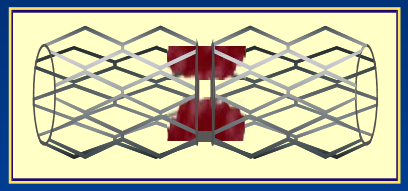
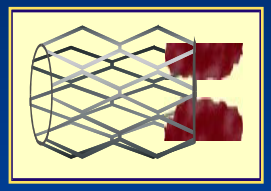
PCI for
In-stent Restenosis

Patterns of ISR

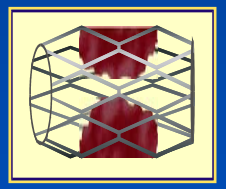
FOCAL



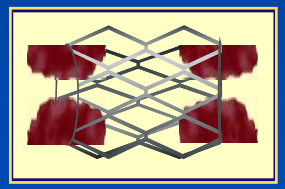
Articulation or Gap



Margin

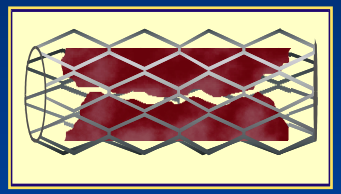


Focal Body

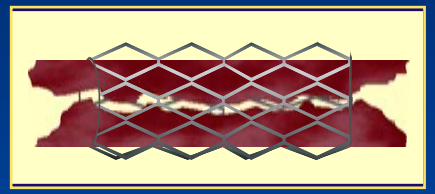


Multifocal

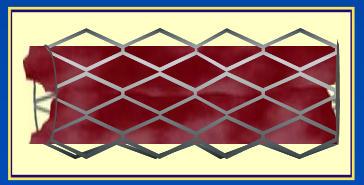
DIFFUSE



Intra-stent



Proliferative



Total Occlusion

Mehran R et al. Circulation 1999;100:1872-78

Treatment of ISR

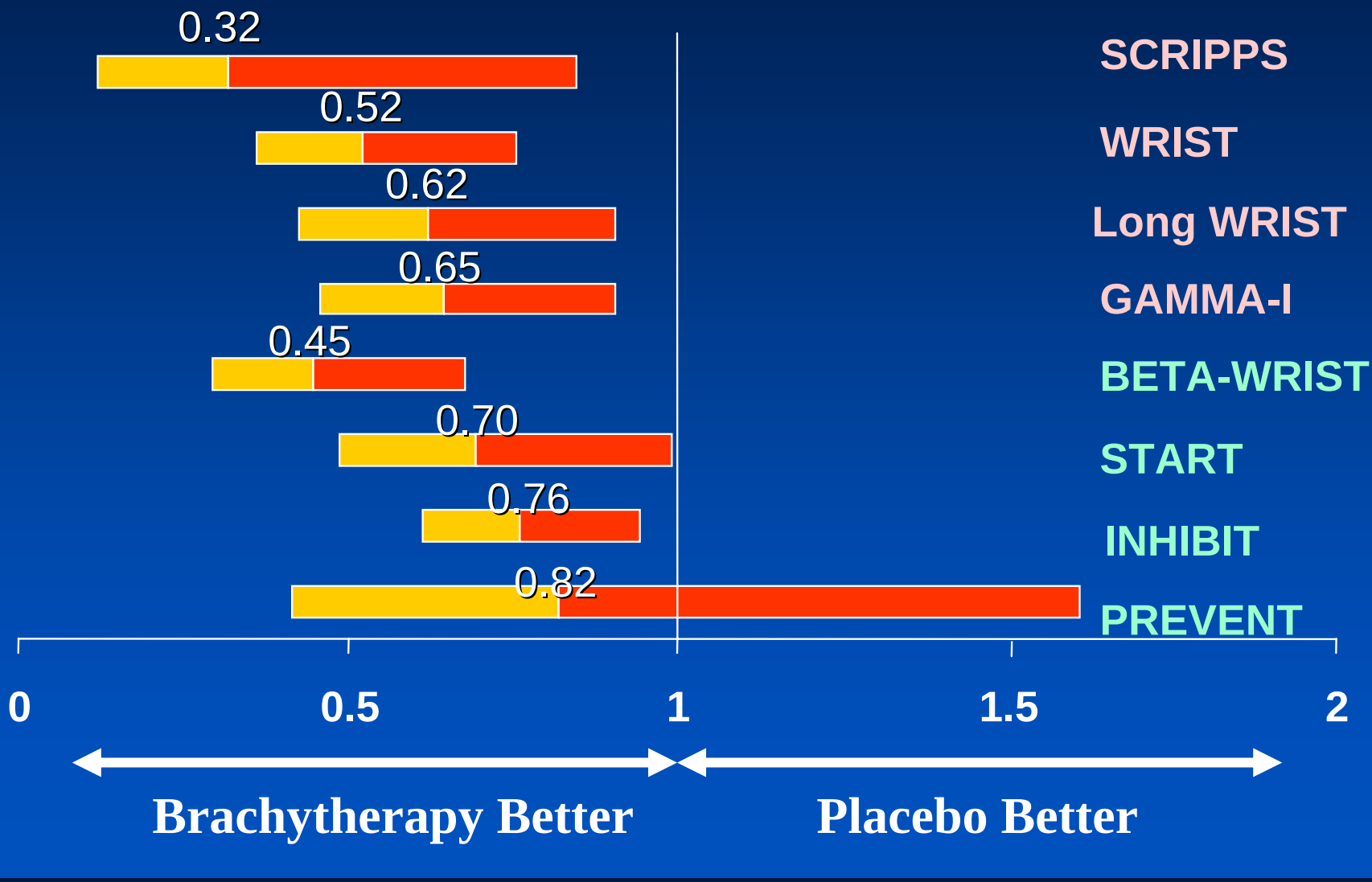
- Balloon angioplasty
- Cutting balloon angioplasty
- Rotablating atherectomy
- Repeat stenting
- Intracoronary brachytherapy
- Drug eluting stent

Not encouraging in diffuse ISR

Intracoronary Brachytherapy

- Most effective therapy of in-stent restenosis before development of drug eluting stent
- Use of source train or balloon with beta or gamma radiation
- Inhibition of neo-intimal growth

Risk Reduction of Brachytherapy



Brachytherapy

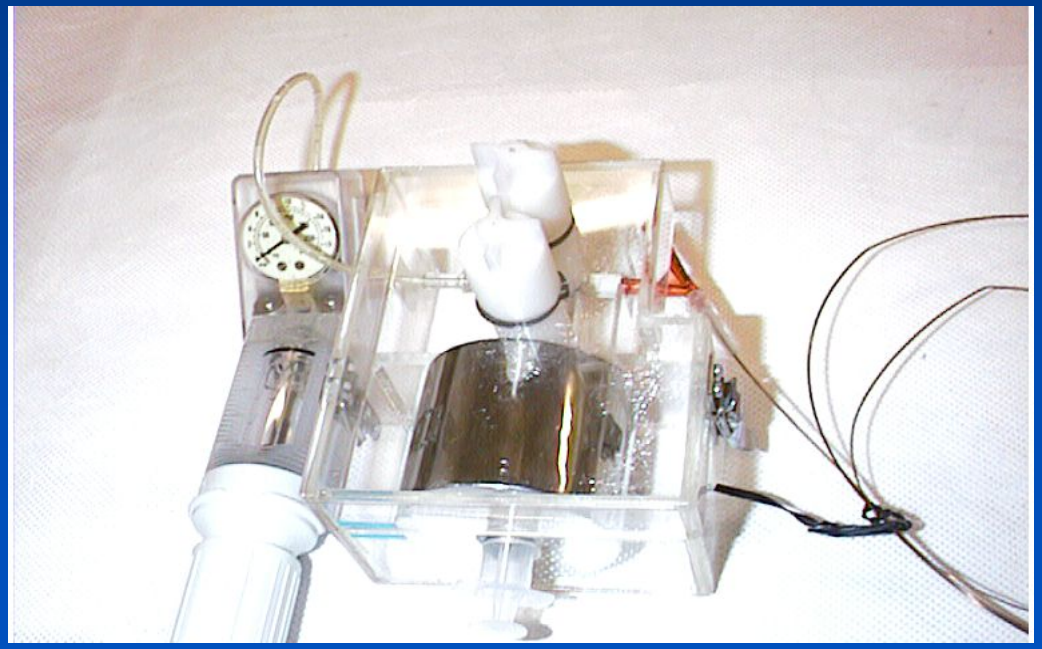
Reported Clinical Trials for ISR

TRIAL	Source	Length (mm)	Pts (n)	Restenosis %	
				Placebo	Treated
SCRIPPS	192Ir	15.3	35	70.5	11.1
WRIST	192Ir	23.7	130	58.3	19
GAMMA 1	192Ir	20.2	252	50.5	21.6
GAMMA 2	192Ir	19	125		23
LONG WRIST	192Ir	32	120	71	32
B-WRIST	90Y	20.6	50		22
START	Sr/90	17	476	42.2	14.2
INHIBIT	P32	17	332	48	16
BRITE	P32	17	26		0

AMC Experience of Brachytherapy

Why 188Re-MAG3 balloon ?

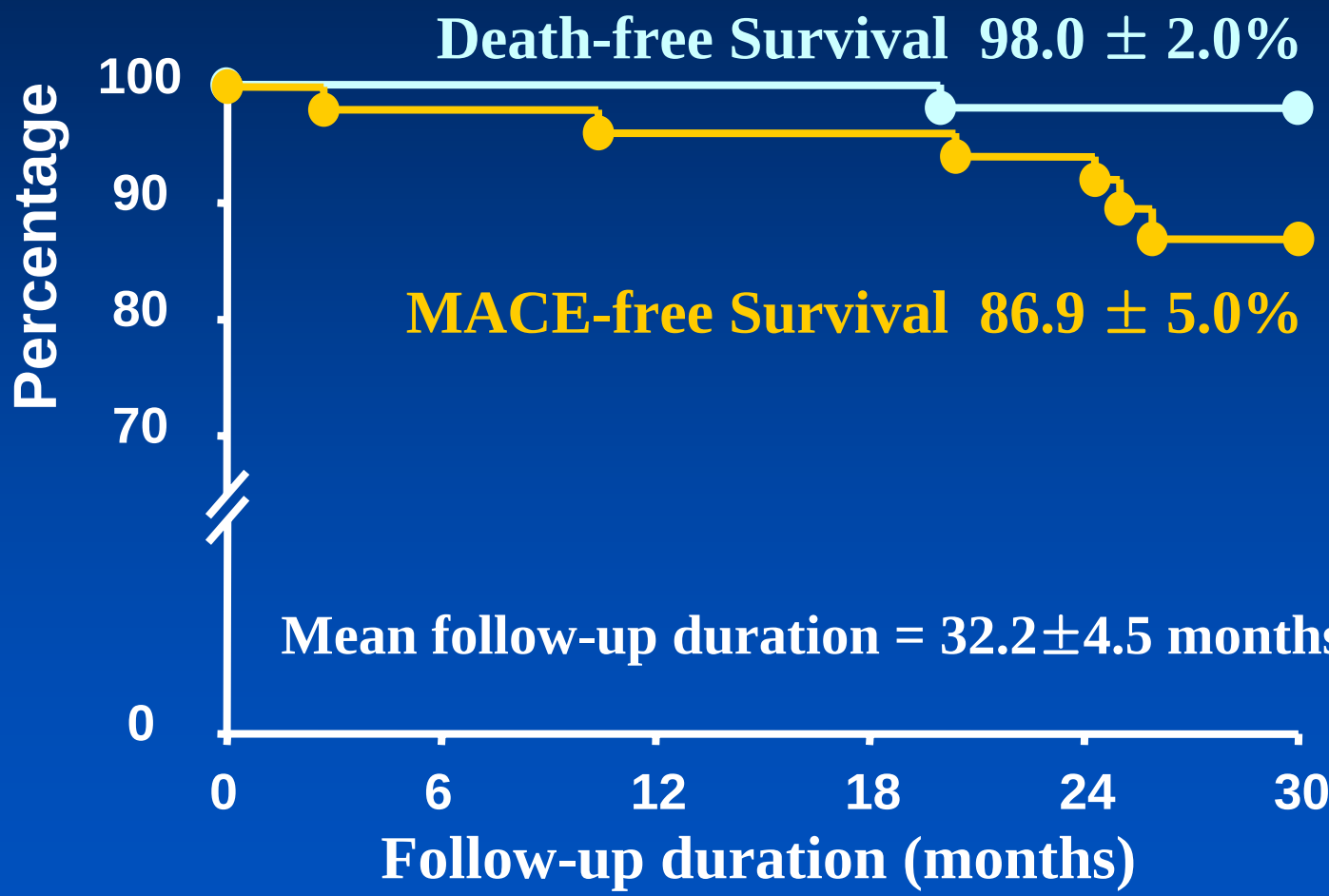
- Cost-effective
- No additional shielding
- Obtained from a Generator



Why 188Re-MAG3 balloon ?

- Centering, Angled lesion
- Beta source with High energy (Max 2.12 MeV)
- Short Half-life (T 1/2 = 17 hrs)
- Negligible radiation exposure
- Very safe

Death & Event-Free Survival after Rotablation and Beta-Radiation with 188Re



Lee SW et al. Int J Cardiol 2005;99:201-205

Effective Pretreatment Methods Before Beta Radiation

Performed Studies in AMC

- Robating atherectomy

  vs. Simple balloon

- Cutting balloon angioplasty

  vs. Simple balloon

Rotablation vs. Simple Balloon

First 50 consecutive patients have been performed rotablation prior to radiation,

- Rota+RT N=50

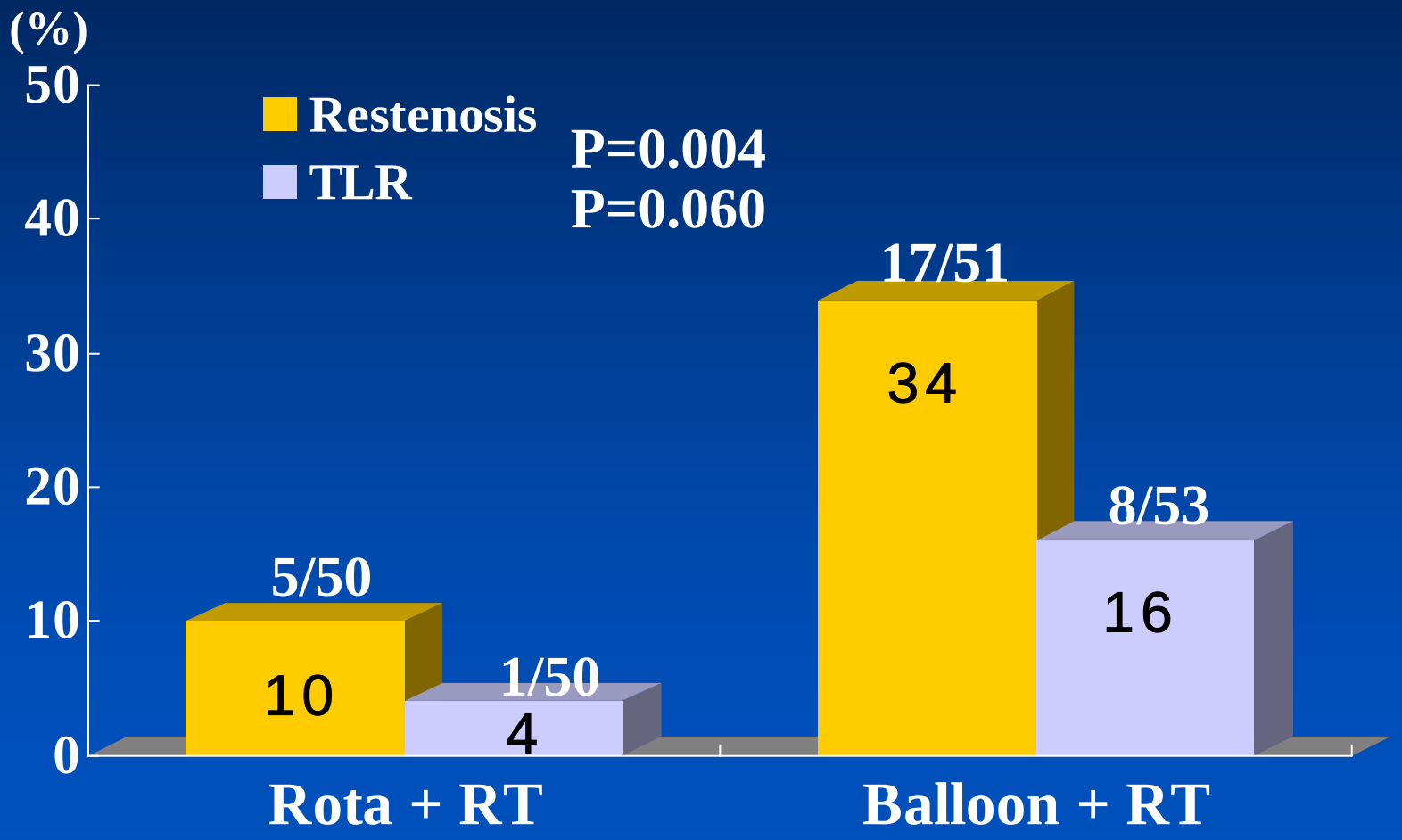
and the remaining 53 consecutive patients received balloon + radiation strategy.

- Balloon+RT N=53

Int J Cardiol (in press)

6-Month Restenosis Rate & TLR

Rota vs. Balloon



Int J Cardiol (in press)

Rotablation vs. Cutting Balloon

- Patients with diffuse in-stent restenois in a native coronary artery (n=113)

Randomization

Rotational atherectomy ± PTCA (n=58, RA group)

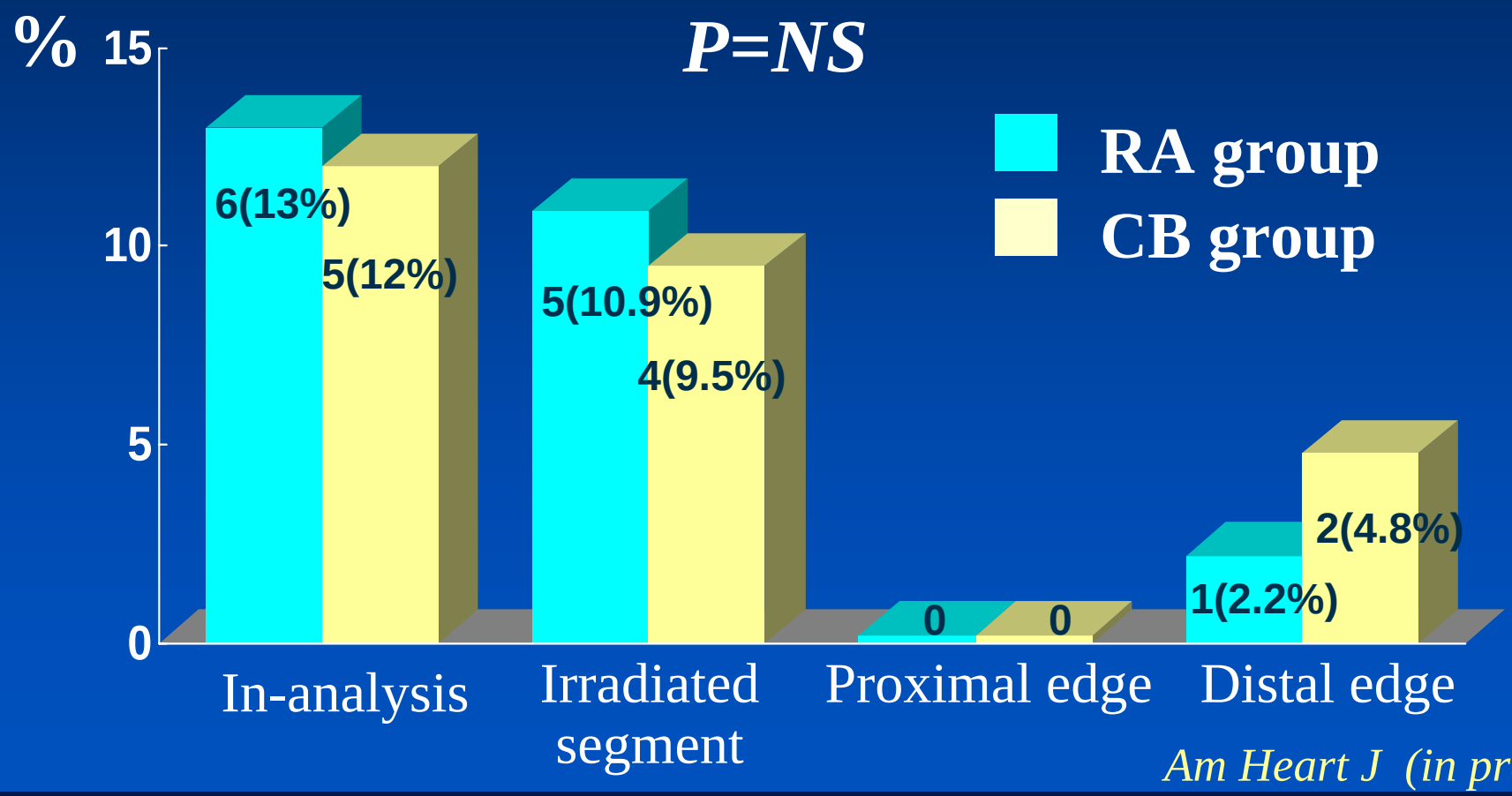
Cutting balloon angioplasty (n=55, CB group)

Beta-radiation therapy using ^{188}Re-MAG$_3$-Filled Balloon

Am Heart J (in press)

Angiographic Restenosis

Rota vs. Cutting



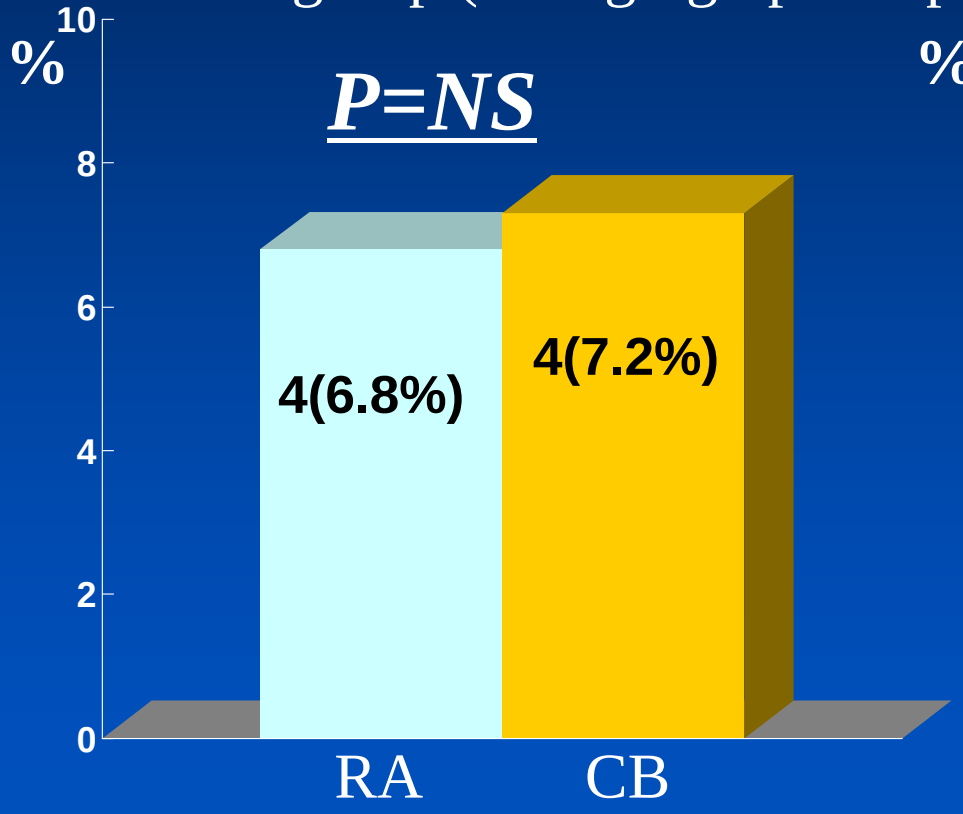
Am Heart J (in press)

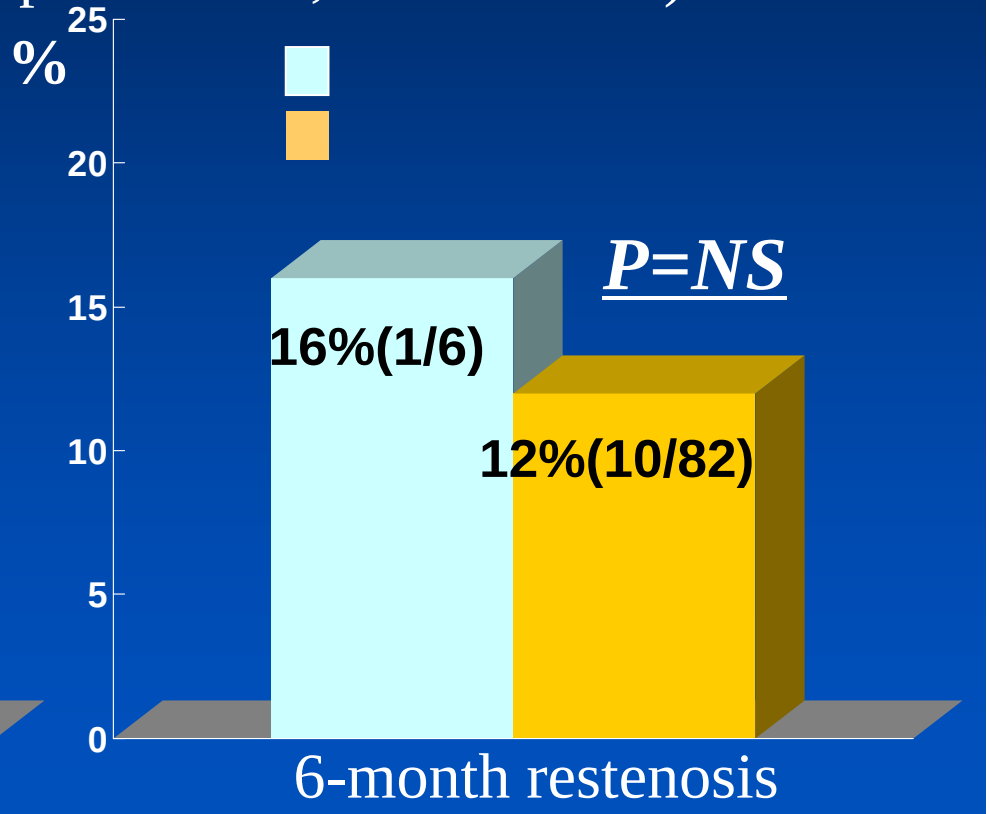
Additional Stenting

Rota vs. Cutting

RA group (3: dissection, 1:hematoma)

CB group (3: angiographic optimization, 1: dissection)





Am Heart J (in press)

9-Month Clinical Outcome

Rota vs. Cutting

	RA group (n=58)	CB group (n=55)	*p*
Stent thrombosis	0	0	NS
MI	0	0	NS
TLR	2(3.4%)	2(3.6%)	NS
PCI	2(3.4%)	2(3.6%)	
CABG	0	0	
Death	0	0	NS

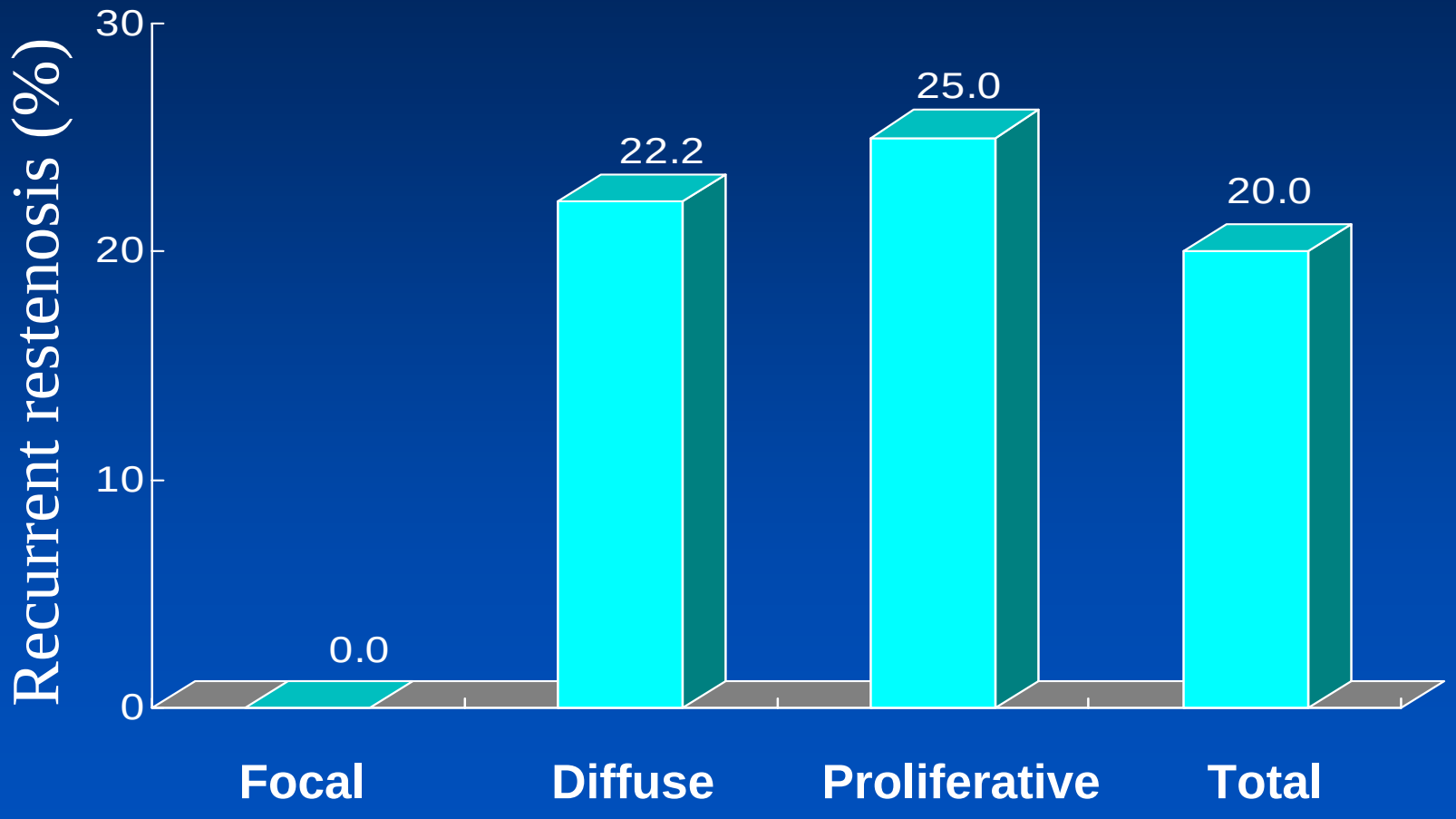
Am Heart J (in press)

Drug-Eluting Stent

New Standard for ISR ?

SES Restenosis after ISR Treatment

Total 53 lesions



Saia F et al. Heart 2004;90:1183

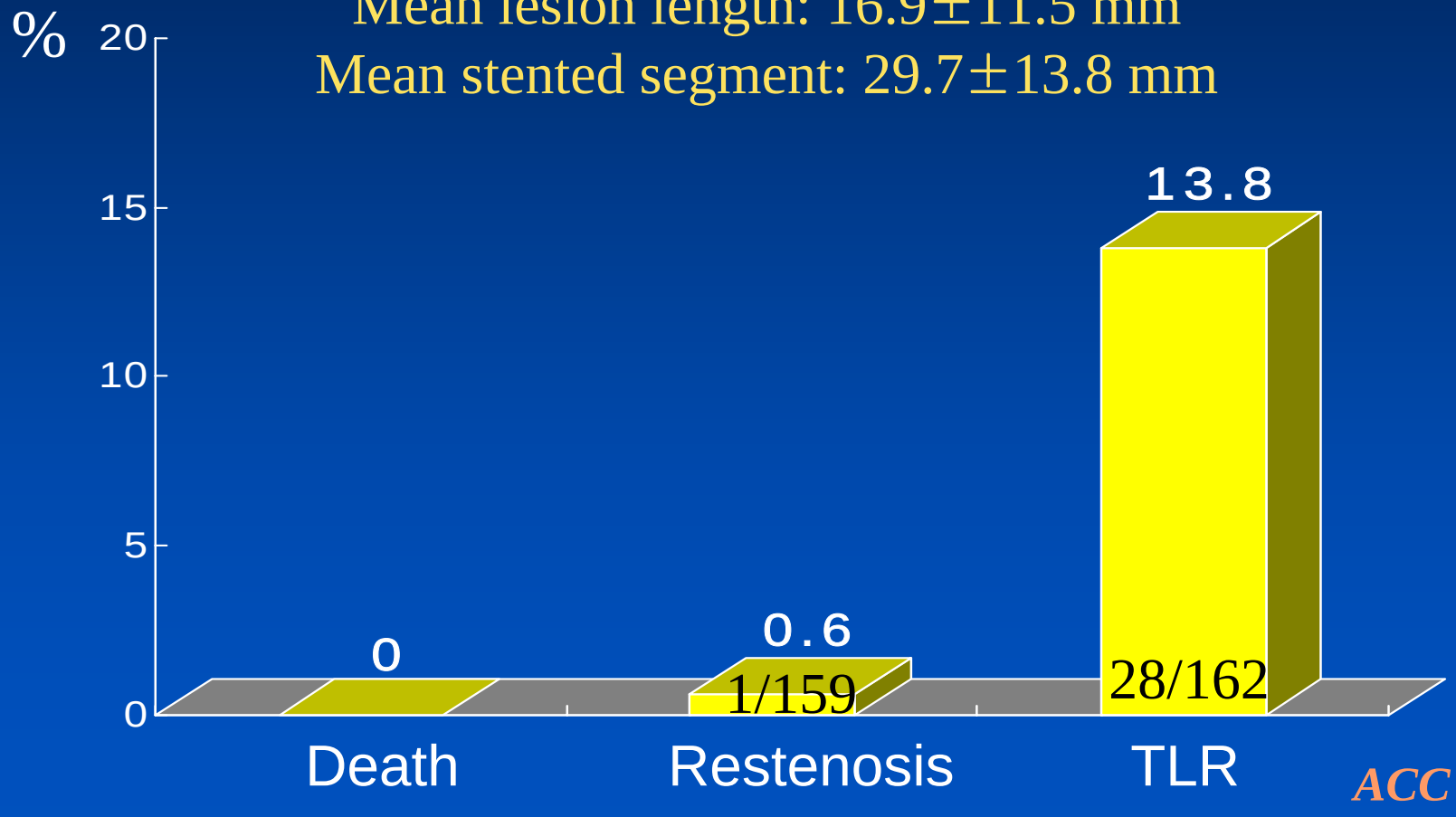
SES for ISR in Milan

Immediate and mid-term results

206 ISR, 159 patients

Mean lesion length: 16.9±11.5 mm

Mean stented segment: 29.7±13.8 mm



ACC 2004

ISR in AMC

183 lesions with DES Implantation From Feb 2003 till Oct 2004

Focal	62 (34 %)
Diffuse	88 (48 %)
Proliferative	19 (10 %)
Total occlusion	14 (8 %)

Lesion length : 27.3 ± 15.3 mm

6-Month Restenosis : 4.9 %

	81 eligible lesions (75%)
Reference vessel (mm)	2.73 ± 0.48
MLD (mm)	2.36 ± 0.60
Late loss (mm)	0.48 ± 0.45
Diameter stenosis (%)	11.6 ± 28.6
Binary restenosis (%)	4 (4.9%)

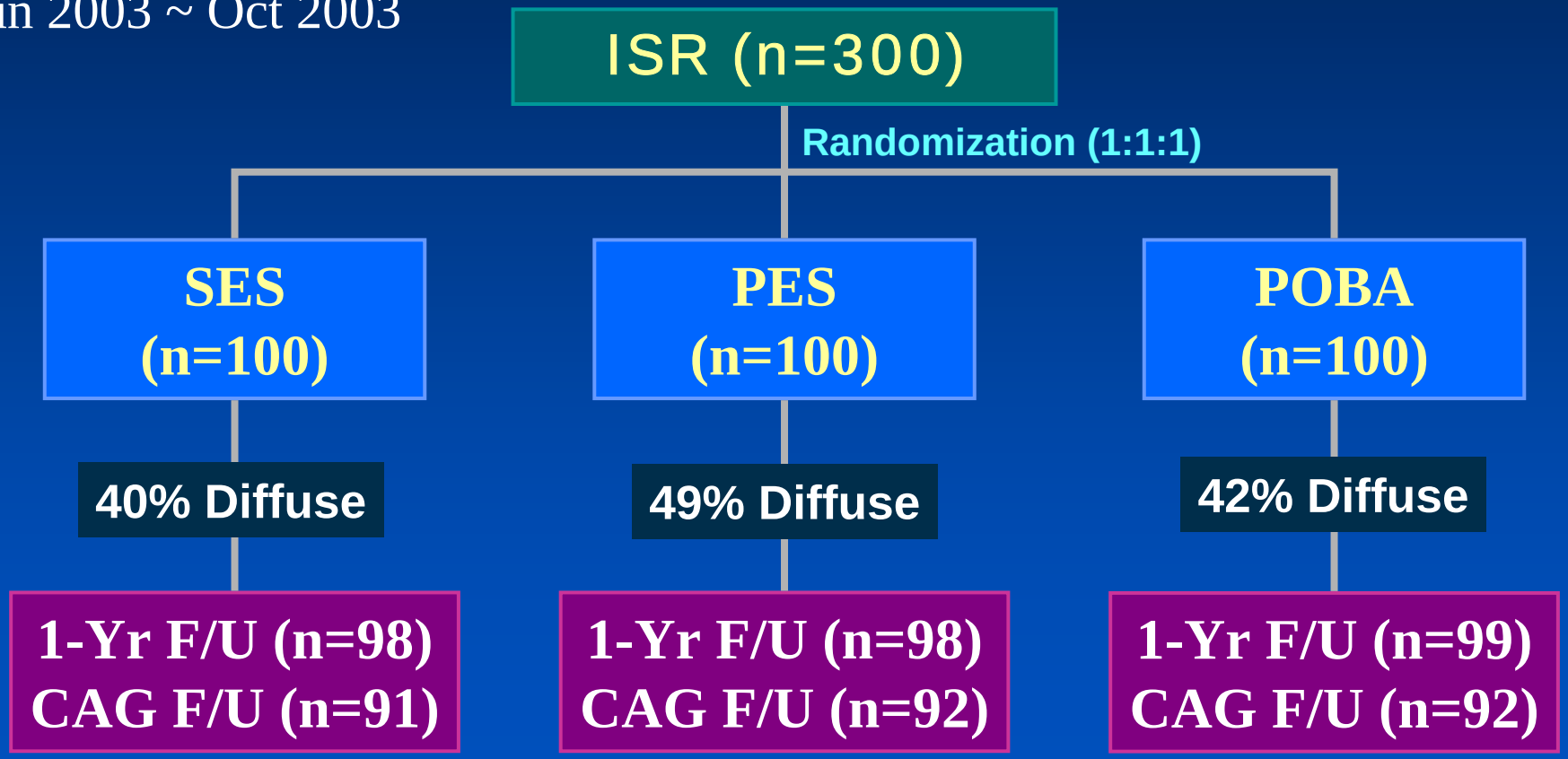
Role of DES for ISR

DES vs. Angioplasty

SES vs PES vs POBA for ISR

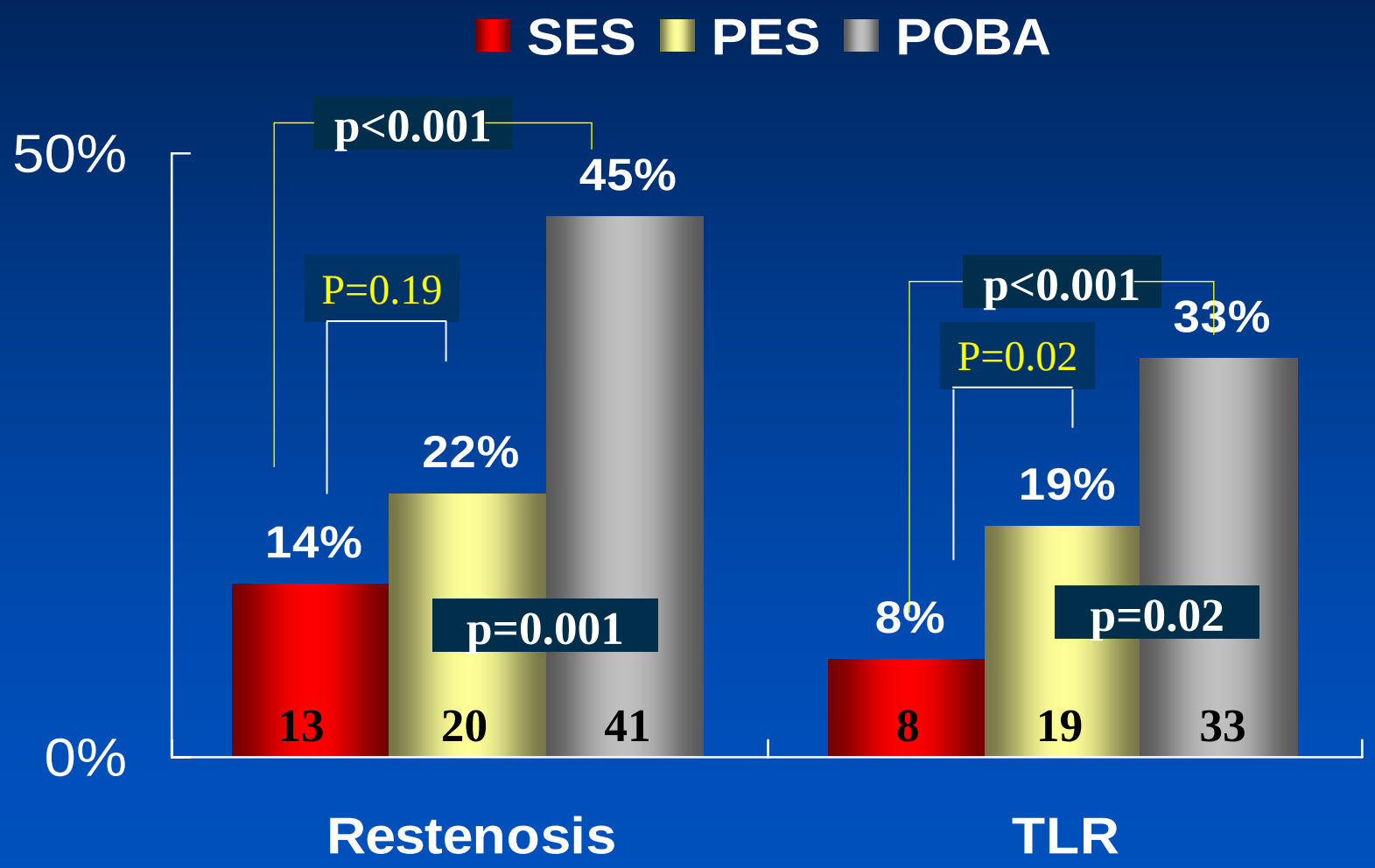
ISAR-DESIRE study

Jun 2003 ~ Oct 2003



A Kastrati et al. JAMA 2005;293:165

Restenosis and TLR Rates



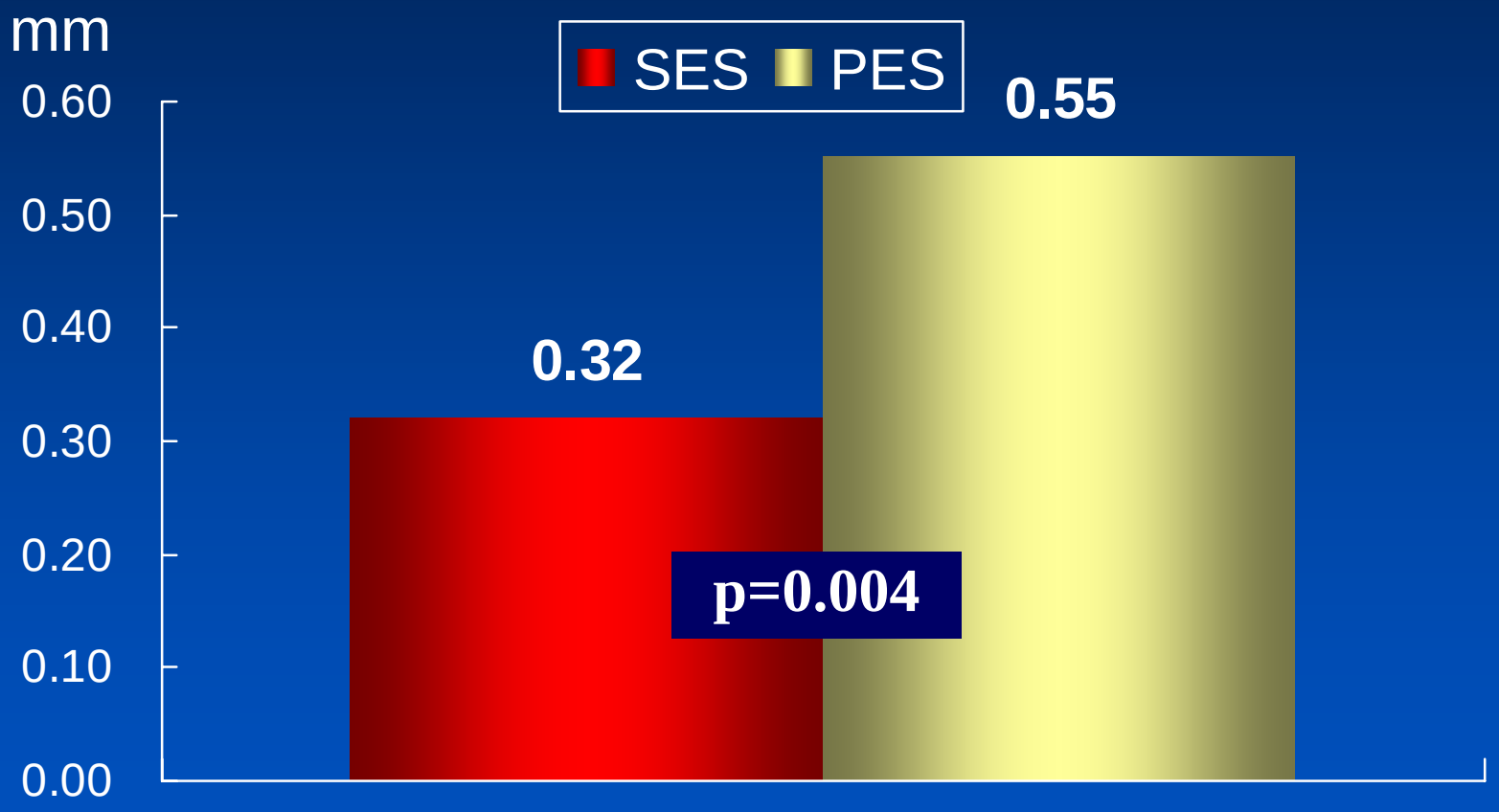
A Kastrati et al. JAMA 2005;293:165

SES vs. PES (QCA at F/U)

	SES (n=91)	PES (n=92)	P value
MLD, mm			
In-segment	**2.12**	**2.02**	**0.23**
In-stent	2.45	2.21	0.05
DS, %			
In-segment	23.1	26.6	0.04
In-stent	12.6	19.6	0.004
Late loss, mm			
In-segment	0.32	0.55	0.02
In-stent	0.10	0.26	0.004
Restenosis, %			
In-segment	**13(14.3%)**	**20(21.7%)**	**0.19**
In-stent	**10(11.0%)**	**17(18.5%)**	**0.15**

SES vs PES

In-segment Late loss of SES and PES



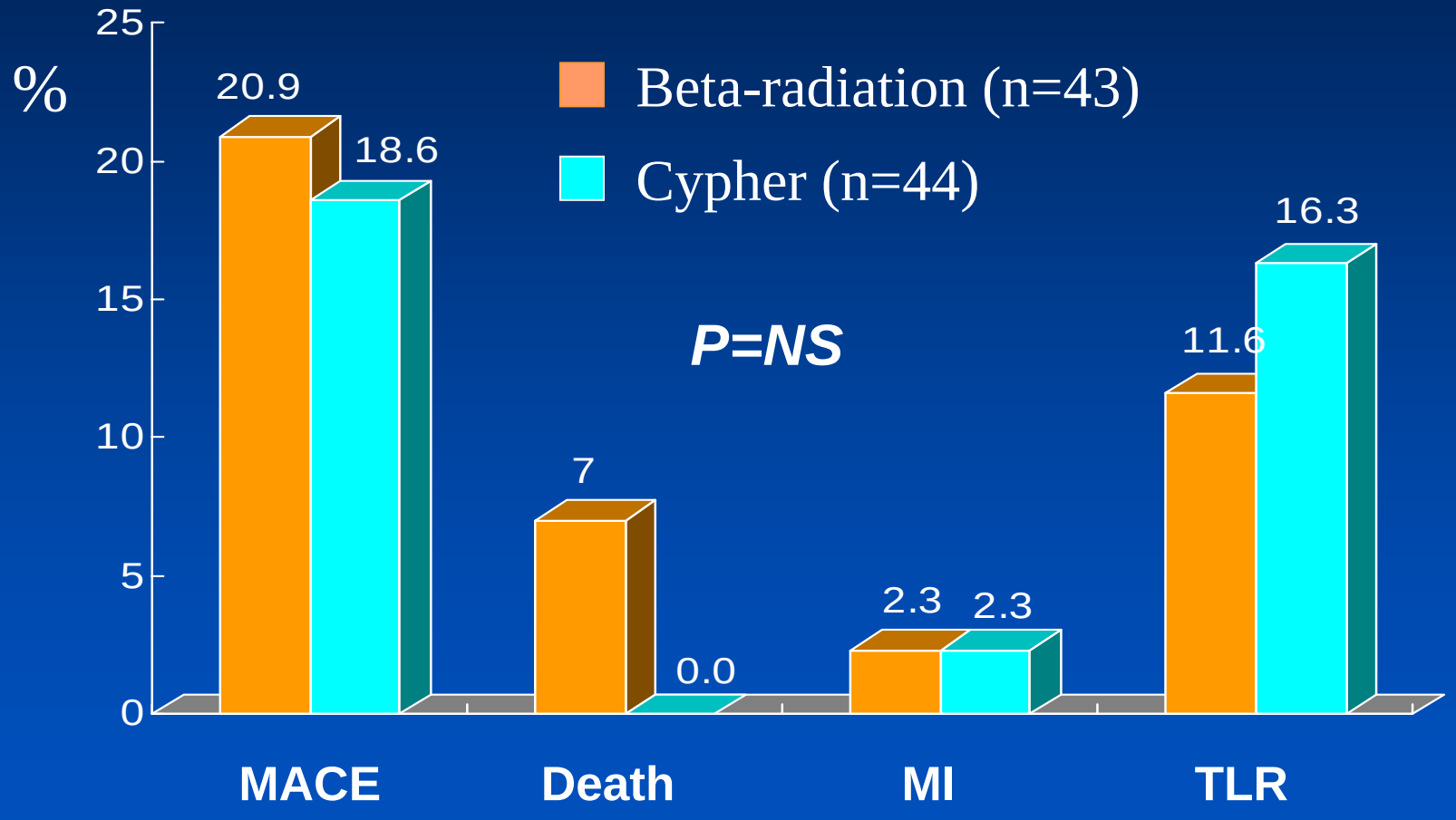
A Kastrati et al. JAMA 2005;293:165

Role of DES for ISR

DES vs. Brachytherapy

Cypher vs. RT for ISR

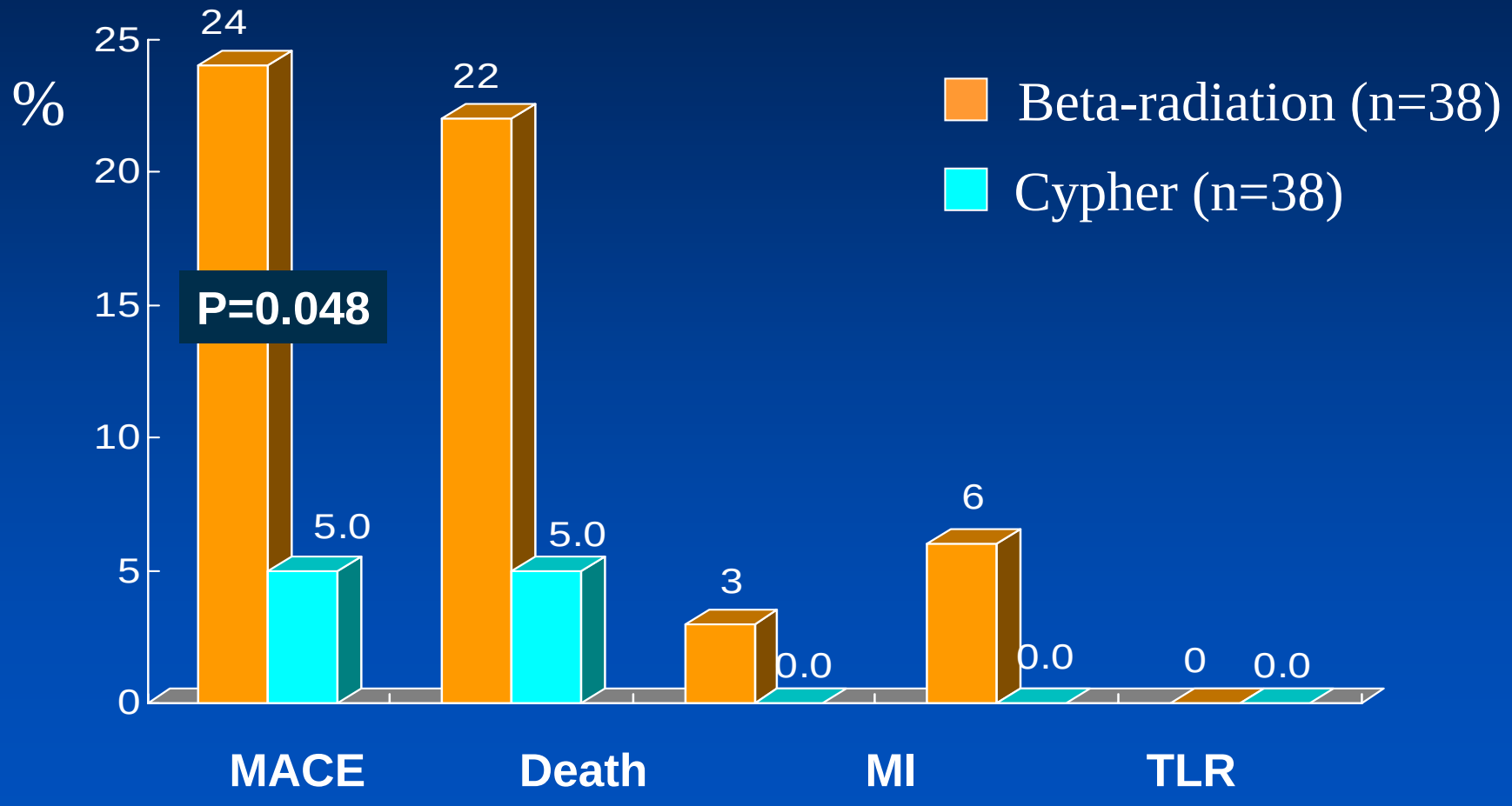
9-Month Outcomes in RESEARCH Registry



Saia F et al. Catheter Cardiovasc Interven 2004;62:283

Cypher vs. RT for ISR

Non-randomized comparison at 11 months

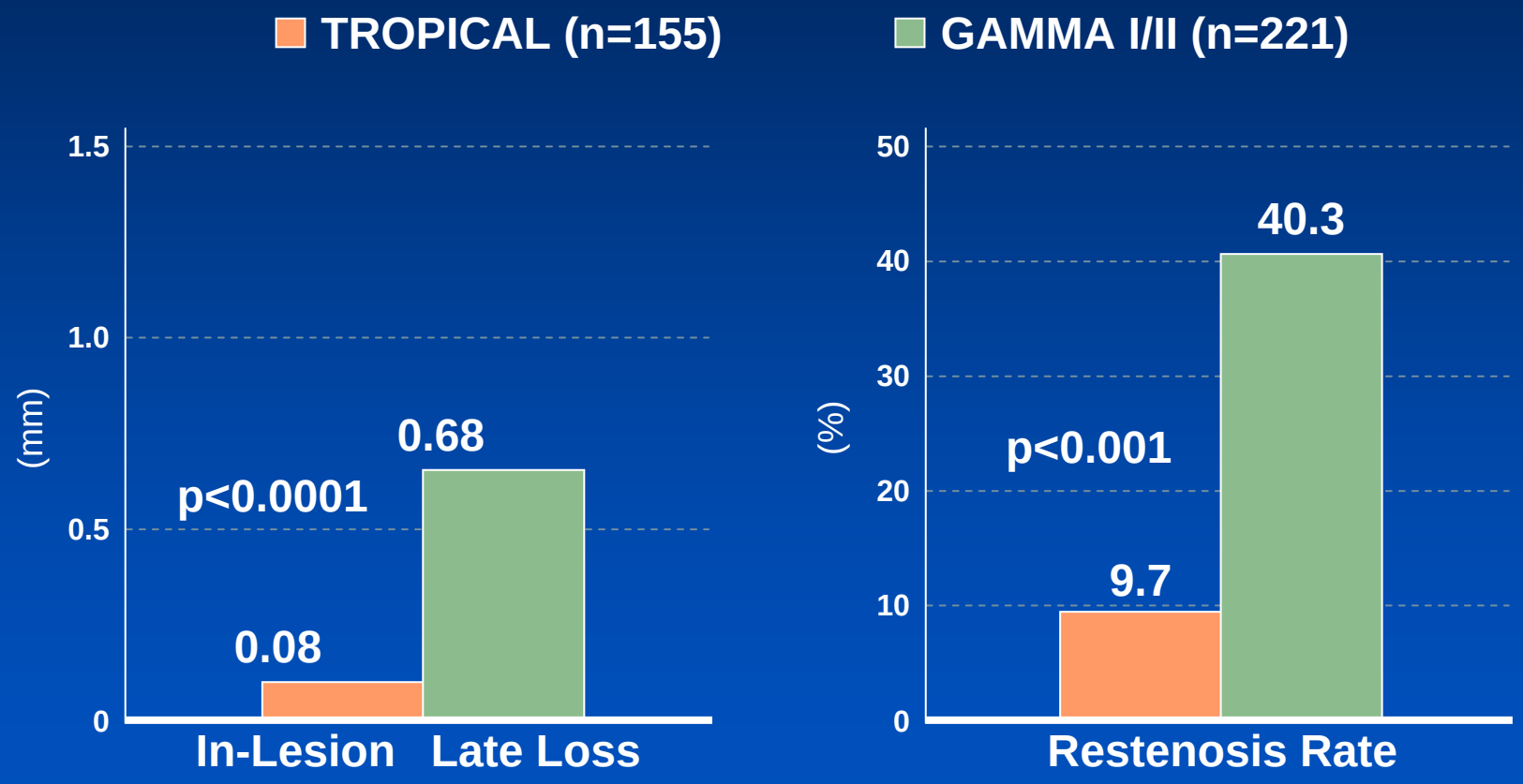


Goy JJ et al. Heart 2004;90:1491

Cypher vs. Gamma Radiation

TROPICAL

CYPHER vs brachytherapy (GAMMA I/II - historical control)

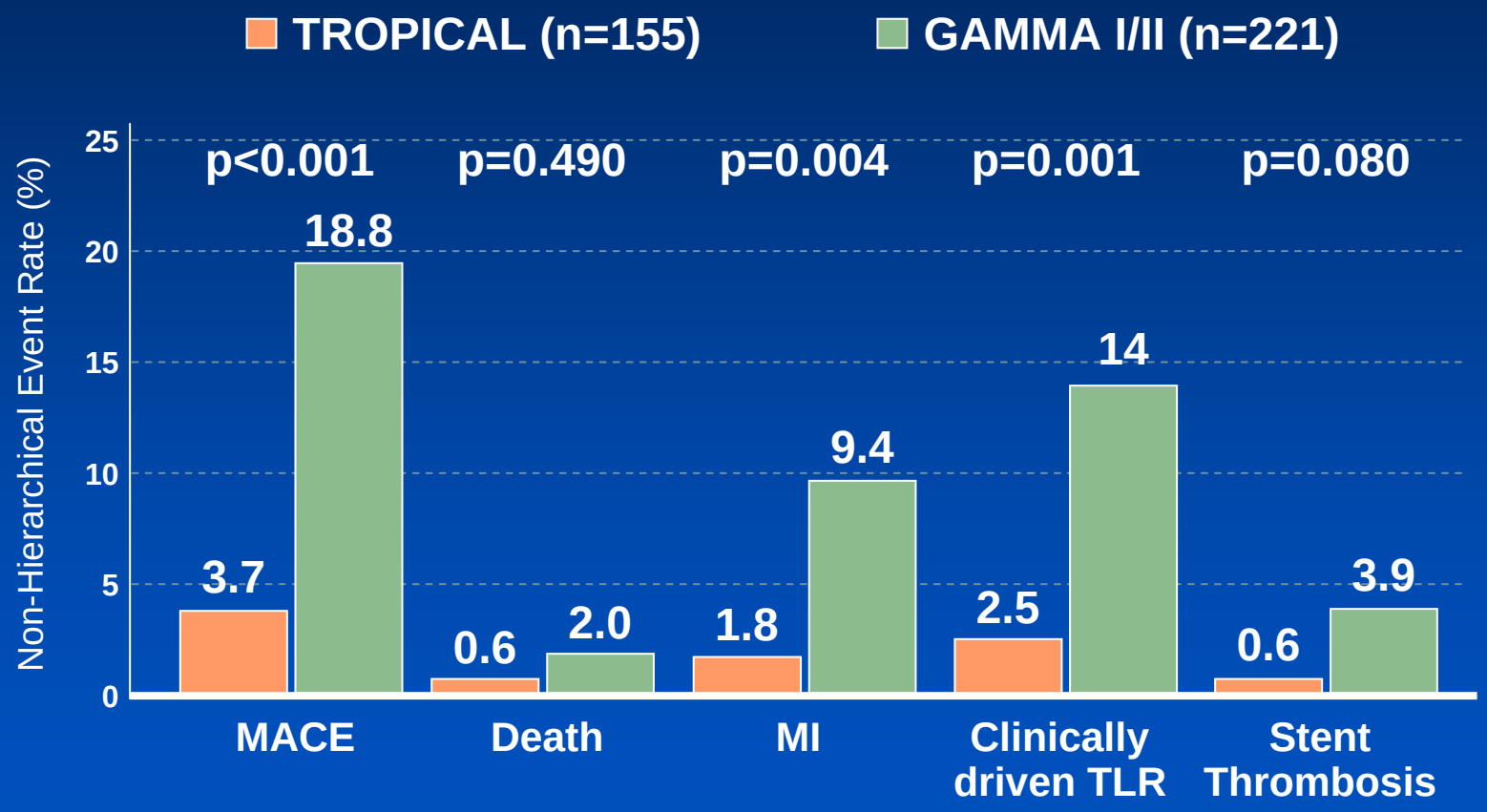


Neumann F-J, Desmet W. Euro PCR 2004.

Cypher vs. Gamma Radiation

TROPICAL

Clinical F/U at 6 Months



Neumann F-J, Desmet W. Euro PCR 2004.

RT vs. Non-polymer PES

In-Stent Restenosis

Matched-pair comparison

Paclitaxel-Eluting Stent Implantation (25 lesions, 22 patients)

Beta-radiation with Beta-Cath Device (Strontium 90) (25 lesions, 25 patients)

Complete lesion coverage with PES ($3.0 mcg/mm^{2)}$)

Radiation dose of ***21.1 ±3.1 Gy at a depth of 2.0 mm*** into the vessel wall

Radke PW et al. European Heart Journal 2004;25:920-5

RT vs. Non-polymer PES

	PES (n=22 pts)	RT (n=25 pts)	p
Age, years	61±10	60±13	0.44
Diabetes, n (%)	5(23)	5(20)	
Hyperlipidemia, n (%)	21(84)	23(92)	
Hypertension, n (%)	17(68)	23(92)	
Type of ISR, n (%)			
Focal	6(24)	6(24)	1.0
Diffuse ISR	12(48)	12(48)	1.0
Proliferative	6(24)	6(24)	1.0
Total occlusion	1(4)	1(4)	1.0

Radke PW et al. European Heart Journal 2004;25:920-5

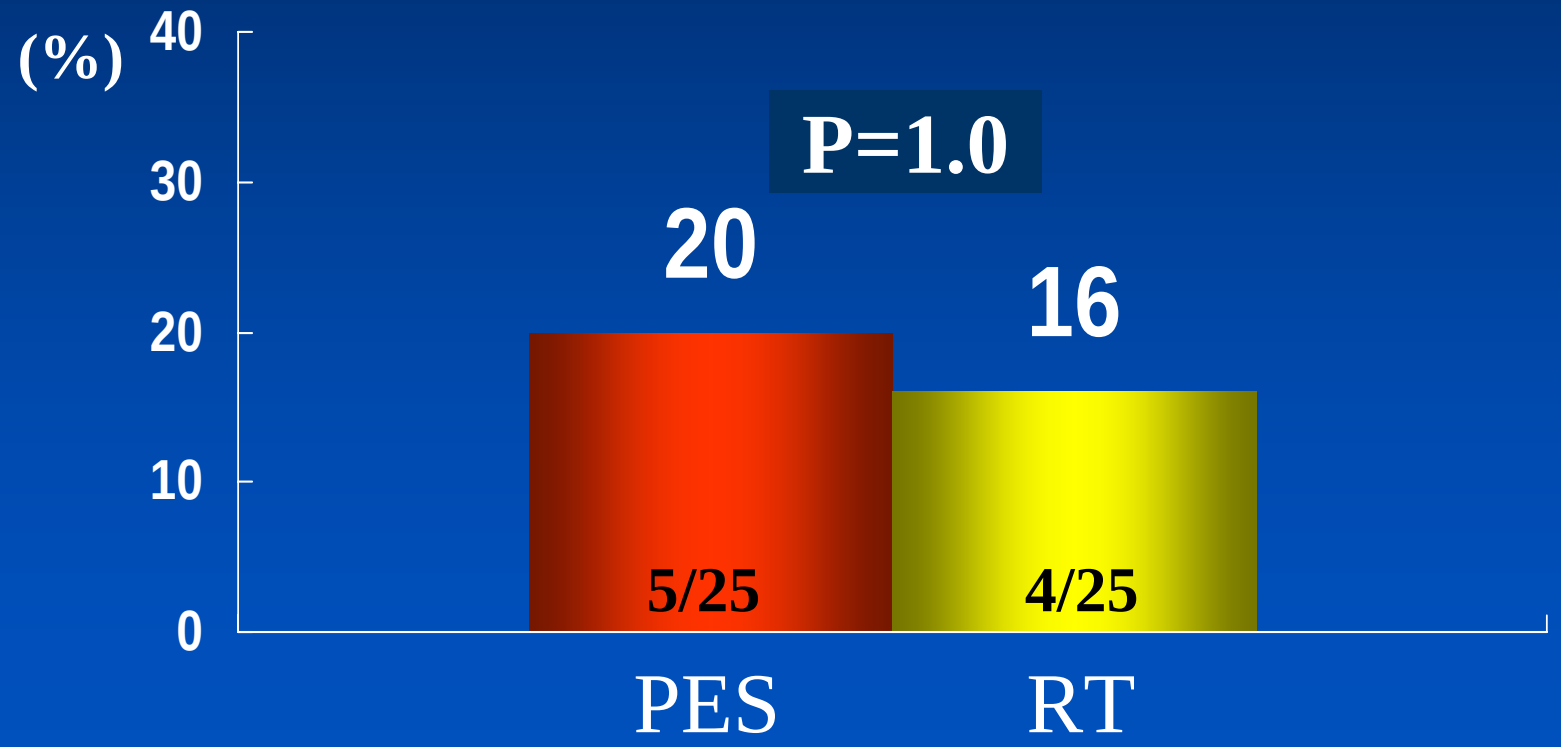
RT vs. Non-polymer PES

	PES (n=25)	RT (n=25)	p
Reference vessel, mm	2.78±0.57	2.76±0.44	0.65
Lesion length, mm	13.3±5.0	12.9±4.8	0.80
Minimal lumen diameter			
Preprocedure, mm	0.91±0.43	0.90±0.28	0.96
Postprocedure, mm	2.26±0.61	2.17±0.37	0.51
Follow-up, mm	1.83±0.67	1.35±0.61	0.16
Acute gain, mm	1.35±0.61	1.26±0.47	0.59
Late loss, mm	0.42±0.50	0.56±0.65	0.47

Radke PW et al. European Heart Journal 2004;25:920-5

RT vs. Non-polymer PES

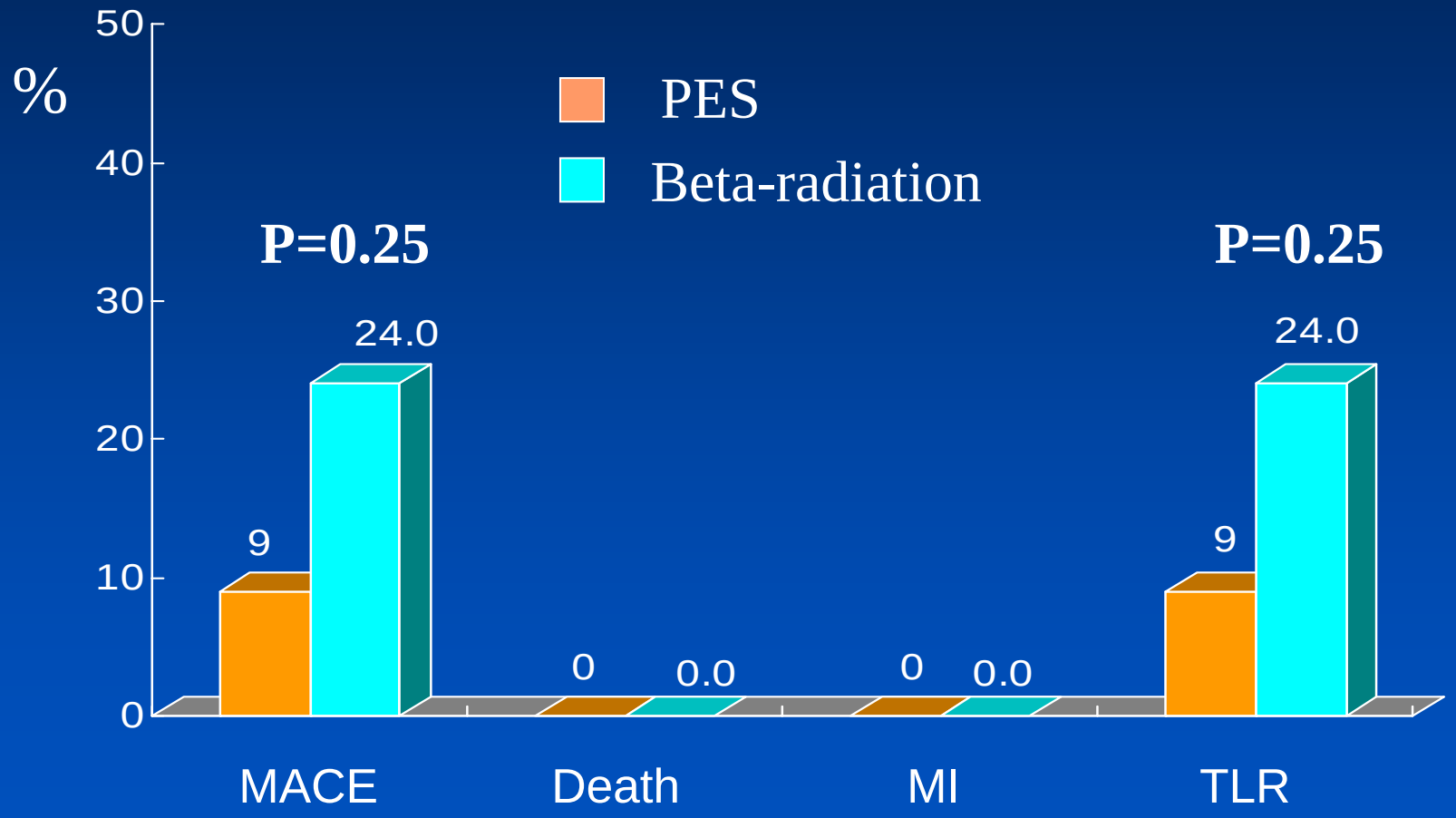
6-Month Restenosis Rate (in-segment analysis)



Radke PW et al. European Heart Journal 2004;25:920-5

RT vs. Non-polymer PES

12-Month Clinical Outcomes

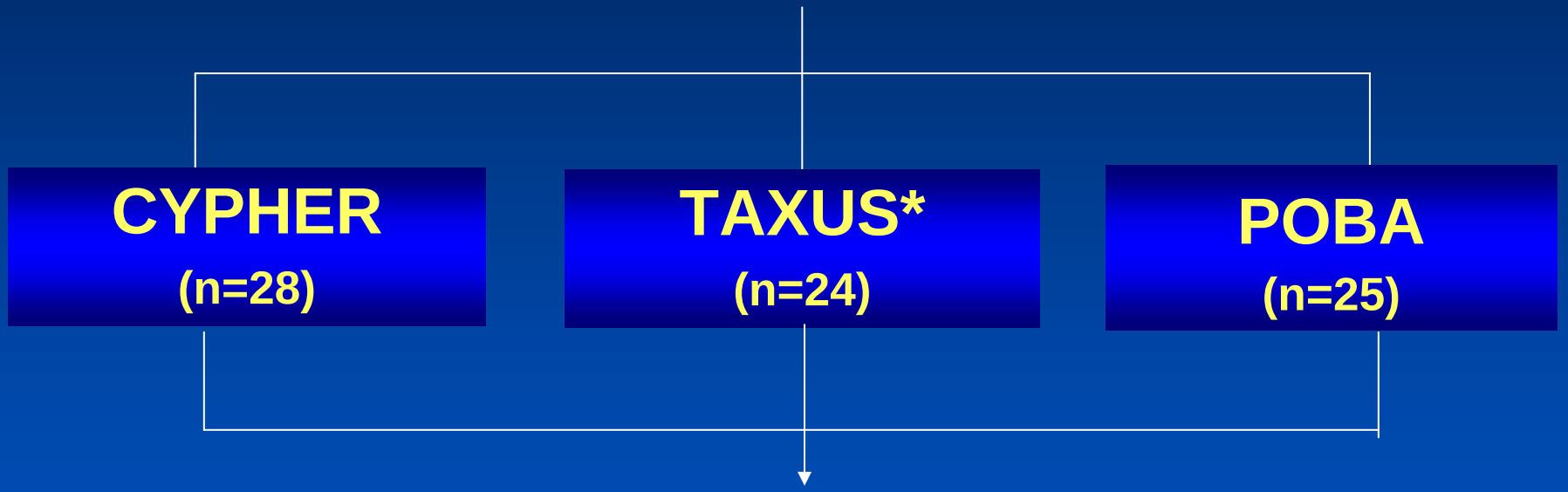


Radke PW et al. European Heart Journal 2004;25:920-5

Matched Comparison

From January 1998 - to April 2003

In-stent restenosis



6-Mo angiographic restenosis(in-segment) & 9-Mo clinical outcomes

***Non-polymer paclitaxel-eluting stent**

Iofina E et al. Catheter Cardiovasc Interv 2005;64:28-34

Baseline Characteristics

	SES (n=28)	PES (n=27)	POBA (n=26)	p
Reference vessel, mm	2.57	2.53	2.47	NS
Lesion length, mm	10.6	13.7	10.6	NS
PreMLD, mm	0.60	0.87	0.63	0.071
PostMLD(in-stent), mm	2.37	2.54	1.78	<0.001
PostMLD(in-lesion), mm	2.17	2.30	1.82	0.005
Focal ISR	8(29%)	6(22%)	8(31%)	0.346
Diffuse intrastent	13(46%)	13(48%)	11(42%)	0.615
Proliferative ISR	3(11%)	7(26%)	5(19%)	0.352
Total occlusion	4(14%)	1(4%)	2(7%)	0.375

Iofina E et al. Catheter Cardiovasc Interv 2005;64:28-34

Randomized Comparison of RT vs. SES for Diffuse ISR from Multicenter Study in Korea

Compared the efficacy and safety of sirolimus-eluting stent implantation versus β-radiation therapy with ^{188}Re-MAG$_3$- filled balloon for diffuse ISR in a prospective randomized manner.

SES vs. Brachytherapy

From March 2003 to July 2004

Diffuse ISR (n=129)

Randomization (1:1)

Cutting balloon angioplasty

Sirolimus-Eluting Stent (n=65, SES group)

* **Coronary Brachytherapy (n=64, RTx group)**

Angiography follow-up
Clinical follow-up

* One patient failed to receive RT due to isotope spillage before RT

Baseline Demographics

	SES	RTx	P
Patients	65	64	
Age, yr	60.5±9.3	59.1±8.3	0.420
Male	50 (76.9)	52 (81.3)	0.546
Hypertension	41 (63.1)	33 (51.6)	0.186
Diabetes mellitus	20 (30.8)	20 (31.3)	0.953
Hypercholesterolemia (total cholesterol ≥ 200 mg/dL)	5 (7.7)	5 (7.8)	0.980
Current smoking	21 (32.3)	15 (23.4)	0.367
Left ventricular EF, %	58.4±7.8	59.0±9.1	0.722

Baseline Demographics

	SES	RTx	P
Patients	65	64	
Clinical manifestation			0.183
Stable angina	31 (47.7)	38 (59.4)	
Acute coronary syndrome	34 (52.3)	26 (40.6)	
Multi-vessel disease	32 (49.2)	22 (34.4)	0.228
Target vessel			0.205
Left anterior descending	39 (60.0)	32 (50.0)	
Left circumflex artery	9 (13.8)	6 (9.4)	
Right coronary artery	17 (26.2)	26 (40.6)	

Baseline QCA Results

	SES	RTx	P
Patients	65	64	
Reference diameter, mm	2.98±0.58	2.88±0.54	0.325
Lesion length, mm	30.0±11.2	31.9±16.2	0.447
MLD, mm	0.83±0.44	0.79±0.38	0.626
DS, %	71.2±13.9	72.3±12.7	0.666

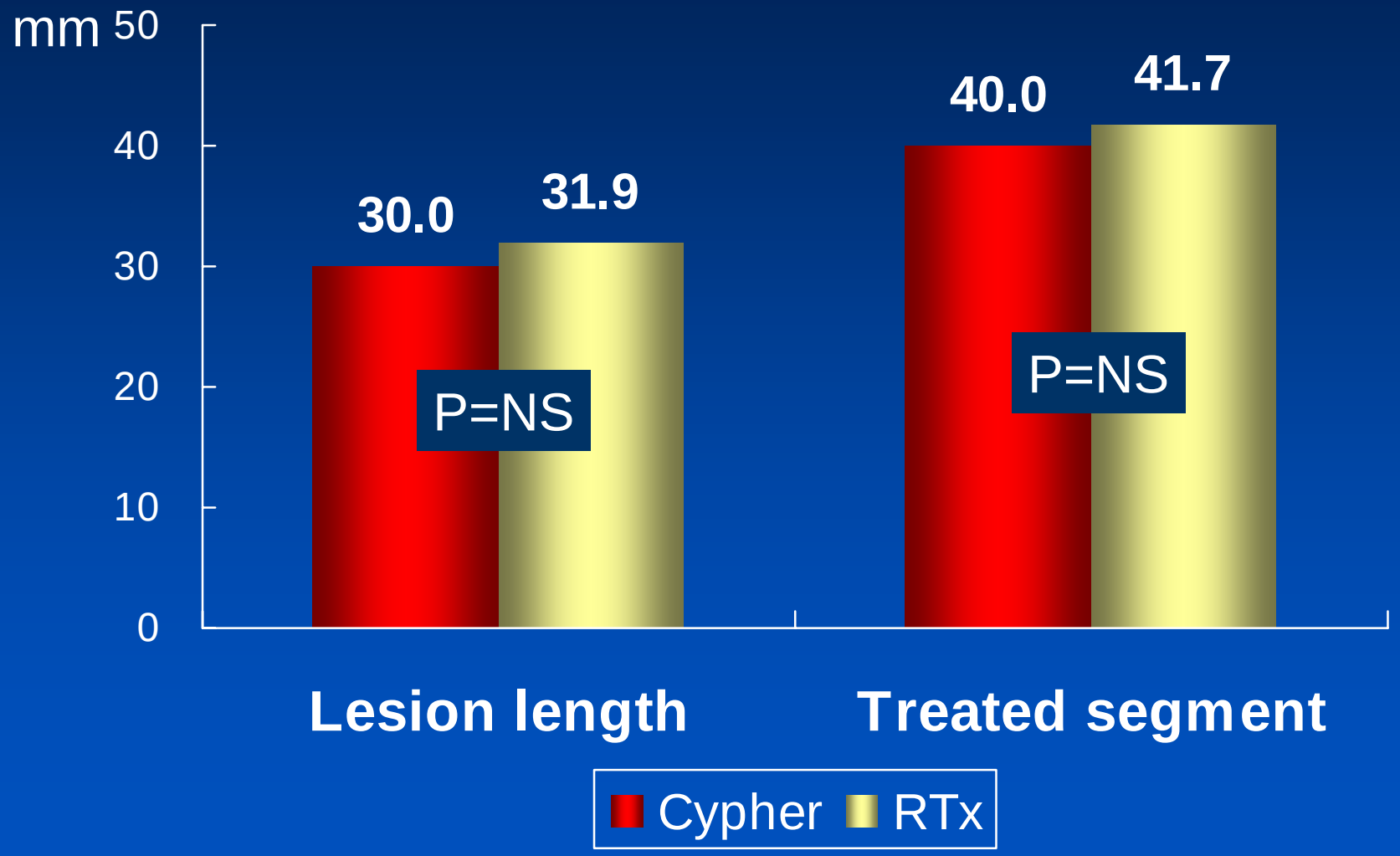
Procedural Findings in RTx Group

Beta-radiation therapy	n=64
Radiated segment, mm	41.7±15.0
Overlap of balloon	16 (25)
Fractionation	54 (84.3)
Exposure time, sec	265.3±178.3
Additional stenting (BMS:4, SES:7)	11 (17.2)

Procedural Findings in SES Group

SES implantation	n=65
Stents used	106
Stent overlapping	35 (53.8)
Stents per lesion	1.6±0.7
Total stent length, mm	40.0±13.7
Final balloon size, mm	3.3±0.4
Inflation pressure, mm	15.2±3.8

Lesion Length & Treated Segment



QCA Results after Procedure

	SES	RTx	P
Patients	65	64	
MLD, mm	2.97±0.54	2.52±0.50	<0.001
DS, %	-0.6±13.0	11.7±12.9	<0.001
Acute gain, mm	2.12±0.57	1.73±0.52	<0.001

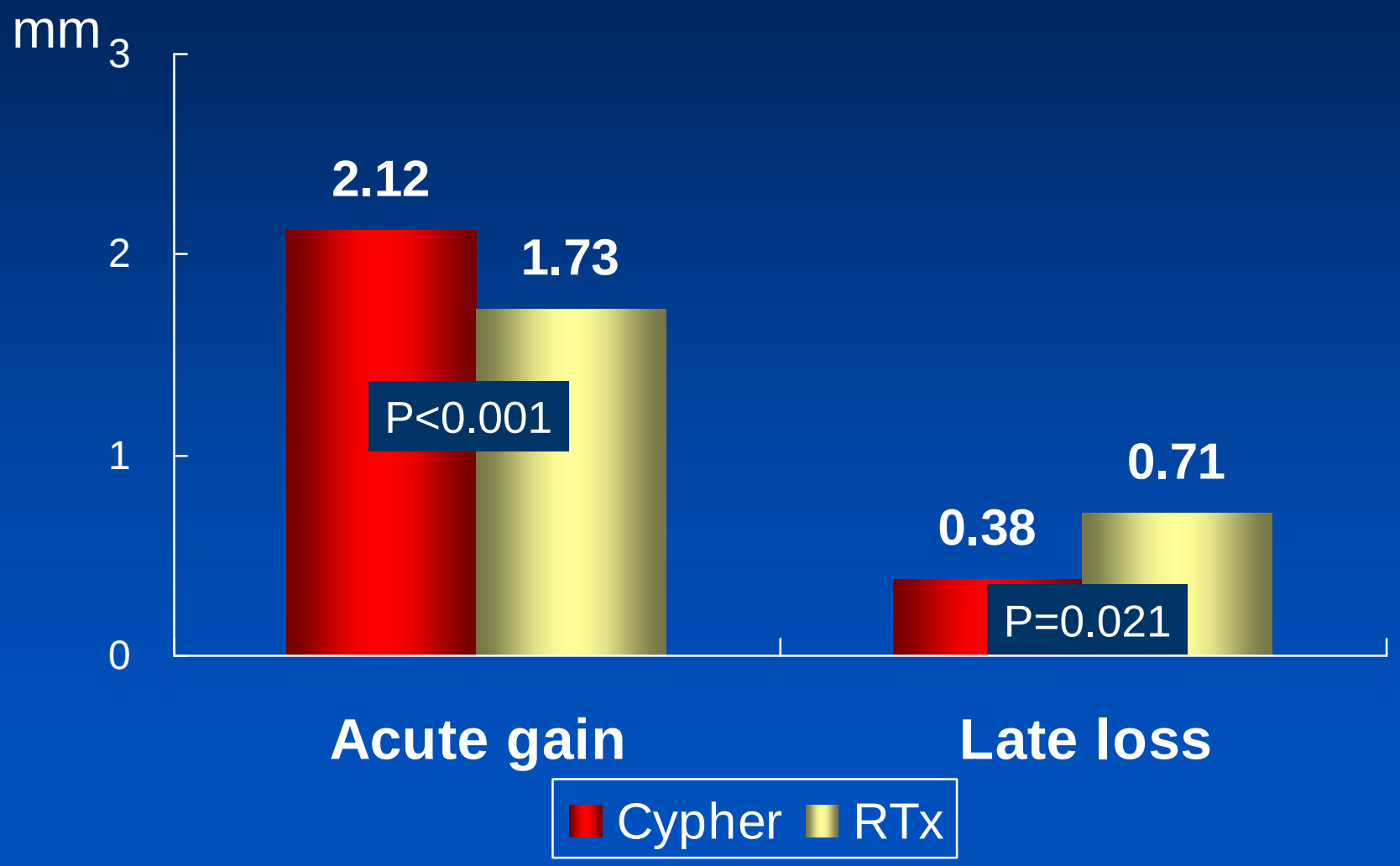
In-Hospital Outcomes

	SES	RTx	P
Patients	65	64	
Angiographic success	63 (97)	58 (91)	0.164
Death	0	0	1.0
Myocardial infarction	1 (1.5)	2 (3.1)	0.619
Q-MI	0	0	
Non-Q MI	1 (1.5)	2 (3.1)	
Stent thrombosis	0	0	1.0
TLR	0	0	1.0

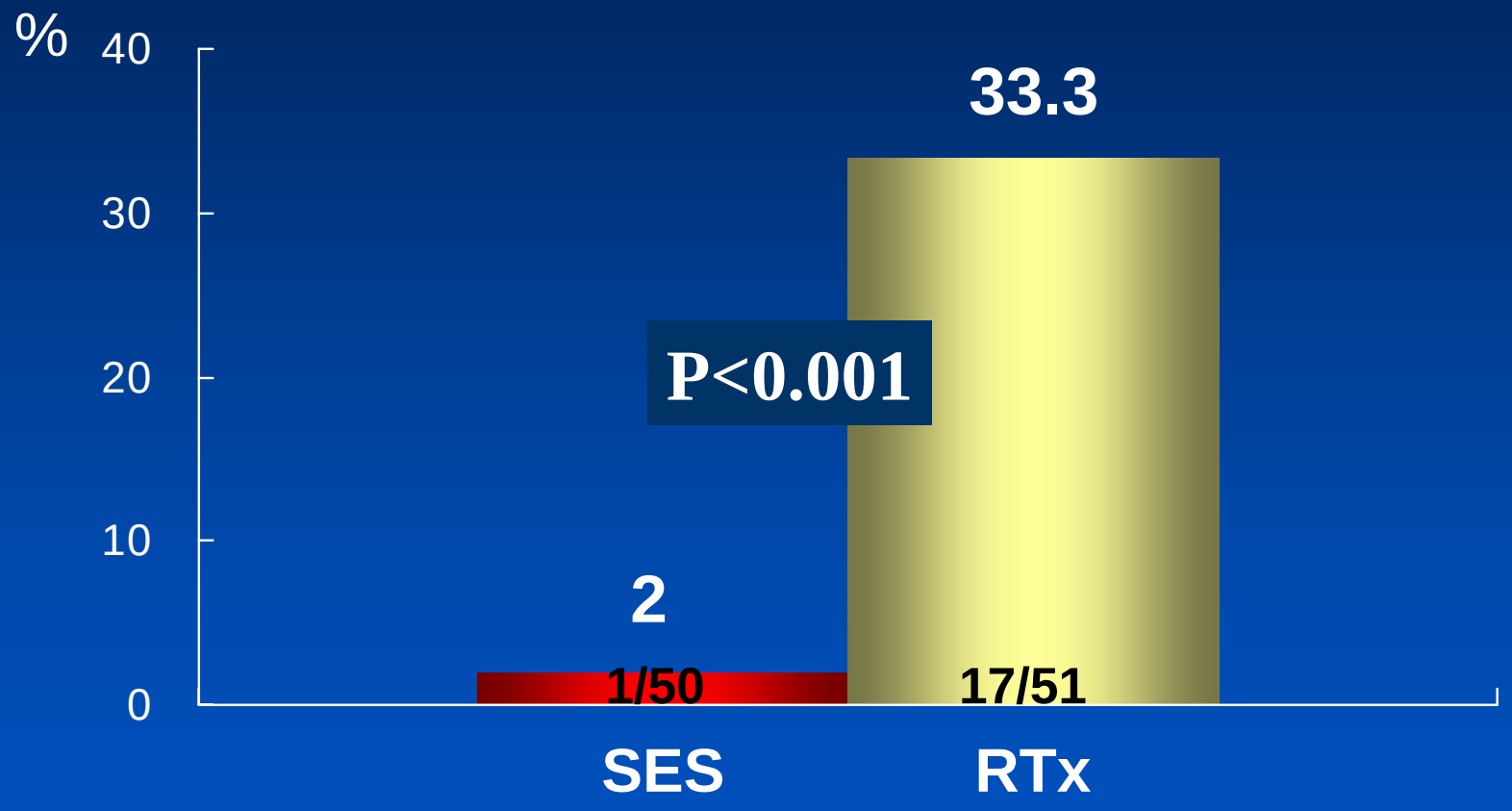
QCA at Follow-up

	SES	RTX	P
Angio F/U rate	50/64 (78%)	51/62 (82%)	
Reference, mm	2.87±0.50	2.72±0.41	0.113
MLD, mm	2.66±0.67	1.74±0.81	<0.001
DS, %	6.89±20.25	32.77±28.20	<0.001
Late loss, mm	0.38±0.57	0.71±0.84	0.021

Acute Gain & Late Loss



Restenosis Rate at 6 Months



Clinical Outcomes at 9 Months

	SES	RTx	P
Patients	57	57	
Death	0	0	1.0
MI	0	0	1.0
Stent thrombosis	1 (1.7%) *	0	1.0
TLR	2 (3.5%)	9 (15.8%)	0.053
MACE	2 (3.5%)	9 (15.8%)	0. 053

* Late stent thrombosis, 6 months after index procedure

Restenosis Pattern and TLR

Sirolimus-Eluting Stent (restenosis: 1 patient)

Distal focal ISR involving distal edge

Cutting balloon

The other 1 TLR was due to late stent thrombosis

Coronary Brachytherapy (restenosis: 17 patients)

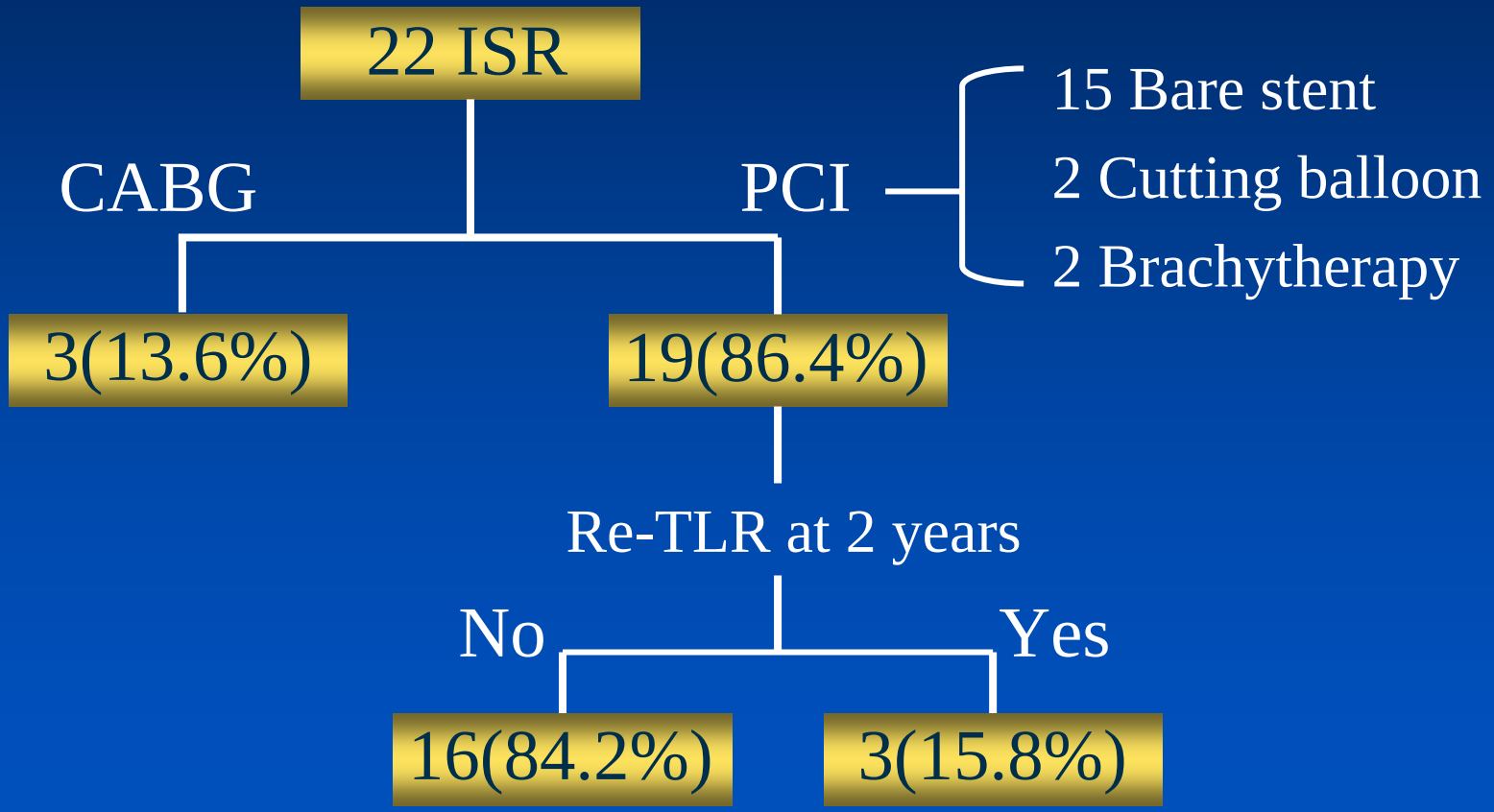
Focal ISR : 9
Diffuse ISR : 4
Total occlusion : 4

SES implantation : 8
CABG :1

Treatment for DES Failure

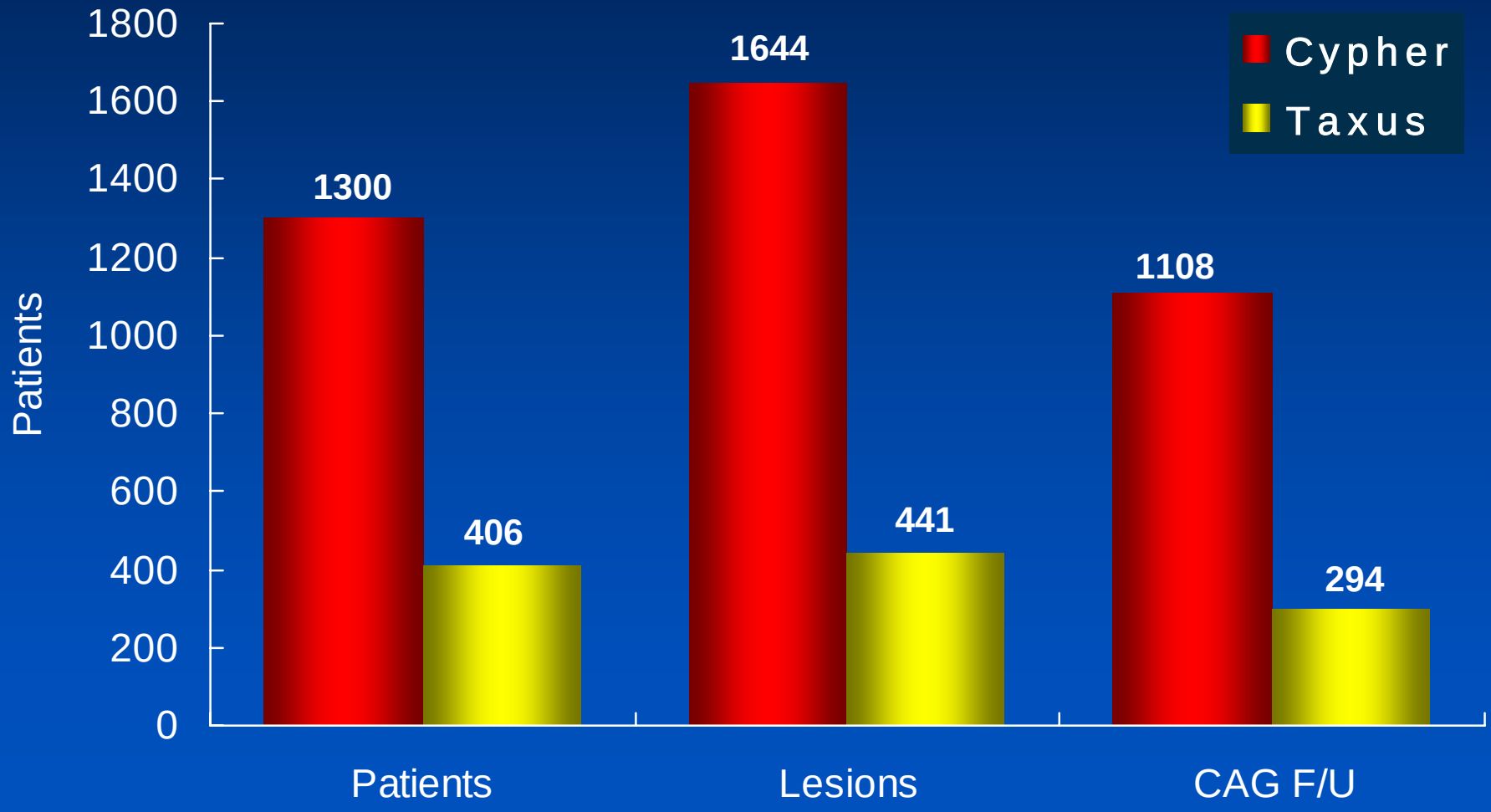
Fate of ISR in DES

22 ISRs of 528 patients in SIRIUS



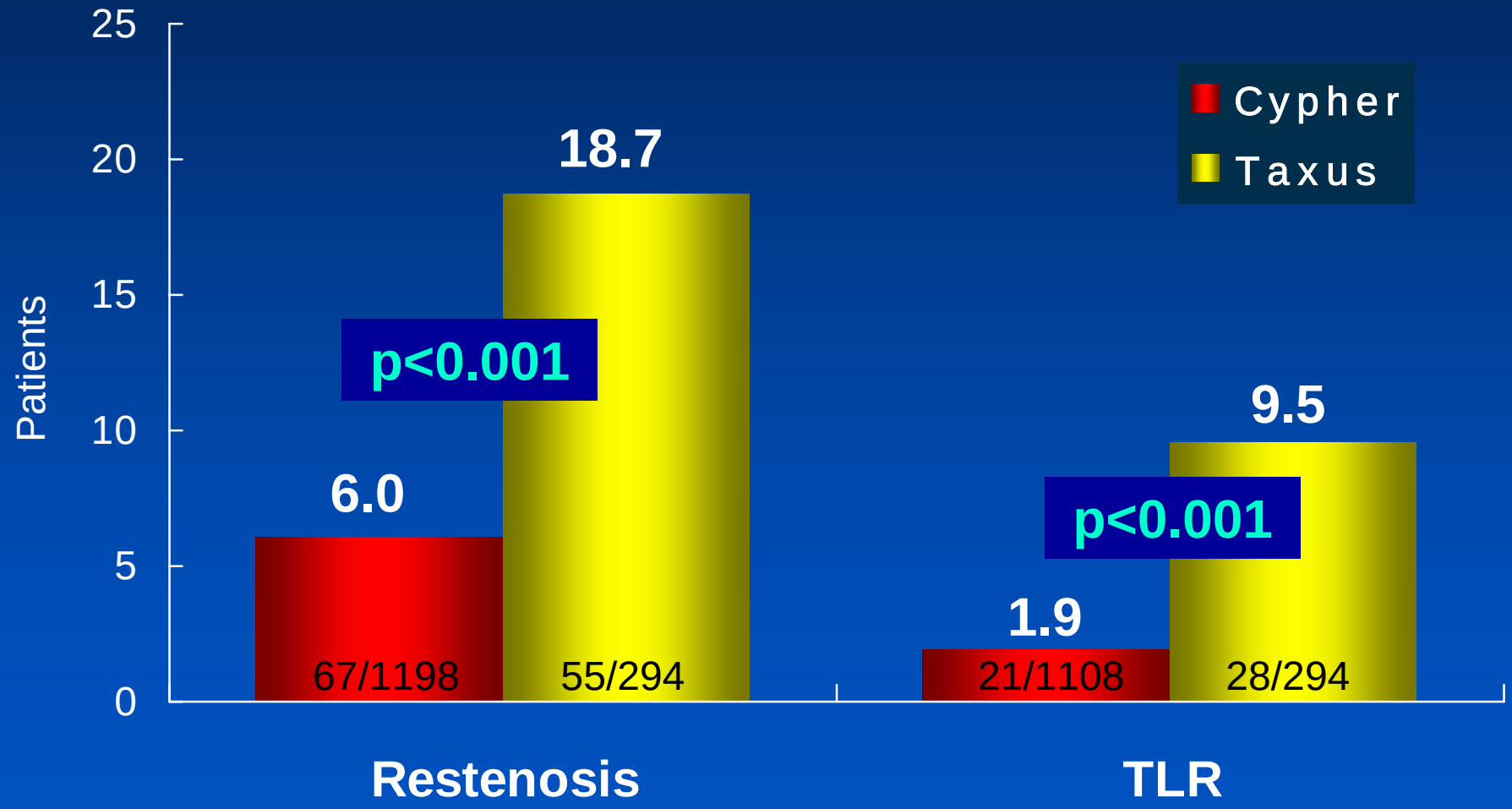
DES Implantation in AMC

Feb 2003 ~ Nov 2004



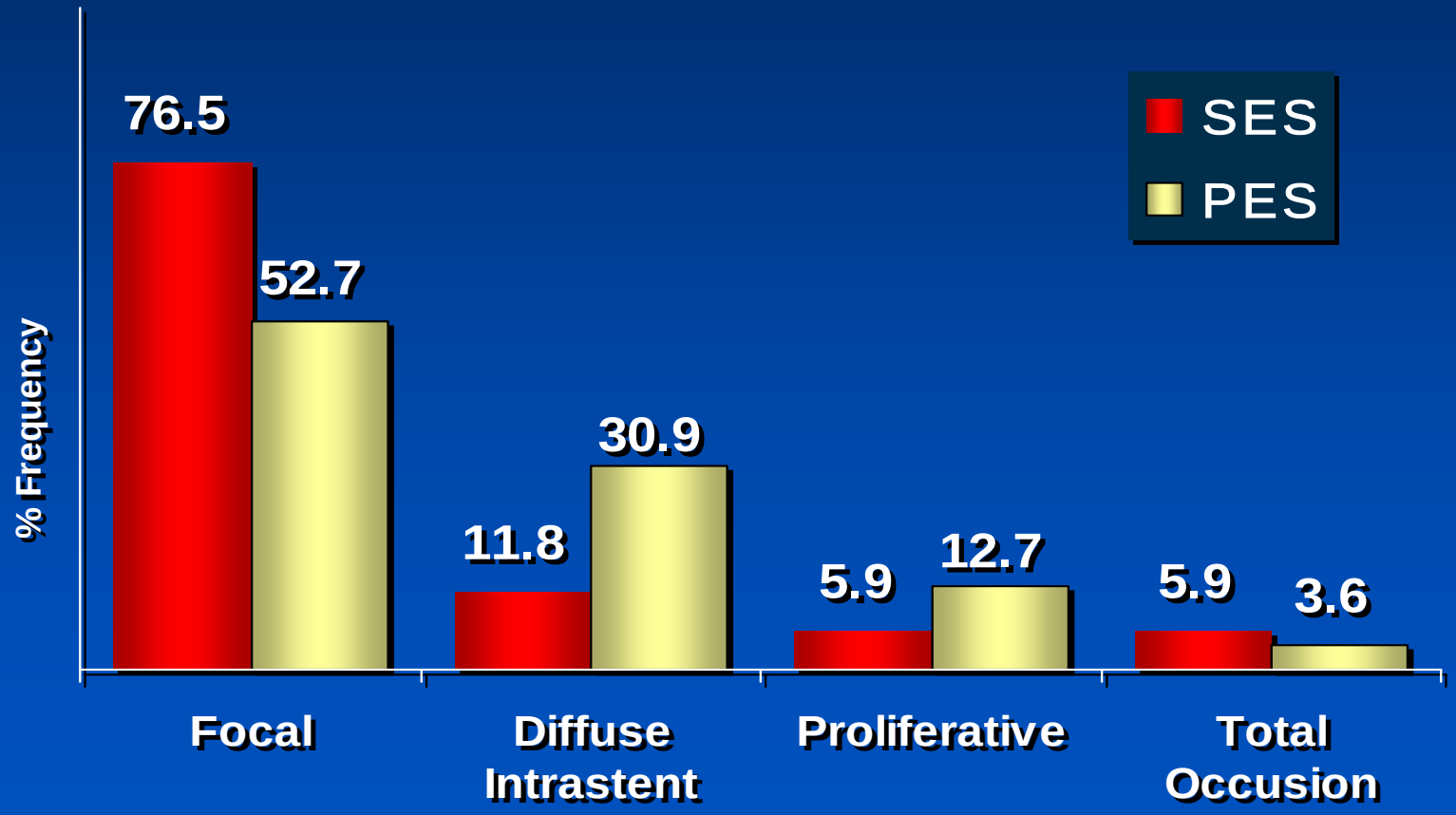
ISR after DES Implantation

Feb 2003 ~ Nov 2004



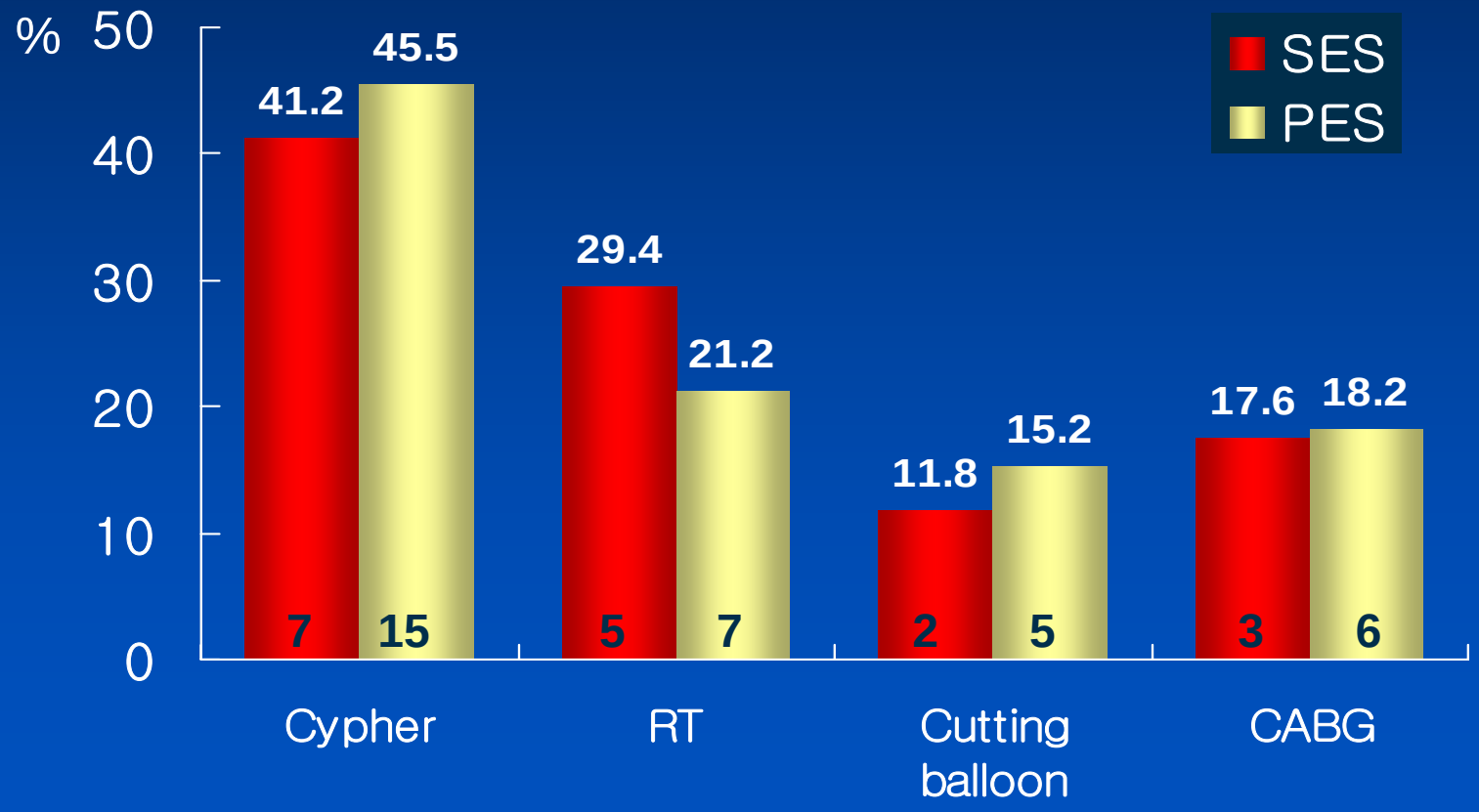
Patterns of ISR

Total 67(SES) / 55 (PES) restenosis lesions



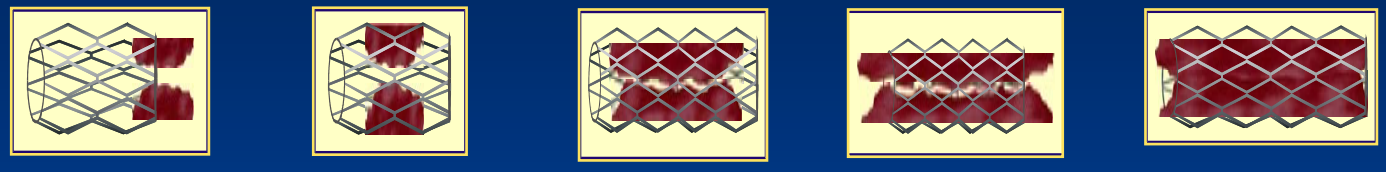
Treatment for DES failure

Total 17 (SES) / 33 (PES) TLRs



ISR patterns and TLR strategies

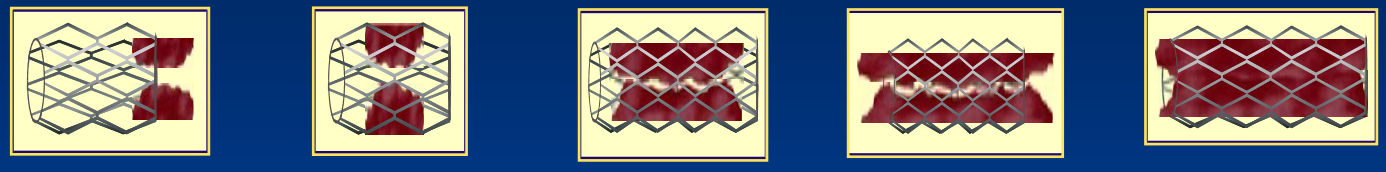
Total



Cypher	13	14	3	2	0	**32 (50.8%)**
RT	0	4	5	3	0	**12 (19.0%)**
Cutting	1	7	1	0	0	**9 (9.5%)**
CABG	2	2	2	2	2	**10 (15.9%)**
	16 (25.4%)	**24 (42.9%)**	**11 (17.5%)**	**7 (11.1%)**	**2 (3.2%)**	**63**

ISR patterns and TLR strategies

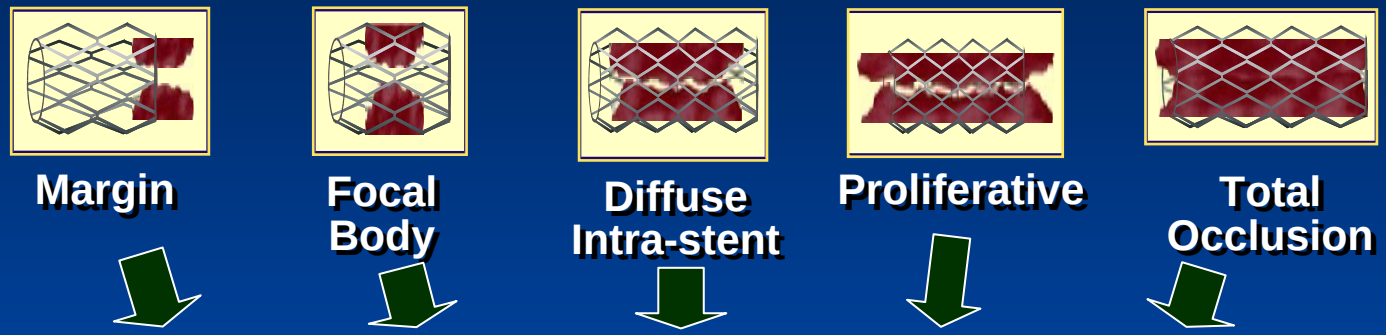
SES



Cypher	7	0	0	0	0	**7 (41.2%)**
RT	0	2	2	1	0	**5 (29.4%)**
Cutting	1	1	0	0	0	**2 (11.8%)**
CABG	1	0	1	0	1	**3 (17.6%)**
	9 (52.9%)	**3 (17.6%)**	**3 (17.6%)**	**1 (5.9%)**	**1 (5.9%)**	**17**

ISR patterns and TLR strategies

PES



Cypher	1	10	3	1	0	**15 (45.5%)**
RT	0	1	4	2	0	**7 (21.2%)**
Cutting	0	4	1	0	0	**5 (15.2%)**
CABG	2	1	0	2	1	**6 (18.2%)**
	3 (9.1%)	**16 (48.5%)**	**8 (24.2%)**	**5 (15.2%)**	**1 (3.0%)**	**33**

Conclusions

- Focal ISR pattern was most frequent after SES implantation and was easily treated by repeat SES stenting or cutting balloon.
- Until now, no statement can be made regarding the most appropriate treatment strategy for SES failure.
- Therefore, treatment decision should depends on each patient and each lesion.