



Q&A WITH DR. SIMONIAN

By Jana Acciacca

Gregory Simonian, MD is Chief of Endovascular Studies at Hackensack University where he has recently finished preliminary research on a new therapy for deep vein thrombosis (DVT) that could potentially reinvent the way we treat the disease. Publisher Jana Acciacca recently spoke with Dr. Simonian to get a better understanding of the impact that his findings may have on both patients and physicians alike.

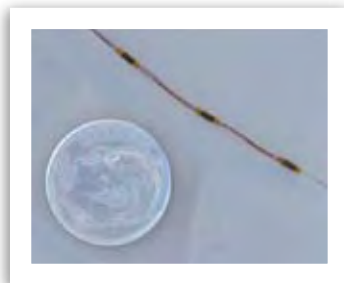
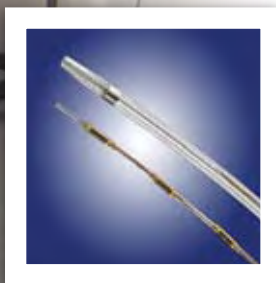
Being new to this arena, can you help me understand how DVT has traditionally been treated and the different approaches that have been taken?

The traditional standard of care for DVT (and to some degree peripheral thrombotic disease “PTD”), in general was limited to the use of blood thinners, leg elevation and anti-coagulation drugs. While anti-coagulants like Warfarin prevent further clotting and reduce the chance of pulmonary embolism (PE), they do not remove the existing thrombus. There is

mounting evidence that failure to substantially remove the clot can permanently damage the delicate but important valves inside the veins. Failure of these valves over time can lead to a condition called post thrombotic syndrome (PTS). Chronic pain, swelling and discoloration of the legs are symptoms of this condition.

Over the past decade, percutaneous interventions have been used to treat extensive upper limb DVT. The most common method is catheter-directed thrombolysis (CDT) where a side-hole catheter is placed across the occluding thrombus and a thrombolytic (clot dissolving) drug is infused to re-liquefy the clot. While effective, the patient must be observed in an intensive care unit during therapy for two or three days and there is a risk of bleeding with long exposure to thrombolytic agents. Mechanical thrombectomy catheters have also been used to break up or macerate the clot. These devices can re-establish blood flow after two or three hours of treatment in the cath lab. However, complete clot removal is difficult and the mechanical action can damage blood cells or cause pieces of clot to break away and embolize downstream. Recently, the EkoSonic Endovascular System, developed by EKOS, accelerates CDT through a combination of mechanical ultrasound energy and a drug delivery catheter. We have been using the EKOS system for over two years at Hackensack University and this new approach has given us very favorable results.

In short, EKOS’ ultrasound accelerated CDT provides rapid dissolution of the clot and the patient gets quick relief with minimal time and discomfort. Post-treatment Day 1: Patient has a hot, swollen leg, and Day 2: Patient finds a significant decrease in pain and discomfort. This rapid dissolution provides both short-term and long-term benefits for patients and for medical economics. Patients are treated and released in less time and, perhaps most important, fewer patients are seen again for the same symptoms at a later date.





What makes ultrasound accelerated CDT so different from mechanical thrombectomy?

There are a few different strategies for mechanical thrombectomy. One product uses a high-pressured jet at the tip of its catheter to create a vacuum that aspirates the clot. To avoid kidney problems from hemolysis there is a time

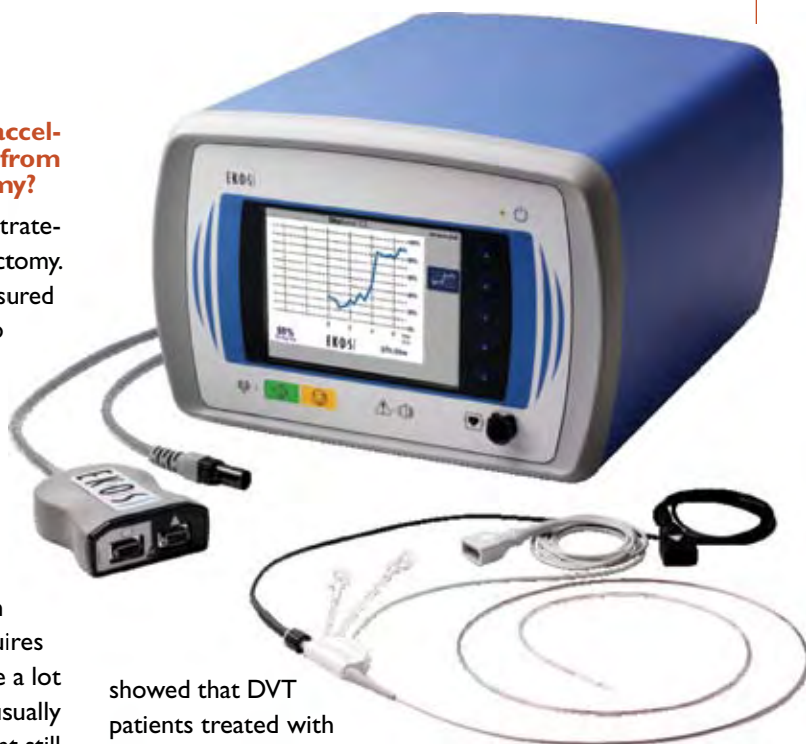
limit associated with the use of this type of device. Another device is designed to infuse thrombolytic drugs into a short section of clot isolated between two balloons while a rotating wire situated between them beats or whips the clot. The process usually requires multiple, sequential treatments and can very likely leave a lot of the clot behind. These mechanical therapies are usually supplemented with overnight CDT anyway, so the patient still spends 2-3 hours in the cath lab plus an overnight stay.

EKOS' approach is to use ultrasound to accelerate thrombolysis. This particular form of CDT could be called a "hybrid concept" as it combines a gentle ultrasound mechanical action with thrombolytic drugs to provide a gentler and more therapeutically efficient way to re-liquefy the clot. The ultrasound does not break up the clot. Instead the ultrasound energy alters the shape of the fibrin skeleton of the clot making it more porous and therefore, more permeable. The acoustic energy also creates a pressure wave that pushes the drug away from the catheter into the clot. It's like syrup permeating a melting snow cone instead of pouring syrup over an ice cube. The drug works on a larger surface area within the clot, not on the external surface area of the clot. Because the clot melts rather than breaks, we see less distal embolization.

In my opinion, the benefits of the EKOS system are most promising because you no longer have to use two methods: mechanical thrombectomy and CDT; instead, EKOS can be used as a stand alone treatment.

You mentioned that it significantly lowered both the amount of drugs and time needed to reach the desired outcome so a patient can be released. How does this happen?

During the two decades that CDT has been utilized, techniques have improved and drug choices have increased. In the National Venous Registry (Mewissen, 1999), patients treated for DVT with CDT, had average treatment time of 50 hours. In a more recent retrospective registry Johns Hopkins University (Grunwald, 2004), average CDT infusion times had dropped to 36 hours. This year a multi-center registry (Parikh, 2008)



showed that DVT patients treated with the EKOS EndoWave system were infused an average of 24 hours and 70% of these patients had complete resolution of their clot. When compared to similar patients in the Grunwald study, EKOS treated patients were infused with half the drug dose and in half the time.

You are involved in an observational study on accelerated CDT which you are very excited about. Can you tell us a little about the study and what it could mean to the treatment of DVT and PE?

EKOS has continued to evaluate ways to further improve their product, one aspect being the actual ultrasound signal. The original design emitted ultrasound, pulse parameters with constant frequency, width and intensity. EKOS engineers postulated that constantly varying the pulse parameters might cause the irregular mesh of clot fibrin to be even more permeable. The result, the EkoSonic Mach 4 system was introduced in July 2008. Believed to be four times faster than standard CDT, the enhanced performance of the Mach 4 device is being evaluated at Hackensack University along with over 10 other study sites in the TERAS Trial (Thrombolysis with EKOS ultrasound for the Resolution of Arterial and Venous occlusions Study).

Next on the horizon, EKOS is in the midst of their third generation of devices and are already looking at the fourth, fifth and sixth generations.

Publisher's Note: In the interest of full disclosure, Dr. Simonian is a principle investigator in the TERAS Trials supported by EKOS Corporation.