IVUS Pre and Post PCI

Gary S. Mintz, MD

Cardiovascular Research Foundation

Randomized FFR Trials in Non-LMCA Lesions

- **DEFER showed that it was safe to defer PCI in lesions with an FFR >0.75**
  - *Bech et al. Circulation 2001;103:2928-34*
  - *Pijls et al. J am Coll Cardiol 2007;49:2105-11*
- **FAME-I showed that treating lesions with an FFR >0.80 with first generation DES was harmful and that a deferred PCI strategy was safer and cost-saving**
  - *Tonino et al. N Engl J Med. 2009;360:213-24*
  - *Pijls et al. J am Coll Cardiol 2010;56:177-84*
  - *Fearon et al. Circulation 2010;122:2545-50*
- **FAME-II showed that deferring PCI in lesions with an FFR <0.80 was harmful compared to optimal medical therapy. While more expensive at the beginning, the cost of this strategy decreased by 50% at 1 year. In addition, FAME-II confirmed the findings of DEFER**
  - *De Bruyne et al. N Engl J Med 2012;367:991-1001*
  - *Fearon et al. Circulation 2013;17:1335-40*
  - *De Bruyne et al. N Engl J Med 2014;371:1208-17*

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

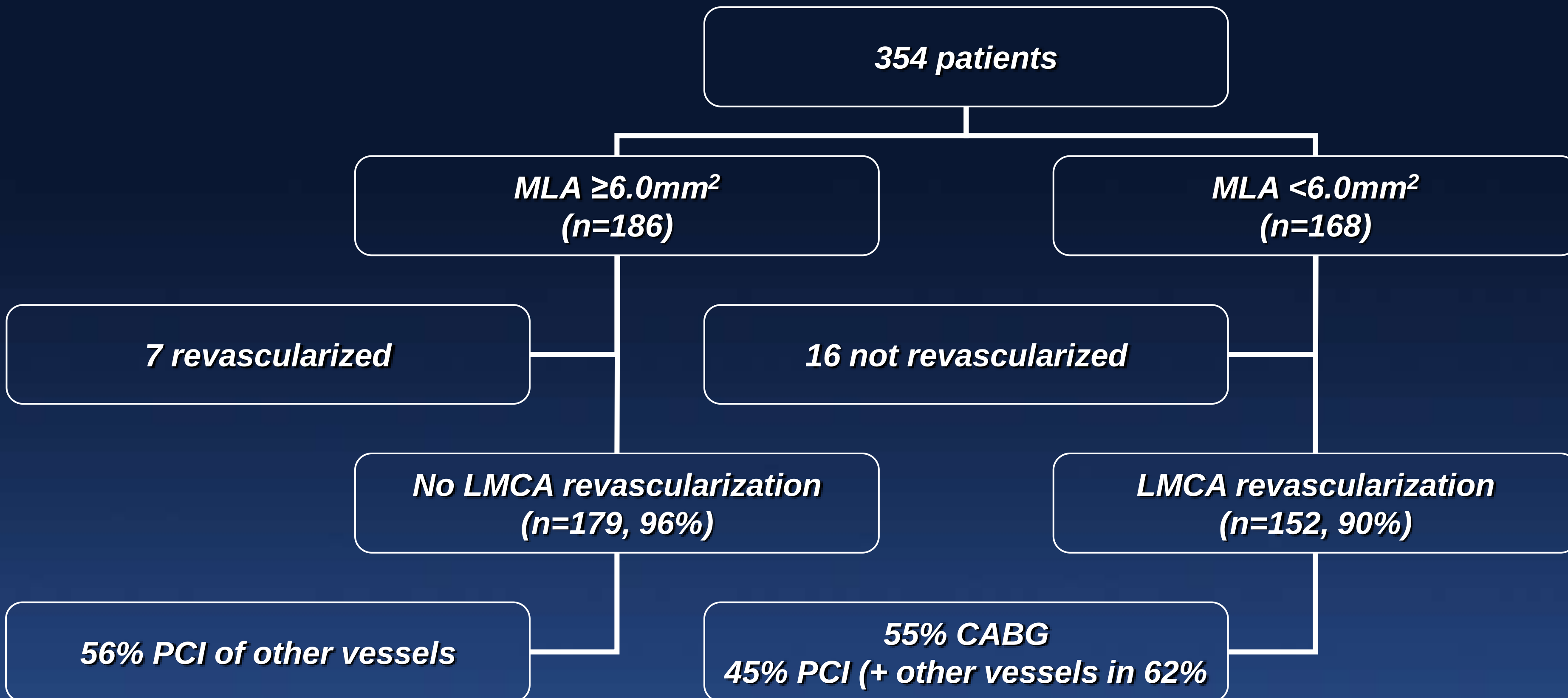
Reference	Versus	# of lesions	% abn	Inclusion criteria	Mean MLA (mm^2)	MLA cut-off (mm^2)	Other independent IVUS anatomic determinants	PPV	NPV
Abizaid AJC 1998	CFR<2.0	112	40%		4.4	4.0			
Nishioka JACC 1999	SPECT	70	65%		4.3	4.0			
Takagi Circulation 1999	FFR<0.75	51	49%		3.9	3.0			
Briguori AJC 2001	FFR<0.75	53	23%	40-70% DS	3.9	4.0	Lesion length	46%	96%
Takayama CCI 2001	FFR	14	50%	>2.5mm vessels	3.5		MLA divided by lesion length		
Lee AJC 2010	FFR<0.75	94	40%	30-75% DS <3mm vessels	2.3	2.0	Lesion length Plaque Burden		
Kang Circ Interv 2011	FFR<0.8	236	21%	30-75% DS	2.6	2.4	LAD Plaque burden	37%	96%
Ahn JACC Interv 2011	SPECT	170	26%		2.1	2.1		39%	91%
Kang AJC 2012	FFR<0.8	784	29%	30-90% DS		2.4	LAD Lesion length Plaque rupture Plaque burden	48%	90%
Ben-Dor EuroInterv 2011	FFR<0.75	92	19%	40-70% DS >2.5mm vessels	3.6	2.8	Lesion length		
	FFR<0.8					3.2			
Ben-Dor CRM 2012	FFR<0.8	205	26%	40-70% DS >2.5mm vessels		3.1			
Koo JACC Interv 2011	FFR<0.8	267	33%	30-70% DS Proximal or Mid	3.0	3.0	Proximal or Mid LAD	47%	
Gonzalo JACC 2012	FFR<0.8	51	46%	40-70% DS	2.6	2.4		67%	65%

Reference	Versus	# of lesions	% abn	Inclusion criteria	Mean MLA (mm^2)	MLA cut-off (mm^2)	Other independent IVUS anatomic determinants	PPV	NPV
Waksman JACC 2013	FFR<0.8	334	25%	40-80% DS >2.5mm vessels	5.6	3.1	LAD Plaque burden	40%	83%
Stone TCT 2013	FFR<0.80	544	31%	40-80% DS >2.75mm vessels		2.9	LAD vs LCX RCA vs LCX	47%	81%
Kwan CMJ 2012	FFR<0.8	169	59%	40-99% DS LAD	3.0	3.0	Plaque burden	84%	82%
Chen IJC 2013	FFR<0.8	323	54%	≥40% DS	2.9	3.0	Plaque burden LAD	73%	76%
Yang CCI 2014	FFR<0.8	206	44%	40-70% DS Prox/mid LAD >3.0mm vessel	3.1	3.2 (Prox) 2.5 (Mid)	Lesion length		
Kang JACCInterv 2013	FFR<0.8	493 males	43% males	>30% DS LAD	2.6	2.5		63% male	81% male
		207 females	27% females		2.5	2.5		42% female	93% female
Lopez-Palop REspCard 2013	FFR<0.8	61	49%	40-70% DS ≥20mm length	2.7	3.1	Lesion length	67%	93%
Naganuma CRM 2014	FFR<0.8	169	30%	40-70% DS	3.0	2.7	Plaque burden	59%	90%
Voros AJC 2014	FFR<0.75	323	27%	40-99% DS	3.7	2.7		39%	93%
Cui CMJ 2013	FFR<0.8	206	26%	40-70% DS >2.5mm vessels	3.9	3.2	Plaque burden	53%	85%
Han Cardiology 2014	FFR<0.8	169	39%		3.1	2.8		49%	73%
Koh JACCInterv 2012	FFR<0.8	38	37%	40-70% DS Ostial MV		3.5		69%	87%
		55	27%	40-70% DS Ostial SB				<50%	

Five studies have highlighted the inaccuracy of angiography in the assessment of LMCA disease

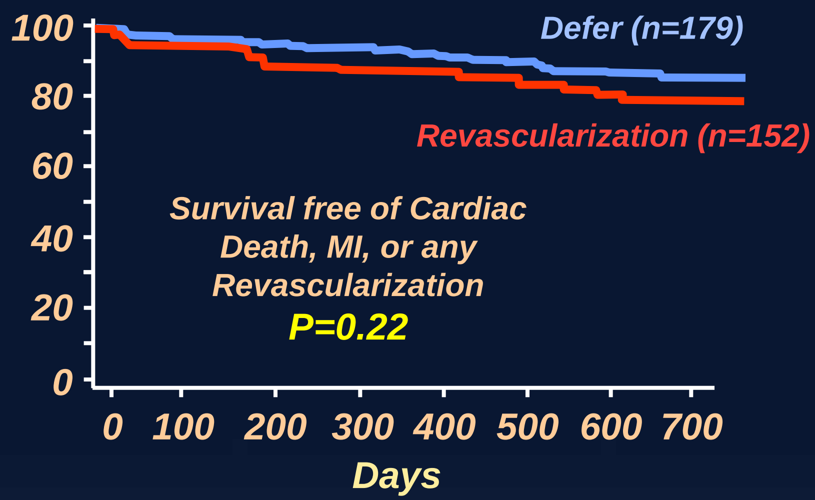
- CASS Registry Studies
  - Fisher et al. Cathet Cardiovasc Diagn 1982;8:565-75
  - Cameron et al. Circulation 1983;68:484-489
- Lindstaedt et al. Int J Cardiol 2007;120:254-61
  - In 51 patients unanimous correct assessment of LM severity by 4 experienced interventional cardiologists was only 29%
- Hamilos et al. Circulation 2009;120:1505-12
  - In 209 patients two reviewers either (1) disagreed whether the LM was significant (26%) or (2) agreed, but were wrong in their assessment when compared to FFR (23%)
- Chakrabarti et al. Circ Cardiovasc Interv 2014;7:11-8
  - 11.2% (17 out of 152) pts with "core laboratory" LM disease were listed as normal in the NCDR, whereas 56.7% (177 out of 312) pts that were listed as having LMCA disease in the NCDR had no LM lesion by core laboratory analysis

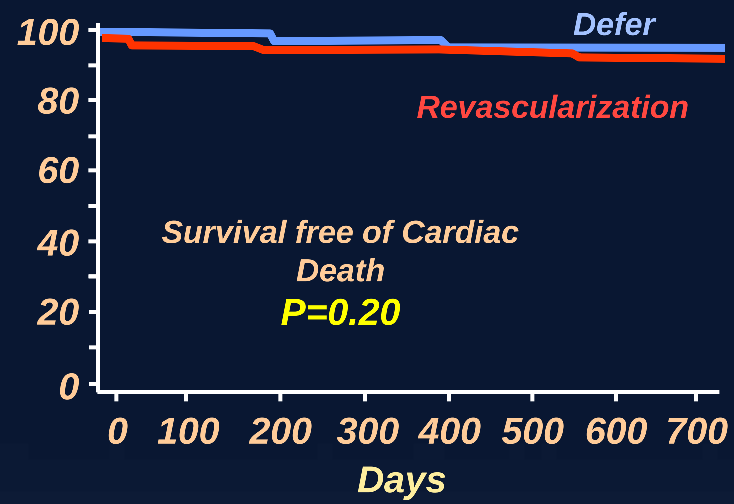
Prospective application of predefined IVUS criteria for revascularization of intermediate LM lesions: Results at 2 years from the LITRO study



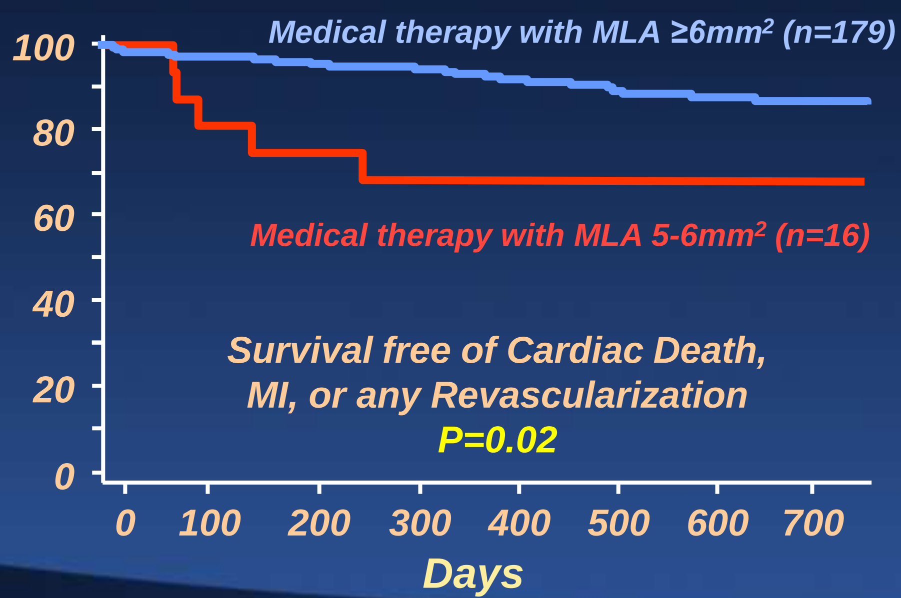
De La Torre Hernandez et al. J Am Coll Cardiol 2011;58:351-8

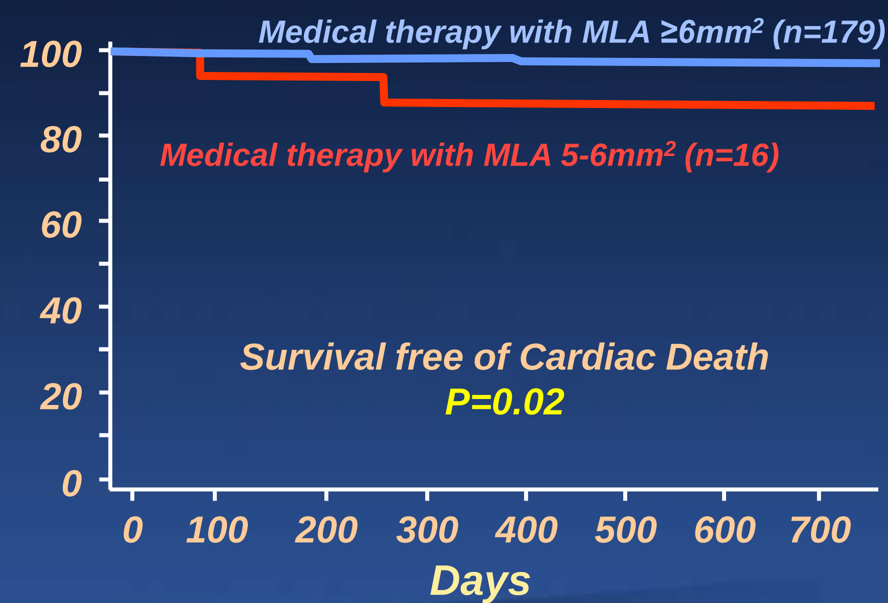
Clinical Outcome of Pts With vs Without Revascularization





Clinical Outcome of Pts Treated Medically According to MLA





De La Torre Hernandez et al. J Am Coll Cardiol 2011;58:351-8

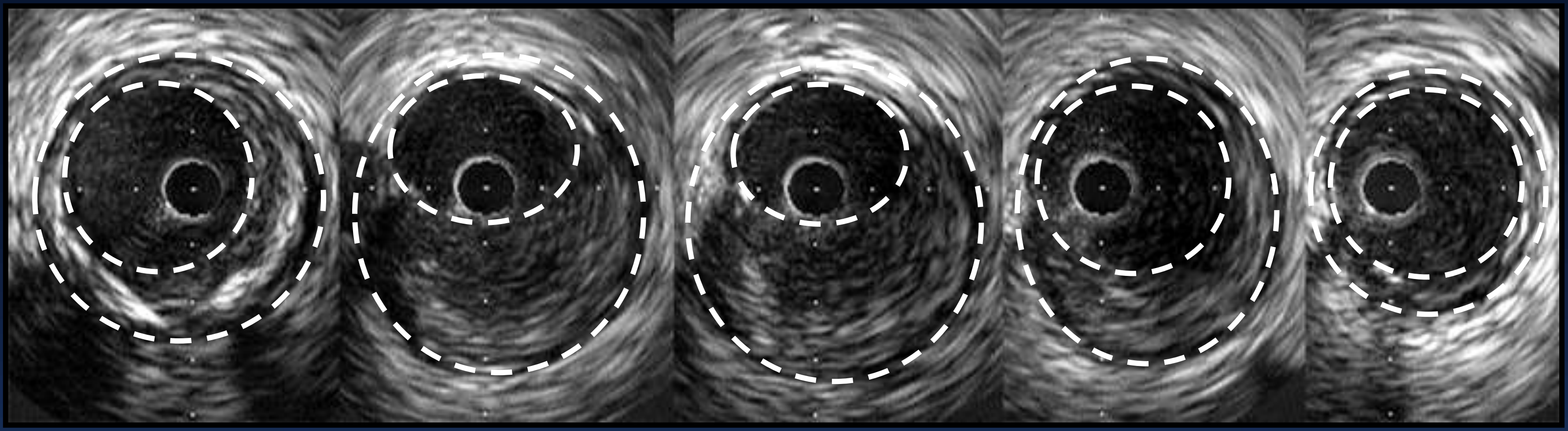
CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

Stent Length and Size Selection

- **Using pre-intervention IVUS, identify proximal and distal reference segments as the landing zones**
  - *Largest lumen with smallest plaque burden in the same coronary artery segment*
  - *Avoid segments with calcium (especially a lot of calcium). Calcium at a stent edge can lead to dissections as well as stent edge underexpansion that can be difficult to correct without causing reference segment trauma*
- **Measure the distance between the two landing zones to determine lesion and stent length**
- **Correlate the IVUS and the angiographic images to facilitate stent placement**

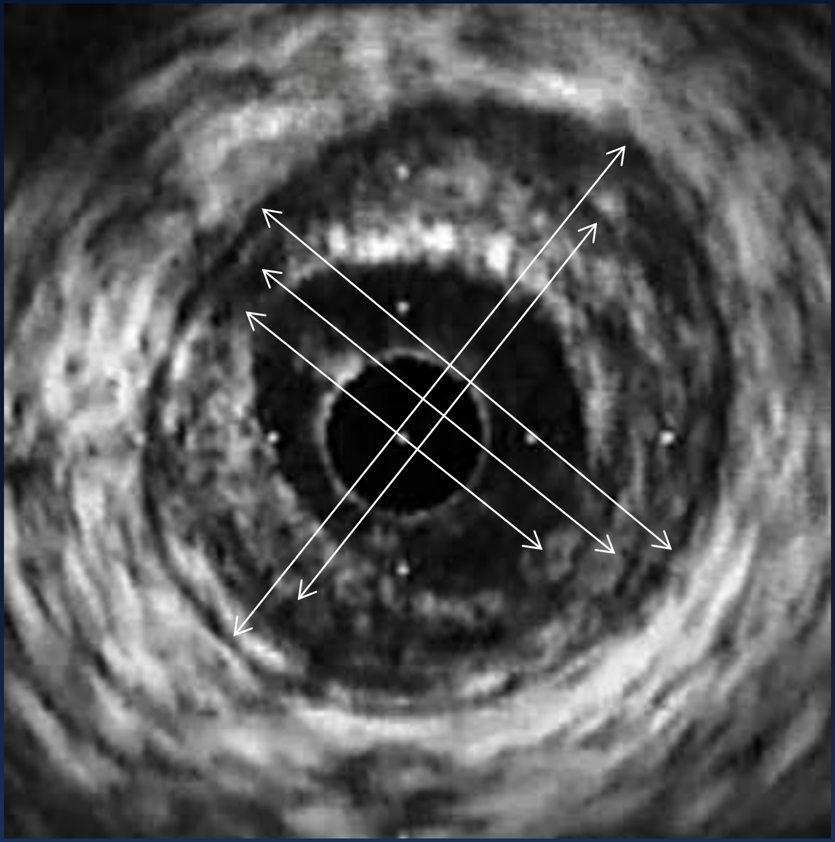
Proximal reference

Distal reference



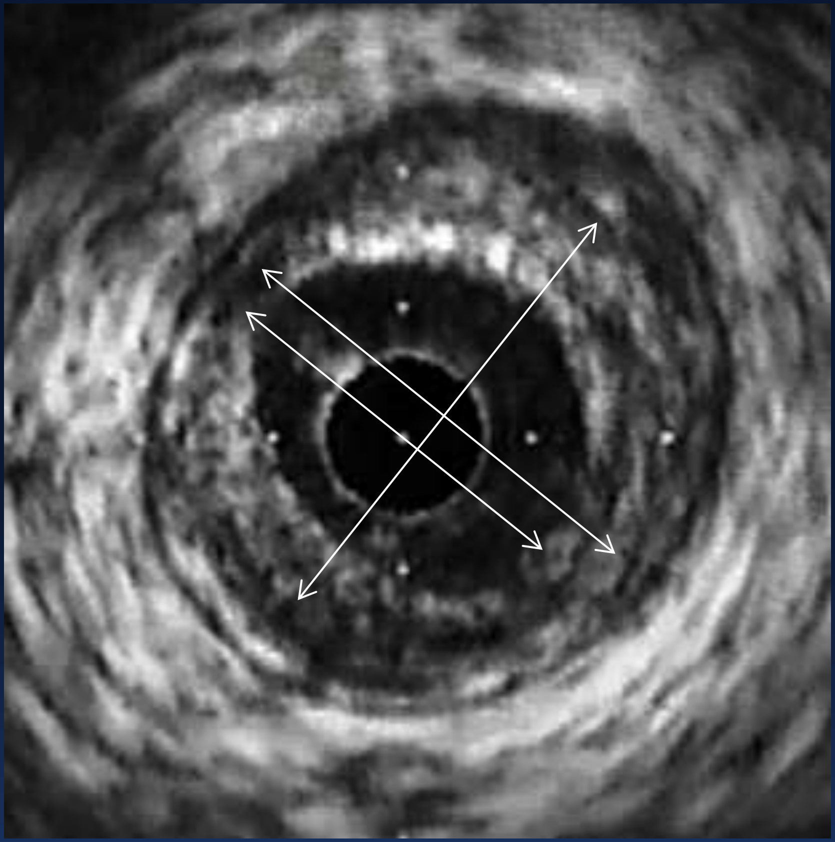
0 → *3mm* → *12mm*

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation



Increasingly aggressive

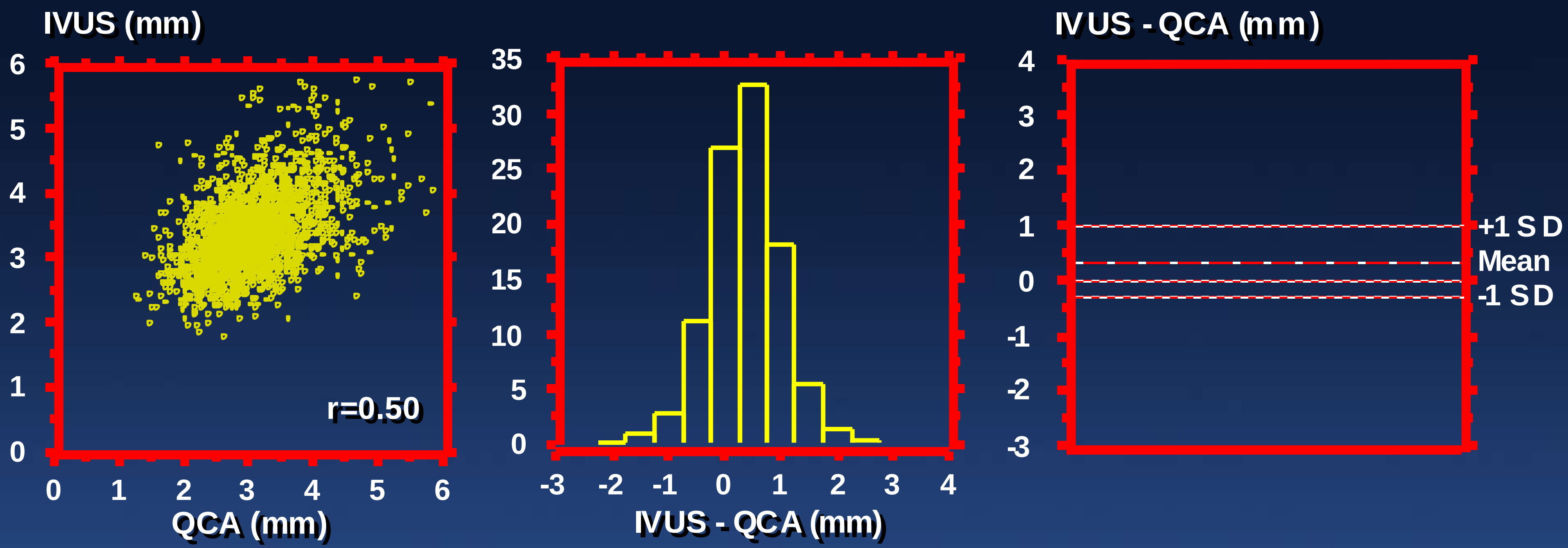
- Largest reference lumen whether proximal or distal
- Midwall
- Media-to-media



Increasingly aggressive ↓

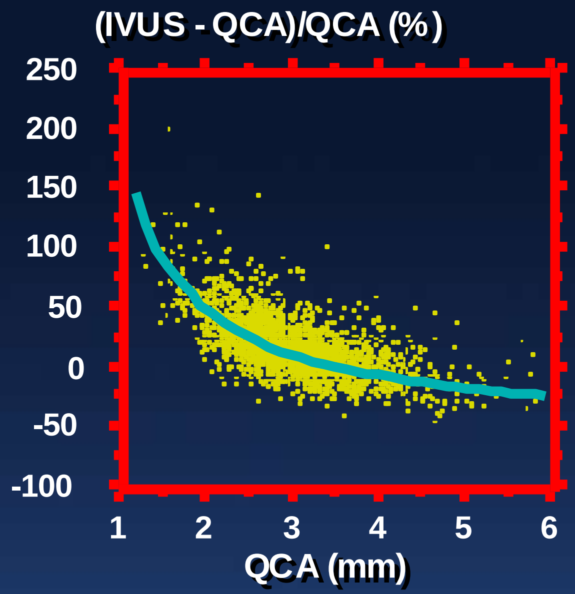
- ***Largest reference lumen whether proximal or distal***
- ***Midwall***
- ***Media-to-media <u>(typically discounted by approximately 0.5mm)</u>***

Even just using the largest reference lumen diameter, IVUS stent sizing is more accurate and typically larger than angiographic stent sizing



The impact is greater in smaller vessels

Stent size	MSA at 100% expansion	MSA at 80% expansion
2.0 mm	3.1 mm^2	2.5 mm^2
2.25 mm	4.0 mm^2	3.2 mm^2
2.5 mm	4.9 mm^2	3.9 mm^2
3.0 mm	7.1 mm^2	5.7 mm^2
3.5 mm	9.6 mm^2	7.7 mm^2
4.0 mm	12.6 mm^2	10.0 mm^2

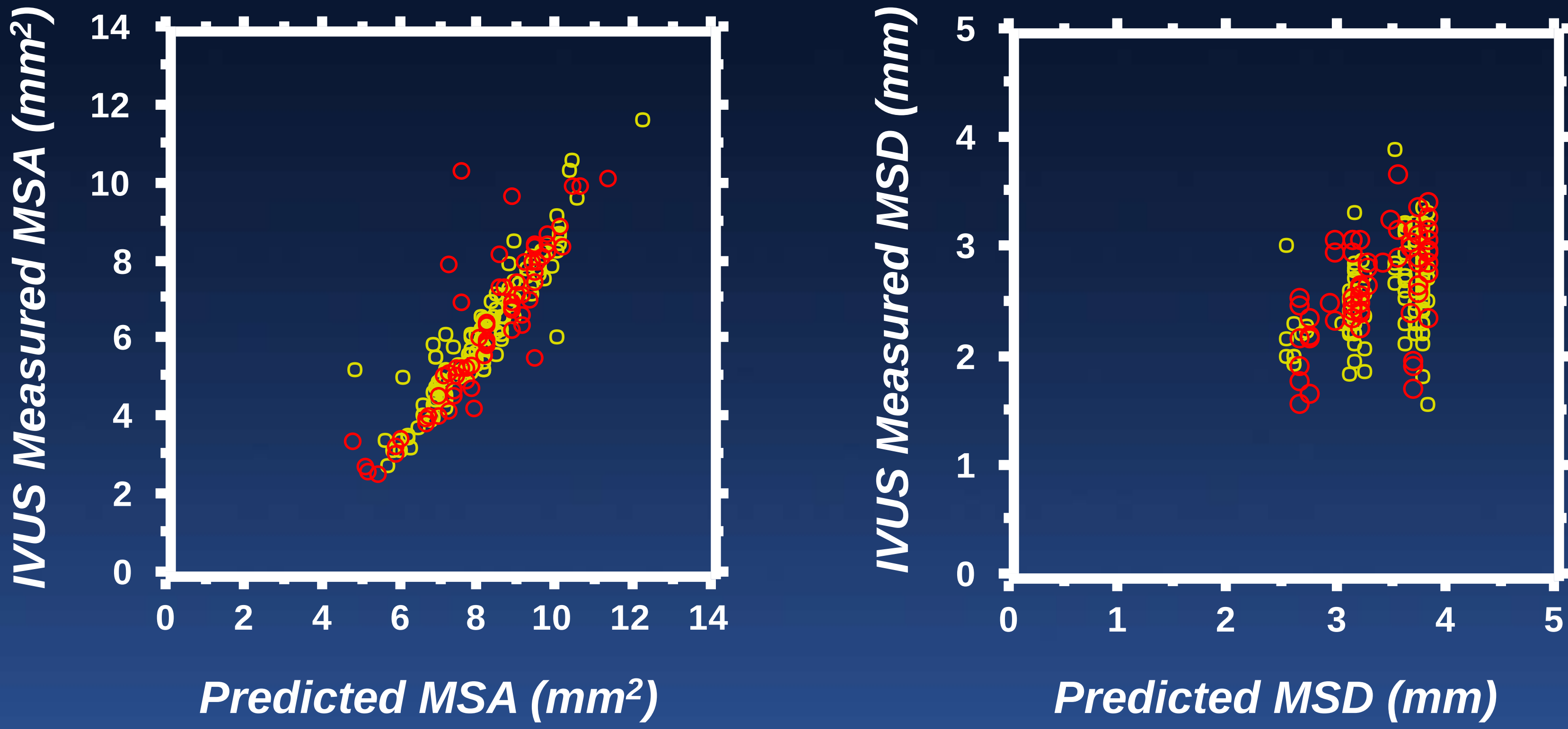


IMHO, too much time and energy is spent worrying about stent size selection and not enough about stent optimization

- Stents come in (mostly) 0.5mm size increments – not in 0.1mm size increments
- The various approaches result in almost the same stent size selection
- Stent size selection is only the first step, and stent optimization is only partly dependent on stent sizing.
- Iterative post-stent imaging with post-dilation using higher pressures and/or larger balloon sizes is the key to optimizing expansion along with assessing stent edges and correcting complications.

Manufacturer's Compliance Charts Cannot Be Used to Guarantee Adequate Stent Expansion

Comparison of IVUS-measured minimum stent diameter (MSD) and minimum stent area (MSA) with the predicted measurements from Cypher in yellow, n=133) and Taxus in red, n=67). DES achieve an average of only 75% of the predicted MSD (66% of MSA)



de Rebamar Costa et al. Am J Cardiol 2005;96:74-8

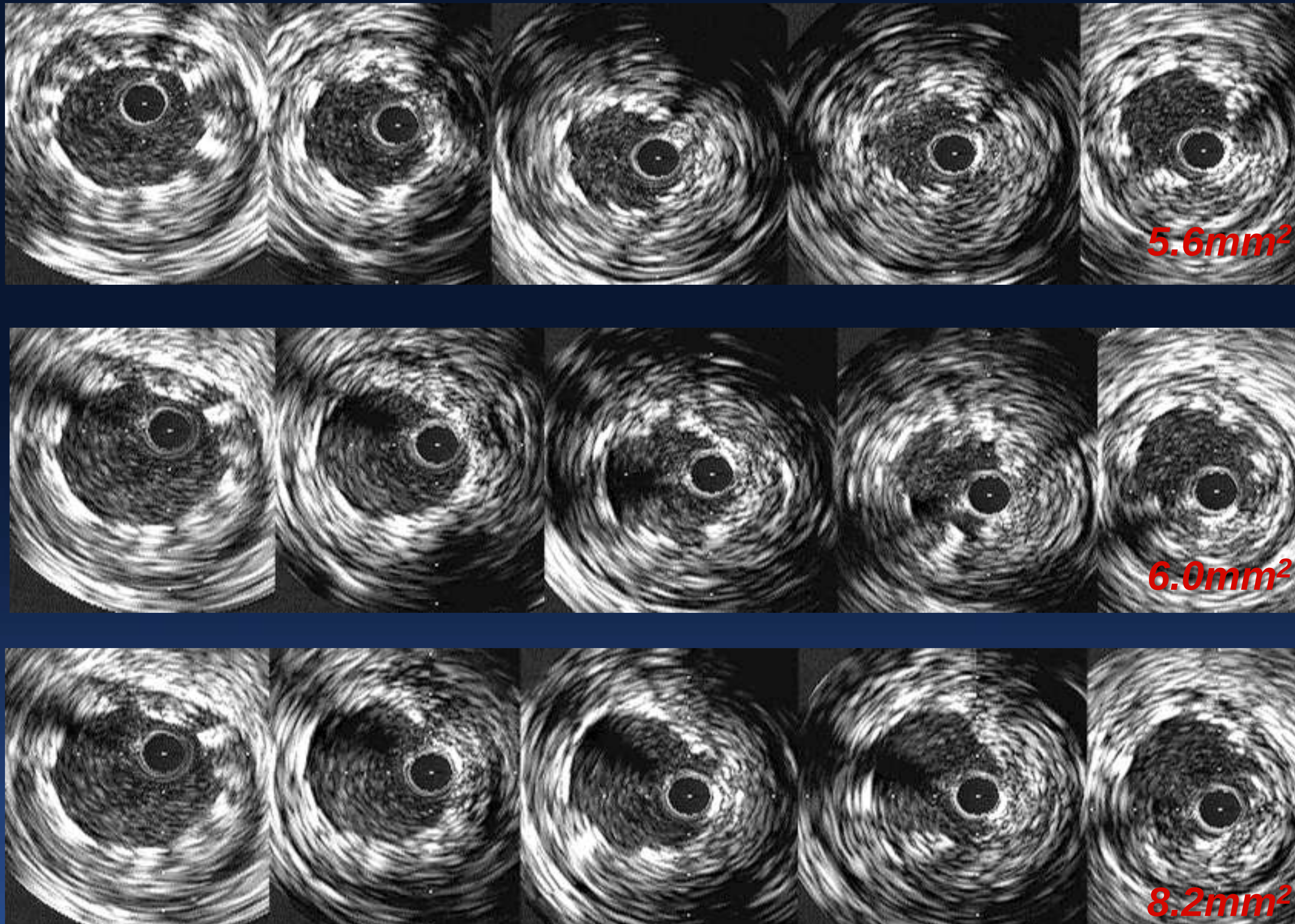
de Rebamar Costa et al. Am Heart J 2007;153:297-303

He et al. Am J Cardiol 2010;105:1272-5

3.5mm
16atm

4.0mm
10atm

4.0mm
16atm



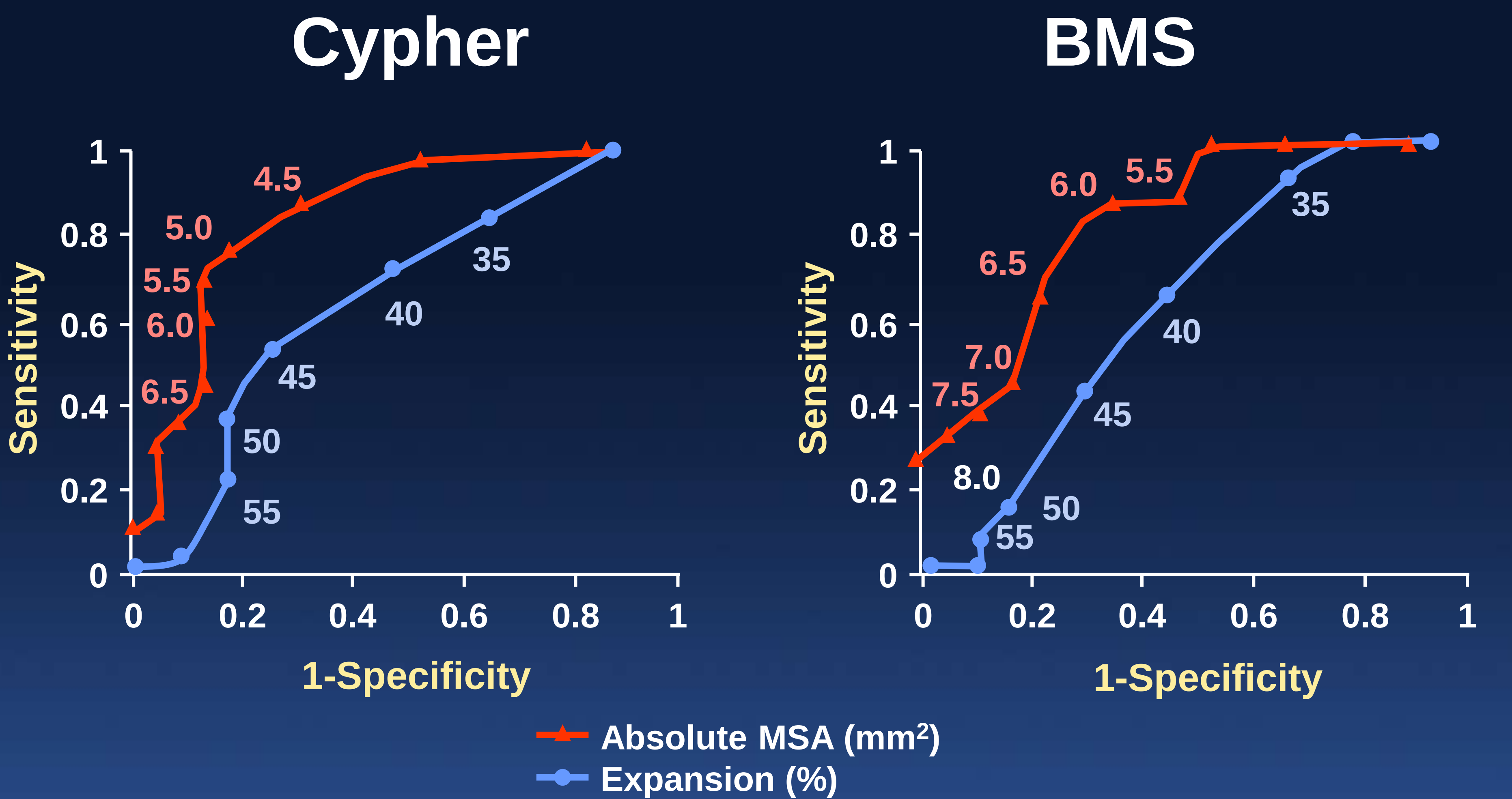
0 → 3.0 → 12.0mm

IVUS Predictors of BMS Early Thrombosis & Restenosis

	Early Thrombosis	Restenosis
Small MSA or underexpansion	•*Cheneau et al. Circulation 2003;108:43-7*	•*Kasaoka et al. J Am Coll Cardiol 1998;32:1630-5* •*Castagna et al. AHJ 2001;142:970-4* •*de Feyter et al. Circulation 1999;100:1777-83* •*Sonoda et al. J Am Coll Cardiol 2004;43:1959-63* •*Morino et al. Am J Cardiol 2001;88:301-3* •*Ziada et al. Am Heart J 2001;141:823-31* •*Doi et al. JACC Cardiovasc Interv. 2009;2:1269-75*
Edge problems (geographic miss, secondary lesions, large plaque burden, dissections, etc)	•*Cheneau et al. Circulation 2003;108:43-7*	•*Sakurai et al. Am J Cardiol 2005;96:1251-3* •*Liu et al. Am J Cardiol 2009;103:501-6*
Stent length		•*Kasaoka et al. J Am Coll Cardiol 1998;32:1630-5* •*de Feyter et al. Circulation 1999;100:1777-83*

IVUS Predictors of DES Early Thrombosis & Restenosis

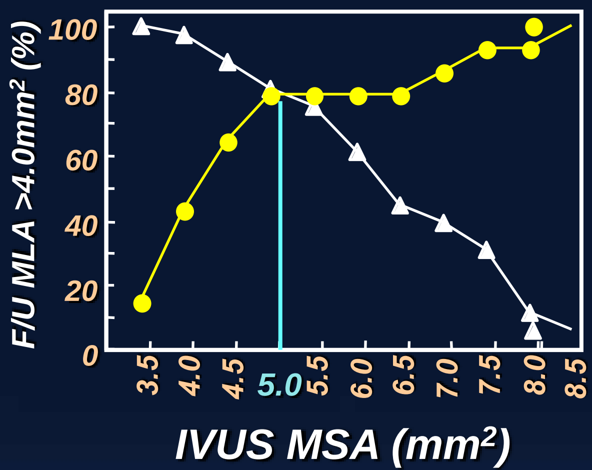
	Early Thrombosis	Restenosis
Small MSA or underexpansion in stable lesions **Small MLA in ACS/MI lesions**	•*Fujii et al. J Am Coll Cardiol 2005;45:995-8* •*Okabe et al. Am J Cardiol. 2007;100:615-20* •*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34* •*Choi et al. Circ Cardiovasc Interv 2011;4:239-47*	•*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 2014;83:873-8*
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* •*Kang et al. Am J Cardiol 2013;111:1408-14* •*Kobayashi et al. ACC2014*



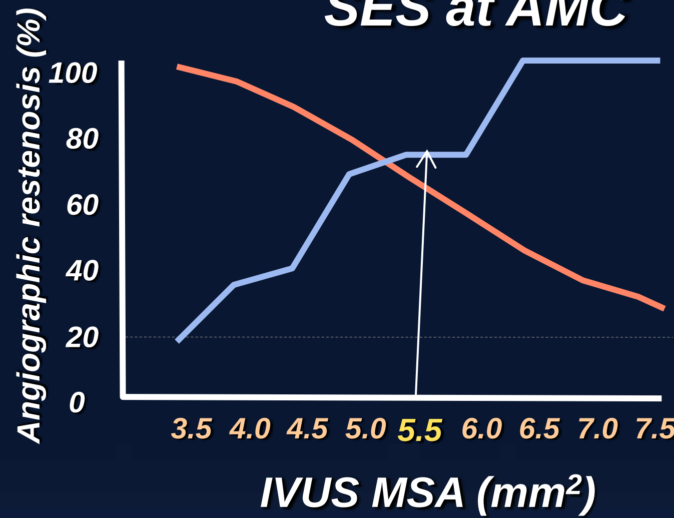
Sonoda et al. J Am Coll Cardiol 2004;43:1959-63

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

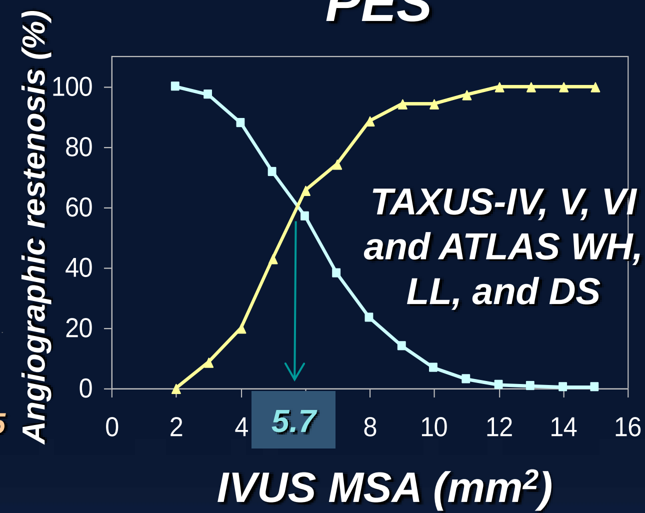
SES in SIRIUS



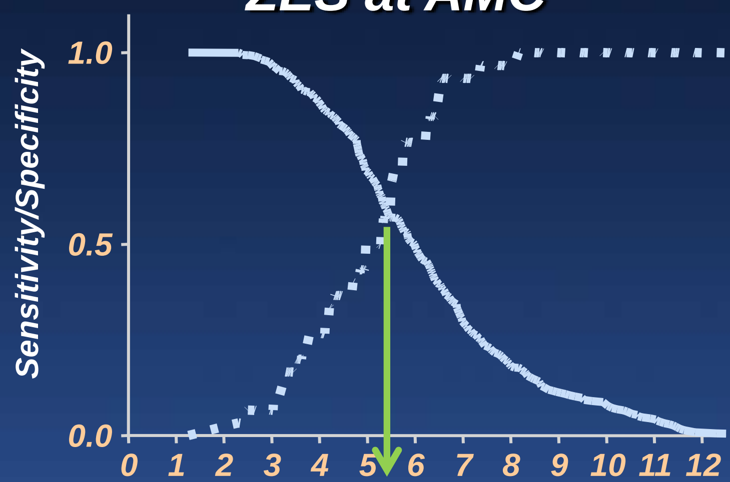
SES at AMC



PES

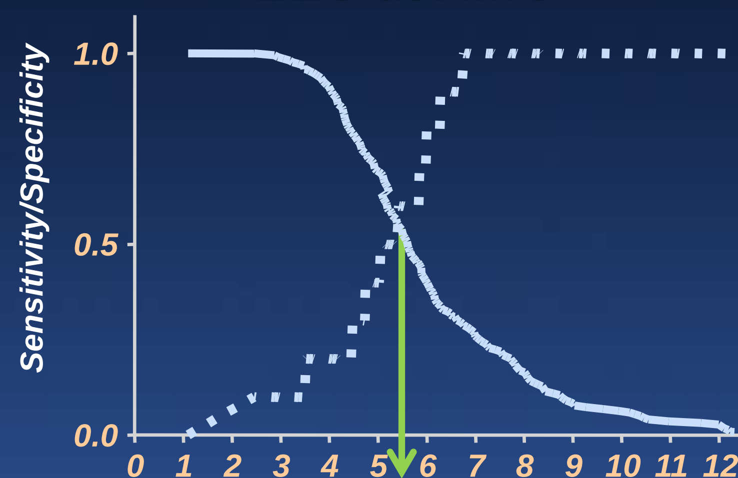


ZES at AMC



MSA 5.3mm²

EES at AMC

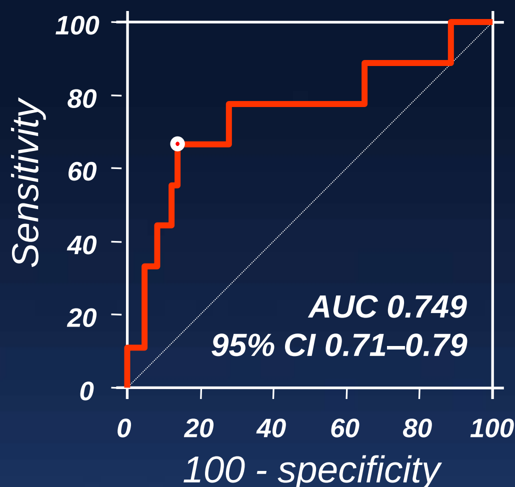


MSA 5.4mm²

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
Song et al. Cathet Cardiovasc Interv 2014;83:873-8

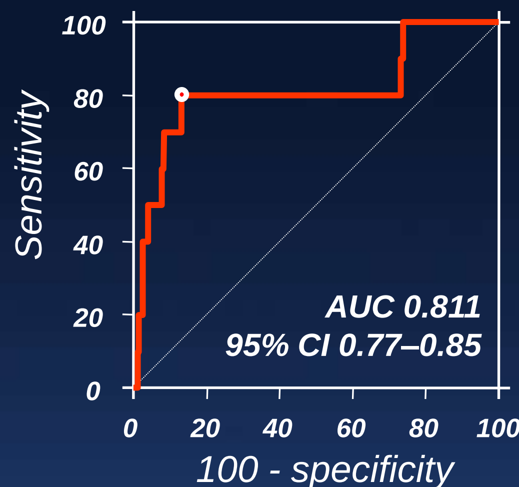
IVUS Predictors of Edge Restenosis after Second Generation DES

433 E-ZES



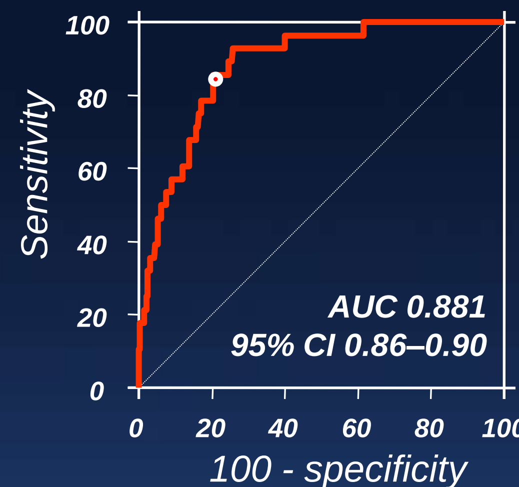
Plaque burden=56.3%
Sensitivity 67%
Specificity 86%

422 R-ZES



Plaque burden=57.3%
Sensitivity 80%
Specificity 87%

813 EES



Plaque Burden=54.2%
Sensitivity 86%
Specificity 80%

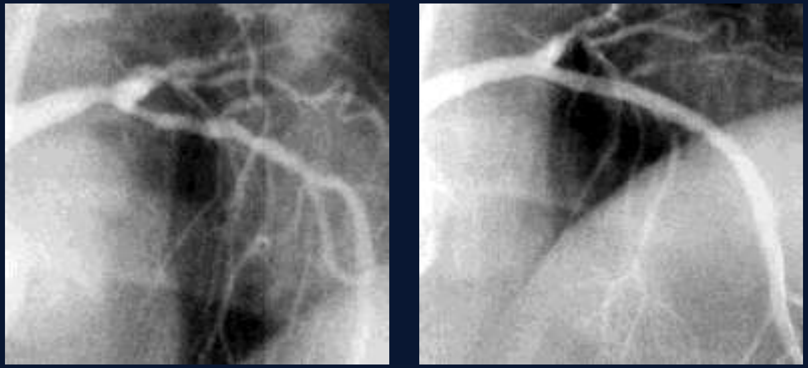
Kang et al. Am J Cardiol 2013;111:1408-14

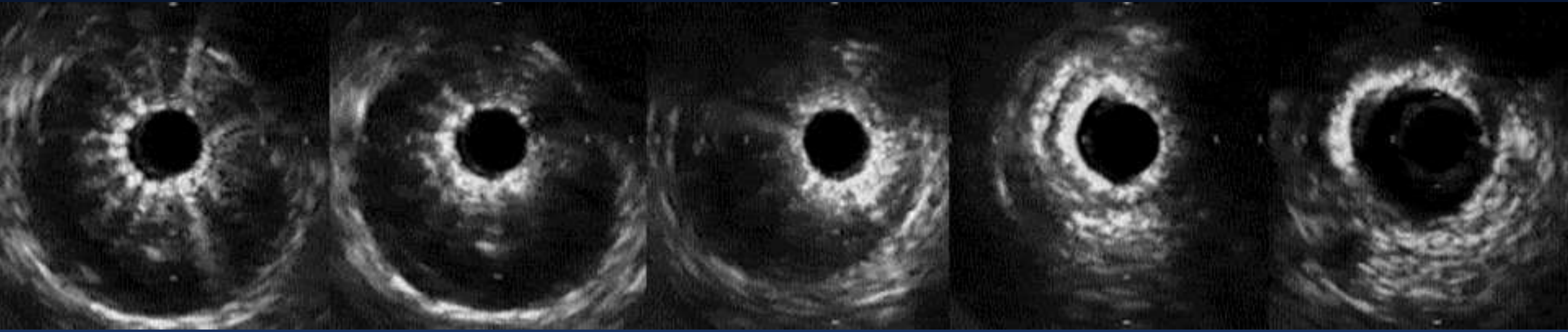
CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

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, & VI & 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 mos – 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*
- Although acute malapposition was detected in 10.5% of 1982 pts in ADAPT-DES, it was not associated with advere events at either 30 days or 2 years.
  - *Sousa et al. ACC2014*

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation



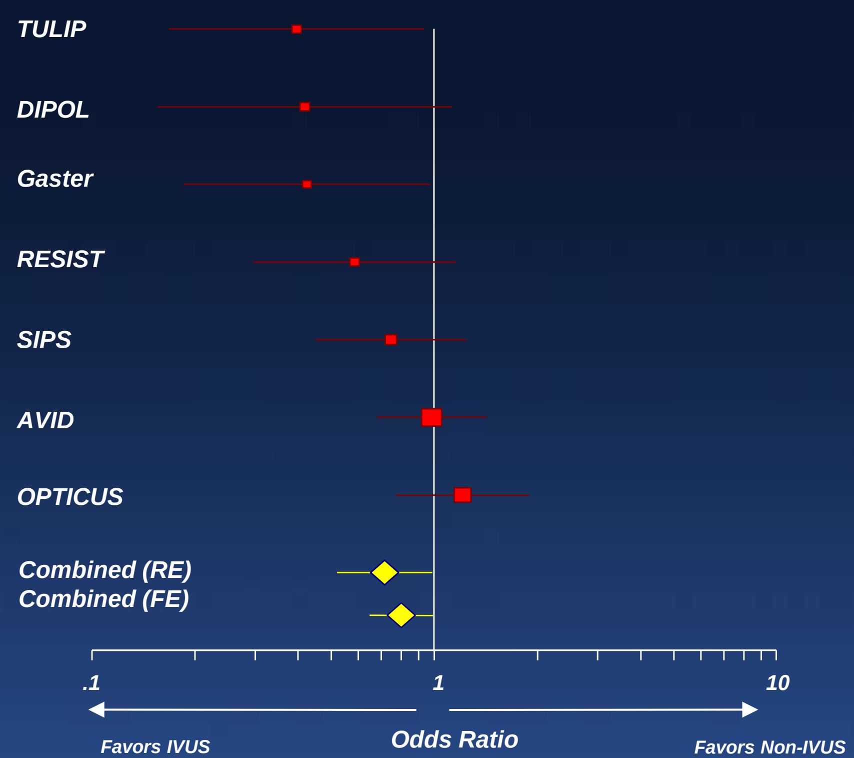


Meta-analysis of Randomized Trials of IVUS vs Angiographic Guided BMS implantation (n=2193 pts)

IVUS guidance was associated with significantly lower rate of

- *Angiographic restenosis (22.2% vs. 28.9%; OR 0.64, p=0.02)*
- *Repeat revascularization (12.6% vs. 18.4%; OR 0.66, p=0.004)*
- *Overall MACE (19.1% vs. 23.1%; OR 0.69, p=0.03)*
- *But no significant effect on MI (p=0.51) or mortality (p=0.18).*
- *ST was not reported*

MACE



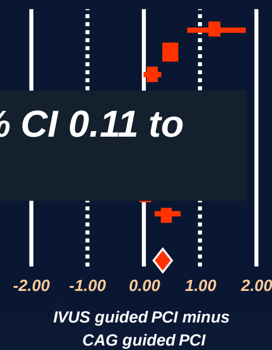
Parise et al. Am J Cardiol. 2011;107:374-82

Four meta-analyses have assessed IVUS vs angiography-guided DES implantation

					HR (p-values)					
Reference	**Yr**	**RCT**	**Non-RCT**	**Pts**	**MACE**	**Death**	**MI**	**ST**	**TLR**	**TVR**
Zhang et al Eurointervention	2012	1	10	19,619	0.87 (p=0.008)	0.59 (p<0.001)	0.82 (p=0.13)	0.58 (p<0.001)	0.90 (p=0.3)	0.90 (p=0.2)
Propensity score matched sub-analysis			6	5,300	0.86 (p=0.06)	0.73 (p=0.04)	0.63 (p=0.01)	0.57 (p=0.004)	0.85 (p=0.3)	0.94 (p=0.6)
Klersy et al Int J Cardiol	2013	3	9	18,707	0.80 (p<0.001)	0.60 (p<0.001)	0.59 (p=0.001)	0.58 (p=0.007)	0.95 (p=0.8)	
Jang et al. JACC Cardiovasc Interv	2014	3	12	24,869	0.79 (p=0.001)	0.64 (p<0.001)	0.57 (p<0.001)	0.59 (p=0.002)	0.76 (p=0.01)	0.81 (p=0.01)
Propensity score matched sub-analysis			9	13,545	0.79 (p=0.01)	0.58 (p=0.01)	0.56 (p=0.04)	0.52 (p=0.004)	0.85 (p=0.3)	0.93 (p=0.3)
Ahn et al. Am J Cardiol	2014	3	14	26,503	0.74 (p<0.001)	0.61 (p<0.001)	0.57 (p<0.001)	0.59 (p<0.001)	0.81 (p=0.046)	0.82 (p=0.022)

Implanted Stent Number

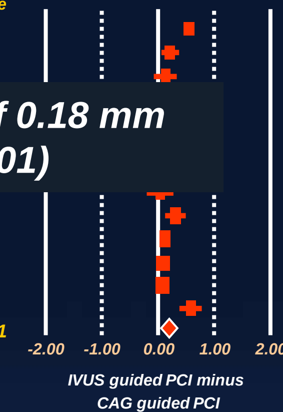
	Std diff in means	Standard error	Vari-ance	Lower limit	Upper limit	Z-value	P value
Ahn SG et al. (2013)	1.200	0.238	0.057	0.733	1.667	5.041	0.000
Ahn JM et al. (2013)	0.477	0.036	0.001	0.408	0.547	13.407	0.000
Chen SL et al. (2012)	0.134	0.080	0.006	-0.022	0.291	1.681	0.093
Youn YJ et al. (2011)	0.371	0.113	0.013	0.149	0.593	3.277	0.001
Random Effect Model	0.269	0.080	0.006	0.112	0.426	3.360	0.001



0.27 more stents per lesion (95% CI 0.11 to 0.43, P<0.001)

Implanted Stent Length

	Std diff in means	Standard error	Vari-ance	Lower limit	Upper limit	Z-value	P value
Ahn SG et al. (2013)	0.500	0.036	0.001	0.430	0.570	14.016	0.000
Chen SL et al. (2012)	0.167	0.080	0.006	0.010	0.324	2.088	0.037
Chieffo A et al. (2013)	0.106	0.105	0.011	-0.100	0.311	1.007	0.314
Park KW et al. (2012)	0.278	0.057	0.003	0.167	0.390	4.889	0.000
Roy P et al. (2008)	0.095	0.048	0.002	0.001	0.188	1.989	0.047
Witzenbichler B et al. (2012)	0.085	0.022	0.000	0.042	0.128	3.844	0.000
Yoon YW et al. (2013)	0.047	0.047	0.002	-0.045	0.140	1.005	0.315
Youn YJ et al. (2011)	0.521	0.114	0.013	0.298	0.745	4.569	0.000
Random Effect Model	0.175	0.048	0.002	0.080	0.271	3.618	<0.001



Mean difference in stent length of 0.18 mm (95% CI 0.08 to 0.27, P<0.001)

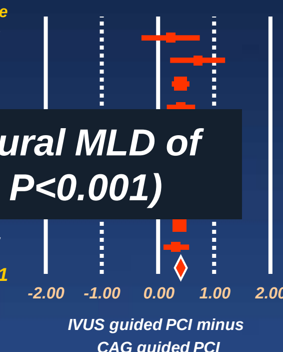
Mean Stent Diameter

	Std diff in means	Standard error	Vari-ance	Lower limit	Upper limit	Z-value	P value
Ahn SG et al. (2013)	0.484	0.223	0.050	0.048	0.920	2.174	0.030
Ahn JM et al. (2013)	0.467	0.036	0.001	0.398	0.537	13.134	0.000
Chen SL et al. (2012)	0.195	0.080	0.006	0.038	0.352	2.439	0.015
Claessen BE et al. (2011)	0.250	0.061	0.004	0.131	0.369	4.122	0.000
Witzenbichler B et al. (2012)	0.553	0.023	0.001	0.509	0.597	24.557	0.000
Youn YJ et al. (2011)	0.343	0.113	0.013	0.122	0.565	3.034	0.002
Chieffo A et al. (2013)	0.243	0.105	0.011	0.037	0.449	2.311	0.021
Random Effect Model	0.328	0.054	0.003	0.221	0.435	6.015	<0.001

Mean difference in stent size of 0.33 mm (95% CI 0.22 to 0.44mm, P<0.001)

Minimal Lumen Diameter

	Std diff in means	Standard error	Vari-ance	Lower limit	Upper limit	Z-value	P value
Agostoni et al. (2005)	0.208	0.267	0.071	-0.316	0.732	0.779	0.436
Ahn SG et al. (2013)	0.667	0.225	0.051	0.225	1.108	2.958	0.003
Chen SL et al. (2012)	0.369	0.081	0.006	0.211	0.527	4.582	0.000
Chieffo A et al. (2013)	0.363	0.106	0.011	0.156	0.570	3.437	0.001
Youn YJ et al. (2011)	0.270	0.113	0.013	0.048	0.491	2.389	0.017
Random Effect Model	0.335	0.034	0.001	0.269	0.400	9.981	<0.001



Mean difference in post-procedural MLD of 0.34 mm (95% CI 0.27 to 0.40, P<0.001)

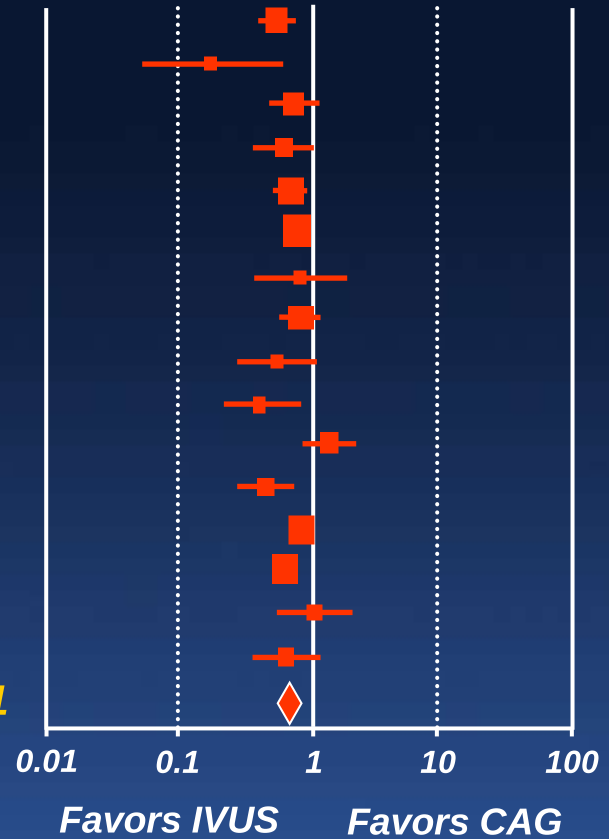
Ahn et al. Am J Cardiol 2014;113:1338-47

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

Major Adverse Cardiovascular Events

	Odds Ratio	Lower limit	Upper limit	Z-value	P value
Ahn JM et al. (2013)	0.555	0.400	0.772	-3.499	0.000
Ahn SG et al. (2013)	0.174	0.050	0.604	-2.755	0.006
Chen SL et al. (2012)	0.759	0.503	1.146	-1.312	0.190
Chieffo A et al. (2013)	0.673	0.374	1.211	-1.321	0.186
Claessen BE et al. (2011)	0.755	0.566	1.009	-1.900	0.057
Hur SH et al. (2012)	0.851	0.706	1.026	-1.689	0.091
Jakabcin J et al. (2010)	0.906	0.388	2.118	-0.227	0.820
Kim JS et al. (2011)	0.889	0.599	1.318	-0.587	0.557
Kim JS et al. (2013)	0.598	0.287	1.247	-1.370	0.171
Kim SH et al. (2010)	0.436	0.223	0.852	-2.430	0.015
Park KW et al. (2012)	1.434	0.872	2.358	1.421	0.155
Park SJ et al. (2009)	0.466	0.271	0.802	-2.755	0.006
Roy P et al. (2008)	0.877	0.677	1.137	-0.991	0.322
Witzenbichler B et al. (2013)	0.649	0.514	0.819	-3.631	0.000
Yoon YW et al. (2013)	1.097	0.556	2.167	0.268	0.789
Youn YJ et al. (2011)	0.664	0.354	1.246	-1.276	0.202
Random Effect Model	**0.735**	**0.637**	**0.849**	**-4.197**	**<0.001**

Odds Ratio and 95% CI

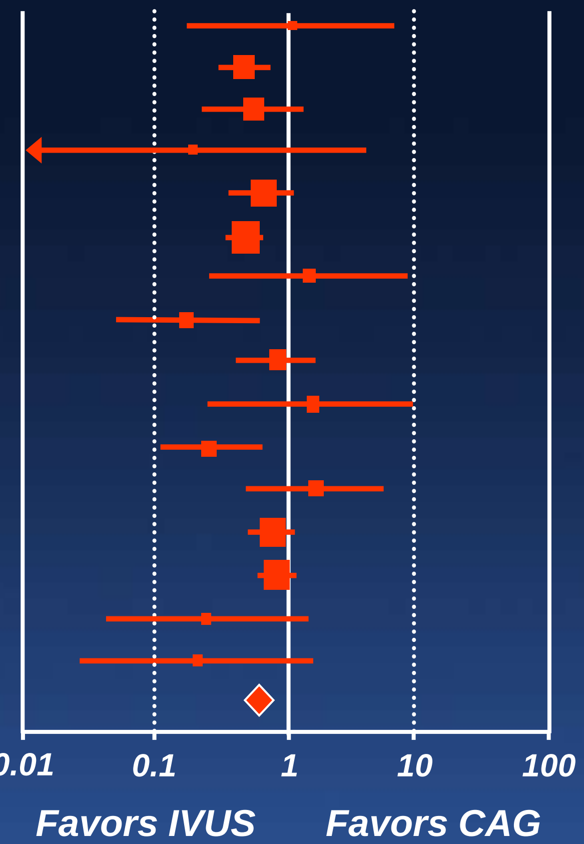


Ahn et al, Am J Cardiol 2014;113:1338-47

Death

	Odds Ratio	Lower limit	Upper limit	Z-value	P value
Ahn JM et al. (2013)	1.095	0.174	6.898	0.097	0.923
Ahn SG et al. (2013)	0.477	0.301	0.756	-3.152	0.002
Chen SL et al. (2012)	0.554	0.216	1.422	-1.227	0.220
Chieffo A et al. (2013)	0.198	0.009	4.170	-1.041	0.298
Claessen BE et al. (2011)	0.656	0.376	1.147	-1.478	0.139
Hur SH et al. (2012)	0.486	0.358	0.661	-4.604	0.000
Jakabcin J et al. (2010)	1.515	0.259	8.874	0.461	0.645
Kim SH et al. (2010)	0.172	0.050	0.590	-2.802	0.005
Kim JS et al. (2011)	0.857	0.425	1.725	-0.433	0.665
Kim JS et al. (2013)	1.578	0.254	9.784	0.490	0.624
Park SJ et al. (2009)	0.259	0.107	0.629	-2.982	0.003
Park KW et al. (2012)	1.673	0.506	5.533	0.844	0.399
Roy P et al. (2008)	0.791	0.539	1.160	-1.200	0.230
Witzenbichler B et al. (2013)	0.875	0.636	1.204	-0.818	0.413
Yoon YW et al. (2013)	0.248	0.039	1.587	-1.472	0.141
Youn YJ et al. (2011)	0.210	0.026	1.698	-1.463	0.143
Random Effect Model	**0.613**	**0.478**	**0.786**	**-3.861**	**<0.001**

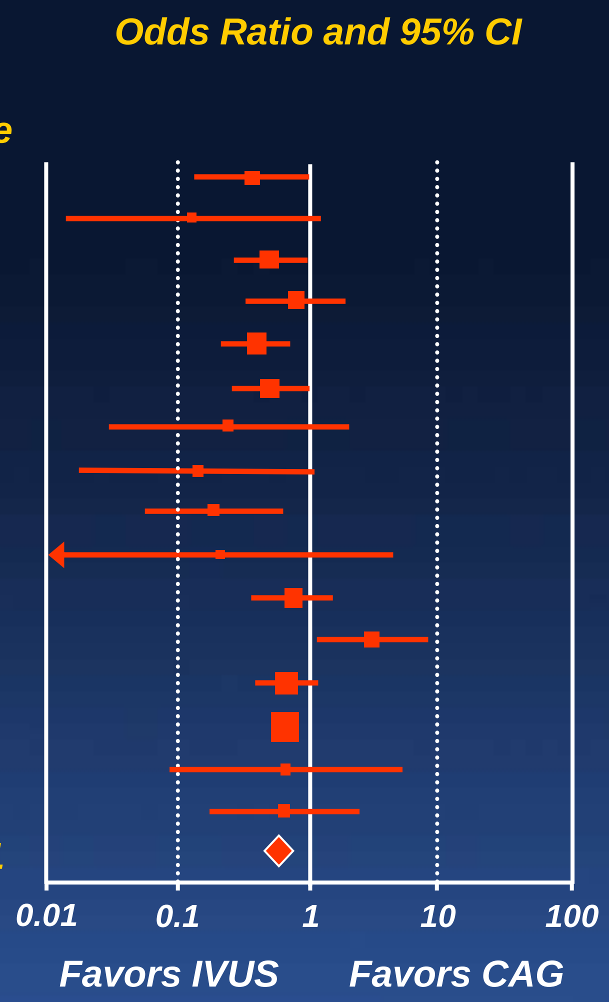
Odds Ratio and 95% CI



Ahn et al, Am J Cardiol 2014;113:1338-47

Myocardial Infarction

	Odds Ratio	Lower limit	Upper limit	Z-value	P value
Ahn JM et al. (2013)	0.373	0.131	1.061	-1.849	0.064
Ahn SG et al. (2013)	0.126	0.014	1.154	-1.233	0.067
Chen SL et al. (2012)	0.494	0.257	0.948	-2.120	0.034
Chieffo A et al. (2013)	0.810	0.338	1.941	-0.472	0.637
Claessen BE et al. (2011)	0.399	0.214	0.744	-2.893	0.004
Hur SH et al. (2012)	0.497	0.247	1.004	-1.949	0.051
Jakabcin J et al. (2010)	0.242	0.028	2.094	-1.288	0.198
Kim SH et al. (2010)	0.139	0.017	1.150	-1.830	0.067
Kim JS et al. (2011)	0.189	0.054	0.665	-2.596	0.009
Kim JS et al. (2013)	0.209	0.010	4.414	-1.006	0.315
Park SJ et al. (2009)	0.757	0.369	1.550	-0.762	0.446
Park KW et al. (2012)	3.043	1.125	8.234	2.191	0.028
Roy P et al. (2008)	0.670	0.369	1.218	-1.313	0.189
Witzenbichler B et al. (2013)	0.660	0.508	0.858	-3.110	0.002
Yoon YW et al. (2013)	0.666	0.083	5.317	-0.383	0.701
Youn YJ et al. (2011)	0.640	0.167	2.458	-0.650	0.516
Random Effect Model	**0.571**	**0.435**	**0.751**	**-4.011**	**<0.001**

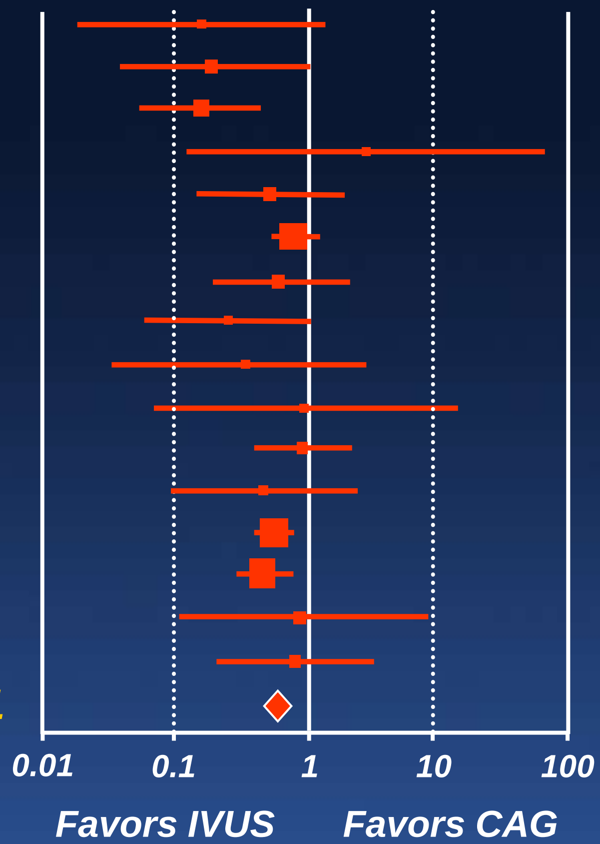


Ahn et al, Am J Cardiol 2014;113:1338-47

Definite or Probable Stent Thrombosis

	Odds Ratio	Lower limit	Upper limit	Z-value	P value
Ahn JM et al. (2013)	0.163	0.017	1.557	-1.575	0.115
Ahn SG et al. (2013)	0.199	0.037	1.079	-1.872	0.061
Chen SL et al. (2012)	0.164	0.055	0.489	-3.240	0.001
Chieffo A et al. (2013)	3.009	0.121	4.609	0.672	0.501
Claessen BE et al. (2011)	0.553	0.149	2.051	-0.885	0.367
Hur SH et al. (2012)	0.855	0.558	1.308	-0.723	0.470
Jakabcin J et al. (2010)	0.653	0.184	2.314	-0.661	0.509
Kim SH et al. (2010)	0.263	0.059	1.179	-1.745	0.081
Kim JS et al. (2011)	0.332	0.033	3.300	-0.941	0.347
Kim JS et al. (2013)	1.000	0.070	4.371	0.000	1.000
Park SJ et al. (2009)	1.000	0.406	2.465	0.000	1.000
Park KW et al. (2012)	0.498	0.091	2.719	-0.804	0.421
Roy P et al. (2008)	0.583	0.392	0.867	-2.666	0.008
Witzenbichler B et al. (2013)	0.497	0.289	0.855	-2.529	0.011
Yoon YW et al. (2013)	1.000	0.106	9.393	0.000	1.000
Youn YJ et al. (2011)	0.854	0.210	3.468	0.825	0.825
Random Effect Model	**0.592**	**0.468**	**0.750**	**-4.358**	**<0.001**

Odds Ratio and 95% CI



Ahn et al, Am J Cardiol 2014;113:1338-47

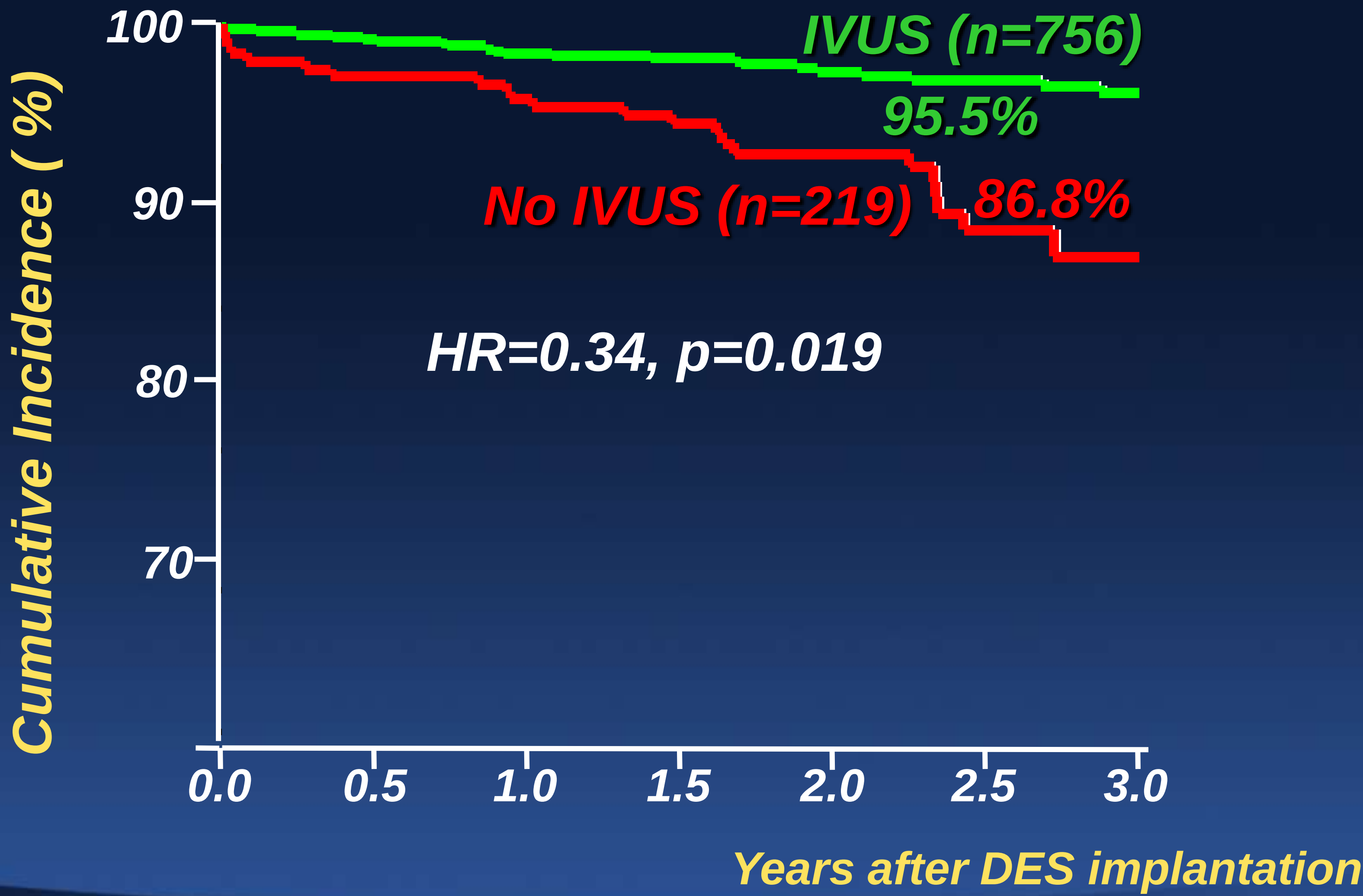
More recent published studies assessing benefit of IVUS

Reference	Lesion subset	Stats	# Pts	Endpoint
Patel et al. Cath Cardiovasc Interv, in press	Ostial	Propensity score matched	225	MACE (HR=0.54, p=0.04)
De la Torre Hernandez et al. JACC Cardiovasc Interv 2014;7:244-54	LM	Propensity score matched	505 pairs	ST (0.6% vs 2.2%, p=0.04) MACE (11.7% vs 16.0%, p=0.04, especially distal lesions treated with 2 stents: 16.7% vs 41.0%, p=0.02)
Gao et al. Patient Pref Adherence 2014;8:1-11	LM	Propensity score matched	291 pairs	MACE (16.2% vs 24.4%, p=0.014)
Hong et al. Am J Cardiol 2014;114:534	CTO	Propensity score matched	201 pairs	ST (0% vs 3%, p=0.014)
Singh et al. Am J Cardiol 2015, in press			377,096 angio vs 24,475 IVUS	In-hospital mortality (0.4% vs. 0.8%, P<0.001)

Studies showing NO benefit of IVUS

Reference	Lesion subset	Stats	# Pts	Endpoint
Fröhlich et al. JAMA Intern Med. 2014;174:1360-1366	All	Propensity score	803 pairs	also no benefit for FFR-guidance

All-cause mortality after LMCA DES implantation: Impact of IVUS guidance

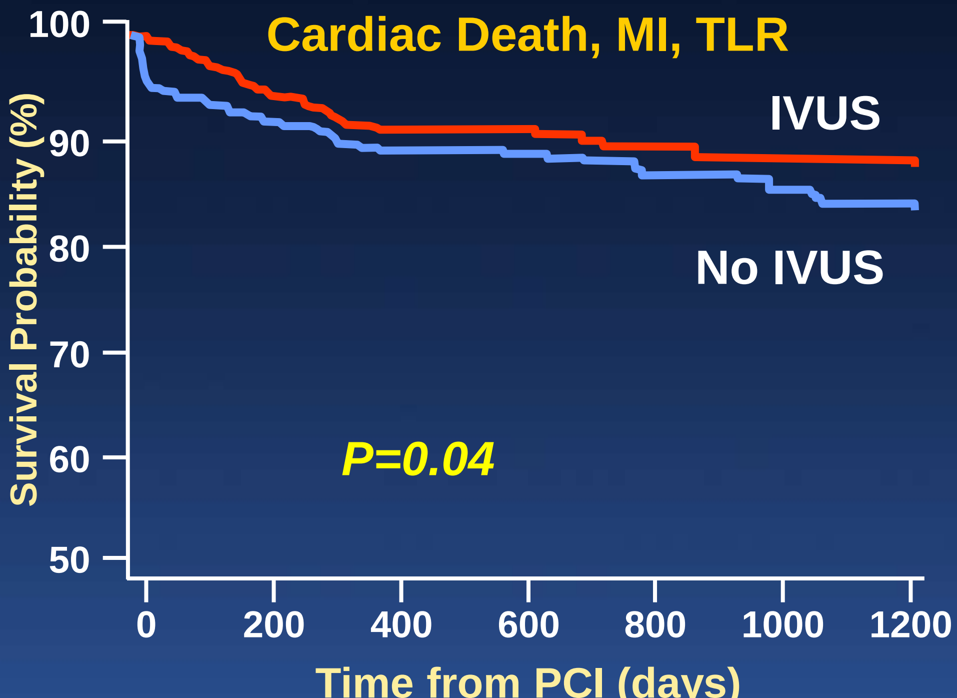


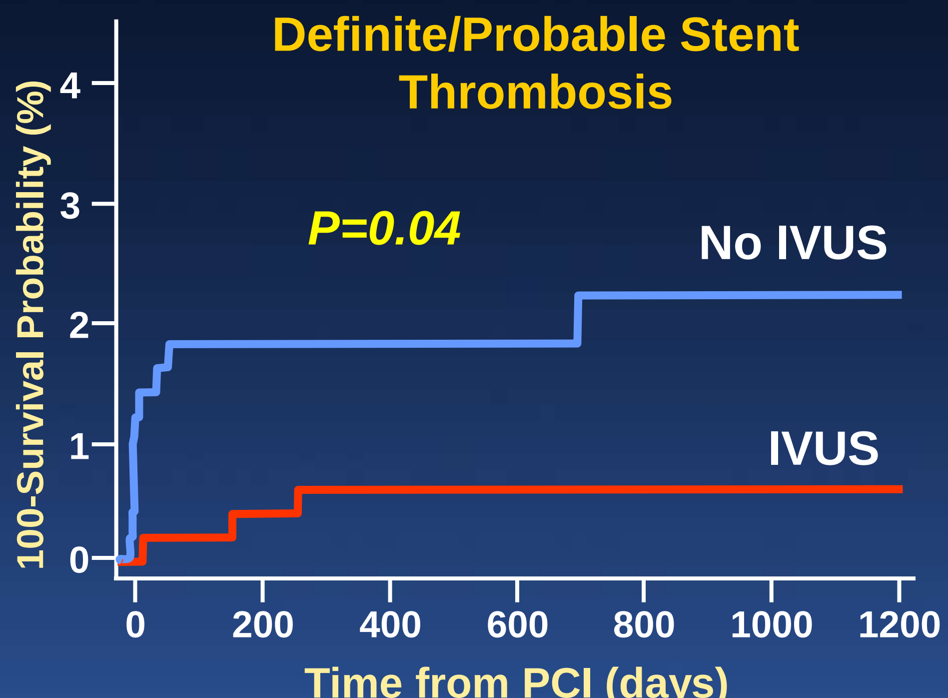
Park et al. Circ Cardiovasc Intervent 2009;2:167-77

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

Impact of IVUS Guidance of Unprotected LM Propensity Matched 1010 pts from 4 Registries

- *Distal LM lesion ~60%, 2 stent technique ~13%*
- *IVUS guidance was an independent predictor of MACE*





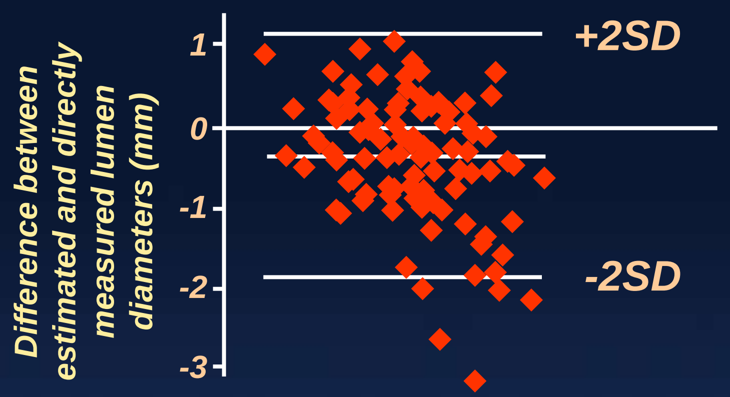
De la Torre Hernandez et al. J Am Coll Cardiol 2014:244-54

Comparison of 1-year clinical outcomes between IVUS-guided versus angiography-guided implantation of DES for LMCA lesions: A single-center analysis of a 1,016 pt cohort

	IVUS	No IVUS	P
Overall	**337**	**679**	
Cardiac death	1.8%	6.2%	0.002
STEMI	1.2%	3.4%	0.004
TLR	2.4%	9.4%	<0.001
Stent thrombosis	0.6%	2.7%	0.026
MACE	14.8%	27.2%	<0.001
Propensity Score Matched	**291**	**291**	
Cardiac death	12.4%	15.1%	0.023
STEMI	1.0%	3.4%	0.05
TLR	2.7%	8.2%	0.004
Stent thrombosis	0.3%	2.4%	0.075
MACE	16.2%	24.4%	0.014

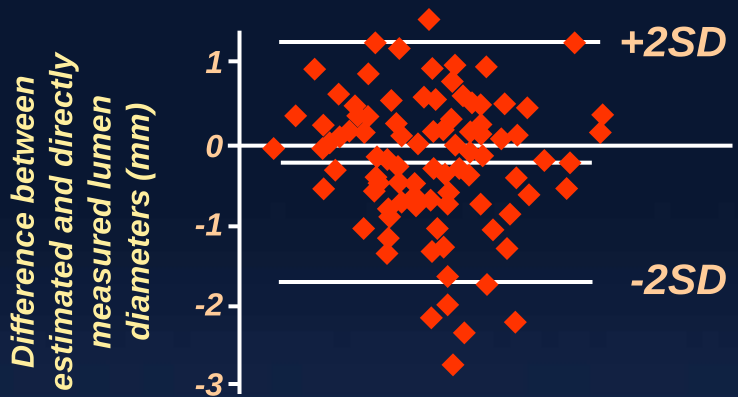
Gao et al. Patient Pref Adherence 2014;8:1-11

Evaluation of the LAD from the LM-LCX Pullback



	Sensitivity	Specificity
Plaque burden >40%	59%	45%
Plaque burden >70%	78%	42%

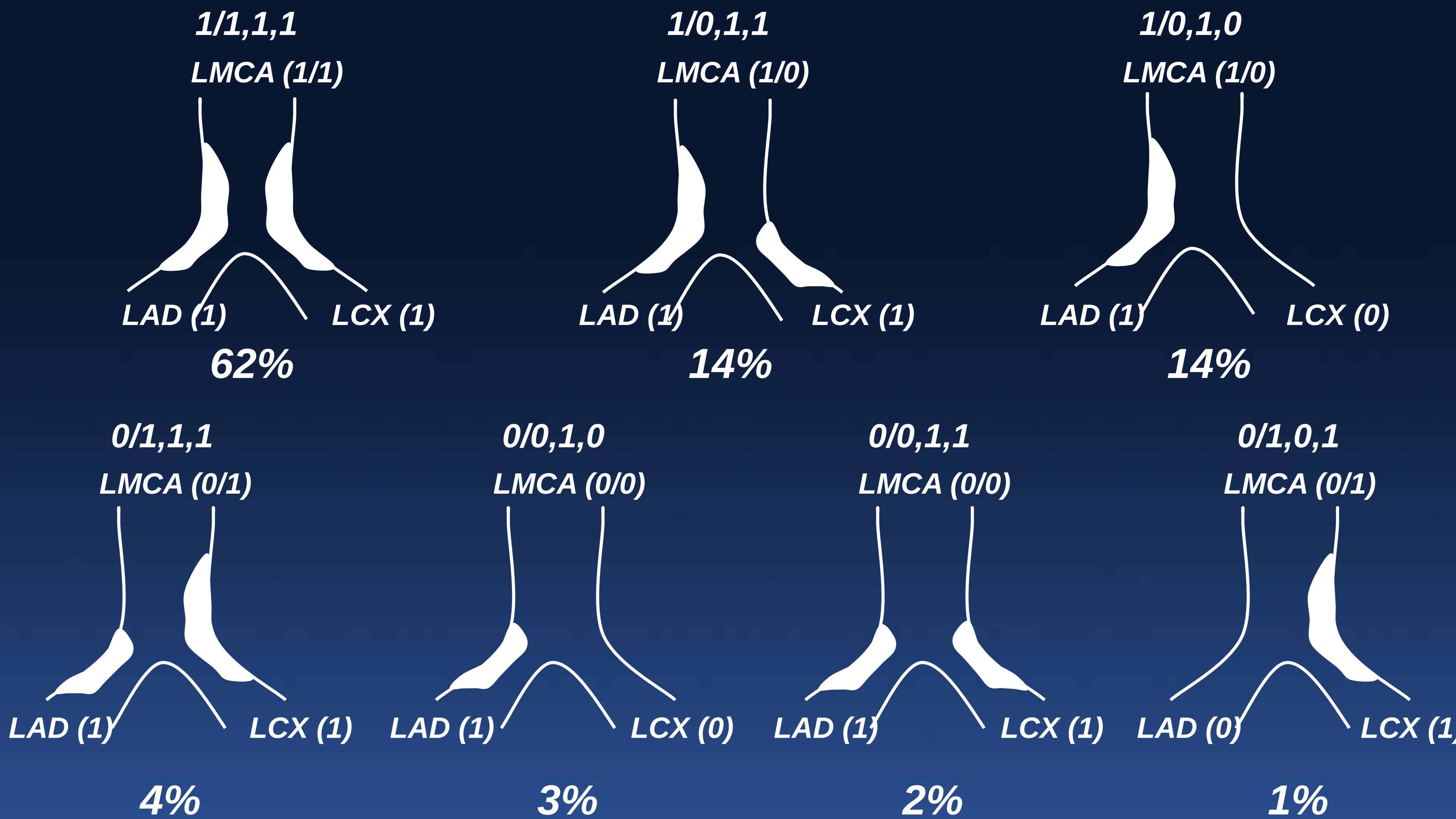
Evaluation of the LCX from the LM-LAD Pullback



	Sensitivity	Specificity
Plaque burden >40%	67%	55%
Plaque burden >70%	88%	42%

Oviedo et al. Am J Cardiol 2010;105:948-54

IVUS plaque distribution in 140 distal LMCA bifurcation lesions

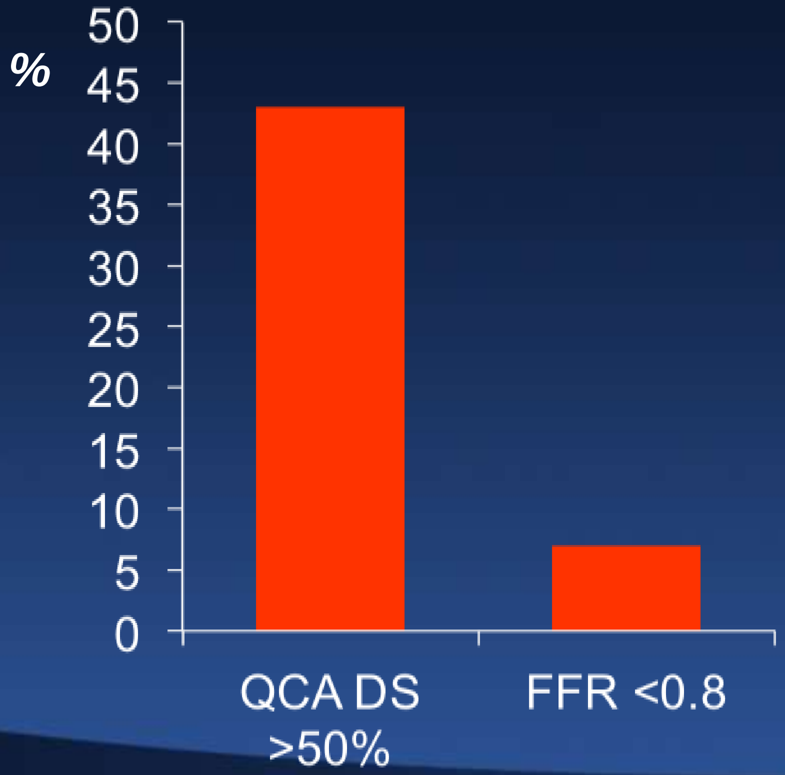


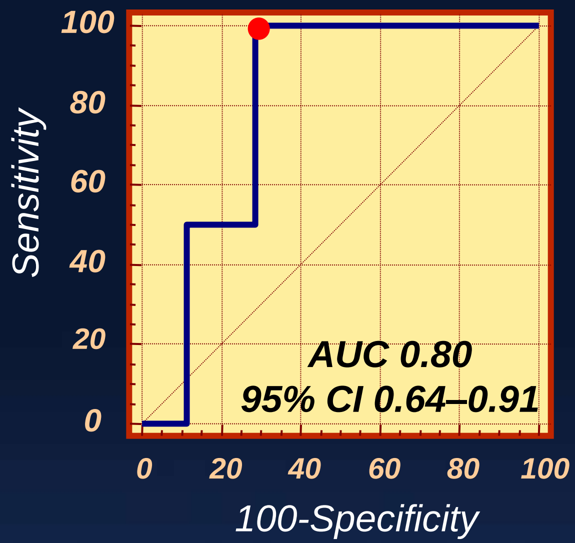
Oviedo et al. Circ Cardiovasc Interv. 2010;3:105-12

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

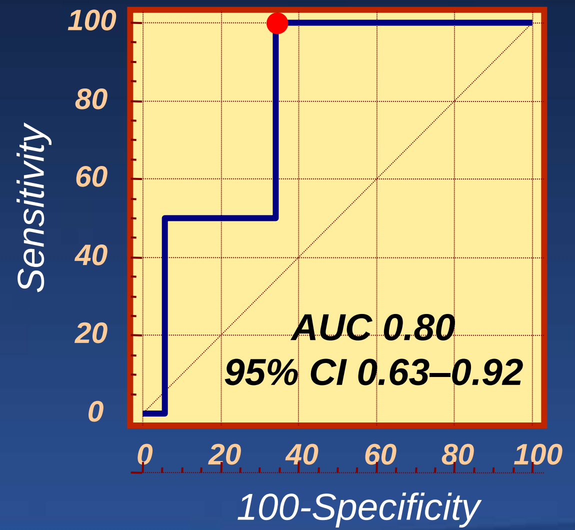
Oviedo et al. Circ Cardiovasc Interv. 2010;3:105-12

43 LMCA bifurcation lesions with a pre-PCI LCX ostial DS<50% were treated by single-stent cross-over





MLA <3.7mm²
- Sensitivity 100%
- Specificity 71%
- PPV 16%
- NPV 100%

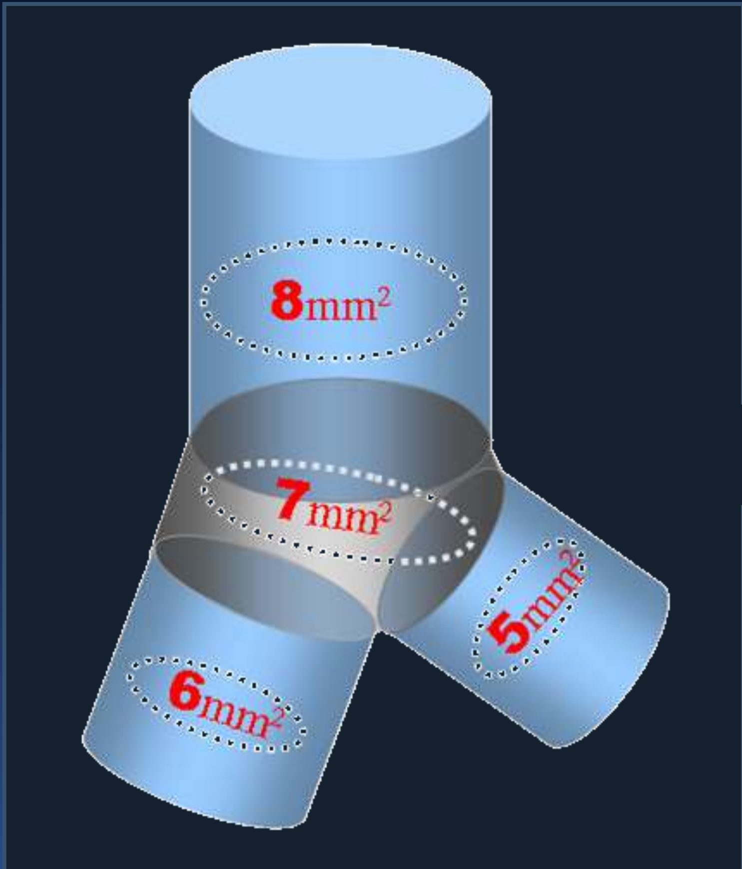


Plaque Burden >56%
- Sensitivity 100%
- Specificity 65%
- PPV 14%
- NPV 100%

Kang et al. Catheter Cardiovasc Interv 2014;83:545-52

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

Criteria for Stent Underexpansion at the Distal LMCA Bifurcation (n=403)

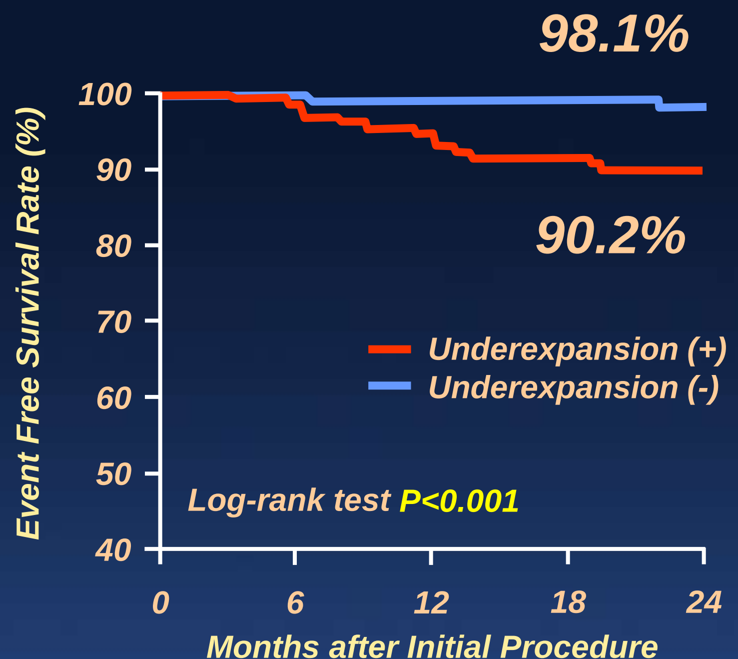


- MACE-free survival was lower in pts with underexpansion vs those without underexpansion (89.4% vs 98.1%)
- TLR-free survival was lower in patients with underexpansion vs no underexpansion (90.9% vs 98.5%)
- Although acute malapposition was observed in 28 pts, malapposition was not related to MACE at follow-up

Kang et al. Circ Cardiovasc Interv. 2011;4:562-9

MACE-free and TLR-free Survival

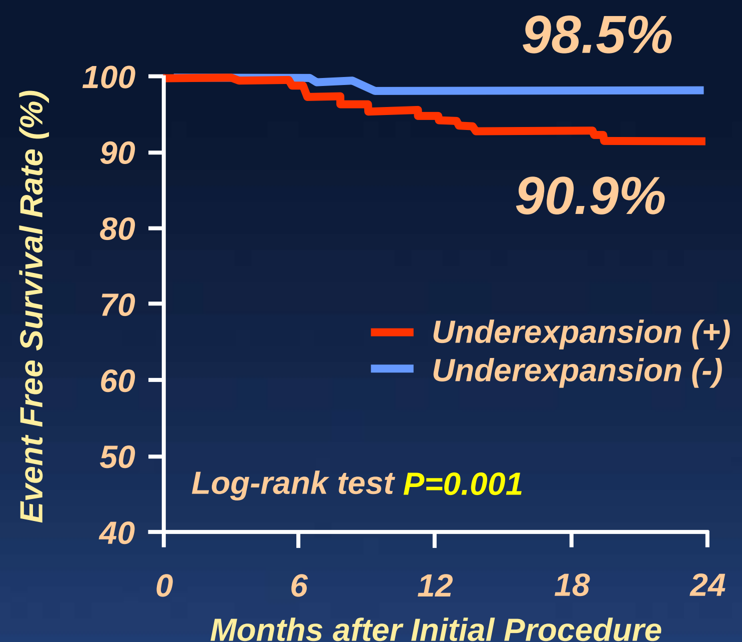
MACE



No. at risk

	0	6	12	18	24
Underexpansion (+)	133	131	126	121	75
Underexpansion (-)	260	260	255	246	129

TLR



No. at risk

	0	6	12	18	24
Underexpansion (+)	133	131	126	121	75
Underexpansion (-)	260	260	255	246	129

Kang et al. Circ Cardiovasc Interv. 2011;4:562-9

Stent Coverage of the Ostium in 199 LMCA treated with DES

- Strut protrusion into the aorta was seen in 68%, with a protrusion length of 3.4±1.7mm
- Incomplete stent coverage of the ostium was seen in 23%, with a length of uncovered ostial segment of 2.3±1.3mm and a residual plaque burden of 38±12%
- Acute malapposition was seen in 18.8%
- Only 1.2% of LMCA developed ostial restenosis; this was not related to strut protrusion or ostial coverage or acute malapposition

Kang et al. Am J Cardiol 2013;111:1401-7

Randomized IVUS vs Angiographic Guided CTO Intervention

467 patients with CTO were initially screened

Exclusions
- Wiring failure - 61 patients
- Refusal of study enrollment - 4 patients

A total of 402 pts were finally enrolled after successful guidewire-crossing

1:1 randomization

IVUS-guided group (n=201)

1:1 randomization
R-ZES vs. N-BES

Angiography-guided group (n=201)

IVUS-guided group (n=231)

Angiography-guided group (n=171)

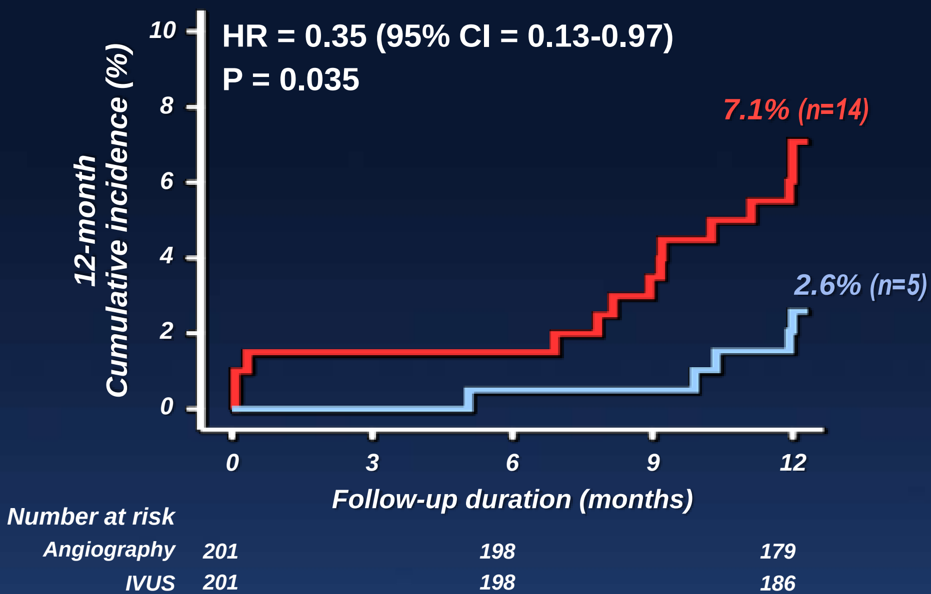
Primary endpoint was a composite of cardiac death, MI, or TVR at 12 months

Jang et al. TCT2014

Primary endpoint (Cardiac death, MI, TVR)

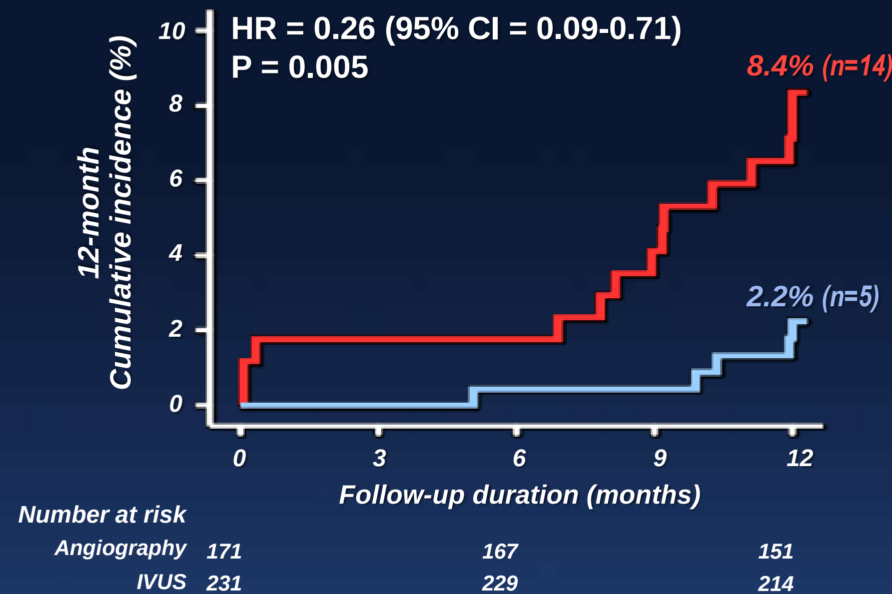
Angiography-guided group
IVUS-guided group

Intention to Treat



	IVUS	Angio	P-value
Cardiac death/MI	0%	2%	0.045
TVR	2.6%	5.2%	0.186

Per Protocol



	IVUS	Angio	P-value
Cardiac death/MI	0%	2.3%	0.019
TVR	2.2%	6.1%	0.049

Jang et al. TCT2014

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

ADAPT-DES

Assessment of Dual AntiPlatelet Therapy with Drug-Eluting Stents

8,575 pts prospectively enrolled

No clinical or anatomic exclusion criteria

Succesful and uncomplicated PCI with ≥1 non-investigational DES

↓

Pre-specified IVUS vs no IVUS substudy

↙ ↘

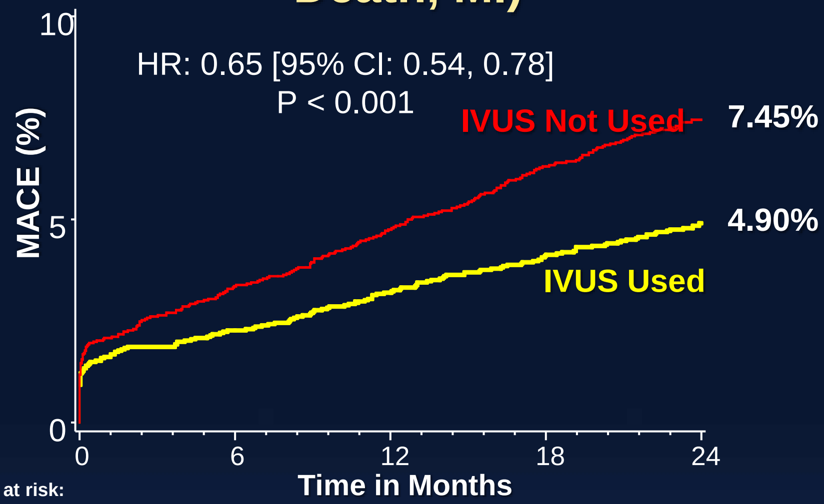
IVUS: 3349 pts | **No IVUS: 5234 pts**

↓ ↓

Clinical FU at 30 days, 1 year, 2 years

Two year follow-up data from ADAPT-DES (3361 pts treated with IVUS-guidance vs 5221 pts treated with angiographic guidance)

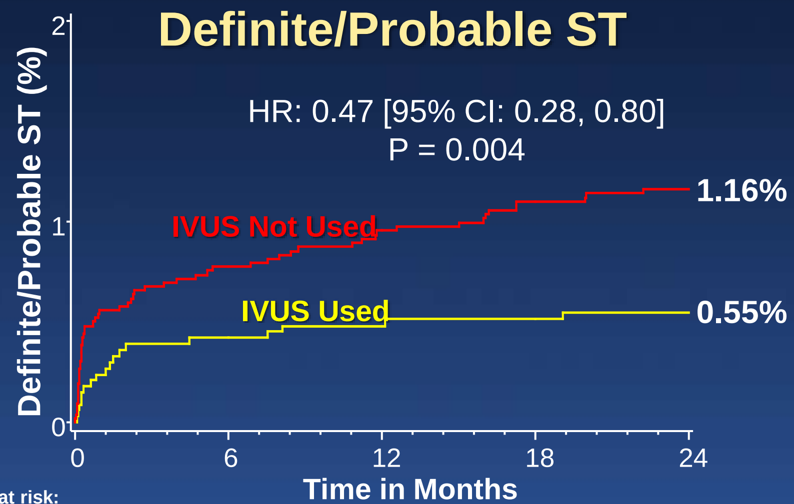
MACE (Definite/Probable ST, Cardiac Death, MI)



Number at risk:

IVUS Used	3361	3206	3117	2988	1739
IVUS Not Used	5221	4912	4740	4537	2177

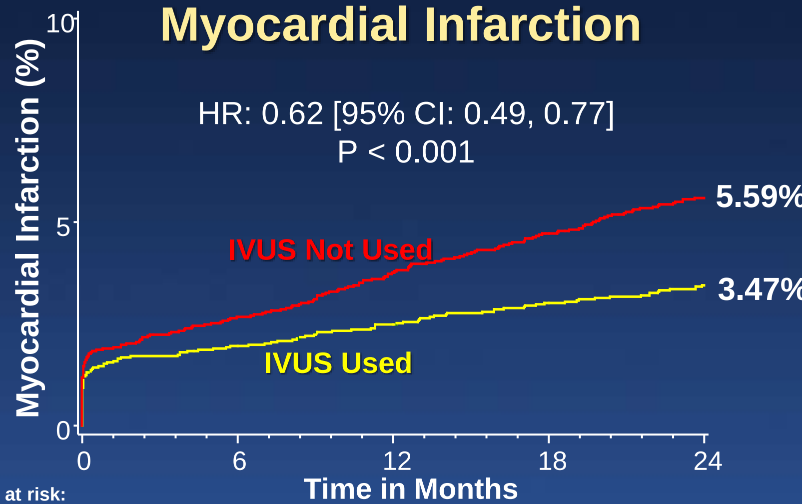
Definite/Probable ST



Number at risk:

IVUS Used	3361	3260	3182	3065	1791
IVUS Not Used	5221	5019	4886	4713	2279

Myocardial Infarction



Number at risk:

IVUS Used	3361	3209	3120	2991	1739
IVUS Not Used	5221	4916	4744	4541	2179

Maehara et al. J Am Coll Cardiol 2013;62:B21-B22

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

Conclusions

- In the cath lab you have two basic decisions:
  - Should I treat this patient/lesion?
  - How can I do the best job possible because a better acute result is tied to a better long-term outcom?
- Use FFR to assess non-LMCA lesion severity
- Use IVUS (or FFR) to assess LMCA lesion severity
- Use IVUS to optimize stent implantation