Executive Summary
Appropriate patients may be eligible for mechanical thrombectomy whether or not they have previously received intravenous t-PA, and whether or not they presented to a center capable of this specialized technique. Based on several recent randomized controlled trials, mechanical treatment reduces long-term disability in properly selected patients with acute ischemic stroke due to large vessel occlusions. Estimates of the “Number Needed to Treat” (NNT) are on the order of 5 or less. Few medical therapies offer such a low NNT. However, intra-arterial thrombectomy is a highly specialized technique that is available at only a limited number of centers. Hospitals that are unable to perform intra-arterial thrombectomy should develop protocols and transfer arrangements in preparation for patients that will meet treatment criteria. Systems of care should be put in place by institutions, state health authorities and local EMS agencies; individual emergency physicians at hospitals not capable of performing thrombectomy should not be expected to invent a process from scratch for each individual patient. These preparations will enable emergency physicians to have the highest likelihood of being able to offer state of the art therapy for AIS, even if patients present to a facility with limited stroke treatment resources.

Introduction
Stroke is the fifth leading cause of death in the U.S. and a leading cause of long-term disability. The majority of acute strokes are ischemic in etiology, rather than hemorrhagic. The optimum treatment for patients with acute ischemic stroke (AIS) remains uncertain. This stems from variability in patient presentations and includes some of the following characteristics:

- Elapsed time since symptom onset
- Severity of neurologic deficits at presentation
- The use of different scales to evaluate stroke severity (i.e., NIH Stroke Scale, modified Rankin Score)
- Responses to re-vascularization with tissue plasminogen activator (t-PA)
- Variability in systems of care at hospitals where acute ischemic stroke patients initially present

Mechanical thrombectomy (“clot retrieval”) represents a treatment option for a select subset of patients with AIS. Recent trials evaluating mechanical thrombectomy have provided new evidence regarding efficacy, resulting in a favorable opinion regarding this therapy. The aim of this statement is to provide practicing emergency physicians updated data to inform their decision regarding mechanical thrombectomy for certain AIS patients. Appropriate patients may be eligible for mechanical thrombectomy whether or not they have previously received intravenous t-PA, and whether or not they presented to a center capable of this specialized technique.

Evidence Synopsis
Systemic (or intravenous) thrombolysis often fails to reperfuse the brain distal to occluded cerebral blood vessels in patients with AIS, particularly from proximal occlusions of the internal carotid artery or the first segment of the middle cerebral artery. Mechanical thrombectomy devices received approval of the Federal Drug Administration (FDA) in 2005. Initial randomized
controlled trials evaluating these devices failed to demonstrate improved patient outcomes. Critics of these initial studies cited the fact that they included patients who were treated too late for mechanical thrombectomy to be effective, and that first generation devices had suboptimal effectiveness. In addition, a number of trials compared pharmacologic attempts at thrombolysis to mechanical or intra-arterial therapy and these were neutral.

Newer devices, particularly stent-retrievers, were developed and demonstrated improved and faster vessel re-canalization when compared to first generation devices. As a result, additional clinical trials were developed to determine whether patients with persistent proximal arterial occlusions benefit from mechanical therapy in addition to receiving intravenous t-PA?

Several of these trials were reported at scientific meetings in late 2014 and published in 2015. Two were stopped early after an interim data analysis demonstrated efficacy of intra-arterial thrombectomy. All three trials demonstrated a large effect size reducing disability (modified Rankin Score) and, in some studies, mortality. Though different imaging protocols were used across the trials, all required the documented presence of a large vessel occlusion on vascular imaging. The largest trial (MR-CLEAN) was designed to test clot retrieval AFTER intravenous t-PA had been administered. The median onset to t-PA time in MR-CLEAN was 88 minutes from onset, whereas in routine clinical practice most U.S. stroke patients are currently treated between 120 to 150 minutes from onset.

The implications of these three latest trials for emergency physicians are concordant. If your hospital is equipped to provide mechanical treatment following stroke, this appears to be a reasonable treatment option and should be instituted as promptly as possible for patients meeting local inclusion criteria. If your hospital is not equipped to promptly provide mechanical treatment following stroke, it appears that patient outcomes can be improved by prompt transfer of patients with large vessel strokes to facilities that can rapidly and capably offer arterial reperfusion with intra-arterial thrombectomy. It is important to ensure conditions (e.g., geography, weather) allow such patients to arrive at endovascular centers within approximately 4.5-6 hours from onset (Different trials evaluated various time intervals). Such transfers can be expedited when prior arrangements and transfer agreements between hospitals and EMS agencies have been created. Some hospitals are located in regions where access to advanced centers within 4.5-6 hours of onset is not feasible.

Only a limited number of medical centers are currently equipped and capable of offering this therapy. In addition, it is important to note that endovascular treatment IS NOT a substitute for prompt intravenous thrombolysis – this should occur as rapidly as possible for eligible patients. Neurons die rapidly from the time of onset of AIS. Importantly, the current studies did not omit t-PA for patients treated with intra-arterial thrombectomy. The vast majority of patients in the three recent positive trials of intra-arterial thrombectomy received IV t-PA prior to mechanical treatment. Each recent trial used different advanced imaging techniques to select patients – at the minimum a CTA should demonstrate a large artery occlusion.

Conclusions
Mechanical treatment reduces long-term disability in properly selected patients with acute ischemic stroke due to large vessel occlusions. Estimates of the “Number Needed to Treat” (NNT) are on the order of 5 or less. Few medical therapies offer such a low NNT. However, intra-arterial thrombectomy is a highly specialized technique that is available at only a limited number of centers. Hospitals that are unable to perform intra-arterial thrombectomy should develop protocols and transfer arrangements in preparation for patients that will meet treatment criteria. These preparations will enable emergency physicians to have the highest likelihood of being able to offer state of the art therapy for AIS, even if patients present to a facility with limited stroke treatment resources.