# Rethinking IVUS and Physiologic Lesion Assessment

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# Introduction

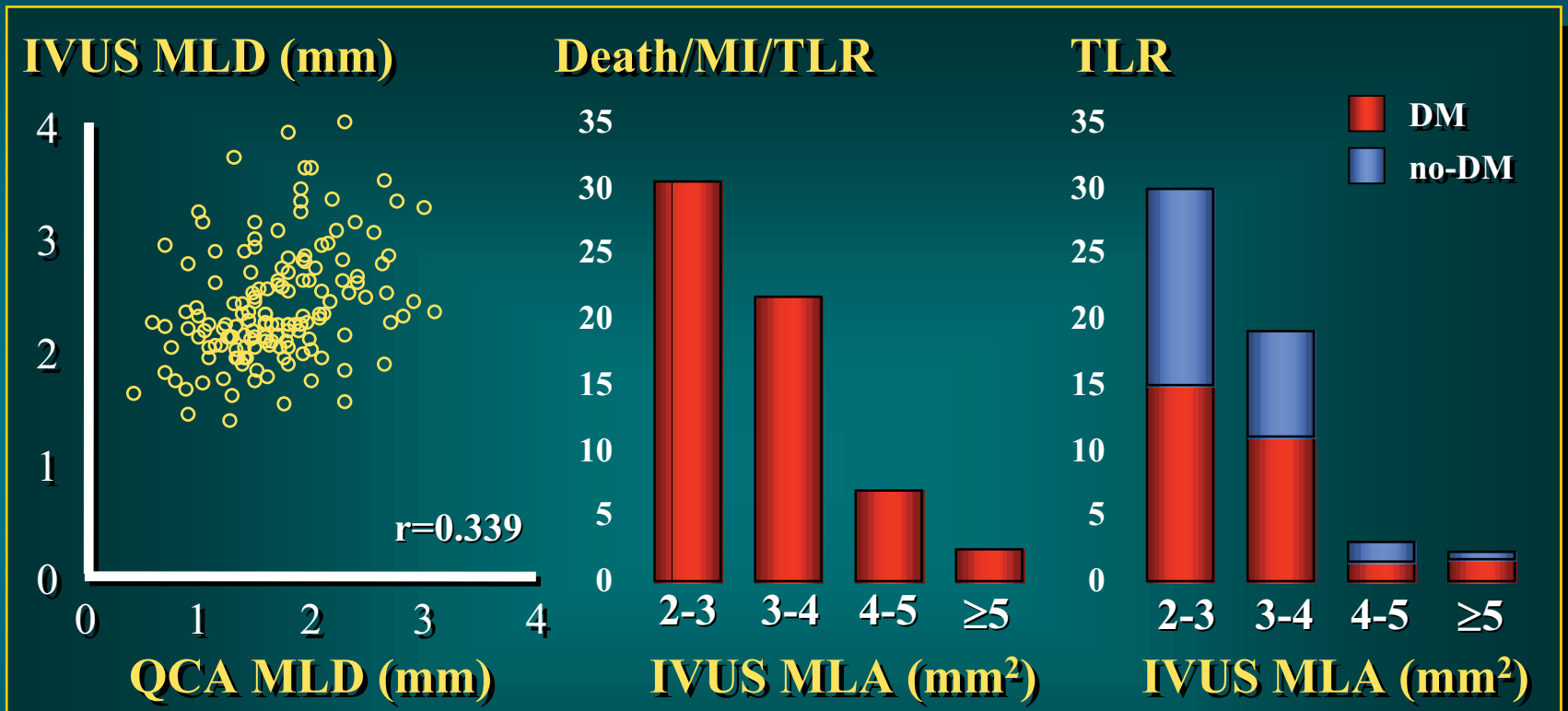
Most of the concepts used in IVUS-guided intervention are no different from those used in angiography-guided intervention. However, unlike angiography, IVUS is actually able to make precise measurements and assess lesion morphology.

- Weigh potential problems (i.e. LM disease, significant proximal or distal disease)
- Assess lesion severity
- Assess unusual lesion morphology (i.e., aneurysms, calcium, thrombi, in-stent restenosis, etc.)
- Measure vessel size
- Measure lesion length
- Determine and fine-tune the the final result of interventions
- Assess complications

# IVUS Criteria for a 'Significant' Stenosis

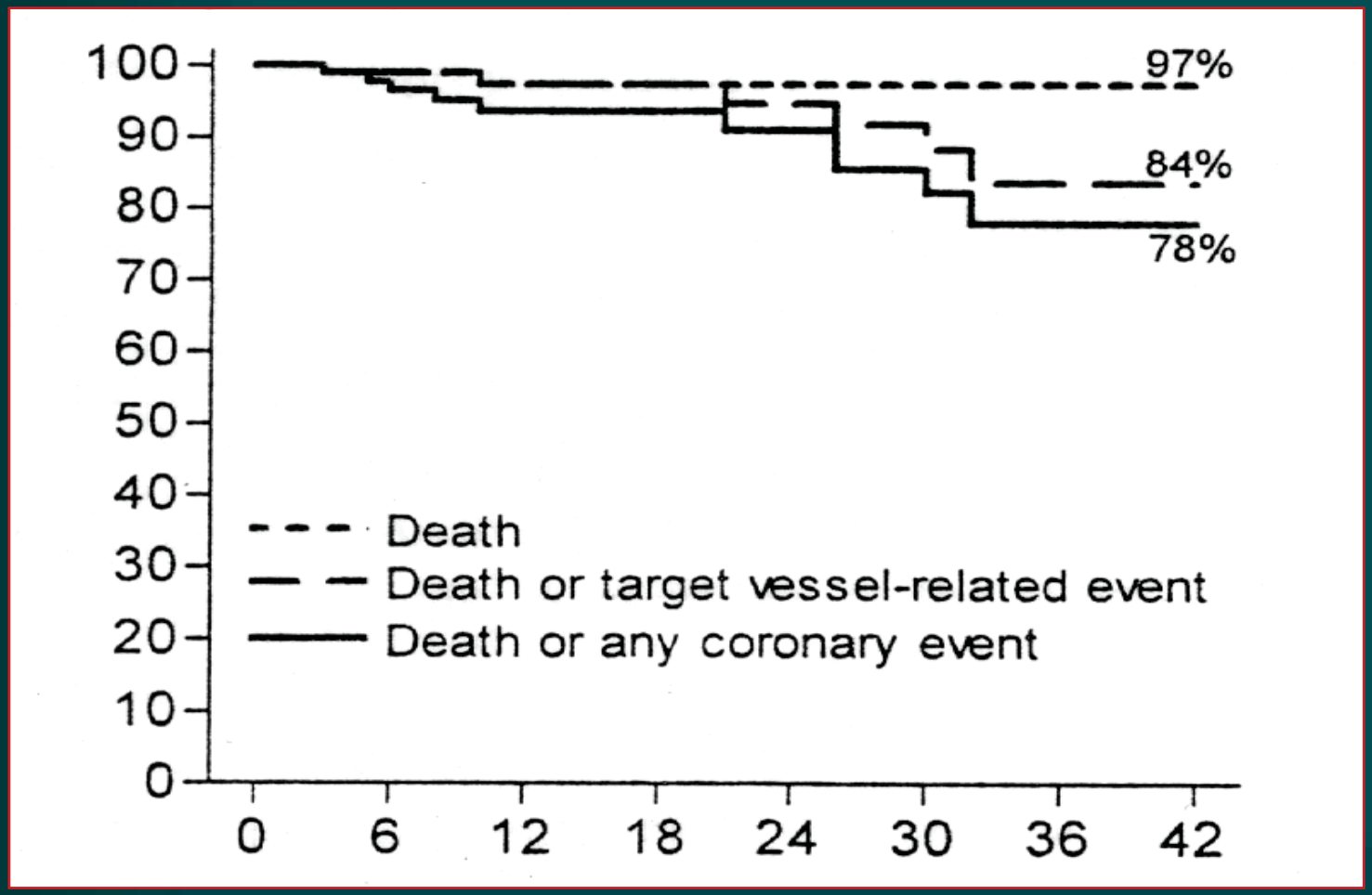
- Most authorities feel that a lumen area less than 4.0 $mm^2$ in a proximal epicardial artery ***excluding the Left Main*** is a flow limiting stenosis

# Clinical Follow up in 357 intermediate lesions in 300 patients deferred intervention after IVUS imaging




- Death/MI/TLR @ (mean) 13 mos = 8% overall (2% death/MI and 6% TLR)
- Death/MI/TLR @ (mean) 13 mos = 4.4% in lesions with MLA >4.0mm$^2$
- Only independent predictor of death/MI/TLR was IVUS MLA (p=0.0041)
- Independent predictors of TLR were DM (p=0.0493) and IVUS MLA (p=0.0042)

# Event-free survival after deferred PCI in pts with intermediate stenosis and FFR ≥0.75

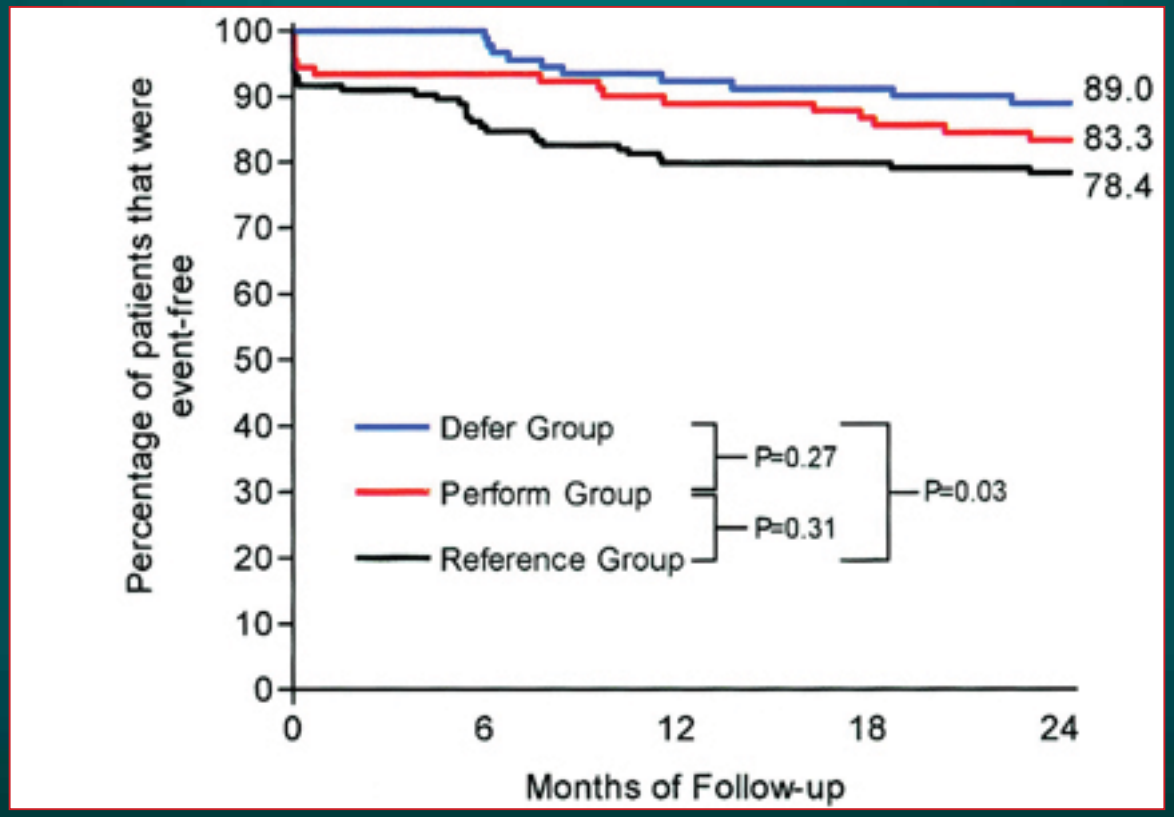



Months after deferral

*(Bech et al. JACC 1998;31:841-7)*

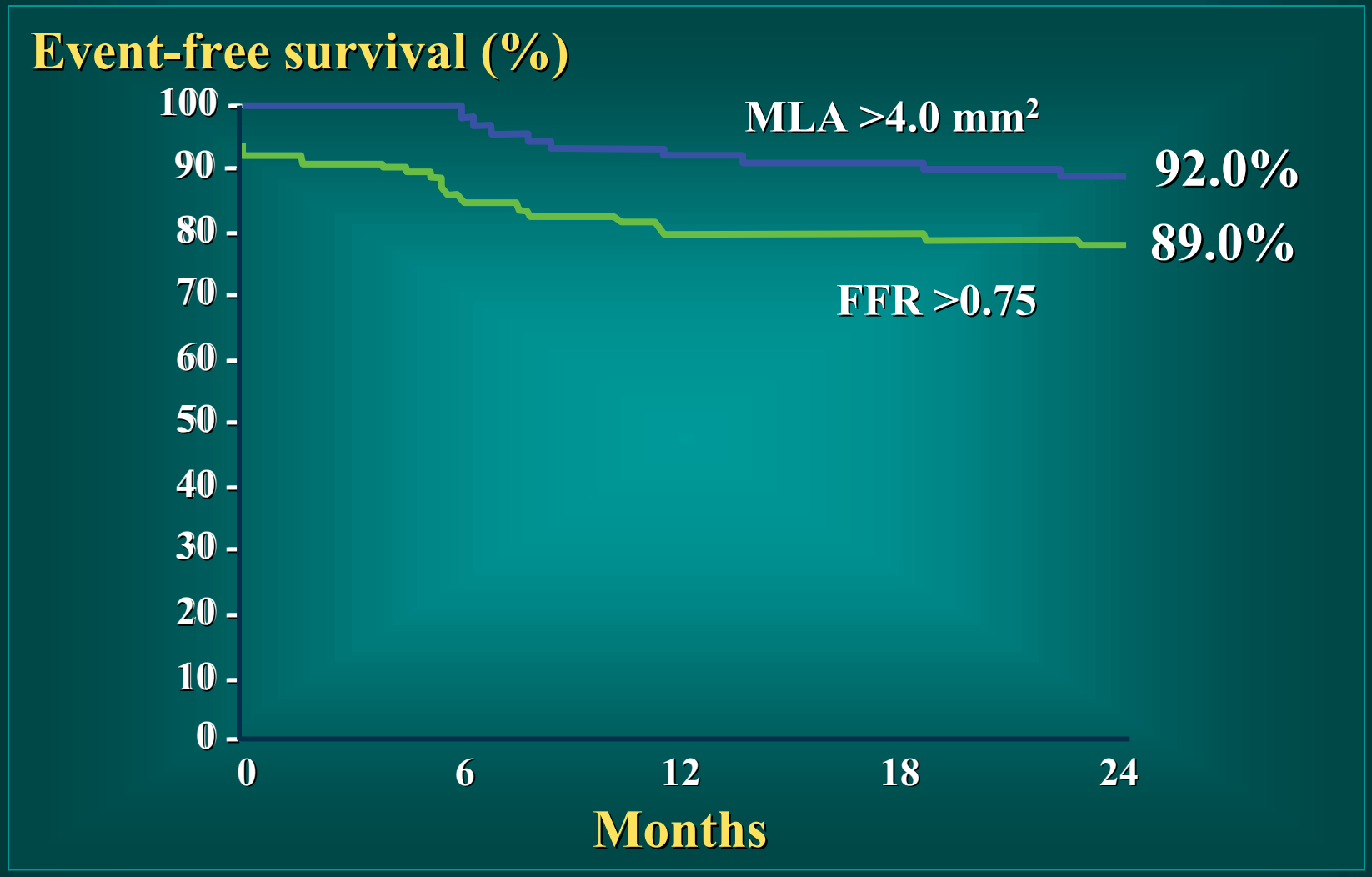
# The DEFER Study

**In 325 patients without documented ischemia in whom PTCA was planned, FFR was measured. If FFR was >0.75, patients were randomized to deferral of PTCA (Defer group; n=91) or performance of PTCA (Perform group; n=90). If FFR was <0.75, PTCA was performed as planned (Reference group; n=144).**



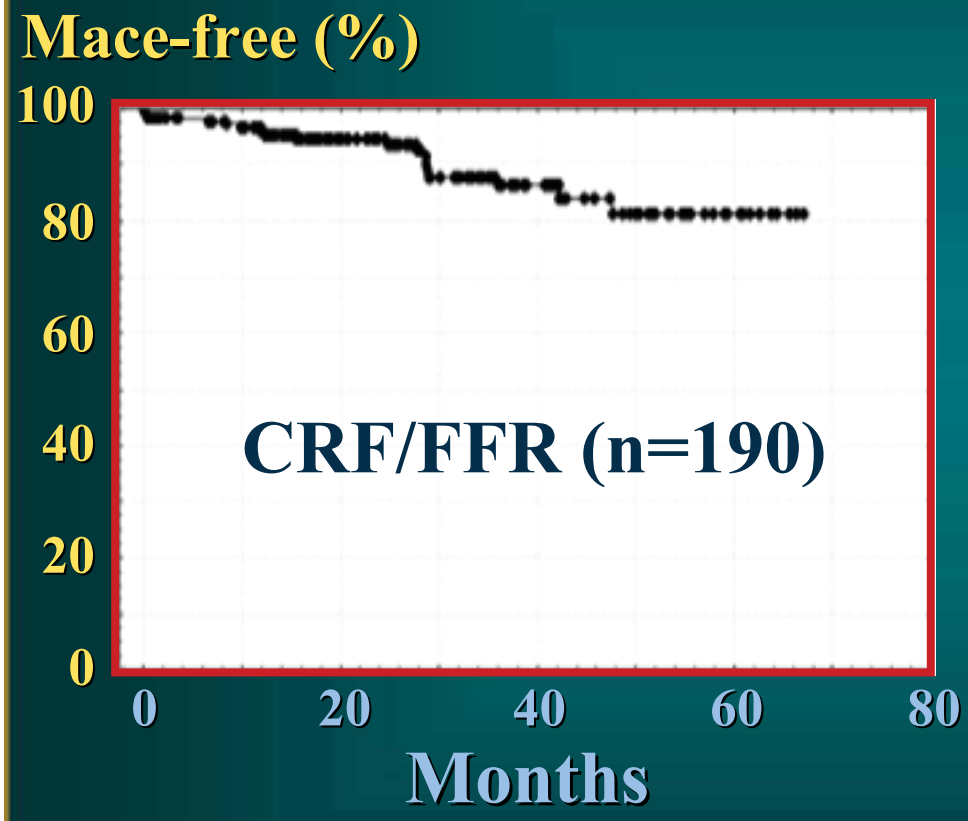

*(Bech et al. Circulation 2001;103:2928-34)*

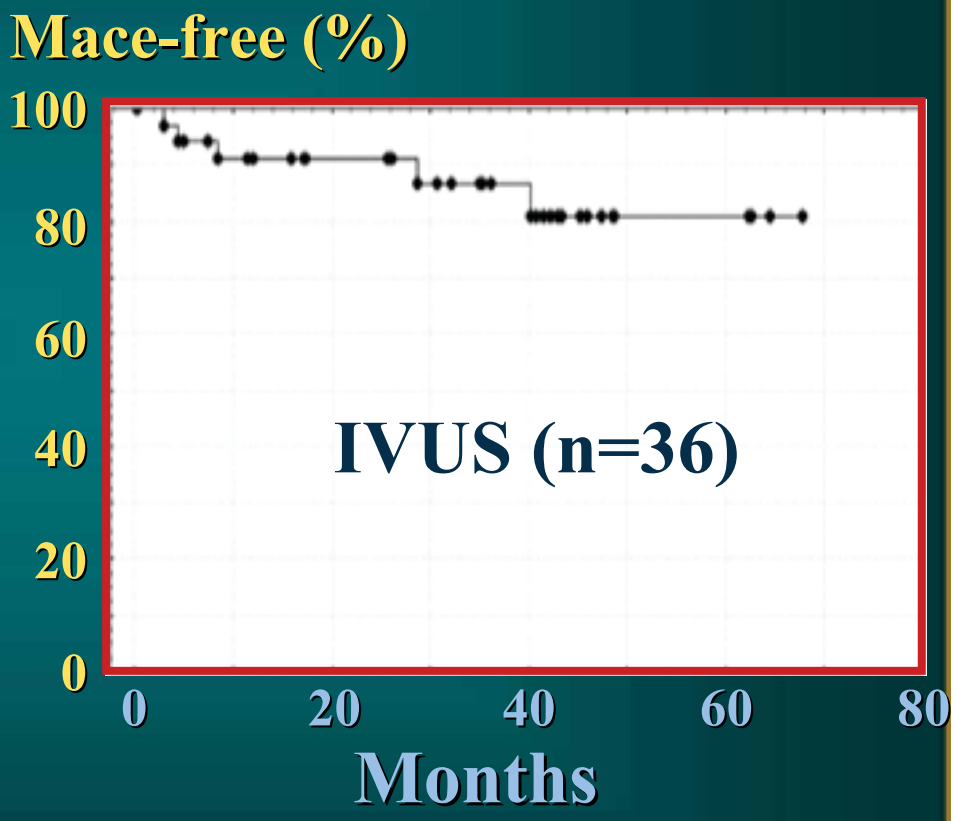
# Event-Free Survival Curve of Patients with Intermediate Lesions and Deferred Procedures




*(Abizaid AS, et al. Circulation 1999;100:256-261)*
*(Bech G, et al. Circulation 2001;103:2928-2934)*

# Single institution experience of CRF/FFR and IVUS in intermediate lesions



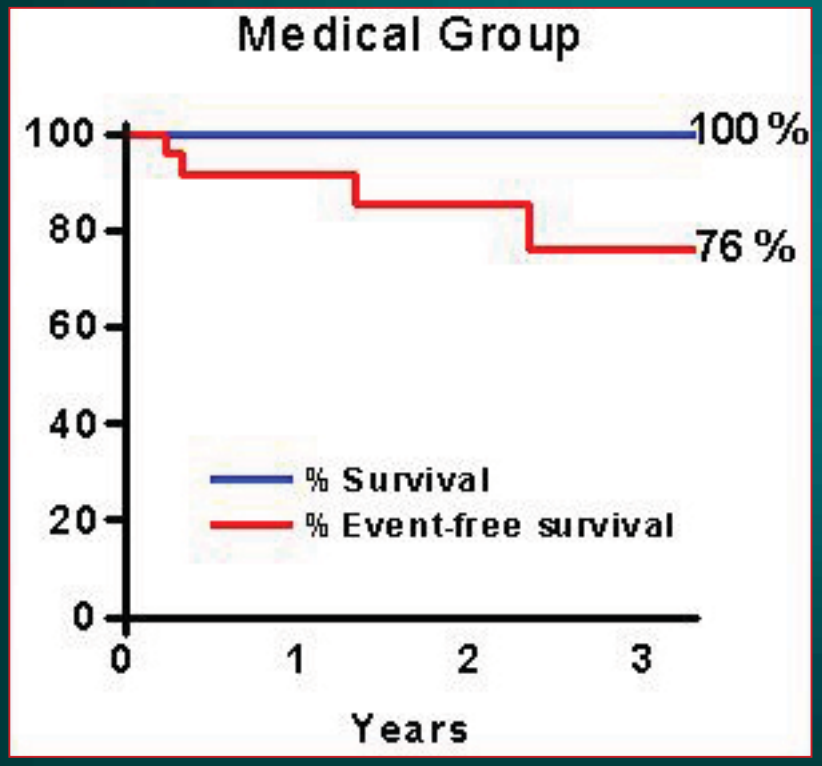



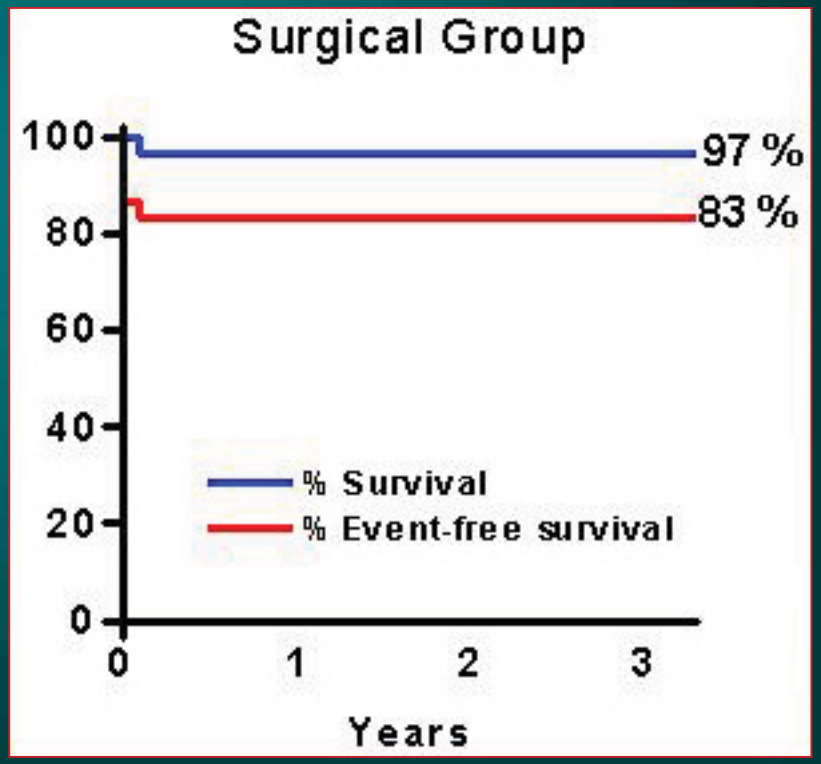

*(Hodgson JMcB, et al. ACC 2003)*

# FFR in LM disease

**N=24**
**FFR ≥0.75**
**(16 Med Rx only, 1 AVR, 7 PCI of another lesion)**

**N=30**
**FFR <0.75**

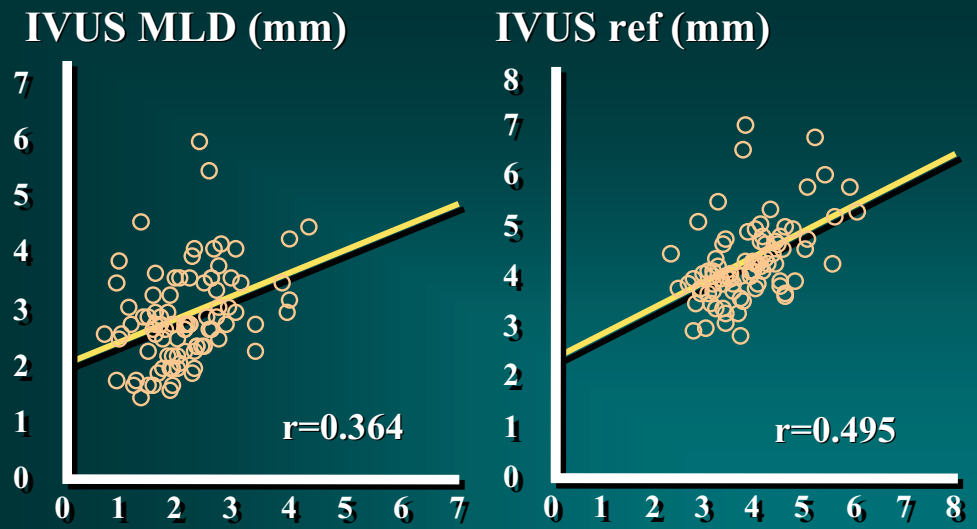



*(Bech et al Heart. 2001;86:547-52)*

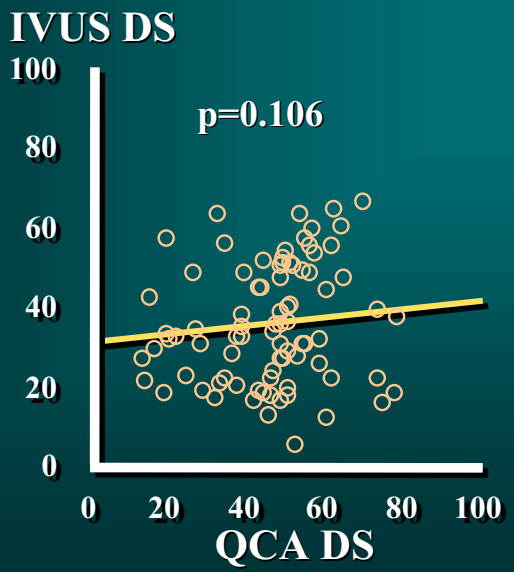
# Suggested IVUS Criteria for a 'Significant' LMCA Stenosis

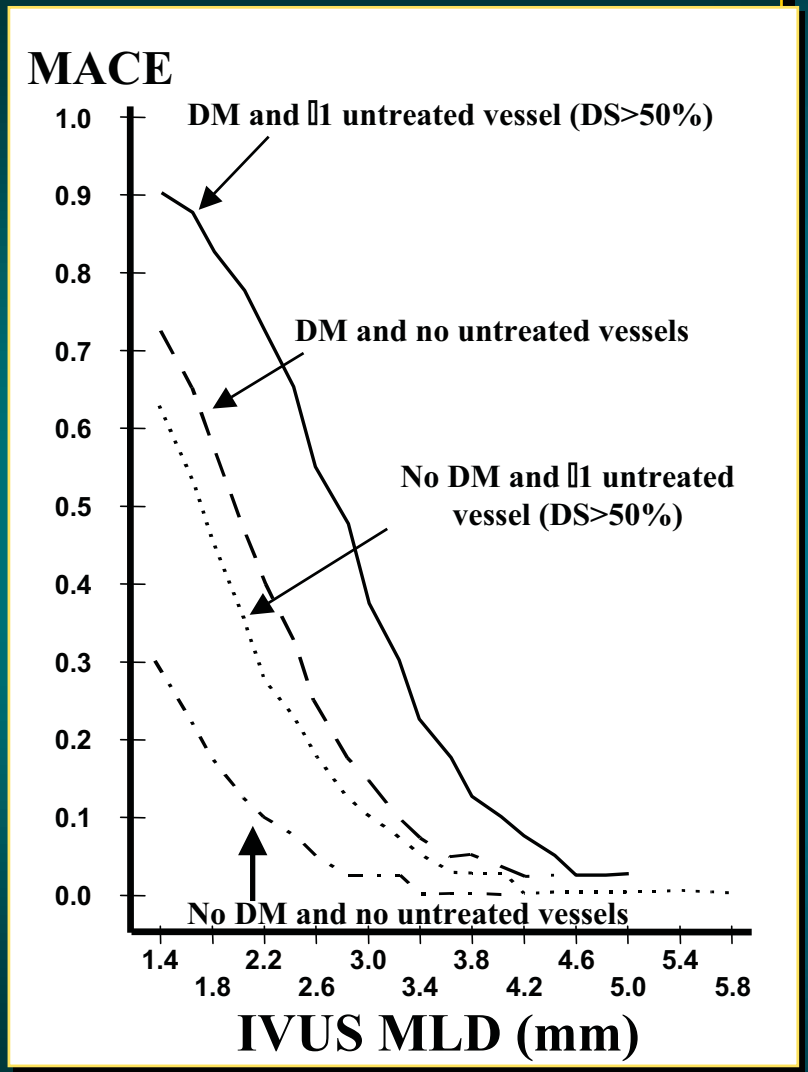
- Most IVUS LMCA studies show either insignificant disease or critical disease, only a minority require careful quantification
- Although there are no prospective studies, the following criteria for a significant LMCA stenosis are suggested
  - Lumen diameter stenosis <50% as measured by IVUS vs the reference
  - Lumen CSA <6.0mm$^2$ - because. . .
    - In general, the sum of the lumen areas of the two daughter vessels (LAD and LCX, each of which should be 4.0mm$^2$) = 150% of the parent (LM)
    - This correlates with a LM FFR <0.75.







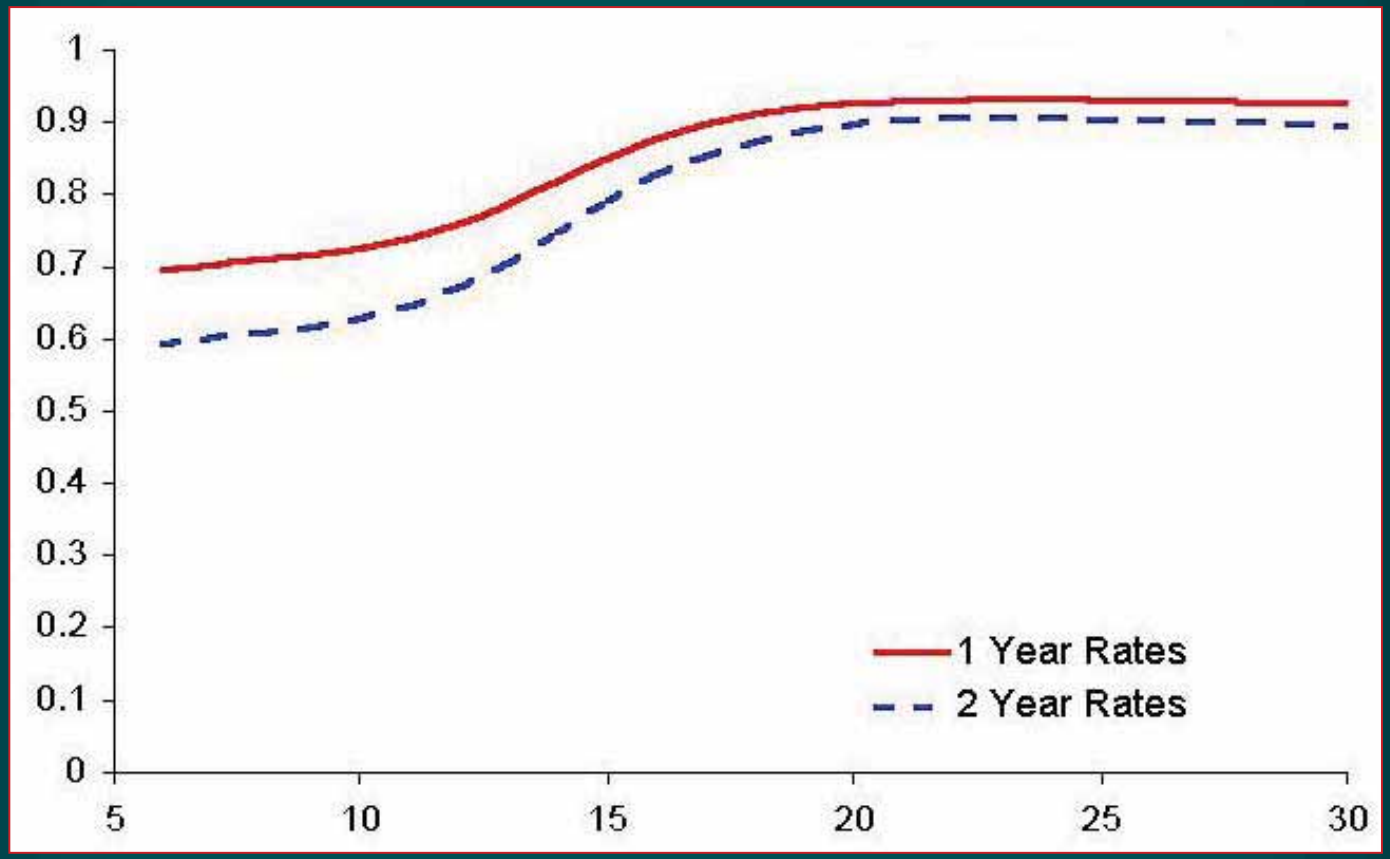



*Independent predictors of MACE @11.7 months: DM (P=0.004), any untreated lesion >50% (p=0.037), and IVUS MLD (P=0.005).*

# 107 pts with angiographically normal or mildly diseased LM

## Event-free survival




## IVUS Minimum lumen area ($mm^2$)

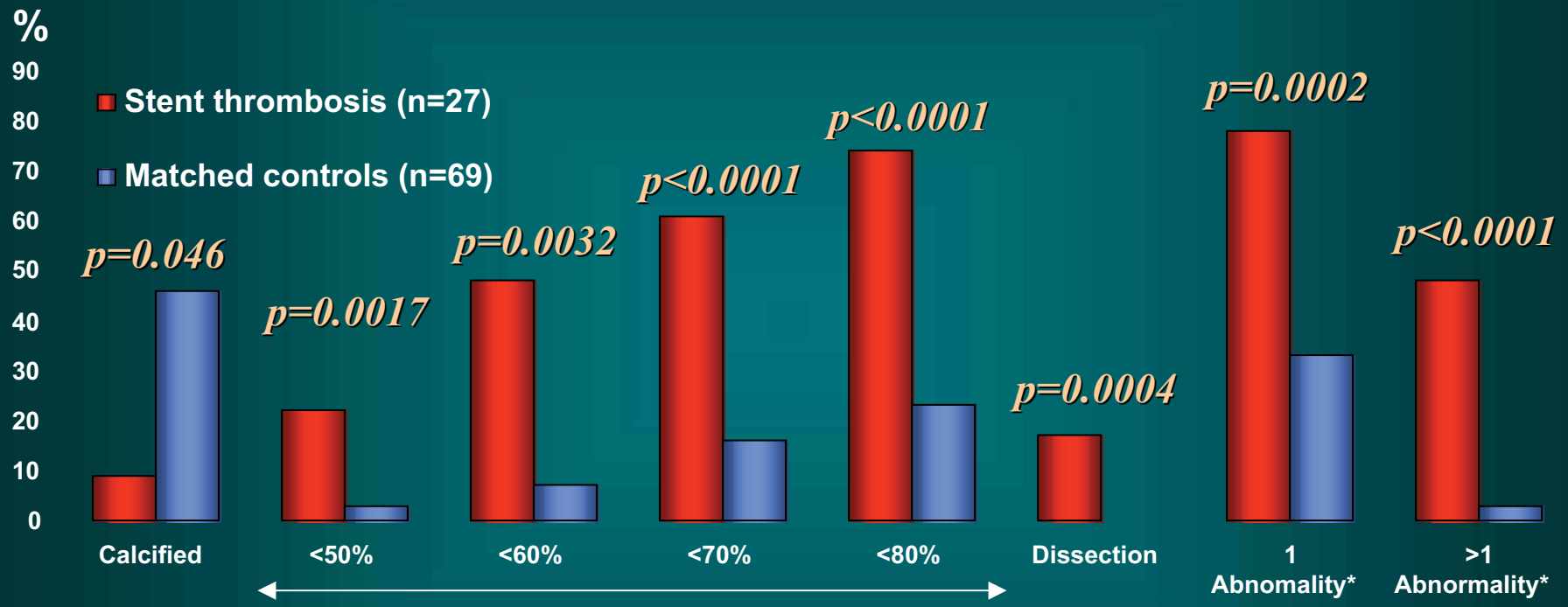
**Only the presence of diabetes mellitus (p=0.014) and IVUS MLA (p=0.015) were independently associated with future adverse events**

***(Ricciardi et al. Am Heart J, in press)***

# Unusual Lesions

- Aneurysms
- Filling  Defects
- Acute Coronary Syndromes
- Spontaneous Dissections

# IVUS Predictors of Stent Thrombosis (27/7484=0.4%)

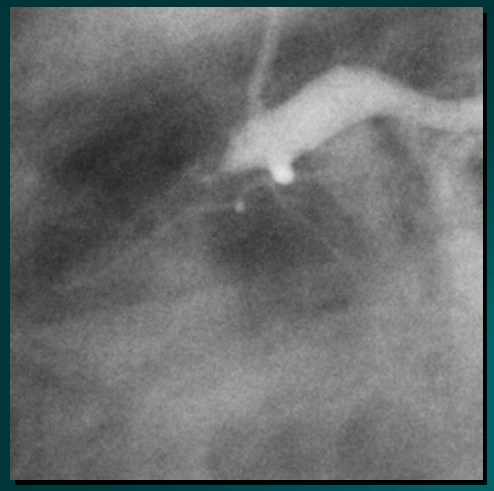



(MSA=6.4 vs 7.7mm$^2$, p=0.047)

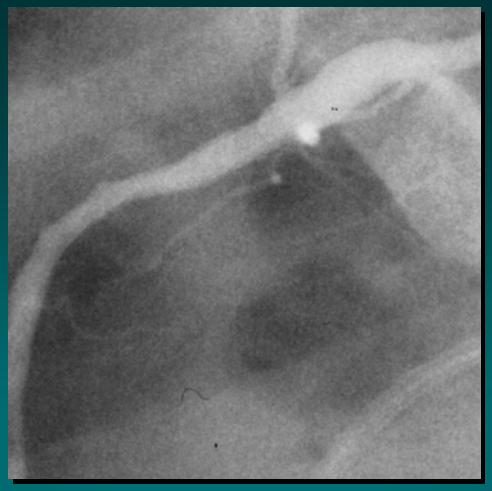
***Expansion defined as<90% of reference lumen or <80% if MLA>9.0mm$^2$)**

*Cheneau et al. Circulation 2003;108:43-47*

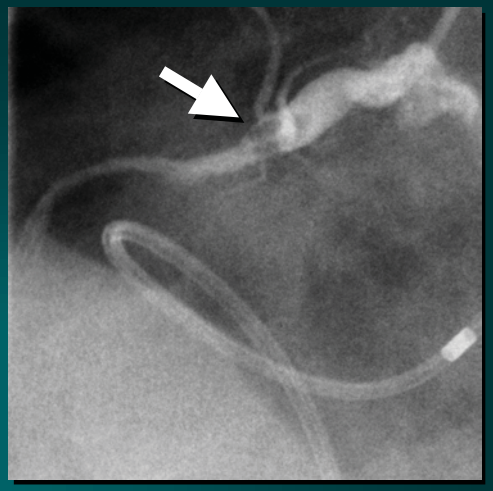
# Crushed stent leading to subacute thrombosis



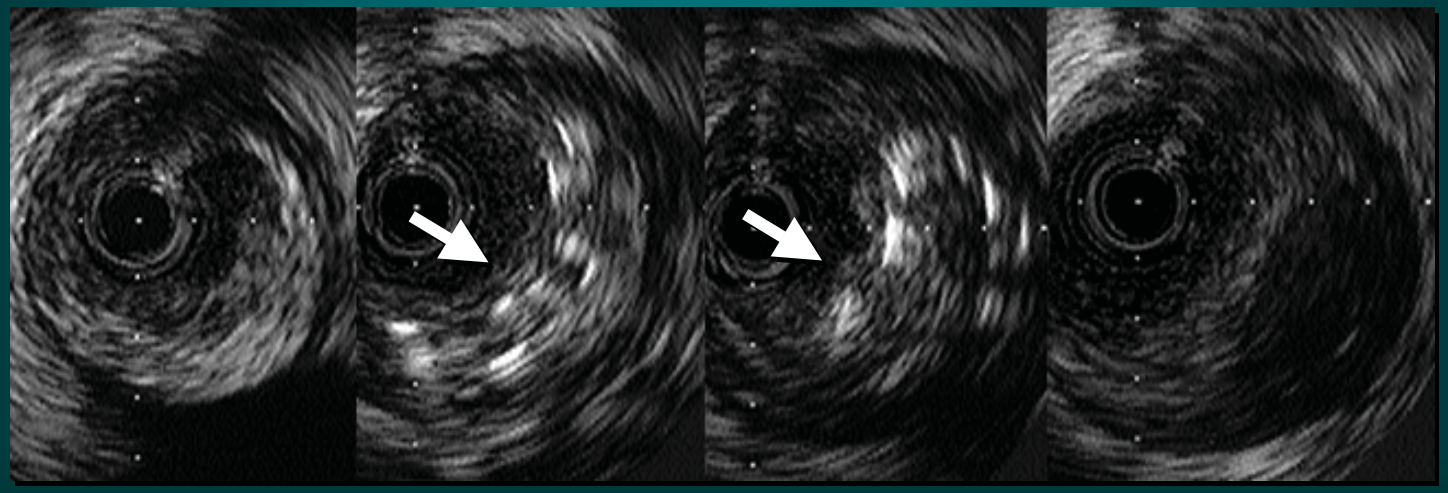
Pre-intervention



s/p JJIS+PTCA

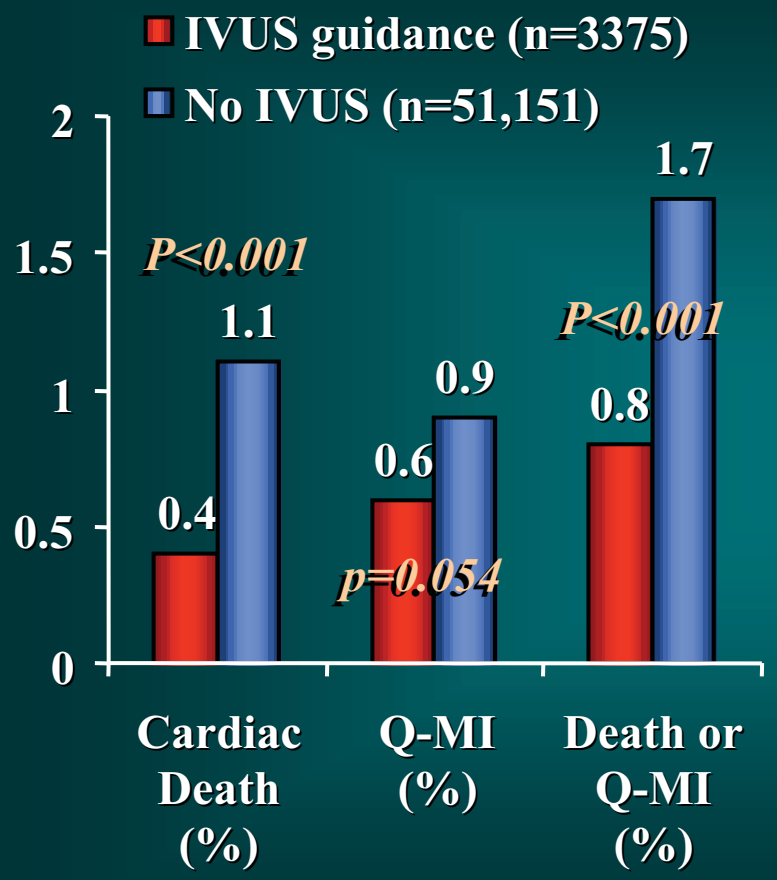


2 week follow-up



0 → 4mm → 20mm

# CENIC* registry report of 54,524 patients treated with stent implantation between 1997-2001



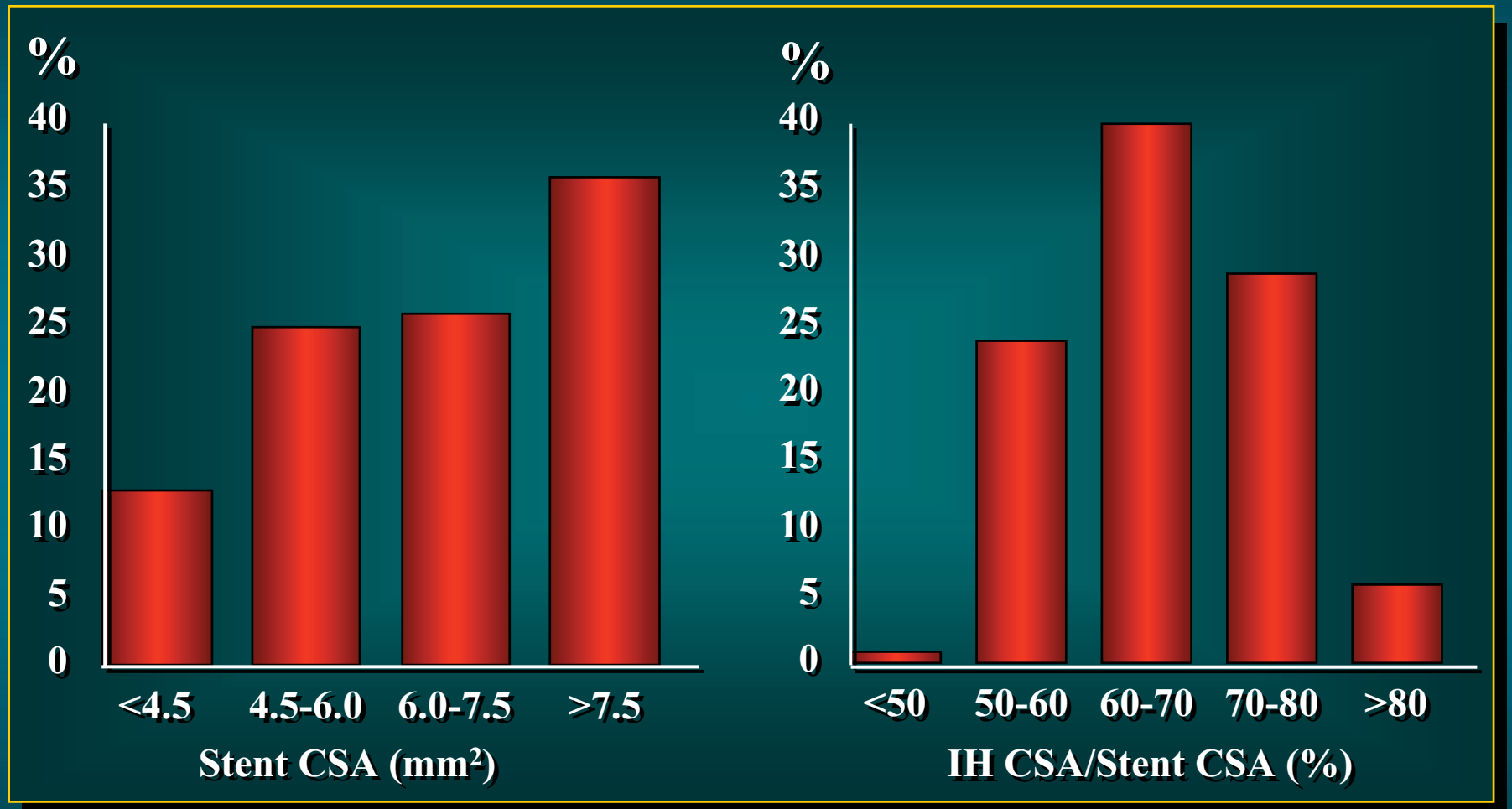

- IVUS guided patients had less diabetes, more USA, lower EF, more complex lesions (LAD, $B_2$/C, $Ca^{++}$, thrombus), and lower post-PCI DS
- IVUS guidance was an independent predictor of Death/Q-MI (OR=0.47)

* Brazilian Society of Interventional Cardiology Registry - CENIC

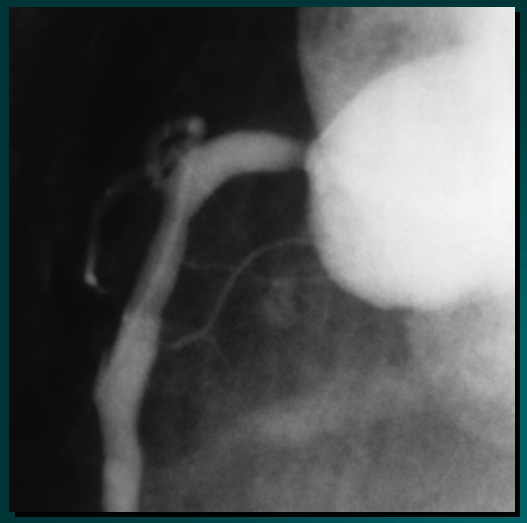
# Approach to the Patient with In-Stent Restenosis

- Does the in-stent restenosis lesion need to be treated?
  - Analysis of 142 patients with 150 intermediate ISR lesions (Angio DS 40-75%: 34% had DS >50% and 17% had a positive exercise thallium). Repeat PCI was deferred if the IVUS MLA measured >3.5mm$^2$ regardless of symptoms, noninvasive testing, or angiographic findings. At follow-up that averaged 32 months, only 10% of patients had events; and the two year EFS was 96.5%. (Nishioka et al AHA 2002)
- Is there a mechanical problem with the stent that needs to be addressed? (IVUS is especially important if restenosis is early and IVUS not performed at implantation)
- Is the in-stent restenosis confined to the stent or does it involve the reference segments?

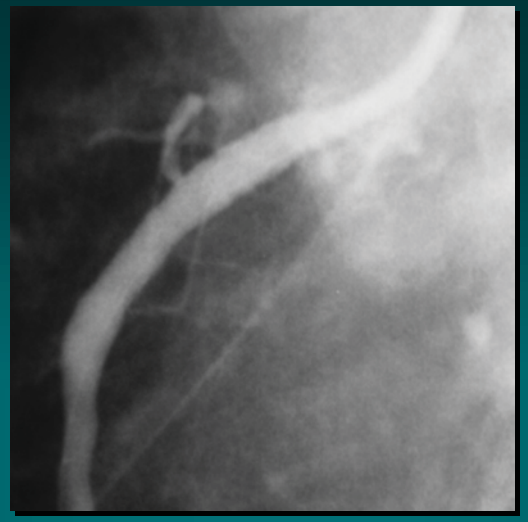
# Analysis of 1089 consecutive patients with in-stent restenosis



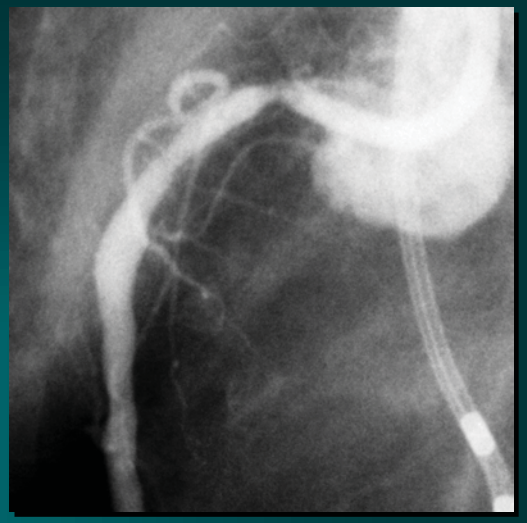

*4-5% of cases had "unrecognized mechanical complications"*



Pre-intervention

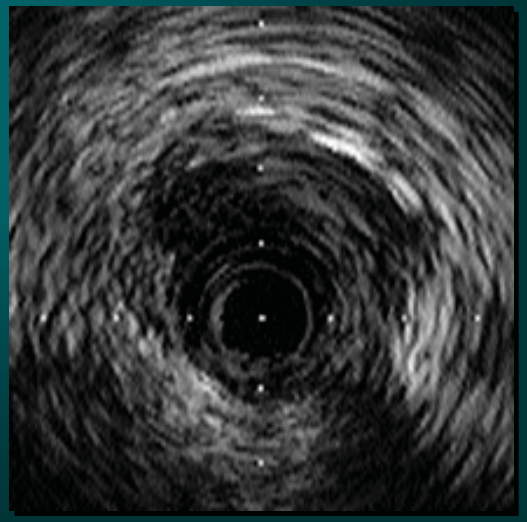


Post JJIS

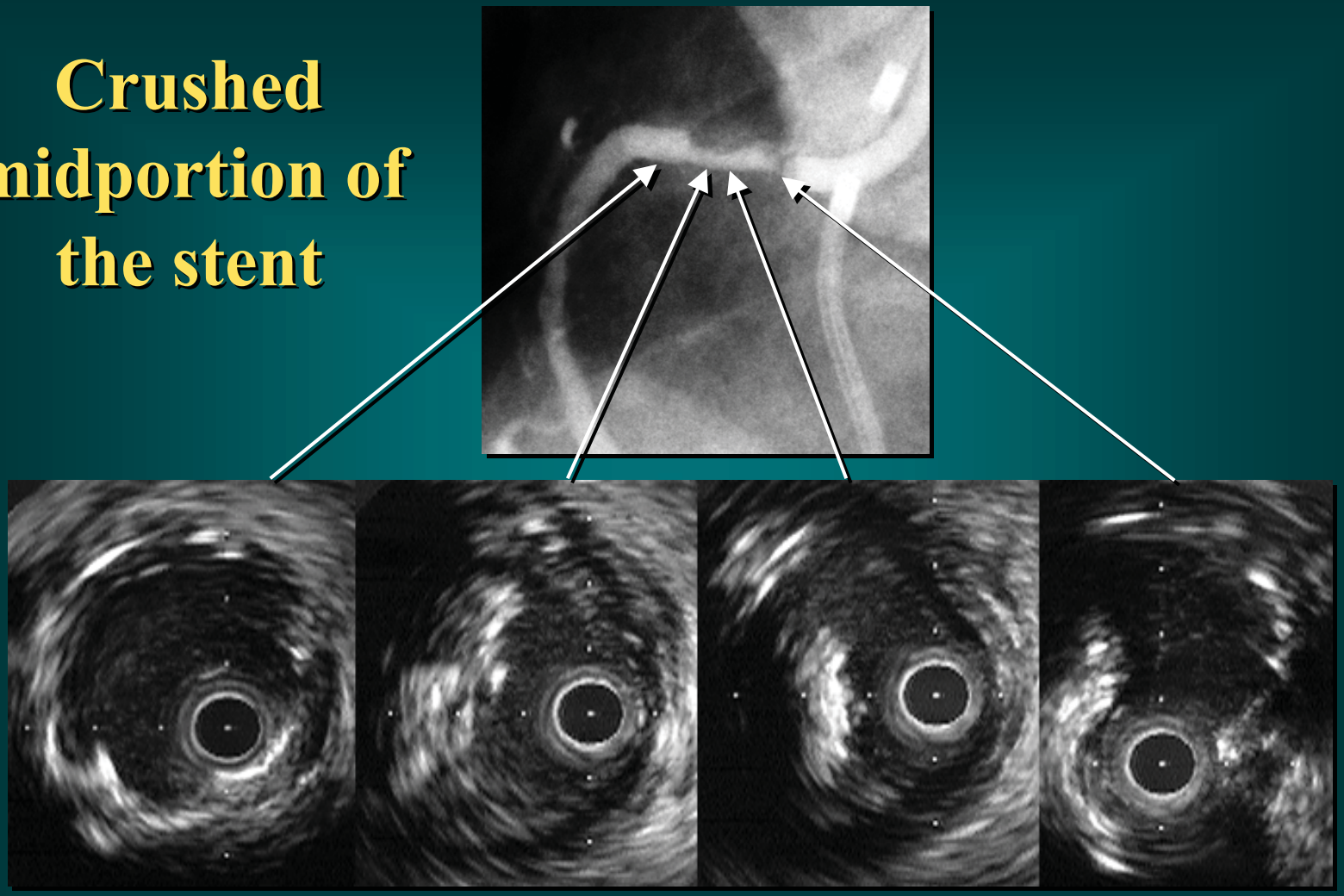


2 month F/U

# Ostial RCA stenosis treated with stenting - BUT the stents missed the ostium

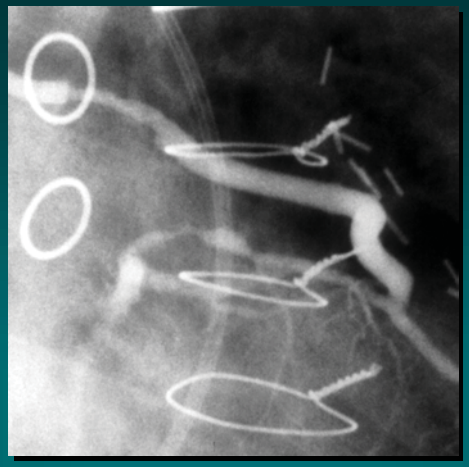


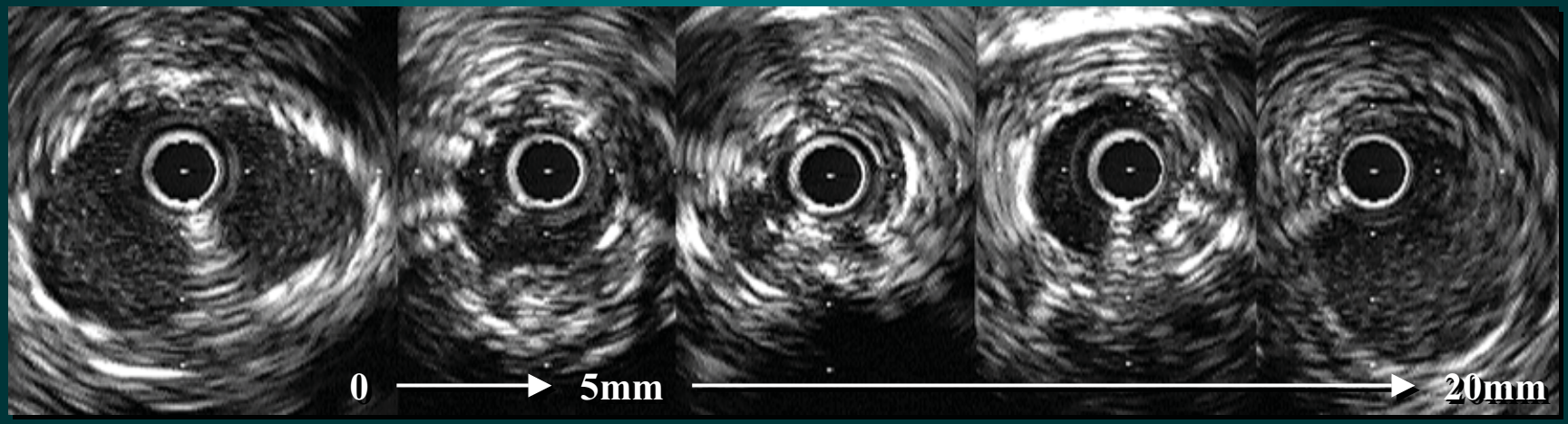
# Crushed midportion of the stent



Distal edge Distal body Central articulation Proximal edge

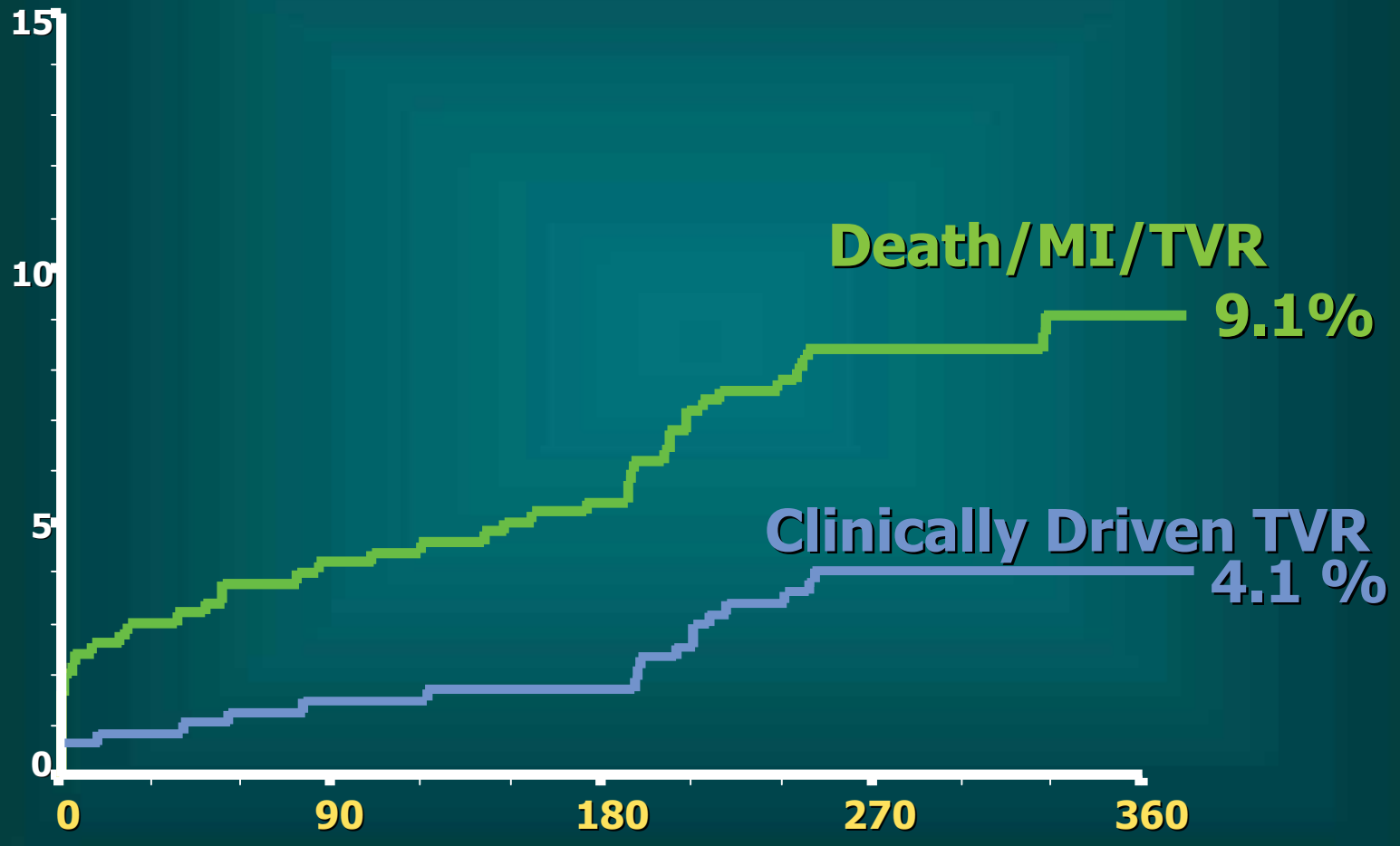
# Unexpanded stent in vein graft





# How may this all change in the world of drug-eluting stents???

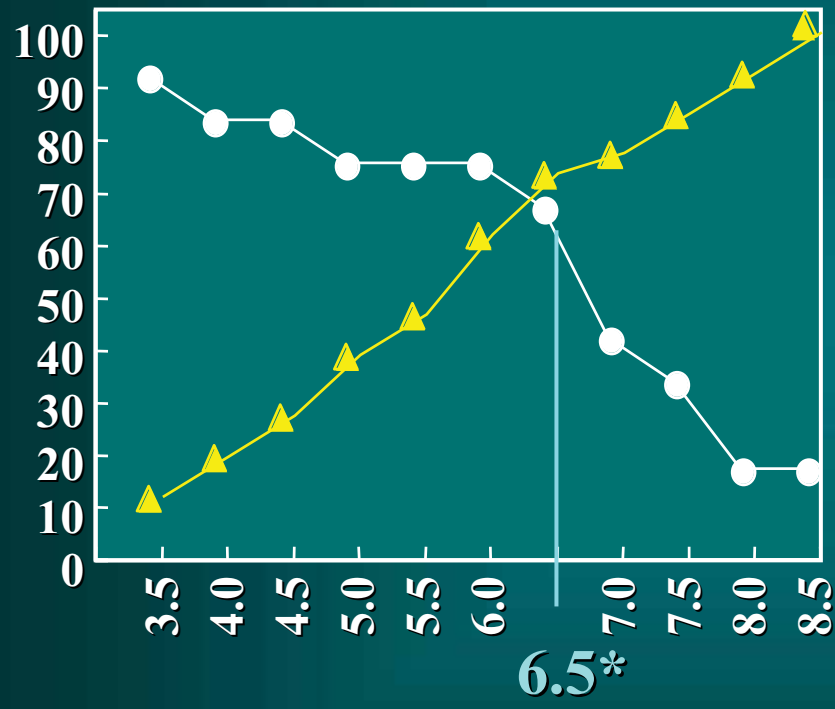
# Cumulative incidence of death, MI, or TVR in the RESEARCH Registry



- TLR after DES appears to be lower than events after an intervention is deferred based on physiologic lesion assessment or IVUS guidance.
- Therefore, if cost is not an issue does it make sense simply to treat intermediate lesions with DES?

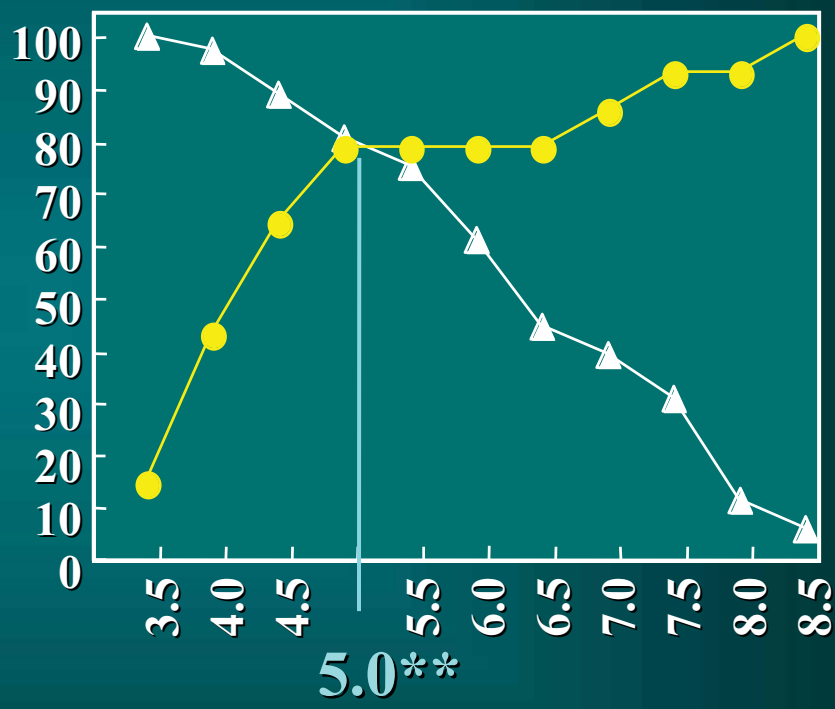
# "Optimal" MSA (from SIRIUS)

## Bare Metal Stents




*predictive value=56%

## Cypher




**predictive value=90%

*(Sonoda et al. J Am Coll Cardiol 2004; in press)*

- **Follow-up angiograms were available in 238 patients with 441 lesions in the RESEARCH Registry. Binary restenosis rates were**

| | |
|---|---|
| Treatment of in-stent restenosis | 19.6% |
| Ostial location | 14.7% |
| Diabetes mellitus | 14.3% |
| Stent length >26mm | 13.9% |
| Reference diameter <2.17mm | 10.3% |
| Non-LAD lesion location | 10.8% |

*Lemos et al. Circulation. 2004;109:1366-7*

- **Restenosis rates of DES bifurcation stenting was 25.7% (17/66 with angiographic follow-up): 14 at the ostium of the side branch and 4 in the main branch.**

*Colombo et al. Circulation. 2004;109:1244-9*

# IVUS analysis of SES Failures @ LHH

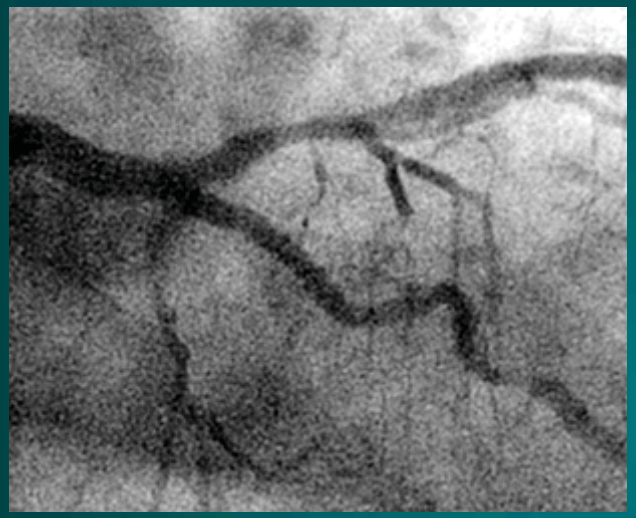
- 32 patients with Cypher stent target vessel failure with IVUS performed at implantation, at follow-up, or both
  - 4 stent thrombosis (1 death, 2MI), 3 new lesions, 22 intra-stent restenosis, 5 stent edge restenosis, and 1 missing stent
- IVUS findings
  - Underexpansion (MSA<5.0mm$^2$) in 16 patients (especially in bifurcation lesions) including 2 stent thrombosis patients
  - Residual dissection in 2 stent thrombosis patients - one also had an unrecognized perforation
  - Significant negative remodeling in 4 of 5 stent edge restenoses
  - No stent seen in one patient

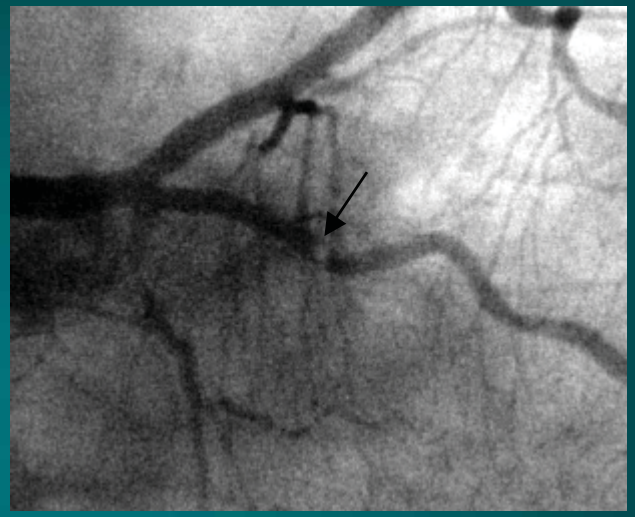
*Takebayashi et al. Unpublished Observations*

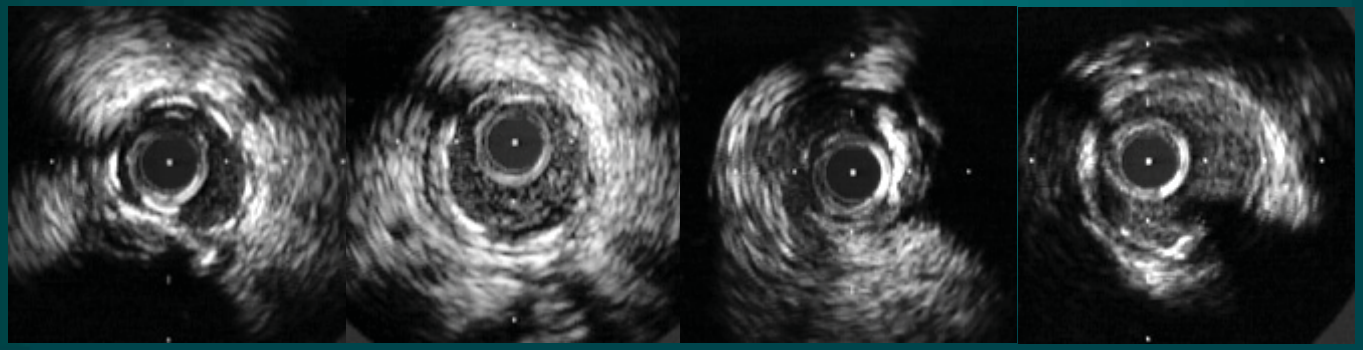
# IVUS analysis of SES Failures @ LHH

| | ISR (n=21) | No-ISR (n=21) | p |
|---|---|---|---|
| MSA ($mm^2$) | 4.4±1.6 | 6.5±1.6 | <0.01 |
| <5.0 $mm^2$ | 18 | 6 | |
| <4.0 $mm^2$ | 11 | 0 | |
| <3.0 $mm^2$ | 8 | 0 | |
| IH CSA ($mm^2$) | 1.3±1.2 | 0.2±0.4 | <0.01 |

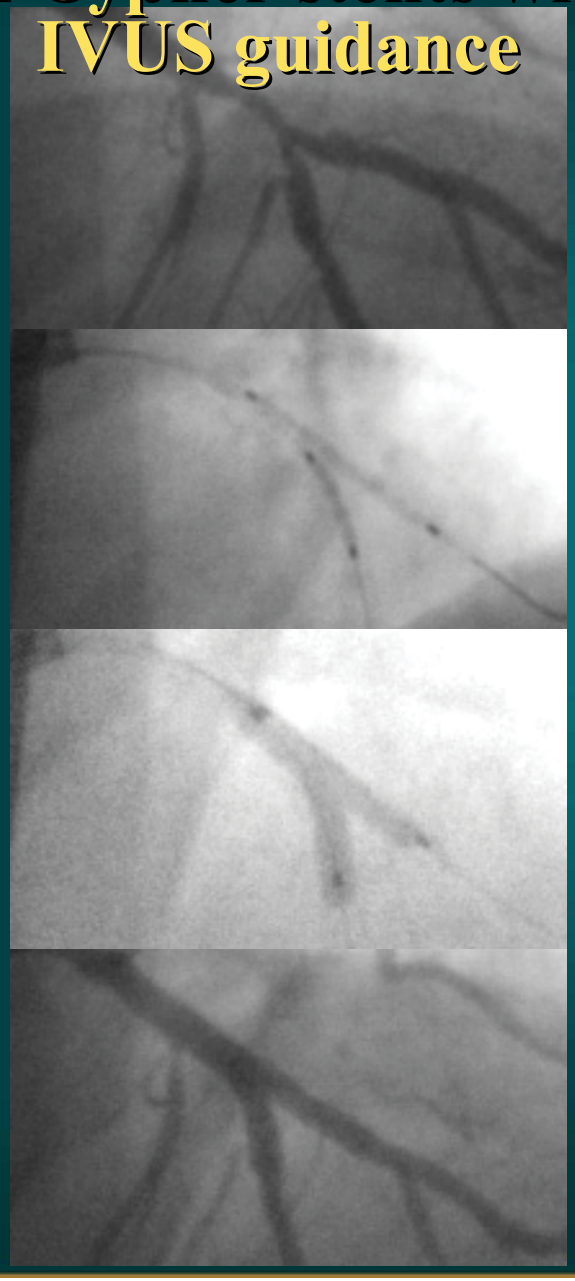
# Stent thrombosis after DES



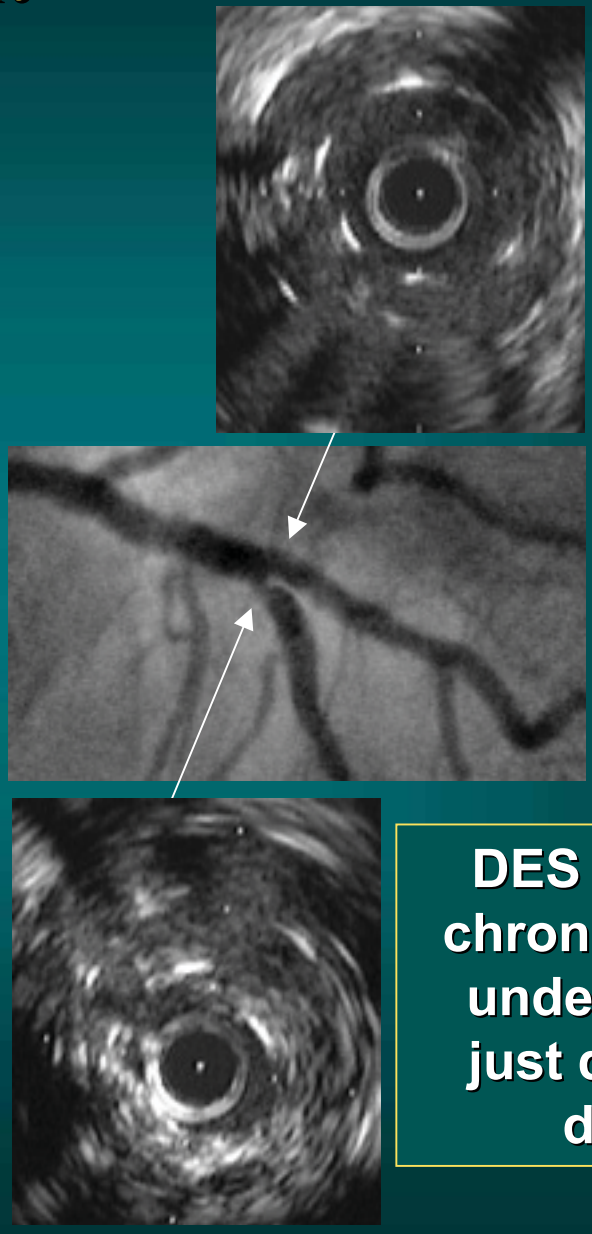




# Bifurcation stenosis treated with 2 Cypher stents without IVUS guidance



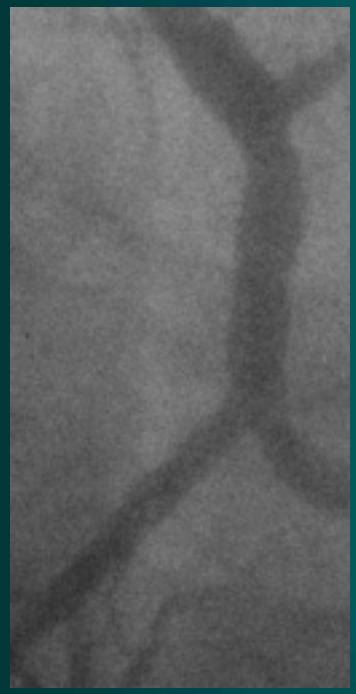
## 7-month Follow-up



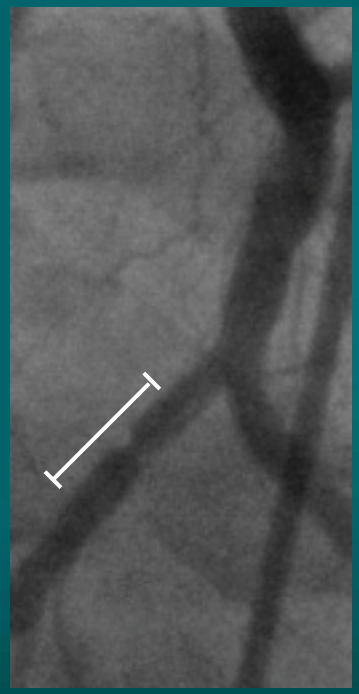
DES “failure” 2º chronic LAD stent underexpansion just distal to the diagonal

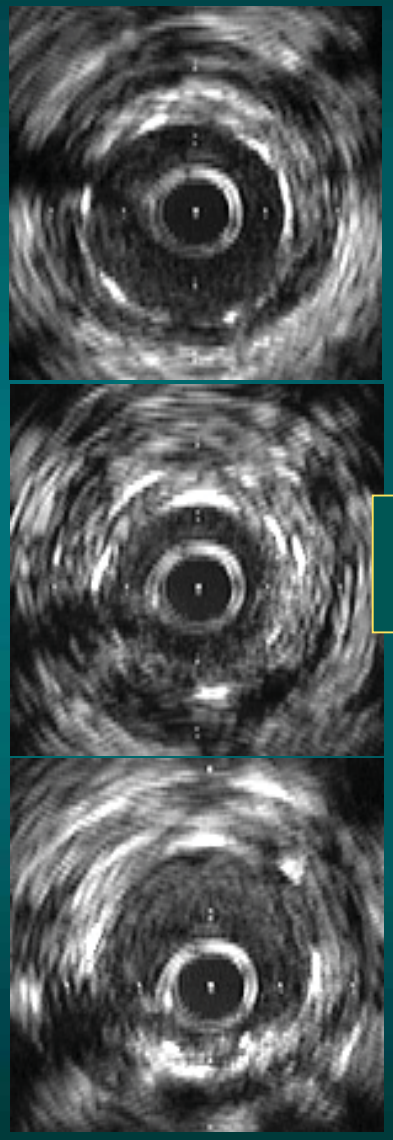
# DES Failure 2° Stent Underexpansion in a Diabetic

Post 3.0x18
and 3.0x8
Cypher stents



8 Months Later



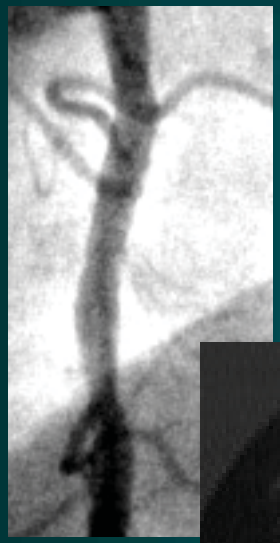


Proximal

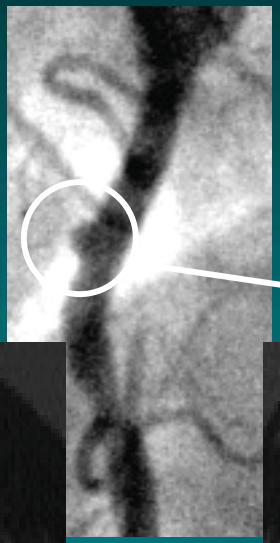
Stent CSA = 5.2mm²
MLA= 3.7mm²

Distal

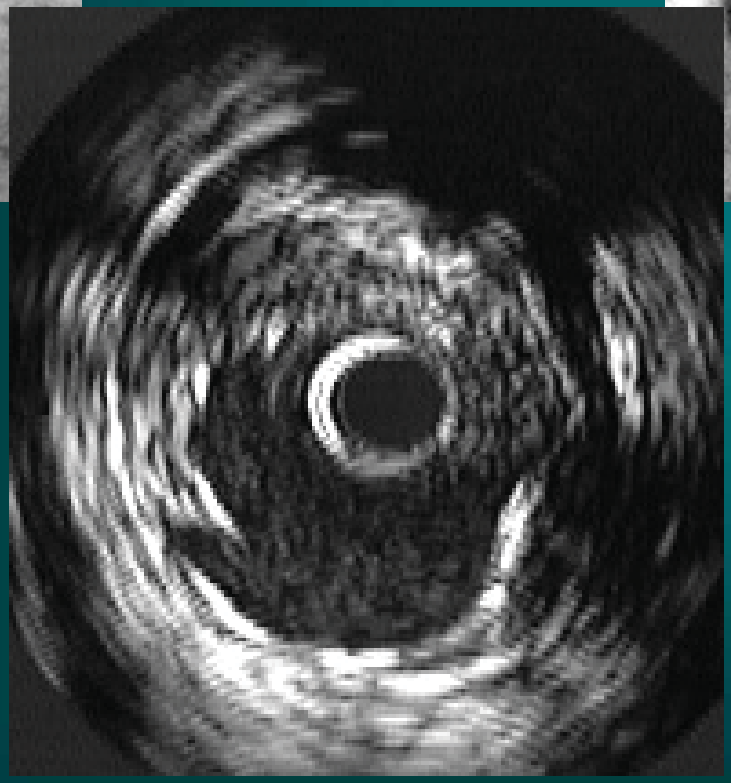
# Late Malapposition

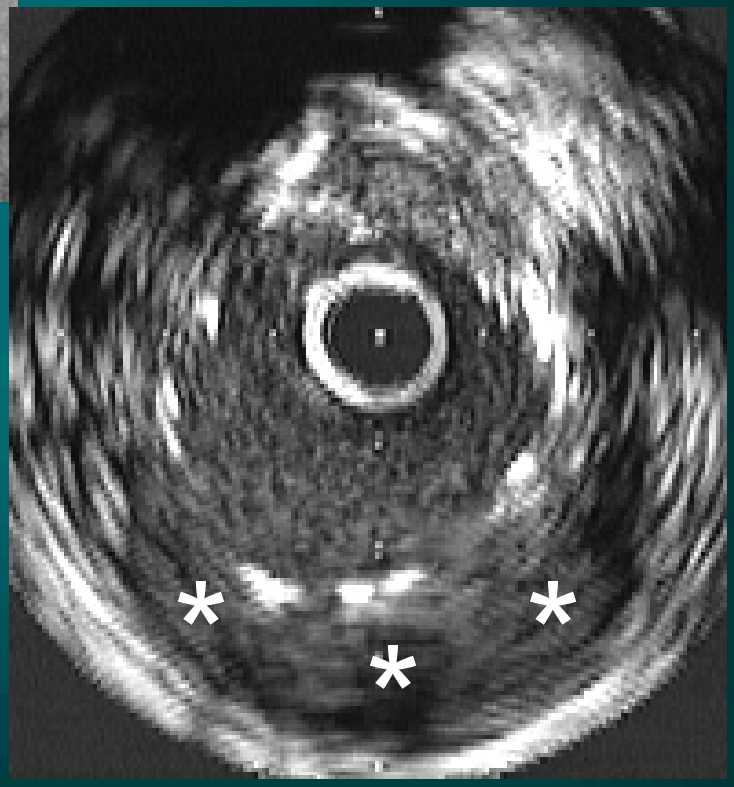


After Stenting



10 Months Later





# Treatment of in-stent restenosis

| | Sao Paulo (n=25) | Rotterdam (n=16) | Taxus-III (n=28) |
|---|---|---|---|
| Drug | Sirolimus | Sirolimus | Paclitaxel |
| Recurrent ISR | 20% | 50% | |
| VBT failure | 0% | 25% | |
| #DES | 1 or 2 | 1-5 | 1 or 2 |
| ISR Pattern | | | |
| Diffuse/proliferative | 68% | 62% | 61% |
| Total occlusion | 0% | 19% | 4% |
| %IH | 1.8%@12mos* | 1.1%@4mos | 11.8%@6mos |
| MACE or recurrence | 4% | 38%** | 29%*** |

*Excludes one patient with angiographic recurrence

***One 2° IH accumulation in a gap between 2 drug-eluting stents***

**Two events occurred in VBT failure patients

****Three in bare metal stents or in gap between drug-eluting stents***

# Treatment of in-stent restenosis at LHH

- 41 patients with in-stent restenosis treated with sirolimus-eluting stents and IVUS
- Recurrence in 10 patients
  - Gap between multiple stents was seen in 3 recurrent and 1 non-recurrent lesion
  - Stent underexpansion (MSA <5.0mm$^2$) in 8/10 recurrence in-stent restenosis lesions (80% vs 12/38 [38%] of non-recurrent lesions, p=0.02)
    - 6/10 (60%) recurrent lesions had a MSA <4.0mm$^2$ vs 8/38 (18%) non-recurrent lesions (p=0.02)
    - 4/10 (40%) recurrent lesions had a MSA <3.0mm$^2$ vs 4/38 (11%) non-recurrent lesions (p=0.03)
  - Gap between SESs was detected in 3/10 recurrent lesions: vs 1/38 non-recurrent lesion (p=0.005). In these 4 cases the SES gap was not detectable angiographically, and it measured <1mm in length by IVUS.

*Fujii et al. Circulation 2004;109:1085-1088*

# Conclusions. . .

- In bare metal stents, as many as 30% of in-stent restenosis lesions have underexpanded stents or mechanical complications
- A smaller minimum stent area is acceptable in DES vs BMS.
- In the BMS patients the predictive value of "6.5mm$^2$" was only 56% indicating that many other factors (e.g., diabetes, lesion location, etc.) influence the minimum lumen area at follow-up.
- In Cypher patients the predictive value of "5.0mm$^2$" was 90% indicating that stent underexpansion was the ***main*** determinant of the MLA at follow-up. Thus, because DES suppresses the neointimal response, the frequency of mechanical problems as causes of DES failure is likely to increase. This may be especially an issue in bifurcation stenting where there is little data on the adequacy of stent expansion in both branches.
- As in bare metal stents, a single cut-off value for an optimum MSA may be too simplistic. A DES MSA> 5.0mm$^2$ may be necessary in high risk patient and lesion subsets where IVUS will have a role
- Not all ISR patients need to be treated.
- Complete lesion coverage and adequate stent expansion are important in the DES treatment of ISR.

# Clinical Utility (I)

- The clinical utility of IVUS in the drug-eluting stent era may depend on the rate of device adoption.
- In the setting of *selective* adoption, IVUS may be useful in avoiding DES implantation by identifying patients and lesions that do not need stenting or that will do well with only bare metal stents - *and in optimizing their results*.
  - Non-diabetics
  - LCX and RCA location
  - Lesion length
  - Vessel size
  - Non-ostial location
  - Optimum final stent CSA

# Clinical Utility (II)

- In the setting of complete adoption, current IVUS uses include
  - Diagnostic imaging
  - Optimizing stent expansion, especially in high risk patient and complex lesion subsets where a MSA of 5.0mm$^2$ may not be sufficient
  - Determining which ISR patients need to be treated
  - Assuring full lesion coverage without underexpansion or gaps between multiple DES during the treatment of ISR
  - Assessment of patients who fail DES implantation or have other unusual findings.