

Madigan Army Medical Center Clinical Practice Guidelines

Stroke (Acute) Management

Department of Medicine/Neurology
Madigan Army Medical Center
Maintained by Quality Services Division
Clinical Practice and Referral Guidelines Administrator

Last Review for this Guideline: **April 2010**
Clinical Guidelines require review every three years

Core Document

TITLE: CLINICAL MANAGEMENT GUIDELINE FOR THE USE OF THROMBOLYTIC THERAPY FOR THE ACUTE STROKE TREATMENT, MADIGAN ARMY MEDICAL CENTER

GUIDELINE: [Madigan Stroke Treatment Protocol](#)

INDICATIONS FOR THE CLINICAL GUIDELINE: An acute ischemic stroke is when the blood flow to a part of the brain is interrupted. This interruption of blood flow is usually due to a blood clot. Tissue Plasminogen Activator or tPA is a medication that can dissolve blood clots. This medication has been shown when given to patients with acute ischemic stroke to improve their outcome when assessed three months later. tPA is a very strong blood thinning medication and bleeding into the brain or in other regions of the body can result as a side effect of its use. Due to the fact that this drug may significantly help but also harm patients very specific criteria are used to identify those patients most likely to benefit and those in whom the risk may be too great to warrant its use. The following guideline should be used when evaluating patients with acute ischemic stroke for consistency in care and to maximize clinical outcome.

METRICS: THE KEY ELEMENTS OF THE CLINICAL GUIDELINE THAT WILL BE USED TO MONITOR PROVIDER ADHERENCE TO THE CLINICAL GUIDELINE.

1. The [thrombolytic therapy checklist](#) must be carefully completed. Patient must meet all inclusion criteria and none of the exclusion criteria to be an eligible candidate.
2. Patients must have the clinical diagnosis of an ischemic stroke with a measurable neurologic deficit and time onset of their symptoms must be well established and within 180 minutes of administering therapy.
3. Signed [Informed Consent Form](#) must be obtained from the patient or family member.
4. [Followup guidelines](#) for neurological checks with vital signs q 30 min. for 6 hours and q 1 hr for 18 hours must be followed.

DATE: Published: December 1998, Revised: September 1999, May 2003, May 2007, April 2010

AUTHORS:

Please contact the administrator for information regarding the authors of this clinical guideline.

AREAS OF DISAGREEMENT: There was some controversy over several issues. These included whether or not to include clinical signs of a large stroke as one of the exclusion criteria, who should actually administer the drug, and who should be responsible for the interpretation of the CT scan. These issues were resolved with multi-disciplinary input and it was decided that we would not include clinical signs of a large stroke as exclusionary criteria as it was not one of the exclusionary criteria used in the NINDS trial. It was determined that we would not limit the administration of the drug to any particular subspecialty group as this might prohibit individuals from getting the drug who would benefit and finally it was determined that a staff Radiologist would be responsible for the interpretation of the CT scan as per guideline Medicare requirements.

PUBLISHED GUIDELINES OF CARE AND OTHER REFERENCES UPON WHICH THE CLINICAL GUIDELINE IS BASED:

Tissue plasminogen activator for acute ischemic stroke, The National Institute for Neurological Disorders and Stroke, tPA Study Group, NEJM (24): p 1581, Dec 14, 1995 (NINDS).

Intravenous thrombolysis with recombinant tissue plasminogen activator for acute hemispheric stroke, The European Cooperative Study, (ECASS), JAMA 274(13): p 1017, Oct. 4, 1995.

Randomized controlled trial of streptokinase, ASA and combination of both in treatment of acute ischemic stroke, Multicenter Acute Stroke Trial- Italy (MAST-I) group. Lancet 346: p 1509, Dec. 9, 1995.

Thrombolytic therapy with streptokinase and acute ischemic stroke, Multicenter Acute Stroke Trial-Europe Study Group. NEJM 335(3): p 145, Jul 18, 1996.

Streptokinase for acute ischemic stroke with relationship to time of administration, The Australian Streptokinase Study Group. JAMA 276(12): p 961, Sep 25, 1996.

Conditions that mimic stroke in the ED: implications for acute stroke trials. Arch Neurol 53(11): p.1119, Nov 1995.

Guidelines for thrombolytic therapy for acute stroke: a supplement to the Guidelines for the management of patients with acute ischemic stroke. (American Heart Association Guidelines). Circulation 94: p.1176, 1996.

CLINICAL PRACTICE RECOMMENDATIONS:

The following exclusion/inclusion criteria form must be completed in total.

1. THROMBOLYTIC THERAPY CHECKLIST FOR ISCHEMIC STROKE.
2. TREATMENT AND FOLLOWUP GUIDELINES, FLOWSHEET, PATIENT INFORMATION SHEET AND INFORMED CONSENT FORM.

KEY POINTS: There are no key points for this clinical guideline.

IMPACT STATEMENT TO THE INSTITUTION:

This guideline provides a unified multidisciplinary consensus approach to the use of a new and somewhat controversial drug for acute ischemic stroke. It helps insure that patient selection for this drug will be optimized so that those who are most likely to benefit from its use may be selected from the large number of stroke patients evaluated at our institution. It will impact Neurology, the Emergency Department, Radiology, Neurosurgery and the Intensive Care Unit primarily but also any other providers who are involved in caring for patients with stroke.

LINKS WITHIN THE MAMC INTRANET: This clinical guideline should be published on the MAMC Intranet.

METHODS OF PROVIDER EDUCATION:

1. Department Chiefs will notify their departments of the guideline and emphasize the use of the guideline.
2. The guideline will be listed on the Intranet. Flowsheet, Treatment Guidelines
3. Patient "Stroke Packets with hard copies of these forms and guidelines will be available in the

Neurology Clinic and the Emergency Room.

4. The practice guideline will be published for use for providers in our regional care facilities for reference.

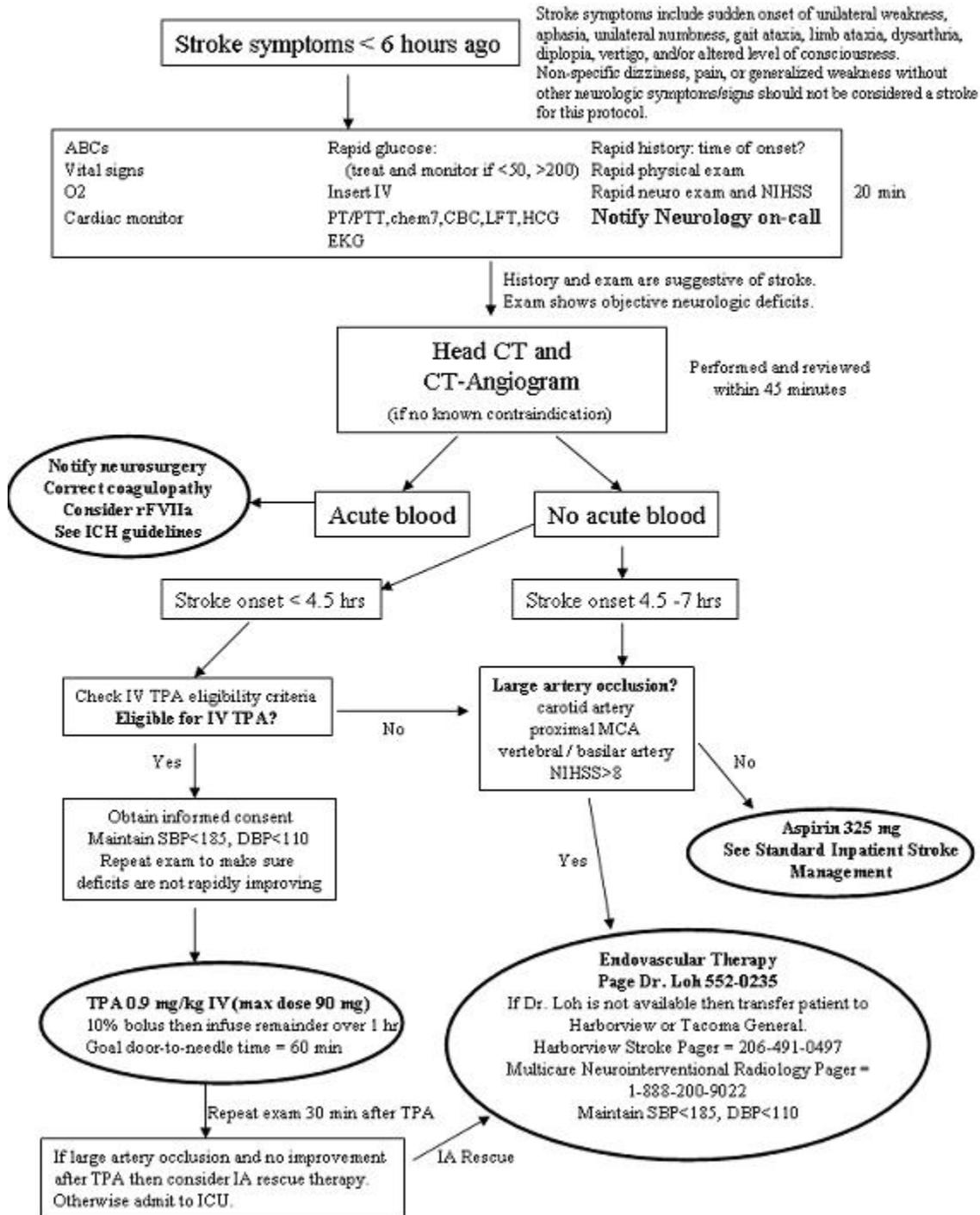
METHODS OF PATIENT EDUCATION: There are no patient education materials for this clinical guideline.

REVISION FREQUENCY: The clinical guidelines committee will review this guideline of care for use of tissue plasminogen activator for acute ischemic stroke annually. Revisions deemed necessary by the authors based upon future clinical trials, updated treatment guidelines or outcomes of metric audits will be forwarded to the clinical guidelines committee when the need is determined.

Addendum: Attached to this document for the provider use is a detailed patient addendum to MAMC Informed Consent Form and a Team Information Sheet. This addendum to the Informed Consent should be used in conjunction with the guideline MAMC consent form as well as the Team Education Sheet intended for physician and provider education. The therapeutic guideline is listed in both a flow sheet format as well as a textual format.

Clinical Guideline

Madigan Acute Stroke Therapy Protocol



Metrics

1. The [Thrombolytic Therapy Checklist](#) must be carefully completed: patient must meet all inclusion criteria and none of the exclusion criteria to be an eligible candidate.
2. Patients must have the clinical diagnosis of an ischemic stroke with a measurable neurologic deficit and time onset of their symptoms must be well established and within 180 minutes of administering therapy.
3. Signed [Informed Consent Form](#) must be obtained from the patient or family member.
4. [Follow up guidelines](#) for neurological checks with vital signs q 30 min. for 6 hours and q 1 hr for 18 hours must be followed.

THROMBOLYTIC THERAPY CHECKLIST FOR ISCHEMIC STROKES

INSTRUCTIONS: All of the YES boxes and all of the NO boxes must be checked before thrombolytic therapy can be given.

Inclusion Criteria (all Yes boxes must be checked before treatment):

YES

- Age 18 years or older.
- Clinical diagnosis of ischemic stroke causing a measurable neurologic deficit.
- Time of symptom onset well established to be less than 270 minutes before treatment would begin.

Exclusion Criteria (all NO boxes must be checked before treatment):

NO

- Evidence of intracranial hemorrhage on noncontrast head CT.
- Only minor or rapidly improving stroke symptoms (NIHSS<4).
- High clinical suspicion of subarachnoid hemorrhage even with normal CT.
- Active internal bleeding (eg. Gastrointestinal bleeding or urinary bleeding within last 21 days).
- Within 3 months of intracranial surgery, serious head trauma, or previous stroke.
- Within 14 days of major surgery or serious trauma.
- Recent arterial puncture at noncompressible site.
- Lumbar puncture within 7 days.
- History of intracranial hemorrhage, arteriovenous malformation, or aneurysm.
- Witnessed seizure at stroke onset.
- Recent acute myocardial infarction.
- Pregnancy or partuition within previous 30 days.
- Baseline labs glucose<50 or >400, Hct<25.
- On repeated measurements, systolic pressure >185mmHg or diastolic pressure>110mmHg at the time of treatment, requiring IV drip medication to reduce blood pressure to within these limits.
- Inability to obtain informed consent from patient or family member.
- Known bleeding diathesis, including but not limited to
 - Platelet count<100,000/mm³
 - Patient has received heparin within 48 hours and had elevated activated partial thromboplastin time (greater than upper limit of normal for laboratory).
 - Recent use of anticoagulant (eg. Warfarin sodium) and elevated prothrombin time>15 seconds

CT Scan Exclusion:

- Blood of any degree.
- Mass effect with obvious early edema (>1/2 of the MCA distribution or >1/3 of a hemisphere).

Additional exclusion criteria for patients receiving rTPA for onset of symptoms from 3 to 4.5hrs:

- Age > 80.
- NIHSS > 25.
- Previous stroke **AND** diabetes.
- On anticoagulation therapy regardless of PT/PTT/INR value.

Consent for Treatment of Acute Ischemic Stroke with tissue Plasminogen Activator

What is a stroke?

A stroke is a problem with the tubes or vessels bringing blood to the brain and results in injury to the brain. There are two main types of stroke, those associated with rupture of the blood vessels (hemorrhagic strokes) and those associated with the blockage of blood vessels (ischemic strokes).

What happens in an acute ischemic stroke?

In an acute ischemic stroke, the blood flow to a part of the brain is interrupted because of sudden blockage of a blood vessel. The blockage is usually due to a blood clot and starves the brain of needed oxygen and nutrients. The center of the starved area may die quickly, and the surrounding area may die slowly over hours.

What is tissue plasminogen activator or tPA?

tPA is a medication that can dissolve blood clots. Because of its strong blood thinning action, bleeding into or around the brain can result as a side effect of its use. (6% risk). Bleeding can also occur in other parts of the body. (Approximately 5% risk)

How can tPA help someone with an acute ischemic stroke?

tPA can sometimes dissolve the clot that is blocking the blood vessel and causing the ischemic stroke. If it does so, the blocked blood vessel reopens, allowing the previously starved brain to receive blood flow again with oxygen and nutrients. If the clot is dissolved soon enough, some or all of the brain may be rescued from the threatened injury. Rescuing brain that was starved may decrease the amount of disability that results from the ischemic stroke.

Do all stroke patients get this treatment?

No. Specific criteria are used to carefully identify those patients most likely to benefit and to avoid serious side effects. If a patient does not fulfill all of the selection criteria, the risks of tPA are higher and the chance of benefitting is lower.

What are the potential benefits?

The potential benefits are all related to an increased chance of having a good outcome, namely little or no disability remaining after recovery from the stroke. If stroke patients meet all the criteria, their chance of having a good outcome increases from 29% without tPA to 41% with tPA. Thus, even though the chances of a good outcome are improved, over half of the stroke patients who are given tPA will still have disability from their stroke. A good outcome is not guaranteed.

***For those receiving tPA at 3 to 4.5 hours after stroke onset:** A study in 2008 showed that more patients had a favorable outcome when given tPA between 3 and 4.5 hours after stroke onset. (52.4% for tPA vs. 45.2% for placebo). However, tPA is **not** FDA approved for use at 3 to 4.5 hours.

What are the potential risks?

The major risk of tPA therapy in stroke patients is that they will bleed into the injured area of the brain, causing a worsening of their condition and even death. The chance of serious bleeding into the stroke area is less than 0.6% in stroke patients not treated with tPA versus 6.4% in those who get tPA. In other words, tPA increases about 10 times the chance of a bleed that can worsen a patient’s condition. Overall, mortality rates are unchanged. About 20% of patients will die within 30 days of their strokes, regardless of tPA.

***For those receiving tPA at 3 to 4.5 hours after stroke onset,** the risk of having significant intracranial bleeding is 2.4% for tPA vs. 0.2% for placebo. Overall mortality did not differ significantly between the tPA group and the placebo group. There is no difference in the rate of other adverse events.

What tests will be done?

No testing beyond what would be routine in a patient with stroke will need to be done. These standard tests include blood work and imaging, including a CT scan of the head to make sure no hemorrhage nor early severe signs are present before administering tPA therapy. A repeat CT scan and further blood testing may be performed depending on how the patient responds to treatment.

I understand that the results of tPA treatment for stroke cannot be guaranteed. I have read and understand the above. My physician has offered to answer all inquiries concerning the proposed treatment with tPA. I understand that I am free to withhold or withdraw consent to the proposed treatment with tPA at any time.

Witness:	Signature of person giving consent:
Date and Time signed:	Relationship to patient (if applicable):

TREATMENT AND FOLLOWUP GUIDELINES FOR THROMBOLYTIC THERAPY FOR ACUTE ISCHEMIC STROKE

TREATMENT

1. tPA 0.9 mg/kg total or max 90 mg.
2. Give 10% bolus.
3. Give remaining 90% with a constant infusion over 60 minutes without interruption.

FOLLOWUP

General patient management guidelines and other therapy

1. Admission to ICU for 36 hours
2. No IV heparin or antiplatelet drugs during the infusion or for 24 hours following onset of symptoms
3. Neuro checks with vital signs q 30 mins for 6 hours and q 1 hr for 18 hours
4. Cardiac monitoring
5. Appropriate measures to control blood pressure within acceptable limits
6. Avoid NG tube, blood draws and invasive lines of procedures for 24 hours if possible.
7. Inform Neurosurgery of events.

THROMBOLYTIC THERAPY FOR ACUTE ISCHEMIC STROKE: GUIDELINE

EMS

1. Alert hospital of possible stroke patient.
2. Rapid transport to hospital.

DOOR

Phase I - 10 minutes from arrival

1. Assess ABCs, vital signs.
2. Provide oxygen therapy.
3. Obtain IV access: obtain blood samples; order CBC, electrolytes, coagulation studies.
4. Check blood sugar; treat if indicated.
5. Perform general neurological screening assessment.
6. Alert members of the stroke team: Neurologist, Radiologist, CT technician.

Phase II - 25 minutes from arrival

1. Review patient history.
2. Review strict inclusion/exclusion criteria.
3. Perform quick head to toe physical examination.
4. Perform neurological examination.
5. Order an urgent, non-contrast CT scan (door to CT scan performed goal less than 25 minutes from arrival).

6. Read CT scan by a radiologist or neurologist (door to CT read goal less than 45 minutes from arrival).

REVIEW DATA

1. Review CT exclusions (stat reading by radiologist or neurologist)
2. Repeat neurological examination: are deficits variable or rapidly improving?
3. Re-review thrombolytic inclusion and exclusion criteria: are they all met?

DECISION - Patient remains candidate for Thrombolytic Therapy - yes or no?

DRUG

1. Obtain informed consent. Review risk and benefits with patient and/or family member.
2. Begin thrombolytic treatment (door to treatment goal less than 60 minutes).
3. Follow treatment plan as outlined on previous page.
4. Admit to ICU.

INTRACEREBRAL HEMORRHAGE MANAGEMENT: GUIDELINE

1. If clinical suspicion of ICH (example: neurological deterioration, new headache, acute hypertension, or nausea/vomiting) discontinue tPA.
2. Perform a stat CT Scan for any neurological deterioration.(notify neurosurgery if bleed present)
3. Order stat lab; PT/PTT, platelet count, fibrinogen, and Type and Cross for 4 units.
4. Prepare for administration of 6-8 units of cryoprecipitate and factor VIII.
5. Prepare for administration of 6-8 units of platelets.

Target times will not be achieved in all cases but represent goals (if time delays are predicted by waiting for the physical presence and evaluation of a Neurologist rTPA can be given if all other criteria are met)

Table NINDS - Recommended Stroke Evaluation Targets for Potential Thrombolytic Candidates*

	Time Target
Door to doctor	10 minutes
Door to CT ¹ completion	25 minutes
Door to CT read	45 minutes
Door to treatment	60 minutes
Access to neurological expertise [#]	15 minutes
Access to neurosurgical expertise [#]	2 hours
Admit to monitored bed	3 hours

*Target times will not be achieved in all cases, but they represent a reasonable goal.

¹CT indicates computed tomography. [#]By phone or in person.

Team Education Sheet
Thrombolytic Therapy for Acute Ischemic Stroke

The National Institute of Neurological Disorder and Stroke Study group (NINDS) has published data that thrombolytic therapy when used in acute ischemic stroke, can improve neurological function at 90 days if given to a select group of patients. (1)

Five randomized trials concerning thrombolytic therapy in acute stroke have been published. Results are conflicting. 4 of 5 of these published studies have demonstrated negative results increasing the mortality rate. Only the NINDS trial demonstrated benefit when thrombolytic therapy was used for acute ischemic stroke.

It is very important that strict adherence to inclusion and exclusion criteria are followed as outlined in the NINDS trial.

The potential benefits related to thrombolytic therapy and to ischemic stroke are related to an increased chance of having a good outcome (little or no disability remaining after recovery from the stroke at 90 days). If stroke patients meet all inclusion/exclusion criteria listed, their chances of having a good outcome increase from 29% without tPA to 41% with tPA.

There was no difference in mortality between the placebo group and the group treated with tPA.

The major risk of tPA therapy in stroke patients is intracranial bleeding. The chance of serious bleeding into the stroke area is less than 0.6% in stroke patients not treated with tPA versus 6.4% in patients treated with tPA. Approximately 20% of patients will die within 30 days of their stroke regardless of tPA therapy. Approximately 5% will bleed somewhere else in the body.

The American Heart Association (AHA), the American Academy of Neurology (AAN) and the American College of Emergency Physicians (ACEP) have all endorsed thrombolytic therapy for acute ischemic stroke in a select group of patients.

Many disorders can mimic acute ischemic stroke. Even well trained stroke teams have reported misdiagnosis rates of up to 20%. (6) Be careful.

Disorders which present similar to acute ischemic stroke are: hemorrhagic stroke, cerebral or cervical trauma, meningitis/encephalitis, hypertensive encephalopathy, intracranial mass and tumor, acute subdural or epidural hematoma, seizure with persistent neurological signs (Todd's paralysis), migraines with persistent neurological symptoms, metabolic disorders such as hyperglycemia, hypoglycemia, post cardiac arrest ischemia, or drug overdose.

As you can see from the data, "A Quick Fix for Strokes" as published in Time magazine, Sept 16, 1996, is quite an overstatement. The majority of stroke patients **will not** be candidates for thrombolytic therapy because of the strict inclusion and exclusion criteria, which must be followed. Teamwork is definitely needed in order to meet the time constraints required in diagnosing and administering thrombolytic therapy for acute ischemic stroke.

1. *tissue Plasminogen Activator for Acute Ischemic Strokes*, The National Institute for Neurological Disorders and Stroke, tPA Study Group, NEJM 333 (24): Page 1581, Dec 14, 1995 (NINDS)
2. *Intravenous Thrombolysis with Recombinant Tissue Plasminogen Activator for Acute Hemispheric Stroke*, The European Cooperative Acute Stroke Study , (ECASS), Hacke, W., et al, JAMA 274(13): pg 1017, Oct 4, 1995.
3. *Randomized Control Trial of Streptokinase, ASA and combination of both in treatment of acute ischemic stroke*, Multicenter Acute Stroke trial-Italy (MAST-I) group, Lancet 346:1509, Dec 9, 1995.
4. *Thrombolytic Therapy with Streptokinase and Acute Ischemic Stroke*, Multicenter Acute Stroke Trial-Europe Study Group, NEJM 335(3): pg 145, Jul 18, 1996.
5. *Streptokinase for Acute Ischemic Stroke with Relationship to Time of Administration*, Donnan, D, et al, For the Australian Streptokinase Study Group, JAMA 276(12): pg. 961, Sep 25, 1996
6. *Conditions that Mimic Stroke in the ED: Implications for Acute Stroke Trials*, Libman, R.B., et al, Arch Neurol 53(11): pg 1119, Nov 1995.