Modern approach to stroke imaging in light of all the new evidence

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University of Calgary
Single biggest disclosure

- It is all about teamwork
- The work that I am presenting here involves so many people that I can even list them in a single slide.

If I have seen further than others, it is by standing upon the shoulders of giants.

(Isaac Newton)
Other disclosures

• Co-PI: ESCAPE, SWIFT PRIME
• Core Lab: REVASCAT
• Consultant: Covidien, Stryker
• IP: mCTA
• Chair exec cttee: HERMES collaboration
1. The only thing that (currently) works for acute ischemic stroke is:
OPENING THE OCCLUDED VESSEL
Everything else are just steps along the way

- Determining the size of the penumbra does not improve patient outcome
- Figuring out whether the NIHSS is 17 or 19 does not improve patient outcome
2. For patients with acute ischemic stroke due to anterior circulation proximal vessel occlusion: endovascular thrombectomy is now the standard of care

- ASPECTS > 5
- Onset to groin < 6 hours ????
- Proximal vessel occlusion: what is proximal
A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke


Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection


Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke


Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke


Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke


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Study Design

To compare the functional outcomes in AIS subjects treated with either IV t-PA alone or IV t-PA in combination with Solitaire device.

Design
Global, multi-center, prospective, randomized, open, blinded endpoint (PROBE) IDE Study

Target Vessel
Intracranial ICA, M1 of MCA, and carotid terminus

Randomization
1:1

IV t-PA alone vs. IV t-PA + Solitaire

Primary Endpoint
90-day global disability assessed via the blinded evaluation of modified Rankin scale (mRS)

Follow-Up
27 hours, 7-10 Days/Discharge, 30 Days, 90 Days

National PIs
Drs. Jeffrey Saver, Mayank Goyal, Elad Levy and Vitor Mendes Pereira
Prof. Chris Diener and Alain Bonafe

The trial enrolled 196 patients between Dec 2012 and Nov 2014.
Patients were equally randomized to 98 in Control and 98 in Intervention arm.
Trial was officially stopped on Feb 4, 2015 due to crossing of a predefined efficacy boundary.
Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials


Findings We analysed individual data for 1287 patients (634 assigned to endovascular thrombectomy, 653 assigned to control). Endovascular thrombectomy led to significantly reduced disability at 90 days compared with control (adjusted OR 2.49, 95% CI 1.76–3.53; p<0.0001). The number needed to treat with endovascular thrombectomy to reduce disability by at least one level on mRS for one patient was 2.6. Subgroup analysis of the primary endpoint showed no heterogeneity of treatment effect across prespecified subgroups for reduced disability (p_{interaction}=0.43). Effect sizes
3. Opening vessels saves brain
4. Infarct size correlates with outcome
Original Contribution

Intra-Arterial Therapy and Post-Treatment Infarct Volumes
Insights From the ESCAPE Randomized Controlled Trial

Fahad S. Al-Ajlan, MD; Mayank Goyal, MD; Andrew M. Demchuk, MD; Priyanka Minhas, MD; Farahna Sabiq, MD; Zarina Assis, MD; Robert Willinsky, MD; Walter J. Montanera, MD; Jeremy L. Rempel, MD; Ashfaq Shuaib, MD; John Thornton, MD; David Williams, MB, PhD; Daniel Roy, MD; Alexandre Y. Poppe, MD; Tudor G. Jovin, MD; Biggya L. Sapkota, MD; Blaise W. Baxter, MD; Timo Krings, MD; Frank L. Silver, MD; Donald F. Frei, MD; Christopher Fanale, MD; Donatella Tampieri, MD; Jeanne Teitelbaum, MD; Cheemun Lum, MD; Dar Dowlatshahi, MD; Jai J. Shankar, MD; Philip A. Barber, MD; Michael D. Hill, MD, MSc; Bijoy K. Menon, MD, MSc; for the ESCAPE Trial Investigators

Background and Purpose—The goal of perfusion therapy in acute ischemic stroke is to limit brain infarction. The
5. DEAD BRAIN IS DEAD BRAIN
6. Time is brain
Time to Reperfusion and Good Clinical Outcome: IMS3

ICAT, M1, and M2 Cases with Reperfusion with 95% confidence bands (p=0.0045)

Observed values shown as horizontal bars for every ~20 subjects
Figure 1: Estimated probability of good clinical outcome based on time from stroke onset to final DSA run in the STAR registry.

STAR study: workflow paper: published in Stroke
Analysis of Workflow and Time to Treatment on Thrombectomy Outcome in the ESCAPE Randomized Controlled Trial

Running title: Menon et al.; Workflow and time in the ESCAPE trial

Bijcy K. Menon, MD\textsuperscript{1,19}; Tolupe T. Sajobi, PhD\textsuperscript{1,19}; Yukun Zhang, MSc\textsuperscript{2}; Jeremy L. Rempel, MD\textsuperscript{3}; Ashfaq Shuaib, MD\textsuperscript{4}; John Thornton, MD\textsuperscript{5}; David Williams, MD\textsuperscript{6}; Daniel Roy, MD\textsuperscript{7}; Alexandre Y. Poppe, MD\textsuperscript{8}; Tudor G. Jovin, MD\textsuperscript{9}; Biggya Sapkota, MD\textsuperscript{10}; Blaise W. Baxter, MD\textsuperscript{11}; Timo Kringis, MD\textsuperscript{12}; Frank L. Silver, MD\textsuperscript{13}; Donald F. Frei, MD\textsuperscript{14}; Christopher Fanale, MD\textsuperscript{14}; Donatella Tampieri, MD\textsuperscript{15}; Jeanne Teitelbaum, MD\textsuperscript{16}; Cheeun Lun, MD\textsuperscript{17}; Dar Dowlatshahi, MD\textsuperscript{18}; Muneer Eesa, MD\textsuperscript{19}; Mark W. Lowerson, PhD\textsuperscript{18}; Noreen R. Kamal, PhD\textsuperscript{1}; Andrew M. Demchuk, MD\textsuperscript{1,19}; Michael D. Hill, MD\textsuperscript{1,19}; Mayank Goyal, MD\textsuperscript{1,19}

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SWIFT PRIME (under review at Radiology)
Absolute difference in chances of good outcome between treated and not treated, by TOR

2 hours: ARD 33%
6 hours: ARD 6.5%
Almost 7% decrease per hour treatment delay
p=0.038
Revascularization

Probability of mRS 0-2
-5% every 30'

Time from symptoms to revascularization (minutes)
We know

• For patients with prox vessel occlusion tPA is not very effective
• For these patients, endovascular treatment is VERY effective: NNT of ~4
• Does the rate of good outcome with IVtPA also reduces with time for patients with prox. Vessel occlusion?
We know

- For patients with prox vessel occlusion tPA is not very effective
- For these patients, endovascular treatment is VERY effective: NNT of ~4
- Massive delays in drip-and-ship
- We have an approximate idea of rate of decrease of good outcomes over time…endovascular
- Similarly the rate of good outcome with IVtPA also reduces with time

I am not going to show you OLD data from the IV tPA trials:
   WHY: Because these were not patients who were likely to be eligible for endovascular treatment.

Instead:
I am going to show you the control arm of HERMES
7. Randomness is a powerful beast
Fooled by Randomness
The Hidden Role of Chance in Life and in the Markets

Author of The Black Swan
Nassim Nicholas Taleb
Variability of results of recent acute endovascular trials: a statistical analysis

Mayank Goyal, Bijoy K Menon
Figure 1: Forest Plot showing effect sizes (rate ratios with 95% confidence intervals) in the five recently published clinical trials showing benefit of endovascular treatment over control. Pooled estimate of effect size is generated using a random effects model.

<table>
<thead>
<tr>
<th>Study</th>
<th>RR (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR CLEAN (n=500)</td>
<td>1.71 (1.25, 2.32)</td>
<td>23.99</td>
</tr>
<tr>
<td>ESCAPE (N=316)</td>
<td>1.81 (1.36, 2.42)</td>
<td>27.15</td>
</tr>
<tr>
<td>REVASCAT (n=206)</td>
<td>1.55 (1.06, 2.27)</td>
<td>15.91</td>
</tr>
<tr>
<td>SWIFT PRIME (n=196)</td>
<td>1.70 (1.23, 2.33)</td>
<td>22.56</td>
</tr>
<tr>
<td>EXTEND-IA (N=70)</td>
<td>1.79 (1.12, 2.85)</td>
<td>10.38</td>
</tr>
<tr>
<td>Overall (I-squared = 0.0%, p = 0.979)</td>
<td>1.71 (1.47, 1.99)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis
Figure 2: Forest Plot showing effect sizes (rate ratios with 95% confidence intervals) after excluding the phase 2 b EXTEND IA trial. The pooled estimates of effect per random effects model are the same as in figure 1.

<table>
<thead>
<tr>
<th>Study</th>
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<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR CLEAN (n=500)</td>
<td></td>
<td>1.71 (1.25, 2.32)</td>
<td>26.77</td>
</tr>
<tr>
<td>ESCAPE (N=316)</td>
<td></td>
<td>1.81 (1.36, 2.42)</td>
<td>30.30</td>
</tr>
<tr>
<td>REVASCAT (n=205)</td>
<td></td>
<td>1.55 (1.06, 2.27)</td>
<td>17.75</td>
</tr>
<tr>
<td>SWIFT PRIME (n=196)</td>
<td></td>
<td>1.70 (1.23, 2.33)</td>
<td>25.18</td>
</tr>
<tr>
<td>Overall (I-squared = 0.0%, p = 0.938)</td>
<td></td>
<td>1.71 (1.46, 2.00)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis
**Figure 6:** Hypothetical Forest Plot showing effect sizes (rate ratios with 95% confidence intervals) in the five recently published clinical trials assuming that two patients in the endovascular arm in each trial who do well with treatment die due to random chance.

<table>
<thead>
<tr>
<th>Study</th>
<th>RR (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR CLEAN (n=500)</td>
<td>1.66 (1.22, 2.27)</td>
<td>24.26</td>
</tr>
<tr>
<td>ESCAPE (N=316)</td>
<td>1.77 (1.32, 2.37)</td>
<td>27.51</td>
</tr>
<tr>
<td>REVASCAT (n=206)</td>
<td>1.48 (1.01, 2.18)</td>
<td>15.88</td>
</tr>
<tr>
<td>SWIFT PRIME (n=196)</td>
<td>1.64 (1.19, 2.26)</td>
<td>22.63</td>
</tr>
<tr>
<td>EXTEND-IA (N=70)</td>
<td>1.61 (0.98, 2.63)</td>
<td>9.71</td>
</tr>
<tr>
<td><strong>Overall (I-squared = 0.0%, p = 0.969)</strong></td>
<td><strong>1.65 (1.42, 1.92)</strong></td>
<td><strong>100.00</strong></td>
</tr>
</tbody>
</table>

**NOTE:** Weights are from random effects analysis.
Study

<table>
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<tbody>
<tr>
<td></td>
<td></td>
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</tr>
<tr>
<td>MR CLEAN (n=500)</td>
<td>1.71 (1.25, 2.32)</td>
<td>35.78</td>
</tr>
<tr>
<td>ESCAPE (N=316)</td>
<td>1.81 (1.36, 2.42)</td>
<td>40.49</td>
</tr>
<tr>
<td>REVASCAT (n=206)</td>
<td>1.55 (1.06, 2.27)</td>
<td>23.73</td>
</tr>
<tr>
<td>Overall (I-squared = 0.0%, p = 0.814)</td>
<td>1.71 (1.42, 2.06)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis

Study

<table>
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<tr>
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</tr>
<tr>
<td>SWIFT PRIME (n=196)</td>
<td>1.70 (1.23, 2.33)</td>
<td>68.49</td>
</tr>
<tr>
<td>EXTRNd-IA (N=70)</td>
<td>1.79 (1.12, 2.85)</td>
<td>31.51</td>
</tr>
<tr>
<td>Overall (I-squared = 0.0%, p = 0.859)</td>
<td>1.72 (1.33, 2.14)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis
8. The brain is not the heart
People on wait list | Median days until transplant
---|---
Kidney | 87,895
Liver | 16,108
Heart | 3,209
Kidney/pancreas | 2,246
Lung | 1,802
Pancreas | 1,398
Intestine | 258
Heart/lung | 69

26,213 transplants were performed in the United States last year between January and November.

Wait list numbers are as of 10 a.m. Wednesday; days until transplant are the most recent available for each organ.
9. We really don’t understand brain eloquence
1. The only thing that (currently) works for acute ischemic stroke is: **OPENING THE OCCLUDED VESSEL**
2. For patients with acute ischemic stroke due to anterior circulation proximal vessel occlusion: endovascular thrombectomy is now the standard of care
3. Opening vessels saves brain (reduces infarct)
4. Infarct size correlates with outcome
5. Time is brain
6. **DEAD BRAIN IS DEAD BRAIN**
7. Randomness is a powerful beast
8. The brain is not the heart
9. We really don’t understand brain eloquence
Recent trials

• ESCAPE by far the fastest
  – CT head to recan median of 84 min
• SWIFT PRIME second fastest but on average slower by 20 min
• Median time in SWIFT PRIME: CT head to CTP post processing: 24 minutes
• CT based patients in general faster than MR based patients (overall in the 5 trials very few patients were treated using MRI; was not permitted in ESCAPE) for most centers across the world
IMAGING

- CT ONLY
- CT + CTA
- CT + CTA + CT PERFUSION
- MRI: DIFFUSION PERFUSION

BALANCE BETWEEN TIME SPENT, LOCAL INFRASTRUCTURE, COMFORT LEVEL IN DECISION MAKING

‘Perfection in imaging takes time and resources’
Acute Stroke Intervention Results: The “Denominator” Fallacy

M. Goyal

It is common these days to have conversations at meetings related to outcome of endovascular procedures for acute stroke. The correct way from a societal perspective would be, how many patients of the 200 had good outcome irrespective of whether they got endovascular treatment. On the basis of current literature and imaging-based patient selection paradigms, it seems likely that the “best” patients would get chosen for endovascular treatment with very low risks and very high likelihood of good outcome; 60 of 200 is better than that at City B (9% good outcome rate; 18 of 200). However, even that is not a totally correct statement.
Imaging two cities: Gotham city and Metropolis

- Both have
  - Similar population
  - Similar demographics
  - Let us say: each year both cities have 200 people who have acute ischemic stroke due to M1 occlusion
Gotham city......batman....bat-extractor

- Use simple technology and patient selection
- CT, CTA
- Take 120 out of the 200 to endovascular
- 60 have a good outcome
- 50%: 60/120 have a good outcome
Metropolis......superman.....Krypton-decimator

• Complicated MR based selection
• Spend 60 min imaging
• Take 20 patients for endovascular
• 18 (90%) have a good outcome
What can one conclude

• Metropolis has better outcomes than Gotham city: 90% vs 50%
• Metropolis’ patient selection /interventionists /devices are better than Gotham city
THE TRUTH IS:

- Gotham city: 60 out of 200: 30% had a good outcome
- Metropolis: 18 out of 200: 9% had a good outcome

CLEARLY FROM A SOCIETAL PERSPECTIVE: GOTHAM CITY IS BETTER
Comments and Opinions

Ischemic Stroke Tissue-Window in the New Era of Endovascular Treatment

Michael D. Hill, MD, MSc; Mayank Goyal, MD; Andrew M. Demchuk, MD; Marc Fisher, MD, PhD

Epoch 1: Onset-to-imaging

P(imaging eligibility)

onset-to-imaging time (hrs)
MRI

- Impractical in the real world
- Takes too long
- Diffusion imaging clearly the best for measuring core
- However, CTA much better for evaluating vessels including collaterals
- MR perfusion imaging has the same problems
MR compatible pacemaker etc.
MR compatible tPA pumps etc.
Better sequences to compensate for patient motion
Perfusion Imaging in Acute Ischemic Stroke: Let Us Improve the Science before Changing Clinical Practice

Reperfusion is the only proved effective therapy for patients with acute ischemic stroke (1). There is an urgent need for improvement in acute stroke care, as only 15%-20% of patients, at best, are eligible for intravenous tissue plasminogen activator (tPA), and many patients so treated do not achieve good clinical outcome (2,3). This need has resulted in an enormous amount of research about developing better methods of revascularization and neuroprotection and designing better imaging paradigms for patient selection. A key element of these advanced imaging paradigms is perfusion imaging.

We intend to bring focus on the extent of our current knowledge on the imaging triaging of acute ischemic stroke patients by using perfusion imaging and to make recommendations for practice and clinical research. Our position is that perfusion imaging should not be used outside of clinical studies seeking to establish the utility of these in animals. In a series of experiments in cats, Hossman et al (7) reported the restoration of electrical activity in individual neurons with the restoration of cerebral blood flow. They also found that the longer the duration and the greater the depth of ischemia, the less likely that electrical function would return. The threshold level for neuronal dysfunction in these studies was a cerebral blood flow (CBF) of approximately 20 ml/100 g/min. Tissue with a value above this CBF threshold level never infarcts; this region was defined as benign oligemia. These animal experiments also demonstrated the dynamic nature of the ischemic penumbra: Without reperfusion, the infarct core expands into the penumbra over time (4,8).

**Imaging of Core, Penumbra, and Benign Oligemia**

Over the past 20 years, we have developed good imaging methods to defin-
Advanced modality imaging evaluation in acute ischemic stroke may lead to delayed endovascular reperfusion therapy without improvement in clinical outcomes

Kevin N Sheth,¹ John B Terry,²,³ Raul G Nogueira,⁴,⁵ Anat Horev,⁶ Thanh N Nguyen,⁷ Albert K Fong,⁸ Dheeraj Gandhi,⁹ Shyam Prabhakaran,¹⁰ Dolora Wisco,¹¹ Brenda A Glenn,⁴,⁵ Ashis H Tayal,¹² Bryan Ludwig,²,³ Muhammad Shazam Hussain,¹¹ Tudor G Jovin,⁶ Paul F Clemmons,¹³ Carolyn Cronin,¹ David S Liebeskind,⁸ Melissa Tian,¹² Rishi Gupta⁴,⁵

556 patients were analyzed. Mean age was 66±15 years and median National Institutes of Health Stroke Scale score was 18 (IQR 14–22). NCT was used in 286 (51%) patients, CTP in 190 (34%) patients, and MRI in 80 (14%) patients. NCT patients had significantly lower median times to groin puncture (61 min, IQR (40–117)) compared with CTP (114 min, IQR (81–152)) or MRI (124 min, IQR (87–165)). There were no differences in clinical outcomes, hemorrhage rates, or final infarct volumes among the groups.
Advanced imaging

- CTP in MRCLEAN (334)
  - Patient selection based on CTP?

<table>
<thead>
<tr>
<th>(N)</th>
<th>acOR (shift in mRs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (500)</td>
<td>1.67 (1.21 – 2.30)</td>
</tr>
<tr>
<td>With CTP (334)</td>
<td><strong>1.4</strong> (1.0 – 2.1)</td>
</tr>
<tr>
<td>No CTP (166)</td>
<td><strong>2.5</strong> (1.4 – 4.5)</td>
</tr>
</tbody>
</table>
Advanced imaging

- CTP in MRCLEAN (N=175)
  - Substudy in 175 CTP patients (source images available)
  - “Mismatch” using EXTEND IA criteria

<table>
<thead>
<tr>
<th>(N)</th>
<th>aOR (mRs0-2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (175)</td>
<td><strong>1.63</strong> (0.94-2.81)</td>
</tr>
<tr>
<td>Mismatch (102)</td>
<td><strong>1.40</strong> (0.67-2.89)</td>
</tr>
<tr>
<td>No mismatch (73)</td>
<td><strong>1.85</strong> (0.76-4.45)</td>
</tr>
</tbody>
</table>

- ‘no interaction between mismatch and treatment allocation on the full mRS scale endpoint (P=0.62) nor on the dichotomized endpoints of mRS 0-2 (P=0.46)’
Analysis of Workflow and Time to Treatment and the Effects on Outcome in Endovascular Treatment of Acute Ischemic Stroke: Results from the SWIFT PRIME Randomized Controlled Trial

Mayank Goyal, MD, FRCPC
Ashutosh P. Jadhav, MD, PhD
Alain Bonafe, MD
Hans Diener, MD
Vitor Mendes Pereira, MD
Elad Levy, MD
Blaise Baxter, MD
Tudor Jovin, MD
Reza Jahan, MD

Purpose:
To study the relationship between functional independence and time to reperfusion in the Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke (SWIFT PRIME) trial in patients with disabling acute ischemic stroke who underwent endovascular therapy plus intravenous tissue plasminogen activator (tPA) administration versus tPA administration alone and to investigate variables that affect time spent during discrete steps.

Materials and
Data were analyzed from the SWIFT PRIME trial, a global
<table>
<thead>
<tr>
<th>mRS 0-2 rates</th>
<th>Solitaire</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfusion imaging mandated</td>
<td>54.1%</td>
<td>28.1%</td>
</tr>
<tr>
<td>Perfusion imaging likely used for decision making</td>
<td>61.3%</td>
<td>38.6%</td>
</tr>
<tr>
<td>Perfusion images after randomization: likely not used</td>
<td>57.9%</td>
<td>28.6%</td>
</tr>
<tr>
<td>Perfusion imaging not performed</td>
<td>60.0%</td>
<td>27.3%</td>
</tr>
</tbody>
</table>

Additionally workflow when using perfusion imaging was slower. CT to CTA: median 9 minutes  
CT to post processed CTP: 22 minutes
Time intervals in subjects investigated by CT and CTA vs. CT alone in IMS3
When you put this together

• Small core
• Patient worth fighting for
• Natural history likely to be bad
• WORK LIKE CRAZY TO ACHIEVE RECANALIZATION
• Don’t waste time on extensive imaging and post processing
When you put this together

- Small core
- Patient worth fighting for
- Natural history likely to be bad
- WORK LIKE CRAZY TO ACHIEVE RECANALIZATION
- Don't waste time on extensive imaging
When you put this together

- Small core
- Patient worth fighting for
- Natural history likely to be bad
- WORK LIKE CRAZY TO ACHIEVE RECANALIZATION
- Don’t waste time on extensive imaging and post processing
Determination of core on NCCT

- ASPECTS
  - problems:
    1. difficult to see changes in early stages
    2. interobserver variability
    3. lack of precision

- Can these be solved?
  - HIGH QUALITY CT HEAD
  - Correlation with collaterals
  - Think BAYESIAN: doesn’t matter if ASPECTS is 8 or 9 or 10 from a decision making perspective
The Three C’s for Imaging Selection

Clot (size/location)

Core (size/severity)

Collaterals
Understanding Alberta Stroke Program Early CT Score (ASPECTS)

Alberta Stroke Program Early CT score (ASPECTS) is a 10-point quantitative topographic CT scan score. ASPECTS was developed to offer the reliability and utility of a standard CT examination with a reproducible grading system to assess early ischemic changes on pretreatment CT studies in patients with acute ischemic stroke of the anterior circulation. ASPECTS CT score is simple and reliable. We describe the use of ASPECTS in detecting early ischemic signs on NCCT brain scan.
Core

• Can one really determine the core
• Dead brain is dead brain
• Moving target for measurement
• What is dead now vs. what is going to be dead in the next 30 min vs. 60 min vs. 90 min

WHAT IS THE LEVEL OF PRECISION REQUIRED
THINK BAYESIAN
CTA collaterals and baseline DWI volume

Souza LCS et al. AJNR epub

Absent >50% M2 MCA
Diminished >50% M2MCA
Diminished <50% M2MCA
Normal
Increased

11% 23%
Multiphase CTA
PATENT PENDING
Our prospective study: PROVE-IT *(Precise and Rapid assessment of collaterals using multi-phase CTA in the triage of patients with acute ischemic stroke for IV or IA Therapy (PRoVe-IT))*

- **Objectives:**
  - Determine if collateral assessment on multi-phase CTA helps in predicting which patients will achieve major neurological improvement with early recanalization.
  - Evaluate if collateral assessment on multi-phase CTA is non-inferior to perfusion CT in predicting which patients will achieve major neurological improvement with recanalization therapy.
  - Identify potentially modifiable determinants associated with good leptomeningeal collateral status in patients presenting with acute ischemic stroke.
Multiphase CTA

Multiphase CT Angiography: A New Tool for the Imaging Triage of Patients with Acute Ischemic Stroke

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Purpose:
To describe the use of an imaging selection tool, multiphase computed tomographic (CT) angiography, in patients with acute ischemic stroke (AIS) and to demonstrate its interrater reliability and ability to help determine clinical outcome.

Materials and Methods:
The local ethics board approved this study. Data are from the pilot phase of PROveIT, a prospective observational study analyzing utility of multimodal imaging in the triage of patients with AIS. Patients underwent baseline unan-
NCCT/MCTA: 98 minutes from onset 78 WF, NIHSS 18; R hemisphere CT ASPECTS score is 8. Proximal right M1 MCA occl

MCTA: a one phase delay, with similar extent and prominence to contralateral side.

A CBF-defined: infarct core is 113 mL (blue) and mismatch ratio (blue/pink areas) is 1.7; this indicates the patient should not undergo treatment.

MCTA and perfusion CT imaging incongruent for treatment decision.

F/U MR DWI: small infarct, M1 MCA clot recanalized
Are all swans white

- You go out looking
- You look at 10,000 swans which are all white: can you conclude that all swans are white
However you need to see only one black swan to conclude that not all swans are white
From two months ago

• NIH 18
• Otherwise healthy
• Eligible for trial
• 65 min from onset
Parallel processing
Team divides: one part goes to talk to family; I go to angio
Patient starts improving
NIH down to 3
We go back and look at the CT perfusion.
Analyze the data many different ways.

Here is the summary:

We looked at the CTP in detail after the procedure. Analyzed it many different ways.

Tmax > 10s volume = 170cc
Tmax > 6s volume = 201cc

CBF < 6 = 160cc
CBF < 35% = 185cc
24 hour diffusion imaging
NIHSS zero
Discharged home on day 3
Case 2
F/80, presents with LEFT hemispheric syndrome, 90 minutes from onset and NIHSS 18
**IV+IA:**
(successful recanalization without clinical improvement)
**Futile recanalization:** 24 hr NIHSS 25 and subsequent mRS 6
Male/59, left M1, Onset to CTP = 2hrs30mins; CTP-to-TICI-3 Reperfusion = 43 mins; Admission NIHSS = 9; 24 hour NIHSS = 1, 90d mRS = 1

CBF < 12; rCBF < 0.30 CBF < 7.0; rCBF < 0.18 Tmax > 16s

Infarct if not reperfused

Tmax > 9s

24 hr f/u
Female/79, right M2, Onset to CTP = 1hr16mins; CTP-to-TICI-2b Reperfusion = 50mins;
Admission NIHSS = 16; 24 hour NIHSS = 2, 90d mRS = 1

CBF < 12; rCBF < 0.30

CBF < 7.0; rCBF < 0.18 Tmax > 16s

Tmax > 9s infarct if not reperfused

24 hr f/u
RESULTS

Continuous-time analysis

Stronger, significant association between CTP-to-reperfusion time and optimal threshold for Tmax and CBF parameters ($p<0.01$)

CBV did not show a relationship ($p>0.05$)

In press: Stroke
$T_{max} > 16s / \text{rel CBF} < 0.20$

$T_{max} > 12.5s / \text{rel CBF} < 0.30$

$T_{max} > 9.5s$

- Ischemic core if reperfused in 90 mins
- Ischemic core if reperfused in 180 mins
- Ischemic core if treated and not reperfused
Acute stroke, Bayes’ theorem and the art and science of emergency decision-making

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Recent Endovascular Trials: Implications for Radiology Departments, Radiology Residency, and Neuroradiology Fellowship Training at Comprehensive Stroke Centers

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Endovascular treatment of acute ischemic stroke is undergoing a paradigm shift similar to the one observed in interventional cardiology for patients with acute myocardial infarction (AMI). Specifically, for patients with AMI, process improvements in communication among the various medical specialties involved and improved decision analysis (EXTEND-IA, or Extending the Time for Thrombolysis in Emergency Neurologic Deficits–Intra-Arterial, was a phase IIIB study with reperfusion and/or National Institutes of Health Stroke Scale at 24 hours as the primary outcome; however, this trial also reported the 90-day outcome as their secondary
Some thoughts to leave you with

- Speed is of essence
- Decision making is essentially dichotomous
- The currency you spend is neurons
- Arbitrarily: 10 million neurons: 5 min of imaging, post-processing and decision making
- Perfection is the enemy of neurons