Public Health Impact of Stroke

- 4th leading cause of death in US, #2 worldwide
- #1 cause of Disability! Most prevalent neurologic condition, most common discharge diagnosis to nursing homes and rehab
- 5 million Americans currently living with the effects of stroke
- > $70 Billion Annually in US in 2012
- WHO (2002) 15.3 million stroke and 5.5 million deaths per year
- WNY is 25% higher than national rate with one regional zip code at 200%

Classification of Stroke

- Ischemic (80%)
  - ICAD
  - Lacunar
  - Carotid Occlusive disease (25%)
- Hemorrhagic (20%)
  - Intracerebral hemorrhage
  - Subarachnoid hemorrhage
Stroke Treatment Options in 2013

• ASA within 24-48 hrs is recommended
• IV rtPA in appropriate patients (<3-4.5 hours)
• IA thrombolysis: an option in major MCA stroke patients <6 hours if not IV rtPA candidates (dose not determined and NOT FDA approved)
• Mechanical thrombectomy devices can be offered in carefully selected patients and should continue to be studied in randomized trials

IV tPA and Large-Vessel Occlusion (35-40% of Ischemic Stroke)

• Clinical response to thrombolysis is influenced by the site of occlusion
• Rate of recovery from IV tPA by occlusion
  • 33% for distal MCA occlusion
  • 15% for proximal MCA occlusion
  • 0% with ICA-T occlusions
• Mortality of LVO

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>53%</td>
</tr>
<tr>
<td>MCA</td>
<td>27%</td>
</tr>
<tr>
<td>Basilar Artery</td>
<td>89-90%</td>
</tr>
</tbody>
</table>

AHA/ASA Stroke Guidelines Stroke 2013
What’s A Retrievable Stent?

2015: Endovascular vs Best Medical Therapy

- 5 major studies evaluating the role of endovascular therapy in stroke treatment
  - MR CLEAN
  - EXTEND-IA
  - ESCAPE
  - SWIFT PRIME
  - REVASCAT
- Endovascular Therapy within 6 hours, NIHSS >7
- ALL 5 trials stopped because of significant benefit in the Endovascular arms
SWIFT PRIME
Medtronic-US

• Proximal anterior circulation occlusion
• Randomized patients who received IV-tPA to undergo endovascular therapy with Solitaire or continue receiving IV-tPA alone

• RESULTS:
• Endovascular showed improvement in mRS at 90 days
  • 60.2% vs 35.5%, P<0.001
• No significant differences in mortality or the occurrence of symptomatic ICH
• NNT = 4
Future of Stroke Imaging

The greatest challenge is to show that advanced neuroimaging, used as a biomarker to select patients for reperfusion therapy (in an extended time window), improves patient outcomes.

Advanced Imaging
Advanced Imaging

- Dynamic Studies capturing one cycle of the full transit of a contrast bolus through the tissue
- Physiologic Imaging: Transit Time, Blood Flow, Blood Volume
  - Parenchyma (Capillary phase NOT large vessels)
  - Intravascular surrogate for Intracellular process (not biological, Xenon)
- Ability to distinguish core (infarcted tissue) from penumbra (salvageable tissue)
- Individualize stroke treatment

Buffalo Protocol

- NIHSS and CTSS (CTA head and neck and CTP)
  - Intervention based on perfusion parameters, clinical exam, and Time of Onset
  - MRI if no obvious deficit on CTP
- Post intervention CT/ LCI /MRI GRE
- CTP POD #1, NIHSS at 24hrs
- MRI at 3-5 days
- Discharge disposition, NIHSS and mRS
- CT or MRI at 1-3 months, mRS and NIHSS
- All patients collected in prospective registry
Neuro One Protocol

- Perfusion
  - 50 cc at 5cc/s, 19 volumes
  - Equivalent to 1.5 NCCT Rad Dose
CT Perfusion Models (4 min processing time)

- Maximum Slope
- Deconvolution
  - Parametric $R(t)$ has specific distribution
  - Non-parametric – $R(t)$ is an unknown
    - Transform – Fourier
    - SVD
  - Delay Invariant Deconvolution (SVD+)
- Bayesian
CT Perfusion Parameters

- CBF mL blood/100g brain tissue/min
- CBV mL blood/100g brain tissue
- Mean transit time (MTT)
- Time to peak (TTP)
- Delay Map

<table>
<thead>
<tr>
<th>Condition</th>
<th>rTTP</th>
<th>rCBF</th>
<th>rCBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Art stenosis/ocl with comp</td>
<td>Prolongd</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Oligemic</td>
<td>Prolongd</td>
<td>&gt; 60%</td>
<td>&gt; 80%</td>
</tr>
<tr>
<td>Tissue at risk</td>
<td>Prolongd</td>
<td>&gt; 30%</td>
<td>&gt; 60%</td>
</tr>
<tr>
<td>Dead tissue</td>
<td>Strong Prolongd</td>
<td>≤ 30%</td>
<td>&lt; 30-40%</td>
</tr>
</tbody>
</table>

Tomovsk V, Mager 2000, Koenig 2001

Cerebral Perfusion

- CBF = 50-60 mL/100 g/min, normal
- CBF = 35: protein synthesis ceases, oligemic stage, tissue can survive.
- CBF = 20: disturbance of synaptic transmission, loss of function (still viable)
- CBF = 10: irreversible cell death
Heiss and Rosner (1983)

Reliability?
• Penumbra/Core – volume mismatch
• Clinical Exam/Core – appropriate for patient selection
Defuse 3- Thrombectomy for Stroke at 6-16 hours with selection by Perfusion Imaging

- NEJM 2018: 378:708-18
- Multicenter, randomized, MCA or ICA, Primary outcome mRS at 90 days
- Less than 70 cc core, and Ratio of >1.8

**RESULTS:**
- Terminated Early for efficacy (92 endo and 90 BMT)
- mRS 0-2 (45% vs 17%)
- 90 day mortality (14% vs 26%)
- No sign difference in sICH (7% vs 4%)

**DAWN**
- Age: > 18
- NIHSS: >= 10
- Vessel: ICA/M1
- LSN: 6-24
- CTP Core: <20, <30, <50
- CTP Ratio: none

**DEFUSE 3**
- Age: 18-90
- NIHSS: > 6
- Vessel: ICA/M1
- LSN: 6-16
- CTP Core: < 70
- CTP Ratio: > 1.8
Clinical History

- 50 yo who woke up with left hemiplegia, dysarthria, and facial droop.
- NIHSS = 16.
- PMH - Anxiety disorder, tobacco dependence, alcohol dependence
Deployment of TREVO retrieval device

1st pull of the microcatheter with the retrieval device
Total intervention time ~20 min

Complete recanalization TIMI 3 after 1 pull
Clinical History

• 75 yo WM last seen normal at 10 pm,  ? Issues at 2 am, awoke thrashing at 4 am with Right gaze preference and left HP
• NIHSS 18

• in the angio suite – the patient could lift his Rt arm antigravity, improved gaze, NIHSS 16 to 5 immediately

• POD#1 NIH -3
• POD#2– NIH -0
Future Advanced Imaging Considerations

- Improvements in validation studies and/or deterministic models (Xenon?)
- Define Futility Thresholds for grey and white matter
- Validation of Semi automated methods across vendor platforms and modalities
- Applications to other organ systems
- Generation of Physiologic Maps from Angiography
Speed to Reperfusion is Critical

- Even though physiologic imaging allows more people to be offered treatment at later time points, realize...
- IT IS STILL A RACE
- Streamlining Stroke triage from ambulance to CTP has helped tremendously