Imaging Criteria for Selection of Acute Stroke Patients: Is ASPECTS enough?

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Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Toshiba – Honorarium</td>
</tr>
<tr>
<td></td>
<td>Medtronic - Honorarium</td>
</tr>
</tbody>
</table>
Improved Recanalization Rates with New Technology

Saver JL, Stroke 2013;44:270-277
What’s a retrievable stent, anyway?
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
- EVT within 6 hrs, NIHSS >7
- ALL 5 trials stopped because of significant benefit in the Endovascular arms
<table>
<thead>
<tr>
<th></th>
<th>Nat Hx</th>
<th>NINDS</th>
<th>MR CLEAN</th>
<th>EXTEND-IA</th>
<th>ESCAPE</th>
<th>SWIFT PRIME</th>
<th>REVASCAT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong># pts</strong></td>
<td>178</td>
<td>333</td>
<td>500</td>
<td>70</td>
<td>315</td>
<td>196</td>
<td>206</td>
</tr>
<tr>
<td><strong>Median NIHSS</strong></td>
<td>16-20</td>
<td>14</td>
<td>17</td>
<td>13</td>
<td>16</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td><strong>TICI 2b-3</strong></td>
<td></td>
<td></td>
<td>58.7%</td>
<td><strong>86%</strong></td>
<td>72.4%</td>
<td><strong>88%</strong></td>
<td>65.7%</td>
</tr>
<tr>
<td><strong>sICH</strong></td>
<td>6%</td>
<td></td>
<td>7.7%</td>
<td>0%</td>
<td>3.6%</td>
<td>0%</td>
<td>4.9%</td>
</tr>
<tr>
<td><strong>mRS (0-2)</strong></td>
<td>&lt;5%</td>
<td>39%(vs 26%)</td>
<td>32.6%</td>
<td><strong>72%</strong></td>
<td>53%</td>
<td><strong>60%</strong></td>
<td>43.7%</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td>80%</td>
<td>17%</td>
<td>18.9%</td>
<td>9%</td>
<td>10.4%</td>
<td>9.2%</td>
<td>18.4%</td>
</tr>
<tr>
<td>Imaging Selection Criteria</td>
<td>MR CLEAN</td>
<td>EXTEND-IA</td>
<td>ESCAPE</td>
<td>SWIFT PRIME</td>
<td>REVASCAT</td>
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<td></td>
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<tr>
<td>Small core</td>
<td>Not required</td>
<td>RAPID perfusion infarct $&lt;70$ mL (relCBF$&lt;30%$ threshold)</td>
<td>ASPECTS score $6-10$</td>
<td>ASPECTS score $6-10$ on NCCT or DWI, RAPID perfusion infarct $&lt;50$ mL (relCBF$&lt;30%$ threshold)</td>
<td>ASPECTS score $&gt;6$ on NCCT, ASPECTS score $&gt;5$ on DWI (NCCT ASPECTS $&gt;8$ for age $80-85$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penumbra</td>
<td>Not required</td>
<td>Target mismatch: RAPID perfusion ischemic core mismatch ratio $&gt;1.2$, absolute mismatch $&gt;10$ mL ($T_{max}&gt;6$ s threshold)</td>
<td>Not required</td>
<td>Target mismatch: RAPID perfusion penumbra/infarct ratio $&gt;1.8$, penumbra absolute volume $&gt;15$ mL ($T_{max}&gt;6$ s threshold) - $T_{max}&gt;10$ s Lesion $\leq 100$ mL</td>
<td>Not required (clinical/core mismatch [NIHSS$&gt;5$])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Collaterals</td>
<td>Not required</td>
<td>Not required</td>
<td>Adequate collateral circulation defined as some filling of 50% or greater of the ischemic territory pial circulation beyond occlusion on CT angiography (preferably multiphase CTA)</td>
<td>Not required</td>
<td>Not required</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 32.6\% vs 19.1\% | 71\% vs 40\% | 53\% vs 29.3\% | 60.2\% vs 35.5\% | 43.7\% vs. 28.2\% |
Why are these trials different than previous randomized trials of EVT vs BMM?

- Confirmation of large vessel occlusion before randomization
- Use of retrievable stents in the majority of patients
Certain endovascular procedures have been demonstrated to provide clinical benefit in selected patients with acute ischemic stroke. Systems of care should be organized to facilitate the delivery of this care.
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.

The Future of Stroke Imaging: What We Need and How to Get to It
Carlos Leiva-Salinas and Max Wintermark
Stroke 2010;41:S152-S153
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)
Imaging Strategies

• NCCT, ASPECTS (eASPECTS)
• Physiologic Imaging (CT Perfusion, MR Perfusion)
• Vascular Study to measure clot length (THERAPY)
• Collateral Imaging
• TCD
• Parametric Imaging
NCCT

- NCCT remains sufficient at identifying contraindications to fibrinolysis
  - Widespread, fast, low cost
- Rule out Hemorrhagic Stroke
- 6 hours before reliable changes, edema vs core?
- > 1/3 MCA EIC on NCCT predicts functional outcome and risk of ICH
  - Sensitivity 65%, Specificity 65%

Guidelines for the Early Management of Patients With AIS
Stroke 2014
Schellinger, 2010, Neurology; Fiebach et al., 2002, Stroke
Alberta Stroke Program
Early CT Score (ASPECTS)

• Standardize the detection and reporting of the extent of EIC on NCCT
• Scoring system of 1 or 0 for 10 predefined locations
• C- Caudate, I- Insularribbon, IC- Internal Capsule, L- Lentiform nucleus, and M1 to M6 MCA territories
• < 8 is correlated with both poor functional outcome and sICH

http://www.aspectsinstroke.com
MRI

- DWI – Diffusion Weighted Imaging
  - Sensitivity 90%, Specificity 95%
  - Within min of onset of sx
  - Small lesions
  - NOT all completed stroke (includes irreversible and reversible regions)

- GRE
  - Rule out ICH

- FLAIR
  - Importance to calculate Final Infarct Volume at 3-5 days

Schellinger, 2010, Neurology; Fiebach et al., 2002, Stroke
CTA/MRA

- Length of a clot within the MCA is inversely related to the success of recanalization with IV tPA
- Helps with identification of cause and can predict severity of stroke (Carotid)

Impact of Clot Burden on Success Rate of IV tPA

CTA Collaterals

http://www.aspectsinstroke.com
N.Y. stroke center installs Toshiba Aquilion One CT

Millard Fillmore Gates Circle Hospital in Buffalo, N.Y., has installed a Toshiba America Medical Systems’ Aquilion One dynamic volume CT system at its Kaleida Health Stroke Center.

The Aquilion One can image the entire brain and show real-time brain function in less time than traditional multi-detector CT systems, according to Toshiba.

The 189-bed acute care medical center is home to a multi-disciplinary team trained in stroke care that comprises the hospital’s Kaleida Health Stroke Center. It is the first stroke center in the United States to offer dynamic volume CT, the Tustin, Calif.-based Toshiba said.
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
Aquilion One Protocol (1 min acquisition)

- CT Head w/o
- Perfusion
  - 50 cc at 5cc/s  19 volumes
    - 1 is mask
Time/Tissue Attenuation Curve
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 Insensitive Deconvolution (SVD+)
- Bayesian
CT Perfusion Parameters

- CBF $\text{mL blood/100g brain tissue/min}$
- CBV $\text{mL blood/100g brain tissue}$
- 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/occl with comp</td>
<td>Prolonged</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Oligemic</td>
<td>Prolonged</td>
<td>&gt; 60%</td>
<td>&gt; 80%</td>
</tr>
<tr>
<td>Tissue at risk</td>
<td>Prolonged</td>
<td>&gt; 30%</td>
<td>&gt; 60%</td>
</tr>
<tr>
<td>Dead tissue</td>
<td>Strong prolonged</td>
<td>&lt; 30%</td>
<td>&lt; 30-40%</td>
</tr>
</tbody>
</table>

Tomandl, 2003; Mayer 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)

Duration of Ischemia for Infarction

CBF (ml/min/100g) vs. time (min)
Time is Brain

- Reperfusion can lead to complete regeneration of neuronal function
- Infarct replaces penumbra at a rate that depends on degree of collateral circulation
- Different for different areas of tissue at risk
- Different for grey and white matter
- Different for each and every person being evaluated and potential treated!!!

- CTP at two different time points to assess Stroke Evolution
Reliability?

Differences in CT Perfusion Maps Generated by Different Commercial Software: Quantitative Analysis by Using Identical Source Data of Acute Stroke Patients

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Makoto Sasaki, MD, PhD
Kei Yamada, MD, PhD
Suketaka Morishima, MD, PhD
Hidetsuna Utsunomiya, MD, PhD
Hiroki Shirato, MD, PhD
Kuniaki Ogawara, MD, PhD

Purpose: To examine the variability in the qualitative and quantitative results of computed tomographic (CT) perfusion imaging generated from identical source data of stroke patients by using commercially available software programs provided by various CT manufacturers.

Materials and Methods: Institutional review board approval and informed consent

Radiology 254(1): Jan 2010
Extend IA

- EVT within 6 hours of stroke onset.
- Advanced Imaging
  - Core (rCBF < 30%) < 70 mL
  - Penumbra (Tm > 6s)
  - Mismatch (> 1.2 and > 10mL larger than core)
    - Campbell *Stroke* 2012
- Mortality was higher in patients with an Core volume >70 mL as compared with those with a volume <70 mL, 35% (12/34) versus 9% (13/141), respectively ($P<0.005$)
EXTEND IA

• Strong benefit for EVT if favorable mismatch and core <70 mL
• Near complete reperfusion (≥90%) in target mismatch patients was strongly tied to favorable clinical outcome (regardless of the treatment strategy)
• Lack of reperfusion was associated with death or dependence in 70% of patients.
SWIFT PRIME

- ASPECTS $\geq 6$
- NIHSS $>7$
- EVT within 6 hrs
- Advanced Imaging:
  - Core $< 50$ ml ($rCBF < 30\%$, Tm$>10$)
  - Penumbra (Tm $>6$)
  - Mismatch ($>1.8$ and $> 15$ mL larger than core)
REVASCAT

- EVT within 8 hrs
- NCCT-based patient selection, only requiring ASPECTS score of ≥6
- Significant discrepancies were observed between the centralized core laboratory ASPECTS and the investigators’ ASPECTS
• ASPECTS > 5
• NIHSS > 5
• Mod to Good CS on CTA (> 50% filling)
• Favor EVT
  - ASPECTS and collateral scores were highly correlated
  - Higher Clot Burden (CBS) demonstrated more treatment effect
Study Methods: Workflow

NCCT/DWI:
<1/3 MCA Territory

CTA/MRA:
ICA-T and/or MCA-M1
(Tandem Occlusions Allowed)

RAPID CTP/DWI CIM:
A. ≥80 y/o:
   1. NIHSS ≥10 + core <21cc
B. <80 y/o:
   2. NIHSS ≥10 + core <31cc
   3. NIHSS ≥20 + core <51cc

1:1 Randomization:
- CIM subgroup
- ICA-T vs M1
- 6-12 vs 12-24h

Control
90-day mRS
- U-W mRS
- mRS 0-2

Thrombectomy

- Age ≥18
- NIHSS ≥10
- Pre-mRS 0-1
- TSLW to Randomization: 6-24h
## Co-primary endpoints

<table>
<thead>
<tr>
<th></th>
<th>Trevo</th>
<th>MM</th>
<th>Treatment benefit (95% CI)</th>
<th>Bayesian probability of superiority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 90 weighted mRS</td>
<td>5.5 ± 3.8</td>
<td>3.4 ± 3.1</td>
<td>2.1 (1.20, 3.12)</td>
<td>&gt;0.9999*</td>
</tr>
<tr>
<td>Day 90 mRS (0-2)</td>
<td>48.6%</td>
<td>13.1%</td>
<td>35.5% (23.9%, 47.0%)</td>
<td>&gt;0.9999*</td>
</tr>
</tbody>
</table>

**NNT for 90-day functional independence = 2.8**

*Similar to p<0.0001*
Secondary effectiveness endpoints

**Pre and 24 hour median core size**

- **Trevo**
  - Pre: 9
  - 24 Hours: 8
- **MM**
  - Pre: 11
  - 24 Hours: 22

*P = 0.02*

**NIHSS early responders**

- **Trevo**
  - 47.7%
- **MM**
  - 19.2%

*P < 0.001

140% Improvement
BUFFALO Decision Making for Acute Stroke Intervention

- Functional Imaging (SVD+)
  - Estimate of Penumbra by manual selection of ROI defined as rCBF of < 80% or significantly increased MTT (> 150%)
  - rCBV > 50% (CBV > 2 mL/100g)

- And

- Clinical Exam – NIHSS >7 unless receptive language

- Clinical Exam / Core assessment
Clinical History

- 50 yo who woke up with left hemiplegia, dysarthria, and facial droop.
- NIHSS = 16.

- PMH - Anxiety disorder, tobacco dependence, alcohol dependence
Dual Run Microcatheter beyond the occlusion
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
• 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
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
Collateral Score Grading

• Best method is debated (Menon AJNR 2011)
• Tan ANJR 2009 method…
  - 0 for absent surface vasculature
  - 1 for 0 - 50% vasculature
  - 2 for 50 - 100% vasculature
  - 3 for normal or supra-normal surface vasculature of the MCA territory
Collateral state and the effect of endovascular reperfusion therapy on clinical outcome in ischemic stroke patients

Johannes C. Gerber¹, Marketa Petrova², Pawel Krukowski¹, Matthias Kuhn³, Andrij Abramyuk¹, Ulf Bodechtel⁴, Imanuel Dzialowski⁵, Kay Engellandt¹, Hagen Kitzler¹, Lars-Peder Pallesen⁴, Hauke Schneider⁴, Ruediger von Kummer¹, Volker Puetz⁴ & Jennifer Linn¹

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Brain and Behavior, 2016; 6(9), e00513, doi: 10.1002/brb3.513
Gerber 2016

- Retrospective review of 180 pts from 1/10-12/12
- Selection:
  - Imaging criteria: no ICH, < 1/3 on NCCT, CTA with large vessel
  - tPA when appropriate
  - ICA, M1, M2
Gerber 2016

• Baseline characteristics
  - Median NIHSS 17 (1-34)
  - 60% IVT bridging
  - 88% of EVT were gen anesthesia
  - EVT: CAS (25%), Asp (51%), ST (39%) – half of which was combo asp, IA (3%), IA combo
    • EVT stopped at TICI 2b or 3 or after 2 hrs
  - Onset to angio (250 min), CT to angio (114 min)
  - 90 day mRS <3 (31%)
  - 90 day mRS = 6 (20%)
The objective of the study was to identify thresholds of NCCT-ASPECTS and CTA CS that best predict ischemic core volume threshold of <50mL quantified by CTP among patients with AIS.
• Thresholds of NCCT-ASPECTS of 9 and CS of 3 with high specificity for finding patients with AIS with core volumes considered ideal for revascularization (<50 ml)
• Threshold of NCCT-ASPECTS of 6 and CS of 1 had a high specificity for identifying patients with AIS with core volumes that made them suboptimal candidates for revascularization (> 50 ml)
• ASPECTS and CS lack sensitivity to estimate true core volume.
Future Advanced Imaging Considerations

- Standardize definition of core, perfusion, mismatch, and CS
- Interrelationships and thresholds between different core measurements (ASPECTS, CBF, CBV) and FIV
- Define Futility Thresholds
- Validation of Semi automated methods across vendor platforms and modalities
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
Need to Improve the Process

For each 1-hour increase in stroke onset to TICI 2b/3 reperfusion, odds of good clinical outcome decreased by 38%.

Menon et al. Stroke 2014
See. Diagnose. Treat.
SUMMARY

• We have established that endovascular treatment adds major benefit

• Challenge:
  • Rapidly offer endovascular treatment to all eligible stroke patients with large vessel occlusions
  • Use of Physiologic Imaging when available to increase eligibility for treatment and improve pt selection
  • ASPECTS is reasonable surrogate when physiologic imaging is not available but may not appropriately represent volume of core
  • Improve workflow efficiencies to decrease time from arrival to clot removal

• RESULT: Better Outcomes
Thank you!
Questions?