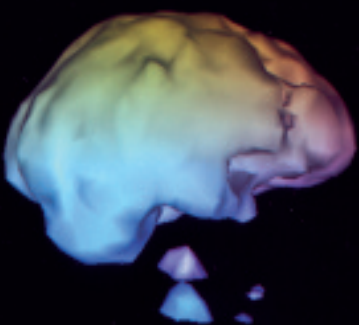
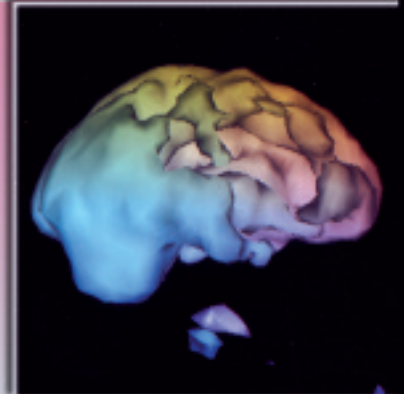
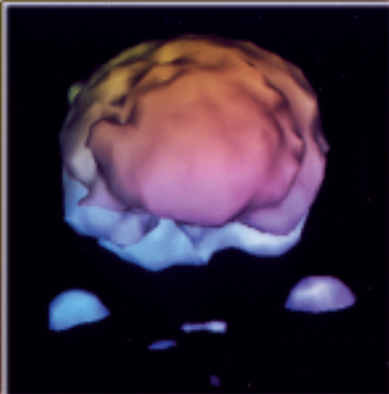
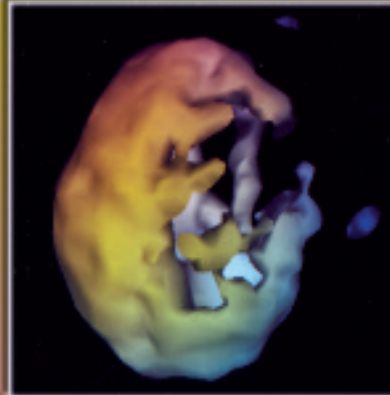
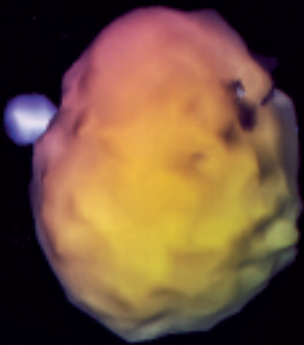
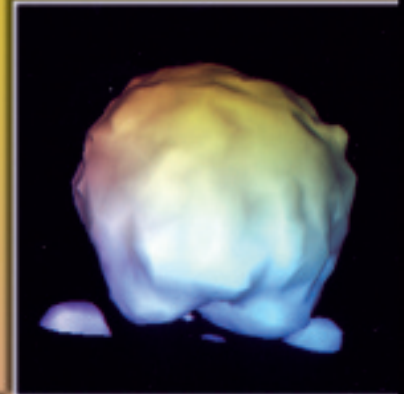
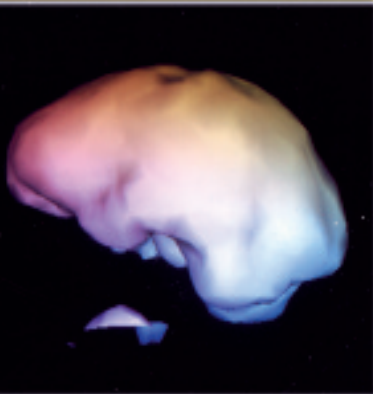


JANUARY 2007

# NNI JOURNAL

VOL. 3 • ISSUE 1



The  
*neuro*logical  
choice.

# Celebrating Progress



*Stanley N. Cohen, M.D.*



*John A. Anson, M.D.,  
F.A.C.S.*

*With 2006 coming to a close, the editors would like to use this time to reflect on the past year and begin to plan for 2007. This year has been marked with many successes for The Nevada Neurosciences Institute at Sunrise and for the NNI Research Foundation. We set very high goals in the areas of patient care, research and education. In looking back, we take great pride in our accomplishments in all three areas.*

*In the field of patient care, our most outstanding achievement was receiving JCAHO certification as a Primary Stroke Center, the only hospital in Southern Nevada to achieve this status. Led by Dr. Scott Selco, Director of Stroke Care at Sunrise, and a team of very dedicated neurologists, neurosurgeons, neuroradiologists and neurological nurses, Sunrise Hospital and Medical Center was able to demonstrate the ability to deliver a level of care to stroke patients that rivals the care given at any major medical center in the country.*

*Participation in cutting edge clinical research is one way to assure that our patients are receiving the latest medical and surgical treatments available. We now have several clinical trials in neurology and neurosurgery active in the Las Vegas area. There are currently four trials ongoing in stroke prevention, five trials in acute stroke treatment, five trials in dementia, one study in neuro-oncology, one in treatment of headache, and one in the surgical management of spinal disorders.*

*Outstanding medical education is a cornerstone in assuring that medical care in our community is of the highest quality. We are proud of our role in contributing to neuroscience education during this past year. The NNI at Sunrise together with the NNI Research Foundation were able to organize several educational opportunities including monthly Neurology/Neurosurgery Grand Rounds with featured topics that included cerebrovascular disease, movement disorders, headache, epilepsy, and interventional neuroradiology. For future topics and dates, please consult our web page at [www.sunrisecme.com](http://www.sunrisecme.com). The educational highlight of the year was our all-day conference held last April attended by 150 medical professionals. From the positive feedback we received, we are currently planning our second annual conference, on March 31, 2007, at the Red Rock Resort and Casino. Registration information for the conference is available on the web page.*

*While we take pride in our successes this past year, the editors are particularly encouraged with the development of the **NNI Journal**. In this issue, we have a paper on the Pearls and Pitfalls in Treating Intracerebral Hemorrhage contributed by Dr. Brett Cucchiara from the University of Pennsylvania. Dr. Jason Garber prepared an update on innovations in motion preservation spinal surgery. Drs. Lindsey Blake and Stanley Cohen wrote on the use of CT perfusion in the management of difficult cerebrovascular cases. We are currently preparing our next issue to be published in April 2007. We look forward to providing the same high quality papers on relevant topics in the field of neuroscience with each coming issue.*

**Stanley N. Cohen, M.D.**

**John A. Anson, M.D., F.A.C.S.**



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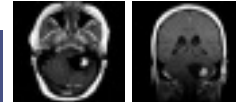
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### On The Cover

*Images from a SPECT scan before and after Diamox administration. In the third row, the images on the left is pre-Diamox. It shows a small right hemispheric deficit. After the Diamox, there is a large defect in the right MCA distribution indicating impaired cerebrovascular reserve.*

# Intracerebral Hemorrhage: Pearls and Pitfalls

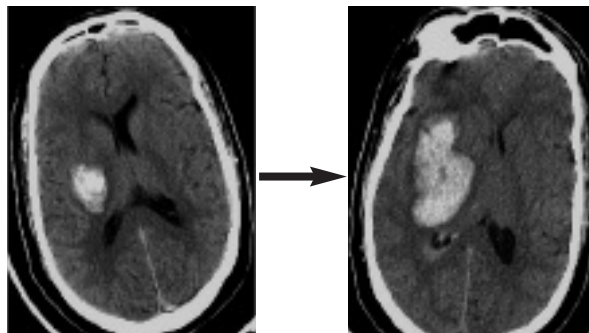


Only since the mid-1970s, when the first CT scanners became available, have clinicians had the ability to accurately diagnose intracerebral hemorrhage (ICH) non-invasively. Much of what we know about ICH, therefore, has been learned in just the last 30 years – a somewhat remarkable commentary on a disease that affects an estimated 63,000 patients per year and is associated with tremendous morbidity and mortality.<sup>1</sup> It may well be that we have only now engaged the steep part of the learning curve about this disease. In this brief collection of pearls and pitfalls, I highlight a few aspects of ICH which I consider either essential to clinical practice, or representative of important new concepts about this disease.

## **Pearl:**

***Patients with early acute ICH have not just “had a bleed” – they are bleeding.***

There is still a tendency to think of intracerebral hemorrhage as an instantaneous process, analogous to a balloon popping. However, it is now clear that within the first few hours after symptom onset, most patients with ICH have active continued bleeding into the brain parenchyma. (**Figure A**) This was shown most elegantly in a study by Brott et al using serial CT scanning of patients with acute ICH.<sup>2</sup> Of patients who presented within 3 hours of symptom onset, 26% had a greater than one-third enlargement in the size of their ICH when the CT was repeated 1 hour later, and an additional 12% had enlargement over the next 20 hours. A subsequent study pooling this data with the results from additional studies found that 72.9% of patients scanned within 3 hours of symptom onset had some degree of hemorrhage expansion at 24 hours.<sup>3</sup> Contrast extravasation, likely representing ongoing bleeding, has been demonstrated in 46% of acute ICH patients undergoing CT angiography.<sup>4</sup> Not surprisingly, hemorrhage expansion is independently associated with subsequent disability and mortality.



**Figure A**  
A 45 year old man presented with mild left hemiparesis. He had significant neurologic deterioration in the Emergency Department. CT scan at presentation (left) and one hour later (right) shows dramatic hematoma enlargement.

## **Pitfall:**

***The earlier a patient presents, the greater the danger of early hemorrhage expansion.***

This is the corollary to the Pearl presented above. Hemorrhage enlargement is an early process, occurring largely within the first 3-6 hours after symptom onset. Enlargement after 24 hours is relatively uncommon. Thus, the patient presenting immediately after symptom onset, even those with relatively minor neurologic deficits, must be assumed to be unstable. Further, any therapies implemented with a goal of stopping hemorrhage expansion must be started in the hyperacute phase. For instance, if blood pressure lowering is pursued in an attempt to prevent hemorrhage expansion, it should begin immediately in the Emergency Department, not the following morning when the patient is seen on rounds in the ICU.

## **Pearl:**

***Intracerebral hemorrhage is a treatable disease.***

Evidence is accruing that much can be done to help the patient with intracerebral hemorrhage. Therapeutic interventions ranging from intensive supportive care in a specialized stroke or neurointensive care unit to aggressive procoagulant therapy have been shown to improve outcome.<sup>5-7</sup> For example, recombinant activated factor VII (rFVIIa), a procoagulant agent, was recently shown in a randomized, controlled trial to dramatically reduce hemorrhage expansion and improve functional outcome in patients with spontaneous ICH treated within 4 hours of symptom onset.<sup>6</sup> In this study, 400 patients with acute ICH were randomly assigned to placebo or one of three doses (40 ug/kg, 80 ug/kg, and 160 ug/kg) of rFVIIa. Patients were required to undergo CT scanning within 3 hours of symptom onset, and to receive study drug within one hour of the CT. Hematoma



*Brett Cucchiara, M.D.*

expansion on follow-up CT at 24 hours, the primary outcome measure, was significantly reduced in the rFVIIa treated groups. Further, there was a significant absolute mortality reduction of about 10%, and a significant reduction in death or disability of about 15% (secondary outcomes). Thromboembolic adverse events were increased in rFVIIa compared to placebo treated patients (7% vs. 2%). These results have prompted a larger, phase III study which is nearing completion.

**Pearl:**

***Diagnostic investigation in an older person with hypertension and a deep intracerebral hemorrhage is unlikely to be revealing.***

A common issue facing clinicians is the decision about what diagnostic tests to order in the individual patient with spontaneous ICH. MRI with or without MR angiography, CT angiography, and catheter angiography may all have a role in select patients. These tests are often used to identify abnormalities, such as arteriovenous malformations and tumors, which may have significant management implications. But who should get what test? As a general rule, several factors can be used to assess the likelihood that these tests will provide relevant additional information. These include the age of the patient, the presence of pre-existing hypertension, and the location of the intracerebral hemorrhage. (**Table 1**)

Zhu et al examined the role of diagnostic catheter angiography in patients with spontaneous ICH.<sup>8</sup> In their study, they prospectively examined 206 consecutive patients using brain CT and catheter angiography. An underlying vascular abnormality was identified more frequently in patients 45 years of age and in those without pre-existing hypertension. More specifically, the yield of angiography in patients 45 years of age and without preexisting hypertension was 48% with putaminal, thalamic, or cerebellar ICH and 65% with lobar ICH. In contrast, the yield in patients > 45 years of age and with pre-existing hypertension was 0% with putaminal, thalamic, or cerebellar ICH and 10% with lobar ICH. (**Figure 1**)

Tayal et al examined the role of

**TABLE 1**

	<b>Expand Diagnostic Testing</b>	<b>Limit Diagnostic Testing</b>
Age	Young	Old
Pre-existing Hypertension	Absent	Present
ICH Location	Lobar	Deep or Cerebellar

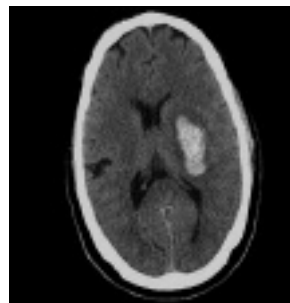
MRI in hospitalized patients with spontaneous deep (basal ganglia or thalamus) ICH.<sup>9</sup> Of 228 patients with deep ICH over a 15 year period at their institution, 97 underwent brain MRI. In only 3/97 (3.2%) did the MRI suggest a diagnosis other than hypertension – 2 cases of amyloid angiopathy and 1 case of moyamoya disease. Thus, MRI in the hospitalized patient with a deep ICH is very low-yield.

**Pitfall:**

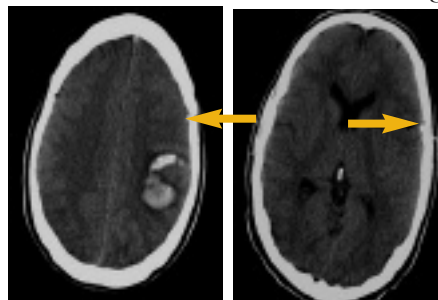
***Don't forget cerebral vein thrombosis as a cause of ICH.***

A frequently overlooked cause of ICH is cerebral vein thrombosis (CVT). CVT typically causes lobar as opposed to deep hemorrhage, often affecting the temporal lobe when the vein of Labbe is affected. Venous infarction may also be present. Diagnosis can be challenging. More than half of patients with CVT report the subacute onset of neurologic symptoms,<sup>10</sup> which is extraordinarily uncommon in patients with other causes of ICH. Other clues to the diagnosis include a prodrome of headache and visual symptoms and the presence of risk factors for a hypercoagulable state. Imaging studies showing bilateral lesions, the combination of infarct and hemorrhage, or infarctions not in an arterial distribution also suggest CVT. Rarely, a thrombosed cortical vein is visible on CT. (**Figure 2**) More typically, MR venography, CT venography, or catheter angiography is required to confirm or exclude the diagnosis.

CVT is not caused by hypertension, nor is there a role for blood pressure lowering in its management. Evidence suggests that patients with



**Figure 1**  
Head CT demonstrates a deep ICH in the left putamen. In an older patient with hypertension, additional diagnostic evaluation is likely to be unrevealing.



**Figure 2**  
Head CT demonstrates a thrombosed superficial cerebral vein (arrow) in addition to a lobar ICH.

CVT treated with anticoagulation have improved outcome, even in the presence of hemorrhage. Though this is not entirely without controversy, most experts would immediately start intravenous heparin or low molecular weight heparin in a patient with ICH confirmed due to CVT.<sup>11</sup> Given that this treatment is the exact opposite of therapy for most patients with ICH, accurate diagnosis is clearly essential, and a high-index of suspicion necessary.

**Pitfall:**

**The patient with cerebellar hemorrhage needs immediate neurosurgical consultation.**

Surgical treatment for supratentorial intracerebral hemorrhage remains controversial, with a recent large randomized controlled trial showing no overall benefit.<sup>12</sup> However, patients with cerebellar hemorrhage represent a unique population for which consensus expert opinion favors a clear role for surgery.<sup>13</sup> Two factors account for this. First, mass effect resulting from cerebellar hemorrhage can result in direct brainstem compression and, due to compression of the fourth ventricle, acute obstructive hydrocephalus. In these situations, rapid and unpredictable clinical deterioration can occur.<sup>14</sup> Second, because the cerebellar hemispheres are superficial, surgical decompression may be undertaken without significant injury to surrounding eloquent brain tissue, and patient outcomes may be remarkably good. The combination of these two factors can be synthesized into a simple clinical rule: cerebellar hemorrhage = immediate neurosurgical evaluation. In hospital settings without neurosurgical coverage, rapid transport to a facility with this capability is indicated. Detailed schemes to assist in clinical decision making regarding surgical intervention in patients with cerebellar hemorrhage have been published, but are beyond the scope of this article.<sup>13, 15</sup>

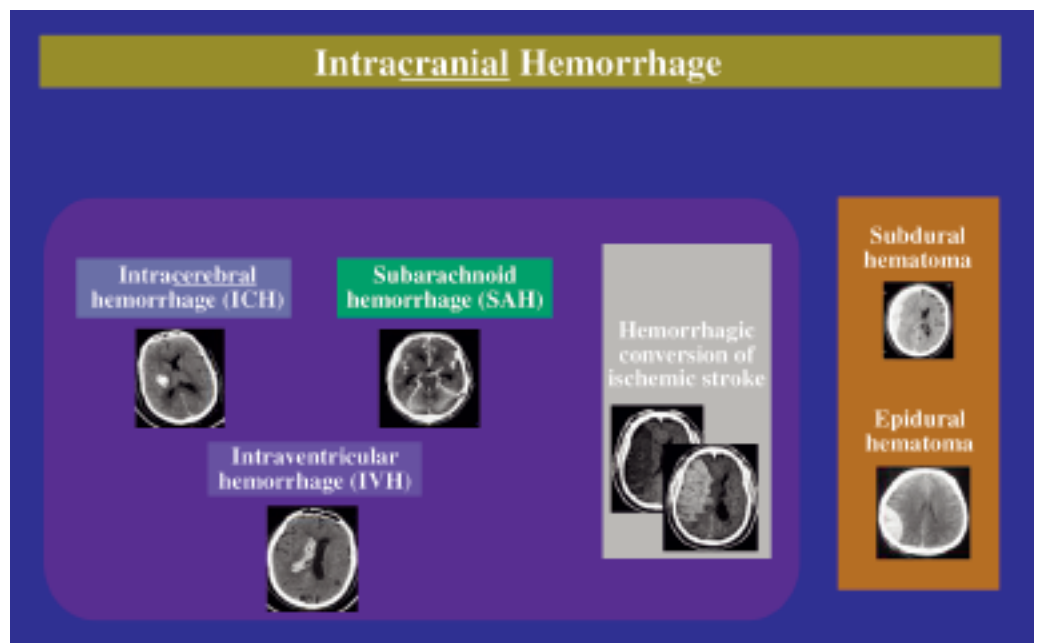
**Pitfall:**

**The terms intracranial hemorrhage, intracerebral hemorrhage, and hemorrhagic stroke are often used interchangeably – and incorrectly.**

Intracranial hemorrhage refers to any bleeding within the cranial vault, and includes subdural and epidural hematomas, in addition to intracerebral hemorrhage and subarachnoid hemorrhage. Intracerebral hemorrhage refers specifically to bleeding within the brain parenchyma, as for example a typical hypertensive hemorrhage. While the term hemorrhagic stroke can be used to refer to either of the above, but may also be used in reference to an ischemic stroke into which bleeding occurred. Because the term “hemorrhagic stroke” is open to different interpretations, it is best avoided. (Figure 3) An ischemic stroke into which bleeding has occurred is best described as hemorrhagic conversion.

**REFERENCES**

1. American Heart Association. Heart Disease and Stroke Statistics - 2006 Update. Circulation 2006;113:e85-e151.
2. Brott T, Broderick J, Kothari R, Barsan W, Tomsick T, Sauerbeck L, Spilker J, Duldner J, Khoury J. Early hemorrhage growth in patients with intracerebral hemorrhage. Stroke 1997;28(1):1-5.
3. Davis SM, Broderick J, Hennerici M, Brun NC, Diringer MN, Mayer SA, Begtrup K, Steiner T. Hematoma growth is a deter-



**Figure 3**  
A 45 year old man presented with mild left hemiparesis. He had significant neurologic deterioration in the Emergency Department. CT scan at presentation (left) and one hour later (right) shows dramatic hematoma enlargement.

minant of mortality and poor outcome after intracerebral hemorrhage. *Neurology* 2006;66(8):1175-81.

4. *Becker KJ, Baxter AB, Bybee HM, Tirschwell DL, Abouelsaad T, Cohen WA.* Extravasation of Radiographic Contrast Is an Independent Predictor of Death in Primary Intracerebral Hemorrhage. *Stroke* 1999;30(10):2025-2032.
5. *Diringer MN, Edwards DF.* Admission to a neurologic/neurosurgical intensive care unit is associated with reduced mortality rate after intracerebral hemorrhage. *Crit Care Med* 2001;29(3):635-40.
6. *Mayer SA, Brun NC, Begtrup K, Broderick J, Davis S, Diringer MN, Skolnick BE, Steiner T.* Recombinant activated factor VII for acute intracerebral hemorrhage. *N Engl J Med* 2005;352(8):777-85.
7. *Varelas PN, Conti MM, Spanaki MV, Potts E, Bradford D, Sunstrom C, Fedder W, Hacein Bey L, Jaradeh S, Gennarelli TA.* The impact of a neurointensivist-led team on a semiclosed neurosciences intensive care unit. *Crit Care Med* 2004;32(11):2191-8.
8. *Zhu XL, Chan MSY, Poon WS.* Spontaneous Intracranial Hemorrhage: Which Patients Need Diagnostic Cerebral Angiography?: A Prospective Study of 206 Cases and Review of the Literature. *Stroke* 1997;28(7):1406-1409.
9. *Tayal A UK, Gupta R, Kromer H, Vora N, Jovin T, Wechsler L, Hammer M.* MRI in deep nuclear intracerebral hemorrhage is over utilized and has low yield. *Stroke* 2006;37(2):675.
10. *Ferro JM, Canhao P, Stam J, Bousser M-G, Barinagarrementeria F,* for the II. Prognosis of Cerebral Vein and Dural Sinus Thrombosis: Results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke* 2004;35(3):664-670.
11. *Stam J.* Thrombosis of the Cerebral Veins and Sinuses. *N Engl J Med* 2005;352(17):1791-1798.
12. *Mendelow AD, Gregson BA, Fernandes HM, Murray GD, Teasdale GM, Hope DT, Karimi A, Shaw MD, Barer DH.* Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomized trial. *Lancet* 2005;365(9457):387-97.
13. *Mathew P, Teasdale G, Bannan A, Oluoch-Olunya D.* Neurosurgical management of cerebellar haematoma and infarct. *J Neurol Neurosurg Psychiatry* 1995;59(3):287-92.
14. *St. Louis EK, Wijidicks EF, Li H.* Predicting neurologic deterioration in patients with cerebellar hematomas. *Neurology* 1998;51(5):1364-1369.
15. *Kirollos RW, Tyagi AK, Ross SA, van Hille PT, Marks PV.* Management of spontaneous cerebellar hematomas: a prospective treatment protocol. *Neurosurgery* 2001;49(6):1378-86; discussion 1386-7.

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## CEREBROVASCULAR CASE CONFERENCE

**January 19, February 2 & 16, March 2 & 16**

Neurologists, neurosurgeons, interventional radiologists, and other health care providers interested in the management of cerebrovascular disease are invited to attend.

We encourage presentation of interesting or challenging cases for discussion.

For more information, call Dr. Cohen at 731-8115.

**Sunrise Hospital Physician's Conference Room**

**7:00 AM to 8:00 AM**

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# Using Technology to Improve Outcomes with Thrombolysis

*"The neurologic armamentarium should be aimed before it is fired"*  
DR. WILLIAM OLDENDORF, circa 1980

In 1995, the results of the two NINDS trials using intravenous tPA (IV tPA) to treat acute ischemic stroke reported their final results demonstrating, for the first time, the potential for significantly reversing the effects of ischemic stroke.<sup>1</sup> Within one year, the FDA approved IV tPA for use in treating acute ischemic stroke in the United States. Over a decade later, despite the potential for dramatic reversal of a devastating illness, the use of a thrombolytic intervention has failed to gain widespread support.

There are many reasons for the limited application of this intervention. One of the main reasons given for failing to administer the drug, even in stroke centers with systems in place to give the drug in a timely fashion, is the limited time window. While the NINDS trials demonstrated benefit of IV tPA when given in the first 3 hours, the analysis of the data indicated a decrease in efficacy with each passing minute and no benefit once the 3 hour limit was passed. The European tPA trials and the Atlantis trials each failed to show efficacy when the window for use was at 5 or 6 hours.<sup>2,3</sup> However, the pooled analysis of IV tPA trials suggested the potential for benefit out to 4.5 hours after stroke onset. This has not been proven in a prospective trial.

Trials using interventions to recanalize vessels in acute stroke other than IV tPA demonstrated the potential for tissue salvage well beyond the 3 hour window. A trial using an intra-arterial thrombolytic agent demonstrated positive benefits of the agent up to 8 hours after stroke onset.<sup>4</sup> Based on positive clinical trials, a clot retrieval device, the MERCI device, was recently approved by the FDA.<sup>5</sup> It is being used up to 6 hours after stroke onset with promising results.

Efforts to recanalize an occluded vessel after ischemic stroke, whether with an intravenous thrombolytic, intra-arterial thrombolytic, or a mechanical device, has potential for serious, and potentially life threatening side effects. Within the first 3 hours, the benefits clearly outweigh the risks. In order to extend the window and keep the risk/benefit ratio favoring

aggressive intervention, steps must be taken to improve patient selection. The neurologic armamentarium must be aimed better.

In the ideal world, we would have a technology that would allow us to select patients for a potentially dangerous intervention who would have the greatest amount to gain (large amounts of tissue at risk with minimum unsalvageable tissue), eliminate patients who have nothing to gain despite low risk (stroke mimics), and have pause before treating patients where the area of damage is so great before treatment that any potential gain will still leave a severely devastated patient. In this paper, we will discuss the application of a readily available technology, multimodal computerized tomography (CT) scanning, that has the potential to dramatically improve patient selection for recanalization therapy.



*Stanley N. Cohen, M.D.*



*Lindsey Blake, M.D.*

## Case 1

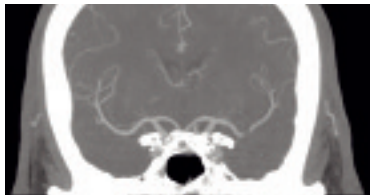
Mr. A was a 61 year old male who was in his usual state of health on the day of admission. It was his custom to arrive at his office at 6:00 AM, before his co-workers arrived at 8:00 AM. At 8:15, his co-workers found him on the floor of his office with mild to moderate right hemiparesis and moderately impaired speech. At the instruction of his family physician, the coworkers bypassed a local hospital and took the patient to our emergency room, about an hour and a half away. The family doctor notified the stroke team and we were awaiting his arrival. Unfortunately, by the time he arrived at 10:45 AM, he was globally aphasic and unable to give any history.

In the emergency room, the patient was awake, alert and very cooperative with the examination. His general medical examination was unremarkable. His neurologic examination was positive for a global aphasia, mild right hemiparesis involving face, arm and

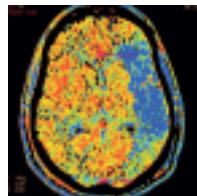


leg and impaired sensory response on the right side of his body.

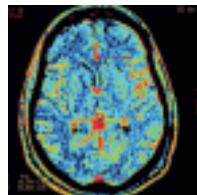
After appropriate blood work, chest x-ray and electrocardiogram, the patient was sent for a stat non-contrast CT of the head, a CT angiogram of the brain, and a CT perfusion of the brain. The non-contrast CT of the brain was entirely normal. The CT angiogram demonstrated a flow gap in the left middle cerebral artery (MCA), in the M1 branch (**Figure 1**). On the CT perfusion scan, the mean transit time scan (MTT) was markedly abnormal in the left MCA distribution, corresponding to the patient's clinical picture and his CT angiography abnormality (**Figure 2**). The cerebral blood volume (CBV) scan demonstrated no abnormality (**Figure 3**).



**Figure 1**  
CT angiogram of the brain, coronal view, demonstrating the distal portions of the bilateral internal carotid arteries, proximal anterior cerebral arteries, and middle cerebral arteries (MCA). The left MCA has a flow gap.



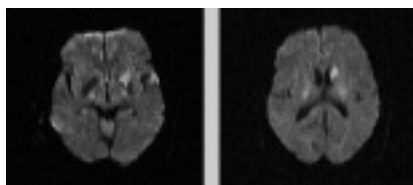
**Figure 2**  
CT mean transit time image showing a delay in a large portion of the middle cerebral artery distribution on the left.



**Figure 3**  
CT cerebral blood volume scan showing normal blood volume in the left MCA distribution.

Because the patient was young and previously healthy, under 6 hours after stroke onset, and because the large mismatch between MTT and CBV scans with an approachable MCA blockage demonstrated on CT angiography, we elected to take this patient to the angiography suite for IA tPA. By the end of the procedure, the vessel was re-canalized.

Clinical examination the next morning found the patient with a minimal speech deficit and normal motor and sensory examinations. The magnetic resonance imaging (MRI) of the brain showed several small hyperintensities on diffusion weighted imaging consistent with distal embolization from the lesion in the M1 segment after it broke up. (**Figure 4**).



**Figure 4**  
MRI diffusion weighted images showing hyperintensities at the cortex and basal ganglia regions (left image) and in the left caudate nucleus (right image).

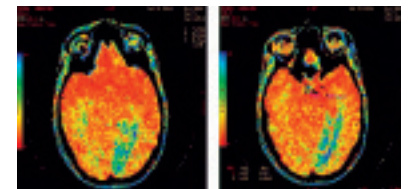
### Case 2

Ms. P was a 22 year old previously healthy female

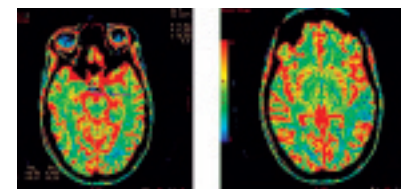
who awoke from an afternoon nap, walked into the her living room, and, while talking to her roommate, developed sudden onset of dizziness, visual disturbance, and problems using her right arm. When the symptoms didn't improve, she came to the Emergency Department about 2 hours after symptom onset. Non-contrast CT was normal. The emergency room physician found a very anxious woman but without hard abnormalities on his examination. He suspected a stroke mimic. Neurology consultation was called about 2 hours 45 minutes after onset. The examination was positive for a slight right pronator drift and a possible partial right field cut. Multimodal CT scanning was performed. The non-contrast CT of the brain and the CT angiogram were normal. The MTT was abnormal demonstrating low flow in the left posterior cerebral artery distribution (**Figure 5**). The CBV was read as normal (**Figure 6**).

A stroke mimic was ruled out. Because of her young age, prior good health, large mismatch on imaging, we treated with IV tPA despite being about 30 minutes beyond the approved 3-hour window. Post-procedure, the patient did well. The MRI scan done the next day showed a small hyperintensity in the left thalamus (**Figure 7**).

Subsequent work-up revealed a patent foramen ovale. She was entered into the CLOSURE 1 trial and randomized to device placement. At one year after her stroke, her exam was positive for a mild sensory abnormality in her right hand.



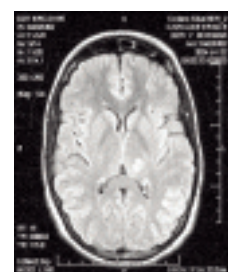
**Figure 5**  
CT mean transit time images demonstrating delay in the left posterior cerebral artery distribution.



**Figure 6**  
CT cerebral blood volume images demonstrating normal blood volume.

### Case 3

Ms. M was a 78 year old female in her usual state of health when, while playing bridge with friends, developed sudden onset of weakness in her right hand and an



**Figure 7**  
MRI FLAIR sequence demonstrating hyperintensity in the left thalamus.

inability to speak. By the time she arrived in the Emergency Department 30 minutes later, her neurologic exam returned to normal. Emergency non-contrast CT of the brain was normal. She was still in the Emergency Department 8 hours later, awaiting an inpatient bed, when she developed sudden onset of right hemiplegia, global aphasia, and decreased level of consciousness. Stat CT scan revealed a new partial loss of the insular ribbon on the left. MTT showed delayed flow through a large portion of the MCA distribution. CBV was decreased in an identical region. Despite the large size of the lesion and the absence of a mismatch between the MTT and the CBV, we administered IV tPA in under 45 minutes after stroke onset (**Figures 8 and 9**).

CT scan done the next day showed a large hypodensity involving the same region as was seen in the MTT and CBV scans (**Figure 10**). The patient developed massive edema and died 3 days later.

## Discussion

A CT protocol for imaging acute stroke should address four key questions in order to triage patients to the appropriate treatment.

1. Is there hemorrhage?
2. Is there an arterial thrombus that can be targeted for treatment?
3. Is there a core of irreversible ischemic tissue?
4. Is there associated penumbra of ischemic but potentially salvageable brain?

Multimodal CT scanning attempts to answer these important questions utilizing three separate components: non-contrast CT of the brain, CT angiography, and CT perfusion imaging. This imaging battery provides an outstanding opportunity to give the treating doctor critical information needed to make decisions about vascular lesion location, degree of tissue injury and degree of tissue at risk but not yet irreversibly injured. The battery can be administered to the majority of stroke patients, adding about 15 minutes to the imaging time compared to the non-contrast CT alone.

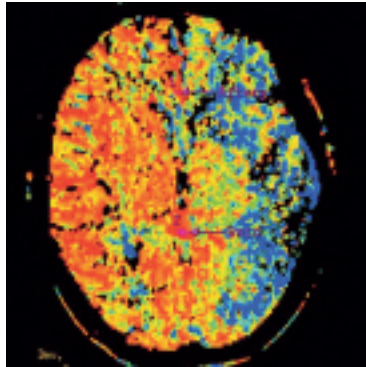
The primary role of non-contrast CT is to distinguish

between hemorrhagic and ischemic stroke. CT findings in early acute ischemic stroke are often absent or subtle and include: loss of the insular ribbon, obscuration of the lentiform nucleus, cortical low density with blurring of the gray-white interface, sulcal effacement, and the hyperdense MCA sign. CT without contrast can also exclude some stroke mimics including tumor, vascular malformations, hydrocephalus and extra-axial fluid collections. The presence of hemorrhage, a well defined ischemic stroke greater than one-third of the MCA territory, and stroke mimics are considered contraindications to thrombolytic treatment.

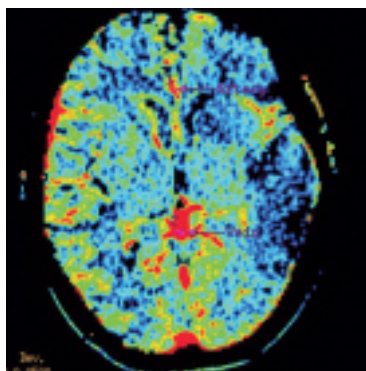
CT angiography and CT perfusion scanning requires administration of a large bolus of contrast material. With careful clinical screening, most patients can receive the contrast without waiting for the results of the blood urea nitrogen and creatinine tests to be completed. The CT angiogram is routinely obtained from the aortic arch to the skull vertex. CT angiography can demonstrate cervical and intracranial arterial patency and we find it useful in localizing the level of occlusion.

CT perfusion (CTP) is the final step in the imaging evaluation of acute stroke. In CTP a rapid bolus infusion of contrast material is given through a large bore needle in an antecubital vein. The bolus passes through the cerebral vascular bed and temporal changes in parenchymal attenuation are demonstrated with multidetector CT. A linear relation exists between contrast concentration and attenuation. CTP provides information on the cerebral blood flow (CBF) MTT, and CBV. The MTT is defined as the average of the transit time of blood through a given brain region. CBF is the volume of blood moving through a given volume of brain per unit time. The CBV measures the amount of blood in a given volume of brain.

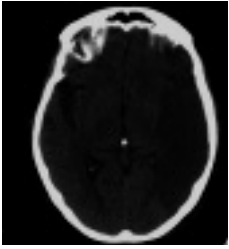
If tissue is at risk but still viable (penumbra), the vessels in the region will dilate, maintaining the total blood volume at a normal or increased level, but have prolonged MTT. If the tissue is no longer viable, the vessels will not dilate and the CBV will be decreased



**Figure 8**  
CT mean transit time showing delay in a large portion of the left MCA distribution.



**Figure 9**  
CT cerebral blood volume images demonstrating marked decrease in the left MCA distribution.



**Figure 10**  
Non-contrast CT of the brain showing low attenuation in a large portion of the left MCA distribution.

and have matched MTT and CBF deficits. Potentially salvageable tissue at-risk will demonstrate a mismatch between the smaller central core of decreased CBV compared to the larger surrounding MTT and CBF abnormalities. These patients are potentially good candidates for aggressive management.. General

guidelines for CTP interpretation are found in **Table 2**.

**TABLE 2. Guidelines for CTP interpretation.**

- Matched MTT and CBF defect:  
No treatment
- Large MTT defect with larger CBF abnormality:  
Possible treatment based on size and time of symptom onset
- Small MTT defect with larger CBF abnormality:  
Potential good candidates for treatment depending on time after ictus

CT perfusion imaging has been shown to be equivalent with MRI diffusion and perfusion studies in identifying cerebral penumbra in acute ischemic stroke.<sup>6</sup> The advantages of multimodal CT imaging compared to multimodal MRI imaging include:

1. Multimodal CT imaging can be performed on fast multislice CT scanners currently available near many large hospital emergency departments.
2. Less scanning time is required compared to MRI.
3. Less patient cooperation is required for the CT, and can be easily performed on critically ill patients.
4. Patients with pacemakers and other metal implants can be tested.

Disadvantages of multimodal CT compared to MRI include:

1. CTP can only image 4 slices of the brain, so the clinician must know which slices to choose to see the lesion before the scan is done.
2. CTP does not adequately image the posterior fossa.
3. Multimodal CT requires administration of potentially nephrotoxic contrast material.
4. Small lesions, such as lacunar infarctions, will not be visualized.

5. Exposure to ionizing radiation.
6. Post processing is labor-intensive.

The 3 cases described are good examples of the useful information the treating physician can get in a timely fashion. In the first case, we were able to determine that the patient had a very large region at risk but that it was still viable. Additionally, were able to determine that the blockage was in a vessel that could easily be reached by our interventional radiologist.

In the second case, we were able to determine that the patient had true ischemia and not a stroke mimic. We saw a large area of brain that was at-risk but still viable. In this case, the imaging gave us confidence to use the IV tPA off-label to potentially salvage an important portion of her left hemisphere.

In the third case, we saw that the patient had a very large ischemic area with no mismatch. This is considered a “malignant MCA syndrome.” Preliminary data suggest that when the core of infarction is this large, the patient will do poorly even if there is a mismatch and tPA is given. Because the patient fell within the guidelines for giving tPA, and because the data defining the malignant MCA syndrome are preliminary, we felt giving the tPA was appropriate though unlikely to help. In the future, when the malignant MCA syndrome is better defined, multimodal CT will be able to help spare patients from futile interventions.

Multimodal CT imaging is a rapid, convenient, safe method of imaging acute stroke. It provides critical information for selecting appropriate patients for more aggressive management. However, many questions are still unanswered and ongoing clinical trials will prove if our assumptions about the clinical utility of these techniques are of real value. Until the data are available, using imaging to deny treatment to patients who fall within the guidelines for intervention is not appropriate. However, it may be reasonable at this time to use these techniques to offer more aggressive management to properly selected and informed patients.

## REFERENCES

1. CT cerebral blood volume images demonstrating marked decrease in the left MCA distribution.
2. Hacke W, Kaste M, Fieschi C, et al. randomized double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke. *Lancet*, 1998. 352: 1245-1251.

3. *Clark WM, Wissman S; Albers GW; Jhamandas JH, Madden KP; Hamilton S; for the ATLANTIS Study Investigators.* Recombinant Tissue-Type Plasminogen Activator (Alteplase) for Ischemic Stroke 3 to 5 Hours After Symptom Onset: The ATLANTIS Study: A Randomized Controlled Trial. *JAMA* 1999;282:2019-2026.
4. *del Zoppo GJ, Higashida R, Furlan A, et al.* PROACT: a phase II randomized trial of recombinant pro-urokinase by direct arterial delivery in acute middle cerebral artery stroke. *Stroke*, 1998. 29: 4-11.
5. *Smith WS, Sung G, Starkman S, et al.* Safety and Efficacy of Mechanical Embolectomy in Acute Ischemic Stroke Results of the MERCI Trial. *Stroke*, 2005;36:1432-1440.

6. *Wintermark M, Reichhart M, Thiran JP, et al.* Comparison of admission perfusion computed tomography and qualitative diffusion- and perfusion- weighted magnetic resonance imaging in acute stroke patients. *Stroke*, 2002;33:2025-2031.

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# Dynamic Stabilization of the Lumbar Spine: Past, Present and Future Innovations



The lumbar spine and its components are still not completely understood. Consequently our ideas about lumbar functional anatomy and dynamic force distribution have recently changed due to an increasing number of biomechanical studies and computer models which have specifically focused on characterizing dynamic patterns and force distribution of the lumbar spine in motion.<sup>5</sup>

Despite frequent success in patient care, today's standard spine techniques are not as consistently successful as most physicians would like.<sup>3</sup> Clinical trials examining the success of lumbar fusion procedures report a success rate up to 80%.<sup>1,8</sup> Although numerous lumbar fusion techniques have been developed and refined, it is difficult to achieve 100% success rates. Furthermore, spine surgeons have observed the phenomenon of adjacent segment-related complications in their fusion patients. Adjacent segment level disease occurs at the level above or below a fusion in the spine, producing subsequent pain. While the cause of this observed phenomenon is uncertain, one potential explanation stems from the fact that while a large percentage of the axial spinal load can be removed from a damaged segment with traditional fusion techniques, the forces must translate elsewhere in the spine. In general, they are transferred to adjacent levels.<sup>6</sup> Though the adjacent levels appeared clinically asymptomatic prior to surgery, it is hypothesized that the transfer of additional forces over time can cause adjacent disk disease and subsequent degeneration. Studies of other weight bearing joints such as the knee, have shown well documented evidence that abnormal load transmissions have a high correlation with degenerative joint changes.<sup>7,9</sup> Additional hypotheses have suggested that adjacent segment disease in the spine results from genetic factors and is less influenced by loading patterns. However, results from this hypothesis lack supportive evidence from controlled clinical trials.

In response to the relative limitations of fusion procedures, emerging technology in the lumbar spine is focusing on motion preservation via dynamic stabilization. The biomechanical concept centers on the stabilization of lumbar mechanical forces that can be

distributed to adjacent segments in a more controlled, natural fashion. As we continue to see more advances in the treatment of lumbar spinal disease into the 21st century, we wish to review the newest developments, and future innovations in the treatment of lumbar spinal degenerative disease. These technological advances in motion preservation may indeed become the next frontier in spine surgery.



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(pictured above)  
John S. Thalgott, M.D.,  
Madilyne Fogarty, B.S.  
and  
Steven P. Caiazza, B.S.*

Although the concept of dynamic stabilization has been inspired by the research and forward thinking of many innovators, one of the most often mentioned is Dr. Manohar Panjabi. He is credited with the concept of the neutral zone theory and instability hypothesis.<sup>12</sup> This theory depends upon the existence of 4 spinal dynamics; the neutral position, the range of motion, the neutral zone, and the elastic zone. By definition, the neutral position is the posture of the spine which reduces the collective internal stresses to the lowest possible state. The range of motion is the entire range of the physiological intervertebral motion; the neutral zone is described as the range of flexible motion within which spinal motion is achieved with minimal internal resistance; and the elastic zone is the part of the range of motion that goes beyond the neutral zone and approaches the physiological limit.

Through a series of studies Panjabi successfully presented experimental evidence to support the existence of the neutral and elastic zones, and used these zones to describe the effects of injury, muscle force, and instrumentation on the human spine. Panjabi concluded that damaged, unstable joints are painful because of uncontrolled motion (particularly in the event of repetitive micromotion) and a reduction of their neutral zones.<sup>12</sup> When a patient's neutral zone is reduced, 'natural' motion often extends into the boundaries of the elastic zone, and can cause pain. Panjabi hypothesized that pain experienced from an injured joint can be reduced by stabilizing the damaged segments, reducing micromovements, and restricting

motion to the neutral zone.

In order to solve the problems defined by the Neutral Zone theory and the issue of adjacent segment disease, a successful posterior dynamic stabilization device must allow retention of physiologic motion while eliminating painful pathologic motion. Ideally a mechanism would block range of motion from positions that are painful or positions that push tissues beyond their elastic range. To achieve this goal successful devices and techniques may include facet joint distraction, disk distraction, disk decompression, and neural protection by widening the canal/foramina.

Although dynamic stabilization devices are relatively new to the US market, they have been used as an alternative to lumbar fusion for over a decade outside of North America. What follows is a categorized survey of the first few devices that broke into the market, the technology that is currently on the market, and a few of the devices that are rapidly barreling down the pipeline.



The Wallis interspinous block

### Wallis

The Wallis (Abbott Spine, Bordeaux, France) is a polyetheretherketone (PEEK), interspinous block that is held in place with a flat Dacron cord. Its

original design was developed in 1986 and consisted of a titanium block. In the US, its current design is still limited to investigational use. The device is intended to treat massive herniated discs, discectomy for herniation of a transitional disc with sacralization of L5, degenerative disc disease at a level adjacent to a previous fusion, and isolated Modic I lesion leading to chronic low-back pain.<sup>14</sup> A clinical report indicates that this device is relatively easy to revise, and that patients who undergo discectomy with the Wallis have better clinical results than patients who undergo discectomy alone.<sup>14</sup> Biomechanical studies have demonstrated that the device has no effect on intradiscal pressures or motion at adjacent segments.<sup>4</sup>



The Diam silicone interspinous spacer

### Diam

The Diam (Medtronic, Inc., Minneapolis, MN) is an “H” shaped silicone interspinous spacer designed for patients experiencing

spinal stenosis. The spacer is covered by a polyethylene coat and is secured in place with two mesh bands: one placed around the spinous process above and one around the spinous process below. Unlike many other devices that act as a spring to dampen motion, the Diam acts more as a cushion that absorbs compressive forces. Previous studies in Europe have implanted the device above fusion levels to prevent adjacent segment disease.<sup>2</sup> No clear conclusions were made with respect to Diam’s ability to reduce adjacent segment disease. The device began investigational device exemption (IDE) clinical trials in 2006. Due to the device’s relatively new status, there is very limited literature on biomechanical testing or clinical results.



The Dynesys system device for treating spinal stenosis

### Dynesys

The Dynesys system (Zimmer Spine, Warsaw, IN) was designed to correct spinal stenosis with degenerative spondylolisthesis.<sup>13</sup>

The system consists of polyethylene-terephthalat cords which are threaded through polycarbonate urethane tube-shaped spacers and anchored to the pedicle with titanium alloy pedicle screws. Insertion is done through a posterior incision, and requires decompression at stenotic levels.<sup>13</sup> Once implanted, the polyester cords provide tensile forces to reduce movement in flexion, and the non-rigid urethane tubes resist compressive forces to prevent excessive motion in extension.<sup>13</sup> The device does not provide much support for lateral bending or axial twisting.<sup>10</sup> Often, when fusion is not successful in cases rigid fixation treatments, patients experience screw loosening from micromotion.<sup>16</sup> Although screw loosening was an expected complication with this device, a 2-year clinical trial reported screw loosening to be comparable to rigid fixation.<sup>13</sup> Instead, the success of the device seems to be most dependent on careful adherence to the device’s technical guidelines, specifically with respect to the length of the plastic spacers. Spacers which are too short may not provide enough support to reduce stenosis, and spacers which are too long can cause focal kyphosis, which is often associated with poor patient outcomes.<sup>11</sup> Biomechanical studies also reported that biomechanical patterns of motion are dependent on the length of the plastic tubing.<sup>10</sup> The device has been used in Europe since 1994, and was approved for use in the

US by the FDA in 2005. Clinical studies have not produced evidence that the device effectively prevents adjacent segment disease.<sup>15</sup>



The Stabilimax pedicle screw-based system

### **Stabilimax NZ**

Stabilimax NZ™ (Applied Spine Technologies, New Haven, Connecticut) is a pedicle screw-based system consisting of 3 components: the pedicle screws, the ball and socket connectors, and the dual spring connectors. The pedicle screws anchor the device to the vertebrae and are made of a titanium alloy. The ball and socket connectors attach to the pedicle screws, and allow motion while offloading the pedicle screws. The dual spring connector consists of two concentric springs which are wrapped in a protective, biocompatible polytetrafluoroethylene (ePTFE) sheath; one of the springs is resistant to compression in order to reduce vertebral extension, and the other is resistant to stretching in order to reduce vertebral flexion. The device was designed by Dr. Panjabi to follow the laws of the neutral zone theory, and has recently begun IDE clinical trials. There is currently no data to summarize the devices performance in vivo.



The Total Facet Arthroplasty System

### **Total Facet Arthroplasty System (TFAS)**

The Total Facet Arthroplasty System (TFAS) (Archus Orthopedics, Redmond, Washington) is a metal, artificial facet system, designed for patients with moderate to severe spinal stenosis. The system consists of two bearing surfaces. The first is fixed to the cephalad pedicles and articulates over the second which is fixed to the caudal pedicles. It is anchored by pegs passing into the vertebral body along the same course as pedicle screws and glued into the vertebral body. Motion is achieved by a sphere sliding along a curved plate. Patients are currently being enrolled into a US investigational study. The device can be used with up to 3 consecutive decompressions, but only one TFAS implant can be used per patient. Biomechanical studies have revealed that TFAS behaves very similar to the intact spine in flexion, extension and lateral bending, however the neutral zone was significantly increased in axial rotation.<sup>18</sup>



The Total Posterior System

### **Total Posterior System (TOPS)**

A total posterior element replacement system, the TOPS (Implant, Inc., Milford, Connecticut) system is anchored by devices much like pedicle screws. The entire posterior elements are removed and the device implanted. Within a plastic-like cover are “bumpers” that allow, but limit, the extent of rotation and extension. Investigation with this device is being planned, and likely to include FDA clinical trials.



The Coflex system

### **Coflex**

The Coflex™ (Paradigm Spin LLC, New York, New York) is a titanium alloy, U-shaped device with two sets of wings extending from the superior and inferior arms of the U. The bone facing surfaces are serrated to prevent migration, and the wings are positioned such that they securely hug the narrow portion of the spinous process. The device is inserted through a posterior midline incision, and requires removal of the interspinous ligament. Formally known as the “Interspinous U,” the Coflex has been in use outside the US since 1995. Despite an 11 year history of use, there is very little literature available on clinical success and biomechanical studies. The device is currently being used in the US in IDE clinical trials.

### **X-STOP**



The X-STOP titanium implant

The X STOP (St. Francis Medical Technologies, Inc., Alameda, CA) is a titanium implant that consists of an oval spacer and wing assembly. The device is designed to limit extension of the vertebrae, and reduce symptoms of stenosis. It is implanted through a posterior incision and fits between the spinous processes of the lumbar spine. The lateral wings prevent anterior and lateral migration, and the supraspinous ligament prevents posterior migration.<sup>19</sup> Although the device has clinical results which are comparable to surgical decompression alternatives, the risks associated with X STOP appear to be much lower. Clinical studies have reported average surgical times as low as 54 minutes, minimal blood loss, and average hospital stays of less than 24 hours in most patients.<sup>19</sup> Lower risks and speed of



recovery makes the device ideal for older patients. Biomechanical studies have shown that the X Stop does not alter the loading of adjacent segments, which may reduce the likelihood of adjacent segment disease.<sup>17</sup> Although there are minimal data on revision cases, the device is expected to perform well in revision procedures because it is implanted close to the skin, and it is not meant to fuse to the spine. The device was FDA approved in 2005 for use in one or two levels in the lumbar spine. It does not function well at L5-S1 due to limited space for the implant.

## Conclusion

In comparison to rigid fusion, dynamic stabilization technology may allow improved patient outcomes, the preservation of motion, and a reduction in adjacent segment disease. Although a single system has yet to prove that it is successful in all three qualifications, there are several promising devices that are currently under investigation, and the early results suggest a possible role in the management of degenerative disorders of the lumbar spine.

## REFERENCES

1. Anjarwalla NK, Morcom RK, Fraser RD Supplementary stabilization with anterior lumbar intervertebral fusion: A radiologic review. *Spine*. 2006;31,1281-1287.
2. Caserta S., La Maida, G.A., Misaggi, B., Peroni, D., Pietrabissa, R., Raimondi, M.T., Redaelli, A. Elastic stabilization alone or combined with rigid fusion in spinal surgery: a biomechanical study and clinical experience based on 82 cases. *European Spine Journal*. 2002;11,S192-197.
3. Castro I., Santos, D.P., Christoph, D.H., Landeiro, J.A. The History of Spinal Surgery for Disc Disease: An illustrated timeline. *Arq Neuropsiquiatr*. 2005;63,701-706.
4. Christie S. D., Song, J.K., Fessler, M.D. Dynamic Interspinous Process Technology. *Spine*. 2005;30,S73-S78.
5. Dubousset J., Spinal Instrumentation, Source of Progress, but Also Revealing Pitfalls. *Bulletin de l'Academie nationale de medecine*. 2003;187,523-533.
6. Hilibrand A. S., Robbins, M. Adjacent segment degeneration and adjacent segment disease: the consequences of spinal fusion? *Spine Journal*. 2004;4,190S-194S.
7. Holt K. G., Wagenaar, R.C., Kubo, M., LaFiandra, M.E., Obusek, J.P. Modulation of force transmission to the head while carrying a backpack load at different walking speeds. *Journal of Biomechanics*. 2005;38,1621-1628.

8. Laurie SW, Kablan LB, Mulliken JB, et al. Donor-site morbidity after harvesting rib and iliac bone. *Plast Reconstr Surg*. 1984;73,933-938.
9. Moglo K. E., Shirazi-Adl, A. Biomechanics of passive knee joint in drawer: load transmission in intact and ACL deficient joints. *Knee*. 2003;10,265-276.
10. Niosi C. A., Zhu, Q.A., Wilson, D.C., Keynan, O., Wilson, D.R., Oxland, T.R. Biomechanical Characterization of the three-dimensional kinematic behaviour of the Dynesys Dynamic Stabilization System: an in Vitro Study. *European Spine Journal*. 2006;15,913-922.
11. Nockels R. P., Dynamic Stabilization in the Surgical Management of Painful Lumbar Spinal Disorders. *Spine*. 2005;30,S68-S72.
12. Panjabi M. M., The Stabilizing System of the Spine. Part II. Neutral Zone and Instability Hypothesis. *Journal of Spinal Disorders & Techniques*. 1992;5,390-396.
13. Schnake K. J., Schaeren, S., Jeanneret, B, Dynamic Stabilization in Addition to Decompression for Lumbar Spinal Stenosis with Degenerative Spondylolisthesis. *Spine*. 2006;31,442-449.
14. Senegas J. Mechanical Supplementation by non-rigid Fixation in Degenerative Intervertebral Lumbar Segments: the Wallis System. *European Spine Journal*. 2002;11,S164-S169.
15. Sengupta D. K., Dynamic Stabilization Devices in the Treatment of Low Back Pain. *Orthopedic Clinics of North America*. 2004;35,43-56.
16. Sengupta D. K., Point of View: Dynamic Stabilization in Addition to Decompression for Lumbar Spinal Stenosis with Degenerative Spondylolisthesis. *Spine*. 2006;31,450.
17. Wiseman C. M., Lindsey, D.P., Fredrick, A.D., Yerby, S.A. The effect of an interspinous process implant on facet loading during extension. *Spine*. 2005;30,903-907.
18. Zhu Q. A., Larson, C.R., Sjøvold, S.G., Rosler, D.M., Keynan, O., Wilson, D.R., Cripton, P.A., Oxland, T.R. Biomechanical Evaluation of the Total Face Arthroplasty System (TFAS): an in Vitro Human Cadaveric Model. In: 51st Annual Meeting of the Orthopaedic Research Society), Vancouver, BC, Canada 2005.
19. Zucherman J. F., Hsu, K.Y., Hartjen, C.A., Mehalic, T.F., Implicito, D.A., Martin, M.J., Johnson, D.R., Skidmore, G.A., Vessa, P.P., Dwyer, J.W., Puccio, S.T., Cauthen, J.C., A Multicenter, Prospective, Randomized Trial Evaluating the X STOP Interspinous Process Decompression System for the Treatment of Neurogenic Intermittent Claudication: Two-Year Follow-Up Results. *Spine*. 20005;30,1351-1358.

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# Featured Image: Cerebellar Hemangioblastoma



## History

The patient is a 45 year-old female who presented with a 3-1/2 week history of headache and dizziness. In the days prior to admission she experienced progressive nausea and vomiting. Examination revealed decreased right finger-to-nose motor coordination and wide-based ataxia.

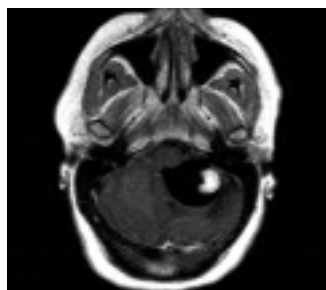
## Diagnosis

Left Cerebellar hemangioblastoma

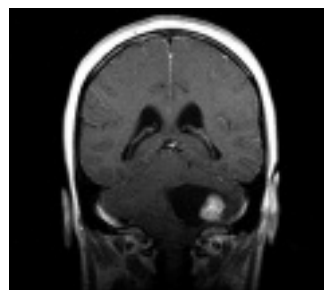
## Discussion

Hemangioblastoma, also known as Capillary Hemangioblastoma, is a WHO classification Grade I tumor of uncertain histogenesis. They are benign, slow growing, highly vascular lesions found most commonly in the posterior cranial fossa (85-95%). It is the most common posterior fossa tumor in adults after metastasis. Hemangioblastomas may also arise in the spinal cord (1-3%), supratentorial compartment, optic nerve, peripheral nerves, and soft tissues of the extremities. There is a slight male predominance and usually appear in the 3rd and 4th decades.

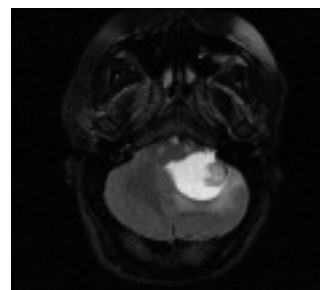
Though its etiology is unclear, a genetic component is strongly suggested by its association with clinical syndromes such as Von Hippel-Lindau disease (VHL). As many as 40% of hemangioblastomas are associated with VHL. Manifestations of VHL include hemangioblastoma (most common), retinal angiomas, pheochromocytoma, renal cell carcinoma, and other visceral tumors. VHL is an autosomal dominant disorder involving a deletion of the VHL tumor suppressor gene leading to overproduction of vascular endothelial growth factor (VEGF).



**Figure A**  
Axial T-1 weighted post contrast MR1



**Figure B**  
Coronal T-1 weighted post contrast MR1



**Figure C**  
Axial T-2 weighted MR1

## Clinical Findings

The clinical manifestation of Hemangioblastoma depends on the tumor's location, size and growth patterns. Common presenting symptoms include those of cerebellar dysfunction such as ataxia and discoordination, or symptoms of increased intracranial pressure related to cerebral spinal fluid flow obstruction. Patients may also experience headaches, lightheadedness, numbness, weakness, and nausea/vomiting. Hemangioblastomas may produce erythropoietin resulting in polycythemia.

## Pathology

Gross examination shows as a well-circumscribed, highly vascular red nodule usually within the wall of a cyst. Microscopically, extensive vasculature with normal endothelium is present along with large stromal cells. These stromal cells have numerous lipid-containing vacuoles creating a "clear cell" morphology. The vacuoles impinge on the borders of enlarged, hyperchromatic nuclei creating a scalloped appearance. Little or no mitotic activity is seen.

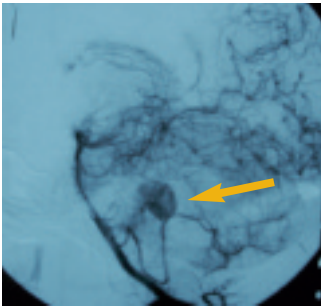
## Imaging Findings

The diagnostic imaging of choice is contrast-enhanced MRI. Hemangioblastomas are classically seen on T-1 post contrast MRI as a cystic posterior fossa intra-axial mass with a solid enhancing mural nodule (**Figure A and B**). Because these are highly vascular tumors, the mural nodule may demonstrate vascular flow voids from enlarged feeding arteries and draining veins. The cyst fluid usually demonstrates low T-1 and increased T-2 signal similar to cerebral spinal fluid (**Figure C**). Angiography typically shows hypervascularity of the mural nodule and avascularity of the cystic



*Lindsey Blake, M.D.*  
(pictured) and  
*Aaron Anderson*

portion of the tumor (**Figure D**). Predominantly solid hemangioblastomas are less common. The differential diagnosis includes: cystic metastases (seen in older adults), pilocytic astrocytoma (seen in children), glioblastoma, cavernous malformations (typically containing old hemorrhage), and cysticercosis (usually multiple smaller cysts with calcification on CT). Complete neural axis imaging is beneficial to rule out multiple lesions in cases where metastasis or VHL is suspected.



**Figure D**  
Lateral Cerebral Angiogram demonstrating enhancing hypervascular mural nodule

## Treatment

Treatment consists of surgical excision of the nodule and drainage of the cyst. Preoperative endovascular embolization has been used to aid surgical resection by reducing intraoperative blood loss. Though benign, up to 25% of hemangioblastomas recur. Adjuvant radiation therapy is indicated in cases of incomplete surgical resection or positive surgical margins. Recurrence is less common in non-VHL patients. Prognosis is generally good with approximately 85% ten-year survival.

**Dr. Lindsey C. Blake** is a fellowship trained neuroradiologist who joined **Radiology Specialists** in 1995. Dr. Blake is currently the Director of Neurointerventional Radiology at Sunrise Hospital.

**Aaron Anderson** is a third-year medical student at **Touro University Nevada College of Osteopathic Medicine**.

## NEUROSCIENCE GRAND ROUNDS

**Jan. 24** "Advances in Neuroradiology: Imaging in the 21st Century"

**Dr. William Orrison, MD**

6:30 PM to 9:30 PM • CME: 1 Hour • No Tuition

Location: TBA

Registration: via the web at: [www.sunriseecme.com](http://www.sunriseecme.com)

**Feb. 28** "Advances in Treating Dementia"

**Dr. Sabbaugh**

6:30 PM to 9:30 PM • CME: 1 Hour • No Tuition

Location: TBA

Registration: via the web at: [www.sunriseecme.com](http://www.sunriseecme.com)

**Mar. 31** **ANNUAL NEUROSCIENCE CONFERENCE**

"Advances in Neurosciences: Update 2007"

**Multiple local and national speakers**

7:30 AM to 5:00 PM • CME: 7.5 Hours

Tuition: Variable depending on early vs. late registration – see web page

Location: Red Rock Hotel and Casino

Registration: via the web at: [www.sunriseecme.com](http://www.sunriseecme.com)

**SAVE  
THE DATE**

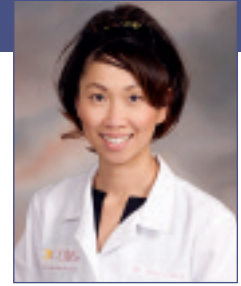
# Questions on Traveling with Medications? Look No More



Due to potential homeland security threats and current conditions in other countries worldwide, the United States Transportation Security Administration continues to amend travel regulations. These enhanced security measures have created uncertainty and confusion amongst travelers with disabilities and medical conditions. We are now expected to be vigilant in the latest air travel guidelines.

According to the Transportation Security Administration, you do not need a letter from your

doctor to avoid hassle. Instead, make sure your medications are properly labeled with a professionally printed label identifying the medication and manufacturer's name or pharmaceutical label. The name on the prescription medicine must also match the name on the passenger ticket.



*Dr. Bess Chang*

**The following is a re-configured list taken from the Transportation Security Administration website ([www.tsa.gov](http://www.tsa.gov)):**

	Carry-On	Checked
Properly labeled prescription medication matching the name on the passenger ticket.	Yes	Yes
No more than 4 oz. of non-prescription liquid medication (i.e. saline solution, eye care products, KY Jelly, cough syrup, gel cap type pills).	Yes	Yes
Bug & mosquito spray & repellents.	No	Yes
Eyeglass Repair Tools- including screw drivers.	Yes	Yes
Wheelchairs with gel cushioned seats/pads.	Yes	Yes
Walking Canes (allowed in carry-on baggage once they have been inspected).	Yes	Yes
Diabetes- liquid or gel low blood sugar treatments, including juice-up to 5 oz.	Yes	Yes
Injection- Related Supplies/Equipment- injection dispensing products; jet injectors; pens; infusers; unlimited number of unused syringes when accompanied by injection medication; lancets; blood glucose meters, blood glucose meter test strips, pumps and pump supplies. These items must be inspected.	Yes	Yes
Ostomy Scissors- All scissors with blades 4 inches or less.	Yes	Yes
Prosthetic Device Tools and Appliances- including drills and drill bits, allen wrenches, pull sleeves used to put on or remove prosthetic devices, if carried by the individual with the prosthetic device or his/her companion.	Yes	Yes
Baby formula and food, breast milk and other baby items-These are allowed in your carry-on baggage or personal items. You can take these through the security checkpoints and board your plane. However, you must be traveling with a baby or toddler. All items will be inspected.	Yes	Yes

**For storage of injection medications, please note the following:**

<ul style="list-style-type: none"> <li>Opened bottles of insulin can be kept non-refrigerated for up to 1 month.</li> </ul>	<ul style="list-style-type: none"> <li>Betaseron in a pre-filled syringe is usually kept refrigeration free.</li> </ul>	<ul style="list-style-type: none"> <li>Avonex in a powder form can be kept non-refrigerated for up to 30 days.</li> </ul>
<ul style="list-style-type: none"> <li>Copaxone in a pre-filled syringe can be kept non-refrigerated for up to 7 days.</li> </ul>	<ul style="list-style-type: none"> <li>Avonex in a pre-filled syringe can be kept non-refrigerated for up to 12 hours.</li> </ul>	<ul style="list-style-type: none"> <li>Rebif in a pre-filled syringe can be kept non-refrigerated for up to 30 days.</li> </ul>

Lastly, please keep in mind that medications and related supplies are normally X-rayed. If you do not wish for your medications and supplies to be X-rayed, you must ask the security officers for visual inspection before the screening process begins. It is advisable to keep your medication supplies in "easy to see" pouch/bag because any items which cannot be cleared visually will be X-rayed. Re-pack your own medication

to prevent contamination and damage after the completion of the visual inspection.

*Have a safe and happy travel!*

*For more updated detailed information, please log onto the Transportation Security Administration website ([www.tsa.gov](http://www.tsa.gov)).*

**Dr. Bess Chang** is a neurologist with **Clinical Neurology Specialists in Henderson, Nevada.**



**Editor's Note:** The following listing includes neuroscience trials that have local Investigational Review Board approval. The editors encourage all local investigators to submit their research studies for listing in the next issue. We hope that by making physicians in the region aware of research opportunities for their patients, we can improve quality of care for patients and help make the local investigators more successful in patient recruitment. To submit a study for publication in the next issue, please contact Elizabeth White at 702-851-5413.

## Stroke - Prevention

### 1. Secondary Prevention of Small Subcortical Stroke (SPS3)

#### **Primary Objective**

To look for the best way to prevent a second stroke and cognitive decline in patients with symptomatic small subcortical strokes (lacunar strokes). This is a prospective randomized comparison of aggressive blood pressure management vs. standard blood pressure management. We will also compare antithrombotic therapies: aspirin alone vs aspirin plus clopidogrel.

#### **Sponsor**

University of Texas Health Science Center at San Antonio funded by a grant from NINDS.

#### **Duration**

Up to 3 years of active participation for subjects. Seen weekly for up to 3 months, then quarterly.

#### **Target Population**

We are recruiting patients with MRI documented lacunar infarction occurring in the last 6 months.

Men and Women age 45 and older.

Absence of cortical ischemia, carotid stenosis or major cardioembolic source.

#### **Principal Investigator**

Stanley N. Cohen, MD

#### **Contact Person**

Rob Phoenix, RN - (702) 731-8291

#### **Status**

Recruitment ongoing.

### 2. Insulin Resistance Intervention After Stroke (IRIS)

#### **Primary Objective**

To determine if pioglitazone, compared with placebo, is effective in lowering the risk for a second stroke or myocardial infarction among non-diabetic men and women with a recent ischemic stroke and insulin resistance.

#### **Sponsor**

Yale New Haven University funded by a grant from NINDS.

#### **Duration**

Up to 3 years of active participation for subjects. Subjects will be seen on the average of quarterly.

#### **Target Population**

We will recruit patients with insulin resistance according to an index HOMA blood test with a recent (within 6 months) non-embolic ischemic stroke.

Men and women age 45 or older who are not diabetic.

#### **Principal Investigator**

Stanley N. Cohen, MD

#### **Contact Person**

Rob Phoenix, RN - (702) 731-8291

#### **Status**

Recruitment ongoing.

### 3. A Randomized Multicenter Clinical Trial of Unruptured Brain AVMs (ARUBA)\*

#### **Primary Objective**

To determine whether conservative medical management or interventional treatment (with endovascular procedures, neurosurgery, or radiotherapy, alone or in combination) results in better long term outcomes for patients with unruptured brain AVMs.

#### **Sponsor**

Columbia University funded by a grant from NINDS.

#### **Duration**

Patients will be followed for 5 years or until they reach an endpoint.

### **Target Population**

Patients discovered to have unruptured AVMs that are considered eligible for an intervention or for medical management.

### **Principal Investigator**

Stanley N. Cohen, MD

### **Contact Person**

Rob Phoenix, RN - (702) 731-8291

### **Status**

Approved. Recruitment to start in September 2006.

## **4. A prospective, multicenter, randomized, controlled trial to evaluate the safety and efficacy of the STARFLEX® Septal Closure System versus best medical therapy in patients with a stroke and/or transient ischemic attack due to presumed paradoxical embolism through a patent foramen ovale. (CLOSURE I)**

### **Primary Objective**

To determine whether the STARFlex® Septal Closure System (STARFlex) will safely and effectively prevent a recurrent embolic stroke/transient ischemic (TIA) and mortality in patients with a patent foramen ovale (PFO) and to demonstrate superiority of the STARFlex device compared to best medical therapy.

### **Sponsor**

The device manufacturer, NMT.

### **Duration**

24 months

### **Target Population**

Documented TIA or stroke and a PFO, with or without atrial septal aneurysm in the absence of any other potentially embolic source or cause of stroke or TIA.

Men and women age 18 to 60.

### **Principal Investigator**

Scott Selco, MD

### **Contact Person**

Rob Phoenix, RN - (702)-731-8291

### **Status**

Recruitment ongoing.

## **Stroke - Acute Treatment**

### **1. A randomized, double blind, placebo controlled study of Ancrod (Viprinex) in Subjects beginning treatment within 6 hours of the onset of acute ischemic stroke**

#### **Primary Objective**

To determine whether Ancrod begun intravenously within 6 hours after stroke onset confers statistically significant benefit in reducing the incidence of disability at 90 days.

#### **Sponsor**

Neurobiological Technologies

#### **Duration**

Up to 90 days post qualifying event.

#### **Target Population**

Men and women age 18 or older with an acute ischemic stroke with onset of symptoms within 6 hours.

#### **Principal Investigator**

Scott Selco, MD

#### **Contact Person**

Rob Phoenix, RN - (702) 731-8291

#### **Status**

Recruitment ongoing at Sunrise Hospital.

### **2. A prospective, randomized, double blind, placebo controlled, single bolus, multinational, multicenter, parallel group, dose ranging study of desmoteplase in the indication of acute stroke (DIAS-2)**

#### **Primary Objective**

To evaluate if desmoteplase, a derivative of vampire bat venom that acts as a thrombolytic agent, can improve outcome in acute ischemic stroke in the 3 to 9 hour window after stroke onset when the imaging studies demonstrate a significant ischemic penumbra.

#### **Sponsor**

Forest Laboratories

#### **Duration**

Up to 90 days post qualifying event.

#### **Target Population**

Men and women age 18 or older with an acute ischemic stroke onset of symptoms from 3 to 9 hours and imaging evidence of a mismatch between core infarction and ischemic penumbra.

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**Principal Investigator**

Scott Selco, MD

**Contact Person**

Rob Phoenix, RN - (702) 731-8291

**Status**

Recruitment ongoing at Sunrise Hospital.

### 3. Randomized, double blind, placebo controlled, multi centre, parallel groups confirmatory efficacy and safety trial of activated factor VII (NovoSeven/Niastase®) in acute intracerebral haemorrhage

**Primary Objective**

To evaluate the safety and efficacy of rFVIIa in reducing disability and improving clinical outcomes by preventing early hematoma growth in patients with acute intracerebral hemorrhage.

**Sponsor**

NovoNordisk

**Duration**

Up to 90 days post qualifying event.

**Target Population**

Non traumatic intracerebral bleed within 3 hours of onset.

Men and women 18 years or older

**Principal Investigator**

Scott Selco, MD

**Contact Person**

Rob Phoenix, RN - (702) 731-8291

**Status**

Recruitment ongoing at Sunrise Hospital.

### 4. Interventional Management of Stroke (IMS III)\*

**Primary Objective**

To determine if ischemic stroke subjects with a baseline NIH stroke scale  $\geq 10$  treated with recombinant tissue plasminogen activator (rt-PA) utilizing a combined approach to recanalization started within 3 hours of onset, are more likely to have a favorable outcome at 3 months, as defined by a modified Rankin score of 0-2, as compared to subjects treated with standard IV rt-PA alone.

**Sponsor**

NIH/NINDS

**Duration**

Up to 3 months post qualifying event.

**Target Population**

Acute ischemic stroke treated within 3 hours on symptom onset.

Men and women age 18 and older.

**Principal Investigator**

Scott Selco, MD

**Contact Person**

Rob Phoenix, RN - (702) 731-8291

**Status**

Approved: Recruitment to start in August 2006.

### 5. A phase II, multi-center, two-part study to evaluate the safety and efficacy of V10153 in acute ischemic stroke.

**Part A-An open label, dose escalation, single-dose administration evaluation of the safety of four dose levels of V10153**

**\*Part B-A randomized, double-blind, placebo-controlled evaluation of the safety and efficacy of a single dose of V10153**

**Primary Objective**

Part A: To establish the safety of four dose level (1, 2.5, 5 and 7.5 mg/kg) of V10153 in patients with acute ischemic stroke.

\*Part B: To confirm safety and assess cerebral recanalization rates of fixed dose of V10153 and placebo in patient with acute middle cerebral artery territory stroke.

**Duration**

30 days

**Target Population**

Men and women age 18 or older. Onset of stroke symptoms within 3 to 9 hours of initiation of treatment.

NIHSS  $>5$ - $=20$

CT scan to show findings of early ischemic changes and an ASPECT score of between 5 and 10 inclusive.

**Principal Investigator**

Scott Selco, MD

**Contact Person**

Rob Phoenix, RN - (702) 731-8291

**Status**

Part A-recruitment is ongoing.

Part B-will recruit at conclusion of Part A.

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## Neuro-Oncology

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### 1. A Study of Brain Tumors. A database for patients with brain tumors\*

#### **Primary Objective**

To develop a comprehensive brain tumor database that includes clinical, imaging and tumor tissue features to provide: molecular characterizations of tumor and correlation of tumor genetic expression/genomics with clinical features and imaging characteristics.

#### **Duration**

1 visit

#### **Target Population**

Any patient with histopathological diagnosis of a CNS tumor or about to undergo a procedure where histopathology will become available.

#### **Principal Investigator**

Marcus Erling, MD

#### **Contact Person**

Rob Phoenix, RN - (702)-731-8291

#### **Status**

Recruitment ongoing at Sunrise Hospital.

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## Migraine/Headache

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### 1. Implantable Stimulator for Migraine

#### **Primary Objective**

To evaluate the safety and efficacy of occipital nerve stimulation using on implantable device for migraine prevention and treatment.

#### **Sponsor**

Advanced Bionics Corporation

#### **Duration**

Approximately 4 years. The majority of visits are within the first 14 months of the trial. Patients will see both the surgeon and the neurologist during this time.

#### **Target Population**

Adults 18-64 years of age with an established diagnosis of migraine and who have tried 2 or more acute medication regimens for migraine and preventative migraine from 2 separate classes of drugs.

#### **Principal Investigator**

Benjamin Venger, MD

#### **Contact Person**

Elizabeth White - (702) 851-0877

#### **Status**

Approved. Enrollment closed.

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## Dementia

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### 1. A Multi-Center, Double-Blind, Placebo-Controlled Therapeutic Trial to Determine Whether Natural Huperzine A Improves Cognitive Function

#### **Primary Objective**

Can the medication Huperzine A, a natural cholinesterase inhibitor, improve brain function in patients with Alzheimer's Disease?

#### **Target Population**

We are recruiting patients age 55 and older who have been diagnosed with probable Alzheimer's disease. Patients cannot be currently taking any cholinesterase inhibitors, however Namenda is acceptable.

Patients must take study drug twice a day during the (7) seven-month study period. Cognitive and memory assessments will be conducted as well. Patients must have a study partner who can accompany them to all (9) nine clinic visits.

#### **Principal Investigator**

Charles Bernick, MD

#### **Contact Information**

University of Nevada School of Medicine, Research Department. (702) 671-5015

### 2. Alzheimer's Disease Neuroimaging Initiative (ADNI)

#### **Primary Objective**

The goal of this study is to determine whether imaging of the brain every six months can help predict the onset and monitor the progression of Alzheimer's disease. The imaging methods used will be Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) scans. In addition to neuroimaging, the study will test blood and, for some participants, cerebrospinal fluid (from lumbar puncture) to determine if biomarkers can predict and monitor the disease.

#### **Target Population**

Researchers are looking for persons who are between 55 and 90 years of age who:

- Are in good general health with no memory problems, OR
- Are in good general health with memory problems or concerns, OR
- Have a diagnosis of early Alzheimer's disease

All patients must be willing to undergo MRI and/or



PET scans. Some participants will be asked to consent to a lumbar puncture (LP). Patients from all groups must have a study partner who is able to accompany them to all clinic visits. During some of the clinic visits, cognitive and memory assessments and blood draws will be performed. Participants will receive monetary compensation for their participation.

**Principal Investigator**

Charles Bernick, MD

**Contact Information**

University of Nevada School of Medicine, Research Department (702) 671-5015

**3. A Randomized, Double-Blind, Placebo-Controlled Trial of Valproate to Attenuate the Progression of Alzheimer's Disease**

**Primary Objective**

The purpose of this study is to evaluate whether chronic use of divalproex sodium (Valproate) is able to change the progression of Alzheimer's Disease (AD).

**Target Population**

We are recruiting Alzheimer's patients between the ages of 55 and 90. Patients cannot have a history of seizure disorders or a clinically significant stroke. Subjects on a stable dose of a cholinesterase inhibitor (Exelon, Reminyl, or Aricept) will be eligible for the study.

Patients must be willing to take the study drug over a course of 26 months. Participation includes 12 clinic visits, some of which involve cognitive and memory assessments and blood draws. A study partner must accompany the patient to all visits.

**Principal Investigator**

Charles Bernick, MD

**Contact Information**

University of Nevada School of Medicine, Research Department (702) 671-5015.

**4. A Double-Blind, Phase II Safety and Efficacy Evaluation of ONO-2506PO in Patients with Mild to Moderate Alzheimer's Disease**

**Primary Objective**

The purpose of this study is to evaluate the safety and effectiveness of ONO-2506, an investigational medication that may help to treat the symptoms of

mild to moderate Alzheimer's disease.

**Target Population**

We are recruiting patients between the ages of 50 and 90 who have been diagnosed with mild to moderate Alzheimer's Disease. The use of Aricept or Exelon is acceptable.

There are a total of (13) clinic visits over approximately 60 weeks. A study partner must accompany the patient to all clinic visits. The clinic visits include cognitive and memory assessments, ECGs, and blood draws.

**Principal Investigator**

Charles Bernick, MD

**Contact Information**

University of Nevada School of Medicine, Research Department (702) 671-5015

**5. A Double-Blind, Randomized, Placebo-Controlled Study of the Efficacy, Safety, and Tolerability of 8-Week Treatment of Rozerem 8 mg (QHS) in Sleep Disturbed, Community Dwelling, Mild to Moderately Severe Alzheimer's Disease Subjects**

**Primary Objective**

Evaluate the safety, efficacy and tolerability of Rozerem in sleep disturbed Alzheimer's Disease patients.

**Target Population**

We are recruiting patients 55 years and older who have been diagnosed with mild to moderate Alzheimer's Disease. Patients must have sleep problems. Females must be post-menopausal. Patients must be capable of self-locomotion and cannot have history of significant stroke, vascular dementia or severe renal dysfunction or disease.

Patients must be able to take the study drug for 8 weeks and must have a habitual bedtime of between 8 pm and midnight. All patients must have a caregiver who resides in the same home. Assessments include cognitive and memory tests, physical examination, laboratory tests, and an ECG recording.

**Principal Investigator**

Charles Bernick, MD

**Contact Information**

University of Nevada School of Medicine, Research Department (702) 671-5015

*\*indicates recruitment has not yet started.*

# Collaboration works.



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