Revascularization in Acute Stroke

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TOSHIBA STROKE RESEARCH CENTER
Conflicts

• EKOS – med advisor
• Primus Medical – med advisor
• Sylva Medical - ?
• Toshiba Medical Systems - research grants
FIBRINOLYTICS (INTRAVENTOUS)

tPA for acute ischemic stroke. NINDS trial

624 patients with ischemic stroke within 3 hours

Intravenous tPA (0.9 mg/kg) vs placebo

Follow-up 3 months

Improvement at 24 h
- tPA: 47%
- Placebo: 39%

Favorable outcome at 3 m (Rankin scale)
- tPA: 42%
- Placebo: 27%

Intracerebral hemorrhage
- tPA: 6.4%
- Placebo: 0.6%

Death at 3 m
- tPA: 17%
- Placebo: 21%
FIBRINOLYTICS (INTRA-ARTERIAL)

Prolyse in Acute Cerebral Thromboembolism (PROACT) I

54 patients with occlusion of middle cerebral artery within 6 hours of onset

Intraarterial rPro UK (6mg) vs placebo

- Recanalization: 58% vs 14.3%
- Hemorrhagic transformation: 15.4% vs 7.1%

Follow-up: 3 months
FIBRINOLYTICS (INTRA-ARTERIAL)

Prolyse in Acute Cerebral Thromboembolism (PROACT) II

180 patients with occlusion of middle cerebral artery within 6 hours of onset

Intraarterial Prourokinase (9mg) vs placebo

Follow-up
3 months

Recanalization
Prourokinase 66%
Placebo 18%

Hemorrhagic transformation
Prourokinase 10%
Placebo 2%

Favorable outcome
Prourokinase 40%
Placebo 25%
Time vs bleeding
Radiographic Evaluation

- CT head
  - Rapid evaluation for ICH
  - Hypodensity < 1/3 effected hemisphere
- Cerebral perfusion
  - MRI diffusion perfusion
  - CT perfusion
  - CT angiogram
Triage

- 0-3 hrs NIHSS<10 IV tPA
  - Unless angular artery, speech
- 0-3hrs NIHSS>10 IA lysis +/- mechanical
- 3-6 IA lysis +/- mechanical
- Over 6 hours guided by perfusion imaging
- Posterior circulation
  - Will treat up 12 – 24 hours
  - MRI dependant
CONFLICT
OF
KNOWLEDGE VS EVIDENCE
82 yo WM, NIHSS 18, Crescendo TIA, hemiparesis unchanged for 30 hours
Cerebral Angiogram
L CAS
48 hours post
Outcome

- Remarkable improvement
  - NIHSS 4 at 24h
  - NIHSS 1 at DC minimal speech problems
CT perfusion Post Rx
Don’t Try This at Home
Pre Diamox

Post Diamox
CBV

Pre Diamox

Post Diamox
Hemispheric Ischemia
Pre Treatment
**Technique**

- Time is Brain
- Local anesthesia
- General anesthesia
- 6 F guide sheath is placed in the femoral artery
- Arch
- Selective angiogram
Technique (continued)

- Target SL-10
- A microcatheter angiogram
- Infusion thrombolytic of choice (retavase 1 U aliquot, max 4 U)
Be Patient, Let Drug Work
Can Take 60 min
Can’t Wait - Snare
Target Coil Retriever
72 yr Black female
Acute Hemiplegia
72 yr female
72 yr female post angioplasty
Concentric Retriever System

Thrombus Retriever X5
Basilar Case Study
31 year old male
Baseline NIHSS Score - 10
Symptom Onset to Treatment - 4h 30min
Basilar Case Study

NIHSSS 24 hours  0
30 days        0
mRS            90 days  0
**MERCI® Trial Summary**

121 Patients Enrolled

- 7 Patients Not Treated (Balloon Guide placed)

114 Patients Treated

114 Patients with Revascularization Data

- 30 Day Follow-Up
  - mRS n = 109
- 90 Day Follow-up
  - mRS n = 98

114 Patients with Revascularization Data

- 30 Day Follow-Up
  - mRS n = 109
- 90 Day Follow-up
  - mRS n = 98
Baseline NIH Stroke Scale Scores

(n=113*)

*Baseline NIHSS not recorded for 1 Patient
MERCI TRIAL

• Symptoms 0-8 hours
• Not just MCA and Vert (proact)
• Toughest lesions - carotid T
Occlusion Location/Vessels Treated
(n=114)

- MCA (65) 57%
- Isolated ICA (22) 19%
- ICA T (15) 13%
- VB (12) 11%
Successful Revascularization by Vessel

- ICA and ICA T (ICA/MCA/ACA) occlusions were combined into the ICA group

Overall (61/114) 54%
ICA* (21/37) 57%
MCA (33/65) 51%
Vert Bas (7/12) 58%

* ICA and ICA T (ICA/MCA/ACA) occlusions were combined into the ICA group
Device-Related Complications

3.5% (4/114)

Two Dissection/Vessel Perforation:

- Patient had evidence of a bleed on CT following treatment with the Retriever, snare and balloon angioplasty
- Patient had evidence of contrast extravasations on angiography following treatment with the Retriever
- Merci Retriever tip detached in both patients
Hemorrhage Rate
Within 24 Hours

• Symptomatic Hemorrhage Rate
  – Retriever Treatment Alone 8% (9/114)
  – Retriever Plus (IA lytic/snare/etc.) 5% (5/97)
  – Retriever Plus (IA lytic/snare/etc.) 24% (4/17)

• Symptomatic Hemorrhage by Clot Location
  – Middle Cerebral (n = 65) 5% (3/65)
  – ICA/ICA-T (n=37) 16% (6/37)
  – Vertebrobasilar (n=12) 0%

Asymptomatic Hemorrhage 29% (33/114)
90-Day Modified Rankin Score

Revascularized vs. Unrevascularized

- Recan:
  - mRS 0-2: 53%
  - mRS 3-5: 16%
  - Death: 31%
  - Total: n= 51

- Non-Recan:
  - mRS 0-2: 6%
  - mRS 3-5: 32%
  - Death: 62%
  - Total: n= 47
90-Day Modified Rankin Score

Revascularized vs. Unrevascularized

<table>
<thead>
<tr>
<th>Score</th>
<th>Recan</th>
<th>Non-Recan</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRS 0</td>
<td>14%</td>
<td>4%</td>
</tr>
<tr>
<td>mRS 1</td>
<td>10%</td>
<td>32%</td>
</tr>
<tr>
<td>mRS 2</td>
<td>16%</td>
<td></td>
</tr>
<tr>
<td>mRS 3-5</td>
<td>29%</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>31%</td>
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n= 51
n= 47
# MERCI® Primary Endpoints

<table>
<thead>
<tr>
<th></th>
<th><strong>Revascularization</strong>*</th>
<th><strong>Serious Complications</strong> (Device Related)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total n=114</td>
<td>53.5% (61)</td>
<td>3.5% (4)</td>
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<tr>
<td></td>
<td>p &lt; 0.0001†</td>
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<tr>
<td></td>
<td>95% Confidence Interval: 44.4% to 62.7%</td>
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† p-value for showing superiority over a 18% success rate using the exact binomial test

* Revascularization defined as TIMI II/III flow achieved in the target vessel(s) with the Retriever alone (no adjunctive treatment).
Problems

- Rotate Device to Get it to engage clot
- Radial outward force
Primus

Device straightened
Actuated, for site access

Device deployed
Snare deployed for clot removal
Primus

- Clot model invivo
- Not yet in humans
- Promising device
- Spring effect

Captured clot
TIME TO REVASCULARIZATION
The EKOS 2.5Fr SV Microcatheter Delivery Tip
EKOS Ultrasound Infusion Catheter
Phase I Ischemic Stroke Clinical Data

- N = 30
- Anterior circulation < 6 hours
- Posterior circulation < 24 hours
- UK, rPA, tPA

Results
- No adverse events related to EKOS catheter
- Avg time to recan = 46min*

*Mahon, et.al, AJNR Mar 2003
## Recanalization Result

<table>
<thead>
<tr>
<th>All MCA Occlusions</th>
<th>EKOS* 11 patients</th>
<th>PROACT II** 104 patients</th>
<th>EMS 10 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI 3 @ 1 hr</td>
<td>27%</td>
<td>4%</td>
<td>10%*</td>
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*EKOS = All anterior occlusions

** PROACT II = MCA occlusions only
Complete Recanalization

Complete Recanalization
All Anterior Segments

<table>
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<tr>
<th>Treatment Time (min.)</th>
<th>PROACT II TIMI 3</th>
<th>EMS TIMI 3</th>
<th>EKOS TIMI 3</th>
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<tbody>
<tr>
<td>15</td>
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* Furlan, et. al., JAMA, 1999; 282 (21):2003-11
## Comparisons of Carotid “T” Occlusion Results

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<th>EMS (5)**</th>
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<td><strong>mRS ≤ 2 (good outcome)</strong></td>
<td>29%</td>
<td>0%</td>
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<td><strong>NIHSS ≥ 50% decrease</strong></td>
<td>43%</td>
<td>0%*</td>
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<td>Sx ICH</td>
<td>13%</td>
<td>20%</td>
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1. IMS II (on-going): 0-3 h. window, comparable to NINDS
   - Expands 0-3 h. window market
   - IMS I Trial performed with standard microcatheter
   - Providing direct comparison for EKOS
IMS II Status
Sept 27, 2004

• 13 sites enrolling
  – Goal: 18 centers

• No. patients enrolled: 42
  – No. IV only 14
  – No. IA treated (67%) 28

• Goal: 70
# AJNR Comparisons of Carotid “T” Occlusion Results

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Early indicator of IMS II flow improvement
Tomsick, et. al., 2004 World Stroke Conference

- Angiograms were performed every 15” during procedure to monitor for recanalization

- 62 available angiographic data points available for MicroLysus Catheter and 35 for standard microcatheter thrombolysis
  - 53% MicroLysus efficacy
  - 34% standard catheter efficacy (p=0.07)
**EPAR Emulsionwire Microcatheter**

- 3F windowed microcatheter
- Used with standard 0.014” guidewires
- Graded flexibility
- Wire reinforced proximal segment
- Highly flexible distal 3cm
- Hydrophilic coating
Transient Micro-bubble and Shockwave Generation

Stress Wave

Optical Fiber
Conclusions

• Time is Brain
• Pharmacologic thrombolysis useful
• Mechanical adjuncts can help open vessels faster
• No reimbursement
• Labor intensive patients
• BUT REWARDING
• Team Approach most successful
WHO SHOULD DO THIS?

• Different than coronary intervention, but close
• Dedicate your life to treatment cerebral ischemia

WELCOME TO THE FINAL FRONTIER