ENDOVASCULAR TREATMENT OF ACUTE ISCHEMIC STROKE

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DISCLOSURES

• None relevant to this talk
OBJECTIVES

• Background, patient selection, and imaging in acute stroke
• To understand the past, present, and future of stroke treatment, with emphasis on endovascular therapy
• Endovascular treatment options for acute ischemic stroke
• Up-to-date review of the previous and most recent studies/trials in endovascular stroke treatment
ISCHEMIC STROKE

- 3rd most common cause of death in industrialized nations
- Most common cause of permanent disability
- ~780,000 new or recurrent stroke cases annually
- 30-50% survivors do not regain functional independence
- 15-30% survivors are permanently disabled
- Est. direct cost of stroke for 2008 was ~$65.5 bil and more recently $73 bil
## 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>

PATIENT SELECTION

- **Time since onset**
  - Within 3 - 4.5 hrs: IV tPA [was sole] primary therapy
  - Within 6 hrs + LVO: Endovascular therapy
  - Wake-up strokes require conservative assumption that the ictus coincides with the time that the pt was last seen in a normal state
    - Perfusion imaging?

- **Severity of neurologic deficit quantified by NIHSS**
  - NIHSS >8 or >5 w/aphasic component, considered for endovascular intervention
    - No set consensus, on a case-by-case basis
    - >20: higher incidence of hemorrhagic transformation and worse outcome

- **Age**
  - >80 yo fare poorly w/ endovasc tx, increase risk of poor fxnl outcome and iatrogenic hemorrhage. Although, more recent studies are reassuring.

- **Baseline functional status**
- **Vascular anatomy**
IMAGING

• Non-contrast head CT
  • Exclude hemorrhage
  • ASPECT score – early ischemic changes
  • > 1/3 territory = higher risk

• CTA head/neck

• MRI/DWI, MRA

• MR/CT Perfusion
  • Estimation of tissue at risk (penumbra)
  • Awaiting randomized trials to assess efficacy in > 6 hours or “wake up” strokes

http://stroke.ahajournals.org/content/44/2/570/F1.large.jpg
A 64-year-old man presenting with headache and acute aphasia.

NCCT: No evidence of acute infarction.

CT perfusion: CBF map shows a region of decreased perfusion within the posterior segment of the left MCA territory.

MTT map shows a corresponding prolongation within this same region.

CBV map demonstrates no abnormality, representing a CBV/MTT mismatch.

IV TPA

- 1996- FDA approved IV tPA for AIS within 3 hrs (NINDS & rtPA Stroke Study Group trial.)²
  - First approved treatment for acute stroke that effectively treats the causative vascular occlusion
- 6 major randomized placebo-controlled trials
  - (Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke [ATLANTIS] I and II, European Cooperative Acute Stroke Study [ECASS] I and II, and NINDS I and II) ⁴
- 2775 pts treated with IV rtPA or a placebo within 6 hrs of onset
- Confirmed the benefit up to 3 hrs
  - Suggested potential benefit beyond 3 hrs for some patients
- ECASS III subsequently confirmed benefit of IV tPA in a 3 to 4.5-hr window
IV TPA - LIMITATIONS

- ICA and M1 occlusions have lower rate of recanalization than M2–M4 occlusions \(^1\)
- 52% with NIHSS <10 will reach NIHSS of 1 after IV tPA, but only 8% with NIHSS >20 \(^2\)
- 30% of MCA occlusions recanalize with IV tPA only within 2 hours
- ICA occlusions recanalize only at 1/3 of the rate of MCA occlusions \(^3\)

\(^1\) Del Zoppo Ann Neurol 1992; 32:78-86
\(^2\) NINDS Stroke 1997;28:2119–2125
\(^3\) Linfante Stroke 2002;33:2066-2071
Logistic regression curve representing an estimate of the probability for successful recanalization of occluded vessels by IVT depending on thrombus length.

**IV TPA - LIMITATIONS**

### CONTRAINDICATIONS
- SBP > 185 or DBP > 110 mmHg
- Seizure at onset
  - if residual deficits are due to the postictal state rather than to ischemia. If rapid diagnosis of vascular occlusion can be made, treatment may be given
- Recent surgery/trauma (< 15 days)
- Recent intracranial or spinal surgery, head trauma, or stroke (< 3 mos)
- H/o ICH or intracranial aneurysm, vascular malformation or tumor
  - may consider IV tPA in patients with CNS lesions that have a very low likelihood of bleeding such as small aneurysm or low vascularity tumors
- Active internal bleeding (< 22 days)
  - including arterial puncture at a non-compressible site
- Platelets < 100k, PTT > 40 sec after heparin use, or PT > 15 or INR > 1.7, or known bleeding diathesis
- Suspicion of SAH (imaging or clinical)
- CT findings (ICH, SAH, or major acute infarct signs)
  - hypodense > 1/3 cerebral hemisphere

### WARNINGS
- Stroke severity - too severe (NIHSS > 22)
- Glucose < 50 or > 400 mg/dl
  - if residual deficits are due to the altered metabolic state rather than to ischemia. If rapid diagnosis of vascular occlusion can be made, treatment may be given
- Left heart thrombus documented
- Increased risk of bleeding due to:
  - Acute pericarditis
  - Subacute bacterial endocarditis (SBE)
  - Hemostatic defects including those secondary to severe hepatic or renal disease
  - Pregnancy
  - Diabetic hemorrhagic retinopathy, or other hemorrhagic ophthalmic conditions
  - Septic thrombophlebitis or occluded AV cannula at seriously infected site
- Patients currently receiving oral anticoagulants, e.g., Warfarin (INR > 1.7)
- Advanced age
- Life expectancy < 1 year or severe co-morbid illness or CMO on admission
REPERFUSION STRATEGIES

- **Recanalization or antegrade reperfusion**
  - w/ MAC vs GA

- Global reperfusion (flow augmentation or transarterial retrograde reperfusion)

- Transvenous retrograde reperfusion (flow reversal)

**MAC vs GA**

- Pts who did not receive GA had double the likelihood of reduced disability at 90 days with ET vs no ET
- Almost 3x more likely to achieve functional independence
  - Whereas those who received GA showed "almost no benefit" from the procedure

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>OR without GA (95% CI)</th>
<th>OR with GA (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced disability (mRS shift analysis)</td>
<td>2.13 (1.46 - 3.11)</td>
<td>1.09 (0.69 - 1.71)</td>
</tr>
<tr>
<td>Functional independence (mRS 0 - 2)</td>
<td>2.79 (1.70 - 4.59)</td>
<td>1.09 (0.56 - 2.12)</td>
</tr>
</tbody>
</table>

MAC vs GA - CONSIDERATIONS

- Time to intubate
- Drop in BP during induction
- NPO status; emesis → aspiration
  - Risk vs benefit
- Case-by-case basis
  - Left vs right hemisphere?
  - Aphasia, receptive?
- Discomfort during physical clot extraction
RECANALIZATION/ANTEGRADE REPERFUSION: INTRA-ARTERIAL (IA) THROMBOLYSIS

• Direct injection of tPA into and around the thrombus
• Lower dose with higher local concentration
  • Theoretical reduction in ICH
• Studies have shown higher recanalization rates compared to IV tPA
• Major disadvantages
  • Additional risks of an invasive procedure?
RECANALIZATION/ANTEGRADE REPERFUSION:
IA MECHANICAL THROMBECTOMY

• Advantages:
  • Lessen/preclude use of thrombolytics (reducing risk of ICH)
  • Possible to extend tx window beyond the limit of 6–8 hrs
  • Mechanically fragmenting a clot increases the surface area accessible to thrombolytics and allows inflow of fresh plasminogen, thereby increase speed of thrombolysis
  • More efficient at coping with material resistant to enzymatic degradation (mature clots, cholesterol emboli, calcium, etc.)

• Disadvantages:
  • Navigating mechanical devices into the intracranial circulation?
  • Trauma to the vasculature (vasospasm, vessel dissection, or perforation)
  • Fragmented thrombus causing distal embolization into previously unaffected territories

• **Advantages of mechanical thrombectomy significantly outweigh its disadvantages and risks in appropriately selected patients**
MERCI retriever

FDA approved in August 2004

“Patients who are ineligible for treatment with IV rtPA or who fail IV t-PA therapy are candidates for treatment.”

Flexible nitinol wire with coil loops that is used in conjunction with a microcatheter and an 8-Fr or 9-Fr balloon guide catheter

ENDOVASCULAR THROMBECTOMY

Penumbra System

FDA approved in January 2008

Thrombus debulking and aspiration with a reperfusion catheter that aspirates the clot while a separator device fragments it and prevents obstruction of the catheter.

ENDOVASCULAR THROMBOASPIRATION CAUSE FEWER EMBOLIC EVENTS AND VASOSPASM
Solitaire & Trevo
“Stentriever“:
Self-expandable
Retrievable
Dual functionality:
1) Acts as a temporary intracranial bypass providing immediate flow restoration through the thrombus
2) Acts as a clot retriever, trapping thrombus into its cells allowing for clot removal

Illustration depicting the major steps in evolution of thrombectomy devices, beginning from the first-generation concept to state-of-the-art approaches.

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

**STENTRIEVER (early 2012) 2nd 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.

**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.

**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.

**SOLUMBRA (late 2012)**
- To minimize the distance the stent retriever must travel while engaging the thrombus and mitigate the possibility of losing purchase of the clot, the stent retriever is then pulled directly into a large bore intermediate catheter while maintaining aspiration.

Unlike ACS in which atheromatous plaque rupture is the most frequent culprit, most cases of acute intracranial vascular occlusions are related to an embolus in the absence of any in-situ vascular pathology.

Therefore, PTA with high-pressure balloons and balloon-expandable stents are typically not necessary to recanalize the vessel and may only increase the chance of vessel rupture or dissection.

Need for DAP in setting of infarct +/- tPA.

**THROMBUS ENTRAPMENT**

- NEUROFORM STENT (BOSTON SCIENTIFIC)
- ENTERPRISE STENT (CORDIS, MIAMI LAKES, FLA)
- LEO STENT (BALT EXTRUSION, MONTMORENCY, FRANCE)
- SOLITAIRE/SOLO STENT (EV3)
- WINGSPAN STENT (BOSTON SCIENTIFIC)
MECHANICAL THROMBUS DISRUPTION
- PTA
- Microwire/microcatheter fragmentation

Risks of vessel rupture and distal embolization (generally reserved as salvage therapy)
REPERFUSION STRATEGIES

- Recanalization or antegrade reperfusion
  - w/ MAC vs GETA
- Global reperfusion (flow augmentation or transarterial retrograde reperfusion)
- Transvenous retrograde reperfusion (flow reversal)

GLOBAL REPERFUSION / FLOW AUGMENTATION

- Focuses on increasing CBF to perfuse the tissue bed distal to the occlusive thrombus via leptomeningeal &/or COW collaterals
- May lead to better recanalization rates when used as an adjunct to antegrade reperfusion treatments
  - Improvement in CBF should theoretically result in greater delivery of thrombolytic drugs to the occlusion site, leading to higher recanalization rates
NeuroFlo device
Dual balloon catheter designed for partial occlusion (70%) of the aorta above and below the origin of the renal arteries

*Mechanical flow diversion from the high-resistance lower body to the lower resistance cerebral circulation*

**MECHANICAL FLOW AUGMENTATION**

**PHARMACOLOGIC FLOW AUGMENTATION**

-IV PHENYLEPHRINE

REPERFUSION STRATEGIES

• Recanalization or antegrade reperfusion
  • w/ MAC vs GETA
• Global reperfusion (flow augmentation or transarterial retrograde reperfusion)
• Transvenous retrograde reperfusion (flow reversal)

COMPLETE ARTERIO-VENOUS FLOW REVERSAL

• ReviveFlow system
  • Balloon guide catheter is placed in the cervical ICAs and jugular veins on 1 or both sides
  • Balloons are subsequently inflated, and blood is aspirated via an external pump system from the proximal ICA and infused in the distal internal jugular vein
  • End result is total reversal of the cerebral circulation and perfusion of the venous system with arterial blood into the capillary bed, which is now physiologically proximal to the occluded artery

• Currently undergoing preclinical studies
# Recanalization Scoring

**(Thrombolysis In Cerebral Infarction)**

<table>
<thead>
<tr>
<th>TICI</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No perfusion</td>
</tr>
<tr>
<td>1</td>
<td>Penetration, but no distal branch filling</td>
</tr>
<tr>
<td>2a</td>
<td>Perfusion with incomplete (&lt;50%) distal branch filling</td>
</tr>
<tr>
<td>2b</td>
<td>Perfusion with incomplete (&gt;50%) distal branch filling</td>
</tr>
<tr>
<td>3</td>
<td>Full perfusion with filling of all distal branches</td>
</tr>
</tbody>
</table>
**CLINICAL OUTCOME MEASURE / FUNCTIONAL INDEPENDENCE**

<table>
<thead>
<tr>
<th>Modified Rankin Score (mRs)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms at all</td>
</tr>
<tr>
<td>1</td>
<td>No significant disability despite symptoms; able to carry out all usual duties and activities</td>
</tr>
<tr>
<td>2</td>
<td>Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability; requiring 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 requiring constant nursing care and attention</td>
</tr>
<tr>
<td>6</td>
<td>Dead</td>
</tr>
<tr>
<td>Study</td>
<td>Median NIHSS</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>NINDS (IV tPA)</td>
<td>14</td>
</tr>
<tr>
<td>PROACT II (IA tPA)</td>
<td>17</td>
</tr>
<tr>
<td>MERCI</td>
<td>19</td>
</tr>
<tr>
<td>Multi MERCI</td>
<td>19</td>
</tr>
<tr>
<td>Penumbra Pivotal (mean)</td>
<td>17.6</td>
</tr>
<tr>
<td>TREVO EU</td>
<td>18</td>
</tr>
<tr>
<td>SWIFT (Solitaire® FR)</td>
<td>18</td>
</tr>
<tr>
<td>TREVO 2 (Trevo® Pro)</td>
<td>19</td>
</tr>
</tbody>
</table>

*Courtesy of Stryker Neurovascular*
### MOST RECENT TRIALS

<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>IMS III</td>
<td>No</td>
<td>IA Lytic (138), Merci Retriever® (95), EKOS (22), Penumbra (54), Solitaire FR (5)</td>
<td>38% ICA 44% M1 44% M2 23% multi M2</td>
<td>40.8% (N=415)</td>
</tr>
<tr>
<td>MR RESCUE</td>
<td>No</td>
<td>Merci Retriever® , EKOS, IA Lytic , Penumbra</td>
<td>24% pen (n=34) 27% nonp (n=30)</td>
<td>21% pen (n=34) 17% nonp (n=30)</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>

Courtesy of Stryker Neurovascular
FEW RECENT TRIALS FAILED TO SHOW BENEFIT IN ENDOVASCULAR THERAPY

• IMS III, MR RESCUE, SYNTHESIS-Expansion

• Lessons learned:
  • Imaging to confirm **LVO**
    • IMS III subset analysis showed clinical benefit
  • Imaging to exclude patients with a large infarct core
  • Improve **time** to treatment
  • Use newest devices to improve recanalization rates

• No differences in sICH or mortality
  • Endovascular intervention safe, not associated with increased risk, and performs at least similarly to IV tPA
## MOST RECENT TRIALS

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<td>21% pen (n=34) 17% nonp (n=30)</td>
<td>26% pen (n=34) 10% nonp (n=20)</td>
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<td>60.2% (n=98)</td>
<td>35.5% (n=93)</td>
</tr>
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<td>71% (n=35)</td>
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Courtesy of Stryker Neurovascular
EMS alert to ED – Stroke pt in route by ground or air

Stroke Alert page (ED, Neurologist, NIR)

Rapid assessment by stroke team, labs, NCCT head + CTA head/neck

Multidisciplinary Stroke Team discussion of the case and treatment decision

ICH

LVO and/or > 6 hrs / wake-up stroke

Neurosurgery Consult

No LVO

LVO < 6 hrs

Endovascular; NIR team activated +/- IV tPA

Medical management – ICU

posterior circulation

(??) CTP mismatch: consider endovascular
Acute thromboembolic occlusion of basilar artery is relatively rare (~6-10% of all large vessel strokes)
- Paucity of controlled trials and prospective studies

Levy et al. meta-analysis of case series involving BAO who underwent IAT with UK and/or rtPA (164 pts):
- Thrombus in distal 1/3 of the BA a/w lower mortality rate
  - Distal occlusions (usually embolic etiology) have higher recanalization rates than proximal occlusions (commonly atherothrombotic)

Most stroke experts agree: time window for IAT in the posterior circulation should be longer than the 6-8 hr
- Dire prognosis of untreated lesions
- Lower rate of hemorrhagic transformation
- Though no consensus guidelines exist to define this interval
TIME

- Current recommendation of 120 mins from door-to-treatment is too long
  - Relatively rapid rate of infarct growth and the dramatic effect of infarct volume on clinical outcome
- In order to achieve optimal outcomes in ischemic stroke, door-to-puncture times will ultimately need to be shorter than the 60-min benchmark for tx of AMI
- Should be dispatched to the highest level of care available in the shortest time possible

~12% decline in outcomes for q 30 min delay to puncture
SUMMARY

• Time is Brain
  • In a typical AIS, the brain loses 1.9-million neurons every minute
  • Every hour, the brain suffering a stroke ages nearly 4 yrs
• Acute stroke algorithm and prompt triage are crucial
• CT/CTA +/- CTP are fast and efficacious
• Various endovascular technique and device options
• Advances in [perfusion] imaging + mechanical thrombectomy devices expand the # of candidates that can undergo endovascular intervention
• Unified effort among EMS, ED physicians & RNs, Stroke Neurology, Radiology team, NIR team, Neurosurgery, ICU team
  • Is endovascular therapy effective for treatment of AIS? ✔
  • How can we improve/increase the # of pts that can benefit from ET? □
• Community education and awareness about stroke symptoms and the need to treat them as medical emergencies
CASE ILLUSTRATION #1

• 71-year-old female with h/o A-fib and recent pericardiocentesis with drain placement (which was recently removed) for pericardial effusion. She was last seen in her usual state at 12:07 a.m. At 12:35 a.m. she was found to have left hemiplegia by her nurse, at which time a stroke code was called. NIHSS was 13. MRI/MRA/MR perfusion demonstrates diffusion restriction in the right basal ganglia/lentiform nucleus.

• Clinical-DWI mismatch as well as DWI-PWI mismatch.
Solitaire FR 6mm x 20 mm
Post 1st pass

Post 2nd pass

Post 3rd pass
Post 4\textsuperscript{th} pass; 1\textsuperscript{st} pass with second Solitaire device + 5 mg of IA tPA
FOLLOW-UP

- Successful TICI 3 recanalization
- At 3-month follow up: mRs=0
CASE ILLUSTRATION #2

• 44 yo healthy male last known in his usual state at 22:00. Woke up at 04:30 with left UE plegia and LE paresis. Also found to have left neglect and right gaze preference in the ED. Outside of IV tPA window. NES called promptly at 05:00.
FOLLOW-UP

- Successful TICI 3 recanalization
- Neurologically intact upon discharge home
- 3-month follow up: mRs= 0
CASE ILLUSTRATION #3

• 48 yo male presenting with acute onset of expressive aphasia, right facial droop, and right hemiparesis. Not a IV tPA candidate due to major aortic/cardiac surgery 4 days ago.
FOLLOW-UP

- Successful TICI 2b recanalization
- Significant neurological improvement immediately
- 3-month follow up: mRs= 0
CASE ILLUSTRATION #4

- 62 yo female who developed sudden onset of left sided weakness, left facial droop and slurred speech around 16:10. OSH CT demonstrates dense R MCA sign. IV tPA was started and she was flown to CRMH for further care.
- CTA shows R MCA occlusion with early ischemic changes in the right caudate and lentiform nucleus.
- No significant improvement after IV tPA.
FOLLOW-UP

- Successful TICI 3 recanalization
- No change in neurological status
- Post CT: Hemorrhagic transformation; aICH
- 3-month follow up: mRs= 3; walking w/o assistance, moderate disability. Recent fall with non-displaced sacral fracture.
CASE ILLUSTRATION #5

- 63 yo male found to have acute onset of left facial droop, speech dysarthria, right gaze preference, left hemiplegia in the PACU immediately after knee replacement. Not IV tPA candidate.
FOLLOW-UP

- Successful TICI 3 recanalization
- Neurologically intact upon discharge home
- 3-month follow up: mRs= pending
REFERENCES

9) http://www.ninds.nih.gov/disorders/clinical_trials/IMS-III.htm
THANK YOU!

Questions?

bmpatel@carilionclinic.org