



Research Suggests EKOS Technology May Enhance Effectiveness of Clot-Dissolving Therapy in Peripheral Vascular Occlusion

Addition of Ultrasound Found to Open Vessels More Quickly and More Completely

BOTHELL, Wash., August 16, 2001- Researchers at Cedars Sinai Medical Center have found that the use of EKOS' LYSUS(TM) ultrasound system may hold promise as a means to improve the effectiveness of thrombolytic, or clot-dissolving, drugs for treating blocked arteries in the leg. This condition is known medically as peripheral vascular occlusion (PVO).

The preclinical study, which appeared in a recent issue of the Journal of Endovascular Therapy, compared a combination of ultrasound and drug to drug treatment alone. This study used the clot dissolver urokinase, although research in other models has shown that ultrasound accelerates the action of other clot-dissolving agents as well. The Cedars-Sinai team found that one hour after treatment all of the blood vessels treated with drug and ultrasound were open, compared with only two-thirds of the drug-only arteries. In addition, they found that the ultrasound group had less clot remaining in the artery wall and had dramatically fewer embolizations. These are pieces of clot that break away and may lodge in blood vessels elsewhere in the body. All of the differences between the ultrasound and nonultrasound groups were statistically significant.

"Ultrasound-enhanced thrombolysis clearly produced more rapid and more complete clot dissolution than drug therapy alone," said Robert Siegel, M.D., director of the cardiac noninvasive laboratory at Cedars-Sinai in Los Angeles. "Further study is needed to ensure that the approach achieves the desired clinical results, but we believe this could be an important step towards improving the safety, effectiveness and expanded application of clot-dissolving therapy in patients with PVO."

Clearing Away More Clot

To evaluate the effects of the different treatment approaches, the researchers studied the arteries in two ways. First they used angiography, a type of X-ray that shows how well blood is flowing through the vessel. This is the standard method for studying clot-dissolving treatment. Then the Cedars-Sinai team went a step further and looked directly at the inside of the blood vessel using a small fiberoptic camera placed in the artery. This technique is called angiосcopy.

The dual approach of studying blood flow with angiography and directly visualizing the interior of the artery with angioscopy is useful because angiography shows functional improvement but does not provide detailed information about the condition of the blood vessel wall. Angioscopy, on the other hand, shows just how cleanly the clot has been cleared away. This is important because often a vessel may appear to be completely open when viewed by angiography but may actually have many remnants of clot left when viewed angioscopically. Leftover clot is deleterious not only because it can embolize but also because it acts as an anchor for new clot formation that, over time, can once again interrupt blood flow through the vessel. Therefore, reducing the amount of residual clot both minimizes embolic complications and helps improve long-term outcomes by preventing reblockage.

In the current study, angioscopy showed that the inside of the vessels treated with ultrasound and drug had virtually no clot remaining, while the drug-only group had persistent clot fragments even in the vessels that were considered open by angiographic evaluation. The extent to which ultrasound improved the removal of clot surprised even the researchers.

"We were quite impressed with the condition of the vessel wall when ultrasound was used compared to when it was not," Dr. Siegel noted. "The difference was dramatic, with the ultrasound-treated vessels appearing much cleaner and more pristine."

The LYSUS System

The LYSUS system consists of a catheter that is placed directly at the treatment site. A drug or therapeutic molecule, such as a clot dissolver, is infused through the catheter to the tip, where a tiny ultrasound transmitter is located. The system allows ultrasound and agent to be administered simultaneously, enhancing movement of the therapy into target tissue.

EKOS began clinical testing of its LYSUS system for PVO in 1999 using an early prototype of the device. The company expects to resume and expand this effort within the next year using an updated design. In addition to its potential application in PVO, the LYSUS system is currently undergoing clinical evaluation in conjunction with clot-dissolving therapy for the treatment of ischemic, or clot-induced, stroke. In May, research presented at the American Society of Neuroradiology (ASNR) meeting demonstrated encouraging early findings in patients treated for this indication.

EKOS Corporation, located in Bothell, Washington, 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.