Experimental Arteriosclerosis Treated by Conventional and Laser Endarterectomy

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Open laser endarterectomy was compared to standard surgical endarterectomy in the rabbit arteriosclerosis model. The aorta was exposed by a thoracoabdominal exploration in 16 rabbits. In Group I (8 rabbits), a conventional endarterectomy (CE) was performed with standard vascular instruments. In Group II (8 rabbits), laser endarterectomy (LE) was performed with an argon ion laser (488 nm and 514.5 nm) at a power of 1.0 W. Aortas were fixed, serially sectioned (6 μm) and stained (H + E) following each procedure. Gross and light microscopic examination revealed identical results for the endarterectomy surfaces of CE and LE. The proper cleavage plane within the media was developed with both techniques and the remaining arterial wall was not damaged with either procedure. The end points of LE were consistently superior to those of CE because of phototherapy fusion. The LE end points were tapered and the intima was fused. Intimal flaps were seen in 2/8 CE experiments and the remaining end points exhibited an uneven transition. LE required an average energy density of 124 ± 9 J/cm². We conclude that LE provides a satisfactory method for the in vivo evaluation of laser radiation upon arteriosclerotic arteries. LE may be the way to begin clinical laser trials.

INTRODUCTION

Experimental [1, 2, 4, 5, 8, 10, 11] and clinical studies [6, 9] have demonstrated the feasibility of laser vaporization of atheromatous plaques by catheter techniques. The problems of the catheter techniques are inadequate target localization and uneven depth of plaque penetration that can lead to perforation, thrombosis, and aneurysm formation [1, 3, 7, 11]. A powerful and potentially destructive device like the laser should not be used in a blind fashion (intraluminal angioplasty) when so little is known about its effects on blood vessels. We have proposed open laser endarterectomy for the in vivo evaluation of laser radiation upon arteriosclerotic arteries [7, 8]. Although a laser can be used for such a precise dissection, the quality of the laser procedure has not been proven. This report compares the open laser and open conventional methods of endarterectomy in an experimental arteriosclerosis model.

MATERIALS AND METHODS

All experiments were performed with the New Zealand white rabbit arteriosclerosis model [7]. The animals received humane care in compliance with the “Principles of Laboratory Animal Care” formulated by the National Society for Medical Research and the “Guide for the Care and Use of Laboratory Animals” prepared by the National Academy of Sciences and published by National Institutes of Health (NIH Publication No. 80-23, revised 1978). Laser experiments were conducted with an argon ion laser (Co-
herent INNOVA 20) with mixed wavelength 488 and 514.5 nm. The laser beam was delivered through a 400-μm quartz fiber optic (QSF 400 Quartz fiber) at a power of 1.0 W. The ends of the fiber optic were freshly cut for each experiment (Radial Fiber optic Cutter, Model F7800 13000). Laser power was monitored from the laser head during each procedure. It was measured from the fiber optic output end prior to each procedure and at the conclusion of each procedure with a Coherent Power Meter, Model 210. Energy delivery was controlled by variation of the duration of exposure.

Sixteen arteriosclerotic rabbits were anesthetized (intramuscular acepromazine 0.5 mg/kg, rompum 3.0 mg/kg, ketamine 50 mg/kg), intubated, and ventilated with a small animal respirator. Additional ketamine (50 mg/kg iv) was administered as necessary during the procedure. A thoracoabdominal exploration was performed to expose the aorta. Regions of arteriosclerosis were identified, heparin (3.0 mg/kg iv) was administered, and proximal and distal vascular control was obtained. A longitudinal arteriotomy was made and the plaque was visualized. In Group I (8 rabbits), an open endarterectomy was performed in the standard fashion [12] using an endarterectomy knife and vascular instruments. A cleavage plane was developed in the media to elevate the plaque and remove the diseased intima. Natural (tapered) end points could not be developed in any of these rabbits, hence, the end points were sharply divided and beveled. In Group II (8 rabbits), an open endarterectomy was performed positioning the fiber tip 1.0 to 2.0 mm from the intima. Laser exposures of 1.0 to 5.0 J were used to create a line of laser craters (0.4 mm diameter to 0.5 mm diameter) at the ends of the atheroma. The craters were connected by continuous wave laser radiation (multiple exposures of 10 to 20 J) to loosen the plaque and the cleavage plane was developed within the media with continuous wave laser radiation (multiple exposures of 10 to 30 J). The plaque was removed and the end points were fused by continuous wave laser radiation (10 to 20 J). The total energy required for each laser endarterectomy was recorded and the surface area of each laser endarterectomy was determined so that energy density (J/cm²) could be calculated for each experiment. Upon completion of the procedure in both groups, the operated segments were removed and the rabbits were sacrificed (barbiturate injection).

The aortic segments were rinsed in Ringer's lactate solution and cut into three specimens (proximal end point, surface, distal end point) under a dissecting microscope. The specimens were pinned flat on Teflon blocks (using Minuten insect pins), fixed in 3% glutaraldehyde in phosphate buffer at 4°C for 24 hr, and rinsed in phosphate buffer. They were dehydrated and processed using a Fisher Histotech processor, removed from the Teflon blocks, and imbedded in paraffin. They were serially sectioned at 6 μm using an AO rotary microtome and stained with hematoxylin and eosin.

The endarterectomy surfaces and end points were scored according to gross and light microscopic appearance. For the surface; 1 was arterial perforation; 2 was within the wrong cleavage plane; 3 was a rough surface; and 4 was a smooth surface. For the end points; 1 was arterial perforation; 2 was an intimal flap; 3 was a rough transition; and 4 was a smooth transition.

RESULTS

Endarterectomy was successfully performed with both techniques according to gross appearance. The end points of the laser endarterectomies were more even and more well defined than the end points of the conventional endarterectomies (Fig. 1, 2).

In Group I (conventional endarterectomy) the plaques were found to readily separate from the media once the proper cleavage plane was found. There was no damage to the remaining layers of the vessel wall. The cleavage plane was just beneath the internal elastic lamina in all 8 experiments and a satisfactory endarterectomy surface was seen
FIG. 1. Appearance of an arteriosclerotic rabbit aorta following conventional endarterectomy. The surface (open arrow) is smooth and glistening. The distal end point (closed arrow) appears ragged and uneven.

FIG. 2. Appearance of an arteriosclerotic rabbit aorta following argon ion laser endarterectomy. The surface (open arrow) is smooth with residual blood clots along the surface. The distal end point (closed arrow) is fused to the vessel wall.
after each procedure (Fig. 3). The plaques were diffuse, i.e., extended the length of the aorta so natural tapered end points could not be developed. Since the end points were sharply divided, most exhibited rough transitions (Fig. 4) and in two instances, distal intimal flaps were seen (Fig. 5).

In Group II (laser endarterectomy) the proper cleavage plane within the media was developed in all 8 experiments with minimal carbonization of the remaining tissues. The endarterectomy surfaces were free of debris and the elastic fibers of the media were not disrupted by laser radiation (Fig. 6). No intimal flaps were seen at the end points. The end points were fused by phototherapy and 5/8 distal end points showed a smooth transition (Fig. 7).

The results of the experiments are summarized in Tables 1 and 2. The conventional endarterectomy and laser endarterectomy surfaces achieved identical scores (mean 3.6). The laser end points were consistently superior to the sharply divided end points (mean score 3.6 and 2.8, respectively). The difference between the scores of the laser and conventional end points was significant, $P < 0.05$, by the Wilcoxon Rank Sum test. Open laser endarterectomy required an average energy density of $124 \pm 9 \text{ J/cm}^2$ (mean $\pm$ SEM).

**DISCUSSION**

The present study shows that argon ion laser endarterectomy is superior to standard endarterectomy in the rabbit model. By serially sectioning each aorta, we were able to confirm the gross observations that the proper cleavage plane within the media was established with both techniques. The endarterectomy surfaces were free of debris and the elastic fibers of the media were not disrupted. The laser end points were consistently superior to the sharply divided end points and, in a chronic experiment, the sharply divided end points would most likely have required

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**FIG. 3.** Longitudinal section of an arteriosclerotic rabbit aorta following conventional endarterectomy. High power ($\times 140$) magnification demonstrates that the internal elastic lamina has been removed. The remaining elastic fibers of the media retain their normal appearance and the integrity of the artery has not been compromised. Hematoxylin and eosin.
**FIG. 4.** Longitudinal section of an arteriosclerotic rabbit aorta following conventional endarterectomy. Low power (×45) magnification of a distal end point. The transition from media (open arrow) to intima (closed arrow) is abrupt but there is no separation of the layers. Hematoxylin and eosin.

**FIG. 5.** Longitudinal section of an arteriosclerotic rabbit aorta following conventional endarterectomy. Low power (×45) magnification of a distal end point. The intima (closed arrow) is separated from the media (open arrow). This will result in a distal intimal flap. Hematoxylin and eosin.
FIG. 6. Longitudinal section of an arteriosclerotic rabbit aorta following argon ion laser endarterectomy. High power (×140) magnification shows that the intima and internal elastic lamina have been removed. The remaining elastic fibers of the media have retained their normal architecture. Hematoxylin and eosin.

FIG. 7. Longitudinal section of a distal end point following argon ion laser endarterectomy. Low power (×45) magnification of a distal end point demonstrates the tapered transition from media (open arrow) to intima (closed arrow). The surface is smooth with modest carbonization. Vacuolization is seen in the superficial layers of the media and intima where the arterial wall has been fused by laser radiation. Hematoxylin and eosin.
sutures to prevent distal intimal flaps. The laser offers a distinct advantage for endarterectomy because phototherapy fusion of end points allows the surgeon to actually "weld" the intima for a secure and smooth transition.

In a previous study [8], we have shown that open laser endarterectomy offers superior results to intraluminal laser angioplasty and laser angioscopy. The angioplasty method resulted in uneven plaque penetration leading to perforation and early thrombosis. The angioscopy technique allowed us to visualize the plaque, but we could not accurately direct the angle of laser exposure. Only open endarterectomy allowed complete control of the lesion and the laser for optimum exposure. The argon ion laser was chosen for the initial study of laser endarterectomy because it produces a beam within the visible spectrum which can be directed through a fiber optic. These characteristics make it easy to accurately direct energy to the target and observe if there is any scatter or transmission. By radiating a discrete area with a known power and energy, we could determine energy density parameters for the tissue, i.e., arteriosclerotic rabbit aortas. We consider energy density, rather than total energy delivered to be the important determinant of tissue response to the laser. The mean energy density of 124 ± 9 J/cm² required in this study would be expected to vary with the severity of arteriosclerosis encountered and probably would be much higher for arteriosclerotic human arteries which are thicker than rabbit aortas and generally have more severe fibrosis and calcification. The rabbit aorta, however, is comparable in size and character to human coronary arteries and may be predictive of energy requirements for the laser treatment of coronary artery disease.

The plaques in the rabbit model tend to be composed chiefly of foam cells and are largely confined to the intima. We have been able to demonstrate fibrosis and moderate calcification [7] in our models, but we have not been able to approach the severe calcification often seen in human arteriosclerosis. Since no ideal animal model exists, early clinical trials of the laser have been proposed [6, 9]. We have shown that a standard surgical procedure, open endarterectomy, can be performed with the laser. Open laser endarterectomy offers a uniform technique for the study of laser radiation upon arteriosclerotic arteries and may be the safest way to begin clinical trials.

### Table 1

**RESULTS OF CONVENTIONAL ENDARTERECTOMY**

| Expt | Atheroma       | Size (cm²) | Surface | End points |
|------|----------------|------------|---------|------------|
| 1    | Mod-severe     | 1.2        | 3       | 3          |
| 2    | Mod            | 1.5        | 3       | 3          |
| 3    | Mod            | 2.0        | 4       | 2          |
| 4    | Mild-mod       | 2.0        | 4       | 3          |
| 5    | Mild-mod       | 1.2        | 4       | 3          |
| 6    | Severe         | 2.7        | 4       | 3          |
| 7    | Mod-severe     | 4.0        | 4       | 2          |
| 8    | Mod            | 5.9        | 3       | 3          |

*Note: Surface: 1 = perforation; 2 = wrong cleavage plane; 3 = rough surface; 4 = smooth surface. End points: 1 = perforation; 2 = intimal flap; 3 = rough transition; 4 = smooth transition.*

### Table 2

**RESULTS OF ARGON ION LASER ENDARTERECTOMY**

| Expt | Atheroma     | Power | Size | Energy density (J/cm²) | Surface | End points |
|------|--------------|-------|------|------------------------|---------|------------|
| 1    | Severe       | 1.0   | 1.0  | 134                    | 4       | 3          |
| 2    | Mod-severe   | 1.0   | 1.5  | 147                    | 4       | 4          |
| 3    | Severe       | 1.0   | 3.0  | 93                     | 4       | 3          |
| 4    | Mild         | 1.0   | 1.2  | 107                    | 4       | 4          |
| 5    | Mild-mod     | 1.0   | 1.2  | 111                    | 3       | 3          |
| 6    | Mod          | 1.0   | 1.0  | 127                    | 4       | 4          |
| 7    | Mod-severe   | 1.0   | 1.0  | 170                    | 3       | 4          |
| 8    | Mild-mod     | 1.0   | 1.0  | 104                    | 3       | 4          |

*Note: Surface: 1 = perforation; 2 = wrong cleavage plane; 3 = rough surface; 4 = smooth surface. End points: 1 = perforation; 2 = intimal flap; 3 = rough transition; 4 = smooth transition.*

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