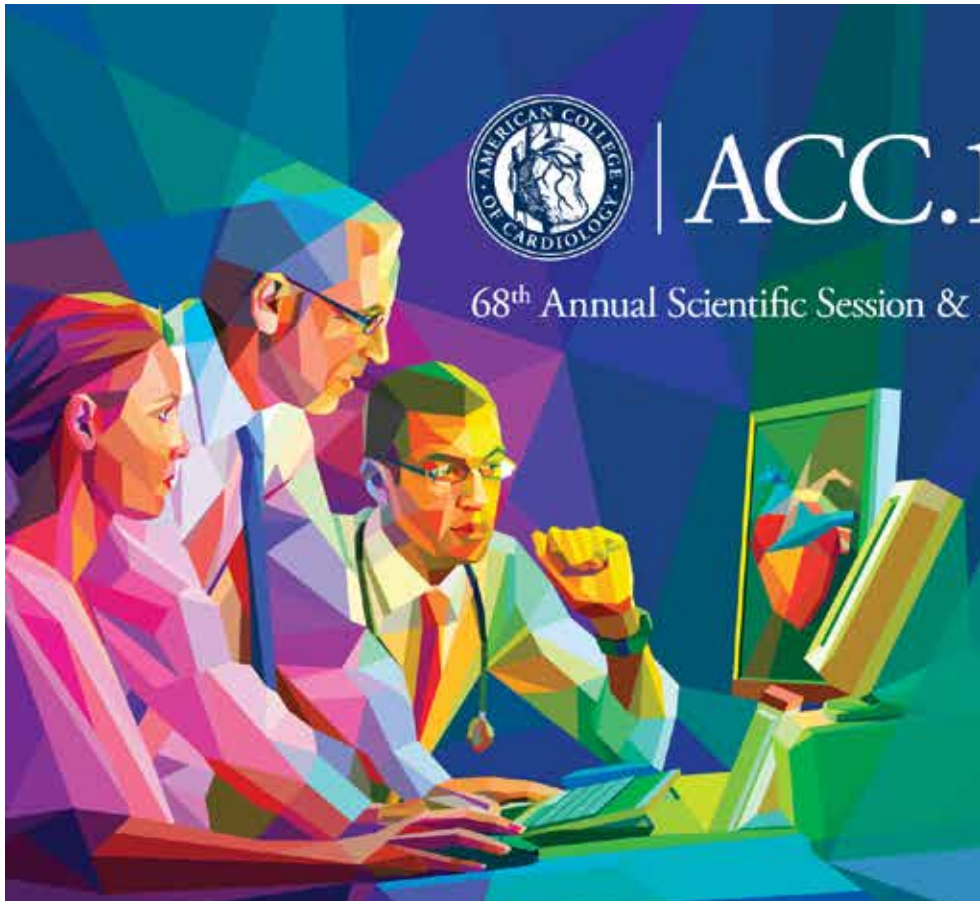

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68th Annual Scientific Session & Expo

NEW ORLEANS
MARCH 16 - 18
2019

DEFINE PCI

Blinded Physiological Assessment of Residual Ischemia after Successful Angiographic PCI

Allen Jeremias, MD, MSc

On behalf of Justin Davies, Manesh Patel, Gregg Stone and the DEFINE PCI Investigators

DEFINE PCI

Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship	Company
• Institutional Educational Grants	• Volcano/Philips • Abbott Vascular
• Consulting Fees/Honoraria	• Volcano/Philips • Abbott Vascular • Opsens • Boston Scientific • Chiesi • Astra Zeneca

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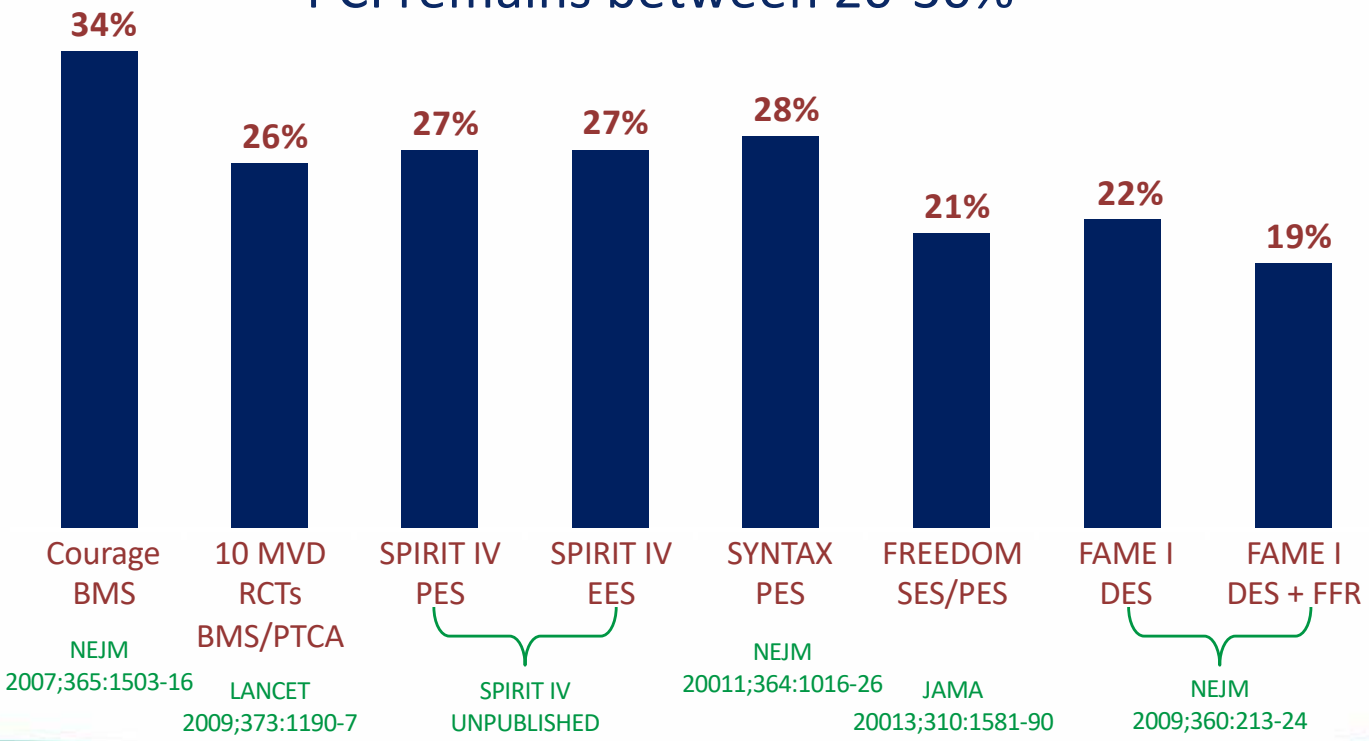
Background (I)

Recurrent Angina at 1 Year After PCI remains between 20-30%



Courtesy of Dr. Gregg Stone

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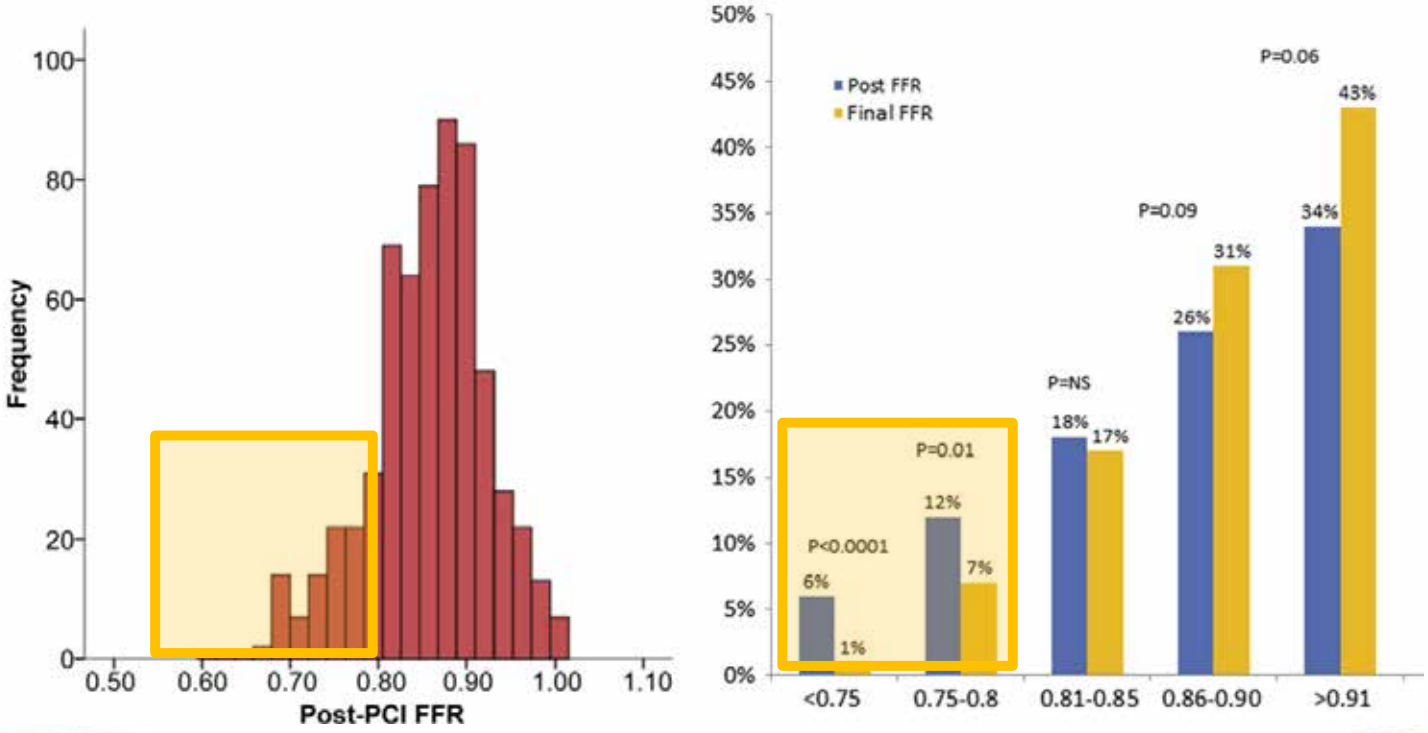
Background (II)

Post PCI ischemia based on FFR ≤0.80 occurs in 10-20% of cases



Lee JM., et al. *J Am Coll Cardiol Intv*. 2018;11:2099–109.
Agarwal SK, et al. J Am Coll Cardiol 2016;9:1022-31.

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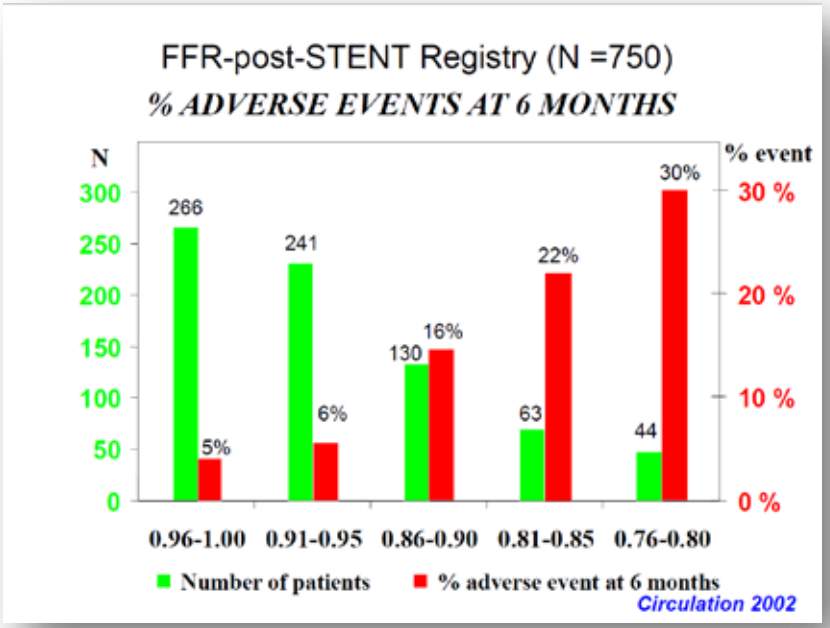
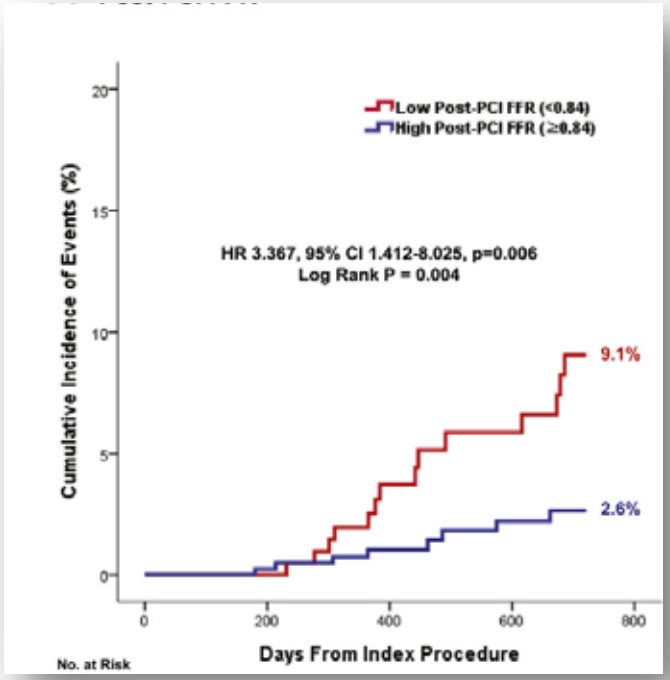
DEFINE PCI

Background (III)

Low post-PCI FFR is related to adverse events





Pijls N., et al. *Circulation*. 2002;105:2950-54.
Lee JM., et al. *J Am Coll Cardiol Intv*. 2018;11:2099–109.

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Study Objectives

How often do patients leave the cardiac cath lab with significant residual ischemia (i.e. iFR ≤0.89), despite angiographically satisfactory results?

Why are the post PCI values ≤0.89?
Missed focal lesion ('physiologic miss'), stent related, diffuse disease

What is the impact of residual ischemia on patient outcomes?
MACE, recurrent angina, and quality of life
(ongoing follow-up)

DEFINE PCI

Study Endpoints

Primary Endpoint

- Rate of residual ischemia (iFR ≤0.89) after operator-assessed angiographically successful PCI (residual DS<50% in any treated lesion)

Secondary Endpoints

- Correlation between iFR ≤0.89 and coronary stenosis >50%
- Differentiation of the cause for impaired iFR (categorized as stent related, distant focal stenosis, or diffuse atherosclerosis)
- Proportion of cases in which the iFR would become non-significant if a focal stenosis demonstrated by iFR pullback were treated with PCI
- Predictors of impaired post PCI iFR

DEFINE PCI

Study Leadership

Study Chairman
- Gregg W. Stone, Columbia University Medical Center

Principal Investigators
- Allen Jeremias, St. Francis Hospital, Roslyn, NY
- Justin Davies, Imperial College London
- Manesh Patel, Duke Health Care System

Steering Committee
- Habib Samady, Emory University
- Andrew Sharp, Royal Devon and Exeter
- Arnold Seto, VAMC, Long Beach, CA

Clinical Events Committee
- Cardiovascular Research Foundation, New York, NY; Steven O. Marx, MD, chair

Physiology Core Laboratory
- Allen Jeremias, Cardiovascular Research Foundation, New York, NY
- Akiko Maehara, Cardiovascular Research Foundation, New York, NY
- Mitsuaki Matsumura, Cardiovascular Research Foundation, New York, NY

Angiography Core Laboratory
- Ziad Ali, Cardiovascular Research Foundation, New York, NY

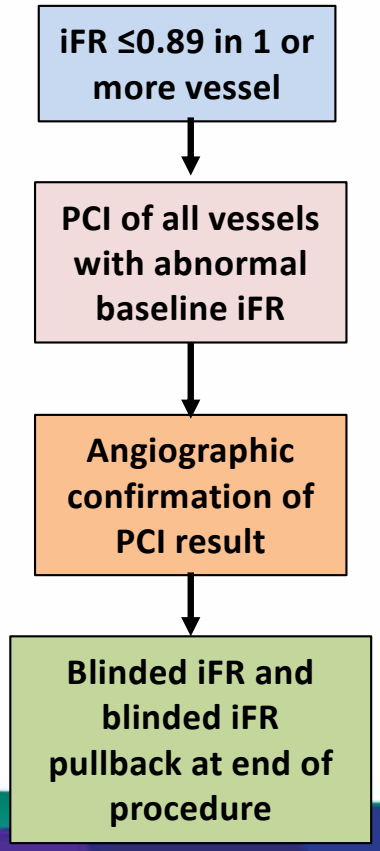
Sponsor
- Philips/Volcano, Amsterdam, The Netherlands

DEFINE PCI

International, prospective, observational multi-center study

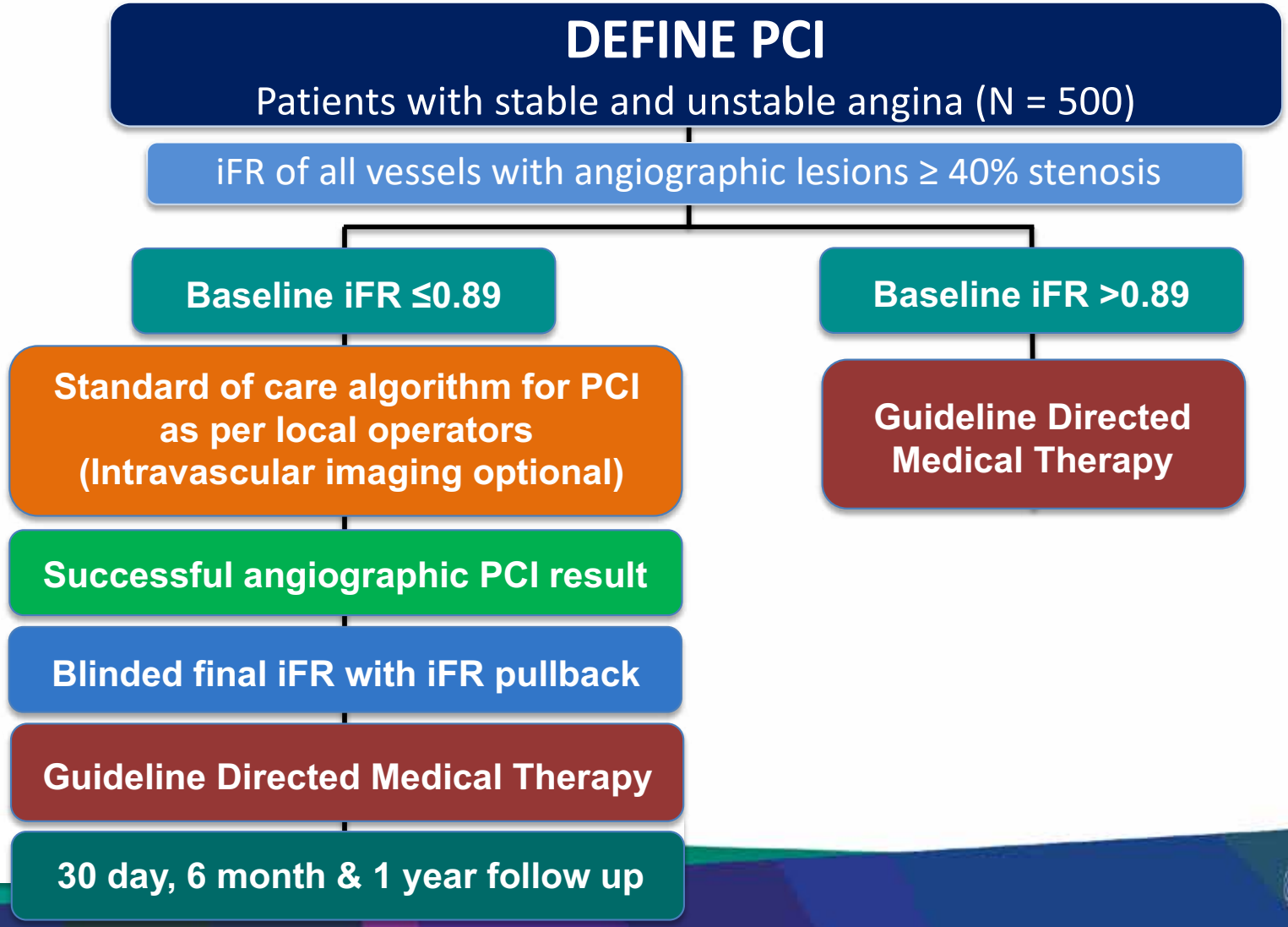
Inclusion Criteria

- Pts with stable or unstable angina
- Lesions of ≥40% angiographic severity
- Single vessel CAD with long lesion (≥20 mm), multi-lesion CAD of a single vessel or multi-vessel CAD
- Pre-PCI iFR performed in all vessels with angiographic lesion severity of ≥40%



Exclusion Criteria

- STEMI within past 7 days
- Cardiogenic shock
- Ventricular arrhythmias
- Prior CABG
- CTO
- EF < 30%
- Severe valvular heart disease
- TIMI flow <3 at baseline or post PCI
- Intra-coronary thrombus on baseline angiography
- Procedural complications


DEFINE PCI
Patients with stable and unstable angina (N = 500)
iFR of all vessels with angiographic lesions ≥ 40% stenosis
Baseline iFR ≤0.89
Baseline iFR >0.89
Standard of care algorithm for PCI as per local operators (Intravascular imaging optional)
Guideline Directed Medical Therapy
Successful angiographic PCI result
Blinded final iFR with iFR pullback
Guideline Directed Medical Therapy
30 day, 6 month & 1 year follow up

DEFINE PCI

DEFINE PCI: Total enrollment 500 pts in 27 US and European Sites

Top 15 Enrolling Centers

67	North Carolina Heart & Vascular (J. Schneider)
50	Essex Cardiothoracic Centre (K. Tang)
40	Royal Bournemouth Hospital (S. Talwar)
36	VU University Medical Center (K. Marques)
32	Midwest Cardiovascular Research Foundation (N. Shammas)
32	Northwell Health (L. Gruberg)
26	Colorado Heart & Vascular (J. Altman)
25	Dartmouth Hitchcock (J. Jayne)
25	VAMC Long Beach (A. Seto)
22	VAMC Atlanta (G. Kumar)
18	AMC Amsterfdam (J. Piek)
17	St. Francis Hospital (R. Schlofmitz)
17	Minneapolis Heart Institute (E. Brilakis)
15	Royal Devon & Exeter (A. Sharp)
13	Stony Brook University Hospital (W. Lawson)

DEFINE PCI

Study Methods (I)

- Blinding was achieved by turning off monitor in procedure room with guidance of measurements by unblinded research staff in control room
- Pullback performed manually under continuous fluoroscopy with bookmarks inserted 5 mm distal and proximal to stent for core lab analysis
- A final drift check was performed and recorded; if drift exceeded >0.02 units, the wire was re-equalized and all measurements were repeated
- All pressure tracings were sent to the physiology and angiography core laboratories at CRF (New York, NY) for centralized independent review

DEFINE PCI

Study Methods (II)

- Each tracing was assessed for quality, including evaluation of aortic and coronary pressure signal for wave-form distortion and ventricularization
- Trans-stenotic pressure gradients in post-PCI iFR pullback were categorized according to their location (distal vessel, stented segment or proximal vessel) and classified into focal lesions or diffuse disease
- Trans-stenotic pressure gradients of ≥0.03 units were categorized as focal lesions when their length was ≤15 mm and as diffuse disease when their length exceeded 15 mm
- The angiographic core laboratory analyzed all angiograms before and after PCI using standard methods

DEFINE PCI

Baseline Patient Characteristics

	N = 500 Patients
Age (years)	66.4 ± 9.9
Male	379 (75.8%)
Diabetes mellitus	169 (33.8%)
Prior PCI	227 (45.4%)
Prior myocardial infarction	134 (26.8%)
Left ventricular ejection fraction (%)	56.3 ± 9.0
Clinical presentation	
Stable angina	212 (42.4%)
Silent ischemia	27 (5.4%)
Unstable angina	155 (31.0%)
NSTEMI	85 (17.0%)
Recent STEMI (>7 days)	21 (4.2%)

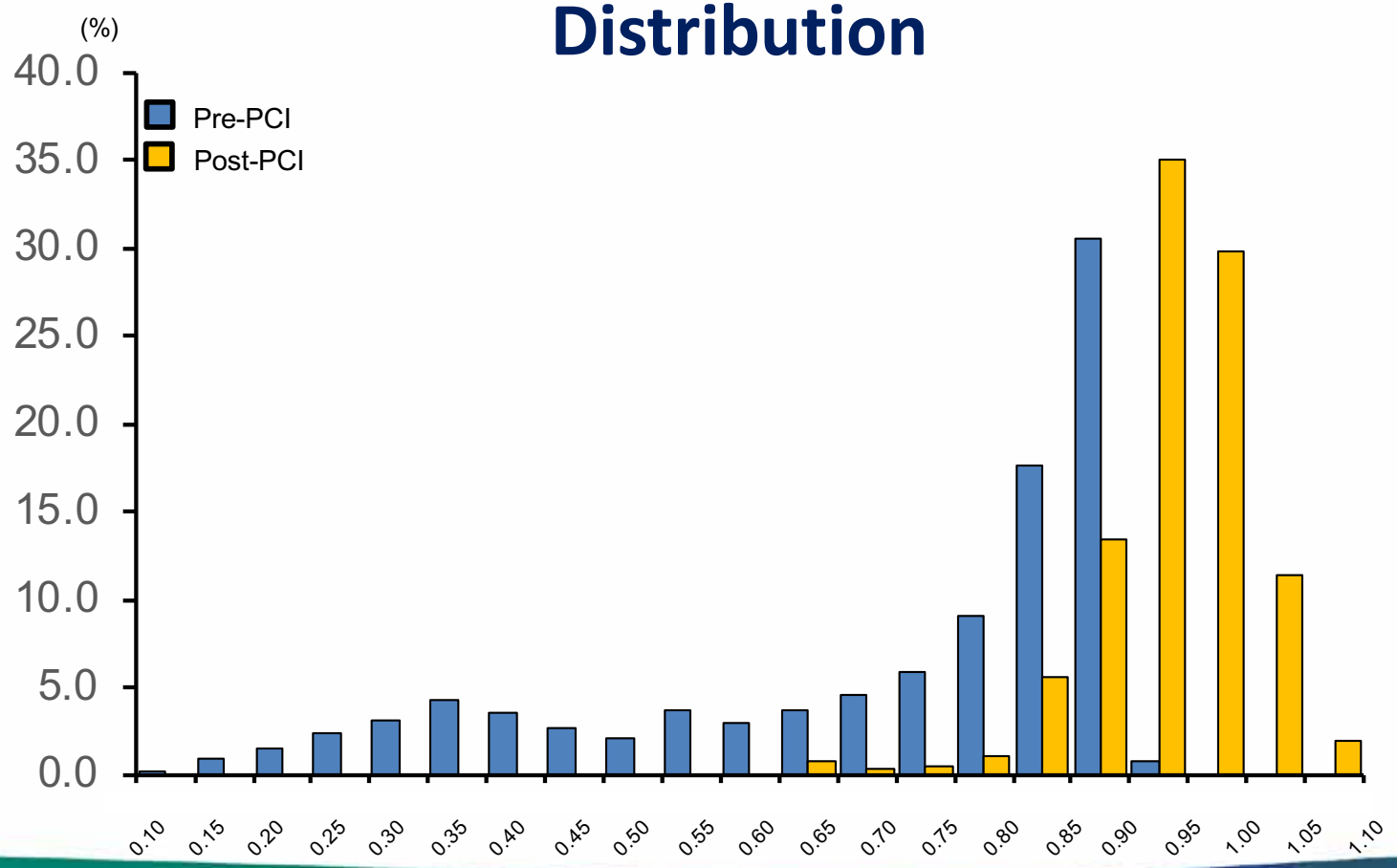
DEFINE PCI

Baseline Procedural Characteristics

	N = 562 Vessels
Left anterior descending artery	342 (60.9%)
Multivessel PCI performed (≥2 vessels)	60 (12.0%)
Bifurcation lesion	188/557 (33.8%)
Lesion length (mm)	23.6 ± 13.6
Pre-PCI diameter stenosis (%)	67.4 ± 11.1
Post-PCI diameter stenosis (%)	24.3 ± 15.0
Post-PCI residual stenosis ≥50%	39/560 (7.0%)
Total number of stents used	1.4 ± 0.8
Total stent length (mm)	32.9 ± 19.5
Maximum device size (mm)	3.3 ± 2.2
Maximum balloon pressure (atm)	17.8 ± 4.0
Post-dilatation performed	324/553 (58.6%)

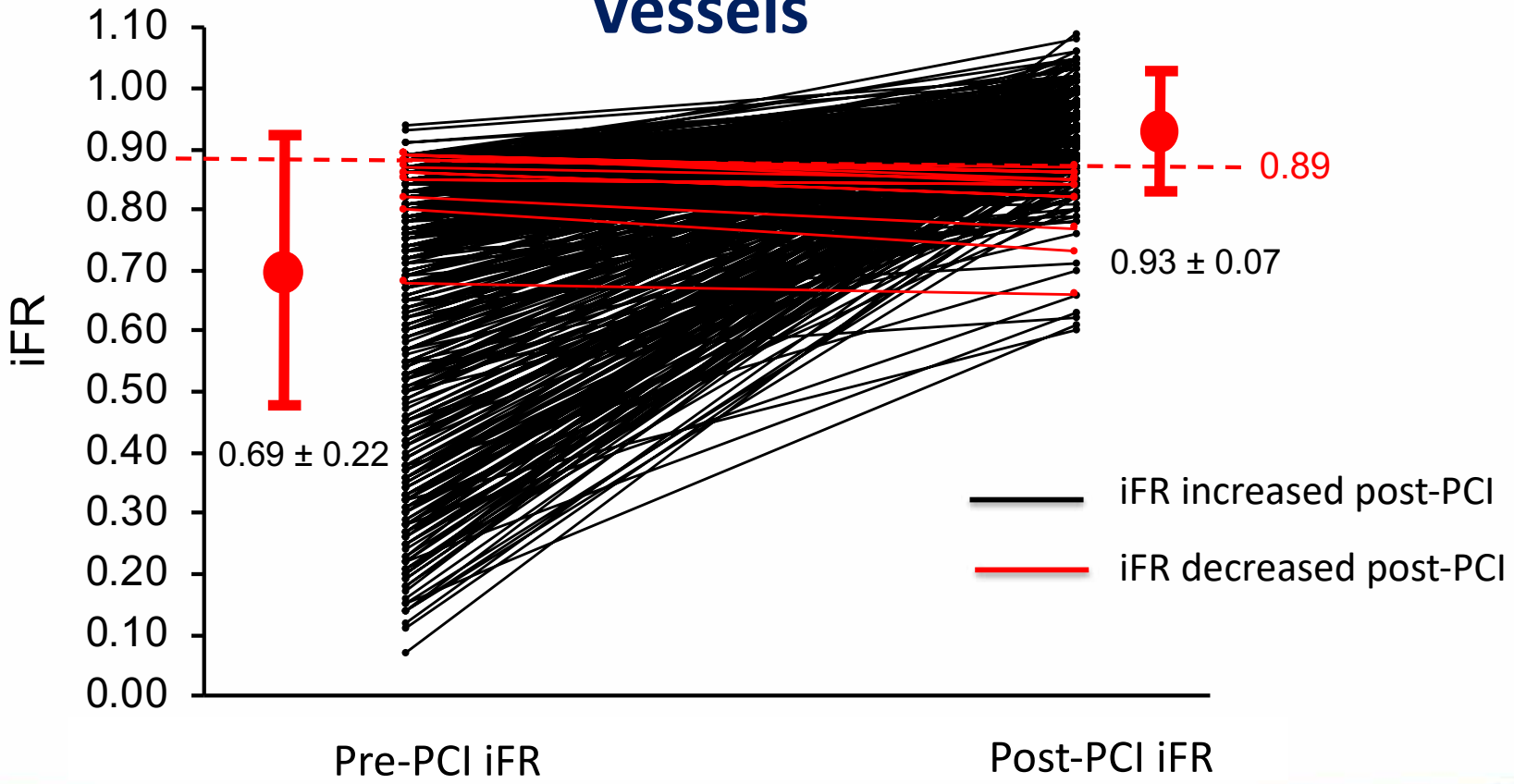
DEFINE PCI

Pre- and Post-Procedure iFR Frequency Distribution



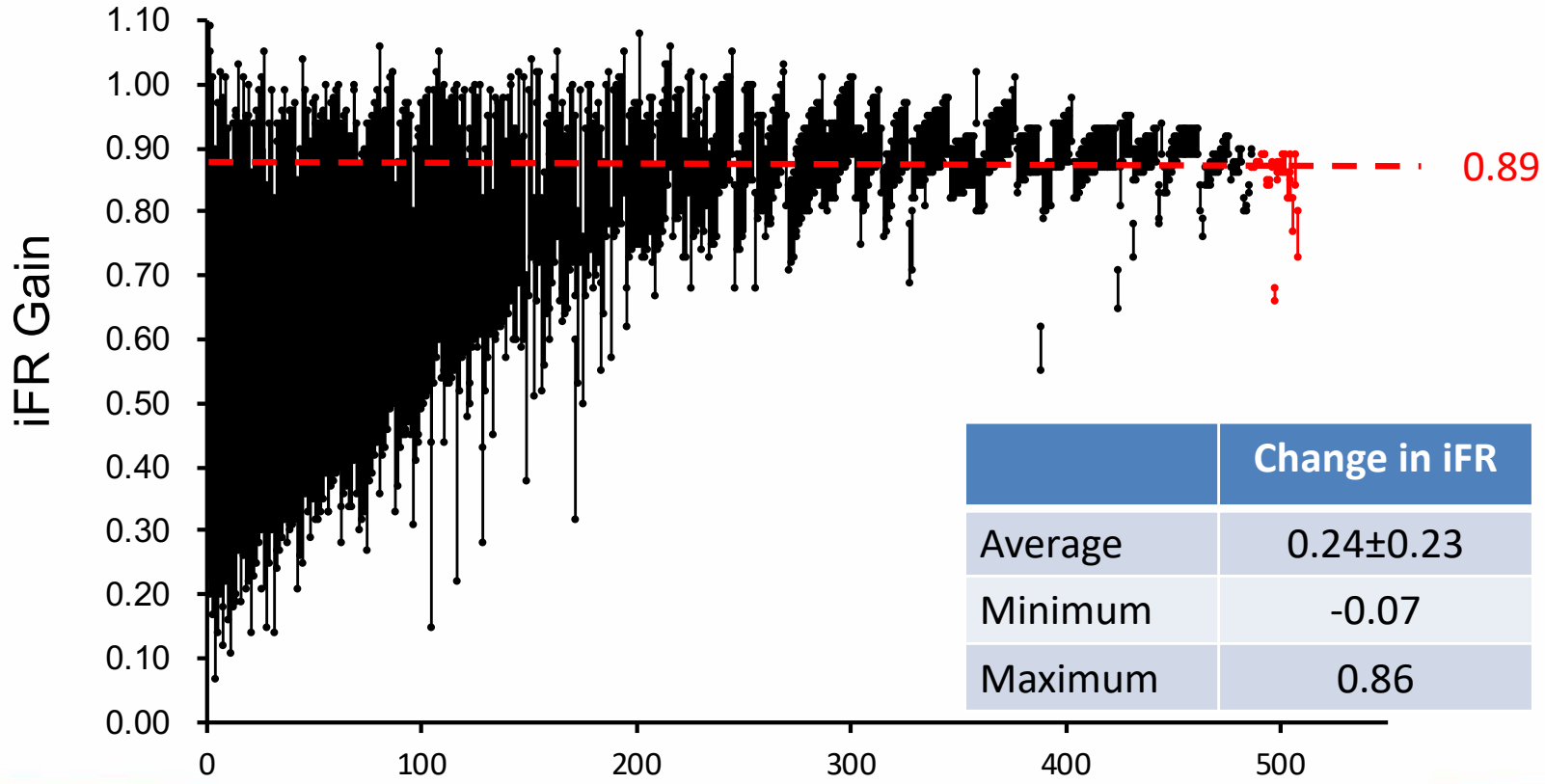
DEFINE PCI

Pre- and Post-PCI iFR in Individual Vessels



DEFINE PCI

iFR Gain in Individual Pts from Pre- to Post-PCI

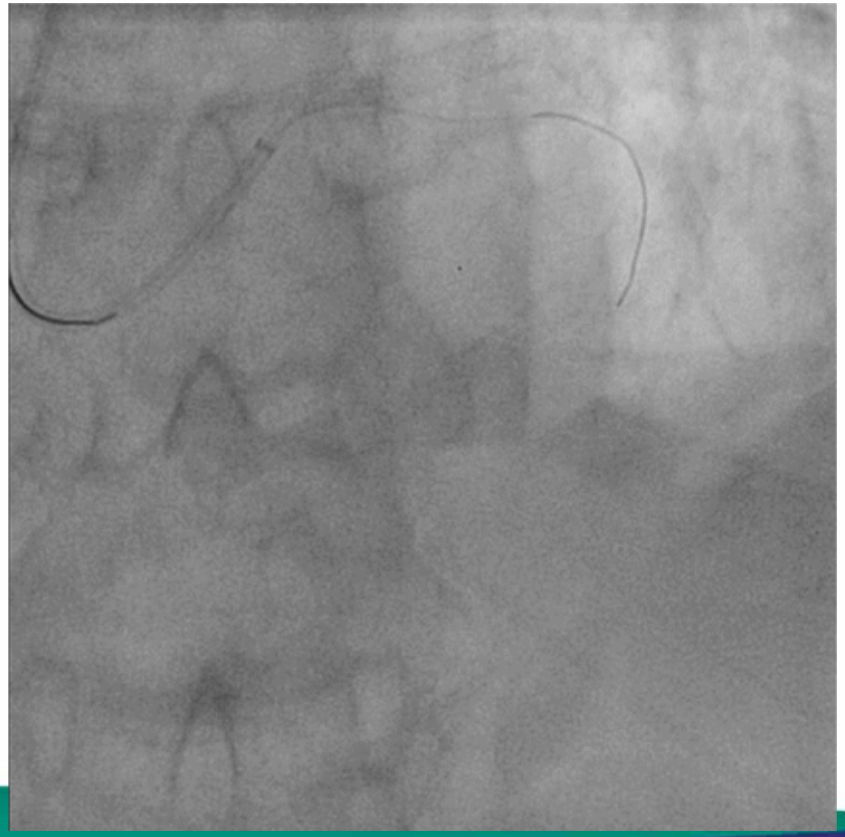


	Change in iFR
Average	0.24±0.23
Minimum	-0.07
Maximum	0.86

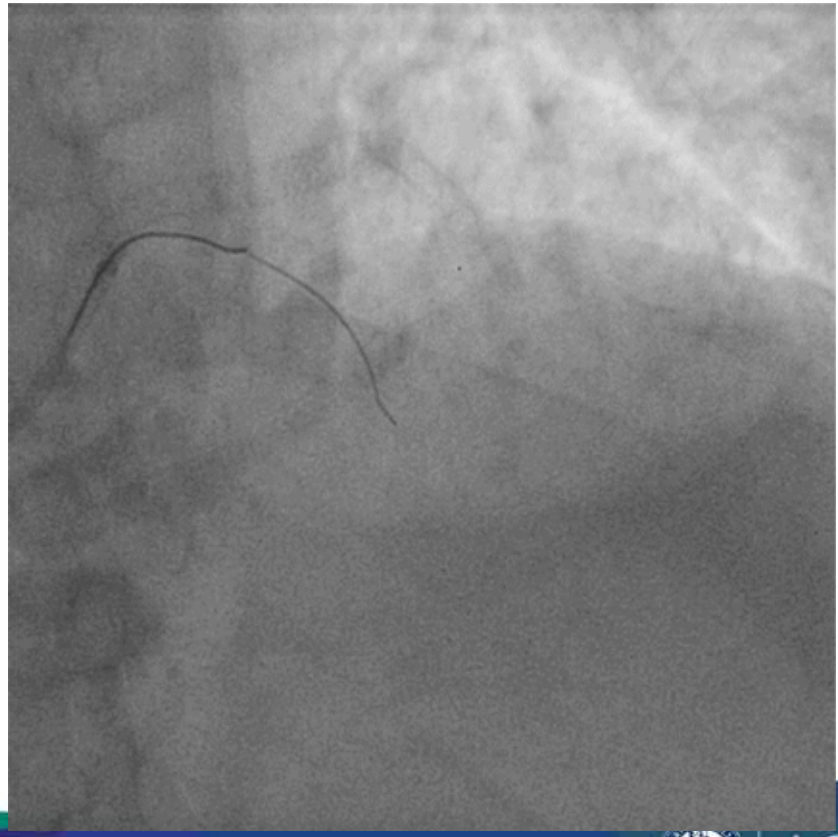
DEFINE PCI

Case Example – Severe LAD Stenosis

Pre Angiogram



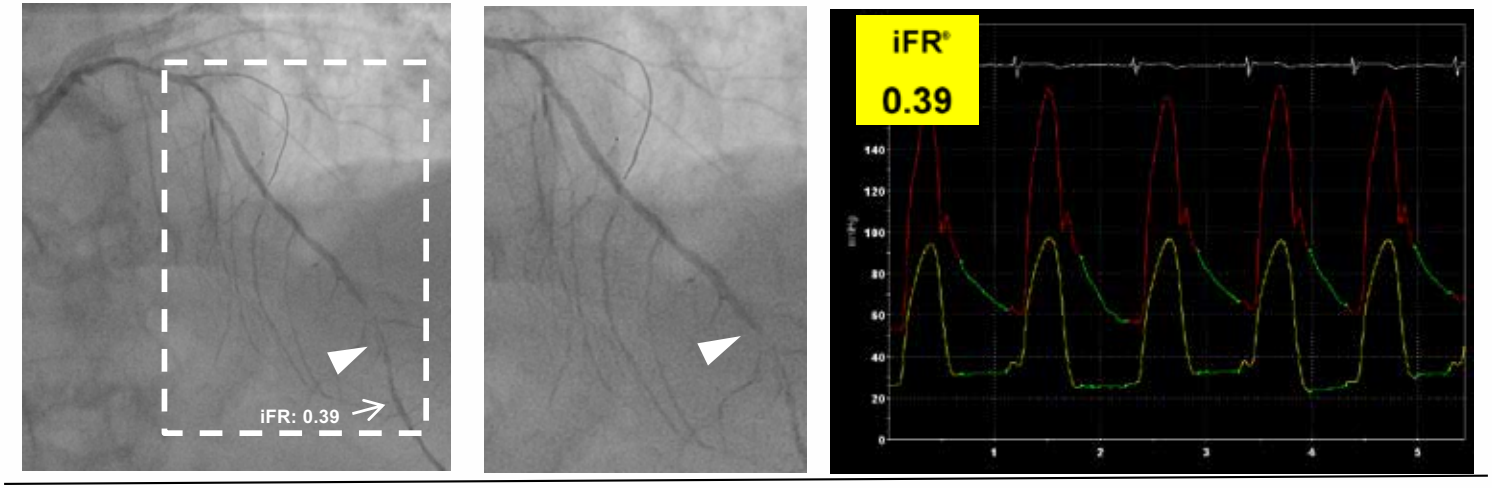
Final Angiogram



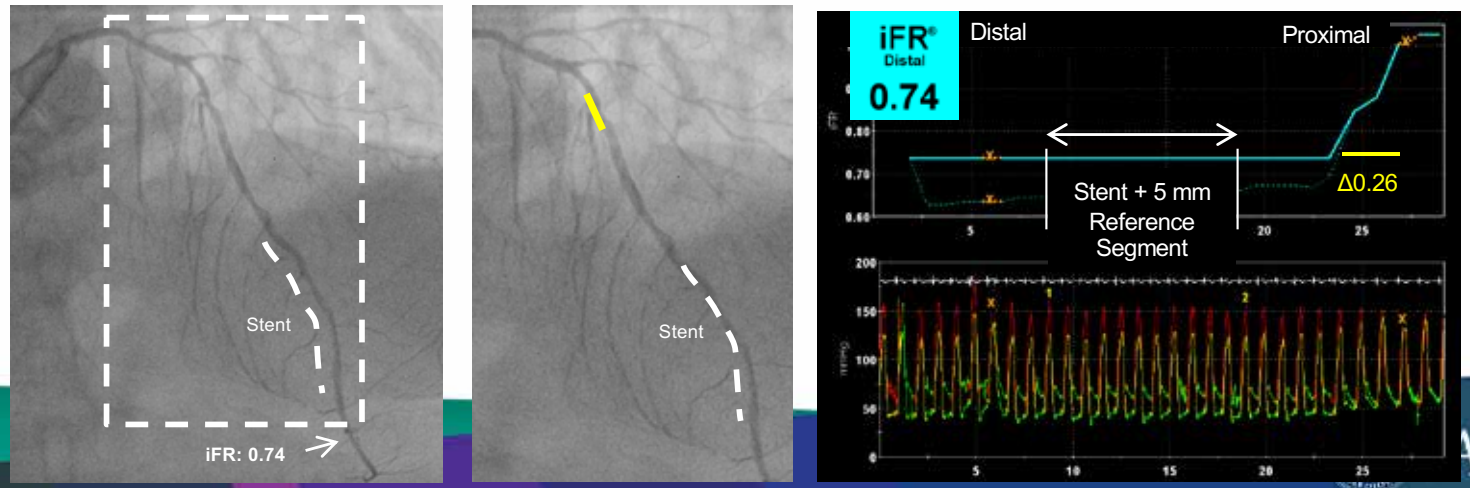
DEFINE PCI

Case Example – Severe LAD Stenosis

Pre-PCI



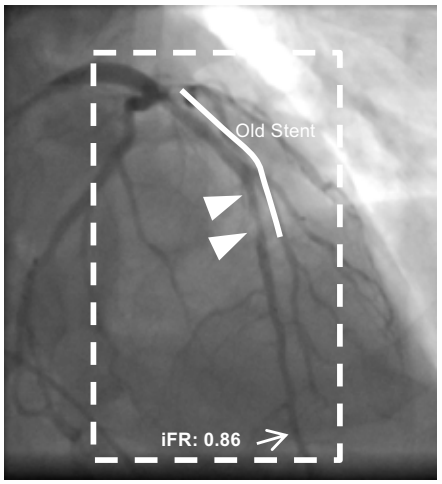
Post-PCI
(Blinded Physiology)

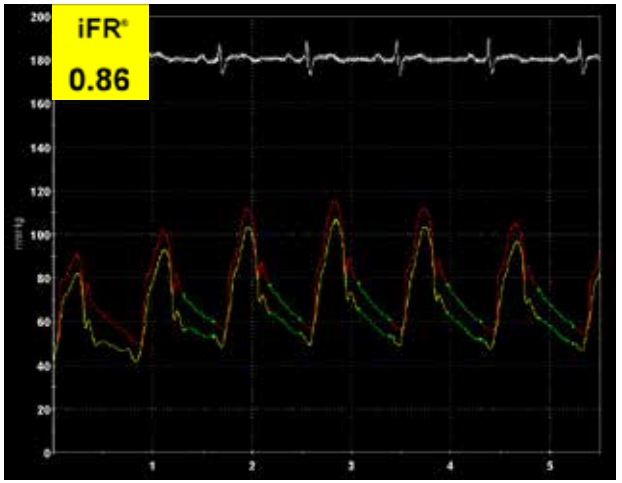


DEFINE PCI

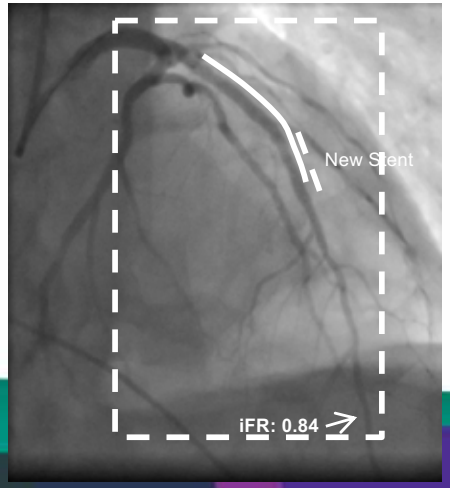
Case Example – Diffuse Disease

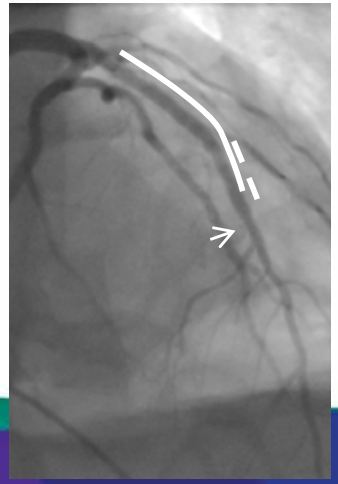
Pre-PCI

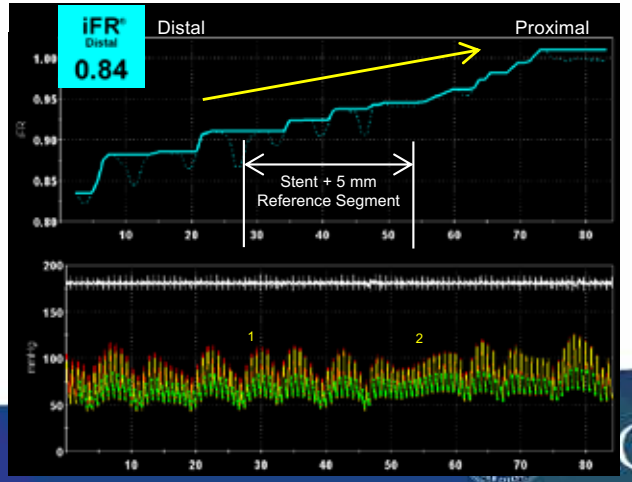




Post-PCI
(Blinded
Physiology)



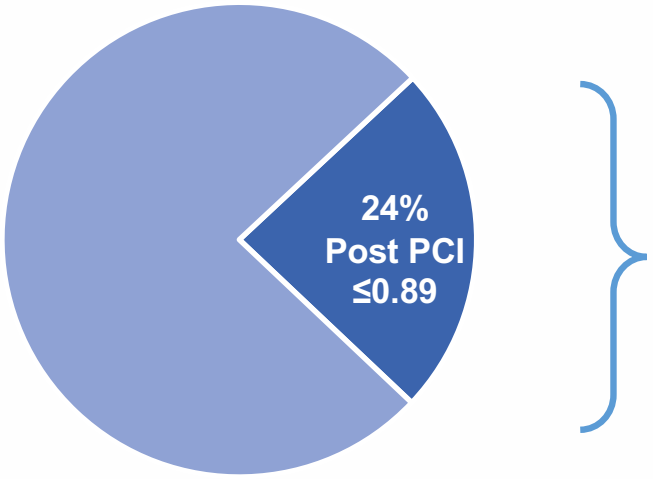




DEFINE PCI

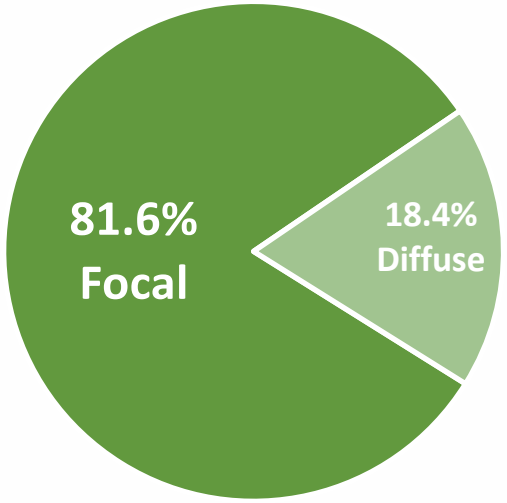
Primary Study Endpoint

480 Patients with Angiographically Successful PCI and qualified iFR pullbacks



■ Post iFR≤0.89 ■ Post iFR>0.89

24% Residual Ischemia (112 patients with Post PCI iFR≤0.89)

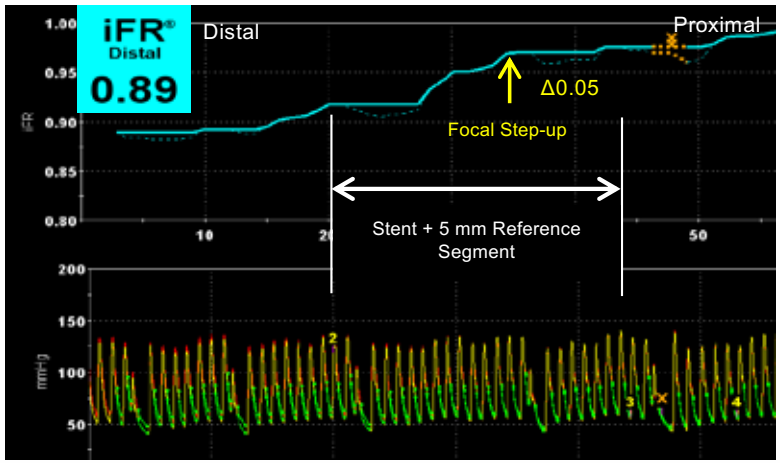


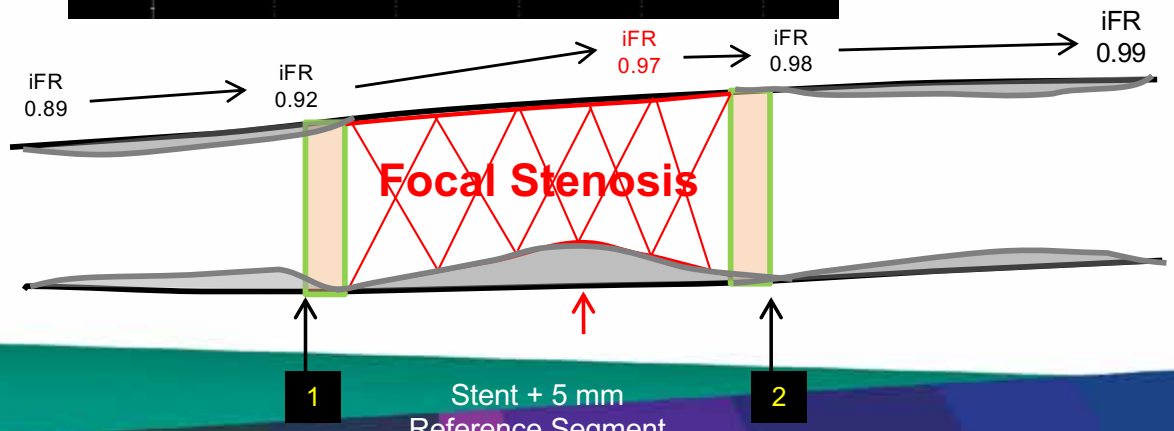
Focal defined as step-up of ≥0.03 units in < 15 mm segment
Diffuse defined as > 15 mm segment

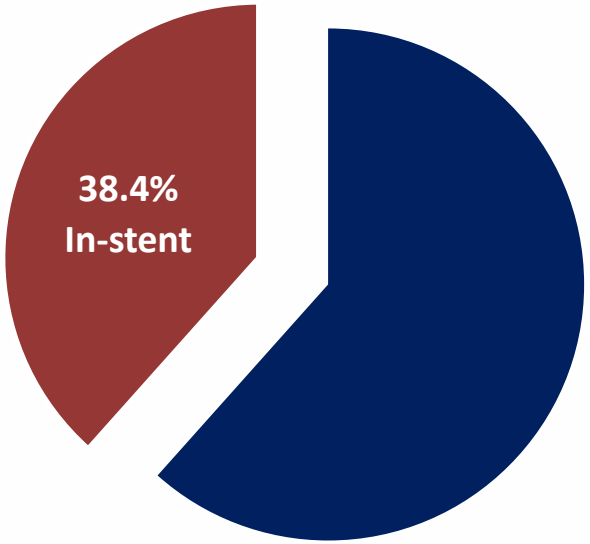
DEFINE PCI

Focal Residual Pressure Gradient in-stent

Among the 93 vessels with focal disease, there were 146 segments (stent, proximal or distal) that had significant residual pressure gradients







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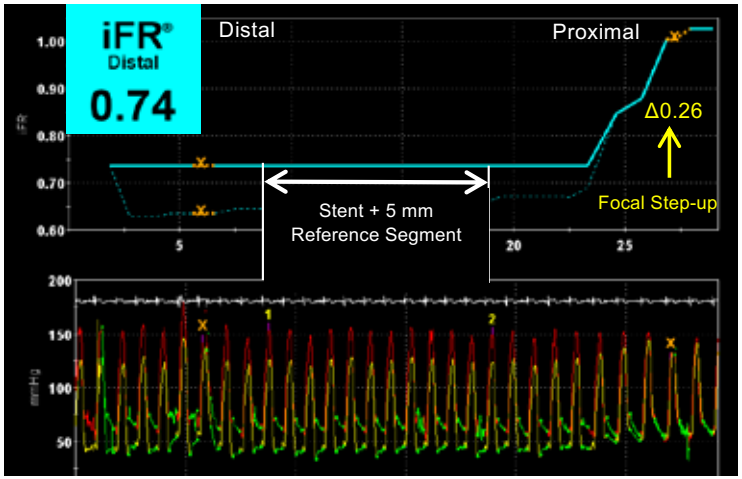
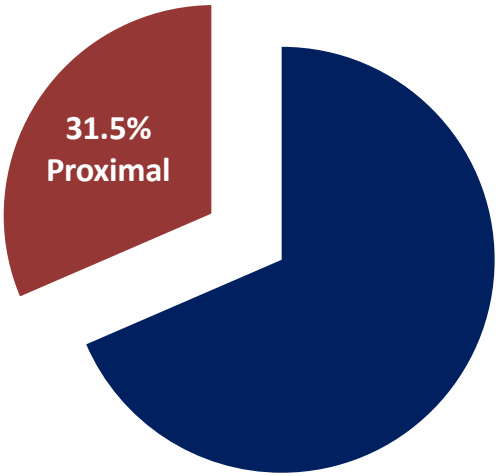
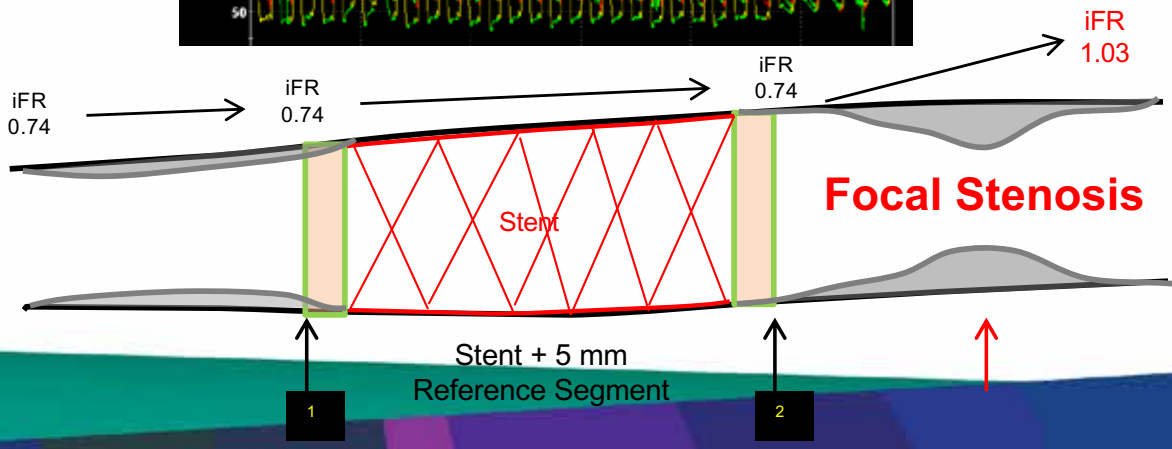
Focal Residual Pressure Gradient Prox to stent

‘Physiologic miss’ occurred in 31.5% of focal lesions proximally







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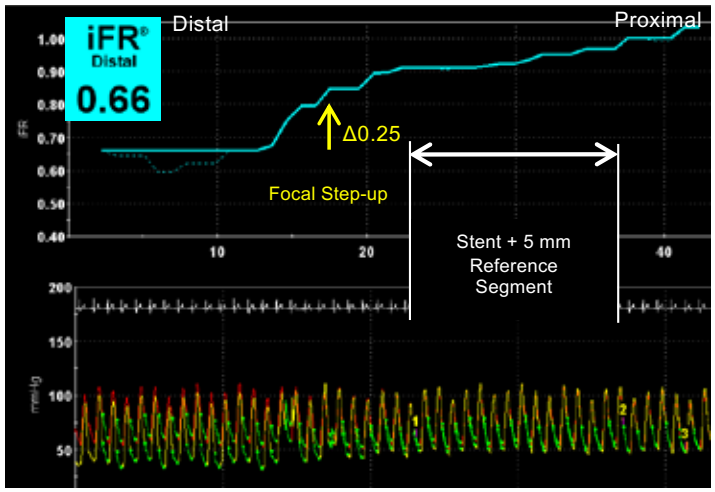
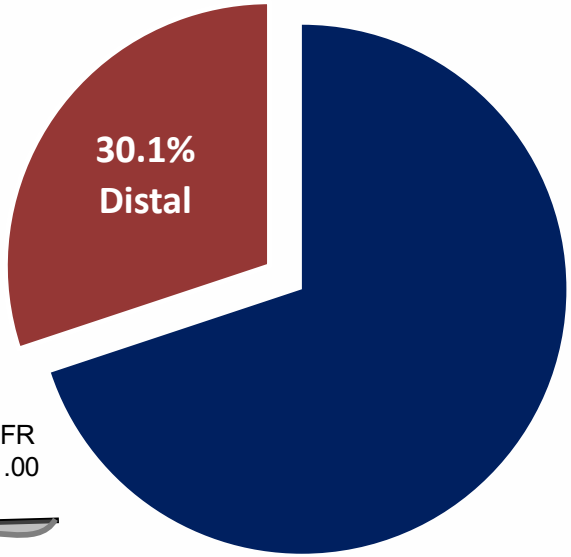
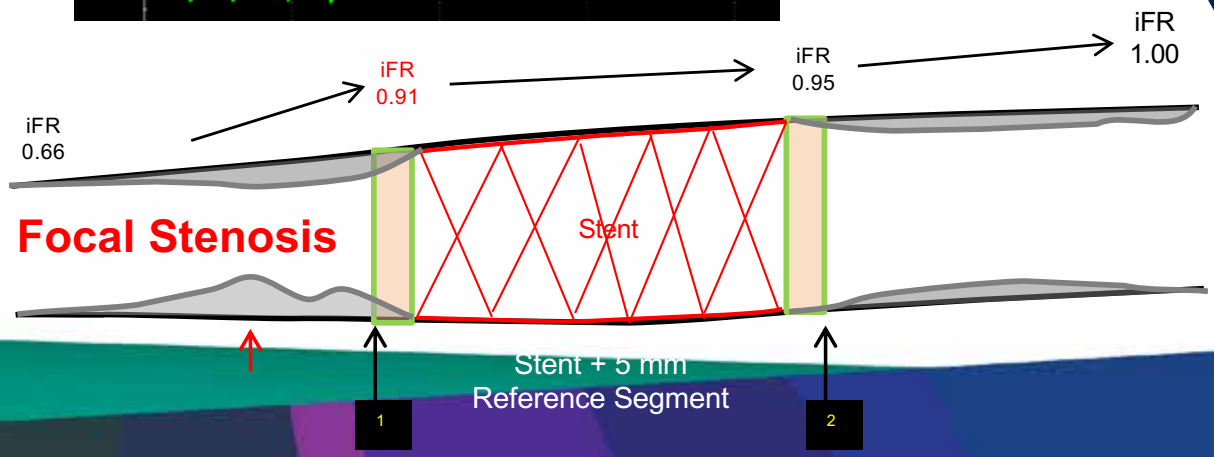
DEFINE PCI

Focal Residual Pressure Gradient Distal to stent

'Physiologic miss' occurred in 30.1% of focal lesions distally







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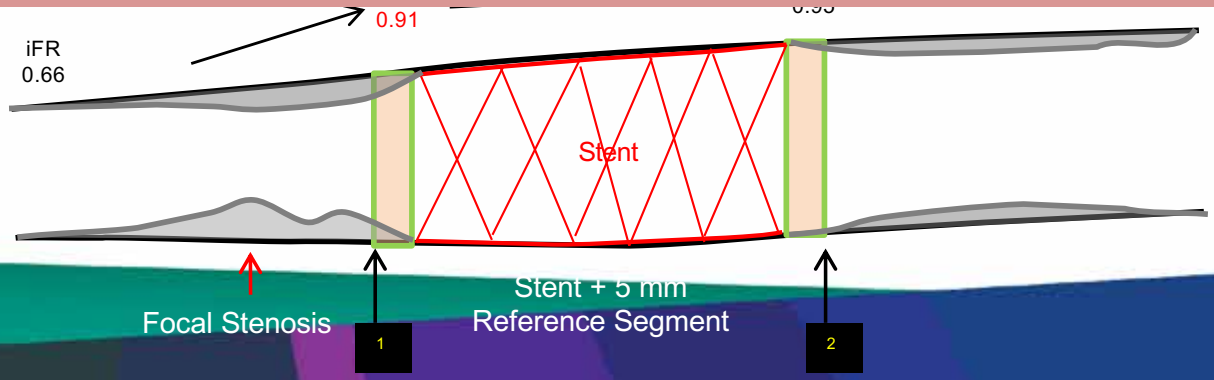
DEFINE PCI

Focal Residual Pressure Gradient Distal to stent

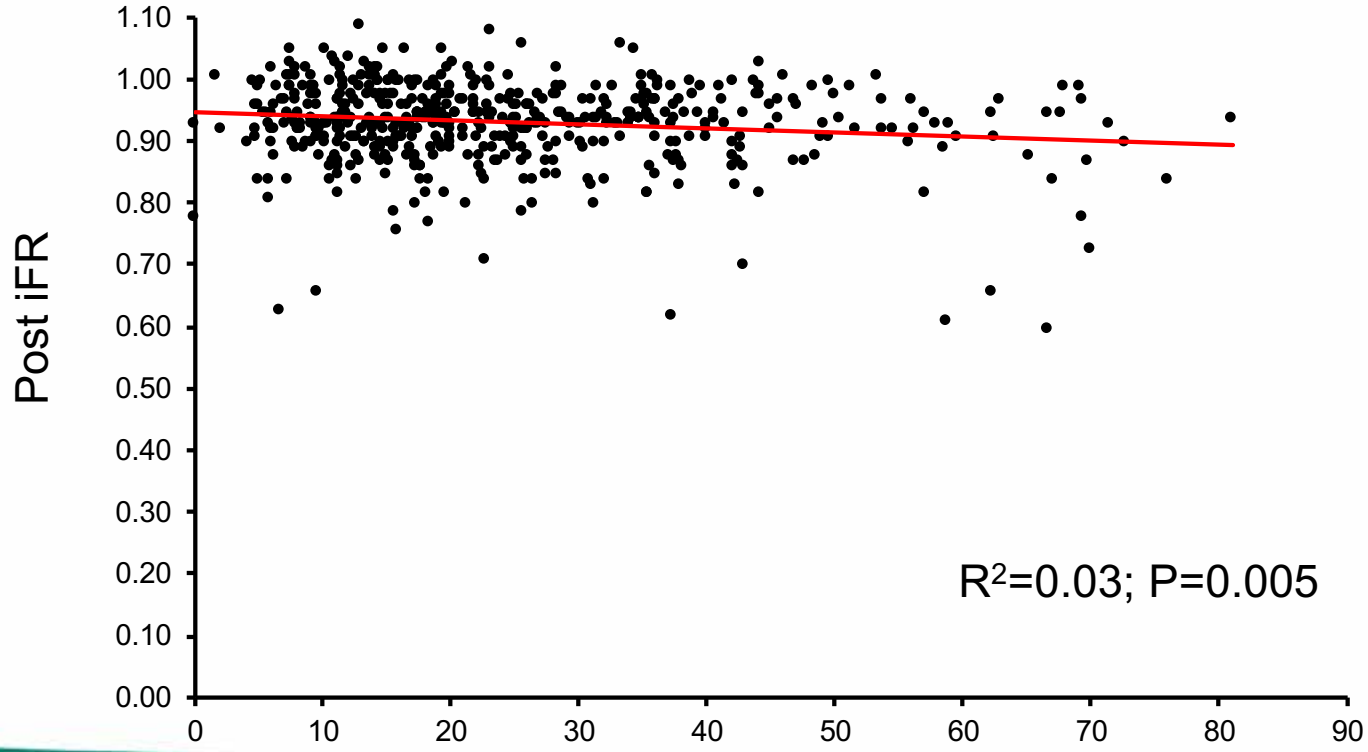
'Physiologic miss' occurred in 30.1% of focal lesions distally

If all residual focal lesions could be treated with additional PCI, the rate of significant ischemia could be theoretically reduced from 24% to 5%



DEFINE PCI

Angiographic diameter stenosis correlates poorly with post PCI iFR



DEFINE PCI

Angiographic diameter stenosis correlates poorly with post PCI iFR

	Residual DS ≥50%	Residual DS <50%	P-Value
iFR ≤0.89	29.7%	21.4%	0.24

Predictors of post-PCI iFR≤0.89 by multi-variate analysis

	OR	95% CI	P-value
Reference Vessel Diameter	0.32	0.18-0.58	0.0002
LAD	5.65	3.07-10.40	<0.0001
Post-PCI DS	1.01	1.00-1.03	0.08

DEFINE PCI

Compared with prior post PCI Physiology studies, DEFINE PCI…

1. iFR used instead of hyperemic physiology
2. Systematic blinded physiology assessment after operator-determined successful PCI
3. Core laboratory assessment of all physiology tracings and angiography images
4. Differentiate focal lesions from diffuse disease
5. Correlate coronary angiography by QCA to vessel physiology
6. Establish the relationship between post-PCI iFR and objective assessment of MACE, recurrent ischemia and quality of life in a blinded fashion

DEFINE PCI

Limitations

1. Whether an iFR pullback pre-PCI would reduce the rate of residual ischemia is unknown
2. Intravascular imaging was not routinely performed, and thus the specific stent-related and untreated lesion-related characteristics that contributed to the decrement in pressure gradient are unknown
3. Given the specific enrollment criteria, the actual proportion of “real-world” cases in which post-PCI physiology could be further optimized with additional PCI remains speculative

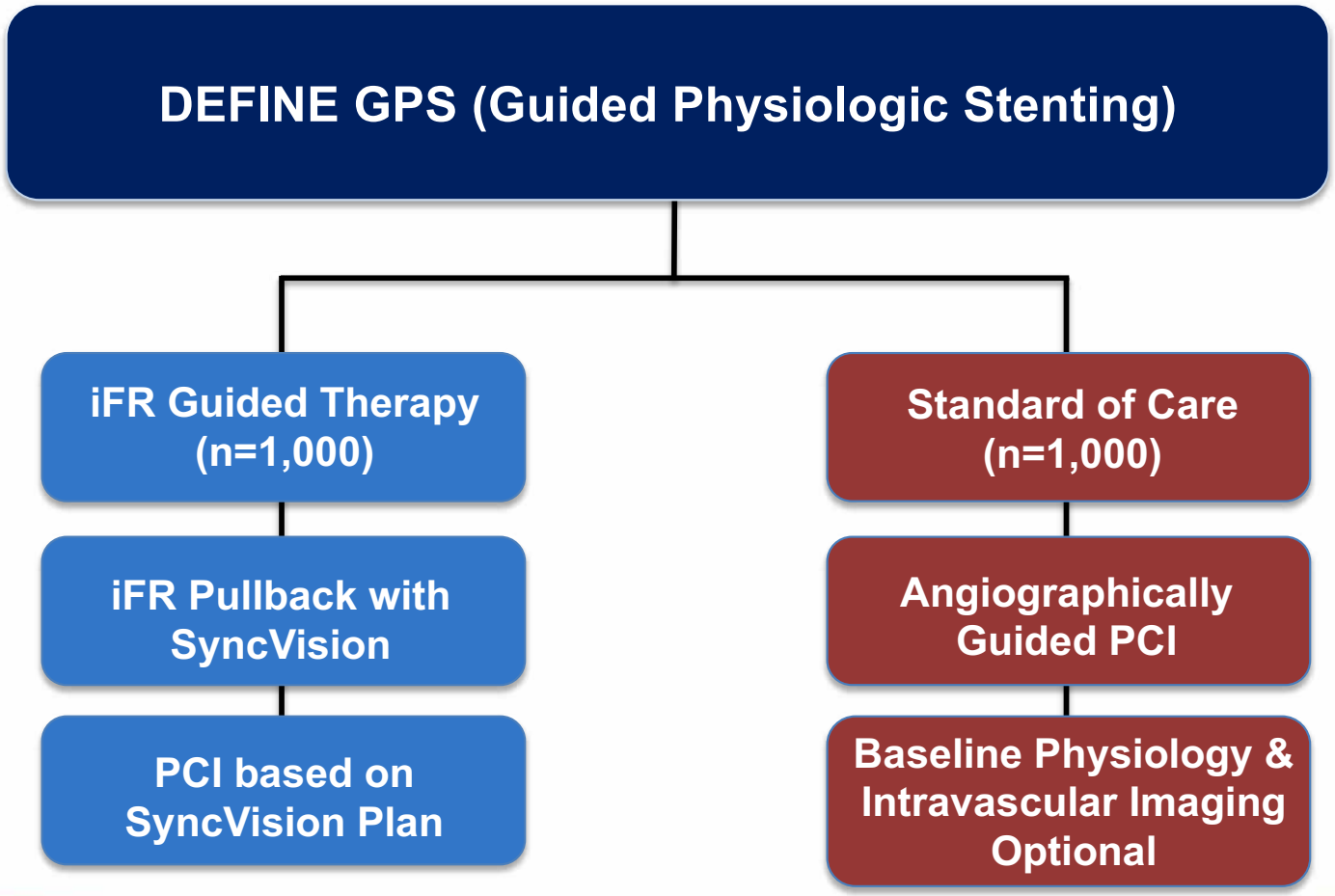
DEFINE PCI

Conclusions

1. Significant epicardial residual ischemia after angiographically successful PCI is not uncommon, occurring in nearly 25% of patients in the present study

2. Post-PCI angiography poorly correlated with physiologic measures

3. In a large majority of cases residual pressure gradients were focal and thus potentially amenable to treatment with additional PCI


DEFINE GPS (Guided Physiologic Stenting)
iFR Guided Therapy (n=1,000)
iFR Pullback with SyncVision
PCI based on SyncVision Plan
Standard of Care (n=1,000)
Angiographically Guided PCI
Baseline Physiology & Intravascular Imaging Optional