Stroke Facts

- About 700,000 Americans each year suffer a new or recurrent stroke
- On average, a stroke occurs every 45 seconds
- Stroke kills more than 150,000 people a year (1 of every 16 deaths)
- No. 3 cause of death (Every 3 to 4 minutes someone dies of stroke)
“Time is Brain”

<table>
<thead>
<tr>
<th></th>
<th>Neurons Lost</th>
<th>Synapses Lost</th>
<th>Myelinated Fibers Lost</th>
<th>Accelerated Aging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per Second</td>
<td>32 000</td>
<td>230 million</td>
<td>200 meters/218 yards</td>
<td>8.7 h</td>
</tr>
<tr>
<td>Per Minute</td>
<td>1.9 million</td>
<td>14 billion</td>
<td>12 km/7.5 miles</td>
<td>3.1 wk</td>
</tr>
<tr>
<td>Per Hour</td>
<td>120 million</td>
<td>830 billion</td>
<td>714 km/447 miles</td>
<td>3.6 y</td>
</tr>
</tbody>
</table>

The following slide describes the emergency strategy for the treatment of patients with acute stroke.

Once the patient arrives to the UCLA Stroke Center, several alternatives for intervention are offered depending on the time and type of vascular occlusion.
Acute Ischemic Stroke

Symptoms 
911 
EMS 
PSC 
Imaging 
IV rTPA 
EMS 
UCLA / Santa Monica UCLA 

Bleed 
Infarct <3 h 
IV rTPA 
Neurosurgery Consult 

Infarct <6 h 
If IV rTPA contraindicated 
Large vessel 
Not improvement 

Infarct >6 h 
If VB stroke 
<6 h coma 
P/D Mismatch 
Consider Mechanical 

IA Therapies: 
IA lysis vs. Mechanical 
Unless match defect or no collateral (T) 

If IA lysis contraindicated 
No proximal vessel occlusion 
Not improvement 

Aortic balloon 
No proximal vessel occlusion
Interventional Management of Stroke

- The following group of slides summarizes the most relevant results of the clinical trials supporting the different current available interventions for acute stroke.
- The first group of slides review the intra-arterial thrombolytic injection and illustrate a clinical case.
IA Thrombolysis

- Based on the observation that large clots tend to respond less to IV rTPA
- There are no guidelines for the use of IA thrombolytics and there is no FDA approved IA drug-lysis
- Prolyse in Acute Cerebral Thromboembolism Trials (PROACT I and II) were the first large trials to investigate the efficacy and safety of IA thrombolysis with prourokinase (proUK)


<table>
<thead>
<tr>
<th></th>
<th>r-proUK n=121</th>
<th>Control n=59</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful Recanalization</td>
<td>66%</td>
<td>18%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Symptomatic Hemorrhage</td>
<td>10%</td>
<td>2%</td>
<td>0.06</td>
</tr>
<tr>
<td>Outcome 90 days (RS less than or equal to 2)</td>
<td>40%</td>
<td>25%</td>
<td>0.04</td>
</tr>
<tr>
<td>Mortality</td>
<td>25%</td>
<td>27%</td>
<td>0.80</td>
</tr>
</tbody>
</table>
53-year-old man with sudden onset of shaking of the left side of the body while he was driving

He tried to pull over the car and hit a telephone pole

Paramedics were called and he was found to have left sided weakness and right gaze deviation

MRI demonstrates a perfusion defect on the right parietal region
Before intervention

Angiogram showing right MCA occlusion and perfusion defect
After intervention

The arrows show the right middle cerebral artery open
Currently only two mechanical devices have FDA approval: the MERCI device and the Penumbra device.
The MERCI device was developed at UCLA and our interventionalists have one of the most extensive experiences in the use of this technique.
IA Mechanical Thrombolysis

Clinical Trials for MERCI approval

MERCI Investigators. Stroke. 2008;39:000-000

Link to movie with procedure
http://www.concentric-medical.com/APM0116_B_L5%20Animation_Short.wmv
MERCI Thrombolysis

- 30 year old female, 2 weeks post partum
- Symptom Onset to Treatment – 5h 37min

Before Intervention: Arrow shows complete occlusion of the left middle cerebral artery.

After Intervention: Arrow shows complete recanalization of the left middle cerebral artery.
Interventional Management of Stroke

- The next slide demonstrates a large mismatch between the brain tissue already stroked and the “penumbra” territory (arrows) susceptible for salvage interventions.
MERCI Thrombolysis

- 41 year old male
- New onset right paralysis and impossibility to speak
- The perfusion study shows in a green triangle the extension of tissue at risk
MERCI Thrombolysis

- Same patient
- Before intervention: Angiography demonstrates left middle cerebral artery occlusion (Arrows)
MERCI Thrombolysis

- Same patient
- After MERCI treatment the brain arteries are open (arrows)
The intervention prevents progression of the stroke. The green triangular area shows the area that could have progressed to stroke with no intervention. Patient recovered function in his right side and regained normal speech.
Interventional Management of Stroke

- The next slide summarizes new technologies undergoing clinical trials for the treatment of acute stroke.
- UCLA is part of two clinical trials using the SENTIS balloon for stroke patients.
Cerebral Perfusion Augmentation

- Preclinical research: Partial aortic balloon occlusion induced 30% increase in cerebral perfusion

- Clinical feasibility studies:
  - 29 patients
  - Up to 12 hours from symptoms onset
  - 60% improved 3 points in NIHSS during treatment and at 24 h

- Ongoing clinical trial:
  - 87 patients enrolled NIHSS 5-18
  - Up to 10 hours from symptoms onset
  - Interim safety: 5.9% mortality in treated group and 19.4% in controls
  - No serious adverse events

Shuaib A. Stroke Conference. February, 2008
Endovascular Treatment of Carotid Disease
81 y/o male

Past history:

- Severe coronary disease with bypass surgery
- Right Carotid surgery in 1986
- Severe shortness of breath x 6 months and episodes of dizziness when standing up

Cardiac Echo:

- Severe cardiac failure
- Severe aortic stenosis (Aortic valve area: 0.4 cm, gradient: 33 mmHg)

Cardiac cath:

- Occlusion of all vein grafts, 4 vessel severe disease only patent mammary to a diagonal branch
- Complete occlusion of the right internal carotid artery
- The arrow shows severe occlusion of the left internal carotid artery (83%)
• The patient has a very high risk to undergo surgery (Carotid endarterectomy CEA) for opening of the severely occluded left carotid artery.

• With that occlusion he could not undergo the aortic valve replacement and coronary surgery necessary to correct his cardiac problems.

• Carotid angioplasty and stenting (CAS) was successfully performed as illustrated in the next slide.

• Patient then underwent a successful cardiac surgery.
Before

Stent in place (arrow)

After (Notice improved caliber of the vessel)
Patient underwent aortic valve replacement and CABG under cardiac arrest

No stroke after 7 months of CAS
Extracranial carotid disease accounts for 25% of ischemic strokes.

CEA is the gold standard for carotid revascularization.

CEA is supported by solid class IA evidence.

- NASCET (North American Symptomatic Carotid Endarterectomy Trial)
- ECST (European Carotid Surgery Trial)
- ACAS (Asymptomatic Carotid Atherosclerosis Study)
- ACST (Asymptomatic Carotid Surgery Trial)
<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Perioperative S/D</th>
<th>Outcome measure</th>
<th>Medical</th>
<th>CEA</th>
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<tbody>
<tr>
<td>NASCET</td>
<td>≥ 70% Symptomatic</td>
<td>5.8%</td>
<td>2yr Ipsilateral stroke/death</td>
<td>26%</td>
<td>9%</td>
</tr>
<tr>
<td>ECST</td>
<td>≥ 70% Symptomatic</td>
<td>6.8%</td>
<td>3yr Ipsilateral stroke/death</td>
<td>26.5%</td>
<td>14.9%</td>
</tr>
<tr>
<td>ACAS</td>
<td>≥ 60% Asymptomatic</td>
<td>2.3%</td>
<td>5yr Ipsilateral stroke/death</td>
<td>11%</td>
<td>5.1%</td>
</tr>
<tr>
<td>ACST</td>
<td>≥ 60% Asymptomatic (utz)</td>
<td>3.1%</td>
<td>5yr Ipsilateral stroke</td>
<td>11% (Deferred CEA)</td>
<td>3.8% (Immediate CEA)</td>
</tr>
</tbody>
</table>

NASCET. NEJM 1991;325:445-453  
ECST. Lancet 1991;337:1235-43  
ACAS. JAMA 1995;273:1421-28  
ACST. Lancet 2004;363:1491-502
<table>
<thead>
<tr>
<th>Registry</th>
<th>Number of patients</th>
<th>30 day S/D rates</th>
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<tbody>
<tr>
<td>CABERNET 1</td>
<td>462</td>
<td>3.9 %</td>
</tr>
<tr>
<td>Boston Scientific™ Filter Wire EX/EZ™ + EndoTex NexStent™</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARCHeR 2</td>
<td>581</td>
<td>6.9 %</td>
</tr>
<tr>
<td>Abbott™ Acculink™ +Accunet™</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CREATE 3</td>
<td>419</td>
<td>6.2 %</td>
</tr>
<tr>
<td>ev3™ Evolution™</td>
<td></td>
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<tr>
<td>CAPTURE 4</td>
<td>3,500</td>
<td>6.3 % (and MI)</td>
</tr>
<tr>
<td>Abbott™ Acculink™ +Accunet™ (Post approval)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BEACH 5</td>
<td>747</td>
<td>5.8 % (and MI)</td>
</tr>
<tr>
<td>Boston Scientific™</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CASES-PMS 6</td>
<td>1,493</td>
<td>5 %</td>
</tr>
<tr>
<td>Cordis™ Angioguard™</td>
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</tr>
</tbody>
</table>

1. Hopkins LN EuroPCR Conference May 24-27, 2005, Paris France
2. Gray WA. J Vasc Surg 2006; 44:258-68
**2008 Stein Oppenheimer Endowment Award**

Drs Gonzalez & Vinuela's

**ENDOVASCULAR STROKE MODEL**

Drs. Nestor Gonzalez and Fernando Vinuela have been selected to receive the 2008 Stein Oppenheimer Endowment Award, a private grant from "Ijane inc."

Stroke is the leading cause of disability and third cause of death in the United States. Much of the research necessary to test new therapeutic strategies for stroke are limited by the current animal models which do not replicate the complexities of human stroke. Drs Gonzalez and Vinuela's awarded proposal of endovascular stroke model will allow for a more accurate simulation of human stroke conditions, utilizing minimally invasive techniques. Scientists and clinicians will benefit from a new model that can be used for molecular studies and new therapy testing.
Links to Additional UCLA Stroke Intervention and Research

- [http://www.stroke.ucla.edu/research](http://www.stroke.ucla.edu/research)
- [http://www.aneurysm-stroke.com](http://www.aneurysm-stroke.com)
- [http://strokeprotect.mednet.ucla.edu](http://strokeprotect.mednet.ucla.edu)