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MEDICAL
CENTER

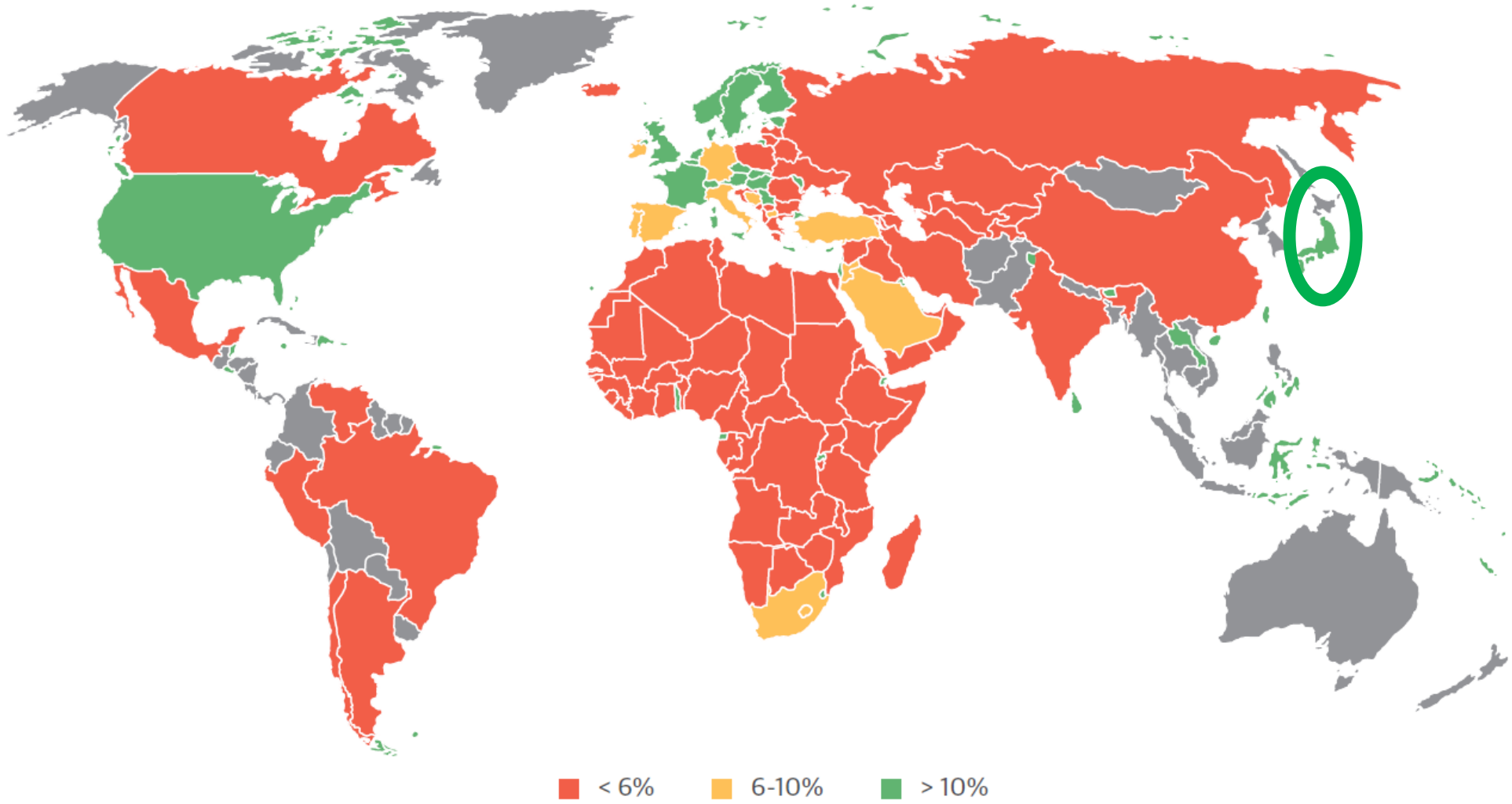
Insight of Physiology in Japan

Shinichiro Yamada, MD, PhD
Kita-Harima Medical Center,
Ono, Japan

Disclosure Statement of Financial Interest

I, [Shinichiro Yamada], DO NOT have a financial interest, arrangement, or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Global Adoption of Coronary Physiology to Guide Revascularization Decision Making in 2016



J-CONFIRM Registry

Long-term outcome of Japanese patients with deferral of COronary iNtervention based on FractIonal flow Reserve in Multicenter registry

Shoichi Kuramitsu, MD, PhD

Kokura Memorial Hospital, Japan

Hitoshi Matsuo, MD, PhD; Hiroaki Takashima, MD, PhD; Hiroyoshi Yokoi, MD; and NobuhiroTanaka, MD, PhD

; **on behalf of the J-CONFIRM registry investigators**

Courtesy of S. Kuramitsu and H. Matsuo

Objectives

We sought to assess clinical outcomes of Japanese patients with deferral of revascularization based on FFR in real-world clinical practice.

Study Design

A prospective, multicenter registry

Inclusion Criteria

1. Patients were clinically suspected of angina pectoris and underwent coronary angiography.
2. Coronary angiography showed more than 50% diameter stenosis by visual estimation and FFR examination was done.
3. Patients fulfilled (1),(2) and any one of the following criteria:

   1) deferred PCI based on FFR >0.80
   2) deferred PCI regardless of FFR <0.80
   3) underwent PCI regardless of FFR >0.80

Exclusion Criteria

1) ST and non-ST elevated myocardial infarction
2) Emergent percutaneous coronary intervention
3) Cardiogenic shock (Killip class IV)
4) Lesion with chronic total occlusion
5) Limited life expectancy due to cancer
6) Inability to give informed consent

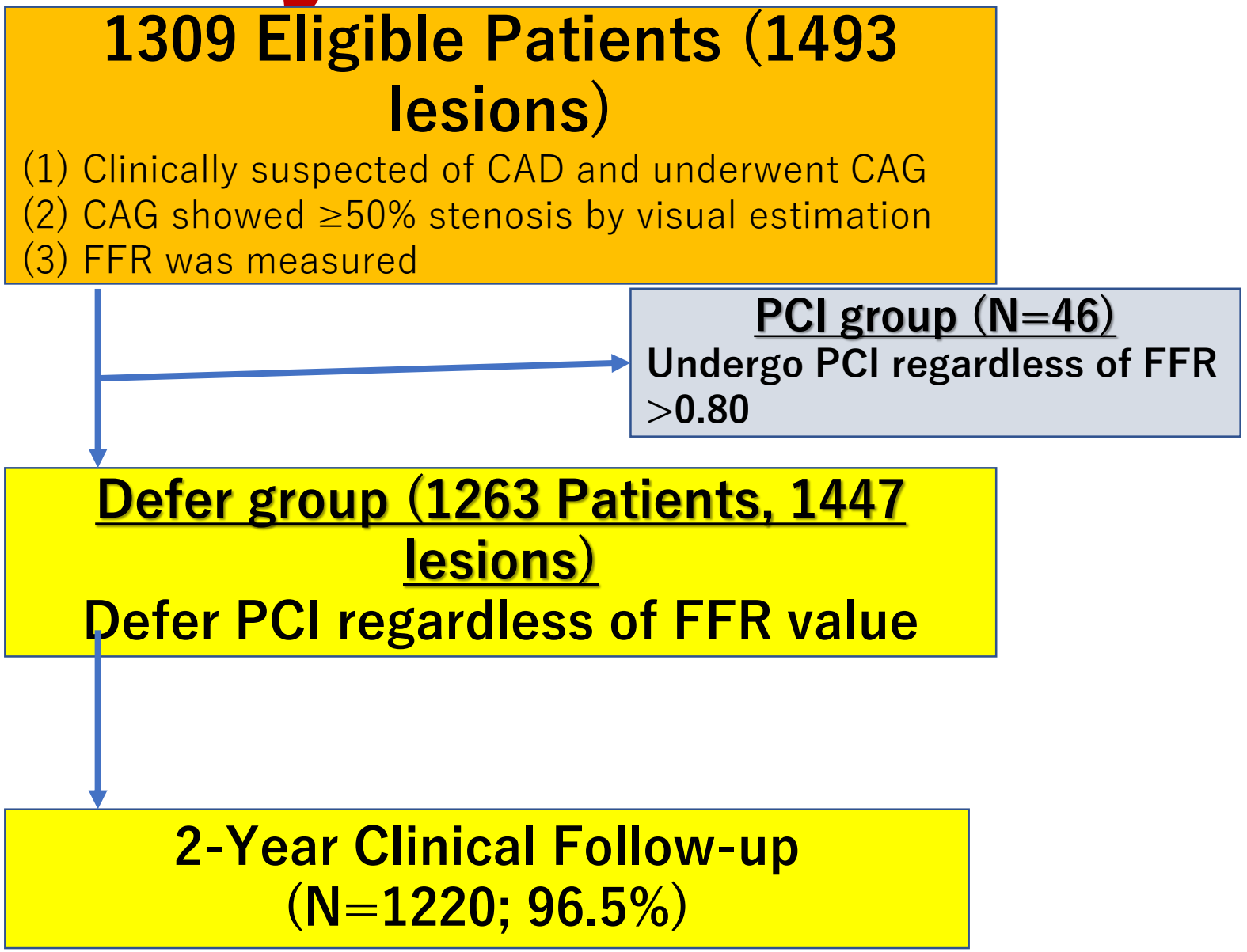
Primary Study Endpoint

- Primary study endpoint was **target vessel failure (TVF) at 2-year**.

- TVF was defined as a composite of cardiac death, target vessel related myocardial infarction (TVMI), and clinically driven target vessel revascularization (TVR).

Results

Study Chart Flow



Clinical Characteristics (1)

No. of patients	1263
Age	70.2 ± 9.7
Male	944 (74.6%)
Risk factors	
Hypertension	969 (76.5%)
Dyslipidemia	809 (63.9%)
Diabetes Mellitus	479 (37.8%)
Current Smoking	403 (31.8%)
Past history	
Prior PCI	**748 (59.0%)**
Prior CABG	33 (2.6%)
Prior MI	**365 (28.8%)**
Prior Stroke	120 (9.5%)
Prior atrial fibrillation	115 (9.1%)
Peripheral artery disease	154 (12.2%)
Hemodialysis	66 (5.2%)
Multivessel disease	310 (21.4%)

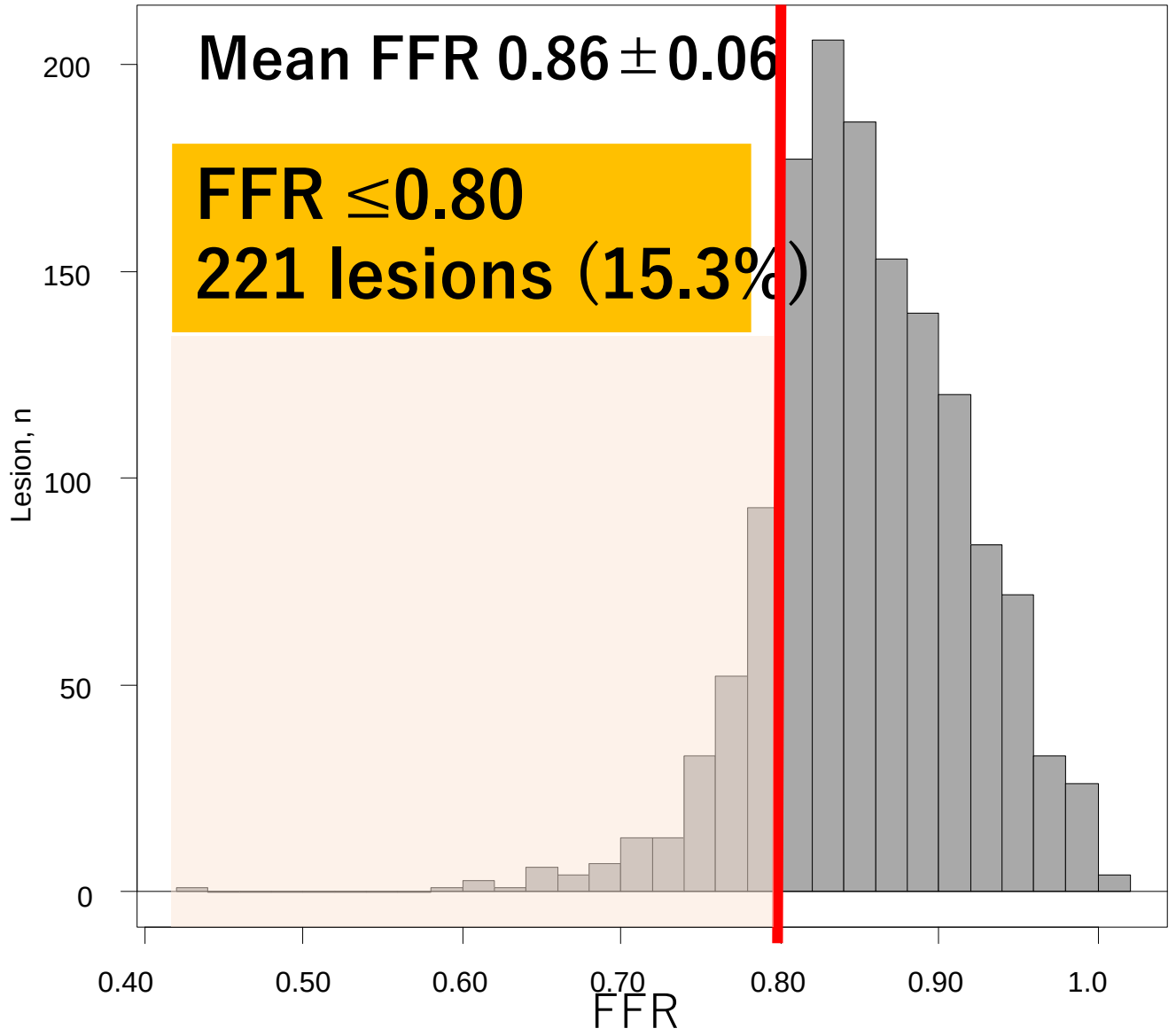
Systolic blood pressure, mmHg	136 ± 22
Diastolic blood pressure, mmHg	73 ± 13
Body mass index, kg/m^2	24.0 ± 4.2
Blood test	
HbA1c (NGSP), %	6.0 (5.6, 6.6)
LDL-C, mg/dl	**98 (78, 118)**
Medication at discharge	
Aspirin	981 (77.5%)
Thienopyridine	650 (51.4%)
ACE-I/ARB	733 (57.9%)
Ca blocker	657 (52.0%)
β blocker	421 (33.3%)
Statin	**816 (64.6%)**
OHA	333 (26.3%)
Insulin	56 (4.4%)

Clinical Characteristics (2)

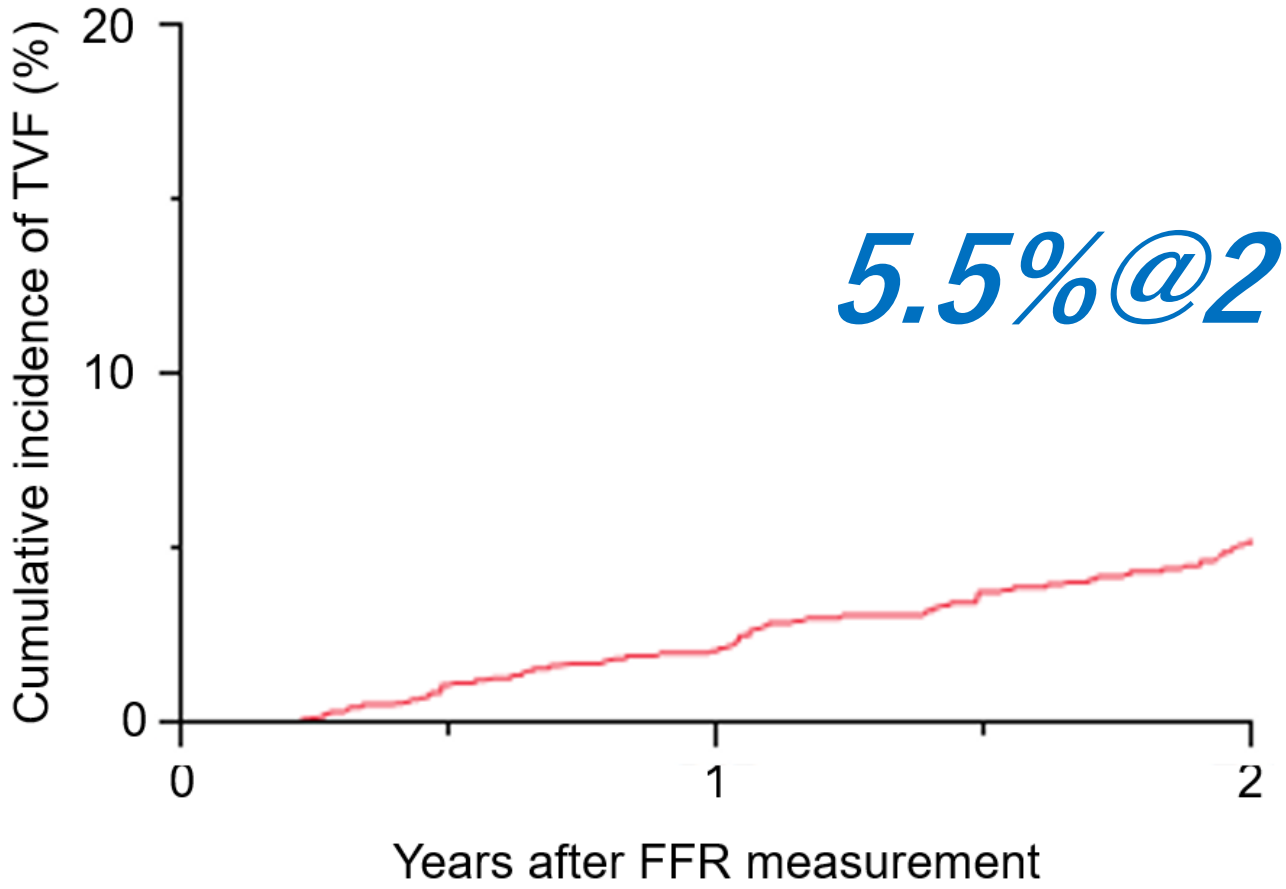
No. of patients	1263
Clinical Presentation	
SAP	**1219 (96.2%)**
UAP	48 (3.8%)
CCS classification	
Asymptomatic	**649 (51.4%)**
Class I	**454 (35.9%)**
Class II	118 (9.3%)
Class III	22 (1.7%)
Class IV	20 (1.6%)
LVEF, %	61 ± 11
Number of FFR measurement	
1-vessel	**1138 (78.6%)**
2-vessel	237 (16.4%)
3-vessel	72 (5.0%)

No. of lesion	1447
FFR Target Vessel	
LAD	703 (48.6%)
LCX	327 (22.6%)
RCA	385 (26.6%)
LMCA	37 (2.6%)
ACC/AHA type	
A	163 (11.3%)
B1	410 (28.4%)
B2	**596 (40.5%)**
C	**271 (19.0%)**
In-stent restenosis	105 (7.3%)
Bifurcation lesion	409 (31.0%)
Moderate to severe calcified lesion	185 (14.0%)
Diameter stenosis, %	**43.1 ± 11.5**
Diameter stenosis >50%	378 (29.0%)
Lesion length, mm	**13.1 ± 6.1**
Lesion length >20 mm	119 (9.0%)

Distribution of FFR Values



Primary Endpoint: TVF at 2 Years

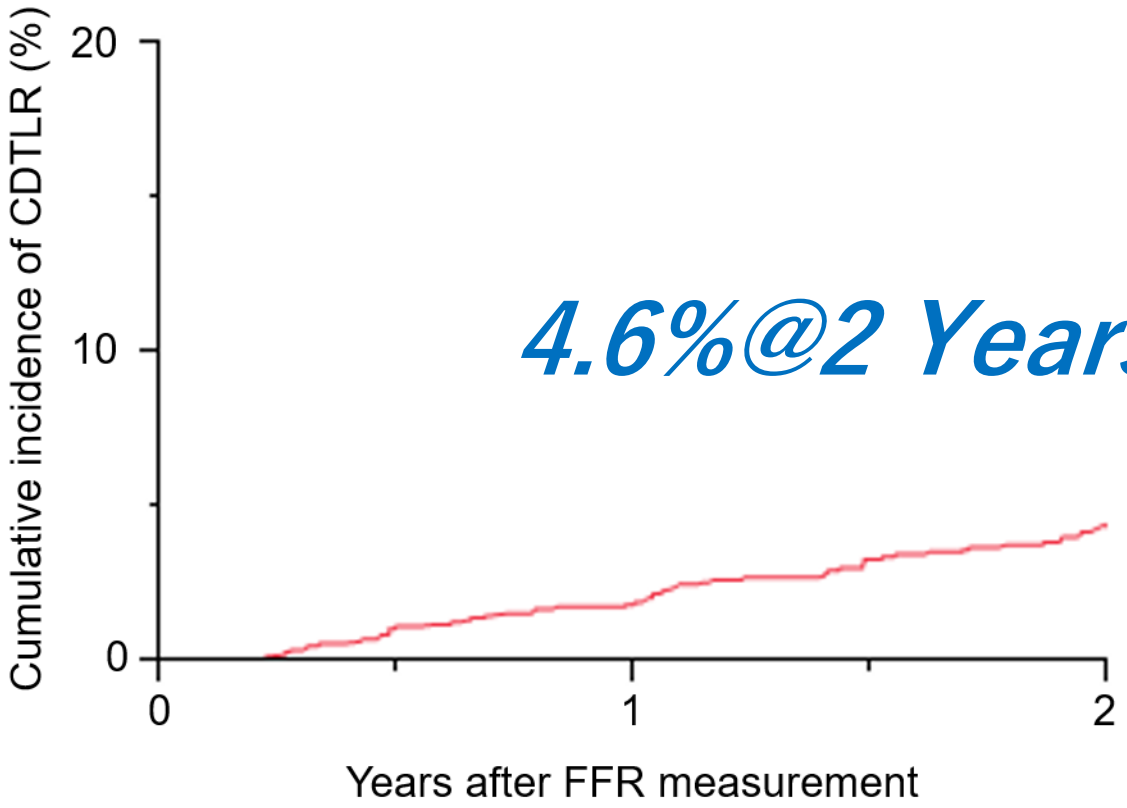


5.5%@2 Years

Years	0	1 Year	2 Years
N of lesions at risk	1447	1368	877
Cumulative incidence	0.0%	2.3%	5.5%

CDTLR and CDTVR at 2 Years

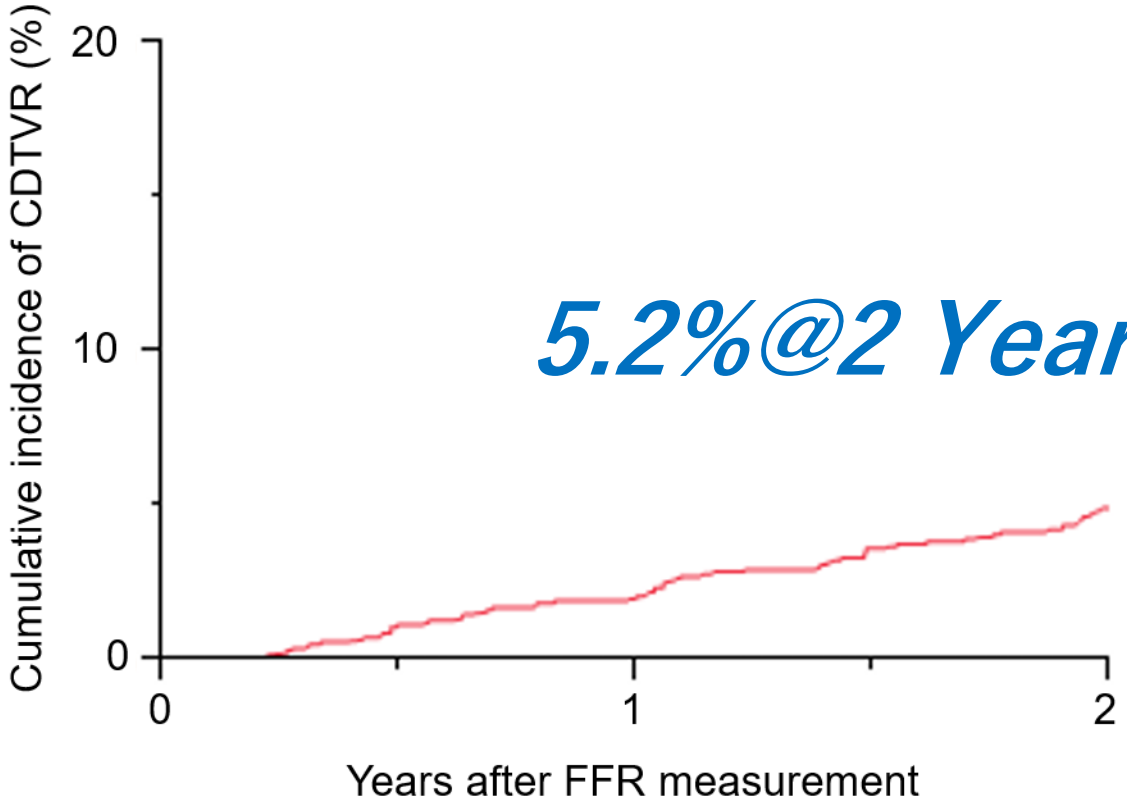
CDTLR



4.6%@2 Years

Years	0	1 Year	2 Years
N of lesions at risk	1447	1371	879
Cumulative incidence	0.0%	2.0%	4.6%

CDTVR

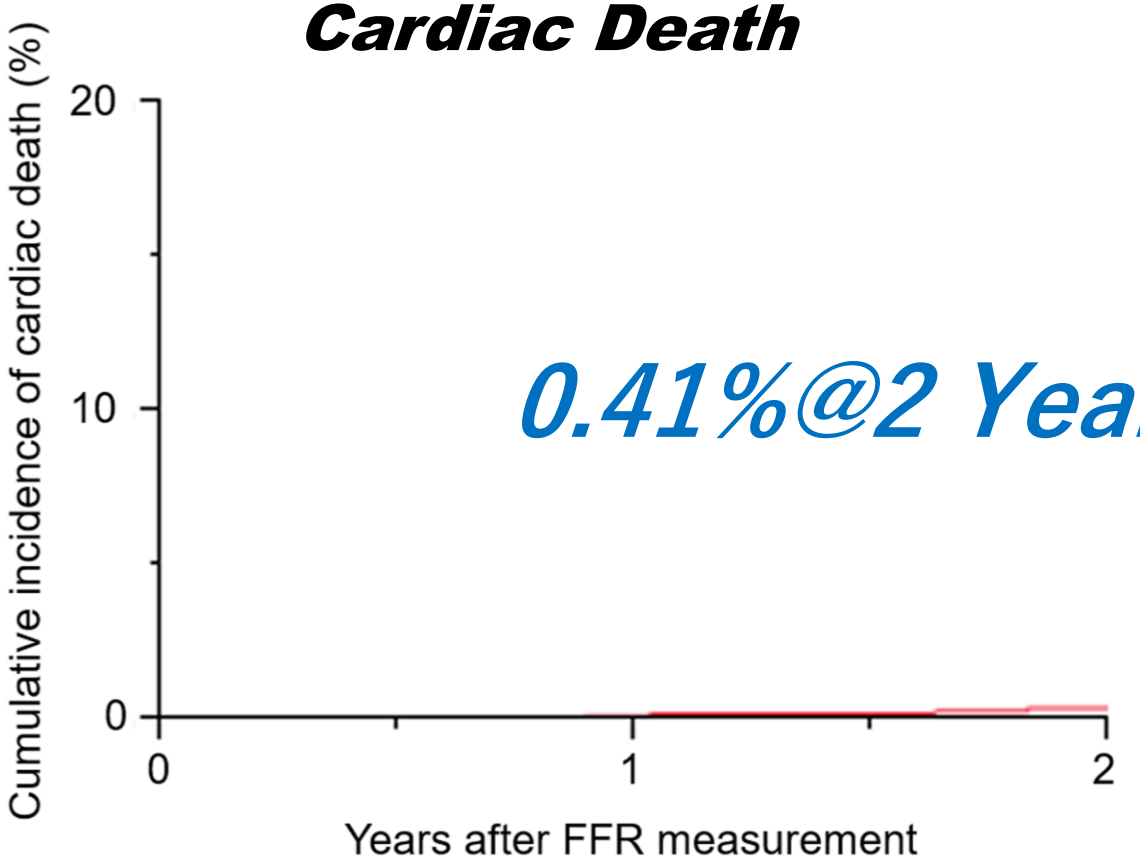


5.2%@2 Years

Years	0	1 Year	2 Years
N of lesions at risk	1447	1368	877
Cumulative incidence	0.0%	2.2%	5.2%

Cardiac Death and MI at 2 Years

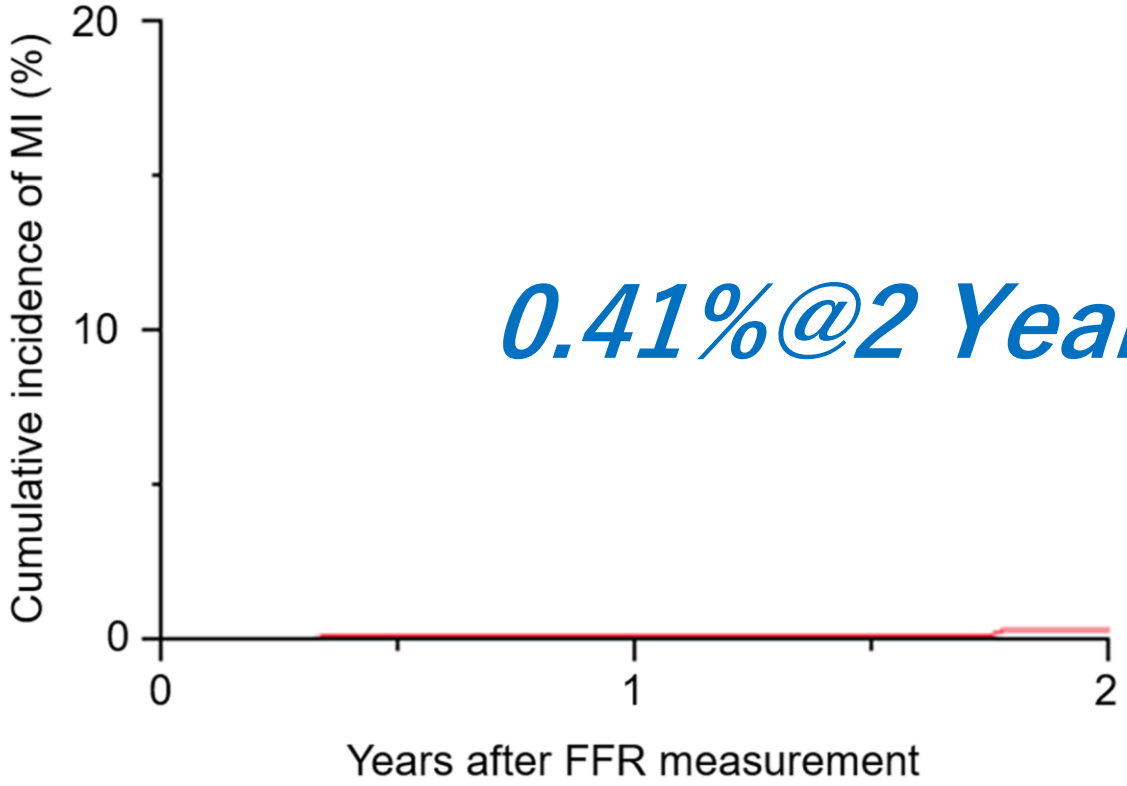
Cardiac Death



0.41%@2 Years

Years	0	1 Year	2 Years
N of patients at risk	1264	1229	819
Cumulative incidence	0.0%	0.16%	0.41%

Myocardial Infarction

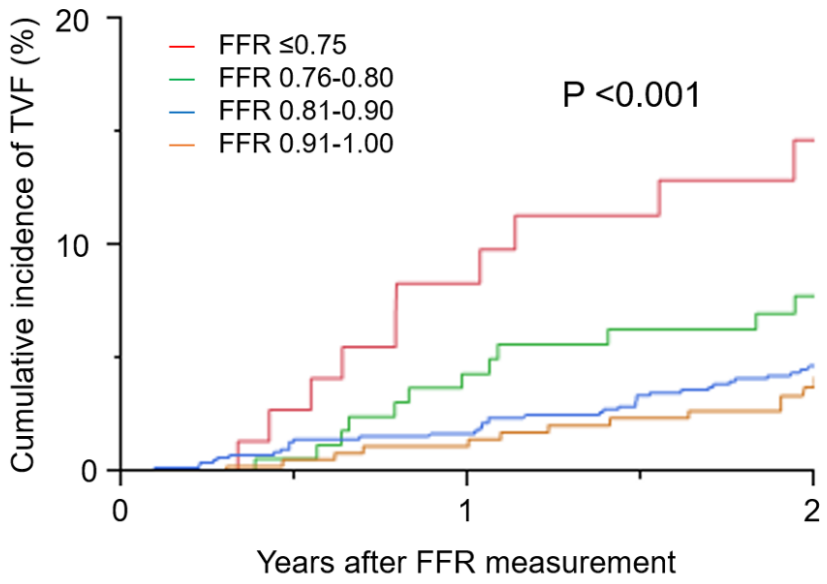


0.41%@2 Years

Years	0	1 Year	2 Years
N of patients at risk	1264	1227	815
Cumulative incidence	0.0%	0.24%	0.41%

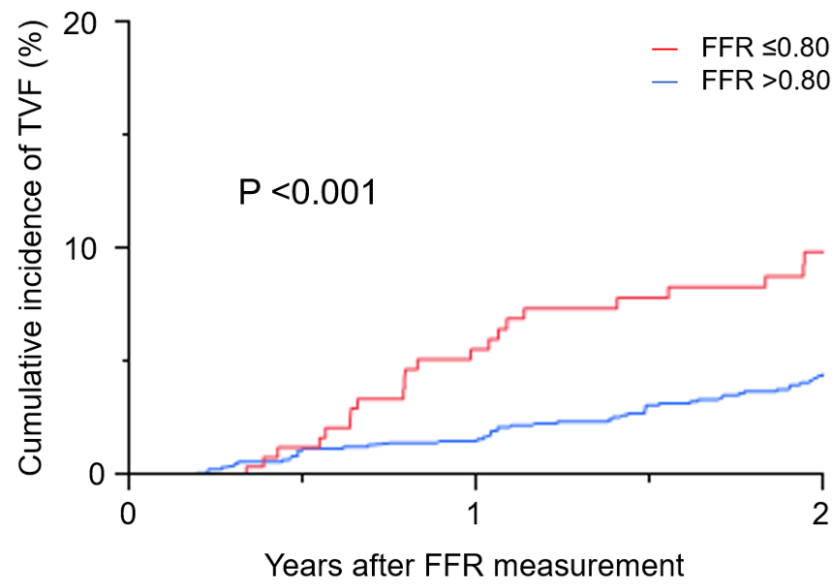
Cumulative Incidence of TVF According to FFR Categories

(A)



Intervals	0	1 Year	2 Years
FFR ≤0.75 group			
N of lesions at risk	72	64	35
Cumulative incidence	0.0%	8.4%	14.7%
FFR 0.76-0.80 group			
N of lesions at risk	161	150	99
Cumulative incidence	0.0%	4.4%	7.8%
FFR 0.81-0.90 group			
N of lesions at risk	872	833	538
Cumulative incidence	0.0%	1.7%	4.7%
FFR 0.91-1.00 group			
N of lesions at risk	342	323	206
Cumulative incidence	0.0%	1.5%	4.2%

(B)



Intervals	0	1 Year	2 Years
FFR ≤0.80 group			
N of lesions at risk	233	213	133
Cumulative incidence	0.0%	5.6%	9.9%
FFR >0.80 group			
N of lesions at risk	1214	1156	744
Cumulative incidence	0.0%	1.7%	4.6%

Predictors of 2-Year TVF

	Multivariable †			
Variables	HR	95% CI*		P value*
FFR (per 0.01 decrease)	1.07	1.04	1.11	<0.001
Target lesion of LMCA	5.89	2.72	12.8	<0.001
Moderately to severely calcified lesion	2.49	1.36	4.58	0.003
Target lesion of LAD	0.42	0.24	0.75	0.003
Hemodialysis	2.90	1.11	7.58	0.03
Target lesion of RCA	1.78	1.02	3.11	0.042

*Based on robust sandwich variance estimates that cluster lesions within the same patients.
† Adjusted for the following variables: FFR (continuous), multivessel disease, percent diameter stenosis (>50% or not), age, and sex.

Study Limitations

- Although this study encouraged all site investigators to enroll consecutive patients deferred PCI based on FFR, it remained unclear whether all eligible patients were enrolled in this study. Therefore, selection bias may exist in this study and have biased the conclusion.

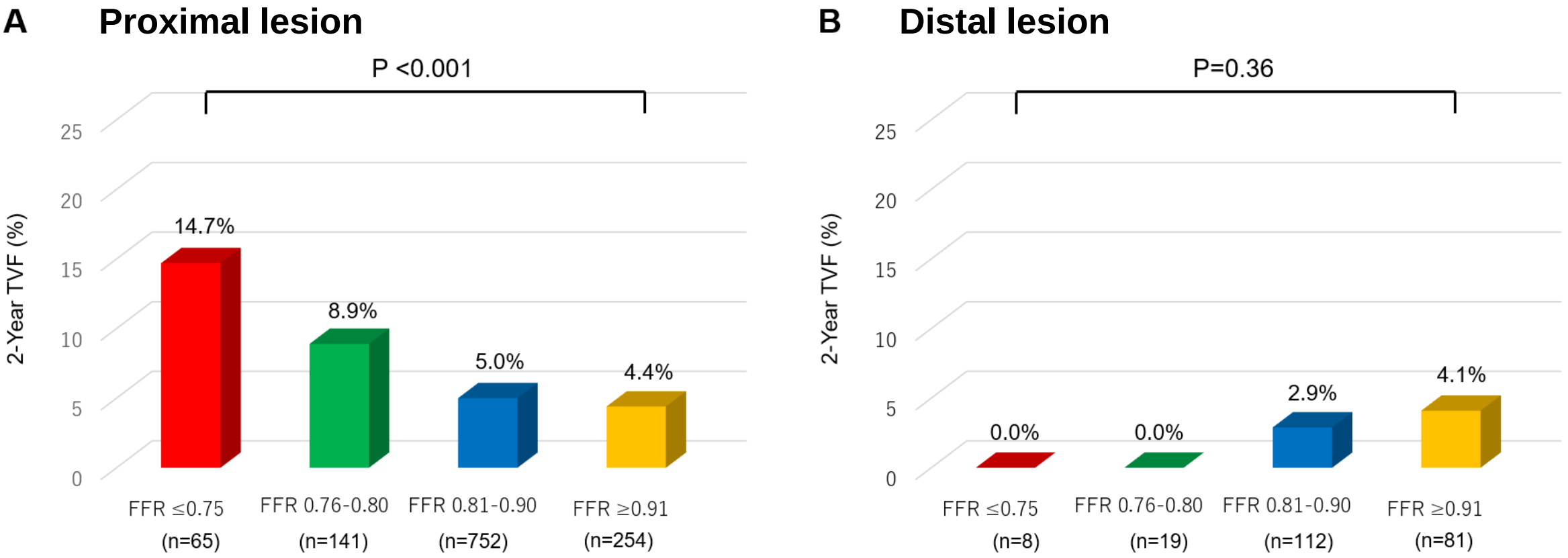
- In the protocol of this study, optical medical therapy (OMT) was recommended after deferral of revascularization based on FFR. Indeed, however, it was left to the local doctor's discretion. Therefore, we did not know whether OMT was done in all patients.

Conclusions

- The J-CONFIRM registry demonstrated the 2-year TVF rate was 5.5% in deferred lesions, highlighting the safety of FFR-based deferral of revascularization in daily practice.

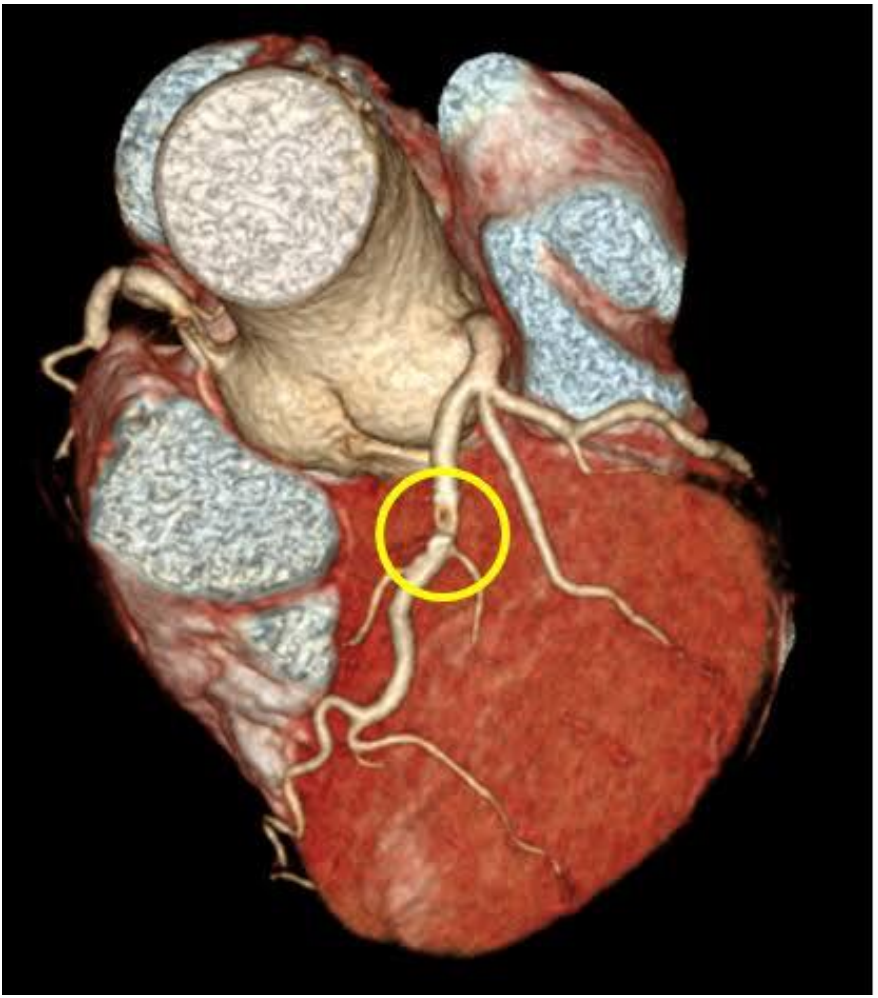
- Careful follow-up may be required in patients with LMCA lesion or moderately to severely calcified lesion.

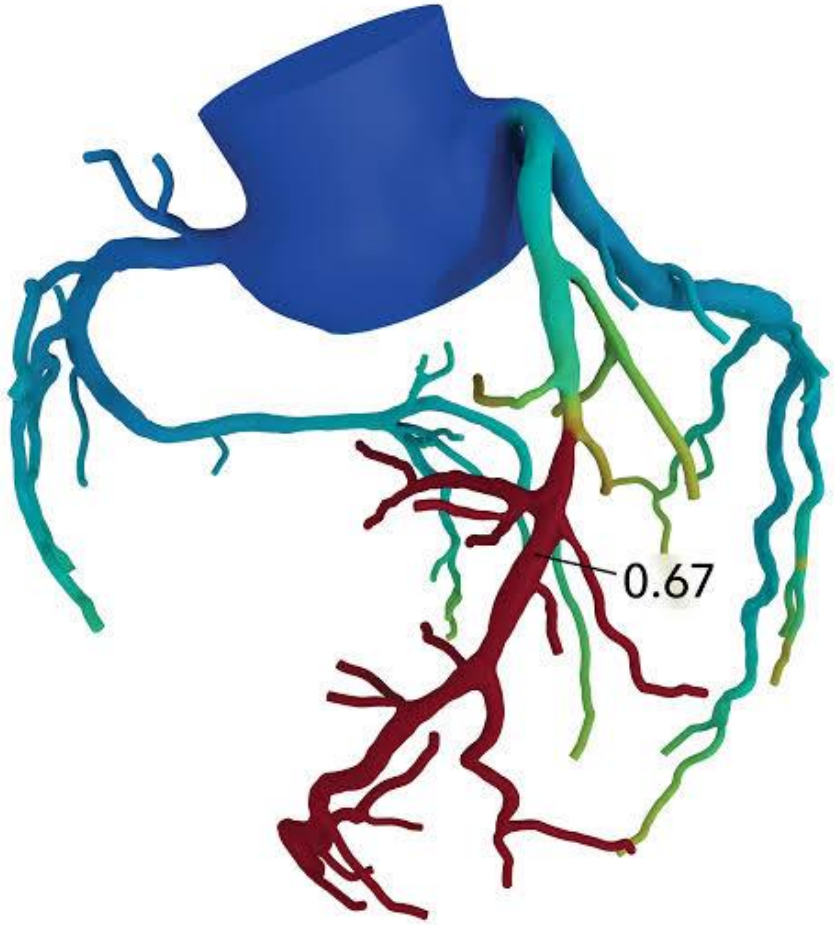
Relationship between FFR Categories and Lesion Location



The lesion location was divided either into **proximal** (referred as segments 1, 2, 5, 6, 7, 11, and 13) or **distal** (3, 4, 8, 9, 12, 14, and 15) segments according to the American Heart Association classification.

FFR CT





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In Japan,

FFR CT is limited

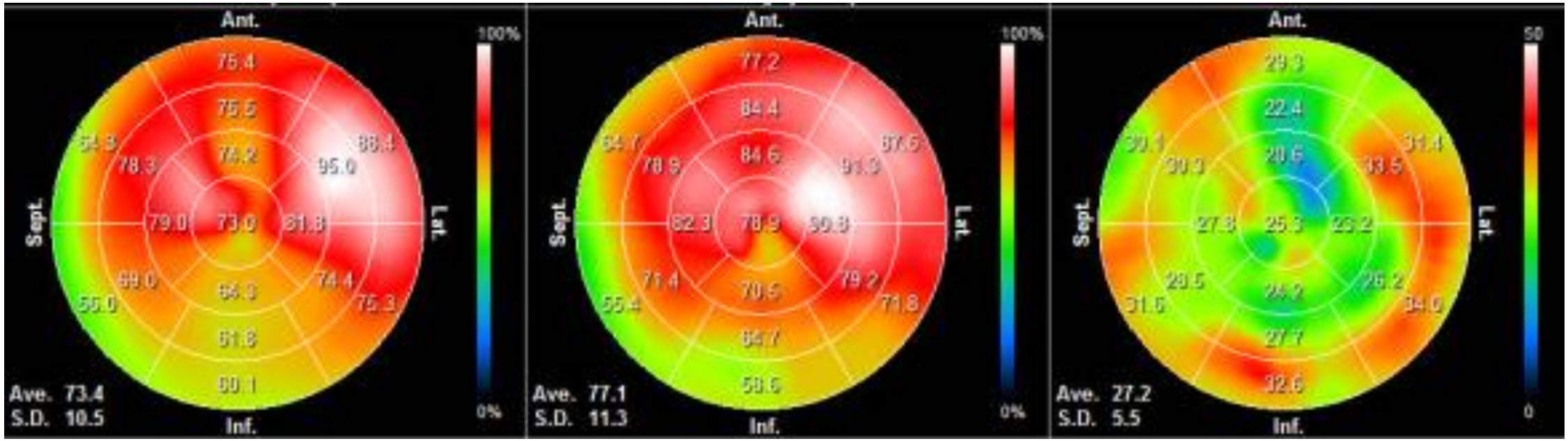
- ✓FFR CT can be done in only certified hospitals.
- ✓If FFR CT is negative, Japanese insurance system prohibits to do any other additional assessments (invasive, non-invasive) within 3 months.

Adenosine stress MPI

Stress

Rest

Washout



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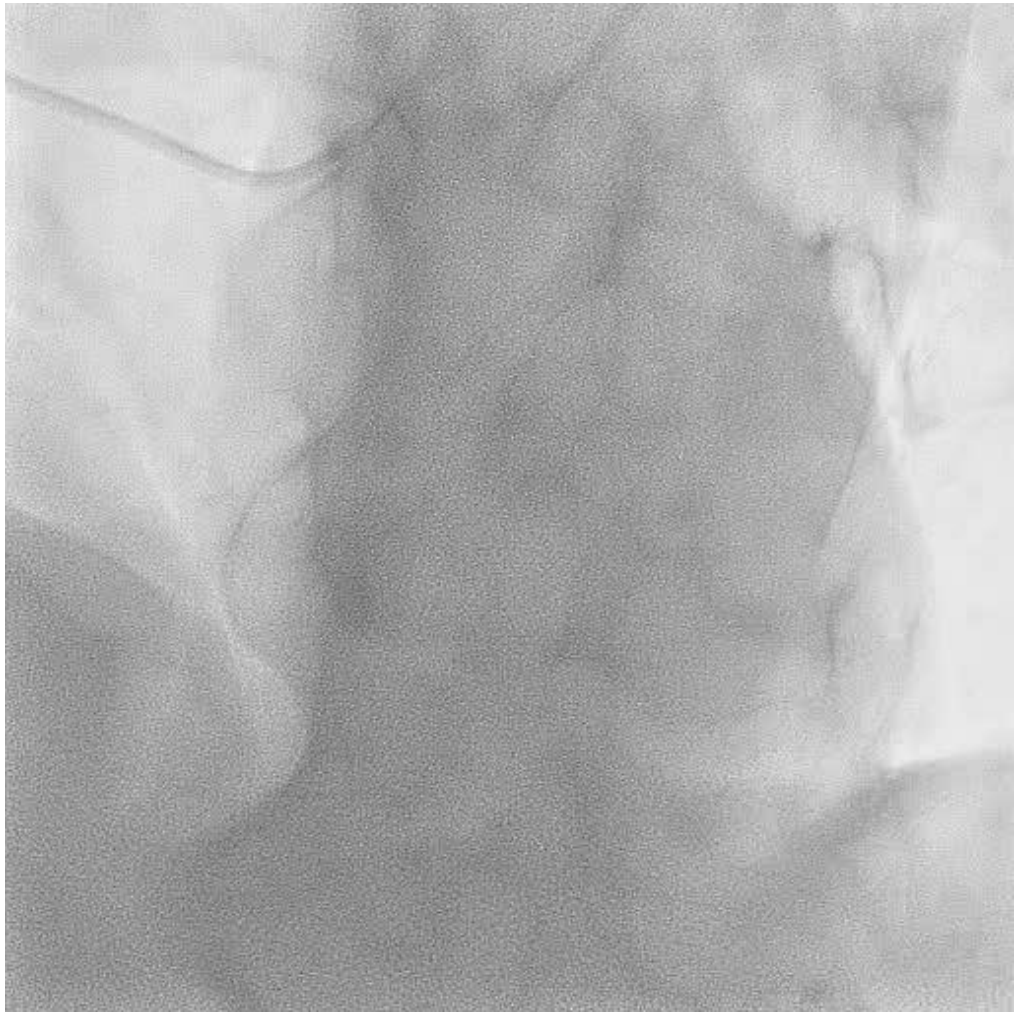
CAG

LCA

CAU

LAO CRA



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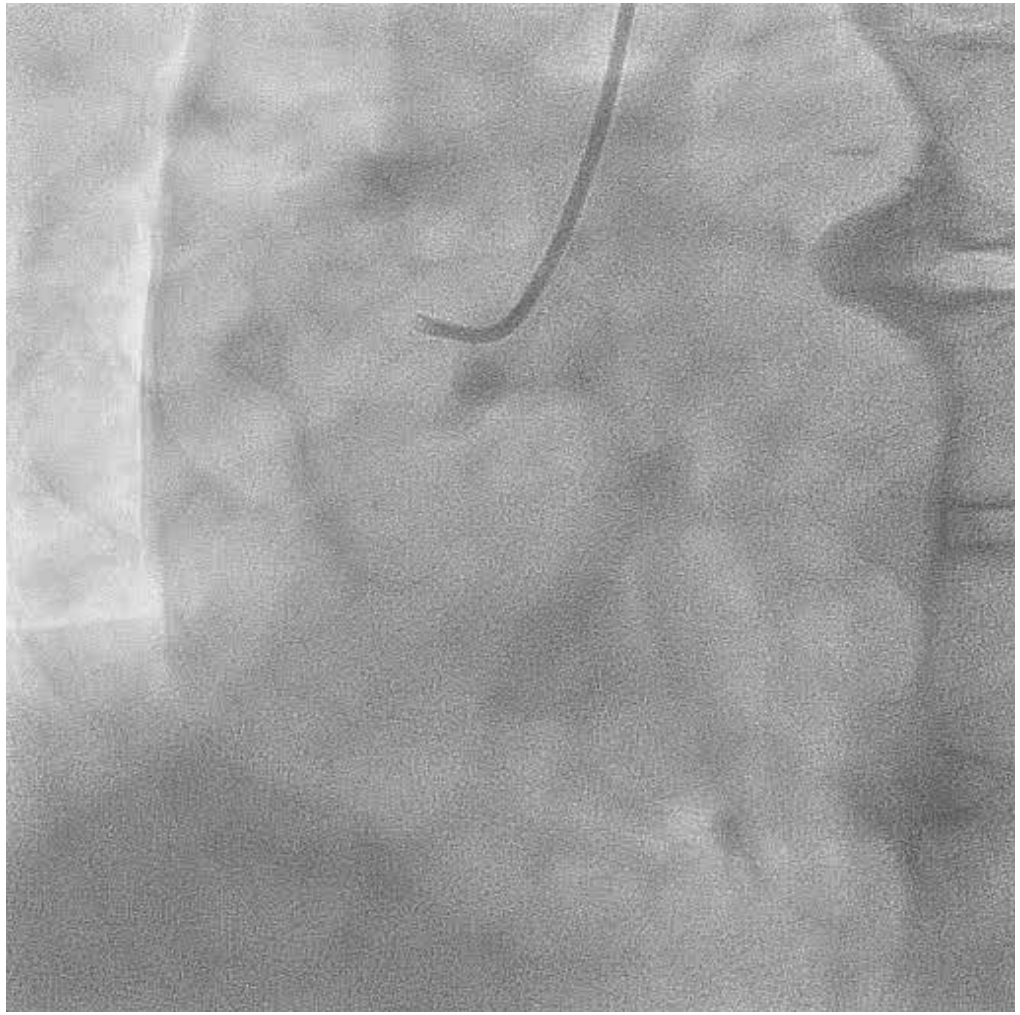
CAG

RCA

CRA



LAO CRA

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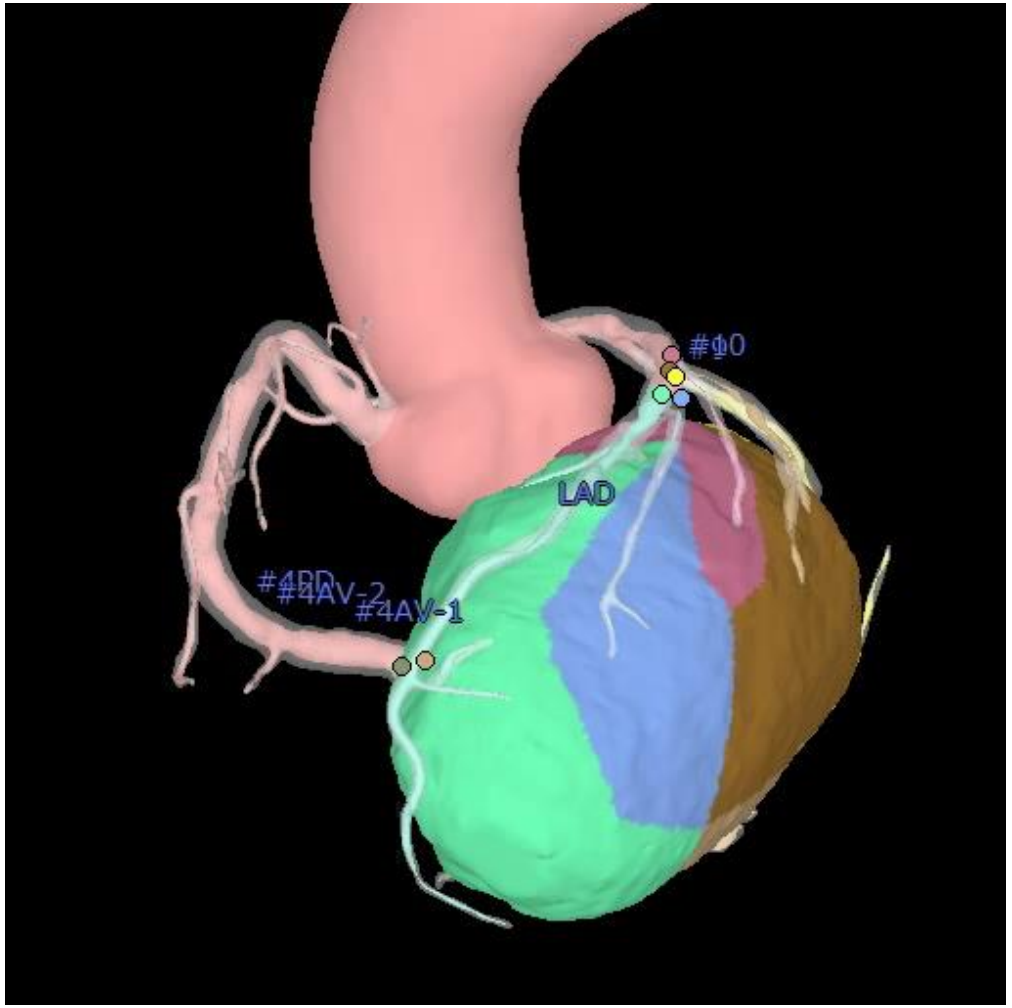
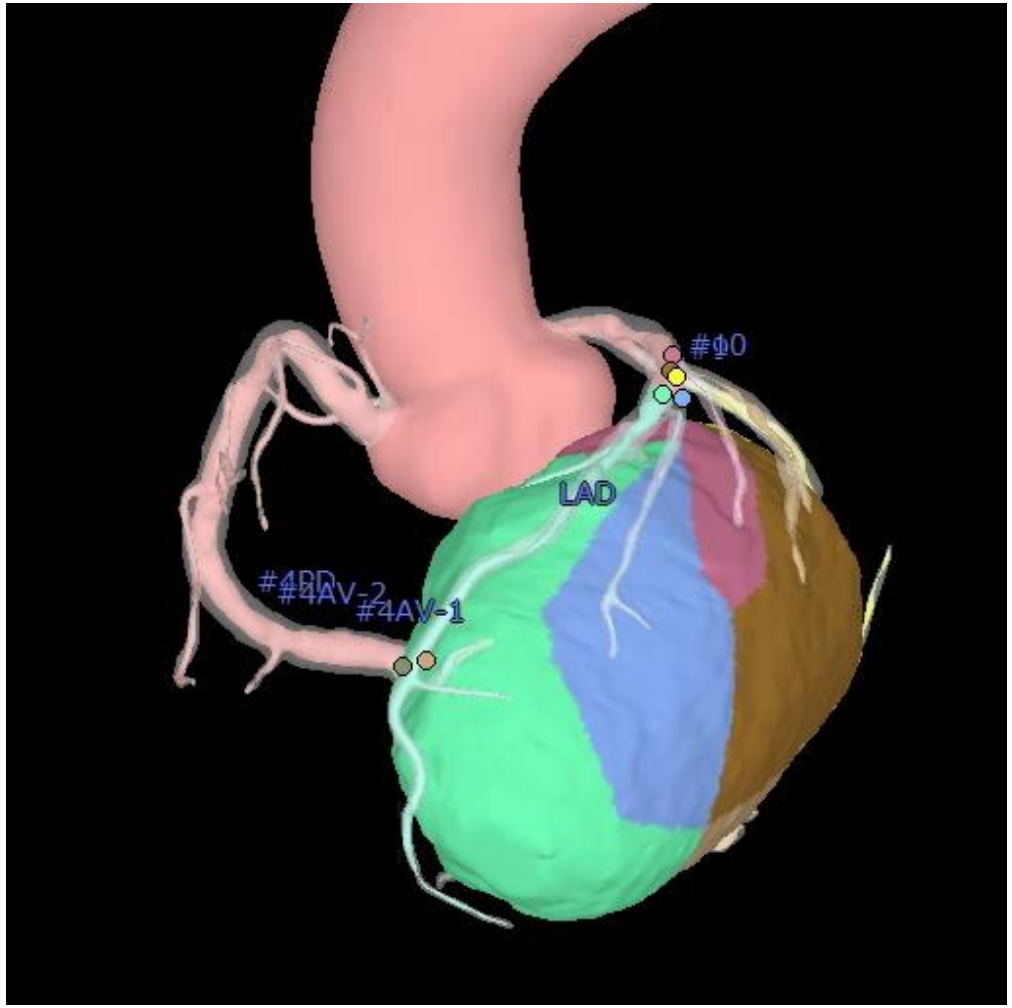
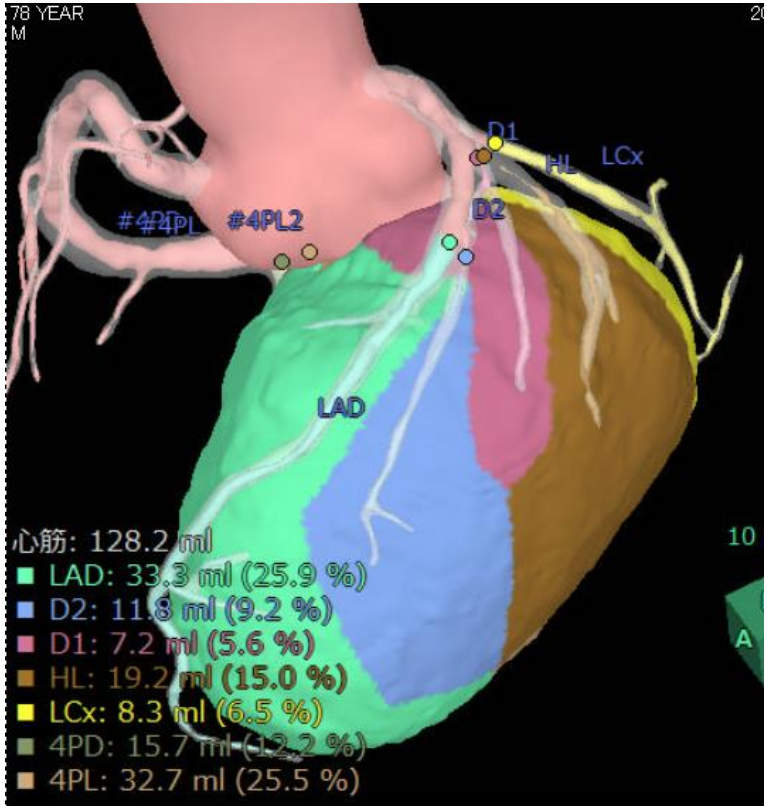
Which lesion(s) should be the target?

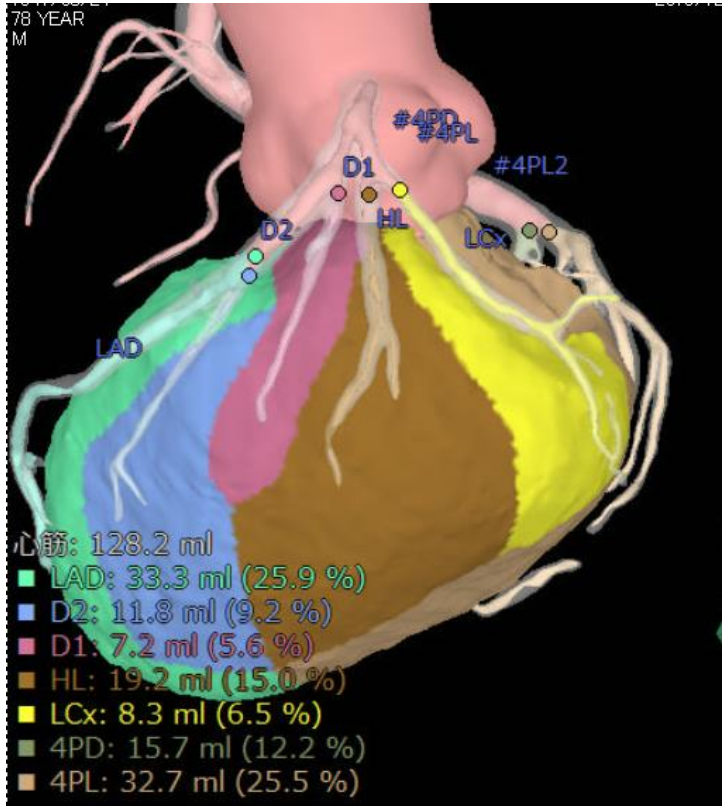
Coronary artery and myocardium territory assessed by CT (Voronoi's method)

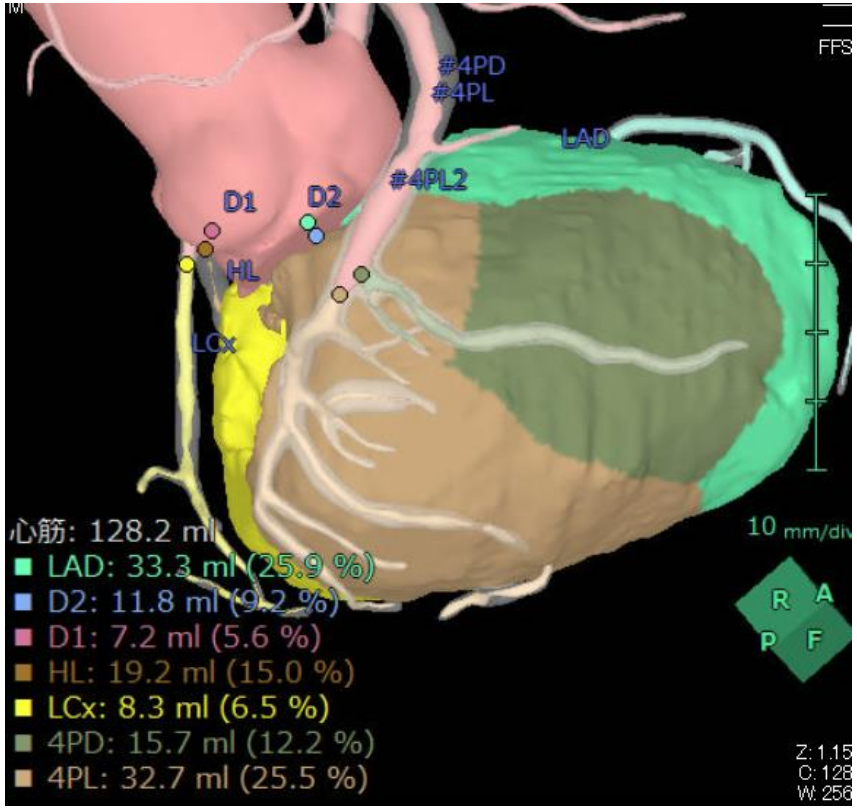




Territory map







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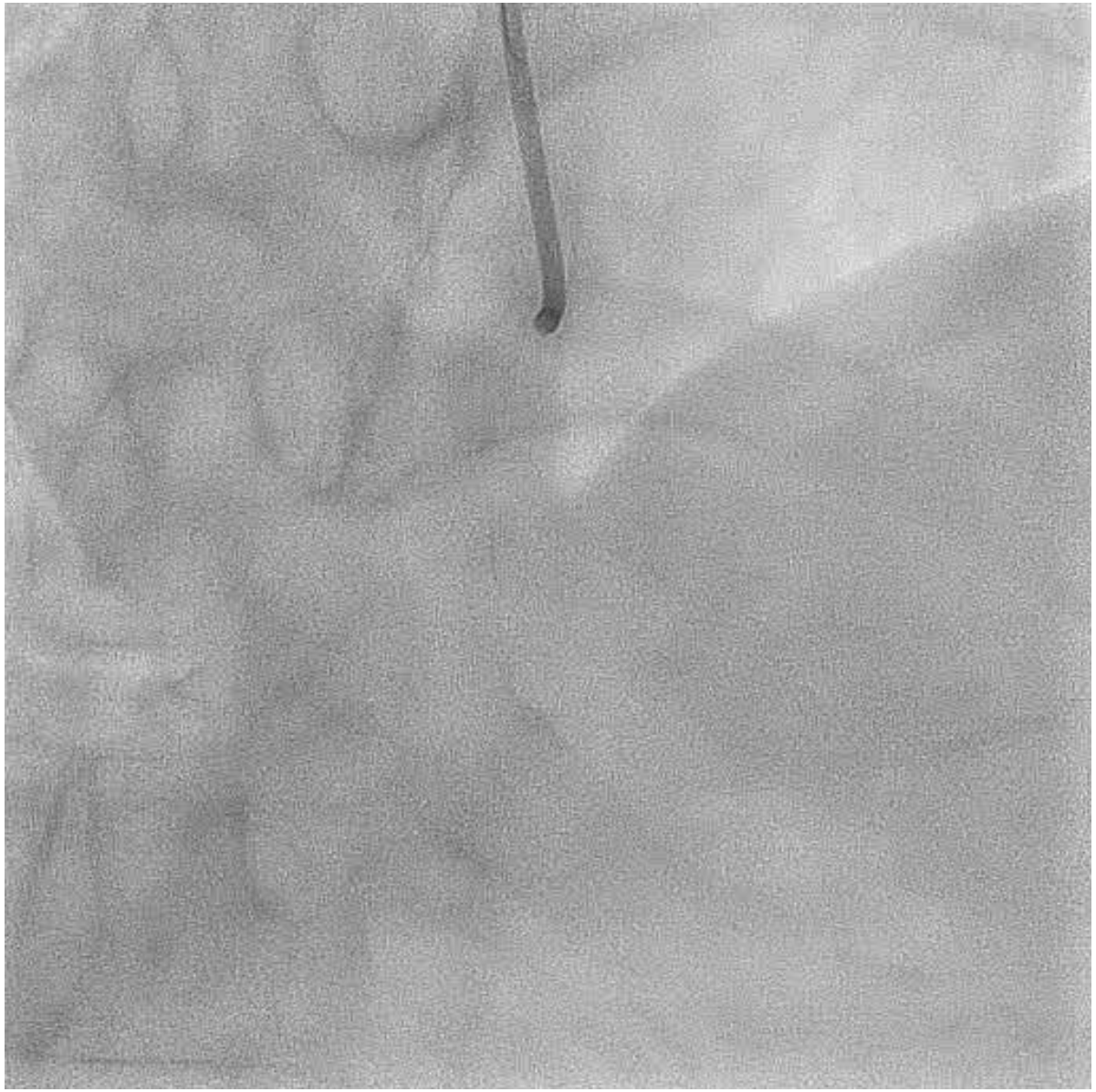
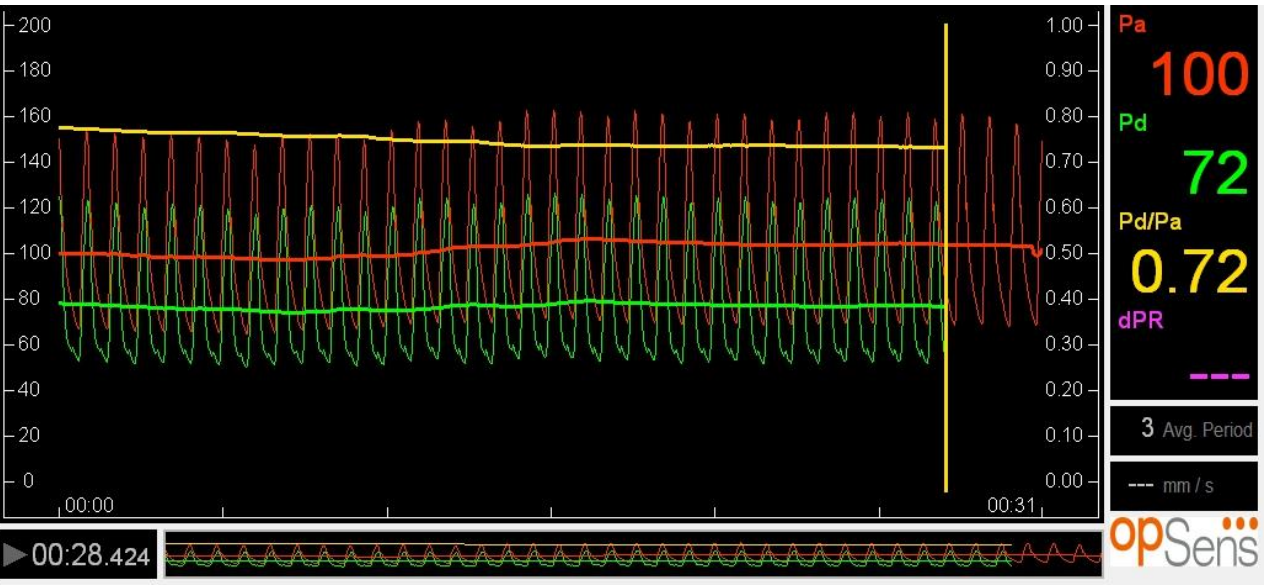
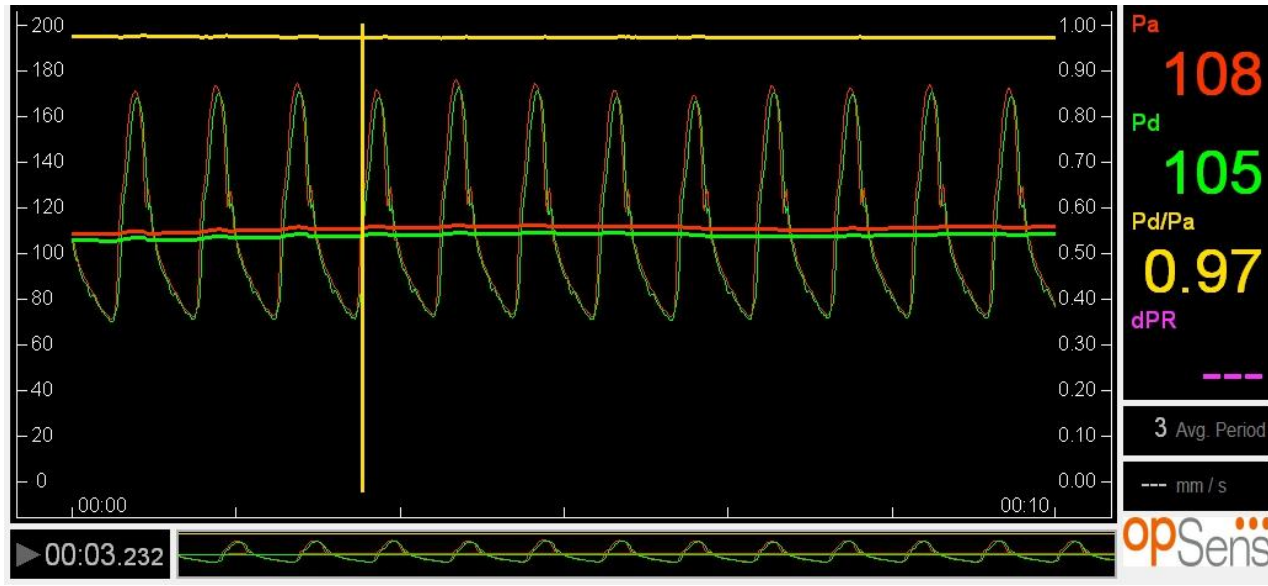


Operator: Yoshiaki Kawase, treated with cutting balloon and DCB

FFR before and after PCI for RCA (4PD)



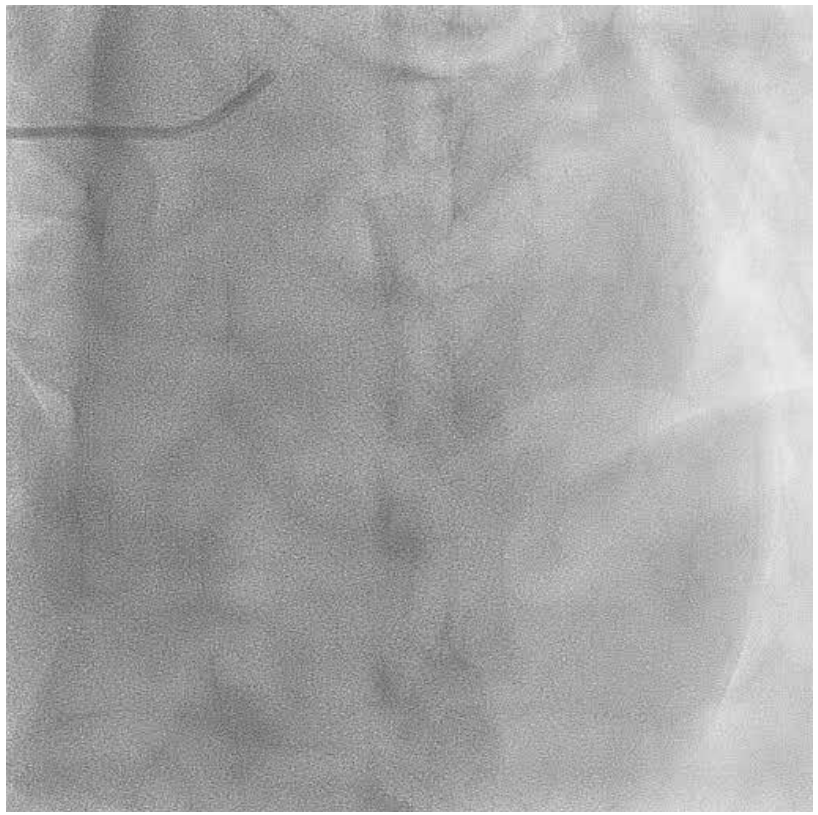


LCA

RAO CAU

CRA

LAO CRA



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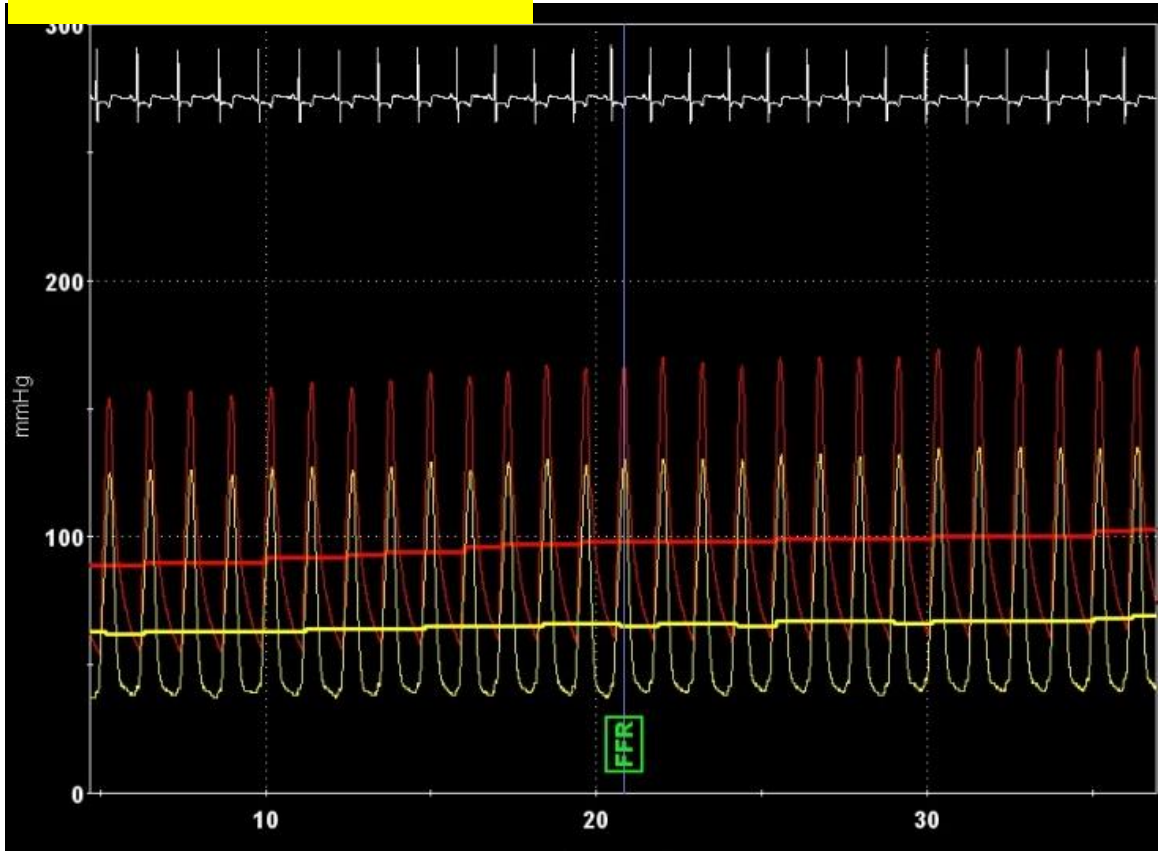
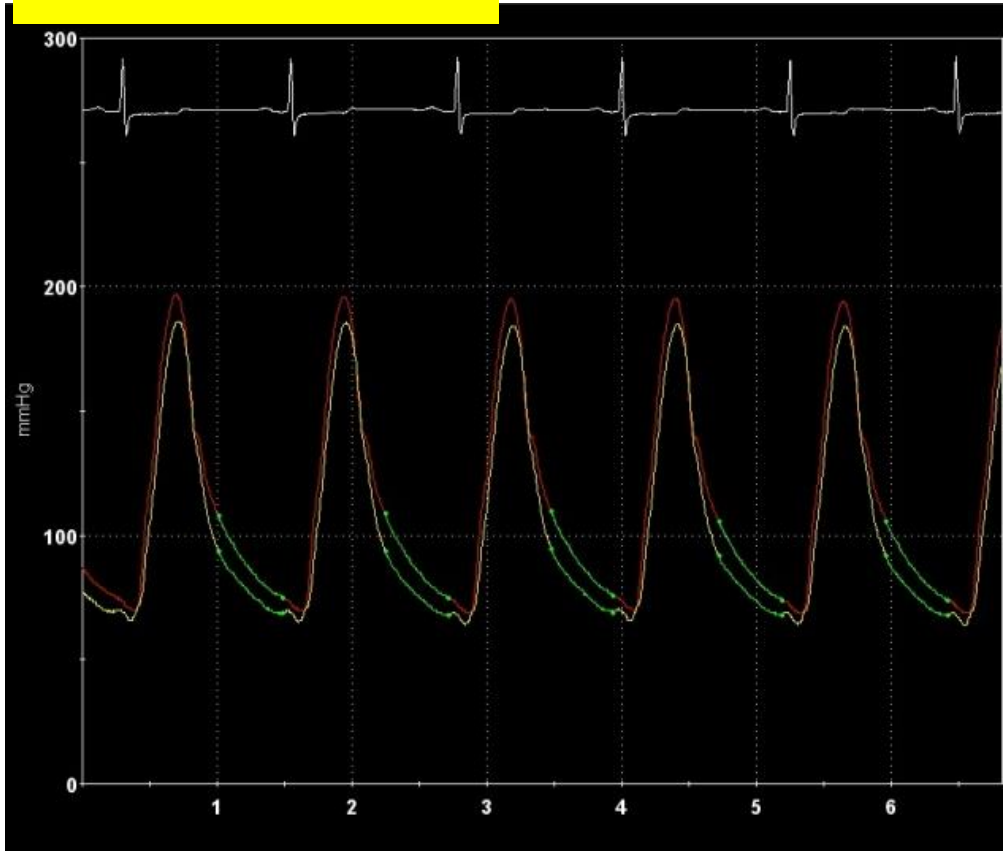
LAD

FFR 0.66



iFR 0.88



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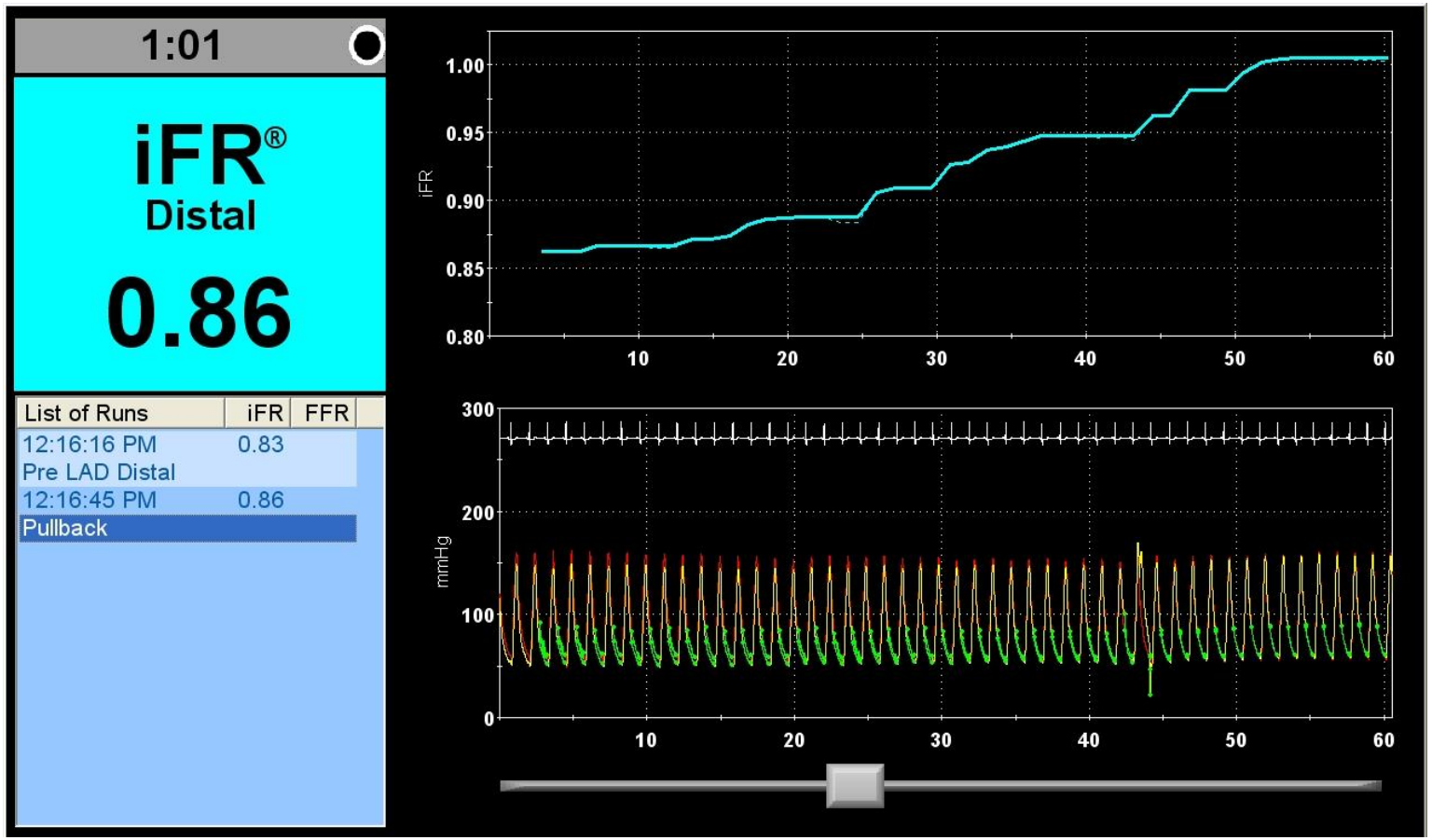
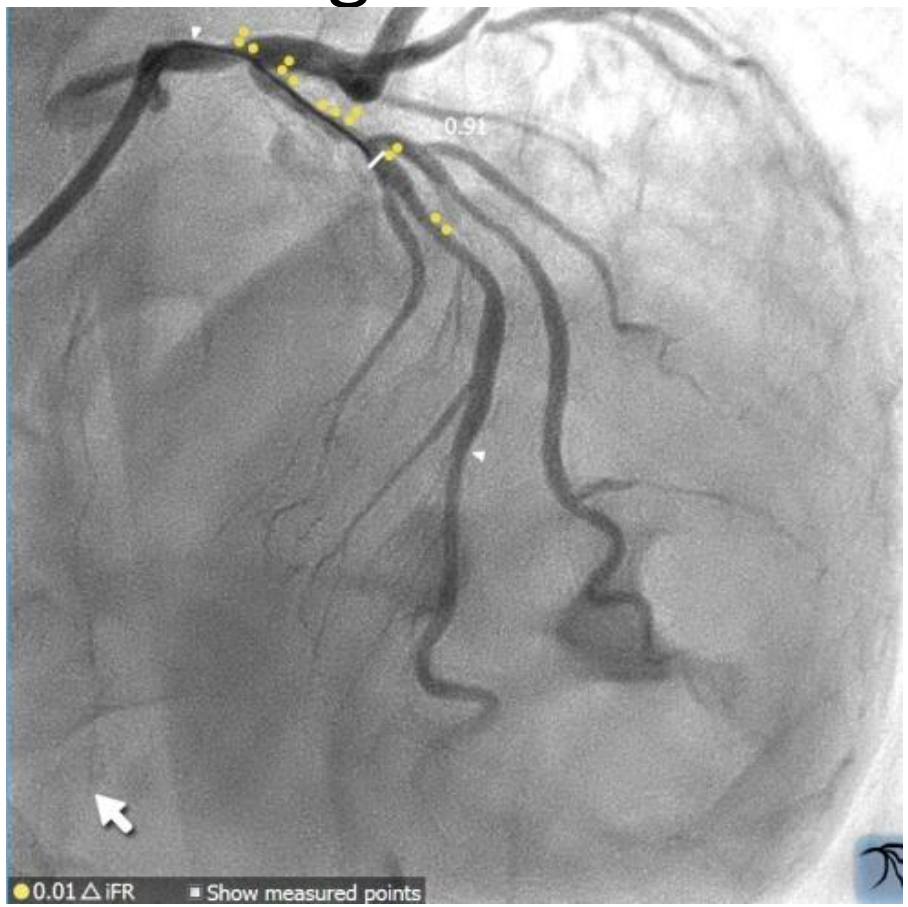
LAD



iFR co-registration



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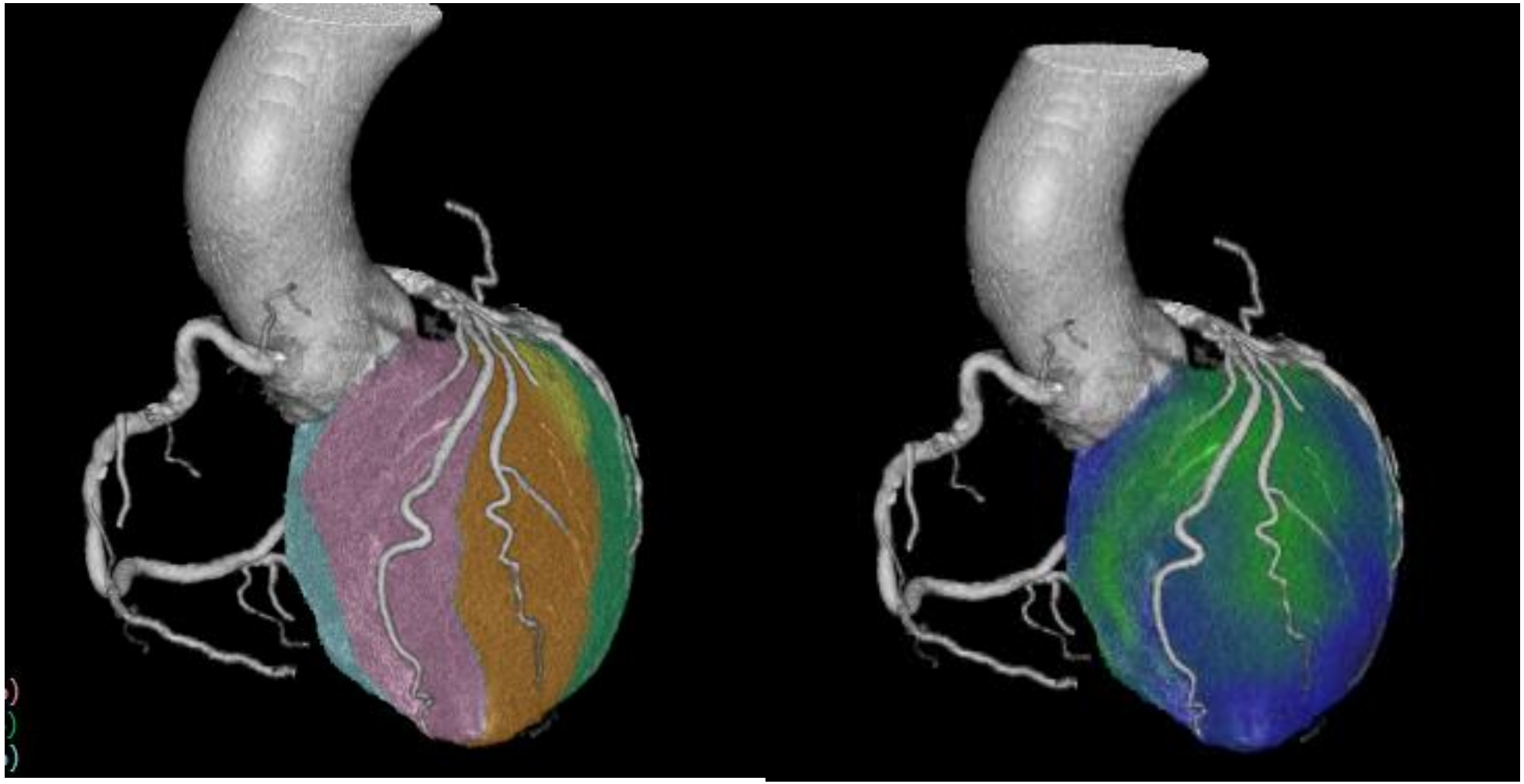
Territory map and CT/SPECT fusion



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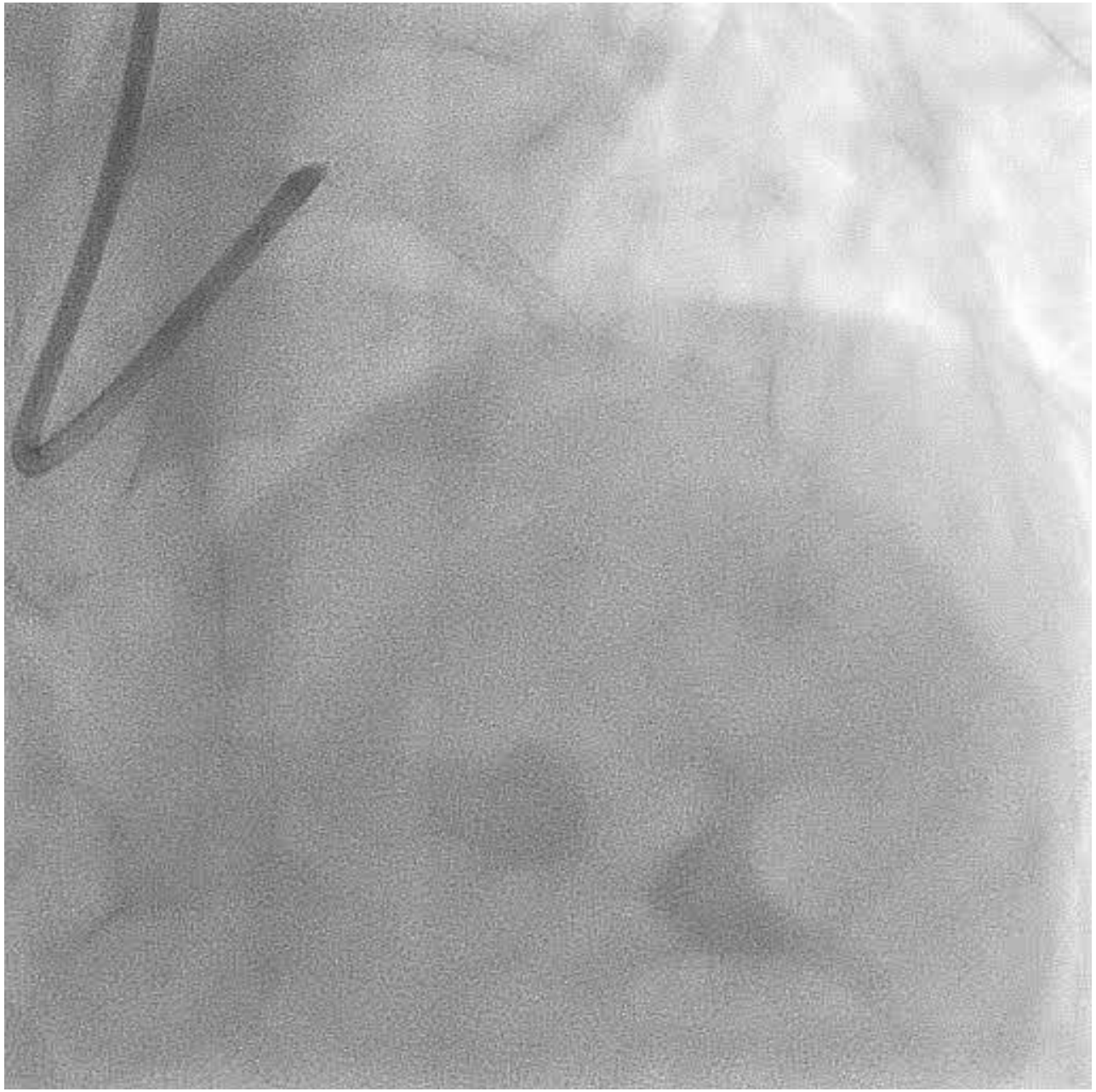
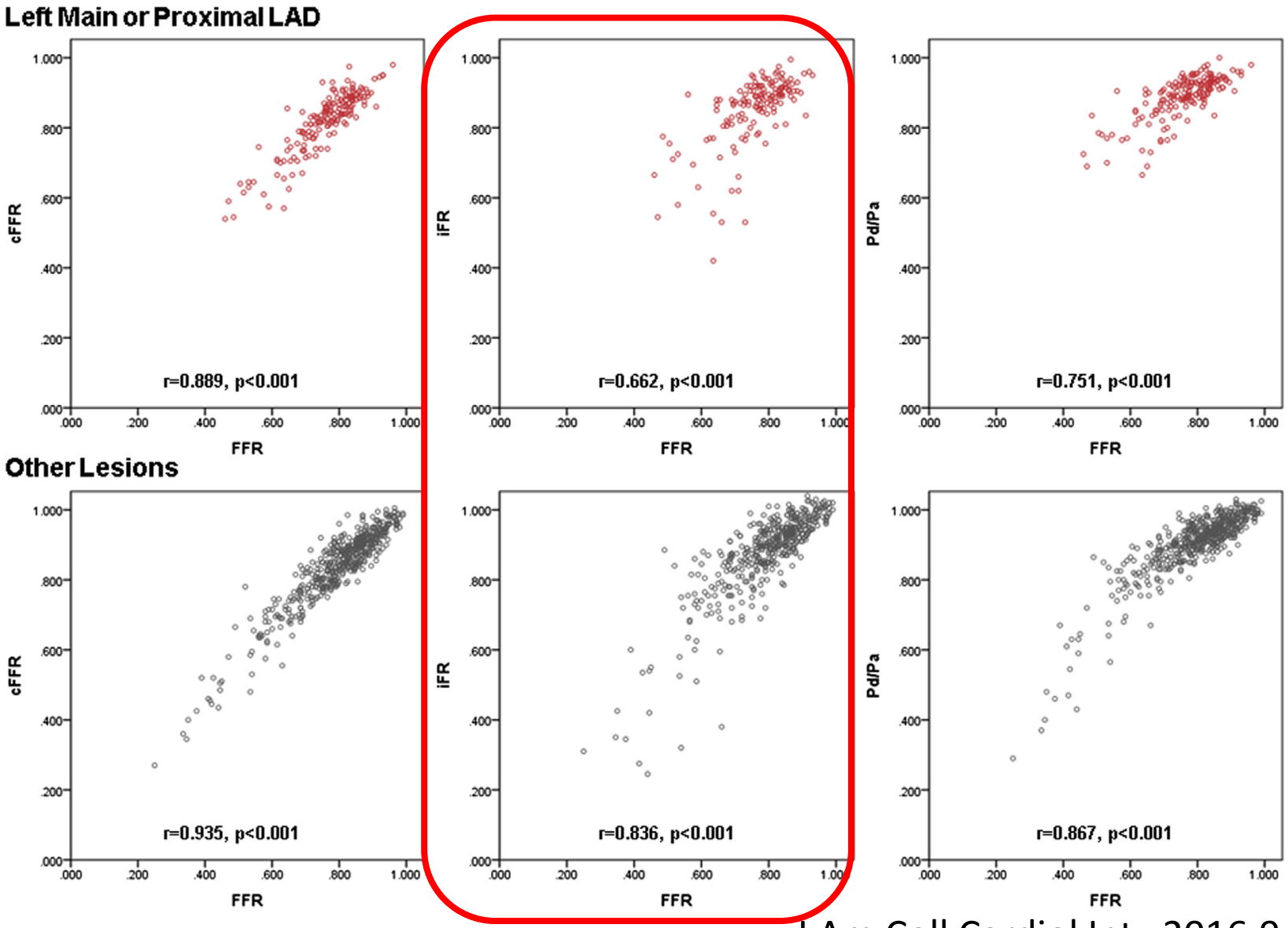


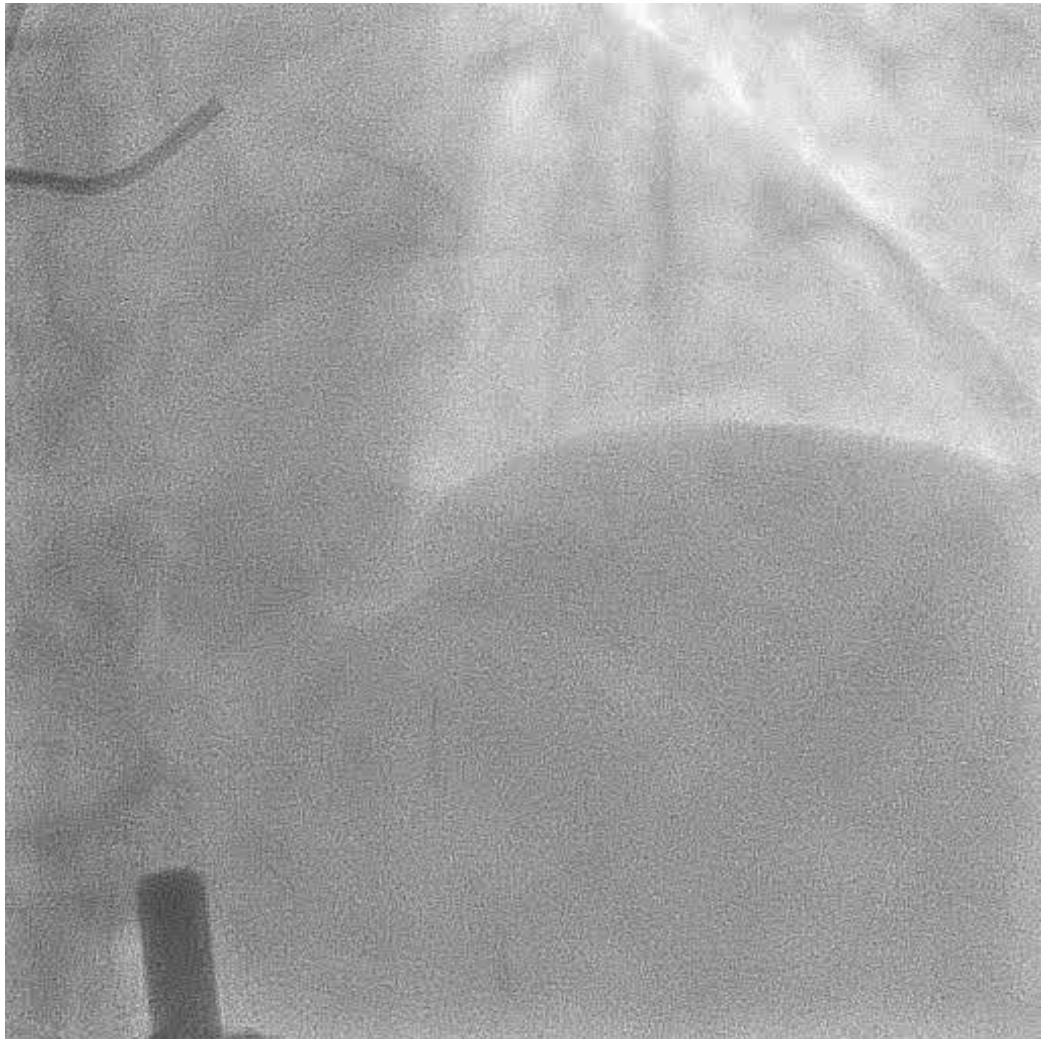
Operator: Hitoshi Matsuo, stent implantation from LAD to LMT

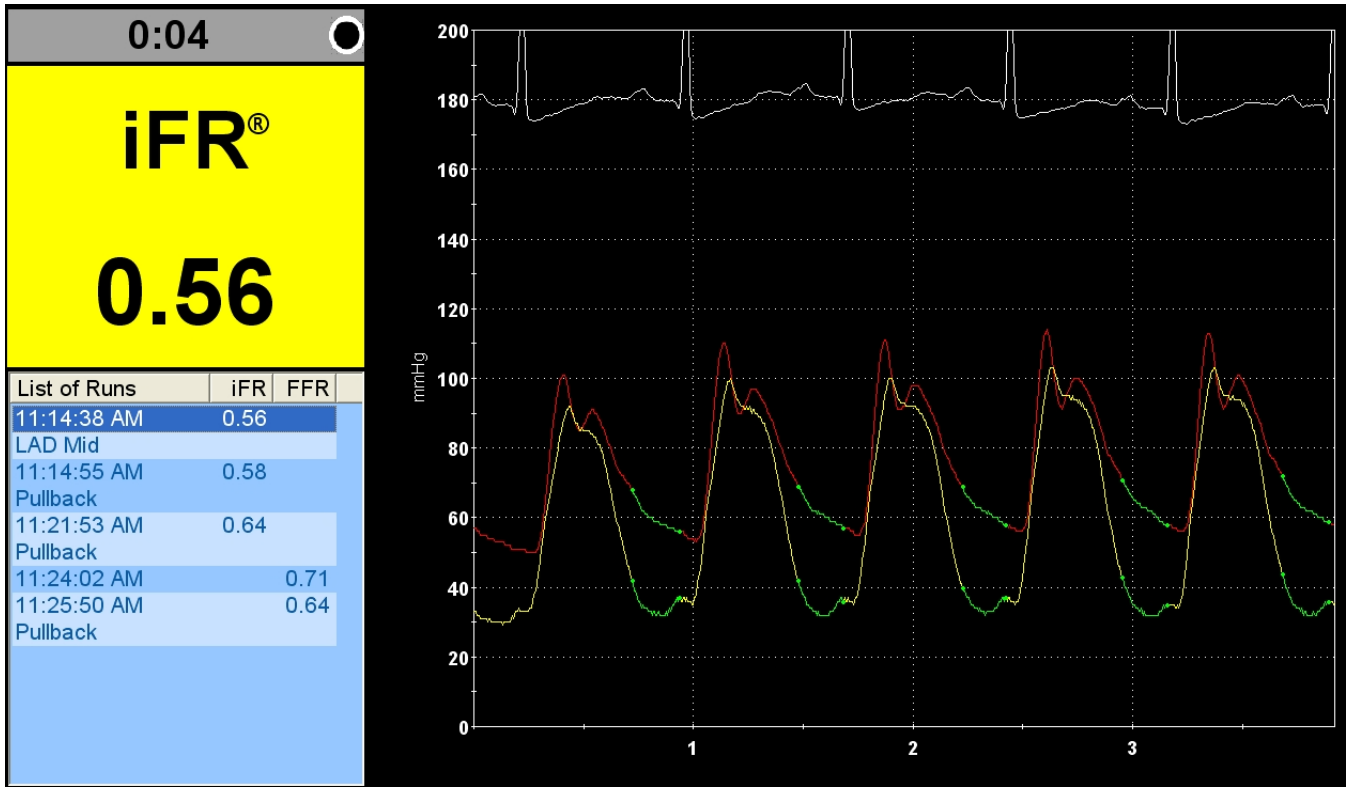
Correlation Between FFR and Adenosine-Free Indices



J Am Coll Cardiol Intv 2016;9:2390

A Case of LAD Disease





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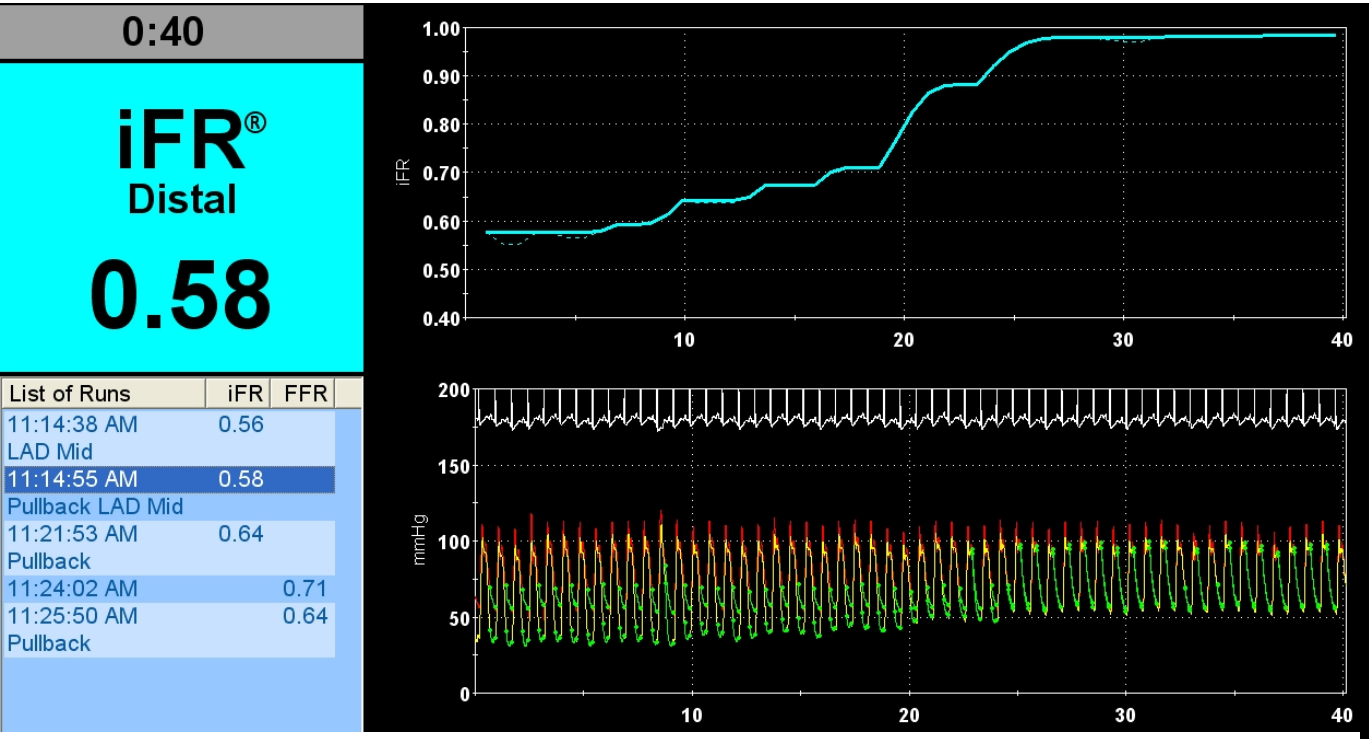
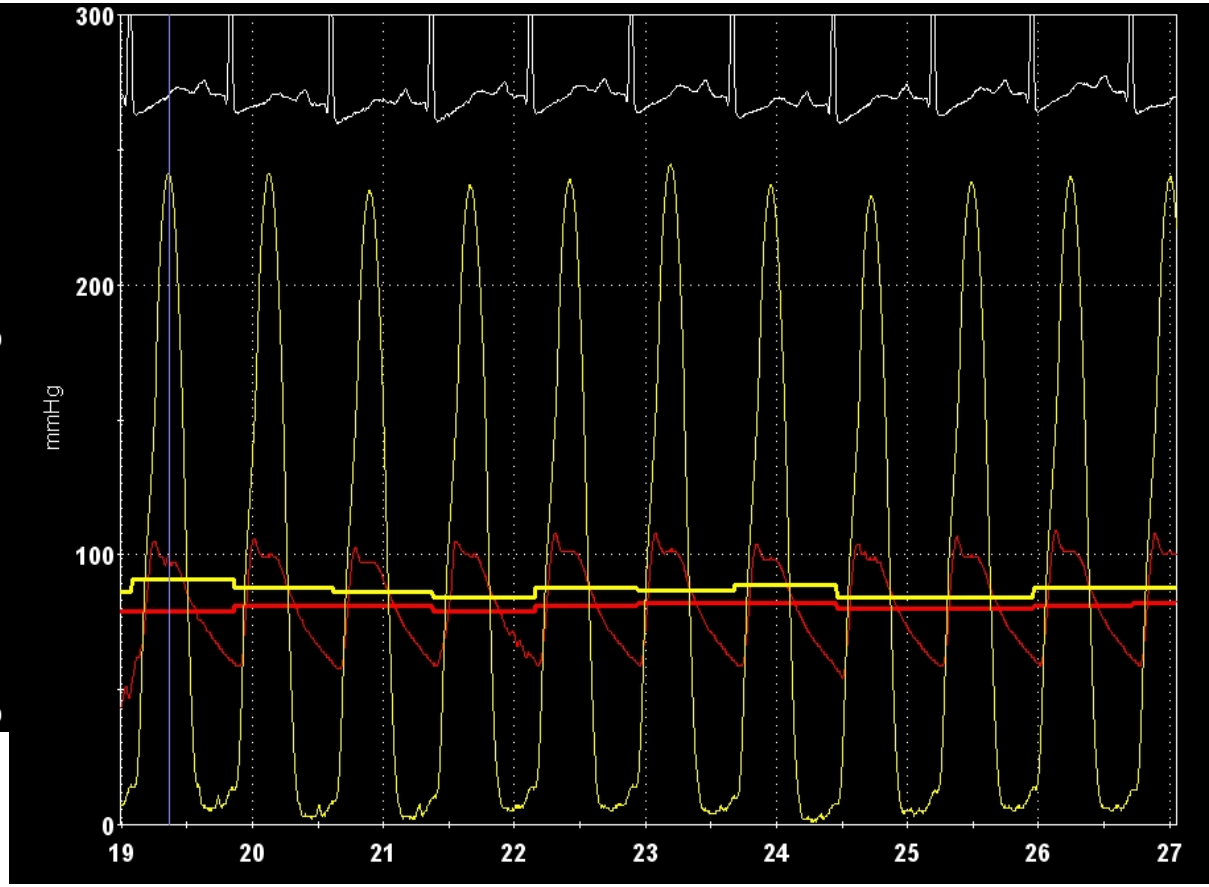
A Case of LAD Disease





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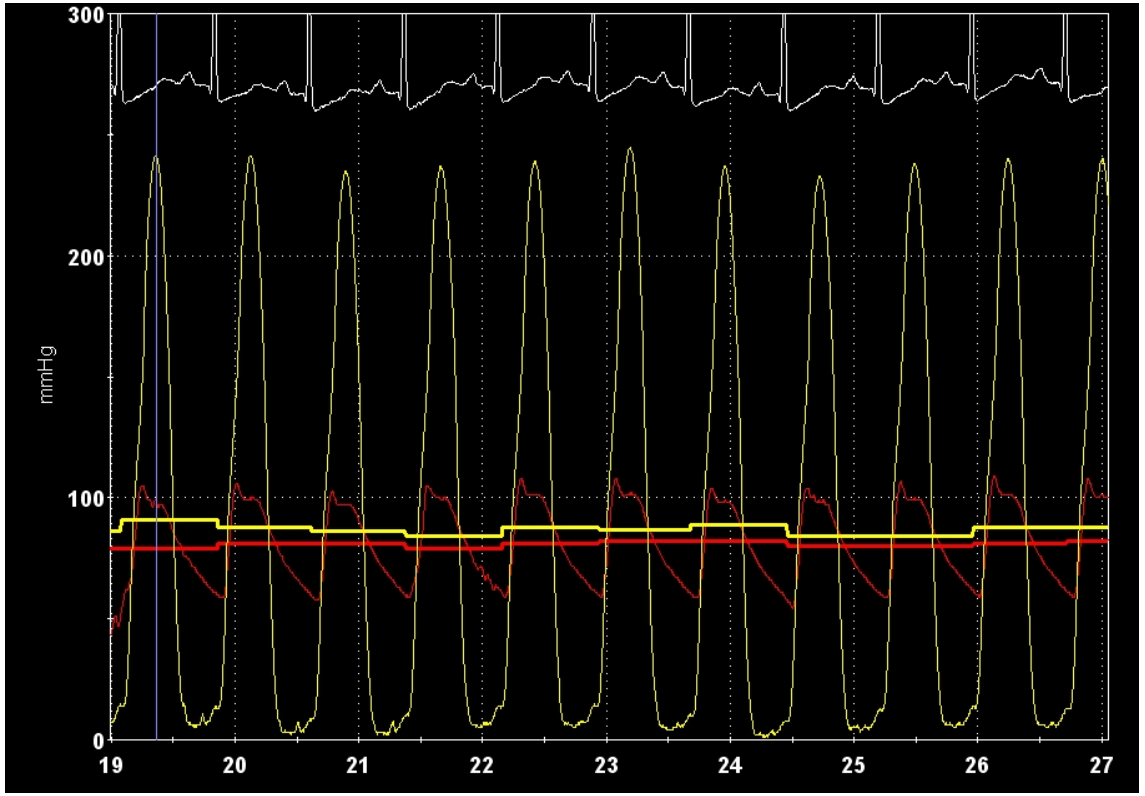
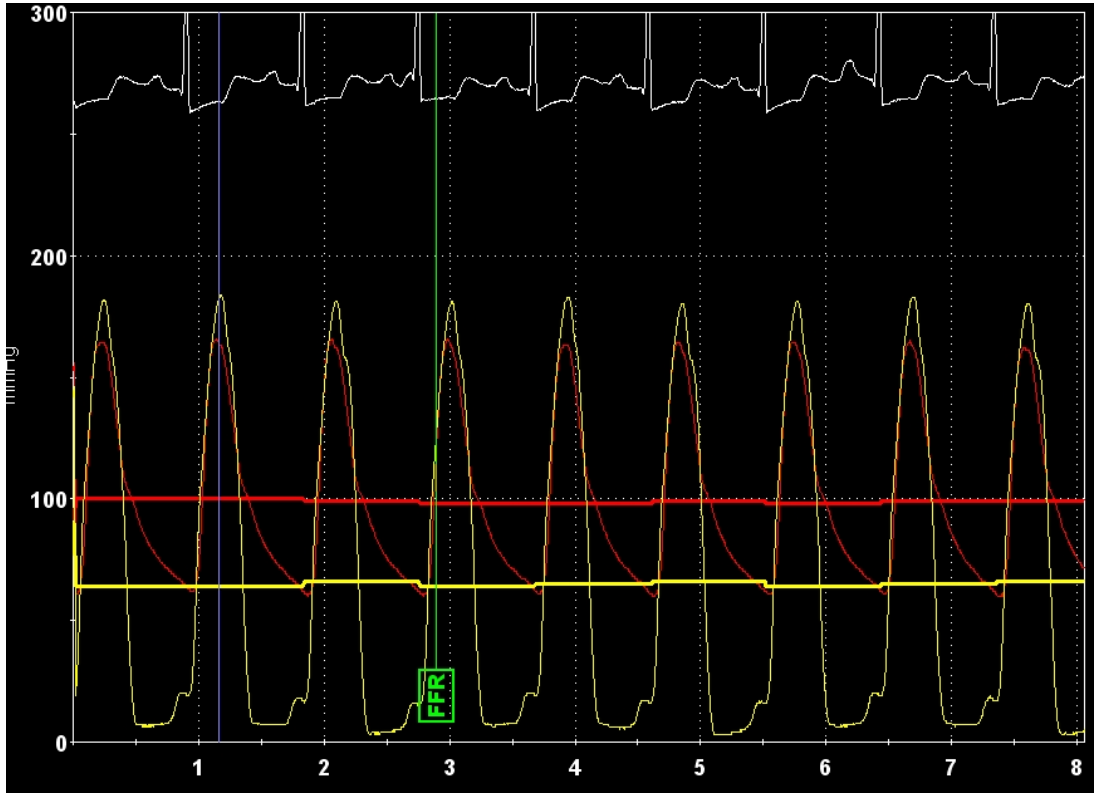
Pre and post administration of oral BB and Cibenzoline

- After (40 days later)





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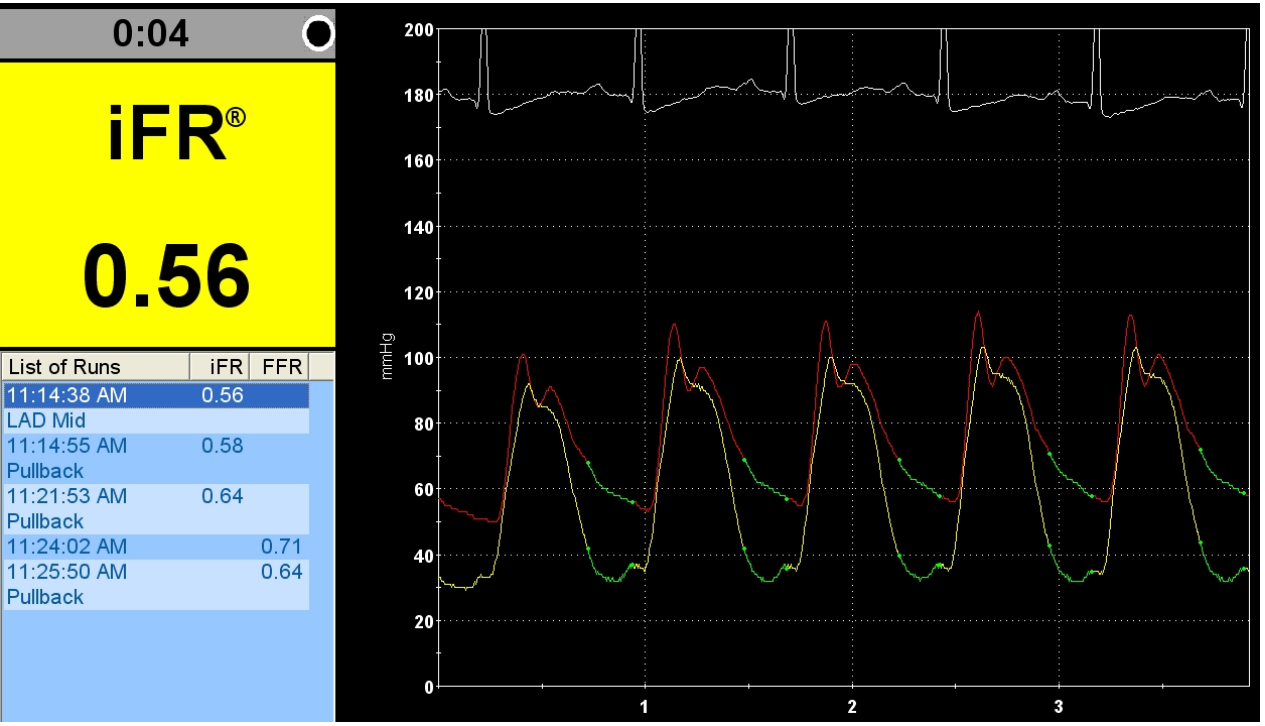
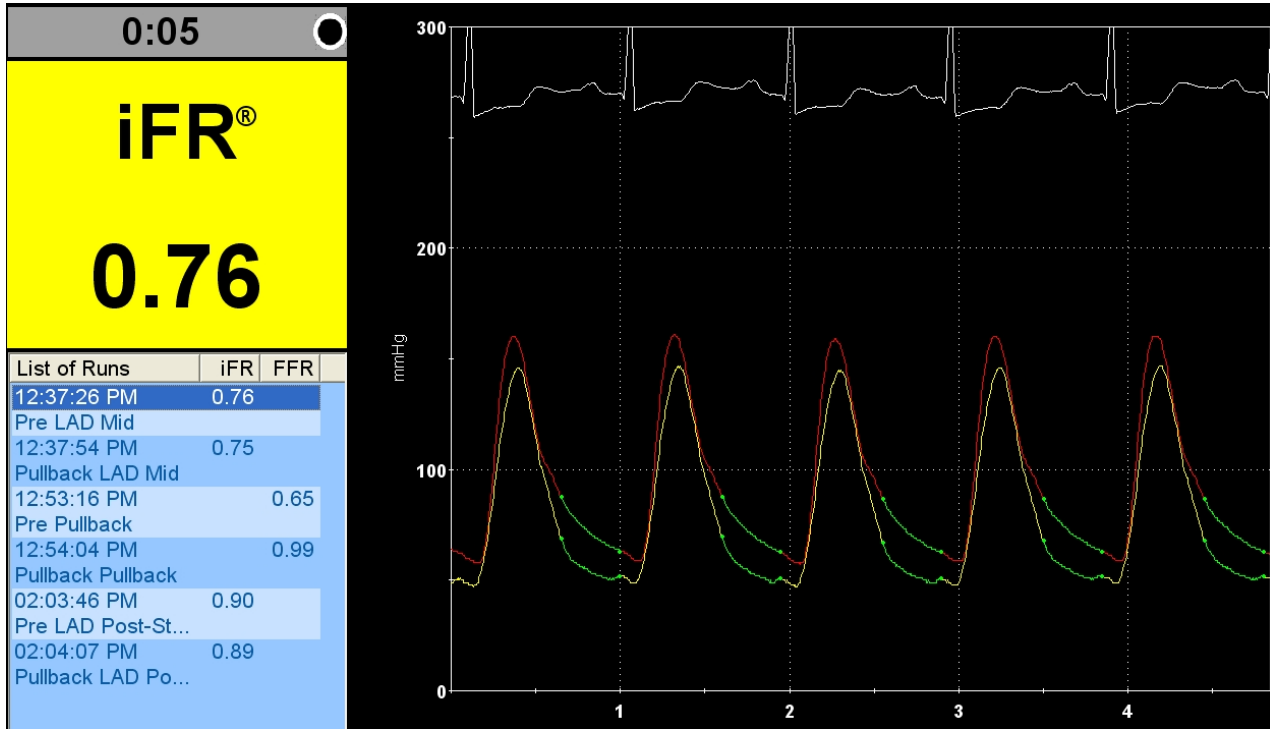
Pre and post administration of oral BB and Cibenzoline

Before

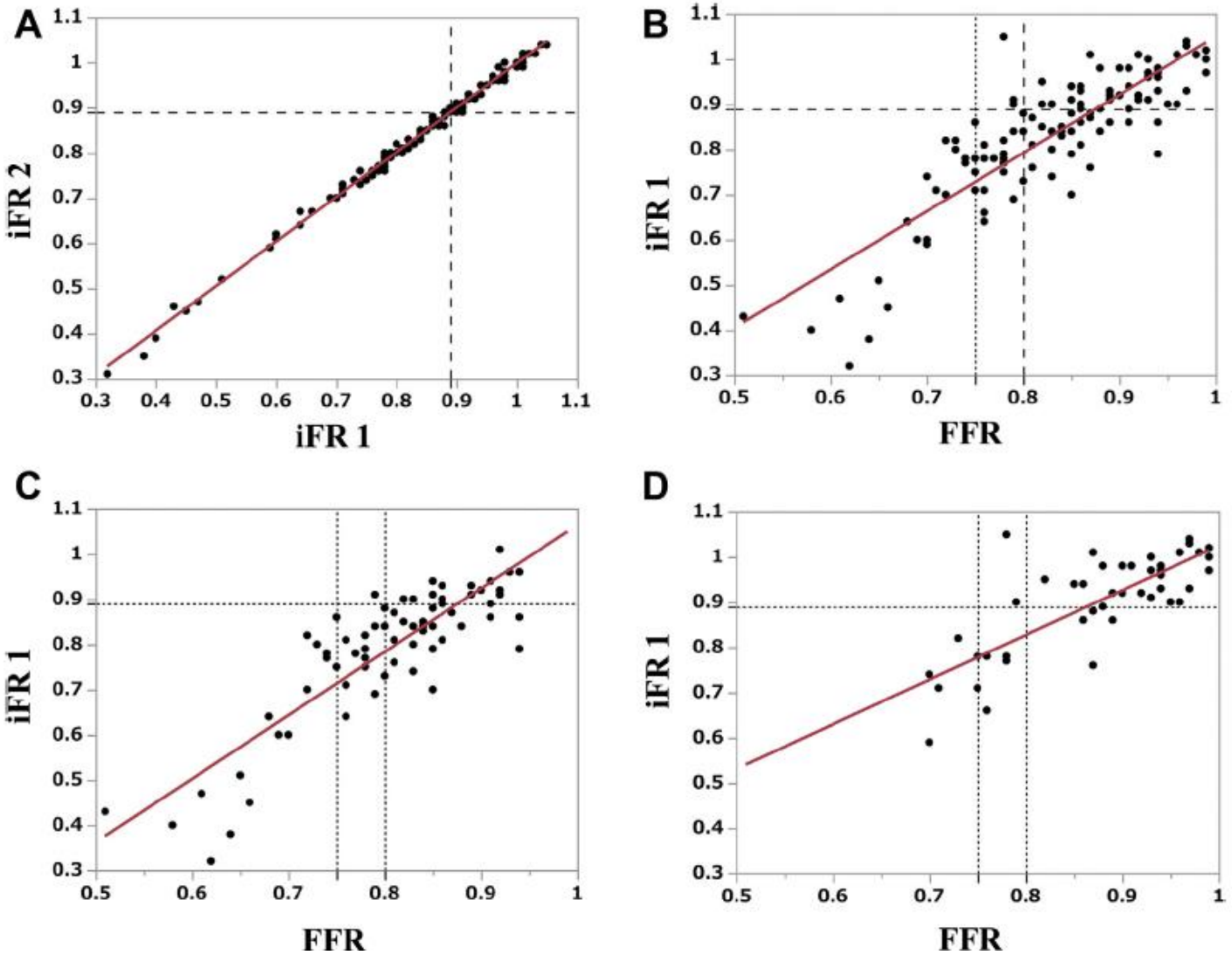


After (40 days later)

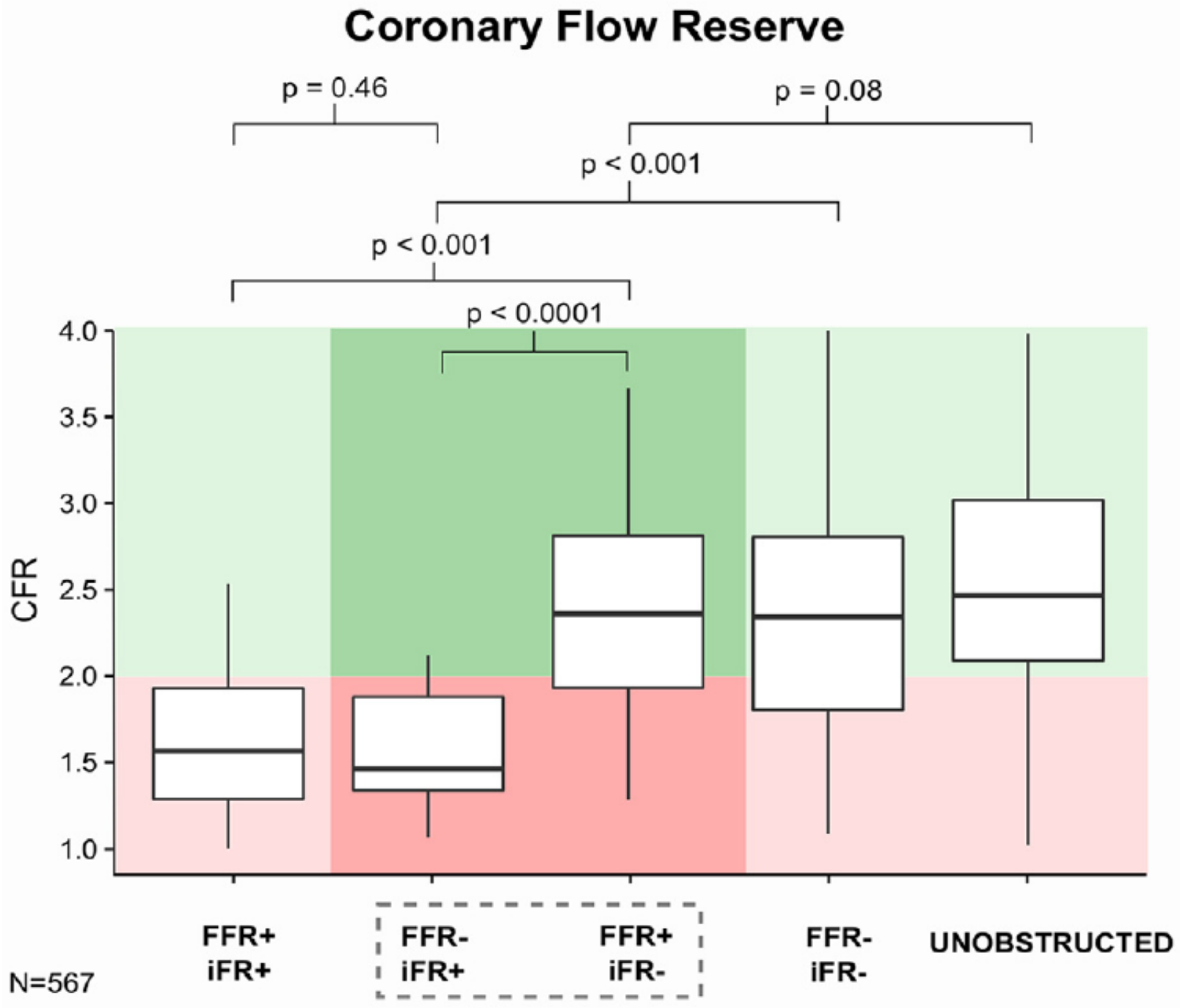


KITA-HARIMA MEDICAL CENTER

Correlation of FFR and resting index (iFR) in patients with severe AS

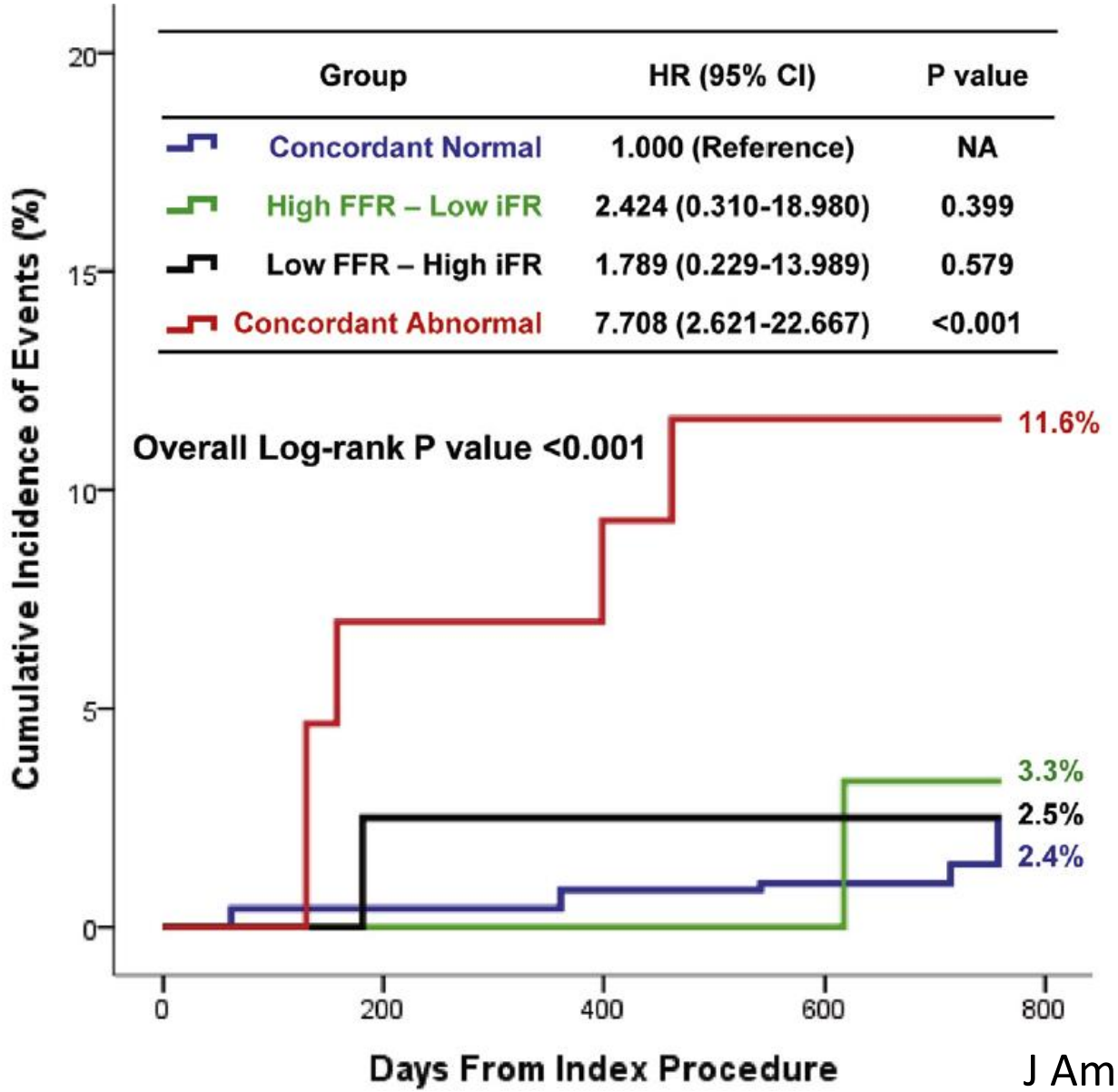


J Am Coll Cardiol Intv 2018;11:2032–40



J Am Coll Cardiol Intv 2017;10:2514

Comparison of 2-Year Clinical Outcomes of Lesions Classified by FFR and iFR in Deferred Lesions



J Am Coll Cardiol Intv 2017;10:2502

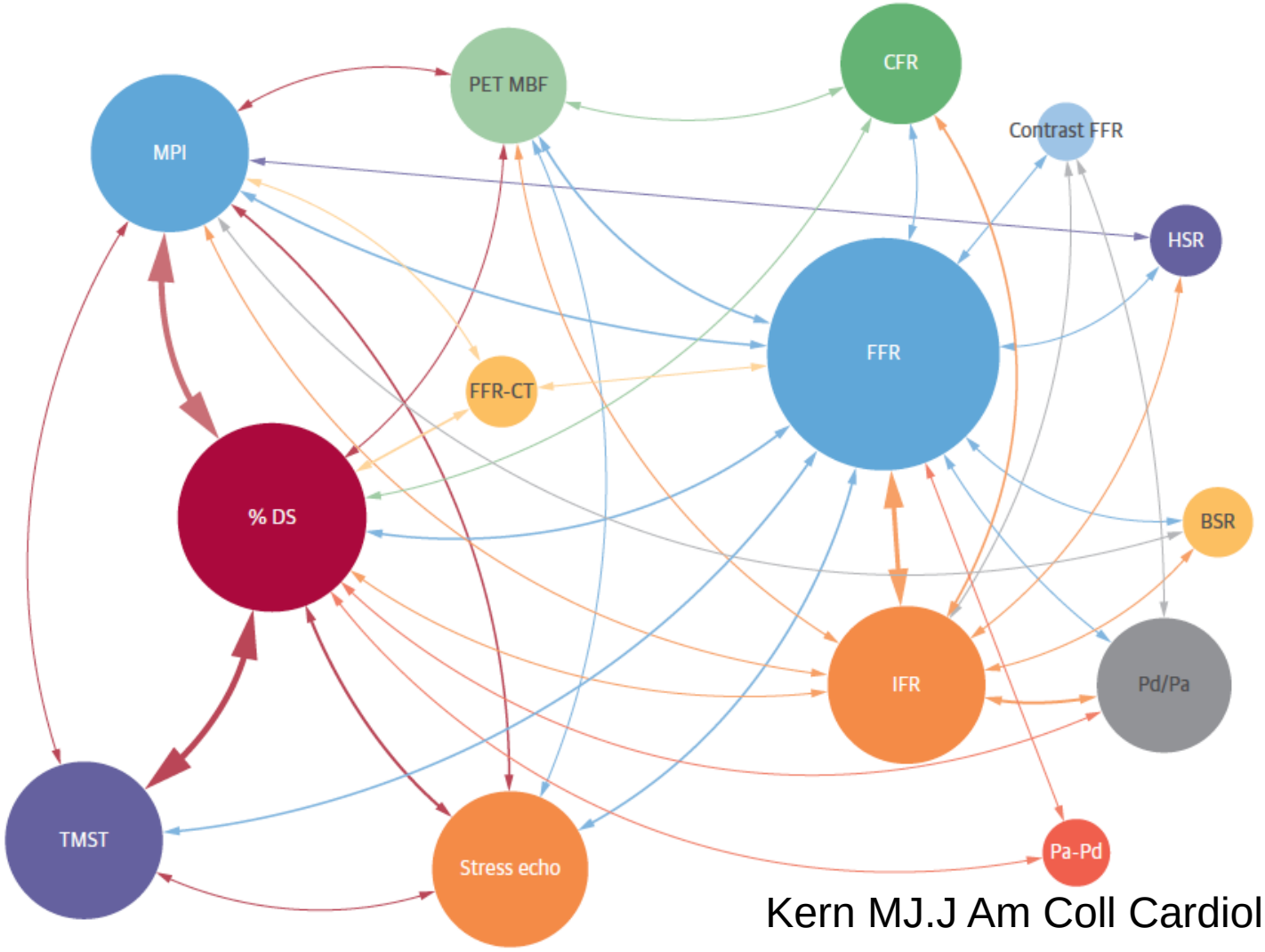
Invasive Coronary Physiology Indices Summary

	FFR	RFR	iFR	dPR	Pd/Pa
Hyperemic y/n	Hyperemic	Non-Hyperemic			
How to calculate	Whole cycle Pd/Pa mean 3 beats	Whole cycle Minimal Pd/Pa 3 beats	End-diastolic Pd/Pa mean 5 beats	Diastolic Pd/Pa mean 5 beats	Whole cycle Pd/Pa mean 3 beats
Company	All	Abbott	Philips	Boston ZEON/Opsens ACIST	All
Cut-off Value	≦0.80	≦0.89			≦0.91

Fractional Flow Reserve

Resting Indices

Chaos?
Physiological Assessment of Coronary Artery Disease



Kern MJ.J Am Coll Cardiol. 2017 Oct 24;70(17):212

Take Home Message

- J-CONFIRM registry demonstrated the safety of deferral PCI especially negative FFR cases
- Territory of coronary artery may be important, and CT territory map might be useful to determine the indication of PCI
- Discordance among various indices of physiology is frequently observed in some clinical setting, and clinical importance of each index is still inconclusive
- Further investigation is needed, and **J-PRIDE registry**, a multicenter registry of various resting indices now started