Invited Case Presentation and Focused Review: Image-guided Intervention

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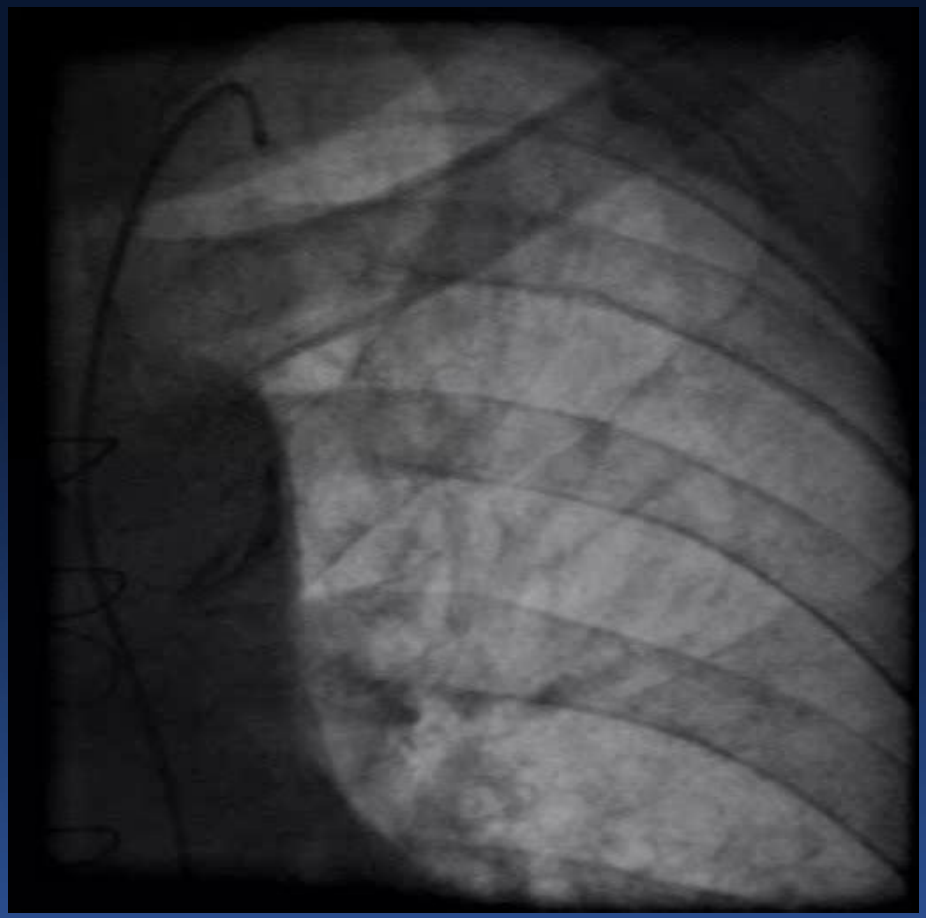
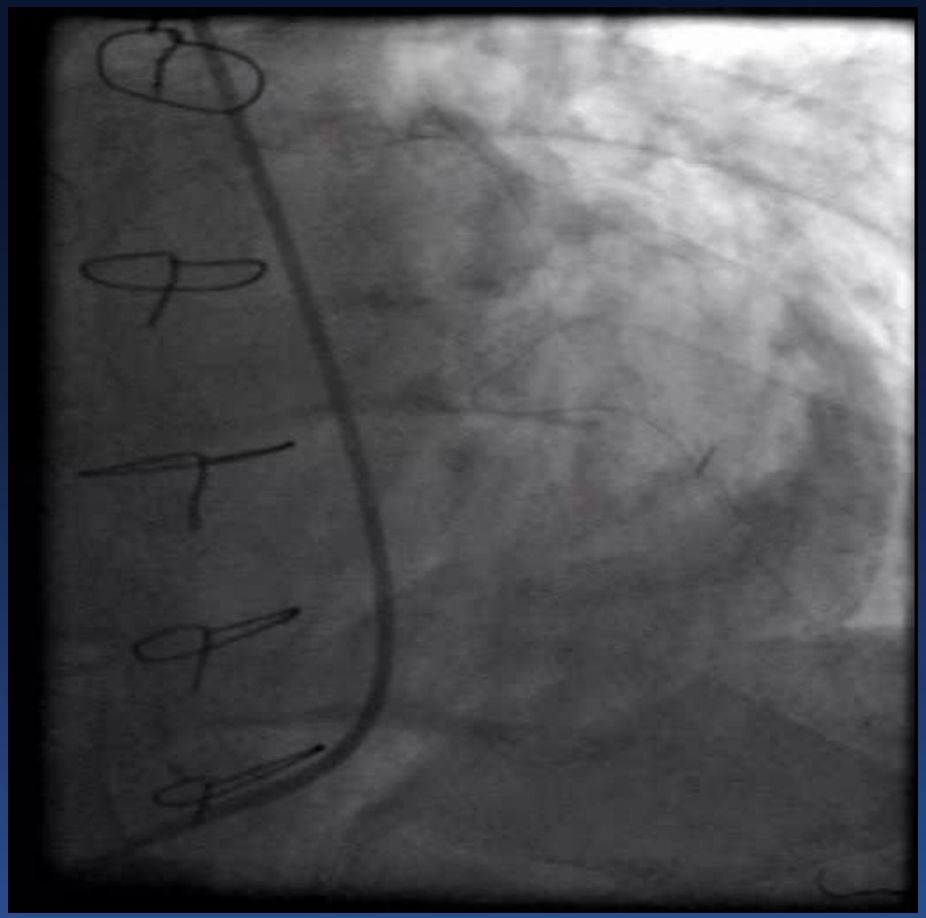
Cardiovascular Research Foundation

Case

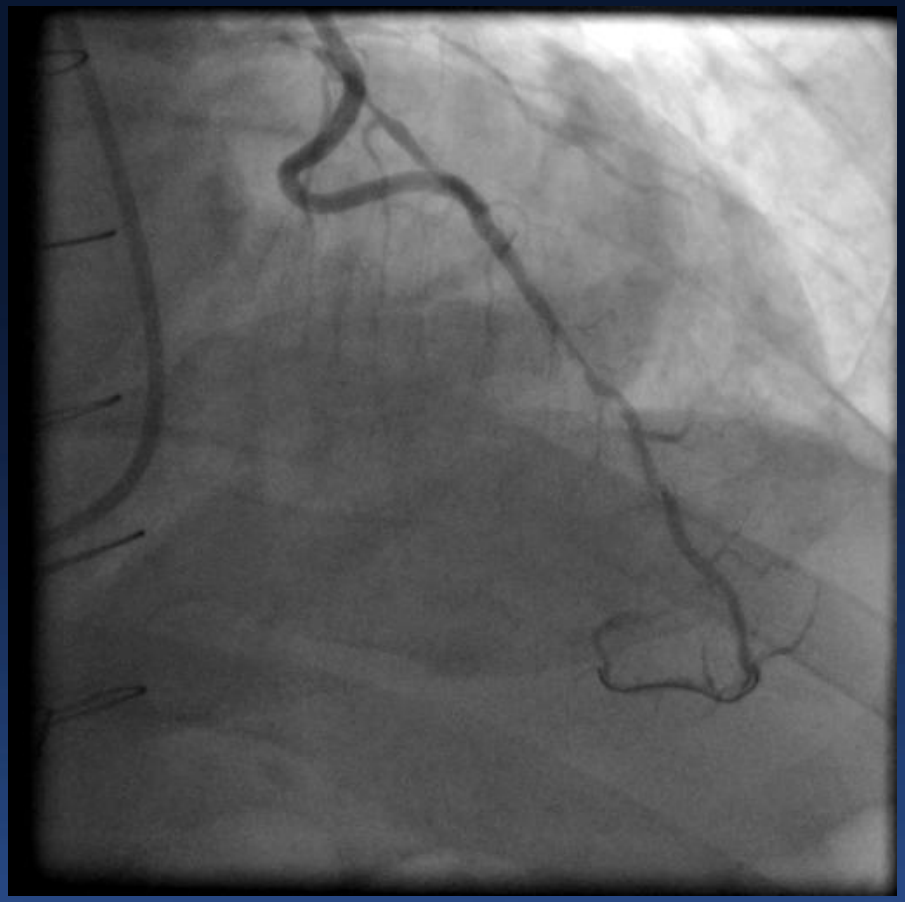
- 75 year old male
- Prior CABG in 1996
- Coronary Risk Factors:
  - Hyperlipidemia, Hypertension

Pre-Intervention

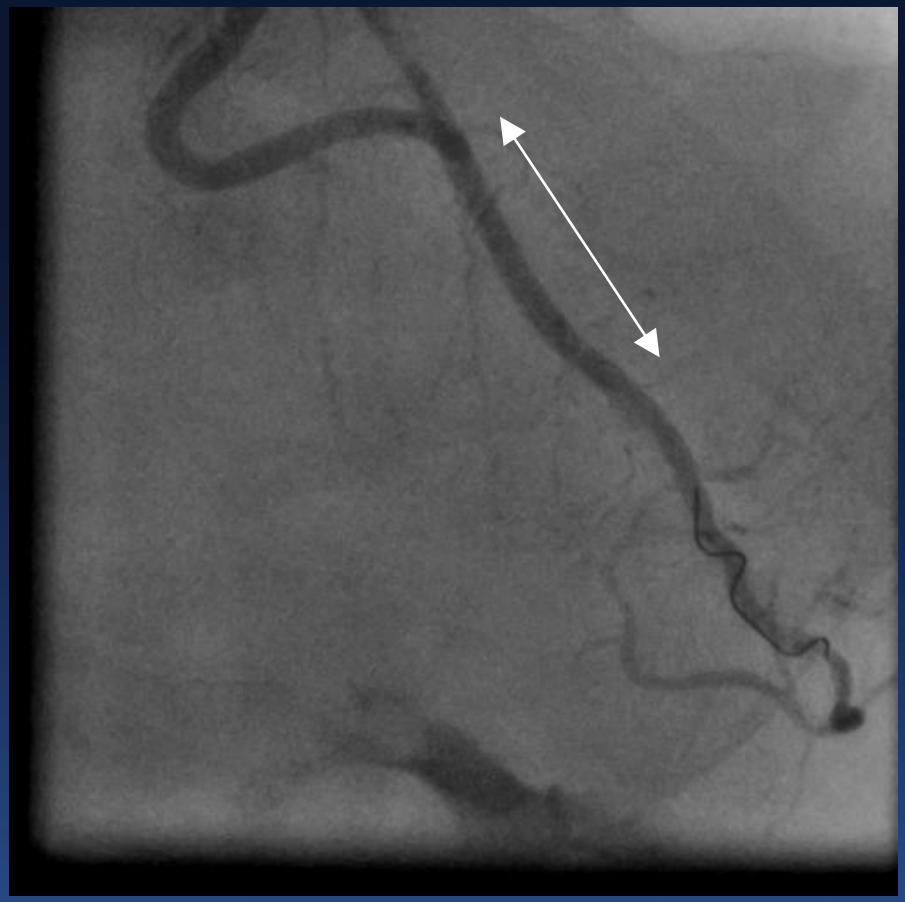




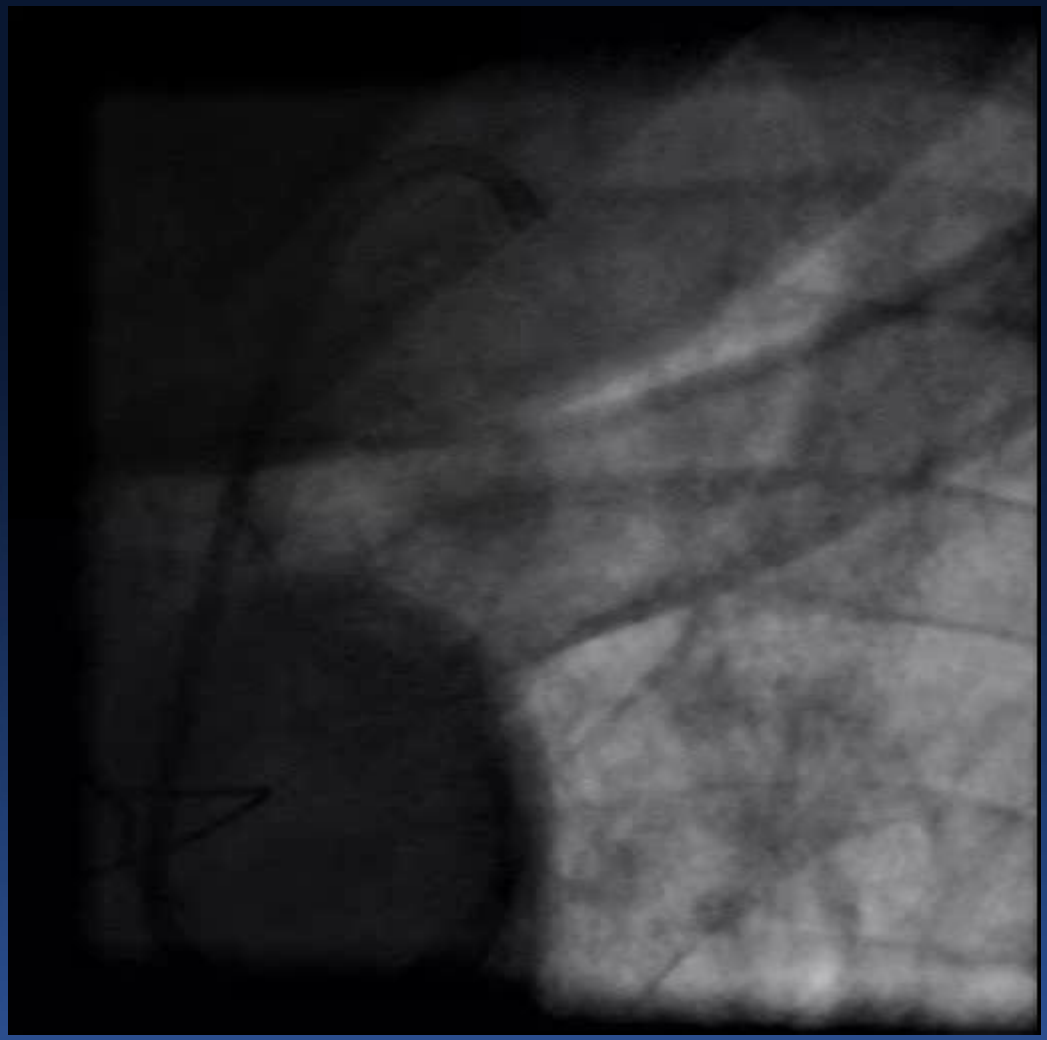
Pre-Intervention



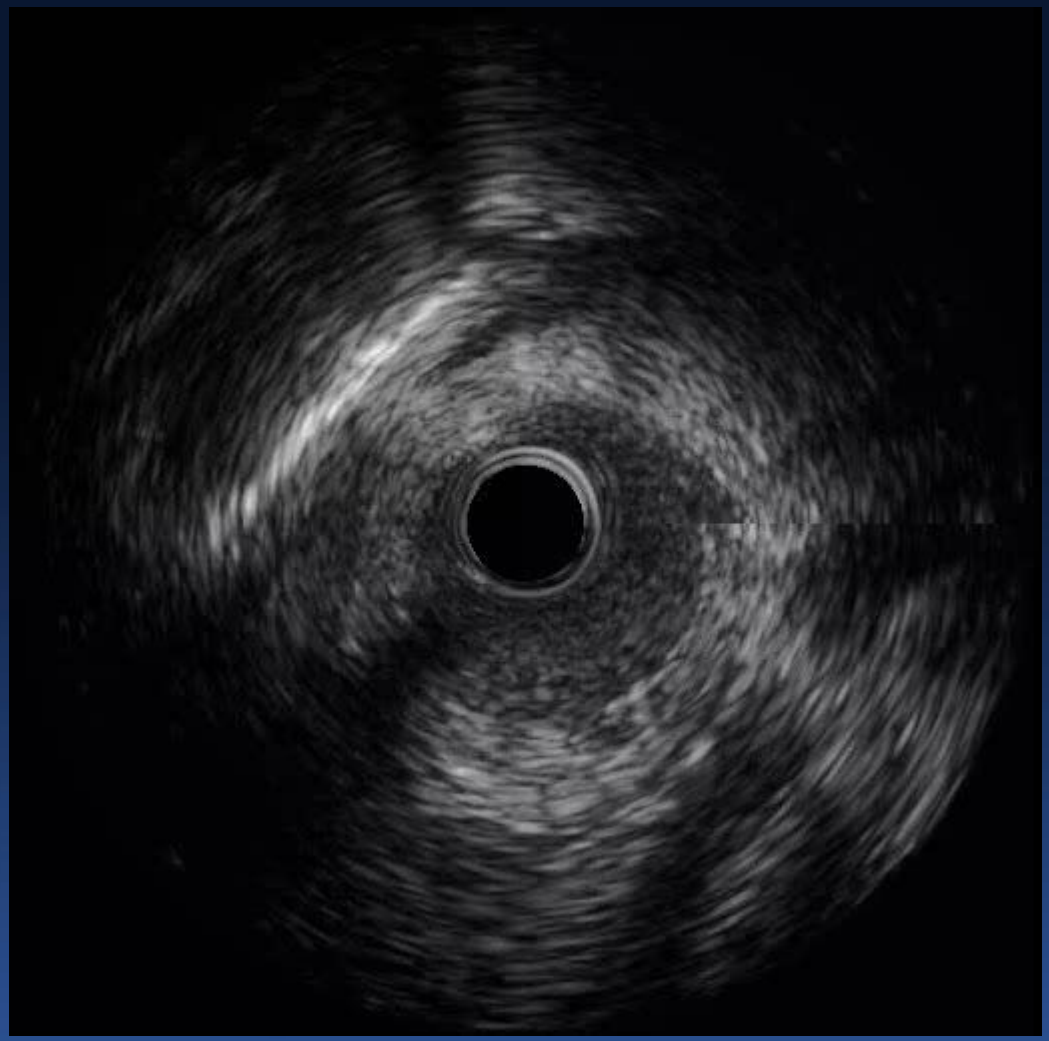
Post-Stent



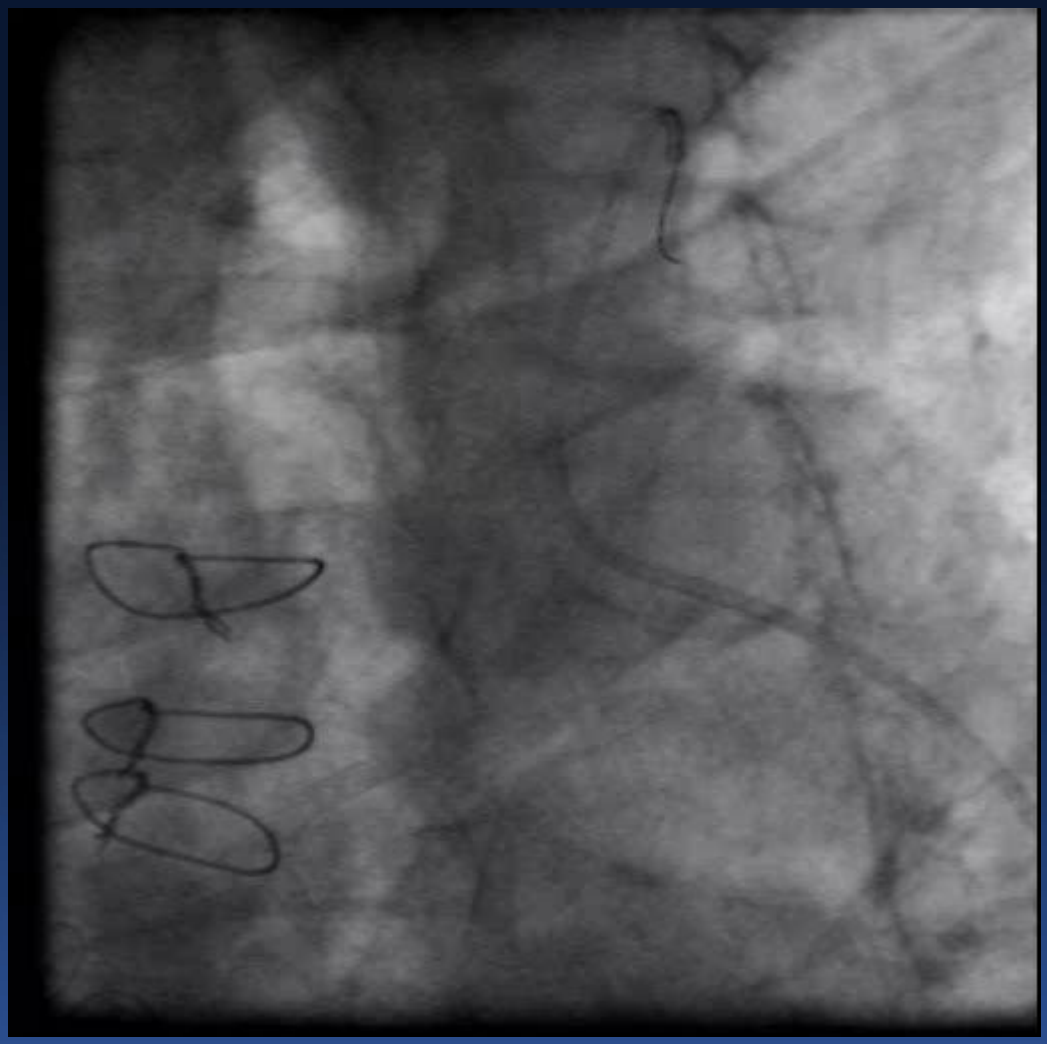
ST Elevation



IVUS - LAD to LIMA



Final



Modalities

- FFR
- IVUS (with or without VH, iMAP, or IB-IVUS)
- OCT
- NIRS (with or without IVUS)
- Some combination of the above
- (ICE or TEE)

Clinical questions

- Is this lesion flow-limiting?
  - Non-LMCA
  - LMCA
- Pre-intervention lesion assessment (ie., what is the culprit?)
- Is this “other” lesion a vulnerable plaque that is at risk for future events?
- What is the likelihood of embolization during stent implantation?
- How do I optimize acute stent results (size, length, expansion, edge coverage)?
- Is this jailed sidebranch significant?
- Why did this stent thrombose or restenose?

Pre-intervention

- Measure vessel size to select stent size
- Identify proximal and distal reference segments or landing zones (largest lumen with least plaque) to select stent length.
- Identify high risk or other unusual morphologies
  - Culprit lesions
  - Plaque at high risk for distal embolization
  - Spontaneous coronary artery dissections
  - Calcific nodules or intracoronary thrombi
  - Mechanical causes of in-stent restenosis

Post-intervention

- Optimize expansion
  - Absolute stent CSA
  - Stent CSA relative to a pre-defined reference
- Full lesion coverage – no geographical miss
- No complications

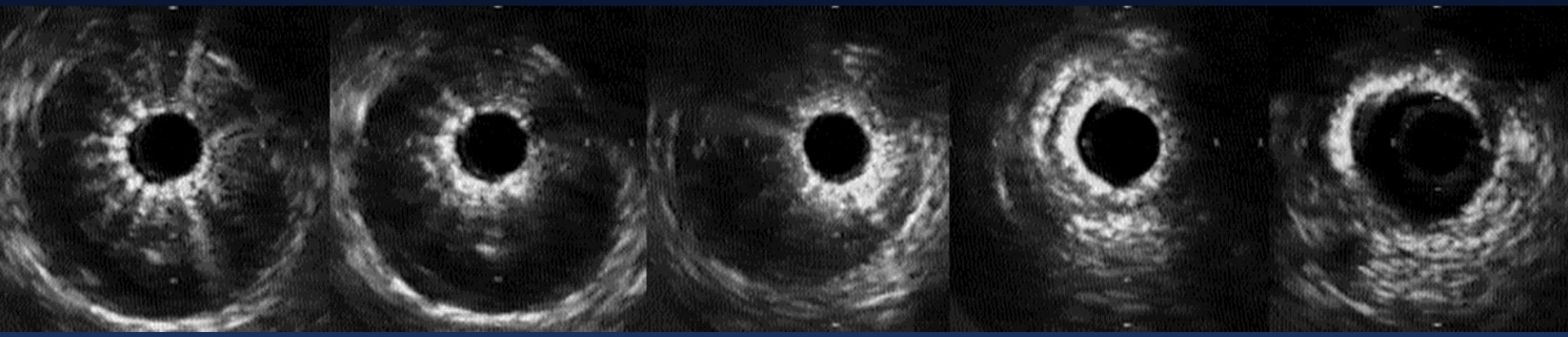
Clinical problem	FFR	IVUS	VH-IVUS	OCT	NIRS
Assessing lesion severity					
Non-LMCA	+				
LMCA	+	+			
Identifying the culprit lesion		±		+	
Identifying vulnerable plaque			+	+	+
Predicting distal embolization		+	+	+	+
Optimizing stent implantation		+		±	
Assessing stent failure		+		+	

IVUS Predictors of DES Early Thrombosis & Restenosis

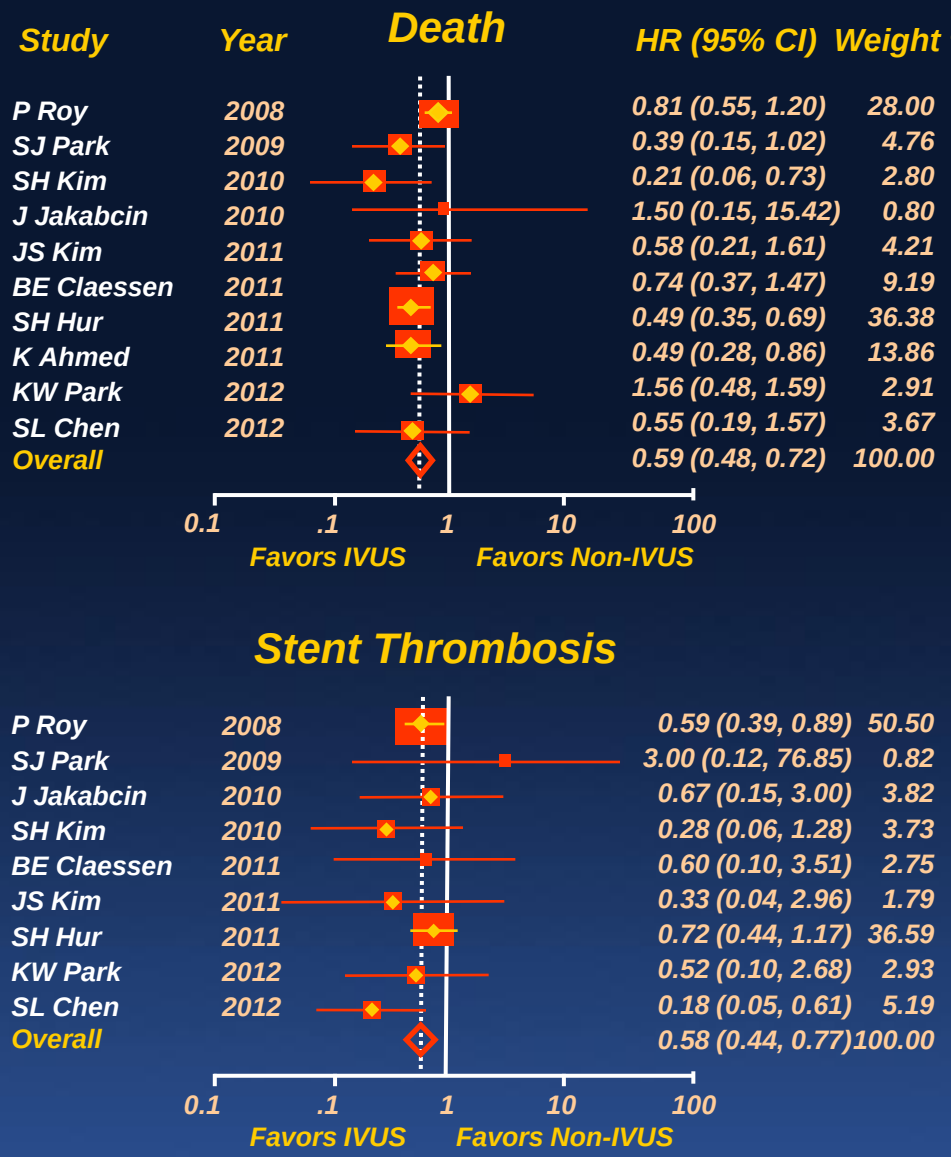
	Early Thrombosis	Restenosis
Small MSA or MLA or underexpansion	•*Fujii et al. J Am Coll Cardiol 2005;45:995-8)* •*Okabe et al., Am J Cardiol. 2007;100:615-20* •*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34* •*Choi et al. Circ Cardiovasc Interv 2011;4:239-47*	•*Sonoda et al. J Am Coll Cardiol 2004;43:1959-63* •*Hong et al. Eur Heart J 2006;27:1305-10* •*Doi et al JACC Cardiovasc Interv. 2009;2:1269-75* •*Fujii et al. Circulation 2004;109:1085-1088* •*Kang et al. Circ Cardiovasc Interv 2011;4:9-14* •*Choi et al. Am J Cardiol 2012;109:455-60* •*Song et al. Catheter Cardiovasc Interv, in press*
Edge problems (geographic miss, secondary lesions, large plaque burden, dissections, etc)	•*Fujii et al. J Am Coll Cardiol 2005;45:995-8* •*Okabe et al., Am J Cardiol. 2007;100:615-20* •*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34* •*Choi et al. Circ Cardiovasc Interv 2011;4:239-47*	•*Sakurai et al. Am J Cardiol 2005;96:1251-3* •*Liu et al.Am J Cardiol 2009;103:501-6* •*Costa et al, Am J Cardiol, 2008;101:1704-11*

Although it was one of the original Colombo criteria, there is little or no data linking *isolated* acute stent malapposition to adverse clinical events including ST and restenosis.

- **Stent malapposition is associated with *less* intimal hyperplasia – the drug can cross small stent vessel-wall gaps**
  - *Hong et al, Circulation. 2006;113:414-9*
  - *Kimura et al, Am J Cardiol . 2006;98:436-42*
  - *Steinberg et al, JACC Cardiovasc Intervent 2010;3:486-94*
  - *Balakrishnan et al., Circulation 2005;111:2958-65*
- **In the integrated analysis of slow release formulation PES in TAXUS IV, V, and VI and TAXUS ATLAS Workhorse, Long Lesion, and Direct Stent Trial, there was no effect of acute stent malapposition on MACE or ST within the first 9 months – whether BMS or DES**
  - *Steinberg et al, JACC Cardiovasc Intervent 2010;3:486-94*
- **In HORIZONS-AMI, acute stent malapposition was detected in 33.8% of 68 lesions treated with PES and 38.7% of 24 lesions treated with BMS (p=0.7). There was no difference in MACE between pts with versus without acute stent malapposition in either BMS or PES cohorts; and acute malapposition was not a predictor of early ST**
  - *Guo et al. Circulation 2010;122:1077-84*
  - *Choi et al. Circ Cardiovasc Interv 2011;4:239-47*
- **Although acute malapposition was observed in 28/403 pts with LMCA lesions treated with DES implantation, malapposition was not related to MACE at follow-up.**
  - *Kang et al. Circ Cardiovasc Interv 2011;4:562-9*



Meta-Analysis of 11 Studies (n=19,619 patients)



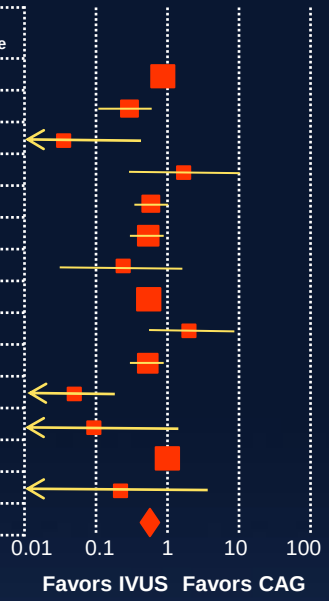
Compared with angiography-guidance, IVUS-guided DES implantation was associated with a reduced incidence of

- ***Death (HR: 0.59, 95% CI: 0.48-0.73, p<0.001)***
- ***Stent thrombosis (HR: 0.58, 95% CI: 0.44-0.77, p<0.0001)***
- ***Major adverse cardiac events (HR: 0.87, 95% CI: 0.78-0.96, p=0.008)***

Zhang et al. Eurointervention 2012;8:855-65

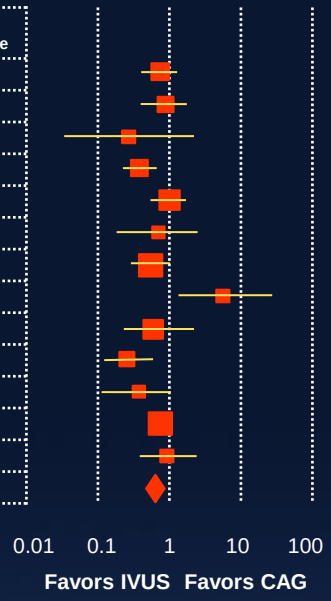
Death from any cause

		OR	Lower	Upper	Z-value	P-value
Roy	2008	0.79	0.54	1.16	-1.20	0.23
MAIN-COMPARE	2009	0.26	0.11	0.63	-2.96	0.00
Kim	2010	0.03	0.00	0.44	-2.57	001
HOME DES IVUS	2010	1.52	0.26	8.87	0.46	0.64
MATRIX	2011	0.53	0.29	0.97	-2.07	0.04
COBIS	2011	0.47	0.26	0.83	-2.62	0.01
Youn	2011	0.21	0.03	1.70	-1.46	0.14
Hur	2012	0.49	0.36	0.66	-4.60	0.00
EXCELLENT	2012	1.84	0.42	7.99	0.82	0.41
Ahn	2012	0.48	0.29	0.79	-2.88	0.00
Patel	2012	0.04	0.01	0.24	-3.66	0.00
Chen	2012	0.09	0.00	1.58	-1.65	0.10
ADAPT-DES	2012	0.88	0.64	1.20	-0.82	0.41
AVIO	2013	0.20	0.01	4.17	-1.04	0.30
Random pooled esttimate		0.50	0.36	0.69	-4.10	0.00



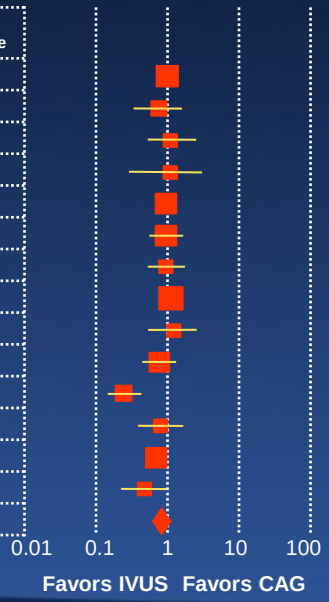
Myocardial Infarction

		OR	Lower	Upper	Z-value	P-value
Roy	2008	0.67	0.37	1.22	-1.31	0.19
MAIN-COMPARE	2009	0.81	0.37	1.75	-0.54	0.59
HOME DES IVUS	2010	0.24	0.03	2.09	-1.29	0.20
MATRIX	2011	0.35	0.18	0.71	-2.96	0.00
COBIS	2011	0.86	0.43	1.72	-0.43	0.66
Youn	2011	0.64	0.17	2.46	-0.65	0.52
Hur	2012	0.50	0.25	1.01	-1.95	0.05
EXCELLENT	2012	5.60	1.16	26.95	2.15	0.03
Ahn	2012	0.60	0.19	1.85	-0.89	0.37
Patel	2012	0.23	0.10	0.53	-3.44	0.00
Chen	2012	0.31	0.10	1.00	-1.97	0.05
ADAPT-DES	2012	0.66	0.51	0.86	-3.11	0.00
AVIO	2013	0.81	0.34	1.94	-0.47	0.64
Random pooled esttimate		0.59	0.45	0.79	-3.63	0.00



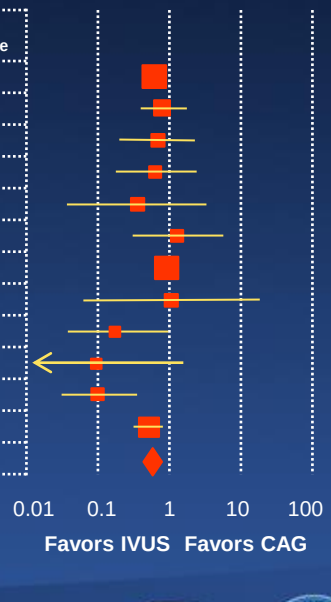
Target vessel revascularization

		OR	Lower	Upper	Z-value	P-value
Roy	2008	0.94	0.68	1.31	-0.37	0.71
MAIN-COMPARE	2009	0.72	0.31	1.67	-0.77	0.44
Kim	2010	1.08	0.45	2.60	0.18	086
HOME DES IVUS	2010	1.00	0.32	3.12	0.00	1.00
MATRIX	2011	0.90	0.62	1.30	-0.57	0.57
COBIS	2011	0.90	0.55	1.47	-0.43	0.67
Youn	2011	0.90	0.46	1.75	-0.32	0.75
Hur	2012	1.09	0.89	1.44	1.04	0.30
EXCELLENT	2012	1.09	0.46	2.58	0.20	0.84
Ahn	2012	0.74	0.46	1.16	-1.31	0.19
Patel	2012	0.24	0.13	0.43	-4.80	0.00
Chen	2012	0.80	0.38	1.71	-0.57	0.57
ADAPT-DES	2012	0.64	0.46	0.88	-2.70	0.01
AVIO	2013	0.46	0.21	0.99	-1.99	0.05
Random pooled esttimate		0.78	0.63	0.96	-2.30	0.02



Stent Thrombosis

		OR	Lower	Upper	Z-value	P-value
Roy	2008	0.58	0.39	0.87	-2.67	0.01
Kim	2010	0.76	0.35	1.67	-0.68	0.50
HOME DES IVUS	2010	0.65	0.18	2.31	-0.66	0.51
MATRIX	2011	0.60	0.15	2.36	-0.74	0.46
COBIS	2011	0.33	0.03	3.30	-0.94	0.35
Youn	2011	1.27	0.28	5.72	-0.31	0.76
Hur	2012	0.85	0.56	1.32	-0.72	0.47
EXCELLENT	2012	1.00	0.06	17.87	0.00	1.00
Ahn	2012	0.17	0.03	0.88	-2.11	0.03
Patel	2012	0.09	0.00	1.65	-1.63	0.10
Chen	2012	0.09	0.03	0.33	-3.63	0.00
ADAPT-DES	2012	0.50	0.29	0.85	-2.53	0.01
Random pooled esttimate		0.55	0.39	0.77	-3.43	0.00



Park et al, unpublished

RESET is a prospective, randomized, open label, multi-center trial to demonstrate non-inferiority of ZES plus 3-mo DAPT vs any other DES plus vs 12-month DAPT. In the pre-specified long lesion subset (lesions requiring a ≥28mm long stent in a vessel with a distal reference diameter ≥2.5mm), pts were randomized to ZES vs EES and then to IVUS-vs angiography-guidance.

	IVUS-guidance	Angiography-guidance	RR	p
N	269	274		
MACE (cardiac death, MI, ST, TVR)	4.5%	7.3%	0.59 (0.28-1.24)	0.16

n=41 cross-over n=13

	IVUS-guidance	Angiography-guidance	RR	p
N	297	246		
MACE (cardiac death, MI, ST, TVR)	4.0%	8.1%	0.48 (0.23-0.99)	0.048

Kim et al., JACC Cardiovasc Interv, in press

ADAPT-DES – IVUS vs No-IVUS Cohort -

Assessment of Dual AntiPlatelet Therapy with Drug-Eluting Stents

8,575 pts prospectively enrolled
No clinical or anatomic exclusion criteria
11 sites in US and Germany

↓

PCI with ≥1 non-investigational DES
Successful and uncomplicated

↙ ↘

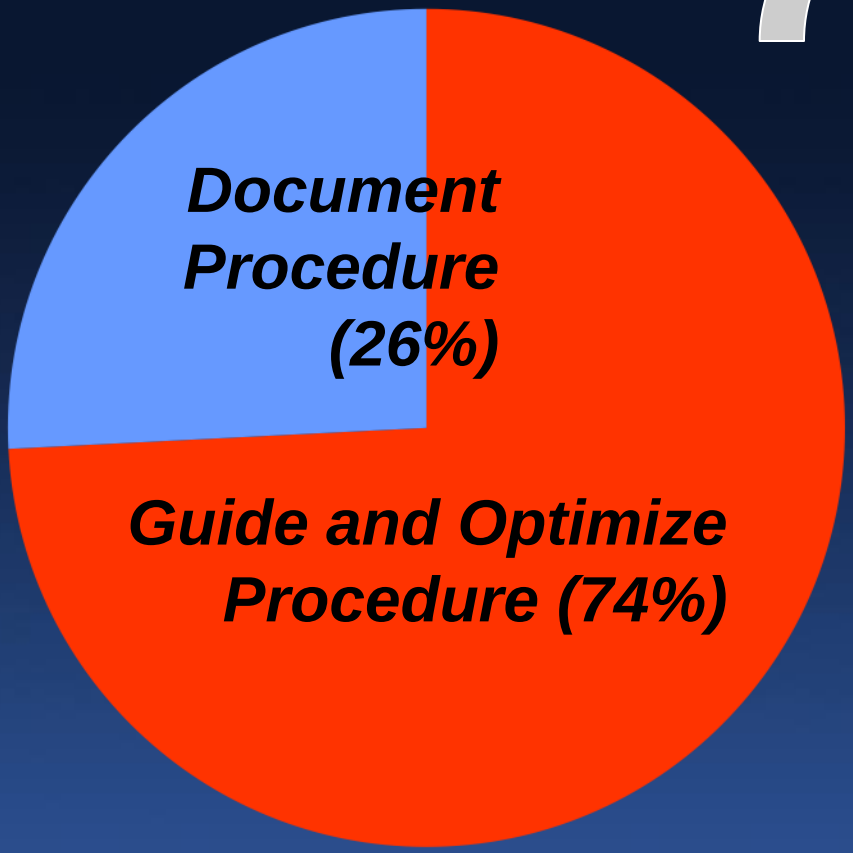
IVUS Use: 3349 pts | **No IVUS: 5234 pts**

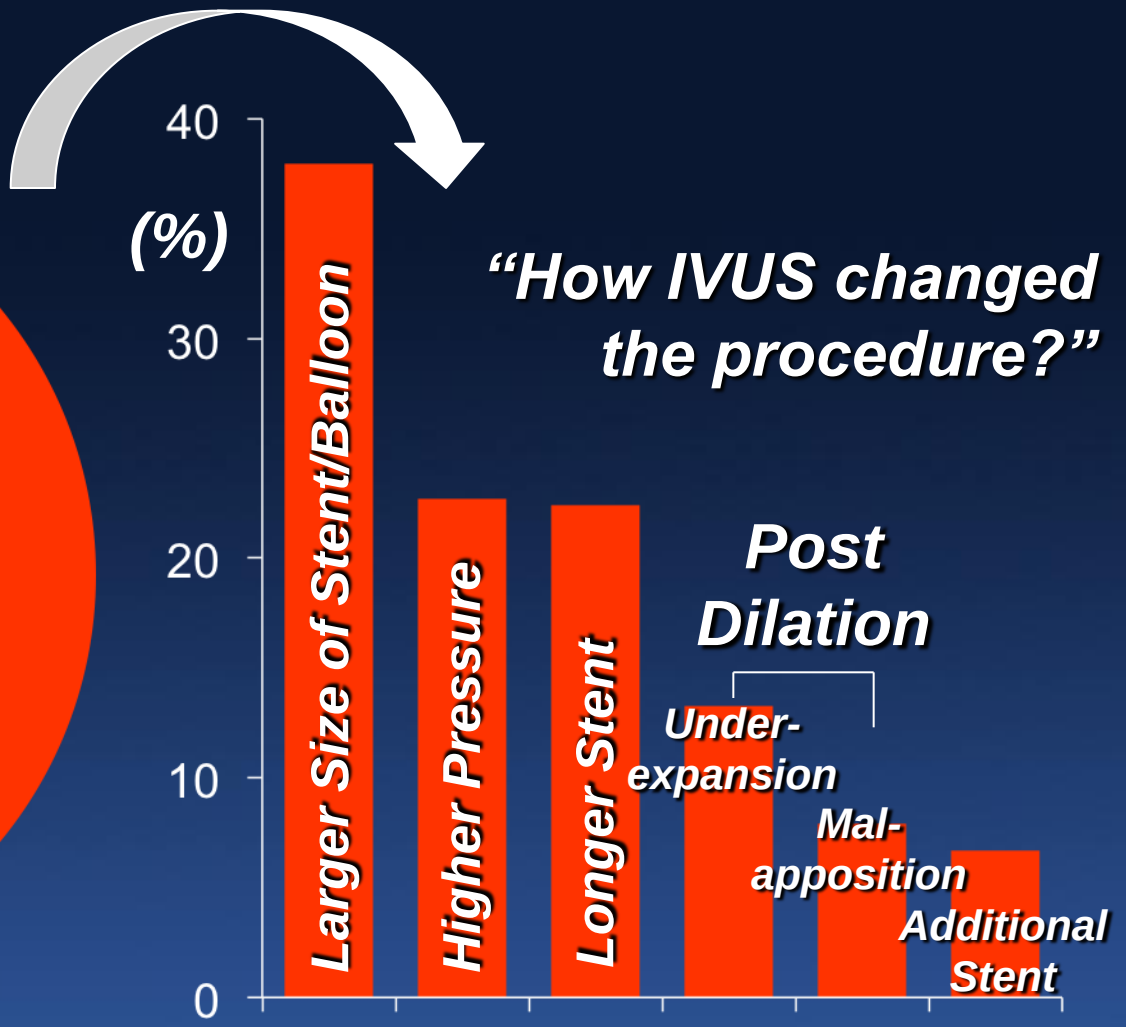
↓ ↓

Clinical FU at 30 days, 1 year

Witzenbichler, et al. TCT2012

Reason for IVUS Use



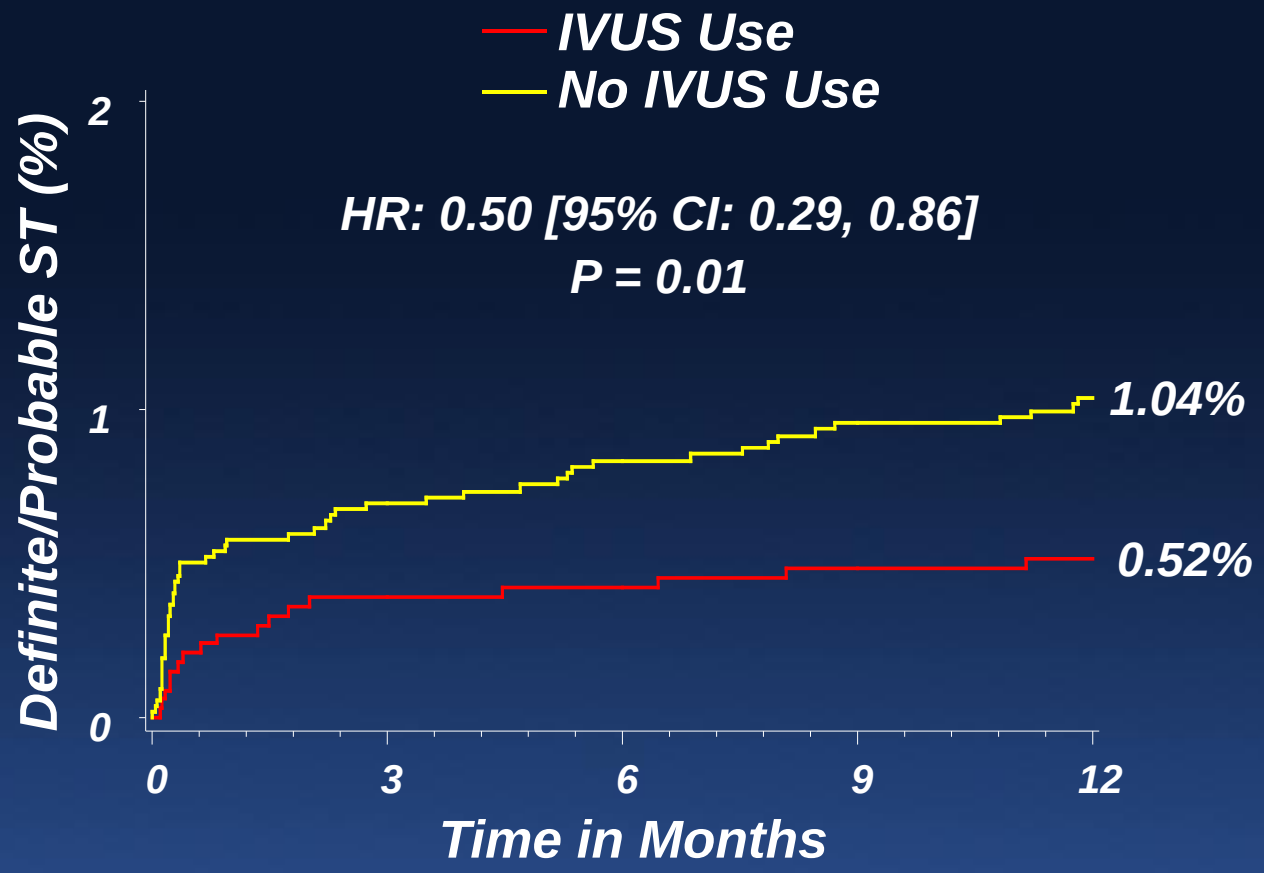


"How IVUS changed the procedure?"

Clinical Outcomes at 1 year

	IVUS n = 3349	No IVUS n = 5234	P Value
Definite/probable ST	0.52% (17)	1.04% (53)	0.011
- Acute<1day	0.06% (2)	0.04% (2)	0.66
- Subacute (1-30day)	0.27% (9)	0.56% (29)	0.051
- Late (>30day to 1yr)	0.25% (8)	0.46% (23)	0.12
All death	1.79% (58)	2.04% (103)	0.40
Cardiovascular death	0.99% (32)	1.35% (68)	0.14
All MI	2.46% (81)	3.68% (188)	0.0022
- Peri-procedural MI	1.26% (42)	1.53% (80)	0.29
- ST-related MI	0.37% (12)	0.59% (30)	0.16
- MI non-ST-related	0.87% (28)	1.58% (79)	0.0054

Relationship between IVUS Use and Definite or Probable ST within 1 year



Number at risk:					
IVUS Use	3349	3251	3221	3197	3023
No IVUS Use	5234	5015	4978	4938	4585

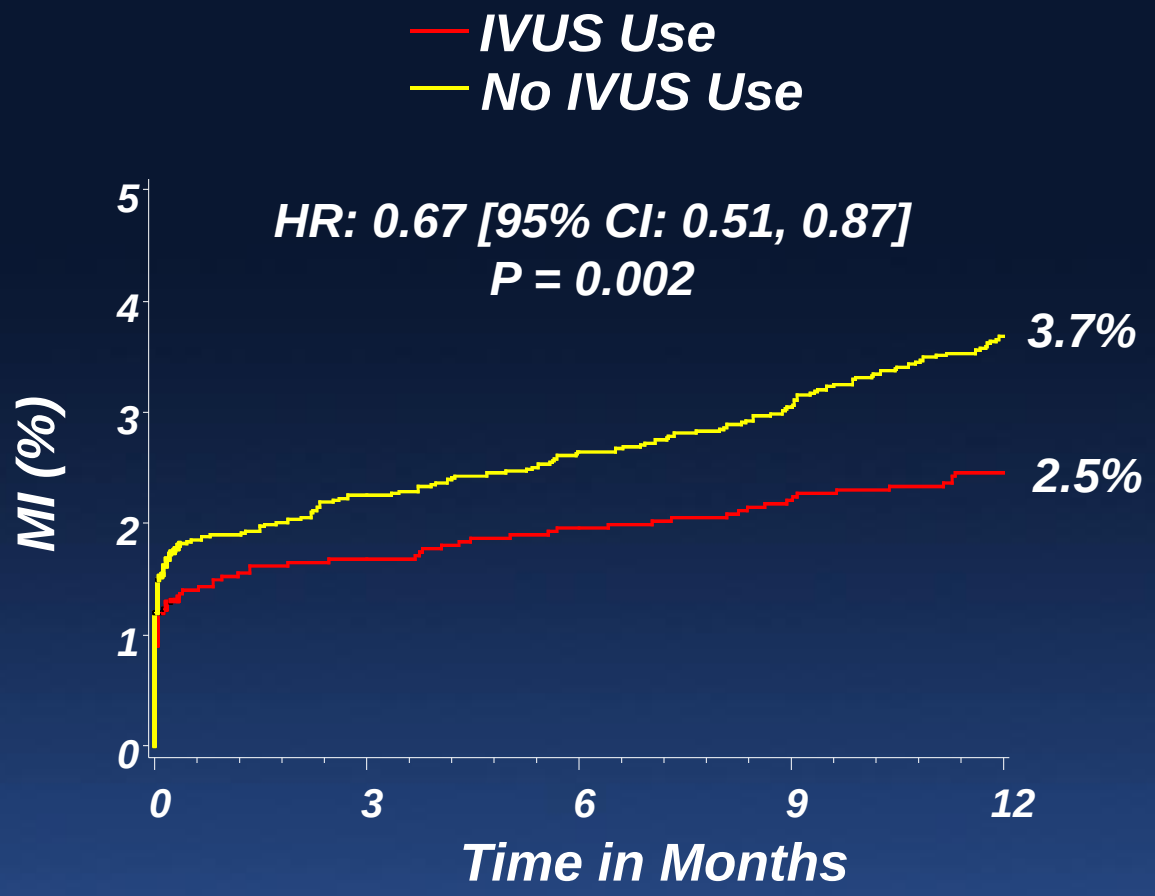
Mutivariable Cox PHR Models of 1-year Stent Thrombosis

Number events=68, Total at risk=8401

	HR [95%CI]	P value
IVUS use	0.37 [0.20, 0.69]	0.0019
PRU>208	2.37 [1.42, 3.96]	0.0009
Diabetes	1.65 [1.00, 2.70]	0.048
STEMI presentation	2.76 [1.51, 5.05]	0.0010
EES use	0.49 [0.30, 0.82]	0.0065
Total stent length (mm)	1.01 [1.00, 1.02]	0.019
Max stent diameter (mm)	0.60 [0.35, 1.02]	0.058
On DAPT at MACE	1.80 [0.92, 3.55]	0.087

Other non significant covariates entered to the model: ARU≥550
Model c-statistics=0.483

Relationship between IVUS Use and MI within 1 year



Number at risk:					
IVUS Use	3349	3209	3171	3141	2969
No IVUS Use	5234	4932	4882	4830	4460

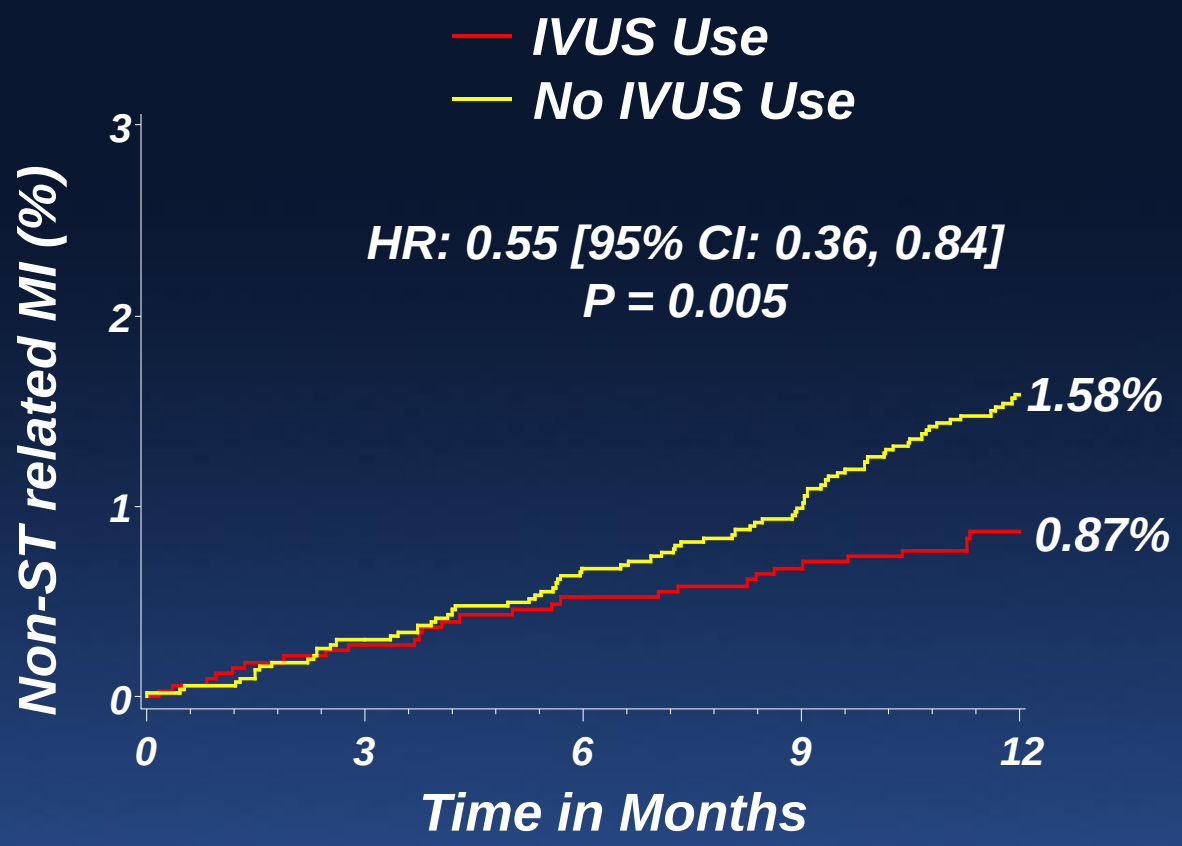
Mutivariable Cox PHR Models of 1-year MI

Number events=269, Total at risk=8547

	HR [95%CI]	P value
IVUS use	0.65 [0.49, 0.87]	0.0034
Cr Clearance <60 ml/min	1.64 [1.19, 2.27]	0.0025
Three vessel CAD	1.57 [1.22, 2.02]	0.0005
Diabetes	1.48 [1.15, 1.89]	0.0021
Acute coronary syndrome	1.41 [1.10, 1.80]	0.0064
Prior MI	1.35 [1.04, 1.75]	0.023

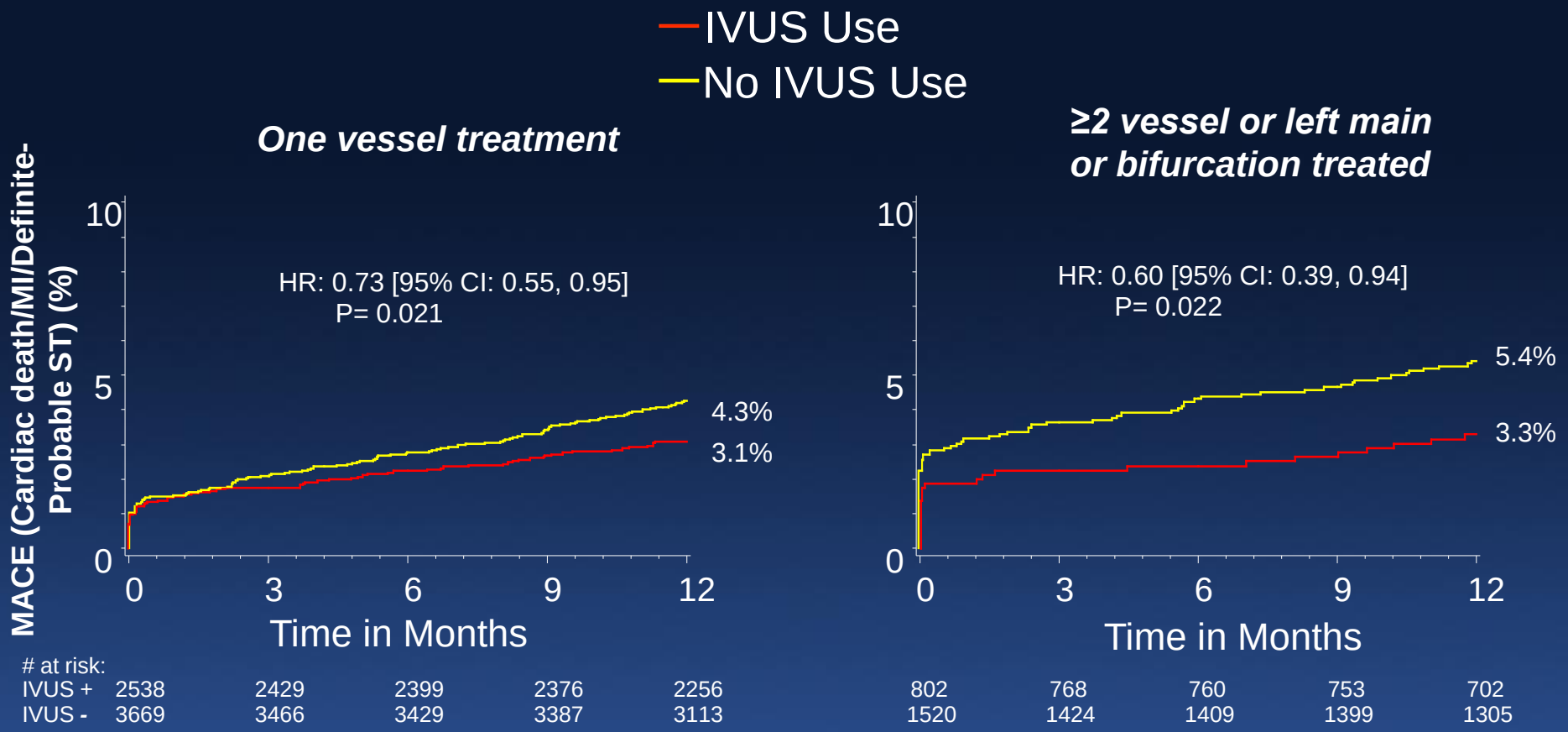
Other non significant covariates entered to the model: Male, Hemoglobin (g/dL)

Relationship between IVUS Use and MI not related to ST within 1 year



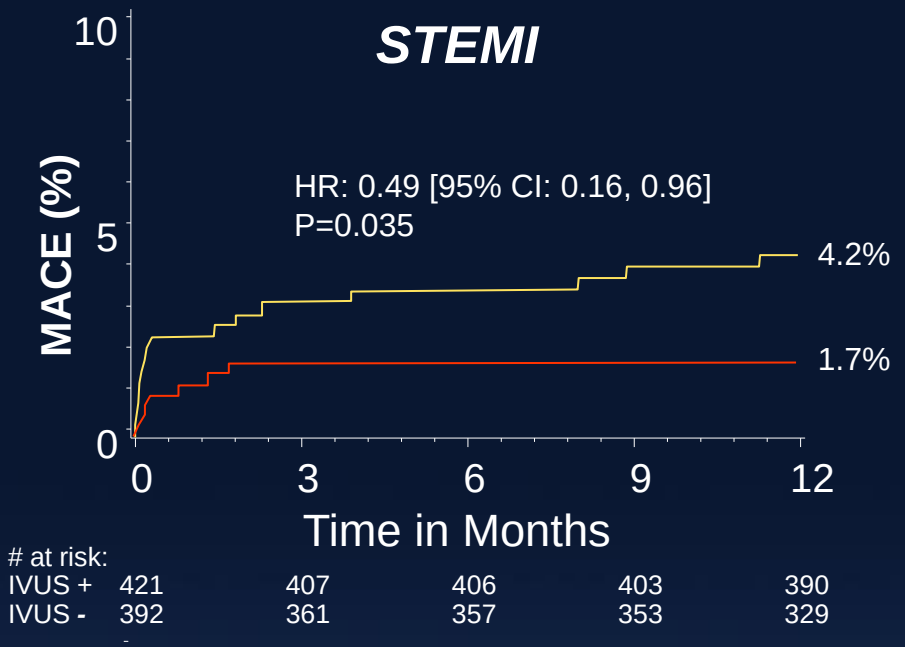
Number at risk:					
IVUS Use	3349	3253	3216	3188	3015
No IVUS Use	5234	5024	4974	4925	4555

Impact of Complexity of Procedure on MACE



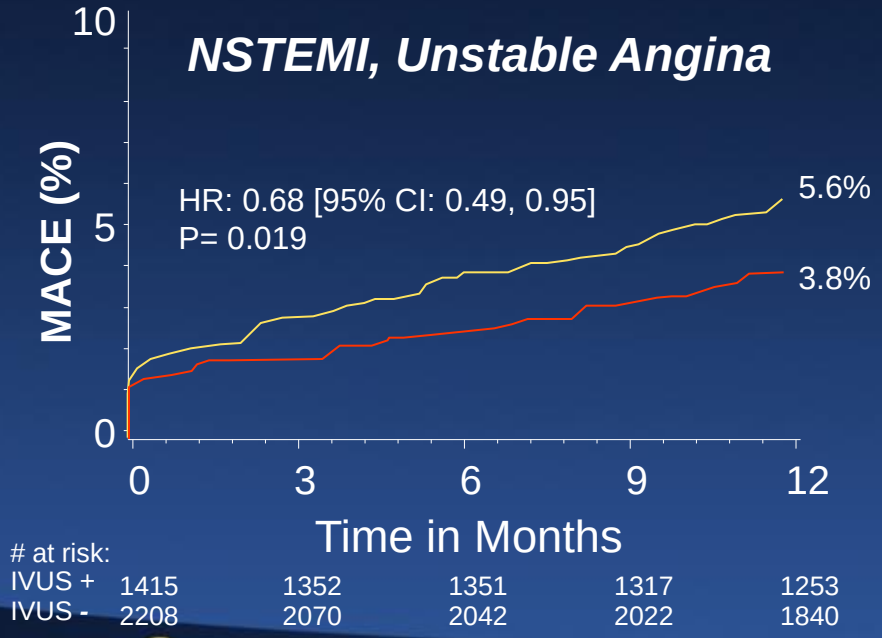
TCT2012

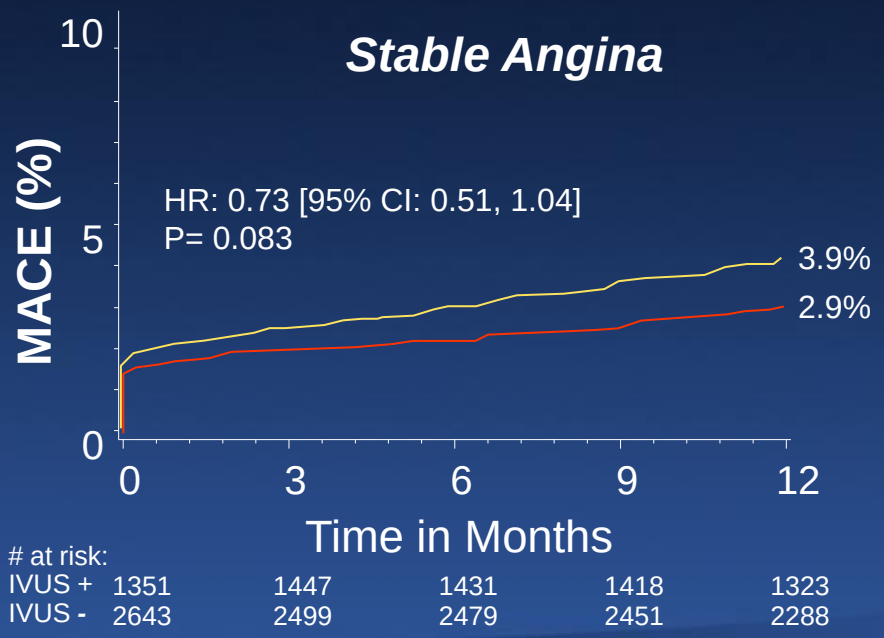
Impact of Patient Presentation on MACE



IVUS Use

No IVUS Use





Comparison of pts undergoing PCI with "OCT guidance" vs angiographic guidance at three high-OCT-volume Italian centers: CLI-OPCI Study

One year outcomes	OCT	Angiography	p
#	335	335	
Death	3.3%	6.9%	0.035
Cardiac death	1.2%	4.5%	0.010
MI	5.4%	8.7%	0.096
TLR	3.3%	3.3%	1
Definite ST	0.3%	0.6%	0.6
Cardiac death/MI	6.6%	13.0%	0.006
Cardiac death/MI or repeat revascularization*	9.6%	15.1%	0.034

Even after accounting for baseline and procedural differences (OR=0.49, p=0.037)

Prati et al. Eurointervention 2012;8:823-9

Randomized comparison of IVUS vs OCT-guided stenting with blinded cross-over imaging (n=70) showed that IVUS was superior and indicating that there is a need for a new paradigm for OCT-guided stenting

	IVUS	OCT	P-value
Final inflation pressure, atm	16.1±4.7	13.5±3.4	0.03
Final balloon diameter, mm	3.2±0.4	3.4±0.6	0.3
Proximal edge			
Plaque burden, %	37.1±10.1	45.7±10.9	0.001
Plaque burden >50%	8.6%	31.4%	0.04
MSA, mm^2	7.1±2.1	6.1±2.2	0.04
Focal expansion	80±13%	65±14%	0.001
Distal edge			
Plaque burden, %	33.3±6.4	40.3±8.8	<0.001
Plaque burden >50%	2.9%	11.4%	0.4

All OCT findings including the frequency of stent malapposition and the percentage of cross sections with malapposed strute were not significantly different between the groups.

Habara et al. Circ Cardiovasc Interv 2012;5:193-201

For OCT to replace IVUS in guiding stent implantation. . .

- Pre-intervention
  - Develop a new paradigm for selecting stent length and diameter, a paradigm that does not rely on visualizing true vessel dimensions as a point of reference
  - Or abandon pre-intervention imaging. . . a step backward. . . and only perform post-stent OCT
- Post-intervention
  - Develop endpoints for optimal stent implantation endpoints, ideally with robust outcomes data similar to IVUS. Some may be similar to IVUS, but others will be different.
  - Identify major complications that are not detectable angiographically or using IVUS and that impact on patient outcomes

Stent expansion

Geographical miss

Findings not seen on IVUS

Malapposition

Tissue protrusion

Edge dissections

So what is the problem?

- **Cost**
  - **While it may be reasonable to do FFR or IVUS or OCT or NIRS, it is not reasonable to do FFR and IVUS and OCT and NIRS; and we do not have a single system/catheter that can do them all.**
  - **Some imaging devices are more expensive than stents. . . at least in some countries**
- **Education**
  - **For many reasons – including, but not only user-unfriendliness of the technologies – it has been difficult to educate the interventional community on the appropriate indications, interpretations, and uses of even one of these modalities, let alone all of them.**

Solution: Cath-lab based imaging program

- **Director**
- **Dedicated Technicians, Nurses, and/or Fellows**
- **Procedure standards**
- **Image acquisition protocol(s)**
- **Reports**
- **Housekeeping issues**

- ***Visit a busy lab to see how it integrates imaging into clinical practice***
- ***Attend course(s)***
- ***Attend live case demonstrations Review studies more than once***
- ***Show cases in weekly cath conference***
- ***Learn from the technicians***
- ***Do more cases***