Endovascular Therapy:
A New DAWN in Acute Stroke Care

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Beth Israel Deaconess Needham Grand Rounds
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Presenter Disclosure Information

David Eric Searls, MD

Financial Disclosure: None
Objectives:

- Review recent data supporting the use of endovascular thrombectomy in patients with acute ischemic stroke due to a large vessel occlusion for patients presenting less than 6 hours from LSW, and those presenting from 6 to 24 hours from LSW.

- Understand role of advanced brain imaging for selecting patients for endovascular thrombectomy.

- Contrast time- vs. tissue (imaging)-based selection of potential candidates for endovascular thrombectomy.
Stroke Is An Emergency
Estimated Pace of Neuronal Loss in Typical Large Vessel Supratentorial Acute Ischemic Stroke

<table>
<thead>
<tr>
<th></th>
<th>Neurons Lost</th>
<th>Synapses Lost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Per second</strong></td>
<td>32,000</td>
<td>230 million</td>
</tr>
<tr>
<td><strong>Per minute</strong></td>
<td>1.9 million</td>
<td>14 billion</td>
</tr>
<tr>
<td><strong>Per hour</strong></td>
<td>120 million</td>
<td>830 billion</td>
</tr>
</tbody>
</table>

Stroke, 2006;37(1):263
The major goal of acute stroke management is resuscitation of the penumbral tissue.
Ischemic Penumbra

No reperfusion

Timely reperfusion
The major goal of acute stroke management is resuscitation of the penumbral tissue

- If reperfusion of the penumbra occurs rapidly, neurons recover & the patient improves

- With no reperfusion, a time-related cascade converts ailing neurons in salvageable penumbral tissue to permanent infarction
10-25% of stroke patients have preceding TIAs

Cumulative Risk for stroke after TIA
- 1st month = 8%
- 1st year = 12%
- 5 years = 30%

TIAs present golden opportunities for intervention to prevent future strokes
Approaches To Acute Therapy

- **Reperfusion**
  - IV thrombolysis (TPA)
  - Endovascular
    - Intra-arterial thrombolysis
    - Mechanical disruption of the clot
    - Trevo
    - Solitaire

- **Antiplatelets or Anticoagulation**
IV t-PA is Standard of Care for:

1: For most eligible acute ischemic stroke patients presenting within 3 hours of stroke symptom onset

2: For some patients presenting within 3 to 4.5 hours from stroke onset
What else can be offered besides IV TPA?
Era of Highly Effective Revascularization Therapy
Stent retriever with thrombus
Stroke Terms

- LVO (Large Vessel Occlusion)
- M1 and M2 segment of MCA
- ASPECTS score
- TICI score
- CT perfusion
The MCA is divided into 4 segments:
- M1 – from origin to bifurcation
- M2 – from bifurcation to circular sulcus of the insula where it bends to continue as M3
- M3 – opercular branches within the Sylvian fissure
- M4 – branches from the sylvian fissure to cortex
Advanced Neuroimaging

Confirm location & type of stroke,
may provide clues to stroke cause,
may reveal penumbra,
& help identify mechanical thrombectomy candidate
Pre-treatment Ischemic Core a Powerful Determinant of Outcome in Acute Ischemic Stroke

ASPECTS image scoring evaluates for ischemic core
Examine all the images at the ganglionic and supra-ganglionic levels.

Take off 1 pt from 10 for every region that is affected.

**ASPECTS**
- 8-10 Small core.
- 6-7 Moderate core.
- 0-5 Large core.
CTA brain
## TICI Score

<table>
<thead>
<tr>
<th>Grade 0</th>
<th>No perfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Penetration with minimal perfusion</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Partial perfusion</td>
</tr>
<tr>
<td>2a</td>
<td>Only partial filling (2/3) of the entire vascular territory is visualized</td>
</tr>
<tr>
<td>2b</td>
<td>Complete filling of all of the expected vascular territory is visualized, but the filling is slower than normal</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Complete perfusion</td>
</tr>
</tbody>
</table>
CT Perfusion Imaging

Mean Transit Time

Cerebral Blood Volume
Conventional Angiogram: Right MCA occlusion prior to treatment
### Good Outcome (%) at 90 days

<table>
<thead>
<tr>
<th>Trial</th>
<th>Control</th>
<th>Endovascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRCLEAN Non-con CT</td>
<td>19%</td>
<td>33%</td>
</tr>
<tr>
<td>REVASCAT ASPECTS ≥6</td>
<td>28%</td>
<td>44%</td>
</tr>
<tr>
<td>ESCAPE ASPECTS ≥6 CTA collaterals</td>
<td>29%</td>
<td>53%</td>
</tr>
<tr>
<td>SWIFT PRIME ASPECTS ≥5, 85% had penumbral imaging</td>
<td>36%</td>
<td>60%</td>
</tr>
<tr>
<td>EXTEND-IA CT Perfusion RAPID (100%)</td>
<td>40%</td>
<td>71%</td>
</tr>
<tr>
<td>THERAPY CTA clot ≥ 8 mm</td>
<td>30%</td>
<td>38%</td>
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New Randomized Clinical Trials of Endovascular Therapy: TIME

<table>
<thead>
<tr>
<th>Study</th>
<th>Onset-groin</th>
<th>Reperfusion</th>
</tr>
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<tbody>
<tr>
<td>MRCLEAN</td>
<td>260 min</td>
<td>355 minutes</td>
</tr>
<tr>
<td>REVASCAT</td>
<td>269 min</td>
<td>241 min</td>
</tr>
<tr>
<td>ESCAPE</td>
<td>Onset-1st reperfusion 241 min</td>
<td></td>
</tr>
<tr>
<td>SWIFT PRIME</td>
<td>Onset-groin 224 min</td>
<td></td>
</tr>
<tr>
<td>EXTEND-IA</td>
<td>Onset-groin 210 min, reperfusion 248 min</td>
<td></td>
</tr>
<tr>
<td>THERAPY</td>
<td>Onset-groin 226 min</td>
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Endovascular
Control

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Hermes Meta-analysis Shows Benefit for Mechanical Thrombectomy

Figure 1: Scores on the modified Rankin Scale at 90 days
Distribution of scores at 90 days in the intervention and control groups in the overall trial population (A) and for patients treated with, or ineligible for, intravenous alteplase (B). Distributions for other subgroups shown in appendix pp 5-11.

Figure 2: Forest plot showing adjusted treatment effect for mRS at 90 days in prespecified subgroups with p values for heterogeneity across subgroups.
- cOR: common odds ratio. mRS: modified Rankin Scale. ASPECTS: Alberta Stroke Program Early CT score.
- NIHSS: National Institutes of Health Stroke Scale.
Hermes Meta-analysis Shows Benefit for Mechanical Thrombectomy

- Pooled analysis of 1287 patients from 5 recent trials
- Functional independence (mRS 0-2) at 3 months, 46% vs 26%
- For every 100 patients treated with endovascular therapy
  - 38 patients will have less disabled outcome
  - Including 20 more functionally independent

Risks of Mechanical Thrombectomy

ICH
Due to mechanical perforation, reperfusion, or use of anticoagulants
4.4% (vs. 4.3% in the medical arm)

New infarct
Due to clot fragmentation or artery-to-artery embolism
~ 0 to 4%
TICI 2B/3 reperfusion had better outcomes

Faster reperfusion had better outcomes
Time is still important . . .

Every 1 minute delay in reperfusion
1/100 patients has increased 3-month disability

Every 6 minute delay
2/100 are functionally dependent at 3 months
Era of Highly Effective Revascularization Therapy

Stent retrieval option for selected adults ≥ 18 years with:

- LVO
- NIH stroke scale 6 or higher
- ASPECTS score ≥ 6
- Symptom to groin puncture time < 6 hours
- Pre-stroke mRS ≤ 1
EVT within 6h may be considered on a case-by-case basis in the following scenarios:

Contraindications to IV t-PA
Occlusions of M2 MCA, ACA, PCA, VA, or BA
Pre-stroke mRS>1
ASPECTS<6
NIHSS<6
Case 1:  
66 year old woman who fell taking out trash

- 10:00 on 4/18/16 was LSW – Witnessed fall
- NIHSS 7 at community hospital
- Past Medical History: Atrial fibrillation, HTN
- Meds: None
- VS: BP 170/82  HR 88
- CT brain: No hemorrhage or early infarct signs
  ASPECTS score 10
- 13:25 iv TPA started
- CTA brain performed: Right MCA occlusion
Case 1:

14:15: Arrives at BIDMC ED
NIH stroke scale 9
1  eye deviation to the right
2  left homonymous hemianopsia
1  left facial palsy
1  left arm drift
1  left leg drift
2  left hemisensory loss
Repeat CT Brain: ASPECTS score 9, no hemorrhage
ASPECTS = 10 (Eligible for ESCAPE Trial)
ASPECTS = 0 (NOT Eligible for ESCAPE)
Conventional Angiogram: Right MCA occlusion prior to treatment at 15:30
Case 1: MRI Brain - DWI
Case 1: Discharge exam

NIHSS 0

- MS: alert and oriented x3, intact language
- CN: intact facial strength, no dysarthria, VFFTC
- Motor: full strength of all four limbs
- Sensory: intact sensation
What if patient with LVO presents more than 6 hours from stroke symptom onset?

- DEFUSE 3 Trial
- DAWN Trial
DEFUSE 3: Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

- Patients randomized to either Endovascular thrombectomy and best medical management versus best medical management alone
- Blinded outcome assessment
## DEFUSE 3: Thrombectomy for Stroke at 6 to 16 hours with Selection by Perfusion Imaging

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
<th>Imaging Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Key Inclusion Criteria</strong></td>
<td></td>
</tr>
<tr>
<td>Presentation consistent with an anterior circulation ischemic stroke</td>
<td>ASPECT Score ≥ 6 on non-contrast CT head</td>
</tr>
<tr>
<td>Age 18-90 years</td>
<td>MR or CT angiography shows an ICA or MCA-M1 occlusion</td>
</tr>
<tr>
<td>Baseline NIHSS ≥ 6</td>
<td>Target mismatch on CTP or PWI (RAPID):</td>
</tr>
<tr>
<td>Pre-stroke mRS 0-2</td>
<td>- Ischemic core &lt; 70mL</td>
</tr>
<tr>
<td></td>
<td>- Mismatch ratio ≥ 1.8 and mismatch volume ≥ 15 mL</td>
</tr>
<tr>
<td></td>
<td>- Or DWI lesion &lt; 25 mL if obtained within 60 mL of CTA/MRA</td>
</tr>
<tr>
<td>Endovascular treatment feasible within 6-16 hours from LKW</td>
<td></td>
</tr>
<tr>
<td><strong>Key Exclusion Criteria</strong></td>
<td></td>
</tr>
<tr>
<td>Treatment with tPA &gt; 4.5 h or thrombectomy &lt; 6 h from LKW</td>
<td>Evidence of intracranial tumor, acute intracranial hemorrhage, or AVM</td>
</tr>
<tr>
<td>Stroke in multiple locations or suspected bacterial endocarditis</td>
<td>Significant mass effect with midline shift</td>
</tr>
<tr>
<td>Concurrent other serious illness or life expectancy &lt; 6 months</td>
<td>Evidence of ICA flow-limiting dissection or aortic dissection</td>
</tr>
<tr>
<td>SBP &gt; 185 / DBP &gt; 110 mmHg not treatable with medications</td>
<td>Occlusions in multiple vascular territories</td>
</tr>
<tr>
<td>Contraindications for contrast, incl. refractory iodine allergy</td>
<td>Intracranial stent implanted in the same vascular territory that would</td>
</tr>
<tr>
<td></td>
<td>preclude safe deployment / removal of the neurothrombectomy device</td>
</tr>
</tbody>
</table>
DEFUSE 3: EVT associated with significantly lower disability scores at 90 days

Table 2. Clinical and Imaging Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Endovascular Therapy (N=92)*</th>
<th>Medical Therapy (N=90)</th>
<th>Odds Ratio or Risk Ratio (95% CI)†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary efficacy outcome: median score on modified Rankin scale at 90 days (IQR):‡</td>
<td>3 (1–4)</td>
<td>4 (3–6)</td>
<td>2.77 (1.63–4.70)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Secondary efficacy outcome: functional independence at 90 days — no. (%)¶</td>
<td>41 (45)</td>
<td>15 (17)</td>
<td>2.67 (1.60–4.48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Safety outcomes — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death at 90 days</td>
<td>13 (14)</td>
<td>23 (26)</td>
<td>0.55 (0.30–1.02)</td>
<td>0.05</td>
</tr>
<tr>
<td>Symptomatic intracranial hemorrhage¶</td>
<td>6 (7)</td>
<td>4 (4)</td>
<td>1.47 (0.40–6.55)</td>
<td>0.75</td>
</tr>
<tr>
<td>Early neurologic deterioration</td>
<td>8 (9)</td>
<td>11 (12)</td>
<td>0.71 (0.30–1.69)</td>
<td>0.44</td>
</tr>
<tr>
<td>Parenchymal hematoma type 2</td>
<td>8 (9)</td>
<td>3 (3)</td>
<td>2.61 (0.73–14.69)</td>
<td>0.21</td>
</tr>
<tr>
<td>Imaging outcomes**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median infarct volume at 24 hr (IQR) — ml</td>
<td>35 (18–82)</td>
<td>41 (25–106)</td>
<td>—</td>
<td>0.19</td>
</tr>
<tr>
<td>Median infarct growth at 24 hr (IQR) — ml</td>
<td>23 (10–75)</td>
<td>33 (18–75)</td>
<td>—</td>
<td>0.08</td>
</tr>
<tr>
<td>Reperfusion &gt;90% at 24 hr — no./total no. (%)</td>
<td>59/75 (79)</td>
<td>12/67 (18)</td>
<td>4.39 (2.60–7.43)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Complete recanalization at 24 hr — no./total no. (%)</td>
<td>65/83 (78)</td>
<td>14/77 (18)</td>
<td>4.31 (2.65–7.01)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TICI score of 2b or 3 — no./total no. (%)</td>
<td>69/91 (76)</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>
DEFUSE 3: EVT associated with significantly lower disability scores at 90 days

Figure 2. Scores on the Modified Rankin Scale at 90 Days.
Evaluating Perfusion Mismatch
DAWN Trial: Thrombectomy 6 to 24 Hours After Stroke with a Mismatch between Deficit and Infarct

- Randomized patients to either EVT and best medical management versus best medical management alone
- Blinded assessment of end points
DAWN Inclusion Criteria

- Occlusion of Intracranial Internal Carotid artery or M1 segment of MCA
- Last known well 6 to 24 hours earlier
- Age ≥ 18
- Prestroke mRS 0 - 1
DAWN: Mismatch between severity of clinical deficit and infarct volume

- **Group A:**
  - > 80 years
  - NIHSS ≥ 10
  - Infarct volume < 21 mL

- **Group B:**
  - < 80 years
  - NIHSS ≥ 10
  - Infarct volume < 31 mL

- **Group C:**
  - younger than 80 years
  - NIHSS > 20
  - Infarct volume 31 to 50 mL
DAWN: EVT group had significantly lower disability scores at 90 days compared medical therapy only group

<table>
<thead>
<tr>
<th>Table 2. Efficacy Outcomes.*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome</strong></td>
</tr>
<tr>
<td>Primary end points</td>
</tr>
<tr>
<td>Score on utility-weighted modified Rankin scale at 90 days§</td>
</tr>
<tr>
<td>Functional independence at 90 days — no. (%)¶</td>
</tr>
<tr>
<td>Secondary end points</td>
</tr>
<tr>
<td>Early response — no. (%)</td>
</tr>
<tr>
<td>Recanalization at 24 hr — no. (%)‡‡</td>
</tr>
<tr>
<td>Change from baseline in infarct volume at 24 hr — ml‡‡</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Infarct volume at 24 hour — ml‡‡</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Grade of 2b or 3 on mTICI scale — no. (%)§§</td>
</tr>
</tbody>
</table>
DAWN: EVT group had significantly lower disability at 90 days compared to medical therapy only group.
Case 2

- 07:20 2/2/18 71-year-old woman found at home with right sided weakness and aphasia
- 22:00 2/1/18 Last known well
- 07:59 2/2/18 BID Needham ED arrival
Case 2

PMH: Hypothyroidism
Meds: Levothyroxine 75 mcg daily
Labs: INR 1.0, glucose 107
    BUN 23, Cr 1.02
Case 2

08:00 2/2/18 CT brain non contrast: Hyperdense left MCA sign
- Hypodensity of left anterior frontal lobe
- ASPECTS score 7

08:03 CTA brain/neck: Occlusion of the M1 segment of the left MCA

08:14 Specialists on Call assessment
- NIH stroke scale 18
Case 2

09:02 2/2/18 Arrival at BIDMC
NIHSS 19

Neuro exam: eyes open
- Left gaze deviation
- Globally aphasic
- Right facial droop, right arm plegic, right leg triple flexion
Case 2

09:16 CT brain non contrast: Hypodensity in left anterior frontal lobe

ASPECTS 6

09:16  CT Perfusion Scan:

- Tmax > 6 secs: 166 mL
- CBF < 30% volume: 56 mL
- Mismatch volume: 110 mL
- Mismatch ratio: 3.0
Case 2: Successful Recanalization

09:38 Conventional Angiogram:
- Complete occlusion of proximal left MCA
- After one pass with Trevo, TICI score 3
Case 2

- 2/04/18 at 12:43am MRI brain without contrast
- Acute infarct left basal ganglia, left insula, left anterior frontal lobe
- Acute infarct right occipital lobe
- Hemorrhagic transformation of left caudate
- Small IVH
Case 2

Discharge Exam:
- Alert and oriented to person, hospital, date
- Mild left gaze deviation
- Able to track examiner
- Follows axial commands
- Non fluent aphasia with phonemic paraphasic errors
Case 2

Discharge Exam:

- Moderate dysarthria
- Right facial droop
- Right arm and leg at least anti-gravity
IV t-PA remains the standard-of-care for most eligible acute ischemic stroke patients presenting within 3h of stroke symptom onset, and for some patients presenting within 3 to 4.5h from stroke onset.

Endovascular thrombectomy, concurrent with IV t-PA or in t-PA ineligible patients, is now the standard-of-care for carefully selected patients with large vessel occlusion presenting within 24h of stroke onset or last known well.
Emergency brain imaging (CT or MRI) is required before IV t-PA or EVT.

Non-invasive vascular imaging (CTA or MRA) is recommended during the initial evaluation, BUT it should not delay IV t-PA (if indicated).

If IV t-PA is initiated before CTA/MRA, obtain vascular imaging quickly after IV t-PA to determine if there is LVO and if EVT is warranted.
Take Home Points

EVT option for selected adults $\geq 18$ years with:

- LVO
- NIH stroke scale 6 or higher
- ASPECTS score $\geq 6$
- symptom to groin puncture time $< 6$ hours
Patients presenting 6 to 24 hours after stroke symptom onset may be candidates for EVT if:

- LVO of intracranial ICA or M1 segment of MCA
- Perfusion CT/MRI brain shows evidence of a perfusion mismatch
- Meets criteria of DEFUSE 3 Trial for patients with LSW 6 – 16 hours or DAWN Trial for patients with LSW 6 -24 hours
- Age ≥ 18

Take Home Points
To achieve expedited care & improve outcomes:

- Rapid identification of LVO
- Rapid transport to EVT-capable Stroke Center
I would like to thank Dr. Magdy Selim and Dr. Marc Fisher for contributing slides to this presentation.