vascular occlusion remains one of the major causes of patient morbidity and mortality, affecting millions of Americans with deadly diseases such as acute limb ischemia, deep vein thrombosis (DVT), acute myocardial infarction, acute ischemic stroke, and pulmonary embolism. However, many of these diseases lack an optimal solution, and in cases such as DVT, there are very few applicable therapies that provide complete treatment in a safe and efficacious way. A new technology, utilized in the OmniSonics Resolution Endovascular System (OmniSonics Medical Technologies, Inc., Wilmington, MA), is based on ultrasonic ablation of thrombus (Figures 1 and 2). This treatment holds promise for providing an alternative therapy with greater benefits, fewer complications, and broader disease applicability than current treatment methods.

THERAPEUTIC APPLICATION OF ULTRASONIC ENERGY

Conte and deLorenzi conducted initial studies in 1940 on the effect of ultrasonic energy on biological tissue. Their work has led to an abundance of new applications and commercial uses for high-frequency ultrasound. One of the most common applications now includes the temporary uses such as the harmonic scalpel (Ethicon EndoSurgery, Cincinnati, OH). In addition, ultrasonic energy is routinely used for disintegration of renal and urethral calculi, aortic valve decalcification, and cataract phacoemulsion procedures. Moreover, significant progress has been made in in vitro, in vivo, and clinical study applications within the last 2 decades, during which ultrasonic energy has been evaluated for thrombus lysis, atherosclerotic debulking, enhanced localized drug delivery, restenosis prevention, and vessel dilation.

Experience with the use of ultrasonic energy on tissues has shown a “bioselectivity” or difference in the susceptibility of different tissues to ultrasonic energy exposure. Elastic tissues (rich in collagen and elastin matrix), such as arteries, veins, aortic valves, and the bladder are very resistant to ultrasonic energy, whereas inelastic tissues, such as atherosclerotic plaque, calcific deposits on the aortic valves, and thrombus are especially susceptible to ultrasonic disruption. This bioselective property of ultrasonic energy may, for example, have advantages over other forms of energy employed for angioplasty (thermal, electromagnetic, and mechanical), which are nonselective and capable of damaging native vessels.

In 1990, Rosenschein et al conducted a feasibility study of ultrasonic angioplasty, demonstrating thrombi disrup-
tion. Rosenschein et al proposed that ultrasonic energy affected thrombus by disrupting the fibrin matrix. This idea was supported by their findings of abundant fibrin fragments and absence of change in red blood cells. These findings were then confirmed in a later study of thrombus ablation in the peripheral arteries. The Rosenschein study also showed the difference in absorption of ultrasound energy and concluded that thrombus, being less inelastic than the artery was affected more by ultrasound. The investigators further analyzed the effect of ultrasound on varying degrees of concentration of hydroxyproline gelatin samples and reinforced their conclusion that the more elastic the sample was, the less effect ultrasound energy had on it. Interestingly, the results of their gelatin model were very much in line with empirical results from thrombus and the vessel samples.

There are many hypotheses as to the fibrinolytic mode of action of ultrasonic energy. Studies conducted over the past few years have identified a series of potential contributors: (1) acoustic cavitation, (2) microstreaming, (3) mechanical effects, (4) intracellular microcurrents, (5) thermal warming, and (6) increased clot permeability. These mechanisms of action vary in importance with the delivery mode and the ultrasound parameters. In the case of intravascular ultrasound-delivery catheters, cavitation, microstreaming, and mechanical effects are the primary mode of action for thrombolysis.

Acoustic cavitation is the formation of vapor-filled “cavities” or microscopic bubbles in a liquid affected by the alternating pressure of ultrasonic energy. The collapse of these microbubbles generates high local pressure charges of up to 20,000 atm that disrupt the target thrombus. The size of the microbubbles is inversely proportional to the frequency of ultrasonic energy. The larger bubbles of lower ultrasound frequencies are thought to produce greater force. A study of the effect of ultrasonic frequency on thrombus disruption showed an inverse logarithmic relation between frequency and thrombus disruption.

APPLICATION OF THEORY TO TECHNOLOGY

There are significant technical issues to be addressed in order to design a device that could utilize the therapeutic properties of ultrasonic energy. By using an external transducer to convert an electric signal into acoustic energy, the catheter’s challenge is to provide an efficient transmission medium to the lesion site. This presents an interesting conundrum because an optimal wave guide would be a solid metal wire with as large of a diameter as possible. Obviously, a large-diameter rod would not provide an ideal interventional device, compromising the physician’s ability to navigate small and tortuous anatomies. Also, bends in a wave guide can “spin off” ultrasonic energy, reducing the efficiency of energy transfer. Another substantial challenge of early devices was their reliance on the conventional approach to deliver energy using longitudinal wave forms, limiting the active section to only the tip of the wire.

The OmniSonics Resolution Endovascular System utilizes OmniWave technology, which enables the creation of a standing transverse wave on the distal section of a small-profile wire. The transverse wave creates ultrasonic energy circumferentially around the wire using very low power. By utilizing a transverse wave, the Resolution Endovascular System expands the “active zone” from just the tip of a wire to a distal section of almost 9 cm and enables the use of a very small and flexible wire, similar in size to regular interventional wires. The proprietary wire design converts the longitudinal motion to transverse motion in the treatment zone, producing an extended region of ultrasonic activation (Figure 3).

THE RESOLUTION ENDOVASCULAR SYSTEM

OmniSonics Medical Technologies recently received FDA clearance for the commercialization of their Resolution Endovascular System, indicated for the treatment of occluded synthetic hemodialysis access grafts. The system has three basic components (Figure 1). The generator sends an electric signal to the handpiece, monitoring and controlling the delivery of acoustic energy.
The handpiece converts the electric signal from the generator to low-power acoustic energy and delivers it down the therapeutic waveguide. At its core, the handpiece is composed of a piezoelectric ceramic and an acoustic horn tuned to resonate at the selected frequency. The therapeutic waveguide generates a transverse acoustic waveform that selectively microfragments the fibrin matrix found in thrombus. The therapeutic waveguide is pre-attached to the handpiece and has an overall length of 60 cm. The proximal section of the waveguide is .025 in, the main barrel .018 in, and the distal segment, called the active zone, is 8.75 cm long with a diameter of .009 in. The oscillation frequency of the waveguide is 20 KHz to maximize the disruptive effect on thrombus. The system has a pump that irrigates fluid down the catheter, a feature that is designed to ensure the system does not produce more than 41º C, which is near the normal internal body temperature of 37º C.

The Resolution System is currently approved by the FDA for declotting hemodialysis grafts. It has been tested in iliofemoral arteries and veins of canine models, and like many other applications before, demonstrated minimal-to-no damage to vessels. In bench studies, 99% of the particulates retrieved were less than 10 µm in size, roughly comparable to red blood cell size. Additionally, canine studies and a clinical study indicated no significant hemolysis as measured by levels of plasma-free hemoglobin, serum haptoglobin, and hematocrit.

FUTURE APPLICATIONS

DVT and peripheral arterial occlusions are logical next steps for the OmniWave technology. There is clear need for a device that can treat the thrombus in DVT patients while maintaining valve functionality and reducing the risks of venous thromboembolism and postthrombotic syndrome. The current DVT “gold standard” treatment is more about prevention and prophylaxis than treatment of the underlying thrombus occlusion. In order to effectively treat DVT patients, physicians require a device that can safely and effectively dissolve or extract thrombus from the veins. Currently available technologies either have safety issues associated with a combined lytic’s hemorrhage risk, or marginal declotting efficacy, particularly when treating larger venous vessel diameters. The potential benefits of ultrasonic energy in treating patients with DVT is significant because it offers a safe and efficacious way to clear thrombus, even when it is “trapped” behind venous valves.

The OmniWave technology is currently being developed for use in the peripheral arterial and venous systems. Among the iterations now being studied for the peripheral device are increased power and efficacy to treat vessel diameters up to 12 mm and clot lengths up to 30 cm. Other areas of focus have been the use of a multilumen catheter for the inclusion of a guidewire lumen to allow physicians to maintain access to the lesion.

Michael J. Hallisey, MD, is from the Center for Minimally Invasive Therapy, Jefferson Radiology, in Hartford, Connecticut. He has disclosed that he is a paid consultant to OmniSonics. Dr. Hallisey may be reached at (860) 246-6589; mhallis@harthosp.org.