The Coaxia Neuroflo Device for Penumbra Augmentation During Acute Stroke

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Presenter Disclosure Information

Name: Mark Reisman, M.D.

Within the past 12 months, the presenter or their spouse/partner have had the financial interest/arrangement or affiliation with the organization listed below.

Nothing To Disclose
Time is Brain!
Acute Stroke Treatment

- **Recanalization:**
  - Thrombolytics, Antithrombotic
  - Mechanical, Laser, Ultrasound

- **Neuroprotectors:**
  - Anti-excitotoxic
  - Anti-inflammatory
  - Anti-apoptotic

- **Manipulation of:**
  - Temperature
  - Blood pressure
  - Oxygen levels
  - Haemodynamics/rheology

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**Graph:**
- Impact
- Minutes
- Hours
- Days

- Excitotoxicity
- Inflammation
- Peri-infarct depolarisations
- Apoptosis

Dirnagl et al. Trends Neurosci 1999
The MRI Approach

DWI abnormality = infarct

DWI/PWI mismatch = penumbra
The NCT/PCT/CTA Approach

**NCT/PCT**
- Hemorrhage
- Sensitive, Early Detection

**PCT**
- Ischemic Injury
- Quantified Infarct

**PCT**
- Perfusion Status
- rCBF
- rCBV
- MTT
- TTP

**CTA**
- Vessel Status
- Large Vessel Intracranial & Extracranial Occlusions
Surrogate Marker for Drug Effect

PCT showing decreased stroke volume with thrombolytic drug
Goal of treatment

Success = \frac{\text{Penumbra} - (\text{Final Stroke Size} - \text{Infarct})}{\text{Penumbra}}
Lausanne Stroke Index =

\[
\frac{\text{Pénombre}}{\text{Pénombre} + \text{Infarctus}}
\]

Favourable prognosis: High LSI

→ considerable improvement of NIHSS

Unfavourable prognosis: Low LSI

→ no improvement of NIHSS

Annals of Neurology 2002;51:417-432
A New Approach to Treating Cerebral Ischemia

- Globally increase cerebral perfusion via partial occlusion of descending aorta
- Utilize extensive cerebral collateral network
- Add volume and flow to the cerebral vasculature without systemic side effects
- Salvage ‘at risk’ tissue immediately (penumbra)
- Minimize risk of hemorrhagic conversion
- No intracranial access required
The Method: Partial Aortic Occlusion with NeuroFlo™

- Temporary, partial occlusion of descending aorta increases flow to carotids
- Dual balloon aortic catheter
- 9 Fr sheath; femoral access
- Balloons advanced to supra- and infra-renal
- Balloons sequentially inflated to 70% luminal occlusion
- 45 minute inflation/treatment

DESIGN / BENEFITS

- Dual balloons and pressure measurements create stable, controllable occlusion
- Cerebral perfusion increases 30% and persists beyond balloon deflation
- Unique, supra- & infra-renal design preserves renal perfusion
Pre-Clinical Proof of Concept: Hemodynamics / Flow

Swine Hemodynamics at 70% occlusion;  n=8

- CBFV increases average >30%
- Minimal systemic effect on MAP, HR and CO

n=8
T=36.1-37.1°C
paCO2 = 27-30 mmHg
Natural Progression of Infarct in Stroke

CoAxia Non-treatment Patient Example (010-007)

<table>
<thead>
<tr>
<th>% Change of summary map (Baseline vs Follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total area</td>
</tr>
<tr>
<td>- 5%</td>
</tr>
</tbody>
</table>
NeuroFlo Effect on Stroke Patient

Pre-NeuroFlo

Post-NeuroFlo

% Change of summary maps (Pre vs Post-NeuroFlo)

<table>
<thead>
<tr>
<th>Total area</th>
<th>“At risk”</th>
<th>“Infarct”</th>
</tr>
</thead>
<tbody>
<tr>
<td>- 54%</td>
<td>- 78%</td>
<td>- 37%</td>
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</table>

“At risk” penumbra resolves to normal
Clinical History

- **Pre-Clinical Studies**
  - Rat, canine, porcine models; various studies
  - Validated perfusion increase w/o systemic effects; optimized design

- **Phase I Stroke** (focus on safety)
  - Conservative, incremental balloon inflation
  - 9 US and European centers; 17 patients

- **Phase II Stroke** (focus on outcome / perfusion)
  - Several minute inflation to target occlusion
  - 5 US centers; 12 patients

- **Phase I Vasospasm** (focus on safety and outcome)
  - Single center (Buenos Aires)
  - Treatment evolved during the study; 24 patient
# Human Feasibility Summary: Ischemic Stroke

<table>
<thead>
<tr>
<th></th>
<th>Total Treatment (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
</tr>
<tr>
<td>Median NIHSS baseline</td>
<td>9.0</td>
</tr>
<tr>
<td>Mean time to treat (hrs)</td>
<td>7.6 ± 2.2</td>
</tr>
<tr>
<td>NIHSS reduction ≥ 3 peri-procedural</td>
<td><em><em>61% (17/28</em>)</em>*</td>
</tr>
</tbody>
</table>

| **24 hours**                     |                        |
| NIHSS reduction ≥ 3 or resolution (24 hr) | **62% (16/26**) |
| NIHSS 0-2 (24 hr)                | **27% (7/26**)         |
| Median NIHSS (24 hr)             | 5.0                    |
| Median NIHSS 30 days             | 5.0                    |

| **30 days**                    |                        |
| % reduction in median NIHSS    | 44%                    |
| mRs ≤ 1 30 days               | **37% (10/27**)        |

*1 patient sedated peri-procedurally

** 2 patients sedated plus 1 missing data point at 24 hrs

*** 2 patients died (unrelated to procedure)
## Human Feasibility Summary: Cerebral Vasospasm

<table>
<thead>
<tr>
<th>Peri-procedural Neurological Improvement</th>
<th>Baseline NIHSS</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean NIHSS reduction</td>
<td>-3.4</td>
</tr>
<tr>
<td></td>
<td>NIHSS reduction ≥ 2</td>
<td>71%</td>
</tr>
<tr>
<td></td>
<td>NIHSS reduction ≥ 4</td>
<td>43%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Perfusion Augmentation</th>
<th>TCD</th>
<th>82%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Angiogram</td>
<td>67%</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>30 Day Neurological Improvement</th>
<th>NIHSS ≤ 2</th>
<th>13/16 (81%)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Modified Rankin ≤ 2</td>
<td>9/10 (90%)</td>
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</table>
## Adverse Events

<table>
<thead>
<tr>
<th>Type of events</th>
<th># patients (%)</th>
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<tbody>
<tr>
<td>No adverse events</td>
<td>9/29 (31%)</td>
</tr>
<tr>
<td>Only non-serious events</td>
<td>12/29 (41%)</td>
</tr>
<tr>
<td>Serious, non-fatal events</td>
<td>6/29 (21%)</td>
</tr>
<tr>
<td>Deaths</td>
<td>2/29 (7%)</td>
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### All events adjudicated by Safety Review Committee:

- No deaths considered to be device- or procedure-related
- 1 serious AE considered procedure-related (groin hematoma)
- 8 non-serious AEs considered procedure-related:
  - 5 groin bleed / hematoma
  - 1 allergic reaction
  - 1 vaso-vagal reaction
  - 1 mild neurologic deterioration
Feasibility Results Have Led to Pivotal Trial

**SENTIS Stroke Trial**
- Pivotal, randomized trial for ischemic stroke is FDA approved and ongoing
- NeuroFlo vs. medical management
- Up to 10 hours post symptom onset
- 90 day neurological recovery as primary endpoint
  - pre and post Tx perfusion imaging data – secondary endpoint
- 40 sites
  - 25 currently in process; seeking up to 15 additional sites
Conclusion

- An interventional treatment for stroke victims beyond the 3 hour tPA window (up to 24 hours if penumbra?)

- Wide availability due to ease of use and early data on safety

- Role for interventional cardiology in acute stroke

*We hope to have more data and acute outcomes to present at TCT 2006*