Endovascular Treatment for Acute Ischemic Stroke: 

*Ready for the PRIME time*

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Baptist Physician Lexington
Disclosures:
SWIFT PRIME site (Medtronic)
Physician Proctor & Speaker Bureau (Medtronic)
Consultant (Stryker)
Stroke

- **Impact**
  - Every 45 seconds someone in the U.S. has a stroke
  - Stroke is #4 cause of death
  - Stroke is #1 cause of adult disability
  - Approximately 87% ischemic

- **Limited treatment options**
  - Intravenous lytic
    - Limitation: must be administered within 4.5 hours of stroke onset
    - Estimated <5% of stroke patients receive IV lytic
  - Mechanical revascularization with Merci®, Penumbra®, Solitaire®, and Trevo® Systems
    - Provide option for patients with large vessel occlusions
Signs of Large Vessel Occlusion (LVO)

• The “no brainer” stroke:
  • Weak or paralyzed on one side of body
  • Facial droop
  • Absent or slurred speech.

• If you have these symptoms, there is a high likelihood of a large vessel occlusion. Transport to hospital capable of performing thrombectomy.
35-40% of Ischemic Strokes are Considered “LVO”

- This subset of ischemic stroke comprises blockages in the:
  - Internal Carotid Artery (ICA)
  - Middle Cerebral Artery (MCA)
  - Vertebral / Basilar Artery

- Patient prognosis with these types of stroke is poor

<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>
Large Vessel Occlusions

Clot Location and Response to IV TPA

- Large vessel occlusions respond poorly to IV TPA
- Clot burden is major determinate of response to IV TPA
- ICA < extensive M1 < min M1 < M2 < M3

Kimura et al. *Eur Neurol* 2009
Goal of Interventional Stroke Therapy

Salvage the Penumbra

Cerebral Perfusion in Acute Stroke: Model

- CBF (CBV) → Energy-dependent autoregulation
- O₂, glucose and ion exchange preserved
- Tissue survives temporarily or permanently

- CBF (CBV) → Nutrient exchange impaired
- Membrane integrity impaired
- Infarction
Fate of the Penumbra?

75 yo WM presents to BHL ED 2 hrs after onset of dysarthria and left facial droop. Because of ‘mild’ deficits (NIHSS 3) the patient was not administered IV tPA. CT Perfusion was performed demonstrating sizeable ischemic penumbra (with relatively small ‘core’ infarct, MRA showed right MCA occlusion.
2 days later, the patient declined the following evening with increasing lethargy, slurred speech, and left sided weakness, requiring PEG placement.
Endovascular Thrombectomy of Cerebral Vessels

• Merci® Retriever

• First surgical device cleared by the FDA for acute ischemic stroke patients in 2005

• Restores blood flow to the brain by physically removing thrombus from the occluded precerebral or cerebral vessel

• Indications for Use:
  • Patients who are ineligible for treatment with intravenous t-PA:
    • outside 4.5 hour window
  • other clinical factors, eg. recent surgery, long-term current use of anticoagulants for atrial fibrillation, allergy to t-PA
  • Patients who have failed (or not responding to) prior intravenous t-PA therapy
Merci Registry

The Largest, Prospective Multi-Center Study of Mechanical Embolectomy for Acute Ischemic Stroke

- Prospective, multi-center study (36 centers)
- 1,000 patients enrolled in 3 years
  - Interim results presented at ISC 2010 analyzed 625 patients
- Inclusion criteria: procedure must have included a Merci Retriever and patient informed consent
- No exclusion criteria
- Interim results validated MERCI and Multi MERCI results in a much larger unconstrained cohort
### Table S4. Thrombolysis in Cerebral Infarction (TICI) Rating Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No perfusion</td>
</tr>
<tr>
<td>1</td>
<td>Perfusion past the initial obstruction but limited distal branch filling with little or slow distal perfusion</td>
</tr>
<tr>
<td>2a</td>
<td>Perfusion of less than 2/3 of the vascular distribution of the occluded artery</td>
</tr>
<tr>
<td>2b</td>
<td>Perfusion of 2/3 or greater of the vascular distribution of the occluded artery</td>
</tr>
<tr>
<td>3</td>
<td>Full perfusion with filling of all distal branches</td>
</tr>
</tbody>
</table>

### Table 14. Modified Rankin Scale (mRS)

<table>
<thead>
<tr>
<th>Score</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms</td>
</tr>
<tr>
<td>1</td>
<td>No significant disability, despite symptoms; able to perform all usual duties and activities</td>
</tr>
<tr>
<td>2</td>
<td>Slight disability; unable to perform all previous activities but able to look after own affairs without assistance</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability; requires some help, but able to walk without assistance</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance</td>
</tr>
<tr>
<td>5</td>
<td>Severe disability; bedridden, incontinent, and requires constant nursing care and attention</td>
</tr>
<tr>
<td>6</td>
<td>Death</td>
</tr>
</tbody>
</table>
Revasc Rates by Final TICI Score
Merci Registry

TICI 2b or higher = 53.7%
Average Procedure Time = 115 minutes
So What’s Next?

- “Stent-retrievers”
- Solitaire® and Trevo®
- Allow for faster and higher recanalization rates, with fewer device deployments (‘passes’), and improved clinical outcomes relative to Merci
Every Minute Counts: Time is Brain

Estimated Pace of Neural Circuitry Loss in Typical Large Vessel, Supratentorial Acute Ischemic Stroke

<table>
<thead>
<tr>
<th></th>
<th>Neurons Lost</th>
<th>Synapses Lost</th>
<th>Myelinated Accelerated Fibers Lost</th>
<th>Aging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per Stroke</td>
<td>1.2 billion</td>
<td>8.3 trillion</td>
<td>7140 km/4470 miles</td>
<td>36 yrs</td>
</tr>
<tr>
<td>Per Hour</td>
<td>120 billion</td>
<td>830 billion</td>
<td>714/447 miles</td>
<td>3.6 yrs</td>
</tr>
<tr>
<td>Per Minute</td>
<td>1.9 million</td>
<td>14 billion</td>
<td>12 km/7.5 miles</td>
<td>3.1 weeks</td>
</tr>
<tr>
<td>Per Second</td>
<td>32,000</td>
<td>230 million</td>
<td>200 meters/218 yards</td>
<td>8.7 hours</td>
</tr>
</tbody>
</table>

IMS I & II Trials showed a 10% decrease in probability of functional independence (mRS 0-2) with every 30 min delay from time of symptom onset to reperfusion.
**Comparison b/w Merci Retriever® and Solitaire®**

<table>
<thead>
<tr>
<th>Devices Used</th>
<th>MERCI®</th>
<th>MULTI-MERCI®</th>
<th>MERCI Registry®</th>
<th>Solitaire™ FR device Retrospective Study²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>141</td>
<td>164</td>
<td>1000</td>
<td>141</td>
</tr>
<tr>
<td>Device Passes</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>1.8</td>
</tr>
<tr>
<td>Procedure Time</td>
<td>87mins</td>
<td>N/A</td>
<td>115mins</td>
<td>40mins</td>
</tr>
<tr>
<td>Mortality</td>
<td>44%</td>
<td>34%</td>
<td>34%</td>
<td>20.5%</td>
</tr>
<tr>
<td>TIMI 2-3</td>
<td>48%</td>
<td>57%</td>
<td>79%**</td>
<td>96%**</td>
</tr>
<tr>
<td>mRS at 90 days (mRS 0-2)</td>
<td>44%</td>
<td>36%</td>
<td>30%</td>
<td>55%</td>
</tr>
</tbody>
</table>

**The Solitaire™ FR device Retrospective data demonstrates higher angiographic and neurological outcomes when compared to these Merci® registries.**

**TICI 2a-3 classification was used**
79 yo WM awoke and walked to bathroom at 9am, wife heard loud noise and went to find husband lying in the floor of bathroom, aphasic and right sided hemiplegic. Transferred to CBH and received full-dose t-PA at 12pm (approx. 3hrs after symptom onset). Initial NIHSS was 24 upon arrival to CBH. CT Perfusion scan shows large area of ischemia in left MCA territory consistent with large vessel occlusion, sent for possible thrombectomy.
Partial flow restoration with Solitaire at 130pm (4.5 hrs after sx onset)
The next day, the patient had regained anti-gravity strength in the right upper and lower extremities and significant improvement in speech (mild-moderate residual expressive aphasia). 24 hr NIHSS had improved to 6 (initial was 24).
Why Use Imaging to Triage Care?

Both patients present around 4 hours after symptom onset, both candidates for IV tPA
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Recent Stroke Trials

- MR CLEAN
- ESCAPE
- EXTEND-IA
- SWIFT PRIME
- REVASCAT
Multicenter (16 Centers in Netherlands), prospective, randomized trial, open label treatment and:
- Blinded assessment of functional outcome at 90 days
- Blinded assessment of neuro-imaging at baseline and follow-up

500 patients randomized to best medical therapy (including IV tPA) or best medical therapy (including IV tPA) plus mechanical thrombectomy with stent retriever (Solitaire). 233 mechanical thrombectomy, 267 to best medical therapy

Masked, web-based, 1:1 random treatment allocation
- Intraarterial treatment (IA thrombolysis, mechanical treatment or both) plus usual care (could include IV tPA)
- Usual care alone (control group)

Inclusion Criteria
- Acute ischemic stroke, Age ≥18, NIHSS ≥2
- Intracranial anterior circulation occlusion (confirmed by CTA)
- Initiation of IA treatment within 6 hours from onset
MR CLEAN

Stent Retrievers were 97% of IAT Treatment in the Intervention Arm

N = 196 patients

Devices Used

- Stent Retrievers: 190 (97%)
- Thrombolysis: 1 (0%)
- Other Mechanical Devices: 5 (3%)
MR CLEAN
Effect Of Intervention On Primary Outcome

Intervention (N=233)
- mRS 0: 3%
- mRS 1: 9%
- mRS 2: 21%
- mRS 3: 18%
- mRS 4: 22%
- mRS 5: 6%
- mRS 6: 21%

Control (N=267)
- mRS 0: 6%
- mRS 1: 13%
- mRS 2: 16%
- mRS 3: 30%
- mRS 4: 12%
- mRS 5: 22%

mRS 0-2
- Intervention: 32.6%
- Control: 19.1%
EXTEND-IA

- **EXTEND IA** – **EXtending the T**ime for thrombolysis in **E**mergency **N**eurological **D**eficits – **I**ntra – **A**rterial

- **Rational:**
  - To select patients with the best chance of benefit from reperfusion (“Dual Target”)
    - Proven major vessel occlusion **AND**
    - Salvageable tissue with ischemic core <70mL (CT perfusion)
  - Treat as fast as possible (no waiting to assess tPA “failure”)
  - Use the most effective device (stent retriever)

- **Methods:**
  - Randomized, open-label with blinded endpoint (PROBE) design
    - Intervention: **Stent Retriever** (Solitaire FR) + IV tPA
    - Control: IV tPA
EXTEND-IA

Inclusion Criteria

- Acute ischemic stroke
- Age \( \geq 18 \) years
- Pre-stroke mRS 0-1
- Intra-arterial clot retrieval treatment can commence (groin puncture) within 6 hours of stroke onset.

Imaging inclusion criteria. Dual target:

- CTA reveals large artery occlusion in anterior anatomy (ICA, M1 or M2)
- Mismatch - Using CT or MRI with a Tmax >6 second delay perfusion volume and either CT-rCBF or DWI infarct core volume.
  - Mismatch ratio of greater than 1.2 and
  - Absolute mismatch volume of greater than 10ml and
  - Infarct core lesion volume of less than 70mL
EXTEND-IA

Only used the *Solitaire Device* for intervention

Devices Used
- Solitaire Device

35/35 (100%)

N= 35 patients
EXTEND-IA

Revascularization in the IV tPA + Endovascular Arm (N=29)

- TICI 2b/3: 86.0%
- TICI 3: 48.0%
EXTEND-IA

*mRS 0-2 at 90-days*

Intervention: N=35

Control: N=35

NNT = 3.2

for independence
EXTEND-IA

Conclusions

- Early mechanical stent thrombectomy after tPA using Solitaire FR led to faster and more complete reperfusion.
- Patients treated with Solitaire spent significantly less time in the hospital or in rehabilitation before returning home (15 vs. 73 days, p=0.006).
- In this population selected for vessel occlusion and salvageable tissue this translated to:
  - Improved early neurological recovery
  - Improved functional outcome at 3 months
  - No safety concerns

- tPA + mechanical stent thrombectomy should be the new standard of care.
SWIFT PRIME – Solitaire FR With the Intention For Thrombectomy as Primary Endovascular treatment for acute ischemic stroke

Purpose:
- To determine if patients experiencing an Acute Ischemic Stroke due to large vessel occlusion, treated with combined IV t-PA and Solitaire FR within 6 hours of symptom onset have less stroke-related disability than those patients treated with IV t-PA alone.

Methods:
- Randomized, open-label with blinded outcome evaluation, parallel group trial
  - Intervention: IV tPA with Solitaire FR Device
  - Control: IV t-PA alone
SWIFT PRIME

[US Enrolling Centers]
101 UCLA/ Ronald Reagan UCLA Medical Center
102 Oregon Health and Science University (OHSU)
103 University of Pittsburgh Medical Center
104 University of Buffalo Neurosurgery, Buffalo General Hospital
105 University of Miami Jackson Memorial Hospital
106 Chattanooga Center for Neurologic Research/ Erlanger
109 Hennepin Country Medical Center
110 Medical College of Wisconsin Froedtert Hospital West
111 Maine Medical Center
113 Ohio Health Research Institute/ Riverside Methodist Hosptial
116 Florida Hospital
117 SUNY Upstate Medical University
118 Promedica Toledo Hospital
120 Central Baptist
121 Cleveland Clinic
122 West Virginia U
123 Providence Brain and Spine Institute
124 University of Massachusetts Medical Center
125 Emory University / Grady Medical Center
126 Rush University Medical Center
129 Saint Lukes
130 St. Jude Medical Center
134 Valley Baptist Medical Center
135 Tenet Hospital System

[EU Enrolling Centers]
201 CHU Montpellier - Hôpital Gui de Chauliac
203 Universitätsklinikum Kiel
204 Hospital Clínico Universitario de Valladolid
206 Klinikum der Johannes Wolfgang Goethe-Universität – Frankfurt
207 Kantonsspitale Aarau
210 Jansen
211 Arenillas du Mesnil de Rochemont
212 Remondes

Participating Centers
Selected 69 sites
Activated 61 sites
Enrolled 39 sites
SWIFT PRIME

mRS 0-2 at 90-days

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>N=98</td>
<td>N=97</td>
</tr>
<tr>
<td>60.2%</td>
<td>35.5%</td>
<td></td>
</tr>
</tbody>
</table>

NNT = 4

P=0.0008
<table>
<thead>
<tr>
<th>Trial</th>
<th>Imaging Required to Confirm Occlusion Prior to Randomization?</th>
<th>Device(s) Used in Intervention Arm</th>
<th>TICI 2b/3 Revascularization Rate in the Intervention Arm</th>
<th>mRS 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Intervention Arm</td>
<td>Control Arm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Intervention Arm</td>
<td>Control Arm</td>
</tr>
<tr>
<td>MR CLEAN</td>
<td>Yes</td>
<td>97% Stent Retrievers, 2% other Mechanical</td>
<td>58.7% (N=196)</td>
<td>33% (N=233)</td>
</tr>
<tr>
<td>ESCAPE</td>
<td>Yes</td>
<td>86% Stent Retriever</td>
<td>72.4% (n=156)</td>
<td>53.0% (n=164)</td>
</tr>
<tr>
<td>SWIFT PRIME</td>
<td>Yes</td>
<td>100% Stent Retriever</td>
<td>88.0% (n=83)</td>
<td>60.2% (n=98)</td>
</tr>
<tr>
<td>EXTEND-IA</td>
<td>Yes</td>
<td>100% Stent Retriever</td>
<td>86.2% (n=29)</td>
<td>71% (n=35)</td>
</tr>
</tbody>
</table>

SWIFT PRIME & EXTEND-IA…Superior recanalization rates and 90 day mRS scores may be attributable to:

1. Utilization of Viability Imaging (ASPECTS and/or Perfusion Imaging)
2. 100% Stent Retrievers
3. Encouraged BCG usage
“The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists”

Endorsed by the:

- American Association of Neurological Surgeons (AANS)
- Congress of Neurological Surgeons (CNS)
- AANS/CNS Cerebrovascular Section
- American Society of Neuroradiology (ASNR)
- Society of Vascular and Interventional Neurology
RECOMMENDATIONS

- Patients eligible for IV-tPA should receive IV-tPA even if endovascular therapy is being considered (Class I)
- Patients should undergo stent retriever endovascular therapy (Class I):
  - Pre-stroke mRS 0-1
  - AIS receiving IV-tPA within 4.5 hours
  - Occlusion of ICA or M1 segment MCA
  - Age ≥ 18, NIHSS ≥ 6, ASPECTS ≥ 6
  - Treatment onset within 6 hours of symptom onset

- Observing patients after IV-tPA to assess for clinical response before pursuing endovascular therapy is NOT required and is NOT recommended
What about patients with LVO that can’t get IV TPA?

**Exclusion Criteria**
- Recent Surgery
- Prior Stroke or Head Trauma prior 3 months
- Prior ICH
- Recent Intracranial or Spinal Surgery
- Anticoagulated (large pop. of our stroke patients are a.fib.)
- Can’t administer within 4.5 hrs of “last seen normal”

**“Relative” Exclusion Criteria**
- GI or Urinary Tract hemorrhage prior 21 days
- Major surgery or major trauma in prior 14 days
- MI in prior 3 months
63 yo WM presented 2 hrs after acute onset of dense left hemiplegia, slurred speech, and left facial droop (NIHSS 17). PMH notable for prior CABG 14 days prior…thus deemed not a candidate for IV tPA therapy. So what should be done…nothing???
Right Carotid

Left Carotid
Rapid improvement on the Cath Lab table, NIHSS had improved from 17 → 2 before leaving the cath lab. NIHSS was normal (17 → 0) the next day.
‘Wake Up’/Unknown Time of Onset Strokes

- 54 year-old female with history of atrial fibrillation, treated with ASA therapy, awoke with symptoms of aphasia and right hemiplegia (NIHSS 22).
- Traditionally do not qualify for any aggressive therapy, patients are not a candidate for IV t-PA therapy.
- At BHL, we utilize CT Perfusion imaging to offer treatment for these patients

- Time-to-Peak CT Perfusion map showing large area of ischemia, shown to be penumbra, involving the left MCA vascular territory.
- Time-to-Peak CT Perfusion map showing large area of ischemia, shown to be penumbra, involving the left MCA vascular territory.

- MRI the next day shows only punctate area of infarction within the left temporal cortex (arrow). The patient returned to 'normal' within 4hrs post-procedure (NIHSS 0).

- The patient was started on oral anticoagulation therapy for her atrial fibrillation and was discharged home.
57 year-old who awoke with slurred speech and left hemiplegia (NIHSS 17)

Not candidate for IV tPA as he was a “wake up” stroke
Acute Carotid Occlusions with Distal Emboli
Presenting NIHSS17 → 0
D/C home the next day
RECOMMENDATIONS

- Endovascular therapy with stent retrievers may be **REASONABLE** in:
  - Anterior circulation occlusions who have contraindications to IV-tPA, stent retriever endovascular therapy completed within 6 hours of symptom onset is REASONABLE (Class IIa)
  - AIS in who have M2/3 MCA occlusion, ACA, VA/Basilar/PCA (Class IIb)
  - Patients < 18 years of age with AIS and LVO that can be initiated within 6 hours of symptom onset (Class IIb)
  - AIS with pre-stroke mRS>1 or NIHSS<6 (Class IIb)
  - Angioplasty/stenting of cervical ICA stenosis or occlusion at the time of thrombectomy may be considered, usefulness is unknown (Class IIb)
  - The effectiveness of endovascular therapy is uncertain in AIS beyond 6 hours (Class IIb)
IMAGING

- If endovascular therapy is contemplated, a non-invasive intracranial vascular study is strongly recommended during the INITIAL imaging evaluation of the acute stroke patient, but should not delay IV-tPA administration (Class I)

- The benefit of additional imaging beyond CT/CTA or MR/MRA, such as perfusion imaging, for selecting patients for endovascular therapy are unknown (Class IIb)
Presenting NIHSS 20

Found ‘down’
Discharged to rehab

NIHSS 20→2

mRS 0 at 30 days
SYSTEMS OF STROKE CARE

- Patients should be rapidly transported to the closest available PSC or CSC (Class I, Level A). In some instances, this may involve air medical transport and hospital bypass.
- Regional systems of care should be developed, consisting of:
  - Healthcare facilities that provide initial emergency care, including of IV-tPA, including PSC, CSC, and other facilities
  - Centers capable of performing endovascular stroke treatment with comprehensive periprocedural care, including CSC and other healthcare facilities
- Endovascular therapy requires the patient to be at an experienced stroke center with rapid access to cerebral angiography and qualified neurointerventionalists (Class I, Level E)
CONCLUSIONS

- Stroke therapy is an evolving field, but we now have techniques and devices, combined with randomized controlled trials that provide:
  
  - Reliable & reproducible recanalization rates
  - Times to recanalization that are exceptional
  - Patient safety profiles that are comparable (if not better) to IV t-PA
  - Triage of patients to determine ‘salvageable’ brain
  - Data to support mechanical thrombectomy with stent retrievers as ‘standard of care’ for large vessel occlusions with severe stroke symptoms and favorable imaging patterns (CT perfusion, ASPECTS).
  - American Heart/American Stroke Society guidelines recommending thrombectomy from “experienced” centers as the standard of care