New Frontiers in Flow Diversion

Disclosures:

Pipeline & Onyx proctor
Advisory Board: Intreped, Premier, Shield project
Principal Investigator: PUPS, Intreped, Swift Prime, Premier, Barrel, Aspire
National PI: Shield trial
Research collaboration: Pipeline Shield Technology Project

Concepts for endovascular treatment of aneurysms

1990 - Coiling
1996 - Stent and Coiling
2011 - Flow Diversion
Before FD we had to overlap low coverage stents “homemade flow diverter”

Flow diverter alone

How to improve our outcomes?


Balloon mounted stent

Flexible self-expanding stent

Flow diverter

CLINICAL STUDIES ON PED:

PITA
*PUFS
*ASPIRE
*INTREPED
*PREMIER
*SHEILD – COMING SOON!

* Trials Rush University participated – “Chicago experience”
Comparison of FD to Stent Coiling

<table>
<thead>
<tr>
<th>Complete occlusion rate</th>
<th>IncasoPED</th>
<th>PUFs</th>
<th>Stent-Assisted Coiling Meta Registry</th>
<th>Neuroform Stent Registry</th>
<th>Enterprise Stent Registry</th>
</tr>
</thead>
<tbody>
<tr>
<td>71% (12-24 mo follow)</td>
<td>86% (12 mo follow)</td>
<td>61%</td>
<td>48.2% (progressive thrombosis at 12.8 mo avg follow)</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>Recurrence rate</td>
<td>0%</td>
<td>14%</td>
<td>27.7%</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>M&amp;M</td>
<td>8.3%</td>
<td>5.6%</td>
<td>5.3%</td>
<td>8.1%</td>
<td></td>
</tr>
<tr>
<td>Neurologic death</td>
<td>3.8%</td>
<td>2.8%</td>
<td>2.1% (periprocedural)</td>
<td>3.2%</td>
<td></td>
</tr>
</tbody>
</table>

1. IntrePED Presentation by Dr. David Kallmes, SNIS Conference, July 28, 2013.

Flow diversion of large and/or giant & wide-necked ICA aneurysms in PUFs

95.2% 5.6%

Aneurysm Occlusion Rate (@5years) M&M

Pooled DATA from PED trials

- 1092 patients – 1221 aneurysms
- 12 mm size – 6mm neck (mean)
- Complete occlusion:
  - 75% 180 days
  - 85.5% 1 year
  - 93.4% 3 years
  - 95.2% 5 years
- Retreatment – 3%
- Major M&M – 7.1%
Complication reported with flow-diversion

- Thromboembolic events
- Delayed aneurysm rupture
- Parenchymal hemorrhages
- Perforators or side branch occlusion
- In-stent thrombosis

Background

Thromboembolism is one of the most common endovascular complications

Factors Contributing to Stent Thrombosis

So what is next in flow diversion?

• Surface modification
• Intravascular Imaging

Low hanging fruit?

• Thromboembolic complications are multifactorial

How to address that?

• Coronary stents have been modified to decrease their thrombogenicity
• Neuro intervention could benefit if implants are less thrombogenic or “more blood compatible”

What is Shield Technology™?

Shield Technology™ is a surface treatment where an inert, synthetic phosphorylcholine (PC) polymer is covalently bonded to the strands that make up the Pipeline braid.
What is Phosphorylcholine (PC)?

- PC is the major component on the surface of red blood cells and therefore treating a device with PC results in physiologic mimicry of the cell membrane.
- PC coatings have been successfully used on implanted vascular devices for over 14 years.

Phosphorylcholine (PC) Coatings:
Synthetic copy of PC headgroup from RBC outer membrane

Thrombogenicity of flow diverters in an ex vivo shunt model: effect of phosphorylcholine surface modification.

CONCLUSIONS:
In this preclinical model, phosphorylcholine modification reduces the platelet-specific thrombogenicity of a flow diverter under physiologically relevant flow with and without DAPT.
We have further identified increased fibrin-driven thrombogenicity associated with FRED relative to PED.
OCT for stent evaluation

Follow up

Strut apposition

Strut coverage
• Optical Coherence Tomography (OCT) is an imaging modality able to provide high-resolution images of vessels in vivo.

• While intravascular ultrasound (IVUS) uses backscattered ultrasound, OCT uses reflected light to create cross sectional images of the vessel.

---

The C7-XR™ OCT Imaging System

- Dual monitors and remote output for multiple sight lines
- Easy mouse and keyboard control
- Multiple export options including DVD/CD
- Small footprint for easy placement

---

Imaging Catheter

- Quick connect hub
- 3 cc gauge syringe
- 0.035″/2.7 Fr with hydrophilic coating
- Guidewire exit port
- 2 cm mini-rail
- Tip marker
- Lens marker
A Simple and Fast Procedure

- Cross with monorail imaging catheter
- Inject 10-12cc of contrast
- The automatically triggered imaging scan is performed in less than five seconds

OCT scan from PCA to Basilar

- Resolution: 100 - 150 µm (axial), 150 - 300 µm (lateral)
- Penetration depth: 4 - 8 mm (IVUS), 1.5 – 2 mm (OCT)
- Scan Area: 6-7 mm (IVUS), 10 - 15 mm (OCT)
- Blood removal: Not required (IVUS), Required (OCT)
Precise Vessel Measurement

MCA – Lenticulostriate perforators

Side branch detection

False lumen

Intima tear
OCT for the evaluation of new generation stents
Bioabsorbable stents.

- The prospective, multicenter, ABSORB study evaluated the safety and efficacy of a fully absorbable everolimus eluting stent (BVS*) for the treatment of de novo single coronary stenoses.
- OCT substudy in Rotterdam after implantation, at 6 months and 2 years.

*Bioabsorbable Vascular Solutions, Inc, an affiliate of Abbott Laboratories, located in Mountain View, CA
Serruys et al. Lancet 2009; 373: 897-910

Stent endothelialization monitored with intravascular imaging and histology in porcine

Results - 4 days
- Endothelialization: FLEX (5 × 12mm) vs. FLEX with Shield (5 × 12mm) vs. Solitaire (5 × 20mm) (1Fr.=0.1mm)

10th Fr. 100th Fr. 200th Fr. 280th Fr.

FLEX 1 Shield 1 Solitaire 1
Endothelialization of device over time in a porcine model