Intra-arterial tPA and Mechanical Thrombectomy

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Disclosures

• Consultant
  – Stryker

• Speaker’s bureau
  – Stryker
  – Penumbra Inc.
  – Genentech Inc.
Objectives

• Review acute stroke treatment options including endovascular stroke
• Discuss data supporting endovascular treatment of stroke
An estimated 795,000 Americans will suffer a new or recurrent stroke this year…

…that’s one every 40 seconds
Stroke

- 4th leading cause of death in US
- #1 cause of adult disability
- Stroke is a growing global epidemic
  - 1 in 6 people will have a stroke
  - 15 million new strokes each year
  - 6 million deaths
  - 30 million survivors with disabilities

*AHA Stroke Facts, 2006*
The Total Estimated Cost of Stroke is $48 Billion

- Lost productivity due to mortality and morbidity: $15 Billion
- Hospitalization Costs: $16 Billion
- Rehabilitation: $4.5 Billion
- Physician Costs: $4 Billion
- Medications & Other Costs: $3.5 Billion

The lifetime cost of stroke to a single patient is more than $140,000
Two Types of Stroke

Ischemic Stroke

Ischemic = type of condition in which oxygen is deficient

Often caused by a blood clot or plaque buildup that blocks blood flow

Hemorrhagic Stroke

Hemorrhage = bleeding

Occurs when a blood vessel ruptures, causing blood to leak into the surrounding tissue
Two Types of Stroke

13% of strokes are hemorrhagic:
• 10% intracerebral
• 3% subarachnoid

87% of strokes are ischemic; only 1% of these patients get intervention.

4 out of every 5 families will be affected by stroke

35-40% of Ischemic Strokes are Considered “Large Vessel”

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

- If left untreated, 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%(^1)</td>
</tr>
<tr>
<td>MCA</td>
<td>27%(^2)</td>
</tr>
<tr>
<td>Basilar Artery</td>
<td>89-90%(^3)</td>
</tr>
</tbody>
</table>

2. Furlan A et al. PROACT II Trial
Physiological Impact of Stroke

Estimated Pace of Neural Circuitry Lost in a Typical Large Vessel Acute Ischemic Stroke

<table>
<thead>
<tr>
<th>Time</th>
<th>Neurons Lost</th>
<th>Synapses Lost</th>
<th>Myelinated Fibers Lost</th>
<th>Accelerated Aging</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 second</td>
<td>32,000</td>
<td>230 million</td>
<td>218 yards</td>
<td>8.7 hours</td>
</tr>
<tr>
<td>1 minute</td>
<td>1.9 million</td>
<td>14 billion</td>
<td>7.5 miles</td>
<td>3.1 weeks</td>
</tr>
<tr>
<td>1 hour</td>
<td>120 million</td>
<td>830 billion</td>
<td>447 miles</td>
<td>3.6 years</td>
</tr>
<tr>
<td>Avg. stroke</td>
<td>1.2 billion</td>
<td>8.3 trillion</td>
<td>4470 miles</td>
<td>36 years</td>
</tr>
</tbody>
</table>

Options for Patients Experiencing an Ischemic Stroke

- **IV tPA**: Gold-standard in ischemic stroke care. Drug is designed to break apart the clot.
- **Medical Management**: Monitor vitals and provide secondary stroke prevention.
- **Endovascular Clot Removal**: Mechanical disruption or removal of the clot using standard endovascular approaches.

Bridging Therapy
Endovascular Therapy-Idea
Endovascular Therapy-Idea

Before

After
Stroke as a Process

Functional tissue

Nonfunctional but reversibly injured tissue

Irreversibly injured tissue

Infarction
Recanalization helps FACT
Impact of Recanalization
Review of Published Data

IV thrombolytics is the first line of therapy
Acute Treatment

• IV t-PA (Gold Standard)
• Key Clinical Trials
  - 0 to 3 hours (1996)
    ○ NINDS IV t-PA
  - 3 to 4.5 hours (2008)
    ○ ECASS III
NINDS IV t-PA (3 months): 0 to 3 hours
Treatment window

- Treatment within the first 3 hours only
  - IV t-PA
- Treatment within the first 4.5 hours
  - IV t-PA

Figure 3: Model estimating odds ratio for favourable outcome at 3 months in rt-PA-treated patients compared with controls by OTT.
Adjusted for age, baseline glucose concentration, baseline NIHSS measurement, baseline diastolic blood pressure, previous hypertension, and interaction between age and baseline NIHSS measurement.
Number of patients who benefit and are harmed per 100 patients treated with t-PA in each time window

<table>
<thead>
<tr>
<th>Treatment time-window (minutes)</th>
<th>Benefit</th>
<th>Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-90</td>
<td>27.8</td>
<td>1.5</td>
</tr>
<tr>
<td>91-180</td>
<td>23.1</td>
<td>2.6</td>
</tr>
<tr>
<td>181-270</td>
<td>16.9</td>
<td>3.4</td>
</tr>
<tr>
<td>271-360</td>
<td>5.2</td>
<td>7.3</td>
</tr>
</tbody>
</table>
Limitations of t-PA

• Time dependent
  – Reduced benefit with increased time
• Not effective for large thrombus
• Risk for systemic hemorrhage
Proximal vessel occlusions do not respond well to IV lytics

FACTS
# Proximal Vessel Occlusion

## Table 2. Baseline Occlusions and Proportional Recanalization

<table>
<thead>
<tr>
<th>Occlusion Location</th>
<th>Recanalization (All)</th>
<th>Recanalization After IV rt-PA</th>
<th>Recanalization After Endovascular Treatment</th>
<th>No Recanalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1-MCA</td>
<td>75.4% (49)</td>
<td>32.3% (21)</td>
<td>43.1% (28)</td>
<td>24.6% (16)</td>
</tr>
<tr>
<td>ICA terminus (T, L) occlusion</td>
<td>43.5% (10)</td>
<td>4.4% (1)</td>
<td>39.1% (9)</td>
<td>56.5% (13)</td>
</tr>
<tr>
<td>M2-MCA</td>
<td>92.3% (12)</td>
<td>30.8% (4)</td>
<td>61.5% (8)</td>
<td>7.7% (1)</td>
</tr>
<tr>
<td>BA</td>
<td>56.0% (14)</td>
<td>4.0% (1)</td>
<td>52.0% (13)</td>
<td>44.0% (11)</td>
</tr>
<tr>
<td>All</td>
<td>67.7% (86)</td>
<td>21.3% (27)</td>
<td>46.5% (59)</td>
<td>32.3% (41)</td>
</tr>
</tbody>
</table>

BA indicates basilar artery; ICA, internal carotid artery; IV, intravenous; MCA, middle cerebral artery; rt-PA, recombinant tissue plasminogen activator.

127 patients evaluated w IV tPA

Impact of Clot Burden on Success Rate of IV tPA

Successful Recanalization

~40% recanalization

Persistent Occlusion

What is TICI Score?

0: No perfusion
1: Perfusion past the initial obstruction but limited distal branch filling with little or slow distal perfusion
2a: Perfusion of less than half of the vascular distribution of the occluded artery
2b: Perfusion of half or greater of the vascular distribution of the occluded artery
3: Full perfusion with filling of all distal branches

• Successful recanalization is considered by most to be TICI 2b or TICI 3
CLINICAL TRIALS
IMS III Trial Design

- Patients must have moderate to severe neurologic deficits
  - NIHSS ≥ 10
- Patients who received IV tPA within 3 hours of symptoms onset were randomized 2:1
  - IV tPA alone
  - IV tPA plus IA therapy
- Primary outcome: mRS ≤ 2 @ 90 days

Broderick, et al. Endovascular Therapy after IV tPA vs tPA alone for Stroke (IMS III). 2013. NEJM
IMS III: Primary Outcome

• mRS ≤ 2
  – 40.8 % with endovascular therapy
  – 38.7 % with IV tPA alone
    95% CI: -6.1% to +9.1%

Broderick, et al. Endovascular Therapy after IV tPA vs tPA alone for Stroke (IMS III). 2013. NEJM
IMS III: Conclusions

- No significant difference in functional independence with endovascular therapy after intravenous t-PA, as compared with intravenous t-PA alone
- No difference in safety

Broderick, et al. Endovascular Therapy after IV tPA vs tPA alone for Stroke (IMS III). 2013. NEJM
IMS III: Patient Tracking

Broderick, et al. Endovascular Therapy after IV tPA vs tPA alone for Stroke (IMS III). 2013. NEJM
IMS III: Patient Tracking

• 434 randomized to IA/IV
  – 11 did not get an angiogram
  – 89 did not get endovascular therapy
• 23.0% of patients in “IA arm” did not get ANY IA therapy

Broderick, et al. Endovascular Therapy after IV tPA vs tPA alone for Stroke (IMS III). 2013. NEJM
IMS III: EVT Rates

• 49% of patients in EVT arm (164/334) were treated with IA tPA +/- ECHOS catheter
  – Not current standard

• 28% of patients (95/334) were treated with MERCI
  – Not current standard

• 77% of patients were treated with obsolete tools!!!!
Need for Quality Revascularization

### Revascularization Predicts Good Outcome For ICA, M1 Occlusion

<table>
<thead>
<tr>
<th></th>
<th>TICI=0</th>
<th>TICI=1</th>
<th>TICI=2a</th>
<th>TICI=2b</th>
<th>TICI=3</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>32</td>
<td>16</td>
<td>67</td>
<td>80</td>
<td>5</td>
</tr>
<tr>
<td>% 90 Day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS 0-2</td>
<td>6.3%</td>
<td>12.5%</td>
<td>19.4%</td>
<td>46.3%</td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>p &lt; .0001</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
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1 Tomsick T. Comparison of outcome by IA approach and interpretation in light of comparative trials. Paper presented at: International Stroke Conference; February 6-8, 2013; Honolulu, HI, USA.
Need for Speed – TIME MATTERS

Final Multivariable Model

<table>
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<tr>
<th>Risk Ratios</th>
<th>95% CI</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Time to Reperfusion (every 30 minutes)</td>
<td>0.90</td>
<td>0.82-0.99</td>
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Every 30 minute delay in reperfusion is associated with a 10% relative reduction in probability of good clinical outcome (mRS 0-2).

Khatri P, Yeatts SD, Mazighi M, et al. Time to angiographic reperfusion is highly associated with good clinical outcome in the IMS III Trial. Paper presented at: International Stroke Conference; February 6-8, 2013; Honolulu, HI, USA.
IMS III: Conclusions

• Basic CT alone is insufficient for selection of patients for IA therapy in most cases
• Interventional techniques yielding a low rate of TICI 2b and 3 flow do not improve outcomes in patients w stroke
  – IA tPA alone
  – MERCI
• Recanalization helps
• Time is brain
News Cycle 2/2013

['Clot-Buster' Drug May Still Be Best Stroke Treatment]

[No Benefit of Endovascular Therapy After Thrombolysis]

[No Advantage for Endovascular Stroke Treatment Over IV tPA]

[Imaging: Endovascular Therapy No Benefit Late After Stroke]
### Need for Quality Revascularization

**Revascularization Predicts Good Outcome For ICA, M1 Occlusion**

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<th>% 90 Day</th>
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<tr>
<td>0</td>
<td>32</td>
<td>3.1%</td>
<td>6.3%</td>
</tr>
<tr>
<td>1</td>
<td>16</td>
<td>12.5%</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>67</td>
<td>19.4%</td>
<td></td>
</tr>
<tr>
<td>2b</td>
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<td></td>
</tr>
<tr>
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<td>5</td>
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<tr>
<th></th>
<th></th>
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• Time is brain
Recent Stroke Trials

- MR CLEAN
- ESCAPE
- EXTEND-IA
- SWIFT PRIME
MR CLEAN
Results of the Multicenter Randomized Clinical trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands

Design

- **502 patient**, 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
- Masked, web-based, 1:1 random treatment allocation
  - Endovascular vs medical management
- **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
Patients were Randomized 1:1

502 Total Patients

97% (190/196) patients → stent retrievers

Baseline CT, CTA
N=502

2 pts withdrew consent

Randomized

Intervention
N=233

IAT never initiated in 17 pts

20 DSA Only

*IAT
N=196

mRS Assessment
N=233

Control
N=267

1 pt received IAT

Standard tx
N=266

mRS Assessment
N=267

Received Therapy

*IAT therapy was performed in 196 of 233 pts

End of Follow Up

7x Higher Odds of Recanalizing with Intra-Arterial Treatment*

Recanalization on CTA after 24 Hours

Control (68/207)  Intervention (141/187)

33%  75%

*Adjusted value odds ratio (95% CI) for "no intracranial occlusion on follow up CT angiography" in the intervention group versus the control group was 6.88 (4.34 to 10.94). Values were adjusted for age, NIHSS at baseline, time from onset to randomization, status with respect to previous stroke, atrial fibrillation, diabetes mellitus and occlusion of the ICAT. Data for follow up CT angiography were not available for 106 patients.
Effect of Intervention on Primary Outcome

Common adjusted odds ratio: 1.67 (95% CI: 1.21 to 2.30)

No Significant Between-Group Difference in the Occurrence of Serious Adverse Events at 90 days (P=0.31)

<table>
<thead>
<tr>
<th>Serious Adverse Events</th>
<th>Intervention (N=233)</th>
<th>Control (N=267)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any serious adverse event</td>
<td>110 (47.2%)</td>
<td>113 (42.3%)</td>
</tr>
<tr>
<td>Parenchymal hematoma type 2</td>
<td>14 (6.0%)</td>
<td>14 (5.2%)</td>
</tr>
<tr>
<td>New ischemic stroke in different vascular territory*</td>
<td>13 (5.6%)</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>25 (10.7%)</td>
<td>41 (15.4%)</td>
</tr>
<tr>
<td>Hemicraniectomy</td>
<td>14 (6.0%)</td>
<td>13 (4.9%)</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within 7 days</td>
<td>27 (11.6%)</td>
<td>33 (12.4%)</td>
</tr>
<tr>
<td>Within 30 days</td>
<td>44 (18.9%)</td>
<td>49 (18.4%)</td>
</tr>
</tbody>
</table>

*P<0.001

MR CLEAN Study Conclusions

• In patients with acute ischemic stroke caused by a proximal intracranial arterial occlusion of the anterior circulation, **intra-arterial treatment** administered within 6 hours after stroke onset was effective and safe.

• This treatment leads to a clinically significant increase in the **functional independence** in daily life by 3 months, without an increase in mortality.

ESCAPE

Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times

M Goyal et. al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke. NEJM published on February 11, 2015
Purpose and Methods

Purpose: To answer the question “Do I take this patient for endovascular thrombectomy?”

Methods:

- 316 patients
- 22 centers in Canada, US, Korea, UK and Ireland
- Randomized, open-label with blinded outcome evaluation, parallel group trial
  - **Intervention:** Endovascular mechanical thrombolysis with an approved approach/device (use of retrievable stents and balloon guide catheters recommended)
  - **Control:** Guideline-based standard of care (IV tPA if <4.5 hrs / stroke unit care)
- Enter consecutive ESCAPE-eligible patients – no “cherry-picking”
- 25 cases sequentially per site
- Choose “small core / proximal occlusion / good collaterals” patients
- Be fast, efficient and safe

M Goyal et. al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke. *NEJM* published on February 11, 2015
Inclusion Criteria

- Acute ischemic stroke
- Age $\geq 18$ years
- Last-seen-well time to randomization $<12$ hours
- ASPECTS $>5$
- Baseline NIHSS $>5$ at time of randomization
- Good functional status: pre-stroke modified Barthel Index $\geq 95$, not living in a nursing home; fully independent
- Confirmed symptomatic intracranial occlusion based on CTA in anterior anatomy (Carotid T/L, M1, 2 or more M2’s not including the anterior temporal artery)
- Moderate to good collaterals on CTA
- Endovascular treatment can be initiated within 60 minutes of baseline NCCT with target CT to first recanalization of 90 minutes

M Goyal et. al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke. *NEJM* published on February 11, 2015
Patients were Randomized 1:1

316 Total Patients

**Intervention**

- Received tPA (n=120)
- Did not receive tPA (n=45)

**Control**

- Received tPA (n=118)
- Did not receive tPA (n=32)

**Allocated to intervention arm (n=165)**

- Did not undergo procedure – no groin puncture (n=4)
- Did not have intracranial angiography (n=2)
- Had TICI 3 on first intracranial angiography (n=2)
- Had TICI 2b on first intracranial angiography (n=6)

**Allocated to control arm (n=150)**

- Cross over from control to endovascular (n=1)

**Received endovascular treatment (n=151)**

- Lost to 90-day follow-up (n=1)

164 evaluable subjects

147 evaluable subjects

86% (130/151) → stent retrievers

Revascularization

M Goyal et al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke. NEJM published on February 11, 2015
90-day mRS

Common adjusted odds ratio: 3.1 (95% CI: 2.0 to 4.7)

M Goyal et al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke. NEJM published on February 11, 2015
## Safety Endpoints/Mortality

<table>
<thead>
<tr>
<th>Serious Adverse Events</th>
<th>Intervention (N=165)</th>
<th>Control (N=150)</th>
<th>Adjusted RR (CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>10.4%</td>
<td>19.0%</td>
<td>0.5 (0.3 to 0.8)</td>
</tr>
<tr>
<td>Large MCA / malignant MCA stroke</td>
<td>4.8%</td>
<td>10.7%</td>
<td>0.3 (0.1 to 0.7)</td>
</tr>
<tr>
<td>sICH (clinically determined at site)</td>
<td>3.6%</td>
<td>2.7%</td>
<td>1.2 (0.3 to 4.6)</td>
</tr>
<tr>
<td>Access site hematoma</td>
<td>1.8%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>MCA perforation</td>
<td>0.6%</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions

• Endovascular thrombectomy is a safe, highly effective procedure that saves lives and dramatically reduces disability WHEN:
  – Patients are carefully selected by imaging to identify proximal occlusions and exclude large core and exclude patients with absent collaterals
  – Treatment is extremely fast with target first slice
    - Imaging to groin puncture <60 minutes
    - Imaging to reperfusion <90 minutes
  – Safe effective technology (retrievable stents) is used

SWIFT PRIME

Solitaire FR with the intention for Thrombectomy as PRIMary Endovascular treatment for acute ischemic stroke

Results of the SWIFT PRIME Trial were presented by Dr. Jeffrey Saver and Dr. Michael D. Hill at the International Stroke Conference in Nashville, TN on Wednesday, February 11, 2015.
Purpose and Methods

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

• **Methods:**
  – Randomized, open-label with blinded outcome evaluation, parallel group trial
    - *Intervention*: IV tPA with Solitaire FR Device
    - *Control*: IV tPA alone
  – 39 enrolling sites in the USA and Europe
  – 196 patients

Results of the SWIFT PRIME Trial were presented by Dr. Jeffrey Saver at the International Stroke Conference in Nashville, TN on Wednesday, February 11, 2015.
Inclusion Criteria

- Acute ischemic stroke
- Age 18-80
- Pre-stroke mRS≤1
- **ASPECTS ≥6**
- Baseline NIHSS 8-29 at time of randomization
- CTA or MRA confirmation of large vessel occlusion in ICA, M1 segment of MCA or carotid terminus
- **Initiation of IV tPA within 4.5 hours of onset of stroke**
- Endovascular treatment can be initiated within 6 hours of onset of stroke symptoms and within 90 minutes from CTA/MRA to groin puncture

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90-day mRS

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### Safety Endpoints/Mortality

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<table>
<thead>
<tr>
<th>Serious Adverse Events</th>
<th>Intervention (N=98)</th>
<th>Control (N=97)</th>
<th>OR (CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (p=0.50)</td>
<td>9.2</td>
<td>12.4</td>
<td>0.72 (0.29 to 1.79)</td>
</tr>
<tr>
<td>Any serious adverse events</td>
<td>35.7%</td>
<td>30.9%</td>
<td>1.24 (0.68 to 2.25)</td>
</tr>
<tr>
<td>sICH at 27 hours</td>
<td>1%</td>
<td>3.1%</td>
<td>0.32 (0.03 to 3.16)</td>
</tr>
</tbody>
</table>
Conclusions

• In AIS patients with confirmed large vessel anterior circulation occlusions treated with IV tPA, rapid treatment with the Solitaire stent retriever lessens post-stroke disability over the entire outcome range and increases the proportion of patients who are alive and independent 3 months after stroke.

• For every two and a half patients treated, one more patient has a better disability outcome.

• For every four patients treated, one more patient is independent at long term follow up.
EXTEND-IA

A randomized controlled trial of endovascular thrombectomy after standard dose intravenous tPA within 4.5 hours of stroke onset utilizing dual target imaging selection
Rationale and Methods

• **Purpose:** 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 IV tPA “failure”)

• **Methods:**
  - Randomized, open-label with blinded endpoint (PROBE) design
    - *Intervention:* endovascular treatment + IV tPA
    - *Control:* IV tPA
  - 70 patients
Inclusion Criteria

• Acute ischemic stroke
• Age ≥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) **AND**
  – Mismatch - Using CT or MRI with a Tmax >6 second delay perfusion volume and either CT-rCBF or DWI infarct core volume
70 Total Patients

Randomized
N=70

Intervention
tPA + Endovascular
N=35

Received Angiogram
N=33

mRS Assessment
N=29

Control
tPA only
N=35

100% (35/35) \rightarrow stent retrievers

IAT never initiated in 2 pts

B.C.V. Campbell et. al. Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection. NEJM published on February 11, 2015
Revascularization in the IV tPA + Endovascular Arm (N=29)

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

B.C.V. Campbell et. al. Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection. NEJM published on February 11, 2015
90-day mRS

Intervention (N=35)
- mRS 0: 26%
- mRS 1: 26%
- mRS 2: 20%
- mRS 3: 17%
- mRS 4: 3%
- mRS 5: 9%

Control (N=35)
- mRS 0: 17%
- mRS 1: 11%
- mRS 2: 11%
- mRS 3: 11%
- mRS 4: 17%
- mRS 5: 11%
- mRS 6: 20%
<table>
<thead>
<tr>
<th>Serious Adverse Events</th>
<th>IV tPA Only (N=35)</th>
<th>IV tPA + Endovascular (N=35)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>20%</td>
<td>9%</td>
<td>0.18</td>
</tr>
<tr>
<td>sICH (SITS MOST)</td>
<td>6%</td>
<td>0%</td>
<td>0.49</td>
</tr>
<tr>
<td>PH</td>
<td>9%</td>
<td>11%</td>
<td>0.99</td>
</tr>
<tr>
<td>Wire Perforation</td>
<td></td>
<td>2.9%</td>
<td></td>
</tr>
<tr>
<td>Emboli</td>
<td></td>
<td>5.7%</td>
<td></td>
</tr>
</tbody>
</table>
Endovascular Therapy-A New Era?

Medscape Medical News > Neurology

Endovascular Stroke Therapy Proven at Last: MR CLEAN Published
Sue Hughes
December 17, 2014

The New York Times

For First Time, Treatment Helps Patients With Worst Kind of Stroke, Study Says

Since then, two other trials evaluating endovascular interventions — ESCAPE (Endovascular Treatment for Small Core and Proximal Occlusion Ischemic Stroke) and EXTEND IA (Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial) — have been stopped after early interim analyses showed benefit in the intervention group.
Triple Win for Clot Retriever Devices in Acute Stroke
— ESCAPE, EXTEND-IA, and PRIME SWIFT trials all showed benefit over thrombolysis alone.

Clot Extractors Shown Beneficial In Stroke Patients

Brain stents show big promise for certain stroke patients
# LVO-Time is Brain

<table>
<thead>
<tr>
<th>STUDY</th>
<th>Time to IVt-PA</th>
<th>Time to Groin</th>
<th>Time to Recan</th>
<th>TICI 2b-3</th>
<th>MRS 0-2 IA</th>
<th>MRS 0-2 Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMS_III</td>
<td>121-122 min</td>
<td>208 min</td>
<td>N/A</td>
<td>40%</td>
<td>40.8%</td>
<td>38.7%</td>
</tr>
<tr>
<td>MR CLEAN</td>
<td>85-87 min</td>
<td>260 min</td>
<td>N/A</td>
<td>58.7%</td>
<td>32.6%</td>
<td>19.1%</td>
</tr>
<tr>
<td>ESCAPE (1)</td>
<td>110-125 min</td>
<td>185 min</td>
<td>241 min</td>
<td>72.4%</td>
<td>53%</td>
<td>29.3%</td>
</tr>
<tr>
<td>EXTEND IA (2)</td>
<td>127-145 min</td>
<td>210 min</td>
<td>248 min</td>
<td>86%</td>
<td>71%</td>
<td>40%</td>
</tr>
<tr>
<td>SWIFT PR. (3)</td>
<td>167.5 min</td>
<td>184 min</td>
<td>213 min</td>
<td>88%</td>
<td>60.2%</td>
<td>35.5%</td>
</tr>
</tbody>
</table>

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HERMES data

Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials
<table>
<thead>
<tr>
<th>Intervention population</th>
<th>Control population</th>
<th>Risk difference (%)</th>
<th>Rate ratio (95% CI)</th>
<th>Odds ratio (95% CI)</th>
<th>Adjusted rate ratio (95% CI)</th>
<th>Adjusted odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRS score reduction (shift analysis; primary outcome)*</td>
<td></td>
<td></td>
<td></td>
<td>2.26* (1.67-3.06); p&lt;0.0001</td>
<td>2.49* (1.76-3.53); p&lt;0.0001</td>
<td>2.49* (1.76-3.53); p&lt;0.0001</td>
</tr>
<tr>
<td>mRS score 0-1 at 90 days</td>
<td>26.9% (170/633)</td>
<td>12.9% (83/645)</td>
<td>14.0</td>
<td>2.00 (1.54-2.60); p&lt;0.0001</td>
<td>2.49 (1.84-3.35); p&lt;0.0001</td>
<td>2.06 (1.59-2.69); p&lt;0.0001</td>
</tr>
<tr>
<td>mRS score 0-2 at 90 days</td>
<td>46.0% (291/633)</td>
<td>26.5% (171/645)</td>
<td>19.5</td>
<td>1.7 (1.41-2.05); p&lt;0.0001</td>
<td>2.35 (1.85-2.98); p&lt;0.0001</td>
<td>1.73 (1.43-2.09); p&lt;0.0001</td>
</tr>
<tr>
<td>NIHSS score 0-2 at 24 h</td>
<td>21.0% (129/615)</td>
<td>8.3% (52/630)</td>
<td>12.7</td>
<td>2.47 (1.79-3.41); p&lt;0.0001</td>
<td>2.91 (2.06-4.12); p&lt;0.0001</td>
<td>2.66 (1.92-3.67); p&lt;0.0001</td>
</tr>
<tr>
<td>Early neurological recovery at 24 h</td>
<td>50.2% (309/616)</td>
<td>21.2% (134/633)</td>
<td>29.0</td>
<td>2.34 (1.91-2.87); p&lt;0.0001</td>
<td>4.04 (2.75-5.93); p&lt;0.0001</td>
<td>2.34 (1.91-2.87); p&lt;0.0001</td>
</tr>
</tbody>
</table>

Data show the proportion of patients with outcome (n/N). unless otherwise stated. NIHSS—National Institutes of Health Stroke Scale. mRS—modified Rankin Scale. *Common odds ratio indicating the odds of improvement of 1 point on the mRS.

Table 2: Efficacy outcomes from the pooled data
HERMES data

Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials
Conclusion and future of therapy

• Conclusion
  – Endovascular therapy for large vessel occlusion stroke is effective
  – Serves as an alternative to IV tPA
    ○ Outside of time window
    ○ Failure of therapy

• Future
  – Extending the time window
    ○ Patient selection based on collaterals/tissue survival
    ○ Neuroprotective agents
Example Case 1

- 60 yo female
- Presentation NIHSS = 18
- Puncture ~ 5 hours from LKN
- TICI 3 in 31 minutes
- Discharge NIHSS = 0 → home
Example Case 2

- 74 yo male
- Presentation NIHSS = 22
- Puncture ~ 15 hours from LKN
- TICI 3 in 20 minutes
- Discharge NIHSS = 2 → rehab
Example Case 3 – Multiple passes

- 42 yo male
- Presentation NIHSS = 19
- Puncture ~ 10 hours from LKN
- TICI 3 in 29 minutes
- Discharge NIHSS = 0 → home