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Thermal Compression and Molding of Atherosclerotic Vascular Tissue With Use of Radiofrequency Energy: Implications for Radiofrequency Balloon Angioplasty

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The combined delivery of pressure and thermal energy may effectively remodel intraluminal atherosclerotic plaque and fuse intimal tears. To test these hypotheses with use of a non-laser thermal energy source, radiofrequency energy was delivered to postmortem human atherosclerotic vessels from a metal "hot-tip" catheter, block-mounted bipolar electrodes and from a prototype radiofrequency balloon catheter. Sixty-two radiofrequency doses delivered from a metal electrode tip produced dose-dependent ablation of atherosclerotic plaque, ranging from clean and shallow craters with histologic evidence of thermal compression at doses <40 J to tissue charring and vaporization at higher (>80 J) doses. Lesion dimensions ranged between 3.14 and 3.79 mm in diameter and 0.20 and 0.47 mm in depth. Tissue perforation was not observed.

To test the potential for radiofrequency fusion of intimal tears, 5 atm of pressure and 200 J radiofrequency energy were delivered from block-mounted bipolar electrodes to 48 segments of human atherosclerotic aorta, which had been manually separated into intima-media and media-adventitial layers. Significantly stronger tissue fusion resulted (28.5 ± 3.3 g) with radiofrequency compared with that with pressure alone (4.8 ± 0.26 g; $p < 0.0001$). A prototype radiofrequency balloon catheter was used to deliver 3 atm of balloon pressure with or without 200 J radiofrequency energy to 20 postmortem human atherosclerotic arterial segments. In 10 of 10 radiofrequency-treated vessels, thermal "molding" of both normal and atherosclerotic vessel wall segments resulted with increased luminal diameter and histologic evidence of medial myocyte damage. In 10 of 10 control vessels treated with balloon pressure alone, vascular geometry and luminal diameter recoiled to predilation values.

Thus, delivery of radiofrequency energy in combination with pressure to atherosclerotic tissue effectively molds atherosclerotic plaque and vessels and produces medial myocyte damage and strong tissue fusion. These observations may have important implications for preventing acute and chronic restenosis after balloon angioplasty.

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Percutaneous transluminal balloon angioplasty is an important and effective treatment of peripheral and coronary vascular disease (1–3). However, its overall efficacy is limited by the relatively high frequency of restenosis in initially successful cases (4) and the lower success rate in totally occluded arteries (5).

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In preliminary studies, laser-thermal angioplasty has been shown to be effective in opening long, stenotic lesions as well as totally occluded vessels (6,7); and there is suggestive evidence in experimental models of atherosclerosis that the use of thermal energy may decrease the incidence of restenosis compared with that of balloon angioplasty alone (8). Studies (9) have also demonstrated the feasibility of fusing or sealing intimal flaps by laser light diffused through an angioplasty balloon. Intimal tears produced by balloon angioplasty may be "fused" back against the vessel wall, thereby decreasing the potential for acute vessel closure and chronic restenosis (9). Laser systems, however, are an expensive and inefficient energy source for heating a small metal probe or the vascular tissue surrounding a balloon catheter.

Radiofrequency energy has recently been shown to be an

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effective energy source for ablation of endocardial arrhythmogenic foci in the treatment of cardiac arrhythmias (10), and, in preliminary studies (11,12), it has been shown to be promising for use in vascular intervention. It is a versatile energy source that is easy to control and less costly than laser energy. The purpose of this study was to assess whether the combination of non-laser thermal energy and pressure could effectively remodel atherosclerotic plaque, fuse intimal tears and alter the luminal geometry of atherosclerotic vessels. The feasibility of using radiofrequency balloon angioplasty to effectively alter vascular luminal geometry was tested in postmortem human atherosclerotic arteries using a prototype radiofrequency balloon angioplasty catheter.

Methods

The radiofrequency energy power unit. This consisted of a Microvasive Bicap electrocautery unit (650 kHz) coupled to a custom-built radiofrequency controller. Because preliminary studies have shown that gold is a superior thermal and electrical conductor that transfers energy more efficiently to tissues than does either stainless steel or platinum, custom-manufactured 1.5 mm diameter gold-tip electrode catheters were used for initial studies of the effects of radiofrequency energy on human and canine aorta. For these studies, radiofrequency energy was delivered from the tip of the electrode catheter through tissue samples to a copper electrode plate.

Human aortic in vitro dosimetric and histologic studies. Forty-three strips of fresh postmortem human atherosclerotic aorta and five strips of canine aorta were used to study the dosimetric, histologic and thermal effects of radiofrequency energy on atherosclerotic plaque and normal aortic wall. Although human samples vary in plaque consistency, ranging from fibrofatty ("soft") to densely fibrotic and calcified ("hard") plaque, all the human samples consisted of fibrofatty plaque except for three heavily calcified samples. The gold-tip electrode catheter was placed perpendicular to the tissue with the tip directly in contact with the endothelial surface, maintaining a constant force on tissue equal to 40 g (or pressure of 2.06×10^6 dynes/cm^2). This force was chosen to approximate the amount produced by a "gentle push on a catheter against a mild resistance." Heparinized whole blood was perfused (5 ml/min) over the point of contact of the catheter tip with tissue. Sixty-two radiofrequency doses ranging from 20 to 85 J were delivered to human atherosclerotic aorta and 100 radiofrequency doses delivered to fresh canine aorta for dosimetric and histologic studies (human: 20 J [n = 12]; 30 J [n = 12]; 50 J [n = 10]; 60 J [n = 12]; 85 J [n = 16]; canine: 20 J [n = 10]; 25 J [n = 10]; 30 J [n = 10]; 40 J [n = 10]; 50 J [n = 10]; 60 J [n = 10]; 65 J [n = 10]; 80 J [n = 10]; 82 J [n = 10]; 85 J [n = 10]). Measurements of gross lesion dimensions were made with use of a microcaliper. Tissues were fixed in formalin and prepared for histologic examination.

Temperature and histologic studies. A second set of experiments was performed to characterize the influence of different biologic media on radiofrequency energy delivery to atherosclerotic tissue, specifically, tissue thermal response and tissue injury. A gold-tip electrode catheter was placed in contact with samples of fresh postmortem human and canine aorta as described previously. Tissue temperatures were measured on the luminal surface at a point 2 mm from the point of contact of the catheter tip with tissue with use of a 22 gauge temperature probe (Cole-Parmer Instrument Co., YSI series 500; time constant = 0.2 s) and a digital thermometer (Cole-Parmer Instrument Co., model 8110-20; range: −25.7 to +103.2°C; resolution: 0.1°C). Heparinized whole blood or saline solution at room temperature was perfused (5 ml/min) at the tissue-catheter tip junction during delivery of 103 doses of 20 to 85 J radiofrequency energy. For temperature studies, 41 doses of 80 J radiofrequency energy were delivered and tissue temperatures were measured every 5 s for 1 min after the start of radiofrequency delivery, as has been previously described (13). The peak rise in tissue temperature was calculated by subtracting the baseline tissue temperature from the peak temperature achieved after radiofrequency delivery. Tissue lesions were again measured and tissue specimens prepared for histologic examination as previously described.

In vitro study of vascular tissue fusion. Because other investigators (14) have shown that heat from neodymium:yttrium aluminum garnet (Nd:YAG) laser light directed through a diffusing lens is capable of "fusing" atherosclerotic aorta that has been mechanically separated along tissue planes, a third set of experiments was performed to determine whether heat generated by a non-laser source produces similar fusion of separated tissue planes. A pair of flat copper electrodes (area 1.63 cm^2) were mounted on a plastic block separated by a 5.08 mm gap (Fig. 1). This electrode configuration was designed to be similar to the electrode configuration of a prototype 4 mm diameter radiofrequency balloon angioplasty catheter. The mounted electrode pair was placed over strips of fresh postmortem atherosclerotic aorta in which the intima-media was manually separated from the underlying media-adventitia (14). A drop of heparinized whole blood was placed between the separated tissue planes and the separated layers reapposed.

The electrode pair was placed on the luminal surface and pressure applied with use of an inverted plastic syringe connected to a standard coronary angioplasty inflating device. Pressure of 5 atm was used to approximate that exerted by an angioplasty balloon. Radiofrequency doses of 200 J were applied to each of 24 specimens from the electrode pair, while pressure on the tissues was maintained for a total of 60 s. The "fused" aortic strips were placed in a device in which one piece of tissue was fixed to a plate and the other tissue flap was connected to a styrofoam cup that was slowly

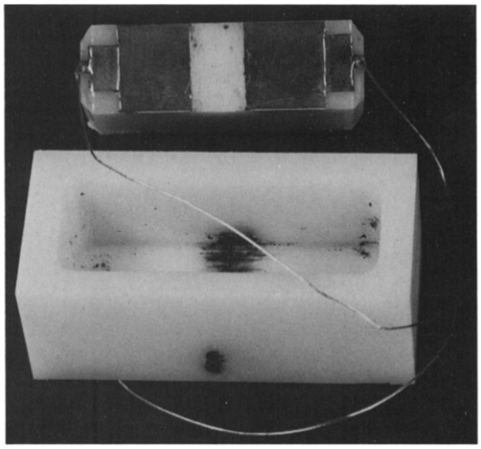
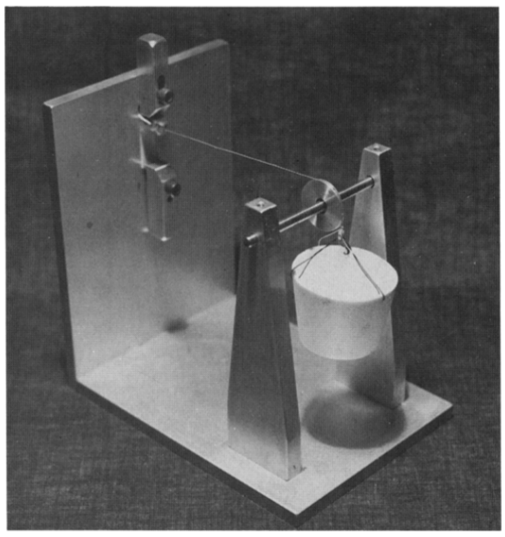


Figure 1. Copper electrodes mounted on a nylon block with surface area and gap width identical to those of the prototype gold-coated 4 mm radiofrequency angioplasty balloon. A strip of postmortem human aorta separated along the intima-media and media-adventitial plane is placed in the chamber and covered by the electrode-mounted block. An inverted syringe and pressure gauge were used to apply 5 atm of pressure to the tissue.

filled with water (5 ml/min) until the tissue planes separated (Fig. 2). The cup was then weighed to measure the weight required to separate the "fused" tissue planes. In addition, 24 control experiments were performed using 5 atm of tissue pressure without delivery of radiofrequency energy.

Radiofrequency-balloon feasibility study. The feasibility of using a prototype radiofrequency balloon angioplasty catheter for recanalizing and molding stenotic atherosclerotic vessels was assessed in 10 samples of intact postmortem human atherosclerotic coronary or peripheral arteries.

Figure 2. Apparatus for measuring weld strengths. One side of the "fused" tissue is affixed to the metal apparatus and the other to a clip attached to a styrofoam cup that is filled with water at a slow, constant rate. The cup is weighed when the tissue separates.



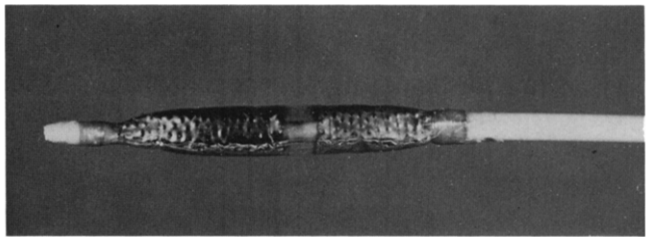


Figure 3. Prototype radiofrequency balloon catheter with gold electrodes.

All arteries had significant intraluminal atherosclerotic plaque without gross evidence of calcification. A prototype 4 mm diameter radiofrequency angioplasty balloon catheter was constructed using gold electrodes separated by a 5.08 mm gap (Fig. 3). The deflated balloon catheter was inserted in each of the 2 to 3 cm long, 3 to 4 mm diameter arterial segments and the tissue and balloon catheter tip placed in a small beaker of blood. For each dilation attempt, the balloon was filled with saline solution and the balloon inflated to 3 atm with use of a standard coronary angioplasty inflation device. Three atmospheres was used because the prototype balloon catheter would not uniformly withstand higher inflation pressures. When balloon pressure reached 3 atm, 200 J of radiofrequency energy was delivered over approximately 30 s. The balloon was then deflated after a total of 60 s. Ten control samples consisted of the adjacent segments of the aforementioned vessels, which were treated with identical balloon inflation duration and pressures but without radiofrequency delivery. The tissues were immediately fixed and histologic evaluation was performed as described.

Effect of radiofrequency energy on cardiac rhythm. Lastly, to assess the arrhythmogenic potential of radiofrequency energy, five doses of 80 J radiofrequency energy were delivered to the epicardial surface of two anesthetized and artificially ventilated, open chest dogs from the gold-tip electrode catheter. Because radiofrequency energy produced interference with electrocardiographic (ECG) recordings, continuous arterial pressures were recorded to monitor the heart rate and rhythm. Animal studies and care conformed to the Position of the American Heart Association on Research Animal Use.

Statistics. Data were expressed as mean values ± SEM and statistical significance was assessed with use of the Student's t test. Statistical significance was assumed at $p < 0.05$.

Results

Human aortic in vitro dosimetric and histologic studies. Figure 4 shows the appearance of characteristic radiofrequency lesions produced in fresh postmortem human atherosclerotic aorta. Radiofrequency energy delivered from a gold-tip electrode pressed against normal canine and human

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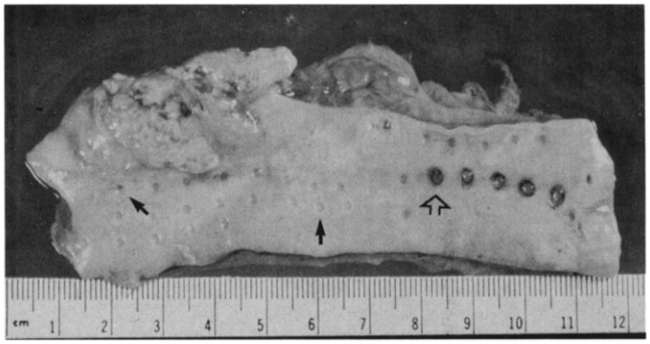

Figure 4. Fresh postmortem human aorta showing characteristic radiofrequency-induced lesions. These consist of discrete, shiny craters in both normal vessel wall and atherosclerotic plaque (**dark arrows**). At higher radiofrequency energy dosages (80 J), the craters develop charred borders (**open arrows**).

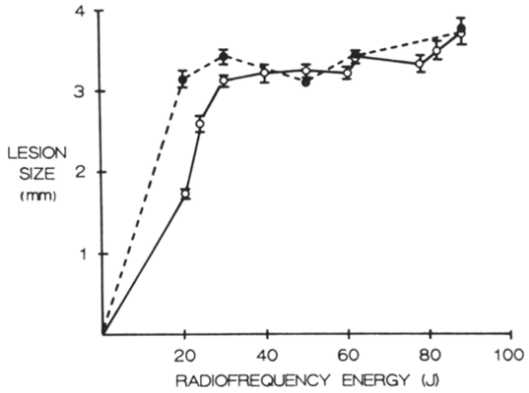

Figure 5. Dimensions of radiofrequency-induced lesions in human (**solid circles**) and canine (**open circles**) aorta plotted as a function of radiofrequency energy dose. No detectable lesions were produced with pressure on the catheter tip without radiofrequency energy delivery.

atherosclerotic vascular tissues produced dose-dependent lesions ranging from sharply defined, shiny appearing tissue craters without gross evidence of thermal charring at doses <40 J (dark arrows) to progressively greater gross and histologic evidence of tissue charring and vaporization at doses >40 J (open arrows). Radiofrequency produced similar appearing lesions in normal aorta and atherosclerotic plaque, which are seen as the lighter, amorphous areas.

Tissue lesion diameter in human and canine aorta plotted as a function of radiofrequency energy dose are shown in Figure 5. Electrode pressure of 2.06×10^6 dynes/cm^2 without delivery of radiofrequency energy did not produce detectable tissue injury. With delivery of 20 to 85 J radiofrequency energy, lesion size in human atherosclerotic aorta ranged between 3.14 and 3.79 mm in diameter and from 0.20 to 0.47 mm in depth. Because of the narrow range of depth measurements, the precise relation of depth to radiofrequency dose could not be accurately determined. Histologic examination of lesions produced with <40 J showed shallow indentations of the luminal surface and the appearance of molding of the collagen fiber network with collagen fibers conforming to the shape of the gold electrode tip with minimal evidence of vaporization (Fig. 6). A more dramatic example of collagen molding in radiofrequency-treated canine aorta is shown in Figure 7. At higher doses (>40 J), lesions showed progressively greater histologic evidence of tissue vaporization and charring; however, not to the extent seen with bare fiber and hot tip laser energy (13). Unlike bare fiber laser energy, radiofrequency produced relatively superficial lesions that did not penetrate beyond the vessel media (Fig. 6).

Radiofrequency energy was capable of ablating all types of atherosclerotic plaque except heavily calcified plaque. There was no difference in the dose-lesion size relation between normal vessel and noncalcified atherosclerotic plaque. Histologic examination of atherosclerotic plaque after radiofrequency ablation showed dose-related surface vaporization with nonspecific damage to the underlying fibrofatty plaque (Fig. 6). This tissue damage is histologically similar to that occurring with necrosis of living tissue.

Temperature and histologic studies. Similar to our previous findings with bare fiber laser energy (13), the presence of blood also enhanced the amount of tissue injury produced by radiofrequency energy. Figure 8 shows the gross appearance of fresh, postmortem human aorta in which radiofrequency lesions were produced in saline solution to the left and in blood to the right. Resulting lesion dimensions in normal canine aorta were significantly increased at all doses tested when radiofrequency energy was delivered in blood compared with saline solution (Fig. 9). After a delivered radiofrequency dose of 80 J to human atherosclerotic aorta, lesion dimensions in blood were significantly larger than those produced in saline solution (3.36 ± 0.139 versus 1.28 ± 0.10 mm; $p < 0.0001$). There was no significant difference in lesion depth in blood compared with saline solution (0.27 ± 0.21 versus 0.21 ± 0.12; $p = 0.15$).

Histologically, the lesions created in saline solution were characterized by local areas of desiccated "indentations" unassociated with charred craters and edges. Lesions created in the presence of blood, however, were characterized by extreme charring of the crater center and edges with extensive dessication. Luminal surface temperatures rose an average of 31.5 ± 1.7°C after deliver of 80 J radiofrequency energy when tissues were perfused with blood as opposed to 14.2 ± 0.8°C when tissues were perfused with saline solution ($p < 0.001$). When radiofrequency energy was delivered in blood medium, a gas pocket formed at the catheter tip-tissue interface, which was possibly a result of vaporization or combustion of the protein components in blood. Gas bubbles were not observed to form when radiofrequency energy was delivered to tissue in saline solution.

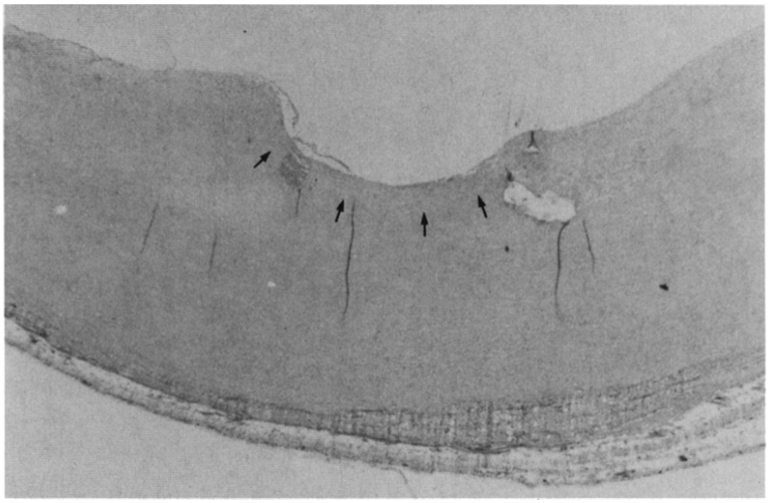

Figure 6. Histologic section of human atherosclerotic aortic lesion produced by 40 J radiofrequency energy. The lower energy level produced sharply defined craters and the luminal surface appears "remodeled." The "indented" area (**arrows**) results from compression of collagen and elastic fibers into a shape that conforms to that of the electrode tip. At this low dose, no vaporization or charring resulted. (Hematoxylin-eosin stain, original magnification ×10, reduced by 13%.)

In vitro study of vascular tissue fusion. Radiofrequency energy, delivered from the previously described block-mounted bipolar electrodes to human aortic tissues dissected along the intima-media and media-adventitial plane, produced strong tissue "fusion" similar to that described with the Nd:YAG laser (14). When 5 atm of pressure was delivered to separated aortic tissue without radiofrequency energy, an average of 4.76 ± 0.26 g was required to separate the "fused" layers. When 200 J of radiofrequency energy was delivered in addition to the 5 atm of pressure, an average of 28.5 ± 3.3 g of weight was required to separate the layers ($p < 0.0001$) (Fig. 10). A representative histologic specimen showing fused tissue layers is shown in Figure 11. Note the smooth approximation of the layers without detectable areas of bonding.

Radiofrequency balloon feasibility study. Ten of 10 human postmortem atherosclerotic vessels treated with 200 J radiofrequency energy and 3 atm of balloon pressure delivered from a prototype radiofrequency balloon angioplasty catheter demonstrated luminal dilation with evidence of thermal molding of plaque and vessel walls. Radiofrequency-treated vessels maintained a firm, fusiform area of dilation with slight tissue blanching at the site of balloon inflation and radiofrequency delivery. In contrast, 10 of 10 adjacent control segments treated with 3 atm balloon pressure alone demonstrated recoil of the vessels to their prior predilation luminal geometry. These noncoagulated control vessels appeared to "collapse" on themselves after balloon removal.

Figure 12 shows a section through a vessel, one segment of which was treated with radiofrequency and balloon pressure (A) and the other was a control segment treated with balloon pressure alone (B). There is stretching and thermal molding of the disease-free wall of the radiofrequency-treated vessel with maintenance of the lumen in the shape of the balloon. There is histologic evidence of compression of atherosclerotic plaque and medial myocyte injury but no gross or histologic evidence of intimal tears, tissue charring or plaque vaporization. In contrast, lacking thermal coagulation and molding, the control arterial wall recoils to its original geometry, presumably because of the inherent elastic properties of the untreated vessel. There is no histologic evidence of medial myocyte damage.

Figure 12C shows a diagram drawn from enlargements of radiofrequency-treated and control vessel segments to further illustrate the luminal changes with and without radiofrequency treatment. The broken lines represent the expected arterial lumen assuming a circular configuration in both cases. Ordinarily, the exposure to formalin will produce a marked inward folding or collapse of the disease-free wall as seen in the control vessel (right). In the radiofrequency-treated vessel (also exposed to formalin), there is a 61% increase in luminal area and 29% increase in internal luminal circumference due to marked outward expansion resulting from balloon stretching and thermal molding of the disease-free wall (left). In contrast, after balloon inflation alone, there was a 24% decrease in luminal diameter and a 24% decrease in internal luminal circumference.

Effect of radiofrequency energy on cardiac rhythm. No arrhythmias were detected with application of the catheter tip to the epicardial surface of the heart without radiofrequency delivery. With radiofrequency current delivery, although there was transient interference with the ECG recordings, the aortic pressure recordings demonstrated that only rare ventricular premature beats occurred despite the production of large areas of epicardial thermal injury (0.8 ± 0.75 premature ventricular beats per radiofrequency dose).

Discussion

This study demonstrates that the combination of pressure and radiofrequency energy effectively produces thermal

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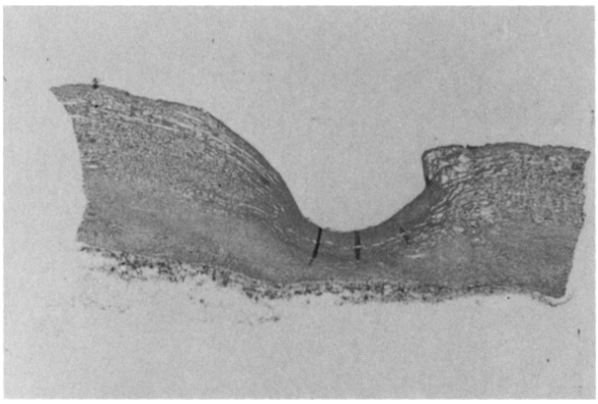


Figure 7. An example of more dramatic "molding" of collagen fibers with radiofrequency energy delivered to canine aorta. (Hematoxylin-eosin stain, magnification ×10).

compression, fusion and molding of atherosclerotic plaque and vessels and may be a promising modality for treating obstructive atherosclerotic vascular disease. Radiofrequency energy is a versatile and economical energy source that produces tissue injury primarily through thermal mechanisms (15,16). When delivered from a gold-tip electrode catheter, radiofrequency energy produced dose-dependent, discrete thermal compression and ablation of atherosclerotic plaque characterized by smooth and shallow tissue lesions. At higher energy levels, radiofrequency produces tissue charring and vaporization, much like laser energy. Also like laser-induced tissue injury, radiofrequency-mediated tissue injury is increased in the presence of blood and decreased in the presence of saline solution. This phenomenon is likely due to a nonspecific thermal enhancing effect of blood in which the protein components of blood are combusted, resulting in increased amounts of heat delivered to tissue. Additionally, a thermal insulating effect of blood may be responsible for the increased tissue injury (13). The understanding of this interaction of radiofrequency energy with blood is of practical importance for determining and modulating the degree of intravascular radiofrequency-induced tissue injury.

Radiofrequency tissue fusion and thermal molding. Radiofrequency energy delivered from an electrode pair in combination with pressure to tissue produces strong tissue fusion of separated intima-media and media-adventitial flaps and may be potentially effective in reducing the frequency of acute vessel closure resulting from balloon angioplasty-induced intimal tears. On the basis of theoretical calculations, a systolic blood pressure of 120 mm Hg with an arterial luminal diameter of 2.5 mm produces an estimated force on an intimal tear of 10 to 15 g. Therefore, our experimentally measured fusion strength after 200 J of radiofrequency energy and 5 atm of pressure should produce fusion strengths well within physiologic limits. Although the exact mechanism of thermal fusion remains unclear, it has been suggested that tissue fusion results from thermal alteration of collagen, resulting in homogenization and interdigitation of collagen fibrils (17).

Radiofrequency energy and balloon pressure delivered from a prototype radiofrequency balloon angioplasty catheter produced thermal molding of atherosclerotic vessels and plaque resulting in firm, fusiform dilation at the balloon site. This result was most likely due to thermal molding and coagulation of proteins because the noncoagulated control vessels, treated with balloon pressure without radiofrequency delivery, recoiled to their predilation geometry, appearing to "collapse" on themselves after balloon deflation. Heat-induced tissue injury, by denaturation of collagen and protein, may also result in decreased elastic recoil of the

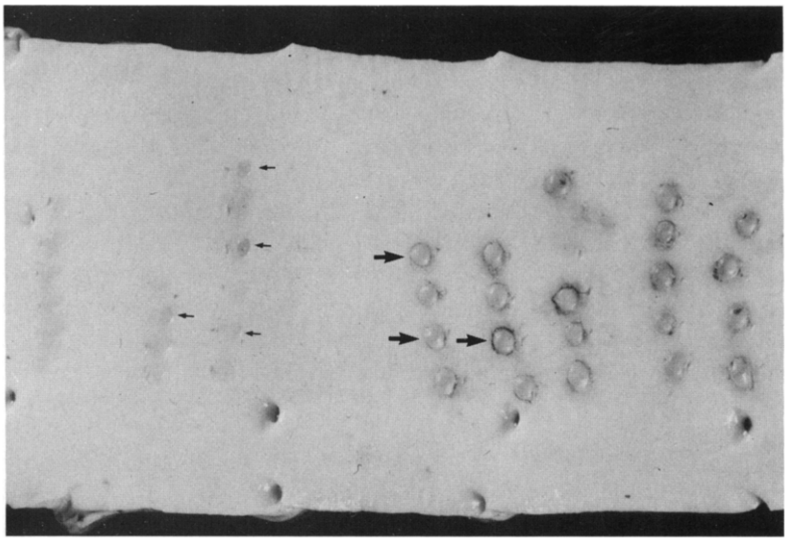


Figure 8. Radiofrequency energy lesions in human aorta superfused with saline solution (**small arrows**) versus heparinized whole blood (**large arrows**). The lesion dimensions produced in whole blood were significantly larger than those produced in saline solution.

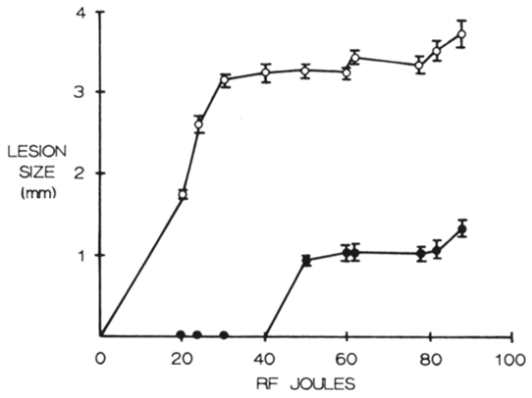
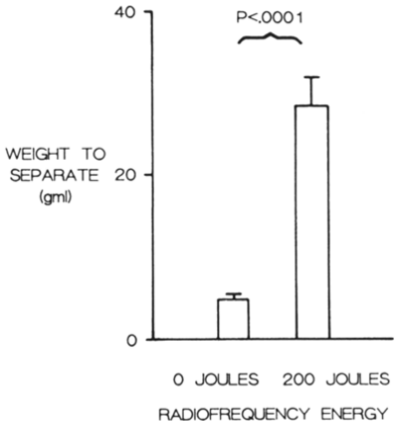


Figure 9. Graph of lesion dimensions produced in canine saline solution (**solid circles**) versus canine blood (**open circles**). At all radiofrequency (RF) energy doses, lesions produced in whole blood were significantly larger than those produced in saline solution.

vessel wall and may also prevent acute vessel spasm. An intriguing possibility for vascular intervention is the use of lower thermal energy to mold and shape rather than ablate atherosclerotic vessels. Protein denaturation may occur at tissue temperatures as low as 42 to 65°C; cell injury, inflammation and repair may occur with temperatures of only 5 to 10° above body temperature (18). Subablation temperatures may produce changes in the protein, collagen and lipid components of the atherosclerotic plaque and the uninvolved vessel wall. Coupled with the pressures exerted by the angioplasty balloon, these phase changes may result in molding of the atherosclerotic plaque and vessel lumen to conform to the balloon shape and size. Because the majority of coronary atherosclerotic lesions are eccentric (19), the potential arises for utilizing subablation temperatures and

Figure 10. Histogram of the weight necessary to separate "fused" aortic tissues. To the left, the weight required to separate tissues pressed together with 5 atm pressure but without radiofrequency energy. To the right, the weight necessary to separate tissues pressed together with 5 atm pressure along with 200 J radiofrequency energy.



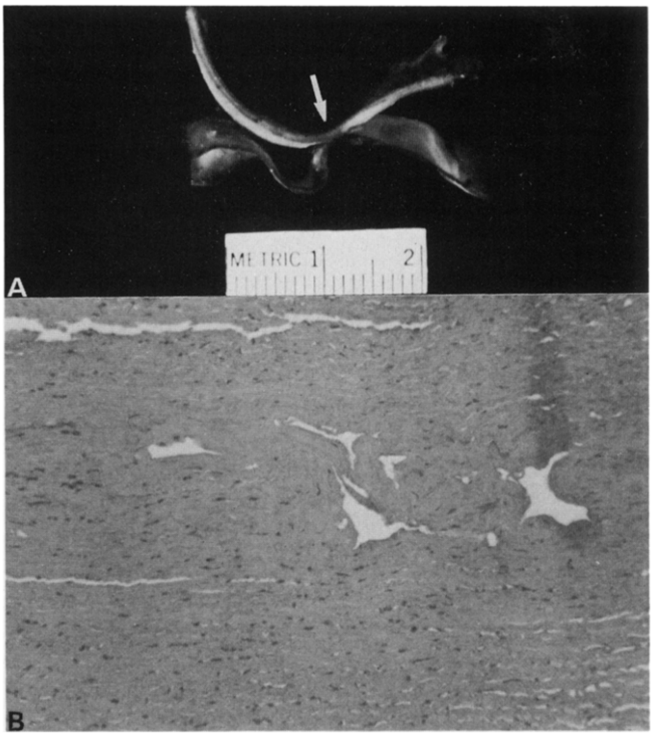


Figure 11. Human aortic tissue fused by radiofrequency energy. **A,** Intimal-medial and medial-adventitial layers are fused (**arrow**) at gap area. **B,** Histologic section through fused zone shows melting together of medial layers. (Hematoxylin-eosin stain, original magnification ×100, reduced by 25%.)

the pressure of the angioplasty balloon to stretch and thermally mold the disease-free portion of the vessel in addition to the atherosclerotic plaque.

In this study, when heated with a radiofrequency angioplasty balloon catheter, the vessel lumen takes on the shape and size of the expanded balloon primarily by stretching and thermal molding of the disease-free wall. Furthermore, if intimal flaps are adequately sealed and low pressure balloon inflation prevents disruption of the internal elastic lamina, the underlying vascular intima and media may not become exposed to circulating blood elements and the stimulus for acute thrombosis and chronic restenosis (that is, exposure of myocytes, fibrocytes and vessel wall collagen to activated platelets) may not be activated. In addition, the absence of tissue charring seen with higher temperatures may also decrease the stimulus for intraluminal thrombosis.

Medial myocyte injury. Radiofrequency energy produced histologic evidence of injury to medial myocytes, cells believed to be responsible for chronic restenosis. Studies have suggested that thermal injury decreases the likelihood of restenosis in a rabbit model of atherosclerosis (8) presumably by injuring cells responsible for the fibroproliferative response. Thus, it is possible that heat delivered to the arterial wall after radiofrequency balloon angioplasty may

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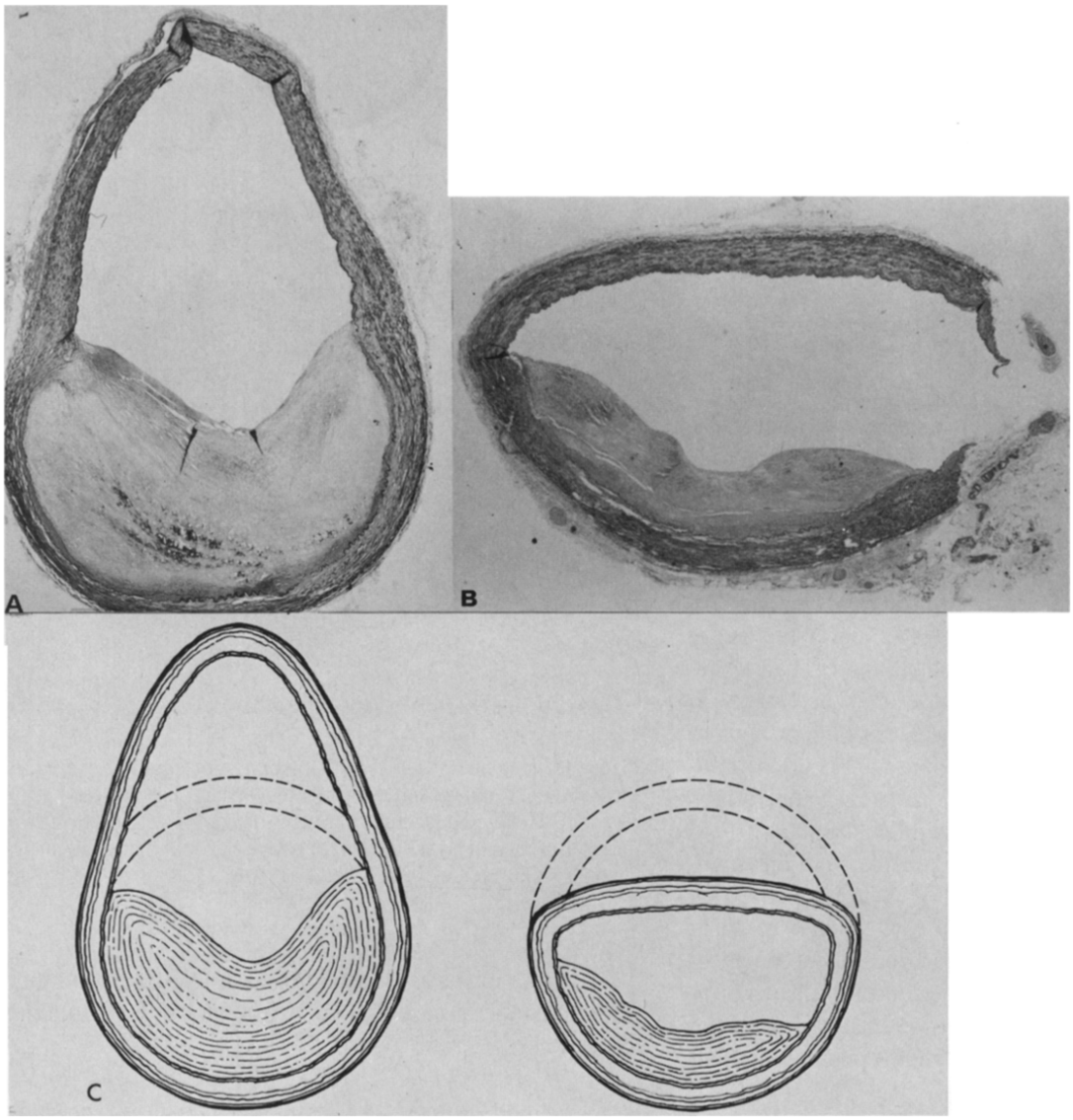

Figure 12. Comparison of the effects of balloon dilation with (**A**) and without (**B**) combined 200 J radiofrequency energy in postmortem human arteries with eccentric atherosclerotic plaque. **A,** The arc of disease-free wall is stretched and thermally molded by the balloon with an excellent luminal area. **B,** In comparison, the same segment of vessel with identical balloon inflation but without radiofrequency thermal energy shows that the noncoagulated vessel is not stretched or molded to the balloon shape. **C,** Schematic diagram drawn from enlargements of radiofrequency-treated (**left**) and control vessels (**right**). Ordinarily, the exposure to formalin will cause a marked inward folding or collapse of the disease-free wall as seen in the control vessel. In the radiofrequency-treated vessels, there is a marked outward expansion (see text). (**A** and **B**, Hematoxylin-eosin stains; original magnification ×10, reduced by 30%.)

decrease the likelihood of chronic, late restenosis by interfering with the capacity of myointimal and fibroproliferative cells to proliferate. These intriguing hypotheses require further validation in clinical trials.

Safety. Radiofrequency current at the frequency described herein may be safer than other electrical energy sources. We observed no significant arrhythmias when we applied radiofrequency energy directly to the beating heart using an energy density far greater than would be used in coronary artery intervention. It is possible, however, that low frequency components delivered during the vulnerable period of the heart may precipitate arrhythmias and radiofrequency current may be best delivered synchronously with the R wave.

Conclusions. The combined delivery of radiofrequency energy and balloon pressure may be a safe and effective modality for percutaneous vascular intervention. The use of lower energy doses along with balloon pressure may result in stretching and thermal molding of both atherosclerotic plaque and disease-free wall resulting in increased luminal area without tissue charring or vaporization. Whether the lower temperatures will prevent the vascular thrombosis and

late development of aneurysms seen with other thermal devices remains to be determined. Long-term animal studies are currently in progress and human clinical trials planned to further test these hypotheses.

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