Ultrasonic Plaque Ablation
A New Method for Recanalization of Partially or Totally Occluded Arteries

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The potential application of ultrasonic energy for ablation of atherosclerotic plaques was studied in human atherosclerotic arteries with continuous and pulsed delivery of energy. With a prototype ultrasonic wire probe (n=79 segments), there was gross reduction in vascular lesions as well as microscopic disruption of fibrous and calcified plaques. Normal portions of vessels appeared unaffected by the application of ultrasound. The prototype ultrasonic wire catheter ablated calcific deposits in less than 10 seconds. With this probe, all 26 complete atherosclerotic occlusions 0.5-5 cm in length were recanalized irrespective of the presence of calcium. Twenty-four of the segments were reopened in less than 20 seconds. By light microscopy, the site of plaque ablation was smooth, concave, and conformed to the shape of the probe tip. In 17 samples, there was evidence of thermal injury, and in six of the 79 samples studied with the prototype probe, there was vascular perforation. No vascular perforation occurred without thermal damage, when pulsed (rather than continuous) ultrasonic energy was used (n=40) or when the duration of application was less than 30 seconds, with power output less than 25 W and with the probe oriented parallel to the wall (n=26). Thus, by modifying the duration, mode, and magnitude of the ultrasonic power output, thermal injury and vascular perforation may be avoided. In vivo intra-arterial ultrasonic angioplasty of a canine chronic femoral fibrocellular occlusion was also performed. A preliminary in vivo study demonstrated feasibility of the percutaneous application of intra-arterial ultrasonic recanalization. Thus, ultrasonic energy appears to have potential as a method for ablation of occlusive atherosclerotic plaque.

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Balloon angioplasty has three unresolved limitations: complete obstructions, multisegment multivessel disease, and late restenosis. To resolve these problems, a variety of new techniques are being investigated, including hot-tip thermal probes, several types of laser radiation methods, atherectomy catheters, and high-speed drills. Each of these technologies also has limitations, principally relating to endothelial damage and perforation.

In the present study, we examine ultrasound as an alternate ablation energy source. Ultrasonic lithotripsy has been shown to be effective in the destruction of renal and ureteral calculi. Surgical ultrasound has also been used for the disintegration of gallstones, for dental plaque removal, in facilitating excision of intracranial and hepatic tumors, and for debridement of heavily calcified cardiac valves. In addition, surgical ultrasound has been shown to be relatively atraumatic to normal tissues, including blood vessels. We, therefore, sought to investigate whether ultrasound energy might be an effective and safe technique for ablation of human atherosclerotic plaque.

Methods
Seventy-nine segments of human atherosclerotic arteries were obtained from 14 individuals. The arteries (coronary, carotid, aorta, iliofemoral, and dorsalis pedis) were obtained within 24 hours of death or amputation. The arteries were dissected free and stored in normal saline at 3°C.

These 79 human atherosclerotic arterial segments were studied with a flexible 2.6F solid wire probe ensheathed in a 7F catheter and a modified Blackstone Model PDX-1 Ultrasonic Lithotripsy generator (115 VAC/50–60 Hz, Jamestown, New York). Each specimen was classified as calcified or noncalcified by gross and histological examination. A vessel was designated as calcified only when the gross inspection was confirmed by histological evaluation. Twenty-six of the segments were totally
occluded, and the ultrasonic probe was applied directly to the occluded lumen. The duration of the application of the solid probe to the occluded vessel segments (n=26) was from 2 to 60 seconds; for 24 segments, it was less than 20 seconds. For the 53 remaining segments, the ultrasound was applied perpendicular to the luminal surface of the atherosclerotic plaque after longitudinally opening each segment. The duration of application to these vessel segments was from 5 seconds to 20 minutes.

The ultrasonic frequency was fixed at 20 kHz. The longitudinal and transverse amplitude of the ultrasonic probe is 50±25 μm. The acoustic power output ranged from 20 to 50 W. G forces at the probe tip range from 0 to 82,000 G, are a function of the power output in watts, and increase as wattage is increased. Pulsed mode ultrasound, with a 50% duty cycle of 20 msec, was applied to 40 segments, and continuous wave ultrasound was applied to the other 39 segments. Normal saline was infused through a guide catheter at a rate of 5 ml/min to prevent heating of the probe during its use. The wire probe was advanced beyond the 7F guiding catheter by a trigger mechanism. In the semiflexible system, the range of applied forces was approximately 40±20 g force (1.38±0.69 kg/cm²) as determined by a dynamometer (PK Neuses Inc, Arlington Heights, Illinois). Precise identification of the site of application of ultrasound energy in the opened arteries was accomplished by marking these sites with India ink.

Analysis of particle size, shape, and counts was made on the effluent from nine of the 26 recanalized total arterial occlusions. The effluents from the vessels during ultrasonic recanalization were collected in sterile plastic containers (Sage Products Inc, Cary, Illinois). Five milliliters from each sample was filtered through an 0.8-μm filter. The filters were then examined with a calibrated microscope.

Preliminary In Vivo Testing

The ultrasonic probe was also tested in one dog with a chronic fibrocellular femoral arterial stenosis. This lesion is generated by removing a 3-ml specimen of autologous subcutaneous fat from the femoral triangle. A pellet is created by wrapping the fat in a 0.25-cm thick by 2-cm long strip of gel foam. This pellet is embolized to the dog's femoral artery through a 7F angiography catheter. A baseline angiogram documented the proximal femoral arterial obstruction. Twelve months later, a repeat angiogram was obtained to confirm a chronic arterial obstruction (Figure 3A). In our study, the ultrasonic probe ensheathed in a 7F catheter was passed percutaneously through an introducer sheath to the femoral arterial obstruction. With angiographic guidance, the probe was passed through the arterial obstruction with pulsed wave ultrasound at 47 W acoustic power output emanating from the transducer horn.

Results

Figure 2A shows a typical light microscopic image of a crater produced by placing the ultrasonic wire probe perpendicular to an atherosclerotic vessel segment. Grossly calcified arterial deposits were visibly reduced in less than 10 seconds. The applied force of the probe ball-tip without the use of ultrasonic energy was not sufficient to open or perforate the vessels studied. The magnitude of applied force did not affect crater size; rather, the ex vivo craters in the plaque conform to the shape of the ultrasonic wire ball-tip. The site of ablation of plaque was always concave, smooth, and conformed to the shape of the probe tip. Plaque ablation occurred in most vessels without other damage. In 10 of 53 cases, the intimal defect extended to the media without extension to the adventitia as shown in Figure 2B.

All 26 complete arterial occlusions, segments 0.5–5 cm in length were recanalized in less than 60 seconds, and 24 of 26 segments were recanalized in less than 20 seconds (Figure 2C). Eighteen of the 19 vessels defined as totally occluded and calcified were also reopened in less than 20 seconds. There were no apparent differences in the time required for recanalization between pulsed mode and continuous mode ultrasound. The rapidity of recanalization was in part mediated by the rate the probe was advanced while the ultrasonic unit was in operation. No thermal injury or perforation was present in these vessel segments.

Figure 2D is illustrative of both thermal damage that occurred in 17 of the 53 longitudinally opened specimens and of the six cases that also had arterial
perforation from intima to adventitia. Fourteen of the 17 examples of thermal injury were associated with the use of continuous wave energy as were all six cases of vessel perforation.

Table 1 summarizes the predisposing factors for ex vivo vessel perforation by the ultrasonic probe. Vessel perforation was always associated with thermal damage, the use of continuous wave energy, a power output of more than 20 W, the application of the probe perpendicular to longitudinally opened segments (rather than to 100% vessel occlusions with the probe applied parallel to the lumen for recanalization), and use of ultrasound for at least 30 seconds (in five of the six cases for more than 60 seconds). Nine vessels had prolonged perpendicular application of the ultrasonic probe from 8 to 20 minutes (8–9 minutes, n=4; 10–11 minutes, n=3; 20 minutes, n=2), without vessel perforation.

Figure 3 demonstrates the effects of ultrasonic angioplasty on an in vivo canine chronic (12-month) arterial fibrocellular occlusion. The lumen was restored with the ultrasonic angioplasty probe. The significant increase in the arterial lumen dimension (arrows) is corroborated by the disappearance of the collateral vessels. Two residual filling defects in the arterial lumen are present. No balloon angioplasty was performed on this vessel. Figure 3C shows the histological findings in the recanalized vessel in which there is a patent lumen with a mild

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<th>TABLE 1. Factors Associated With Ex Vivo Ultrasonic Probe Vessel Perforation (n=6 of 79)</th>
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residual stenosis because of the chronic fibrocellular lesion. No damage to the adjacent normal artery was noted.

The results of ultrafiltration and analysis of the sample saline solutions in which nine different atherosclerotic vessels had been subjected to ultrasound are shown in Table 2. Particle counts between 5 and 10 μm were in excess of 300/ml for all nine samples. Thus, for most samples, 90% of the particle sizes were less than 25 μm. The particles appeared as clear, transparent granules, flakes, and fibers. The majority of particles over 100 μm appeared to be fibers. Such fibers were most likely attributable to "container contamination," unrelated to particle generation from plaque ablation.

**Discussion**

Our study demonstrates for the first time that ultrasonic energy can be used to ablate atherosclerotic plaque. The prototype, specially designed, flexible wire ultrasonic probe demonstrated the capacity to rapidly ablate both fibrous and calcified plaques within seconds. All 26 total arterial occlusions were readily recanalized. Calcific arterial obstructions did not prevent the reopening of total vascular occlusions. This is consistent with previ-
ous experience with renal ultrasonic probes, which are capable of fragmenting calcified renal or ureteral stones in seconds. In the 53 vessel segments that had the probe applied perpendicular to the longitudinally opened artery, a crater was created in the plaque. Consequently, this methodology has potential for both angioplasty of stenotic vessels and restoring patency to total vascular occlusions. Our in vivo study of a canine femoral arterial occlusion demonstrated recanalization of a long narrow arterial stenosis with the prototype ultrasonic angioplasty probe. Angiography showed a reduction in the stenosis as well as disappearance of the collateral vessels after intra-arterial ultrasound.

The mechanisms of surgical ultrasound are believed to be attributable to both mechanical and cavitational effects.13,16,19,23 We theorize that the mechanism responsible for ultrasound ablation of atherosclerotic tissue is similar. The mechanical effect of plaque ablation is likely due to the longitudinal and transverse rapid (20,000 cycles/sec) movement of the probe impacting on the rigid, noncompliant, atherosclerotic portion of the vessel. Normal tissues and blood vessels are not damaged because of the small amplitude (50±25 μm) of motion of the ultrasonic probe. Thus, this mechanism of action or machining of the calcified and fibrous plaque with sparing of the normal vessel is analogous to a cast-cutter. Skin moves out of the way of the teeth of the cast-cutter because of its small amplitude of rotation.16,23 The effects of the ultrasonic probe are also related to cavitation or the generation of vapor-filled voids (bubbles) in tissues, fluids, or cells.16,23 The bubbles generated at the probe tip cause implosions as the bubbles burst. This results in the generation of 1–3 atm pressure. We hypothesize that these implosions facilitate the atherosclerotic plaque disintegration.

There are potential technical problems to overcome before clinical use of the ultrasonic probe for plaque ablation is possible. We have only preliminary studies on the effect of ultrasound on the vascular wall in vivo. However, previous data with similar devices have not demonstrated any significant ultrasonic damage to renal parenchyma or ureteral urothelium.13,14,16 We found that perforation in the ex vivo blood vessel is avoidable with pulsed wave energy, keeping power below 50 W and duration less than 30 seconds. The probe is metallic and must be sufficiently flexible to avoid in vivo vessel perforation. Because sound waves travel linearly, intravascular bends in the probe could cause heat dissipation and reduce the amount of ultrasonic energy delivered. Further, plaque ablation generates microscopic debris. Methods will need to be developed to either aspirate this material or ensure that this debris is too small to cause embolic damage.

The intravascular use of ultrasonic energy represents a new application of this modality. Our findings indicate that ultrasound has significant potential for recanalizing arterial stenosis and complete occlusions. The safe and effective recanalization of total atherosclerotic arterial obstructions would be a major advance in therapy. Further assessment of intravascular ultrasonic energy in vivo is requisite to determine its role among the proliferating new technologies for plaque penetration, ablation, and removal.

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