



Hyperemia Free Indexes:
Algorithms, Diagnostic and Prognostic Performance

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Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship

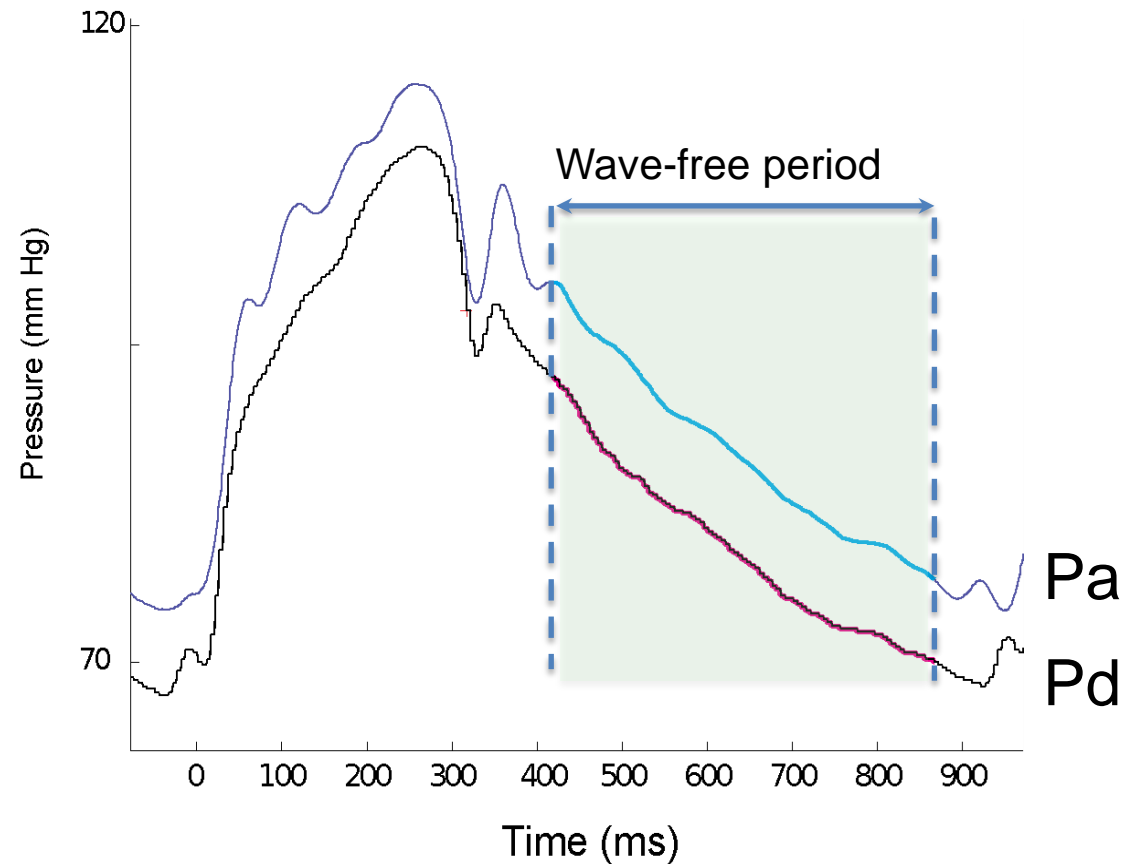
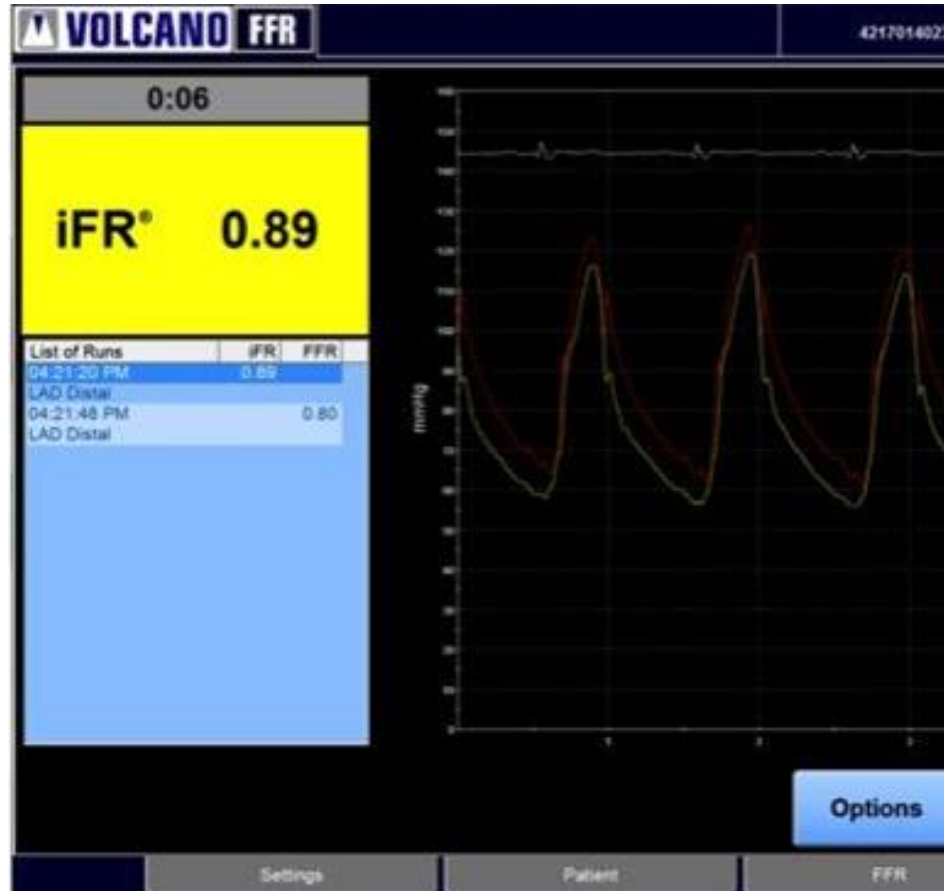
- Consulting Fees/Honoraria

Company

- Zeon Medical Inc,
Phillips volcano
Abott Vascular
Boston Scientific,
Kaneka Medical Inc,
Nihon Medipysics

Definition of iFR:

Instant wave-free ratio across a stenosis during the wave-free period, when **resistance is naturally constant** and minimized in the cardiac cycle



Study Design

DEFINE FLAIR



Coronary stenosis in which physiological severity was in question

1:1 Randomization

Hyperemia

Resting

**FFR-guided
revascularization**

**iFR-guided
revascularization**

FFR >0.8
Defer PCI

FFR ≤0.8
Perform PCI

iFR >0.89
Defer PCI

iFR ≤0.89
Perform PCI

30 day, 1-, 2- and 5-year follow-up

Primary endpoint to be reported at 1-year

MACE composite endpoint of:

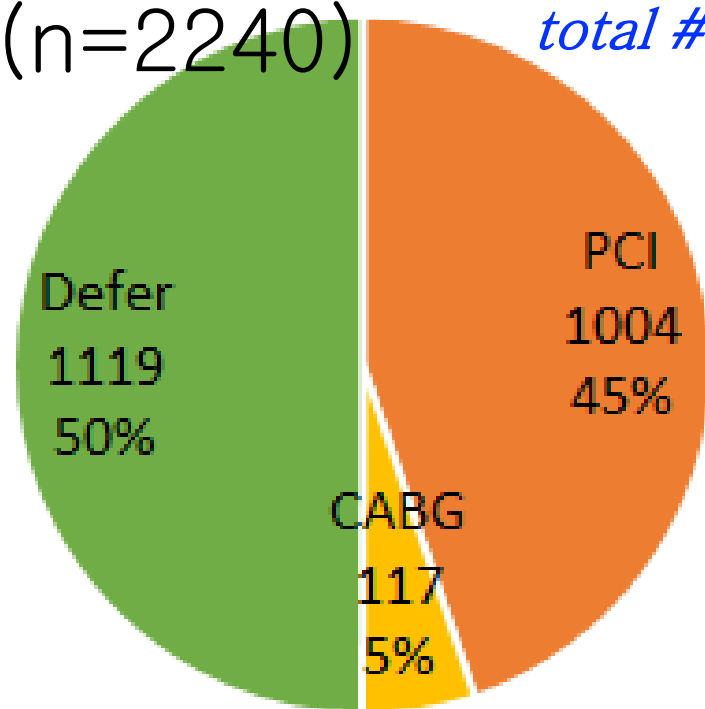
- Death
- Non-fatal myocardial infarction
- Unplanned revascularization

Non-inferiority margin for risk difference: 3.4%

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

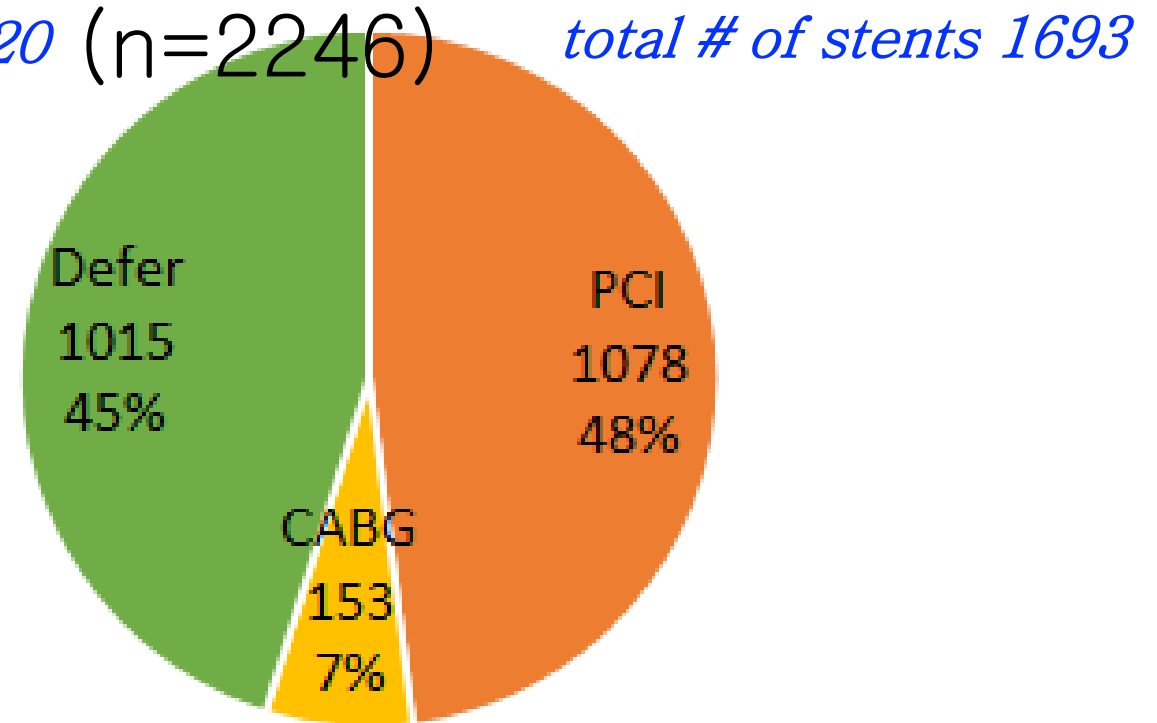
pooled analysis of Define FLAIR and iFR Sweedeheart

iFR guide
(n=2240)



■ PCI ■ CABG ■ Defer

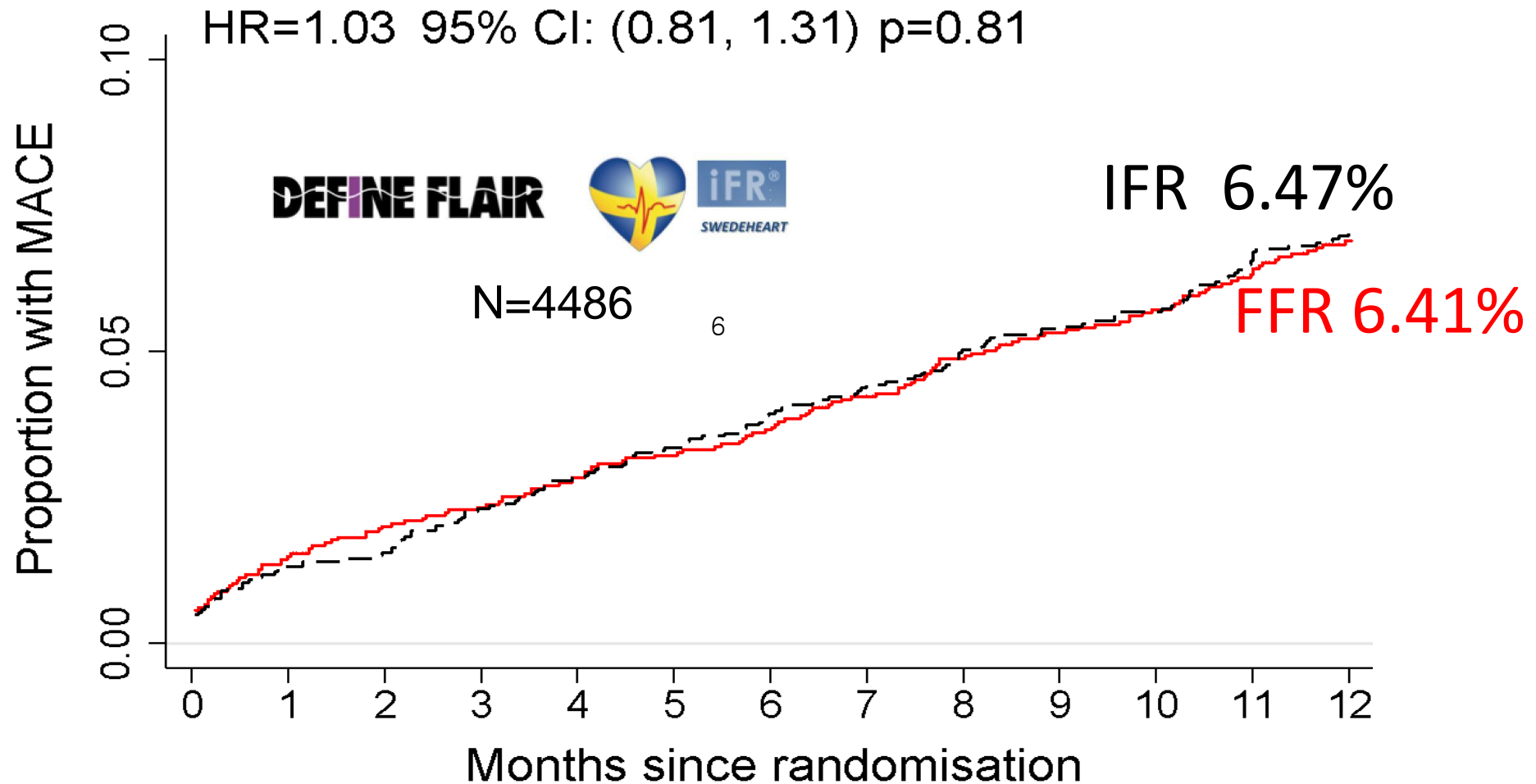
FFR guide
(n=2246)



■ PCI ■ CABG ■ Defer

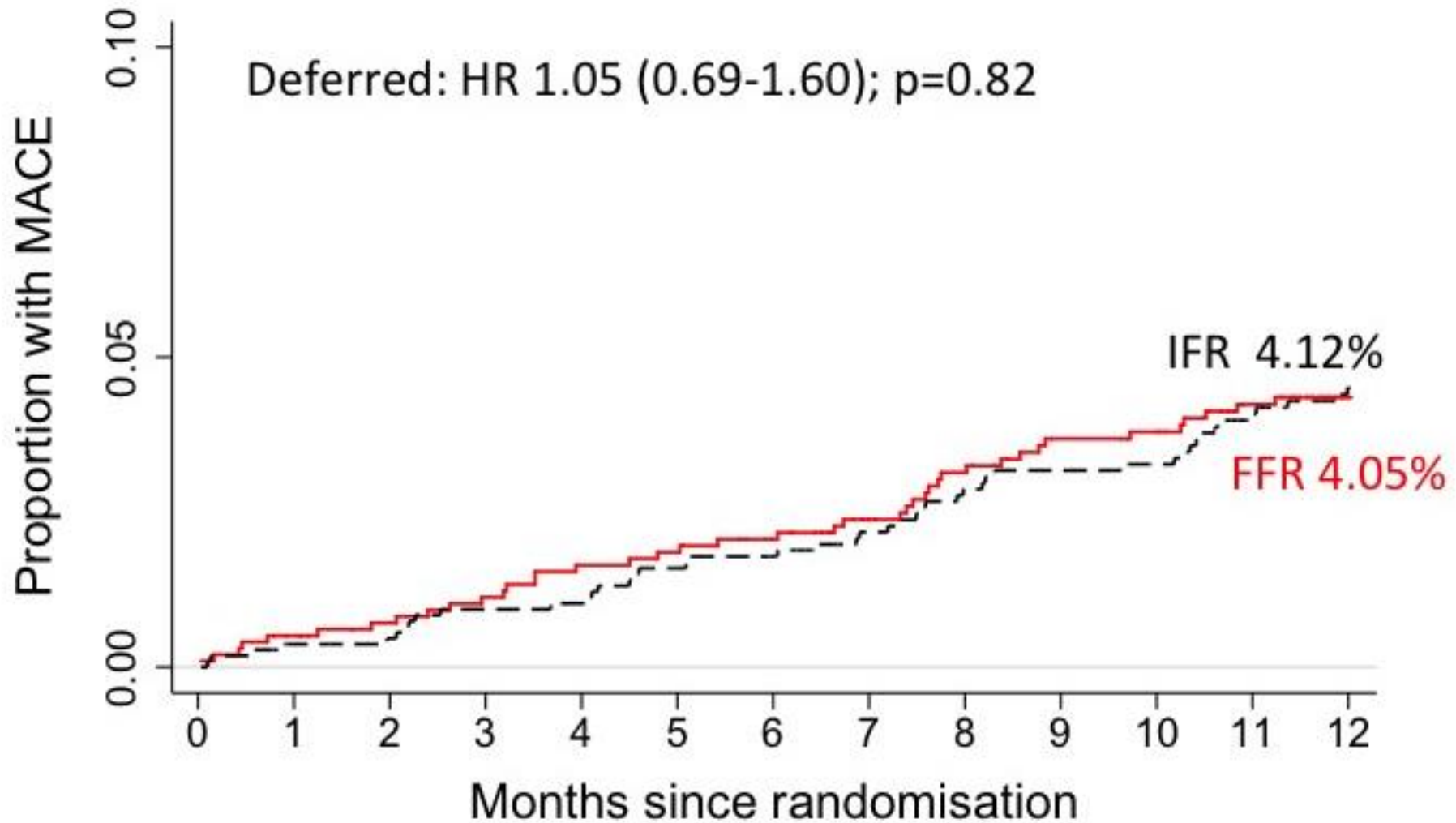
Significantly less revascularisation based on iFR interrogation (P < 0.01)

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



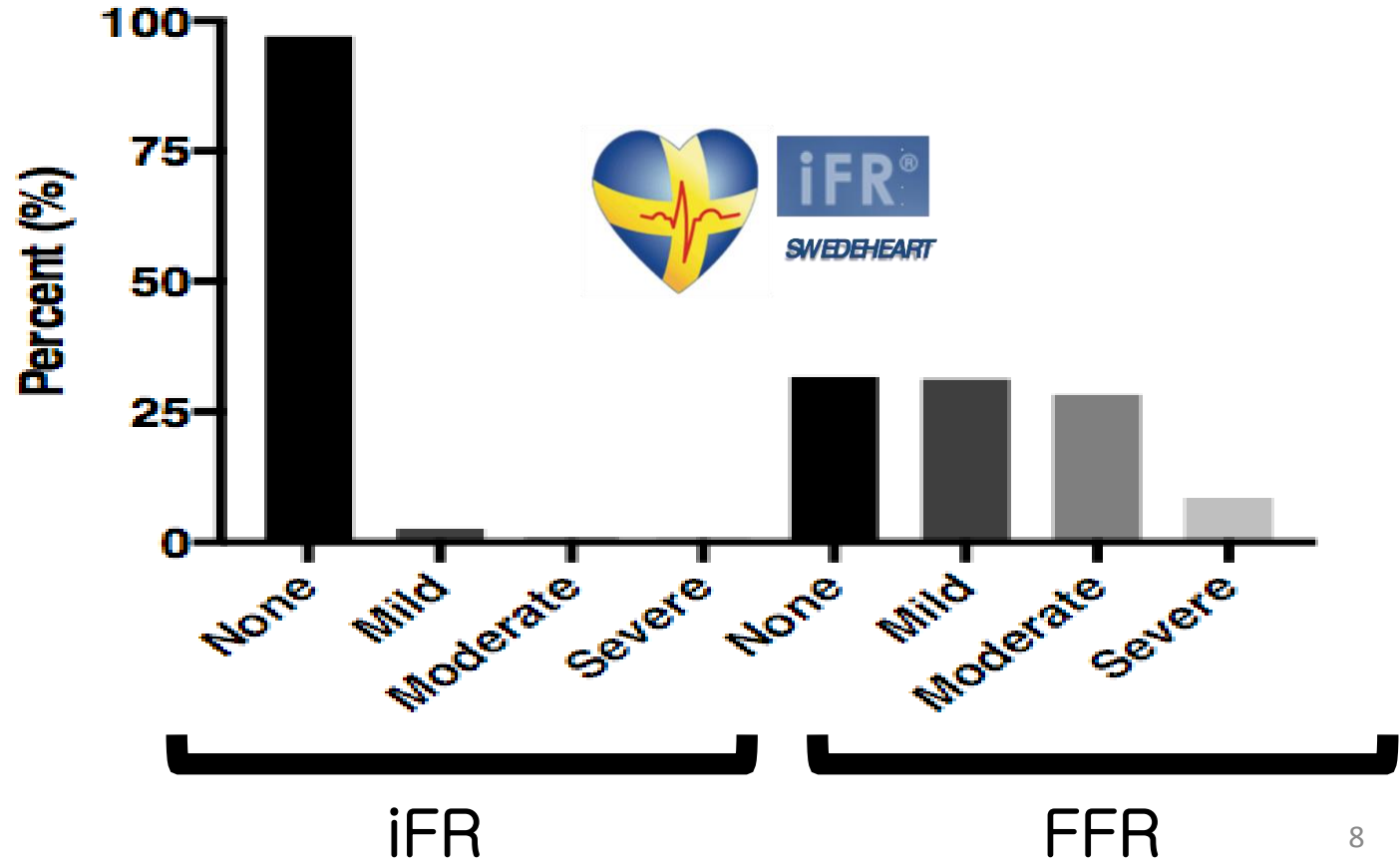
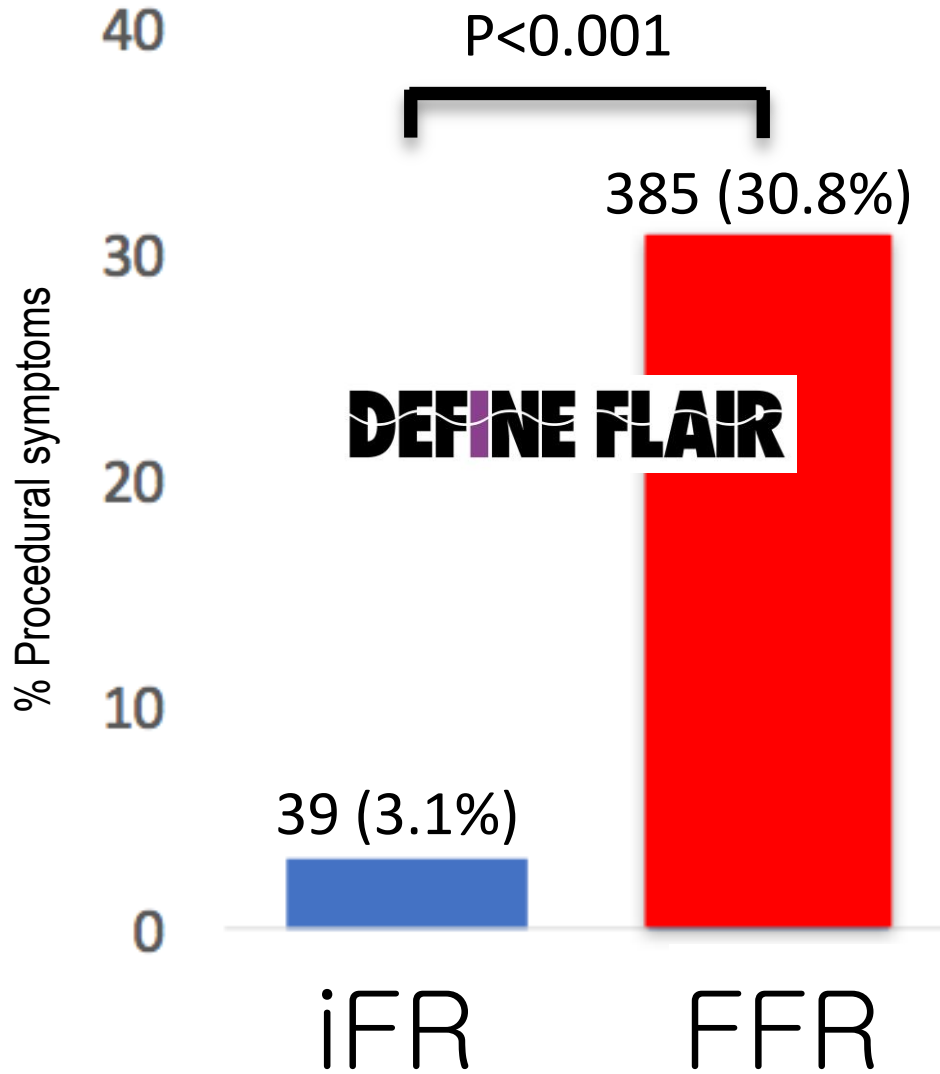
MACE similar and low at 1 year after iFR- and FFR-based decision-making

Pooled data: analysis of deferred revascularisation patients

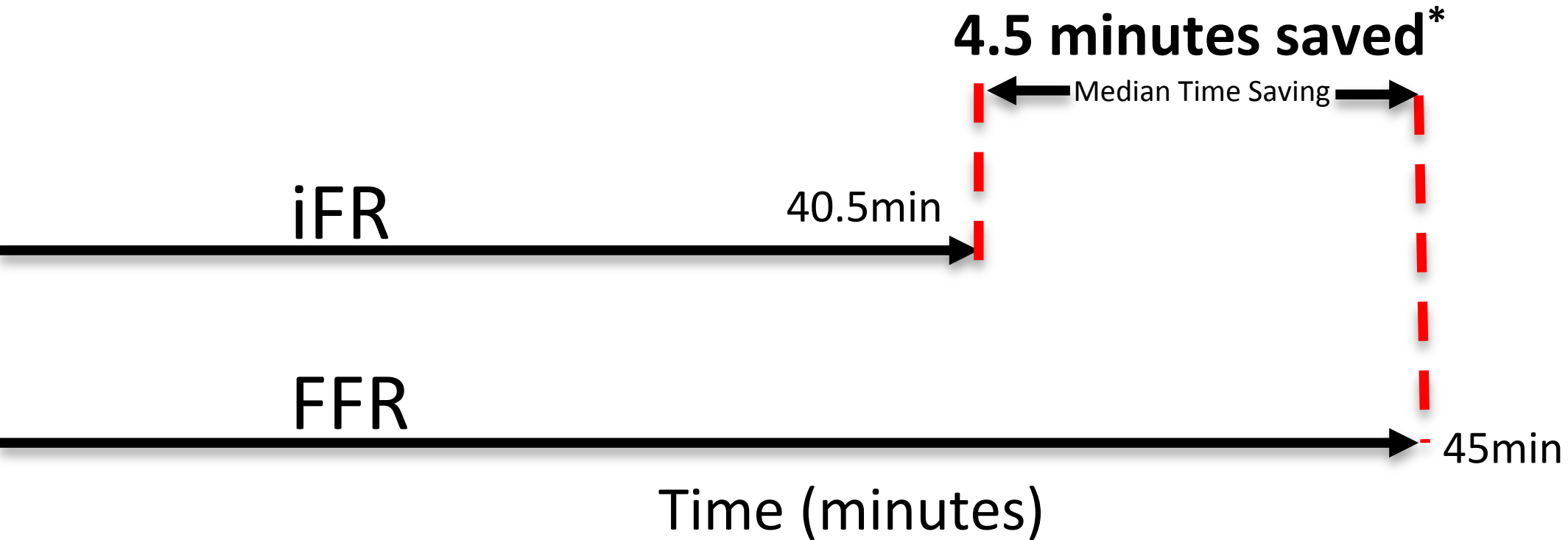


Similar and low MACE rates at 1 year after iFR- and FFR- based deferral

iFR: fewer side effect



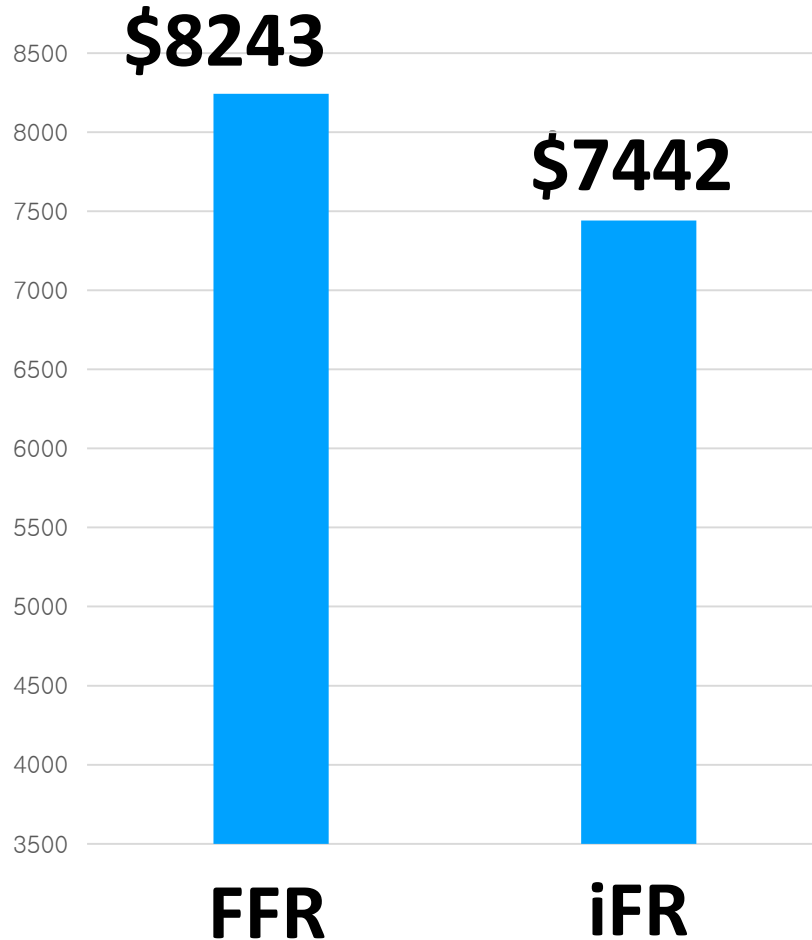
DEFINE FLAIR: iFR guided revascularization reduces procedure time



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

Significantly Lower Cost with iFR

**Adjusted Δ \$896
(p=0.006)**



Shorter procedural duration

No hyperaemic medication

Lower PCI rates

Fewer CABG procedures

Fewer Unplanned PCI (LAD)

ESC Guideline of coronary revascularization (Neumann, Sousa-Uva et al. 2018)

Recommendations on functional testing and intravascular imaging for lesion assessment

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

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When evidence of ischemia is not available, FFR or iwFR are recommended to assess the hemodynamic relevance of intermediate grade stenosis.

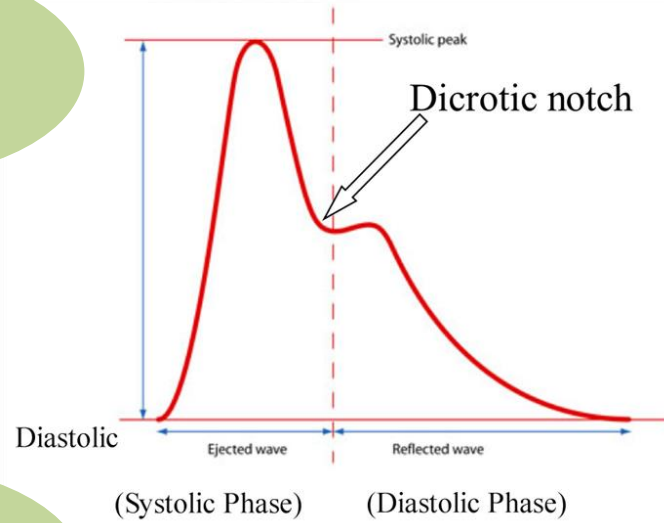
FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; IVUS = intravascular ultrasound; PCI = percutaneous coronary intervention.

^aClass of recommendation.

^bLevel of evidence.

Intracoronary Physiology Indices

iFR



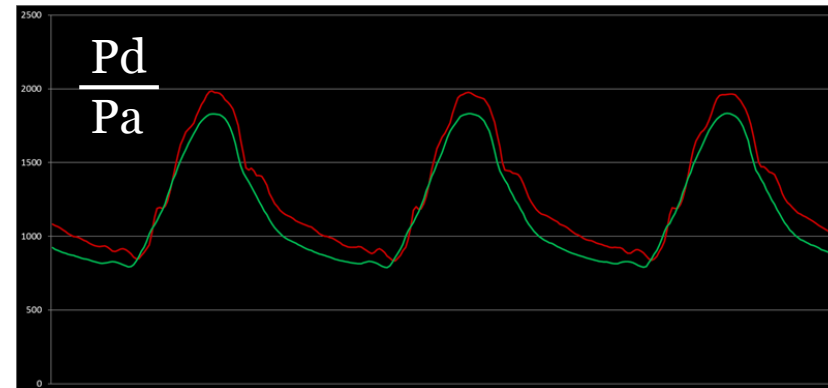
Pd/Pa



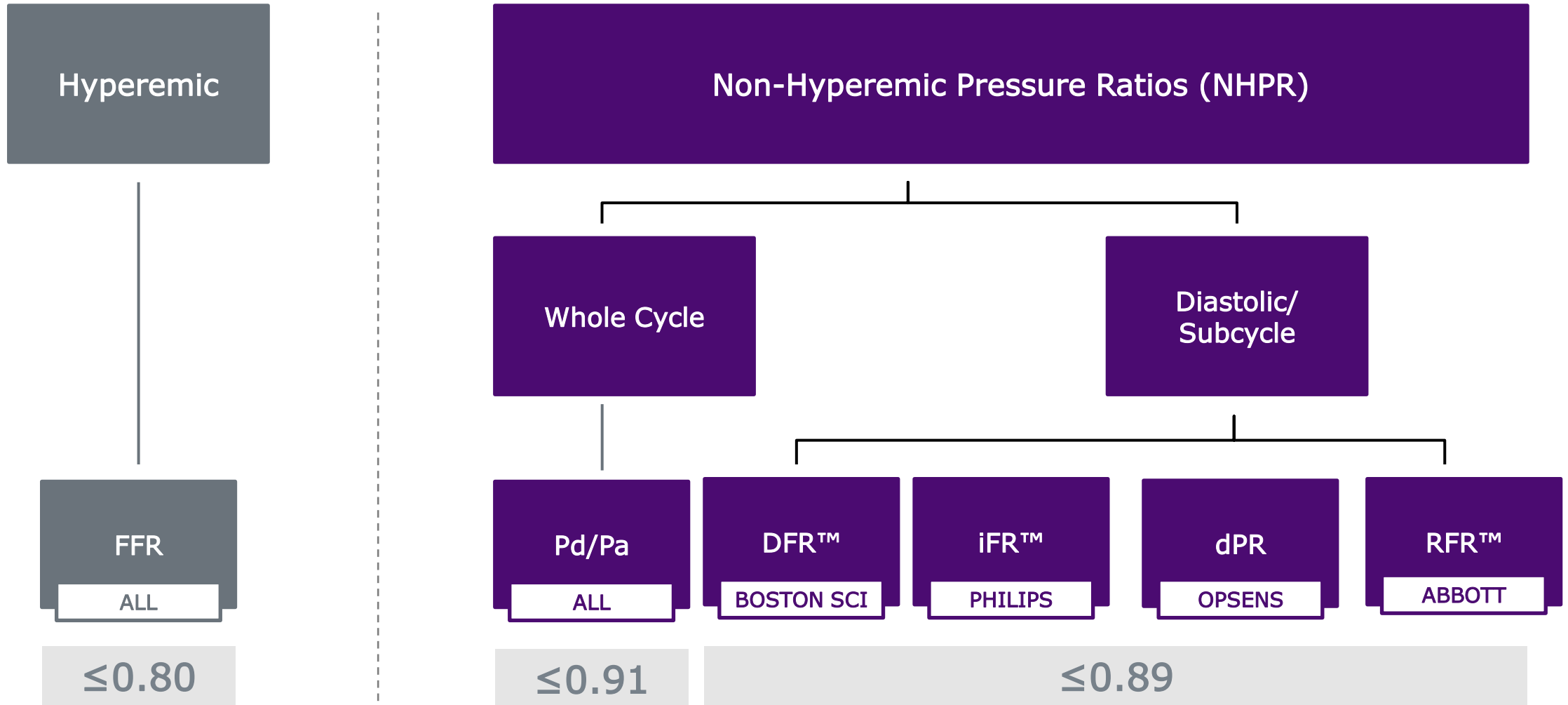
FFR

RFR

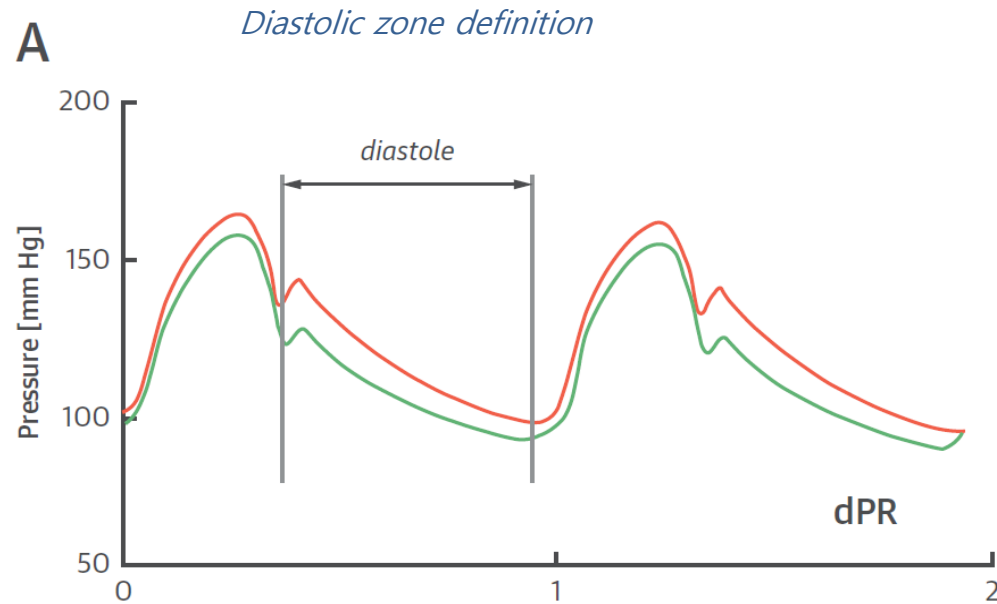
dPR



Options in Coronary Physiology



dPR provided by Opsens

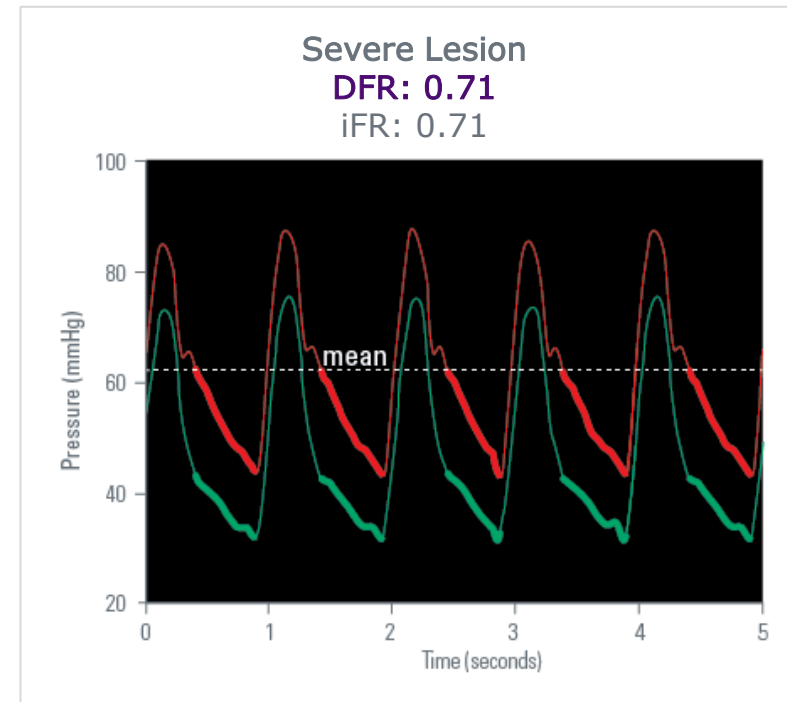
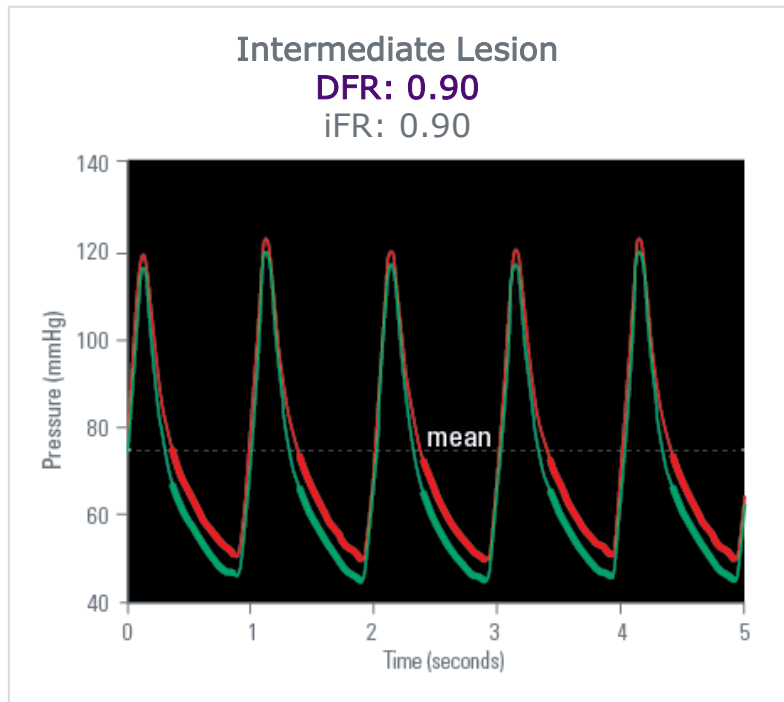


The dPR is shown as the Pd/Pa^* ratio over the entire diastole

* *mean (Pd/Pa)*

- Does not require ECG signal.
- Opsens own signal analysis and dicrotic notch detection method.
- Median value over 4 consecutive heartbeats is regarded as dPR because this allows reliable dPR measurement without the need for analyzing and rejecting heartbeats that are considered as irregular/outliers.

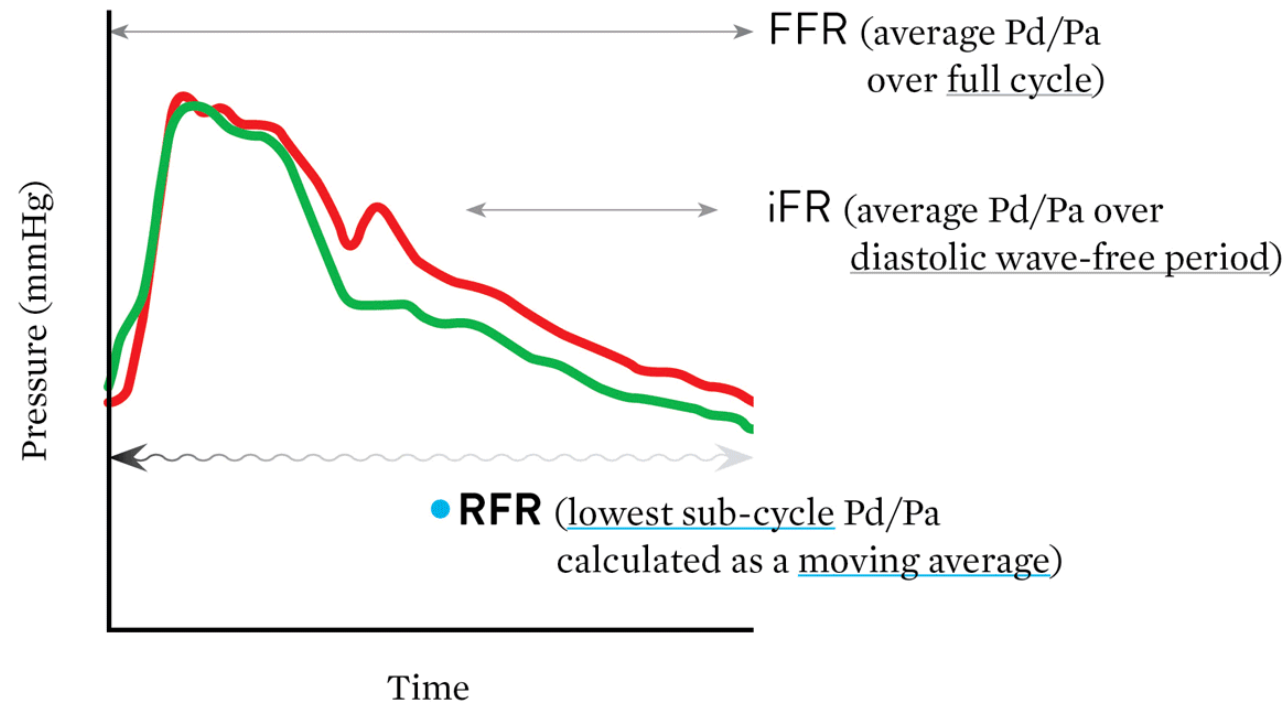
DFR provided by Boston Scientific



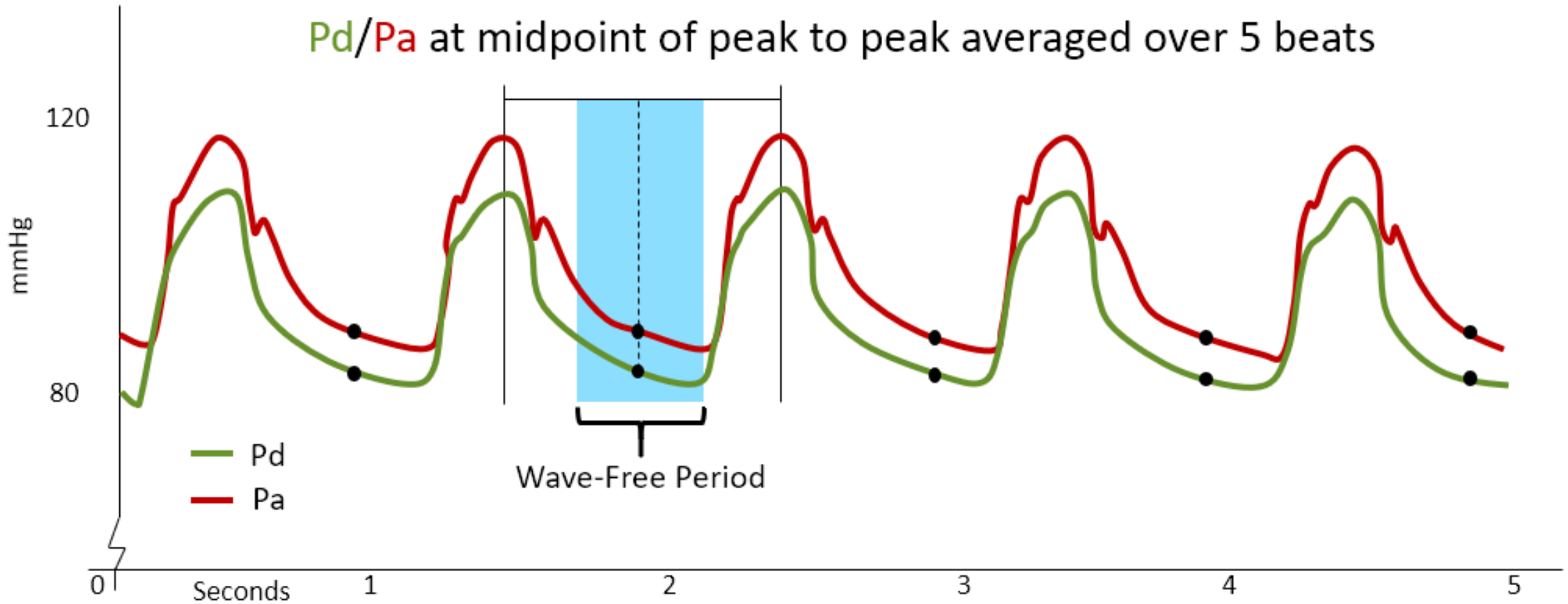
- This e DFR window uses two criteria: **Pa < mean Pa** **AND** **down-sloping Pa**
- No ECG signal required
- 5-beat average in bold = DFR definition

RFR provided by Abbott Vascular

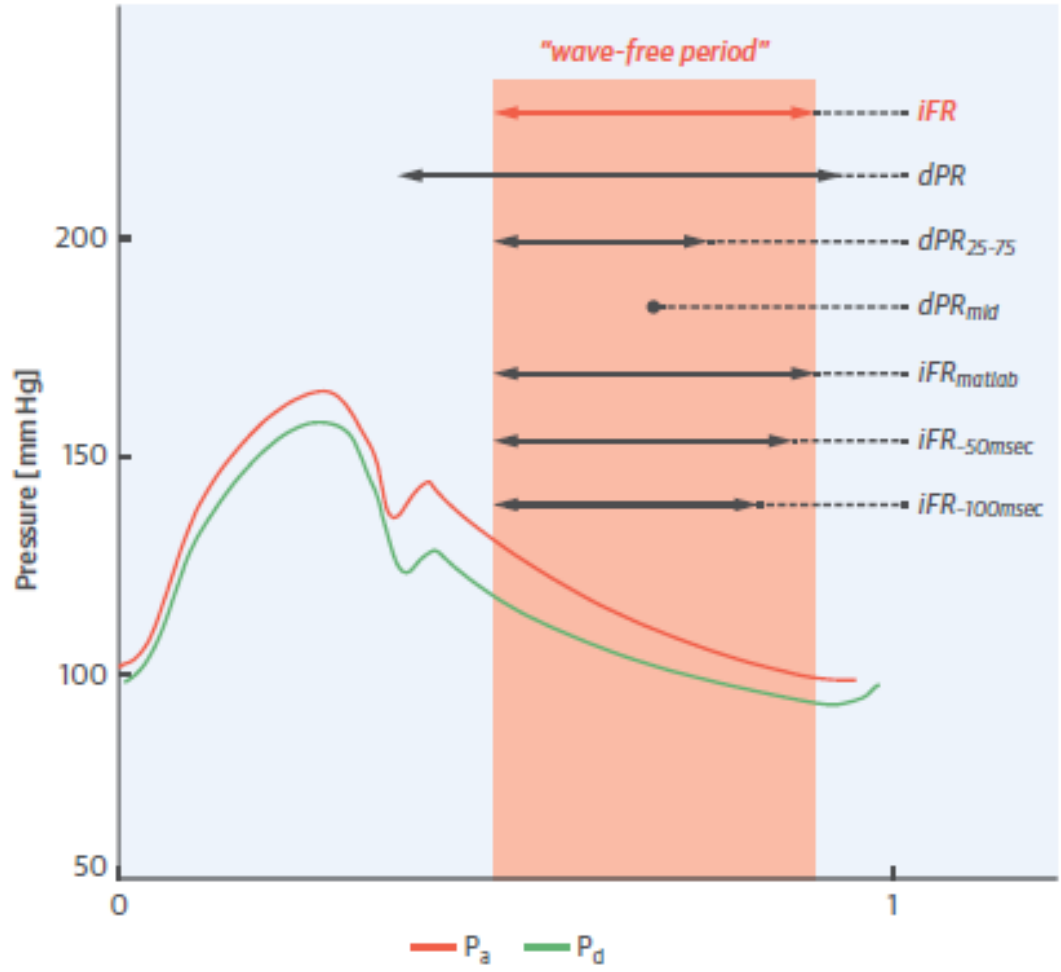
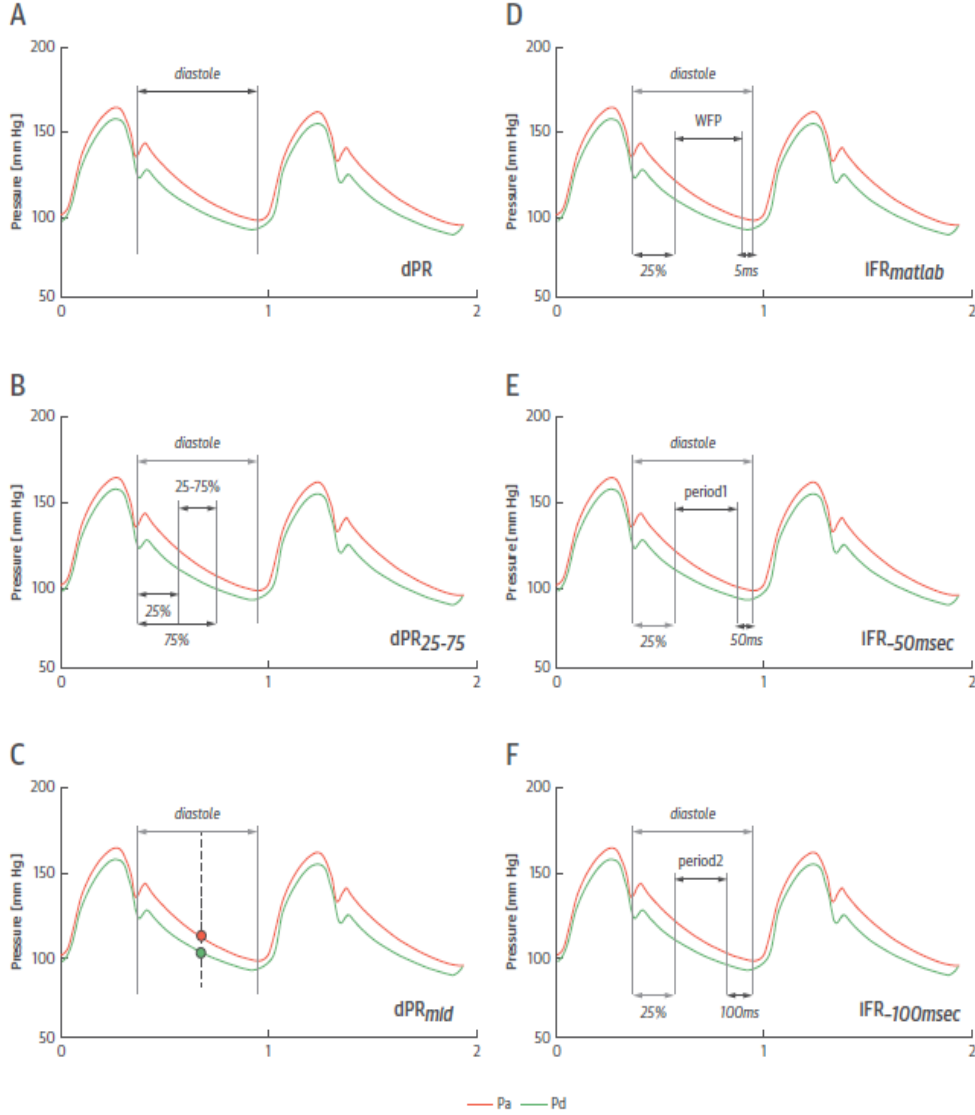
- RFR = Resting Full Cycle Ratio
- RFR is a resting index specifically equipped with abbot vascular pressure wire.
- RFR is defined as the lowest Pd/Pa during whole cardiac cycle. 5 beats averaging value is regarded as the RFR in the single point calculation whereas Beat by beat value is applied to draw the pullback curve of RFR.



ACIST dPR: Algorithm Definition



Comparison of different diastolic resting indexes to iFR



088-96

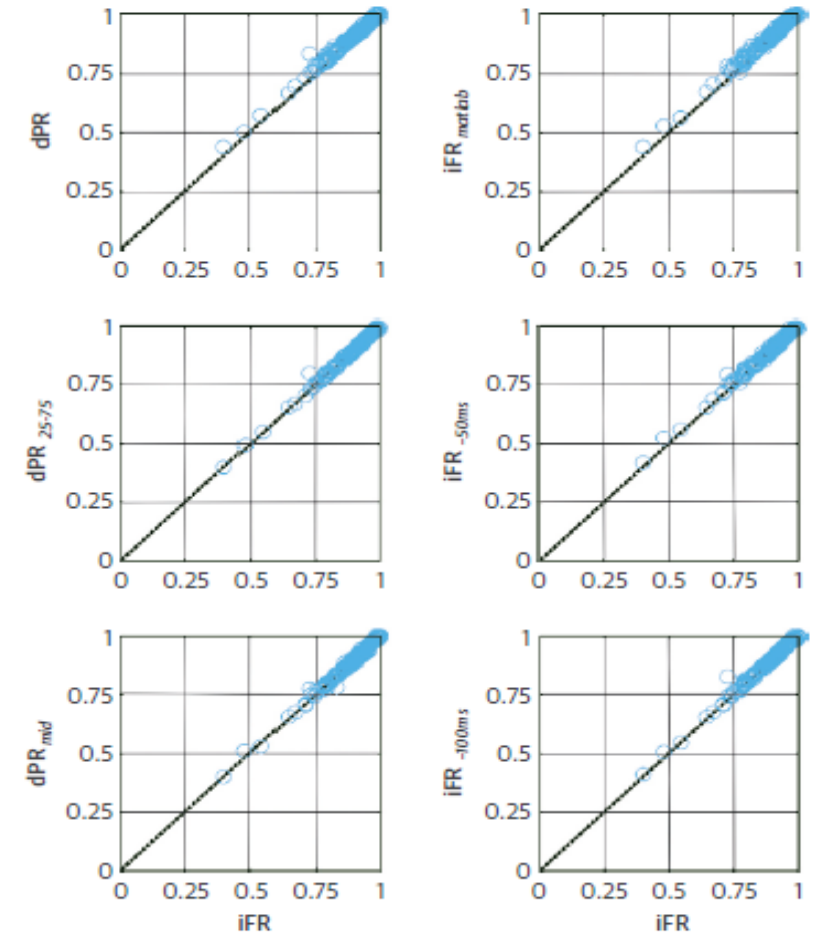
Comparison of different diastolic resting indexes to iFR

TABLE 1 Median Values and Mutual Differences, Spearman's Correlation Coefficients, Coefficients of Determination, and AUC Values of Resting Diastolic Indexes With Respect to iFR

Index	Median (IQR)	Difference With iFR	Spearman's Rho	R ²	AUC
dPR	0.920 (0.880–0.960)	0.0059 ± 0.0108	0.993	0.984	0.997
dPR ₂₅₋₇₅	0.915 (0.870–0.950)	0.0012 ± 0.0065	0.997	0.994	0.999
dPR _{mid}	0.915 (0.870–0.950)	0.0012 ± 0.0081	0.993	0.990	0.997
iFR _{matlab}	0.915 (0.875–0.955)	0.0054 ± 0.0088	0.993	0.989	0.995
iFR _{-50ms}	0.915 (0.870–0.950)	0.0026 ± 0.0083	0.996	0.990	0.998
iFR _{-100ms}	0.915 (0.870–0.960)	0.0009 ± 0.0086	0.996	0.990	0.998

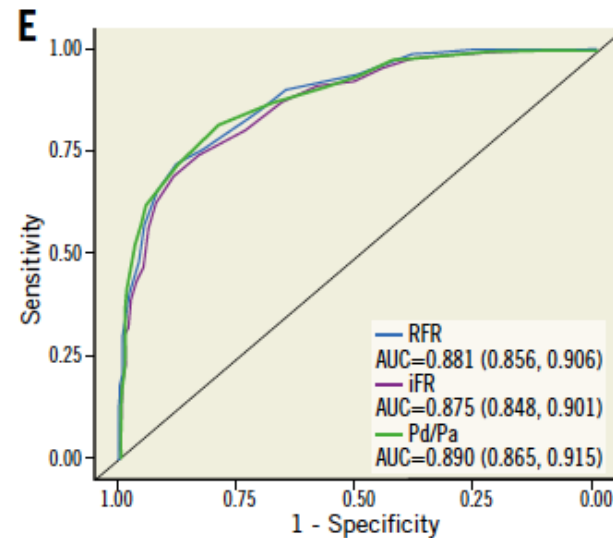
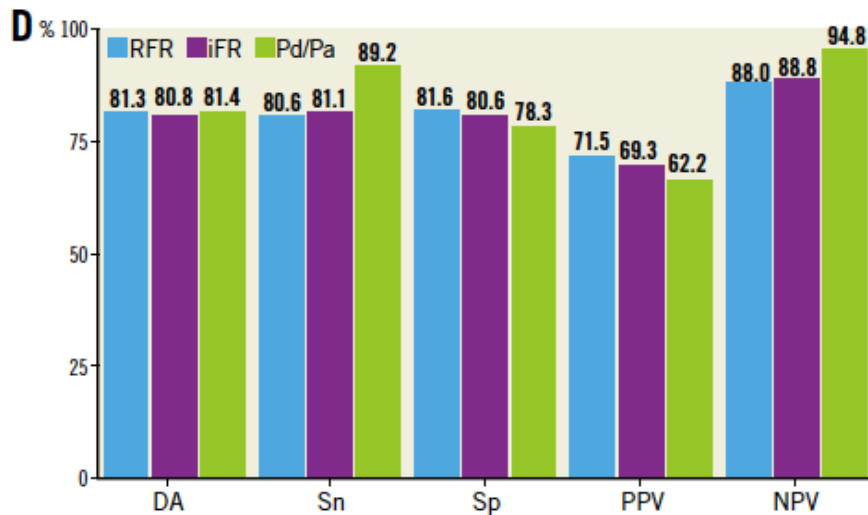
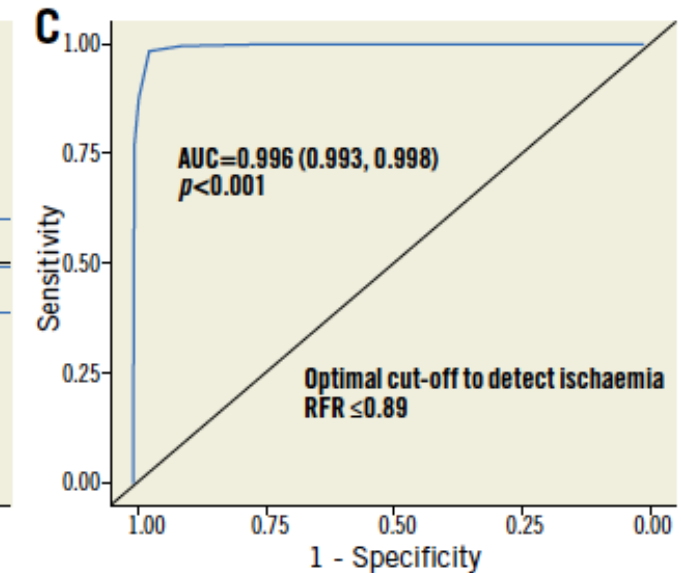
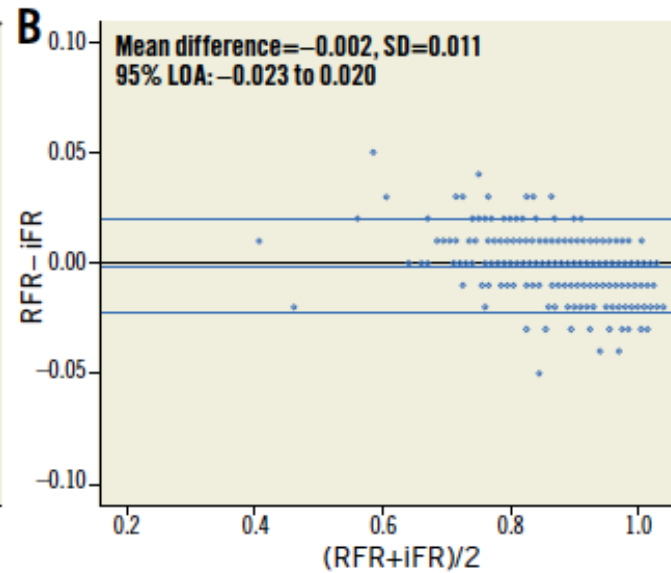
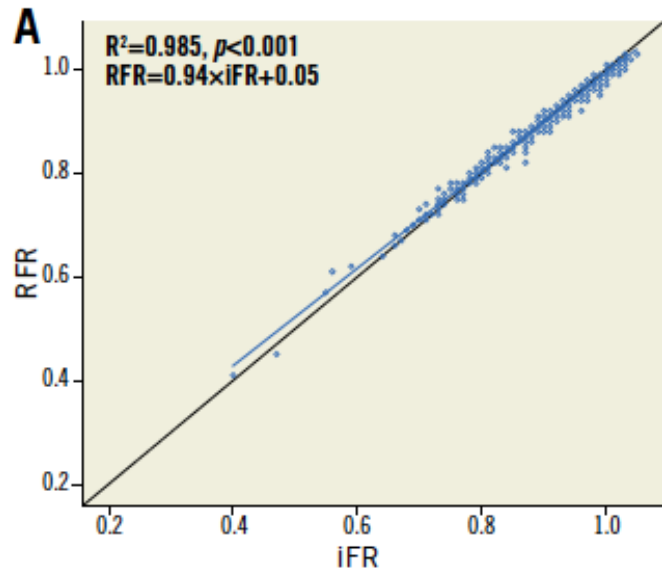
AUC = area under the curve; dPR = diastolic pressure ratio; dPR₂₅₋₇₅ = average Pd/Pa from 25% to 75% into diastole; dPR_{mid} = Pd/Pa at the single point in time at mid-diastole; iFR = instantaneous wave-free ratio; iFR_{-50ms} = average Pd/Pa from 25% into diastole until 50 ms before end of diastole; iFR_{-100ms} = average Pd/Pa from 25% into diastole until 100 ms before end of diastole; iFR_{matlab} = average Pd/Pa from 25% into diastole until 5 ms before end of diastole; IQR = interquartile range; Pa = aortic pressure; Pd = distal coronary pressure.

FIGURE 2 Scatterplots of iFR Versus Different Diastolic Indexes



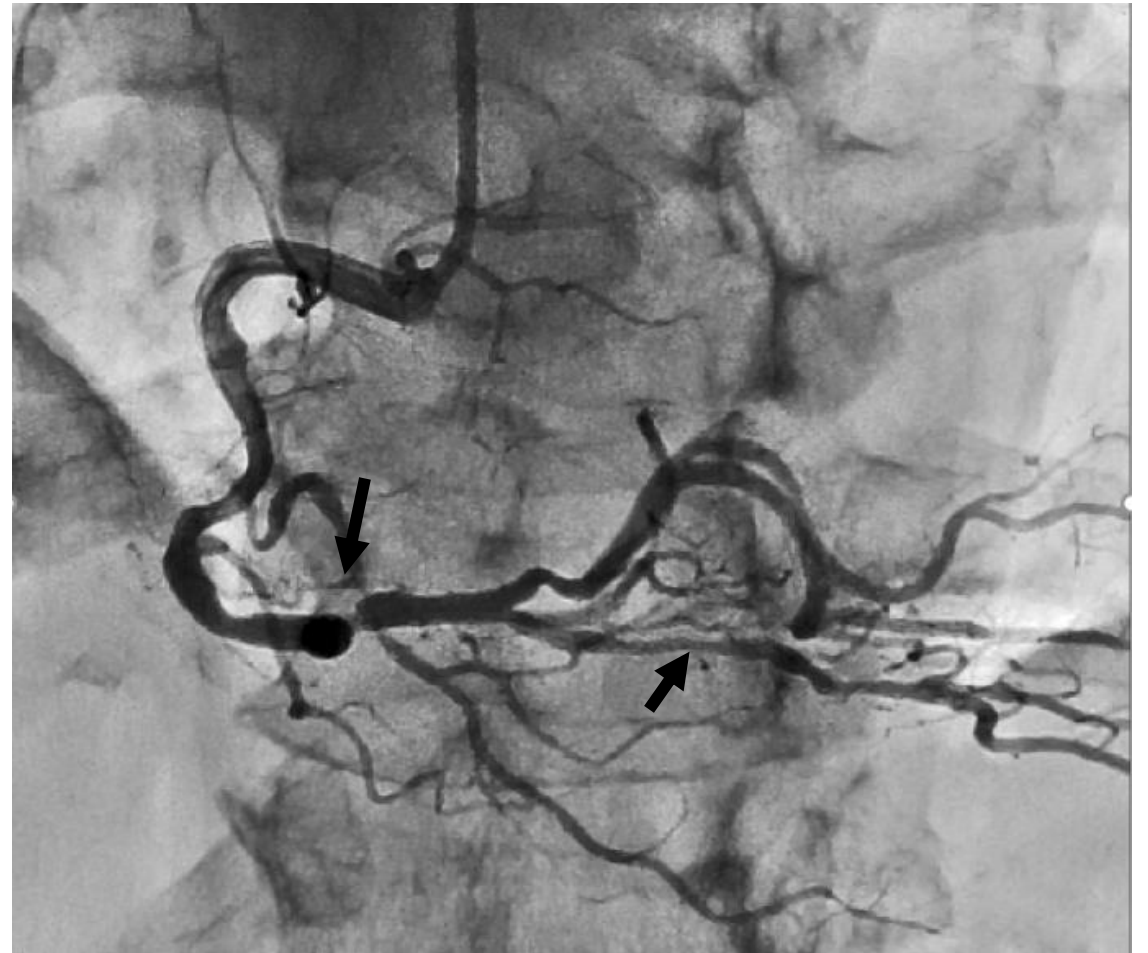
Scatterplots of iFR versus different diastolic indexes. The dashed lines indicate the line of identity. Abbreviations as in Figure 1.

VALIDATE RFR study

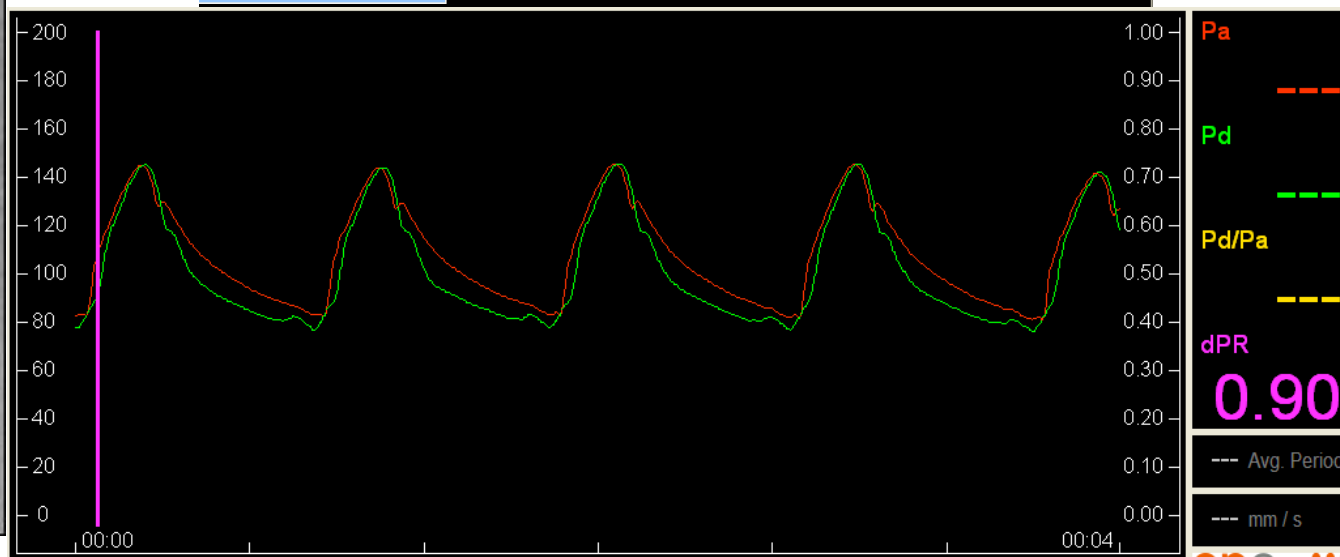
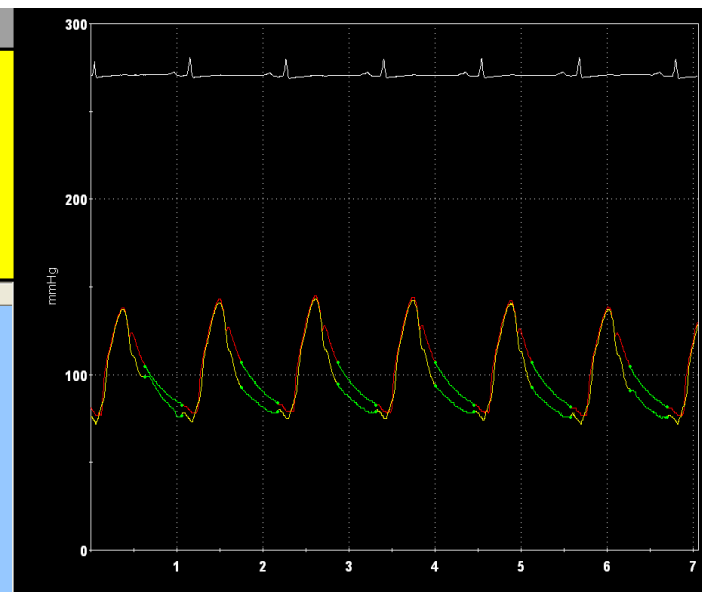
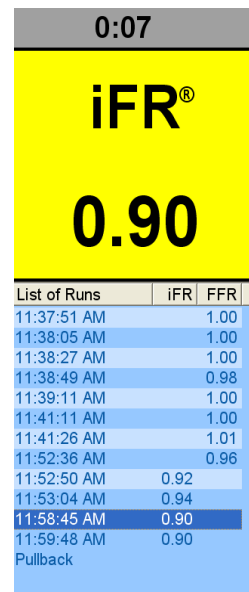


Case 1: 72 y.o. male, atypical chest pain

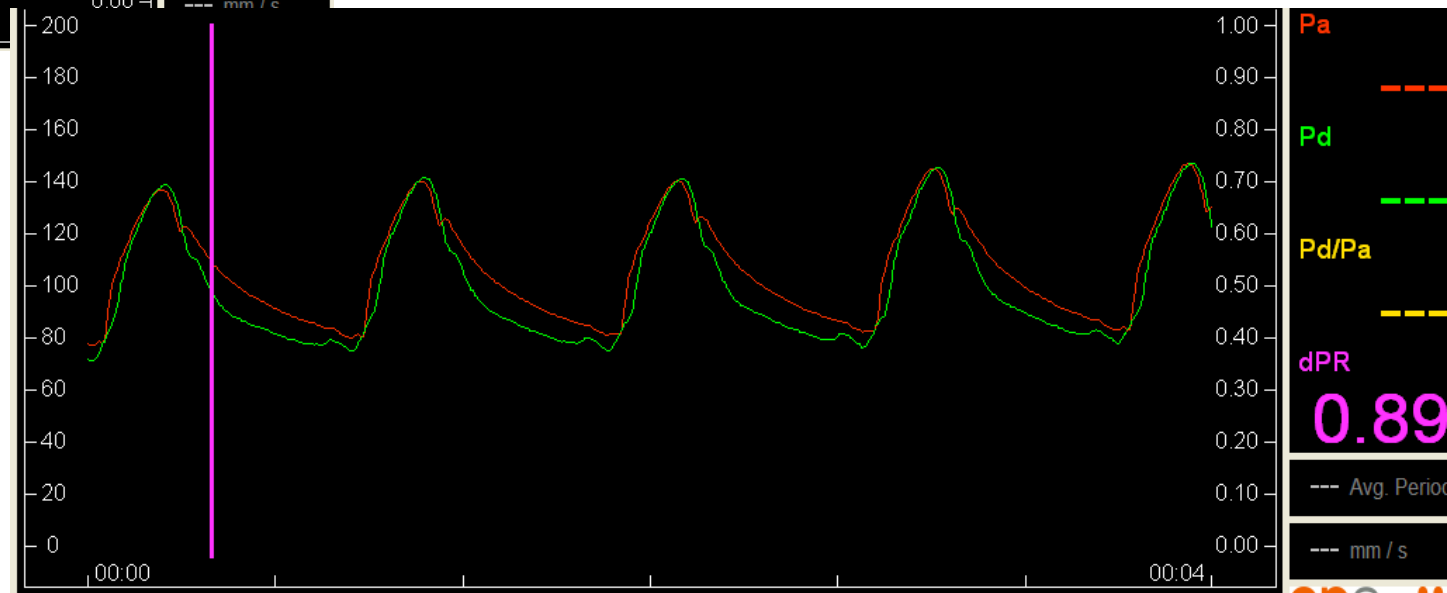
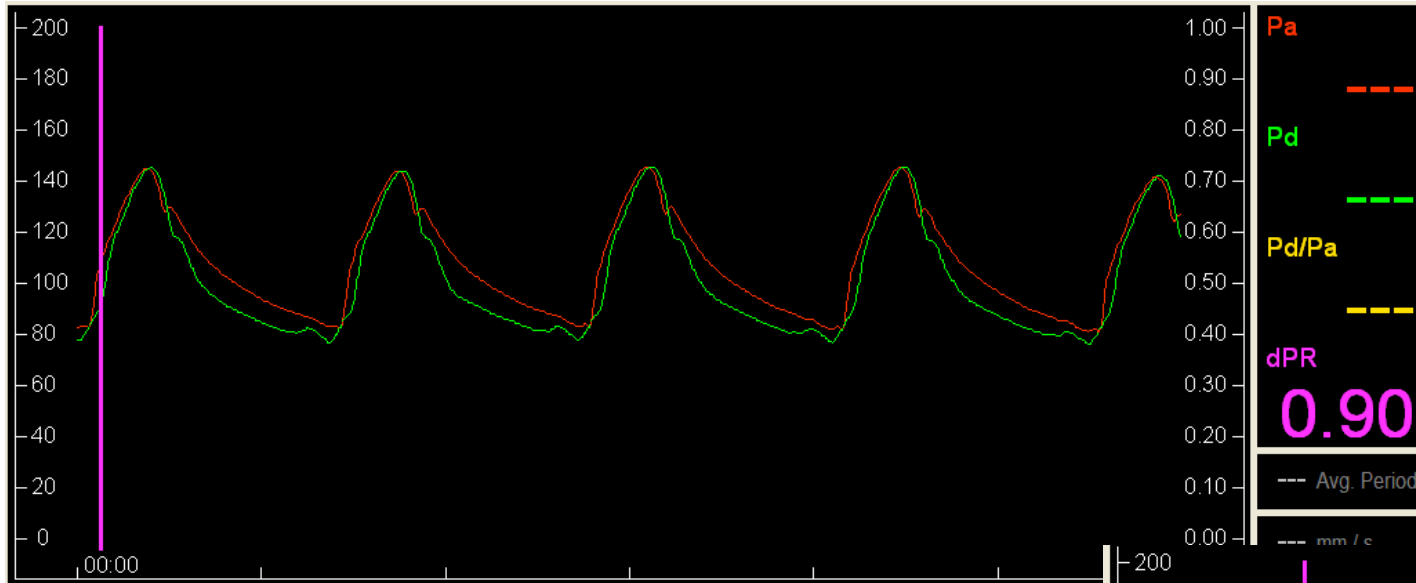
Coronary angiogram showed serial stenosis in RCA



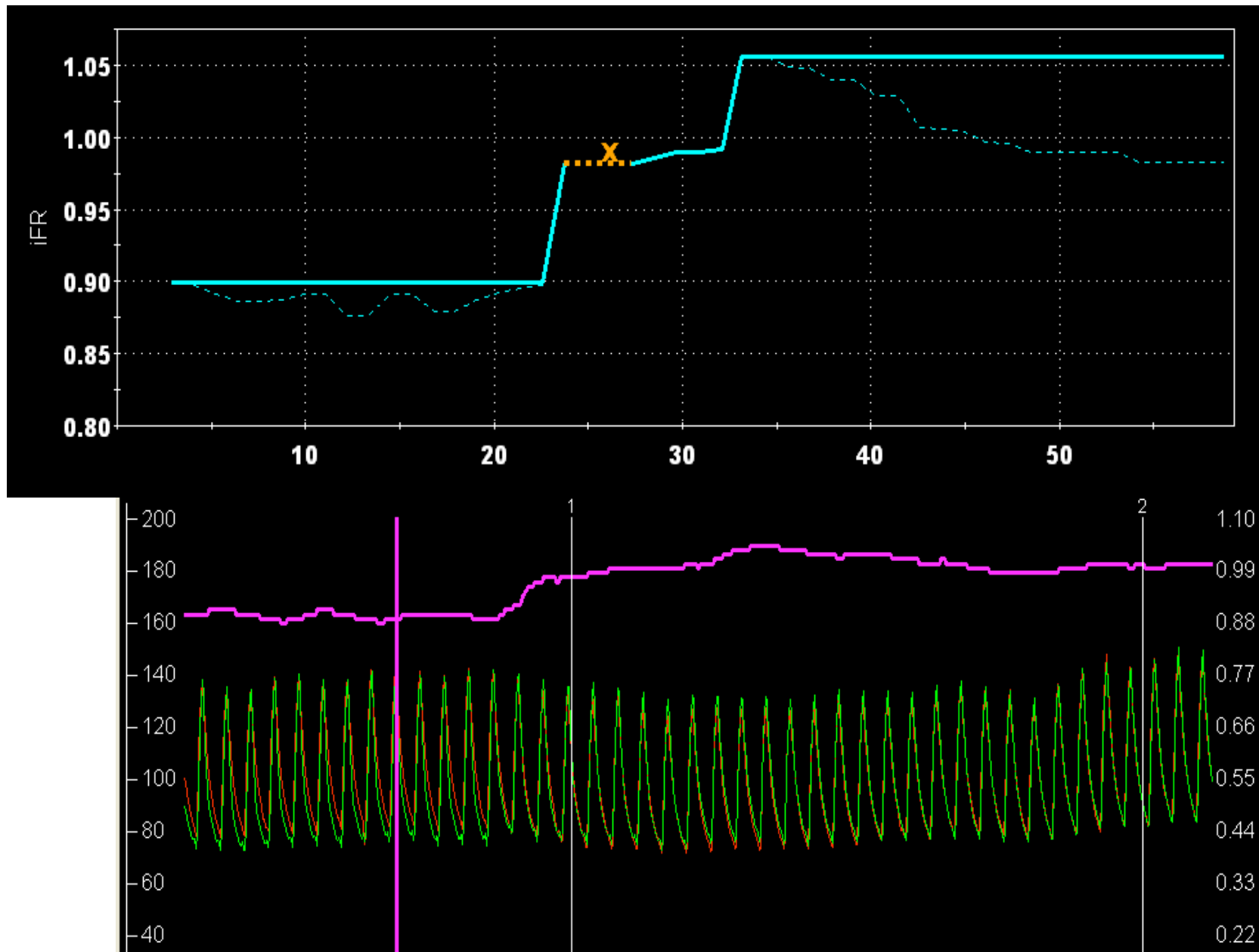
Simultaneous Assessment of dPR and iFR



dPR is reproducible

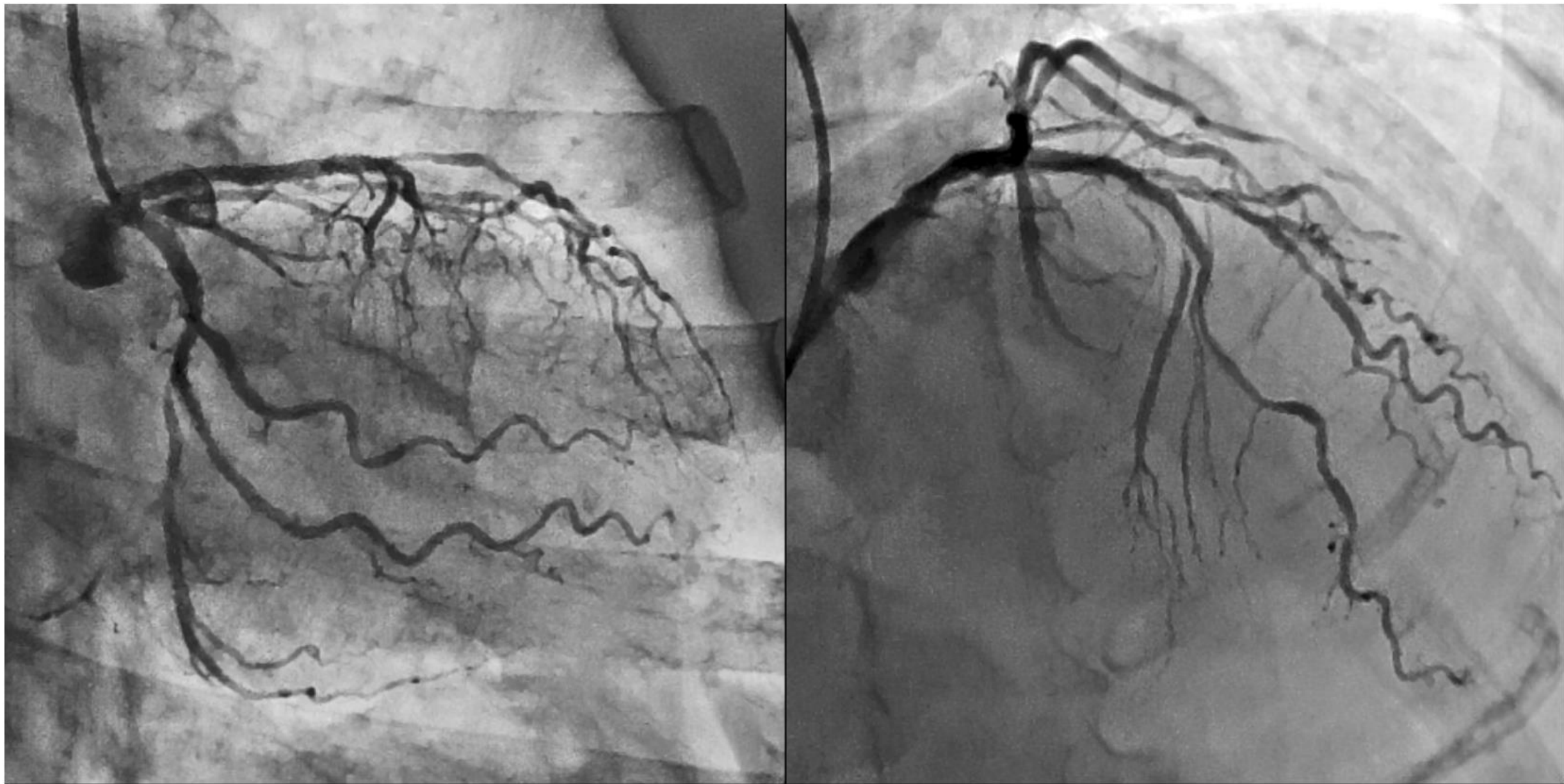


Pullback assessment of iFR and dPR

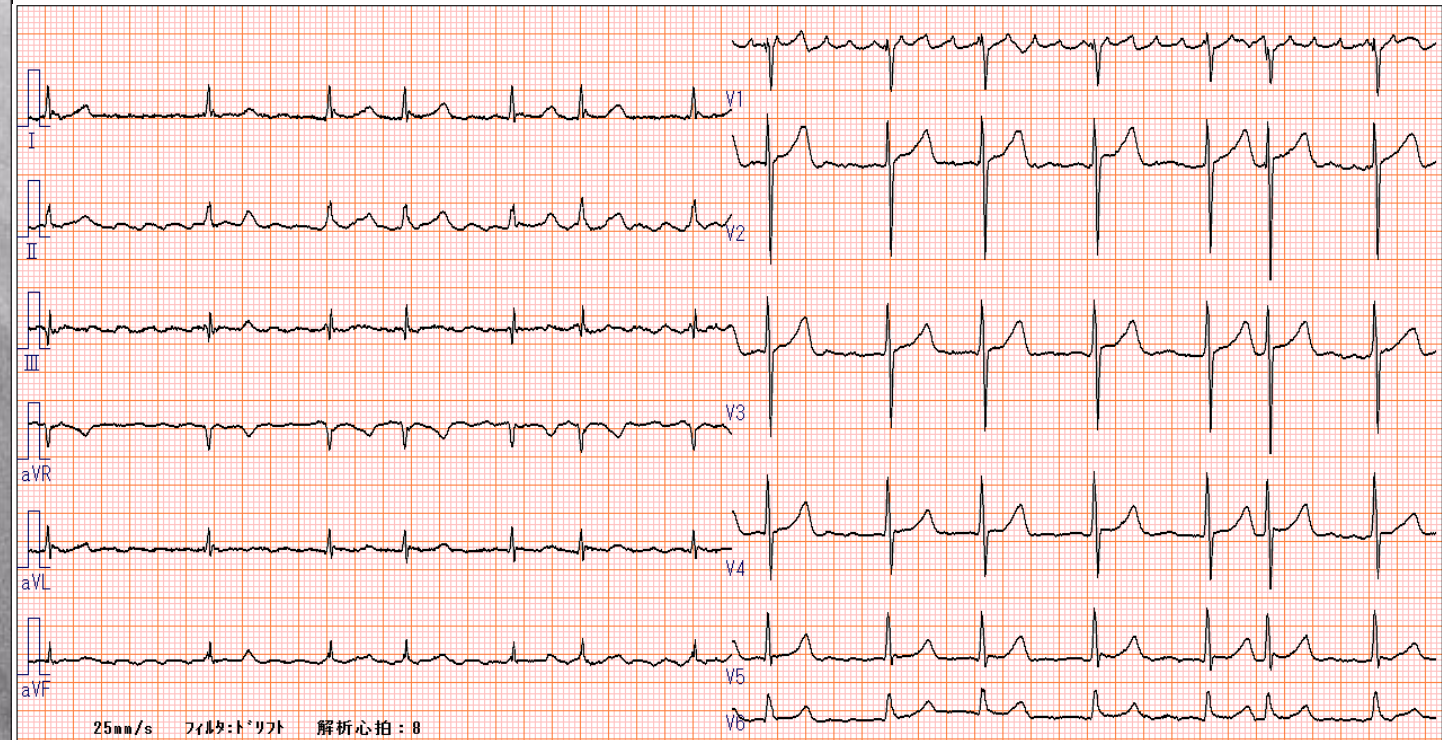
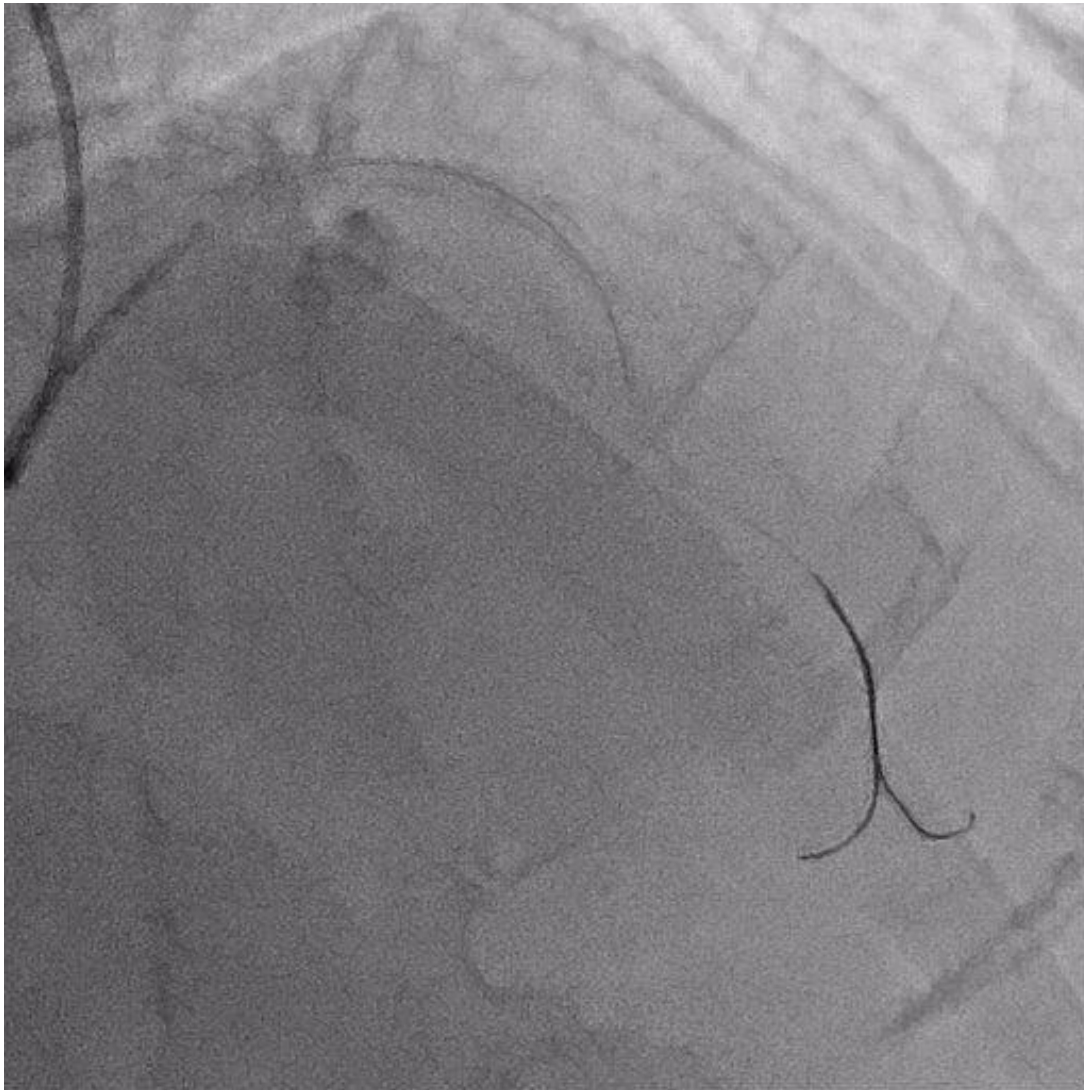


Images shown are the authors' own.

Case 2: 77 y.o. male, angina pectoris



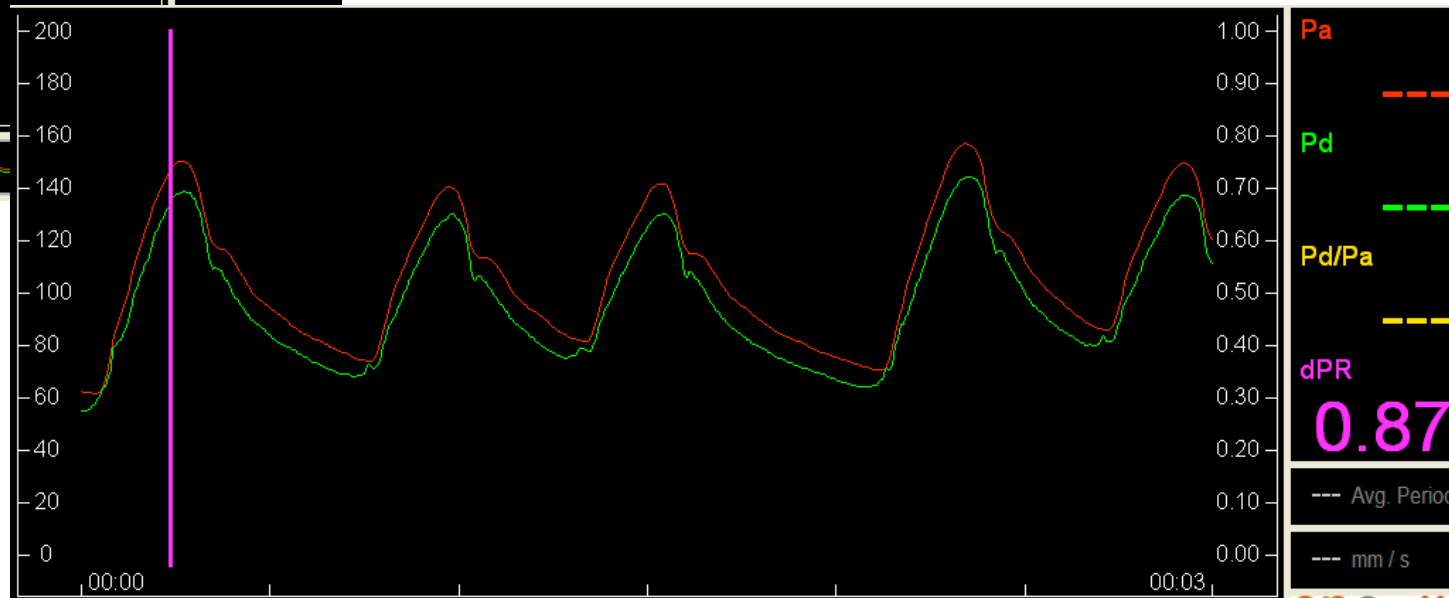
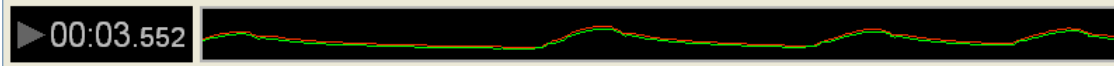
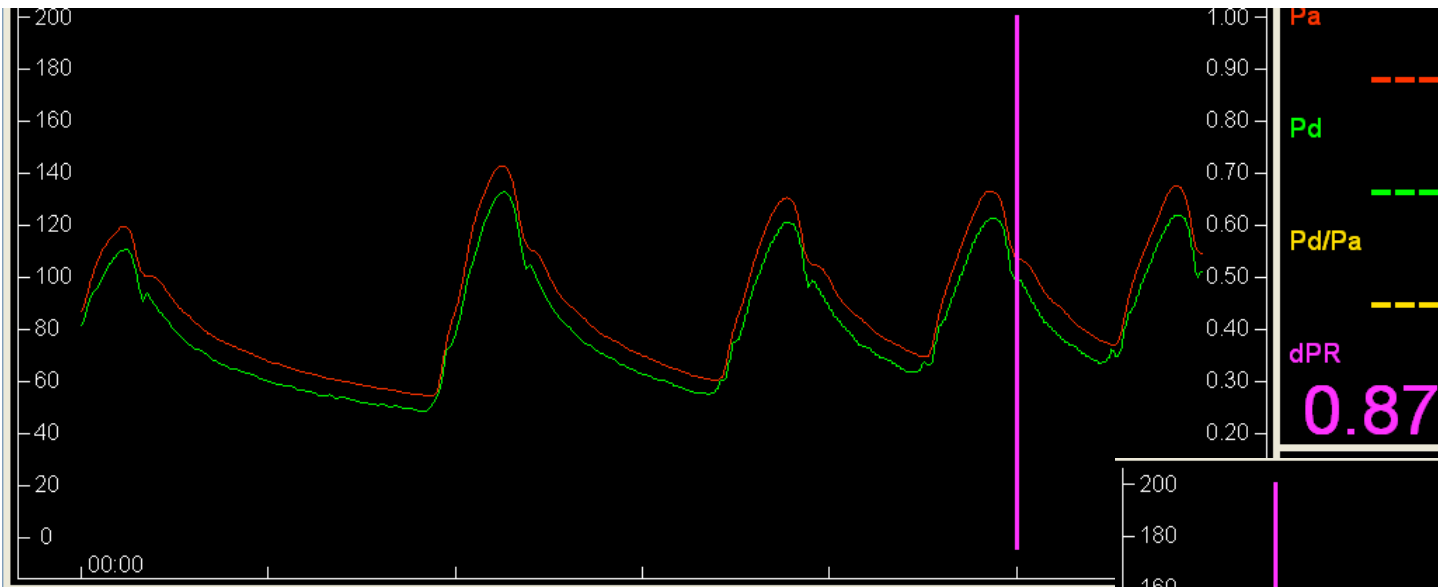
Simultaneous assessment of dPR and iFR in irregular heart beat



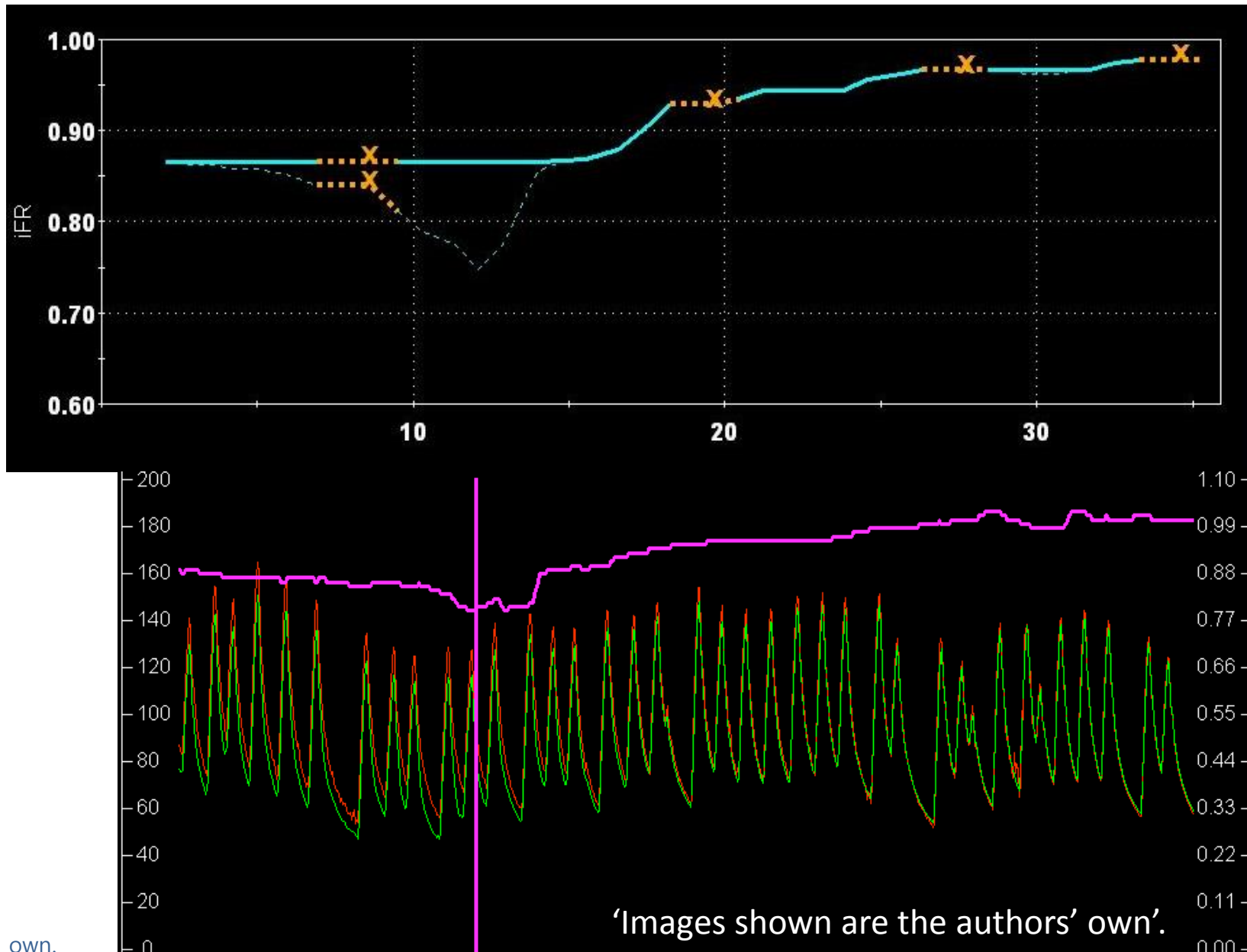
Reproducibility of iFR

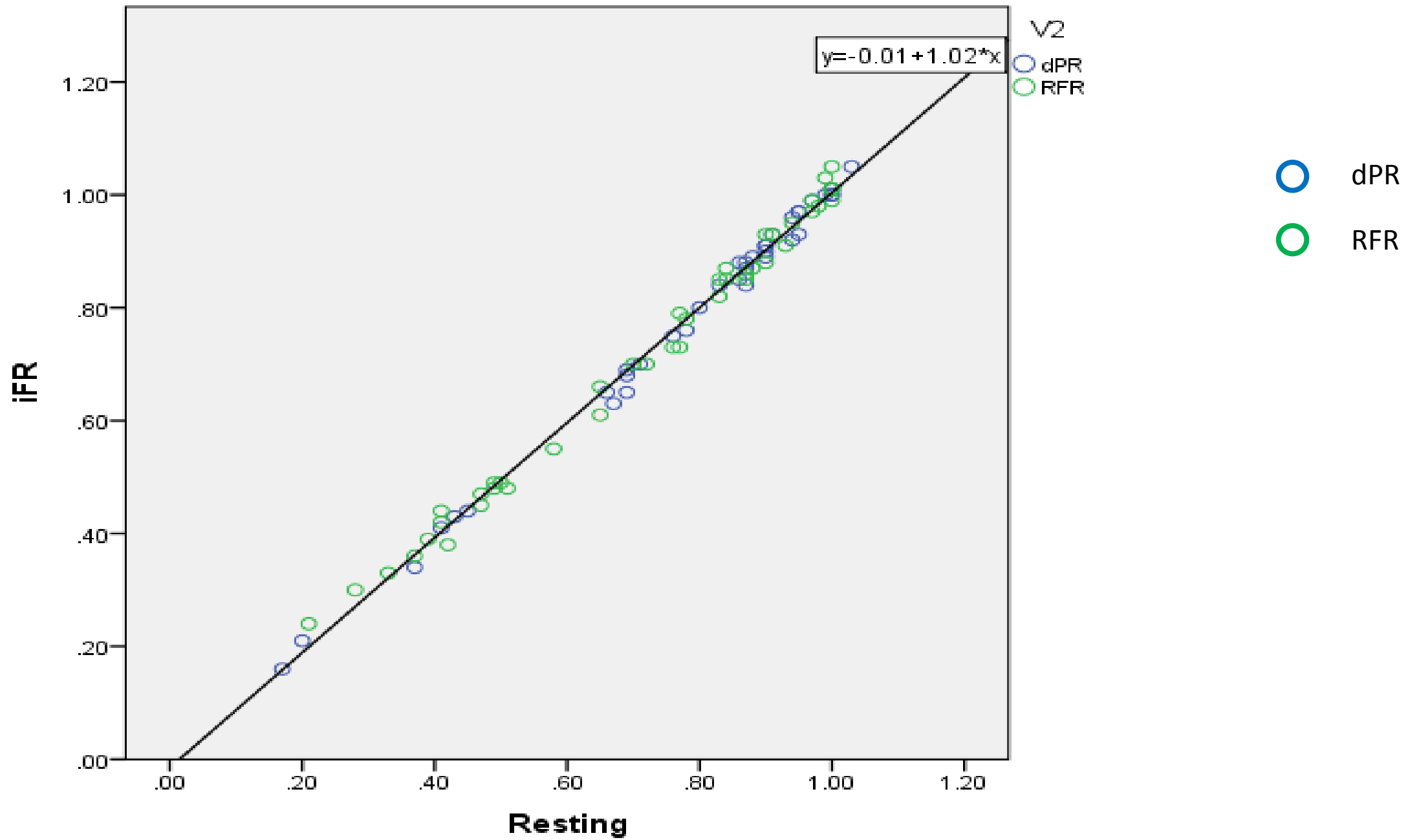


Reproducibility of dPR



Pullback assessment by DPR





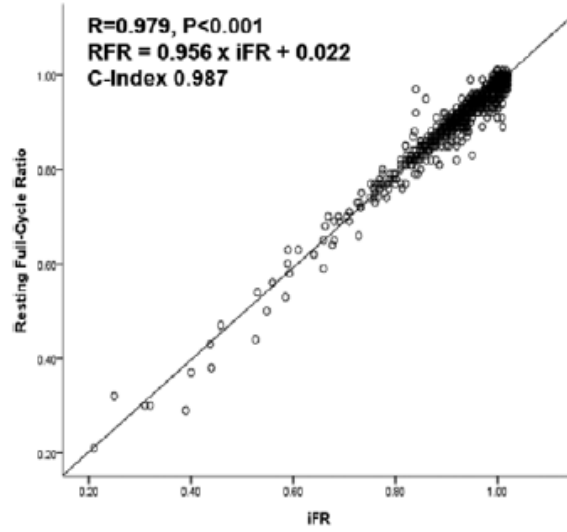
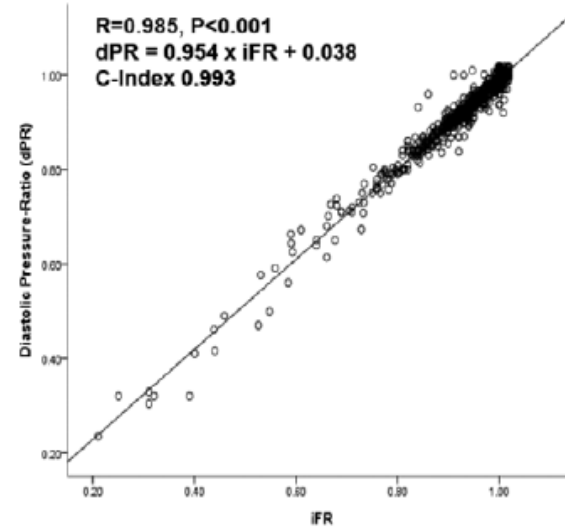
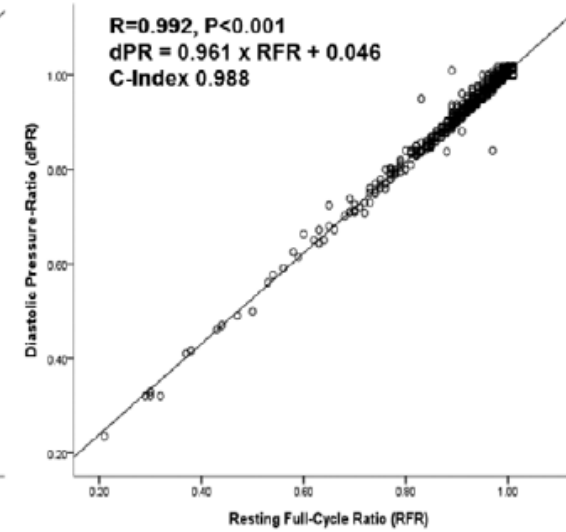
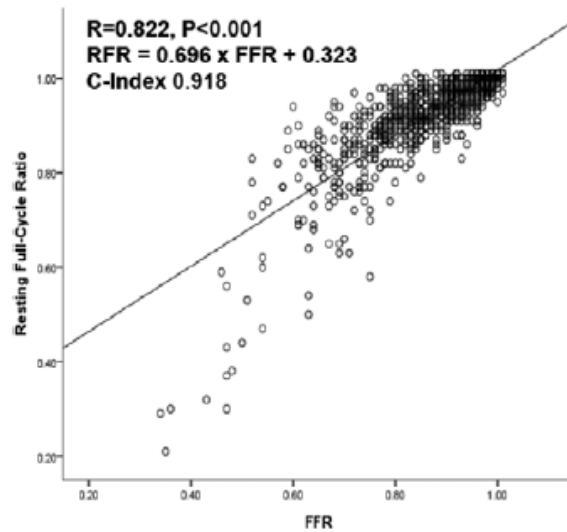
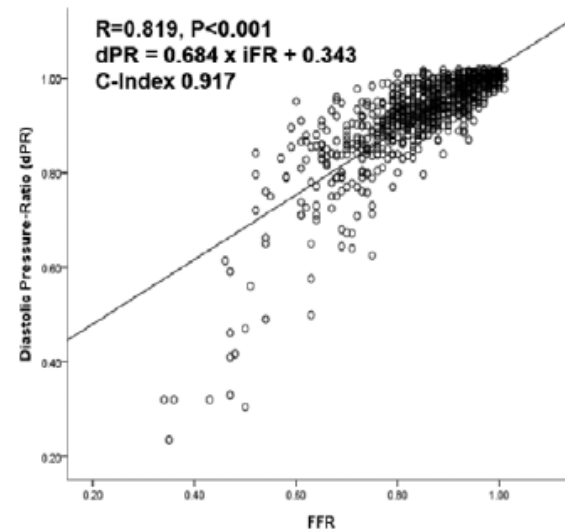
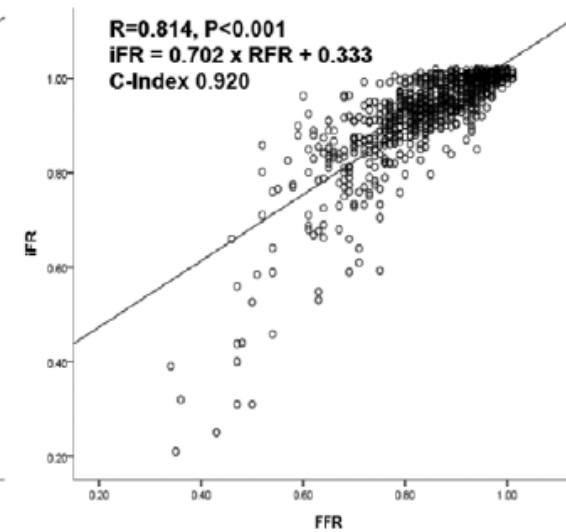
Circulation

ORIGINAL RESEARCH ARTICLE

Physiological and Clinical Assessment of Resting Physiological Indexes

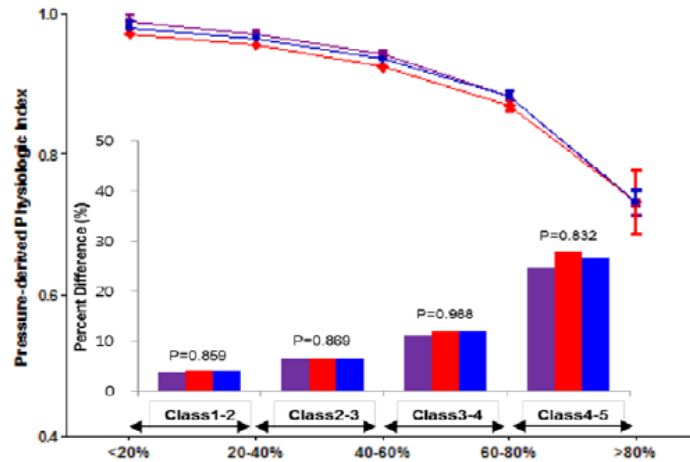
Resting Full-Cycle Ratio, Diastolic Pressure Ratio, and Instantaneous Wave-Free Ratio

Lee JM, Koo BW et al . Circulation 2019; 139:889 – 900

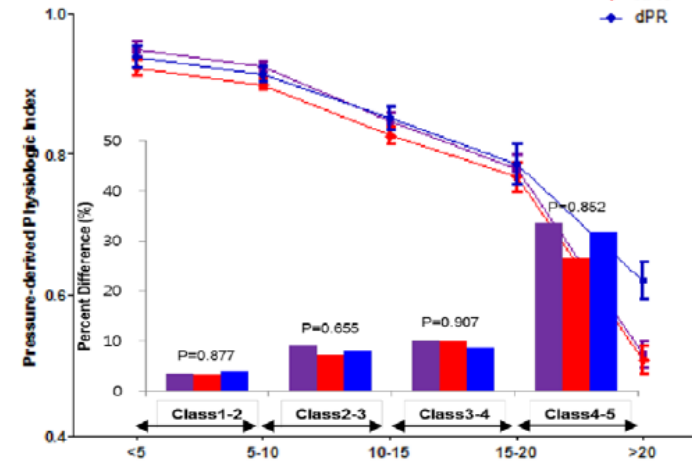
A RFR - iFR**B dPR - iFR****C dPR - RFR****D RFR - FFR****E dPR - FFR****F iFR - FFR**

Resting physiological indexes according to different anatomical and hemodynamic severity.

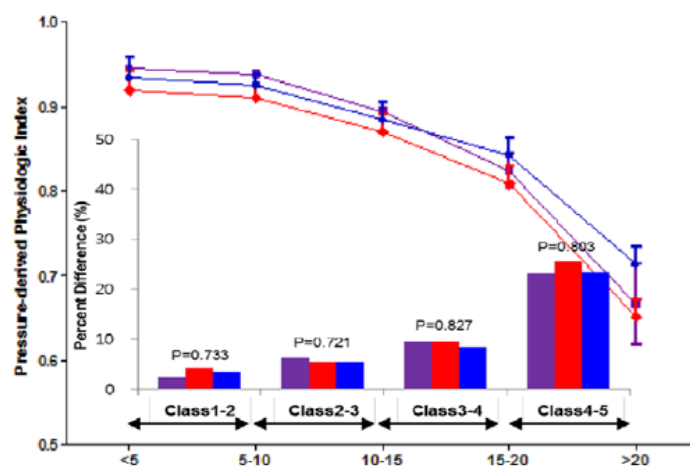
A Diameter Stenosis



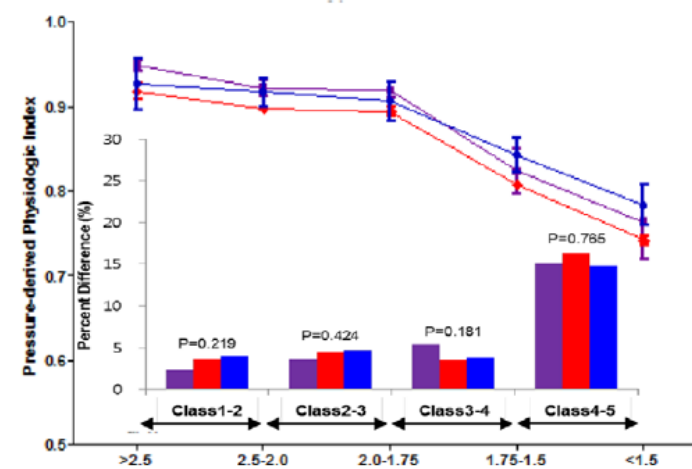
B Basal Stenosis Resistance



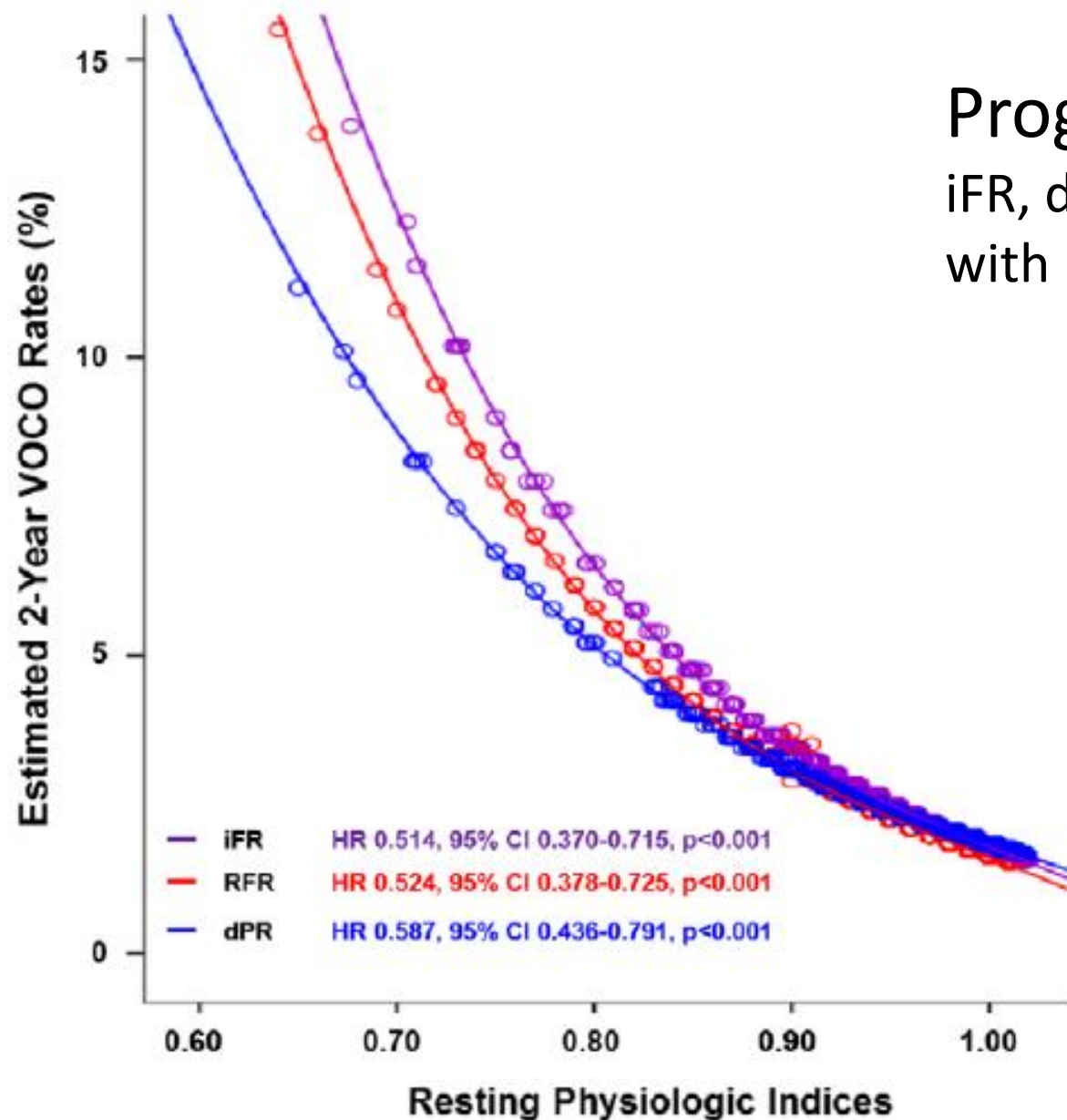
C Hyperemic Stenosis Resistance



D Hyperemic Myocardial Blood Flow



Prognostic value of resting indexes.
iFR, dPR, RFR all showed similar association
with Estimated 2 year VOCO rates.



Take home message

- DEFINE FLAIR and iFR SWEDEHEART study demonstrated the similar outcome with less revascularization, with less cost.
- Deferal by both iFR and FFR are safe.
- Both iFR and FFR are recommended as class IA in ESC revascularization guideline.
- Other resting indexes like dPR, RFR, DFR are numerically identical and prognostically same compared with iFR.
- These newly emerged resting indexes can be used in the same way as iFR.