The Progress in Endovascular Management of Intracranial Aneurysms

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### Device Name

Guglielmi Detachable Coil (GDC), Class III.

| GDC (K951256) | for embolizing certain intracranial aneurysms that - because of their morphology, their location, or the patient's general medical condition - are considered by the treating neurosurgical team to be a) very high risk for management by traditional operative techniques, or b) inoperable. |
**ISUIA 03**

<table>
<thead>
<tr>
<th></th>
<th>Surgery</th>
<th>Endovascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural M&amp;M*</td>
<td>12.6% (Gr. I)</td>
<td>9.1%</td>
</tr>
<tr>
<td>(Gr. I)</td>
<td></td>
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<tr>
<td></td>
<td>10.1% (Gr. II)</td>
<td>9.5%</td>
</tr>
<tr>
<td>(Gr. II)</td>
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</tbody>
</table>

*Endo patients: Older
Larger aneurysms
More posterior circulation

We then did the trials
ISAT

$N=2143$ (AJ Molyneux)

- RPCT: coils vs. clips
- 44 NS centers
- 1994 start
1 Year Follow Up - 1491 Patients

- Relative risk reduction - coils 24.3%
- p<0.001
- Absolute risk reduction 7%
Available Coil Shapes 510K

- Mini Complex
- Complex
- Helical
# Available Coil Shapes 510K

## Platinum Coils

<table>
<thead>
<tr>
<th>Category</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Framing</td>
<td>Cosmos, HyperSoft 3D, Complex</td>
</tr>
<tr>
<td>Filling</td>
<td>VFC, Cosmos, HyperSoft 3D, Helical</td>
</tr>
<tr>
<td>Finishing</td>
<td>HyperSoft, HyperSoft 3D, VFC</td>
</tr>
</tbody>
</table>
New Coil types - Hydrogel 510K

- Hydrosoft and Hydroframe
  - Platinum with hydrogel core
  - Do not expand much, can be retrieved
## Delivery System Comparison

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Coil Attachment Point</th>
<th>Delivery System Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codman Neurovascular</td>
<td></td>
<td>Soft Tube → Hydraulic</td>
</tr>
<tr>
<td>Micrus Endovascular</td>
<td></td>
<td>Wire → Electrolytic</td>
</tr>
<tr>
<td>Boston Scientific</td>
<td></td>
<td>Wire → Electrolytic</td>
</tr>
<tr>
<td>Microvention / Terumo</td>
<td></td>
<td>Wire → Electrolytic</td>
</tr>
<tr>
<td>eV3</td>
<td></td>
<td>Wire → Mechanical</td>
</tr>
</tbody>
</table>
Hydrogel-coated coils versus bare platinum coils for the endovascular treatment of intracranial aneurysms (HELPS): a randomised controlled trial

Philip M White, Stephanie C Lewis, Anil Ghokkar, Robin J Sellar, Hans Nahser, Christophe Cognard, Lynn Forrester, Joanna M Wardlaw, for the HELPS trial collaborators

<table>
<thead>
<tr>
<th>Rupture status</th>
<th>Hydrogel (n/N)</th>
<th>Bare platinum (n/N)</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unruptured</td>
<td>75/105 (71%)</td>
<td>85/111 (77%)</td>
<td>0.77 (0.42–1.41)</td>
<td>0.014</td>
</tr>
<tr>
<td>Ruptured</td>
<td>83/123 (68%)</td>
<td>64/128 (50%)</td>
<td>2.08 (1.24–3.46)</td>
<td></td>
</tr>
<tr>
<td>Aneurysm size (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.0–4.9</td>
<td>27/38 (71%)</td>
<td>27/39 (69%)</td>
<td>1.09 (0.41–2.90)</td>
<td></td>
</tr>
<tr>
<td>5.0–9.9</td>
<td>103/134 (77%)</td>
<td>90/136 (66%)</td>
<td>1.70 (0.99–2.90)</td>
<td>0.458</td>
</tr>
<tr>
<td>10.0–24.9</td>
<td>28/56 (50%)</td>
<td>32/64 (50%)</td>
<td>1.00 (0.49–2.05)</td>
<td></td>
</tr>
</tbody>
</table>

**Interpretation** Whether use of hydrogel coils reduces late aneurysm rupture or improves long-term clinical outcome is not clear, but our results indicate that their use lowers major recurrence.
The most progress has come about from improvements in initial angiographic results through the use of balloon remodeling, adjunctive stent placement, and a wider selection of coils.
New Coil types - Bioactive Coils 510K

• Polyglycolic-Polylactic Acid (PGLA)
  • Incites inflammation and thrombosis
• Matrix Coils
  • Platinum coil with PGLA
  • Packing density decreases over time
• Cerecyte Coils
  • Platinum coils around polyglycolic acid (PGA) filament
• Nexus Coils
  • Platinum coils with PGLA filaments that extend out as small hairs
Bioactive versus Bare Platinum Coils in the Treatment of Intracranial Aneurysms: The MAPS (Matrix and Platinum Science) Trial


MATERIALS AND METHODS: This was a multicenter randomized noninferiority trial with blinded endpoint adjudication. We enrolled 626 patients, divided between Matrix² and bare metal coil groups. The primary outcome was target aneurysm recurrence at 12 ± 3 months.

CONCLUSIONS: Tested Matrix² coils were not inferior to bare metal coils. Endovascular coiling of intracranial aneurysms was safe, and the rate of technical success was high. Target aneurysm recurrence is a promising clinical outcome measure that correlates well with established angiographic measurements.
Cerecyte Coil Trial
Angiographic Outcomes of a Prospective Randomized Trial Comparing Endovascular Coiling of Cerebral Aneurysms With Either Cerecyte or Bare Platinum Coils

Andrew J. Molyneux, FRCR; Alison Clarke, BA; Mary Sneade, BA; Ziyah Mehta, DPhil; Stuart Coley, FRCR; Daniel Roy, MD; David F. Kallmes, MD; Allan J. Fox, MD

Results—Four hundred ninety-four patients were eligible for analysis. Four hundred eighty-one patients underwent coil treatment of their aneurysm, 227 patients with recently ruptured aneurysms and 254 with unruptured aneurysms. Four hundred thirty-three follow-up angiograms were assessed by the core laboratory; 127 of 215 (59%) and 118 of 218 (54%) in the Cerecyte and bare platinum groups, respectively, fulfilled the trial prespecified definition of success, namely that the treated aneurysm showed complete angiographic occlusion, had stable neck remnant, or improved in angiographic appearance compared with the end-of-treatment angiogram ($P=0.17$). Late retreatment was performed in 25 of 452 (5.5%) patients, 17 (7.7%) Cerecyte versus 8 (3.5%) bare platinum ($P=0.064$; range, 4–34 months). The clinical outcomes did not differ between the groups.

Conclusion—There was no significant difference at 6 months in the angiographic outcomes between Cerecyte coils and bare platinum coils when assessed by the core laboratory.
High Recanalization Rate was Observed in Published Coiling Studies Treating Wide-Necked and/or Large and Giant Aneurysms Outcomes

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>Size</th>
<th>100% Occlusion Rate</th>
<th>Neck Remnants</th>
<th>Morbidity</th>
<th>Mortality</th>
<th>Follow-Up Time</th>
<th>Recanalization Rate (# Follow ups)</th>
<th>% Retreat</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISAT¹⁴</td>
<td>2002</td>
<td>1073</td>
<td>Endovascular Arm: 1073</td>
<td>Small: 92.0%</td>
<td>Not Reported</td>
<td>125/801(1 year)</td>
<td>65/801(1 year)</td>
<td>1 year</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Large: 8.0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Berenstein¹⁷</td>
<td>2006</td>
<td>27</td>
<td>Small Wide-Neck: 33%</td>
<td>41%</td>
<td>5.8%</td>
<td>92/801(1 year)</td>
<td>0%</td>
<td>5.3 Months (11/30)</td>
<td>57% (4/7)</td>
<td>12%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>32</td>
<td>Large: 13%</td>
<td>38%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>27% (6/22)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>Giant: 0%</td>
<td>67%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100% (1/1)</td>
<td></td>
</tr>
<tr>
<td>Murayama¹⁵</td>
<td>2003</td>
<td>245</td>
<td>Small Wide-Neck: 41%</td>
<td>46%</td>
<td>4.8%</td>
<td>11 months (489 / 916)</td>
<td>20% (NR)</td>
<td>Not Reported</td>
<td>Not Reported</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>198</td>
<td>Large Wide-Neck: 40%</td>
<td>45%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>35% (NR)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>73</td>
<td>Giant: 26%</td>
<td>64%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>59% (NR)</td>
<td></td>
</tr>
<tr>
<td>Sluzewski¹⁸</td>
<td>2003</td>
<td>31</td>
<td>Very Large and Giant: 51%</td>
<td>48%</td>
<td>15%</td>
<td></td>
<td>18 months (20/29)</td>
<td>69% (20/29)</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td>Gruber¹⁹</td>
<td>1999</td>
<td>19</td>
<td>Very Large: 42%</td>
<td>Not Reported</td>
<td>20%</td>
<td></td>
<td>30 months (14/25)</td>
<td>50% (8/16)</td>
<td>52%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12</td>
<td>Giant: 42%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>67% (6/9)</td>
<td></td>
</tr>
</tbody>
</table>

M&M Range: ISAT: 23% Single Center: 5.8 – 20%
Recanalization Range: 20 – 100% (5.3 – 24.3 month follow-up)
Balloon-assisted Coiling 510K
CONCLUSIONS

- Balloon-assisted coil embolization (BACE) of intracranial aneurysms is associated with a high complication rate.
- The BACE procedure does not improve the occlusion rates of the aneurysms on follow-up evaluation.
CONCLUSION: This largest-to-date literature review and meta-analysis did not demonstrate a higher incidence of thromboembolic events or iatrogenic rupture with the use of adjunctive balloon remodeling compared with unassisted coiling. Balloon remodeling appears to result in higher initial and follow-up aneurysm occlusion rates.
Self-Expanding Stents

- First developed for the treatment of wide-necked intracranial aneurysms
The Neuroform™ Microdelivery Stent System is intended for use with embolic coils for the treatment of wide neck, intracranial, saccular aneurysms arising from a parent vessel with a diameter of ≥2mm and ≤4.5mm that are not amenable to treatment with surgical clipping. Wide neck aneurysms are defined as having a neck of ≥4mm or a dome-to-neck ratio of <2.
### Table 2: Serious Device or Procedure-Related Adverse Events

<table>
<thead>
<tr>
<th>Serious Adverse Event</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Aneurysm Perforation</td>
<td>2 (6.9%)</td>
</tr>
<tr>
<td>Arterial Perforation</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Subarachnoid/Interventricular Hemorrhage</td>
<td>2 (6.9%)</td>
</tr>
<tr>
<td>Thromboembolic Stroke</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Intracerebral Hematoma</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Left Hemiparesis</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Intraparenchymal Bleeding</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Retroperitoneal Hematoma</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Confusion</td>
<td>1 (3.4%)</td>
</tr>
</tbody>
</table>

1 First revision unhappy 12 patients adverse events. The “1” reflects and
Drawbacks - Neuroform

- Open cell has limited support in large coil masses
  - Potentially allowing herniation into the parent vessel
- Early experience demonstrated increased thrombogenicity, requiring pre-treatment of patients with dual anti-platelet agents (aspirin, clopidogrel)
- Resulting in limited use in acute subarachnoid hemorrhage
Enterprise Stent HDE May 2005

- Designed to address the limitations of the open-cell design
- Further support provided to limit coil mass herniation
- Closed-cell design allows for retrieval of stent if necessary

The CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System is intended for use with embolic coils for the treatment of wide-neck, intracranial, saccular or fusiform aneurysms arising from a parent vessel with a diameter of ≥ 3 mm and ≤ 4 mm. Wide-neck is defined as having a neck width ≥ 4 mm or a dome-to-neck ratio < 2.
Enterprise - Closed Cell Design

Neuroform - Semi-open Cell Design
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Study</th>
<th># ANs Treated</th>
<th>Mean AN Size (mm)</th>
<th>Immediate Complete Occlusion %</th>
<th>Follow-Up Occlusion %</th>
<th>Recurrence %</th>
<th>Recurrence % for LG Giant</th>
<th>Follow-Up %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent-Coiling</td>
<td>Stent-Coiling Meta Analysis/ Shapiro et al, 2012&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1517</td>
<td>65% &lt;10</td>
<td>45%</td>
<td>61% (6 mo)</td>
<td>14%</td>
<td>Not Reported</td>
<td>48.5%</td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Mocco et al, 2009</td>
<td>142</td>
<td>55 were &lt;7, 48 were 7-12, 24 were 12-24, 4 were &gt;25</td>
<td>25%</td>
<td>Not Reported</td>
<td>Not Reported</td>
<td>Not Reported</td>
<td>100.0%</td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Mocco et al, 2011</td>
<td>219</td>
<td>46.6% &lt;7, 31.1% 7-12, 16.9% 12-24, 4.6% &gt;24, 0.9% n/a</td>
<td>Not Reported</td>
<td>40% (6 mo)</td>
<td>Not Reported</td>
<td>Not Reported</td>
<td>50.2%</td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Fiorella et al, 2009</td>
<td>302</td>
<td>Of aneurysms with follow up: 97 small, 57 large, 12 Giant</td>
<td>Not Reported</td>
<td>33.1% (12.9 mo avg)</td>
<td>28%</td>
<td>54%</td>
<td>58.5%</td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Piotin et al, 2010</td>
<td>216</td>
<td>9.7</td>
<td>44% (100/216)</td>
<td>Not Reported</td>
<td>15%</td>
<td>33%</td>
<td>52.7%</td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Colby et al, 2011</td>
<td>41</td>
<td>7</td>
<td>43%</td>
<td>Not Reported</td>
<td>15%</td>
<td>Not Reported</td>
<td>86.7%</td>
</tr>
<tr>
<td>Treatment</td>
<td>Study</td>
<td>Avg AN Size (mm)</td>
<td>Patients/ ANs</td>
<td>Follow-up</td>
<td>Overall M&amp;M</td>
<td>Intracranial Hemorrhages</td>
<td></td>
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<td>-------------------</td>
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</tr>
<tr>
<td>Stent-Coiling</td>
<td>Stent-Coiling Meta Analysis/ Shapiro et al, 2012&lt;sup&gt;2&lt;/sup&gt;</td>
<td>63% &lt;10</td>
<td>1517/ Not Reported</td>
<td>Not reported</td>
<td>2.1% mortality, 3.2% delayed TIA/stroke</td>
<td>2.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Mocco et al, 2009&lt;sup&gt;8&lt;/sup&gt;</td>
<td>73%&lt;12</td>
<td>141/142</td>
<td>Not reported</td>
<td>8.8% morbidity, 2.8% mortality</td>
<td>3.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Mocco et al, 2011&lt;sup&gt;9&lt;/sup&gt;</td>
<td>79%&lt;12</td>
<td>213/219</td>
<td>110 (52%)</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Fiorella et al, 2009&lt;sup&gt;10&lt;/sup&gt;</td>
<td>61%&lt;10</td>
<td>284/302</td>
<td>62%</td>
<td>5.3% major stroke/ 3.2% mortality</td>
<td>4 IPH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Piotin et al, 2010&lt;sup&gt;11&lt;/sup&gt;</td>
<td>9.3</td>
<td>216 (with SAC)</td>
<td>53%</td>
<td>7.4% morbidity/ 6.0% mortality</td>
<td>2.8% -ruptured, 0.5% -unruptured</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Colby et al, 2011&lt;sup&gt;12&lt;/sup&gt;</td>
<td>7.0</td>
<td>30</td>
<td>87%</td>
<td></td>
<td>3.3% -SAH peri procedural</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Timeline of Endovascular Development

- **1989**: GDC invented
- **1994**: GDC FDA approval
- **1999**: 3D GDC introduced
- **2004**: Neuroform FDA approval
- **2009**: Enterprise FDA approval
- **2014**: Pipeline FDA approval

Additional events:
- ISUIA
- ISAT
- BRAT
The problem with stent/coil

- Relatively complex procedures
  - 2 microcatheters, multiple devices
  - Configuration at bifurcations often leaves surgeon wanting for better devices
  - Complication rates on the order of 4-8%
- Recanalization rate is high for large aneurysms treated with coiling
Flow Diverters

- Stents with higher metal coverage and lower porosity than traditional intracranial stents
- Aim to
  - redirect flow through the parent vessel away from the aneurysm
  - provide a scaffold for neointimal growth and healing of the vessel wall
Pipeline for Uncoilable or Failed Aneurysms (PUFs)

- 107 patients treated
- Unruptured aneurysm in the ICA from petrous to superior hypophyseal segments
  - $\geq 10$ mm in size and neck $\geq 4$ mm
- 81.8% complete occlusion at 180 days with 5.6% of major complications
- 97.8% successful delivery
Based on PUFS...

- In April of 2011, the Pipeline embolization device gained FDA PMA approval for large or giant wide-necked intracranial aneurysms in the internal carotid artery from the petrous to the superior hypophyseal segments
We then did the trials

Complications associated with Pipeline across different studies

<table>
<thead>
<tr>
<th>Table 2. Reported Clinically Significant Complications, Morbidity, and Mortality Associated with Pipeline Embolization Device Treatment Across Various Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complications</strong></td>
</tr>
<tr>
<td>Mass effect</td>
</tr>
<tr>
<td>In-stent thrombosis</td>
</tr>
<tr>
<td>Perforator occlusion</td>
</tr>
<tr>
<td>Thromboembolic event</td>
</tr>
<tr>
<td>Intracranial Hemorrhage</td>
</tr>
<tr>
<td>Morbidity, n (%)</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
</tr>
<tr>
<td>Morbidity and Mortality, n (%)</td>
</tr>
</tbody>
</table>

*Same patient with more than one complication.
†Mortality case.
Post-market experience with Pipeline

Early Postmarket Results After Treatment of Intracranial Aneurysms With the Pipeline Embolization Device: A US Multicenter Experience

BACKGROUND: The Pipeline embolization device (PED) is the latest technology available for intracranial aneurysm treatment.

OBJECTIVE: To report early postmarket results with the PED.

METHODS: This study was a prospective registry of patients treated with PEDs at 7 American neurosurgical centers subsequent to Food and Drug Administration approval of this device. Data collected included clinical presentation, aneurysm characteristics, treatment details, and periprocedural events. Follow-up data included degree of aneurysm occlusion and delayed (> 30 days after the procedure) complications.

RESULTS: Sixty-two PED procedures were performed to treat 58 aneurysms in 56 patients. Thirty-seven of the aneurysms (64%) treated were located from the cavernous to the superior hypophyseal artery segment of the internal carotid artery; 22% were distal to that segment, and 14% were in the vertebrobasilar system. A total of 123 PEDs were deployed with an average of 2 implanted per aneurysm treated. Six devices were incompletely deployed; in these cases, rescue balloon angioplasty was required. Six periprocedural (during the procedure/within 30 days after the procedure) thromboembolic events occurred, of which 5 were in patients with vertebrobasilar aneurysms. There were 4 fatal postprocedural hemorrhages (from 2 giant basilar trunk and 2 large ophthalmic artery aneurysms). The major complication rate (permanent disability/death resulting from perioperative/delayed complication) was 8.5%. Among 19 patients with 3-month follow-up angiography, 68% (13 patients) had complete aneurysm occlusion. Two patients presented with delayed flow-limiting in-stent stenosis that was successfully treated with angioplasty.

CONCLUSION: Unlike conventional coil embolization, aneurysm occlusion with PED is not immediate. Early complications include both thromboembolic and hemorrhagic events and appear to be significantly more frequent in association with treatment of vertebrobasilar aneurysms.

KEY WORDS: Endovascular treatment, Flow diversion, Intracranial aneurysm, Pipeline device
Post-market experience with PED

Prospective registry at 7 American hospitals

58 aneurysms in 56 patients
- 8 posterior circulation aneurysms

Complications:
- Overall: 6 thromboembolic events, 4 post-procedural hemorrhage, 2 delayed in-stent stenosis
- For posterior circulation aneurysms only: 5 thromboembolic events, 2 fetal hemorrhage

Complication rates higher in posterior circulations!
Retrospective study

Included all patients treated with PED 7/2008 – 2/2013

6 countries, 13 centers

Required minimum 10 PED cases experience per center
  - Included initial experiences of other investigators

793 patients with 906 aneurysms enrolled
### Incidence of delayed aneurysm ruptures in relation to aneurysm size

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>large &amp; giant</th>
<th>large</th>
<th>giant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5/793</td>
<td>5/423</td>
<td>2/357</td>
<td>3/66</td>
</tr>
<tr>
<td></td>
<td>0.6%</td>
<td>1.1%</td>
<td>0.5%</td>
<td>4.5%</td>
</tr>
</tbody>
</table>

**Table:**

- **Total**
  - 5/793, 0.6%
  - 5/423, 1.1%
  - 2/357, 0.5%
  - 3/66, 4.5%

**Graph:**

- Patients without previous subarachnoid haemorrhage (group 1)
- Probability of subarachnoid haemorrhage
- Lines represent different aneurysm sizes:
  - <7 mm
  - 7-12 mm
  - 13-24 mm
  - >25 mm
- p < 0.0001

**Reference:**

Wiebers et al., ISUIA II., THE LANCET
- Vol 362 • July 12, 2003
## Safety outcomes: Intracranial hemorrhage

<table>
<thead>
<tr>
<th>Study</th>
<th>F/u</th>
<th>Total incidence</th>
<th>Clinical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>IntrePED</td>
<td>19.3 months</td>
<td>24/793 (3.0%)</td>
<td>Major 19/793 (2.4%)</td>
</tr>
<tr>
<td>PUFS</td>
<td>6 months</td>
<td>5/107 (4.6%)</td>
<td>Major 2/107 (1.9%)</td>
</tr>
</tbody>
</table>

\[ p = 0.74 \]

Major Events: symptoms present after 7 days
Minor Events: resolved within 7 days

2 non PUFS eligible aneurysms
## Safety Outcomes: Ischemic stroke

<table>
<thead>
<tr>
<th>Cohorts</th>
<th>F/u</th>
<th>Total incidence</th>
<th>Clinical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>IntrePED</td>
<td>19.3 months</td>
<td>51/793 (6.5%)</td>
<td>36/793 (4.5%)</td>
</tr>
<tr>
<td>PUFs</td>
<td>6 months</td>
<td>5/107 (4.6%)</td>
<td>3/107 (2.8%)</td>
</tr>
</tbody>
</table>

- **Major Events:** symptoms present after 7 days
- **Minor Events:** resolved within 7 days

9 non PUFs eligible aneurysms

$p = 0.41$
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Study</th>
<th>% F/u &amp; Duration</th>
<th>Pts</th>
<th>Overall M&amp;M</th>
<th>Intracranial Hemorrhages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pipeline</td>
<td>PUFs</td>
<td>96% / 1 year</td>
<td>107</td>
<td>5.6%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Pipeline</td>
<td>IntrePED</td>
<td>19.3 mo median</td>
<td>793</td>
<td>8.2%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Meta-analysis</td>
<td>Brinjikji W et al 2013</td>
<td>6 mo avg</td>
<td>1651 pts</td>
<td>9%</td>
<td>3%</td>
</tr>
<tr>
<td>Pipeline / Silk</td>
<td>Brinjikji W et al 2013</td>
<td>6 mo avg</td>
<td>1651 pts</td>
<td>9%</td>
<td>3%</td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Fiorella et al, 2009</td>
<td>62% / 13 mo</td>
<td>284</td>
<td>8.1%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Stent-Coiling</td>
<td>Piotin et al, 2010</td>
<td>53% / 14 mo</td>
<td>216 aneurysms</td>
<td>13.4%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Meta-analysis</td>
<td>Shapiro et al, 2012</td>
<td>13 mo avg</td>
<td>1517 pts (763 pts reported M&amp;M)</td>
<td>5.3%</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

Safety profile compared to stent assisted coiling.
Pipeline Embolization Device for Small Intracranial Aneurysms: Evaluation of Safety and Efficacy in a Multicenter Cohort

**BACKGROUND:** To date, the use of the flow-diverting Pipeline Embolization Device (PED) for small intracranial aneurysms (≤ 7 mm) has been reported only in single-center series.

**OBJECTIVE:** To evaluate the safety and efficacy of the PED in a multicenter cohort.

**METHODS:** Five major academic institutions in the United States provided data on patient demographics, aneurysm features, and treatment characteristics of consecutive patients with aneurysms ≤ 7 mm treated with a PED between 2009 and 2015. Radiographic outcome was assessed with digital subtraction angiography. Clinical outcome was measured with the modified Rankin Scale.

**RESULTS:** The cumulative number of aneurysms ≤ 7 mm treated with PED at the 5 institutions was 149 in 117 patients (age, 54 years [range, 29-87 years]; male to female, 1:5.9). Aneurysms were most commonly located in the paraophthalmic segment (67.1%) of the internal carotid artery. Radiographic outcome at last follow-up was available for 123 aneurysms (82.6%), with a complete occlusion rate of 87%. Thromboembolic and symptomatic procedural complications occurred in 8.7% and 6% of the aneurysms treated, respectively. There was 1 mortality (0.9%) unrelated to the PED procedure. Multivariable logistic regression identified size < 4 mm, balloon angioplasty to open the device, and simultaneous treatment of multiple aneurysms as predictors of procedural complications. Good clinical outcome was achieved in 96% of electively treated patients.

**CONCLUSION:** In the largest series on PED for small aneurysms to date, data suggest that treatment with the flow-diverting PED is safe and efficacious, with complication rates comparable to those for traditional endovascular techniques.

**KEY WORDS:** Pipeline embolization device, Small, Aneurysm, Intracranial, Endovascular, Embolization
Treatment of Distal Anterior Circulation Aneurysms With the Pipeline Embolization Device: A US Multicenter Experience

BACKGROUND: Utilization of the Pipeline embolization device (PED) to treat distal carotid circulation aneurysms has not been well studied.

OBJECTIVE: To report the collective experience of using PED to treat distal anterior circulation aneurysms.

METHODS: We retrospectively reviewed clinical and radiographic records of all patients who underwent Pipeline embolization of distal anterior circulation aneurysms at 10 US neurosurgical centers between 2011 and 2013.

RESULTS: Twenty-eight patients (mean age 51.7 years; 18 women) with 28 aneurysms were included in the analyses. Fifteen aneurysms were fusiform, 5 dissecting, and 8 saccular. Average aneurysm size was 12.3 mm; 7 were giant. Twenty aneurysms were located along the middle cerebral artery, 6 along the anterior cerebral artery, and 2 along the anterior communicating artery. PED deployment was successful in 27 patients, with coils utilized in 6 cases. Clinical follow-up was available for an average of 10.7 months (range 3-26). Twenty-seven patients had follow-up neurovascular imaging; 21 aneurysms had complete occlusion, 4 had residual neck filling, and 2 had residual dome filling. Periprocedural complications (<30 days) occurred in 3 patients (10.7%), including 1 case of device failure resulting in stroke. Outcomes were good (modified Rankin Scale score 0 to 2) in 27 patients (96.4%) and fair (modified Rankin Scale 3) in 1.

CONCLUSION: PED can be utilized in the treatment of distal anterior circulation aneurysms with difficult anatomy for conventional surgical or endovascular techniques. Larger-scale studies with long-term follow-up are needed to further elucidate the durability of PED treatment and its effect on perforator-rich vascular segments.

KEY WORDS: Flow diverter, Intracranial aneurysm, Pipeline embolization device
CASE SERIES

Treatment failure of fetal posterior communicating artery aneurysms with the pipeline embolization device

Peter Kan, Edward Duckworth, Ajit Puri, Greg Velat, Ajay Wakhloo

ABSTRACT
Aneurysms that involve the internal carotid artery and posterior communicating artery junction and incorporate a fetal posterior cerebral artery are known as fetal posterior communicating artery aneurysms. We report the outcomes of four patients with fetal posterior communicating artery aneurysms who underwent treatment with the pipeline embolization device with or without adjunctive coil embolization. In our study, all four patients failed to achieve aneurysm occlusion at the last follow-up evaluation. Based on our results, we currently do not recommend the use of the flow diverter for the treatment of fetal posterior communicating artery aneurysms.

fetal PCA who underwent flow diversion treatment with a PED.

METHODS
We report the cases of four patients with fetal PCOMA aneurysms who underwent treatment with a PED. Each of the patients had a PCOMA aneurysm incorporating a fetal PCA (fetal PCOMA aneurysm) treated with a PED, and had at least 12 months of angiographic follow-up. A fetal PCA was defined as one with a primary supply from the ICA on angiography, with an absent P1 segment. Patients with PCOMA aneurysms occurring on the ICA separate from the fetal PCA were excluded. The study was approved by the local institutional
Aneurysm treatment Options have evolved....

1. Clipping
2. Coiling
3. Balloon-assisted coiling
4. Stent-assisted coiling
5. Flow Diverters
6. Second generation microstents
7. Second generation flow diverters
8. Bifurcation stents/devices
The LVIS Device is intended for use with bare platinum embolic coils for the treatment of unruptured, wide neck (neck ≥ 4 mm or dome to neck ratio < 2), intracranial, saccular aneurysms arising from a parent vessel with a diameter ≥ 2.5 mm and ≤ 4.5 mm.
The Neuroform Atlas Stent System is indicated for use with neurovascular embolic coils in patients who are ≥ 18 years of age for the treatment of wide neck, intracranial, saccular aneurysms arising from a parent vessel with a diameter of ≥ 2 mm and ≤ 4.5 mm that are not amenable to treatment with surgical clipping. Wide neck aneurysms are defined as having a neck ≥ 4 mm or a dome-to-neck ratio of < 2.
Liberty
Hybrid approach laser cut- Nitinol Technology
Medtronic Barrel Stent
PulseRider: Neck Reconstruction

Pulsar Vascular Receives CE Mark Approval For PulseRider®
PulseRider® is indicated for use with neurovascular embolic coils in patients $\geq 18$ years of age for the treatment of unruptured wide-necked intracranial aneurysms with neck widths $\geq 4$ mm or dome to neck ratio $< 2$ originating on or near a vessel bifurcation of the basilar tip or carotid terminus with at least a portion of the aneurysm neck overlapping the lumen of the parent artery. The inflow vessels should have diameters from 2.7 mm to 4.5 mm.
Table 18: Aneurysm Occlusion

<table>
<thead>
<tr>
<th>Score</th>
<th>Day Zero n/N (%)</th>
<th>180 Days(^1) n/N (%)</th>
<th>365 Days n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raymond I</td>
<td>18/34 (52.9%)</td>
<td>20/33 (60.6%)</td>
<td>6/8 (75%)</td>
</tr>
<tr>
<td>Raymond II</td>
<td>9/34 (26.5%)</td>
<td>9/33 (27.3%)</td>
<td>2/8 (25%)</td>
</tr>
<tr>
<td>Raymond III</td>
<td>7/34 (20.6%)</td>
<td>4/33 (12.1%)</td>
<td>0/8 (0%)</td>
</tr>
</tbody>
</table>

\(^1\)One enrolled subject had MRA performed instead of an angiogram and is excluded from this analysis.

Table 19: Blinded Core Lab Adjudicated Raymond I and II at 180-Days Follow-Up

<table>
<thead>
<tr>
<th>Raymond Score</th>
<th>180 Days % (n/N)</th>
<th>Lower 80% Confidence Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>I/II</td>
<td>87.9% (29/33(^1))</td>
<td>80.5%</td>
</tr>
</tbody>
</table>

\(^1\)One enrolled subject had MRA performed instead of an angiogram and is excluded from this analysis.

Table 16: Safety Outcome Assessed Based on Neurological Death and Stroke Resulting in mRS \(\geq 3\) at 180 ± 45 Days Follow-Up*

<table>
<thead>
<tr>
<th></th>
<th>% (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological Death</td>
<td>0% (0/34)</td>
</tr>
<tr>
<td>Stroke resulting in mRS (\geq 3)</td>
<td>2.9% (1/34)</td>
</tr>
</tbody>
</table>

*The 90-day mRS was not conducted and only 180-day long-term follow-up was available. The 180-day mRS was assessed by office visit by a non-blinded assessor to the treatment.
WEB (Sequent) Concept

- Intrasaccular

- Microcatheters 0.027 for device ≤ 7 mm to 0.032 compatible for device > 7 mm

- Two layers of Nitinol mesh (216 or 288 wires)

- 3 platinum markers

- Retrievable and detachable

- CE marked
LUNA (Nfocus/Covidien) AES Concept

- The LUNA Aneurysm Embolization System (AES) is a self-expandable, round-ovoid implant with delivery system.

- The implant is made from a double layer of 72 Nitinol wire 25μ. Mesh (144 wires) secured at both proximal and distal ends and clearly marked with radiopaque markers.

- Available size 4.5mm (B) - 8.5mm (G).

- The delivery system provides for distal navigation through a commercially available (0.027 compatible) microcatheter.

- Microcatheter shaft with detachment controlled by operator activation of delivery handle.

- CE marked February 2011.
Flow Re-Direction Endoluminal Device (FRED)

- **Outer layer:**
  - 1 mm cell size
  - 16-wire weave design
- **Inner layer:**
  - 48-wire braid design
  - Attached to outer layer in helix pattern
SURPASS - Safety and Effectiveness of an Intracranial Aneurysm Embolization System for Treating Large or Giant Wide Neck Aneurysms (SCENT)

Surpass is a cobalt-chromium, low porosity (metal surface area coverage 30%), self-expanding tubular-shaped mesh structure with a high pore density (21–32 pores/mm2)
PIPELINE SHIELD

- Pipeline™ device with next generation delivery & Surface modification
Current Status

- PREMIER
- SURPASS
- FRED
- WEBIT
- LIBERTY
- ENTERPRISE II
- BARREL
- LVIS
- ANSWER
- SHIELD
- MEDINA
- BRAVO
- ARTISSE
- LEO
- SILK
- P64
- PCONUS

Years:
- 2015
- 2016
- 2017
- 2018
- 2019
- 2020
Commercially available technologies not available in US
Continued progress towards higher safety and efficacy

- FDA has carefully approved iterative and transformational technologies based on a narrow focus on safety and efficacy
- The clinicians have refined their tool kits based on pragmatic trials and shared learning
- Rigorous post-market data collection can further strengthen this relationship and allow continued delivery of effective and safe therapies for our patients