PCI σε επαναστενωτικές βλάβες

Τσαγάλου Ελευθερία
Επιμελήτρια
Θεραπευτική Κλινική Πανεπιστημίου Αθηνών
DES-ISR by Stent Generation

Number of ISR by DES Generation after Initial Stent Implanting

DES generation  First  Second

(Washington Hospital Center)

Incidence 3-20% (Dangas et al. JACC 2010;56:1897-907)
Clinical Presentation and Outcomes of Coronary In-Stent Restenosis Across 3-Stent Generations

Marco A. Magalhaes, MD; Sa’ar Minha, MD; Fang Chen, PhD; Rebecca Torguson, MPH;


909 patients (1077 ISR lesions)
ISR is not benign…

After matching patients for cardiovascular risk factors, the overall MACE at 3 years was worse for group presenting with ISR compared to the group presenting with de novo coronary artery stenosis (*adjusted HR for clinical presentation of MI).
Mechanisms of ISR

• Biological factors
  Drug resistance
  Hypersensitivity

• Mechanical factors
  Non uniform stent strut distribution
  Stent fractures
  Polymer peeling
  Non uniform drug deposition

• Technical factors
  Incomplete stent expansion
  Stent gaps or “misses” (uncovered lesion segments)
  Barotrauma to unstented segments
**DES In-Stent Restenosis:**

**Focal**
- DES Fracture
- DES Gap
- Geographic Miss
- Uneven/Undelivered Drug
  - Non-uniform Strut Distribution
  - DES Damage
- DES Underexpansion (***)
- Hypersensitivity
- Drug Resistance

**Mechanical Factors**

**Diffuse**

**Biological Factors**

**IVUS / OCT**
**Neointimal Proliferation**

- Predominant Mechanism
- Neointimal hyperplasia (SMC)

**Neoatherosclerosis**
Nakazawa G, Virmani R. J Am Coll Cardiol 2011;57:1314–22

- Fibroatheroma. Lipid-laden Macrophages, calcium (Necrotic Core)
- DES 30%, Earlier than BMS
- Young, Unstable, Time, DES
**Difference of Tissue Characteristics Between Early and Late Restenosis After Second-Generation Drug-Eluting Stents Implantation**

— An Optical Coherence Tomography Study —

Hiroyuki Jinnouchi, MD; Shichio Kuramitsu, MD; Tomohiro Shinzaki; Yusuke Tornoi, MD;

<table>
<thead>
<tr>
<th></th>
<th>Early-ISR (n=30)</th>
<th>Late-ISR (n=23)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUMEN AREA, MM²</td>
<td>1.5±1.0</td>
<td>1.3±0.7</td>
<td>0.65</td>
</tr>
<tr>
<td>NIH AREA, MM²</td>
<td>4.2±2.1</td>
<td>4.1±1.7</td>
<td>0.89</td>
</tr>
<tr>
<td>HOMOGENEOUS INTIMA</td>
<td>8 (26.7)</td>
<td>1 (4.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>LIPID-LADEN</td>
<td>9 (30.0)</td>
<td>16 (69.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>NEOATHEROSCLEROSIS</td>
<td>9 (30.0)</td>
<td>17 (73.9)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
2014 ESC Guidelines on Myocardial Revascularization

IVUS/OCT in ESC guideline 2014

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVUS or OCT to assess mechanisms of stent failure</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>
TREATMENT STRATEGIES

Balloon angioplasty
Focal restenosis
Stent underexpansion

Adjunctive Therapy
Rotational atherectomy
Cutting Balloon
Laser atherectomy
Drug Eluting balloons

1. IN.PACT Admiral is coated with a matrix of paclitaxel and an excipient, urea.

2. The coating comes into contact with water in the bloodstream upon inflation, hydrating the urea, which facilitates the release of paclitaxel at the target lesion.

3. Paclitaxel penetrates the vessel wall, where it remains at a therapeutic dose for over 180 days, addressing the causes of the restenosis.
RIBS V
A Randomized Comparison of Drug-Eluting Balloon vs Everolimus-Eluting Stent in Patients with *Bare-Metal* Stent-In-Stent Restenosis

- **Inclusion Criteria**
  - Informed Consent

- **Randomization**
  - 189 Pts BMS ISR

- **Rx Centralized Stratification**
  - ISR Length & Edge

- **95 Pts DEB**
  - 3 Died
  - 1 Thrombosis
  - 7 Refused
  - 84 Pts Angio FU
  - Mean: 271 days

- **94 Pts EES**
  - 8 Refused
  - 86 Pts Angio FU
  - Mean: 270 days

- **100% Angiographic Success**
- **Angiographic FU**
- **QCA Primary Endpoint**
- *(170 Pts: 92% of Eligible)*
✓ Superior angiographic results in the EES arm
✓ Similar rate of MACE
RIBS IV

(January 2010 – August 2013)

Inclusion Criteria: Informed Consent

309 Pts DES-ISR Randomization

Rx Centralized Stratification: ISR Length & Edge

Xience Prime (Abbott Vascular)

155 Pts EES

100% Angiographic Success

133 Pts Angio FU

155 Pts Clinical FU

4 Died
18 Refused
1 Thrombosis

SeQuent Please (B. Braun)

154 Pts DEB

139 Pts Angio FU

3 Died
12 Refused

154 Pts Clinical FU

QCA Primary End-point (90%)

3-Year Clinical FU (100%)
RIBS IV

3-Year Clinical Follow-up:
Freedom From Death, MI, TLR

Breslow, p = 0.030
Log Rank, p = 0.036

3 Year FU 309 P (100%); FU Time 1057±163 days

Time (years)
Events at Final FU (3 Years)
3 Year FU 309 P (100%); FU Time 1057±163 days

TLR (35)
- EES: 11 (7%)
- DEB: 24 (14%)

TVR (49)
- EES: 17 (11%)
- DEB: 32 (21%)

Intention to Treat
A “class effect” of DEB has not been demonstrated

<table>
<thead>
<tr>
<th>Device</th>
<th>Company</th>
<th>Additive and substance class</th>
<th>Dose [μg/mm²]</th>
<th>Approval</th>
<th>Vessel territory</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low dose</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moxi™</td>
<td>Lutonix, USA</td>
<td>Polysorbate + sorbitol, Surfactant + sugar alcohol</td>
<td>2</td>
<td>CE certified, FDA approval</td>
<td>Peripheral</td>
</tr>
<tr>
<td>Agent™</td>
<td>Boston Scientific, USA</td>
<td>Acetyl tributyl citrate, Plasticiser</td>
<td>2</td>
<td>CE certified</td>
<td>Coronary</td>
</tr>
<tr>
<td>Ranger™</td>
<td>Boston Scientific, USA</td>
<td>Acetyl tributyl citrate, Plasticiser</td>
<td>2</td>
<td>CE certified</td>
<td>Peripheral</td>
</tr>
<tr>
<td>Stealare™</td>
<td>Spectranetics, USA</td>
<td>Polyethylene glycol, Synthetic polymer</td>
<td>2</td>
<td>CE certified</td>
<td>Peripheral</td>
</tr>
<tr>
<td>Elutax SVM™</td>
<td>Aachen Resonance, Germany</td>
<td>none</td>
<td>2.2</td>
<td>CE certified</td>
<td>Coronary/Peripheral</td>
</tr>
<tr>
<td>Danubio™</td>
<td>Minvasys, France</td>
<td>n-Butyl tri-n-hexyl citrate, Plasticiser</td>
<td>2.5</td>
<td>CE certified</td>
<td>Coronary</td>
</tr>
<tr>
<td><strong>Regular dose</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orchid™</td>
<td>Acotec, China</td>
<td>Magnesium stearate, Salt of stearin acid</td>
<td>3</td>
<td>CE certified</td>
<td>Peripheral</td>
</tr>
<tr>
<td>Sequent™</td>
<td>B. Braun, Germany</td>
<td>Iopromide, X-ray contrast medium</td>
<td>3</td>
<td>CE certified</td>
<td>Coronary</td>
</tr>
<tr>
<td>Sequent™</td>
<td>B. Braun, Germany</td>
<td>Resveratrol</td>
<td>3</td>
<td>CE certified</td>
<td>Peripheral</td>
</tr>
<tr>
<td>Pantera Lux™</td>
<td>Biotronik, Germany</td>
<td>n-Butyl tri-n-hexyl citrate, Plasticiser</td>
<td>3</td>
<td>CE certified</td>
<td>Coronary</td>
</tr>
<tr>
<td>Passeo Lux™</td>
<td>Biotronik, Germany</td>
<td>n-Butyl tri-n-hexyl citrate, Plasticiser</td>
<td>3</td>
<td>CE certified</td>
<td>Peripheral</td>
</tr>
<tr>
<td>LEGFLOW™</td>
<td>Cardionovum, Germany</td>
<td>Shellac, Varnish</td>
<td>3</td>
<td>CE certified</td>
<td>Peripheral</td>
</tr>
<tr>
<td>RESTORE™</td>
<td>Cardionovum, Germany</td>
<td>Shellac, Varnish</td>
<td>3</td>
<td>CE certified</td>
<td>Coronary</td>
</tr>
<tr>
<td>AngioSculptX™</td>
<td>Spectranetics, USA</td>
<td>Nordihydroguaiaretic acid, Antioxidant</td>
<td>3</td>
<td>CE certified</td>
<td>Coronary</td>
</tr>
<tr>
<td>Chocolate Touch™</td>
<td>QT Vascular, Singapore</td>
<td>undisclosed</td>
<td>–</td>
<td>CE certified</td>
<td>Coronary/Peripheral</td>
</tr>
<tr>
<td>Advance PTX™</td>
<td>Cook Medical, USA</td>
<td>none</td>
<td>3</td>
<td>CE certified</td>
<td>Peripheral</td>
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<tr>
<td>Dior® II, BioStream™</td>
<td>Eurocor, Germany</td>
<td>Shellac, Varnish</td>
<td>3</td>
<td>CE certified</td>
<td>Coronary</td>
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<tr>
<td>FREEWAY™</td>
<td>Biosensors, Switzerland</td>
<td>Shellac, Varnish</td>
<td>3</td>
<td>CE certified</td>
<td>Peripheral</td>
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<tr>
<td>essential™</td>
<td>iVascular, Spain</td>
<td>undisclosed</td>
<td>–</td>
<td>CE certified</td>
<td>Coronary</td>
</tr>
<tr>
<td>luminor™</td>
<td>iVascular, Spain</td>
<td>undisclosed</td>
<td>–</td>
<td>CE certified</td>
<td>Peripheral</td>
</tr>
<tr>
<td>IN.PACT™ (Admiral, Pacific, Falcon)</td>
<td>Medtronic Vascular, USA</td>
<td>Urea, Endogenous metabolite</td>
<td>3.5</td>
<td>CE certified, FDA approval</td>
<td>Coronary/Peripheral</td>
</tr>
</tbody>
</table>
Sirolimus Eluting Balloons

VIRTUE Sirolimus Eluting Balloon

DEVOIR Sirolimus Eluting Balloon
VIRTUE™ Sirolimus Eluting Balloon

Virtue solves DEB Limus delivery challenge of tissue uptake and long-term elution

Sirolimus tissue concentrations > 300-fold higher in coronary artery treatment site and target concentration maintained for 28 days

# SABRE: Clinical Safety Outcomes 24 Months Follow Up

### Intent to Treat Analysis (ITT)

<table>
<thead>
<tr>
<th></th>
<th>In Hospital 50</th>
<th>30 Days* 50</th>
<th>12 Months 49</th>
<th>24 Months 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Death</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>MI</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>1 (2.0%)</td>
<td>1 (2.1%)</td>
</tr>
<tr>
<td>CABG</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>1 (2.0%)</td>
<td>1 (2.1%)</td>
</tr>
<tr>
<td>TLR</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td><strong>6 (12.2%)</strong></td>
<td><strong>7 (14.6%)</strong></td>
</tr>
<tr>
<td>TLF</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td><strong>6 (12.2%)</strong></td>
<td><strong>7 (14.6%)</strong></td>
</tr>
</tbody>
</table>

### Per Protocol Analysis (PP)

<table>
<thead>
<tr>
<th></th>
<th>12 Months PP 36</th>
<th>24 Months PP 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Death</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>MI</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>CABG</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>TLR</td>
<td><strong>1 (2.8%)</strong></td>
<td><strong>2 (5.7%)</strong></td>
</tr>
<tr>
<td>TLF</td>
<td><strong>1 (2.8%)</strong></td>
<td><strong>2 (5.7%)</strong></td>
</tr>
</tbody>
</table>

*Primary safety endpoint is 30 day TLF

*Adjudicated through May 2016

Values are reported as n (%)
PATENT-C – Clinical Follow up intention to treat

- Coated scoring balloon
- Uncoated scoring balloon

Freedom from MACE (death, MI, stent thrombosis, or TLR)

p=0.01, log-rank

Bioresorbable Vascular Scaffolds for Patients With In-Stent Restenosis

The RIBS VI Study

Freedom from MACE (Cardiac Death, MI, TLR)

1 Year FU (FU Time 361±29 days)

Breslow, p = 0.02
Log Rank, p = 0.03

94%
87%

J Am Coll Cardiol Intv 2017
Conclusions

• Incidence of ISR-DES ranges from 3 to 20% and can occur even 10 years after stent deployment

• It is important to understand the mechanism and phenotype of ISR (use of IVUS, OCT are helpful)

• The efficacy of Drug Eluting Modalities has significantly reduced the utilization of other therapeutic options such as BA, BMS, debulking devices and VBT

• DCB and DES are as effective for BMS-ISR while DES are the preferred strategy for most DES-ISR

• DES and DCB are associated with nearly 10-20% recurrence rate

• Next generation DCB and BVS should be evaluated in randomised trials
Σας ευχαριστώ
Treatment algorithm

**DES ISR**

- FFR (IVUS/OCT)
  - (-)
  - Medical Rx
- Asymptomatic Severity?

**IVUS / OCT**

- Underlying Mechanism
  - Focal
    - Gap
    - Fracture
    - Edge
    - Body
  - DES
- Diffuse
  - Underexpansion?
  - Avoid Geo Miss
  - ↑ Pressure NC BA
  - Cutting/Scoring
  - Optimization
  - 2nd G DES / DEB

**Preferred DES:** Hetero & 2nd G DES

**Favor DEB:** Multiple ST layers, major SB good acute result, short DAT, 1st ISR (?)