IN STROKE, EVERY MINUTE COUNTS: WHEN TIME = BRAIN

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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
What is a Stroke?

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

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

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Can be Small Vessel Disease (SVD) due small penetrating artery atherosclerosis, degradation, or small emboli (clots).
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Hemorrhagic stroke ~10% of all strokes
Blood vessel in brain bursts (aneurysm)
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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
- Blood-deprived area
- Blood flow is obstructed

Hemorrhagic Stroke
- Bleeding area
- A ruptured blood vessel leaks blood into brain

Dissection
**DISSECTED INTERNAL CAROTID ARTERY**

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

**Emboli are formed**
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.

**Normal blood flow**
- Tunica intima
- Tunica media
- Tunica adventitia
- Emboli
- Thrombus
- External carotid artery
- Common carotid artery
- Direction of blood flow
Stroke Location
Anterior Circulation
- from Internal Carotid

Posterior Circulation
- Vertebral-Basilar
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
Time is Brain!
Treatments to Salvage Brain Tissue

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

- Rapid restoration of blood flow most effective
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
Taking Advantage of What’s Already There

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

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

CT imaging with digital subtraction angiography of collateral perfusion during LVO
Pial Collaterals as a Target for Stroke Treatment

Vein

MCA

ACA
Pial Collaterals as a Target for Stroke Treatment
Pial Collaterals as a Target for Stroke Treatment
Pial Collaterals as a Target for Stroke Treatment

Compared constriction of collateral vessel from normal rats vs. hypertension
Collateral Vessel Constriction to Pressure

Active Diameters

% Tone

Inner Diameter (µm)

Pressure (mmHg)

WKY-18wk (n=6)

Percent Tone (%)

Pressure (mmHg)

WKY-18wk (n=6)
Collateral Vessel Constriction to Pressure

**Active Diameters**

![Graph showing active diameters for WKY-18wk (n=6) and SHR-18wk (n=8).](image)

**% Tone**

![Graph showing % tone for WKY-18wk (n=6).](image)
Collateral Vessel Constriction to Pressure

**Active Diameters**

- WKY-18wk (n=6)
- SHR-18wk (n=8)

**% Tone**

- WKY-18wk (n=6)
- SHR-18wk (n=8)
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**

![Graph showing change in CBF](image)

**Effect of Sanguinate on Reperfusion Blood Flow**

![Graph showing change in CBF over time](image)
Sanguinate™ Prevented Stroke Damage to Brain

Effect of Sanguinate on Brain Injury (Infarction)
Support

National Institute of Neurological Disorders and Stroke (NINDS)

National Heart, Lung, and Blood Institute (NHLBI)

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Cipolla Lab

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Zhaojin Li, MS
Thank you!
Questions?
Time is Brain!

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