Five-Year Follow-UP 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

Radiation with ^{188}Re-MAG$_3$-filled balloon after Rotablation for diffuse in-stent Restenosis

Purpose

To evaluate the efficacy and 5-year clinical outcomes of R4 trial

Inclusion Criteria

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

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

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)

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

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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

Antithrombotic Therapy

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

Follow-Up

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

- QCA Analysis

Clinical follow-up at 60 months:

- MACE and other significant events

linical haracteristics (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

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%)

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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	

adiation Coverage

ean Lesion Length		25.6 ± 12.7 mm
ean 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)*

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

Immediate Results

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

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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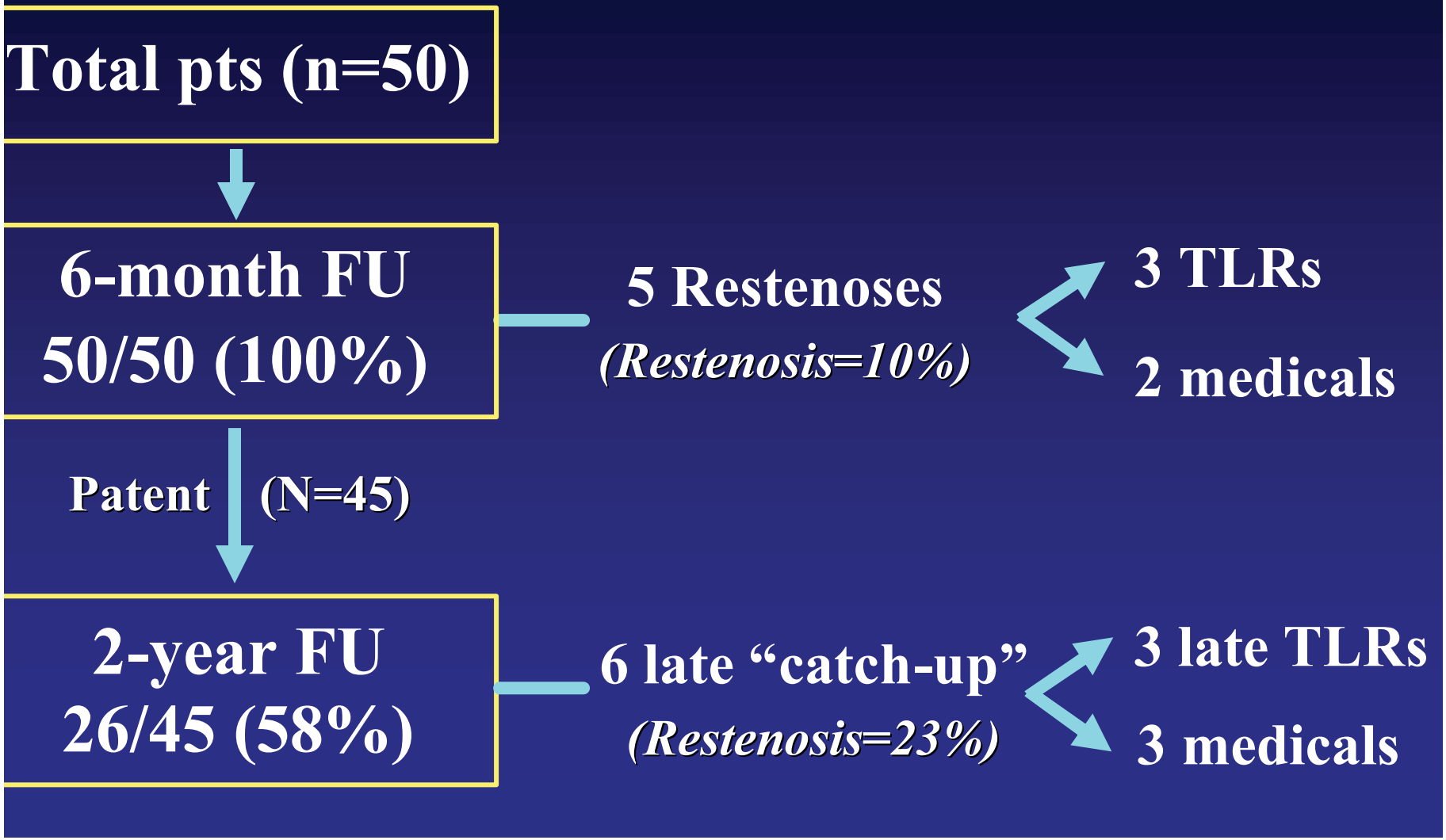
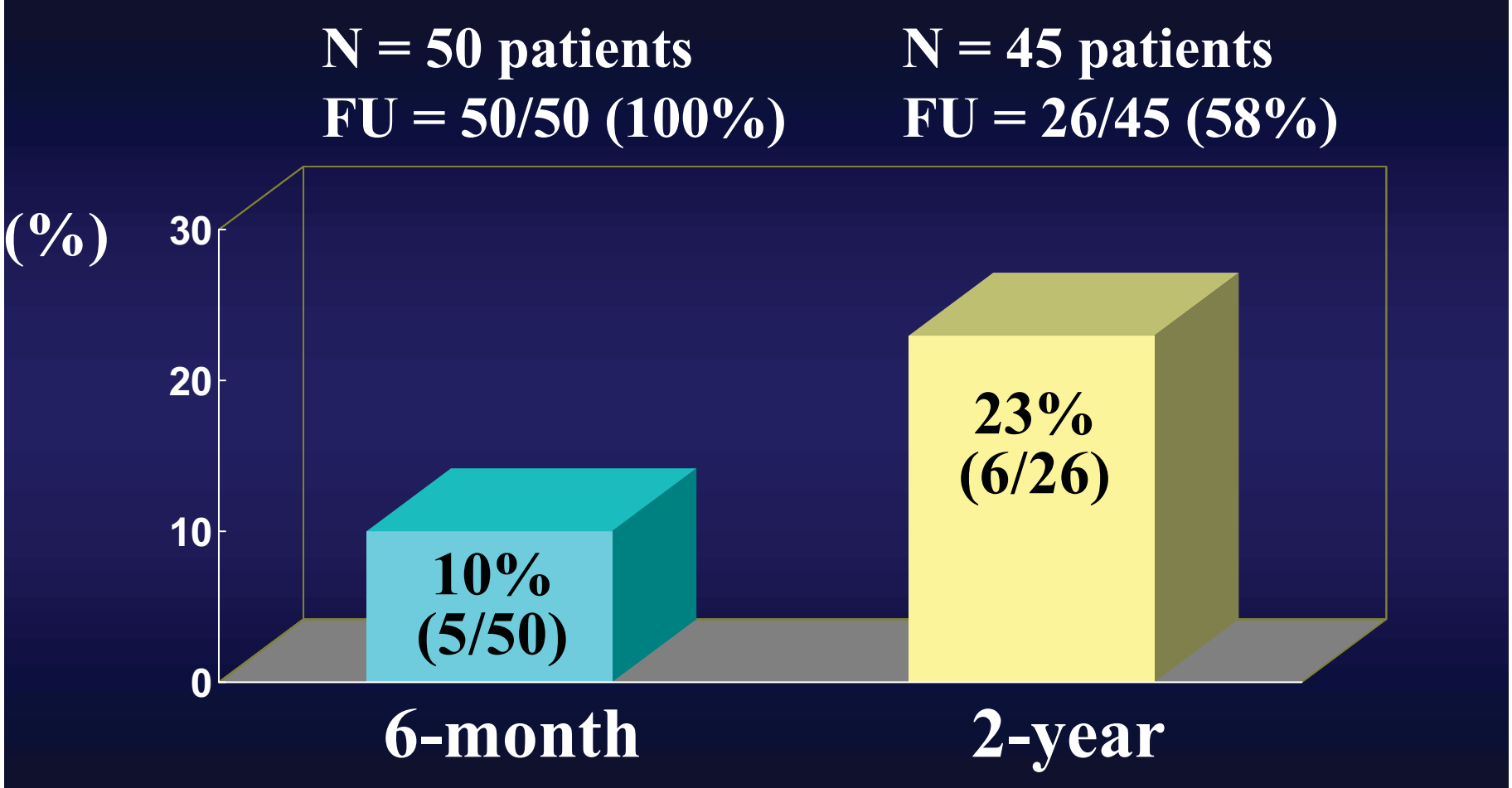
6-month & 2-year angiographic FU



6-month & 2-year angiographic Restenosis Rate



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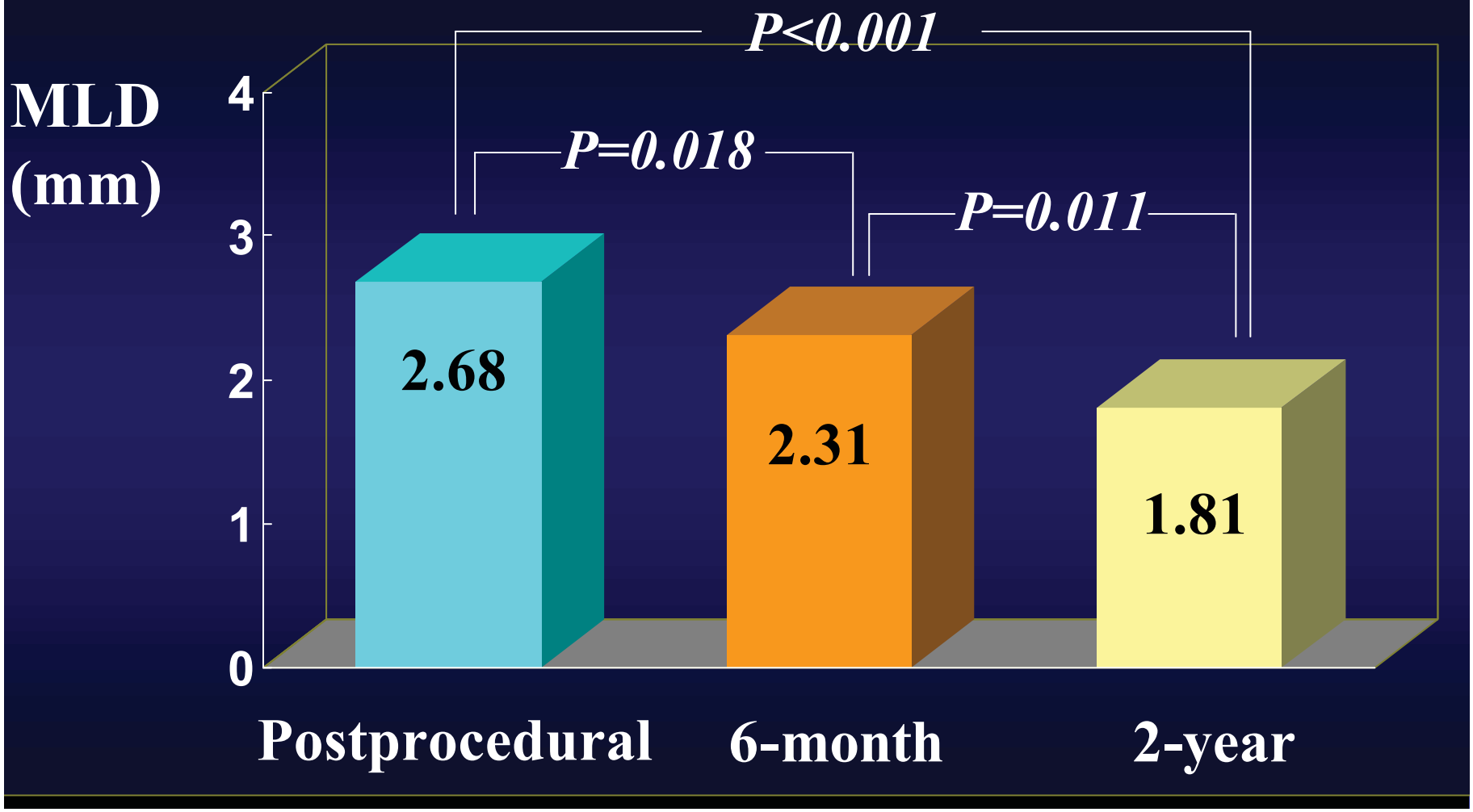
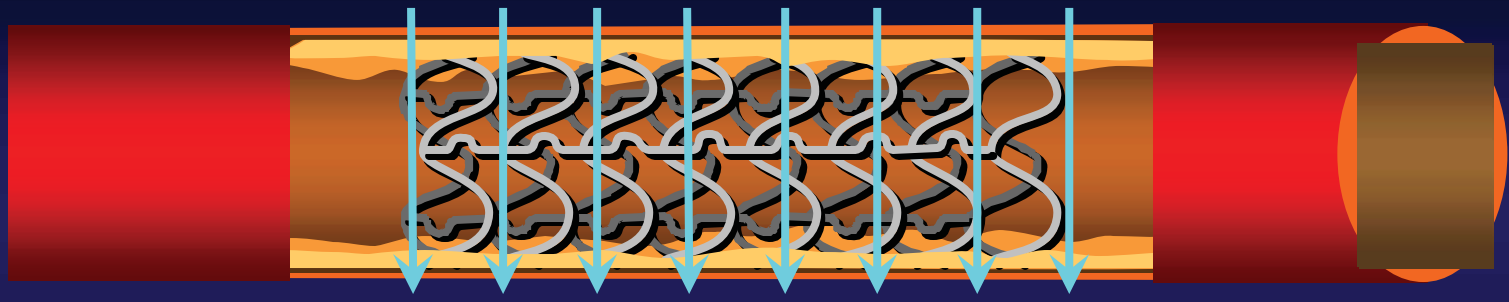
-month & 2-year angiographic M

N=2



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



In-stent segment with 2 mm interval

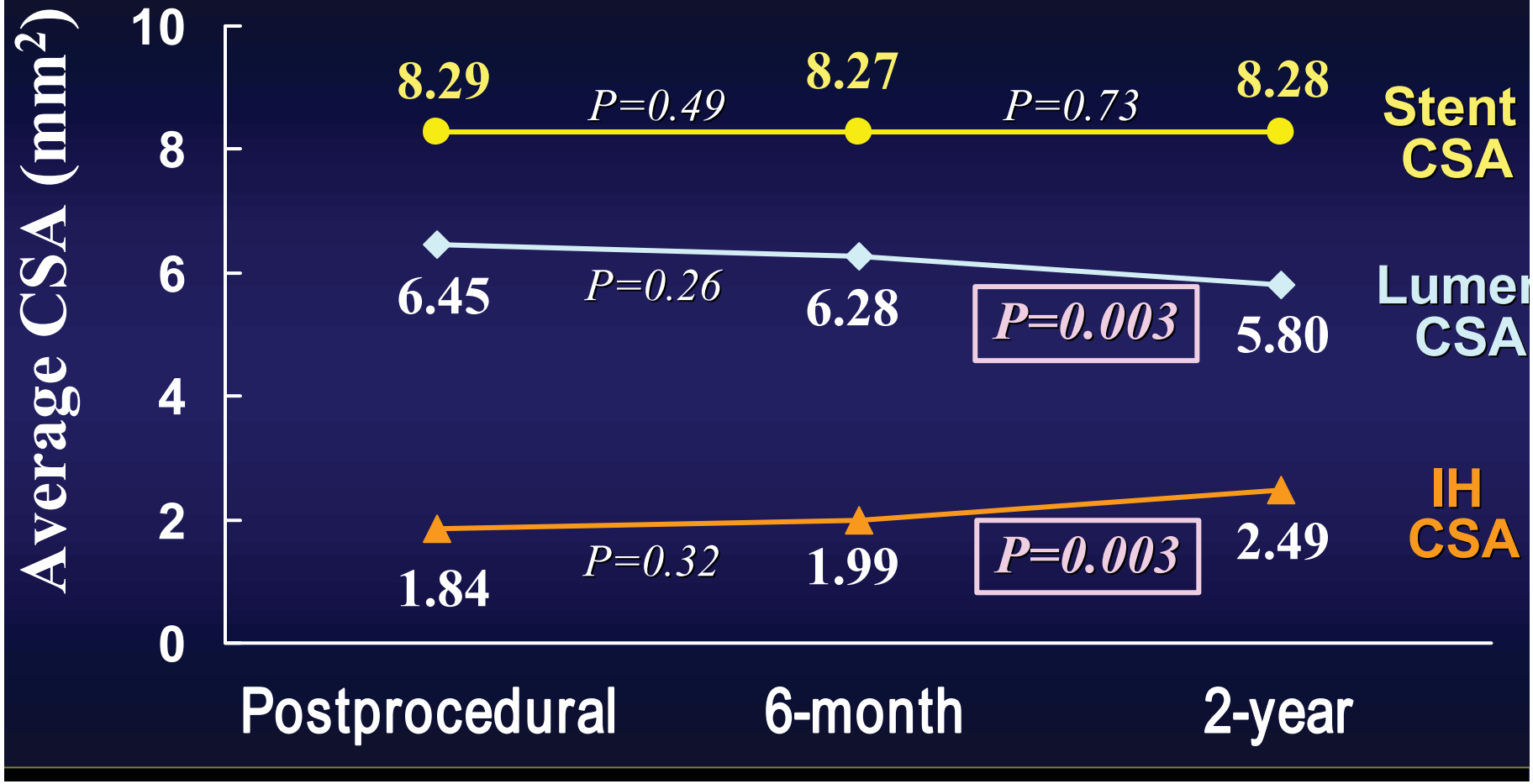
→ Average stent CSA (mm^2)
Average lumen CSA (mm^2)
Average intimal hyperplasia CSA (mm^2)

Of 26 patients, 21 available data were analyzed.

R4 tria

-month & 2-year IVUS Data

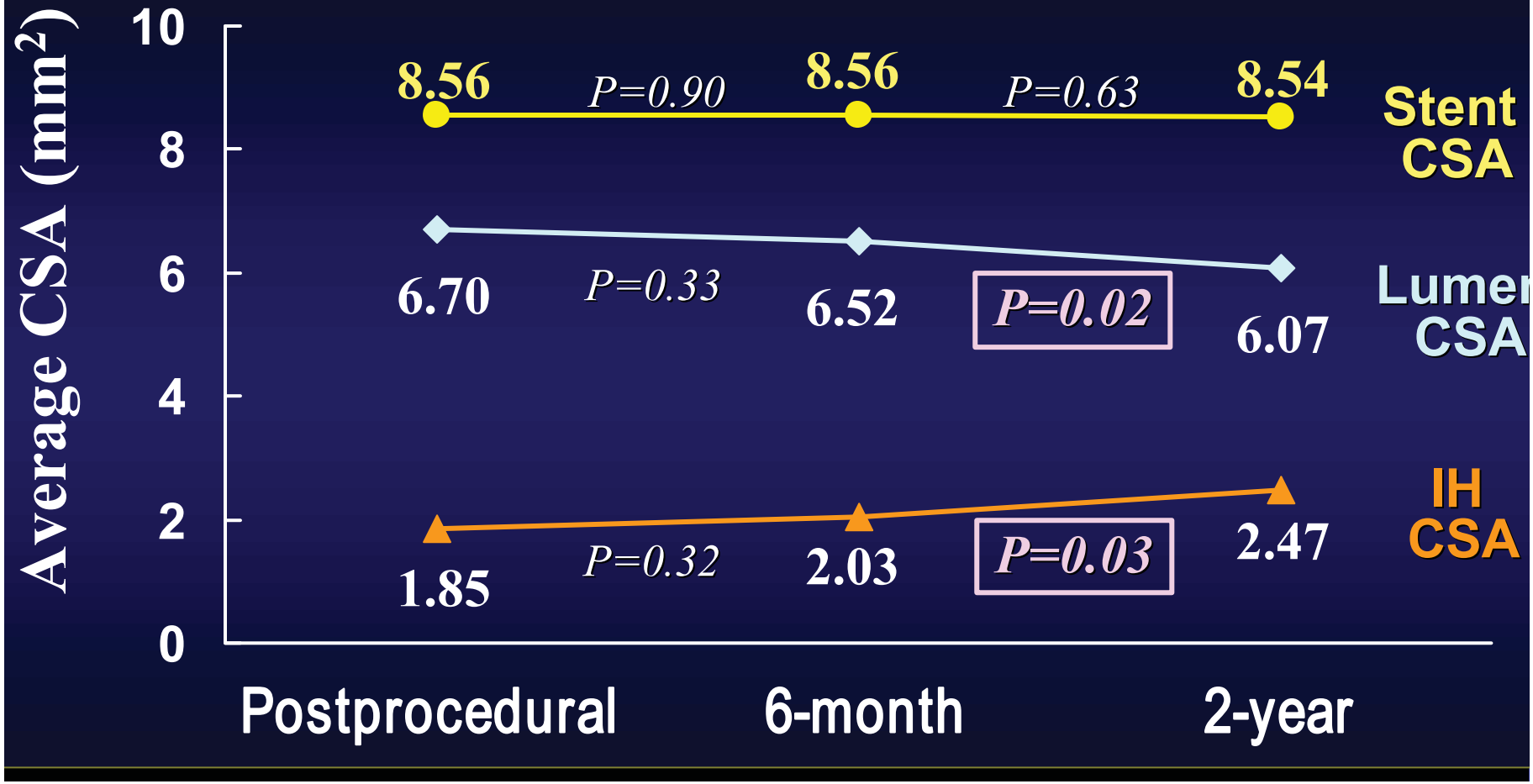
cluding 4 patients with late "catch-up" phenomena (N=



R4 tria

-month & 2-year IVUS Data

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



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

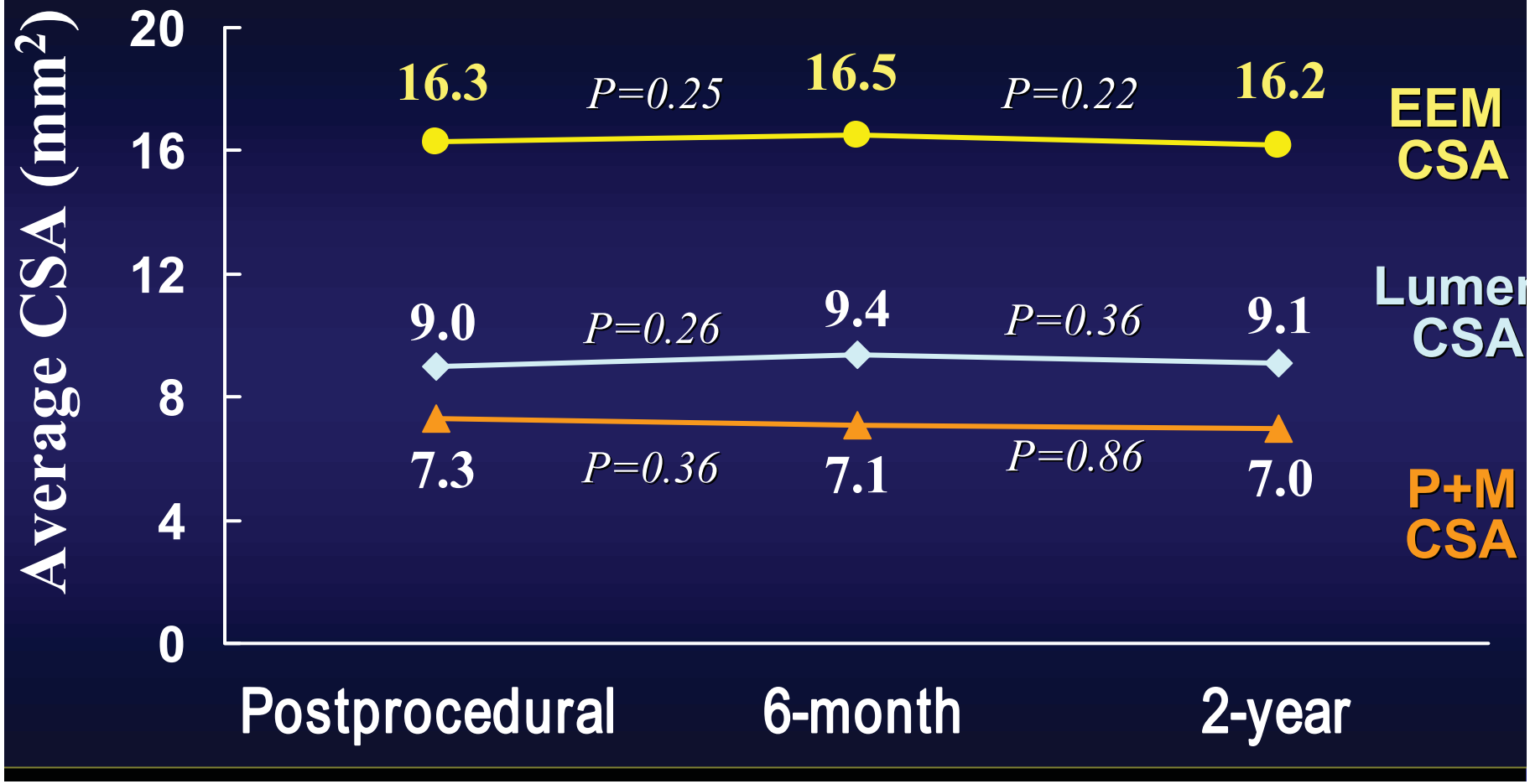
Proximal and distal segment with 2 mm interval from the stent edge

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

R4 tria

6-month & 2-year IVUS Data

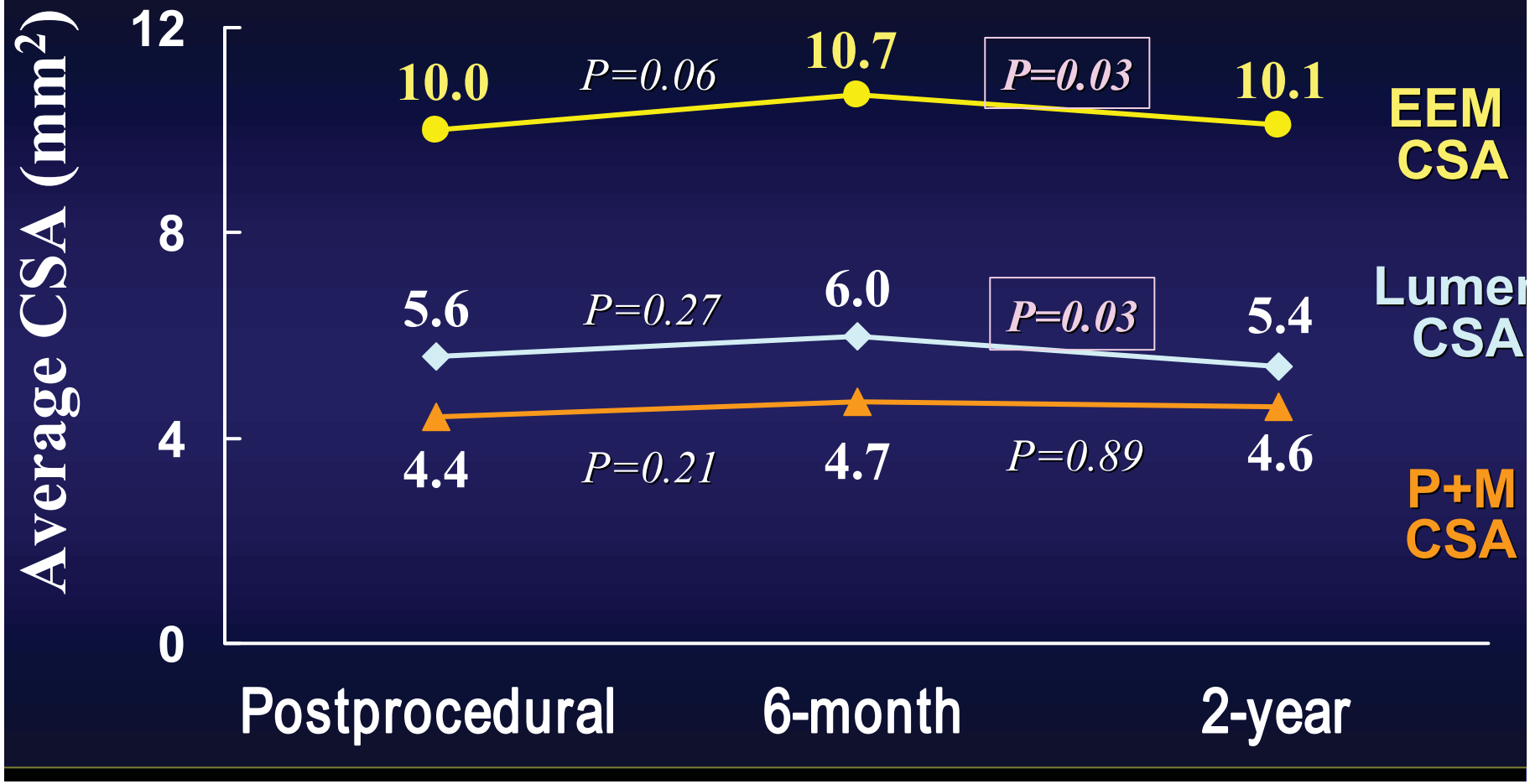
Proximal reference segment (N=17)



R4 tria

-month & 2-year IVUS Data

Distal reference segment (N=17)



ive-Year Clinical Follow-up

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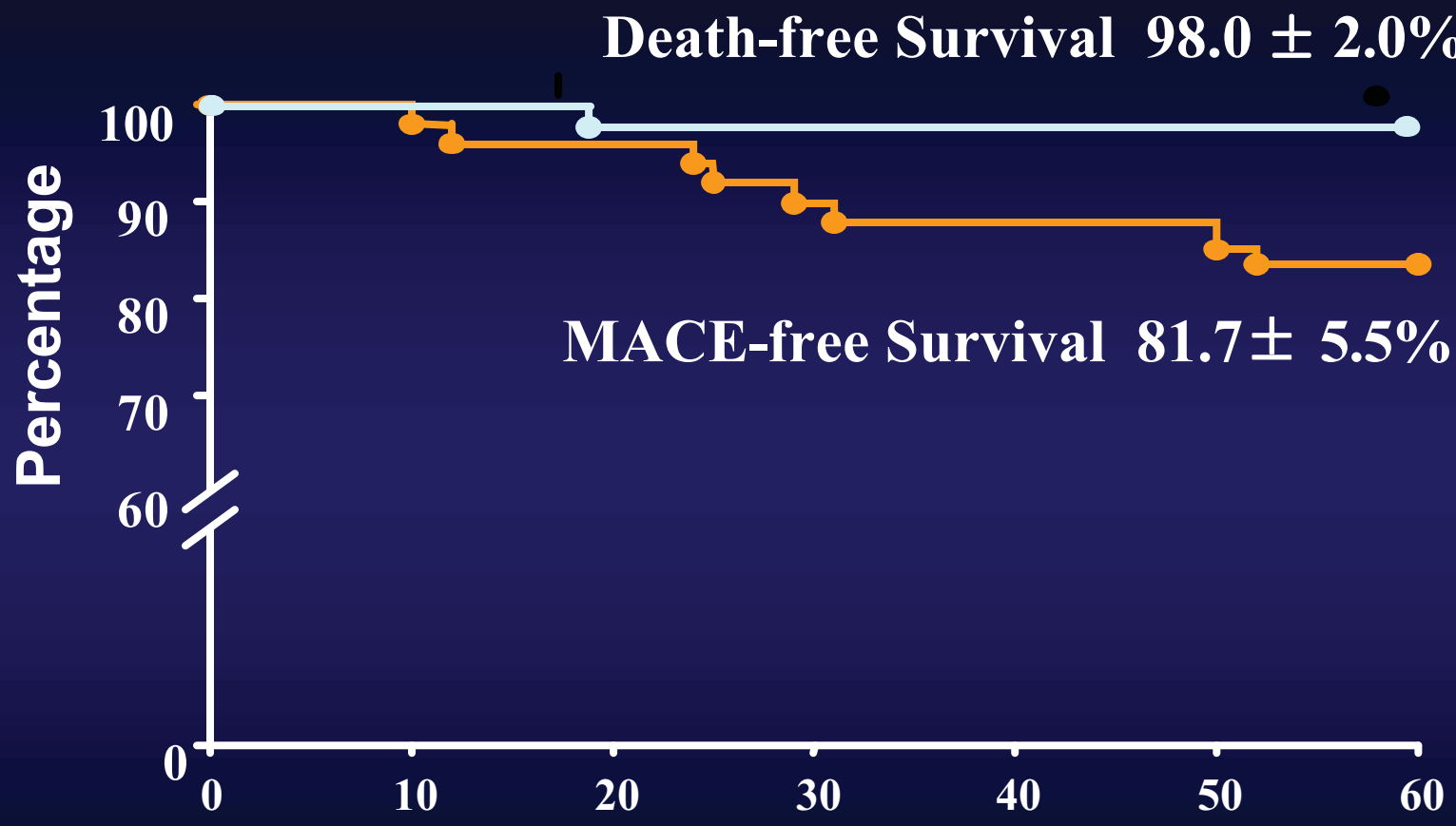
N=50	At 6 month	At 6 to 30 months	At 30 to months
eath	0	1(2%)	0
Noncardiac	0	1(0.1%)	0
Cardiac	0	0	0
on fatal MI	0	0	0
LR	0	6(12%)	2(4%)
te thrombosis	0	0	0
mbined events	0	7(14%)	2(4%)

R4 tria

Death & Event-free Survival



Conclusion

The late catch-up phenomenon might occur between 6 months and 5 years after beta-radiatio

Although long-term (5-year) follow-up show occurrence of late TLR, which may be associat with late restenosis, beta-radiation using a ^{188}R MAG_3-filled balloon after rotational atherecton is associated with sustained favorable outcomes u to 5 years.

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.

There were no routine angiographic follow-up after 2 years, thus clinically driven event do not represent subclinical changes of irradiated segment.