# Imaging Criteria for DES Optimization

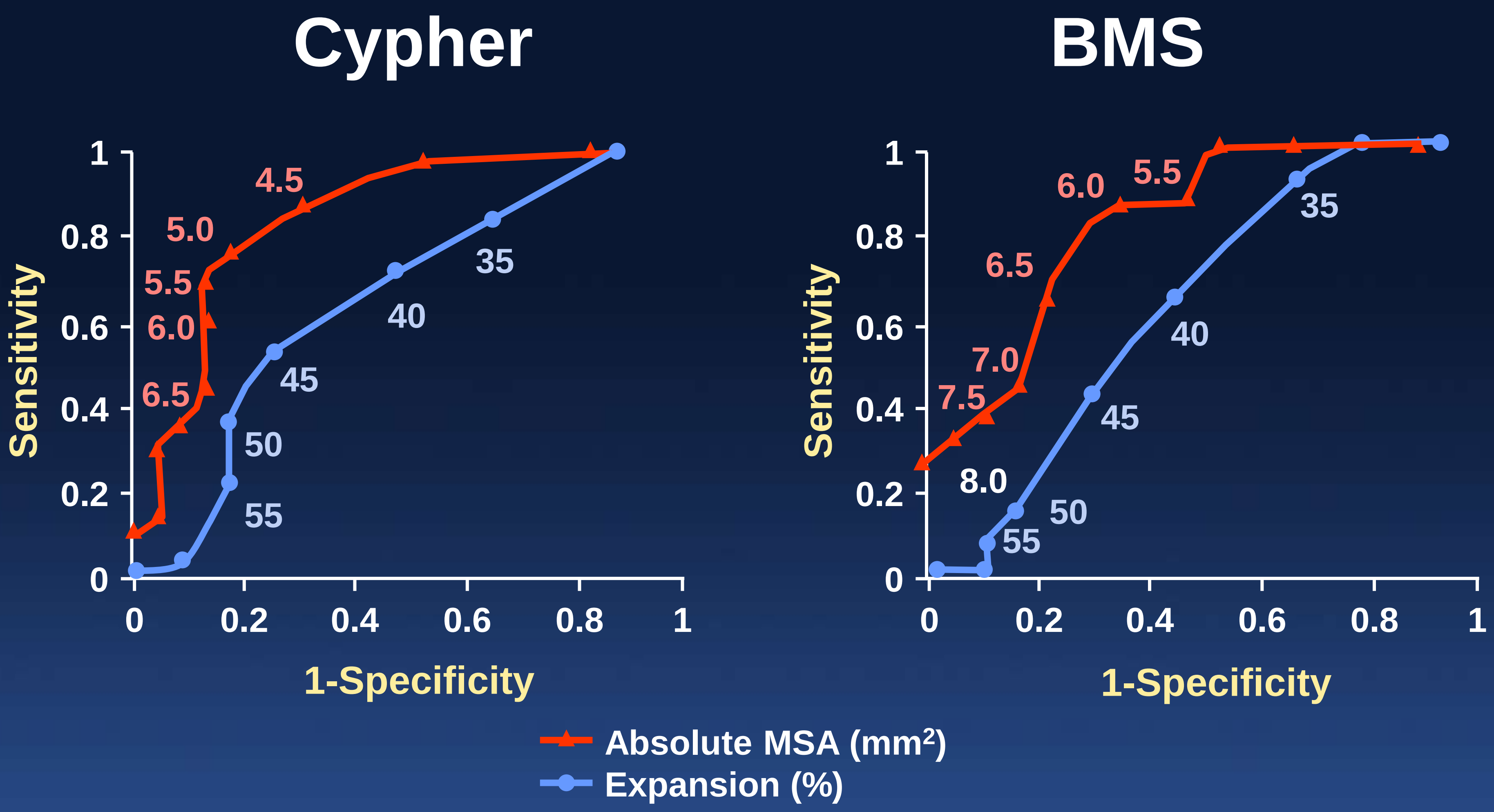
*Gary S. Mintz, MD*

*Cardiovascular Research Foundation*

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

# IVUS Predictors of DES Early Thrombosis & Restenosis

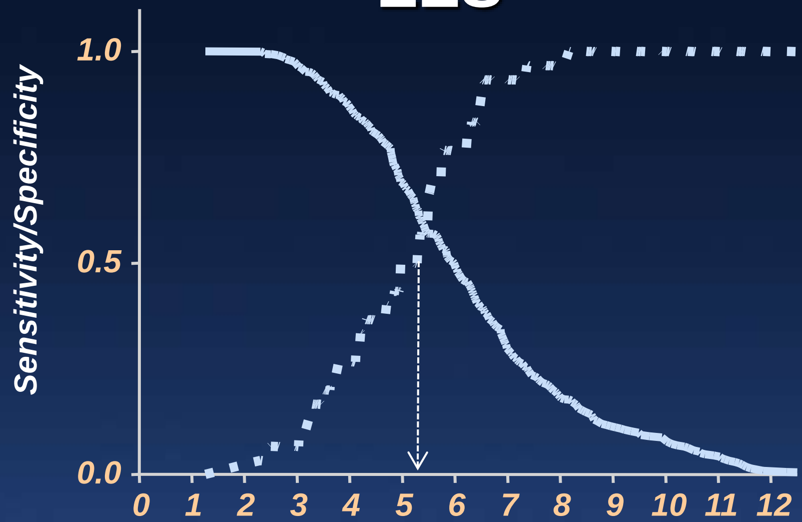
| | Early Thrombosis | Restenosis |
|---|---|---|
| **Small MSA or underexpansion in stable lesions**<br>**Small MLA in ACS/MI lesions (accounting for plaque/thrombus protrusion)** | •*Fujii et al. J Am Coll Cardiol 2005;45:995-8*<br>•*Okabe et al. Am J Cardiol. 2007;100:615-20*<br>•*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34*<br>•*Choi et al. Circ Cardiovasc Interv 2011;4:239-47* | •*Sonoda et al. J Am Coll Cardiol 2004;43:1959-63*<br>•*Hong et al. Eur Heart J 2006;27:1305-10*<br>•*Doi et al JACC Cardiovasc Interv. 2009;2:1269-75*<br>•*Fujii et al. Circulation 2004;109:1085-1088*<br>•*Kang et al. Circ Cardiovasc Interv 2011;4:9-14*<br>•*Choi et al. Am J Cardiol 2012;109:455-60*<br>•*Song et al. Catheter Cardiovasc Interv 2014;83:873-8*<br>•*Kang et al. PLoS One 2015;10(10):e0140421* |
| **Edge problems (geographic miss, secondary lesions, large plaque burden, dissections, etc)** | •*Fujii et al. J Am Coll Cardiol 2005;45:995-8*<br>•*Okabe et al., Am J Cardiol. 2007;100:615-20*<br>•*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34*<br>•*Choi et al. Circ Cardiovasc Interv 2011;4:239-47* | •*Sakurai et al. Am J Cardiol 2005;96:1251-3*<br>•*Liu et al. Am J Cardiol 2009;103:501-6*<br>•*Costa et al, Am J Cardiol, 2008;101:1704-11*<br>•*Kang et al. Am J Cardiol 2013;111:1408-14*<br>•*Kobayashi et al. ACC2014* |
| **Stent length (>40mm)** | | •*Hong et al. Eur Heart J 2006;27:1305-10* |




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

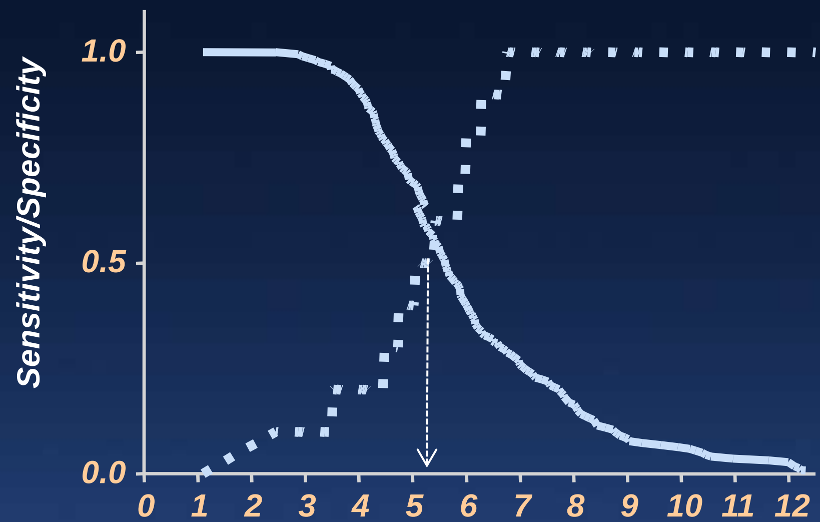
# Predicting Freedom From Angiographic Restenosis with Second Generation DES at AMC

## ZES




***MSA 5.3mm²***

## EES



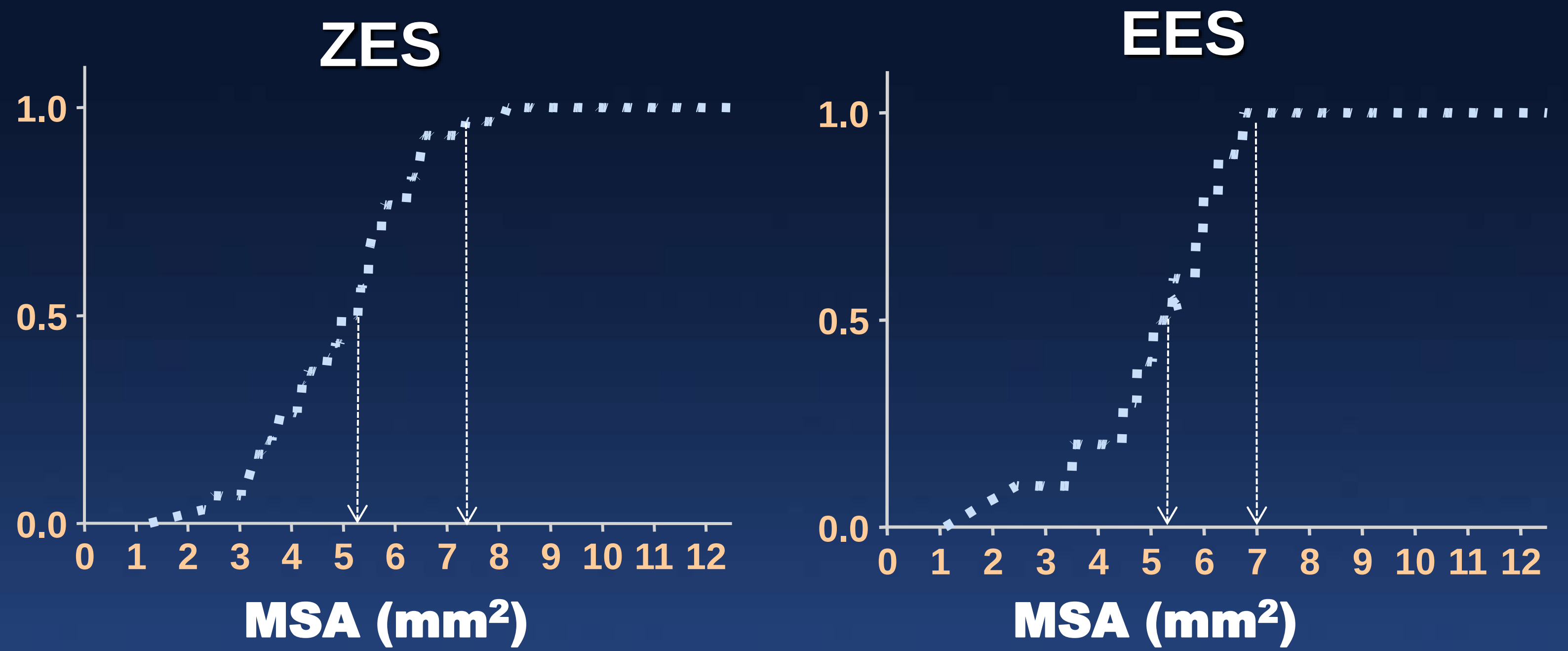

***MSA 5.4mm²***

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

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

By definition, sensitivity/specificity curve analysis "must" identify a single MSA that "best" separates events from no events. However, sensitivity and specificity are not of similar importance when predicting outcomes.

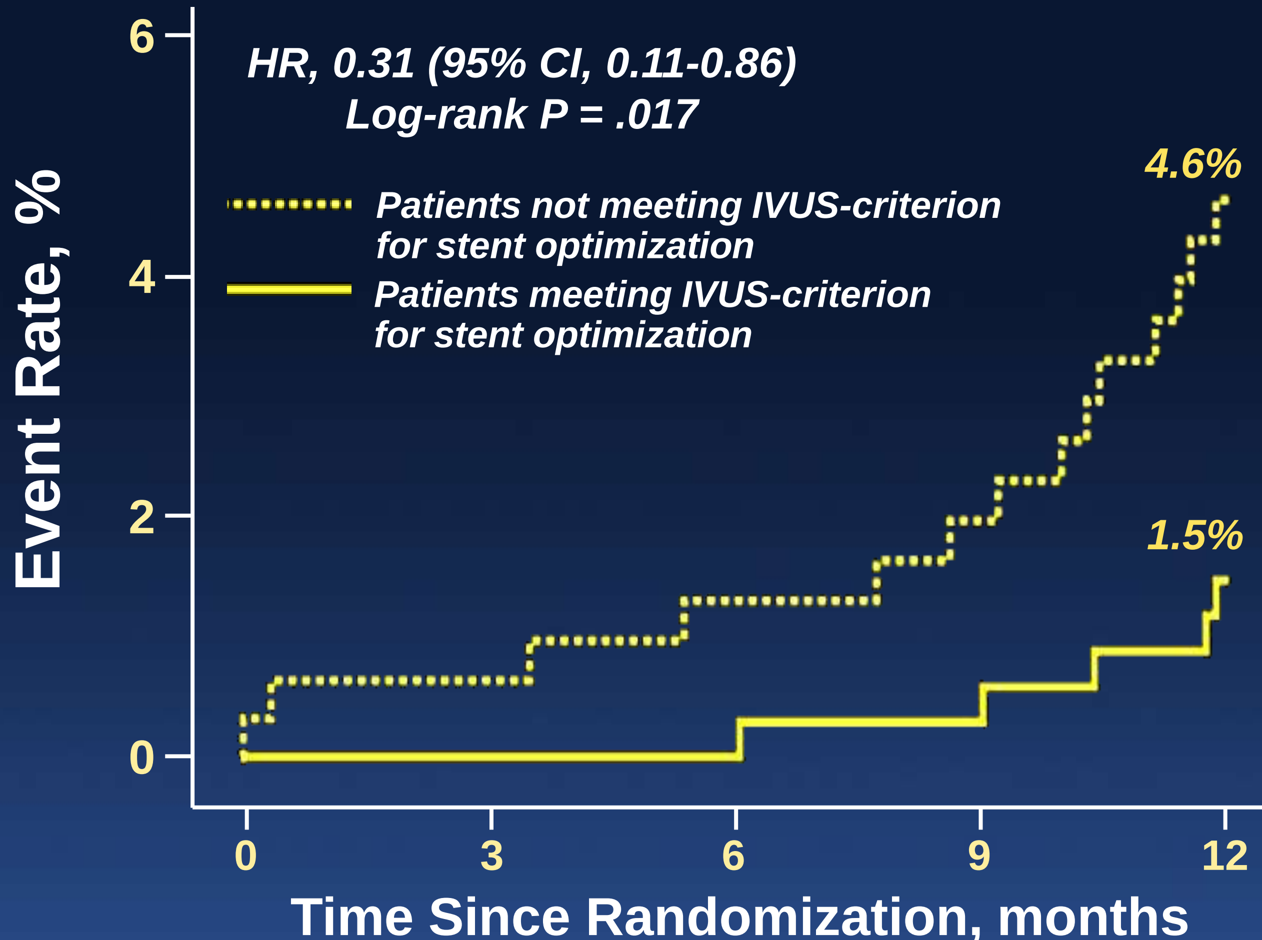
# Predicting Freedom From Angiographic Restenosis with Second Generation DES at AMC




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

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

# IVUS-XPL: Impact of stent optimization
## (in-stent MLA > distal reference)

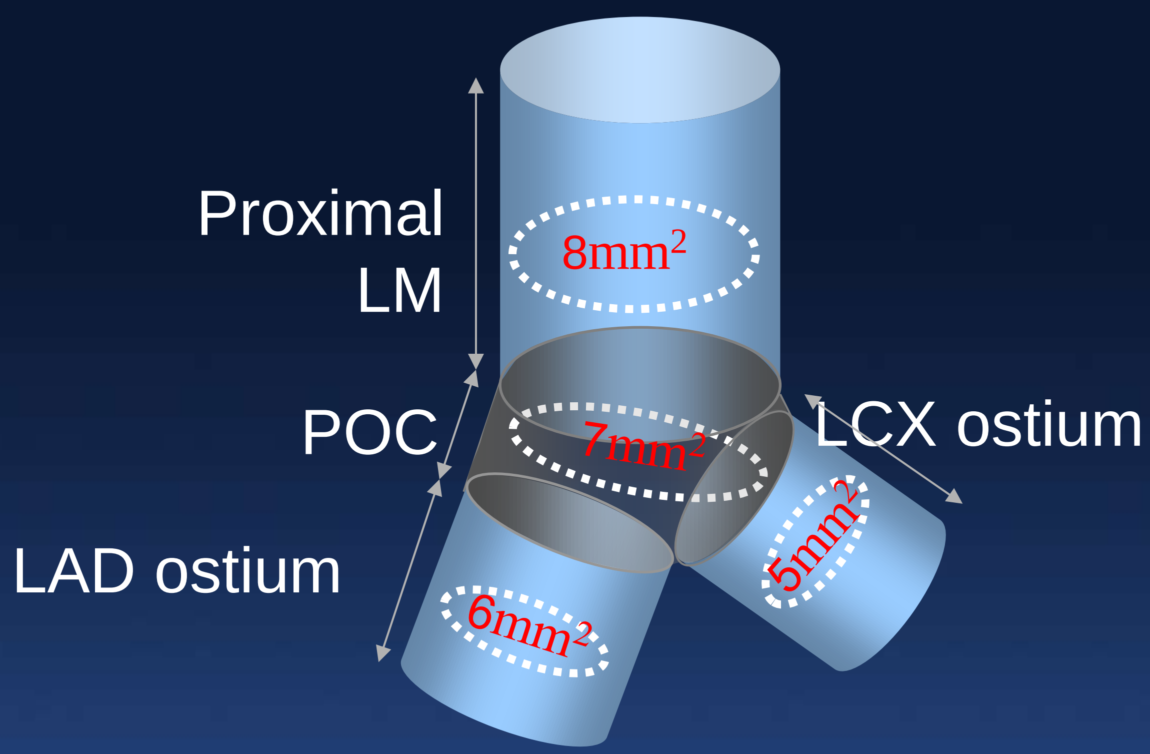



| No. at risk | | | | | |
|---|---|---|---|---|---|
| *Not meeting criteria* | *315* | *299* | *297* | *394* | *285* |
| *Meeting criteria* | *363* | *362* | *345* | *338* | *334* |

*Hong et al. JAMA 2015;314:2155-63*

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

# Criteria for stent underexpansion at the distal LMCA bifurcation (n=403)

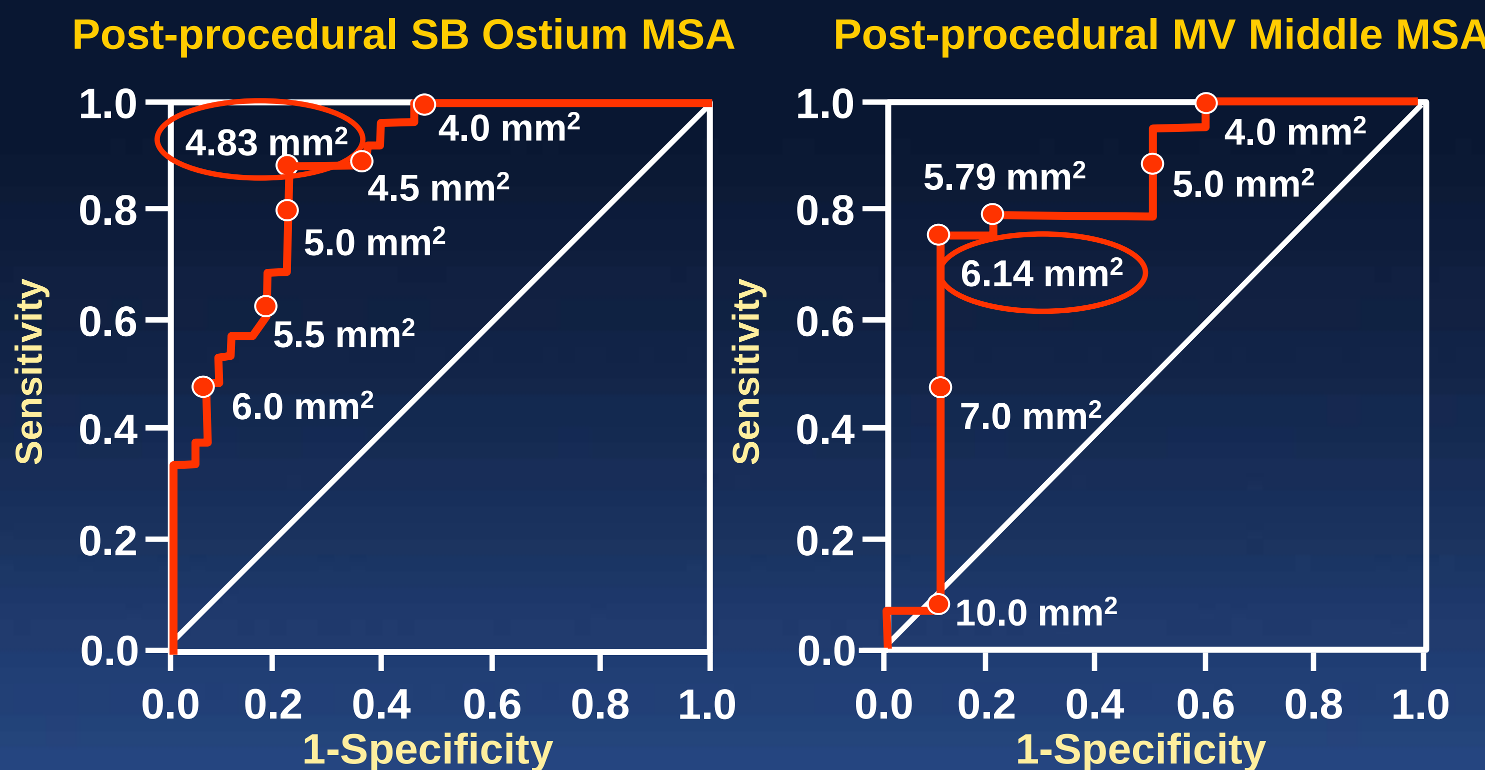



- ***MACE-free survival was lower in pts with underexpansion vs those without underexpansion (89.4% vs 98.1%)***
- ***TLR-free survival was lower in pts with underexpansion vs no underexpansion (90.9% vs 98.5%).***
- ***Although acute malapposition was observed in 28 pts, malapposition was not related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

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

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

# The Optimal Cutoff Value of Post-Procedural MSA to Predict a Follow-up MLA ≥4mm² After Bifurcation T-Stenting




**AUC=0.88 (95%CH=0.80-0.95)**

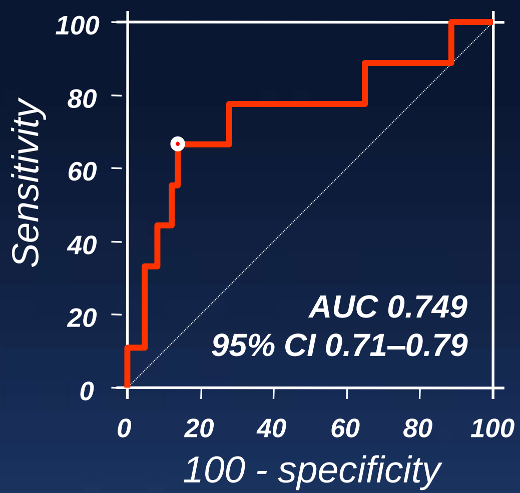
**AUC=0.81 (95%CH=0.64-0.99)**

Hahn et al. *J Am Col Cardiol* 2009;54:110-7

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

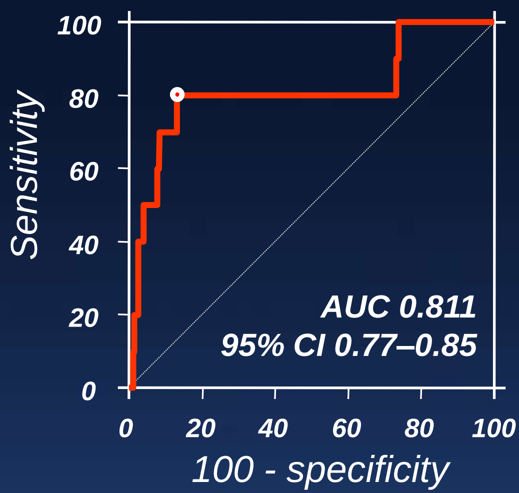
# IVUS Predictors of Edge Restenosis after Second Generation DES

**433 E-ZES**



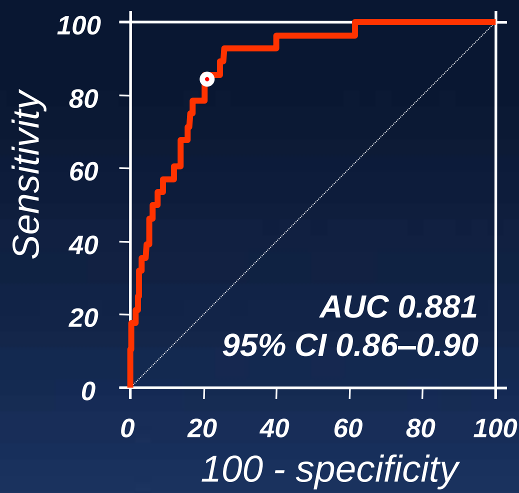

**Plaque burden=56.3%**
**Sensitivity 67%**
**Specificity 86%**

**422 R-ZES**




**Plaque burden=57.3%**
**Sensitivity 80%**
**Specificity 87%**

**813 EES**

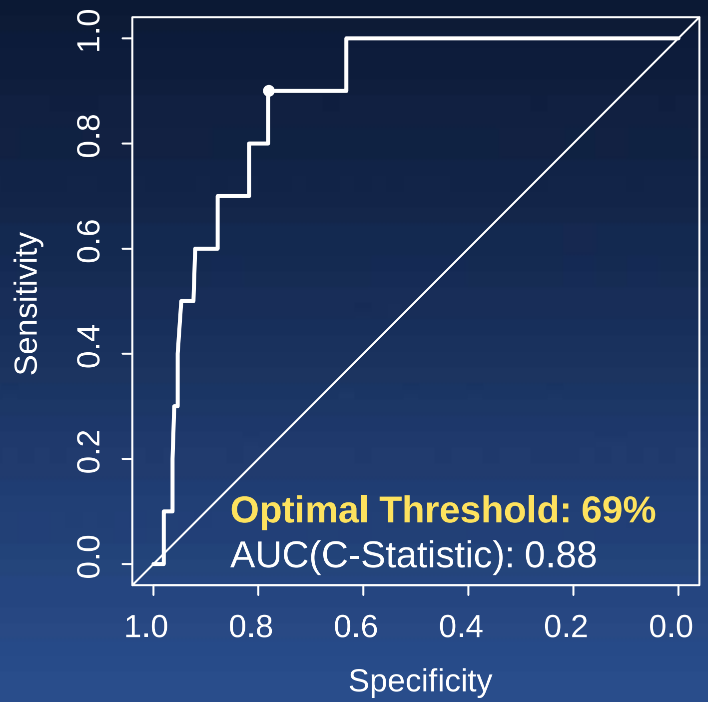



**Plaque Burden=54.2%**
**Sensitivity 86%**
**Specificity 80%**

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

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

# Plaque burden predictor of TCFA in 271 atherosclerotic lesions from 106 fresh coronary arteries in 54 patients at necropsy.




*Inaba, unpublished*

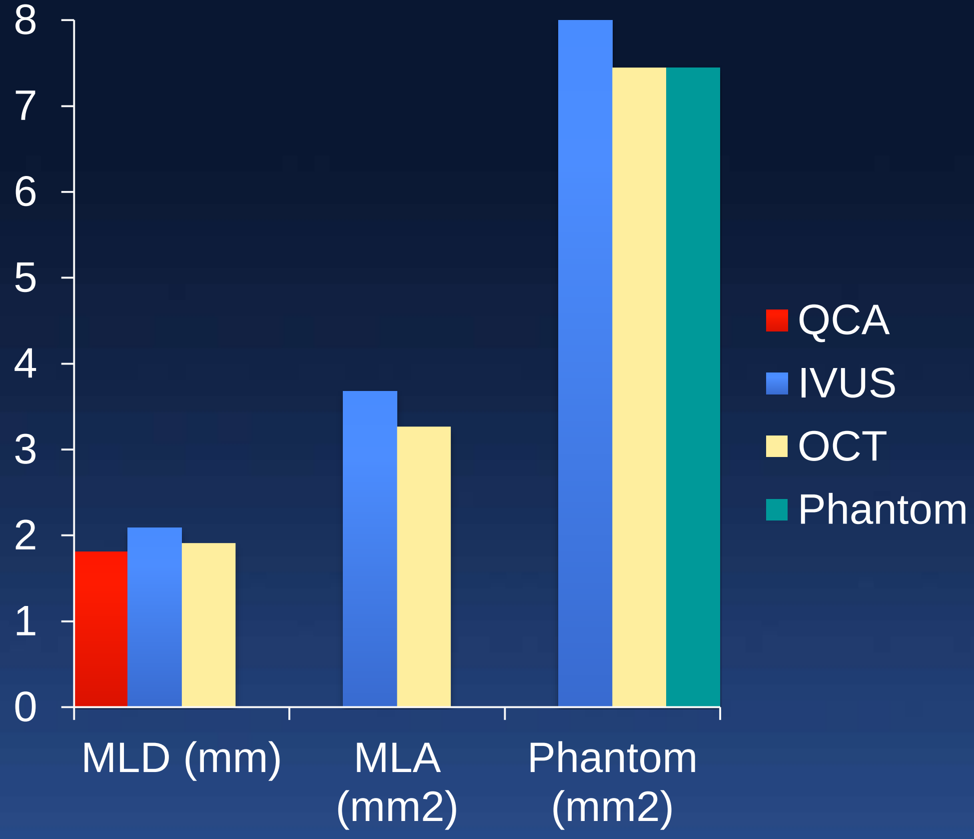
# Edge Dissection in ADAPT-DES

| 1-year events | Dissection (159 pts) | No dissection (1903 pts) | P Value |
|---|---|---|---|
| MACE | 11.48% (18) | 7.97% (148) | 0.097 |
| Cardiac death | 1.91% (3) | 1.44% (26) | 0.6 |
| Peri-procedural MI | 2.52% (4) | 1.16% (22) | 0.14 |
| Clinically driven TLR | 5.8% (9) | 3.1% (68) | 0.067 |
| Stent Thrombosis | 1.28% (2) | 0.53% (10) | 0.2 |

- ***Lesions with 1-year TLR had a smaller effective lumen area at the dissection site (4.8 $mm^2$ [3.4-6.2] vs.6.7 $mm^2$ [4.8-9.2], p=0.03 ) compared to lesions without TLR; however, there was no difference in dissection length or dissection angle.***
- ***By ROC curve analyses, only the effective lumen CSA at the dissection site predicted 1-year TLR with an optimal cut-off of 5.1 $mm^2$ (AUC of 0.73, p=0.05).***

***Kobayashi et al. unpublished***

# **OPUS-CLASS** (OCT Compared With IVUS in 3.0mm phantoms and in 100 pts)

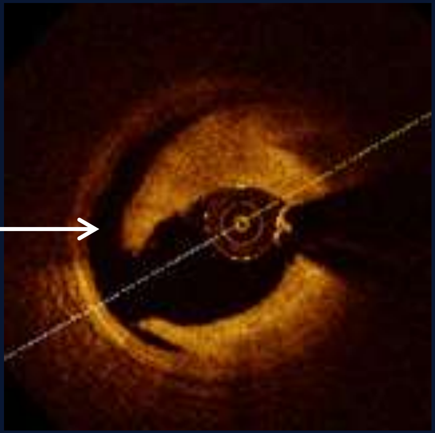



- *IVUS-MLD was significantly greater than OCT-MLD (mean difference of 0.18 mm)*
- *QCA-MLD was significantly smaller than OCT-MLD (mean difference of 0.10 mm).*
- *The difference between IVUS-MLA and OCT-MLA was significantly greater in nonstented vs stented segments (0.56±0.49 $mm^2$ vs. 0.25±0.87 $mm^2$; $p < 0.007$).*

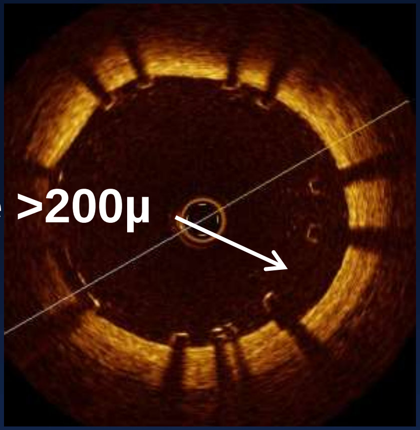
***Kubo et al. JACC Cardiovasc Imaging 2013;6:1095-104***

# *OCT Criteria Tested in the CLIO-PCI II Registry*

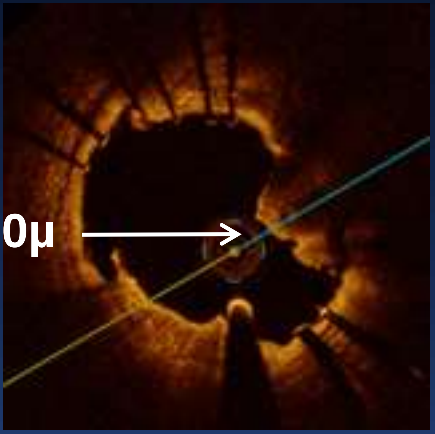
**Edge dissection width >200µ**



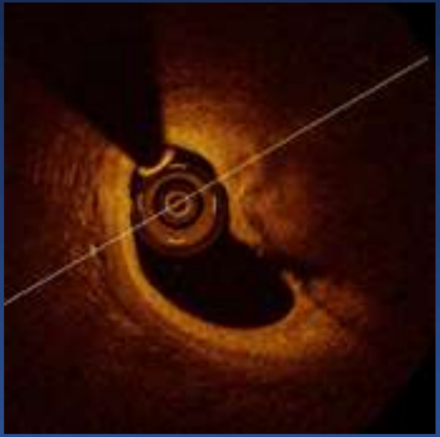
**Stent malapposition distance >200µ**

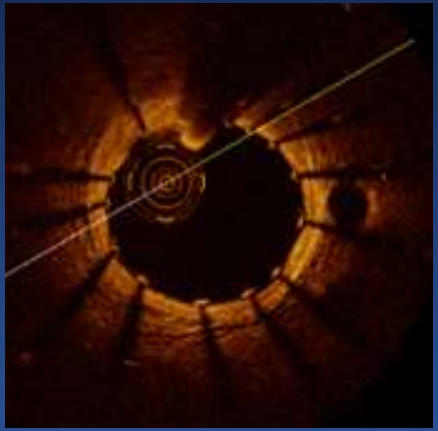


**Thrombus thickness >500µ**



***Residual stenosis adjacent to stent edge: MLA <4.5mm$^2$ in presence of plaque***

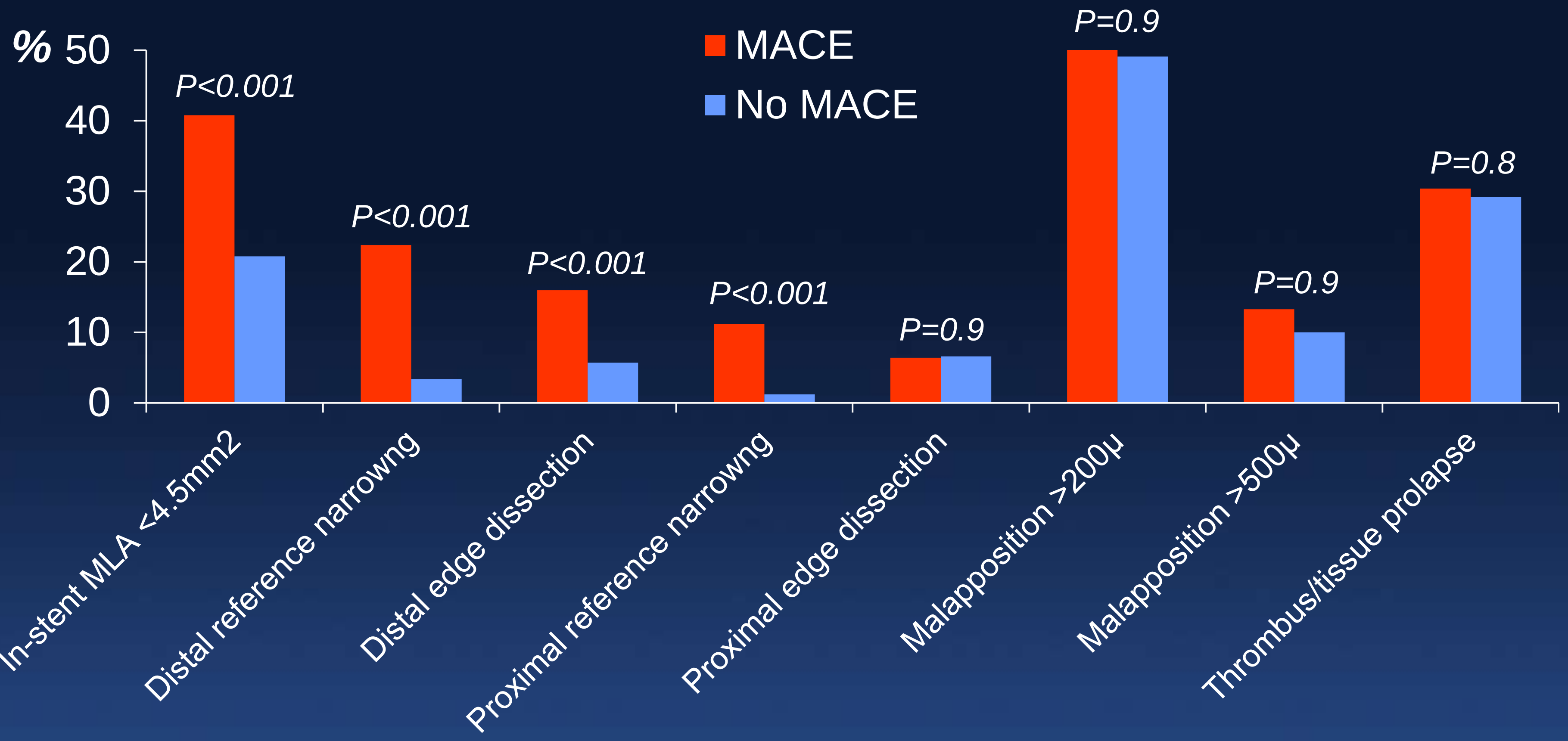




***In-stent MLA <4.5mm$^2$***

*Prati et al. JACC Cardiovasc Imaging 2015;8:1297-305*

# 929 pts (989 lesions) in CLI-OPI II registry
## MACE (death, MI, ST, or TLR in 12.2%) @ 1 yr

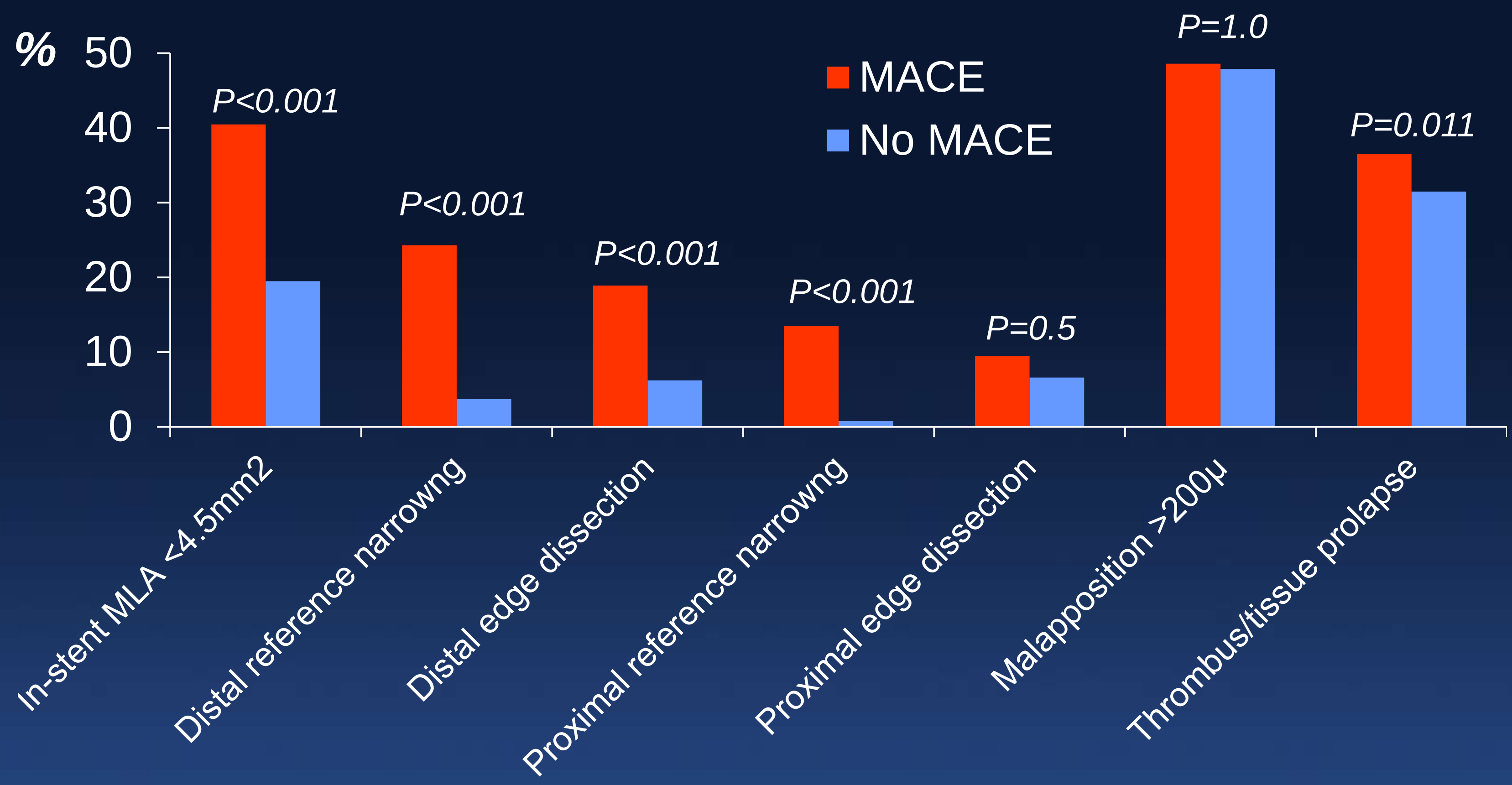



Independent predictors of MACE were in-stent MLA <4.5mm$^2$, proximal or distal reference narrowing, or distal edge dissection

*Prati et al. JACC Cardiovasc Imaging 2015;8:1297-305*

# 507 pts (588 lesions) in CLI-OPI ACS registry

## MACE (death, MI, ST, or TLR in 12.6%) @ 9 mos




***Presence of at least one OCT finding was found to be an independent predictor of worse outcome (HR=4.05, CI 95% 1.8-9.0, p=0.001) - especially the presence of a residual intrastent plaque/thrombus protrusion (HR=2.96, CI 95% 1.4-6.3, p=0.005).***

***Prati et al. unpublished***

# Baseline OCT and 1 year follow-up (900 stents in 786 patients)

| Independent predictors of 1 year events | | | | |
|---|---|---|---|---|
| | Device oriented clinical events | | TLR | |
| | OR | P-value | OR | P-value |
| **Age, years** | | | 0.98 | 0.4 |
| **Male gender** | **3.13** | 0.068 | 36% | |
| **BMS** | **1.75** | 0.005 | 1.80 | 0.002 |
| **Irregular protrusion** | **2.64** | 0.003 | 2.66 | 0.003 |
| **Small MSA** | **2.54** | 0.012 | 2.54 | 0.011 |

- Irregular protrusion = protrusion of material with an irregular surface (>100 microns) into the lumen between stent struts.
- Small MSA defined by ROC analysis = 5.0mm$^2$ for DES (AUC=0.63) and 5.6mm$^2$ for BMS (AUC=0.59)
- Neither edge dissection nor acute malapposition nor relative stent underexpansion predicted events at 1 year of follow-up

*Soeda et al. Circulation 2015;132:1020-9*

# 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 was 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 14.4% of 2072 pts (12.6% pf 2446 lesions) in ADAPT-DES, it was not associated with adverse events at either 30 days or 2 years.**
  - *Wang et al. Unpublished*

# Frequency of acute stent malapposition

| | Study | # | IVUS | OCT |
|---|---|---|---|---|
| Steinberg et al. JACC Cardiovasc Interv 2010;3:486-94 | Combined TAXUS | 1200 | 8% | |
| Guo et a. Circulation 2010;122:10-77-84 | HORIZONS-AMI | 263 | 36% | |
| Van der Hoven JACC Cardiovasc Interv 2008;1:192-201 | MISSION-AMI | 184 | 35% | |
| Wang et al, unpublished | ADAPT-DES | 2446 | 13% | |
| Bezerra et al. JACC Cardiovasc Interv 2013;6:228-36 | | 26 | 42% | 96% |
| Kubo et al. JACC Cardiovasc Imaging 2013;6:1095-1104 | OPUS-CLASS | 100 | 14% | 39% |
| Im et al. Circ Cardiovasc Interv 2014;7:88-96 | | 356 | | 62% |
| Kawamori et al. EHJ Cardiovasc Imaging 2013;14:865-75 | | 40 | | 65% |
| Shimamura et al. EHJ Cardiovasc Imaging 2015;16:23-8 | | 77 | | 100% |
| Soeda et al. Circulation 2015;132:1020-9 | | 1001 | | 39% |
| Prati et al. JACC Cardiovasc Imaging 2015;8:1297-305 | CLI-OPCI-II | 1002 | | 49% |
| Prati et al. unpublished | CLI-OPCI ACS | 588 | | 48% |
| **Overall** | | | **14%** | **49%** |

# Resolution of acute stent malapposition

| | Study | IVUS | | OCT | |
|---|---|---|---|---|---|
| | | ASM | % resolution | ASM | % resolution |
| **Steinberg et al. JACC Cardiovasc Interv 2010;3:486-94** | **Combined TAXUS** | 96 | 55% | | |
| **Guo et a. Circulation 2010;122:10-77-84** | **HORIZONS-AMI** | 94 | 39% | | |
| **Van der Hoven JACC Cardiovasc Interv 2008;1:192-201** | **MISSION-AMI** | 67 | 58% | | |
| **Im et al. Circ Cardiovasc Interv 2014;7:88-96** | | | | 221 | 69% |
| **Kawamori et al. EHJ Cardiovasc Imaging 2013;14:865-75** | | | | 26 | 77% |
| **Shimamura et al. EHJ Cardiovasc Imaging, In Press** | | | | 77 | 68% |
| | | **257** | **50%** | **324** | **69%** |

# Events related to acute stent malapposition

| | Study | | Follow-up | Acute malapposition | No acute malapposition |
|---|---|---|---|---|---|
| Steinberg et al. JACC Cardiovasc Interv 2010;3:486-94 | Combined TAXUS | IVUS | 9 mos | 8.2% MACE | 10.7% MACE |
| Van der Hoven JACC Cardiovasc Interv 2008;1:192-201 | MISSION-AMI | IVUS | 9 mos | 0% ST | 0% ST |
| Guo et a. Circulation 2010;122:10-77-84 | HORIZONS-AMI | IVUS | 13 mos | 0% ST | 0% ST |
| Wang et al. Unpublished | ADAPT-DES | IVUS | 2 yrs | 5.2% MACE (0.65% ST) | 4.5% MACE (0.43% ST) |
| Soeda et al. Circulation 2015;132:1020-9 | | OCT | 1 yr | 4.4% DoCE | 4.8% DoCE |
| Prati et al. JACC Cardiovasc Imaging, in press | CLI-OPCI-II | OCT | 1 yr | 13% MACE | 10% MACE |
| Prati. Unpublished | CLI-OPCI-ACS | OCT | 9 mos | 12.8% MACE | 12.4% MACE |

CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

# Criteria for DES Optimization

- Good expansion
- Absence of geographical miss (covering large plaque burden, lipid rich plaque, etc)
- No complications
- Not greater stent length
- Not plaque/thrombus protrusion – unless it results in a small lumen area (primarily in ACS patients)
- Not malapposition – unless it is associated with underexpansion
- Not asymmetry – unless it is associated with underexpansion