MICROWAVE BALLOON ANGIOPLASTY

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ABSTRACT

Angioplasty of the coronary and peripheral arteries has become standard treatment for obstructive atherosclerotic vascular disease. The major acute problems which are encountered are acute closure of the vessel due to elastic recoil, dissection of the vessel or thrombus. The major long term problem is restenosis. We have evaluated the utility of microwave thermal energy in resolving these problems. In normal and atherosclerotic rabbit models we have demonstrated the feasibility and efficacy of a microwave system to enhance the result of the primary angioplasty procedure. The result at four weeks was also enhanced by microwave energy. Clinical trials are planned to explore the clinical utility of this modality.

Coronary angioplasty has become a standard therapy in the treatment of obstructive coronary artery disease. Coronary angioplasty is performed by positioning a balloon catheter across an area of blockage in the coronary vessel and inflating the balloon. Following balloon deflation the stenosis is reduced with a resultant normalized blood flow pattern. Utilizing this technique success rates of 90% are achieved. There are two major problems that occur using this technique however. The first is that there can be acute disruptions of the coronary artery which develop and which can lead to acute closure of the vessel. These disruptions can be caused by elastic recoil of the artery, by dissection of the arterial wall or by thrombus. If untreated complete occlusion and an acute myocardial infarction may result. The second problem is that of recurrence of stenosis which occurs in approximately 30% of patients. A variety of modalities have been utilized to deal with these problems, including intracoronary stents, (1) mechanical atherectomy devices,(2) and thermal balloon techniques. (3)

We have investigated the potential application of microwave to these problems. The system which is used consists of a microwave generator at a frequency of 2450MHz. The generator is coupled to a cable of 0.23 to 0.35 inches. The design requirement for such a cable is to have the smallest possible diameter which mechanically can be advanced into the tortuous coronary tree yet which at the same time can conduct enough energy to radiate from the antenna. The cable terminates in an antenna which is inserted into the central lumen of a balloon catheter. When the cable is fully advanced the antenna is in the center of the balloon. The balloon catheter has a thermocouple which is coupled to the generator. Temperature rise is determined on line and generator output is controlled by this feedback loop.

Our initial studies using this technology were performed in the iliac arteries of normal rabbits. Following induction of anesthesia, the femoral arteries of the rabbits were isolated and the catheter/cable system was positioned retrogradely in the external iliac artery. The interaction of three variables was evaluated in these studies: the duration of heating and the duration of balloon inflation, the temperature attained and peak balloon inflation pressure.

The period of balloon inflation was either 1 or 2 minutes and the corresponding time of heating was either 30 or 60 seconds. The peak temperature varied from 50°C to 100°C and the peak balloon inflation pressure was either 2 or 5 atmospheres. Following the procedure animals were sacrificed after one week. The arteries were perfusion fixed, sectioned and stained with hemotoxalin and eosin, trichrome, and Verhoff-VonGiesen stains.

The effect of microwave heating was analyzed by evaluating the presence and extent of injury to the media of the vessel and by the extent of intimal proliferation. We did not find that there was a correlation between medial injury or intimal proliferation and either the peak balloon inflation pressure or the time of heating or balloon inflation. We had expected to find an effect related to the duration of heating but did not find so.

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Perhaps a plateau of the heating effect in this model was attained by the 30 second time period. We observed a direct correlation between the extent of medial injury and the peak temperature attained. We also observed an inverse relationship between the extent of medial injury and intimal proliferation. This was important because intimal proliferation is thought to be the cause of restenosis following angioplasty. An example of the difference in response to low temperature and higher temperature is shown in figure 1. In figure 1A an artery which was heated to 50°C for 30 seconds is demonstrated. The media is intact and prominent intimal proliferation is seen. In figure 1B an artery which was heated to 90°C is demonstrated. There is loss of cellularity in the media and replacement by fibrous elements. There is no evidence of intimal hyperplasia. There is a multifactorial causation of intimal hyperplasia. Ingrowth of smooth muscle cells from the media is thought to be one of the mechanisms responsible for mediation of this process, which in turn causes restenosis. We concluded that a selective thermal injury to the media could modify this process.

Our next study was performed in an atherosclerotic rabbit model. Animals were fed a high fat diet. After two weeks on this diet endothelial denudation of the external iliac arteries was performed by positioning a balloon catheter in the external iliac artery, and then pulling it back into the distal aorta thus shearing off the endothelium. This procedure predictably results in an atherosclerotic lesion at the site of denudation. Four to six weeks later these animals were brought back to the laboratory and bilateral femoral artery cutdowns were performed. The balloon catheter/cable system was then positioned in the atherosclerotic external iliac artery. Animals had microwave balloon angioplasty (MBA) performed on one external iliac artery and conventional balloon angioplasty (CBA) performed on the contralateral artery. Each animal thus served as its own control. Angioplasty was performed with a 3mm balloon inflated to 5 atm for one minute. In the animals treated with MBA a similar procedure was performed with the addition of microwave energy for 30 seconds during the inflation. Energy was delivered to raise the temperature, as measured on the balloon surface, to 70°C or 85°C. After treatment of both vessels, angiography was performed and the femoral arteries were ligated.

Four weeks after the angioplasty procedure the animals were brought back to the laboratory. Angiography of the iliac arteries was repeated and the animals were sacrificed. Following perfusion fixation of the iliac arteries, the vessels were excised, fixed, sectioned and stained in the same manner as described above. Histologic analysis and quantitative angiography of the vessels were performed.

Histologic analysis revealed that on the side treated with MBA there was loss of lipid laden cells and replacement in the intima, and in some cases in the media, with a hypocellular fibrotic matrix. The effect of these changes could be considered a "biologic stent". An example of this effect is seen in figure 2. Quantitative angiography of the iliac arteries revealed a significant improvement in the diameter of the arteries treated with MBA at 85°C both immediately and at four weeks. Although there was a trend for benefit immediately post procedure in the animals treated with MBA at 70°C this was not statistically significant. Furthermore, at four weeks there was loss of the immediate benefit in the 70°C MBA vessels and no difference compared to the control arteries treated with conventional angioplasty.

These studies suggest that MBA is technically feasible, and that the initial results of angioplasty are enhanced with MBA. The finding of sustained benefit at four weeks has encouraged us to explore further the potential of this modality in reducing the incidence of restenosis. At the current time, a target temperature of 85°C seems optimal for this effect.

In addition to the above, studies are in progress to evaluate the potential of this technique to treat two additional mechanisms which may decrease coronary flow and lead to unsuccessful angioplasty. In the first study, the ability to seal dissections is being evaluated. Preliminary observation suggests that such tears in the vessel wall can be sealed by microwave thermal energy.

A second problem which can complicate angioplasty is the presence or the development of thrombus at the site of angioplasty. We have performed preliminary studies in which thrombus is induced in the coronary artery of a dog. Following complete occlusion of the coronary artery with thrombus the microwave balloon system was positioned across the thrombosed region. Balloon inflation for 60 seconds and microwave heating to 85°C for 30 seconds were performed. Following a 30 minute period of observation the animal was sacrificed and the artery excised and studied histologically. An example of the effect of such treatment is seen in figure 3. There is thrombus present which is coagulated. A satisfactory lumen shaped by balloon inflation is present in the center of the coagulated thrombus. Thus it may be possible to more effectively treat patients with coronary thrombus, allowing the subsequent resolution of the coagulated and stabilized thrombus.

Our studies have thus led us to the conclusion that MBA is effective in enhancing the primary result of angioplasty. The addition of microwave energy is effective in increasing the diameter of the vessel post angioplasty, in sealing dissections, and seems to be effective in aiding in the resolution of thrombus. The role of microwave angioplasty in reducing the incidence of restenosis is a complex question. The current results, although encouraging, are too preliminary to offer definitive answers.

The MBA system is relatively easy to deploy, and the system is cost effective compared to alternative heating modalities.

Based on these observations, clinical trials are planned to explore the utility of this device in patients.

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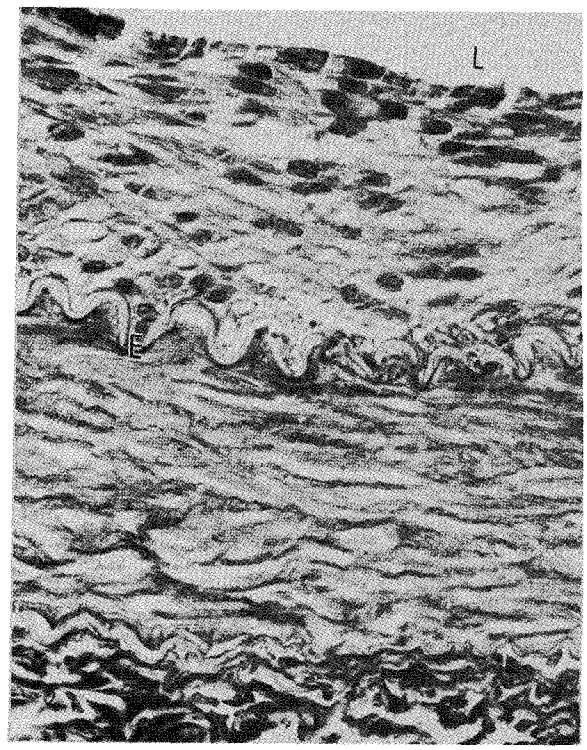

Figure 1A. Normal rabbit iliac artery heated to 50°C for 30 seconds.
L=lumen E=internal elastic lamella

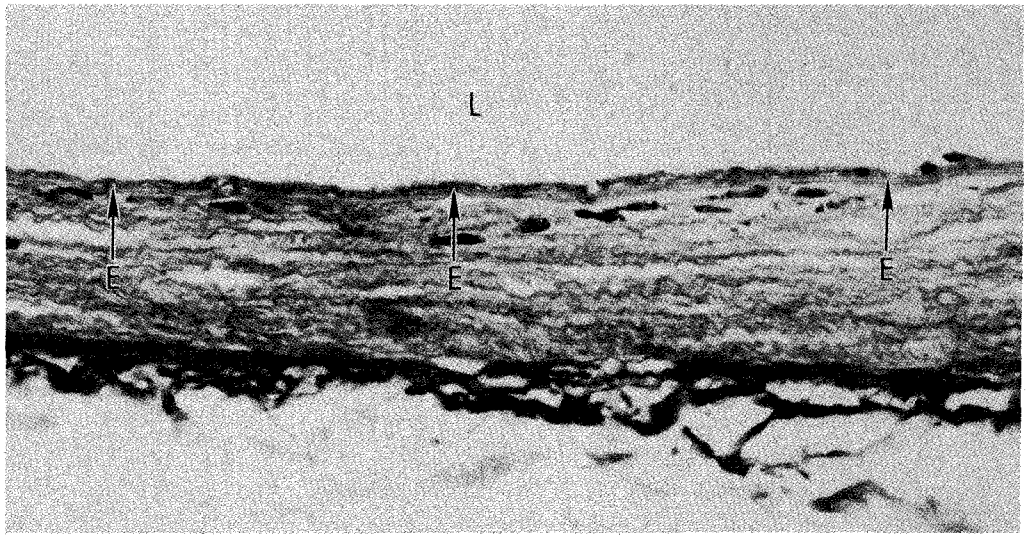

Figure 1B. Normal rabbit iliac artery heated to 90°C for 30 seconds.
L=lumen E=internal elastic lamella

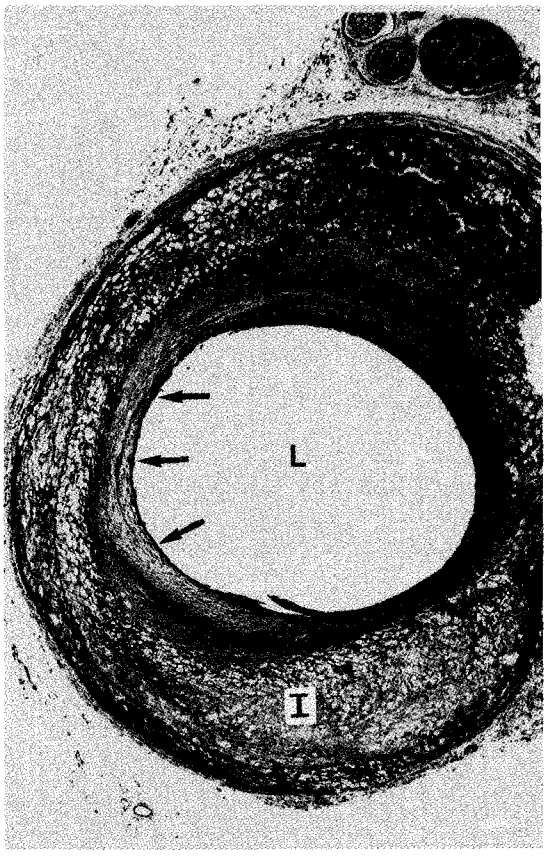

Figure 2. Atherosclerotic rabbit iliac artery heated to 85°C for 30 seconds. Arrows point to the hypocellular fibrotic matrix in the intima.
L=lumen I=intima

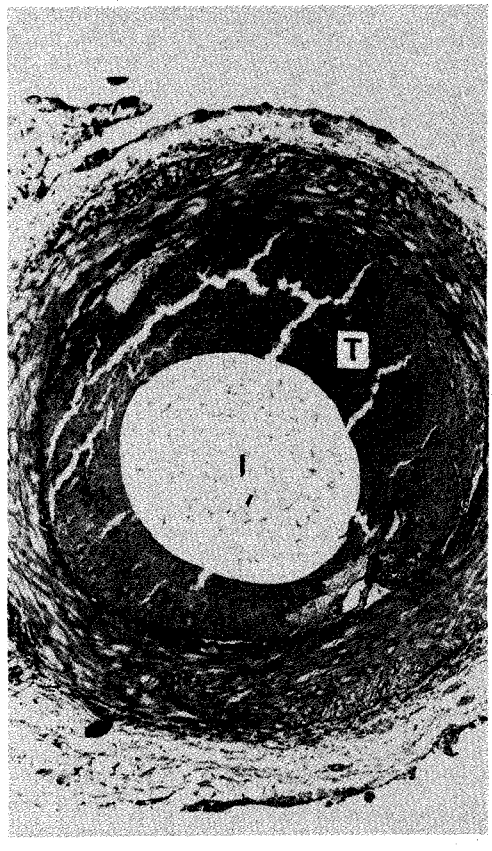

Figure 3. Dog coronary artery with thrombus following microwave balloon angioplasty.
L=lumen T=thrombus