ENDOVASCULAR TREATMENT
OF STROKE

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OUTLINE

• Stroke Center concept
• Treatment Algorithm (VUMC)
• Intra Arterial techniques
• Research and Future Horizons

675km of veins, arteries and capillaries...
VUMC STROKE TEAM

• Nurse Coordinator
• Critical Care/Nursing
• Physical, Occupational, Speech Therapies
• Rehabilitation Medicine
• Neurology
• Radiology
• Neurosurgery
Acute Stroke Algorithm

**HOURS**

0 3 4.5 6 8 12

**Stroke Suspected**
- **Transport to ED**
- **Stroke Team Alert**
  - CT/A Ordered
  - Labs Drawn

**CT/A, MRI..**
- **Ischemic**
  - **IV rt-PA candidate**
    - **IV rt-PA**
      - **Large Vessel Clot?**
        - **Yes**
          - **IA Therapy**
        - **No**
          - **Medical Treatment**

**Bleed**

**Hemorrhage Algorithm**
- **Large Vessel Clot?**
  - **Yes**
  - **No**

(Singer, 2010)
VUMC STROKE TEAM

Notification System (Endovascular perspective)...

Code Stroke pager

Large Vessel Clot

No Large Vessel Clot

Interventional Stroke pager
Endovascular Techniques

- Intra Arterial Thrombolysis
- Mechanical Retrieval
- Suction Thrombectomy
- Angioplasty/Stenting
- Other
Acute Stroke Intervention

Access

bifemoral prep

single wall puncture technique

6 Fr. Shuttle Sheath (90cm)

.035” Bentson wire
Selective Catheterization

5 Fr. Vertebral catheter (110cm)

5 Fr. Vitek catheter (prn)

.035” angled glide wire (stiff)
Acute Stroke Intervention

Clot definition/mechanical disruption

.010” microcatheter (SL-10)

.014 microwire (Transend Platinum)

t-PA/ Reopro

(10mg)
Secondary disruption (prn)

Penumbra System

Merci

balloon/stent
ENDOVASCULAR PHOTO ACOUSTIC RECANALIZATION LASER (EPAR)

- fiberoptic filament to the tip of the catheter
- clot absorption converts photo to acoustic energy emulsifying clot inside catheter
- recanalization 44% with adjuvant therapy, 15% device alone
- approved for further trials but funding was lost
ANGIOJET SYSTEM

• saline jets back into catheter creating a low pressure zone inducing suction

• approved for dialysis grafts, coronary arteries, saphenous grafts, and peripheral vessels

• Thrombectomy in Middle Cerebral Artery Embolism (TIME) trial, 22 patients/3 perforations. Trials stopped.

Courtesy of Possis Medical, Inc, Minneapolis, Minn.
EKOS ultrasound
(Ultrasound Thrombolytic Infusion Catheter)

• ongoing study: Interventional Management of Stroke Trial (IMS III)

• ultrasound increases clot permeability

• recanalization enhanced with IA-tPA

all Courtesy of EKOS Corporation, Bothell, Wash.
MERCI RETRIEVAL SYSTEM

- FDA approved 2004
- MERCI trials consistently demonstrate significantly better outcomes with revascularization
- MR Rescue trial stratifies outcome to presence of penumbra on MRI/CTP...

all Courtesy of Concentric Medical, Inc, Mountain View, Calif.

THE PENUMBRA SYSTEM

- aspiration to remove clot
- FDA approved 2007
- recanalization rate: 81.6%
- symptomatic hemorrhage rate: 11.2%

Courtesy of Penumbra, Inc., Alameda, Calif.

STENT-ASSISTED RECANALIZATION IN ACUTE STROKE

• technically feasible

• self expanding v. balloon mounted

• used when lytics and other techniques fail..

• may represent primary therapy in the future
Endovascular technique

1. Clot definition
2. Wire disruption/IA tPA
   - long/short segment
   - short segment
   - Suction Thrombectomy (Penumbra)
   - Mechanical retrieval (MERCI)
3. Stent Assisted Recanalization
**RECANALIZATION**

- tPA potentiates blood brain barrier disruption hastening vasogenic edema and neurotoxicity.

*Graph showing recanalization rates with and without tPA for different procedures: PROACT II 1999 (14.3%), MERCI 2005 (60%), Multi-MERCI 2008 (68%), Penumbra 2008 (82%).

*Graph indicates that adding tPA increases the recanalization rate for each procedure.*

*tPA potentiates blood brain barrier disruption hastening vasogenic edema and neurotoxicity.*
Symptomatic ICH (IA therapy)

- PROACT II: 15.4% (1999)
- Multi Merci: 9.8% (2008)
- Penumbra: 11.2% (2008)
MULTI MERCI CLINICAL OUTCOME

Recanalized | No Recanalization

Good Outcome: 49% (9.6%) | 90 Day Mortality: 25% (52%)
61 y male

aphasia, right hemiparesis @4pm
61 y male

aphasia, right hemiparesis @4pm
61 y male

aphasia, right hemiparesis @4PM
Uh-oh...
The Galilean Telescope

Spherical plano-convex objective lens

Adjustable tube for focusing

Spherical plano-concave ocular lens

Stopped down due to lens extremities being unusable

Overall length approx 5 feet

The Good
Cheap, simple and easy to produce.
Tolerant of bad lenses

The Bad
Dull image due to poor aperture
Narrow field of view limits magnification <30x
Spherical aberration
Doesn't get much better even if lenses do
Patient Outcomes With Endovascular Embolectomy Therapy for Acute Ischemic Stroke: A Study of the National Inpatient Sample: 2006 to 2008
Waleed Brinjikji, Alejandro A. Rabinstein, David F. Kallmes and Harry J. Cloft

### Table 1. Outcomes

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Endovascular Clot Retrieval</th>
<th>Endovascular Clot Retrieval + Thrombolysis</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>2362</td>
<td>1502</td>
<td></td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>64.8 (34.2)</td>
<td>66.1 (35.4)</td>
<td>0.25</td>
</tr>
<tr>
<td>No. (%) female</td>
<td>1226 (51.9)</td>
<td>796 (53.0)</td>
<td>0.51</td>
</tr>
<tr>
<td>Percent white</td>
<td>76.8</td>
<td>73.9</td>
<td>0.08</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharge to long-term care, no. (%)</td>
<td>1246 (52.7)</td>
<td>737 (49.1)</td>
<td>0.03</td>
</tr>
<tr>
<td>In-hospital death, no. (%)</td>
<td>560 (23.7)</td>
<td>380 (25.3)</td>
<td>0.25</td>
</tr>
<tr>
<td>Morbidity and mortality, no. (%)</td>
<td>1806 (76.4)</td>
<td>1117 (74.4)</td>
<td>0.14</td>
</tr>
<tr>
<td>Mean length of stay (SD)</td>
<td>10.0 (17.8)</td>
<td>10.9 (21.5)</td>
<td>0.15</td>
</tr>
<tr>
<td>Intracranial hemorrhage, no. (%)</td>
<td>366 (15.5)</td>
<td>300 (20.0)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Gastrointestinal hemorrhage, no. (%)</td>
<td>68 (2.9)</td>
<td>39 (2.6)</td>
<td>0.55</td>
</tr>
<tr>
<td>Gastrostomy, no. (%)</td>
<td>360 (15.3)</td>
<td>195 (13.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>Tracheostomy, no. (%)</td>
<td>184 (7.8)</td>
<td>134 (8.9)</td>
<td>0.25</td>
</tr>
<tr>
<td>Mean Charlson Comorbidity Index (SD)</td>
<td>5.3 (5.2)</td>
<td>5.2 (5.2)</td>
<td>0.27</td>
</tr>
</tbody>
</table>
PERSPECTIVE...

• Acute stroke therapy is beneficial when properly orchestrated

• Intra Arterial techniques are beneficial for treating large vessel occlusions

• Intra Arterial tPA improves recanalization rates when coupled with mechanical techniques

• tPA is neurotoxic...
Blood–brain barrier permeability and tPA–mediated neurotoxicity

Rami Abu Fanne, Taher Nassar, Sergei Yarvoo, Anwar Rayan, Itschak Lamensdorf, Michael Karakoveski, Polianski Vadim, Mahmud Jammal, Douglas B. Cines, Abd Al-Rooi Higazi

Department of Clinical Biochemistry, Hebrew University - Hadassah Medical Center, Jerusalem, Israel
Department of Pathology and Laboratory Medicine, University of Pennsylvania, SIBA Stellar-Chance, 422 Curie Boulevard, Philadelphia, PA 19104, USA
QRC-Queeni Research Center, Baka El-Garbiah, Israel
Thrombotech Ltd, Ness Zona, Israel
Pharmaseed Ltd, Ness Zona, Israel

Tissue-type plasminogen activator induces opening of the blood-brain barrier via the LDL receptor–related protein

Manuel Yepes, Maria Sandkvist, Elizabeth G. Moore, Thomas H. Bugge, Dudley K. Strickland, and Daniel A. Lawrence

Department of Vascular Biology, Holland Laboratory, American Red Cross, Rockville, Maryland, USA
Department of Neurology, Georgetown University Hospital, Washington, DC, USA
Department of Biochemistry, Holland Laboratory, American Red Cross, Rockville, Maryland, USA
Proteases and Tissue Remodeling Unit, Oral and Pharyngeal Cancer Branch, National Institute of Dental and Craniofacial Research, NIH, Bethesda, Maryland, USA
OTHER AGENTS...

• Desmoteplase- doesn’t promote neuronal injury in animal model, more fibrin specific, potentially safer, Phase III trials underway..

• Tenecteplase- greater fibrin specificity than tPA, recent trial terminated for slow enrollment, question is still unanswered

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Fibrinogen depleting agents-
supportive evidence lacking...

• Ancrod- pit viper venom

• Batroxobin

Lancet 2006; 368: 1871–78.

Stroke 2010; 41; 707-711
OTHER AGENTS...

Glycoprotein IIb/IIla inhibitors
(limit platelet aggregation)

Eptifibatide (Integrillin)  
Abciximab (ReoPro)

IV/IA dosages still under investigation...
THE NEUROVASCULAR UNIT

- Endothelial cell lining
- Basement membrane
- Pericytes
- Glial cells
Blood Brain Barrier in Acute Ischemia

- disrupted due to endothelial cell death and capillary damage
- recruitment of disautoregulated channels
- biphasic pattern.. 2h and 4-6h
- tPA mediated disruption
1. doesn’t appear to prevent the opening of the BBB
2. free radical scavenger, binds free fatty acids/ metal ions
3. inhibition of lipid peroxidation
Albumin ameliorates tissue plasminogen activator-mediated blood-brain barrier permeability and ischemic brain injury in rats.

Tang J, Li YJ, Mu J, Li Q, Yang DY, Xie P.
Department of Neurology, The First Affiliated Hospital, Chongqing Medical University, Chongqing, China.

Abstract
OBJECTIVE: Tissue plasminogen activator (tPA) may aggravate ischemic neuronal damage after focal cerebral ischemia and increase blood-brain barrier permeability. Human serum albumin has neuroprotective effects on ischemic stroke. However, whether albumin can attenuate the deleterious effects of tPA is yet unknown. METHODS: In the present study, we attempted to determine the effects of albumin on cerebral injury and blood-brain barrier disruption induced by middle cerebral artery occlusion for 2 hours followed by 24 hours of reperfusion and tPA. RESULTS: We found that infarct volume in rats which received saline and tPA was 35.6 +/- 3.8% (mean +/- SEM) and 50.9 +/- 4.5%, respectively. There was significant difference between the two groups (p<0.01). The infarct volume in rats that received tPA with albumin was significantly decreased to 29.2 +/- 3.3% (p<0.05), compared with tPA-only-treated group. Combination therapy using tPA with albumin also improved neurological deficits and reduced brain edema significantly (p<0.05). Relative to tPA-treated group, rats that received combination therapy using tPA with albumin had significantly reduced blood-brain barrier permeability, evaluated by quantitation of Evans blue leakage (p<0.05). CONCLUSION: In acute ischemic stroke, combination therapy using tPA with albumin can attenuate the deleterious effects of tPA.
IHC staining
BARRIER TRANSPORT

- Paracellular aqueous pathway: Water-soluble agents
- Transcellular lipophilic pathway: Lipid-soluble agents
- Transport proteins: Glucose, amino acids, nucleosides, Vinca alkaloids, Cyclosporin A, AZT
- Receptor-mediated transcytosis: Insulin, transferrin
- Adsorptive transcytosis: Albumin, other plasma proteins
Evans blue dye (2%, 2ml/kg), IV
(5min prior to BBBD)

courtesy Edward Neuwelt, MD
Summary...

• Stroke teams can offer improved outcomes if properly organized

• Intra Arterial therapy with and without lytics is superior to IV lytics for large vessel clot

• tPA is neurotoxic, mechanical clot disruption and evacuation decreases the overall dose administered

• New lytics aim to decrease neurotoxicity

• BBB manipulation shows promise in reducing infarct volume
Thanks!

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