IVUS Assessment of the Mechanism of In-stent Restenosis?

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SURE Trial: Restenosis in non-stented lesions

Average of the two image slices with the smallest pre-intervention and follow-up lumen CSA

61 native vessel lesions (26 DCA, 35 PTCA) with complete serial IVUS studies (out of 79 lesions enrolled in the study)

Kimura et al. Circulation 1997;96:475-83
Restenosis in Stented Lesions

\[ \Delta \text{IH or P&M CSA (mm}^2\text{)} \]

\[ \Delta \text{lumen CSA (mm}^2\text{)} \]

\[ \Delta \text{stent or EEM CSA (mm}^2\text{)} \]

Hoffmann et al. Circulation 1996;94:1247-54
Therefore, in-stent restenosis is all intimal hyperplasia.

\[ \Delta \text{lumen CSA (mm}^2\text{)} \]

\[ \Delta \text{Stent CSA (mm}^2\text{)} \quad r=0.212 \]

\[ \Delta \text{lumen CSA (mm}^2\text{)} \quad r=0.967 \]

\[ \Delta \text{IH CSA (mm}^2\text{)} \]

Hoffmann et al. Circulation 1996;94:1247-54
4.4% of cases had "unrecognized mechanical complications"
12% had severe chronic stent underexpansion (<4.5mm²)

Castagna et al. AHJ 2001;142:970-4
Impact of lesion length and final minimum stent area (MSA) on restenosis

<table>
<thead>
<tr>
<th>Length (mm)</th>
<th>MSA (mm²)</th>
<th>Restenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>12.0</td>
<td>1.0</td>
</tr>
<tr>
<td>3.0</td>
<td>7.5</td>
<td>0.67</td>
</tr>
<tr>
<td>7.5</td>
<td>3.0</td>
<td>0.33</td>
</tr>
<tr>
<td>12.0</td>
<td>0.67</td>
<td>0.33</td>
</tr>
<tr>
<td>35</td>
<td>0.33</td>
<td>0.33</td>
</tr>
<tr>
<td>60</td>
<td>0.33</td>
<td>0.33</td>
</tr>
</tbody>
</table>

*No actual observations in this range

de Feyter et al. Circulation 1999;100:1777-83
### Predictors of DES Thrombosis & Restenosis

<table>
<thead>
<tr>
<th>Predictor</th>
<th>DES Thrombosis</th>
<th>DES Restenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Okabe et al., Am J Cardiol. 2007;100:615-20</td>
<td>• Hong et al. Eur Heart J 2006;27:1305-10</td>
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<tr>
<td>large plaque burden, etc)</td>
<td>• Liu et al. JACC Cardiovasc Interv. 2009;2:428-34</td>
<td></td>
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<tr>
<td></td>
<td>• Costa et al, Am J Cardiol, 2008;101:1704-11</td>
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</tbody>
</table>
By definition, sensitivity/specificity curve analysis "must" identify a single MSA that best separates restenosis from no restenosis. This does NOT mean that 5.0-5.5mm² suffices in all pts/lesions.

**Hong et al. Eur Heart J 2006;27:1305-10
***Doi et al. J Am Coll Cardiol Intv 2009 2: 1269-75

Honda & Fitzgerald. J Am Coll Cardiol Intv 2009 2: 1276-8
Predictors of angiographic restenosis in 550 pts with 670 native lesions treated with Cypher stents

**Angiographic restenosis (%)**

<table>
<thead>
<tr>
<th>IVUS MSA (mm²)</th>
<th>&lt;5.5mm²</th>
<th>≥5.5mm²</th>
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<tbody>
<tr>
<td>≤40mm</td>
<td>2.4%</td>
<td>0.4%</td>
</tr>
<tr>
<td>&gt;40mm</td>
<td>17.7%</td>
<td>8.6%</td>
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</table>

*Hong et al. Eur Heart J 2006;27:1305-10*
The Optimal Cutoff Value of Post-Procedural MSA to Predict a Follow-up MLA ≥4mm² After Bifurcation T-Stenting

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 Cordis (Cypher in yellow, n=133) and BSC (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 Heart J 2007;153:297-303)
Comparison of 9-month QCA edge restenosis vs reference lumen area and plaque burden in TAXUS-IV, V, and VI (n=810)

ROC Plot on TAXUS Patients Edge Restenosis using plaque burden index as the Predictor

- Reference lumen area did not affect Taxus edge restenosis (c=0.55)
- Reference plaque burden had a moderate effect on Taxus edge restenosis; a cut-off of 42% best separated edge restenosis from no restenosis (c=0.67)

*(Liu et al, Am J Cardiol 2009;103:501-6)
Underexpansion is often lumped with malapposition - even by people who should know better

**Stent Thrombosis – No single set of predictors**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>JEREBAS (registry)</th>
<th>iAHRMVOU (registry)</th>
<th>WATHER (RCT)</th>
<th>n-CYPHER (registry)</th>
<th>ARRIVE 1 (registry)</th>
<th>Champion et al. (registry)</th>
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<tbody>
<tr>
<td>Advanced age</td>
<td></td>
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<tr>
<td>Risk Non-compliance</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Diabetes</td>
<td>Yes</td>
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<tr>
<td>ACS/AMI</td>
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<td>Yes</td>
<td>No</td>
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<tr>
<td>Rest deficit</td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>RINO LVEF</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Thrombosis</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Calcification</td>
<td>Yes</td>
<td></td>
<td></td>
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<tr>
<td>Total occlusion</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>MVD</td>
<td>Yes</td>
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<tr>
<td>Total extent length</td>
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<tr>
<td>Malapposition</td>
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<td></td>
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<tr>
<td>Number of stents</td>
<td>Yes</td>
<td></td>
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**Summary**

- **Stent thrombosis is multifactorial**
  - Anatomic, clinical, pharmacologic
- **Early stent thrombosis (~ 0.6%) is related to**:
  - Lesion complexity
  - Stent malapposition
  - Variable anti-platelet agent responsiveness
  - Early discontinuation of anti-platelet therapy (strongest risk factor)
- **LST and VLST are rare but serious complications of DES**
  - It was not seen in patients who remain on dual anti-platelet therapy in the RESCUE/ITSEARCH analysis by Cour et al., or the TAXUS meta-analysis (1 patient only)

**Current ESC PCI guidelines now recommend 6-12 months of dual anti-platelet therapy after DES**

- The TAXUS® Express®™ DFU recommends 6 months of dual anti-platelet therapy

AMI = acute myocardial infarction; LVEF = left ventricular ejection fraction; RCT = randomized clinical trial; MVD = multivessel disease

Persistent stent malapposition is associated with less intimal hyperplasia – the drug can cross small stent vessel-wall gaps

**Acute Incomplete DES Apposition and IH**

- Persistent ISA (n=40, 83% decreased in size)
- Completely resolved ISA (n=15)

(Hong et al. Circulation 2006;113:414-9)
(Balakrishnan et al., Circulation 2005;111:2958-65)
Serial angiographic FU of Palmaz-Schatz stents

3 yr FU

Extended FU (7 – 11 yrs)


Kimura et al., Circulation 2002;105:2986-91
Changes in Maximum Yellow Color Grade From Baseline to Follow-Up in DES

*p=0.0008 vs. baseline

mean±SD
Percentage of Patients With Atherosclerotic Changes in DES Versus BMS in Relation to Duration of Implant at Autopsy

Nakazawa et al. J Am Coll Cardiol Img 2009;2:625-8
BMS 57-month follow-up
Analysis of 20 stent fractures in 17 patients

- 15 stent fractures were detected by angiography and IVUS, and 5 were detected only by IVUS
- 15 stent fractures in 13 patients were associated with in-stent restenosis (all focal); and 2 stent fractures in 2 patients were associated with very late stent thrombosis
- Five stent fractures occurred within a coronary aneurysm accompanied by malapposition despite the absence of a coronary aneurysm at index stenting.
  - Comparing stent fractures associated with an aneurysm to ones that did not occur in association with an aneurysm, complete stent fracture was more frequent (100% vs. 27%, p=0.008), and all presented >1 year after index stenting (vs. 33%, p=0.03).

(Doi et al. Am J Cardiol 2009;103:818-23)
Assessment of causes of in-stent restenosis
E diastole
B systole
diastole

C diastole
D systole
diastole

E diastole
B systole
diastole
DES after VBT failure for Rx of BMS Restenosis

2 years later

proximal
9-month minimum lumen area that predicts 3-year MACE-free survival in patients from TAXUS IV, V, and VI

<table>
<thead>
<tr>
<th></th>
<th>BMS</th>
<th>Taxus</th>
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<tr>
<td></td>
<td>C-statistic</td>
<td>Cutoff</td>
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<tr>
<td>Minimum lumen area</td>
<td>0.73</td>
<td>4.0mm²</td>
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n=348

n=351