Management of Acute Ischemic Stroke

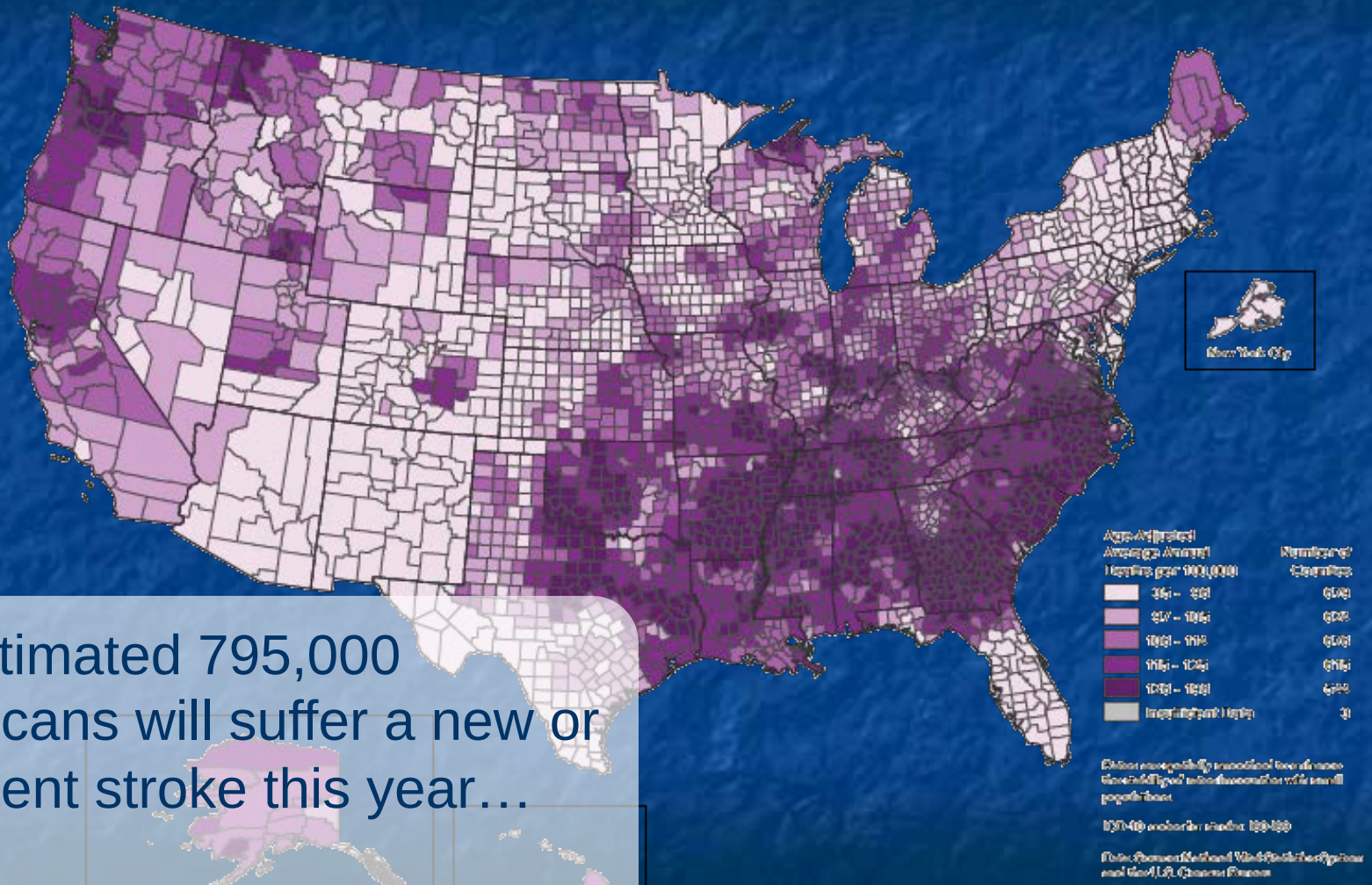
Hamed Farid, MD, MBA

Associate Professor of Radiology and Neurosurgery
Marvin Blaski Stroke Medical Director Endowed Chair, St. Jude Medical Center
Chief, Neurointerventional Radiology

Acute Ischemic Stroke

- Impact
  - #1 cause of adult disability
  - #2 cause of dementia
  - #3 cause of death in the United States
    - 2nd cause of death worldwide

Stroke Incidence



An estimated 795,000 Americans will suffer a new or recurrent stroke this year…

…that's one every 40 seconds

American Heart Association. Heart Disease and Stroke Statistics 2012 Update At-a-Glance.

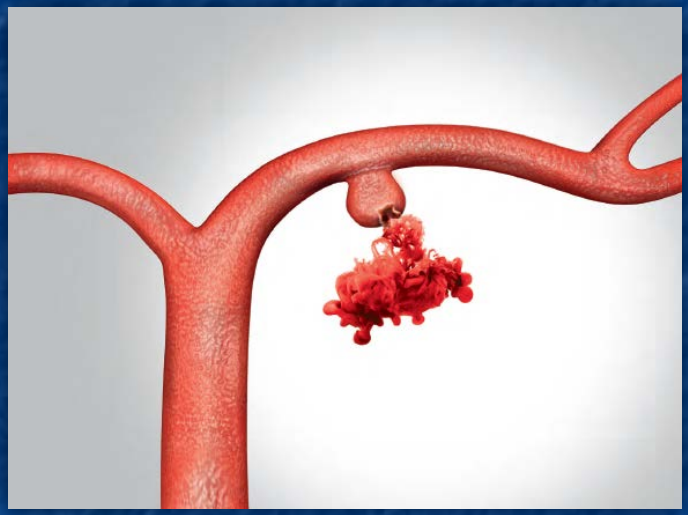
Two Types of Stroke

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



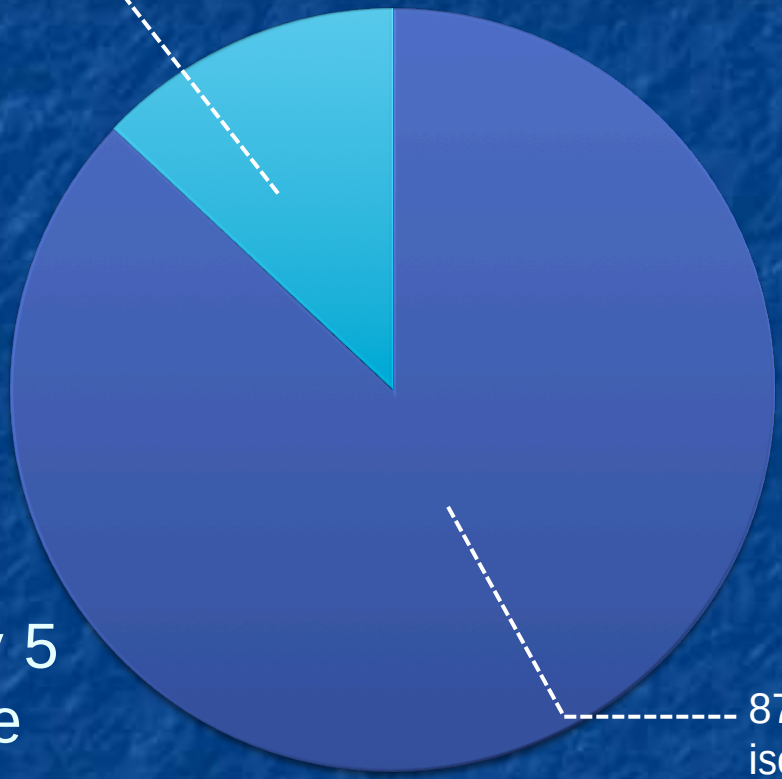
Hemorrhage = bleeding

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 touched by stroke

American Heart Association. Heart Disease and Stroke Statistics 2012 Update At-a-Glance.

35-40% of Ischemic Strokes are Considered "Large Vessel"

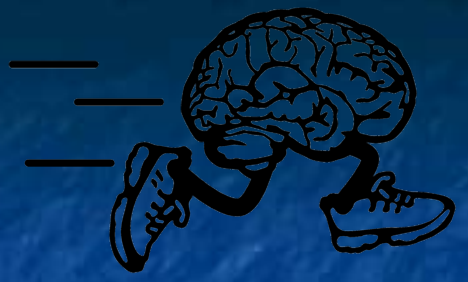
- This subset of ischemic stroke comprises blockages in the:
  - Internal Carotid Artery (ICA)
  - Middle Cerebral Artery (MCA)
  - Vertebral / Basilar Artery

- If left untreated, patient prognosis with these types of stroke is poor

Vessel	Mortality Rate
ICA	53%[1]
MCA	27%[2]
Basilar Artery	89-90%[3]

1. Jansen O, et al.
2. Furlan A et al. PROACT II Trial
3. Brückmann H et al.

Physiological Impact of Stroke

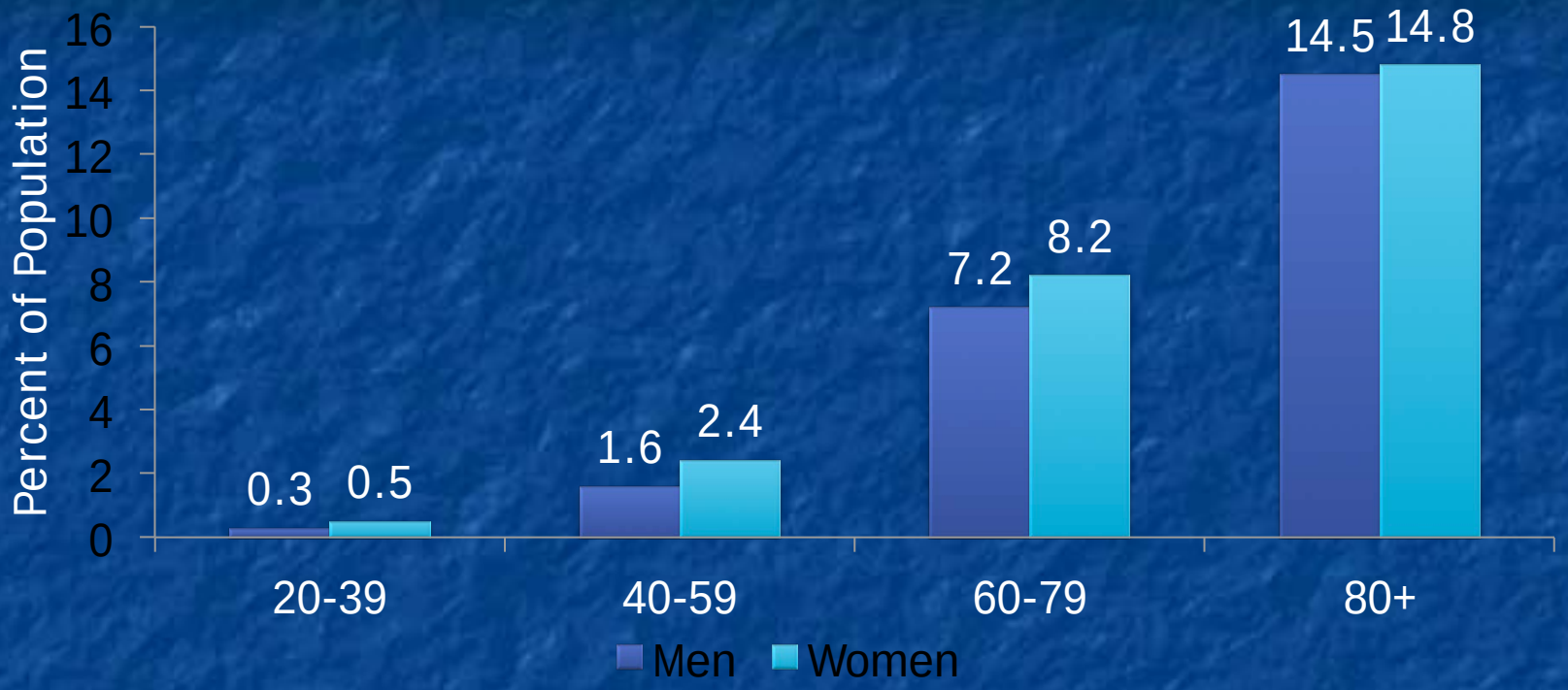


Estimated Pace of Neural Circuitry Lost in a Typical Large Vessel Acute Ischemic Stroke

Time	Neurons Lost	Synapses Lost	Mylinated Fibers Lost	Accelerated Aging
1 second	32,000	230 million	218 yards	8.7 hours
1 minute	1.9 million	14 billion	7.5 miles	3.1 weeks
1 hour	120 million	830 billion	447 miles	3.6 years
Avg. stroke	1.2 billion	8.3 trillion	4470 miles	36 years

Saver, Jeffrey, *Time is Brain – Quantified*. Stroke 2006; 37: 263-266.

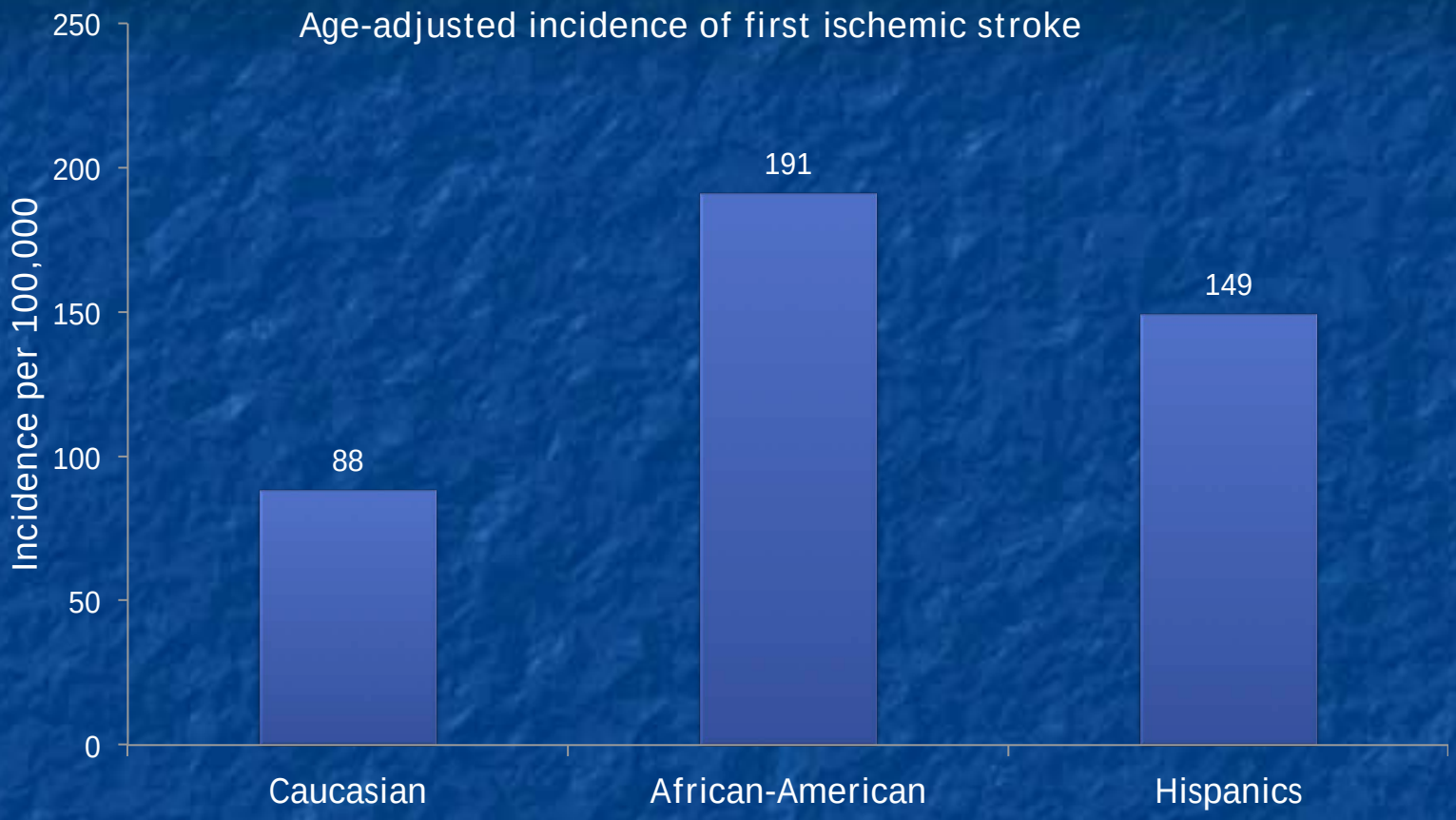
US Prevalence of Stroke by Age and Sex[1]



Stroke kills more women than breast, ovarian, uterine and cervical cancer combined[2]

1. American Heart Association. Heart Disease and Stroke Statistics 2012 Update At-a-Glance.
2. Kochanek KD, et al. Natl Vital Stat Rep. 2011; 59(4):1-68

Race is a Risk Factor for Stroke



African-Americans have a risk of first-ever stroke that is almost twice that of Caucasians

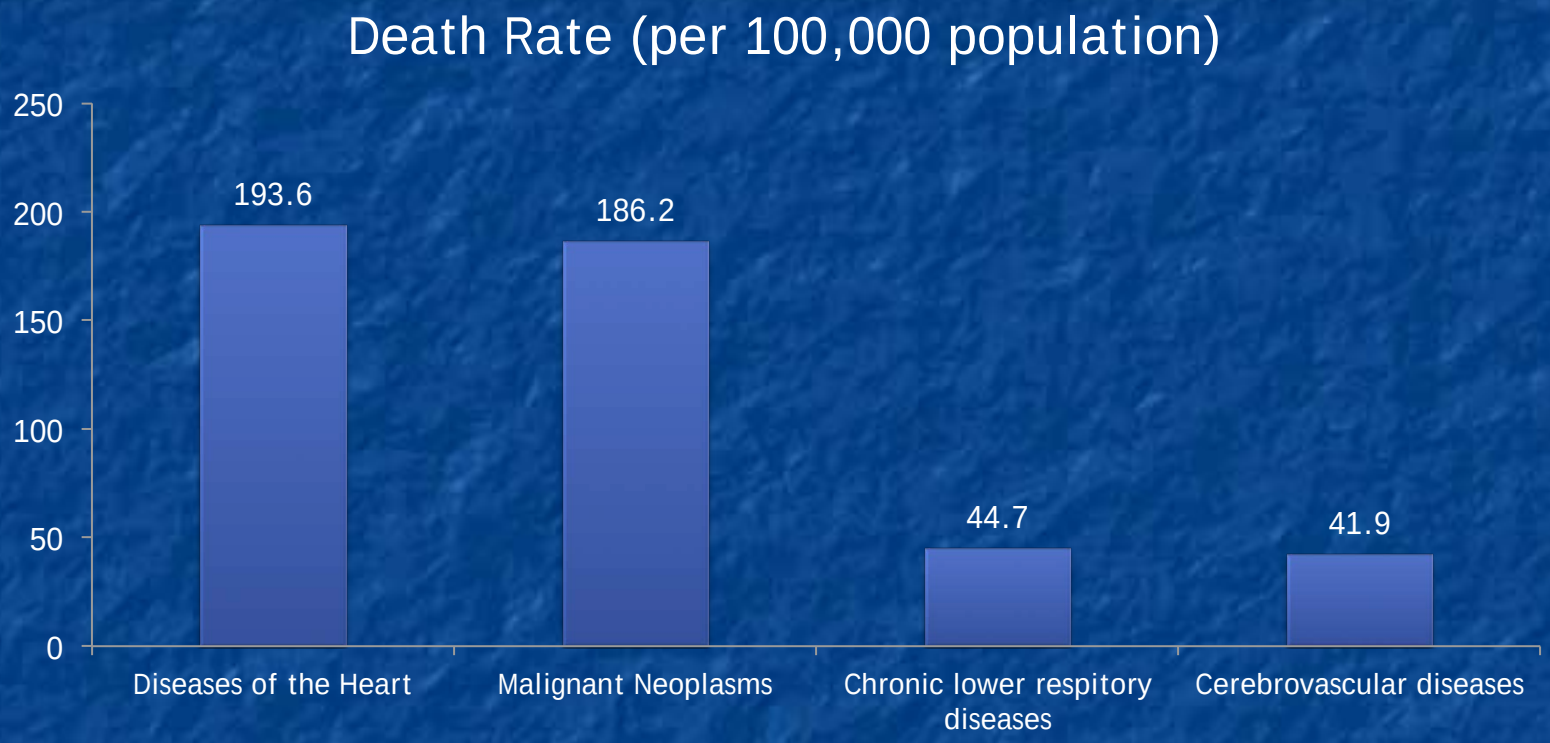
American Heart Association. Heart Disease and Stroke Statistics 2012 Update At-a-Glance.

TIA's (Transient Ischemic Strokes)

- "Mini-Stroke" – symptoms can be similar to a stroke but resolve on their own in a short period of time
- ~5 million Americans have been diagnosed with having had a TIA; true prevalence is probably greater because many TIA's go undiagnosed
- A meta-analysis shows that patients with TIA have a 10-17% risk of stroke within 90 days
- Within 1 year of TIA, ~12% of patients will die

American Heart Association. Heart Disease and Stroke Statistics 2012 Update At-a-Glance.

Stroke is a Leading Cause of Death

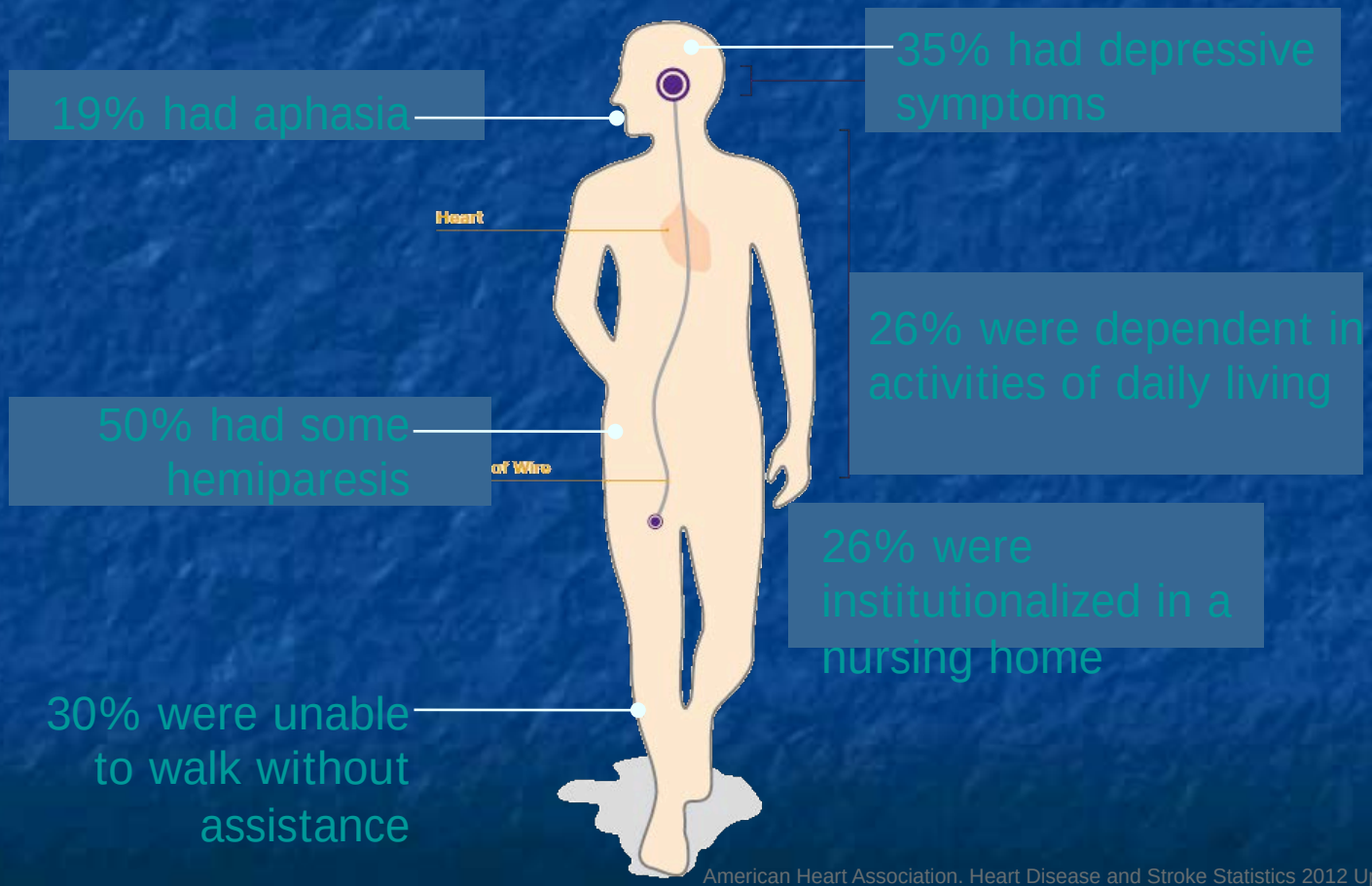


Stroke accounts for 1 of every 18 deaths in the United States, that's 1 every 4 minutes

American Heart Association. Heart Disease and Stroke Statistics 2012 Update At-a-Glance.

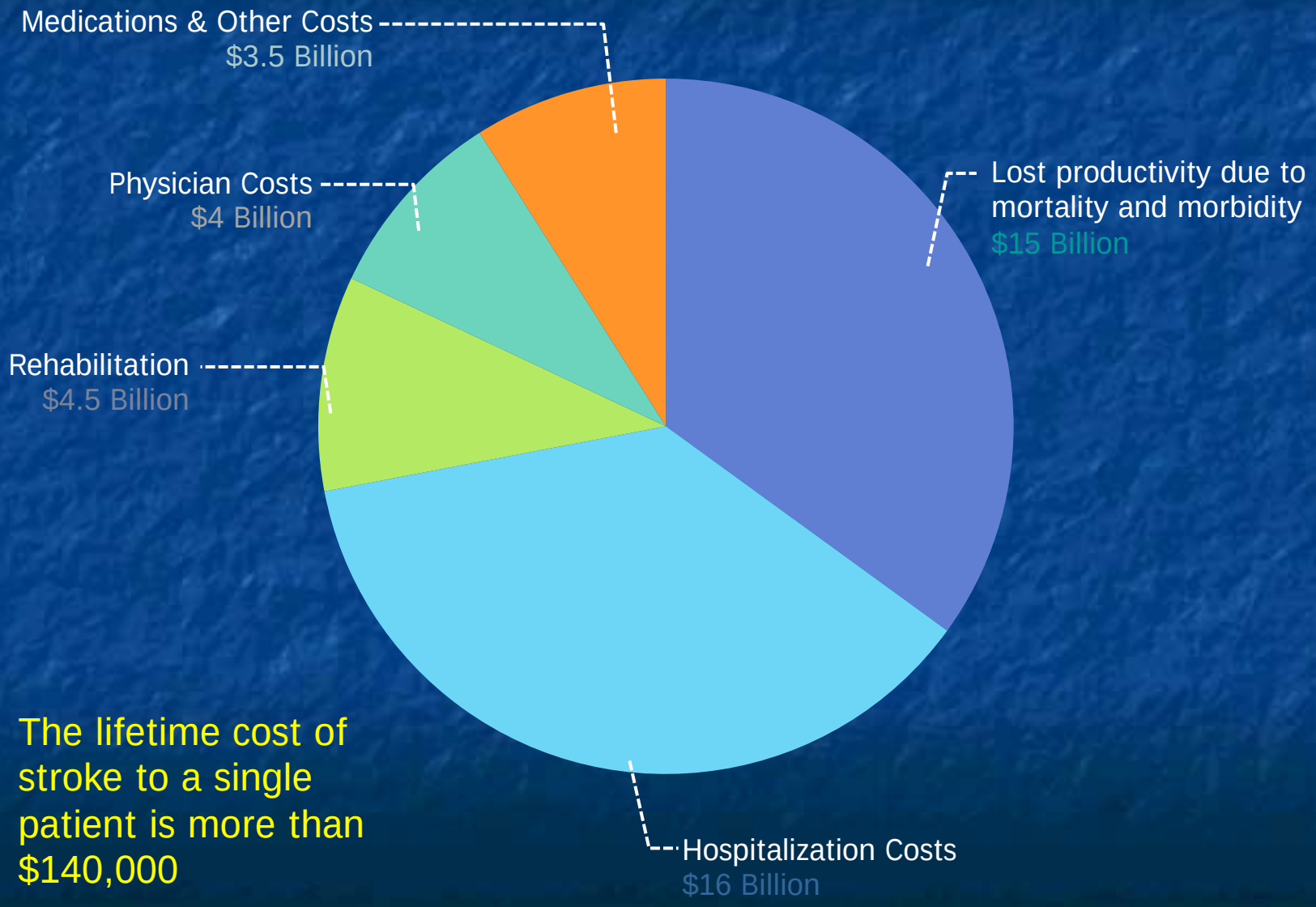
There are Over 7 Million Stroke Survivors...

…two thirds of which are living with moderate to severe disability



American Heart Association. Heart Disease and Stroke Statistics 2012 Update At-a-Glance.

The Total Estimated Cost of Stroke is $48 Billion



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

Risk Factors for Stroke

Hereditary / non-modifiable

- Increasing age
- Family history of stroke
- Prior TIA
- Prior ischemic stroke
- Prior heart attack

Modifiable

- High blood pressure
- High cholesterol
- Smoking / tobacco use
- Diabetes
- Physical inactivity / obesity
- Afib
- Carotid Artery Stenosis
- End-stage renal disease

American Heart Association. Heart Disease and Stroke Statistics 2012 Update At-a-Glance.

- So a stroke comes into the hospital. Now what?

Emergency Medical Services:
American Heart Association Recommendations

- **Onset time of stroke symptoms**
  - Time of onset is very important
  - Clock time at onset of symptoms is preferred over "duration"
- **Notification to hospital of triage**
  - Obtaining telephone numbers of witness or family

National Institute of Neurological Disorders and Stroke (NINDS) Recommended Treatment Times

ED Door-to-MD	10 minutes
ED Door-to-Stroke Team notification	15 minutes
ED Door-to-CT scan	25 minutes
ED Door-to-Drug	60 minutes
ED Door-to-Admission	3 hours

What Are Signs and Clinical Presentation of Stroke?

Symptoms of stroke vary depending on the part of the brain that is affected:

- Sudden numbness or weakness of the face, arm, or leg
- Sudden trouble seeing in one or both eyes
- Sudden confusion or trouble speaking
- Sudden trouble with walking, dizziness, or loss of balance
- Sudden, severe headache with no known cause

Conditions that Mimic Stroke

- Alcohol Intoxication
- Migraines
- Epilepsy
- Psychogenic disorders
- Brain tumor
- Encephalitis
- Vertigo
- Hypo- or Hyperglycemia

Rother, Joachim. Stroke-Mimicking Disorders. Medical Radiology 2006, pp 285-291

Immediate Diagnosis and Management

- **Stat CT Head Scan**
  - Standard diagnostic tool to rule out hemorrhagic stroke
  - Subtle or early signs of infarct
    - Hyperdense vessel sign – indicative of thrombus or embolus
    - Loss of gray-white differentiation
      - Detected in many large vessel anterior circulation occlusions

CT Showing Hyperdense MCA Sign

Courtesy of Ron Budzik, MD, Riverside Methodist Hospital

Immediate Diagnosis and Management

- Lab Work
- EKG
- Maintain O2 saturation ≥ 95%
- Neurological Exam – Stroke Assessment including National Institute of Health Stroke Scale (NIHSS)

Stroke Assessment
National Institute of Health Stroke Scale (NIHSS)

Severity scoring: range 0-42

0 = normal, 42 = worst score

NIHSS is used to measure severity and quantify objective changes in the assessment

1. Level of consciousness, following commands
2. Gaze preference
3. Visual acuity – partial/complete hemianopsia or total blindness
4. Facial palsy – smile/raise your eyebrows

National Institute of Health Stroke Scale (NIHSS) – cont'd

5. Motor arm – hold up your arms for 10 secs
6. Motor leg – hold up your leg for 5 secs
7. Limb ataxia – in 1 or 2 limbs
8. Sensory – do you feel this
9. Best language – aphasia or mute
10. Dysarthria – slurred or unintelligible
11. Extinction/Inattention – to double simultaneous stimulation, partial or profound neglect

NIHSS:
Stroke Severity & Vessel Location

- NIHSS ≥ 12 → 91% Positive Predictive Value of Large Vessel Stroke

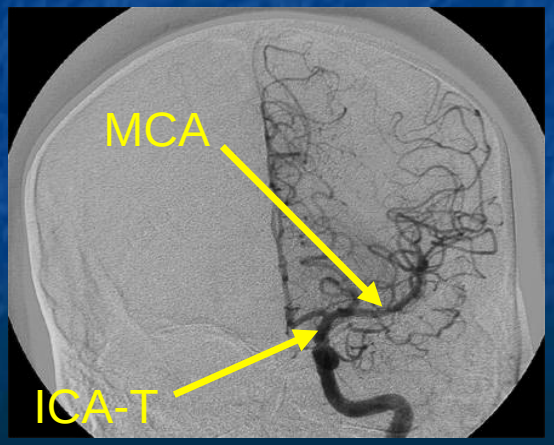
Fischer. *Stroke*. 2005 Oct;36(10):2121-5.

- NIHSS 5-9 → 36% Large Vessel
- NIHSS 10-14 → 44% Large Vessel
- NIHSS 15+ → 100% Large Vessel

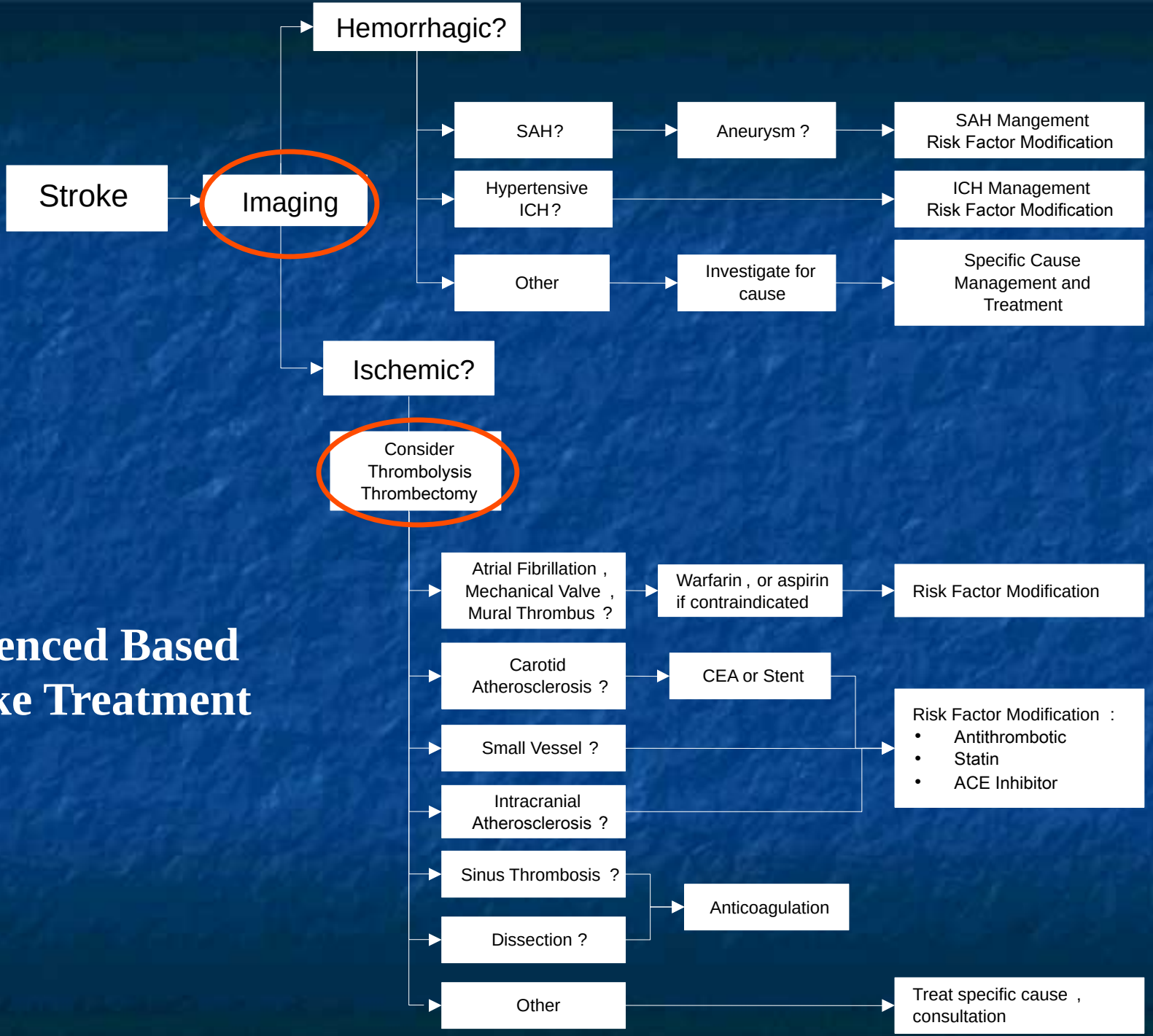
Lewandowski. *Stroke*. 1999 Dec;30(12):2598-605.

Large Vessel Strokes

- ICA, ICA-T, MCA, vertebrobasilar arteries
- Poor natural history in large vessel stroke
- Mortality rates from published literature
  - ICA-T: 53% — Jansen, 1995
  - MCA: 30-35% — Chambers, 1987
  - Basilar: 89-92% — Brückmann H, 1986 & Brandt, 1996



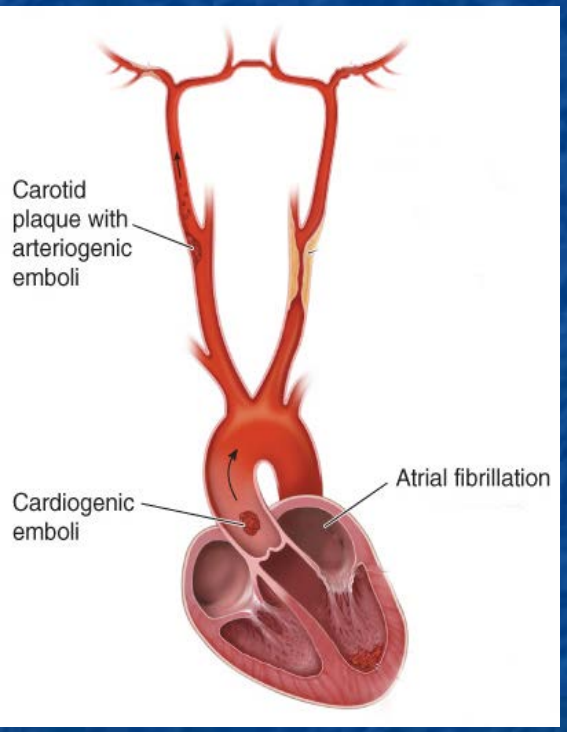
Evidenced Based Stroke Treatment

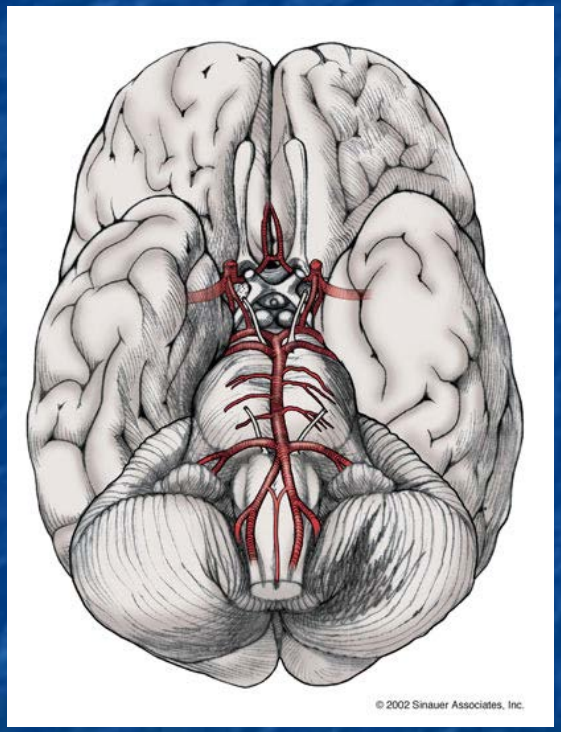


Ischemic Stroke: Basic Criteria for Endovascular Rx

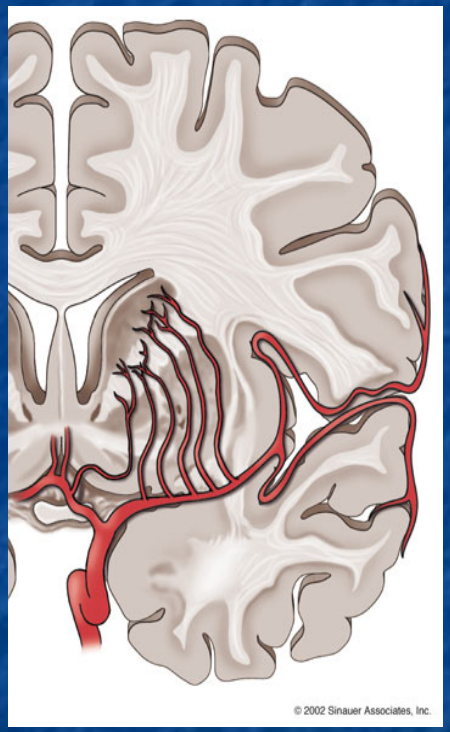
1) Large Vessel Occlusion (CT/MR angiography)

Large Vessel Occlusion



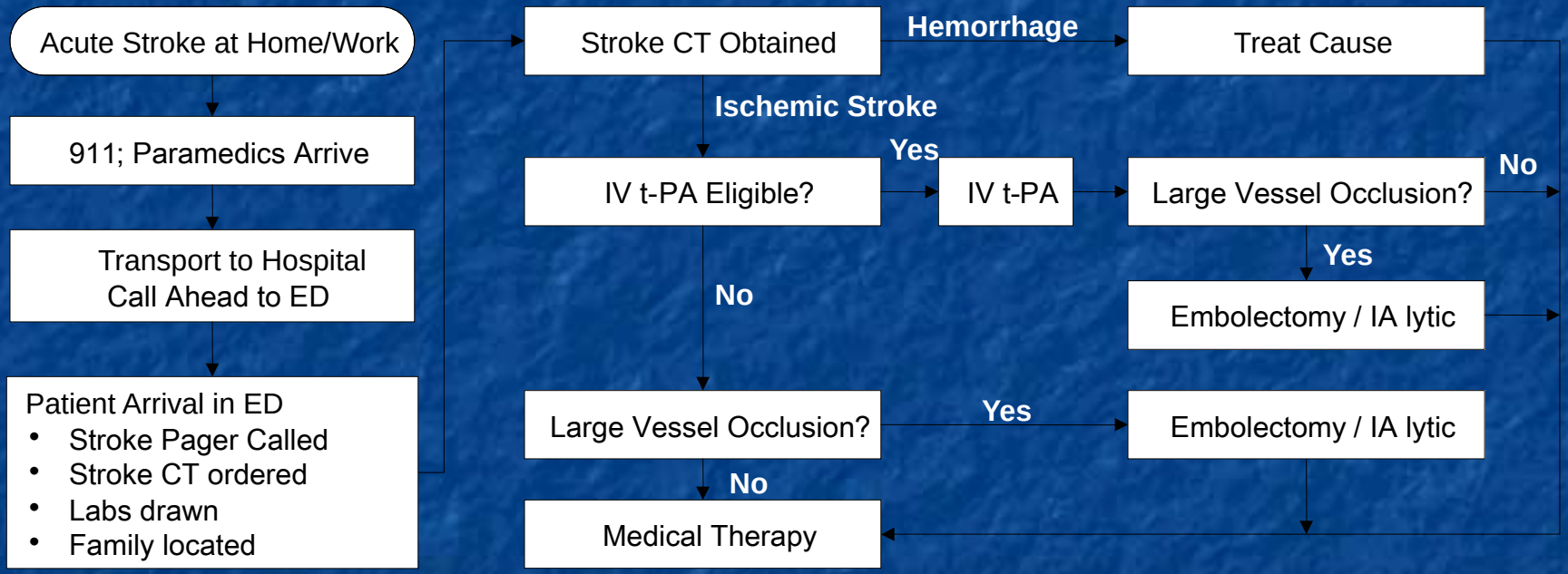


Small Vessel Occlusion



2) Salvageable tissue (time window, imaging studies)

Acute Stroke Protocol



Stroke CT = noncon CT, CTA (chest through brain), CTP, post-contrast CT

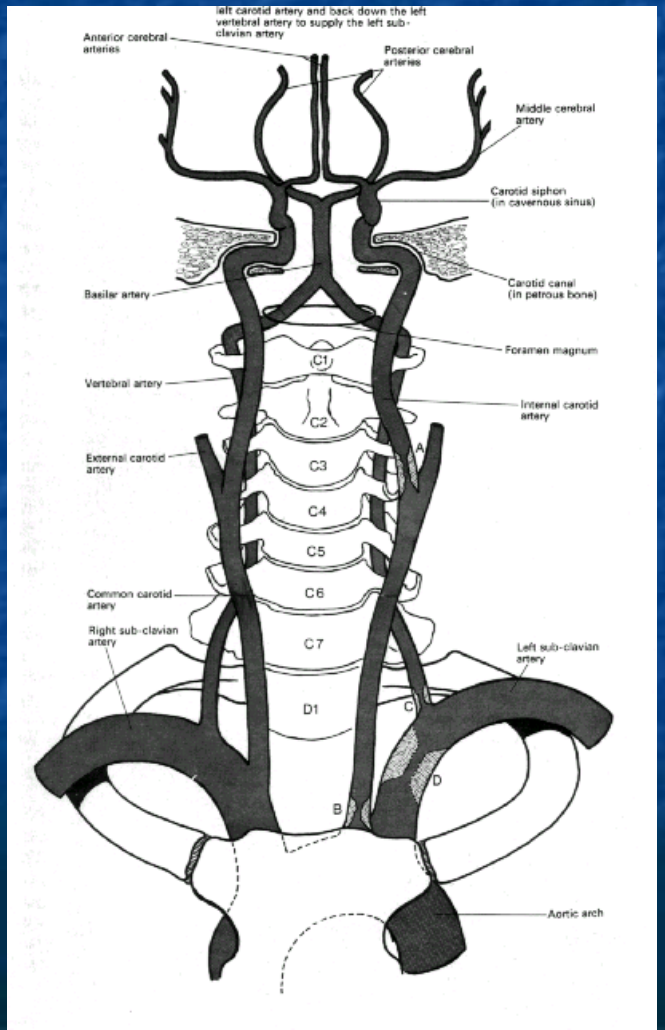
Neurovascular and Spine Associates

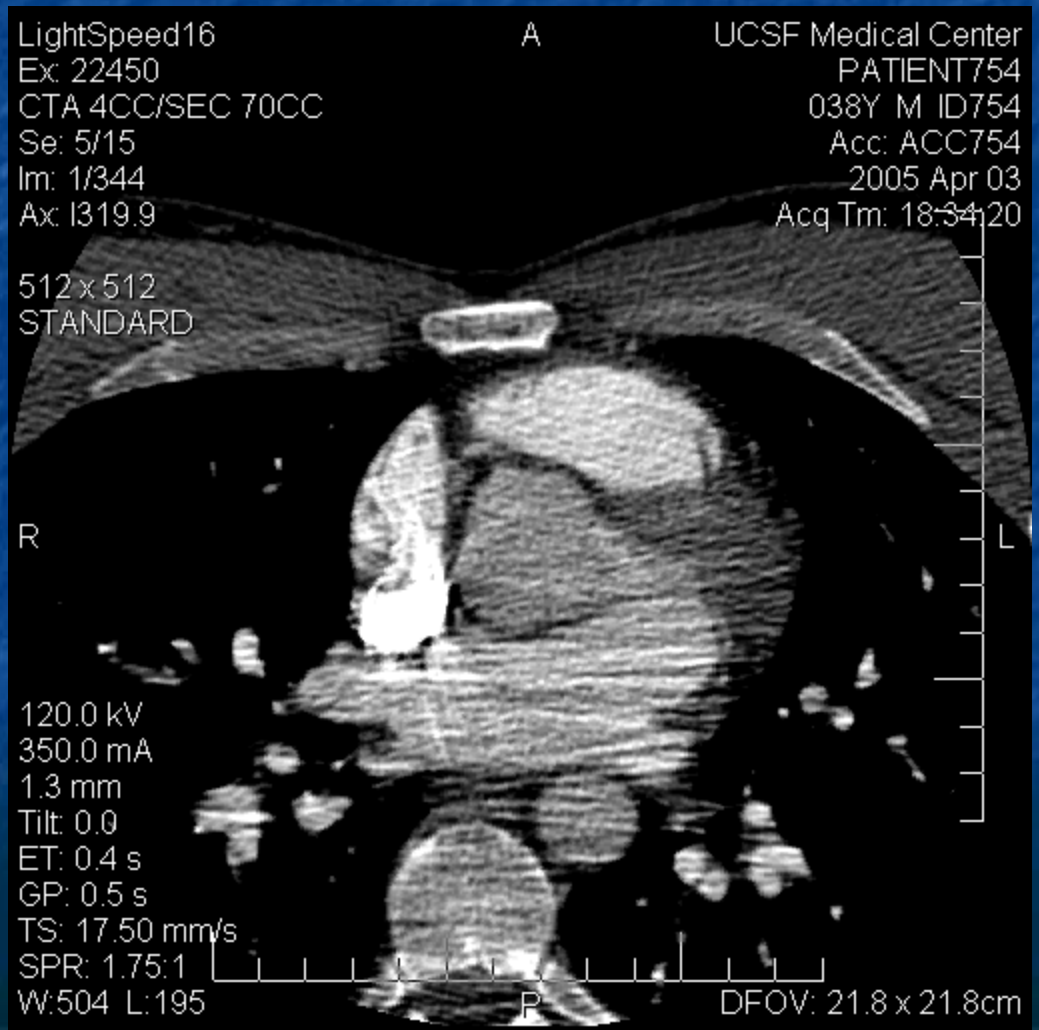
CT Angiography

Intravenous bolus of iodinated contrast is given through peripheral IV. A rapid scan is then performed from the heart to the top of the head, tracking the contrast through the arteries.

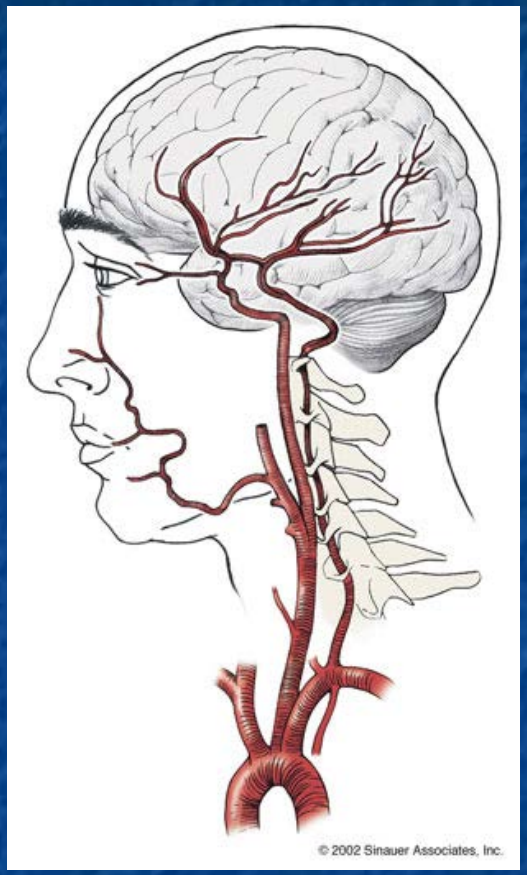
Hemorrhagic Stroke: helps identify aneurysms, vascular malformations

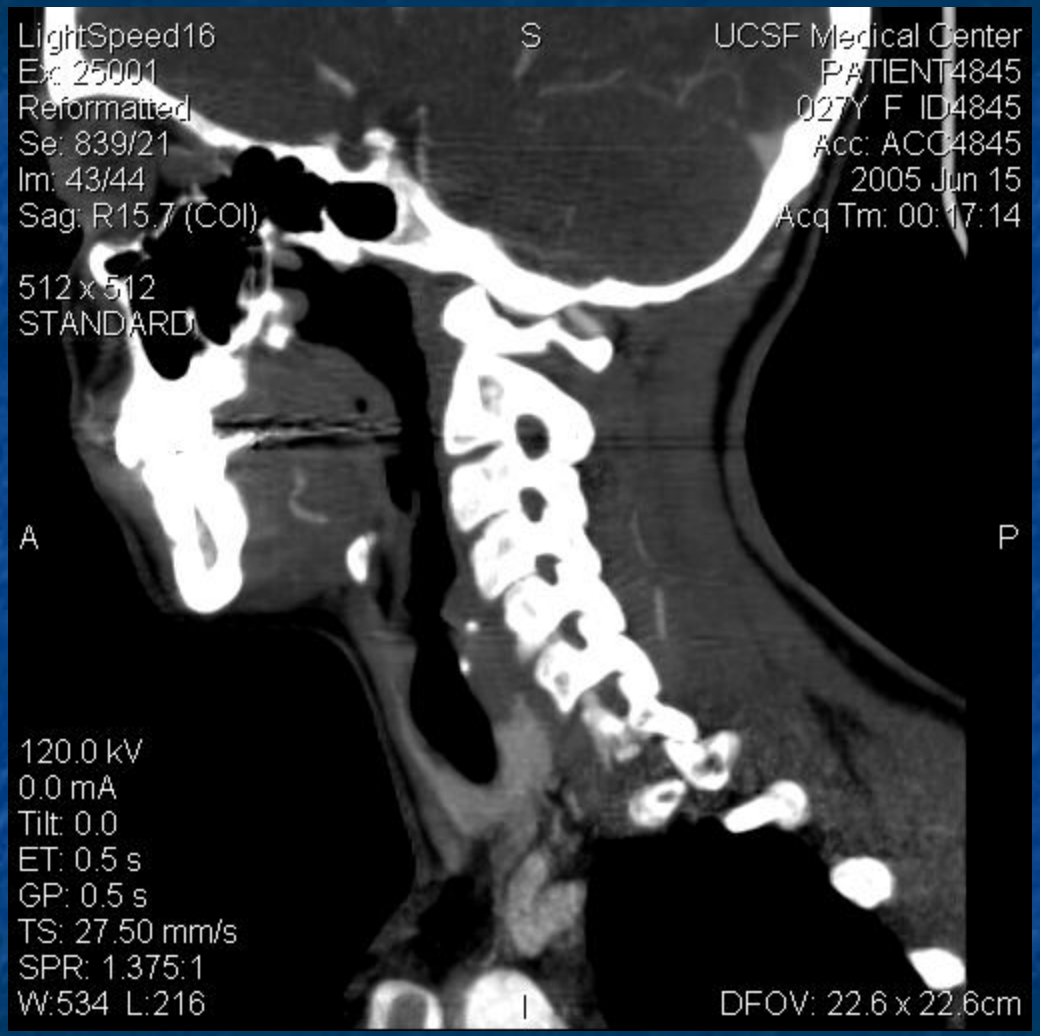
Ischemic Stroke: helps identify large vessel occlusions/stenoses





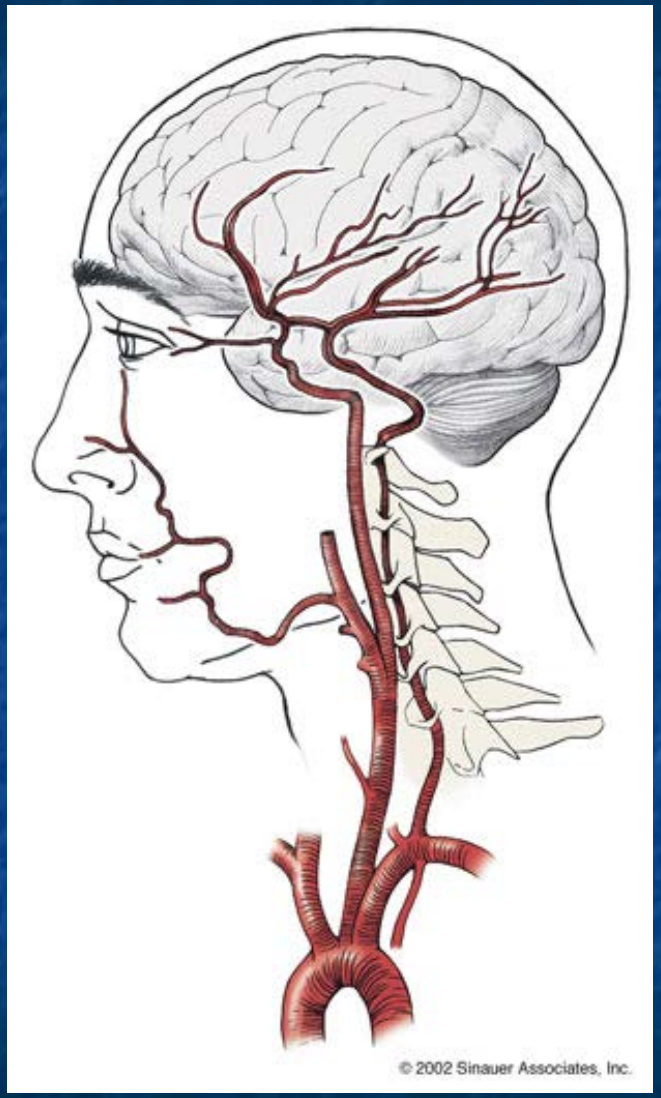
CT Angiography – Extracranial Vessels

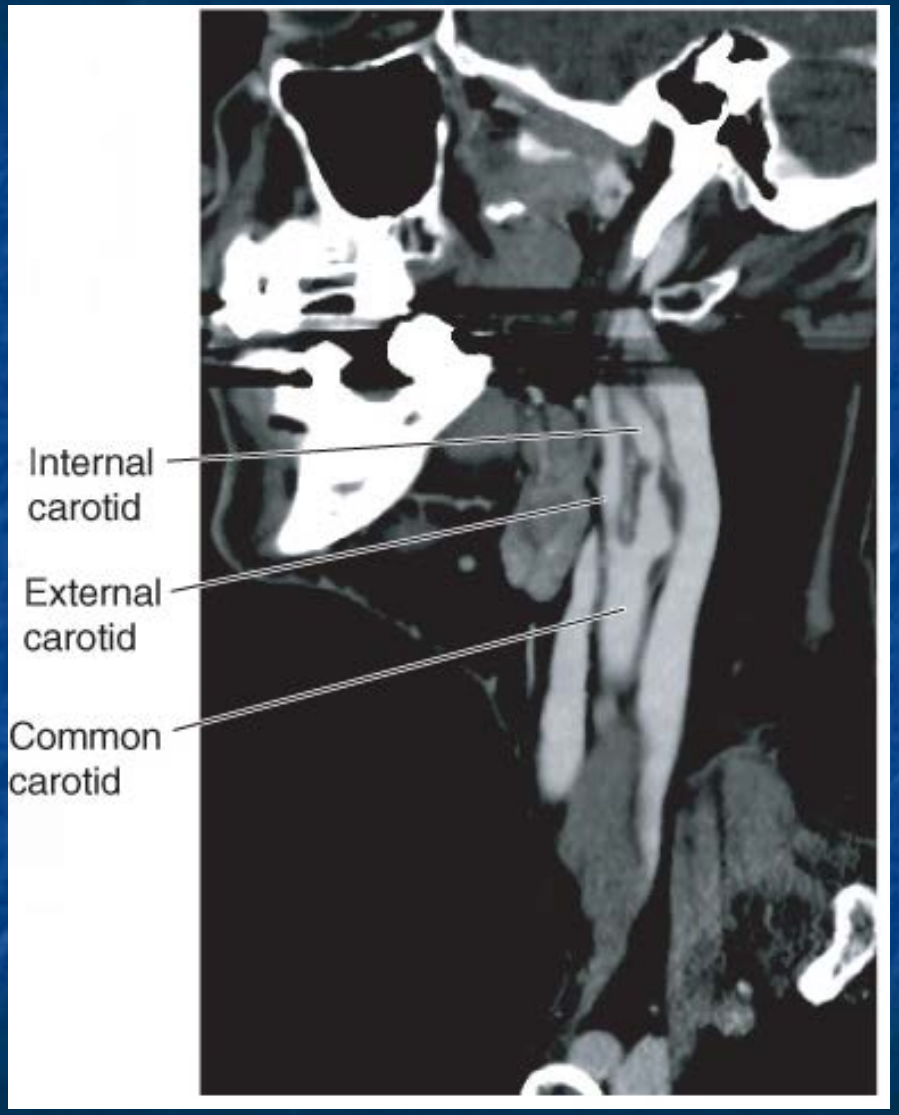




Neurovascular and Spine Associates

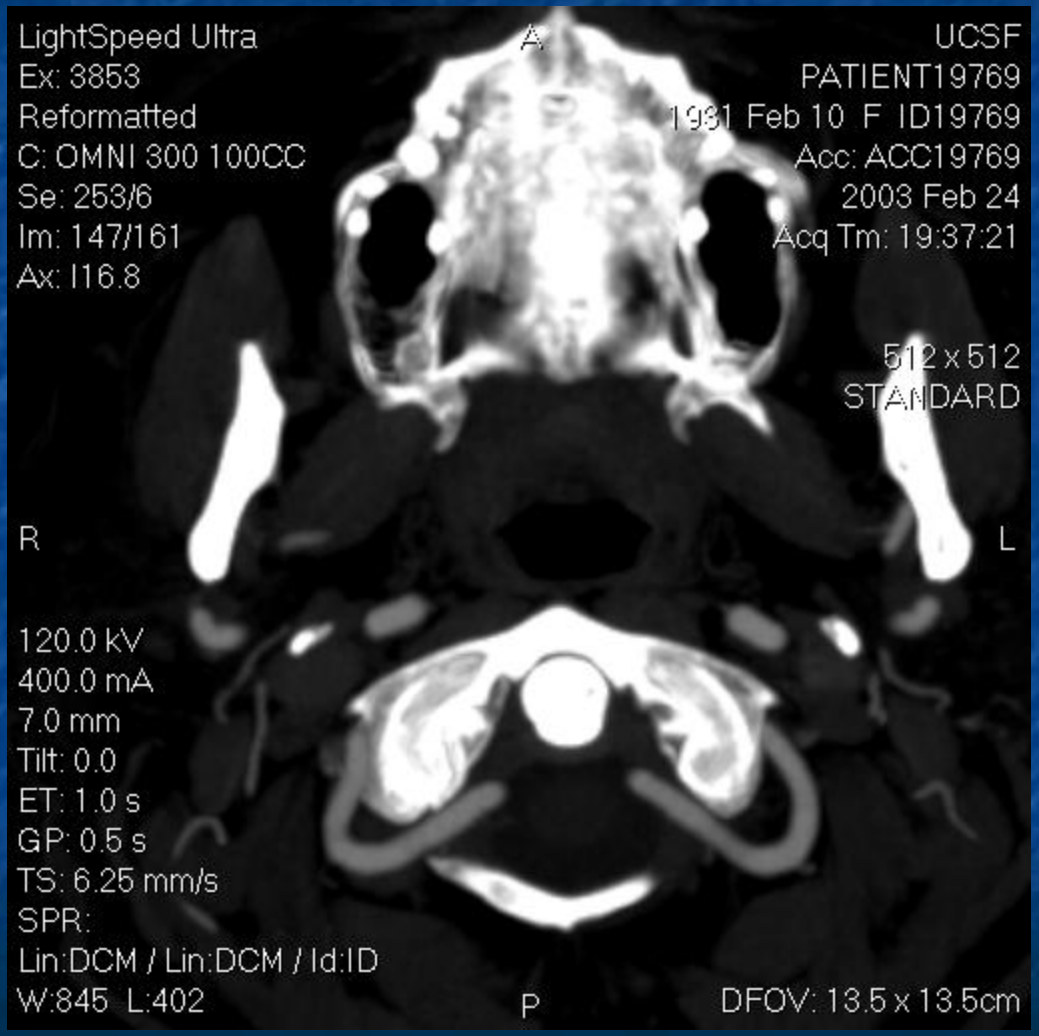
CT Angiography – Extracranial Vessels





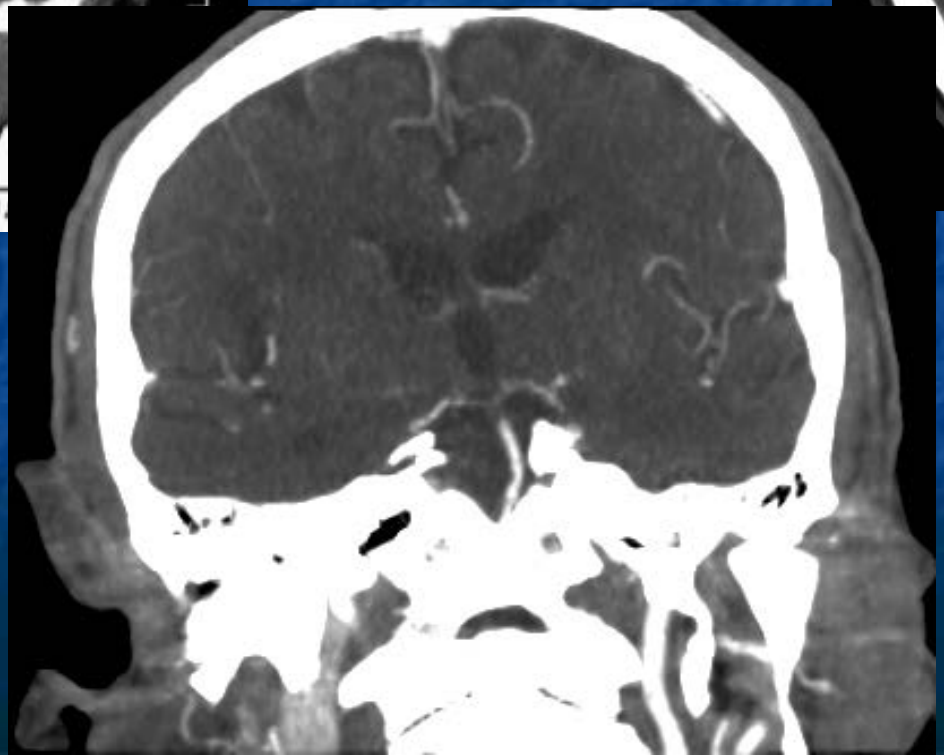
Neurovascular and Spine Associates

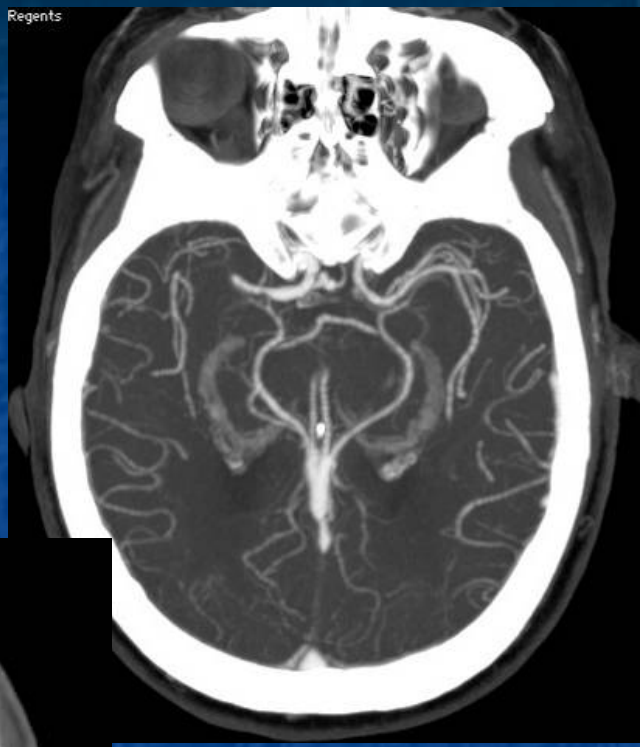
CT Angiography – Intracranial Vessels



Neurovascular and Spine Associates

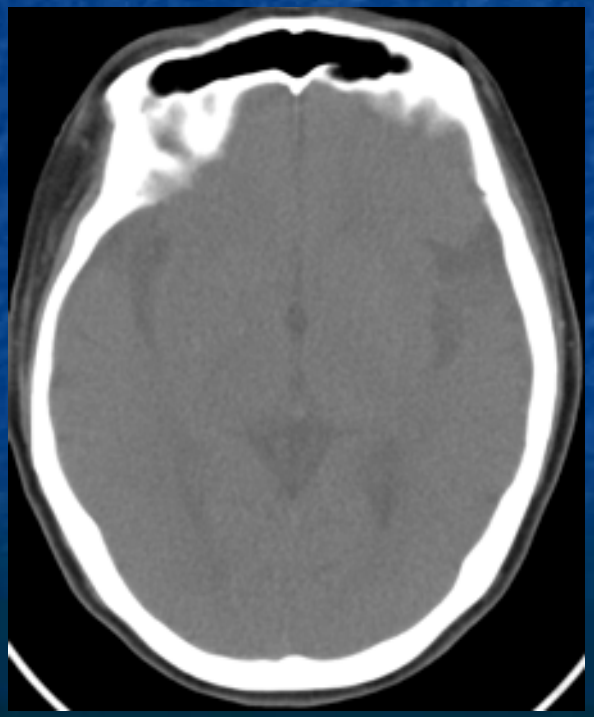
CT Angiography – Intracranial Vessels

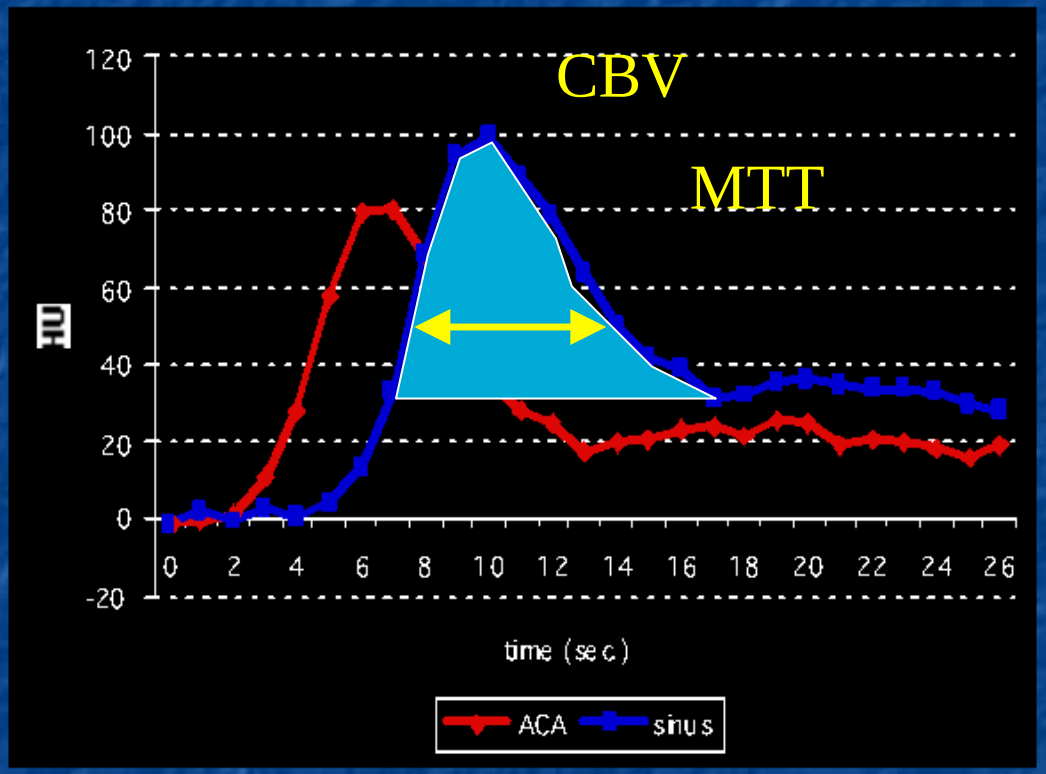




CT Perfusion

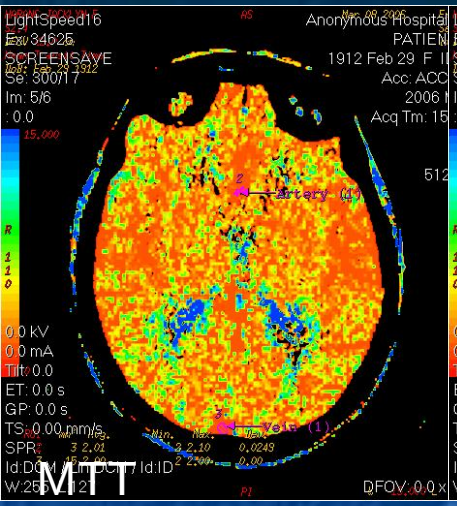
An intravenous bolus of iodinated-contrast is given through a peripheral IV. Serial images are then taken over time at a given location (or “slice”) of the brain, watching the contrast “wash in and wash out.”



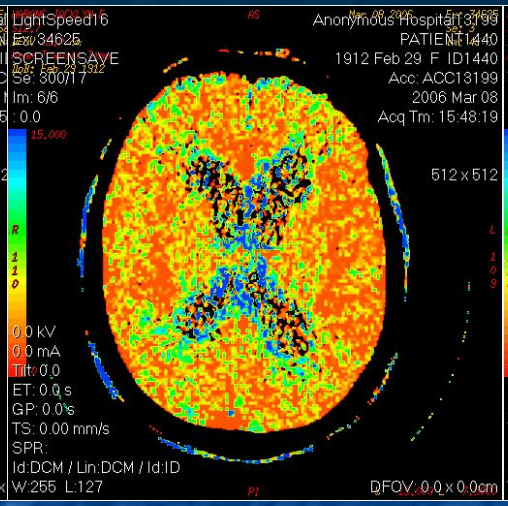


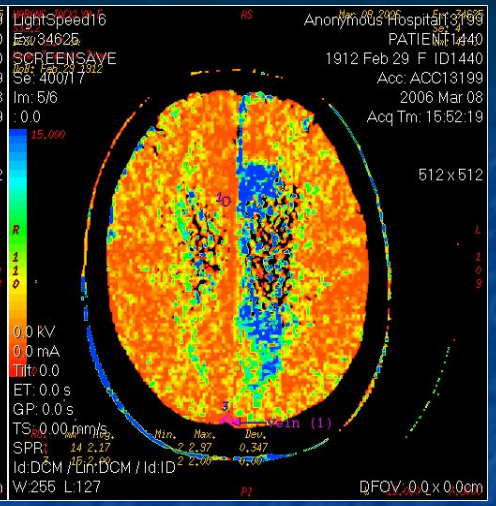
$$\text{CBF} = \frac{\text{CBV (ml/100 gm)}}{\text{MTT (sec)}}$$

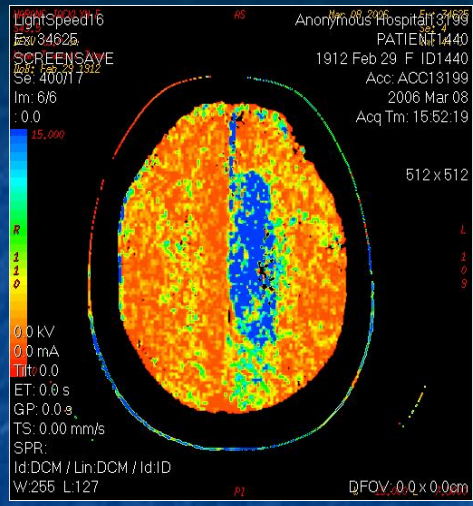
CT Perfusion

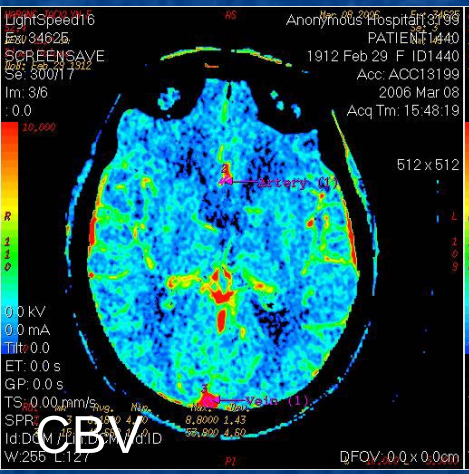


MTT

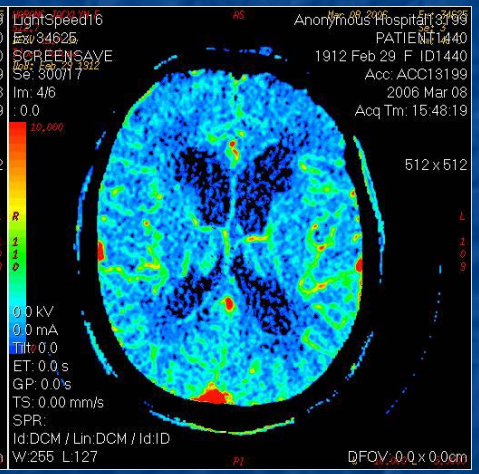


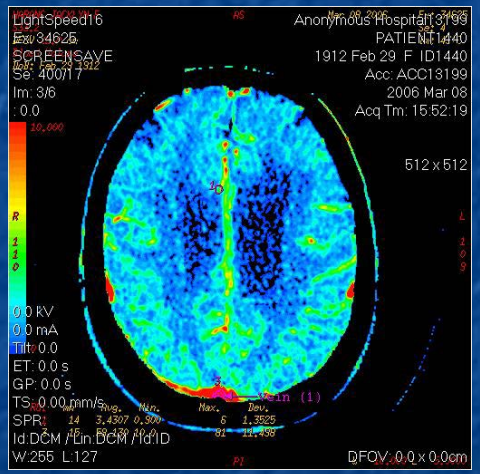


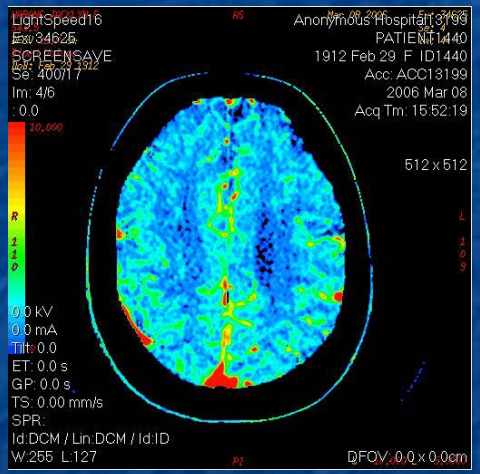




CBV

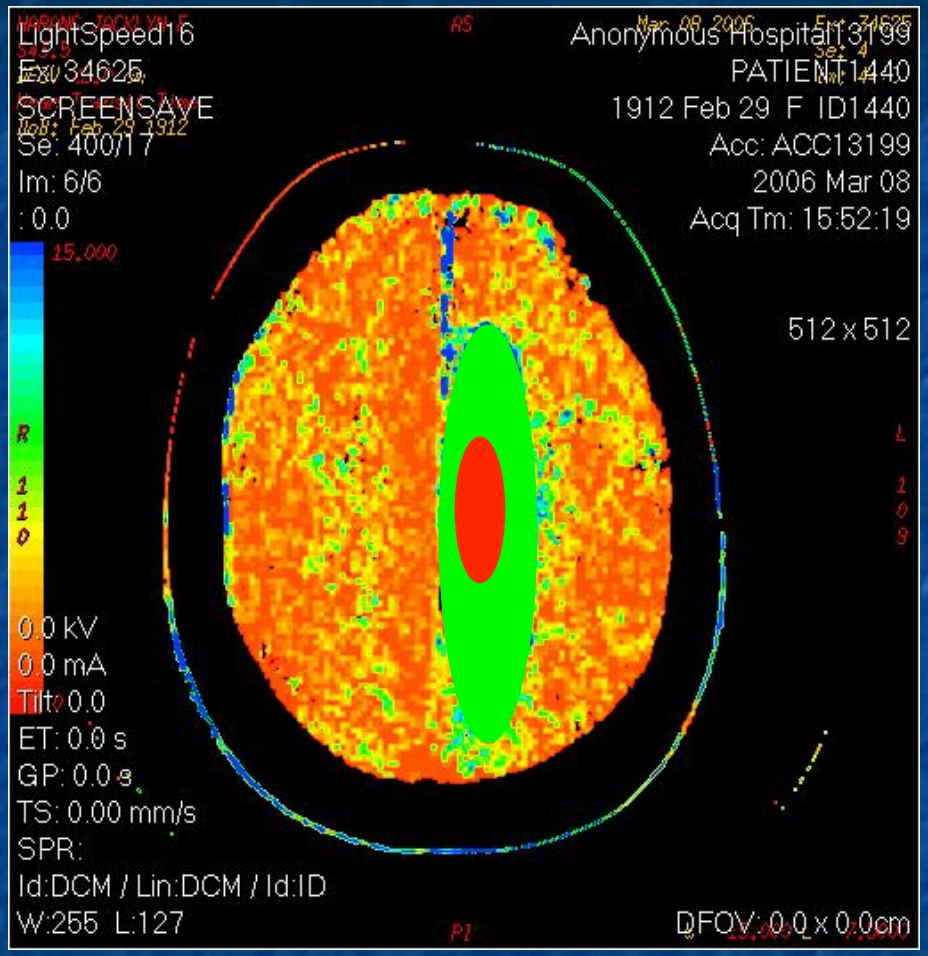




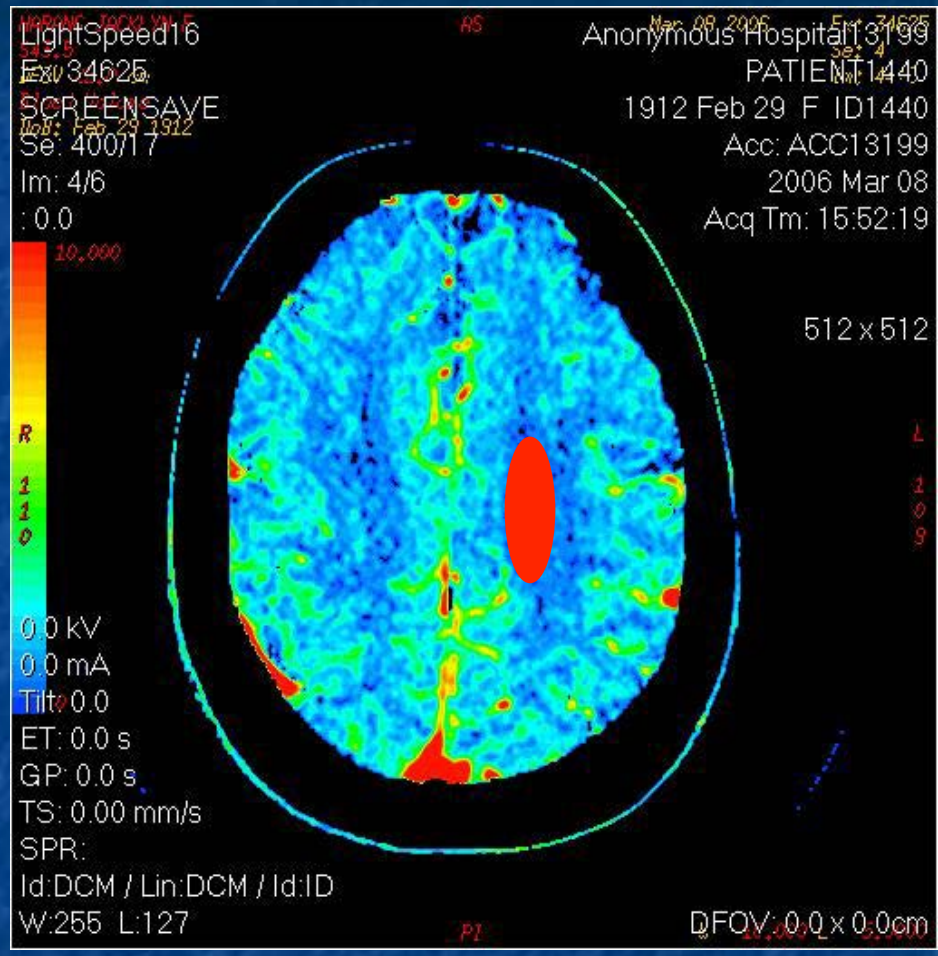


Neurovascular and Spine
Associates

The Ischemic Penumbra



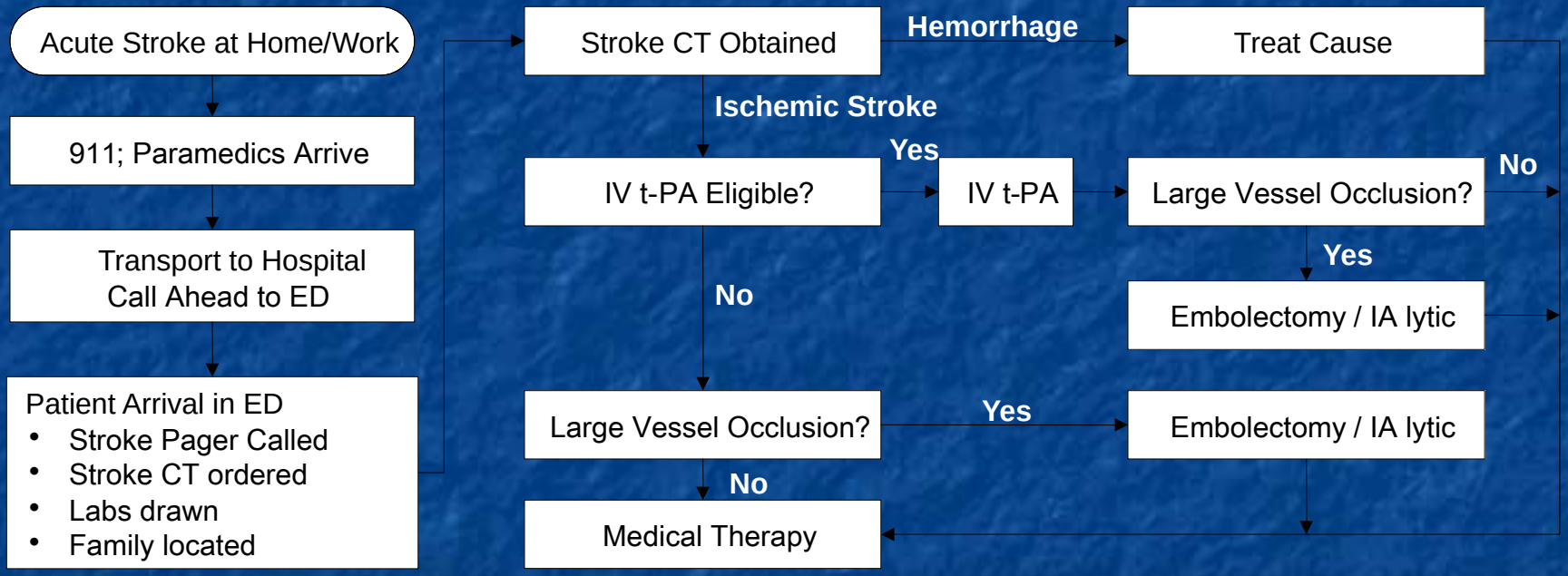
Mean Transit Time



Cerebral Blood Volume

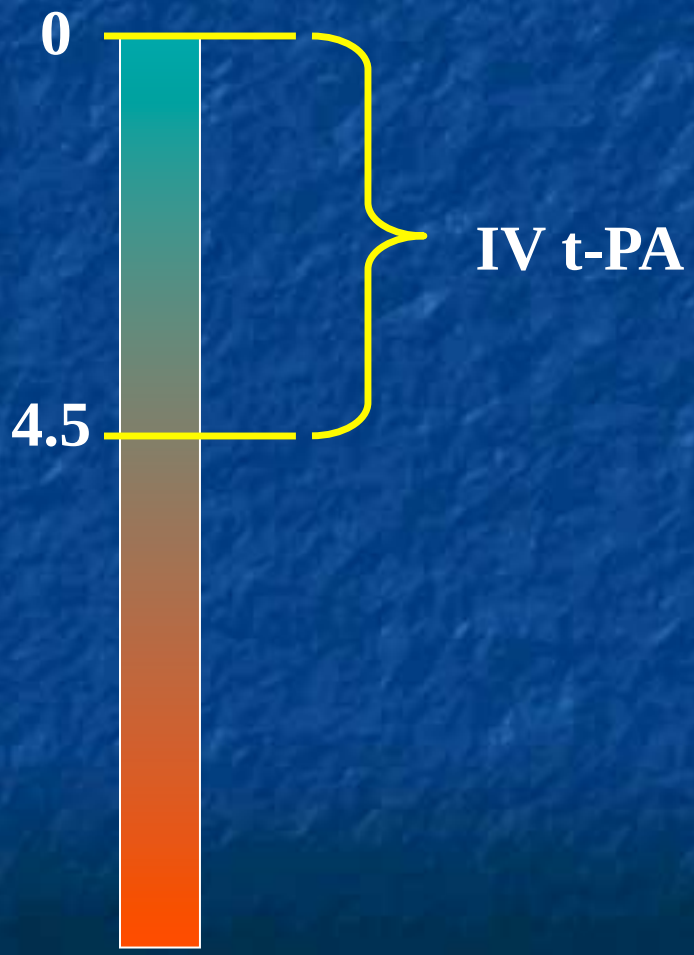
Neurovascular and Spine
Associates

Acute Stroke Protocol



Stroke CT = noncon CT, CTA (chest through brain), CTP, post-contrast CT

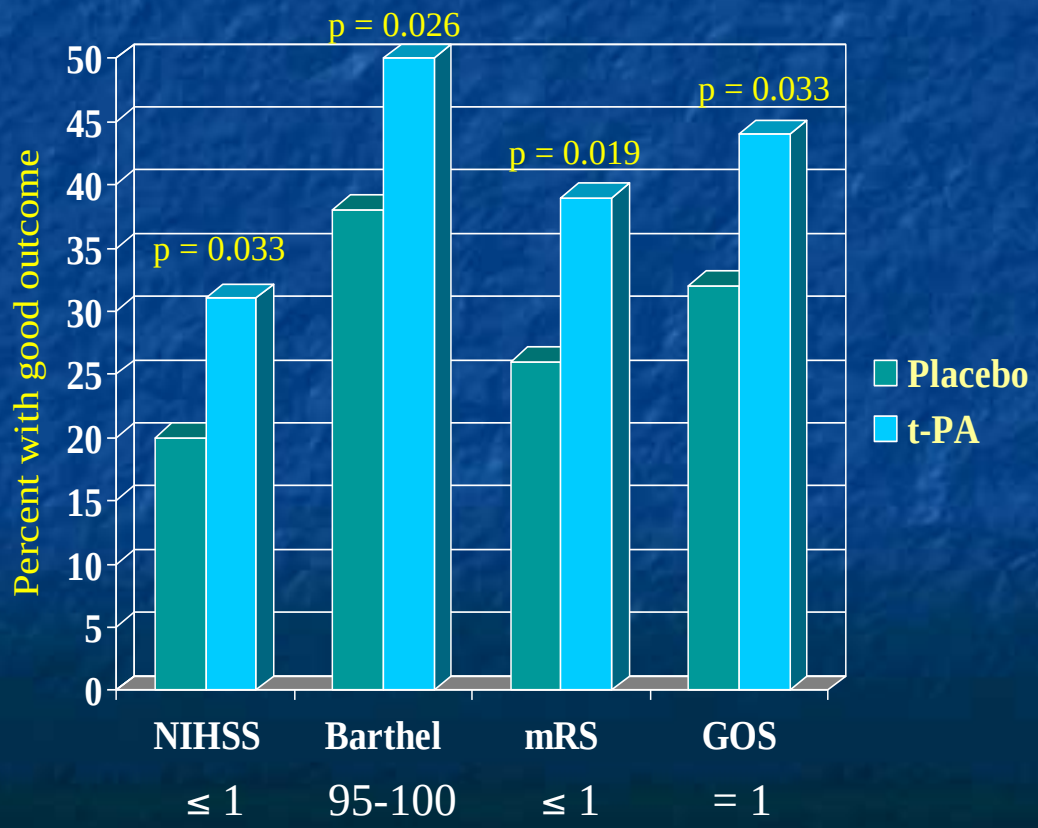
Consider
Thrombolysis
Thrombectomy



Time from stroke symptom onset (hr)

NINDS t-PA Ischemic Stroke

- Intravenous t-PA -vs- placebo (N=312 each group)
  - 0.9 mg/kg t-PA IV (10% bolus, 1 hr infusion)
- within 90-180 mins of symptom onset
- CT exclude hemorrhage

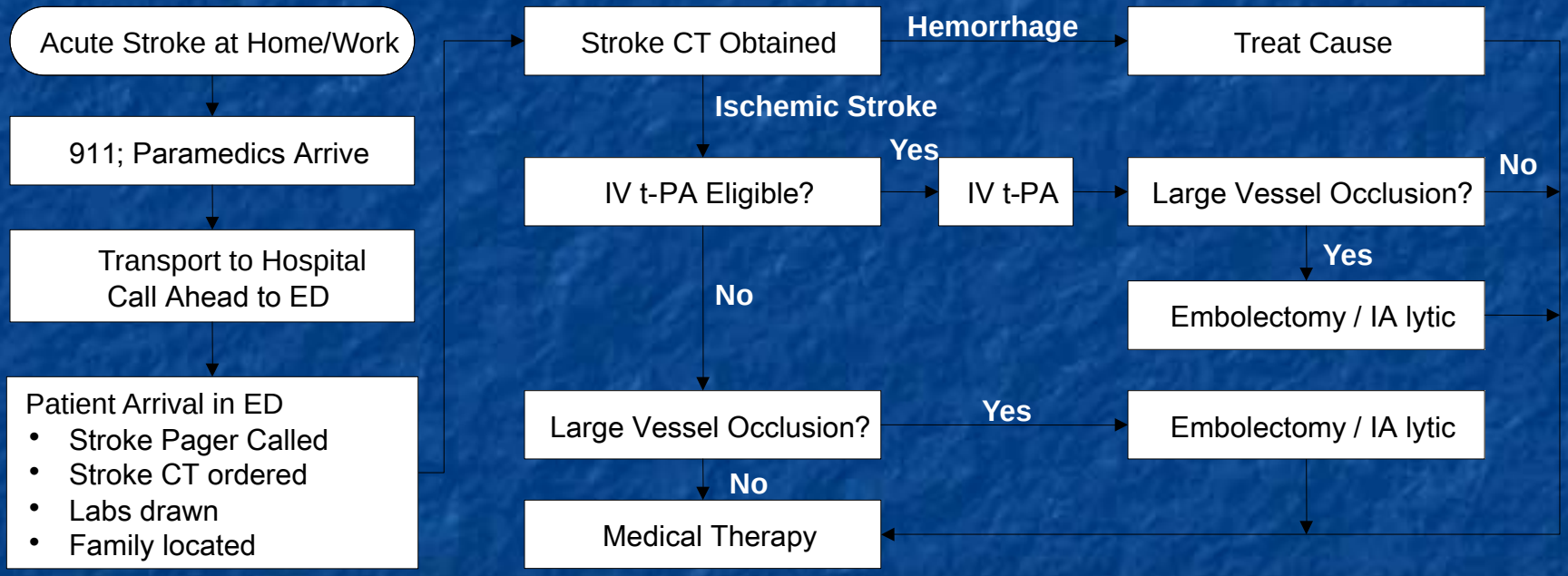


- symptomatic intracranial hemorrhage
  6% -vs- 0.6% (t-PA -vs- placebo)
- 3% hemorrhage-related death

Clinical benefit seen in both large vessel and small vessel stroke syndromes.

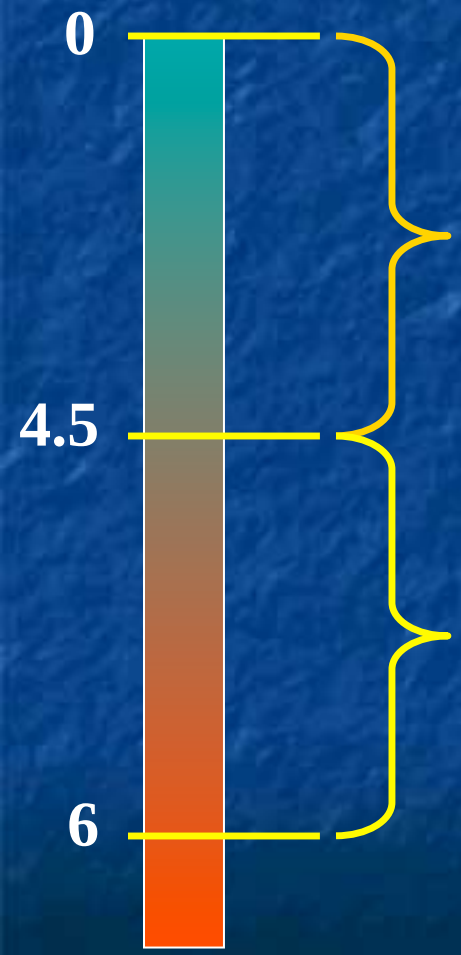
NEJM 333:1581 (1995)

Acute Stroke Protocol



Stroke CT = noncon CT, CTA (chest through brain), CTP, post-contrast CT

Consider
Thrombolysis
Thrombectomy

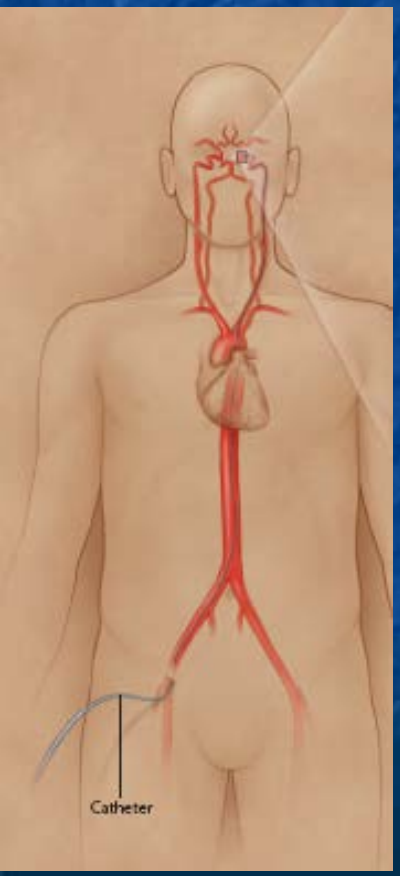


Small and large vessel ischemic strokes.

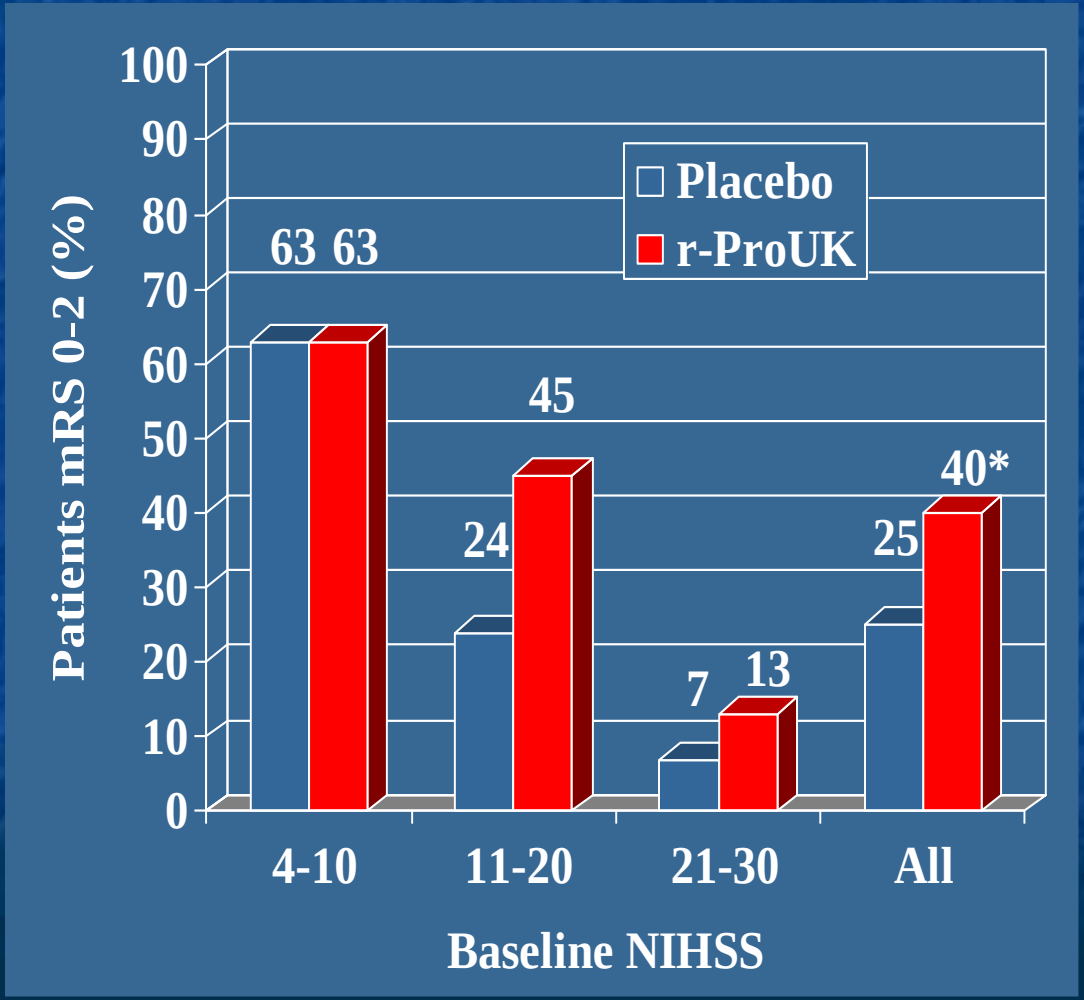
Time from stroke symptom onset (hr)

Intraarterial Thrombolysis – PROACT Trial

180 pts with acute MCA stroke presenting within 3-6 hours randomized 2:1 to IA pro-urokinase or placebo; primary outcome mRS at 90 days



PROACT-II: mRS ≤ 2

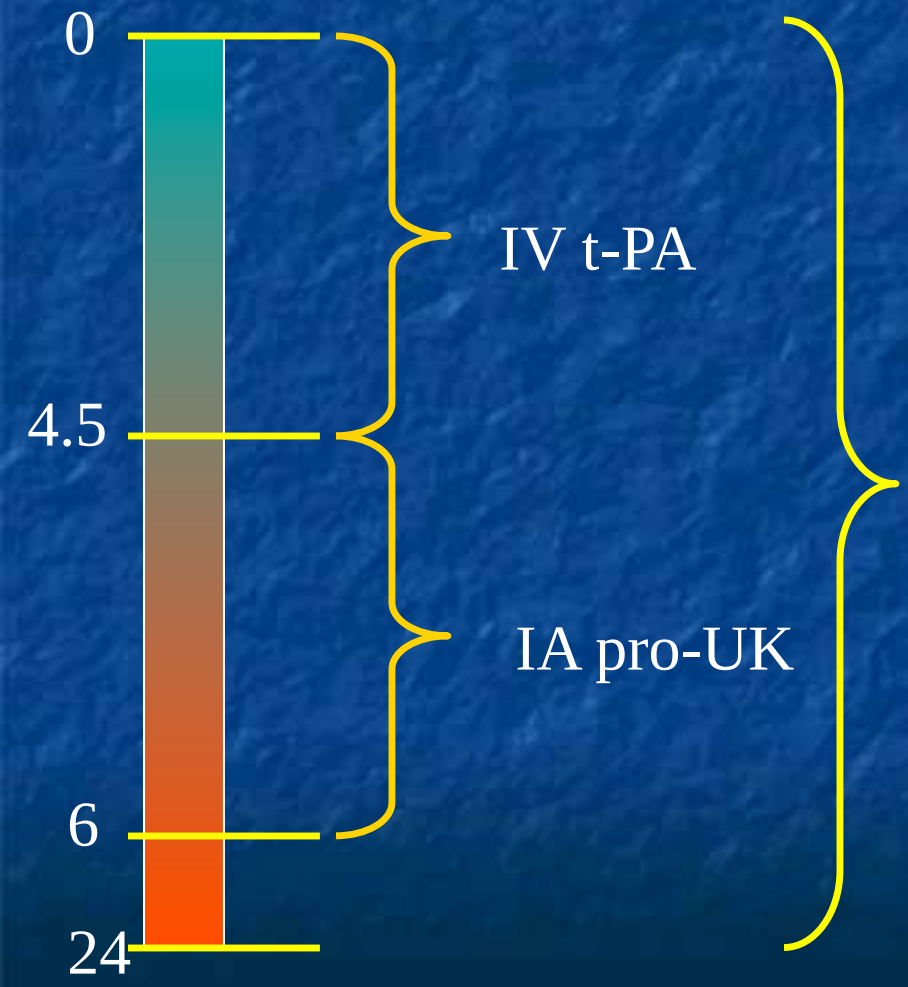


* OR 2.13 (1.02-4.42), p=0.043

PROACT-II: Conclusions

- IA r-ProUK for M1 or M2 occlusions, given under 6 hours, provides 60% relative benefit and 15% absolute benefit (mRS ≤ 2)
- Symptomatic intracranial hemorrhage risk increased (10% IA lytic, 2% control)
- No change in mortality
- MCA recanalization rate 67% (vs. 18% in placebo and ~25-30% with IV tPA alone)
- Natural history of M1/M2 occlusions: 75% disability at 90 days

Consider
Thrombolysis
Thrombectomy



Small and large vessel ischemic strokes.

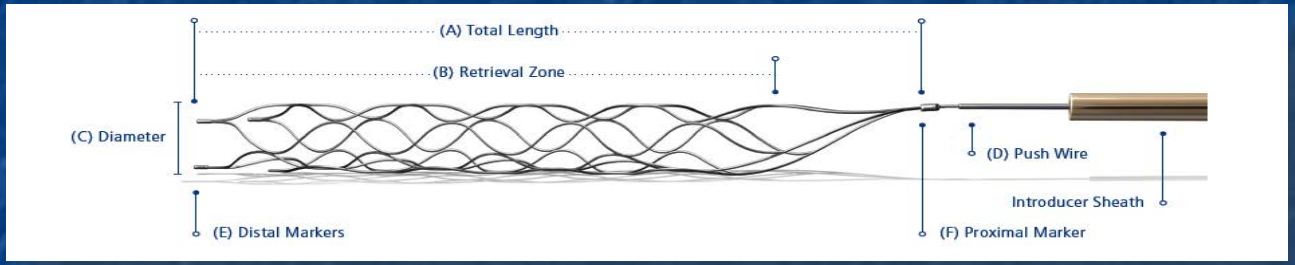
Large vessel ischemic strokes.

Neurovascular and Spine
Associates

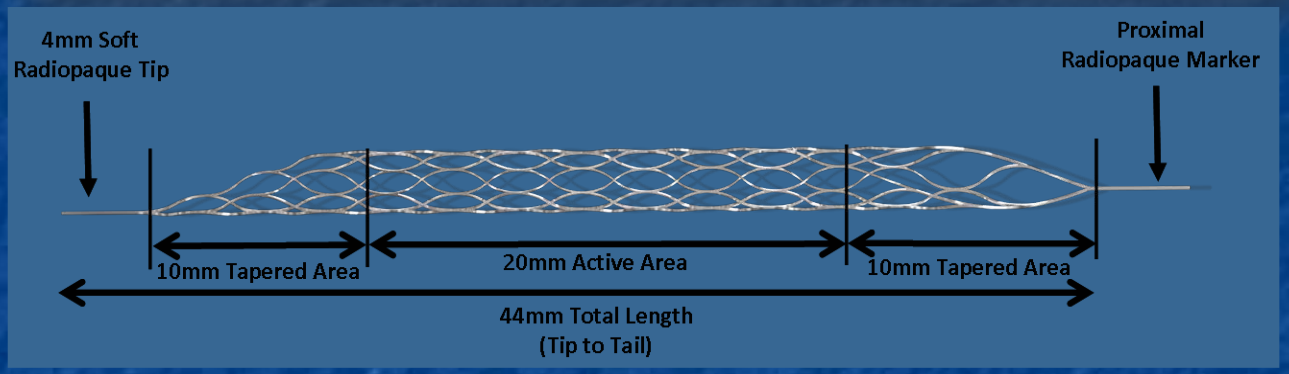
“Stent-retriever”: Self-Expanding Non-Detachable Stent

Newer Technologies = Better Recanalization

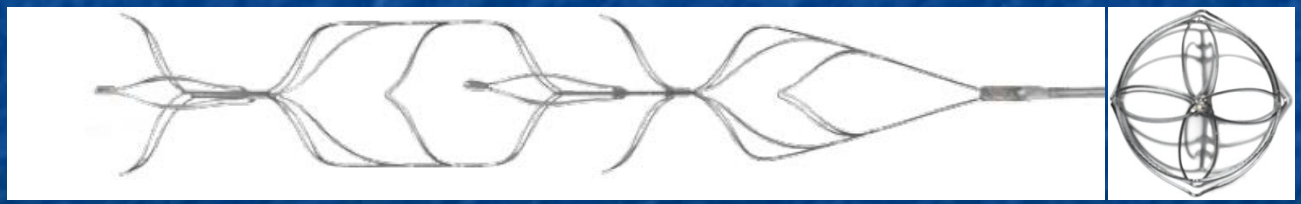
Solitaire FR



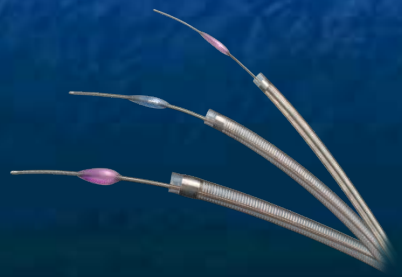
Trevo



Separator 3-D



Penumbra
Max System



	MR CLEAN	ESCAPE	EXTEND-IA	SWIFT PRIME
N	500 patients - 233 IAT - 267 Control	316 - 165 IAT - 150 Control	70 - 35 IAT - 35 Control	196
Device Usage	Open Label - Mostly stent retrievers	Open Label - 86% Stent Retrievers	Solitaire (provided free by Covidien)	Solitaire
Enrollment Time Window	6 hrs from symptom onset	12 hrs from symptom onset	4.5 hrs from symptom onset	6 hrs from symptom onset
Key Selection Criteria	- CTA LVO	- CTA LVO - ASPECTS ≥ 6 - Moderate/ Good Collaterals	- CTA LVO - Mismatch with ischemic core < 70 ml on CTP	- CTA LVO - ASPECTS ≥ 6
Baseline NIHSS	- 17 IAT - 18 Control	- 16 IAT - 17 Control	- 17 IAT - 13 Control	17 both IAT and Control
Median ASPECTS	9 both IAT and Control	9 both IAT and Control	Not applicable	9 both IAT and Control

	MR CLEAN	ESCAPE	EXTEND-IA	SWIFT PRIME
mRS ≤ 2 @ 90 Days	IAT: 32.6% Control: 19.1%	IAT: 53% Control: 29.3% NNT: 4	IAT: 71% Control: 40%	IAT: 61.1% Control: 35.5%
Revas Rate of IAT	58.7% TICI 2b/3	72.4% TICI 2b/3	86% TICI 2b/3	88% TICI 2b/3
Mortality at 90 Days	IAT: 21% Control: 22%	IAT: 10% Control: 19%	IAT: 9% Control: 20%	IAT: 12.2% Control: 25.8%
sICH	IAT: 7.7% Control: 6.4%	IAT: 3.6% Control: 2.7%	IAT: 0% Control: 6%	IAT: 1.0% Control: 3.1%

SWIFT-PRIME

- Multicenter International Randomized Control Trial comparing Solitaire + IV tPA vs. IV tPA alone in patients with large vessel occlusion.

- St. Jude Medical Center was one of only 2 sites in Southern California that was invited to participate in this study.

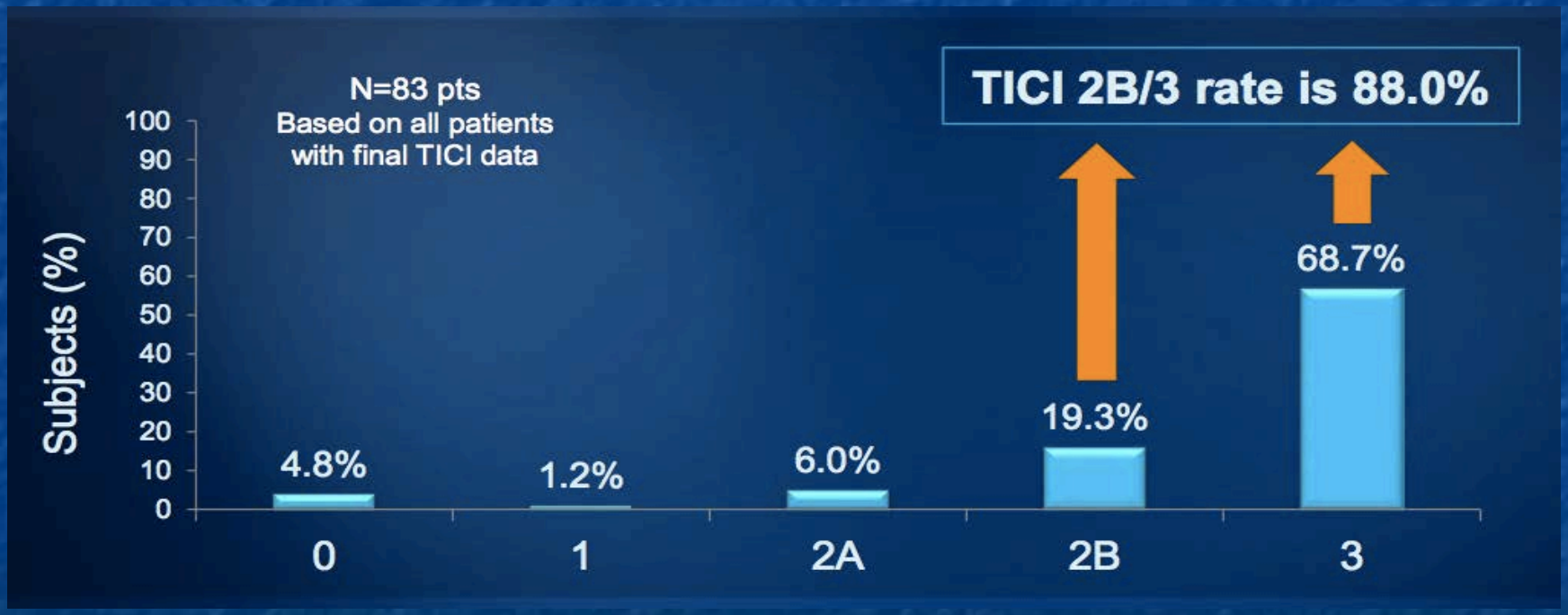
SWIFT PRIME

Key Inclusion Criteria

- Age 18 – 80
- Pre-stroke Modified Rankin Score ≤ 1
- NIHSS 8 – 29 at randomization
- Received IV t-PA within 4.5 hours of stroke onset
- CTA or MRA confirmation of large vessel occlusion (intracranial ICA, M1 or carotid terminus)
- Groin puncture within 6 hours of stroke onset and within 90 minutes* of qualifying imaging

*optimal target: within 70 mins

SPRIME: Reperfusion



SPRIME: Primary endpoint

Functional independence (mRS 0-2) at 90 days	
Solitaire + IV t-PA	59 (60.2%)
IV t-PA	33 (35.5%)

Endovascular Acute Stroke Therapies

- Intra-arterial Thrombolytics (out to ~ 6 hours)
- Mechanical Clot Disruption (out to ~ 24 hours)
  - Retrieval device (e.g., Merci)
  - Suction catheter (e.g., Penumbra)
  - Stent retrieval (e.g., Solitaire, Trevo)
  - Balloon angioplasty and/or stent
  - Clot maceration (microcatheter, microwire)
  - Ultrasound

Acute Stroke – Case 1

30 year old man with neck injury playing tag football

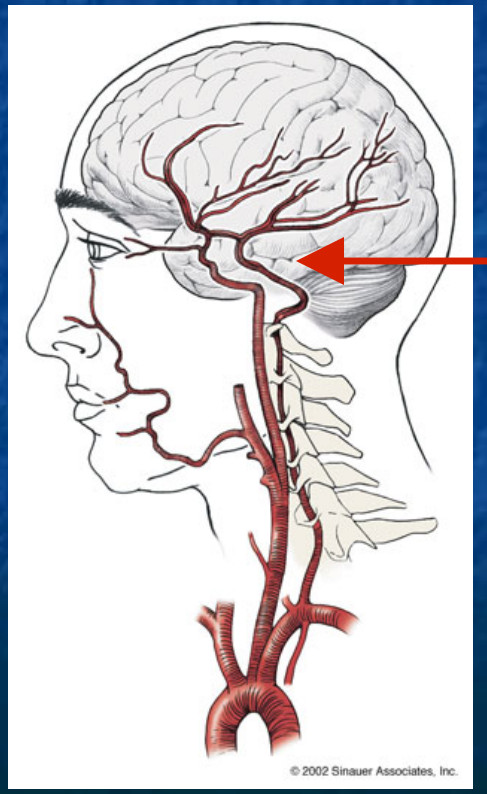
abrupt onset slurred speech and double vision - ? concussion

right arm and leg weakness, tired/sleepy

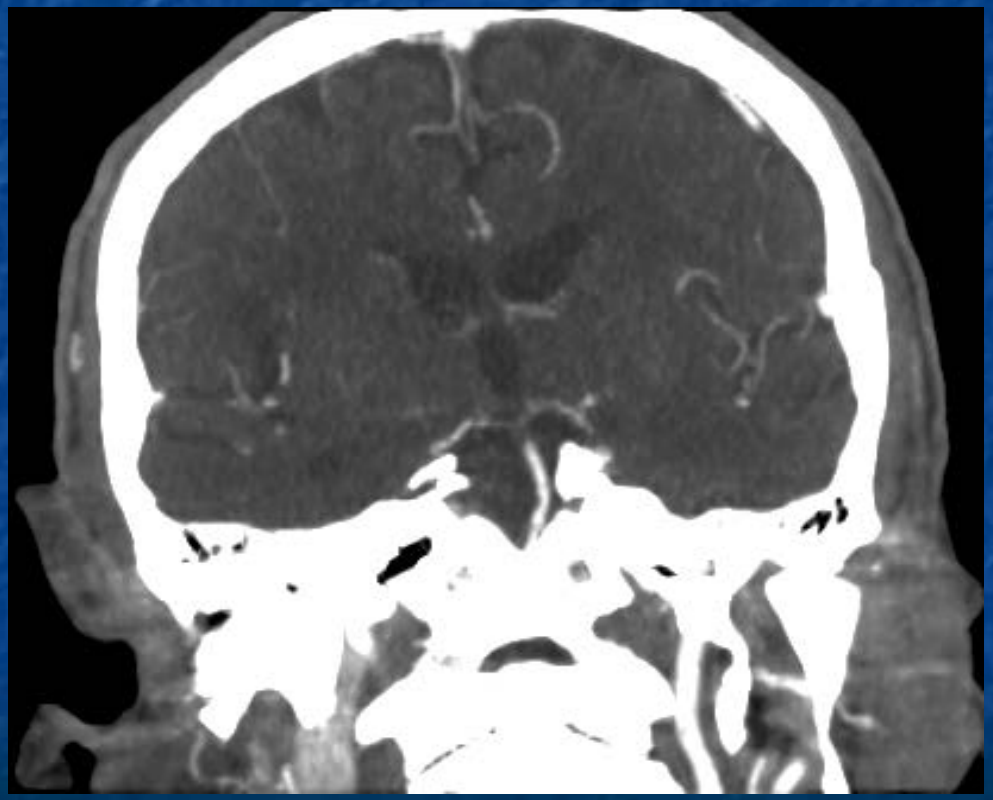
found sleepy but arousable, slurred speech, R lower facial weakness, not moving R arm or leg. Time from onset – 3.5 hours.

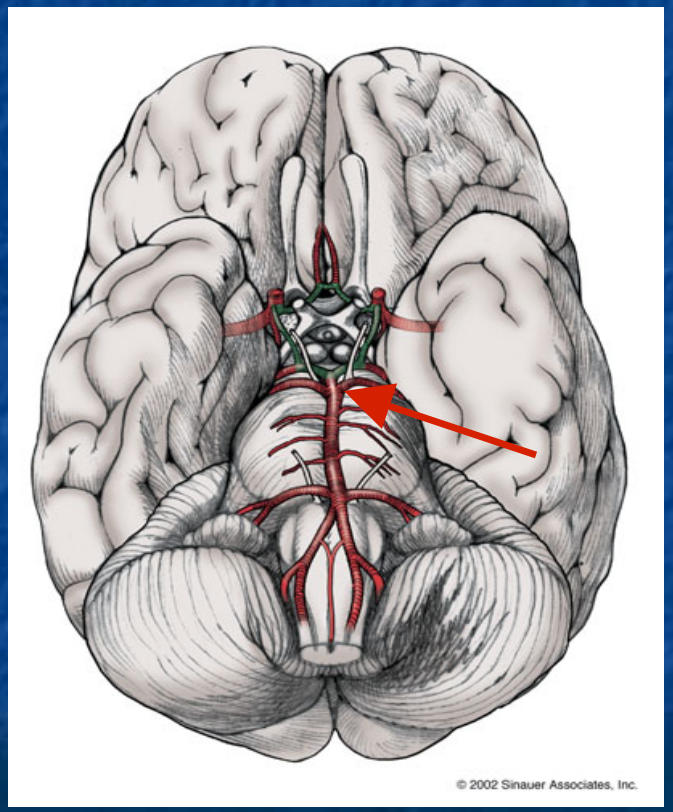
Acute Stroke – Case 1

Taken to St. Jude Medical Center.
Neuro evaluation, non-contrast CT brain



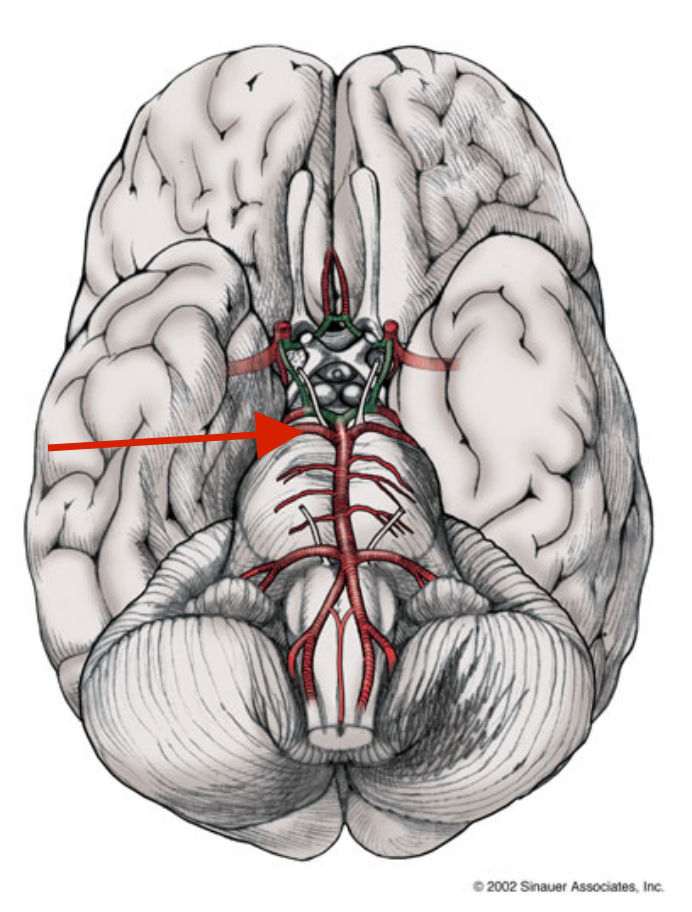
CT Angiography





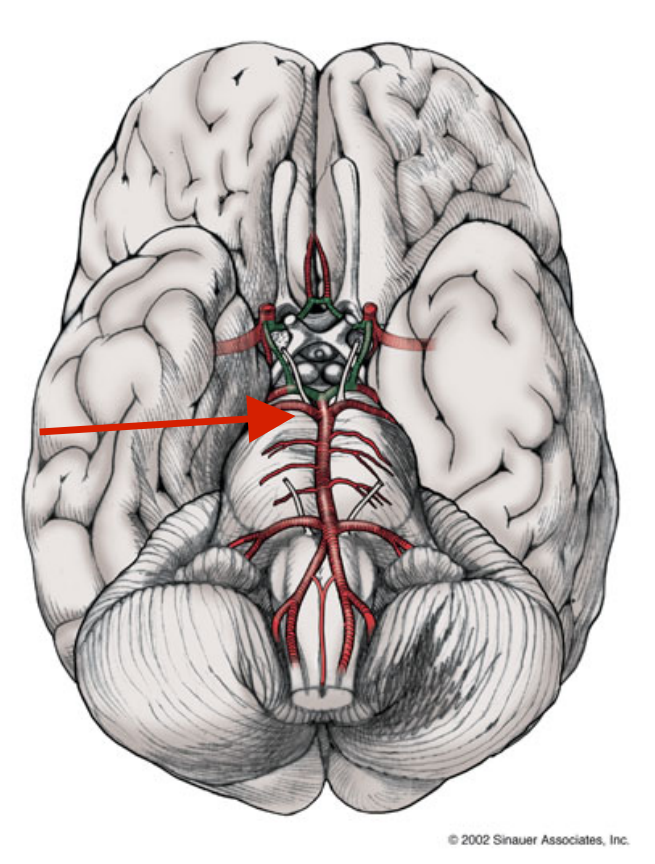
Neurovascular and Spine Associates

Initial Cerebral Angiography



Neurovascular and Spine Associates

Merci® Endovascular Thrombectomy



Neurovascular and Spine Associates

Merci® Endovascular Retrieval System

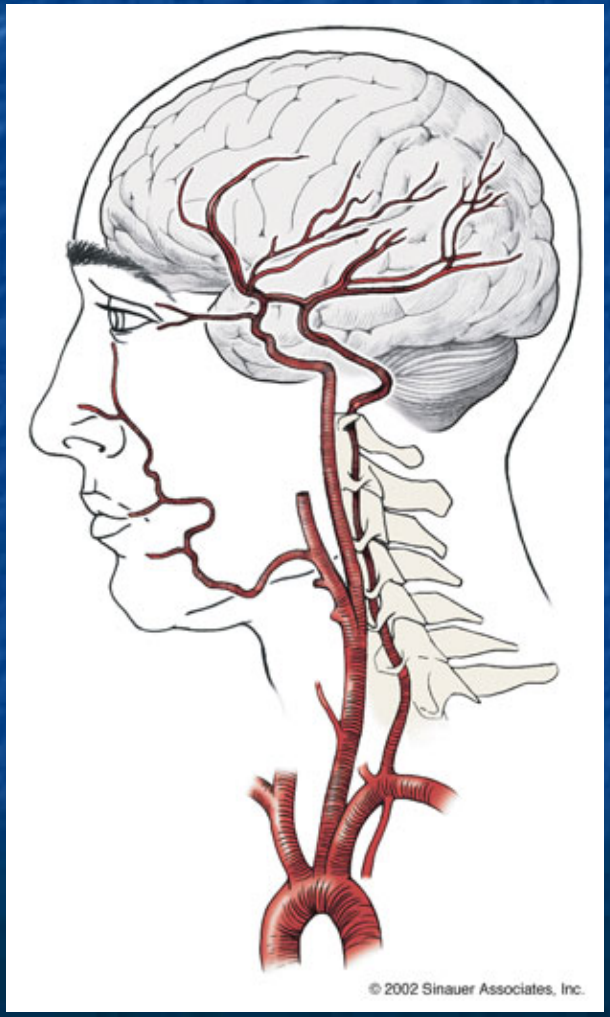
Pre-thrombectomy

Post-thrombectomy

Acute Stroke – Case 1

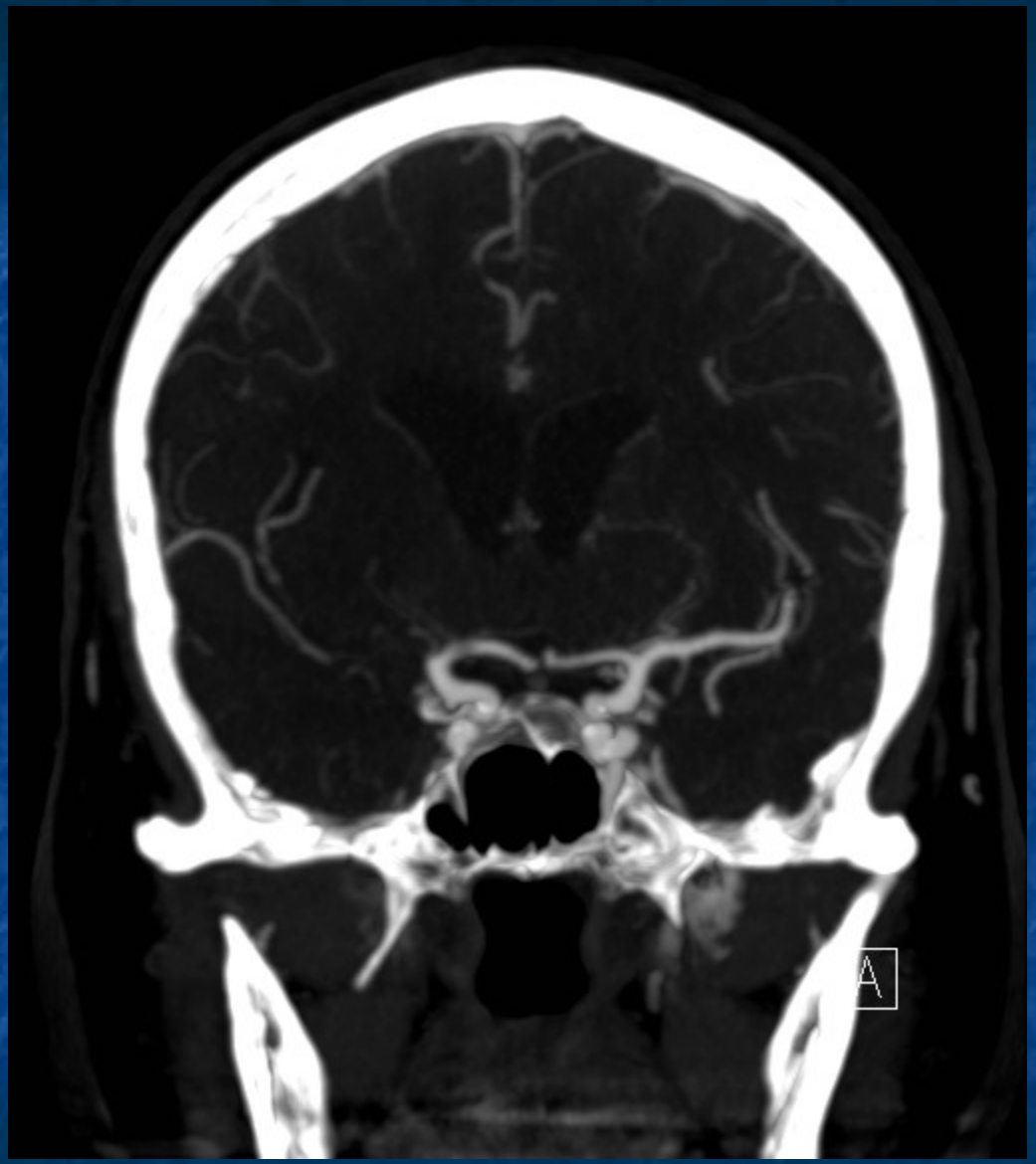
Complete neurologic recovery.

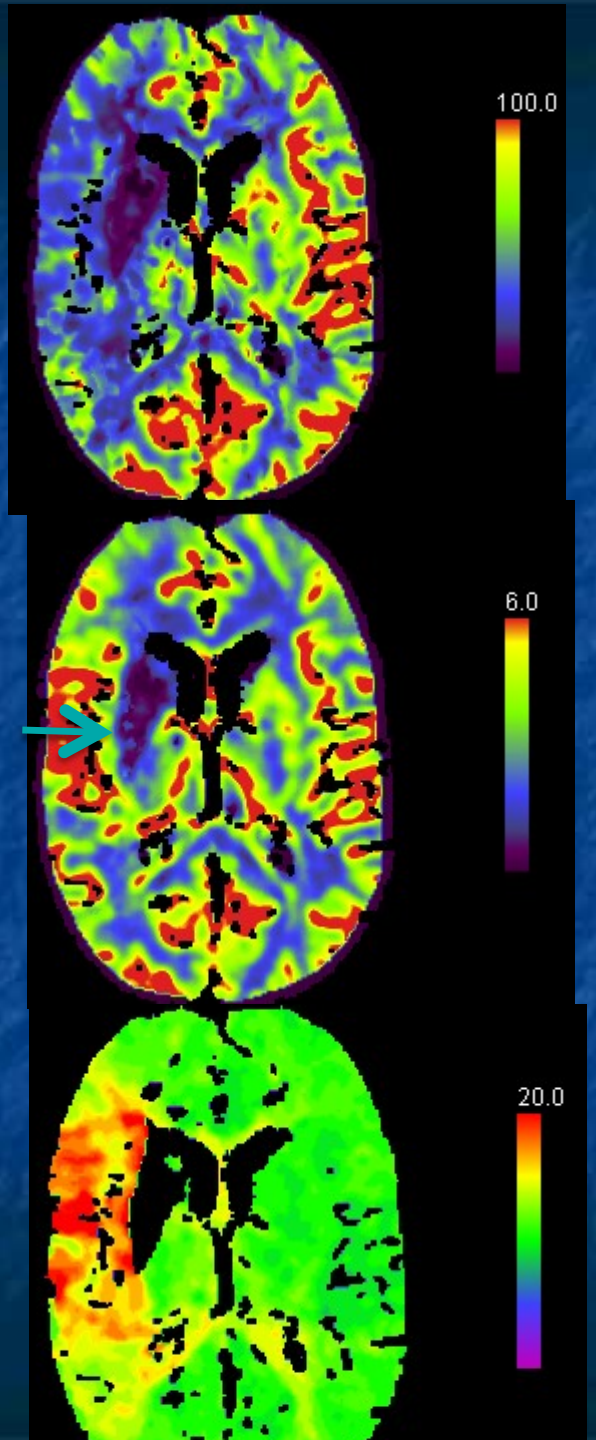
Cause of stroke: dissection of the vertebral artery from neck trauma, complicated by thromboembolism to the basilar tip.

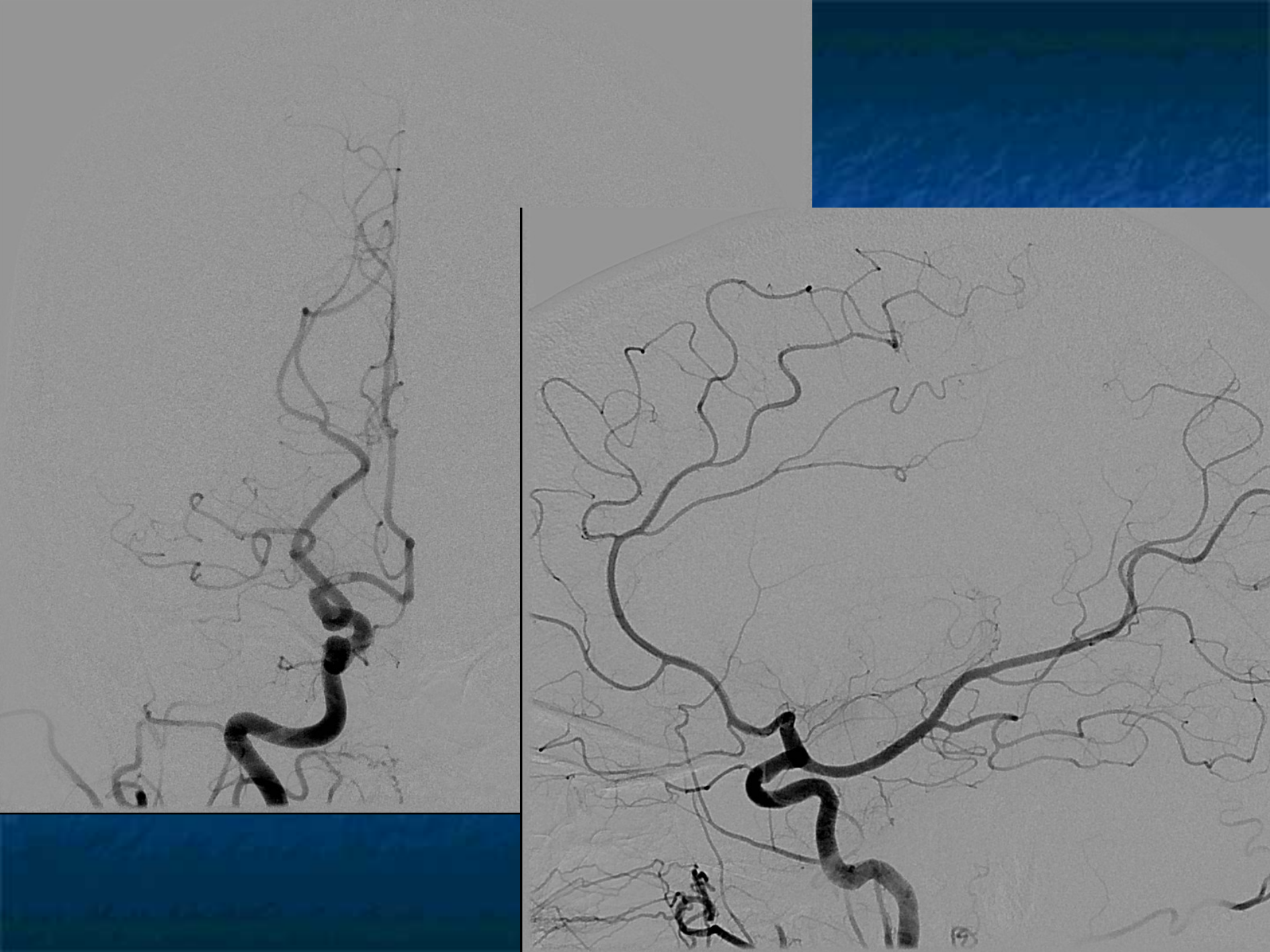


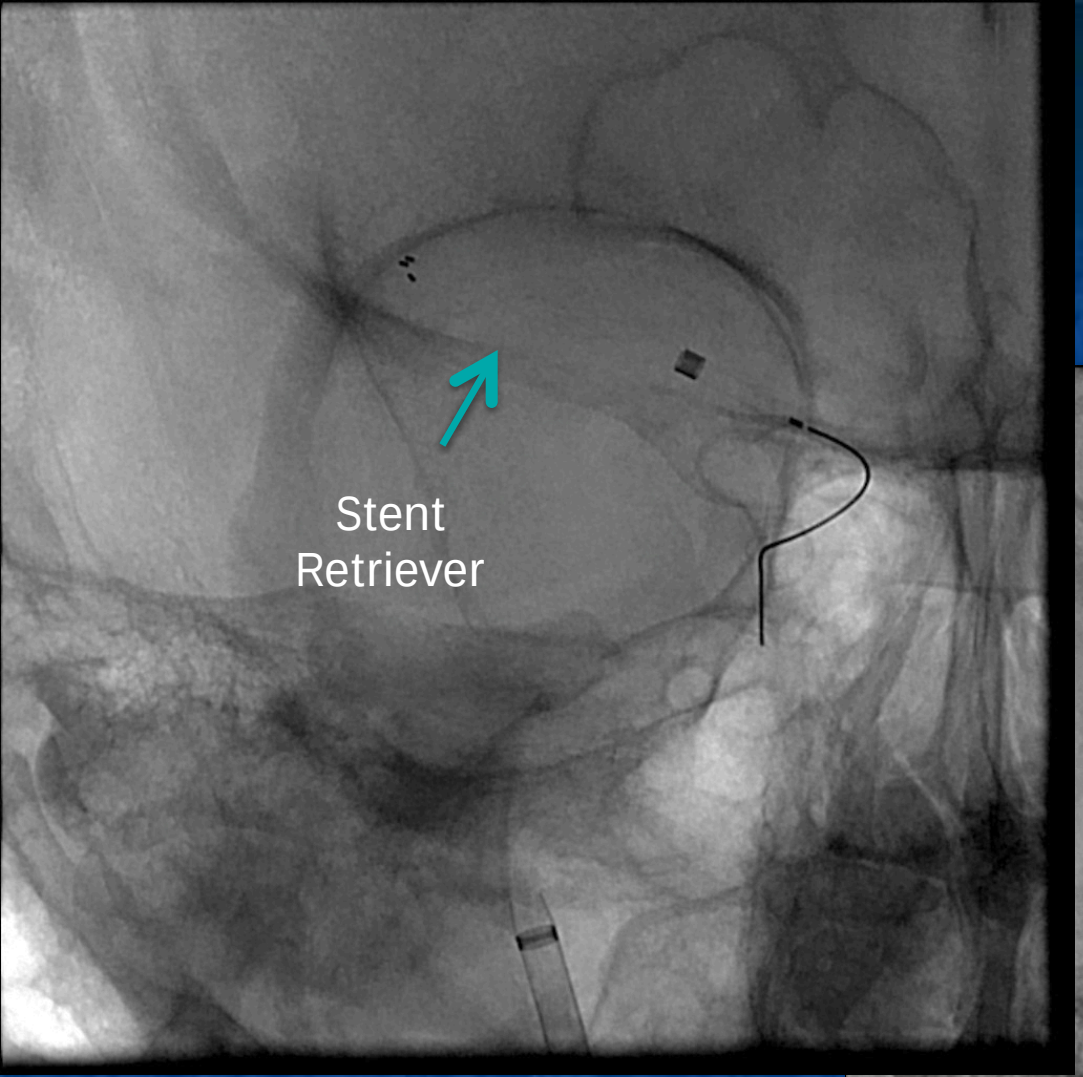
Acute Stroke – Case 2

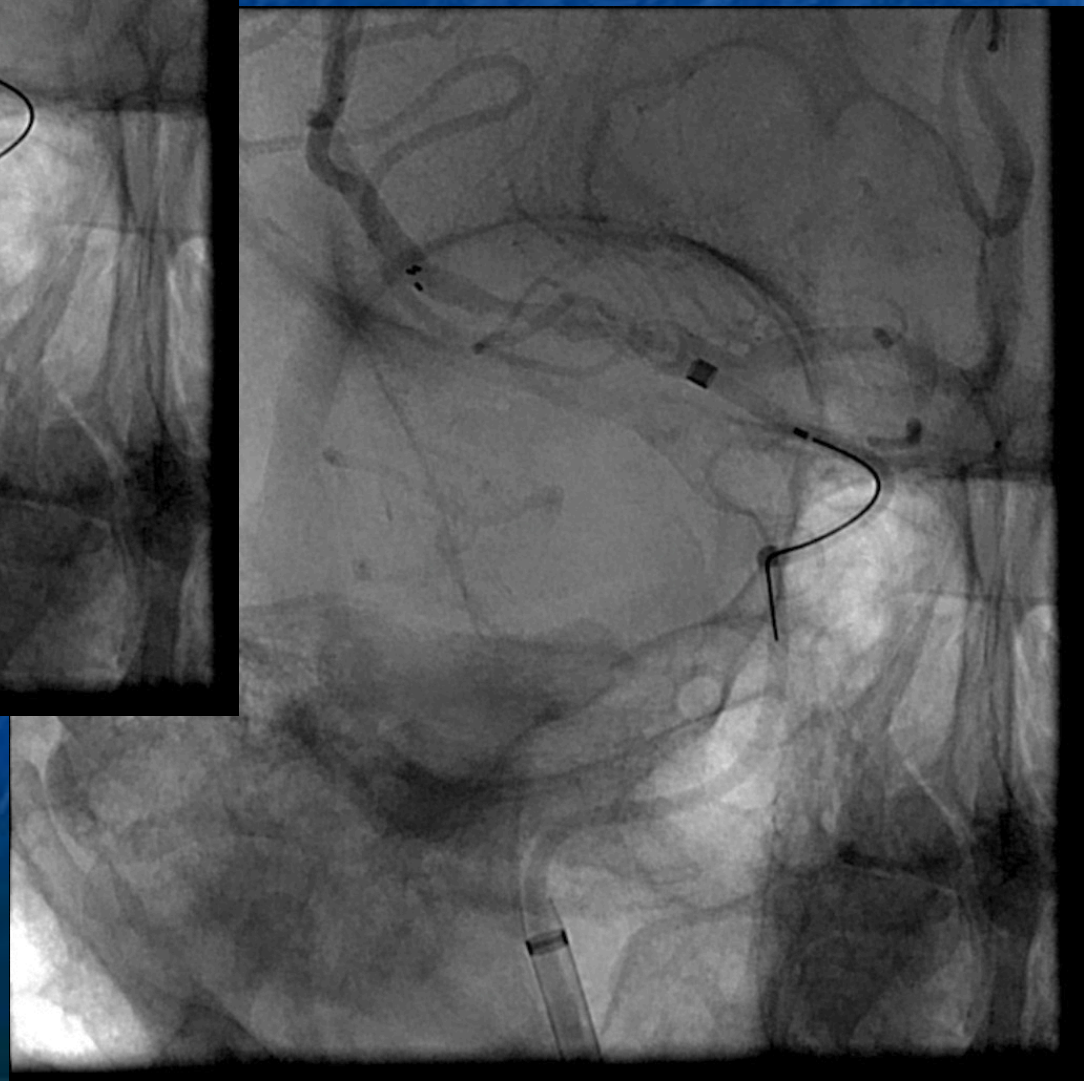
- 72 year old female
- Last known normal at 11 PM last night before going to sleep
- She woke up at 8 AM with left hemiplegia
- CTA/CT Perfusion demonstrates a right MCA occlusion with large penumbra
- NIHSS 12

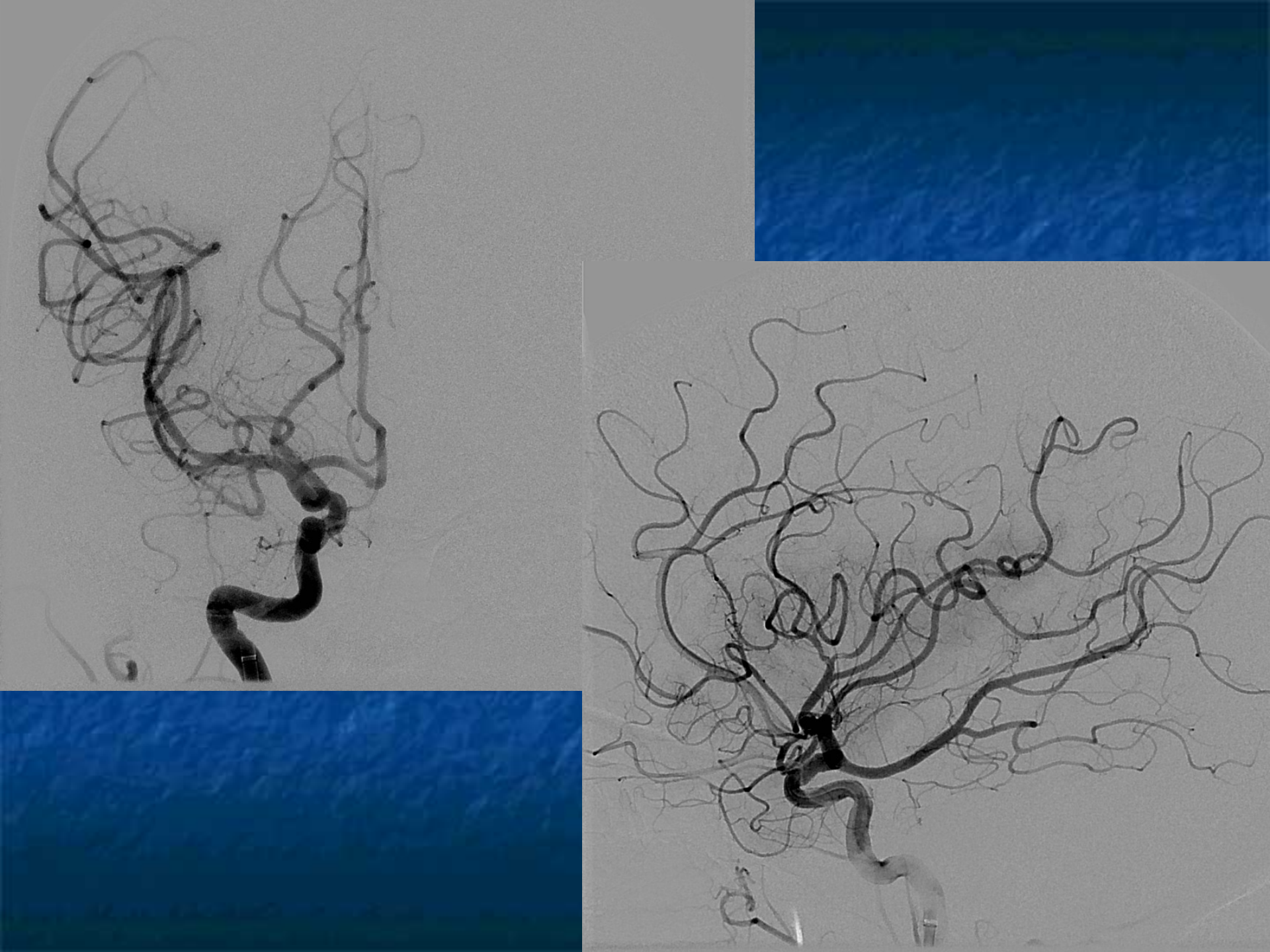



100.0
CBF
6.0
CBV
20.0
TTP

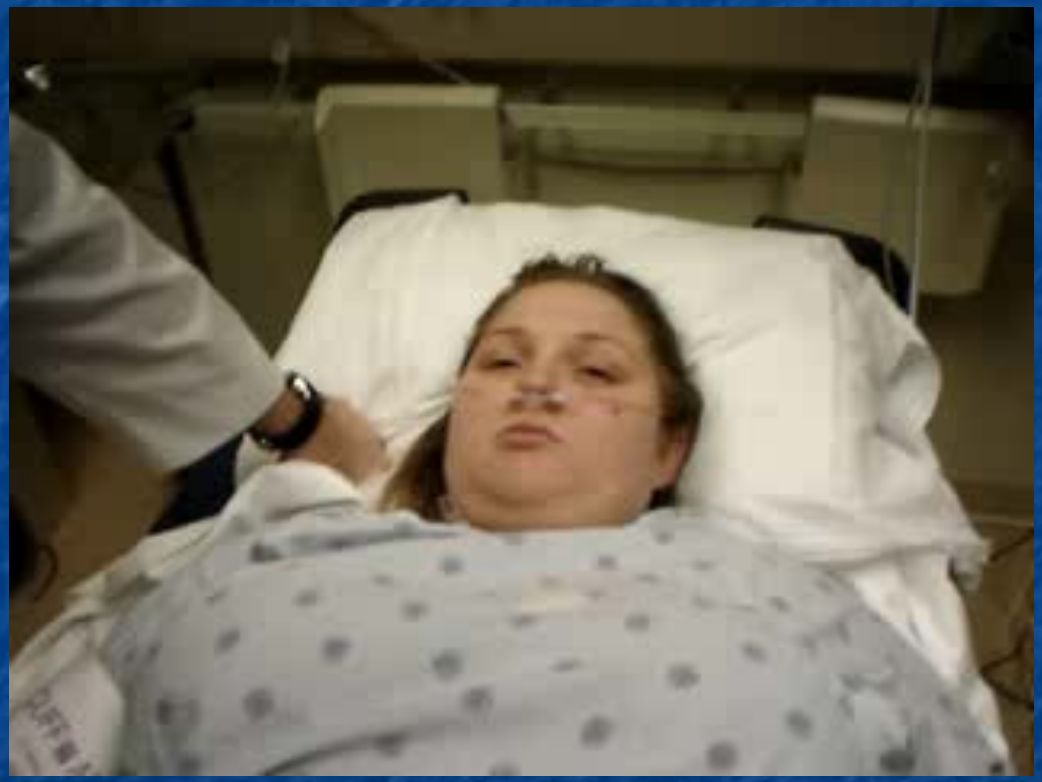



Stent
Retriever



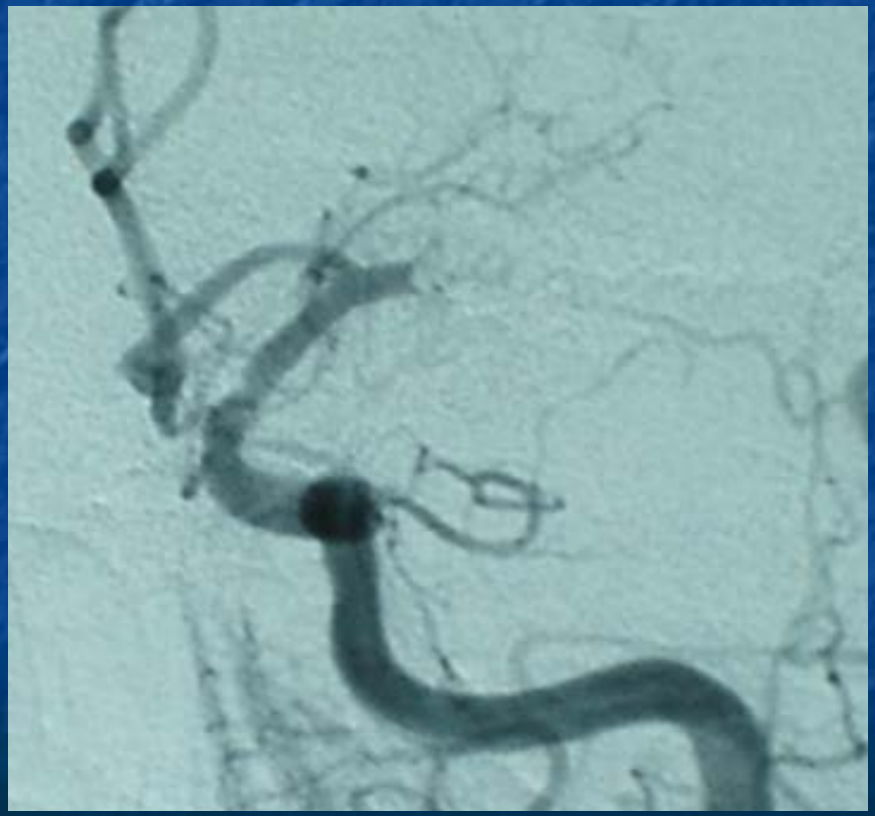


Acute Stroke – Case 3
26 y.o. Female: Left Brain Stroke

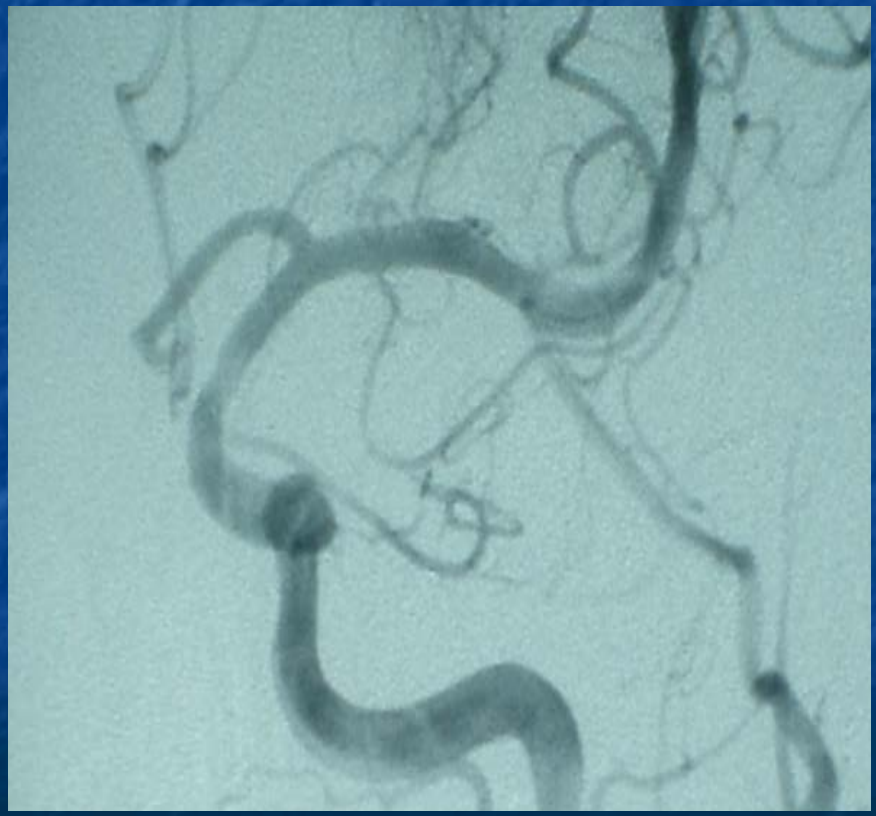


26 yo Female: Left Brain Stroke

Before



After



26 y.o. Female: Left Brain Stroke

Experience with Stent Retrievers

July 2013 – January 2017:

- 161 patients treated with a stent retriever device (Solitaire or Trevo®).
- All selected with CT angiography and CT perfusion studies.
- TICI 2B or 3 recanalization in 90%.
- sICH in 2.0% (4/161), in patients treated with IV tPA + IA tPA as well.
- Early to have long-term clinical outcome data, but f/u in first 128 have shown good outcome (mRS 0-2 at 90 days) in 61%.

Conclusion: Endovascular Therapy in Large Vessel Occlusion

- Acute Ischemic Stroke secondary to large vessel occlusion is a potentially devastating disease for which best treatment remains elusive.

- To promote best possible clinical practice, the administration of interventional stroke treatment should remain in the hands of experienced stroke experts who would maximize data collection to achieve the best possible patient outcomes.

Conclusion: Endovascular Therapy in Large Vessel Occlusion

- Better patient outcomes with interventional stroke therapy:
  - Patient selection using advanced imaging
  - Advanced device technology
  - Faster and more complete recanalization
  - Better time management
    - Getting patients to endovascular capable hospitals
    - Moving patients more efficiently from ER door to recanalization

Thank you

Hamedfarid@gmail.com