IN STROKE, EVERY MINUTE COUNTS: WHEN TIME = BRAIN

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Evie Marcolini, MD

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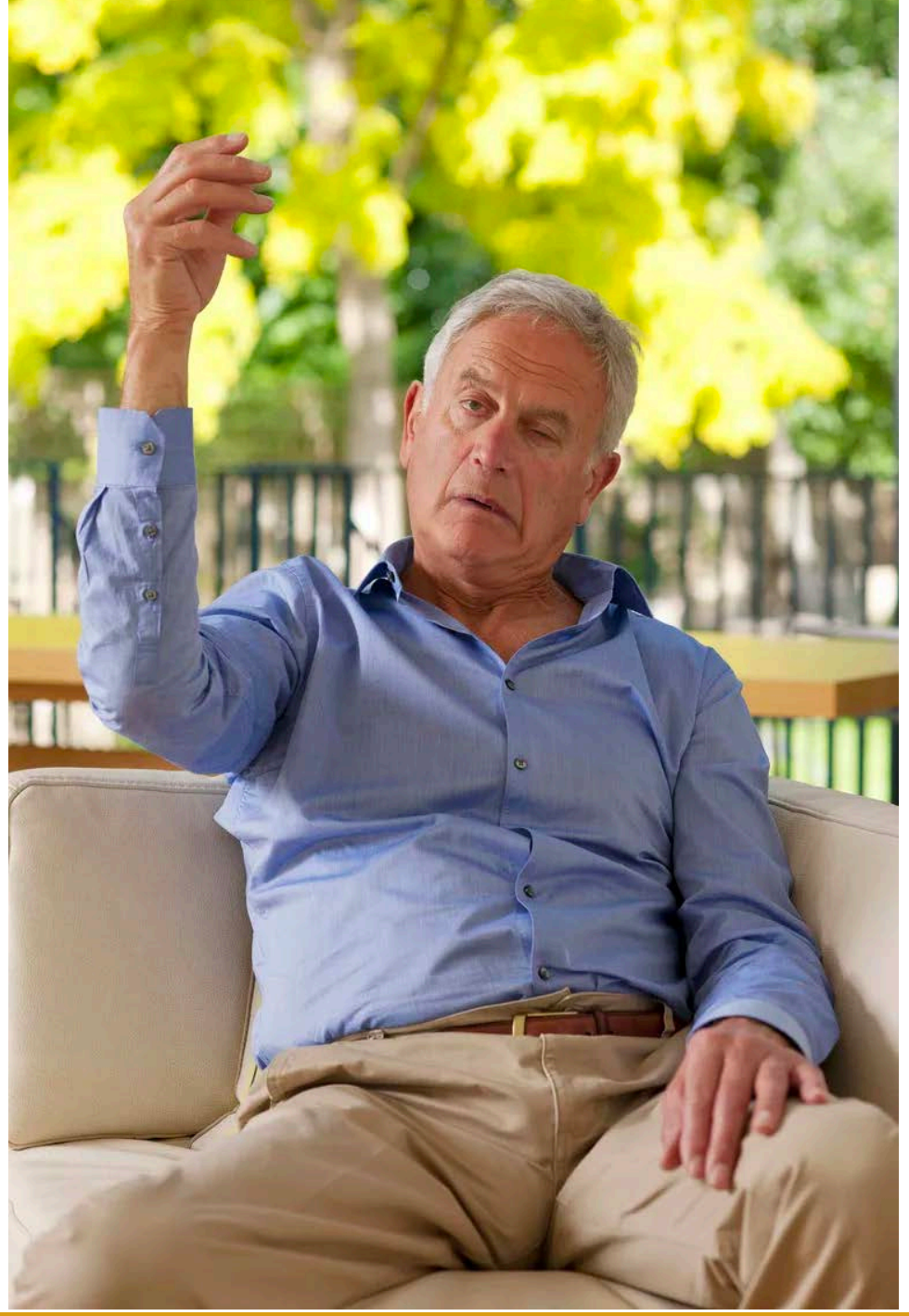


The Impact of Stroke

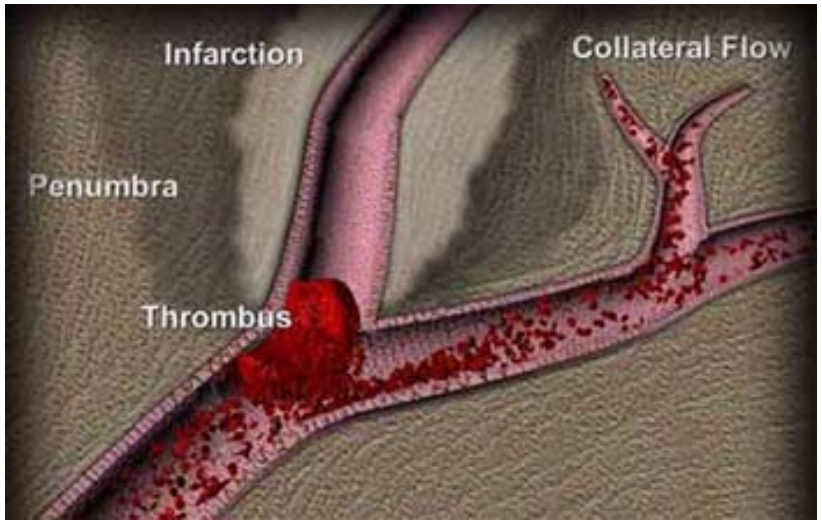
- ~750,000 new strokes diagnosed each year
- Every 45 seconds, someone suffers a stroke
- Every 3 minutes, someone dies from a stroke
- Stroke is the 2nd leading cause of death world-wide
- Stroke is the leading cause of long-term disability

The Impact of Stroke

- ~ 4 million stroke survivors in the US
- Stroke costs an estimated $34 billion/year
- Each year, ~40,000 more women than men have a stroke
- More women than men die from stroke each year

What is a Stroke?

A stroke occurs when blood flow to the brain is interrupted by a blocked or burst blood vessel



Ischemic stroke ~85% of all strokes

Blood vessel in brain blocked by *thrombus* or *embolus*

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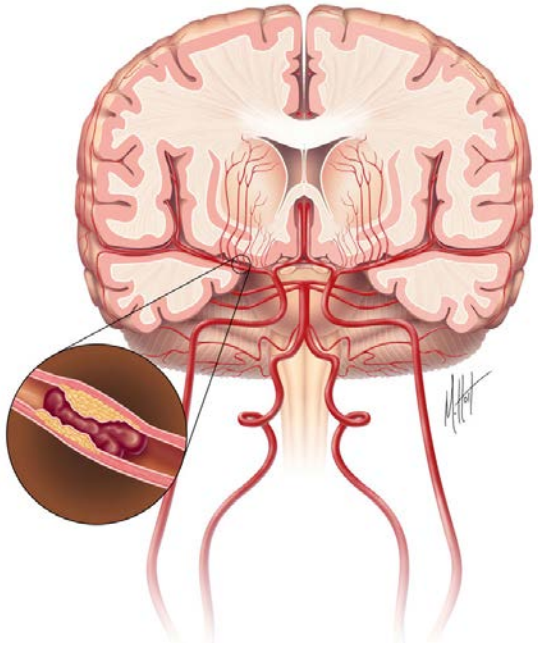

Can be **Large Vessel Occlusion (LVO)** due to atherosclerosis (blockage by fatty deposits) or clot from elsewhere (e.g., heart, atrial fibrillation)

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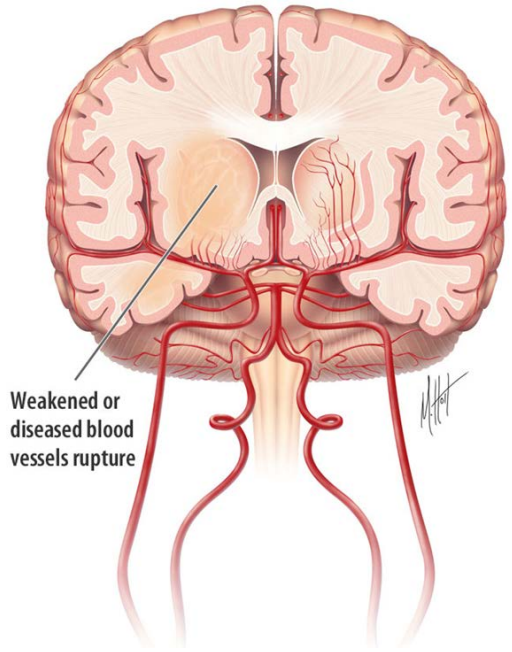
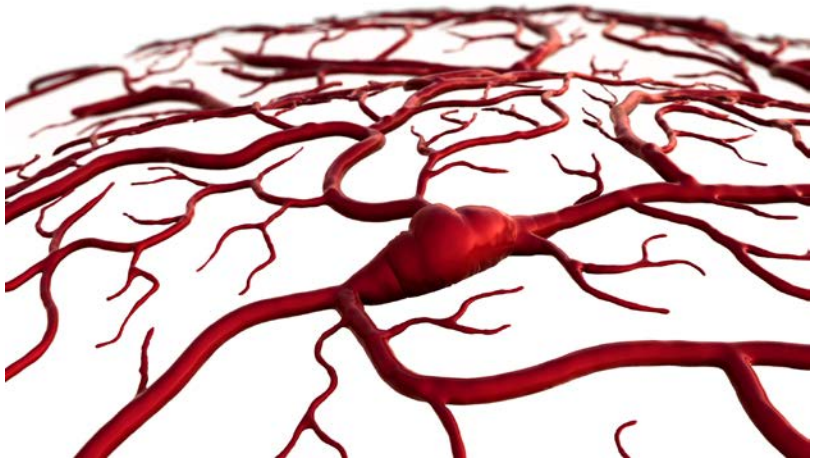


Can be **Small Vessel Disease (SVD)** due small penetrating artery atherosclerosis, degradation, or small emboli (clots)

What is a Stroke?

A stroke occurs when blood flow to the brain is interrupted by a blocked or burst blood vessel



Hemorrhagic stroke ~10% of all strokes

Blood vessel in brain bursts (aneurysm)

What is a Stroke?

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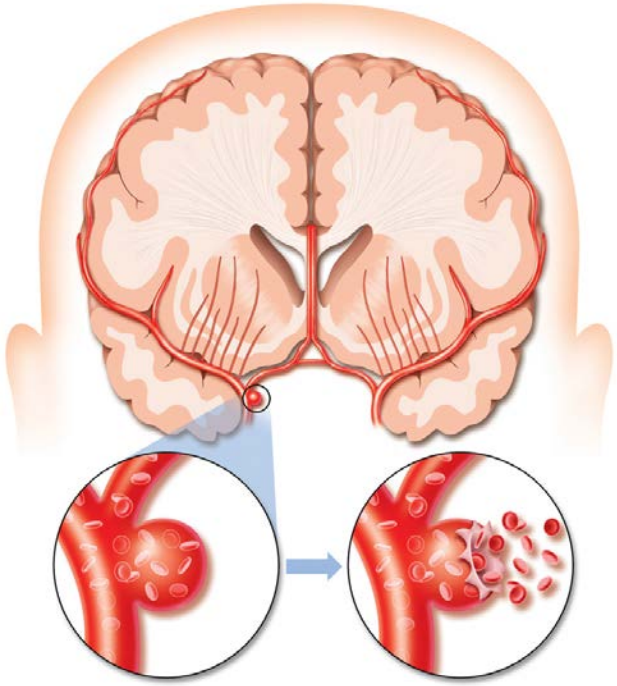


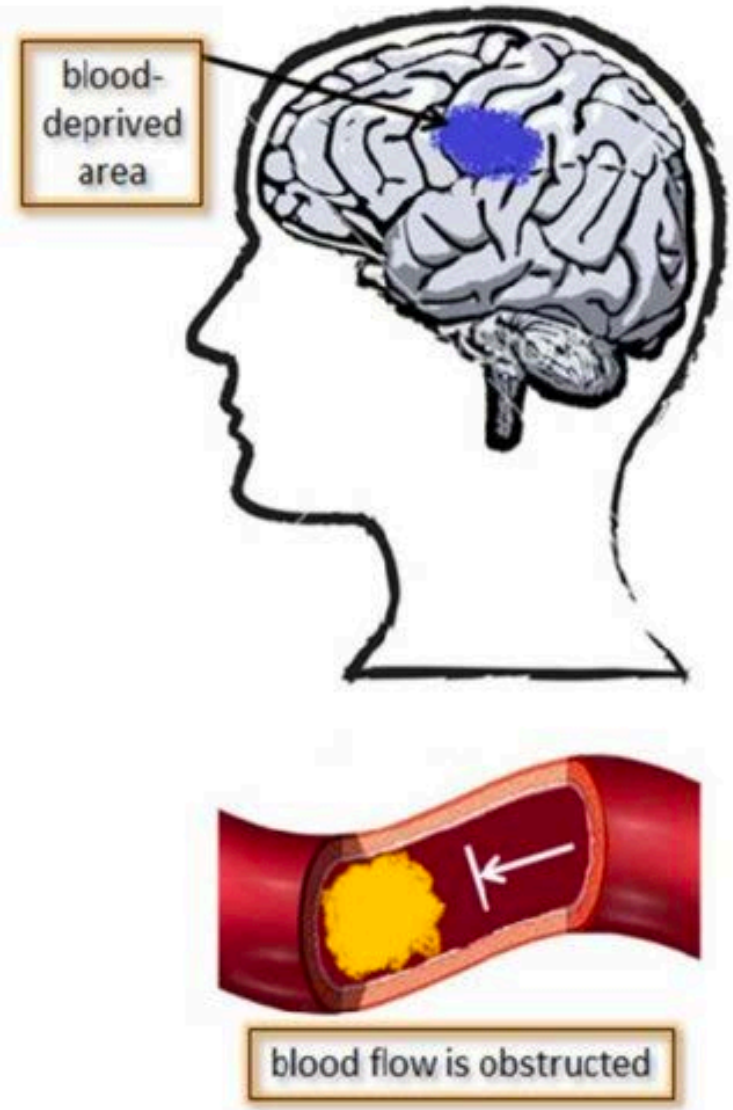
Hemorrhagic stroke ~10% of all strokes

Blood vessel in brain bursts (aneurysm)

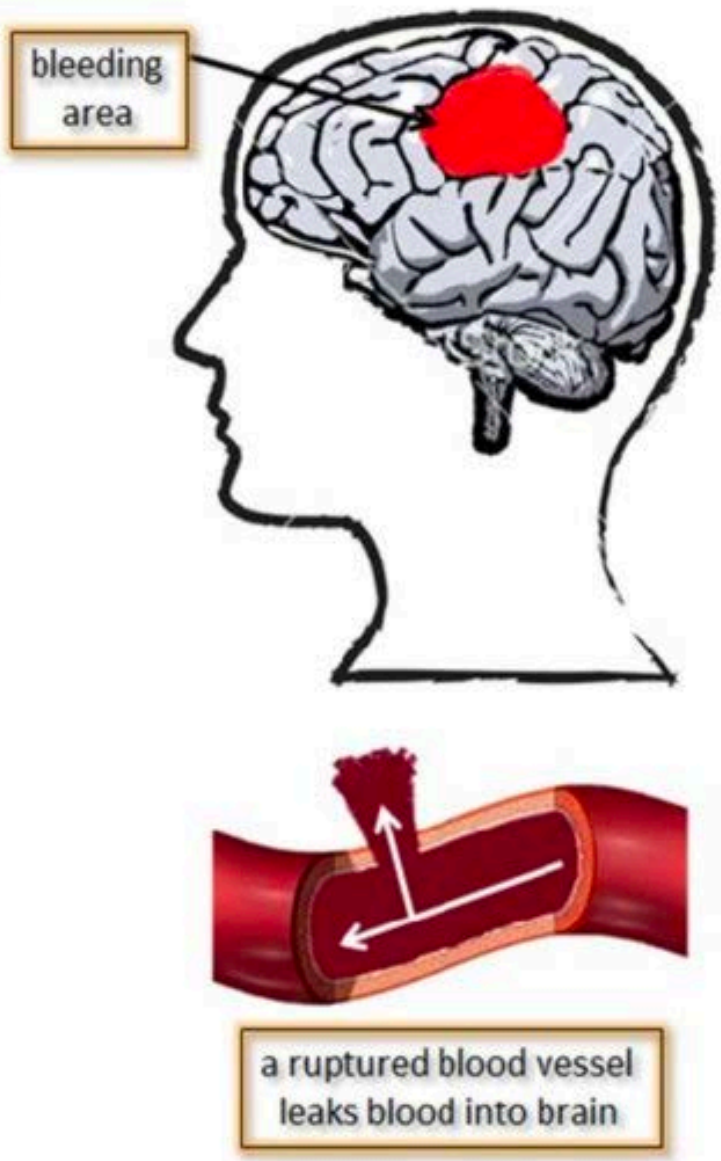
Who is at Risk?

- Hypertension
- Diabetes
- Smoking
- Hyperlipidemia
- Heart diseases
- Sickle cell disease
- Alcohol, cocaine, amphetamines
- Obesity, lack of exercise
- Stress
- Unhealthy diet
- Age and gender
- Race and ethnicity
- Personal or Family history
- Brain aneurysms or AVMs

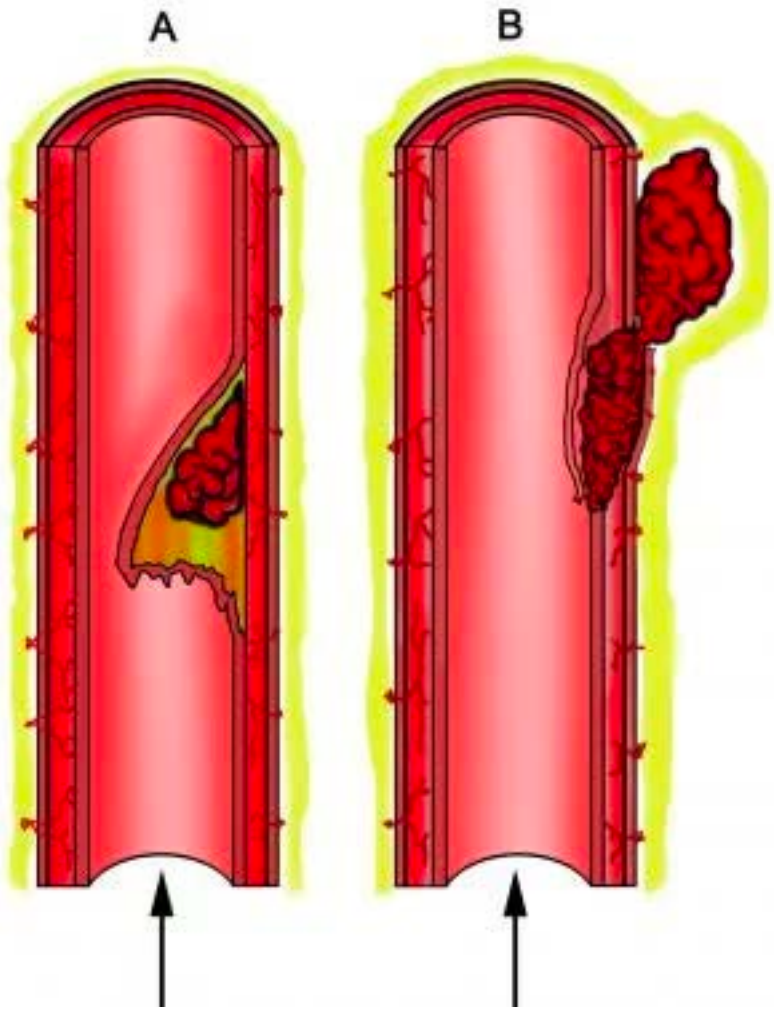
Ischemic Stroke



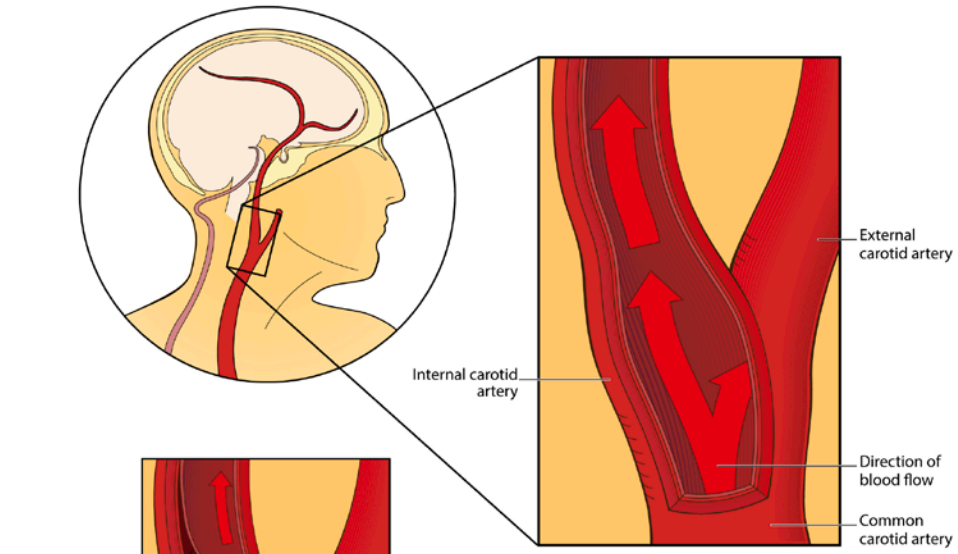
Hemorrhagic Stroke



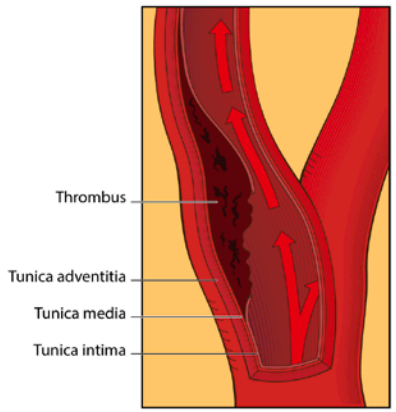
Dissection



DISSECTED INTERNAL CAROTID ARTERY

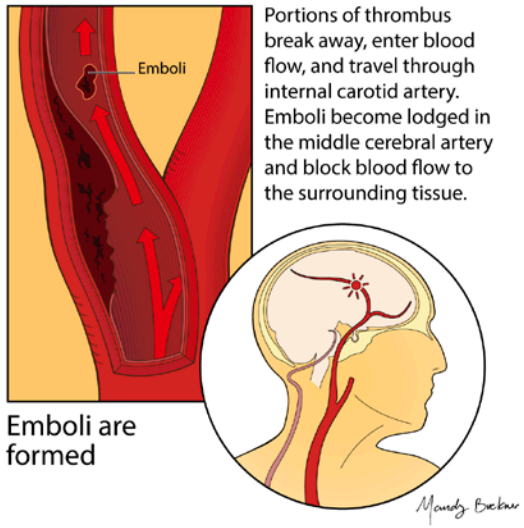


Normal blood flow



Dissected internal carotid artery

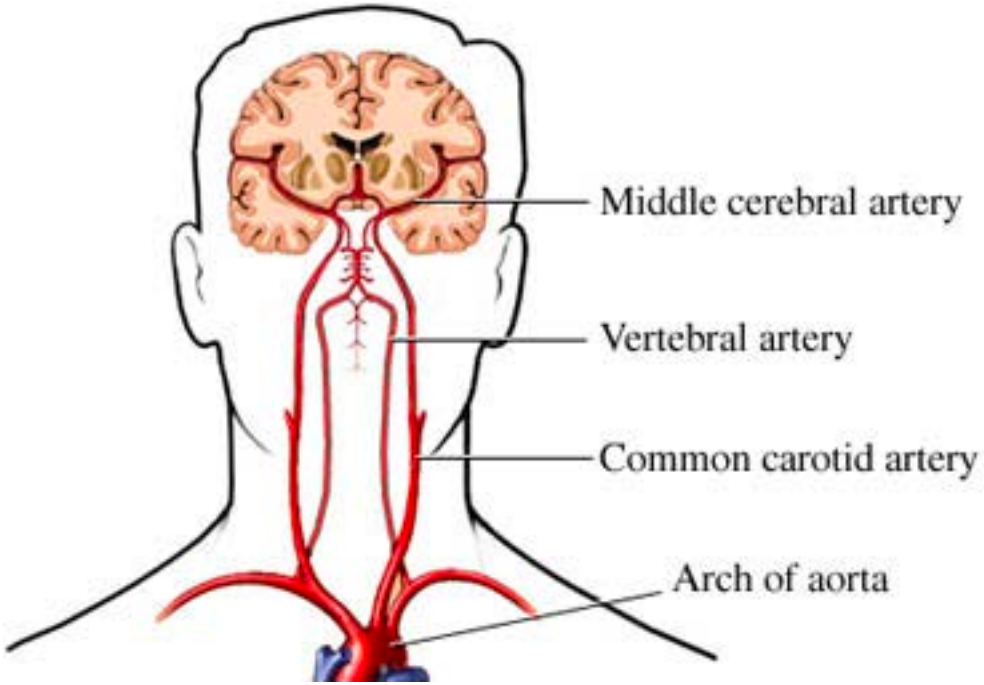
Tunica intima layer of the arterial wall tears. The arterial wall is dissected and a blood clot, or thrombus, forms.

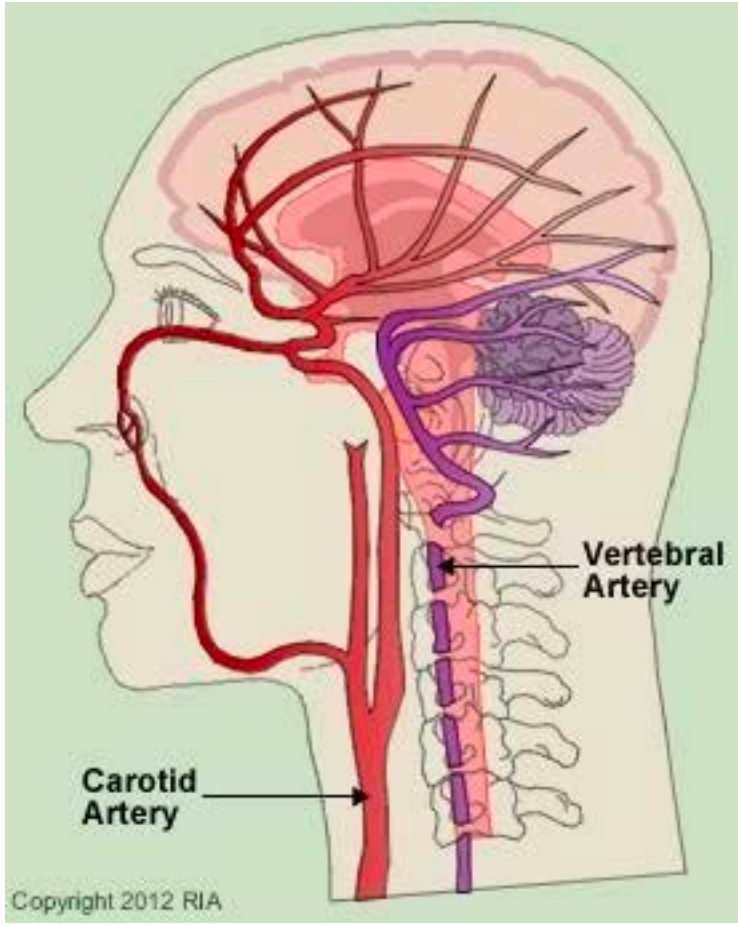


Portions of thrombus break away, enter blood flow, and travel through internal carotid artery. Emboli become lodged in the middle cerebral artery and block blood flow to the surrounding tissue.

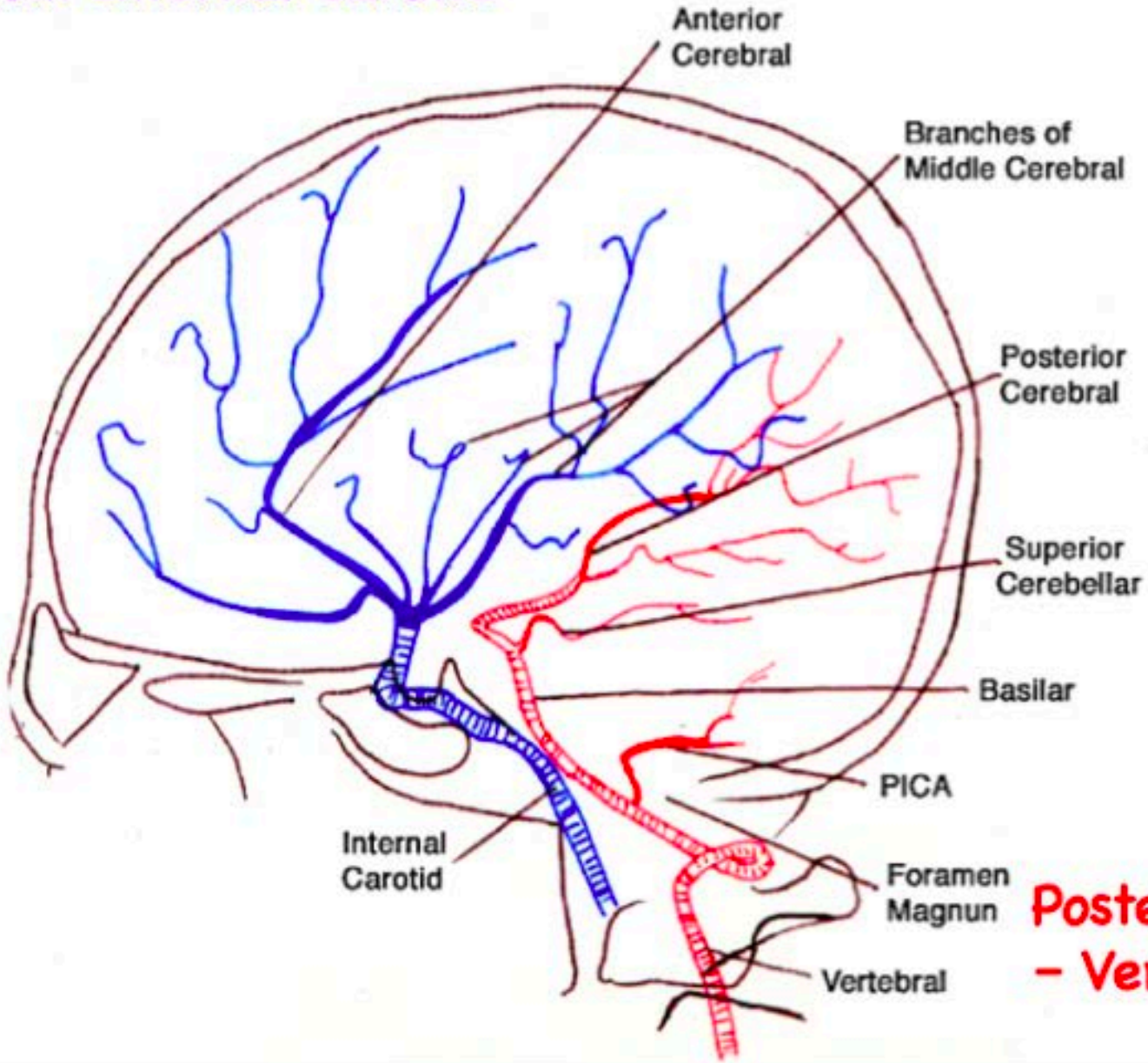
Emboli are formed

Stroke Location

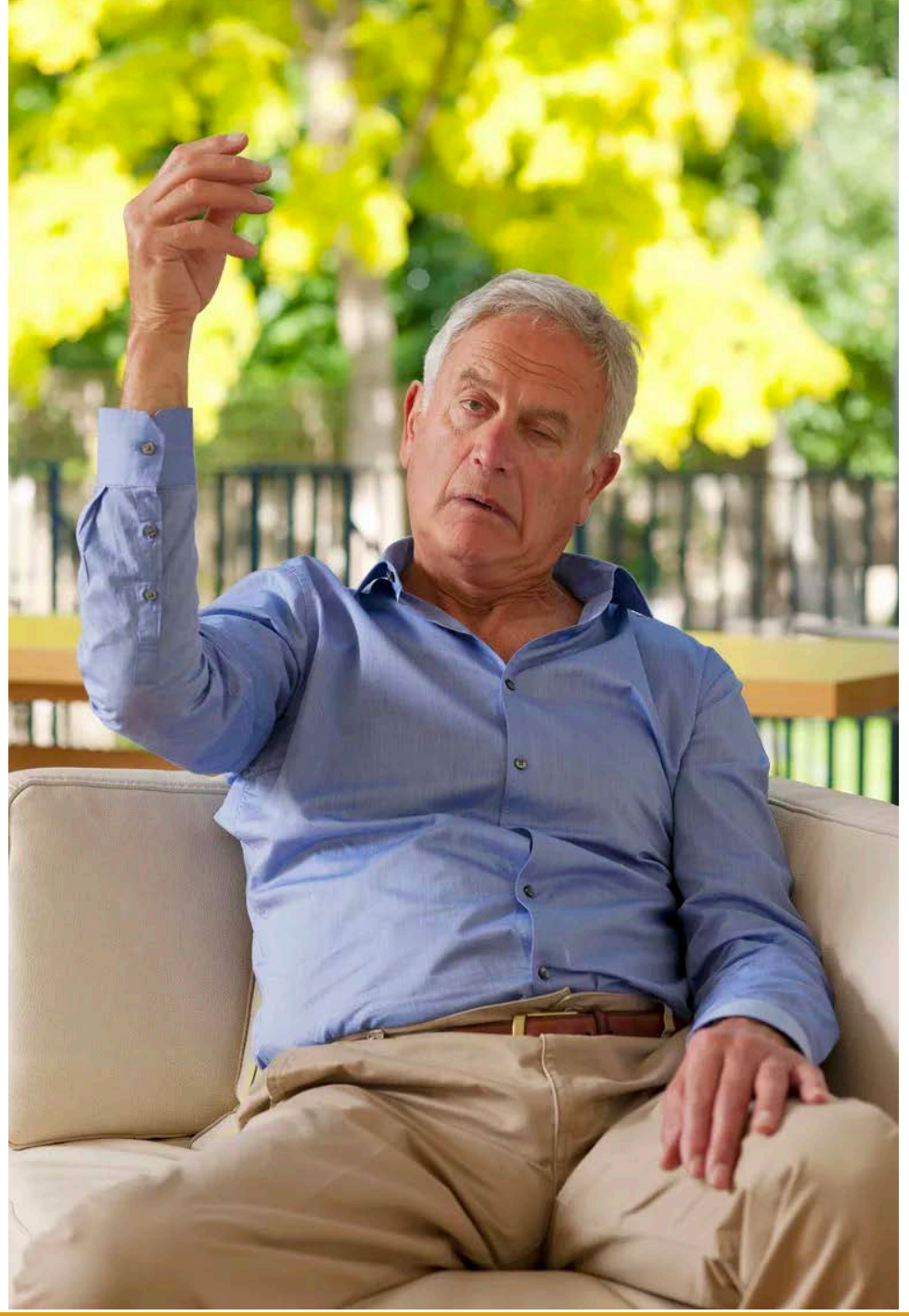




Anterior Circulation
– from Internal Carotid



Posterior Circulation
– Vertebral-Basilar



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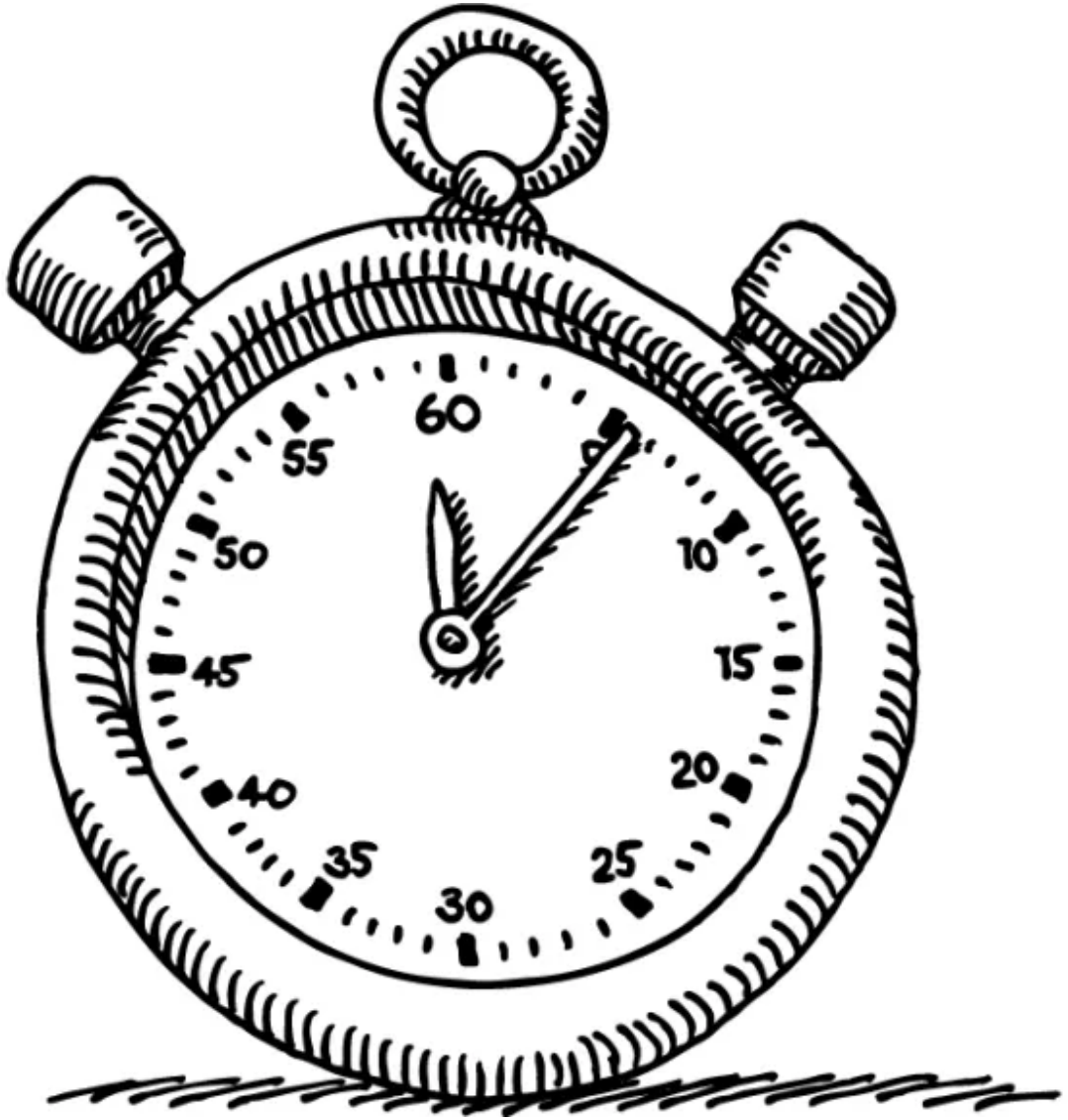
ALL STROKE TYPES HAVE SAME SYMPTOMS!

What to do when you notice signs of stroke

Timing is Everything



Time is Brain!

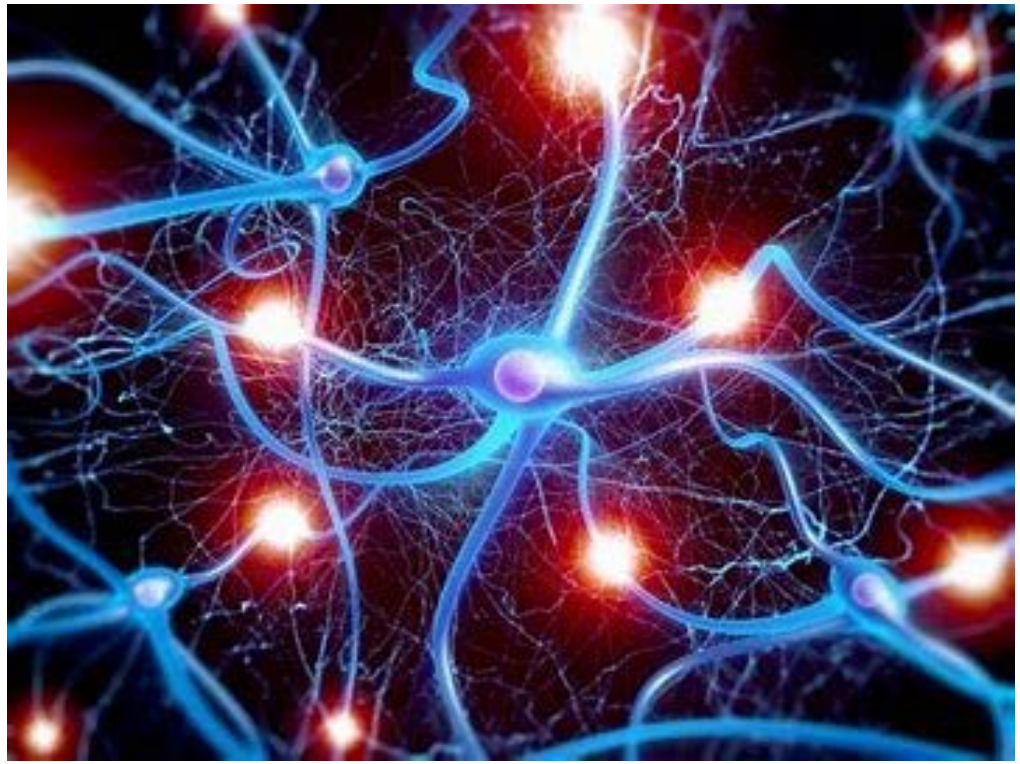
- With a stroke, time lost is brain lost
- It is estimated that 1.9 million neurons are lost every minute of a large vessel occlusion

Time is Brain!

- With a stroke, time lost is brain lost
- It is estimated that 1.9 million neurons are lost every minute of a large vessel occlusion
- **Why?**

Time is Brain!

- Major cell type in brain is *neuron*
- Very high metabolism
- Limited capacity to store energy (unlike muscle)
- Oxygen in blood important and only source of energy
- When blood supply blocked by a stroke, neurons die rapidly



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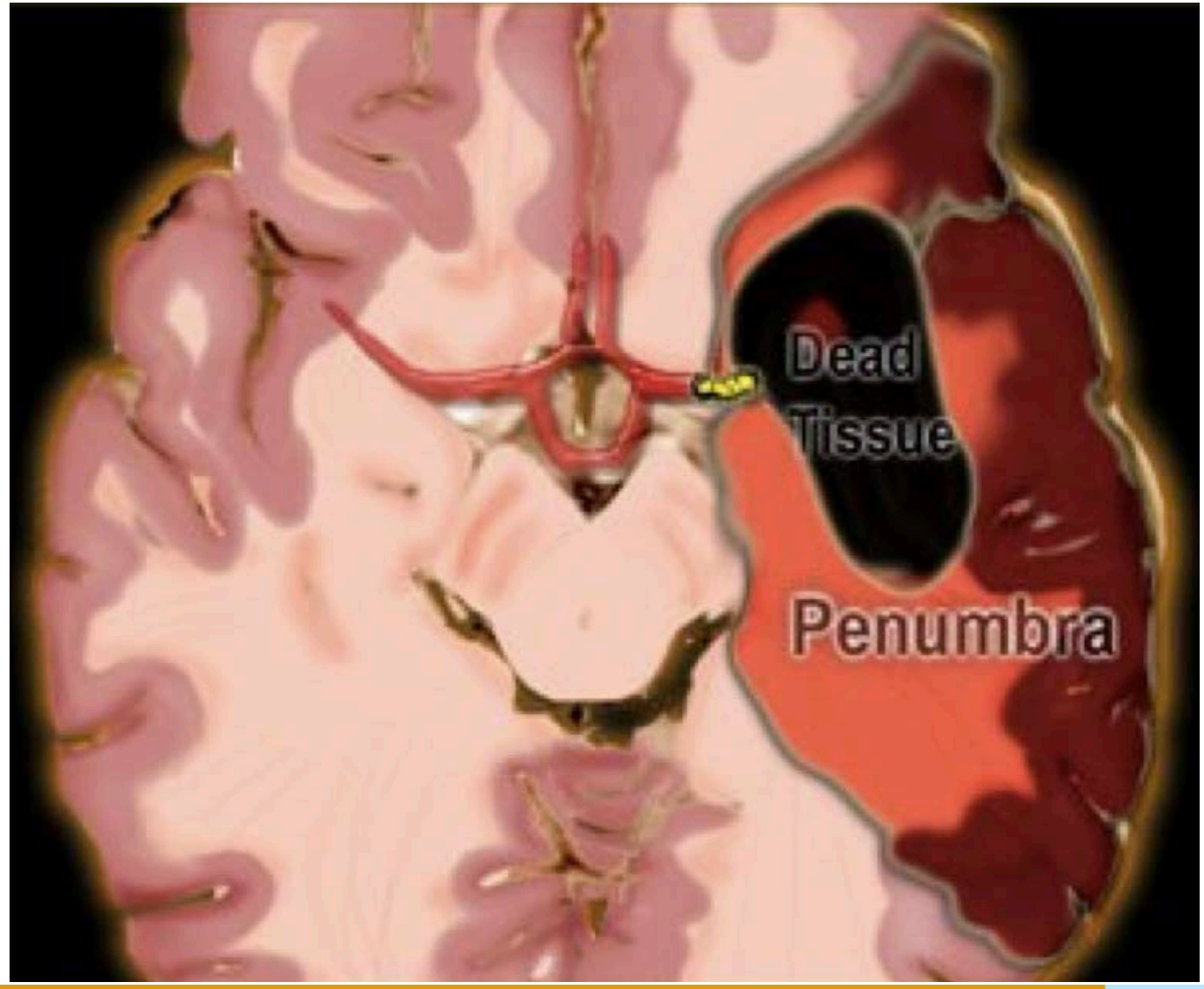
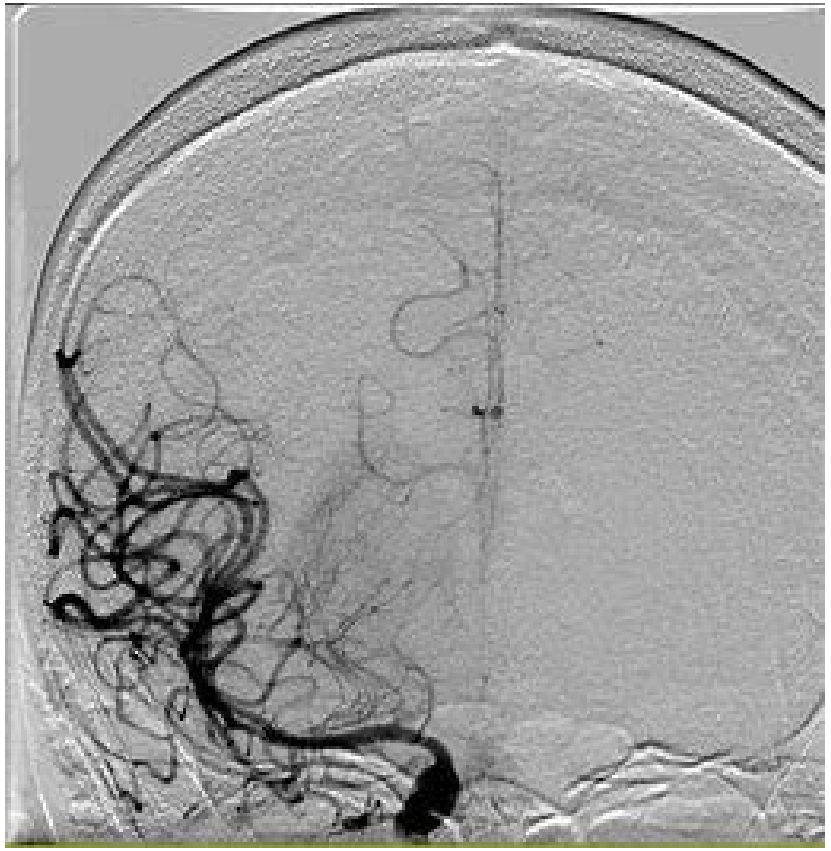


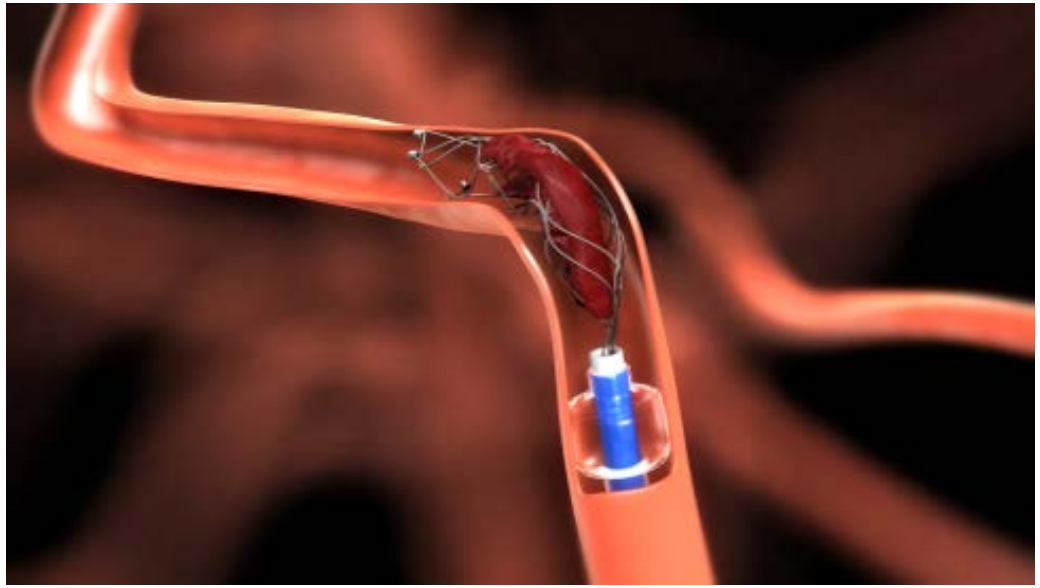
Treatments to Salvage Brain Tissue

- Rapid restoration of blood flow most effective



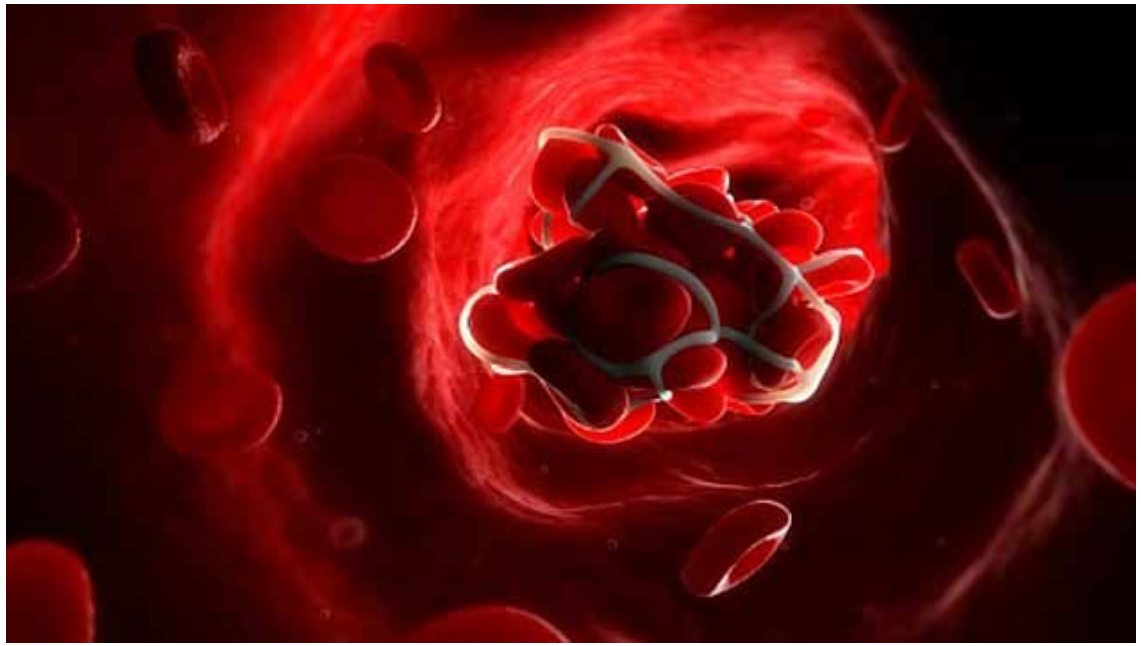
Treatments to Salvage Brain Tissue

- Rapid restoration of blood flow most effective
- Clot removal by endovascular for certain patients with LVO



Treatments to Salvage Brain Tissue

- Rapid restoration of blood flow most effective
- Clot removal by endovascular for certain patients with LVO
- Clot dissolution by tissue plasminogen activator (tPA) for certain patients



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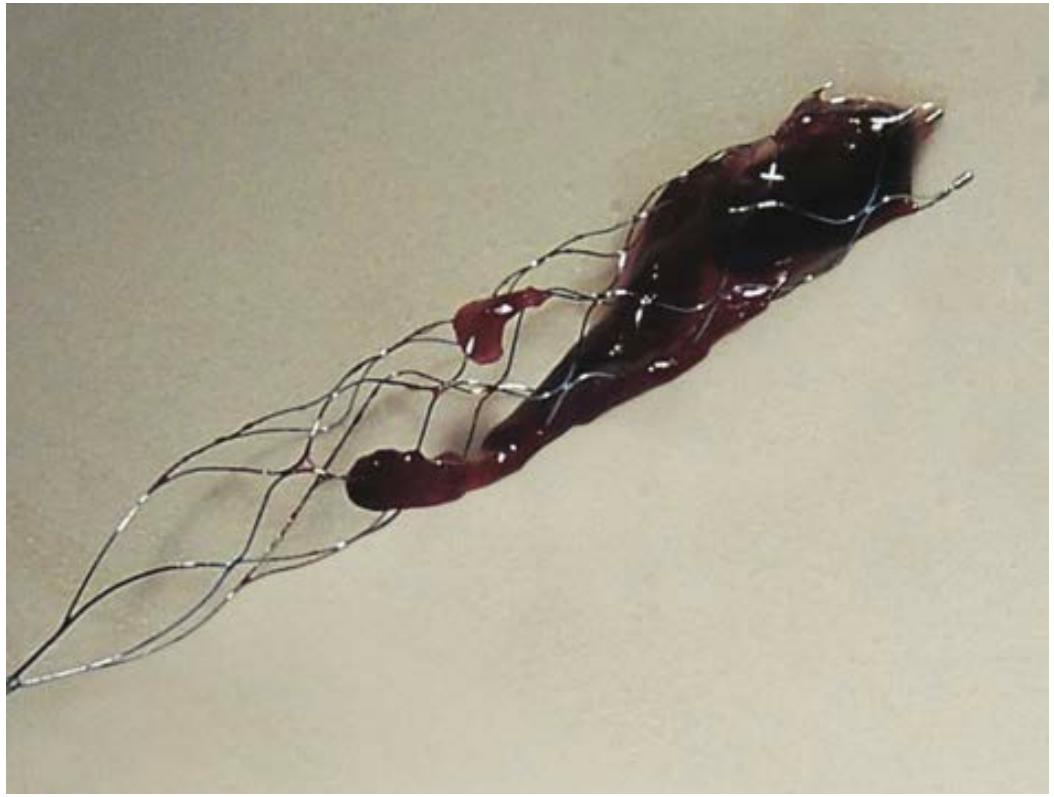
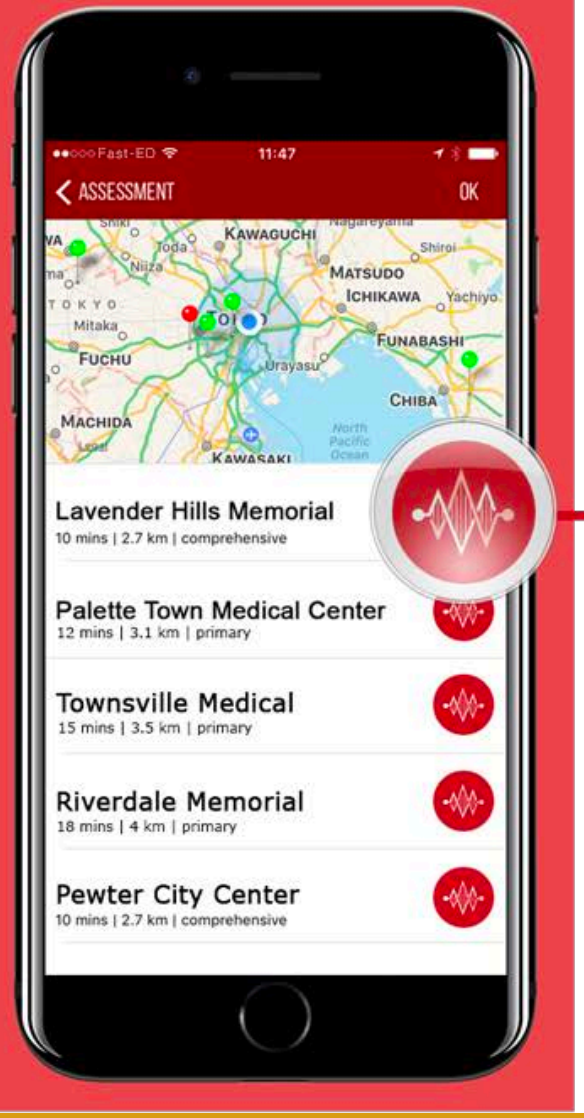
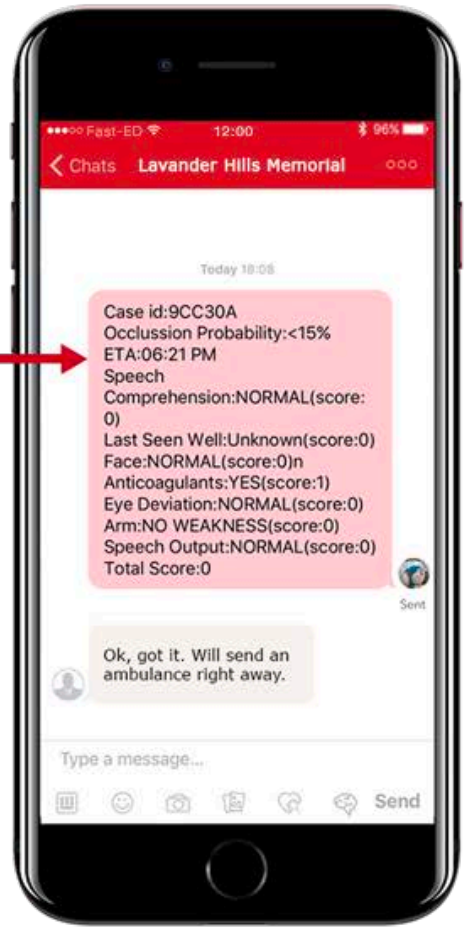
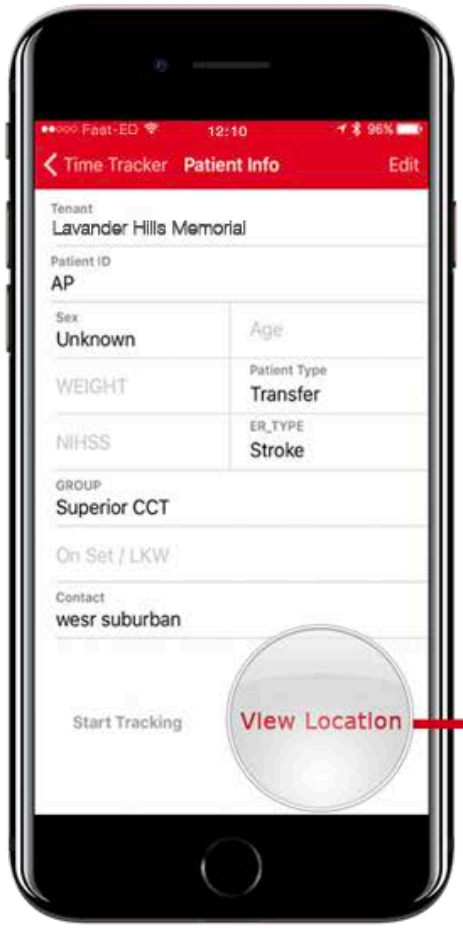
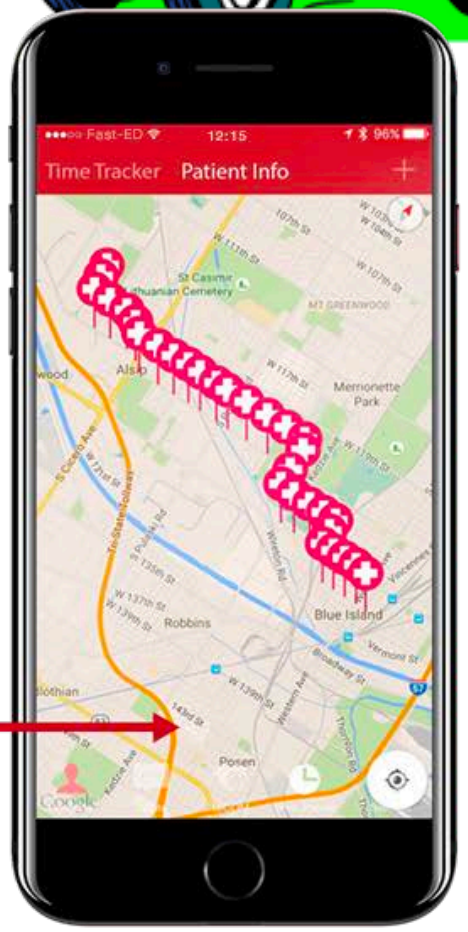



AMBULANCE


Fast-ED 11:47
ASSESSMENT
OK
KAWAGUCHI
MATSUDO
ICHIKAWA
FUNABASHI
FUCHU
CHIBA
MACHIDA
Lavender Hills Memorial
10 mins | 2.7 km | comprehensive
Palette Town Medical Center
12 mins | 3.1 km | primary
Townsville Medical
15 mins | 3.5 km | primary
Riverdale Memorial
18 mins | 4 km | primary
Pewter City Center
10 mins | 2.7 km | comprehensive


Fast-ED 12:00
Chats
Lavander Hills Memorial
Case id:9CC30A
Occlusion Probability:<15%
ETA:06:21 PM
Speech Comprehension:NORMAL(score:0)
Last Seen Well:Unknown(score:0)
Face:NORMAL(score:0)n
Anticoagulants:YES(score:1)
Eye Deviation:NORMAL(score:0)
Arm:NO WEAKNESS(score:0)
Speech Output:NORMAL(score:0)
Total Score:0
Sent
Ok, got it. Will send an ambulance right away.
Type a message...
Send

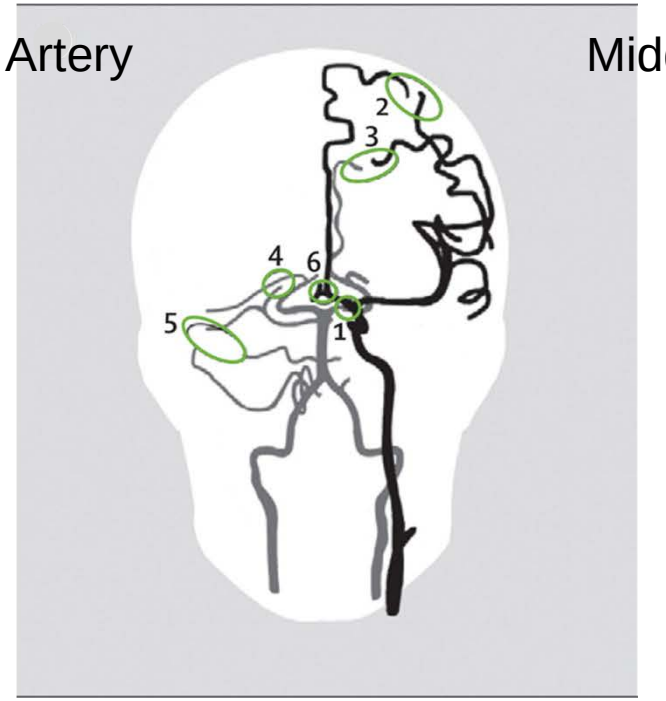

Fast-ED 12:10
Time Tracker
Patient Info
Edit
Tenant
Lavander Hills Memorial
Patient ID
AP
Sex
Unknown
Age
WEIGHT
Patient Type
Transfer
NIHSS
ER_TYPE
Stroke
GROUP
Superior CCT
On Set / LKW
Contact
wesr suburban
Start Tracking
View Location


Fast-ED 12:15
Time Tracker
Patient Info

When was the patient last seen normal?

Current Research on Reperfusion Therapies
Taking Advantage of What's Already There

Anterior Cerebral Artery (ACA)



Middle Cerebral Artery (MCA)

Liebeskind DS. *Stroke* 2003

Current Research on Reperfusion Therapies
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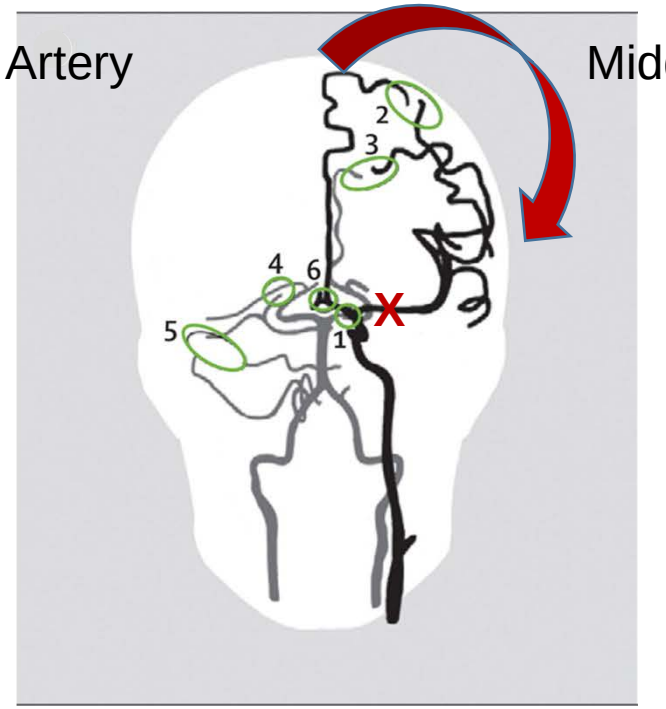
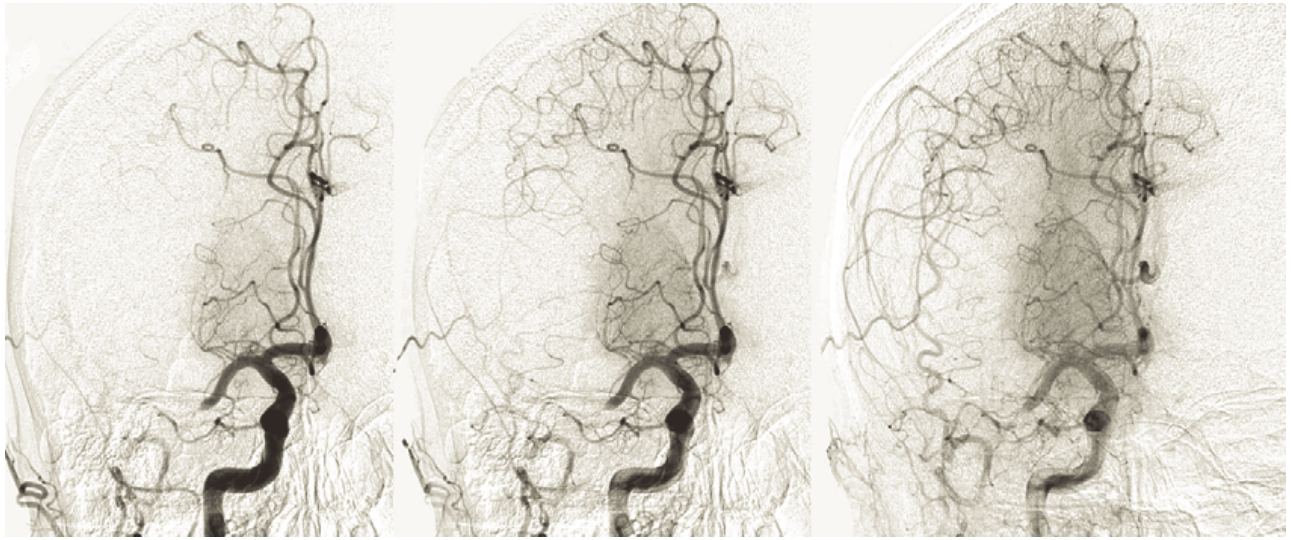


Middle Cerebral Artery (MCA)

Retrograde flow from another vascular territory can sustain blood flow and limit injury from stroke by salvaging brain tissue in penumbra

Liebeskind DS. *Stroke* 2003

Pial Collaterals and Stroke Outcome

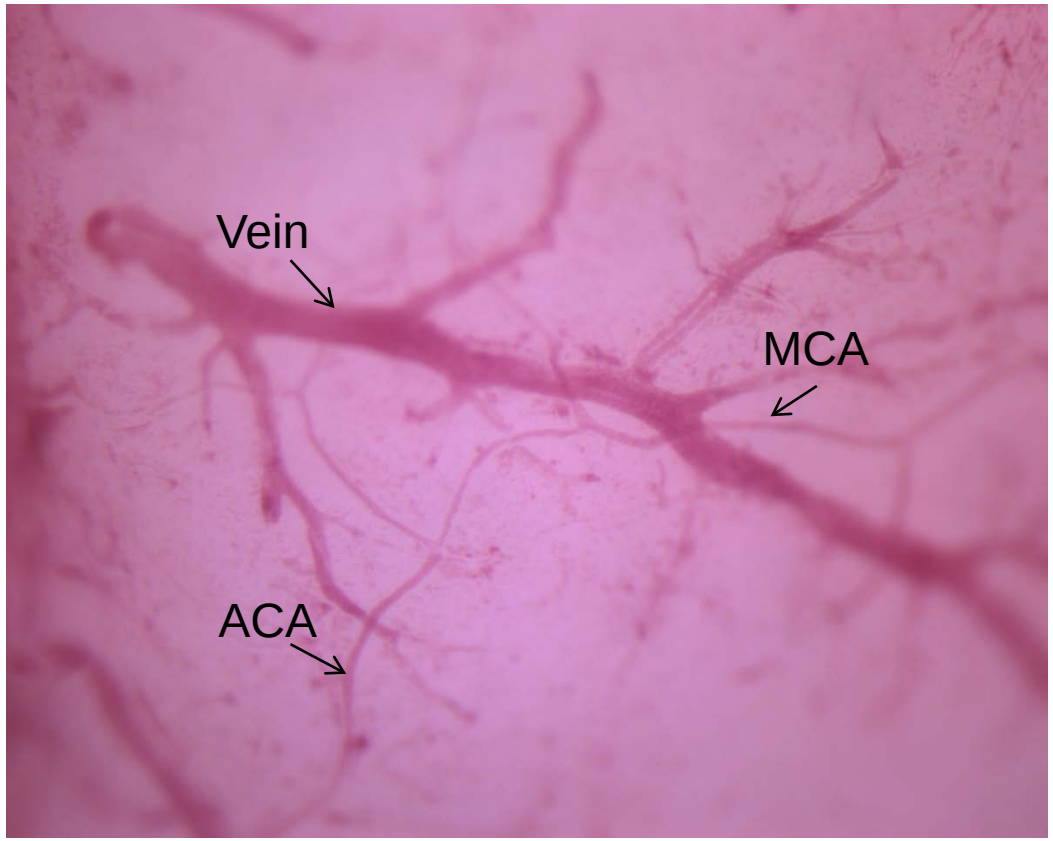


CT imaging with digital subtraction angiography of collateral perfusion during LVO

Collateral status strongest predictor for outcome from stroke:

- Patients with good collaterals = better reperfusion, smaller infarcts and less hemorrhagic transformation
- Patients with poor collaterals = poor outcome even with recanalization

Pial Collaterals as a Target for Stroke Treatment



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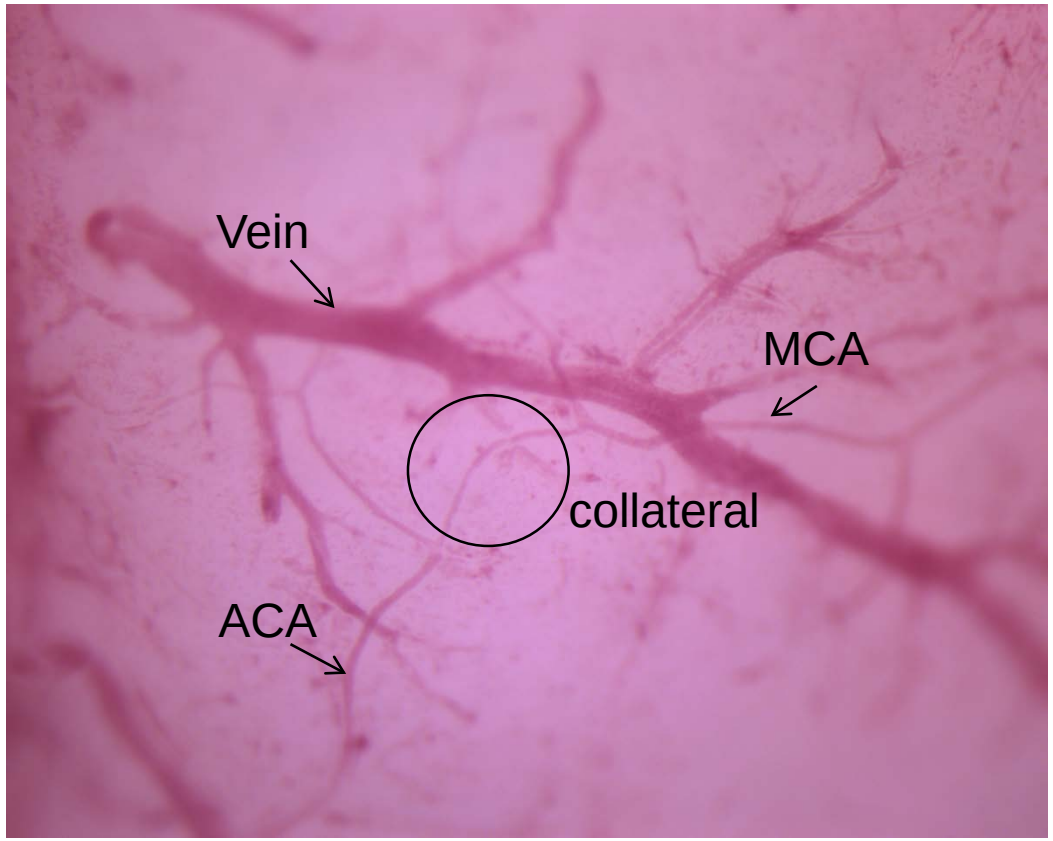

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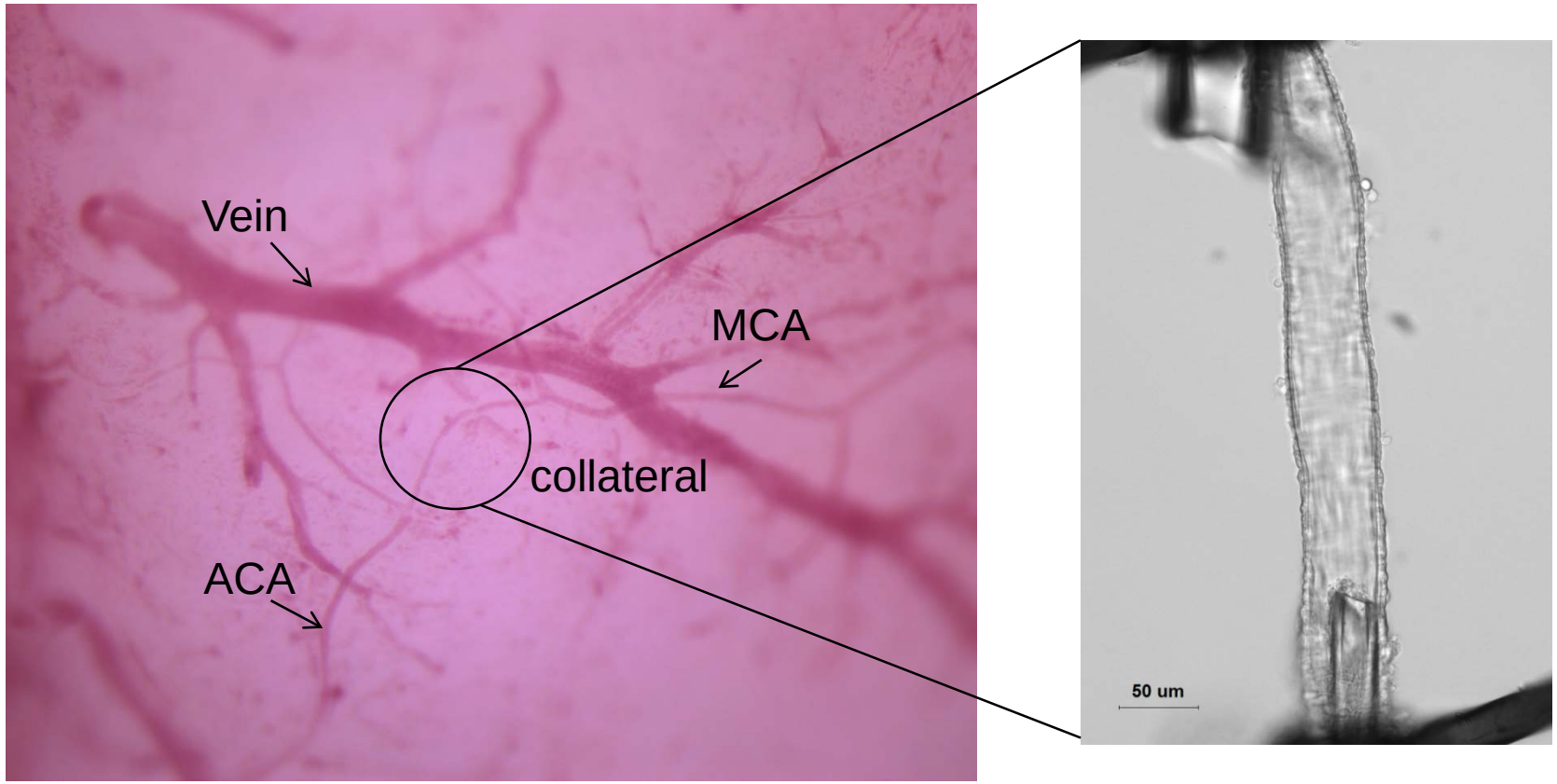

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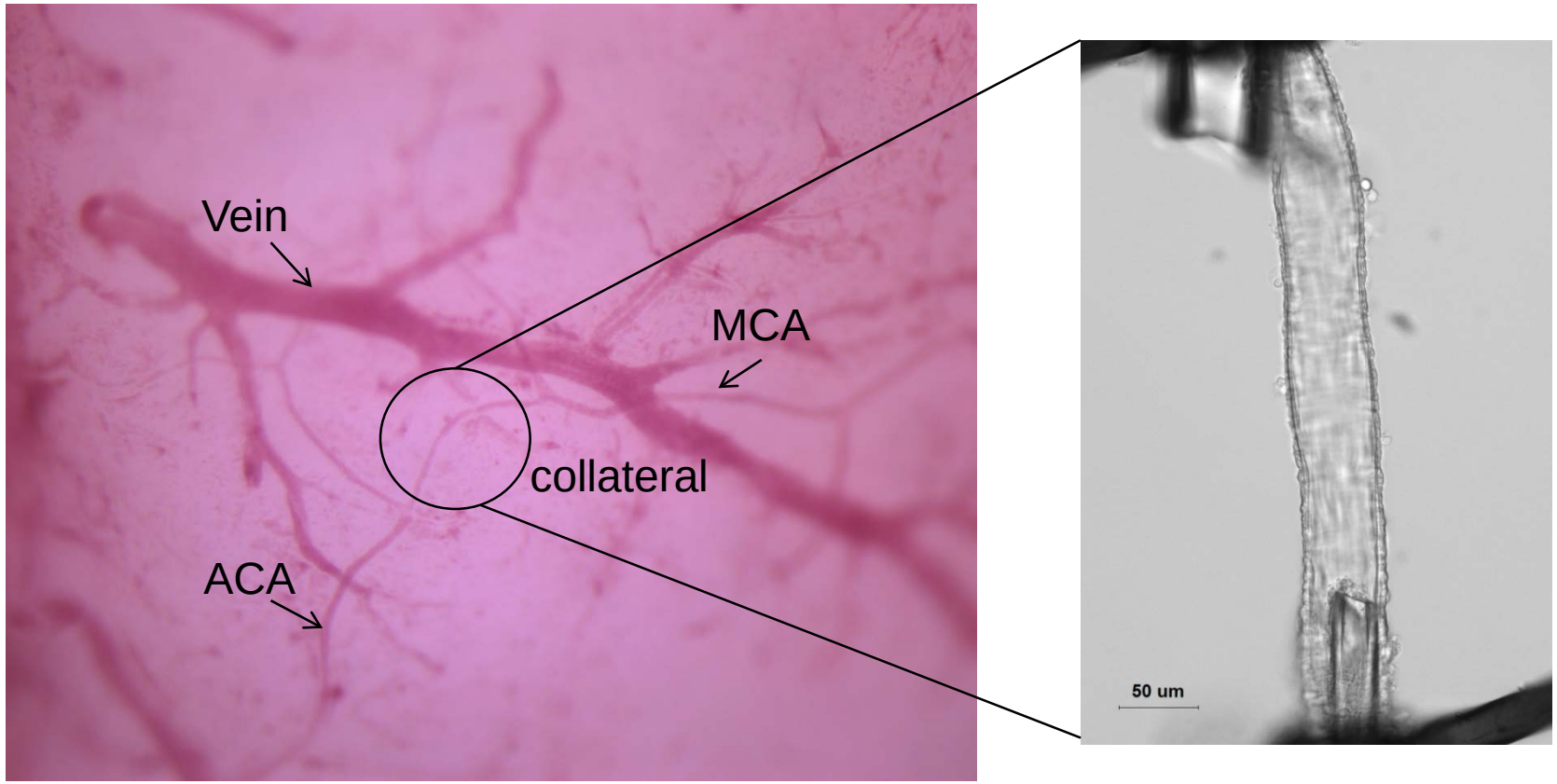
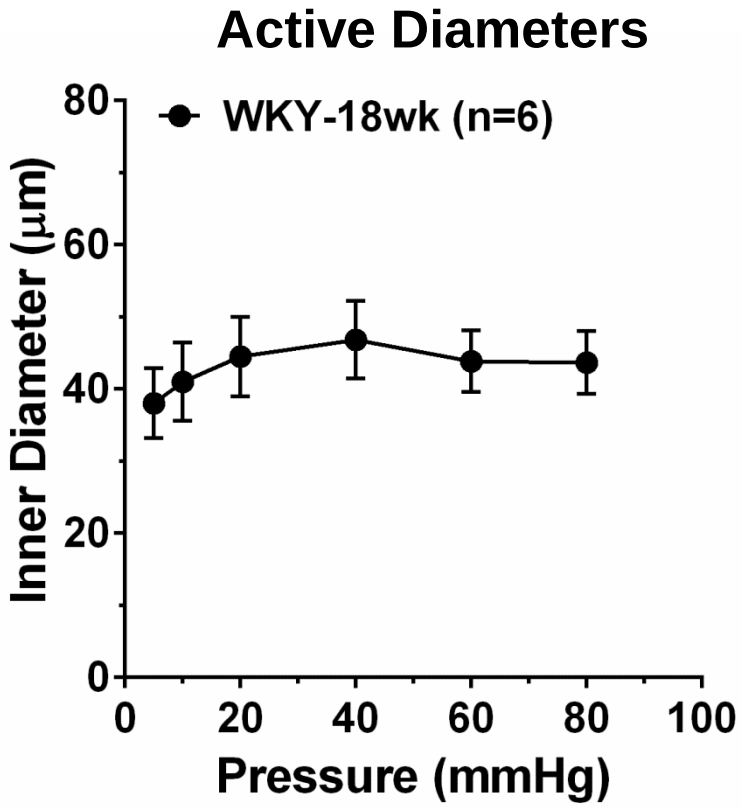
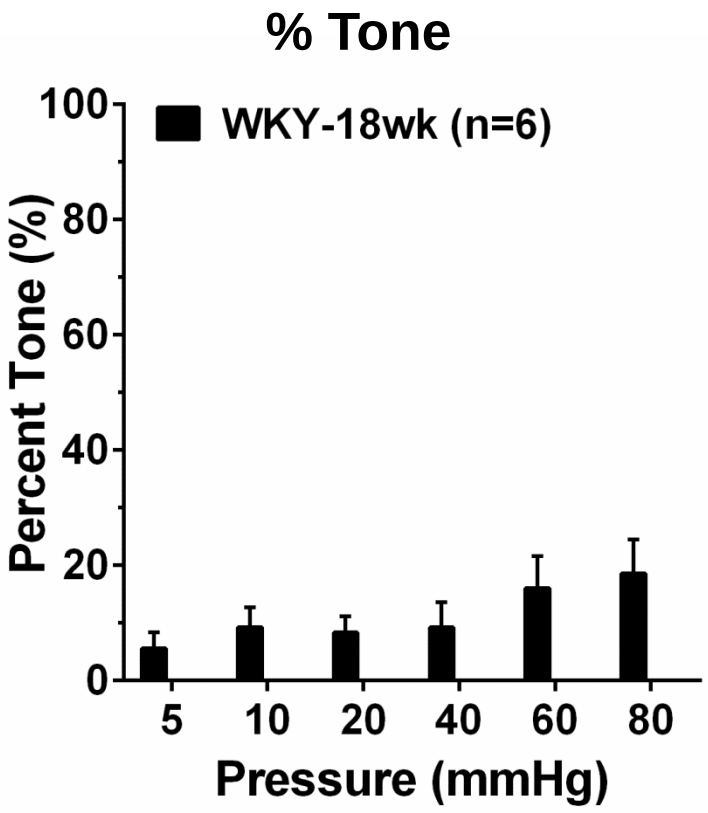


Compared constriction of collateral vessel from normal rats vs. hypertension

Collateral Vessel Constriction to Pressure





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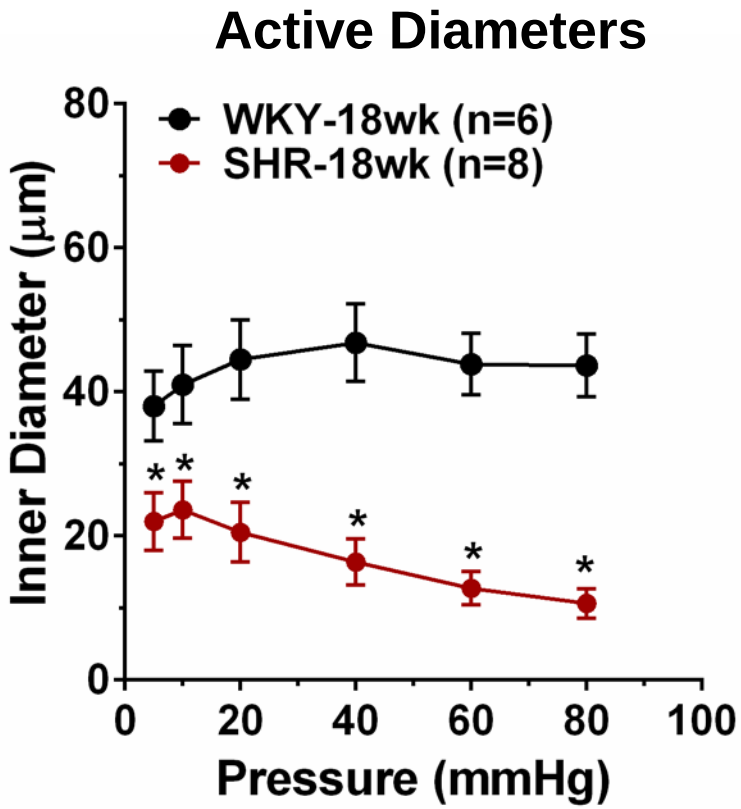

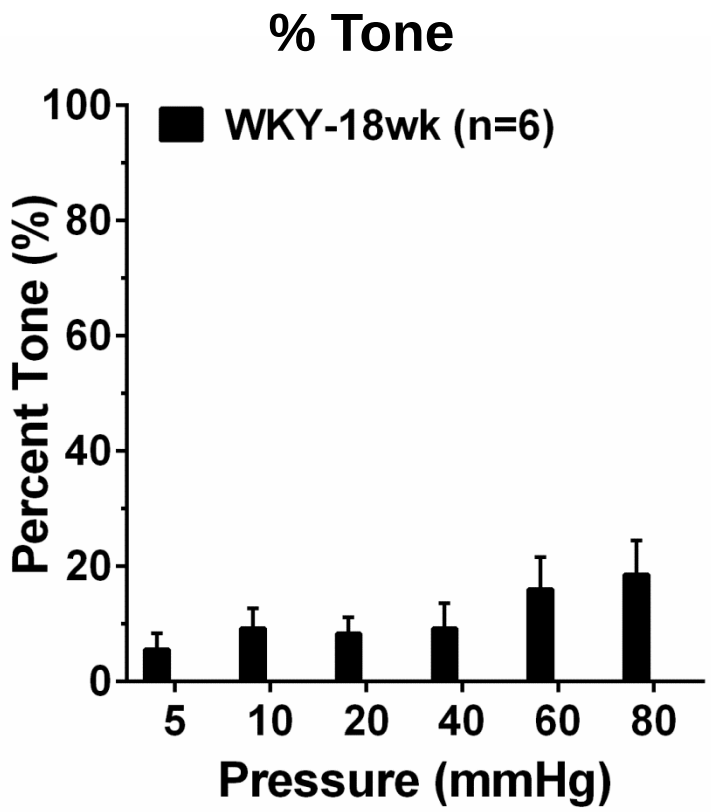

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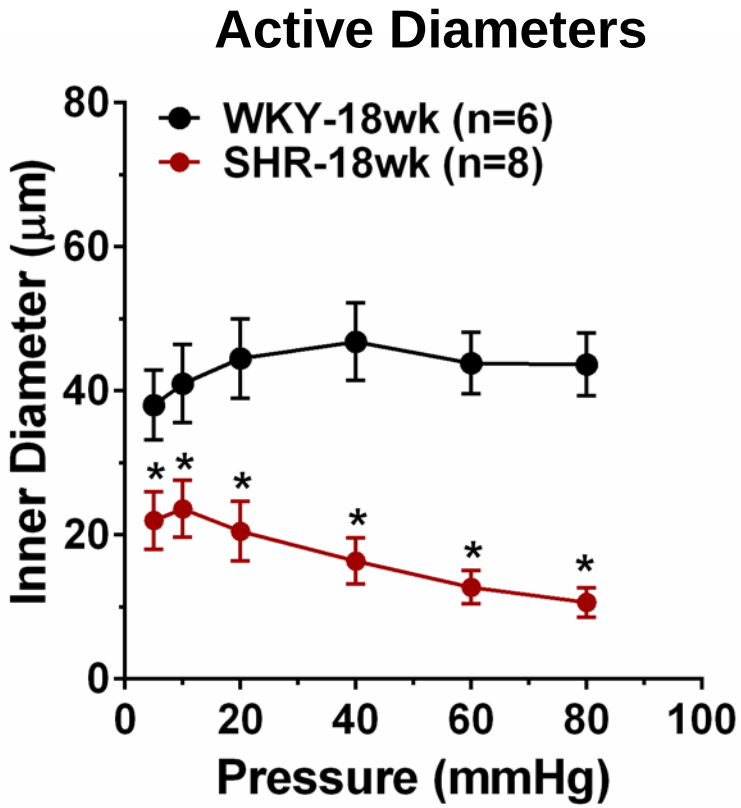
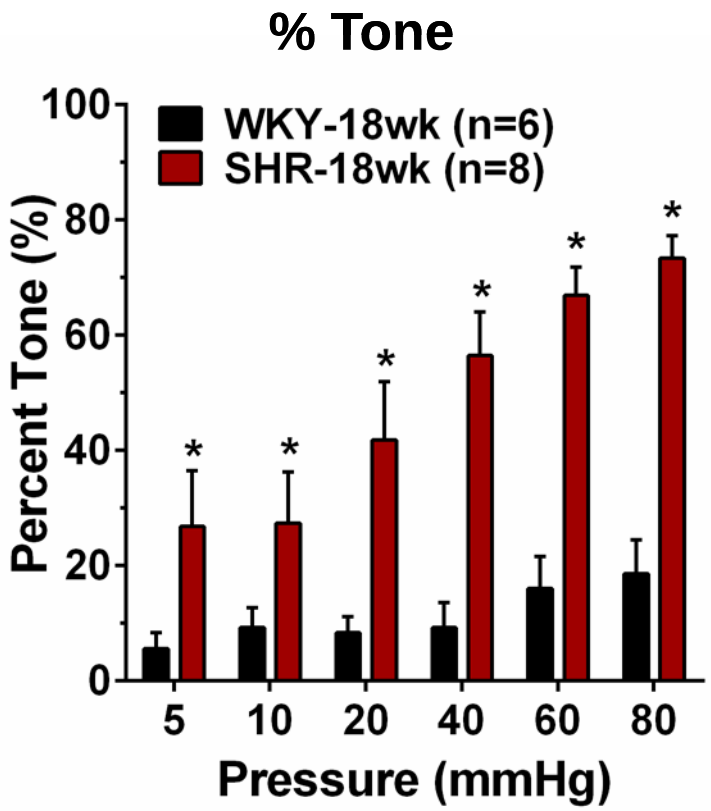


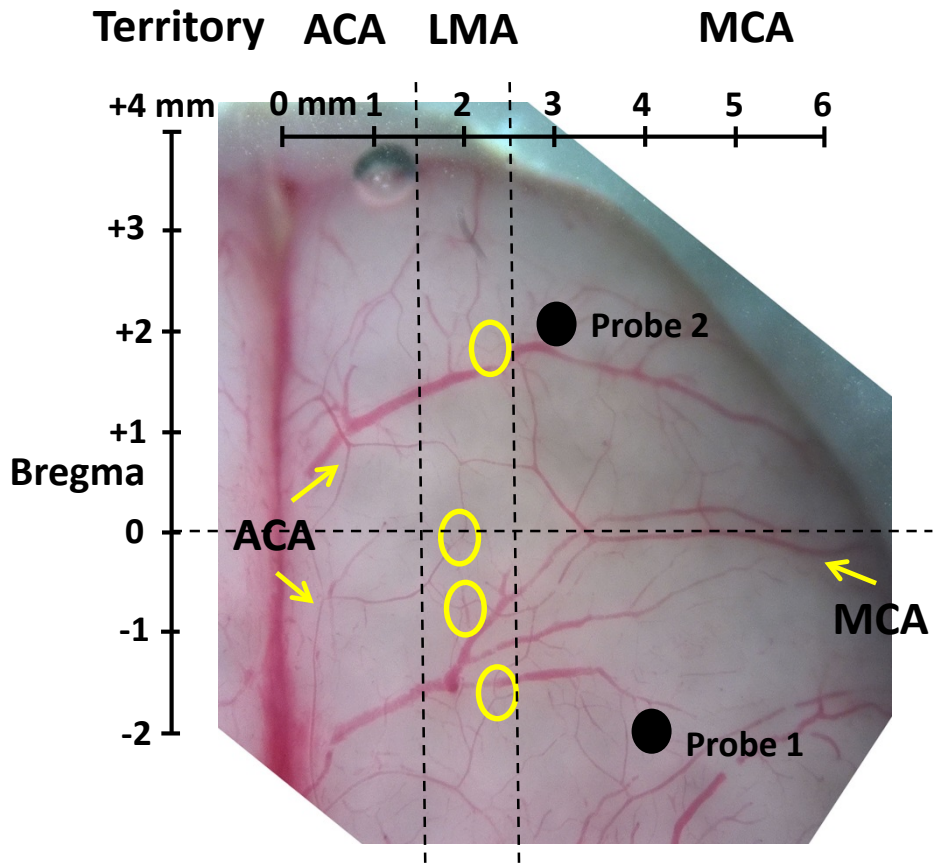


Can collateral flow be increased during stroke to increase salvageable brain tissue and/or buy time?

Rat Model of LVO

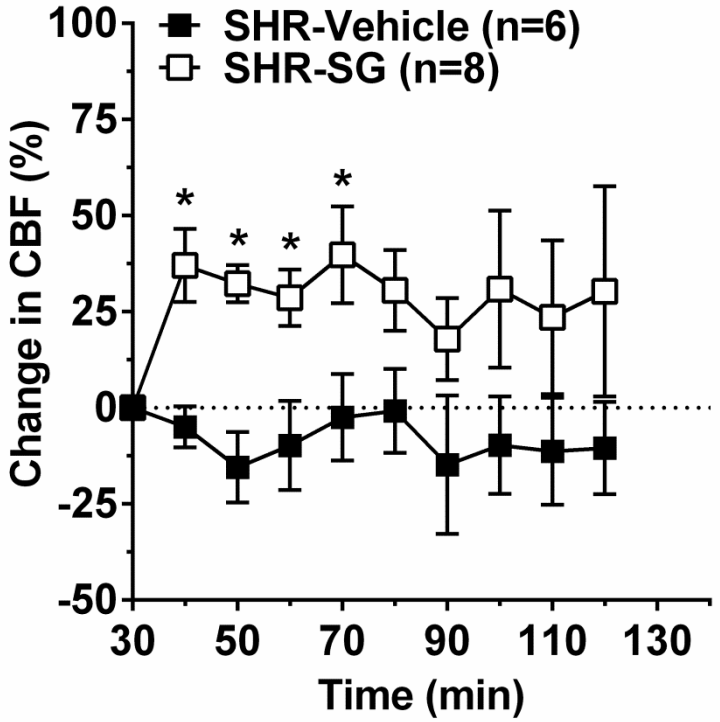
- Approximates clinical stroke
- Induces brain lesions similar to human stroke
- Allows for reperfusion of cerebral blood flow

Multi-site Laser Doppler Measurement of Core and Collateral CBF

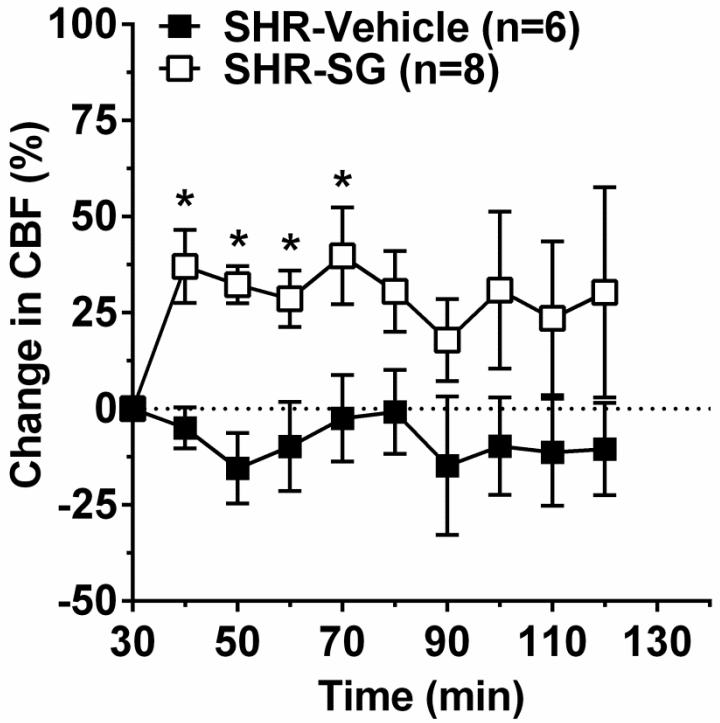


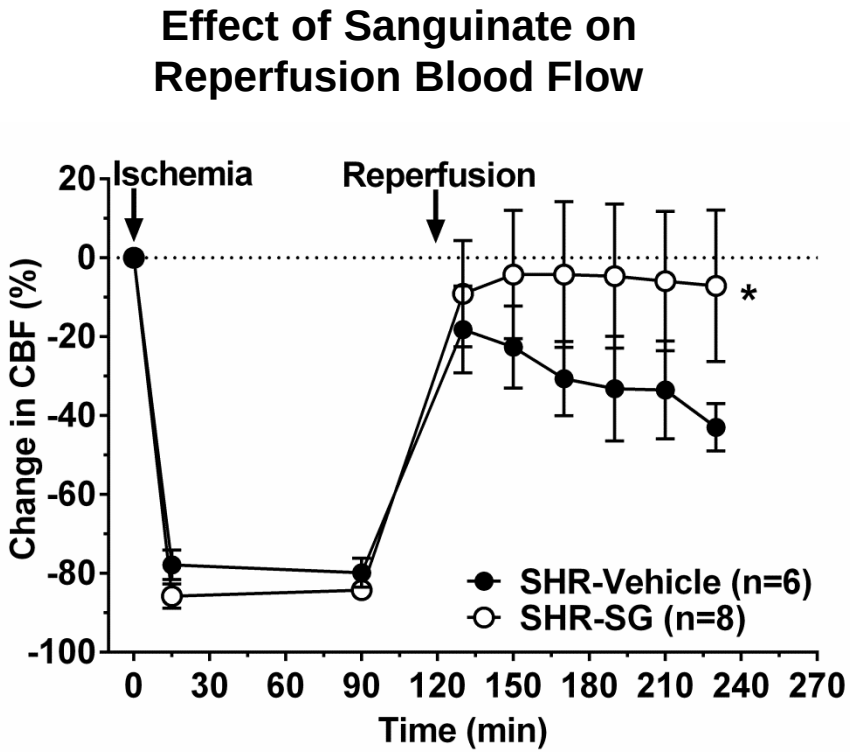
- Two Doppler probes placed on brain
- Allows simultaneous measurement of collateral flow and core infarction
- Measured collateral flow during occlusion with treatment (Sanguinate™)

Sanguinate™ Increased Collateral Flow during LVO



Sanguinate™ Increased Collateral Flow during LVO and Improved Reperfusion





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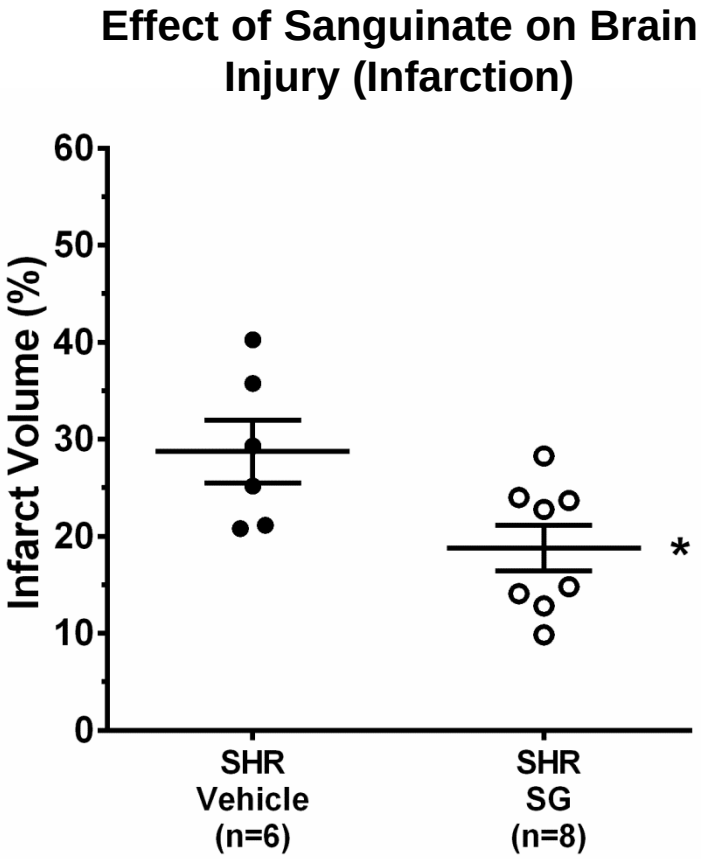
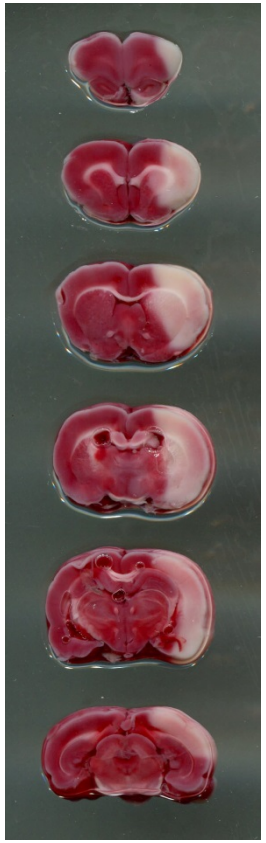
Sanguinate™ Prevented Stroke Damage to Brain





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Support

National Institute of Neurological Disorders and Stroke (NINDS)

National Heart, Lung, and Blood Institute (NHLBI)

Totman Medical Research Trust

Cardiovascular Research Institute of Vermont

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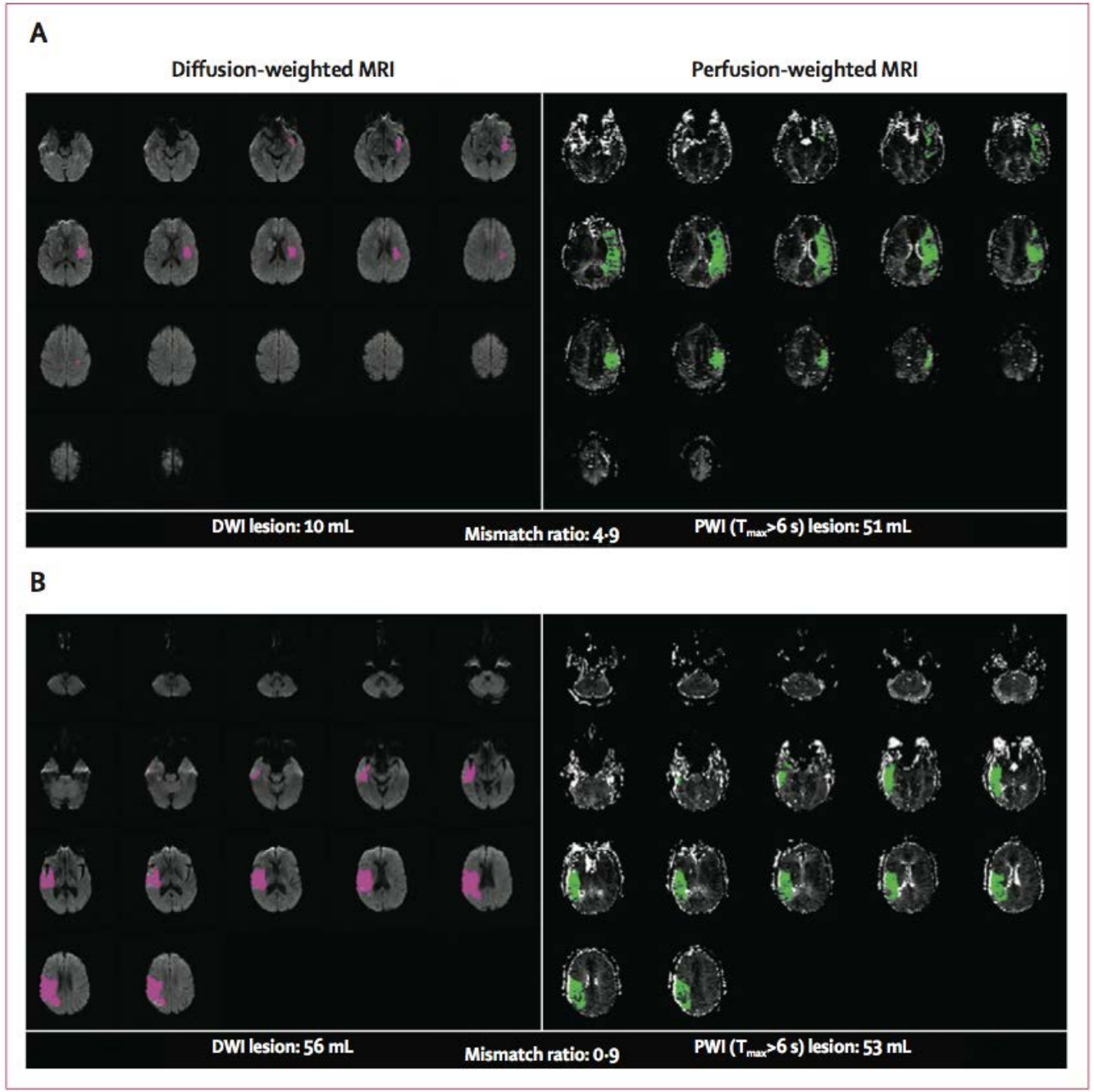
Thank you!

Questions?


A
Diffusion-weighted MRI
Perfusion-weighted MRI
DWI lesion: 10 mL
Mismatch ratio: 4·9
PWI (T_{max}>6 s) lesion: 51 mL
B
DWI lesion: 56 mL
Mismatch ratio: 0·9
PWI (T_{max}>6 s) lesion: 53 mL