STROKE AND THE ROLE OF INTERVENTION IN THE MANAGEMENT OF ISCHEMIC STROKE

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STROKE DEFINITION

- A condition manifested by rapidly developing clinical signs of focal or global disturbance of cerebral function with symptoms lasting 24 hours or longer or leading to death with no apparent cause other than of vascular origin.
- TIA (above lasting less than 24 hours)
- Stroke includes ischemic and hemorrhagic infarction, intracerebral hemorrhage and SAH
- In adults 80-85% of strokes are ischemic
- In children 55% of strokes are ischemic

STROKE STATISTICS

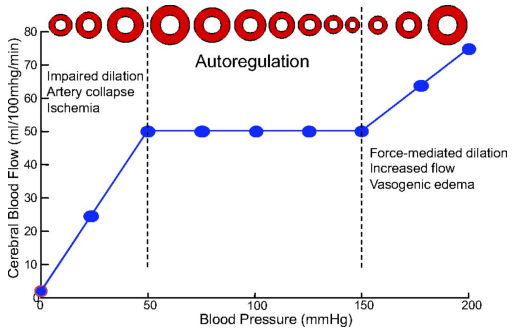
- **WORLDWIDE STROKE KILLS A PERSON EVERY 6 SECONDS**
- **IN THE US SOMEONE HAS A STROKE EVERY 40 SECONDS**
- **IN THE US SOMEONE DIES FROM A STROKE EVERY 4 MINUTES**

STROKE STATISTICS

- #1 Cause of disability among adults in the US
- 795,000 Americans each year suffer a stroke
- 128,000 people/year in US die from a stroke (1/19 deaths)
- #5 cause of death among adults in the US

BASIC PHYSIOLOGY

- The brain contains 2% of total body weight yet receives 20% of the cardiac output (high metabolic activity)
- Cerebral Perfusion Press. = Mean Arterial BP – Intracranial Press.
- Normal CBF 50-65 cc/100g/min
- Normal CPP 70 to 85 mm Hg.
- CBF remains **normal** as **CPP** varies between 60 and 140 mm Hg.
- CPP <20 mm Hg or CBF <20 cc/100g/min becomes critical



ATHEROSCEROTIC DISEASE

- Arterial plaques develop in areas of high vascular wall permeability
- Permeability of the arterial endothelium (vessel lining) is increased by stressors that can include
  - Low density lipoprotein (LDL) serum levels
  - Flow induced mechanical stress
  - Elevated serum cholesterol
  - Elevated homocysteine levels
  - Infection/inflammation
  - Increased permeability allows plasma components accumulate in the enter the vessel wall's subendothelial layer

ATHEROSCLEROTIC DISEASE

- LDL activates subendothelial monocytes which in turn causes fatty streak deposition and induces monocyte conversion into macrophages.
- Macrophages take up LDL which creates foamy cells that go on to die.
- The debris from dead cells leads to more monocyte invasion and faty streak development.
- Smooth muscle cells multiply in this region and collagen deposits form.
- Arteries dilate in response to this wall thickening until they cannot dilate further at which point the arterial lumen begins to narrow.
- Stenosis and plaque instability leads to flow related and thromboembolic related ischemia.

CURRENT EVALUATION PROTOCOL FOR STROKE

- 24 hour ECG monitoring with consideration of ICM device or Holter monitor to better detect atrial fibrillation
- Echocardiogram (TT vs TEE based on cardiologist recommendation)
- Hypercoagulability evaluation
- ASA and Plavix sensitivity testing when indicated
- Serum cholesterol and lipid level evaluation
- BP evaluation
- Toxicity screens when indicated (cocaine, amphetamines)
- Cerebral arterial and venous evaluation (MRA, CTA, and/or catheter angiography)
- Smoking cessation therapy
- Consider evaluation for vasculopathy

DIAGNOSTIC STUDIES FOR ATHEROSCLEROTIC DISEASE

- CT
- CTA
- MR
- MRA
- Duplex carotid ultrasound
- >70% stenosis = Peak systolic velocity >230 cm/s
- Cerebral Catheter Angiography

MEDICAL MANAGEMENT OF ATHEROSCLEROTIC DISEASE

- Risk factor modification
  - Hypertension
  - Diabetes mellitus
  - Hyperlipidemia
  - Tobacco
- Antiplatelet agents
  - Prevents platelet aggregation in vessels
  - Decreases risk of stroke by as much as 30% following a TIA
  - 81 mg vs 325 mg (??)

SURGICAL AND ENDOVASCULAR MANAGEMENT

- NASCET Study (Randomized CEA vs medical management)
  - Patients ≥70% stenosis with TIAs or strokes within 120 days of surgery
    - Absolute risk reduction for ipsilateral stroke at 2 years = 17% in favor of CEA (9% for CEA vs 28% for medical)
  - Patients with 50-69% stenosis
    - 6.7% risk reduction of fatal or nonfatal stroke within 5 years (15.7% for CEA vs 22.2% for medical)
- ACAST Study (Randomized CEA vs medical management)
  - Asymptomatic patients with ≥ 60% stenosis
    - Absolute risk reduction for ipsilateral stroke/death at 5 years of 6.1% (5.1% for CEA vs 11% for medical)

SURGICAL AND ENDOVASCULAR MANAGEMENT

- ICSS Study
  - CEA vs stenting with symptomatic stenosis
    - 120 day results for stroke/death
    - CEA 3.2% vs Stent 4% (no significant difference)
    - Higher risk of fatal MI in stent group
- CREST Study
    - No difference in 30d post procedure stroke rate between CEA and stenting
    - Risk of stroke/death at 4 years higher in stenting group

SURGICAL AND ENDOVASCULAR MANAGEMENT

- EC-IC Bypass Trial
  - Patients with ipsilateral stroke within 3 months of surgery
  - Randomized surgery vs medical management
  - Surgery did not reduce risk of stroke and death
  - Surgical patients had greater rates of perioperative stroke and death
- COSS Study
  - Study stopped early due to better outcomes in medically treated grop

WHAT HAPPENS WHEN MEDICAL AND SURGICAL THERAPY FAIL TO PREVENT NEW AND/OR RECURRENT STROKES?

DEFINING OUR TOPIC

- Stroke can be primarily ischemic or primarily hemorrhagic
- Ischemic strokes can become secondarily hemorrhagic
- Ischemic Stroke
  - Neurologic deficit secondary to reduced blood flow to the brain
    - Average perfusion to brain tissue is 50-54 cc/100g/min
    - Symptomatic Ischemia occurs with CBF < 18-20 cc/100g/min
    - Tissue death (infarction)occurs with CBF < 8-10 cc/100g/min
  - Thromboembolic and hemodynamic etiologies
  - Acute ischemic thromboembolic stroke accounts for 87% of all stroke cases ICA, M1, M2, A1,A2 occlusions account for 33% of all anterior circulation strokes

PATHOGENESIS FOR ISCHEMIC THROMBOEMBOLIC STROKE

- Atherosclerosis with arterial stenosis or occlusion
- Cardiac sourced emboli secondary to valvular, atrial or ventricular abnormalities
- Cardiac sourced paradoxical emboli due to septal defects (PFO)
- Hypercoagulability and subsequent thrombophilia secondary to
  - Inherited thrombophilia
    - Factor V Leiden
    - Prothrombin gene mutation
    - Antithrombin deficiency
    - Protein C deficiency
    - Protein S deficiency
- Acquired thrombophilia
  - Antiphospholipid syndrome
  - Hyperhomocysteinemia
- Post-surgical
- Trauma
- Fractures
- Cancer
- Pregnancy
- Estrogen use
- Vasculopathy

Cryptogenic Stroke and Atrial Fibrillation

- The cause of ischemic stroke often remains uncertain despite a complete diagnostic evaluation in 20-40% of cases; aka: cryptogenic stroke. (NEJM. 2014;370:2478-86)
- Atrial Fibrillation may be a hidden etiology
- Using an insertable cardiac monitor (ICM) rather than routine 24 hour ECG monitoring (current guideline recommendation) Afib has been identified after 6 months in 8.9% of cryptogenic stroke patients vs. a findinb of 1.4% using 24 hour ECG

Cryptogenic Stroke and Patent Foramen Ovale (PFO)

- Foramen Ovale
  - In fetal heart the FO allows flood to enter the left atrium from the right atrium thus bypassing the pulmonary circulation until birth.
  - Not to be confused with *ductus arteriosus* which pre birth connects the pulmonary artery to the descending aorta
- FO closes at birth
- Patent Foramen Ovale (PFO) (10-35% prevalence)
- PFO does not increase the risk of ischemic stroke, but PFO is more prevalent in patients with cryptogenic stroke especially in younger age groups without signs of atherosclerotic disease
- PFO permits venous blood clots that travel to the heart to enter the arterial circulation across the PFO as opposed to normally being absorbed by the pulmonary vasculature

Does PFO Repair Reduce The Incidence of Recurrent Stroke?

- **META-ANALYSIS OF REDUCE TRIAL, CLOSE TRIAL, RESPECT TRIAL (**De Rosa, et al. Annals of Internal Medicine doi:10.7326/M17-3033. January 9, 2018)
- Stroke/TIA
  - Repair group 3.6% vs Medical group 6.3%
- Stroke
  - 1.2% Repair group vs. 4.1% Medical group
- New onset AF/AFL
  - Repair group 4.1% vs 1% Medical group
- Major bleeding
  - 0.9% Repair group vs 1.2% Medical group
- Serious adverse event
  - 25% Repair group vs 24% Medical group
- Greater beneficial effect of repair on ischemic stroke prevention with increasing shunt size in patients with a moderate to large shunt

PATIENT EVALUATION (STEP 1)

- National Institute of Health Stroke Score (NIHSS)
  - Evaluates motor, sensory, visual, speech comprehension
    - 0 No stroke symptoms
    - 1-4 Minor stroke
    - 5-15 Moderate stroke
    - 16-20 Moderate to severe stroke
    - 21-42 Severe stroke

- Predictor of patient outcome **(WITHOUT TREATMENT!!)**
  - NIHSS >16 indicates strong possibility of death
  - NIHSS <6 indicates strong possibility of good recovery
  - An increase of 1 point in a patient's NIHSS decreases the likelihood of an excellent outcome by 17%

PATIENT EVALUATION (STEP 2)

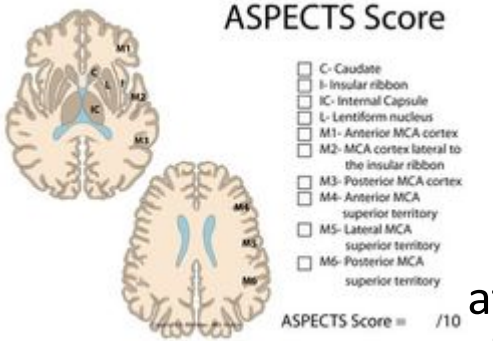
- Determine time of stroke onset
  - Defined as when the patient was last observed to be normal
    - $\leq$ 3 - 4.5 hours
    - When is 6 hour window
- Current medications
  - Antiplatelet
  - Antithrombotic
- Patient medical history
  - Prior strokes
  - Recent surgical procedures
  - Medications
  - Family history of stroke
  - Pregnancy status
  - Neurologic conditions
  - Cardiac conditions
    - Rhythm disturbances
    - Atrial/ventricular dysfunction
    - Septal abnormalities

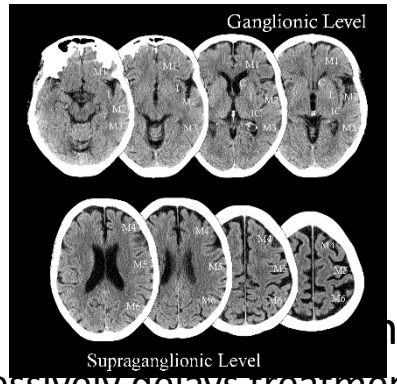
OTHER USEFUL SCORING SYSTEMS

- ABCD2 Score
  - Estimates risk of stroke after TIA
- ASTRAL Score
  - Estimates 90-day outcome after stroke
- CHA2DS2-VASc Score
  - Estimates risk of stroke with atrial fibrillation
- DRAGON Score
  - Estimates long term outcome in patients who are potentially getting iv TPA
- HAT Score
  - Risk of hemorrhage after iv TPA
- mSOAR Score
  - Estimates stroke mortality
- PedNIHSS
  - Pediatric version of NIHSS
- SEDAN Score
  - Estimates risk of symptomatic ICH after iv TPA
- THRIVE Score
  - Estimates prognosis after stroke

PATIENT EVALUATION (STEP 3)

- Emergent Brain Imaging TO EXCLUDE PATIENTS FROM TREATMENT
  - Evaluate patient's brain for:
    - Hematoma (epidural, subdural, subarachnoid, intraparenchymal)
    - Ischemic changes
- Emergent Imaging Modalities
  - CT/CTA with ASPECT Score

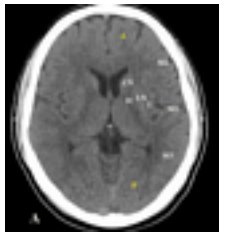


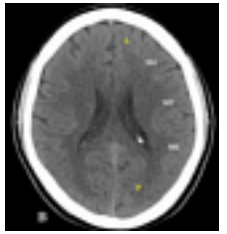


  - MRI/MRA atients ndow)
    - Prior to 6 hour window MR generally excessively delays treatment
    - CORE BUT
    - ADVANCED IMAGING CAN DELINIEATE THE STROKE ***BUT*** IS THIS IMPORTANT FOR EFFICACY AND SAFETY?

Alberta Stroke Program Early CT Score (ASPECT Score; ASPECTS)

- As per Hacking and Sair in Radiopaedia
  - 10 point quantitative CT scan score used in patients with middle cerebral artery (MCA) stroke
  - Segmental assessment of 10 MCA vascular territories is made with 1 point deducted from the initial score of 10 for every region involved
    - Caudate
    - Putamen
    - Internal capsule (any portion)
    - Insular cortex
    - M1: anterior MCA cortex at level of BG on CT (frontal lobe)
    - M2: MCA cortex lateral to the insular cortex at level of BG on CT (anterior temporal lobe)
    - M3: Posterior MCA cortex at level of BG on CT (posterior temporal lobe)
    - M4: Anterior MCA cortex at level of ventricles immediately above BG on CT
    - M5: Lateral MCA cortex at level of ventricles immediately above BG on CT
    - M6: Posterior MCA cortex at level of ventricles immediately above BG on CT





- ASPECTS < 7 PREDICTS WORSE FUNCTIONAL OUTCOME AT 3 MONTHS AS WELL AS SYMPTOMATIC HEMORRHAGE
- PATIENTS WITH ASPECTS < 8 TREATED WITH THROMBOLYSIS DO NOT GENERALLY HAVE GOOD CLINICAL OUTCOMES

TREATMENT FOR PATIENTS PRESENTING ≤ 4.5 HOURS FROM ONSET OF ISCHEMIC SYMPTOMS

- IV-tPA (recombinant tissue plasminogen activator; Alteplase)
  - tPA is naturally encoded by the PLAT gene on Chromosome 8
  - tPA cleaves plasminogen into the protease plasmin
  - Plasmin degrades Fibrin
  - Polymerized Fibrin normally combines with platelets to form a hemostatic clot
- Tissue Plasminogen Activator for Acute Ischemic Stroke. New England Journal of Medicine 1995; 333:1581-1588
  - When compared to patients treated with placebo, those treated with IV-tPA were 30% more likely to have minimal of no disability 3 months following treatment
  - Mortality at 3 months was lower in the tPA treated group (17%) vs the placebo group (21%)
  - Symptomatic intracranial hemorrhage was 6.4% in tPA group vs. 0.6% in placebo group
- In 1996, tPA approved by FDA for treatment of ischemic strokes if administered within 3 hours of symptom onset
- Standard Dosage 0.9 mg/kg not to exceed 90 mg total dose infused over 60 minutes with 10% administered as a bolus over 1 minute.
- 0.6 mg/kg might be just as effective with lower risk of symptomatic intracerebral hemorrhage (1% vs 2.1%) (NEJM 374:2313-2323, 2016)

IV-TPA BEYOND 4.5 HOURS

- EXTEND Trial
  - Australia, New Zealand, Thailand
  - Reported at International Stroke Conference February 2019
- Study used CT and MR perfusion-mismatch (not a time of onset based study)
  - Inclusion criteria were Core <70 ml (median 4 ml) and Mismatch >10ml (median 79 ml)
  - Median NIHSS 11
  - Median LKN 10 hrs (65% were wake up stroke; 10% 4-6 h; 25% 6-9h)
  - 72% had LVO and no thrombectomy
- RESULTS
  - RR 1.44 for mRS 0-1 at 1m and 1.4 for mRS 0-2 at 3m
  - RR 2.6 for early improvement in NIHSS 0-8 group
  - 51% had 90%recanalization and reperfusion
  - No difference in death at 90 days
  - 6% risk ICH (comparable to other studies and did not negate clinical benefits)

iv-tPA INDICATIONS AND CONTRAINDICATIONS

- Inclusion Criteria
  - Time of symptom onset ≤3 hours
  - Diagnosis of ischemic stroke causing measurable neurological deficit (NIHSS >4)
  - Age ≥ 18 years
  - Time of symptom onset <4.5 hours
  - Above plus
  - ≤ 80 years old
  - No history of both diabetes and stroke
  - Patient is not taking Coumadin or any other anticoagulant regardless of INR
  - NIHSS ≤ 25

- Exclusion Criteria
  - Significant head trauma or prior stroke in previous 3 months
  - SAH
  - Prior intracranial hemorrhage
  - Intracranial neoplasm, AVM, aneurysm
  - Recent intracranial or intraspinal surgery
  - Arterial puncture at noncompressible site in previous 7 days
  - Elevated blood pressure (S >185; D>110)
  - Active internal bleeding
  - Blood glucose <50
  - Acute bleeding diathesis including platelet count less than 100K
  - Heparin received within 48 hours resulting in aPTT greater than normal
  - Current use of anticoagulant with INR >1.7 or PT >15
  - Current use of thrombin inhibitors or Factor Xa inhibitors with elevated aPTT, INR)
  - CT demonstrating multilobar infarction (>1/3 cerebral hemisphere; APSECTS <8)

iv-tPA *RELATIVE* CONTRAINDICATIONS

- Minor or rapidly improving stroke symptoms
- Seizure at onset with postictal residual neurological impairments
- Major surgery or serious trauma within previous 14 days
- Recent GI or urinary tract hemorrhage within previous 21 days
- Pregnancy

CAN iv-tPA OUTCOMES BE IMPROVED USING ENDOVASCULAR THERAPY

- <u>Why ask this question?</u>
  - Recanalization rates within 24 hours after the administration of iv-tPA within 4.5 hours of the onset of stroke are only 5-14% for ICA arteries and 20-44% for MCA arteries
  - IV TPA only provides for <40% chance of regaining function after stroke
- Degree of recanalization is related to ultimate infarct volume

• TICI 0	No anterograde flow	166 cc volume infarct
• TICI 1	Penetration with minimal perfusion	145 cc volume infarct
• TICI 2A	Less than 2/3 vascular territory fills	121 cc volume infarct
• TICI 2B	Complete filling; slower than nl flow	54 cc volume infarct
• TICI 3	Complete reperfusion	36 cc infarct volume

RESULTS OF iv-TPA **PLUS** ENDOVASCULAR THERAPY

- **STUDIES**
- Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) NEJM 2015;372:11-20
- 500 patients randomized
  - 233 randomized to endovascular therapy with 196 (84%) actually undergoing endovascular treatment. Retrievable stent used in 82% of IA treatments
  - Patient receives usual customary care (including iv-tPA when indicated). 90% in each group received iv-tPA
  - Age >18
  - Distal ICA, MCA (M1,2), ACA (A1,2) occluded
  - NIHSS ≥2
  - IA therapy initiated within 6 hours after stroke onset included thrombolytic therapy and/or mechanical thrombectomy (aspiration, wire disruption, MERCI, retrievable stent)
- RESULTS
  - No significant difference in adverse events (47% vs 42% control)
  - No difference in mortality (21% vs 22% control)
  - 71% improvement in good neurological outcomes for patients treated with IA + iv-tPA vs iv-tPA alone
  - 33% functional independence in IA group vs 19% in non-IA group (14% absolute difference)
  - It was determined pre-study that a 10% absolute reduction in poor outcome (IA vs non-IA) could save approximately 1% of all new stroke cases from death or disability annually (1% x 800,000 =8,000)
  - No residual occlusion in 75% of IA group vs. 33% of non-IA group
- **THE POSITIVE RESULTS OF THIS STUDY LEAD TO THE TERMINATION OF ALL OTHER ONGOING STUDIES LOOKING AT IV tPA PLUS IA THERAPY**
- **Subgroup Analysis (Lancet. Vol 15. p685. June 2016)**
  - **Beneficial in patients with ASPECT ≥ 5**

ADDITIONAL RESULTS OF iv-tPA **PLUS** ENDOVASCULAR THERAPY

- STUDIES
  - SWIFT PRIME (Global) 6 hours
  - EXTEND IA (Australia, New Zealand) 4.5 hours
  - REVASCAT (Spain) 8 hours
  - ESCAPE (Global) 12 hours
- Each of the above studies compared iv-tPA alone vs iv-tPA plus the Solitaire device within 6-12 hours of stroke onset

STUDY RESULTS

- THROMBECTOMY + IV TPA IS BETTER THAN IV TPA ALONE
- SWIFT PRIME
  - Functional independence (Good Outcome) improved with Solitaire at 90 days (60% vs 35%)
  - Reduction in death with Solitaire (12% vs 9%)
- EXTEND-IA
  - Functional independence improved (71% vs 40% control)
  - IA patients 15 days in hospital or rehab vs 73 days
  - Death reduced (9% vs 20% control)
  - Symptomatic ICH (0% vs 6% control)
- ESCAPE
  - Functional independence improved (53% vs 29% control)
  - Death rate reduced (10% vs 19% control)
- REVASCAT
  - Functional independence improved (44% vs 28% control)
  - No difference in death from stroke (18% vs 16% control)

GUIDELINES FOR STROKE TREATMENT AS A RESULT OF MR CLEAN STUDY (*Ancillary information)

- Patients eligible for IV r-tPA should receive tPA even if IA therapy is being considered **(Pittsburgh Rule: Treat if occlusion is M1 or proximal and NIHSS > 5; If NIHSS is ≤ 5, watch in ICU and treat if worse)***
- Patient should receive endovascular therapy with a stent retriever device if
  - Pre stroke Modified Rankin Scale (mRS) is 0-1 (no symptoms or no significant disability; able to carry out all usual activities despite some symptoms)
  - Acute ischemic stroke receiving IV-tPA within 4.5 hours of onset
  - Occlusion of ICA or proximal MCA (M1)
    - CTA can be useful to rapidly identify these cases when a hyperdense sign does not appear on plain CT imaging
    - Why not ivTPA alone for M2 and beyond? IMS III tPA arm: 40% mortality; STOPStroke Study (no IF tPA or IAT: 41% mortality
    - SMILOS Data For M2 occlusions: Endovascular + ivTPA is better than ivTPA alone (90 day mRS 0-2 73.9% vs 39.4%; 90 day mortlaity 0% vs 24.2%)*
    - Sarraj, et al. JAMA Neurol 2016; EVT superior to Medical management for M2 Occlusion*
  - Age ≥18
  - NIHSS ≥6
  - ASPECTS ≥ 6 Lancet. Vol 15. pp. 685-694, June 2016)
    - Pittsburgh Rule: ASPECTS at the minimum first digit of age or maximum baseline infarct volume = 100 minus age *
  - Groin puncture can occur within 6 hours of symptom onset (JAMA 2016; 316(12):1279-1288 suggests 7.3 hour is acceptable)*

CURRENT STATUS SUMMARY

Jadhav AP, Jovin TG. Endovascular therapy for acute ischemic stroke. The standard of care. Brain Circ 2016;2:178-182

- 5 studies in 2015 demonstrated that outcomes for stroke treated with IV-TPA were improved by adding thrombectomy in properly selected patients (4% good outcome vs 26% good outcome In IMS III study)
- The patient most likely to improve is one with a large vessel proximal occlusion(ICA, ICA terminus and/or M1), significant deficit (mean NIH in studies 15-18, large penumbra, aka: area at risk for infarct but eligible for recovery), small core (infarcted brain volume, aka: ASPECTS >7)
- Time to treatment is also important. In IMS III every 30 minute delay lead to increase in worse outcome (risk ratio 0.85). Patients treated within 300 minutes had 41% good outcome, whereas only 26.5% had good outcomes if they were treated beyond 360 minutes.
- With above treatment, TICI 2b/3 rates are 59-88%

DOES THROMBECTOMY BENEFIT PATIENTS WHO ARE NOT ELIGIBLE FOR IV-TPA?

- HERMES Meta-analysis of 5 randomized studies (Goyal M, et al. The Lancet. 387 (10029):1723-1731, April 2016)
  - 200 IV tPA ineligible patients
  - Thrombectomy benefit was still was statistically significant
- DAWN Study
  - NEXT SLIDE***

CURRENT STATUS SUMMARY

- **DAWN STUDY (NEJM, November 11, 2017)**
  - 206 Patients with intracranial ICA or M1 occlusion
  - Last known normal 6-24 hours earlier
  - Mismatch between severity of clinical deficit and infarct volume
  - Randomly assigned to standard of care(control group) or thrombectomy
  - 90 day functional independence was 49% in thrombectomy group vs. 13% in control group
  - Symptomatic intracranial hemorrhage was 6% in thrombectomy group vs 3% in control group (no statistical difference)
  - 90 day mortality was 19% in thrombectomy group vs 18% in control group

QUESTIONS THAT REMAIN TO BE ANSWERED

Jadhav AP, Jovin TG. Endovascular therapy for acute ischemic stroke. The standard of care. Brain Circ 2016;2:178-182

- What is the ideal imaging modality for assessing patients upon presentation with stroke (CT, CTA, CTP, MR, MRA, MRI DWI)?
- What other occlusion sites (M2, BA) can benefit from endovascular therapy?
- Do patients with fluctuating symptoms or patients with moderate-larger stroke burdens (large core) benefit from IA therapy?

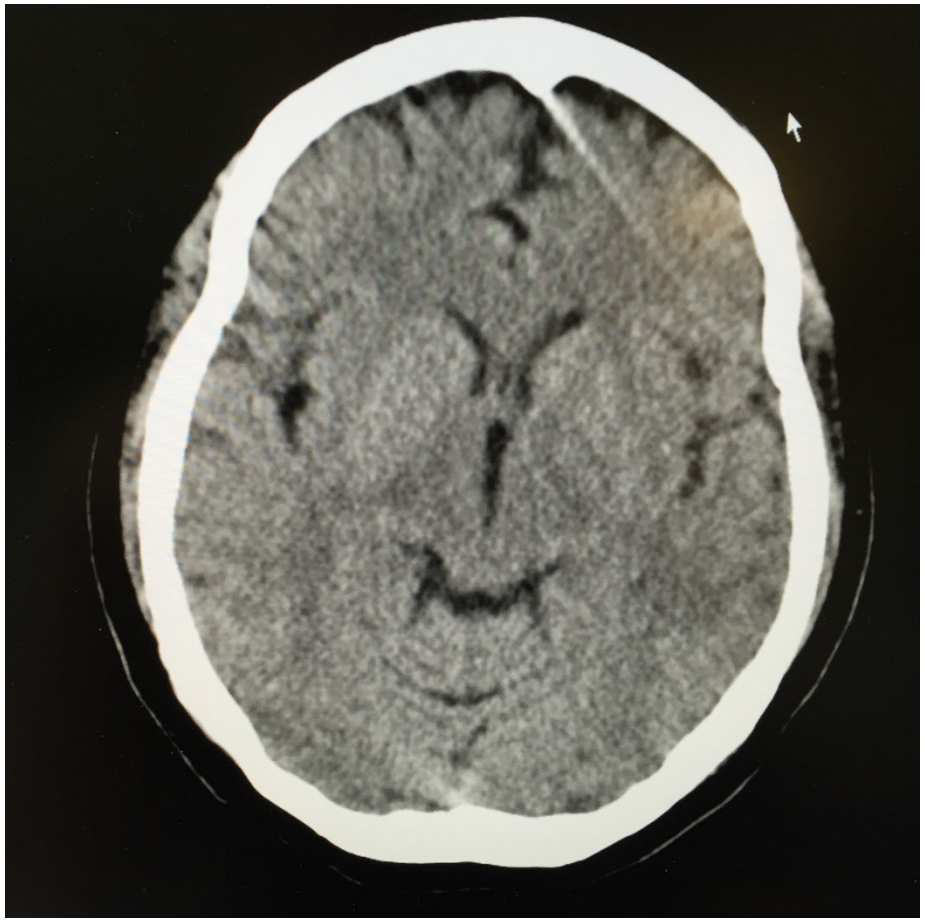
CASE ILLUSTRATION

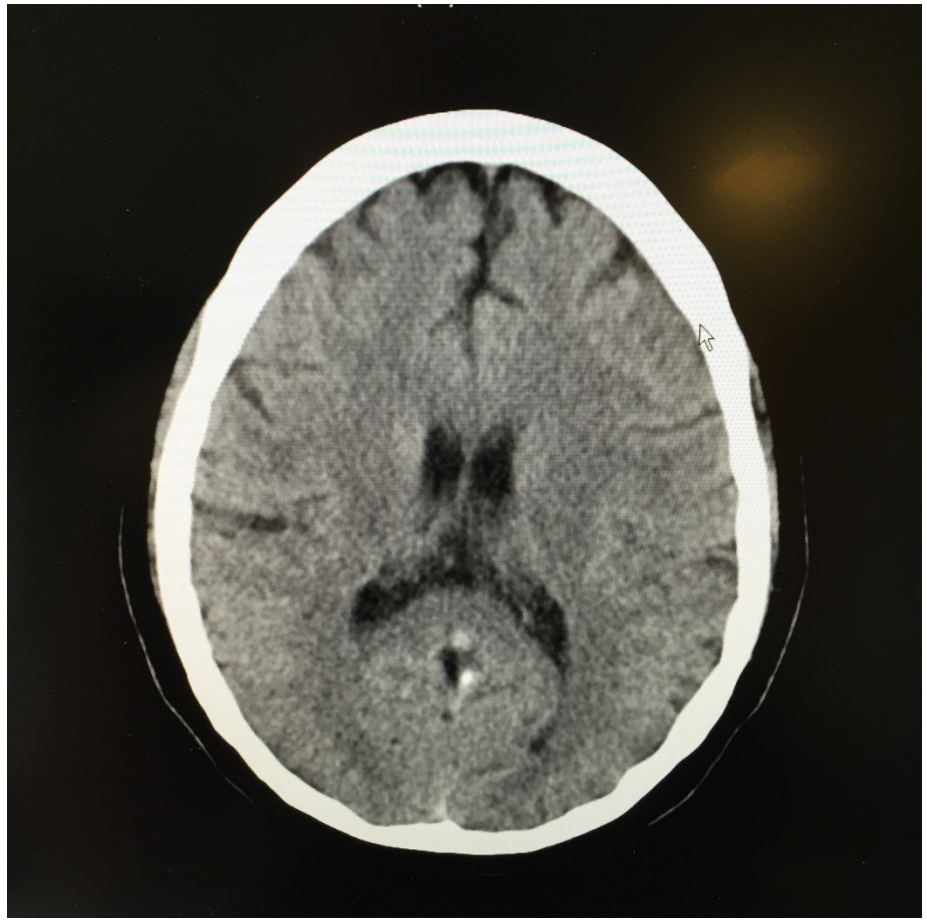
- 44 year old right handed woman presents to ER AT 0910
- Chief Complaint
  - Difficulty speaking. Right sided weakness
- History
  - Husband found wife in bed with difficulty speaking and right sided weakness. Patient was presumed normal at 0600 when she climbed into bed. At 0700 she fell out of bed and was found to be aphasic and plegic on her right side.
- PMH
  - Sleep apnea
  - Migraines
  - Tobacco use
  - Hyperlipidemia
  - Bipolar disorder
  - GERD
- Medications
  - Atenolol
  - Gabapentin
  - Vistaril
  - Lodine
  - Lipitor
  - Lexapro
  - Amerge
  - Migranal
- Exam
  - BP Systolic <150; BP Diastolic <90
  - BMI 42
  - NIH 22 (>21 considered a severe stroke)

CASE ILLUSTRATION

- CT Head
  - No acute findings. No hemorrhage seen. No stroke seen
- Neurology Consult
  - Not an IV-TPA candidate due to unknown time of stroke onset
- Neurosurgery Consult
  - Patient taken emergently to angiography
  - Left ICA and M1 occlusion (TICI 0)
  - Solitaire and suction thrombectomy performed
  - Post procedure TICI 2b-3

CT BRAIN IN ER





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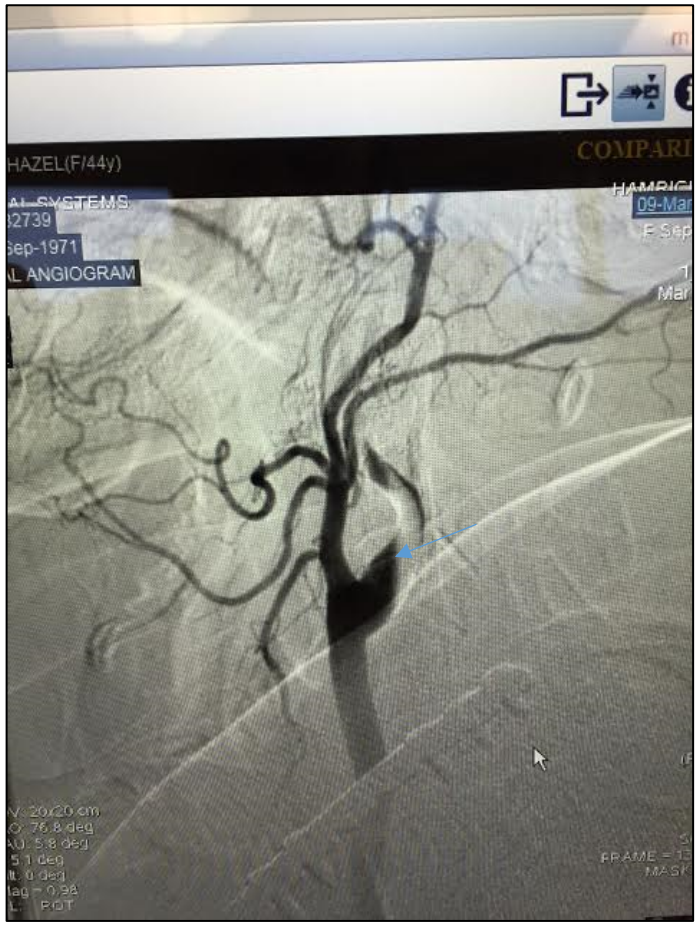
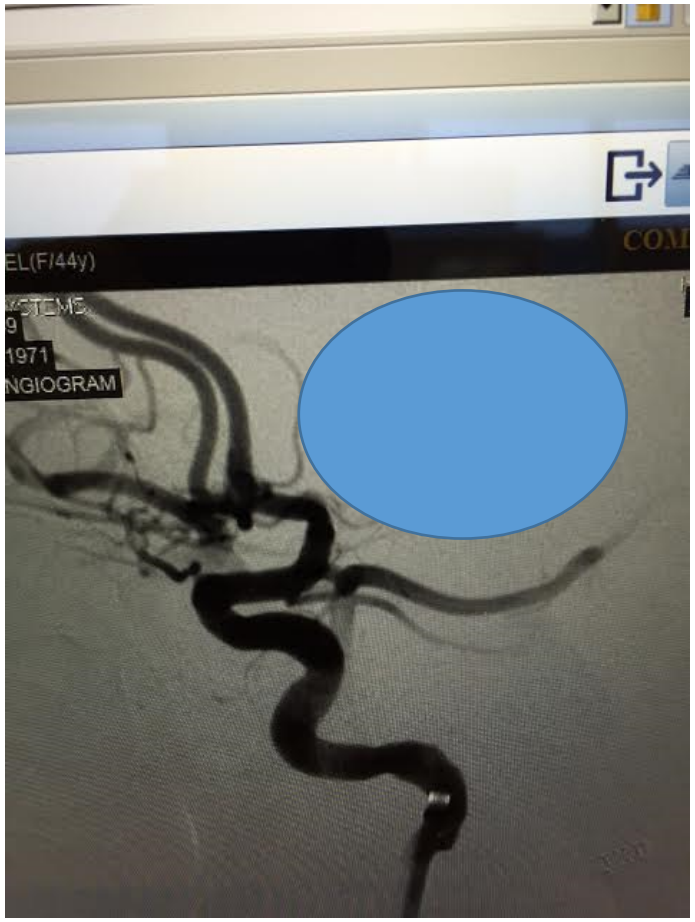
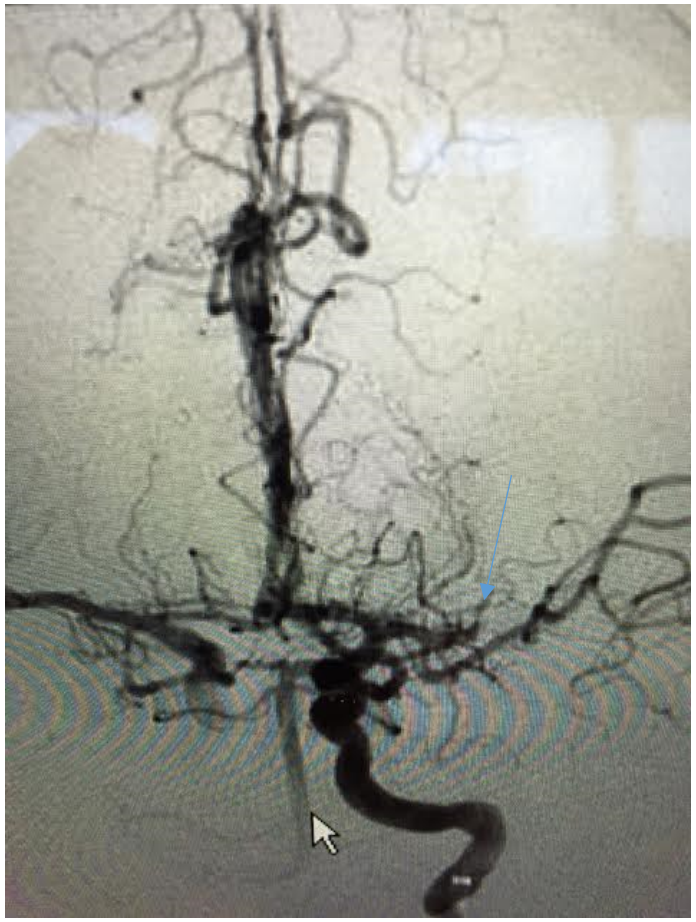
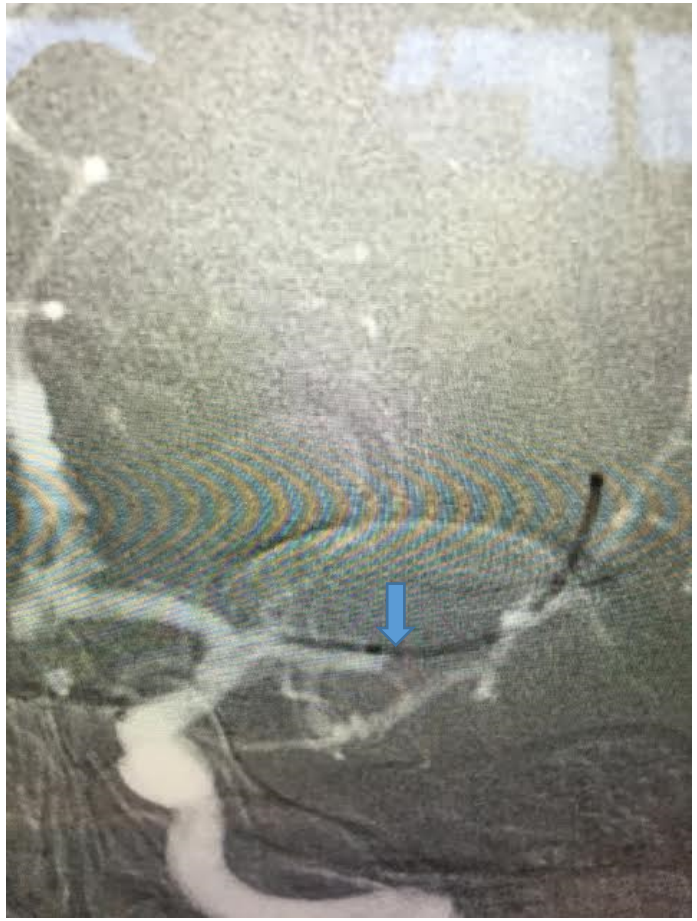


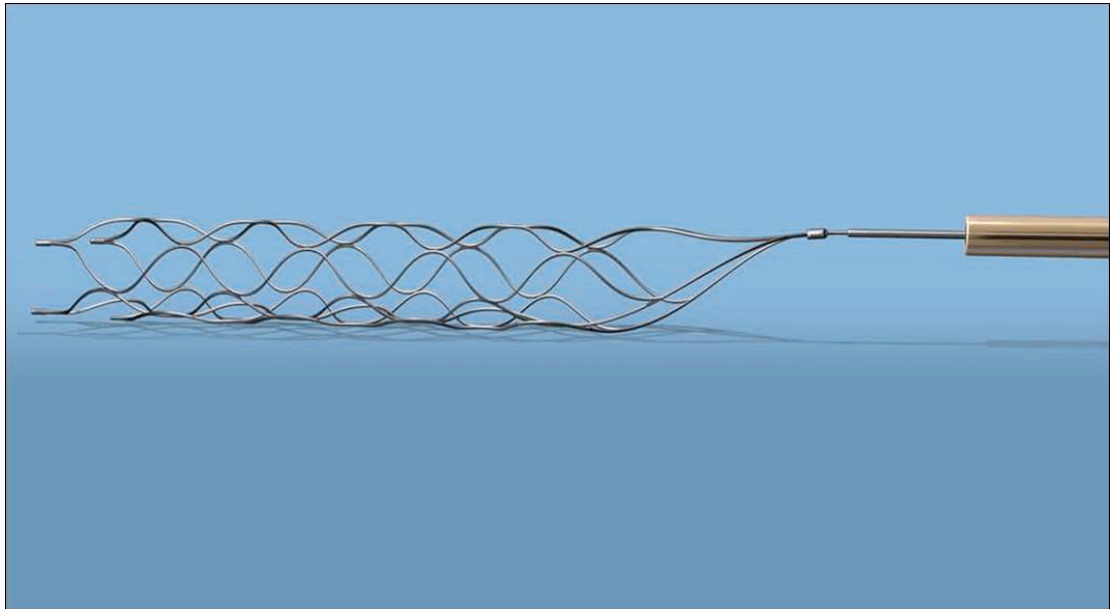


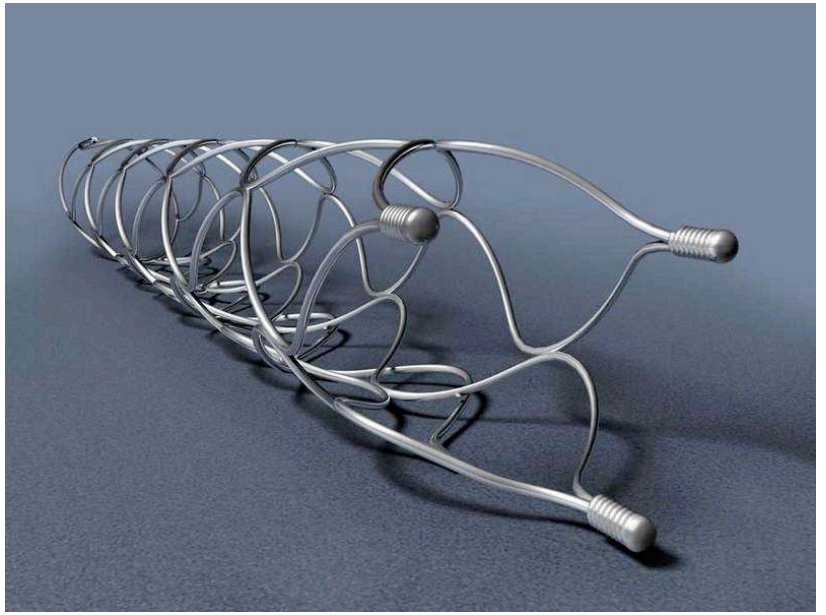


MICROCATHETER PLACED THROUGH OCCLUSION

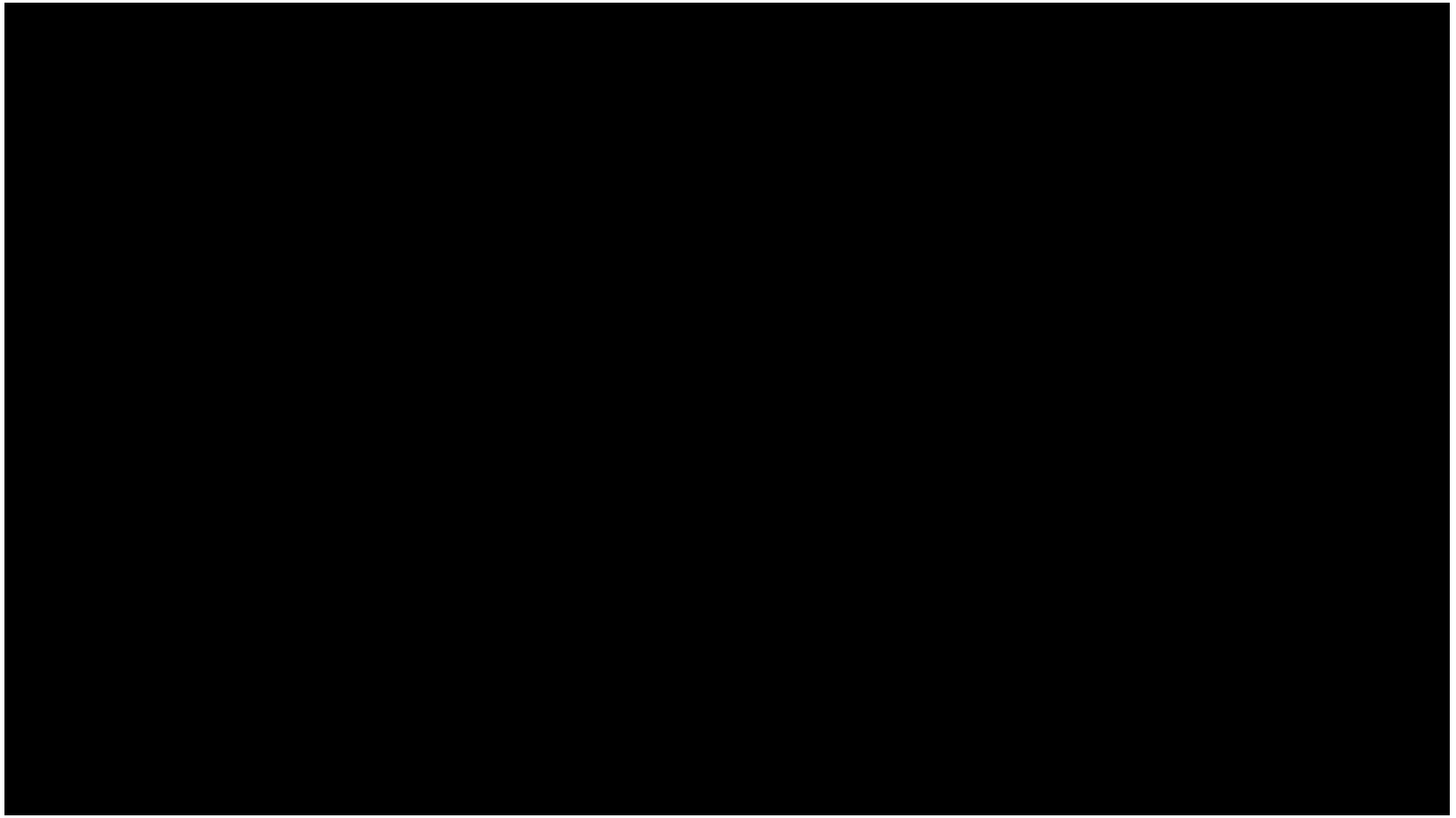


SOLITIARE STENT RETRIEVER
Medtronic
Approved 2012

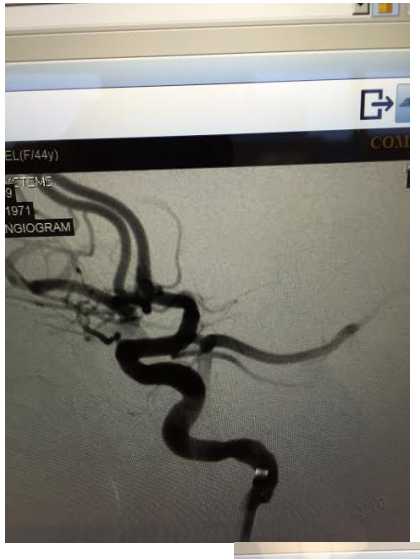


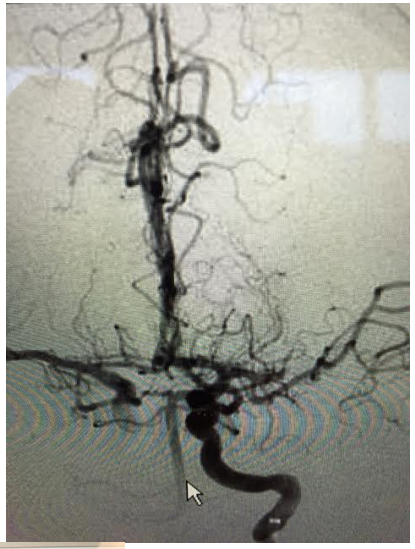


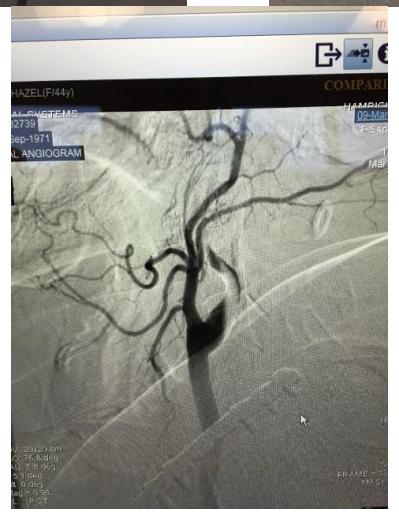
SOLITIARE STENT RETRIEVAL THROMBECTOMY DEVICE ANIMATED VDEO



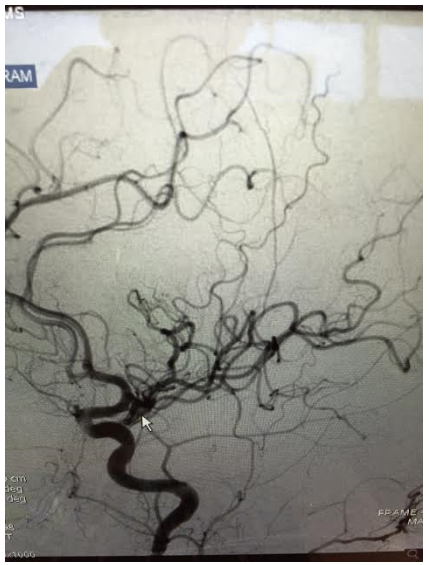
PRE TREATMENT

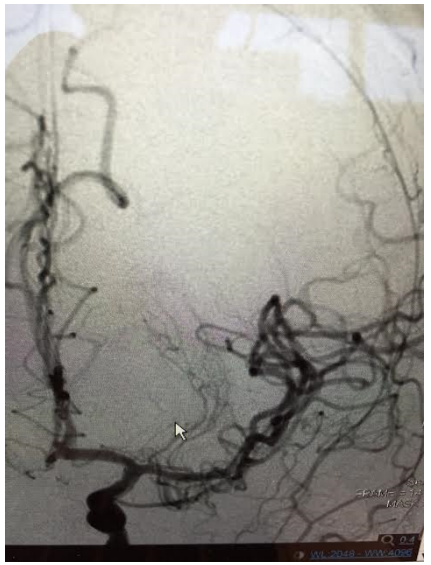


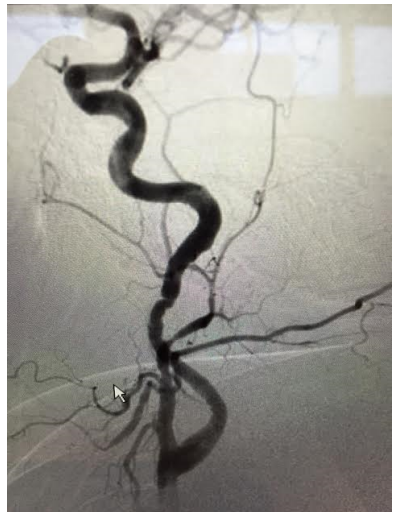




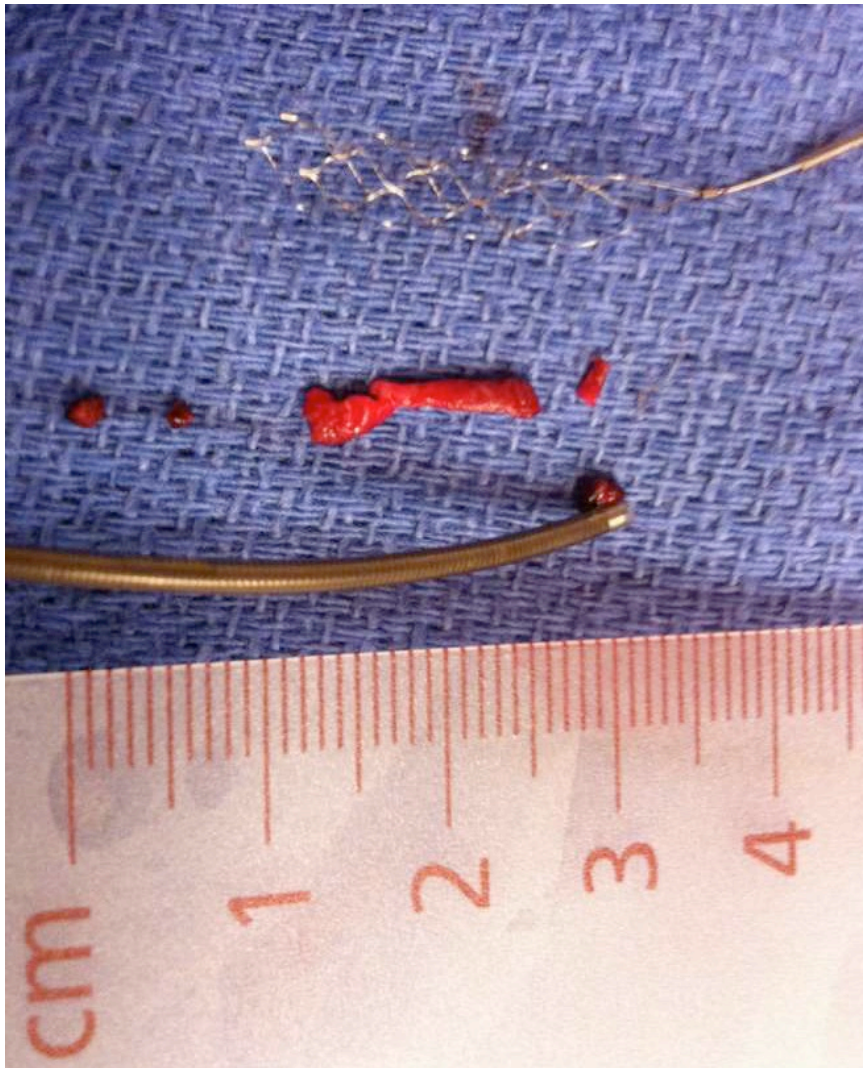
POST TREATMENT



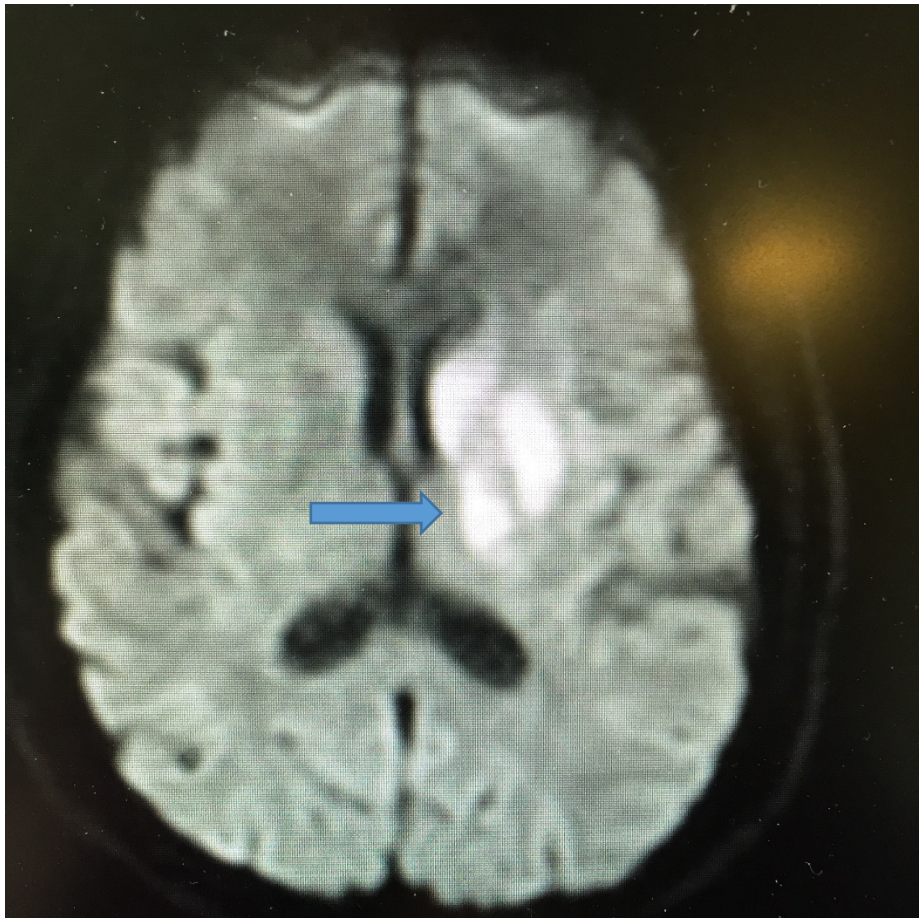


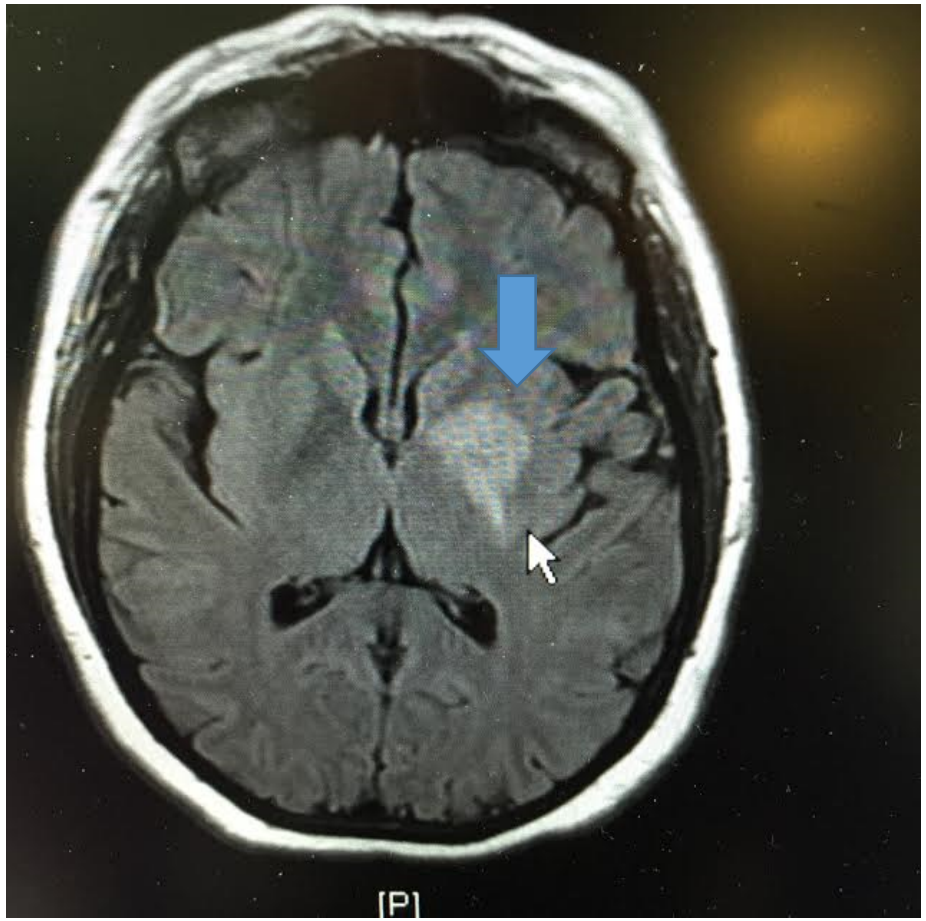


RETRIEVED THROMBUS



MRI BRAIN 24 HOURS POST TREATMENT





WHAT DOES THIS MRI TELL US?

- Caudate and globus pallidus and putamen (basal ganglia) are infarcted
- The vessels that supply these structures (medial and lateral lenticulostriate arteries) are primarily end arteries originating from the A1 segment of the ACA and the M1 segment of the MCA without good sources of collateral blood flow
- Due to lack of collaterals this tissue cannot tolerate arterial occlusion and tissue death develops over a short time period
- The internal capsule appears to be spared (remarkably)
- The remainder of the MCA territory is free of irreversible ischemic changes

HOSPITAL COURSE

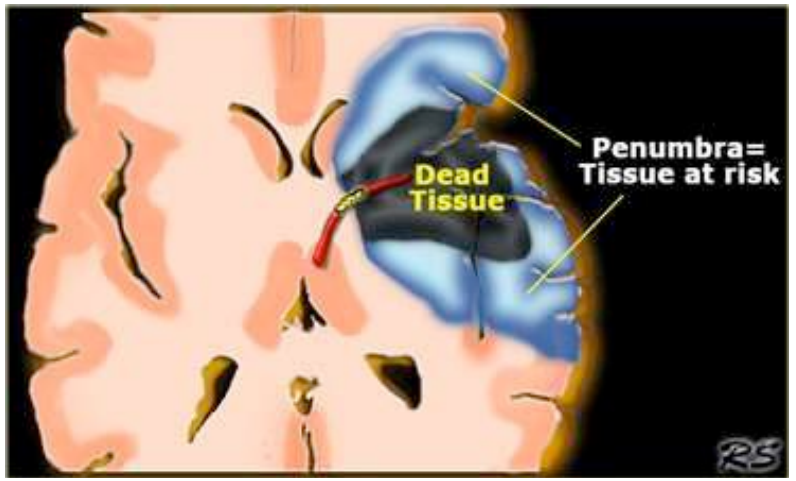
- 7 day hospitalization
- Transesophageal Echocardiogram
  - Normal
- Hypercoagulability evaluation
  - Heterozygous prothrombin gene variant mutation.
  - Placed on ASA
- Discharged from rehabilitation with discharge note stating
  - “She had resolution of her speech deficits and resolution of her right sided weakness. She met all rehabilitation goals and was independent with transfers and ambulation for long distances without device. She is independent with ADLs. She is able to ascend and descend 12 stairs. The patient was discharged home

6 HOURS AND BEYOND

- How do we manage the adult patient who presents with:
  - Ischemic stroke symptoms
  - CT ASPECT ≥6
  - In the time window that would not permit groin puncture by hour 6 from stroke onset
- MRI with DWI imaging and perfusion imaging may hold the key to determining which of these patients might **STILL** benefit from endovascular revascularization using mechanical thrombectomy

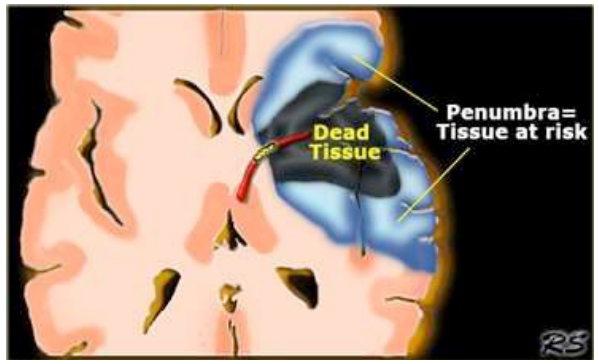
PHYSIOLOGIC TIME VS CHRONOLOGIC TIME

- DEFUSE 2 Study
  - Focused on the issue of physiologic time
  - Core
    - Tissue that will inevitably die and is beyond salvage
  - Penumbra
    - Tissue that is hypoperfused but is not beyond salvage and can survive if normal blood flow is reestablished before the tissue dies.
- GOAL: PRESERVE THE PENUMBRA

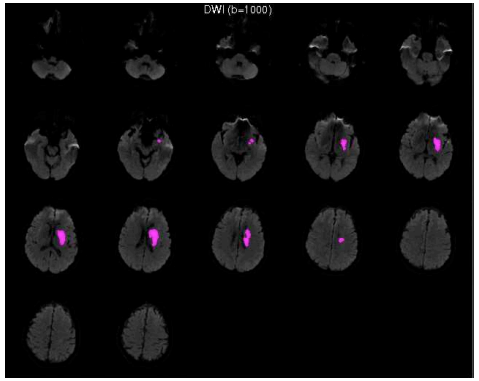


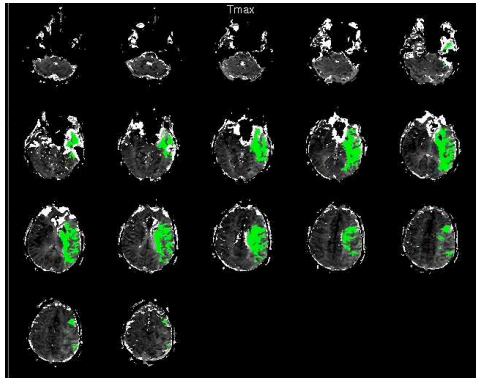
DEFUSE 2

- The ideal candidate for IA therapy despite chronological time from onset of symptoms is the individual with
  - Infarct volume less than 50 cc
  - Perfusion : Diffusion ratio of ≥ 1.8
    - Perfusion = Blood flow
    - Diffusion = Irreversibly damaged brain



- Patients with P:D ratio ≥ 1.8 and M1 or ICA occlusion likely has good collateral blood flow to involved brain tissue





DEFUSE 3 Study (NEJM, Jan 24, 2018)

- PURPOSE: Assess patients in a controlled study to learn if thrombectomy within 6-16 hours of stroke symptom onset is beneficial in patients with less than 70 ml infarct volume and a ratio of ischemic tissue vs infarct volume of 1.8 and an absolute volume of penumbra of ≥15ml
- RESULTS:
  - Thrombectomy + Best Medical was superior to Medical alone with functinal outcome favored by an odds ratio of 2.77)
  - Independent (MRS 0-2) 45% vs 17% at 90 days
  - 90 day mortality 14% vs 26%
  - Symptomatic ICH 7% vs 4%
  - Serious adverse event 43% vs 53%

2017 DAWN Study (DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention)

- PIs: Jovin T and Nogueira R
- Study intervention
- Trevo Stent Retriever plus medical therapy
- Control intervention
- Best medical therapy alone including ivTPA
- Study population:
  - 206 acute stroke patients
  - No upper age limit presenting
  - 6-24 hour time window
  - Proximal anterior circulation occlusions (M1,ICA) and substantial clinical/core mismatch

- STUDY HALTED WHEN INTERIM ANALYSIS OF FIRST 200 PATIENTS PRELIMINARILY DEMONSTRATED SUPERIOR OUTCOMES AT 90 DAYS

DAWN KEY FINDINGS

- Endovascular therapy + Best medical therapy vs. Best medical therapy
- Improved functional independence at 90 days (48.6% vs 13.1%)
- Improved functional independence at 90 days (73% relative reduction in disability at 90 days)
- 1 in 2.8 patients treated with IA retrieval are saved from disability.
- **DAWN STUDY SHOWED SIMILAR RESULTS TO MR CLEAN RESULTS EXCEPT FOR EXENDING TREATMENT WINDOW FOR ENDOVASCULAR THERAPY TO 24 HOURS**

TREATEMENT OF DISTAL THROMBOEMBOLI

- **Grossberg JA, et al Stroke 2018**.
- 69 cases retrospectively reviewed (2010-2015)
  - Occlusion located in ACA and distal to M3
  - Mean age 66.7 +/- 15.8%
  - 57% male
  - Median pre-treatment NIHSS 18
- Distal occlusion was primary treatment site in 45 patients (65%)
- Distal occlusion treatment was rescue after treatment of a proximal site in 23 patients (33%)
- Proximal and distal occlusion was primary treatment site in 1 patient (14%)
- Treatment Modality
  - IV TPA 29 (42%)
  - Stentriever 37 (54%)
  - IA TPA 36 (52%)
  - Aspiration 31 (45%)
- Results
  - TICI 2b-3 in 57 (83%)
  - 3 parenchymal hematomas (4%)
  - 90 day mRS 0-2 in 30%
  - 90 day dead 20%

THANK YOU