All About Delivery
Stroke Care in 2019

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Disclosure

- Relevant financial relationships
  None

- Off-label/investigational uses
  None
Concepts
Large Vessel Occlusion (LVO) Stroke

“An acute vascular occlusion that impairs cerebral perfusion, results in significant clinical deficit, and is accessible for endovascular thrombectomy.”
The Penumbra Concept

Symptoms of stroke

- **Infarction**
  - ↑ Extracellular Ca
  - ↑ Extracellular K
  - ATP failure
  - ↓ Glucose metabolism
  - ↑ Glutamate

- **Ischemia**
  - ↓ O2 delivery
  - ↑ Lactate
  - ↓ Protein synthesis

- **Normal brain**
  - ↑ OEF

**Cerebral Blood Flow** mL/100g/min

6 8 10 14 16 18 20 30 50
The Basis of Acute Stroke Therapy

The “recanalization hypothesis”

Prabhakaran, et al, JAMA 2015
LVO Produces Large Clinical Deficits

NIHSS can predict proximal occlusion

NIHSS (median, first and third quartile, and range) on admission and location of the vessel occlusion as seen on DSA. No oc indicates no occlusion.

Fischer U et al. Stroke 2005
Core Determines Outcome
Collaterals Determine Core

Patients with poor collaterals are especially time sensitive

Fast and Slow Progressors

Souza et al. AJNR 2012
V. Nambiar et al. AJNR 2014
LVO Carries a Huge Burden

<20% of stroke but...

Artwork by Bradley Kaye

Malhotra, et al, Front Neurol, 2017
LVO Carries a Huge Burden

Total Direct Hospital Costs

- LVO
- Non-LVO
Technology Enables Treatment

**MERCI (2004)** 1st GENERATION
Engage the thrombus with deployment of a 'corkscrew' distal tip then remove en bloc. Proximal balloon inflation allowing device retrieval into the guide while minimizing the risk of emboli.

**STRENTIVER (early 2012)**
3rd GENERATION
Engage the thrombus with stent retrieve deployment, which also temporarily restores flow across the occlusion. Proximal balloon inflation allows device retrieval into the guide while minimizing the risk of emboli.

**PENUMBRA (2009)** 2nd GENERATION
The penumbra aspiration system involves maceration of the thrombus with a separator under direct aspiration to prevent showering of fragments. Once the catheter system is delivered to the target vessel, ongoing clot maceration is performed without the need to re-access.

**DAC (2010)**
The DAC is positioned immediately adjacent to the thrombus and aspiration is applied to minimize emboli and optimize the vectors during pulling of the device.

**ADAPT (2013)**
A large caliber aspiration catheter that is advanced up to the thrombus. Direct aspiration is employed to engage and then remove the thrombus.

Spiotta et al, JNIS 2014
Thrombectomy <6hrs
2015: A Time of Revolution

For LVO
Endovascular therapy > best medical therapy

HERMES meta-analysis
Goyal, Lancet 2016
NEJM 2015
LVO Treatment is Powerful

Endovascular Stroke Rx

IV tPA <3hrs

IV tPA <4.5hrs

Statins for stroke prevention

Adapted from Jeff Saver
A Huge Unmet Need

750,000 ischemic strokes /year in the USA 2015

130,000 large vessel occlusions

5,000 thrombectomies 2015

Smith, et al, ISC 2017
Thrombectomy 6-24 hrs
Remember our Progressors…

Patients with poor collaterals are especially time sensitive.

Fast and Slow Progressors
Initial DWI growth rate for the 65 patients with known time of stroke onset. Graphed based on the assumption of infarct volume of 0 ml just prior to symptom onset and linear growth (based on initial findings in Part I of this study). Overall, median initial growth rate was 3.1 ml/h, with a range from 0 ml/h to 117 ml/h. DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging.
Late Window Studies

DWI/PWI and CTP Assessment in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention (DAWN)

- Multicenter randomized controlled trial, funded by industry
- 6-24 hours, NIHSS 10+
- Perfusion evaluation for core volume, graded by age
- Primary outcome: 90 day mRS

Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3 (DEFUSE 3)

- Multicenter randomized controlled trial, funded by StrokeNet
- 6-16 hours, NIHSS 6+
- RAPID software for automated evaluation of penumbra
- Primary outcome: 90 day mRS
Imaging in DAWN, DEFUSE 3

DWI (ADC < 620) volume: 10 ml
Hypoperfusion (Tmax>6s) volume: 76 ml
Mismatch volume: 66 ml
Mismatch ratio: 7.6
Highly Selected Populations

Core threshold
- 50cc for DAWN
- 20cc if >80 yrs old
- 30cc if NIHSS 10-20
- 31-50cc if NIHSS >20
- 70cc for DEFUSE 3

NIHSS threshold
- 6+ for DEFUSE 3
- 10+ for DAWN

Penumbra
- Inferred in DAWN
- Measured in DEFUSE
  - Mismatch ratio ≥1.8
  - Mismatch volume ≥15ml

Nogueira, et al NEJM 2017
Albers, et al NEJM 2018
DAWN Presented at ESOC

DAWN halted early due to efficacy at interim analysis, DEFUSE 3 subsequently halted too.
Outcomes in DAWN, DEFUSE 3

Favorable outcomes in early versus late window stroke trials

Largest treatment effect in the history of stroke trials

Albers, Stroke 2018
Time Remains Essential

Eligible patients remain into late windows, but absolute numbers decrease

Potential thrombectomy candidate

Proportion of patients with viable penumbra

<6hrs

18-24hrs
Time Remains Essential!!

x 200 = USA Stroke Burden
Thrombectomy out to 24 hours is now standard of care
Growing the Red Box

Bridging thrombolysis
EXTEND IA-TNK2

Direct MT
MR CLEAN No-IV
DIRECT-SAFE
DIRECT-MT
SWIFT DIRECT

Neuroprotectants
ESCAPE-NA1

Large Core
TENSION
DEFUSE 4

Low NIHSS
ENDOLOW

Technique
COMPASS

Stroke Systems
RACECAT
System Considerations
Get The Treatment to the People

Pictures from UNICEF
Get The People to the Treatment
Identification of LVO is Key

Comprehensive Stroke Center
Thrombectomy capable

Primary Stroke Center
IV tPA capable

Emergency Medical Services

We have a great responsibility…

Gorelick PB, J Stroke 2013
Current State for LVO Patients

EMS pickup

Primary Stroke Center

Comprehensive Stroke Center

How do we improve this system?

Mohamad et al, ESJ, 2016
Jayaraman et al, JNIS 2016
Parikh NS, et al, Stroke 2018
Option 1: Bypass of PSC

EMS pickup  →  Comprehensive Stroke Center

Primary Stroke Center

Mohamad et al, ESJ, 2016
Jayaraman et al, JNIS 2016
Parikh NS, et al, Stroke 2018
The Bypass Bogey Man

Woooooo....
Field Identification For Bypass

Improving **early identification** in the field

FAST-ED

Artwork by Bradley Kaye
Data is Coming

RACECAT
Direct Transfer to an Endovascular Center Compared to Transfer to the Closest Stroke Center in Acute Stroke Patients With Suspected Large Vessel Occlusion
clinicaltrials.gov/NCT02795962

TRIAGE
TRTreament Strategy In Acute Ischemic larGE Vessel STROKE: Prioritize Thrombolysis or Endovascular Treatment
clinicaltrials.gov/NCT03542188

Froehler, et al, Circulation 2017
Mobile Stroke Units
Mobile stroke units are cost efficient if:
- Operating distance >10 miles
- Population density of >200 inhabitants/mile²

Other “Imaging” by EMS

- Brainscope One
- Cerebrotech Visor
- StrokeFinder MD100
- Infrascanner 2000
Despite the Bogey Man…

…most patients will likely still present locally

1. Bypass radius  (SNIS recommends 30mins radius, AHA 15mins)
2. High threshold field scores  (Moderate strokes will not be bypassed)
3. Population distribution  (suburbs, rural areas, etc.)
4. Slow change  (EMS process, PSC resistance, legislation and regulation)
Option 2: Screening at PSC

EMS pickup

Primary Stroke Center

Comprehensive Stroke Center

Mohamad et al, ESJ, 2016
Jayaraman et al, JNIS 2016
Parikh NS, et al, Stroke 2018
# Selection For Thrombectomy

<table>
<thead>
<tr>
<th>Goal</th>
<th>CT</th>
<th>MRI</th>
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<tbody>
<tr>
<td><strong>1. Exclude hemorrhage</strong></td>
<td>NCCT</td>
<td>GRE</td>
</tr>
<tr>
<td><strong>2. Identify LVO</strong></td>
<td>CTA</td>
<td>TOF MRA, Gad MRA</td>
</tr>
<tr>
<td><strong>3. Assess core</strong></td>
<td>ASPECTS</td>
<td>DWI</td>
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<td><strong>4. Assess penumbra</strong></td>
<td>Multiphase CTA</td>
<td>Automated MRP</td>
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Acute stroke patient presents to Referring Hospital ED

Evaluation (with CTA) for thrombectomy at CSC

Transfer

Evaluation (with CTA) for thrombectomy in PSC ED

Transfer

Keep local stroke care local

Thrombectomy

MApping a Path Forward

- AHA Massachusetts CTA Workgroup formed Nov 2017
  - Surveyed all hospitals in the State

- Developed protocols for CTA dissemination

- Launched Statewide CTA initiative

- Implemented a “federalized” system
  - Each of the 8 thrombectomy-capable sites to implement changes within their own networks
| **Who?** | NIHSS 6+  
|          | LSW <24hrs |
| **What?** | CT head  
|          | CTA head and neck  
|          | Axial MIPS |
| **When?** | 24/7/365 |
| **How?** | Triage determination with receiving hospital |
Interpretation of CTA

CT/CTA reviewed at CSC by care team
 Stroke
 Neuroendovasular
 Neuroradiology

Triage decisions are based upon that review
Pitfall № 1

Quick, let’s hurry back to the ED for tPA/Telestroke/ED Doc evaluation!
Pitfall № 2

Wait, do we have a creatinine on the patient yet?
Metrics for Stroke

EMS
- On-scene time
- Pre-notification

PSC
- % Door to CT <25mins
- % Door to Needle <60mins
- Door to CTA
- Door in Door Out (DIDO)
Metrics Driving System Change
Regionalizing Stroke Care

“E pluribus unum…”

Annual Meeting, Oct 23-25
Marriot Copley Place
thenecc.org
FDA permits marketing of clinical decision support software for alerting providers of a potential stroke in patients identifying LVOs and alerting the relevant specialist with 90 percent sensitivity and specificity, and a median scan to notification time of under 6 minutes.
Network Coordination

Diagnosis
Triage
Decision support

Comprehensive Stroke Center

MASSACHUSETTS GENERAL HOSPITAL
FIREMAN VASCULAR CENTER
CSC Use of PSC Vessel Imaging
Option 3: PSC Thrombectomy

EMS pickup → Primary Stroke Center → Comprehensive Stroke Center

Mohamad et al, ESJ, 2016
Jayaraman et al, JNIS 2016
Parikh NS, et al, Stroke 2018
Penetrance is low:
<1 in 30 thrombectomies is performed by a non-Neurointerventionalist
The Traveling Interventionalist
The Future State?

ONE SIZE DOESN’T FIT ALL
In Conclusion

• Unprecedented change has occurred in acute stroke care
• We have a very powerful treatment for the most affected of the stroke population
• Stroke patients up to 24 hours from their last know well times are candidates for treatment
• We have to improve the systems that triage stroke patients
A rising tide lifts all ships…
Thank you.
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