAD)

Lord J, Tanaka N, Yokoi H, Takashima H, Kikuta Y, Koo BK, Nam CW, Matsuo H, Serruys PW, Escaned J, Patel M, Davies J, *et al.* ACC.18. Submitted

iFR Pullback

Resting physiological indices beyond spot measurement

Decision making at a vessel level

DEFINE FLAIR

iFR® SWEDEHEART

Decision making available at a lesion level

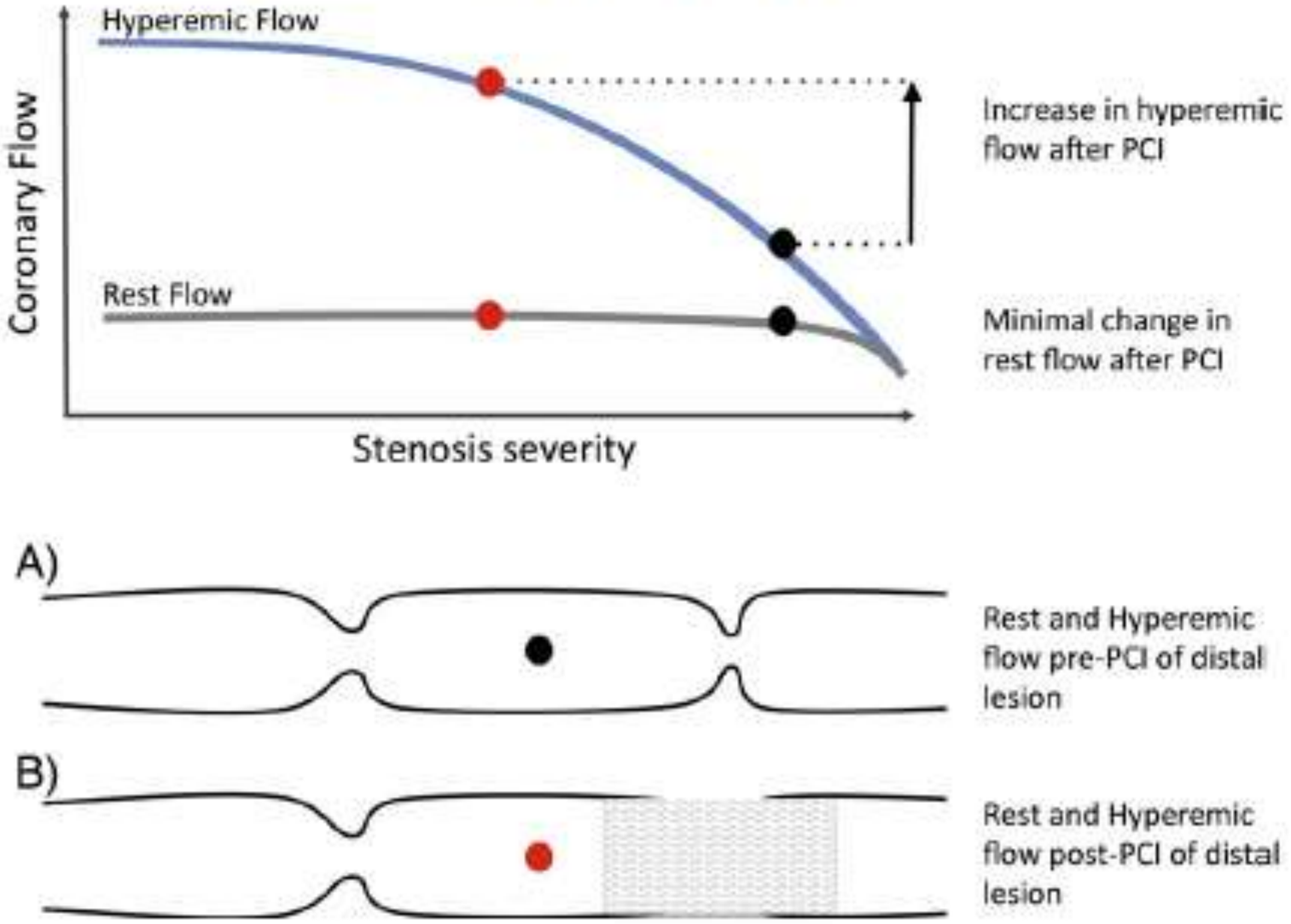
Pre-Angioplasty Instantaneous Wave-Free Ratio Pullback Provides Virtual Intervention and Predicts Hemodynamic Outcome for Serial Lesions and Diffuse Coronary Artery Disease

Sukhjinder S. Nijjer, MB ChB,* Sayan Sen, MBBS, PhD,* Ricardo Petraco, MD,* Javier Escaned, MD, PhD,† Mauro Echavarria-Pinto, MD,† Christopher Broyd, MBBS,* Rasha Al-Lamee, MBBS,* Nicolas Foin, PhD,* Rodney A. Foale, MD,* Iqbal S. Malik, MBBS, PhD,* Ghada W. Mikhail, MBBS, MD,* Amarjit S. Sethi, MBBS, PhD,* Mahmud Al-Bustami, MD,* Raffi R. Kaprielian, MBBS, MD,* Masood A. Khan, MB BChir, MA,* Christopher S. Baker, MBBS, PhD,* Michael F. Bellamy, MBBS, PhD,* Alun D. Hughes, PhD,† Jamil Mayet, MB ChB, MD,* Darrel P. Francis, MB BChir, MA, MD,* Carlo Di Mario, MD, PhD,§ Justin E.R. Davies, MBBS, PhD*

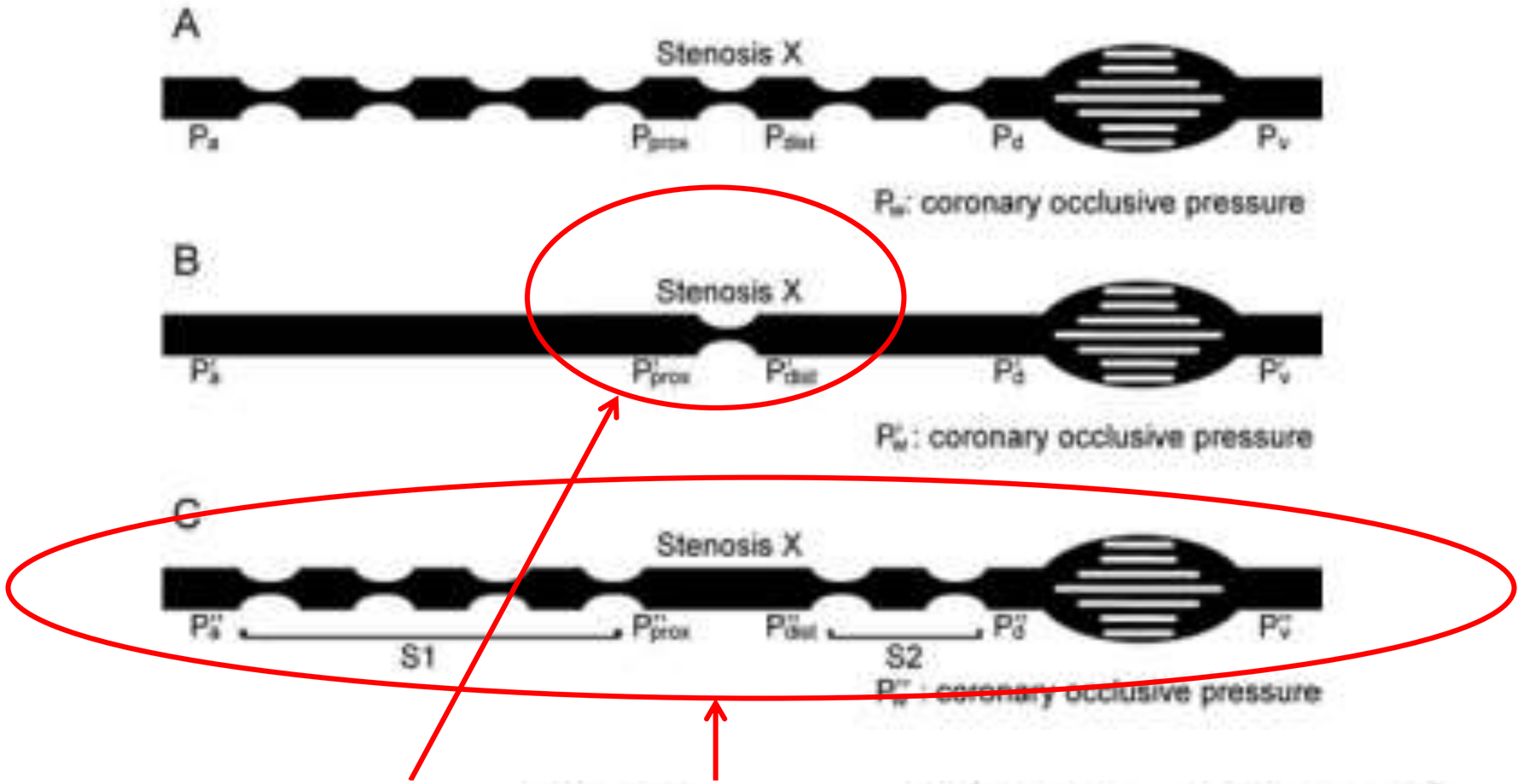
Pre-Angioplasty Instantaneous Wave-Free Ratio Pullback Predicts Hemodynamic Outcome In Humans With Coronary Artery Disease

Primary Results of the International Multicenter iFR GRADIENT Registry

Yuetsu Kikuta, MD,[a,b,*] Christopher M. Cook, MBBS,[a,*] Andrew S.P. Sharp, MD,[c] Pablo Salinas, MD,[d] Yoshiaki Kawase, MD,[e] Yasutsugu Shiono, MD, PhD,[a] Alessandra Giavarini, MD,[f] Masafumi Nakayama, MD, PhD,[g] Salvatore De Rosa, MD, PhD,[h] Sayan Sen, MBBS, PhD,[a] Sukhjinder S. Nijjer, MBChB, PhD,[a] Rasha Al-Lamee, MD,[a] Ricardo Petraco, MD, PhD,[a] Iqbal S. Malik, MBBS, PhD,[a] Ghada W. Mikhail, MBBS,[a] Raffi R. Kaprielian, MBBS, MD,[a] Gilbert W.M. Wijntjens, MD,[i] Shinsuke Mori, MD,[j] Arata Hagikura, MD,[b] Martin Mates, MD,[k] Atsushi Mizuno, MD,[l] Farrel Hellig, MD,[m] Kelvin Lee, MD,[n] Luc Janssens, MD,[o] Kazunori Horie, MD,[p] Shah Mohdnazri, MBBS,[q] Raul Herrera, MD,[d] Florian Krackhardt, MD,[r] Masahiro Yamawaki, MD,[j] John Davies, MBBS, PhD,[q] Hideo Takebayashi, MD, PhD,[b] Thomas Keeble, MD,[q] Seiichi Haruta, MD, PhD,[b] Flavio Ribichini, MD, PhD,[s] Ciro Indolfi, MD, PhD,[h] Jamil Mayet, MBChB, MD,[a] Darrel P. Francis, MB BChir, MA, MD,[a] Jan J. Piek Carlo Di Mario, MD, PhD,[f] Javier Escaned, MD, PhD,[d] Hitoshi Matsuo, MD, PhD,[e,*] Justin E. Davies


Hyperemic Flow
Rest Flow
Coronary Flow
Stenosis severity
Increase in hyperemic flow after PCI
Minimal change in rest flow after PCI
A)
B)
Rest and Hyperemic flow pre-PCI of distal lesion
Rest and Hyperemic flow post-PCI of distal lesion

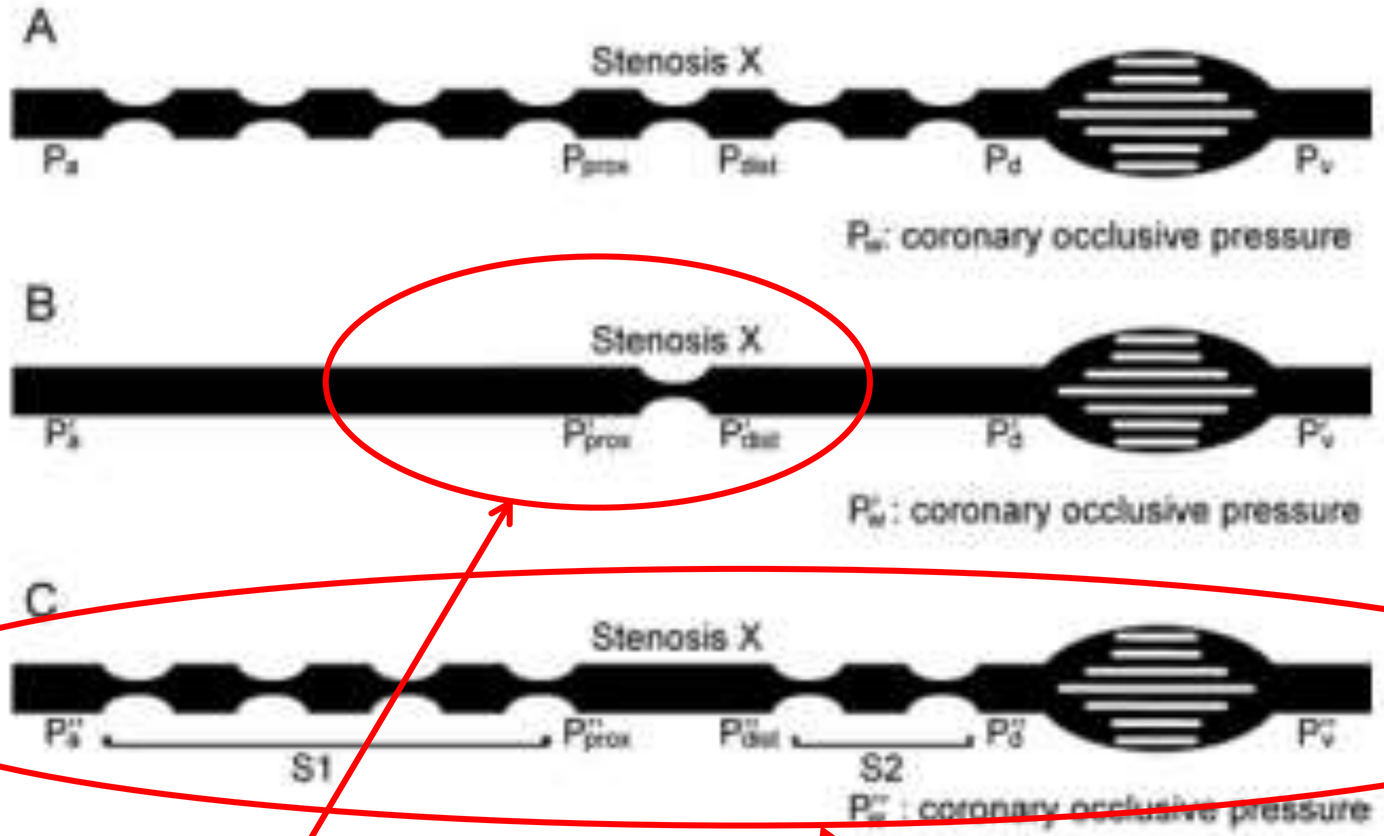
In Vitro Assessment of Mathematically-Derived FFR in Coronary Lesions With More Than Two Sequential Stenoses



$$FFR(X-)_{pred} = \frac{P_d - P_w}{P_a - P_{prox} + P_{dist} - P_w} + \frac{P_w(P_a - P_{prox} + P_{dist} - P_d)}{P_a(P_a - P_{prox} + P_{dist} - P_w)}$$

$$= \frac{P_d - P_w}{P_a - \Delta P - P_w} + \frac{P_w(P_a - \Delta P - P_d)}{P_a(P_a - \Delta P - P_w)} \quad (B)$$

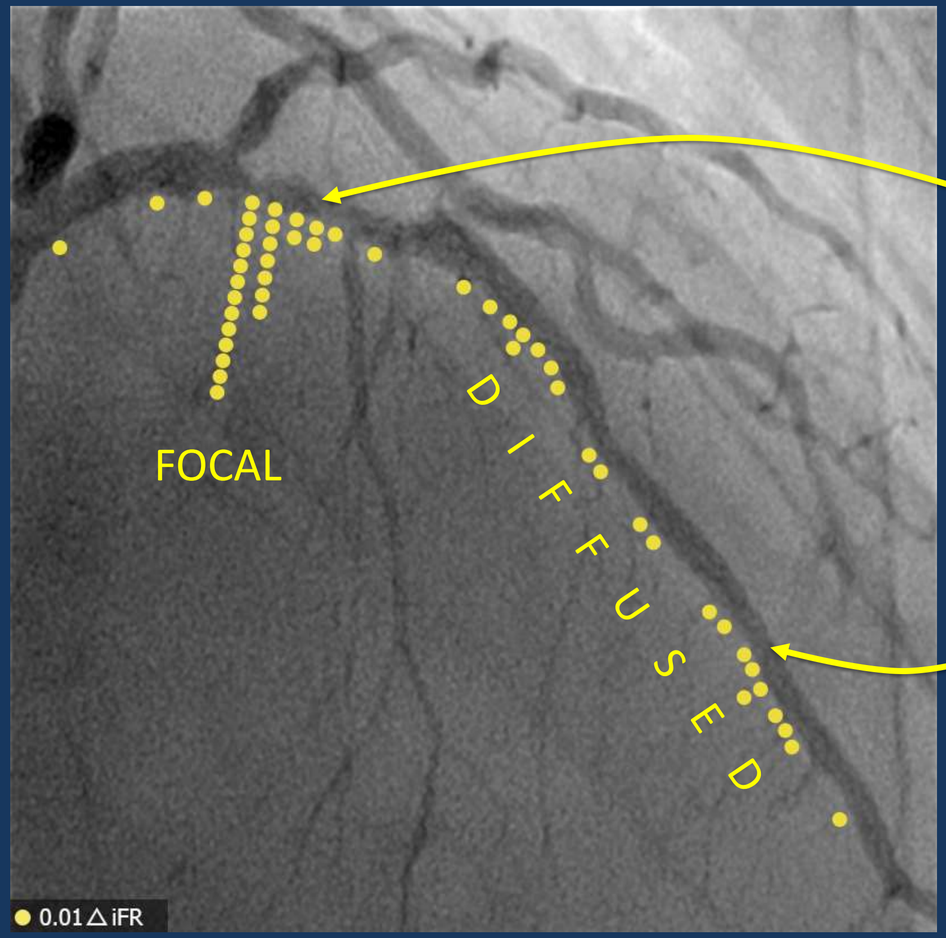
In Vitro Assessment of Mathematically-Derived FFR in Coronary Lesions With More Than Two Sequential Stenoses



$$iFR(X-) = iFRpre + \Delta iFR(X)$$

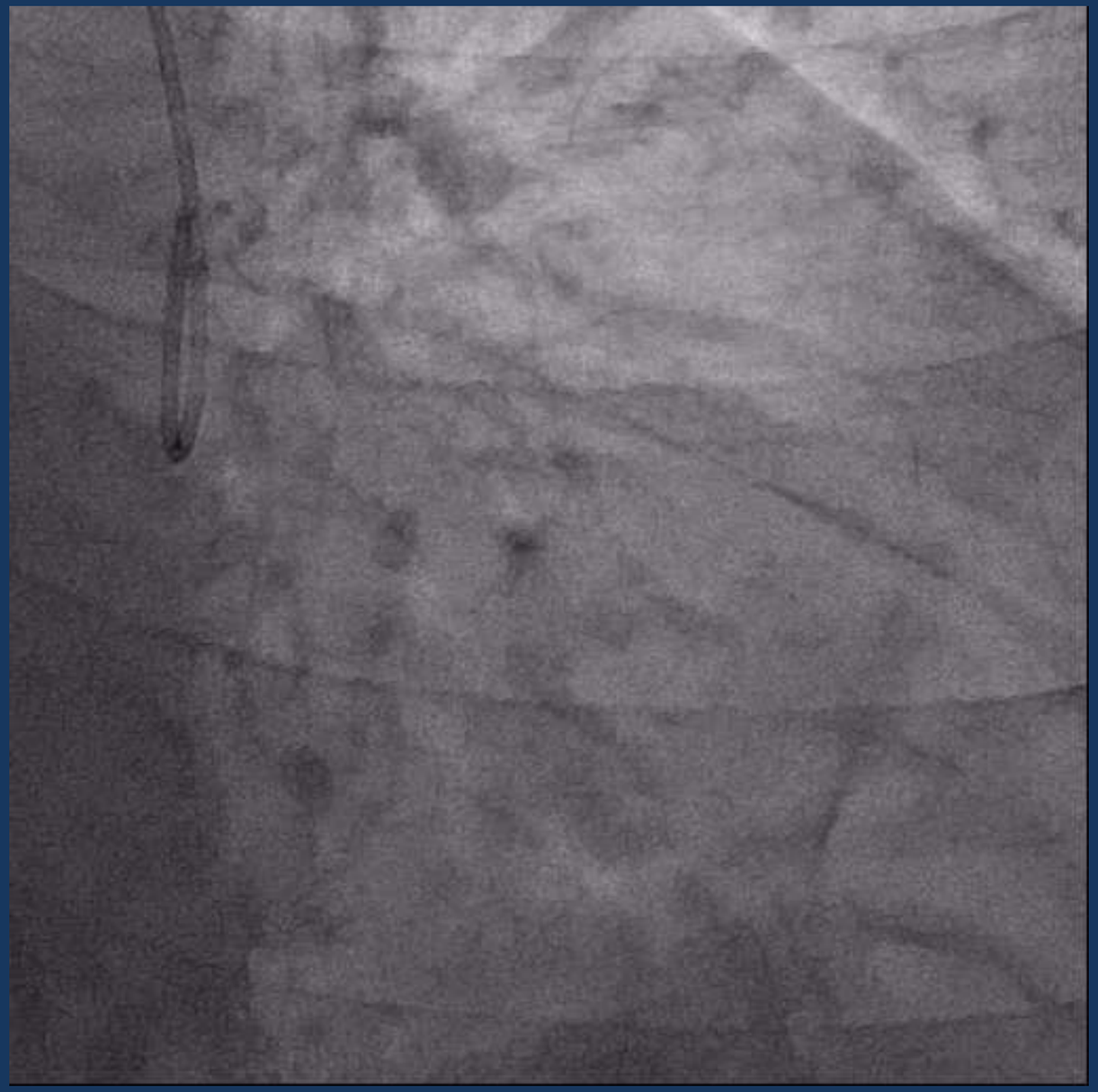
$$iFR\ (X)Pred = 1 - \Delta iFR(X)$$

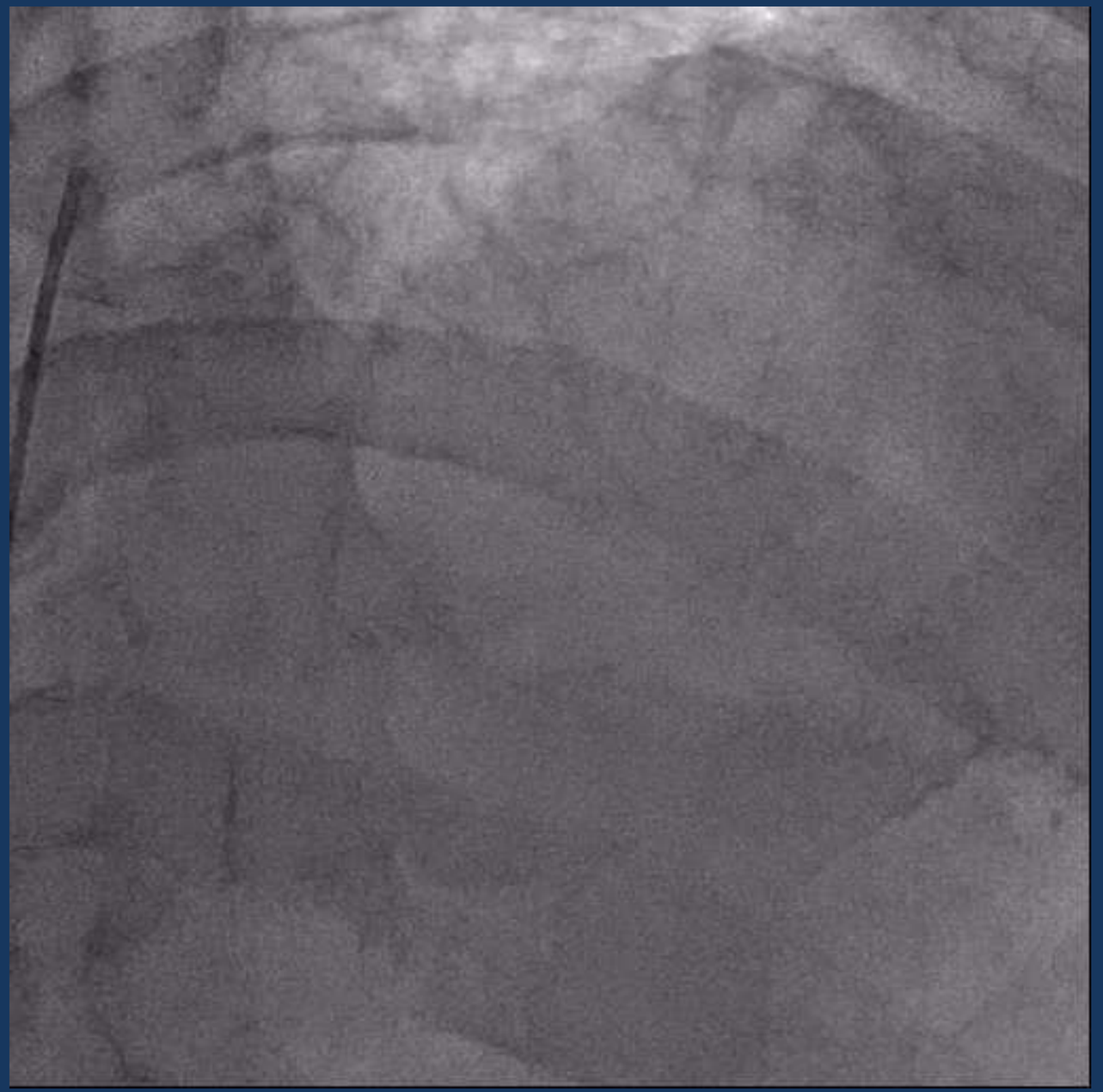
iFR pullback mapping to identify focal and diffuse disease

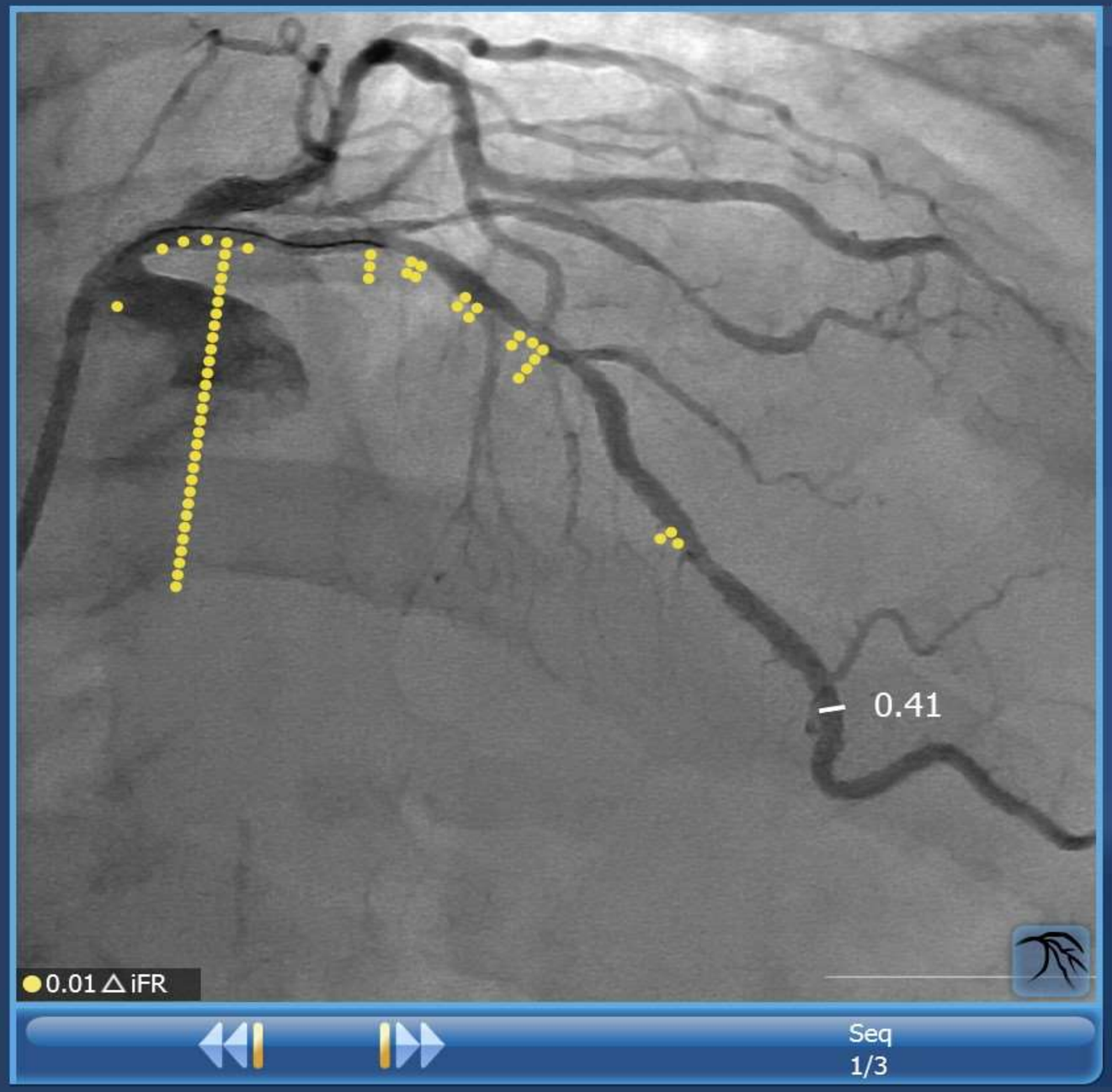


FOCAL
(high pressure drop intensity)

DIFFUSED
(low pressure drop intensity)

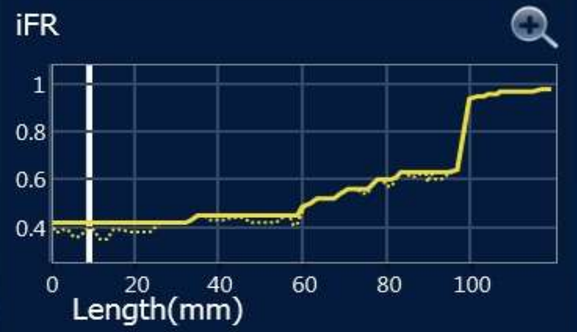






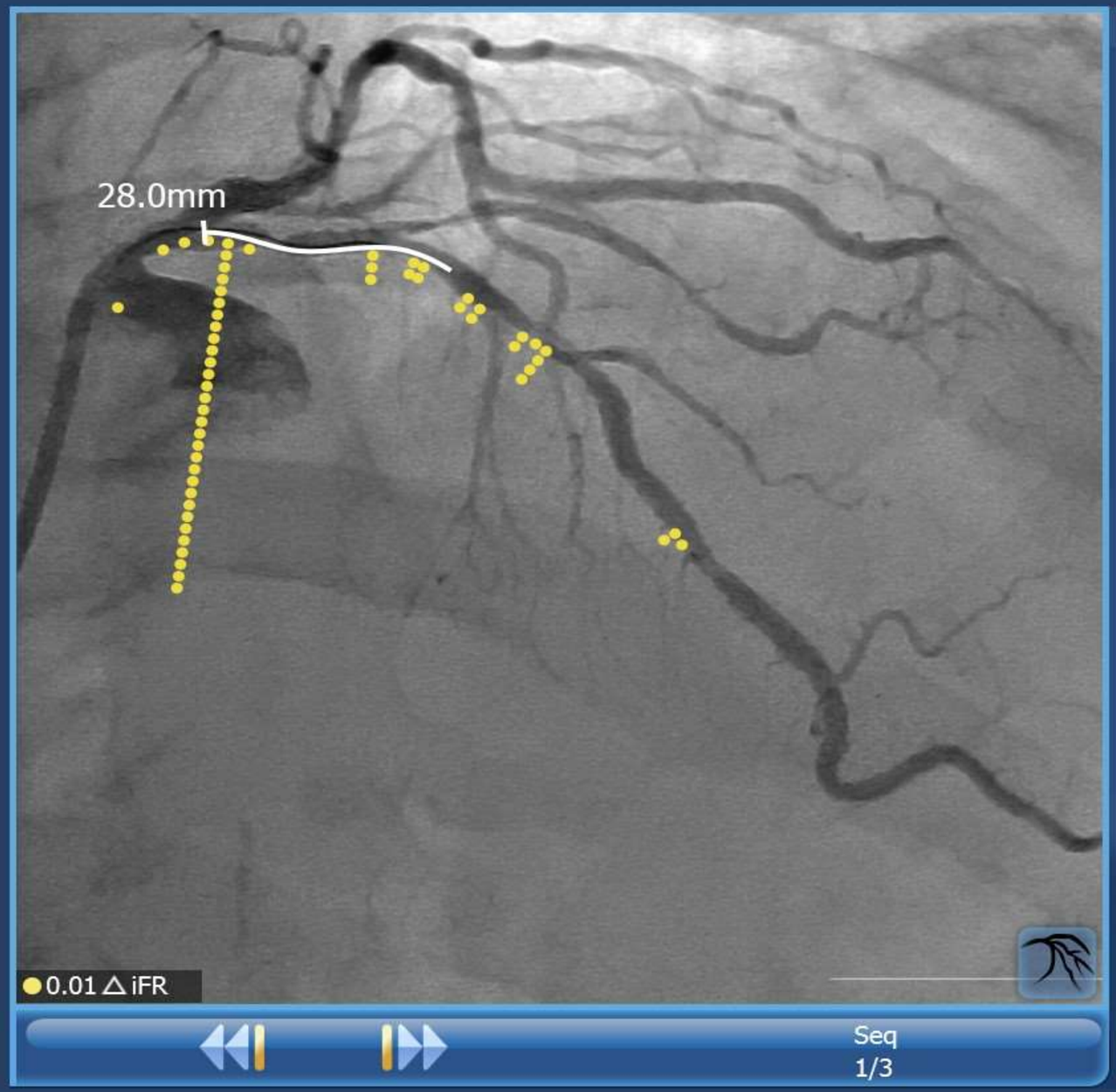
iFR Distal: 0.39

iFR at Cursor: 0.41



VOLCANO

PRECISION GUIDED THERAPY

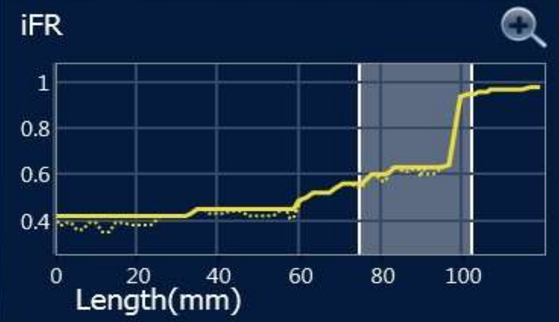


iFR Distal: 0.39

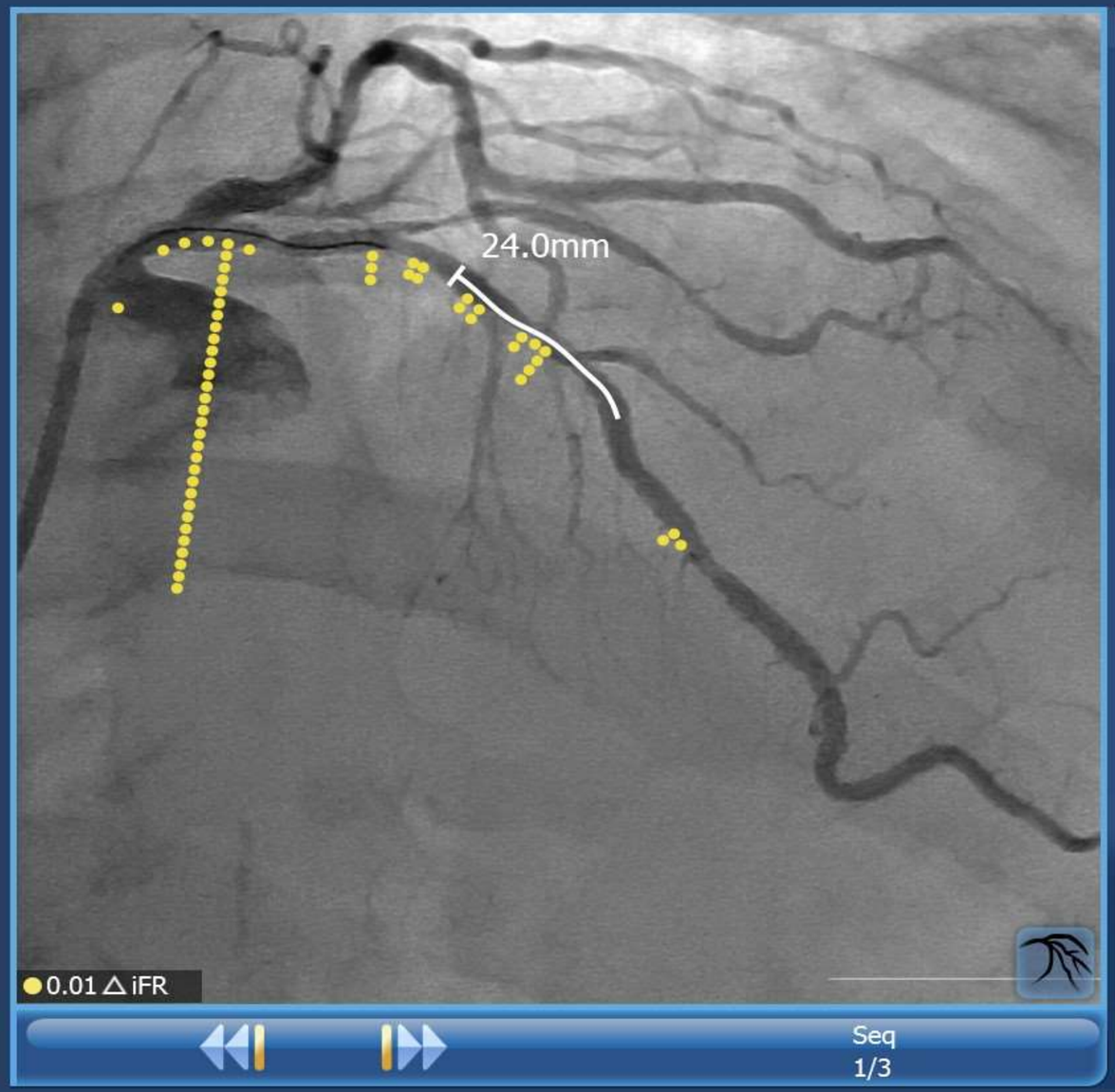
iFR drop in selection : 0.39

Predicted iFR
0.78

Length: 28.0mm



VOLCANO
PRECISION GUIDED THERAPY

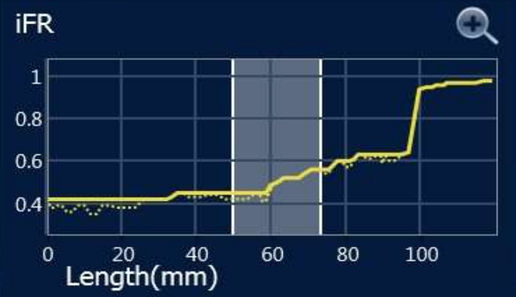


iFR Distal: 0.39

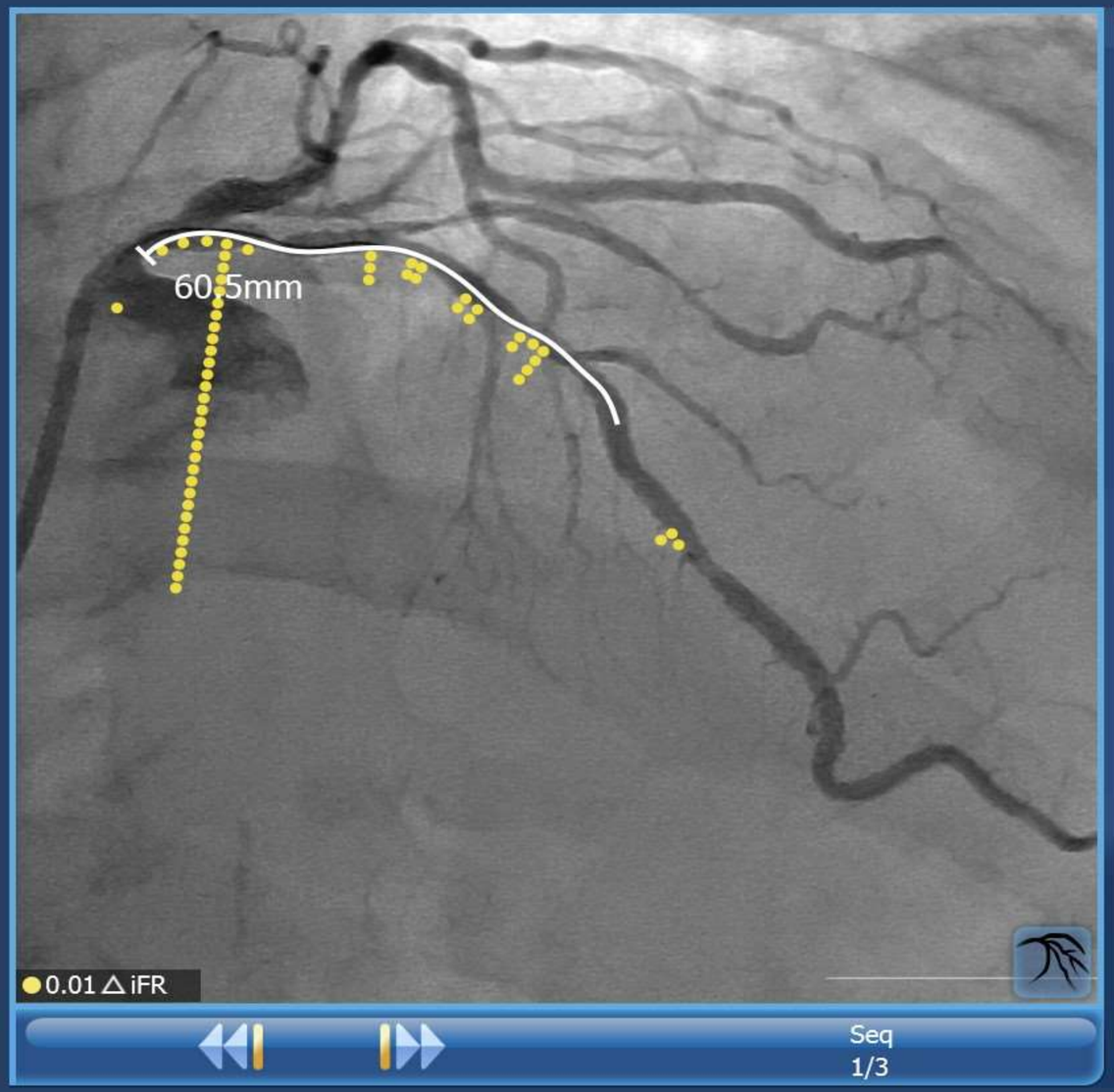
iFR drop in selection : 0.11

Predicted iFR
0.50

Length: 24.0mm



VOLCANO
PRECISION GUIDED THERAPY

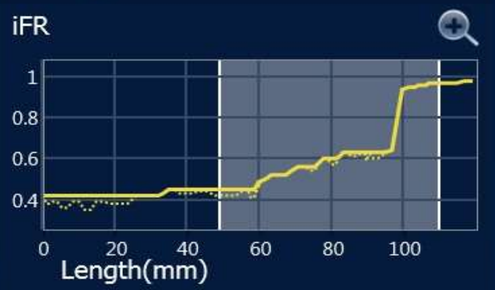


iFR Distal: 0.39

iFR drop in selection : 0.52

Predicted iFR 0.91

Length: 60.5mm



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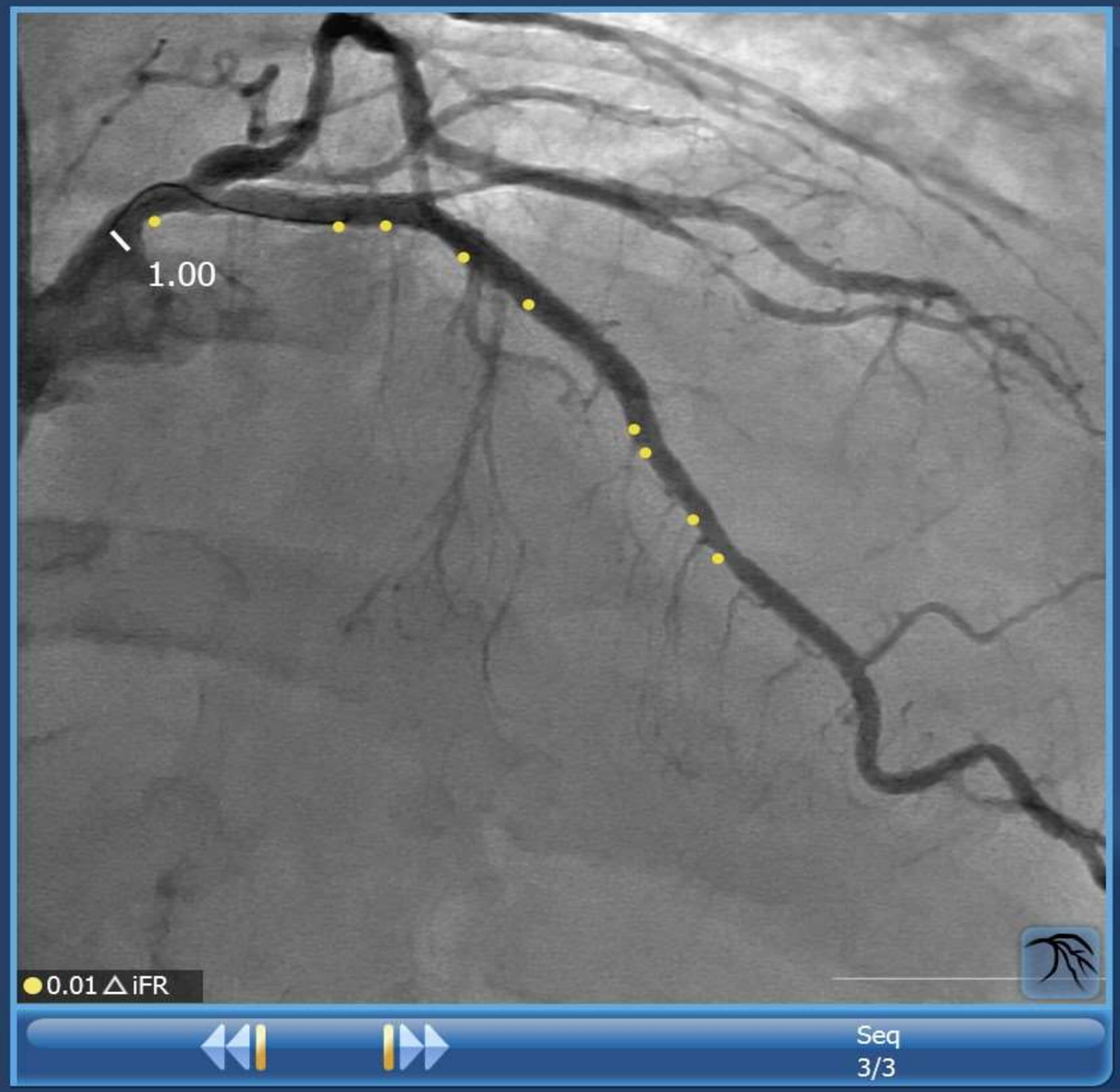
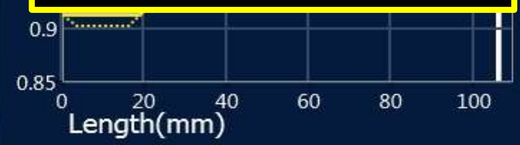


iFR Distal: 0.91

iFR at Cursor: 1.00

post iFR
0.91

Predicted iFR
0.91



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iFR pullback showed an improved accuracy of prediction of physiological outcome

Arthors	Year	Study type	Proximal or distal PCI	Pressure indices	Corrected with	Prediction Overestimations	No of lesions (vessel)
De Bruyne et al.	2000	Animal	Proximal	FFR	Wedge pressure	0.040±0.066	15 (LCx 100%)
De Bruyne et al.	2000	Animal	Distal	FFR	Wedge pressure	0.030±0.040	20 (LCx 100%)
Pijls et al.	2000	Human	Both	FFR	Wedge pressure	0.031±0	32 (NA)
Nijjer et al.	2014	Human	Both	iFR	None	0.016±0.023	32 (LAD 63%)
Kikuta et al.	2018	Human	Both	iFR	None	0.011±0.041	134 (LAD 75%)

FFR mandates Correction in prediction.
You need Occlude the vessel before PCI!

$$FFR(A)_{pred} = \frac{Pd - \left(\frac{Pm}{Pa}\right) Pw}{Pa - Pm + Pd - Pw}$$

$$FFR(B)_{pred} = 1 - \frac{(Pa - Pw)(Pm - Pd)}{Pa(Pm - Pw)}$$

My standpoint 2018 part 1

- iFR and FFR have similar outcomes at 1 year
- Deferral using iFR or FFR is very safe
- iFR is recommended in the US AUC guidelines
- iFR is safer than FFR in LAD deferral
- iFR needs shorter time for evaluation
- iFR is more patient friendly
- iFR deferral is possibly safer in ACS patients

My standpoint in 2018 part 2

- iFR pullback information give us an accurate treatment planning about stent position.

- Co-registration is only possible with iFR

- Based on these data, I believe now,

iFR is enough

Thank you for your attention!!!