Ultrasonic Angioplasty in Totally Occluded Peripheral Arteries
Initial Clinical, Histological, and Angiographic Results

Uri Rosenschein, MD; Leon A. Rozenszajn, PhD; Ludvig Kraus, MD; Charles C. Marboe, MD; James F. Watkins, AB; Eric A. Rose, MD; Daniel David, MD; Paul J. Cannon, MD; and Joseph S. Weinstein, MD

Background. Ultrasonic angioplasty was recently shown to ablate thrombi and atherosclerotic plaques in vitro and to recanalize occluded arteries in experimental animal models. The goal of the present study was to examine the clinical feasibility of ultrasonic angioplasty.

Methods and Results. Intraoperative ultrasonic angioplasty was performed in vivo on totally occluded peripheral arteries (n=7). The ultrasonic angioplasty device consists of a 1.6-mm diameter flexible wire attached to a piezoelectric crystal generating ultrasound at 20 kHz. The controls, totally occluded human atherosclerotic femoral arterial segments (n=6), were crossed mechanically with the ultrasound wire ex vivo but without application of ultrasonic energy. Ultrasonic angioplasty achieved successful recanalization without perforation in all vessels. Angiograms of the treated arteries showed an average lumen patency of 82.5%. Histological examination of the recanalized arteries revealed that the recanalization had taken place through intima diffusely involved with complicated plaque. The treated arteries, compared with the controls, had greater area of recanalized lumen (5.9±1.8 versus 1.7±0.4 mm², p<0.05) and more flow (49.3±16.0 versus 11.8±4.9 ml/min, p<0.03). The damage in treated and control arteries was similar. Size-distribution analysis of the plaque debris from the treated arteries showed that 41±5% of the debris was 0.2–8 μm, 48±8% was 8–30 μm, and the remainder was 30–100 μm. In the mechanically crossed arteries, there was a shift in the distribution to larger size debris with 47±1% greater than 100 μm (p<0.001).

Conclusions. Ultrasonic angioplasty may be a useful clinical method for recanalization of total occlusions in patients with peripheral vascular disease. Ultrasonic energy appears to cause controlled injury to the atherosclerotic intima by selectively disrupting the ultrasound-sensitive occlusion. (Circulation 1991;83:1976–1986)

The development of transluminal balloon angioplasty by Gruentzig et al1,2 heralded a new era in the catheter-based interventional approach to arterial obstructive diseases. The limitations of balloon angioplasty stimulated an explosion of new angioplasty techniques, including laser, ther-
seriously limit attempts to extrapolate experience with new angioplasty techniques from the animal model to clinical practice. The goals of the present study were to examine the clinical feasibility of ultrasonic angioplasty in patients with symptomatic peripheral vascular disease and to determine the effects of ultrasound recanalization on the atherosclerotic arteries.

Methods

Ultrasonic angioplasty was performed during femoral-popliteal bypass surgery by a modification of a protocol previously described for evaluating new angioplasty devices.5

Ultrasonic Angioplasty Device

An experimental ultrasonic angioplasty device described by Rosenschein et al3 was used (Figure 1). Briefly, the device consists of a flexible aluminum ultrasonic transmission wire mechanically coupled at its proximal end to an ultrasound transducer. The transducer consists of piezoelectric elements that convert electrical energy to ultrasonic energy at 20 kHz. Ultrasonic energy is transmitted by the ultrasound wire to the target lesion in the arterial system. The distal end of the ultrasound wire vibrates longitudinally with a displacement amplitude of 150±25 μm. The ultrasound generator was operated in the pulsed mode with a 50% duty cycle to ensure resonance capture. The duration of the pulse was 0.5 second with an interval of 0.5 second.

Study Group

Patients (n=6) with angiographic evidence of total occlusion in the femoral arteries who had been previously selected for femoral-popliteal bypass operation because of severe intermittent claudications or pain at rest were studied. Total occlusion was defined as an occlusion with thrombolysis in myocardial infarction (TIMI) grade 0 or 1 antegrade flow.6,7 All patients were men; the mean age was 65±7 years. Diabetes was present in five, hypertension in three, concomitant coronary artery disease in three, and significant cigarette smoking in four (>10 cigarettes/day). Informed consent for ultrasonic angioplasty was obtained from each patient before the bypass operation. Permission to perform ultrasonic angioplasty was obtained from the Institutional Ethics Committee of the Meir General Hospital and the Israeli Ministry of Health.

Surgical Procedure

All surgical procedures were performed under general anesthesia. The common and deep femoral arteries were exposed in the usual fashion. Of the proximal superficial artery, approximately a 10-cm segment was exposed (about 5 cm longer than usual). A baseline intraoperative peripheral angiogram was obtained. The patients were heparinized (50 IU/kg body wt) before the proximal common femoral artery and deep femoral artery were cross-clamped. An arteriotomy, to be included in the bypass anastomosis, was incised proximal to the occlusion in the common femoral artery. After the ultrasonic recanalization, the surgical procedure was complete in standard fashion.

Ultrasonic Angioplasty Protocol

After the surgical exposure of the femoral artery and the arteriotomy, a 0.035-in. guidewire was introduced through the arteriotomy, and an attempt to penetrate and cross the occlusion was made. A 1.6-mm ultrasound wire, not attached to a catheter system, was then inserted directly into the arteriotomy and advanced under fluoroscopic guidance to

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**FIGURE 1.** Prototype of the ultrasonic angioplasty device used for recanalization of totally occluded peripheral arteries. Device consists of a flexible ultrasound transmission wire (1) coupled at its proximal end to an ultrasound transducer (2) that is powered by an external generator (3). Electrical energy is converted into ultrasonic energy in the transducer and is transmitted by the ultrasound wire to the target lesion in the arterial system.
the site of the lesion. Gentle pressure was applied to effect mechanical recanalization. Only lesions that could not be crossed mechanically, either with the guidewire or the ultrasound wire, were treated with ultrasound. Manual irrigation with saline (<5 ml/min) at the site of the arteriotomy maintained an aqueous medium that ensured ultrasound coupling during the procedure. To maximize patient safety, the endpoint of the experimental procedure was the recanalization of the surgically exposed arterial segment under direct visualization; no effort was made to create a channel through the entire occlusion. Ultrasound was applied in a graded fashion by using a dosimetric matrix beginning at 5 W with increments of 5 W up to a total of 35 W. The applied forward pressure was gentle so that bending of the ultrasound wire was not observed during the procedure. When an obstruction was penetrated at a given power level, this level was held constant. If there was no evidence of penetration at 35 W, the procedure was terminated. The ultrasound wire was passed back and forth through the obstructed segment two to four times. After the procedure, the recanalized segment was ligated and resected just distal to the site of application of ultrasonic energy to permit histological and flow studies and debris collection. When the entire occlusion was located in the surgically exposed arterial segment, a peripheral angiogram was repeated without resection of the recanalized segment.

Two experienced angiographers evaluated the angiograms in a blinded fashion. The maximum percent recanalization (defined by caliper-determined ratio of the diameter of the lumen at the narrowest point relative to that of the adjacent normal diameter) and the length of the involved segment were calculated. In the absence of agreement, the angiograms were reviewed jointly, and a decision was reached by consensus.

Control Group

Totally occluded human atherosclerotic femoral arterial segments (n=6) were obtained during the femoral-popliteal bypass operation. Immediately after the atherosclerotic arteries were dissected, a representative section of each lesion was excised and fixed to document the presence and nature of the total occlusion. The remaining arterial segments were kept in modified Eagle’s medium (Cellgro, Mediatech, Chicago) at 4°C for less than 24 hours. Each of the occluded arterial segments was crossed mechanically with the ultrasound wire but without application of ultrasonic energy. The ultrasound wire was passed back and forth through the occluded segment three times. The flow, histology, and debris in the arterial segments were studied.

Flow Measurements

The recanalized atherosclerotic arterial segments were cannulated and then perfused with saline at a constant pressure of 100 mm Hg. The flow was calculated by averaging triplicate samples of volume collections.

Debris Analysis

The saline flushed from the recanalized arterial segments was collected and filtered serially on preweighed filters of decremental mesh sizes (400-, 100-, 50-, 30-, 8-, and 0.2-μm mesh, Fisher Scientific Co., Pittsburgh). The filters were then dried at 60°C for 3 hours and reweighed (model AB-4, Cristian Becker, Germany). The size distribution of the debris was obtained from the weight difference of the various filters before and after filtration of the debris. The debris was subjected to light and contrast phase microscopy (Photomicroscope, Carl-Zeiss, Inc., Thornwood, N.Y.).

Pathological Analysis

The resected segments of the femoral arteries of all patients were studied in a similar fashion. The length of the recanalized arterial segment was defined as the distance between the entry point and the end of the recanalized lumen. The arterial segments were pressure fixed (100 mm Hg for 20 minutes) with 2.5% gluteraldehyde in 0.1 M phosphate buffer. To minimize the creation of sectioning artifacts and to facilitate the identification of the recanalized lumen, the arterial segments were thoroughly decalcified by immersing them in a 14% HCl solution (Cal-ExII, Fisher Diagnostic, Orangeburg, N.Y.) for more than 5 hours, then trimmed in 5-mm segments, and processed routinely. Five-micron sections were mounted on glass slides and stained with hematoxylin-phlox-
FIGURE 2. Panel A: Diagram illustrating the experimental setup for documenting the production of cavitations by the ultrasonic angioplasty device. Ultrasound imaging transducer (T) is positioned on the wall of an arterial phantom (A). The ultrasound wire (W), positioned in the arterial phantom within the examining plane (dotted area), is the image on display (I). Panel B: Echocardiographic image on display illustrating the distal tip of the ultrasound wire (arrow) during application of ultrasonic energy at a power level less than cavitation threshold (8 W). Cavitations cannot be discerned. Panel C: Echocardiographic image showing that at 12 W, which is the energy level needed for clinical ultrasonic angioplasty, a conically shaped field of cavitations (arrow), which was identified as highly echogenic microbubbles, is emitted from the distal tip of the ultrasonic wire.
ine-saffron or Verhoff–van Gieson’s elastic tissue stain.

The histological sections were subjected to morphometric analysis. The hematoxylin-phloxine-saffron–stained slides were placed on the stage of a projection light microscope (Leitz), and the image, which was enlarged approximately ×200, was projected on a digitizing tablet (Digitizing Table 2210-1212, Numonics Corp., Montgomeryville, Pa). The original lumen (total area enclosed by the internal elastic lamina) and the recanalized lumen (original lumen area less the area of the atherosclerotic plaque) were outlined and measured with an electronic cursor linked to a computer (2-180 Personal Computer, Zenith Data Systems, St. Paul, Minn.) with a commercial software package (SigmaScan, Jandel Scientific, Corte Madera, Calif.). All sections were measured after exclusion of sectioning artifacts, and the average was recorded for each recanalized artery. The percentage of recanalization was calculated according to the following formula: percent recanalization is equal to (area of the recanalized lumen divided by area of the original lumen) multiplied by 100.

The occlusive plaque in each recanalized artery was studied for the presence of calcium deposits, fibrous tissue, old thrombus, fresh thrombus, and fat (extracellular lipid or foam cells).

The extent of arterial wall injury was determined. The circumference of the arterial wall was divided into four equal segments. Each segment was assessed for the presence and degree of injury. A number corresponding to the maximal depth of arterial wall injury was assigned to each segment (medial injury, 1; transmedial injury, 2; adventitial injury, 3; perforation, 4). The score of arterial wall injury was obtained by adding the numbers assigned to each segment. All sections were measured after exclusion of sectioning artifacts, and the average was recorded for each recanalized artery.

**Cavitation Analysis**

To elucidate the mechanism of action of ultrasonic angioplasty, the production of cavitations by the ultrasonic angioplasty device was studied in an arterial phantom. The ultrasound wire was positioned in a 6-mm diameter plastic tube filled with saline at 37°C at a pressure of 1 atm. To image the ultrasound wire, a 7.5-MHz multielement linear array ultrasound imaging transducer was positioned on the wall of the arterial phantom with the ultrasound wire in the plane of examination (Figure 2A). The ultrasound imaging system had a distal resolution less than 0.4 mm, a lateral resolution less than 0.7 mm at focus, maximal depth of 3.2 mm, and a frame rate of 11 frames/sec (Ultraplex, Ulramed Inc., North Branswick, N.J.). To determine the cavitation threshold (i.e., the lower power level at which cavitations are produced), the production of cavitations was studied at different ultrasound intensity output settings (0, 2, 4, 8, 10, and 12 W). Cavitations were identified in the ultrasound image display as highly echogenic microbubbles.

**Thermal Analysis**

The efficiency of ultrasound transmission was assessed by comparing the heat generated in the ultrasound wire with the heat generated in identical wires made of titanium, the metal traditionally used for the construction of ultrasound probes. The ultrasound wires (length, 48 cm; diameter, 1.6 mm) were immersed in saline at 22°C and powered for 300 seconds with 8.7 W of ultrasound. Temperature at the distal tip of the ultrasound wires was continuously measured with a Teflon-coated microthermocoupler (IT-23, Physitemp Instruments, Inc., Clifton, N.J.) attached to a thermometer (BAT-10, Physitemp) with a temperature range of −100°C to 199.9°C and resolution of 0.1°C.

**Statistical Analysis**

Most data were summarized as mean±SEM. Differences between most groups were analyzed with the unpaired two-tailed Student’s t test. The score of arterial wall injury was expressed as the median followed by the range. The wall-injury hypothesis was tested with the Wilcoxon’s ranked-sum test. The plaque debris data were analyzed with ridit analysis to produce means, tolerance intervals, size distribution, and to test the hypothesis. A p value less than or equal to 0.05 was considered significant.

**Results**

In seven of seven totally occluded arteries, in six patients, successful ultrasonic angioplasty (defined as recanalization of the surgically exposed segment of the obstructed artery documented by histology or angiography) was performed without perforations. In two arteries, successful ultrasonic angioplasty was documented by angiography, and in five arteries, the success of the procedure was documented by histological examination of the treated artery. There were no adverse side effects after ultrasonic angioplasty.

Clinical and in vitro data of the patients and the treated arteries are summarized in Table 1. The treated and control arterial segments were similar in length (4.1±0.6 versus 4.0±0.7 cm, p=NS) and in cross-sectional area of the original lumen (19.2±1.5 versus 17.5±2.0 mm², p=NS). Ultrasonic energy application time was 78±14 seconds with ultrasound levels of 12±0.9 W.

**Angiography**

The peripheral angiograms of patients whose entire occlusion was located in the surgically exposed arterial segment (n=2) revealed an average lumen patency of 82.5%. No acute thrombosis, dissection, embolization, or spasm was observed. As a result of the 75% recanalization with TIMI grade 3 antegrade flow in patient 3, the surgical procedure was changed from bypass surgery to arterial endarterectomy. In patient 6, the baseline intraoperative angiograms
**FIGURE 3.** Panel A: *Intraoperative angiogram at baseline shows the target lesion (arrow), which is a subtotal occlusion of the superficial femoral artery.* Panel B: *Intraoperative angiogram after ultrasonic angioplasty reveals 90% lumen patency (arrow), the appearance of a previously occluded side branch (open arrowheads), and a newly implanted saphenous vein graft (solid arrowheads).*

**TABLE 1. Results of Ultrasonic Angioplasty in Totally Occluded Peripheral Arteries**

<table>
<thead>
<tr>
<th>Case</th>
<th>Associated disease</th>
<th>Sonified artery</th>
<th>Recanalized segment length (cm)</th>
<th>% Recanalization (area/diameter)</th>
<th>Arterial wall damage index</th>
<th>Flow (ml/min)</th>
<th>Debris (mg)</th>
<th>Plaque composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CAD/DM</td>
<td>SFA</td>
<td>3.4</td>
<td>13/</td>
<td>0</td>
<td>61</td>
<td>22.2</td>
<td>Ca: Fib: OT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dacron Graft</td>
<td>3.1</td>
<td>91/</td>
<td>0</td>
<td>*</td>
<td>*</td>
<td>FT in graft</td>
</tr>
<tr>
<td>2</td>
<td>DM/HT/SM</td>
<td>SFA</td>
<td>6.0</td>
<td>16/</td>
<td>0</td>
<td>20</td>
<td>31.0</td>
<td>Fib: OT: Ca</td>
</tr>
<tr>
<td>3</td>
<td>DM/SM</td>
<td>CFA</td>
<td>6.3</td>
<td>75/</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>Fib: Fat</td>
</tr>
<tr>
<td>4</td>
<td>CAD/HT/SM</td>
<td>SFA</td>
<td>3.2</td>
<td><em>/</em></td>
<td>1</td>
<td>*</td>
<td>*</td>
<td>OT: Fib: Ca</td>
</tr>
<tr>
<td>5</td>
<td>CAD/HT/SM</td>
<td>SFA</td>
<td>4.7</td>
<td>29/</td>
<td>0</td>
<td>67</td>
<td>36.1</td>
<td>Ca: OT: Fib</td>
</tr>
<tr>
<td>6</td>
<td>DM</td>
<td>SFA</td>
<td>2.0</td>
<td>/90</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td></td>
</tr>
<tr>
<td>Mean±SEM</td>
<td></td>
<td></td>
<td>4.1±0.6</td>
<td>37.5±14.0/82.5</td>
<td>0(0-1)‡</td>
<td>49.3±14.7</td>
<td>20.5±9.6</td>
<td></td>
</tr>
</tbody>
</table>

CAD, coronary artery disease; Ca, calcium deposits; CFA, common femoral artery; DM, diabetes mellitus; Fib, fibrous; Fat, foam cells and/or extracellular lipids; FT, fresh thrombus; HT, hypertension; OT, old thrombus; SFA, superficial femoral artery; SM, smoker.

*Not done due to technical problems.
†The artery was not resected due to successful ultrasonic angioplasty.
‡Median (range).

revealed subtotal occlusion of the superficial femoral artery (Figure 3A). After 2 minutes of treatment with ultrasonic energy, the intraoperative angiogram showed 90% recanalization and the appearance of a previously occluded side branch at the site of the target lesion (Figure 3B).

**Histology**

Histological examination of the treated native arterial segments (n=4) revealed diffuse involvement of the intima with complicated atherosclerotic plaque through which a smooth-walled channel had been created
(19.3±4.9% recanalization). No damage to the media and adventitia, specifically thermal or blast injury, was evident (Figure 4). A thrombotically occluded synthetic graft was treated in patient 1. After application of ultrasonic energy, 91% recanalization was achieved with minimal residual thrombus and no damage to the graft (Figure 5). Total occlusion of the arterial lumen because of atherosclerosis, thrombosis, or both was noted in arterial sections not subjected to recanalization. Morphometric analysis of the arterial segments showed that the cross-sectional area of the ultrasound-induced lumen was greater than that of the mechanically induced control lumen (5.9±1.8 versus 1.7±0.4 mm², p<0.05). The area of ultrasound-induced lumen was greater than that of the ultrasound wire (5.9±1.8 versus 2.0 mm², p<0.005), whereas the area of the mechanically induced control lumen was similar to that of the ultrasound wire (1.7±0.4 versus 2.0 mm², p=NS). Furthermore, a higher percentage of recanalization was achieved in the treated arteries than in the controls (37.5±14.0% versus 10.2±2.6%, p<0.05). Although the incidence of arterial wall injury was higher in the control arteries than in the treated ones (one perforation and two medial injuries versus one medial injury), the difference in the injury score was not significant (1: range, 0–1 versus 0: range, 0–1; p=NS).

**Flow and Debris Analysis**

Before the procedure, angiography showed either minimal or no flow (TIMI grade 0 or 1) through the occluded arteries. After the procedure, the flow through the ultrasound-induced lumen was 49.3±16.0
FIGURE 5. Histological section of a recanalized thrombotically occluded synthetic graft (G). After ultrasonic angioplasty, the recanalized lumen (L) occupies 91% of the area of the original lumen, with minimal residual thrombus (T). Discontinuity in the graft is an artifact.

ml/min compared with 11.8±4.9 ml/min through the mechanically induced lumen (p<0.03).

The plaque debris from the recanalized lumen was composed primarily of amorphous calcified tissue fragments. Analysis of the distribution of the size of the ultrasound-induced plaque debris showed that 41±5% (by weight) was 0.2–8 μm (subcapillary size); 48±8% was 8–30 μm, and the remainder was 30–100 μm. All debris was less than 100 μm. In the mechanically crossed arteries, a shift in the distribution toward larger size plaque debris was noted. Only 5±1% was of subcapillary size, whereas 47±1% was more than 100 μm (p<0.001) (Figure 6).

Cavitation and Thermal Analysis

The cavitational threshold was found to be 8 W. Cavitations were not evident at ultrasound intensities below this level (Figure 2B). At 12 W, which was the mean energy level used clinically, a conically shaped field of cavitations was emitted from the distal tip of the ultrasound wire that reached a maximal distance of 20 mm and a maximal radius of 17 mm (Figure 2C).

The temperature rise at the distal tip of the aluminum ultrasound wires was lower than that of the titanium ultrasound wire (3.1±0.2 versus 6.1±0.5°C).

Discussion

Ultrasonic angioplasty was pioneered in the late 1960s with the development of the first catheter-based systems for intravascular ultrasonic disruption of atherosclerotic plaques and thrombi. Clinical adoption of this new method was slow primarily because conversion of ultrasonic energy to thermal energy in the delivery system resulted in power loss and thermal damage to the arteries. Recently, a number of investigators showed renewed interest in the use of ultrasonic energy for angioplasty. To maximize the transmission of ultrasound and to minimize its dissipation as heat, we used ultrasound wire made of high–mechanical Q aluminum. The mechanical Q of a material is proportional to the ratio of energy stored to the energy dissipated per unit of material volume per cycle of vibration. Thus, the higher the mechanical Q, the less the quantity of ultrasound energy that is dissipated as heat and the lower the attenuation of ultrasound per unit length of ultrasound wire. Aluminum has a higher mechanical Q than does titanium (50,000 versus 24,000), which is traditionally used for the construction of ultrasound probes. We have found minimal conversion of
high-energy ultrasound to heat in the aluminum wires. This observation suggests a high efficiency of ultrasound transmission and lower risk of thermal injury and associated perforations.

In this report, we describe the first clinical study of ultrasonic angioplasty in peripheral vascular disease. Ultrasonic angioplasty was accompanied by successful recanalization of seven totally occluded arterial segments in six patients with symptomatic atherosclerotic lesions. Recanalization with ultrasound resulted in substantial flow and minimal damage to the healthy arterial wall. The treated arteries had a significantly greater area of recanalized lumen, more flow, and smaller-sized plaque debris than did mechanically crossed totally occluded control arteries. These findings suggest that recanalization was achieved by ultrasonic disruption of the occlusive plaque and not solely by mechanical penetration with the ultrasound wire.

The low score of injury to the treated arteries suggests that ultrasound recanalization through the diseased intima was achieved before damage to the media and adventitia occurred. It was recently suggested that injury to the media triggers the marked smooth muscle cell proliferation associated with the restenosis observed after angioplasty. If this is so, then the relatively minimal damage to the media during application of ultrasonic energy suggests a potentially lower restenosis rate after ultrasonic angioplasty.

The small size of the debris from the treated arteries (mean, 18.9 μm) portends a low risk of clinically significant embolization. We had no angiographic evidence of acute embolization in our study. Furthermore, we observed that after ultrasonic angioplasty, an occluded side branch at the site of the target lesion (Figure 3A) had become patent (Figure 3B) rather than filling with disrupted plaque material. The size of plaque debris after ultrasonic angioplasty was similar to that after rotational atherectomy, where the debris appears to have no clinically significant effects on distal perfusion.

Our results are consistent with recent data from experimental animal models and a parallel initial clinical experience in which ultrasonic energy was used successfully and safely for angioplasty. In catheter-based ultrasonic angioplasty systems, the conversion of ultrasound to heat in the delivery system has been a major obstacle that impeded the development of a practical ultrasonic angioplasty system. We found clinical ultrasonic angioplasty not to be accompanied by thermal injury to the treated arteries. This finding confirms our experience in vitro and in vivo and is consistent with the minimal conversion of ultrasound to heat in the ultrasound wire.

**Mechanism**

The amplitude of the longitudinal vibrations at the distal end of the ultrasound wire used in this study was 150 μm. At this amplitude, high-energy ultrasound is capable of fragmenting tissue mechanically. We have demonstrated that the energy level required for successful clinical ultrasonic angioplasty lies above the cavitation threshold. At this level, the ultrasound wire produces a field of cavitations (Figure 2C) with concurrent generation of intense shock waves leading to tissue disruption.

We found that both the area of the recanalized lumen and the flow through treated arteries were greater than those of mechanically crossed control segments. These results would not be expected if recanalization was secondary only to fragmentation by the longitudinal vibration of the ultrasound wire. Rather, they suggest involvement of the shock waves generated in the field of cavitation emitted by the ultrasound wire. We presume, therefore, that both effects—mechanical and cavitational—contribute to the operational mechanism of the ultrasonic angioplasty device.

In this study, the observed larger area of recanalization in the thrombographically occluded graft, compared with the arteries occluded by complicated plaque, is consistent with our previous observations in vivo and in vitro. That thrombi and atherosclerotic plaques are disrupted at different rates. Thrombi appear to disintegrate more rapidly, and the radius of disruption around the ultrasound wire is greater than that of atherosclerotic plaques. Complicated plaques, particularly in the presence of dense fibrous tissue, appear to undergo ultrasonic disruption more slowly, and the disruption occurs in the immediate vicinity of the ultrasound wire. These observations suggest that thrombectomy may be disrupted primarily by the effect of the shock waves produced in the cavitation field, whereas the disruption of fibrous plaques probably involves a greater component of mechanical fragmentation by the vibrating wire. Therefore, the relative contributions of these two components, the cavitations and the mechanical effects, on to the disruption of an occlusion depend on its composition.

**Hypothesis**

Our hypothesis to explain the selectivity of the injury caused by high-energy ultrasound is based on the differences in elasticity between the atherosclerotic plaque and the adjacent media. Collagen, the
major determinant of tissue elasticity, is abundant in muscular arteries mainly in the specialized layer of the media, the internal elastic lamina.27,28 The collagen in atherosclerotic plaques is abnormal in composition and structure.29-31 Micromechanical testing of samples of media and plaques from fresh atherosclerotic arteries from human cadavers indicate that the elasticity of plaques is significantly lower than that of the media.32 When ultrasound waves travel through tissue, the amplitude of the mechanical pressure (i.e., tissue displacement) is proportional to their intensity.33 Therefore, we suggest that a given level of ultrasonic energy exerts a more deforming and disintegrative effect on the atherosclerotic plaque, with the lesser elasticity, than on the arterial wall.

This concept of elasticity-dependent selectivity in tissue disruption is consistent with reports that tissue resistant to high-energy ultrasonic damage has dense collagen matrix (artery,34-36 bladder,37 and aortic valve38), and that tissue that is susceptible to high-energy ultrasonic damage lacks this collagen matrix support (atherosclerotic plaque,3,13,39 thrombus,3,40 liver,34,35 and calcific deposits on the aortic valve38). When ultrasound intensity is raised beyond a threshold level, tissue displacement becomes so large that damage can occur to both plaque and arterial wall.41

Conclusions

The results of this feasibility study suggest that ultrasonic angioplasty is a potentially useful method for clinical recanalization of total occlusions. Ultrasonic angioplasty uses advantageously the differences in the physical properties of the obstructive lesion and the arterial wall to induce controlled injury to the ultrasound-sensitive arterial occlusion. Thus, precise coaxiality of the ultrasound wire and exact focusing and timing of application of ultrasound energy are not crucial in this technique.

Limitations

This study evaluates only the immediate results of ultrasonic angioplasty. The patients were not perfused through reopened arteries, and the in vivo consequences of ultrasonic angioplasty need to be studied. In addition, the ultrasonic angioplasty device we used needs to be refined. Current technology for efficient transmission of high-energy ultrasound dictates the use of solid metal wire; this limits the pliability of the wire’s tip and overall flexibility of the device. More research is warranted that is directed toward developing and identifying materials that will render the ultrasound wire more pliable and flexible while maintaining high efficiency of ultrasound transmission.

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References


KEY WORDS • peripheral vascular disease • atherosclerosis • angioplasty • ultrasound • total occlusion
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