



New Data Point to Utility of EKOS Ultrasound Device for Stroke Treatment

First Clinical Report Suggests MicroLYSUS System Might Help Expand Number of Patients to Benefit from Clot Dissolving Drugs

BOTHELL, Wash., April 27, 2001 - The first clinical experience to evaluate the strategy of combining ultrasound with clot dissolving drugs in acute stroke indicates that this approach may offer new treatment options to patients for whom no effective therapy currently exists. The findings were presented at the annual meeting of the American Society of Neuroradiology, taking place this week in Boston.

In the current research, patients eligible for treatment were those suffering a clot-induced stroke who arrived at the hospital more than three hours after symptom onset and, therefore, were not candidates for currently approved clot dissolving therapy. The study protocol consisted of inserting EKOS' MicroLYSUS™ catheter into the region of the clot and administering a clot dissolver, usually t-PA, together with ultrasound. Angiography was performed to determine the speed and extent of clot dissolution.

In total, 14 patients were treated. Because even high-risk patients were eligible for treatment, many had complex clots that threatened large amounts of brain tissue and carried a high probability of death or significant disability. Among this group were patients with blood clots in the back part of the brain. This is a particularly devastating type of stroke, with a death rate approaching 75 percent and few, if any, medical options.

Researchers found that, at one hour after treatment with the MicroLYSUS device, approximately two-thirds of patients showed evidence of good or complete recanalization, or restoration of blood flow past the point of the clot. Rapid opening of the artery is important to minimize the amount of brain tissue damaged or destroyed and thus limit post-stroke deficit. In terms of clinical outcome, three months after MicroLYSUS treatment 43 percent of patients were able to function independently as assessed by the Modified Rankin Score (MRS), a standard measure of functional status after a stroke. Mortality and intracranial bleeding, the most serious complication of clot dissolving therapy, were comparable to that seen in clinical studies of ischemic stroke patients with equivalent disease. There were no adverse events related to the device itself.

"The patients in this series were all very sick, with an exceedingly poor prognosis prior to treatment," said Wayne Clark, M.D., director of the Oregon Stroke Center and a professor of neurology in OHSU's School of Medicine. "Yet, after intervention with the MicroLYSUS device, nearly half of them survived with normal or nearly normal

neurologic function. While this is still early experience that remains to be confirmed with more study, these are very exciting results."

Expanding Treatment Options

The need for improved treatments for ischemic stroke is compelling. Clots in brain arteries account for approximately 80 percent of the 700,000 strokes that occur each year in the United States alone. Currently, the only approved treatment is intravenous therapy with t-PA administered within three hours of the onset of symptoms. For those who arrive after this window, there are no effective treatments to interrupt the stroke in progress. However, it's estimated that as few as 10 percent of stroke victims arrive at the hospital within three hours and only 2 percent are ultimately treated because of time delays once they reach the emergency room. A key concern in extending the treatment window is the risk of serious drug-related side effects. Researchers believe that by delivering drug directly into the clot, instead of throughout the bloodstream, it may be possible to reduce the amount of drug needed as well as to restore blood flow more quickly. This could result in safer and more effective treatment, and consequently increase the number of patients who could benefit from thrombolytic, or clot dissolving, therapy.

EKOS' MicroLYSUS device is a miniaturized catheter with a tiny ultrasound transducer at the tip that can deliver ultrasound and thrombolytic drug directly into the area of a clot. The device is inserted into an artery in the groin and then threaded up into the brain until it reaches the clot. The ultrasound and drug are designed to be administered simultaneously because it has been shown that ultrasound energy induces a change in the structure of clot that allows the drug to penetrate more efficiently into the internal reaches of the blockage. Laboratory research has shown that this interaction results in more rapid and more complete clot dissolution compared with clot-dissolving drugs alone.

The MicroLYSUS findings presented in Boston represent combined North American experience from four sites: Oregon Health Sciences University in Portland; the School of Medicine and Biomedical Sciences in Buffalo, NY; Vancouver Hospital and Health Sciences Center in British Columbia; and the University of Alberta Medical Center in Edmonton. The current clinical experience was conducted under physician-sponsored investigational new drug (IND) applications. In such cases, individual physicians petition the Food and Drug Administration (FDA) for permission to use an experimental treatment in patients for whom no approved therapy exists. EKOS plans to begin a company-sponsored U.S. phase I stroke study later this year. The MicroLYSUS device is also undergoing evaluation at three sites in Europe.

EKOS Corporation, located in Bothell, Wash., develops proprietary ultrasound-based systems and devices for local drug delivery. Such "active drug delivery" is designed to enhance drug action, reduce dosage requirements and toxicity, and deliver drugs to areas where none can effectively penetrate with standard techniques. EKOS is currently focusing its research and development efforts in the areas of ultrasound-enhanced

thrombolysis for treatment of stroke and peripheral vascular occlusion as well as in gene therapy for prevention of coronary restenosis.