Long-term Outcomes after Treatment of Diffuse In-Stent Restenosis with Rotational Atherectomy Followed by Radiation Therapy with a ^{188}Re-MAG$_3$-Filled Balloon *(R4 trial)*

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R4 trial

*R*adiation with ^{188}*R*e-MAG_3-filled balloon after *R*otablation for diffuse in-stent *R*estenosis

Purpose

To evaluate the efficacy and long-term clinical outcomes of R4 trial

R4 trial

Inclusion Criteria

- Diffuse In-stent Restenosis
  (>10 mm in length)
- Total occlusion

R4 trial

Exclusion Criteria

- LV EF < 30%
- AMI within 72 hours
- Coronary artery spasm
- Creatinine > 3.0 mg/dL
- Concomitant serious disease:
  expected survival < 2 years
- Pregnant woman

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Subject

From March 1999 to February 2000

50 patients (M/F: 42/8, 56 years)

Diffuse ISR

(mean lesion length 25.6±12.7 mm)

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Method

- ^{188}Re-MAG_3-filled balloon after

  Rotational atherectomy with adjunctive balloon angioplasty
- Fractionation allowed if needed
- Single lesion for brachytherapy in patients with multivessel disease
- Long balloon preferred
- Overlapping permitted

R4 trial

How Much to Prescribe?

AMC: ^{188}Re	**15 Gy @ 1 mm depth from balloon / artery interface**
ARREST: ^{192}Ir	12 Gy @ 2mm
ARTISTIC: ^{192}Ir	12-18 Gy @ 2mm for ISR
BERT: ^{90}Sr	12/ 14/ 16 Gy @ 2mm
Beta-WRIST:	20.6 Gy @ 1.2mm for ISR
CURE: ^{188}Re	20 Gy @ balloon surface
START: ^{90}Sr	19-20 Gy @ 2mm for ISR
Perth: ^{188}Re	30 Gy @ 0.5mm for ISR

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Antithrombotic Therapy

- Aspirin 200 mg qd indefinitely
- Ticlopidine 250 mg bid for 1 month
- Cilostazol 100 mg bid > 6 months

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Follow-Up

- Angiographic follow-up at 6 months, and 2 years after brachytherapy

  QCA Analysis

- Clinical follow-up over 30 months:

  MACE and other significant events

R4 trial

Clinical Characteristics (n=50)

Clinical diagnosis (%)	
Unstable angina	33 (66)
Stable angina	17 (34)
Involved artery (%)	
Left Main	1 (2)
LAD	34 (68)
LCX	5 (10)
RCA	10 (20)
LV ejection fraction (%)	60 ± 7

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Lesion Morphology

Mean Lesion Length		25.6 ± 12.7 mm
Length	> 10, ≤ 20 mm	21 (42%)
	> 20, ≤ 30 mm	13 (26%)
	> 30 mm	16 (32%)
*Total occlusion		10 (20%)

R4 trial

Rotablation Procedure

Mean Rotablator burr size	2.06 ± 0.21 mm

Burr Size	1.75mm	8 (16)
	2.0mm	22 (44)
	2.15mm	4 (8)
	2.25mm	10 (20)
	2.38mm	6 (12)

Burr/Artery Ratio	0.7 ± 0.1
Frequency	4.2 ± 1.5

R4 trial

Radiation Coverage

Mean Lesion Length	25.6 ± 12.7 mm
Mean RT Balloon Length	37.6 ± 11.2 mm

Radiation Length	20mm	3 (6)
	30mm	19 (38)
	40mm	21 (42)
	30mm × 2	7 (14)
Overlapping Balloon		7 (14)
Radiation duration		*202 ± 62 sec*
Pressure		*Nominal (6 atm)*

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Procedure-related Data

Reference artery size (mm)	2.89 ± 0.40
MLD (mm)	
Preprocedural	0.60 ± 0.44
Postprocedural	2.68 ± 0.39
Diameter stenosis (%)	
Baseline	79.8 ± 14.1
Final	6.53 ± 12.2
Balloon/Artery Ratio	1.23 ± 0.21
Acute gain, mm	2.08 ± 0.46

R4 trial

Immediate Results

- *Success rate: 100 %*
- *No major procedure related complications*
- *No episode of isotope leakage*

R4 trial

6-month angiographic FU

6-mo angiographic FU rate	50/50 (100%)
F/U MLD (mm)	2.08 ± 0.46
Late Loss (mm)	0.37 ± 0.65
Loss Index	0.17 ± 0.31
Restenosis rate (%)	5/50 (10%)
In-stent	2
Edge	3

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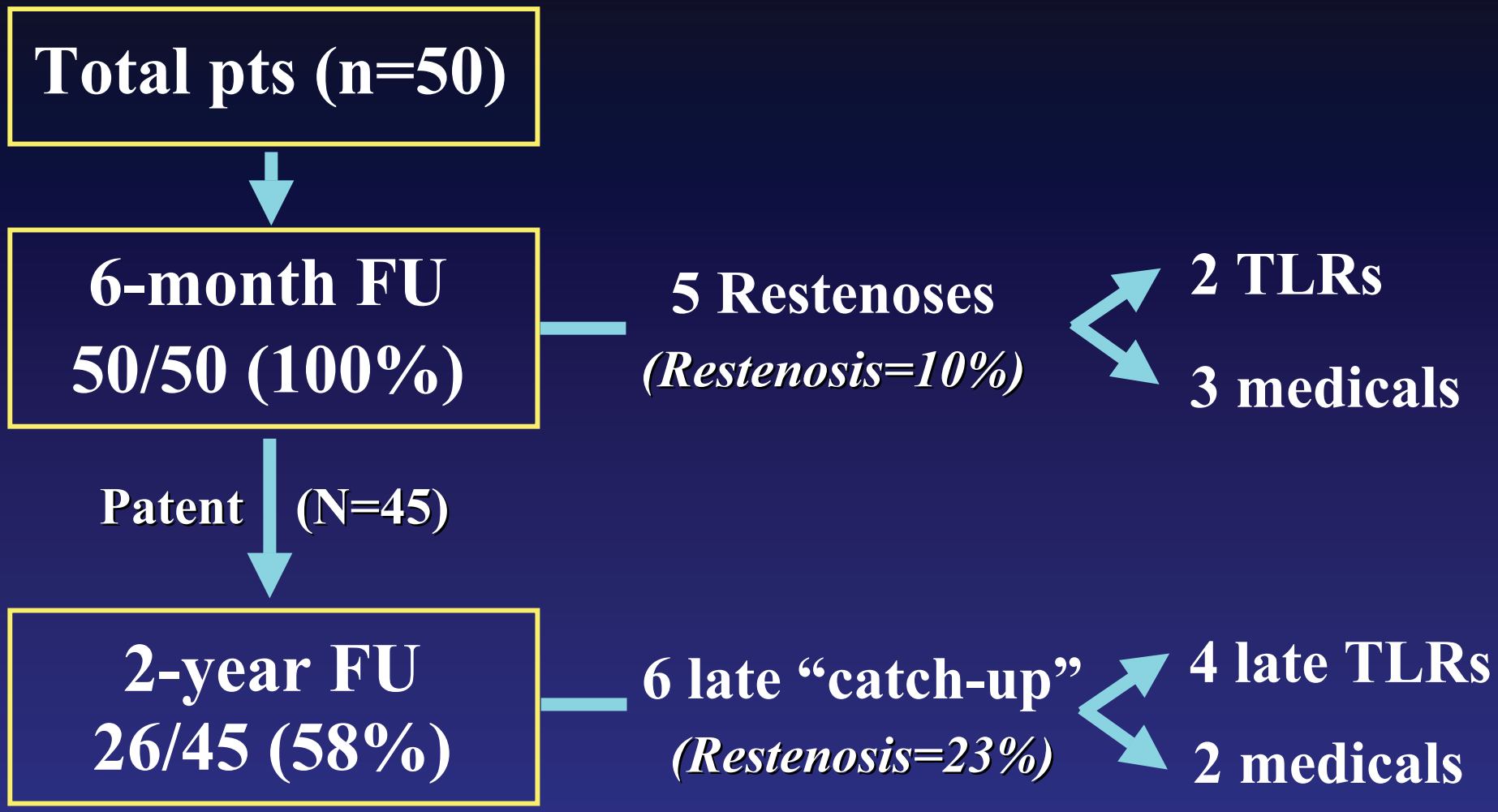
6-month & 2-year angiographic FU



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2-year angiographic Restenosis & TLR Pattern

- *Focal 2*

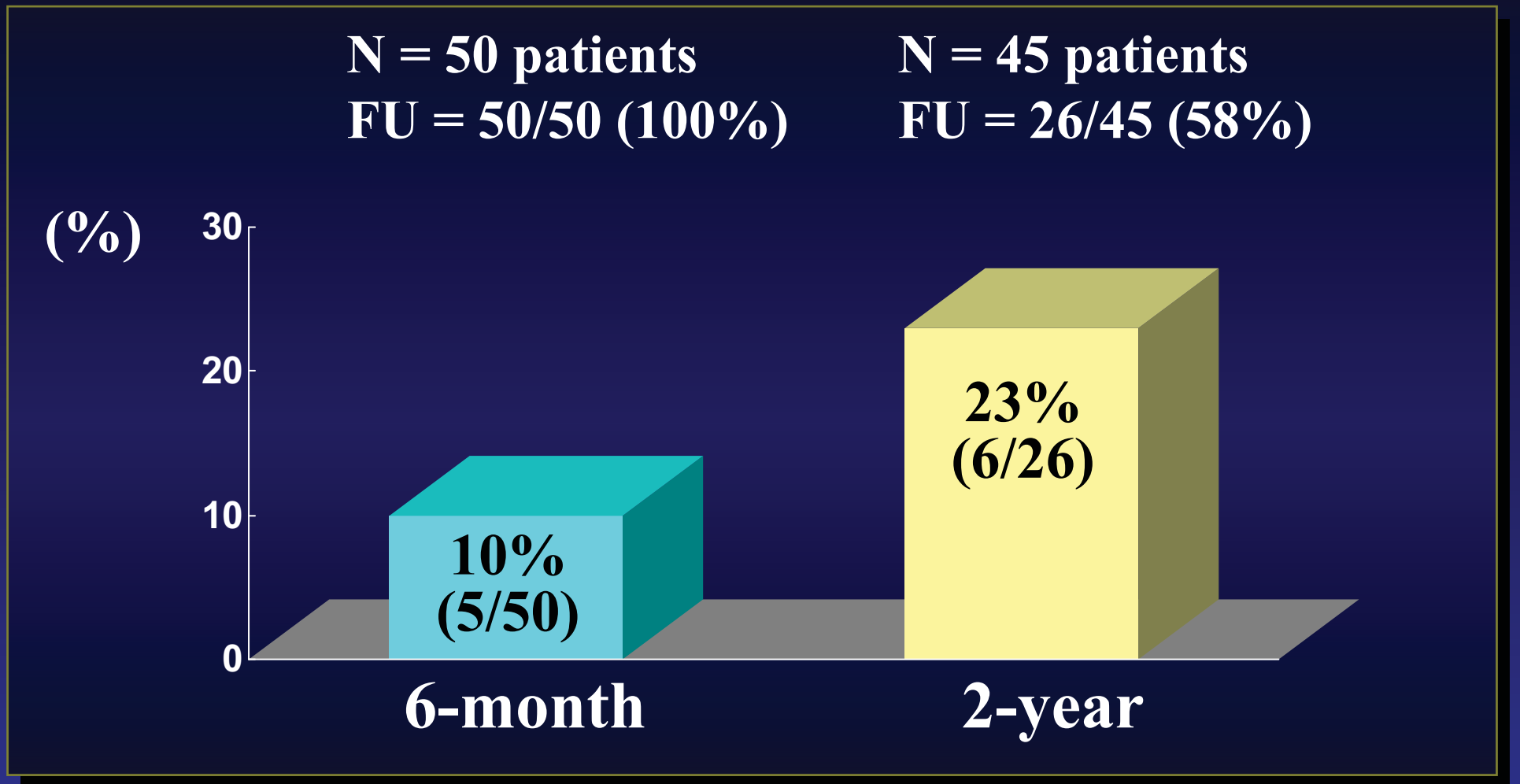
Intrastent	1	→	1	Cutting balloon
Edge	1	→	1	Medical

- *Diffuse 4*

Intra-stent	1	→	1	Medical
Total occlusion	3	→	2	Cutting balloons
		→	1	CABG

R4 trial

6-month & 2-year angiographic Restenosis Rate



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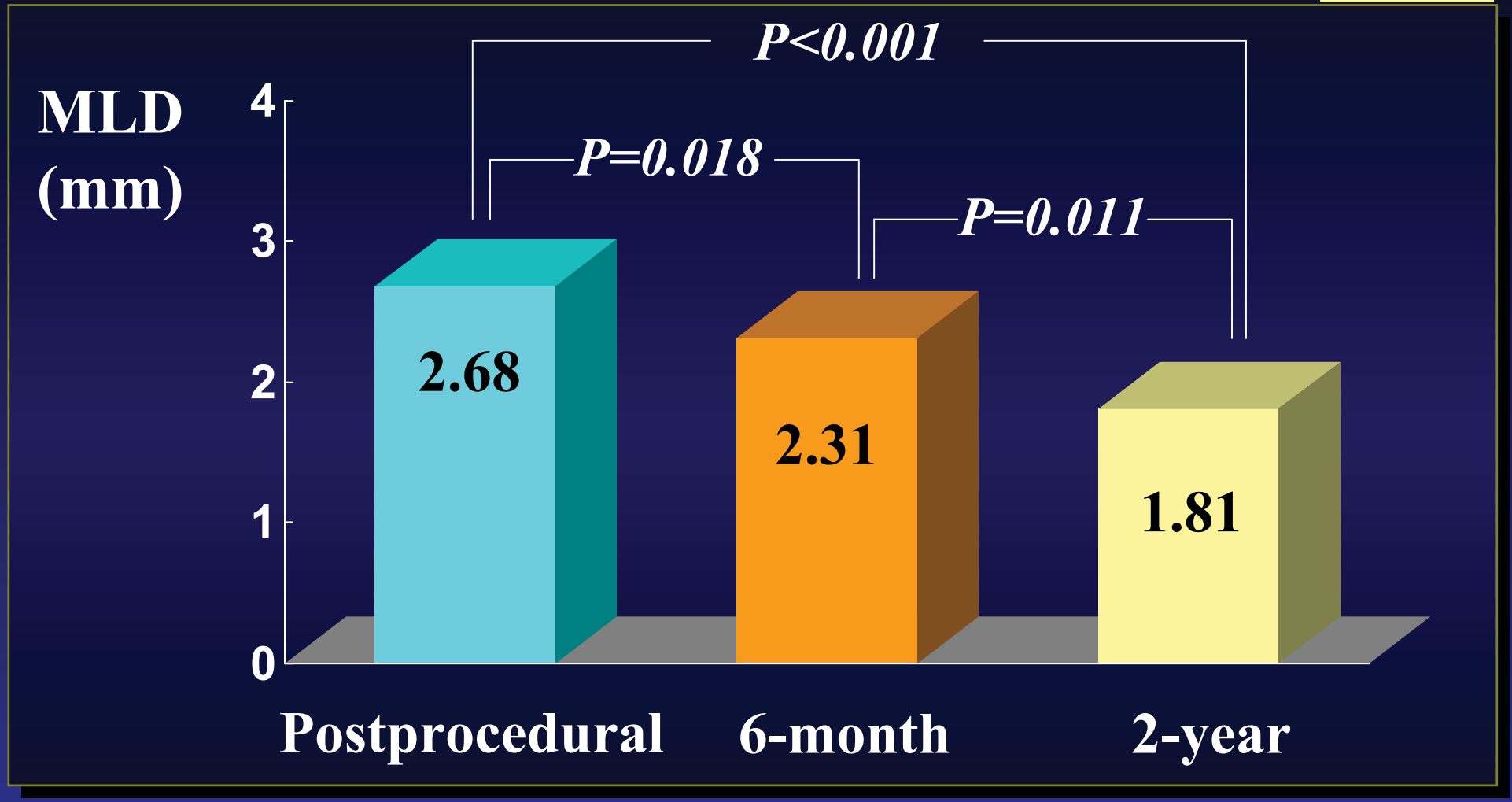
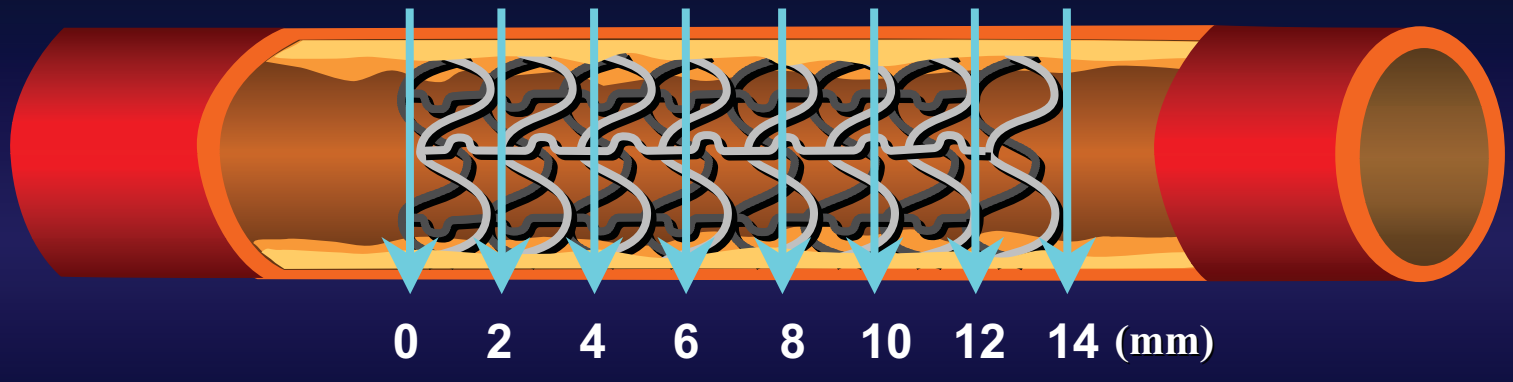
6-month & 2-year angiographic MLD

N=26



Postprocedural, 6-Month, & 2-Year
Quantitative IVUS Measurement



In-stent segment with 2 mm interval

→ **Average stent CSA (mm^2)**

Average lumen CSA (mm^2)

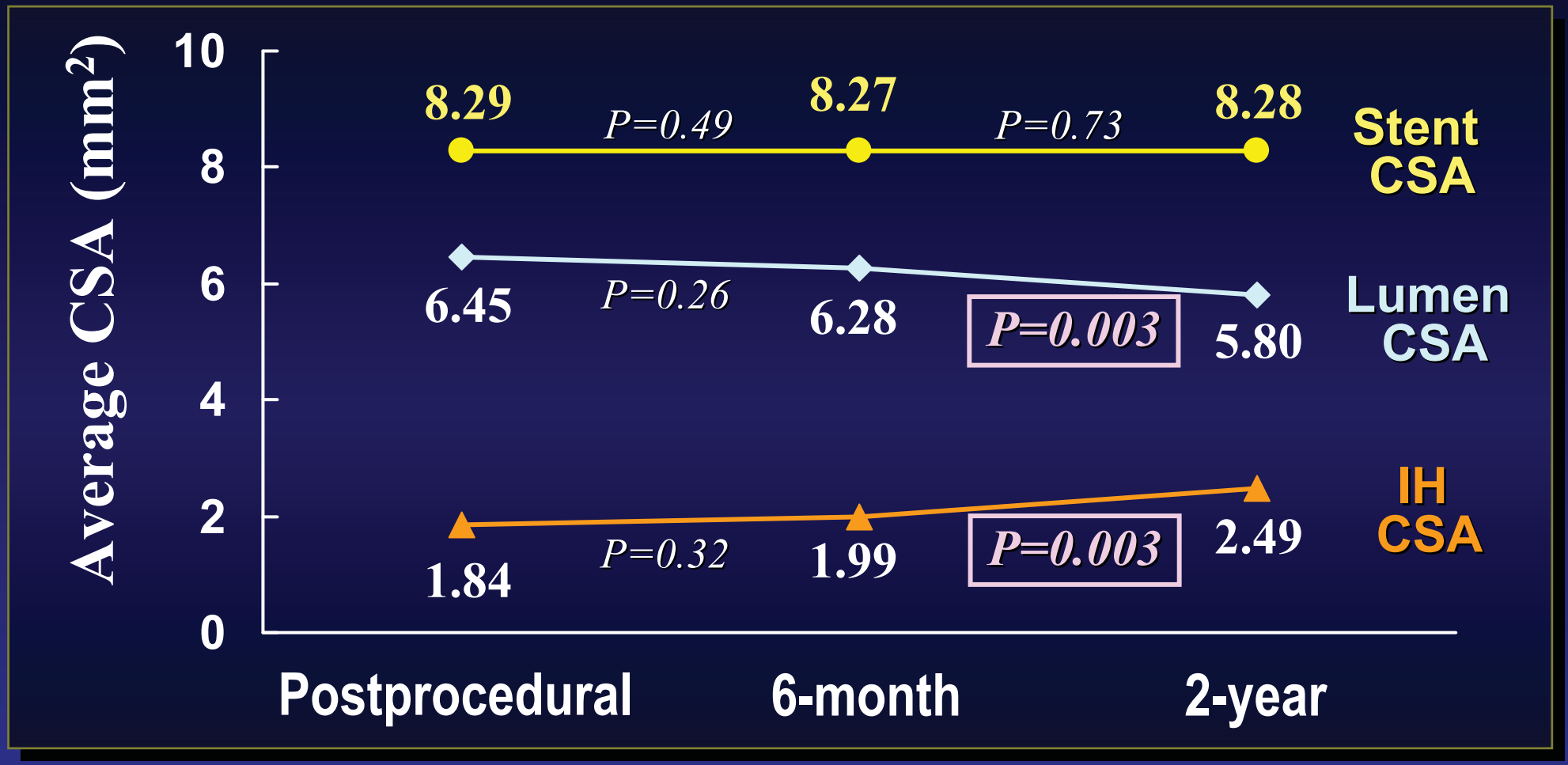
Average intimal hyperplasia CSA (mm^2)

Of 26 patients, 21 available data were analyzed.

R4 trial

6-month & 2-year IVUS Data

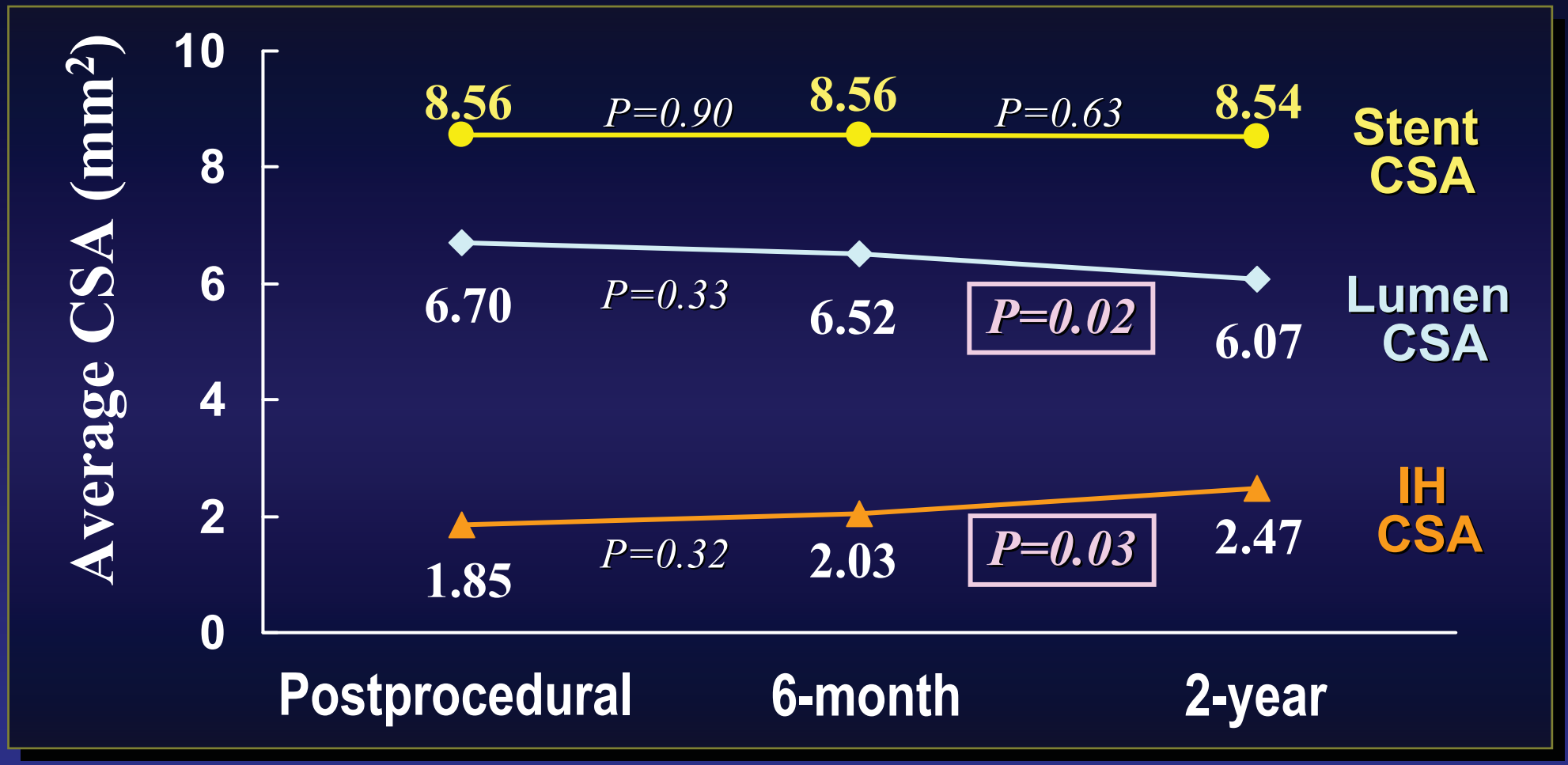
Including 4 patients with late "catch-up" phenomena (N=21)



R4 trial

6-month & 2-year IVUS Data

In patients with patent 6-month & 2-year angiogram (N=17)



Postprocedural, 6-Month, & 2-Year *Quantitative IVUS Measurement*

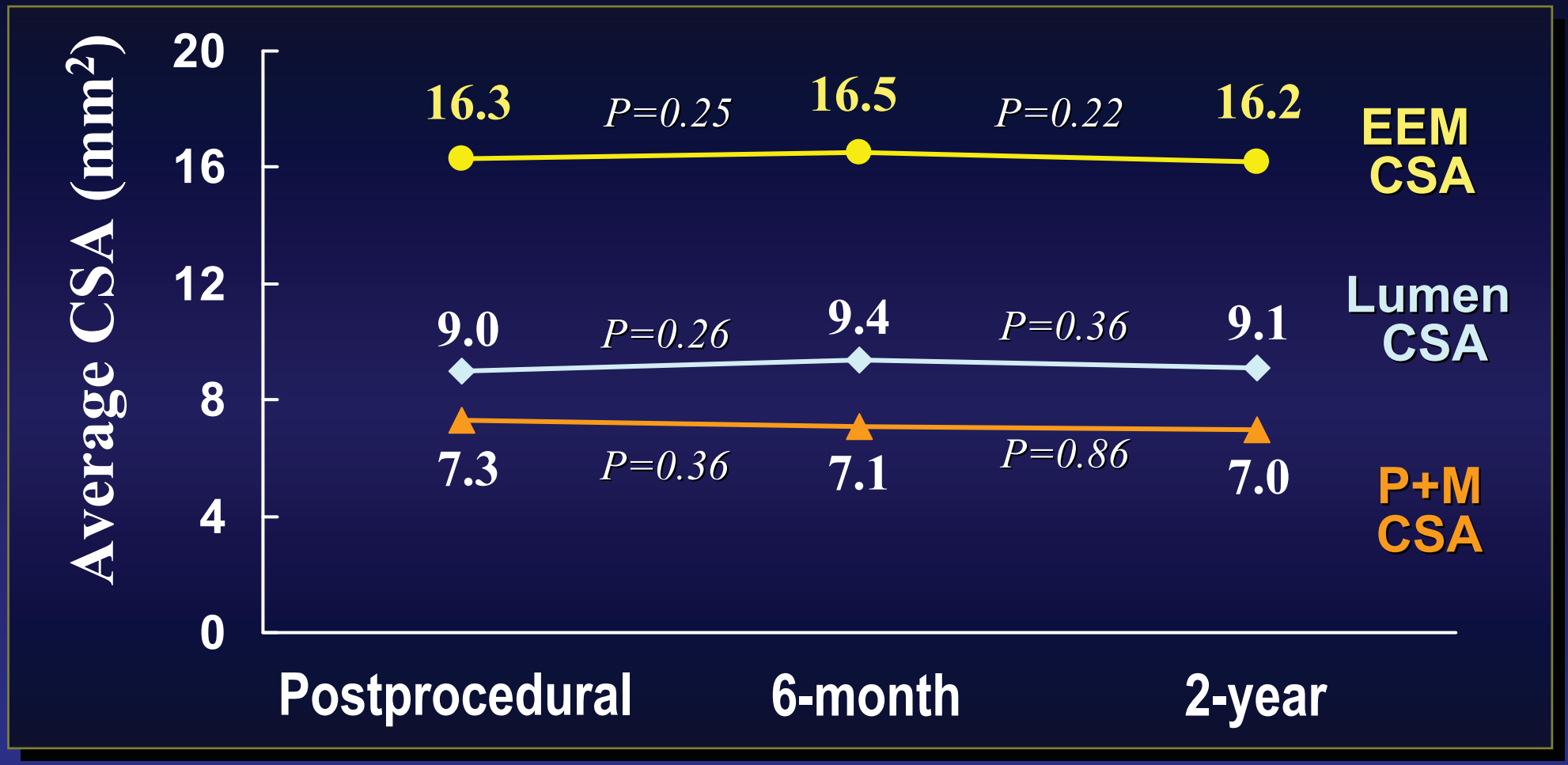
Proximal and distal segment with 2 mm interval from the stent edge

→ **Average EEM CSA (mm^2)**
Average lumen CSA (mm^2)
Average plaque + media CSA (mm^2)
Average plaque burden (%)

R4 trial

6-month & 2-year IVUS Data

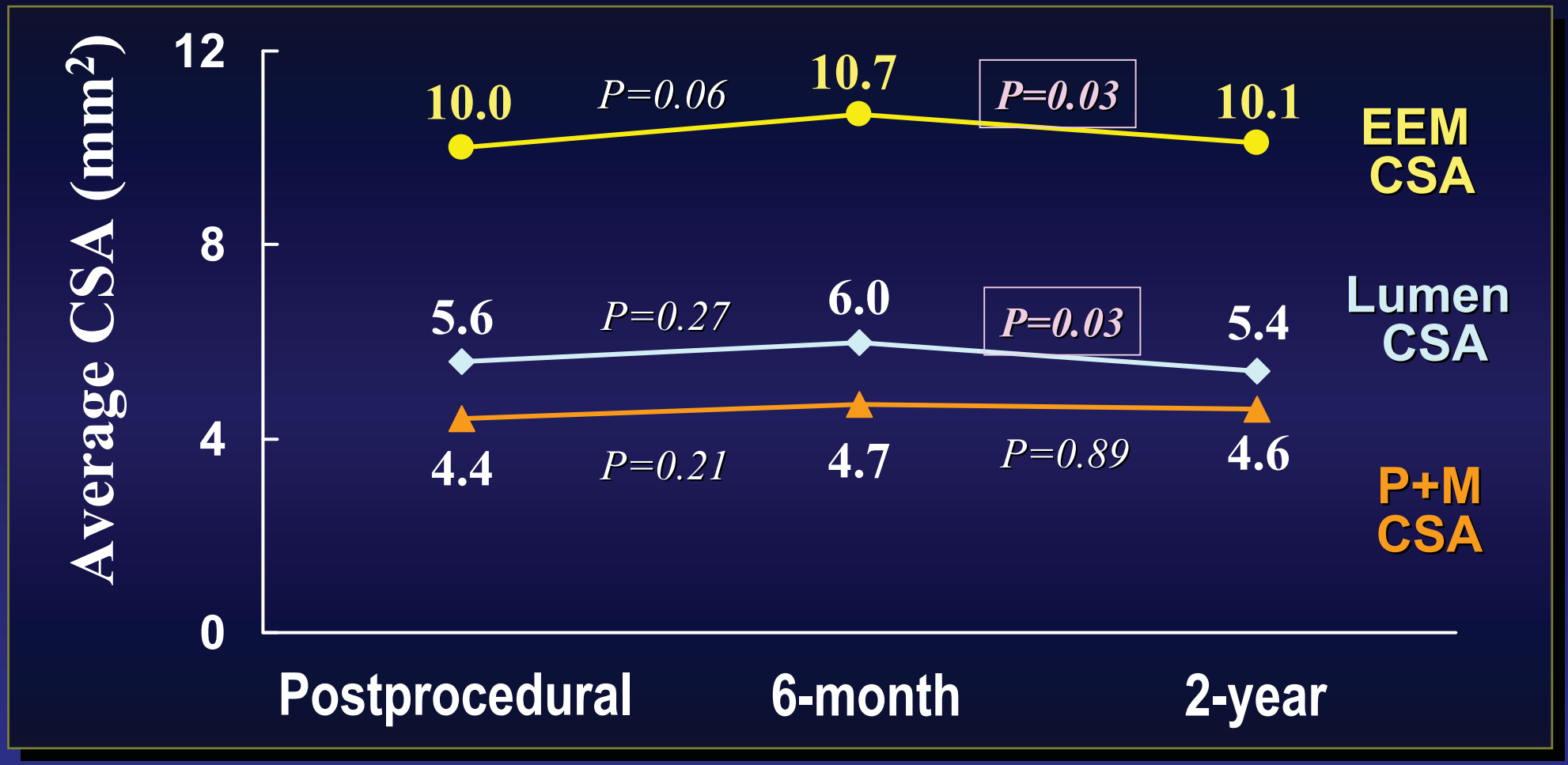
Proximal reference segment (N=17)



R4 trial

6-month & 2-year IVUS Data

Distal reference segment (N=17)



Clinical Follow-up

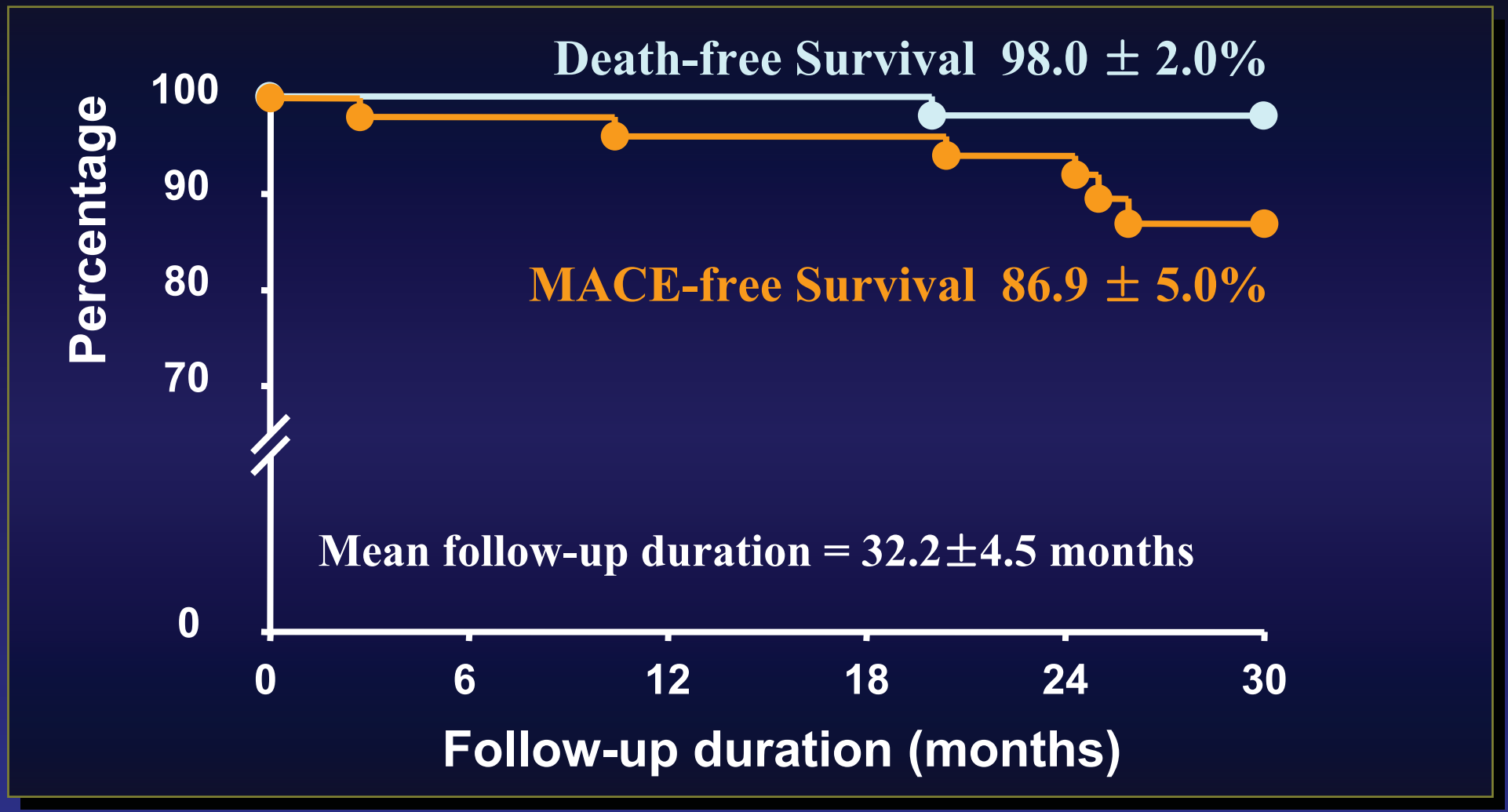
R4 trial

N=50

Mean follow-up duration	32.2 ± 4.5 mo
Symptom Recurrence	4 (8%)
TLR (%)	6 (12%)
Stent	2
CABG	1
Cutting balloon	3
Death	1 (2%), Non-cardiac

R4 trial

Death & Event-free Survival



Conclusion

- Beta-irradiation using a ^{188}Re-MAG_3-filled balloon after rotational atherectomy is safe and feasible in patients with diffuse ISR.
- Long-term angiographic and clinical outcome appears favorable for this highly restenosis prone group.
- *However,* late "catch-up" phenomena were observed in some patients after brachytherapy.

R4 trial

Study Limitations

- The number of study patients is small.
- Because of the lack of a control group, we could not compare the data with other therapeutic modalities.
- 2-year angiographic follow-up rate was relatively low.