Role of IVUS and Benefits in DES Era

Can We Reach Optimal DES Expansion With Conventional Stent Delivery System in Long Diffuse Lesion?

Proven Safety and Best Practice in BES

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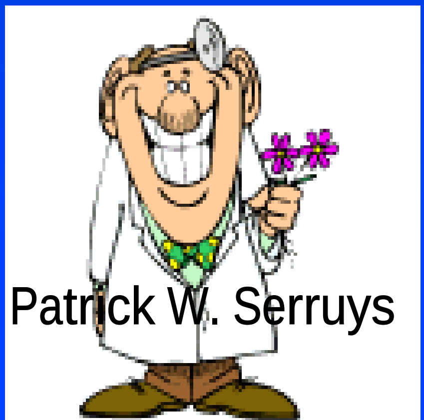
Angioplasty Summit 2007-TCT Asia Pacific

Wednesday, April 25 ~ Friday, April 27, 2007
The Convention Center of Sheraton Grand Walkerhill Hotel, Seoul, Korea

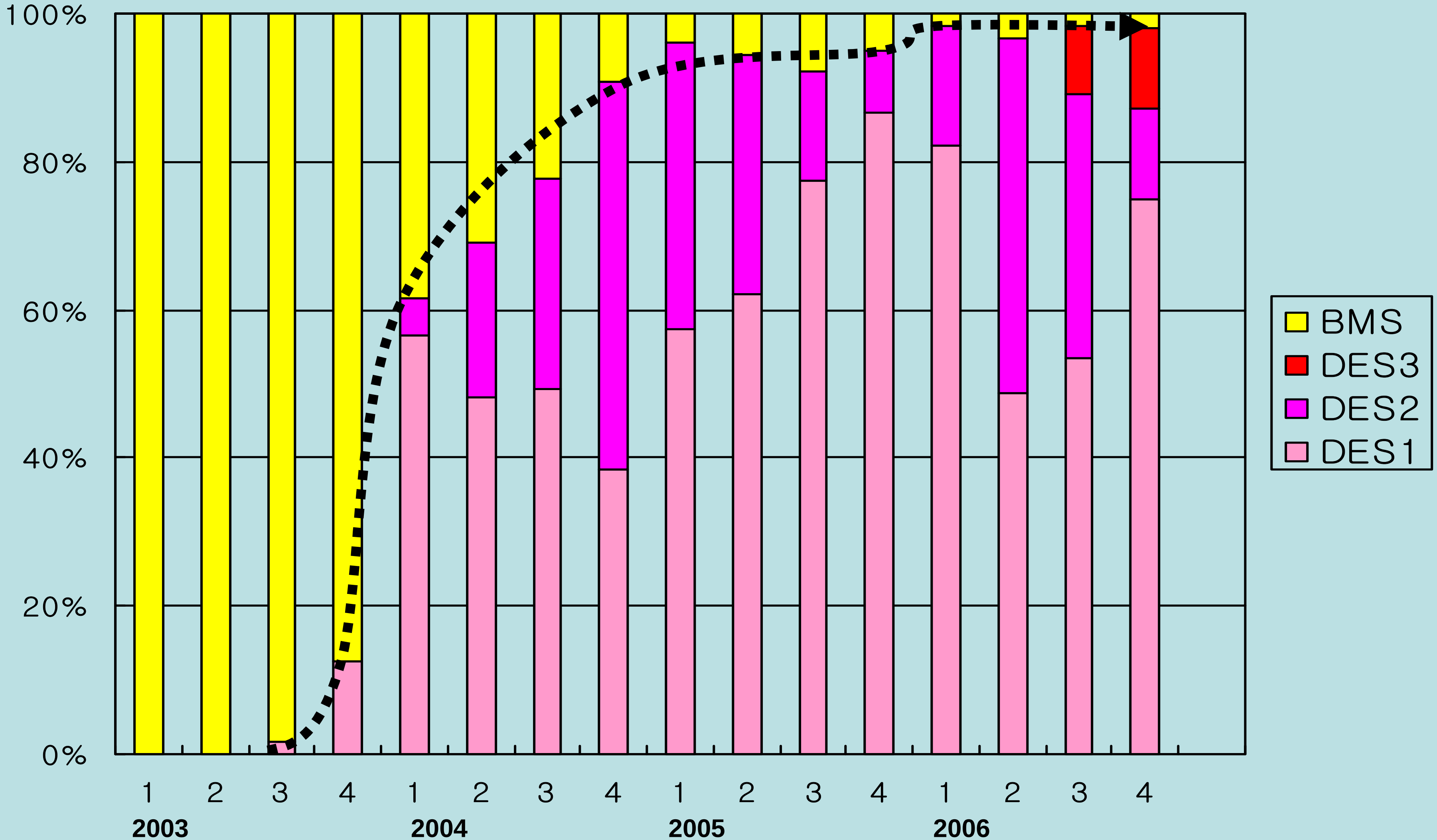
Are Drug-Eluting Stents Changing Your Daily Practice?

After 24 months of DES for all patients, the point of no return has been reached and we will not come back to bare stent.



Thank you

DES Penetration in Ajou University Medical Center



Ajou University Database

DES changes our pattern of PCI

We are getting more aggressive ..

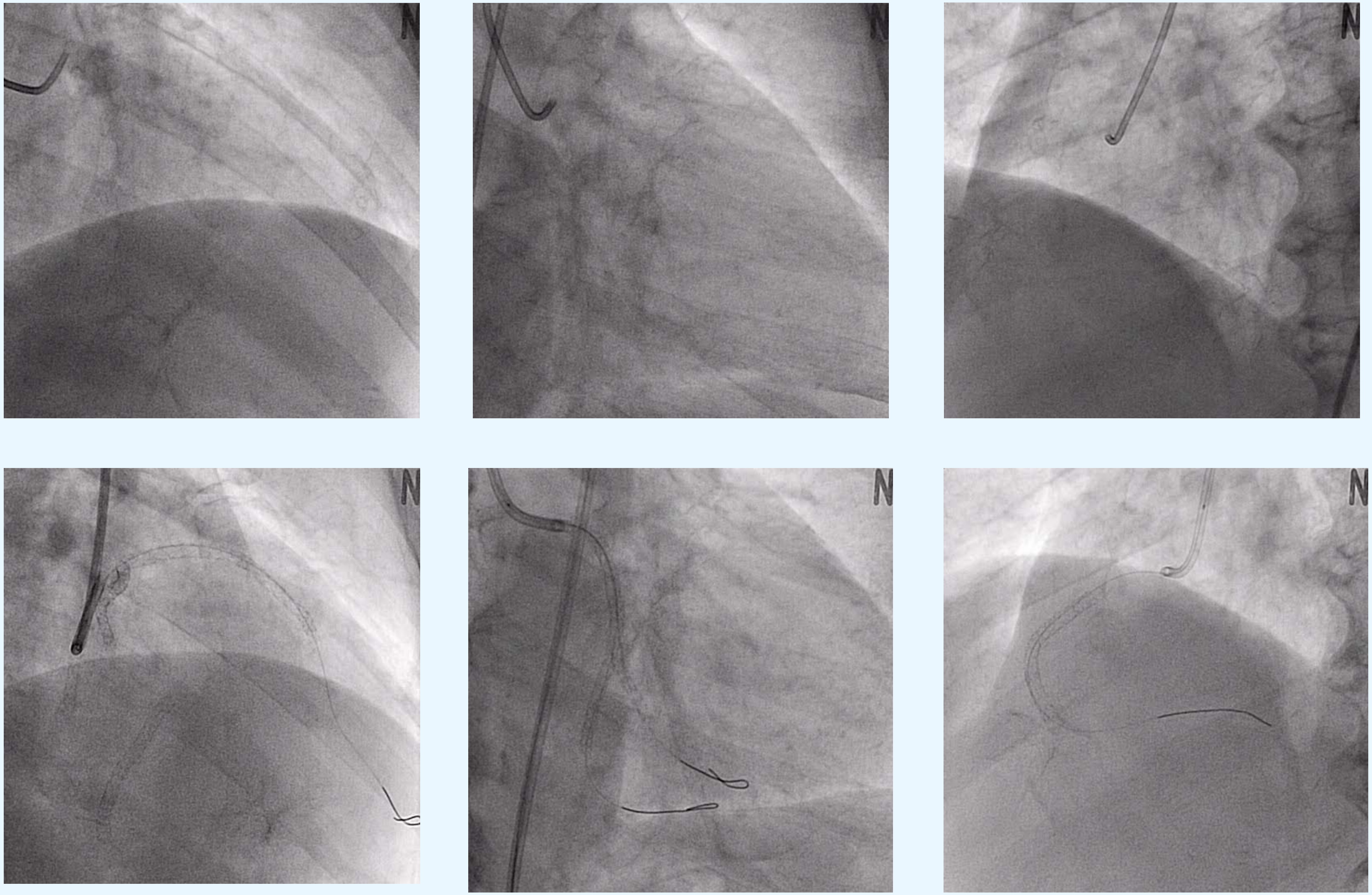
Complex Lesions

Long Diffuse Lesions

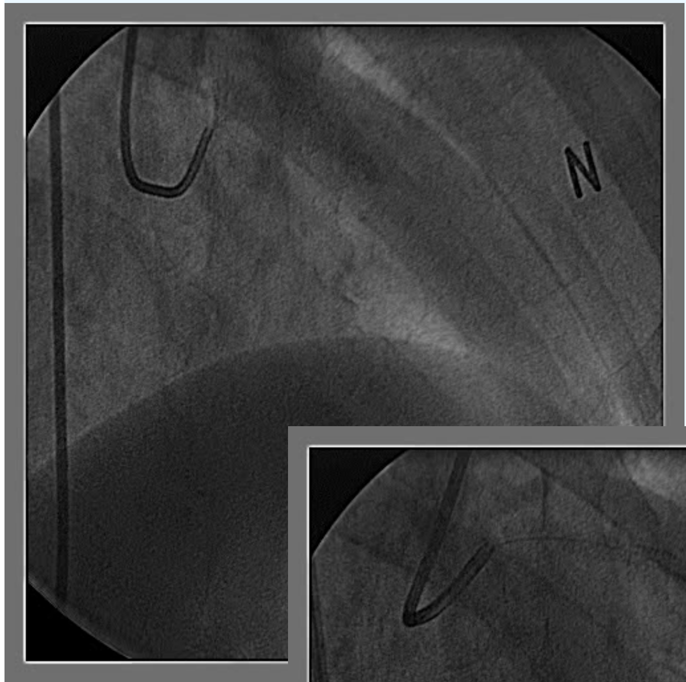
Small Vessels

Diabetic Patients

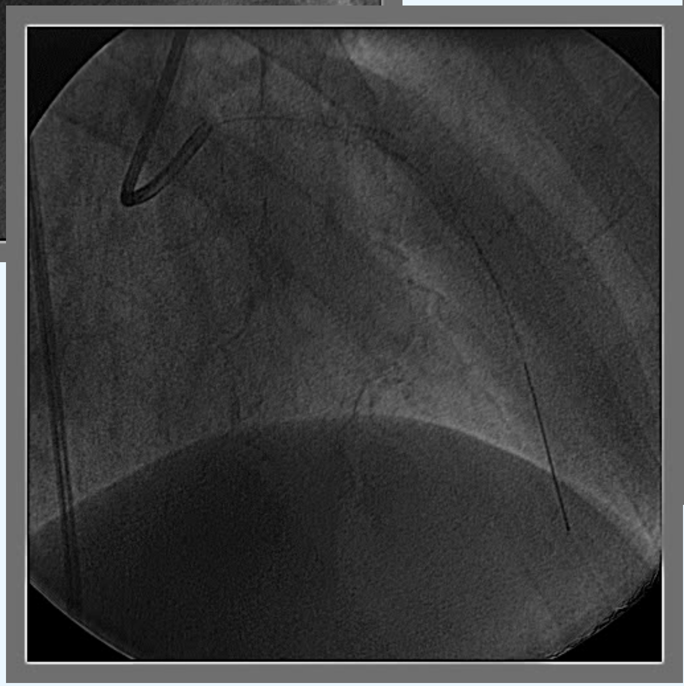
DES Mania .. Metal Jacket



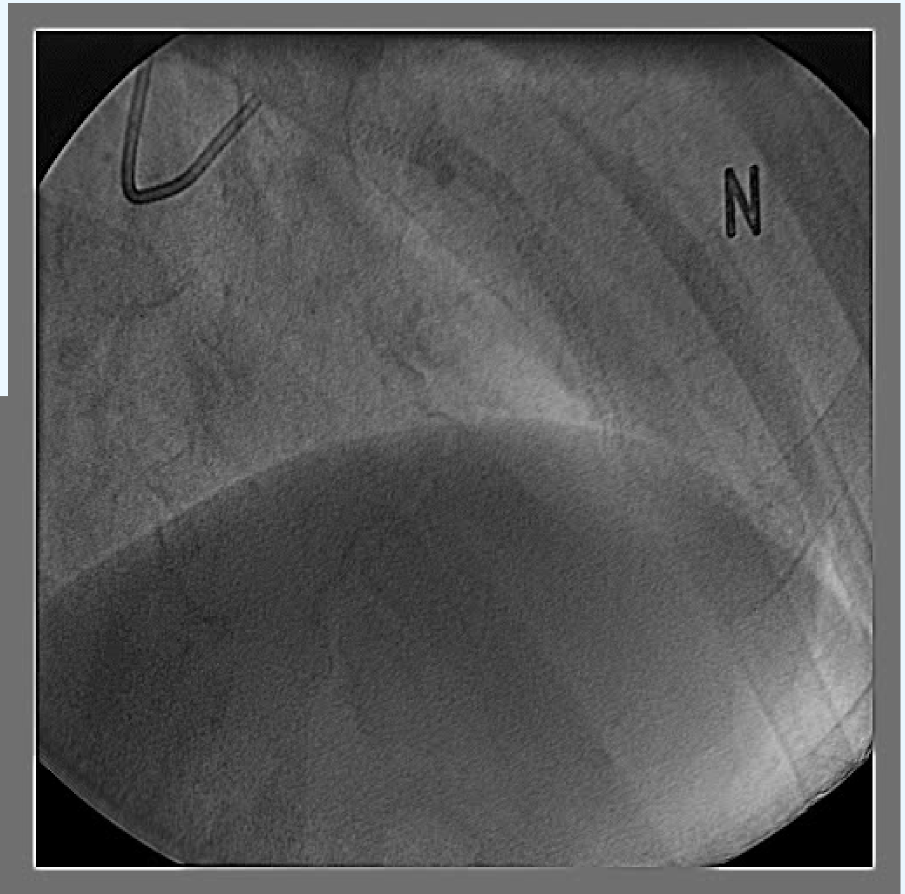
However, Diffuse Restenosis



Pre PCI



Post DES



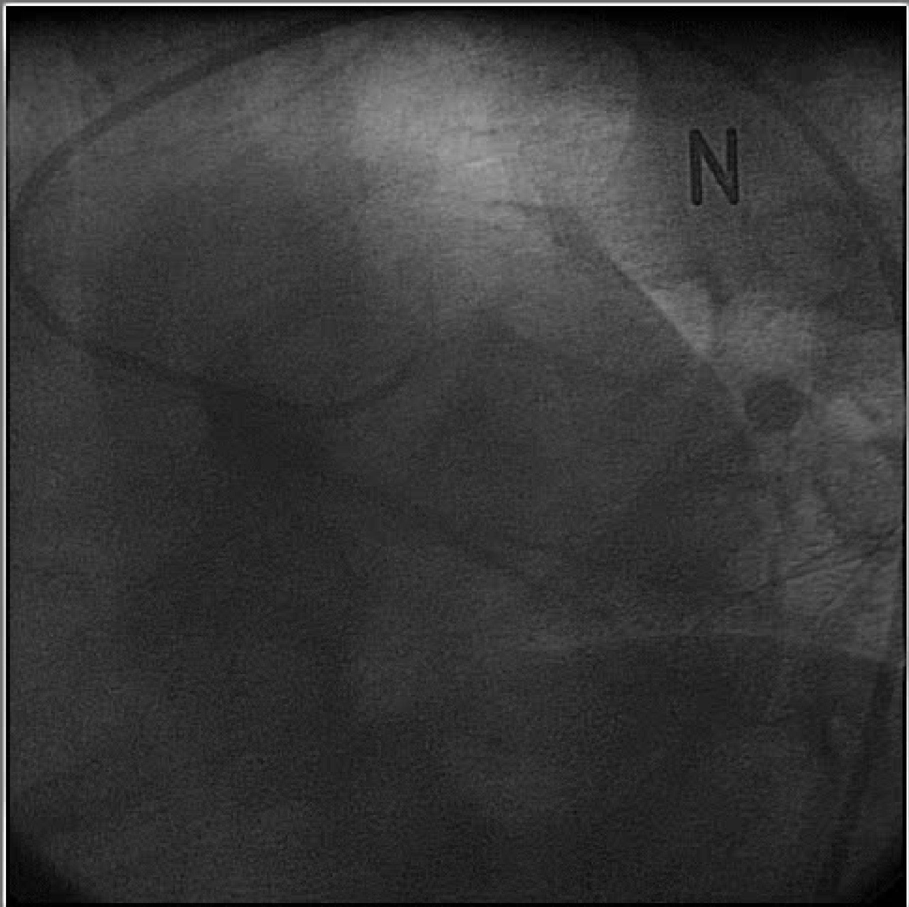
8 months FU

Stent thrombosis

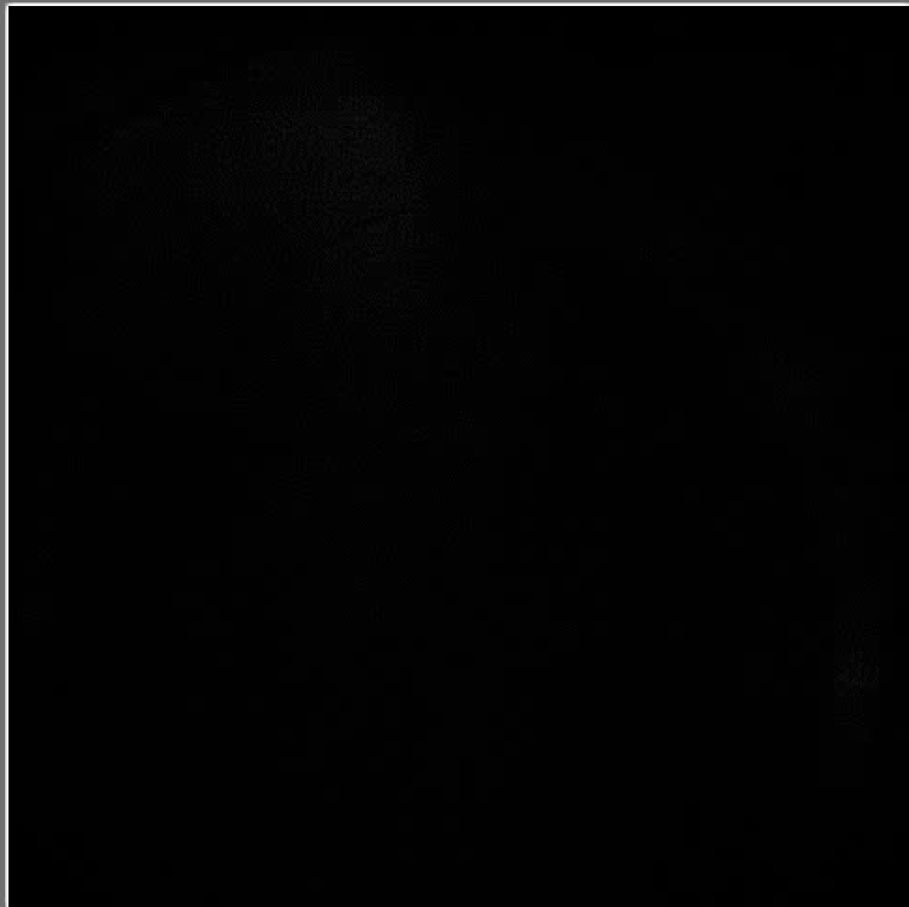
Pre PCI

Post DES

Stent thrombosis

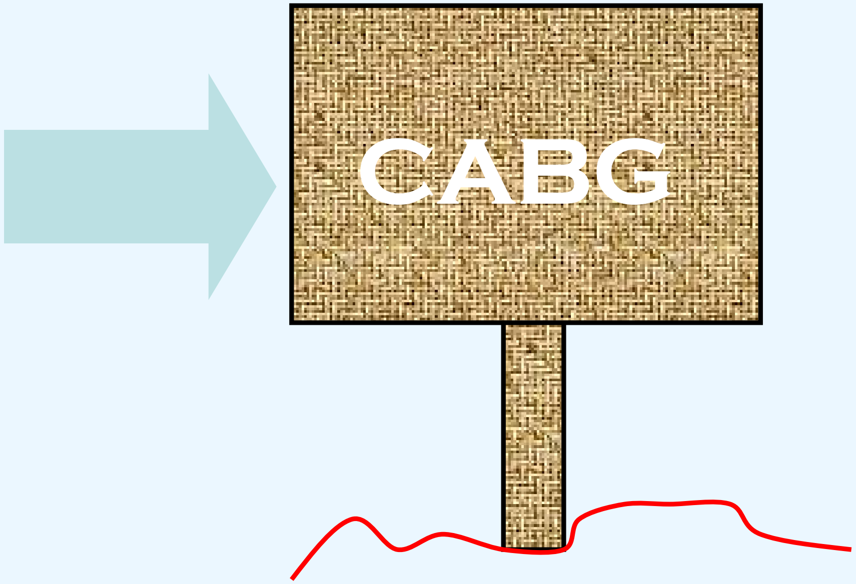


4 days after DES



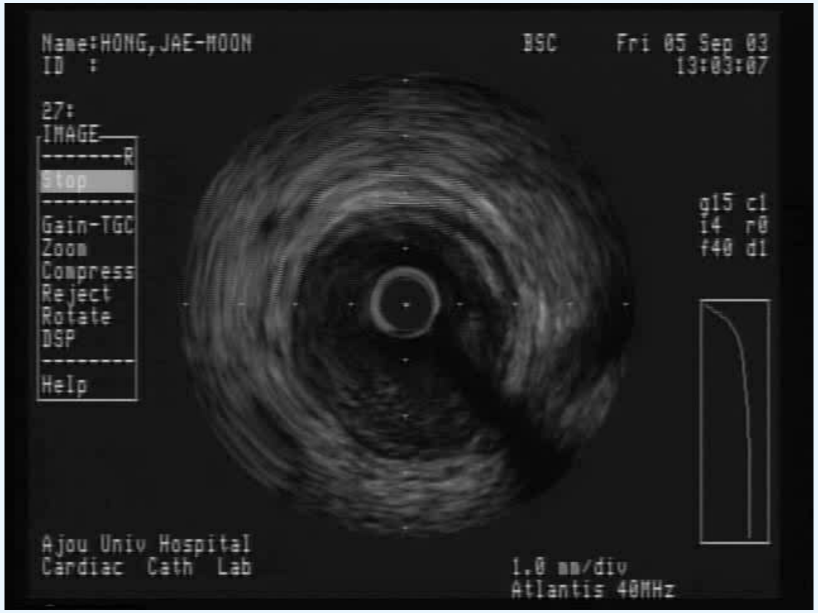
Cutting and HP

Stent thrombosis

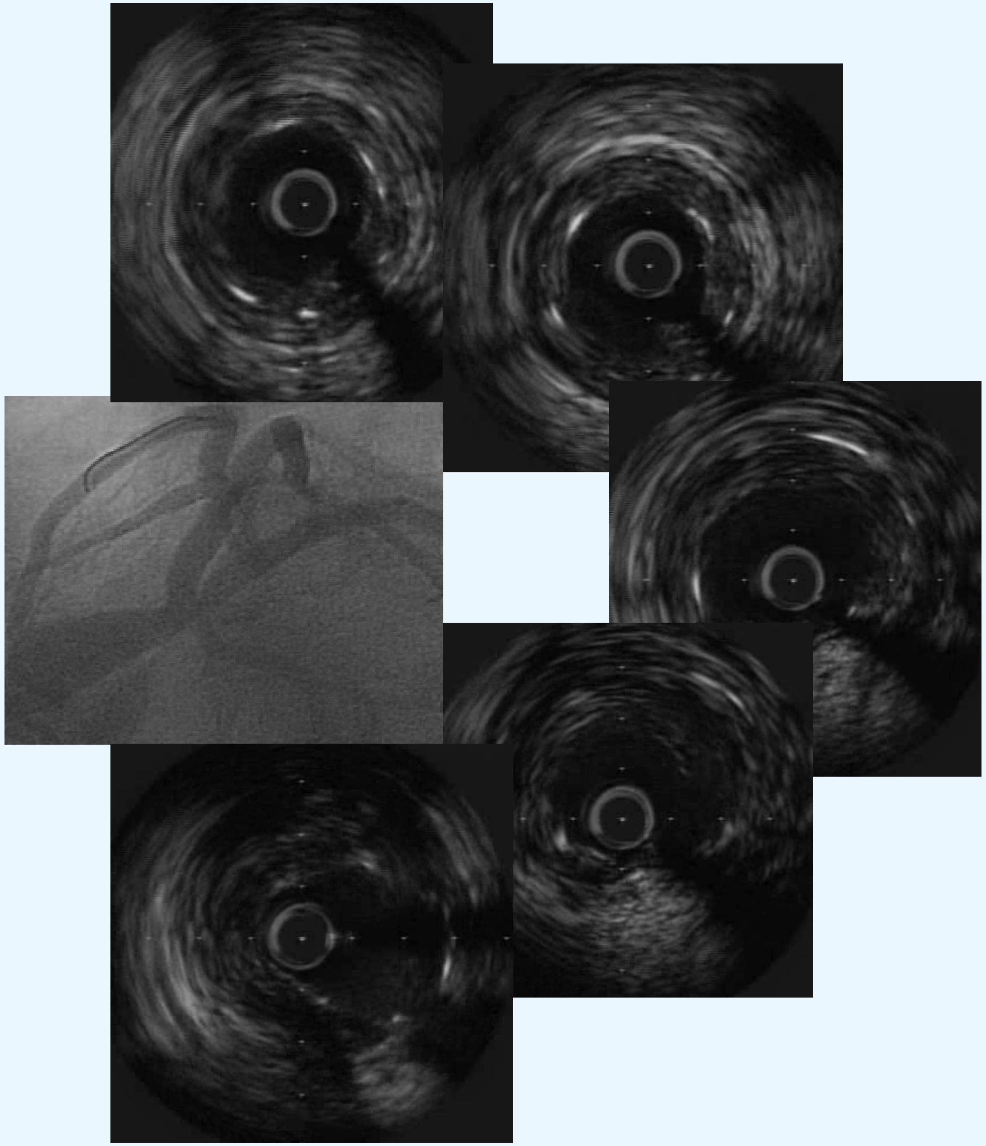


4 days after SAT#1

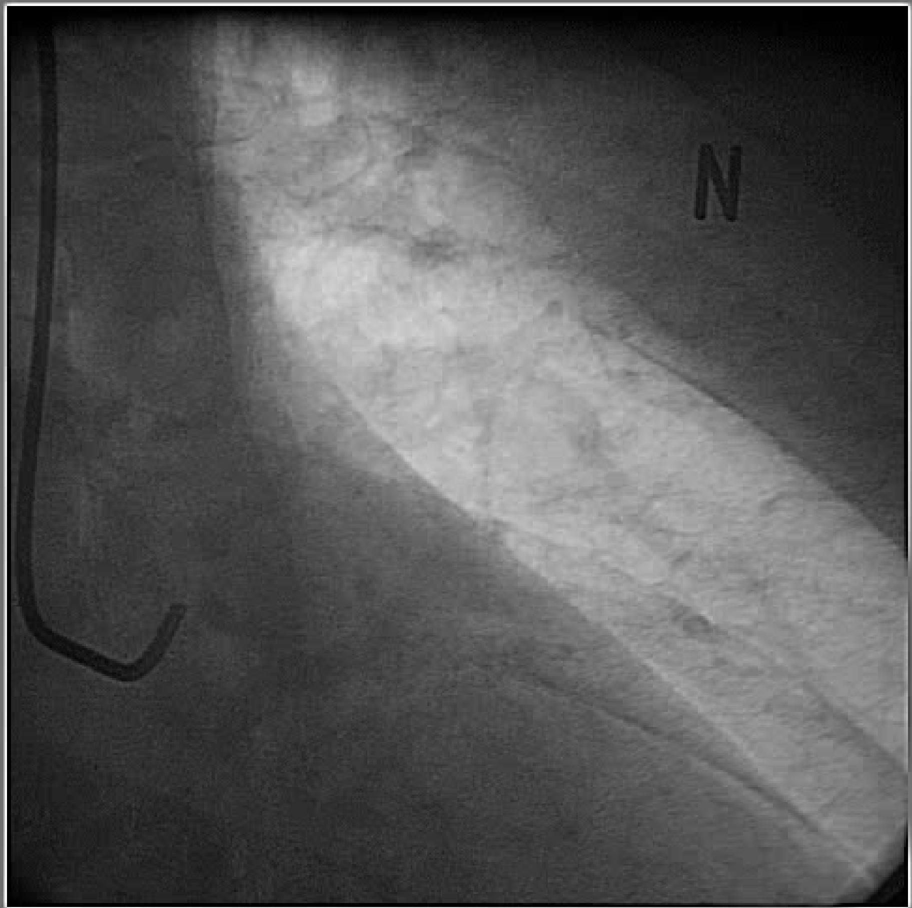
Stent thrombosis



Post DES IVUS



Aneurysm formation

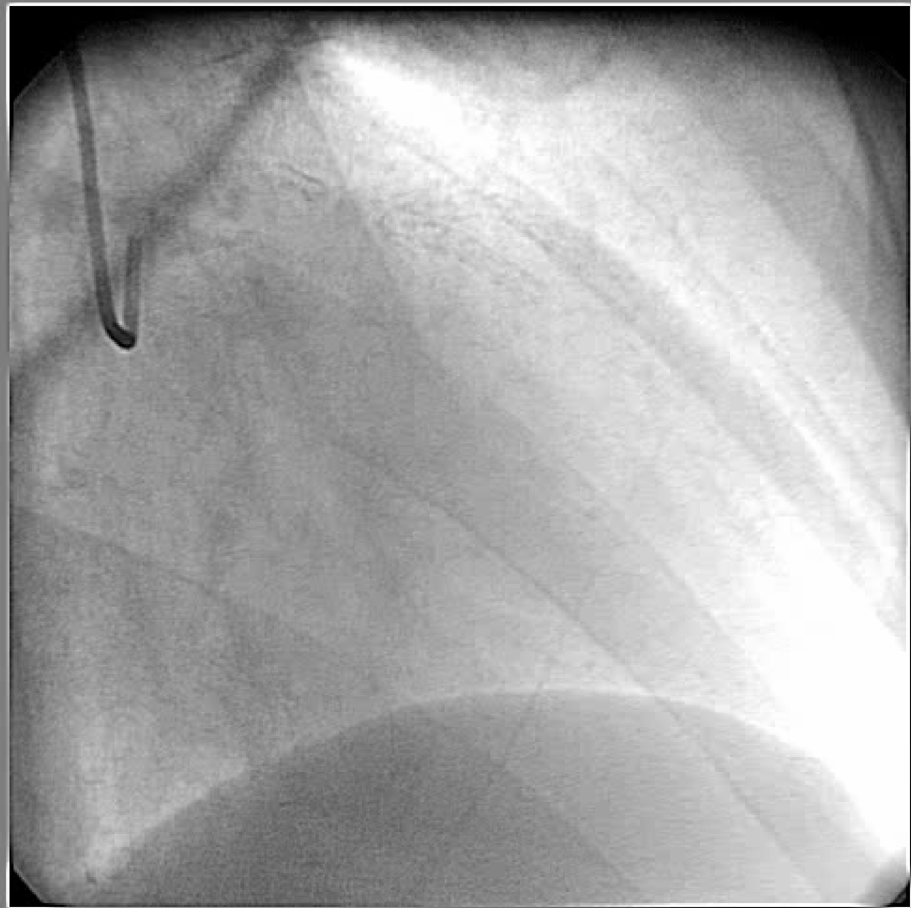


Pre

Crushing

Aneurysm formation

6 months

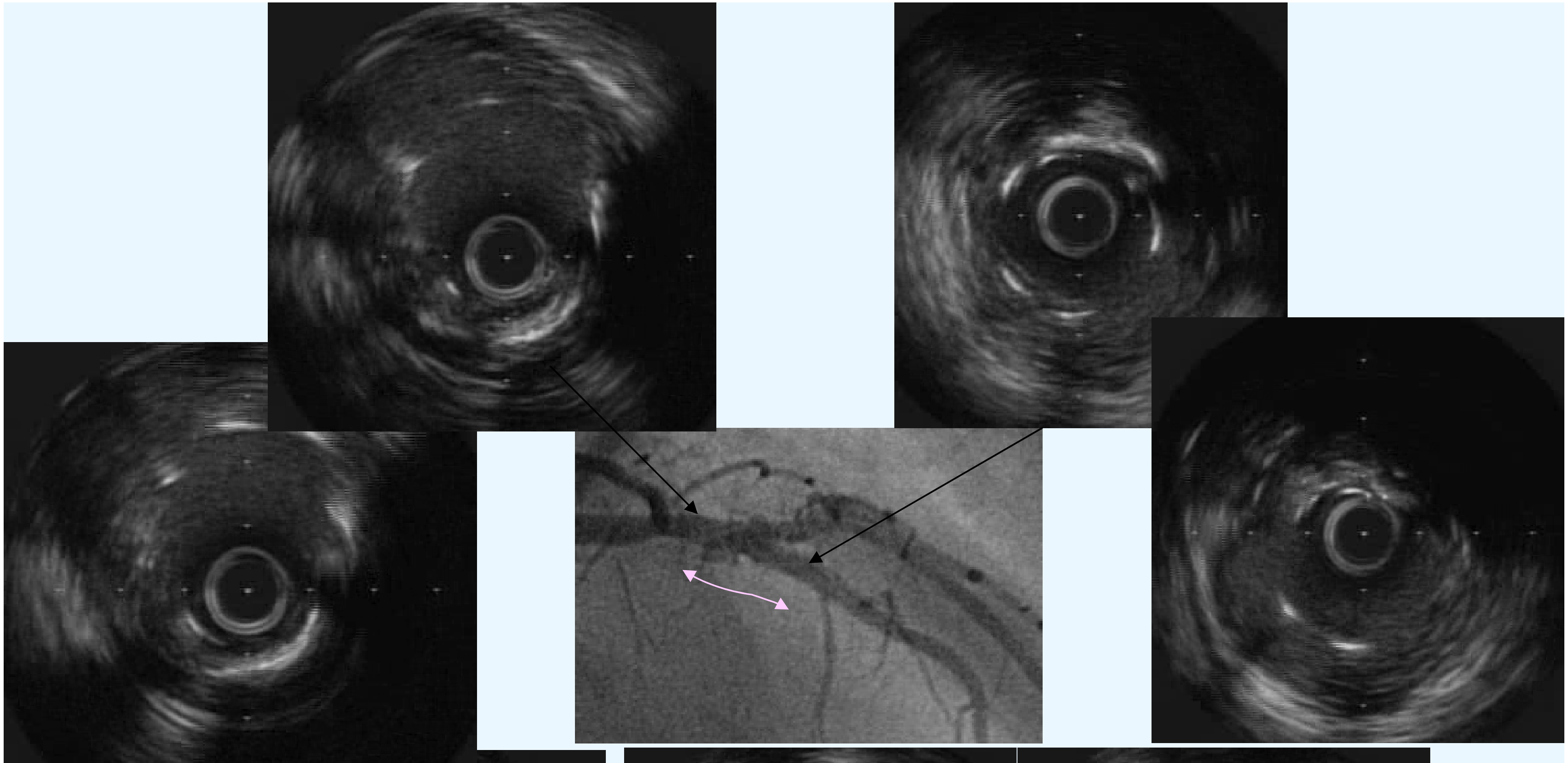


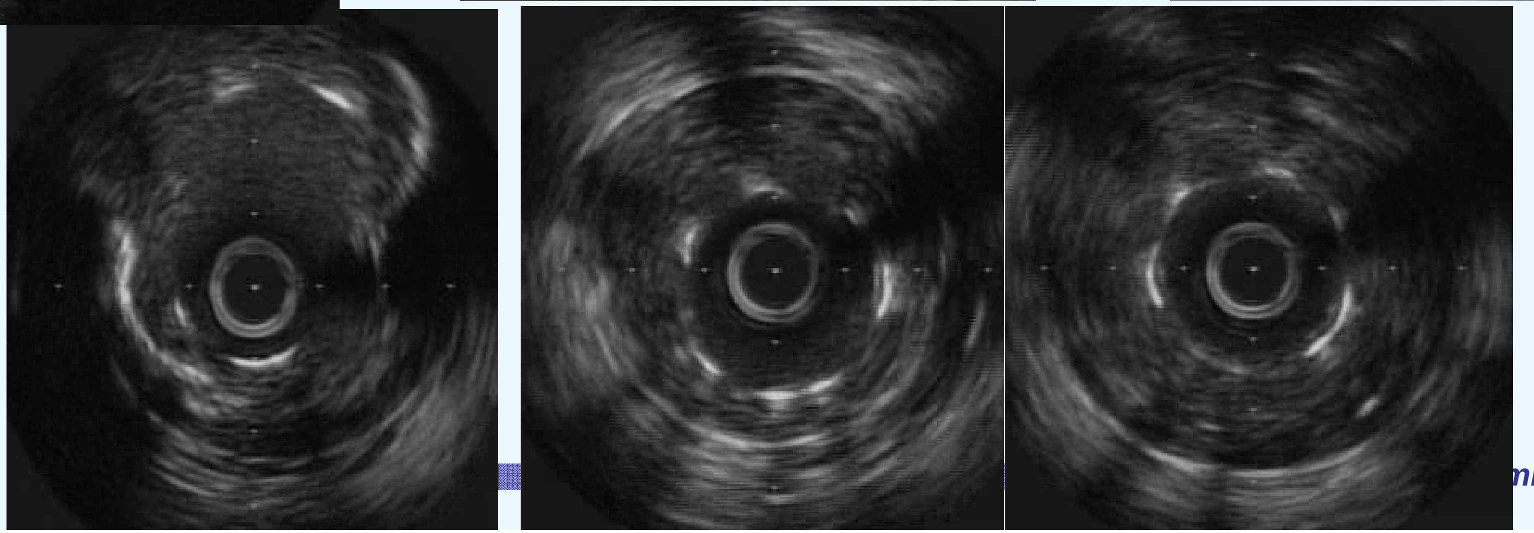
19 months

Aneurysm formation

19 months Post HPB/Kissing

24 months





When is IVUS appropriate?

- Diagnostic procedures
- High risk patients patient and lesion subsets
  - Diabetic patient
  - Ostial lesion
  - Long lesion
  - Small vessel
  - Bifurcation lesion including LM disease
- Treatment of in-stent restenosis
- DES failure

How does one use IVUS during DES implantation

- Identify the proximal and distal reference segments
- Measure
  - The vessel size to select stent size
  - The lesion length to select stent length
- After stent deployment, assess
  - Final stent area, apposition, lesion coverage, and other complications
- Determine whether additional work is required to optimize stent dimensions, completely cover the lesion, or treat complications

Evaluation of Stenosis Severity
Left Main Disease

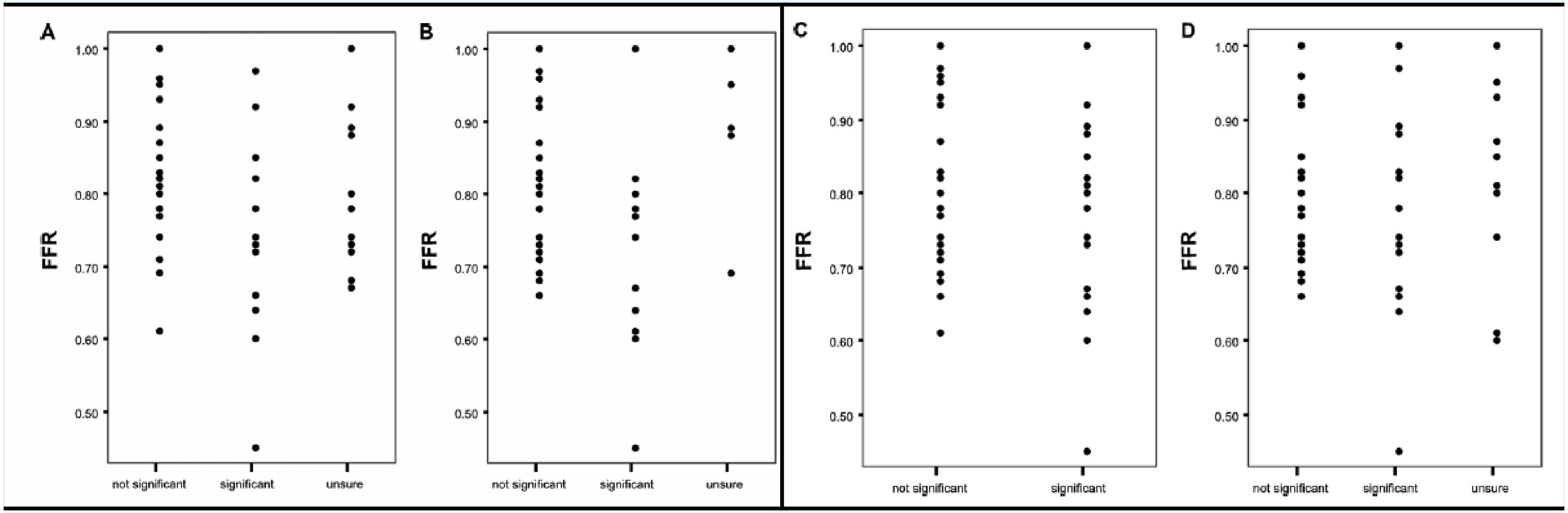
No expert can be perfect with visual assessment…

Visual Angiographic Assessment of Left Main Disease

- To assess the accuracy of visual angiographic assessment of intermediate (40–80% diameter stenosis by angiography) or equivocal left main coronary artery stenoses by experienced interventional cardiologists when taking FFR as the gold standard.
- Angiograms were then reviewed by 4 experienced interventionalists blinded to FFR
- Lesions were visually assessed and their significance classified as ‘significant’, ‘not significant’, or ‘unsure’.

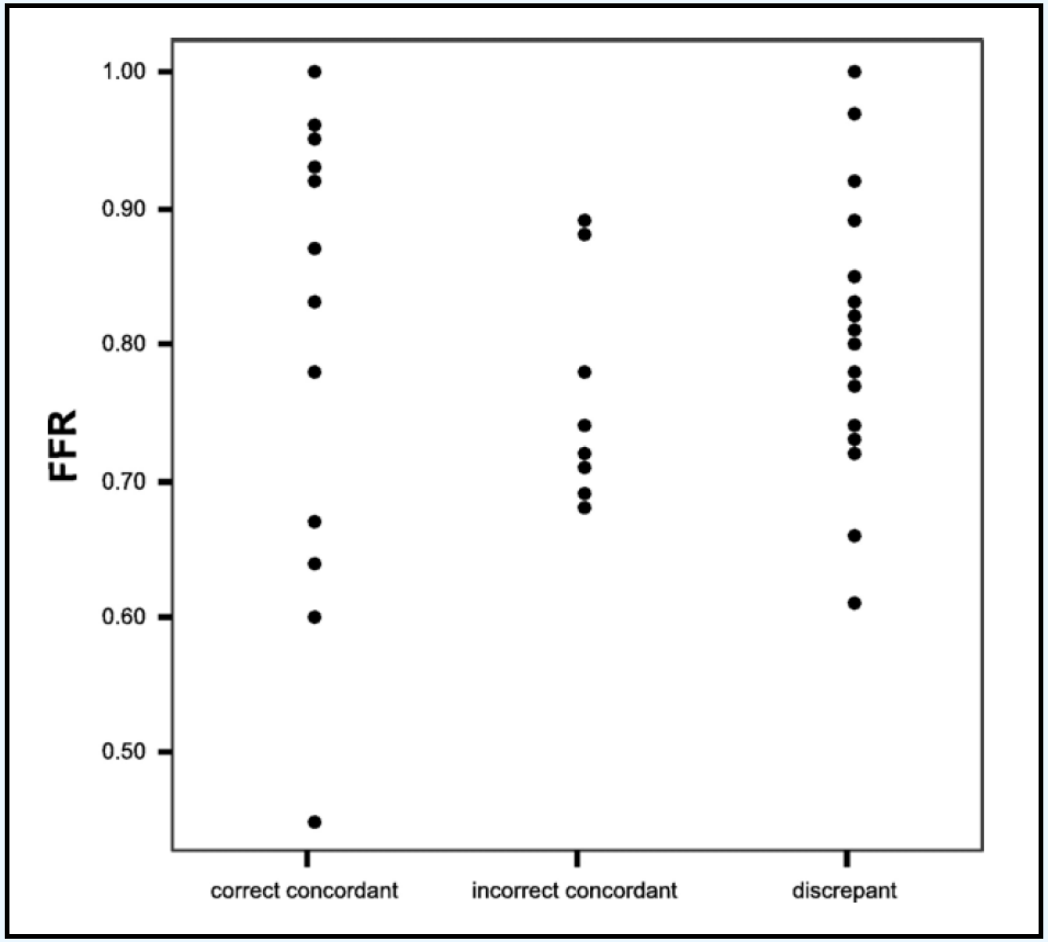
M Lindstaedt et al. Int J Cardiol; 2007 (in press)

Relation between FFR and each reviewer's (A–D) visual assessment of 51 intermediate or equivocal left main stenoses



M Lindstaedt et al. Int J Cardiol; 2007 (in press)

Agreement of concordant classifications (n=25) and discordant classifications (n=26) of reviewers A–D with FFR values



correct=concordant classifications identical to functional significance by FFR
incorrect=concordant classifications different from functional significance by FFR
discrepant=divergent classifications by reviewers

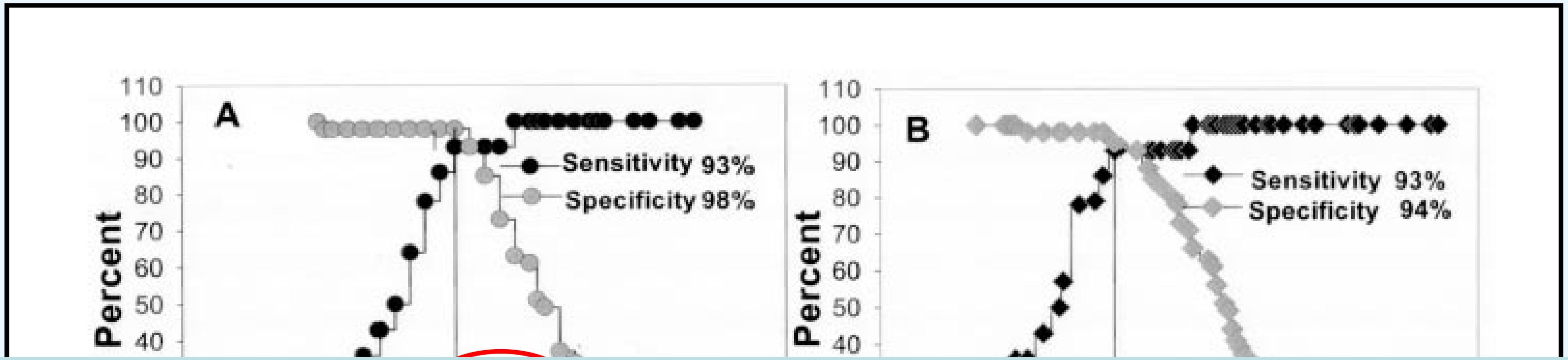
M Lindstaedt et al. Int J Cardiol; 2007 (in press)

Visual Angiographic Assessment of Left Main Disease

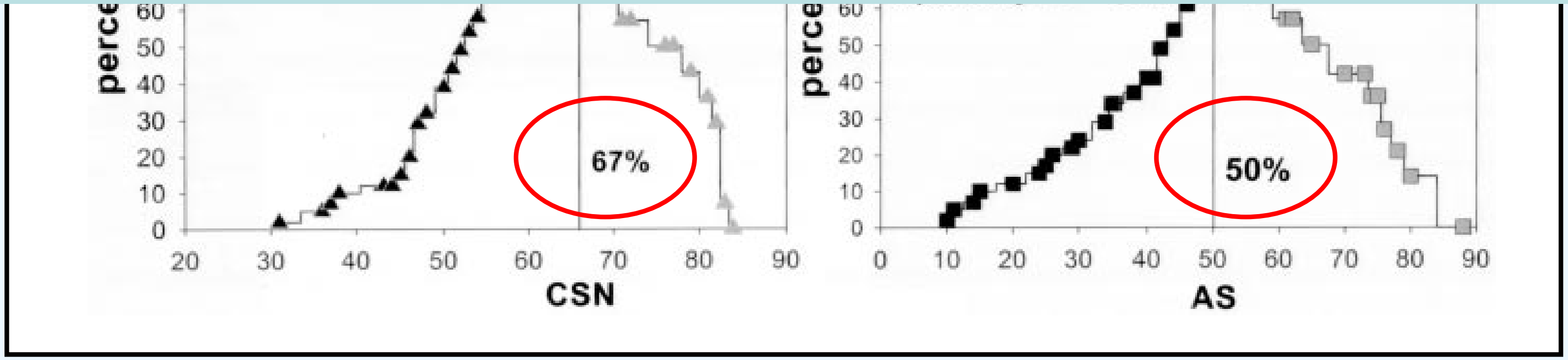
- None of the 4 reviewers achieved correct classification in more than 50% of cases.
- Even on the basis of the most generous of these definitions, there was a concordance of only 49% (25 of 51 lesions) among the reviewers
- An unanimously correct lesion classification was achieved in only 29% (15 of 51 lesions) of all cases.
- Visual assessment resulted in poor sensitivity 38%, specificity 58%, positive predictive value mean 39%, and negative predictive value mean 57%.
- The functional significance of intermediate and equivocal left main stenoses should not be based solely on angiographic assessment even by experienced interventional cardiologists.

M Lindstaedt et al. Int J Cardiol; 2007 (in press)

Ischemic cut point of FFR and IVUS parameters



IVUS MLD and MLA of 2.8 mm and 5.9 mm^2, respectively, strongly predict the physiological significance of an LMCS.

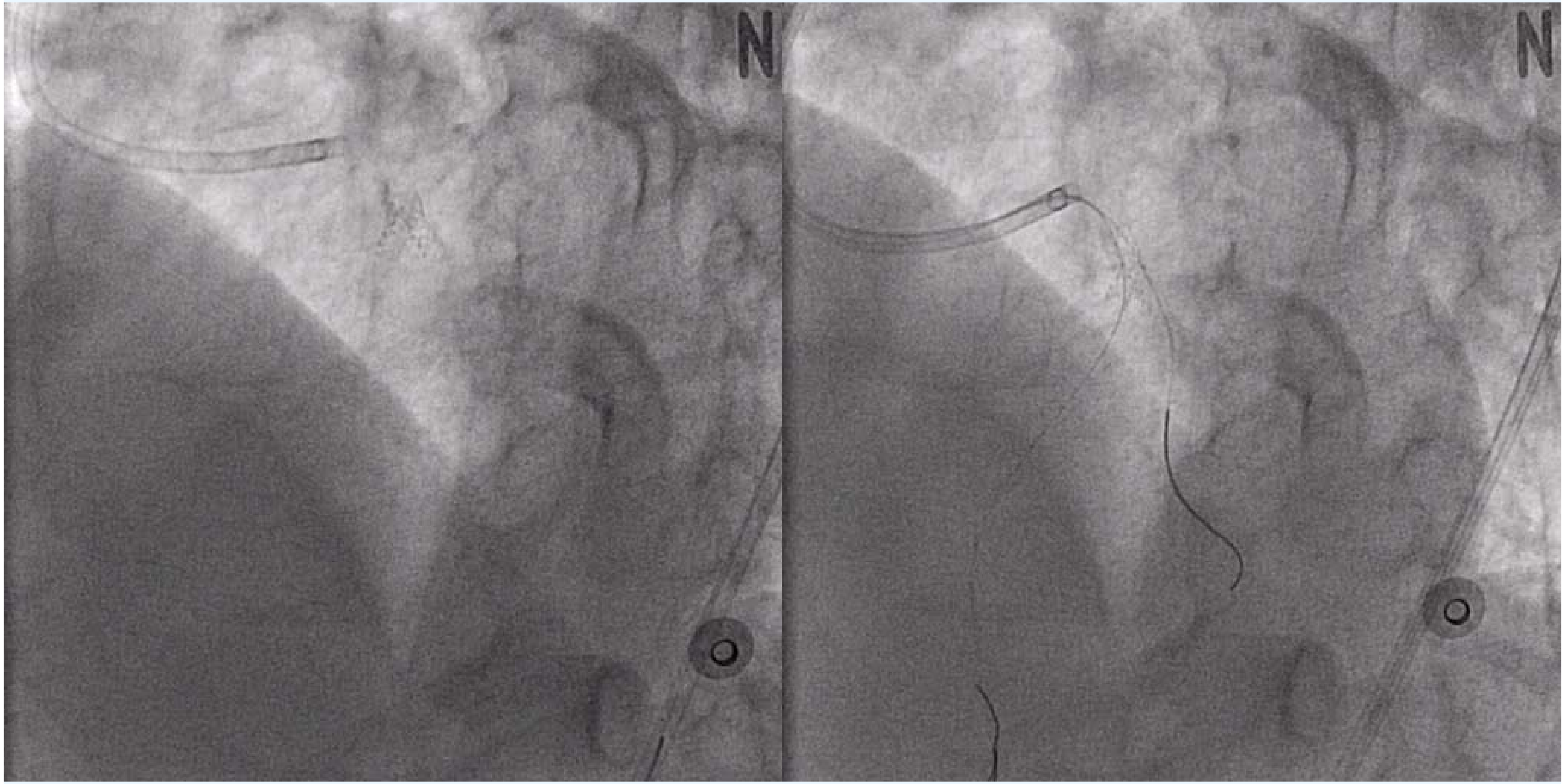


V Jasti et al. Circulation 2004;110:2831-36

Evaluation of Stent Expansion
Bifurcation Lesion

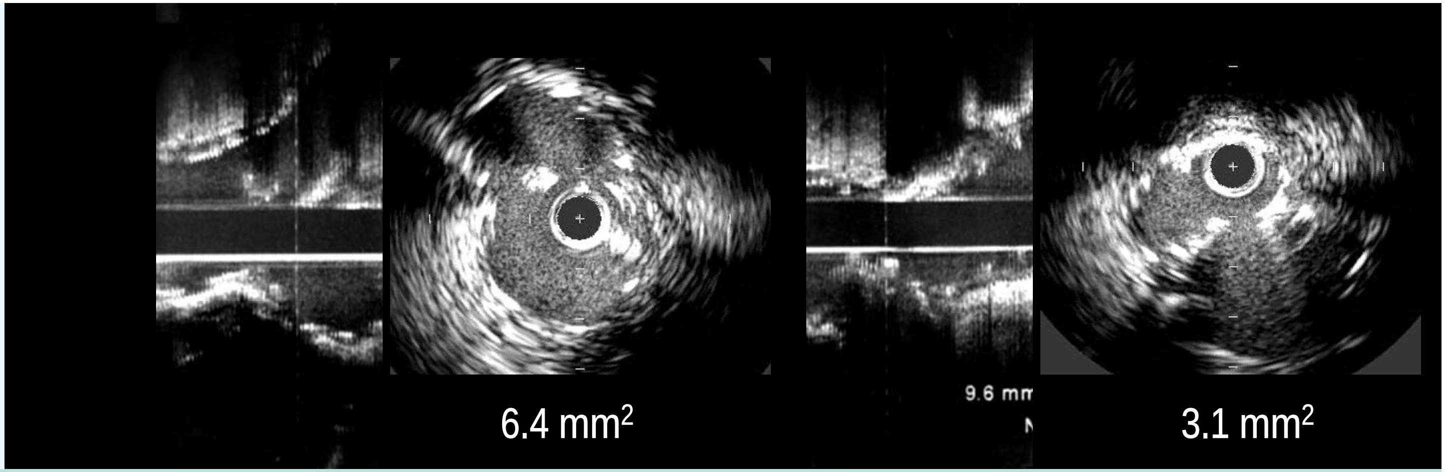
No expert can be perfect with visual assessment…

Any Difference?



NO … ??

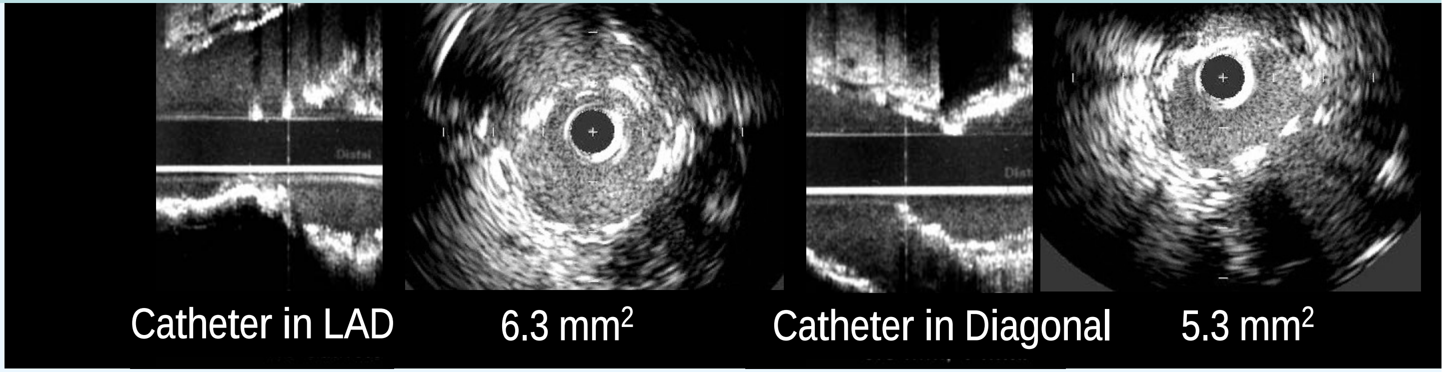
Kissing #1
LAD 3.0x20mm 8atm
DIG 2.5x20mm 8atm
Inflation: Simultaneous
Deflation: Simultaneous



Any Difference?

Yes, Big Difference on IVUS

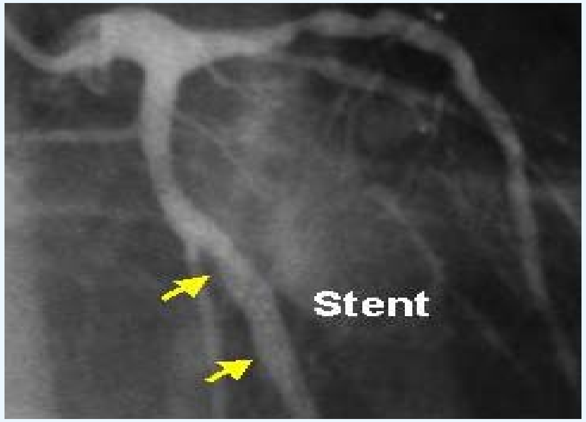
Kissing #3
LAD 3.0x20mm 14atm
DIG 3.0x13mm 8atm
Inflation: DIG→LAD
Deflation: Simultaneous

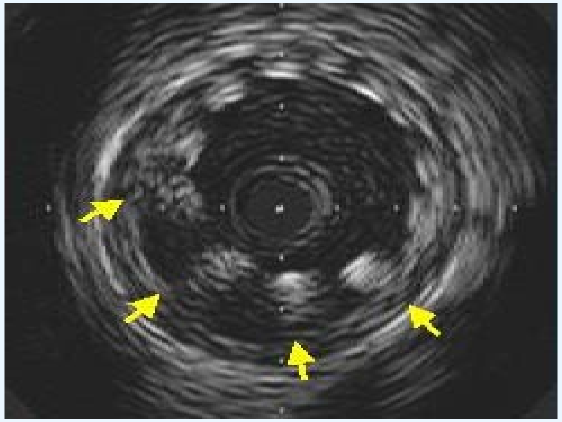


Evaluation of Stent Expansion
Long Diffuse Lesion

No expert can be perfect with visual assessment…

Why is optimal DES expansion and apposition important ..





Under angiography, the stent *appears* fully expanded/apposed

Using IVUS, the stent demonstrates *sub-optimal* expansion/apposition

- Uniform stent apposition facilitates uniform drug absorption into endothelial tissue [2,3,4,5]
- Incomplete apposition may contribute to thrombosis formation & SAT's[1]
- Stent underexpansion may increase risk for restenosis and target vessel revascularization (TVR) [6,7]

1. Cheneau, et al. Circulation 2003;108;43-47
2. Creel, et al. Circulation 2000;86:879.
3. Hwang, et al. Circulation 2001;104:600-605
4. Leon, M. *The basic "tips and tricks" for DES implantation;* TCT 2003 presentation
5. The TAXUS Stent Directions for Use
6. Fitzgerald, et al. Circulation 2000; 102:523-530
7. Fuji, et al. Circulation 2004; 109: 1085-1088

Predictors of Restenosis and Target Vessel Revascularization after SES Implantation

Clinical variables
Diabetes
Angiographic variables
Small reference vessel diameter
Ostial location
Non–left anterior descending artery lesion
In-stent restenosis
Procedural variables
Long stent length
Small stent diameter or minimal stent area (MSA) by IVUS

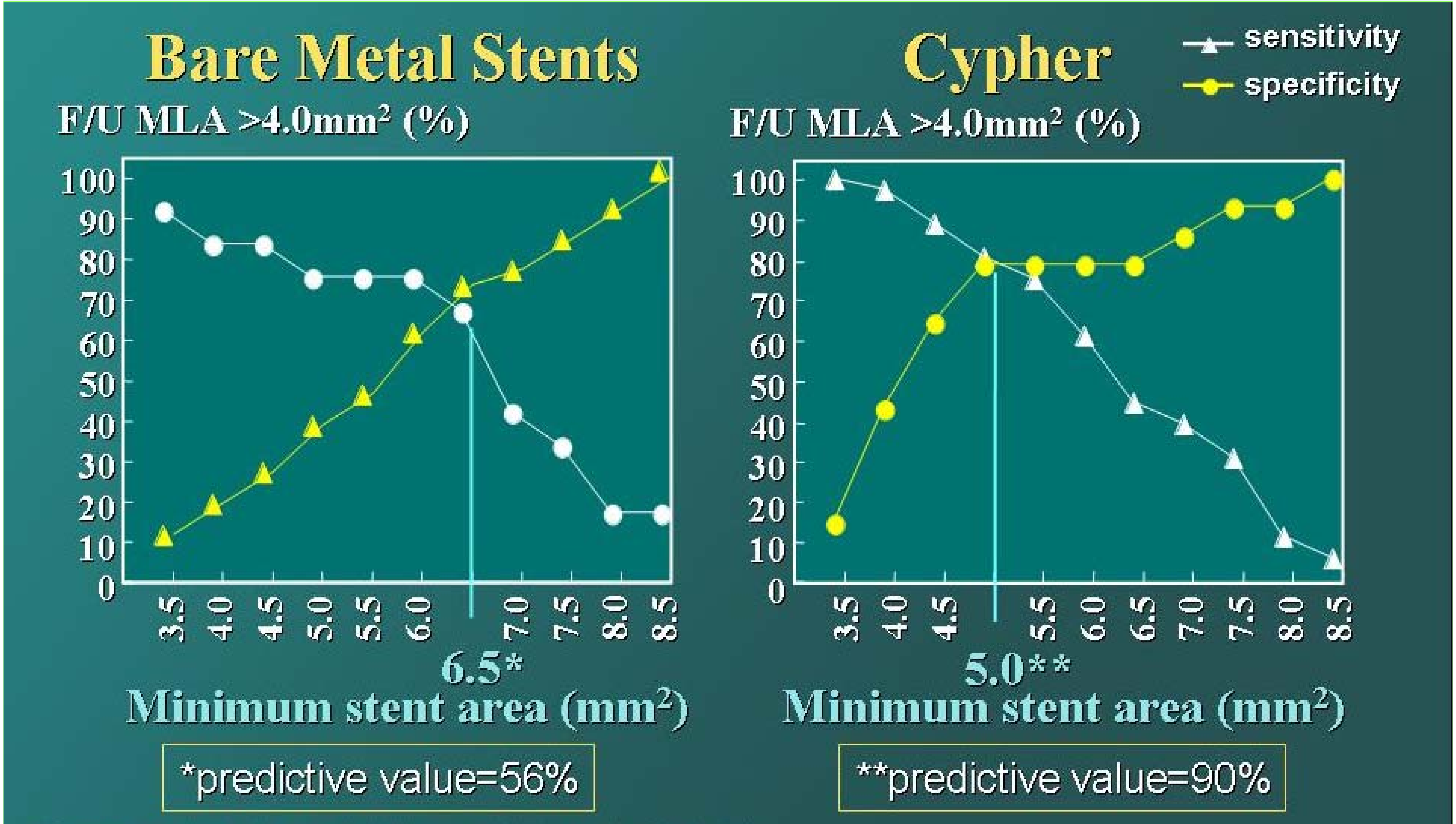
BR Brodie. J Interven Cardiol 2006;19:43–50)

Predictors of Drug-Eluting Stent Thrombosis

Clinical variables	
	Diabetes
	Renal failure
	Low ejection fraction
Angiographic variables	
	Bifurcation lesions
Procedural variables	
	Use of multiple stents
	Use of long stents
	Small final stent area (MSA) by IVUS
	Stent underexpansion
	Residual reference segment stenosis
Postprocedural variables	
	Premature discontinuation of antiplatelet therapy

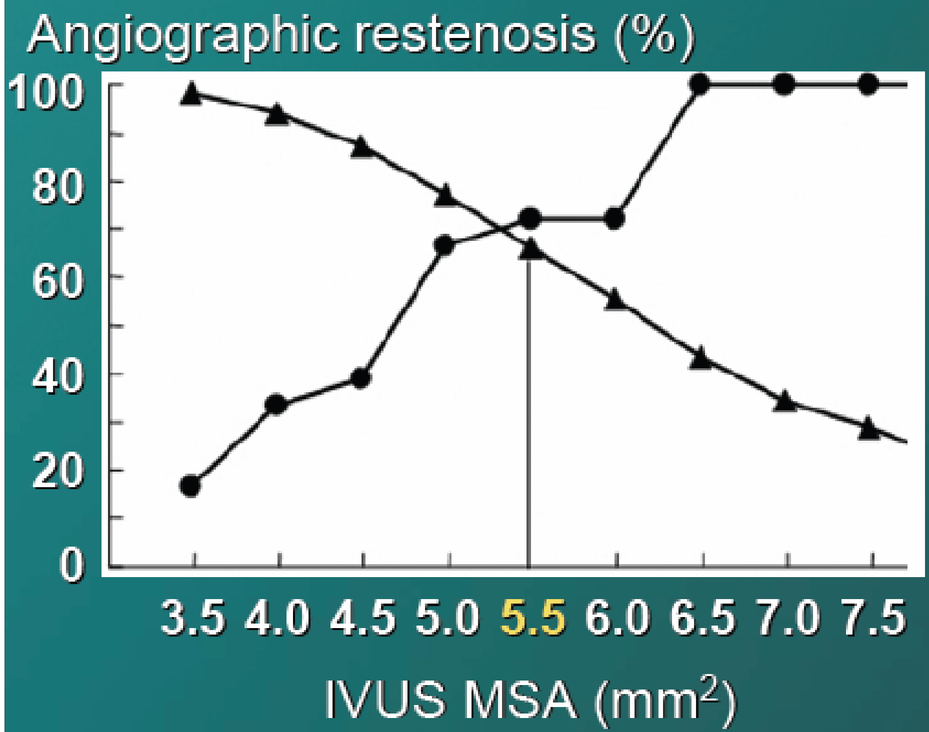
BR Brodie. J Interven Cardiol 2006;19:43–50)

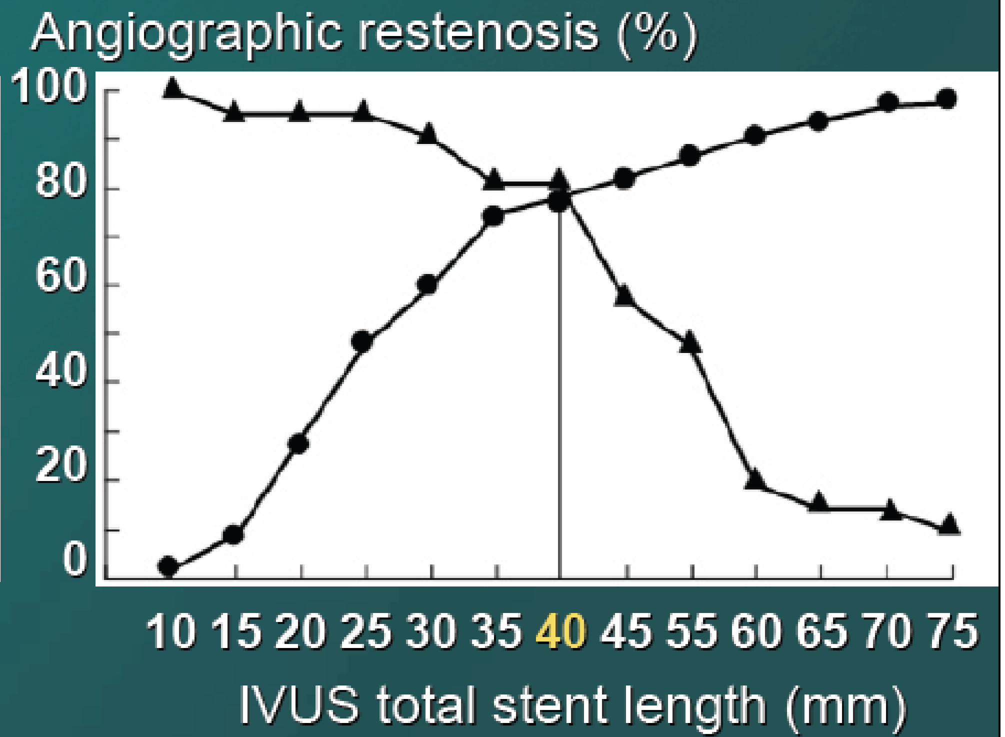
What is the smallest acceptable minimum stent area?



(Sonoda et al. J Am Coll Cardiol 2004;43:1959-63)

Predictors of angiographic restenosis in 550 patients with 670 native artery lesions patients treated with Cypher Stents

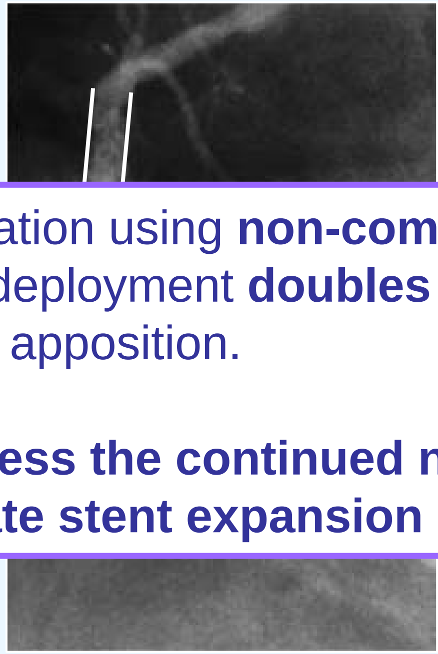


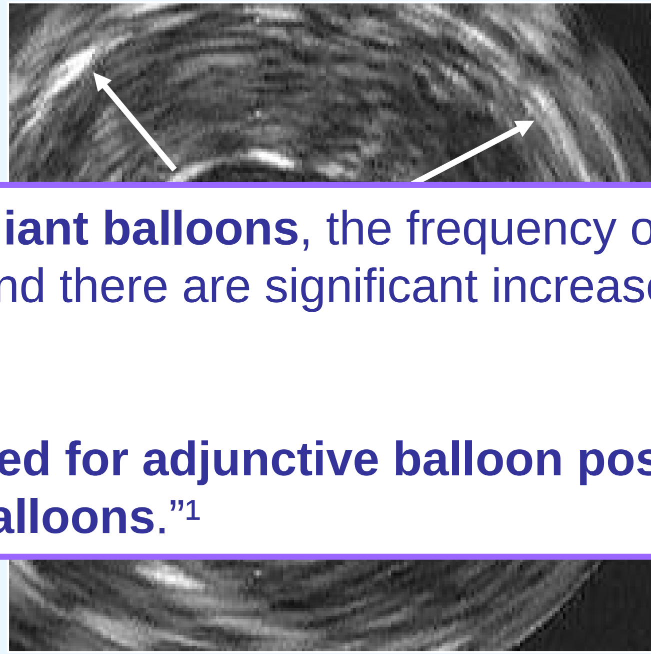


	<5.5mm²	≥5.5mm²
≤40mm	2.4%	0.4%
>40mm	17.7%	8.6%

(Hong et al. Euro Heart J 2006;27:1305-10)

POSTIT Trial
Verification of BMS expansion by IVUS





"With post-dilatation using **non-compliant balloons**, the frequency of achieving optimum stent deployment **doubles** and there are significant increases in MSA – maximum stent apposition.

These data stress the continued need for adjunctive balloon post-dilatation with appropriate stent expansion balloons."[1]

Optimal stent deployment* is only achieved in 29% of patients with current stent delivery systems; usually due to inability of stent delivery balloon to expand fully the stent to nominal size (n=256).

*MSD≥90% of average reference lumen diameter

POSTIT Trial, Brodie et al, Catheterization and Cardiovasc Int 2003;59:184

DES Expansion with Incremental Delivery Pressures

Table 3
Comparison of postintervention IVUS parameters at different delivery pressures

Variable	SES (*n*=46)	PES (*n*=41)	*P* value
14 atm			
Min stent CSA (mm^2)	5.0±1.4	5.6±2.1	.15
Max stent CSA (mm^2)	6.9±1.9	8.0±2.4	.007
Min stent diameter (mm)	2.34±0.33	2.40±0.50	.46
Max stent diameter (mm)	2.93±0.37	3.35±0.50	<.0001
Axial stent symmetry	0.73±0.11	0.69±0.13	.08
Radial stent symmetry	0.80±0.09	0.72±0.09	<.0001
Underexpansion	37/46 (80.4%)	26/41 (63.4%)	.08
20 atm			
Min stent CSA (mm^2)	6.4±1.7	6.0±2.0	.30
Max stent CSA (mm^2)	8.0±1.9	8.4±2.3	.44
Min stent diameter (mm)	2.64±0.34	2.51±0.44	.16
Max stent diameter (mm)	3.20±0.38	3.45±0.48	.01
Axial stent symmetry	0.82±0.11	0.70±0.10	.0004
Radial stent symmetry	0.83±0.08	0.73±0.08	<.0001
Underexpansion	22/46 (47.8%)	9/26 (34.6%)	.28

*** Stent Underexpansion by MUSIC criteria**

A Javaid et al. Cardiovascular Revascularization Medicine 7 (2006) 208– 211

DES Expansion without Postdilation

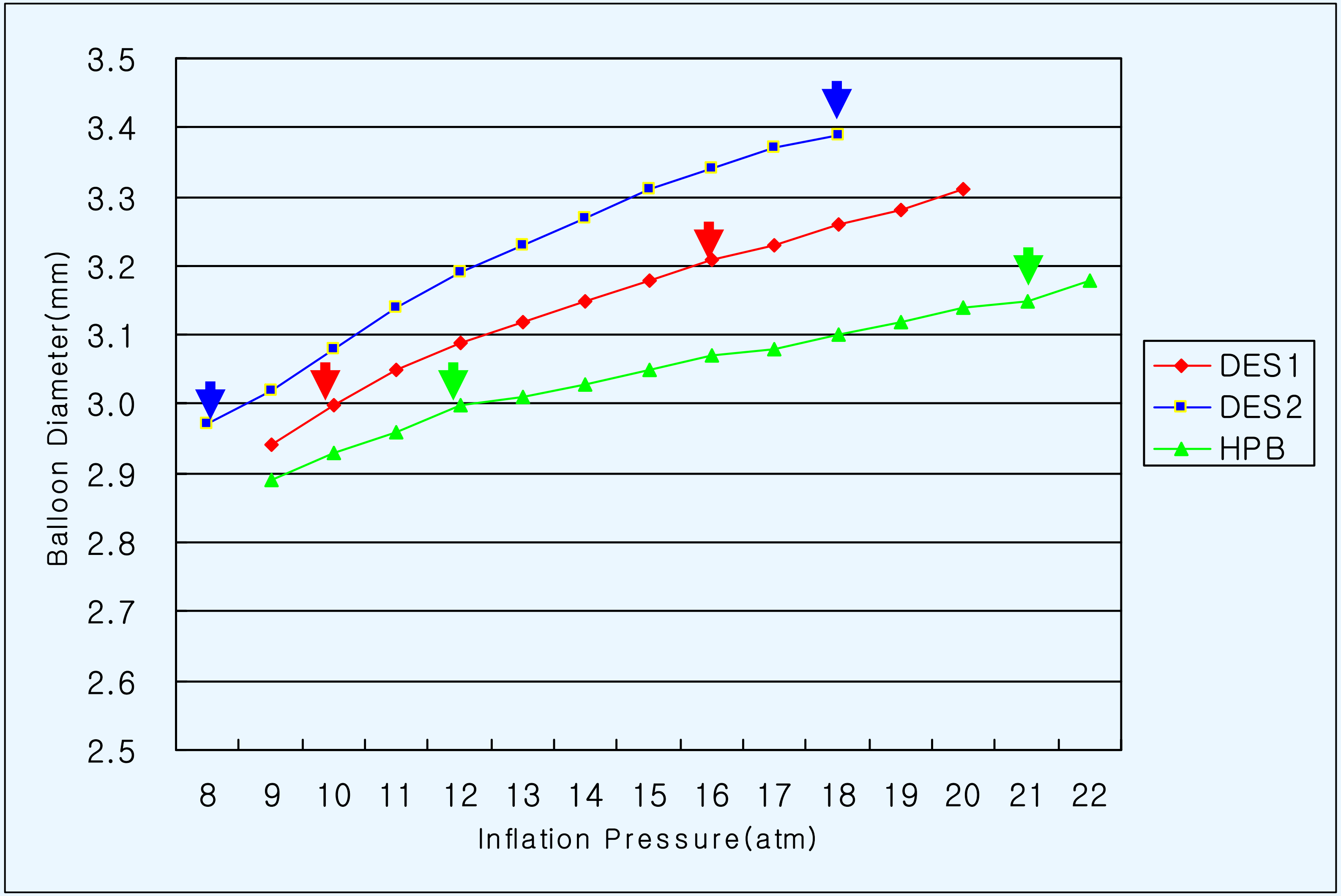
Table IV. IVUS quantitative assessment

	SES (n = 133)	PES (n = 67)	*P*
Reference segment			
area (mm^2)	[illegible]	[illegible]	[illegible]
IVUS/manufacturer's predicted stent diameter (%)	75.6 ± 10.3	74.6 ± 11.0	.5
IVUS/manufacturer's predicted stent cross-sectional area (%)	66.0 ± 16.2	65.4 ± 18.1	.4

- ➢**The DES achieved only 75% of predicted MSD and 66% of predicted MSA.**
- ➢**This was similar form SES and PES.**
- ➢**Furthermore, 24% of SES and 28% of PES did not achieve a final MSA of 5.0 mm^2, a consistent predictor of DES failure.**

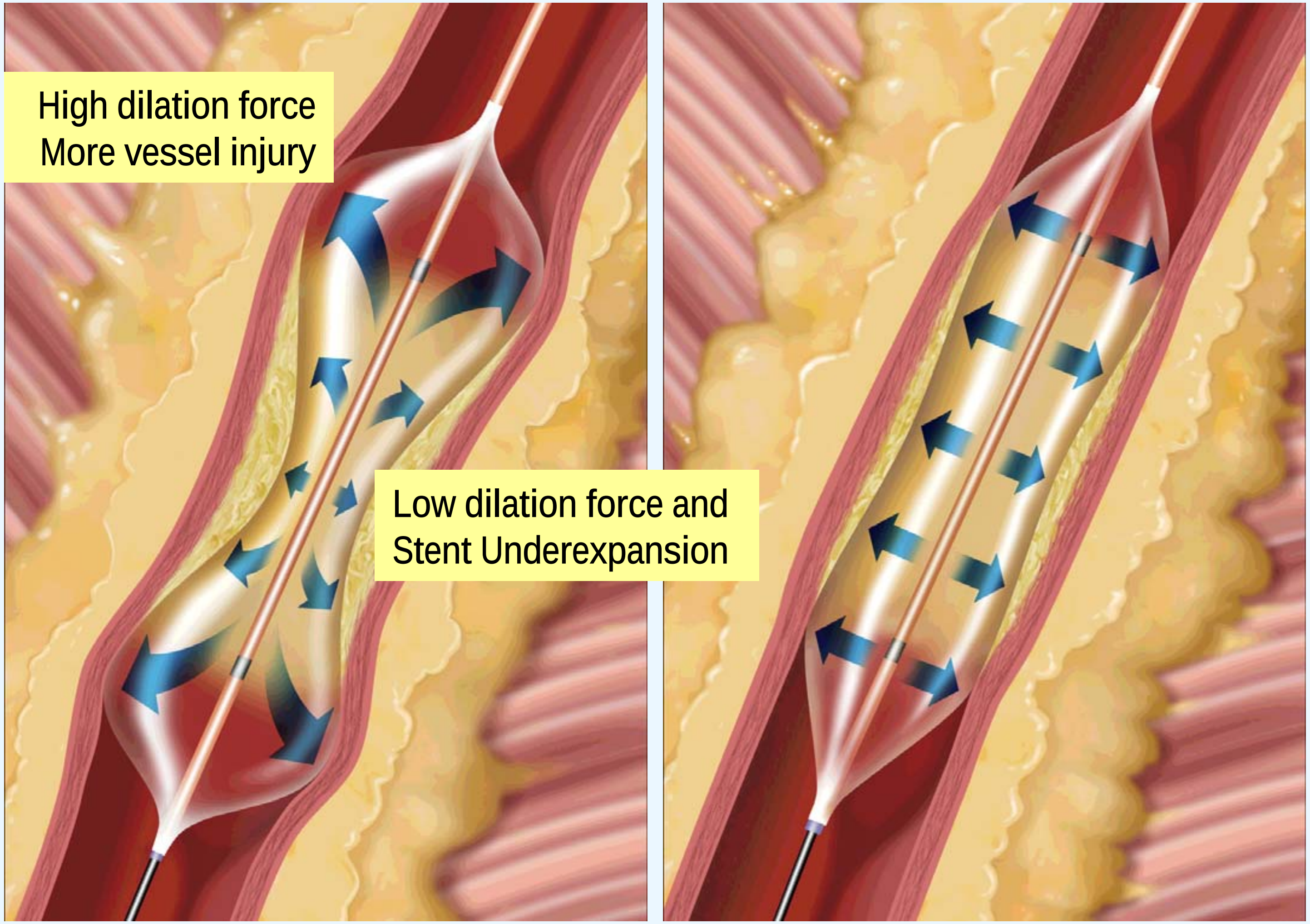
Jose de Ribamar Costaet al. Am Heart J 2007;153:297-303

Compliance of current DES delivery system



Balloon compliance and dilation force

Compliant/Semi-Compliant | **Non Compliant**

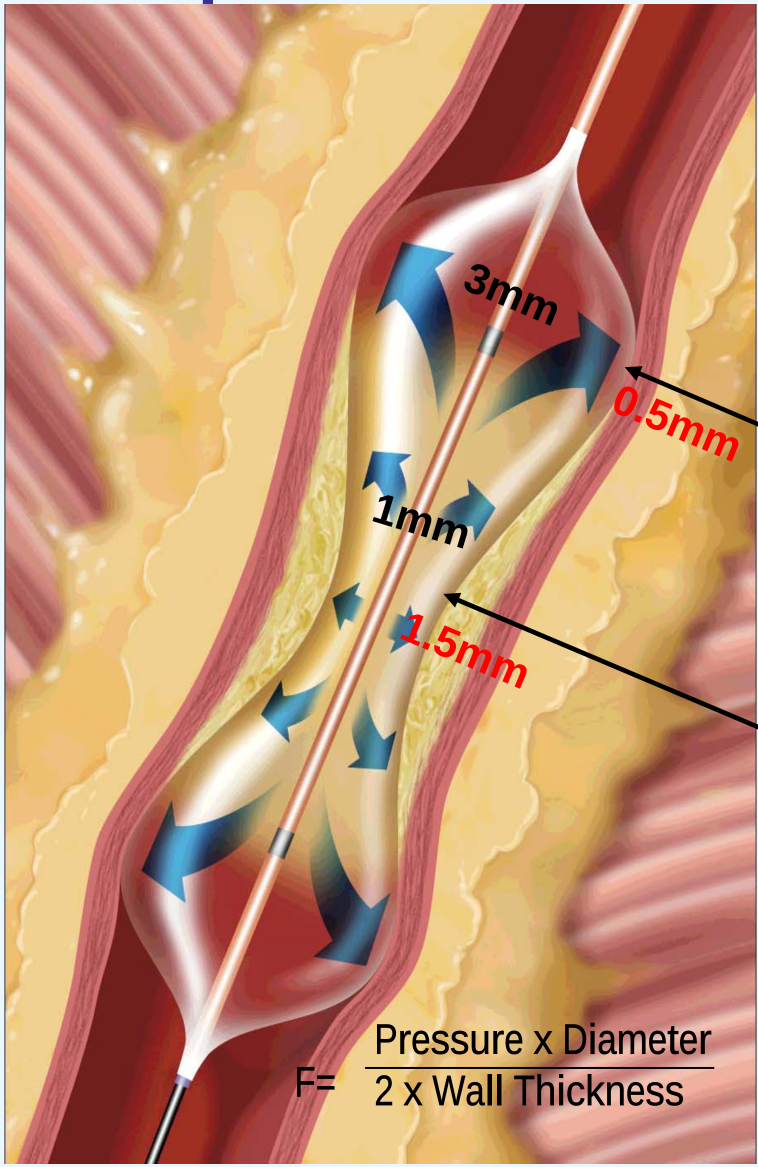


$$F = \frac{\text{Pressure x Diameter}}{\text{2 x Wall Thickness}}$$

Balloon compliance and dilation force

Bench test results may not necessarily be indicative of clinical performance.
Testing completed by Boston Scientific Corporation.
Data on file.

Inflation pressure and dilatation force



Inflation pressure = 10 atm

Dilation force varies from

10x3/2x0.5 = 30 atm

to

X 10 Dilatation Force

10x1/2x1.5 = 3.3 atm

Long Diffuse Lesion
FFR and IVUS-guided DES Implantation

- PCI with current semi-compliant stent delivery system (SDS) in long diffuse lesion may result in stretching of the balloon around the lesion rather than concentrating the force at the lesion and cannot achieve optimal stent expansion at culprit site.

- Visual angiographic estimation of stenosis may poorly correlate with anatomic and physiologic significance.

SJ Tahk, MH Yoon, et al. Aspen 2007

Long Diffuse Lesion
FFR and IVUS-guided DES Implantation

- Evaluate the incidence of suboptimal stent expansion with current drug SDS in long diffuse lesion.
- Evaluate effectiveness of post-stent adjuvant high-pressure non-compliant balloon dilatation.
- Identify the factors which was related with the suboptimal stent expansion.

SJ Tahk, MH Yoon, et al. Aspen 2007

Long Diffuse Lesion
FFR and IVUS-guided DES Implantation

- Inclusion Criteria
  - 41 consecutive angina patients, 47 de novo lesions
  - % DS on QCA >50% with evidence of myocardial ischemia
  - Stent length > 32mm
  - Informed consents for IVUS and FFR measurement.

- Exclusion Criteria
  - Restenotic lesion
  - Acute myocardial infarction or prior myocardial infarction
  - LV dysfunction: LVEF < 55%
  - Left main disease
  - Significant cardiac arrhythmia hampering physiologic study

SJ Tahk, MH Yoon, et al. Aspen 2007

Long Diffuse Lesion
FFR and IVUS-guided DES Implantation

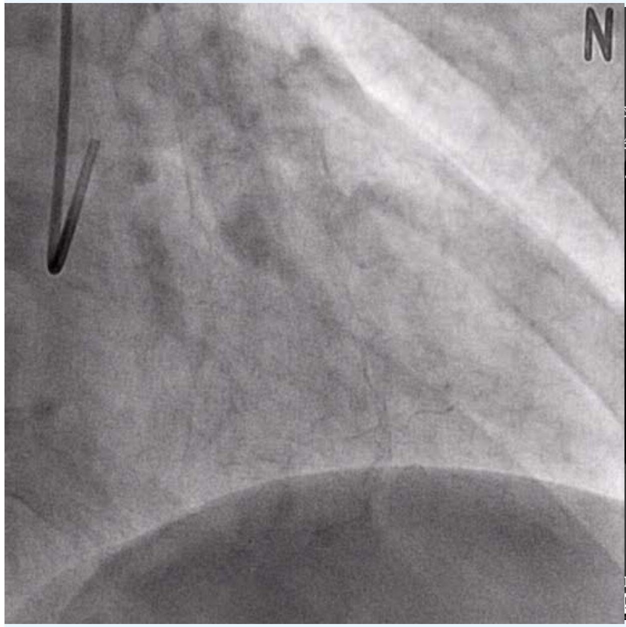
Pre PCI	Stenting with SDS (at RBP: 16-18 atm)	Adjunctive High Pressure (Quantum at 20-22 atm) *if Post Stent FFR<0.95*
IVUS FFR	IVUS FFR	IVUS FFR

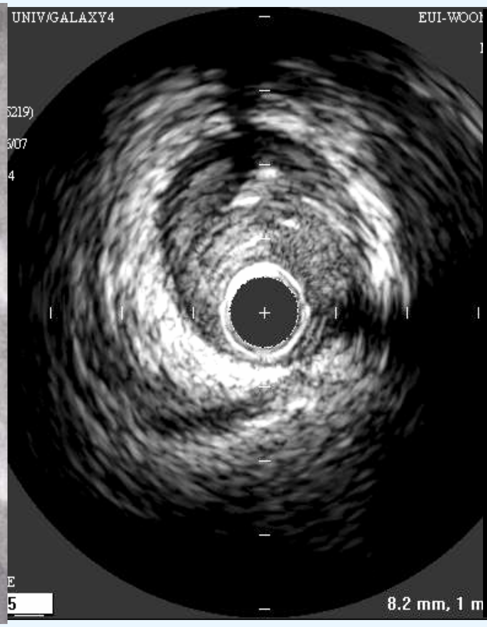
Pressure measurement: RADI Medical System, Uppsala, Sweden

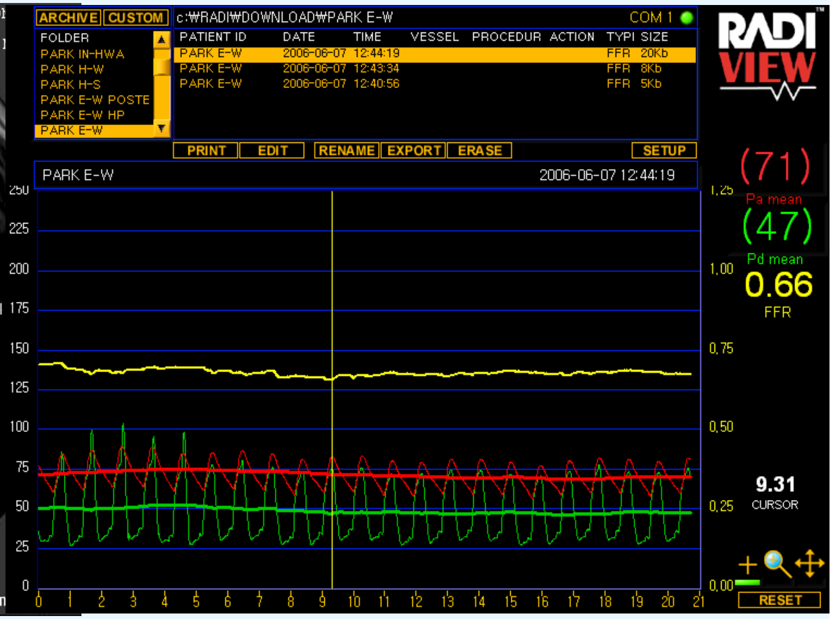
IVUS: 40MHz Atlantis™ SR Pro, Galaxy 2 Ultrasound Imaging System, Boston Scientific Corporation, Natick, MA, USA

SJ Tahk, MH Yoon, et al. Aspen 2007

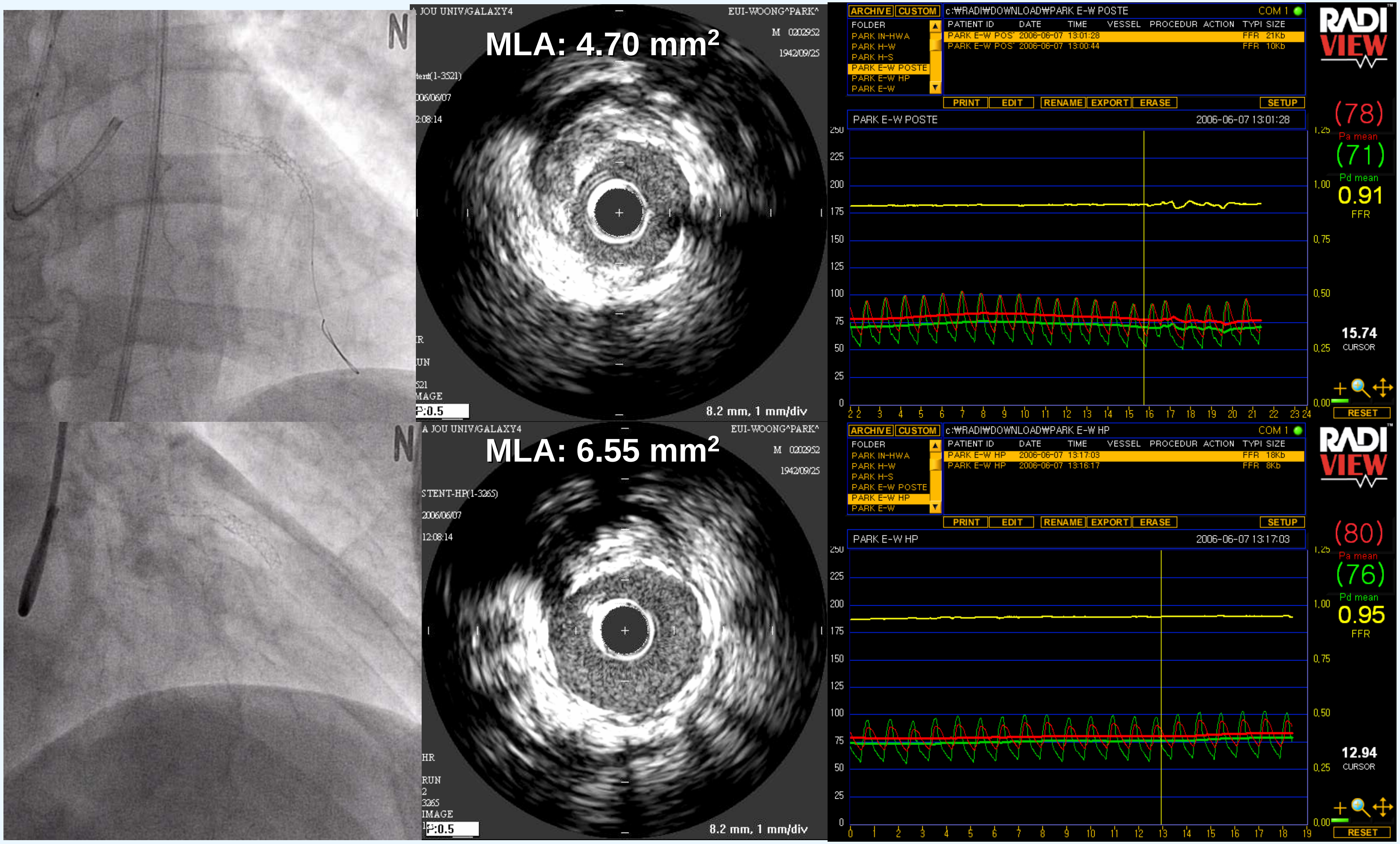
63 y-o Male, Unstable Angina







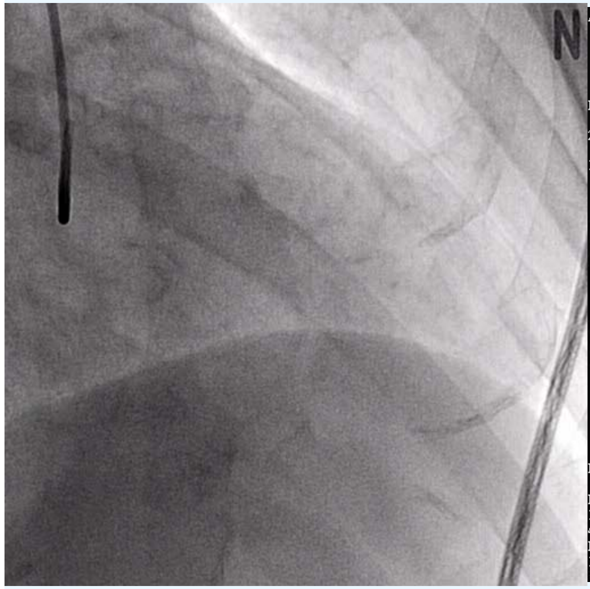
MLD	0.72 mm	MLA	1.15 mm^2
DS	77.0%	%AS	87.6 %
Lesion length	38 mm	Plaque Burden	89.3%

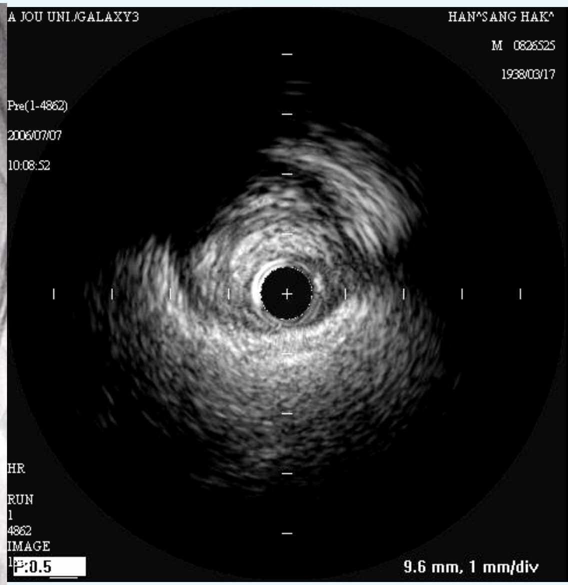


MLA: 4.70 mm²
8.2 mm, 1 mm/div
MLA: 6.55 mm²
8.2 mm, 1 mm/div
PARK E-W POSTE
2006-06-07 13:01:28
(78)
Pa mean
(71)
Pd mean
0.91
FFR
15.74
CURSOR
PARK E-W HP
2006-06-07 13:17:03
(80)
Pa mean
(76)
Pd mean
0.95
FFR
12.94
CURSOR

EY Park

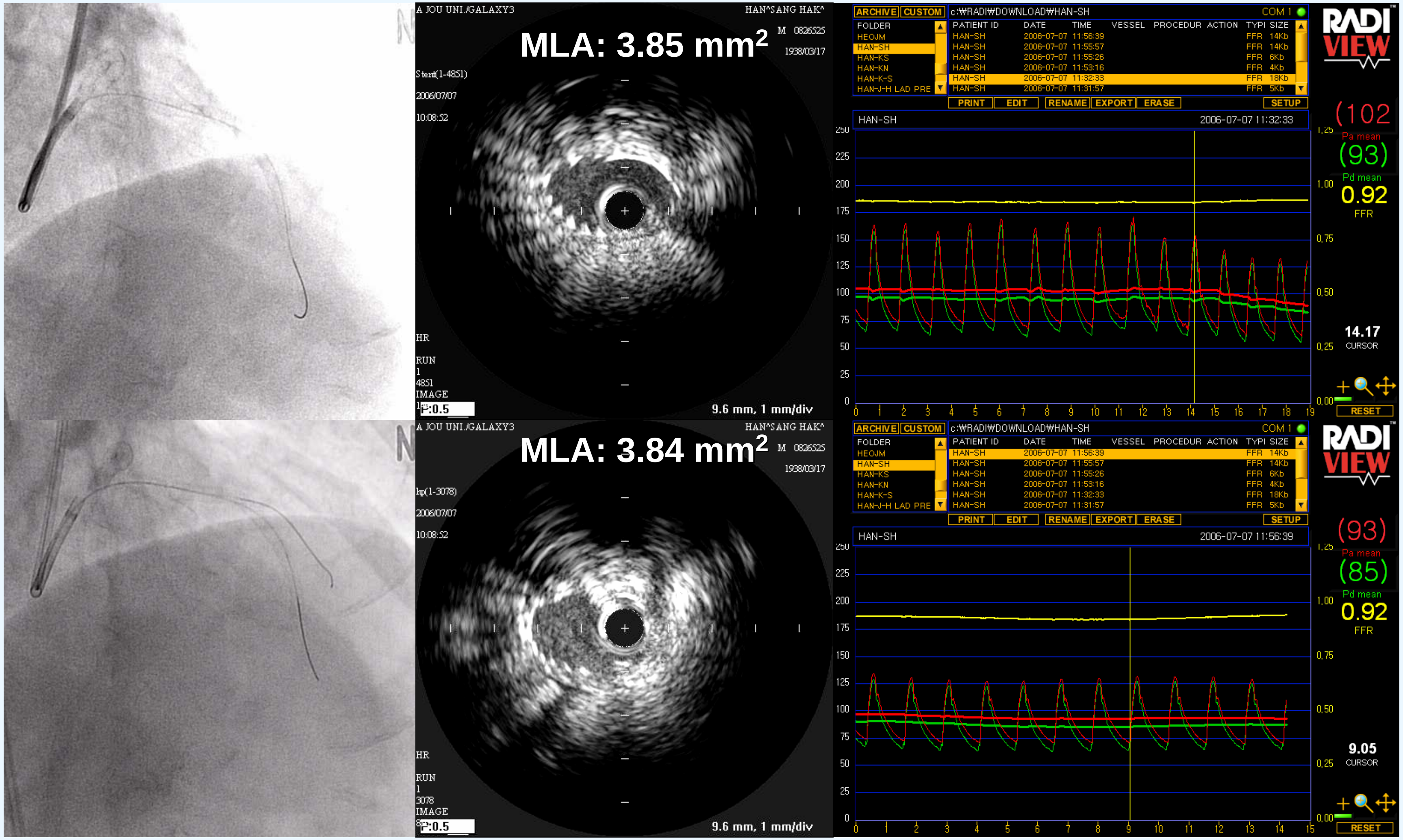
69 y-o Male Stable Angina





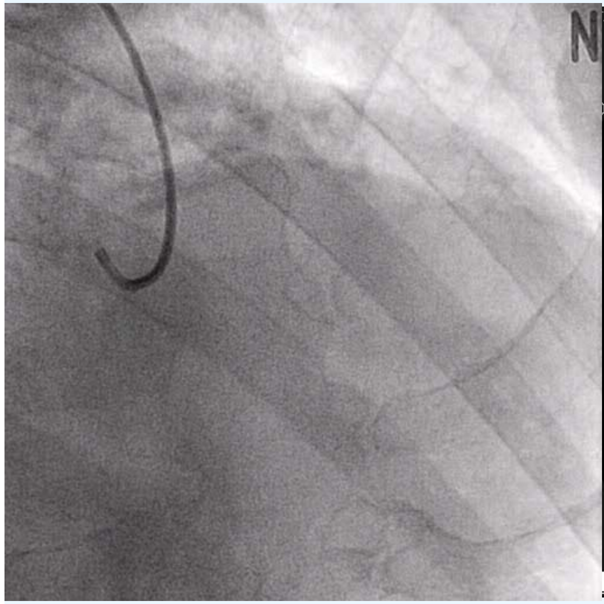
MLD	**0.58 mm**	**MLA**	**0.94 mm²**
DS	**81.0%**	**%AS**	**87.7%**
Lesion length	**61 mm**	**Plaque Burden**	**90.3%**

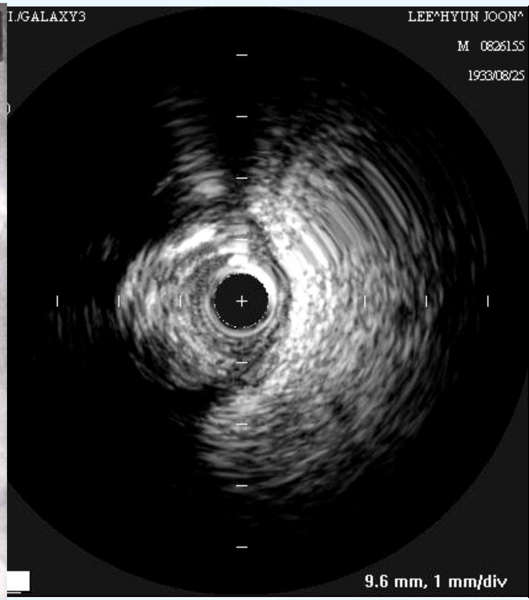
SH Han

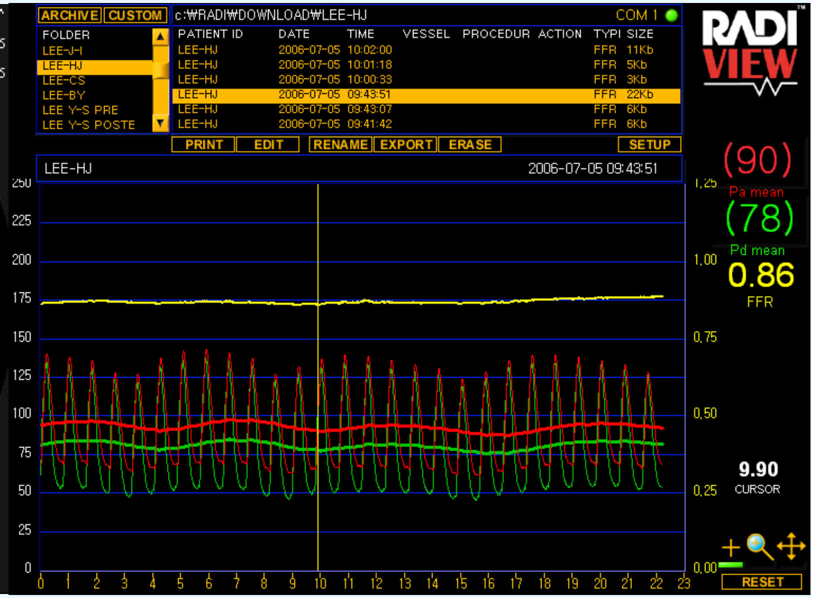


MLA: 3.85 mm²
9.6 mm, 1 mm/div
HAN-SH
2006-07-07 11:32:33
(102)
Pa mean
(93)
Pd mean
0.92
FFR
14.17
CURSOR
RADI VIEW
MLA: 3.84 mm²
9.6 mm, 1 mm/div
HAN-SH
2006-07-07 11:56:39
(93)
Pa mean
(85)
Pd mean
0.92
FFR
9.05
CURSOR
RADI VIEW

72 y-o Stable Angina







MLD	**0.70 mm**	**MLA**	**2.15 mm²**
DS	**77.0%**	**%AS**	**72.7%**
Lesion length	**40 mm**	**Plaque Burden**	**80.5%**

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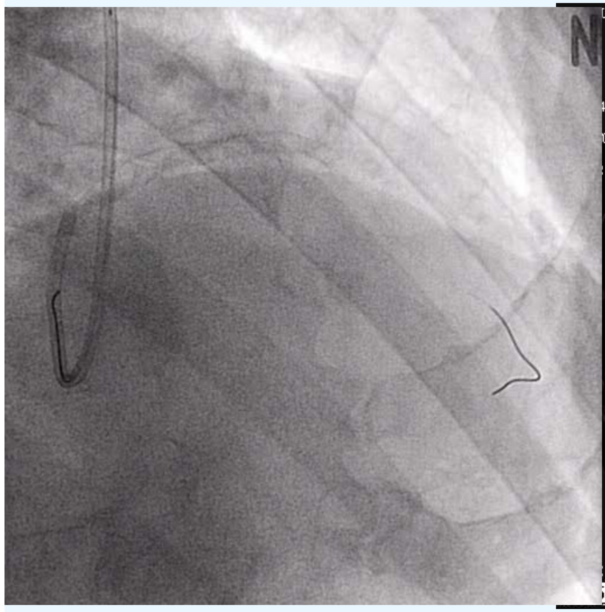
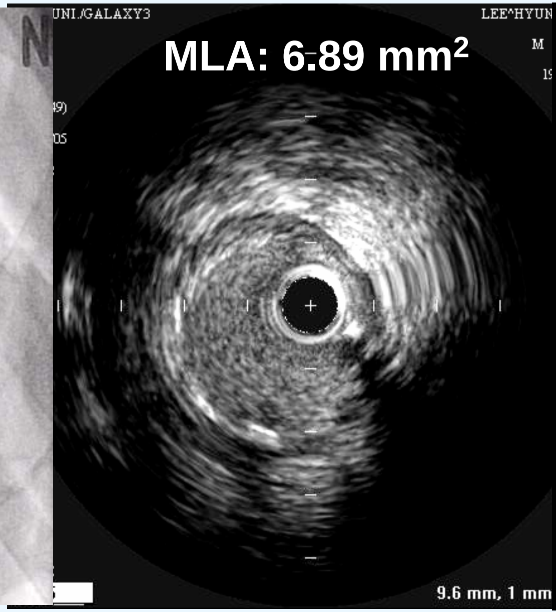
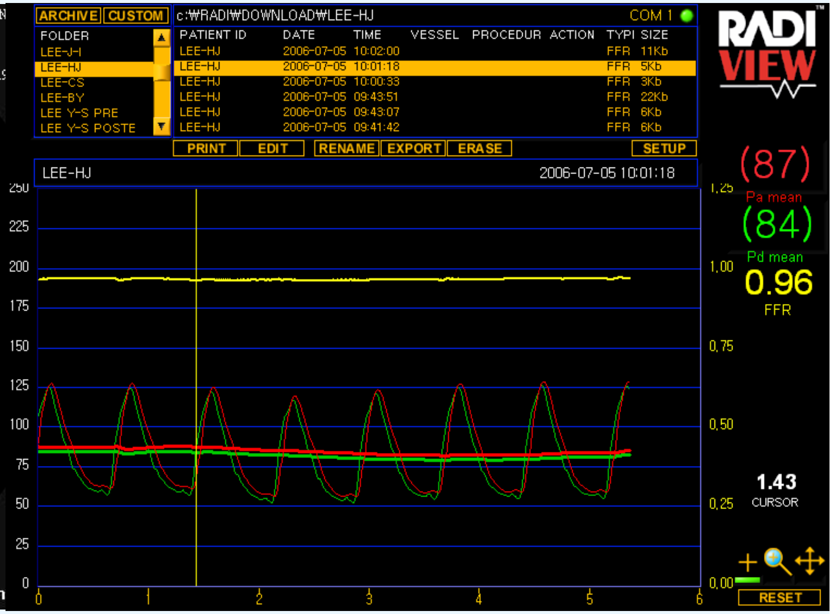



UNI./GALAXY3
LEE^HYUN
MLA: 6.89 mm^2
9.6 mm, 1 mm


ARCHIVE
CUSTOM
c:₩RADI₩DOWNLOAD₩LEE-HJ
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FOLDER
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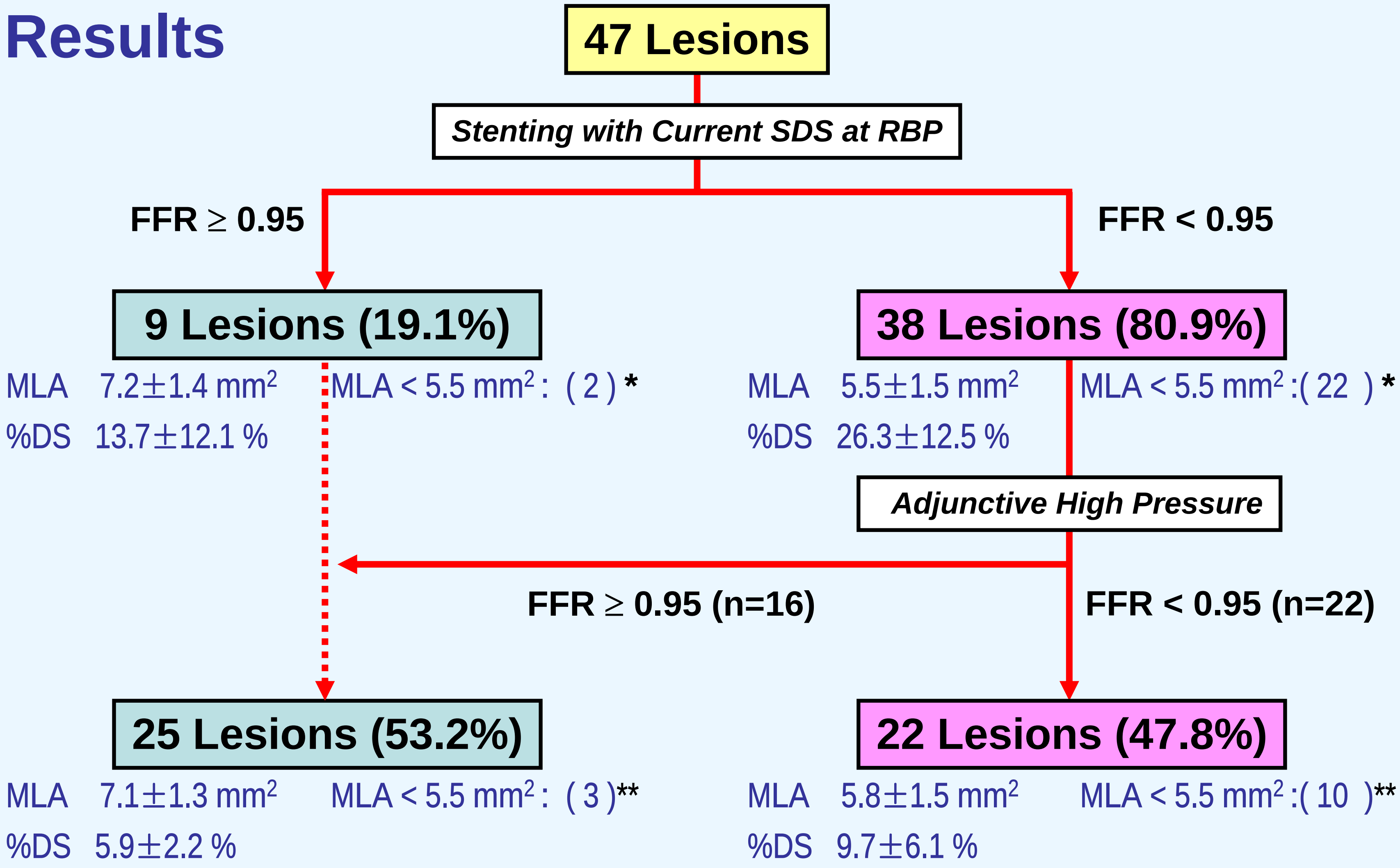
LEE Y-S POSTE
PATIENT ID DATE TIME VESSEL PROCEDUR ACTION TYPI SIZE
LEE-HJ 2006-07-05 10:02:00 FFR 11Kb
LEE-HJ 2006-07-05 10:01:18 FFR 5Kb
LEE-HJ 2006-07-05 10:00:33 FFR 3Kb
LEE-HJ 2006-07-05 09:43:51 FFR 22Kb
LEE-HJ 2006-07-05 09:43:07 FFR 6Kb
LEE-HJ 2006-07-05 09:41:42 FFR 6Kb
PRINT
EDIT
RENAME
EXPORT
ERASE
SETUP
LEE-HJ
2006-07-05 10:01:18
RADI VIEW
(87)
Pa mean
(84)
Pd mean
0.96
FFR
1.43
CURSOR
RESET

HJ Lee

Results



*** 24/47 (52.7%) lesions could not reach MLA>5.5mm^2 on IVIS with SDS at RBP**

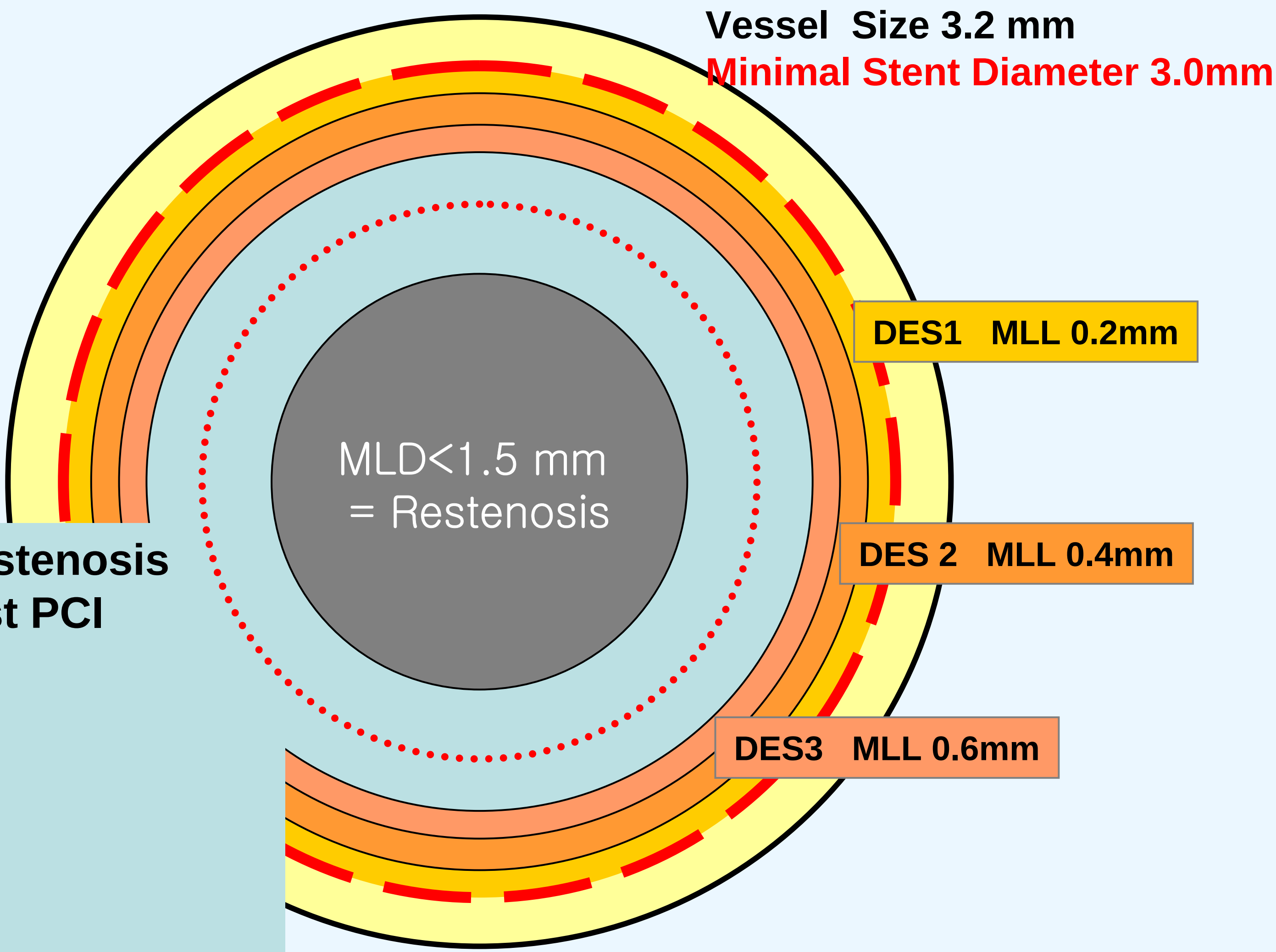
**** 13/47 (27.7%) lesions could not reach MLA>5.5mm^2 on IVIS after HP dilatation**

FFR and IVUS Criteria Reached ..

	Post Stent	Post HP
FFR>0.95	9 (19.1%)	25 (53.2%)
IVUS MSA >5.5mm^2	23 (47.3%)	38 (72.3%)
IVUS MUSIC*	12 (25.5%)	14 (29.8%)

*** Final lumen CSA > 80% of the reference** (or > 90% if minimal lumen CSA was < 9 mm^2)

Late Loss and “Headroom” to Restenosis in Patients FFR≥0.95

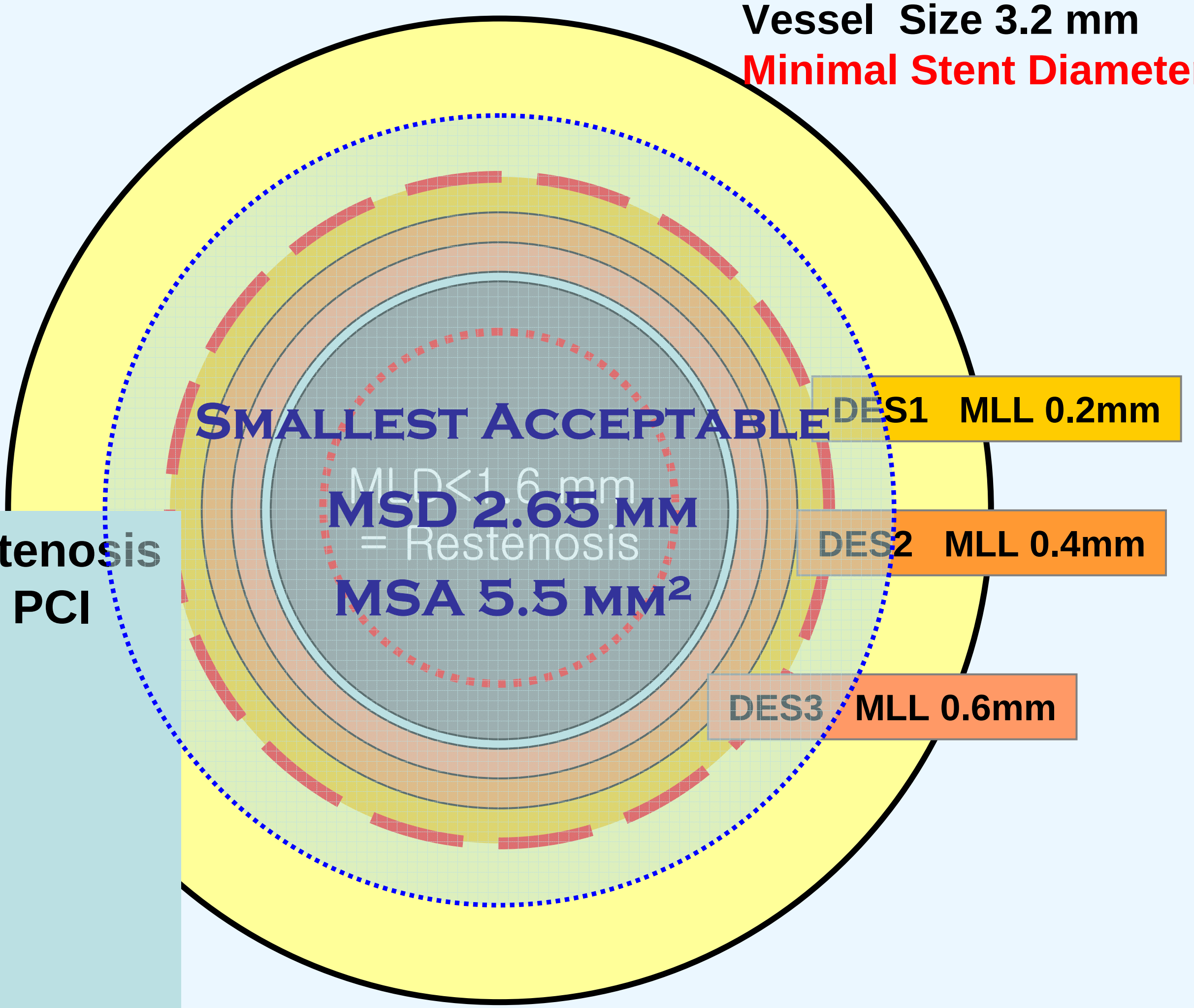


Headroom to Restenosis
1.5 mm after Post PCI

1.3 mm
1.1 mm
0.9 mm

0.5 mm in BMS
RV Size 3.0 mm

Late Loss and "Headroom" to Restenosis in Patients FFR<0.95

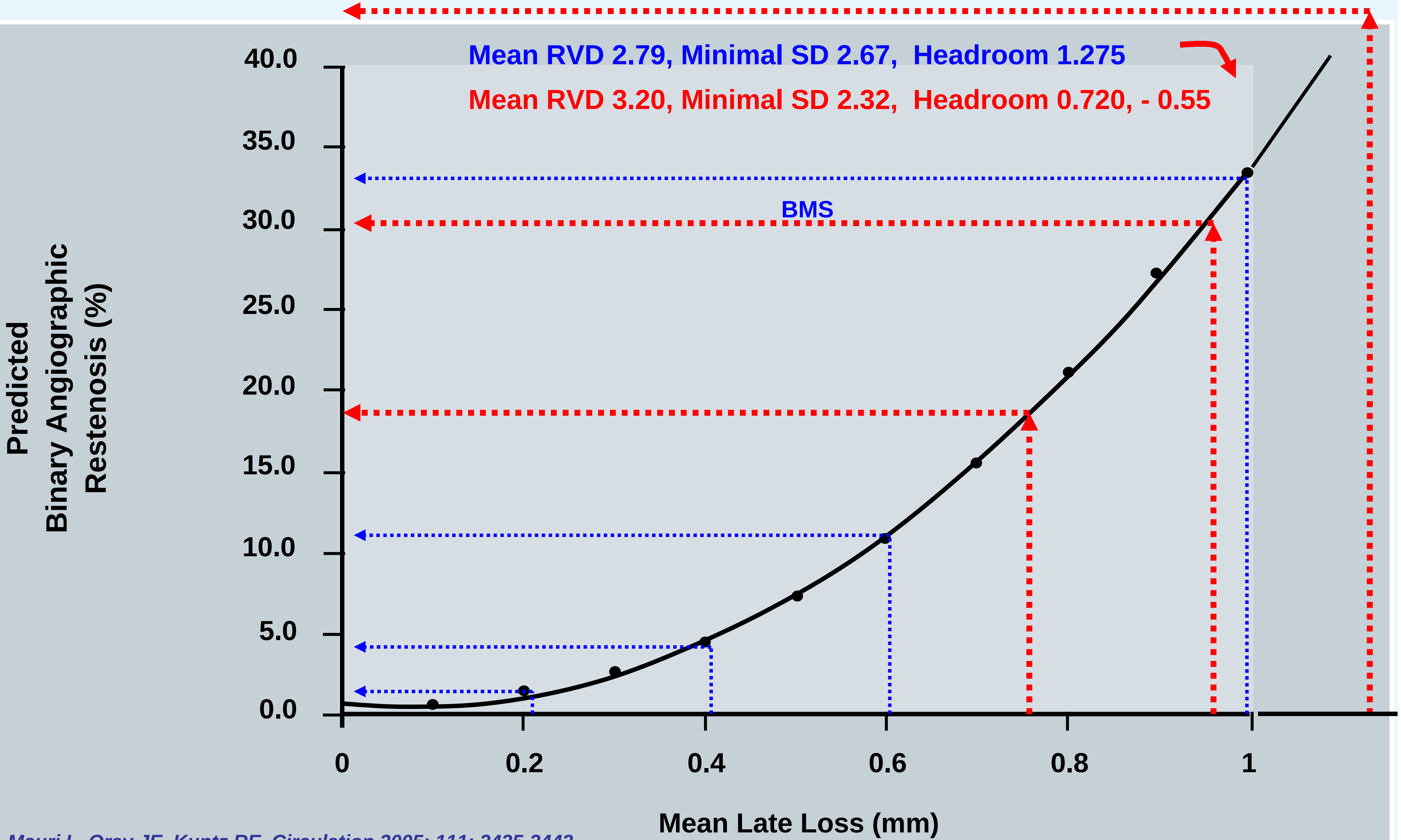


Headroom to Restenosis 0.7 mm after Post PCI

0.5 mm
0.3 mm
0.1 mm

-0.3 mm in BMS
RV Size 3.0 mm

Mean Late Loss and Risk of Restenosis



Mauri L, Orav JE, Kuntz RE. Circulation 2005; 111: 3435-3442

Angiographic and Procedural Findings

	Group A (FFR≥0.95, n=9)	Group B (FFR<0.95, n=38)	p Value
Pre-Stent			
MLD (mm)	0.57 ±0.11	0.59 ± 0.19	0.921
DS (%)	81.1 ± 4.5	81.5 ± 5.4	0.872
Post-Stent			
MLD (mm)	3.09 ± 0.23	2.32 ± 0.46	0.012
DS (%)	13.8 ± 12.1	26.3 ± 12.5	0.014
Reference Diameter (mm)			
Proximal	3.40 ±0.17	3.42 ±0.25	0.776
Distal	2.95 ±0.14	3.0 ±0.29	0.641
Lesion length (mm)	42.8 ±10.4	52.3 ±12.2	0.049
Stent number	1.64 ±0.50	1.95 ±0.55	0.096
Stent length (mm)	46.4 ± 13.9	56.9 ± 15.3	0.047

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IVUS Findings

	Group A (FFR≥0.95, n=9)	Group B (FFR<0.95, n=38)	p Value
Pre-stent			
MLA (mm^2)	2.65 ± 0.68	1.75 ± 0.69	0.001
AS (%)	71.3 ± 9.8	80.0 ± 10.6	0.030
Post-stent			
MLA (mm^2)	7.16 ± 1.64	5.57 ± 1.57	0.005
AS (%)	23.3 ± 12.3	36.2 ± 19.7	0.059
Ref Lumen Area(mm^2)	10.0 ±3.4	8.9 ±1.9	0.176
VA at Lesion(mm^2)	13.0 ±4.2	10.8 ±2.5	0.041
Plaque Burden	78.7 ±6.3	83.7 ±6.5	0.042
Ref Vessel Area (mm^2)	14.6 ± 4.4	13.3 ± 2.9	0.284
Remodeling Index	0.92 ±0.22	0.82 ±0.16	0.140

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Independent Predictor for Suboptimal Stent Expansion (FFR<0.95 or FFR≥0.95)

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	PLAQ_C	.502	1.116	.202	1	.653	1.652
	REMOD_IX	-.120	2.809	.002	1	.966	.887
	ECCENT	-3.706	2.720	1.857	1	.173	.025
	MINLA	-1.482	.685	4.682	1	.030	.227
	ST_LENGT	.019	.041	.213	1	.645	1.019
	Constant	4.057	3.453	1.380	1	.240	57.780

a. Variable(s) entered on step 1: PLAQ_C, REMOD_IX, ECCENT, MINLA, ST_LENGT.

By Multiple binary logistic regression analysis

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Independent Predictor for Suboptimal Stent Expansion (correlation with post-stent FFR)

Coefficients [a]

Model		Unstandardized Coefficients B	Unstandardized Coefficients Std. Error	Standardized Coefficients Beta	t	Sig.
1	(Constant)	.933	.041		22.891	.000
	PLAQ_C	−.012	.012	−.154	−1.010	.320
	REMOD_IX	.001	.032	.005	.036	.972
	ECCENT	.024	.033	.095	.725	.474
	MINLA	.017	.008	.328	2.120	.042
	ST_LENGT	−.001	.000	−.351	−2.364	.024

a. Dependent Variable: FFR_STEN

By Multiple linear regression analysis

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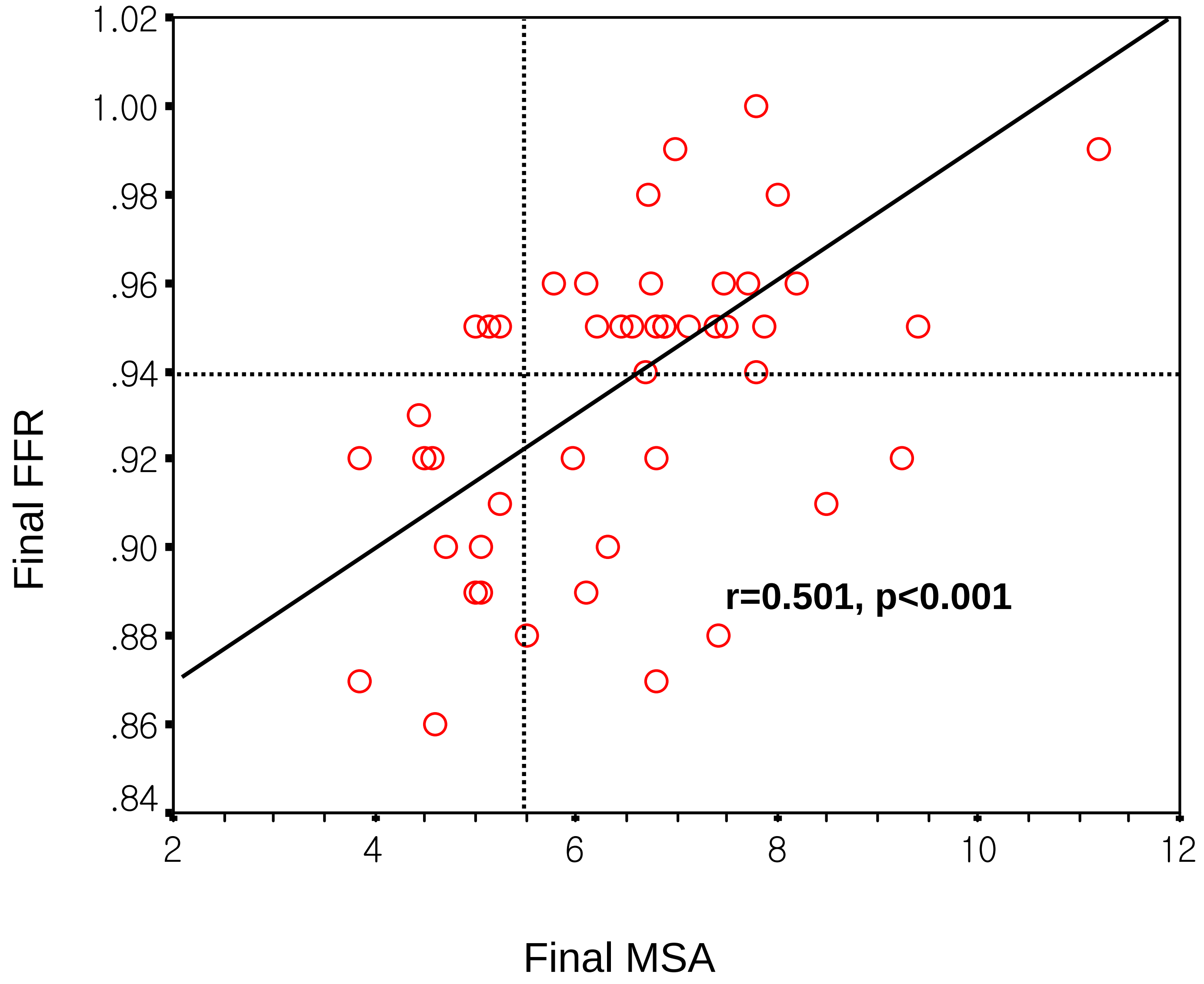
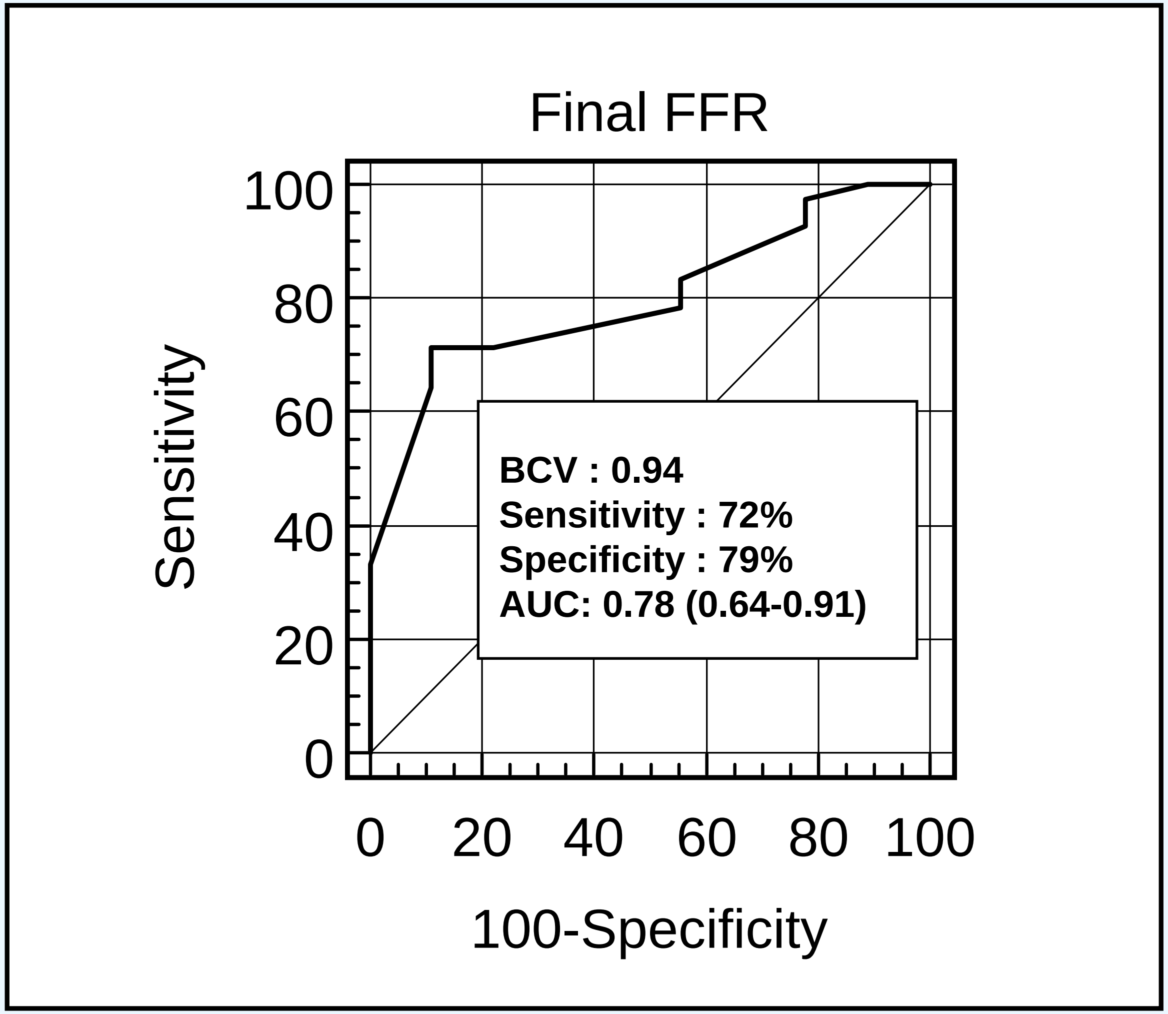
FFR vs. IVUS Minimal Stent Area



The Relation between Final FFR and MSA (BCV of FFR for MSA $\geq$5.5 mm^2)



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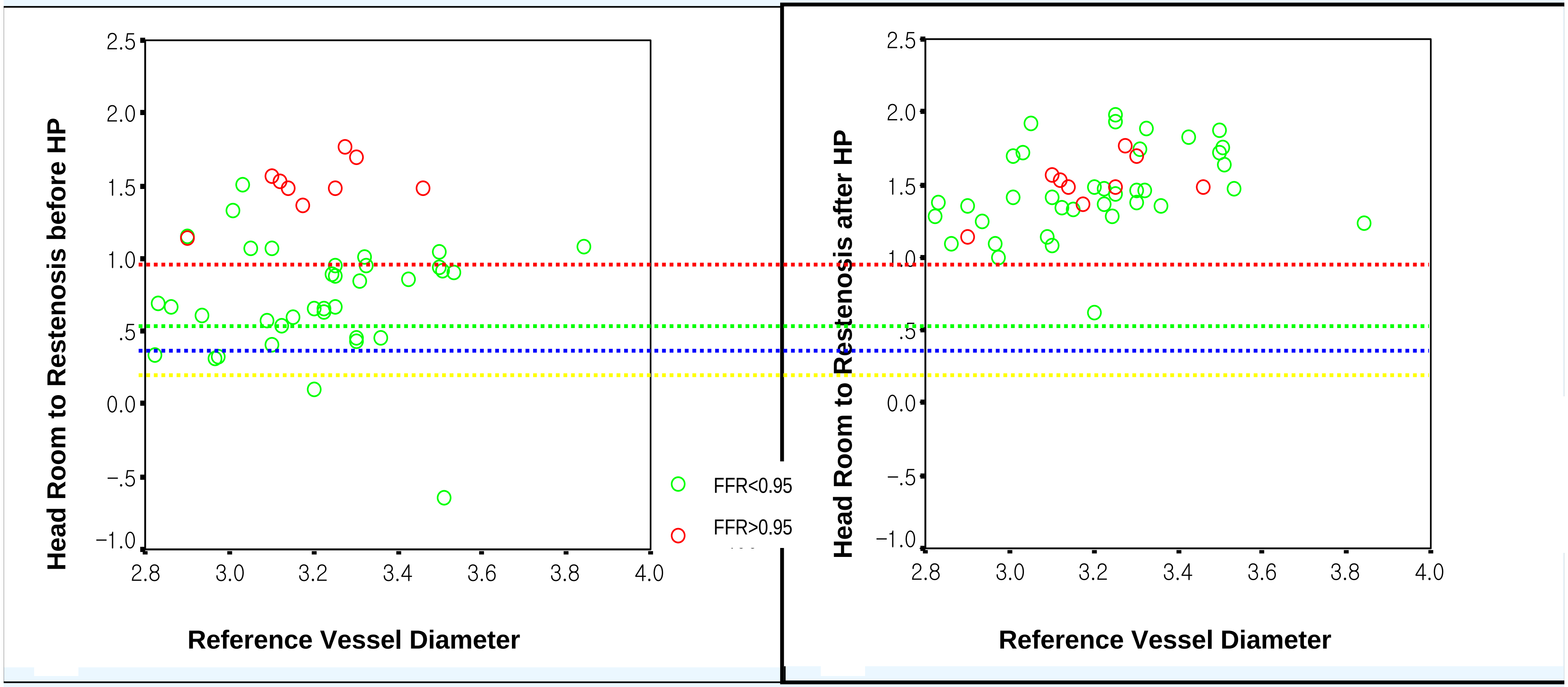
Effect of HP Dilatation on Headroom to Restenosis QCA Analysis



FFR and IVUS Criteria Reached were Inadequate with current SDS even with RBP

	Post Stent	Post HP
FFR>0.95	9 (19.1%)	25 (53.2%)
IVUS MSA >5.5mm^2	23 (47.3%)	38 (72.3%)
IVUS MUSIC*	12 (25.5%)	14 (29.8%)

*** Final lumen CSA > 80% of the reference** (or > 90% if minimal lumen CSA was < 9 mm^2)

- Independent IVUS predictors for suboptimal stent expansion was IVUS minimal lumen area and stent length (lesion length).
- Best cut-off value of FFR for MSA>5.5mm^2 after HP dilatation was 0.94

Conclusion

- Routine adjunctive high-pressure ballooning of DES might be required to achieve optimal functional and anatomic stent expansion, in number of long diffuse coronary stenoses.

- FFR and IVUS-guided PCI could potentially improve the procedural precision and decrease the rate of target vessel failure in DES era. However, the role of physiologic and IVUS study in DES era needs more randomized trials.

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DES Implantation in Long Diffuse Lesion

- Appropriate lesion preparation

- Adjunctive High Pressure Dilatation

DO NOT FORGET OLD LESSONS EVEN IN DES ERA.

- Do not believe your visual estimation

- Please do not avoid modern facilities of convenience