UC Irvine

UC Irvine Previously Published Works

Title

The thrombogenic potential of argon ion laser endarterectomy.

Permalink

<https://escholarship.org/uc/item/5458368p>

Journal

The Journal of surgical research, 42(2)

ISSN

0022-4804

Authors

Pollock, ME
Eugene, J
Hammer-Wilson, M
et al.

Publication Date

1987-02-01

DOI

10.1016/0022-4804(87)90113-2

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at
<https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

The Thrombogenic Potential of Argon Ion Laser Endarterectomy^{1,2}

MARC E. POLLOCK, M.D., JOHN EUGENE, M.D.,³ MARIE HAMMER-WILSON, M.S.,
AND MICHAEL W. BERNIS, PH.D.

Department of Surgery, VA Medical Center, Long Beach, California 90822; University of California, Irvine, California 92717; and The Beckman Laser Institute and Medical Clinic, Irvine, California 92715

Submitted for publication November 22, 1985

The surface thrombogenicity of atheromas, conventional endarterectomy (CE), laser endarterectomy (LE), and laser angioplasty (LA) were compared in the rabbit arteriosclerosis model. Normal ($N = 6$) and arteriosclerotic ($N = 15$) rabbits underwent thoracoabdominal exploration. Multiple CEs and LEs were performed in 12 arteriosclerotic rabbits leaving a segment of intact atheroma between each endarterectomy. Multiple LAs were performed in three arteriosclerotic rabbits. Argon ion laser radiation was used for all laser procedures. Blood (0.05 ml) from normal rabbits was placed on the CE surface, LE surface, LA surface, atheroma, and normal intima and clotting times were determined. Surface thrombogenicity was calculated as the ratio of the clotting time of the CE, LE, LA, or atheroma to normal intima. Surface thrombogenicity was 1.0 ± 0.03 for normal intima (control), 0.58 ± 0.06 for atheromas ($P < 0.001$), 0.46 ± 0.08 for CE ($P < 0.001$ from atheromas), 0.46 ± 0.08 for LE ($P = \text{NS}$ from CE), and 0.27 ± 0.09 for LA ($P < 0.001$ from CE and LE). The thrombogenicity of LE is the same as the thrombogenicity of CE. Both forms of endarterectomy are less thrombogenic than LA in the rabbit model. © 1987 Academic Press, Inc.

Argon ion laser radiation of arteriosclerotic plaques has been shown to leave carbonized debris and thermal disruption of several cell layers beneath the luminal surface [1, 5, 9, 12, 13]. Since atheromas and atheromatous debris (also known as atheromatous gruel), as well as disruption of the endothelial surface predispose to thrombosis [3, 16], the vascular surface following laser angioplasty of arteriosclerosis may be highly thrombogenic. We have attempted to minimize thermal injury to the arterial surface by performing open laser endarterectomy rather than closed laser angioplasty with the argon ion laser [4, 5, 6, 7]. The initial results of laser endarterectomy are comparable, and in some ways superior, to conventional surgical endarterectomy [6]. Yet the influence of

laser radiation upon the atheroma-platelet interaction and the endothelial response to injury may cause the laser surface to be more thrombogenic than the surgical surface. This report evaluates the surface thrombogenicity [19, 23] of argon ion laser endarterectomy in an experimental rabbit arteriosclerosis model.

MATERIALS AND METHODS

Normal and arteriosclerotic New Zealand white rabbits were used in this study. They received humane care in compliance with the Animal Care Committee of the University of California, Irvine and the *Guide for the Care and Use of Laboratory Animals* prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH publication No. 80-23, revised 1978). Under general anesthesia (im acepromazine 0.5 mg/kg, xylazine 30 mg/kg, ketamine 50 mg/kg), 15 rabbits underwent balloon catheter trauma to the thoracoabdominal aorta. They were fed a 2% cholesterol diet for 20 weeks. This regimen pro-

¹ Presented at the Annual Meeting of the Association for Academic Surgery, Cincinnati, Ohio, November 10-13, 1985.

² This work was supported by NIH Grants HL 31318 and RRO 1192.

³ To whom reprint requests should be addressed at 5901 East Seventh Street (112), Long Beach, Calif. 90822.

duces significant arteriosclerosis in 86% of rabbits [4]. The disease is uniform throughout the traumatized aorta. Grossly the intima appears markedly thickened and discolored. Microscopically the atheromas are surrounded by a fibrous cap. They show inflammation, fatty infiltration, and microcalcification with extension into the superficial layers of the media [4].

Argon ion lasers (Coherent INNOVA 20 or Spectra Physics Model 171) with mixed wavelengths 488 and 514.5 nm were used for laser procedures. Laser light was delivered through a 400 μm quartz fiber optic at a power of 1.0 W. Power was measured from the fiber optic output end (Coherent power meter, Model 210) at the beginning and conclusion of each procedure and was continuously monitored from the laser head during laser operation. The ends of the fiber optic were freshly cut and polished for each experiment. The delivery of laser energy was controlled by the duration of exposure and this ranged from 1.0 to 30 sec (1.0 to 30 J). The energy density was approximately 770 W/cm^2 and the spot diameters were approximately 0.5 mm^2 . Six normal rabbits and 15 arteriosclerotic rabbits were anesthetized (im acepromazine 0.5 mg/kg, xylazine 3.0 mg/kg, ketamine 50 mg/kg), intubated, and ventilated with a small animal respirator. Additional ketamine (50 mg/kg iv) was administered during the procedure to maintain anesthesia. A thoracoabdominal exploration was performed. The aorta was isolated and major branches were controlled. No anticoagulants were administered. In the normal rabbits and in 12 arteriosclerotic rabbits, proximal and distal vascular control of the thoracoabdominal aorta was obtained and the aorta was opened longitudinally. Multiple conventional surgical endarterectomies and laser endarterectomies [4] were performed in each of the arteriosclerotic rabbits leaving a segment of intact atheroma between each endarterectomy. Conventional endarterectomy was performed in the standard fashion [20] using an endarterectomy dissector and vascular instruments. A cleav-

age plane was developed just beneath the internal elastic lamina to dissect the atheroma from the arterial wall and the end points were sharply divided. Laser endarterectomy was performed by using individual laser exposures (1.0 to 5.0 J) to create a line of laser craters at the proximal and distal ends of an atheroma. These lines of laser craters were connected by continuous wave laser light (multiple exposures of 10 to 20 J) to loosen the atheroma. The cleavage plane was dissected within the media by continuous wave laser radiation (multiple exposures of 10 to 30 J). When the plaque was dissected free from the atheroma, the end points were welded by continuous wave laser radiation (10 to 20 J).

In the remaining three arteriosclerotic rabbits, vascular control of the common iliac arteries was obtained, an arteriotomy was made in the left common iliac artery, and a balloon catheter was inserted for proximal control. A 5 Fr. catheter was introduced and advanced proximally until an obstructing atheroma was encountered. The exact site of the lesion could be marked for future study because the rabbits were open. The quartz fiber optic was passed through the catheter and 1.0 sec laser exposures were delivered until the plaques were ablated and the catheter could be advanced. Multiple laser angioplasties were performed in each rabbit. Upon completion of laser angioplasties, proximal vascular control was obtained, the fiber optic and the catheters were withdrawn and the aorta was opened longitudinally.

Upon completion of the procedures (endarterectomy or angioplasty), the aortas were rinsed with saline (37°C) to remove blood. Local humidification was provided to the open thorax and abdomen to prevent dessication of the arterial surface. Blood was drawn from normal donor rabbits and 0.05 ml of normal rabbit blood was applied immediately to normal intima (control), intact atheroma, conventional endarterectomy surface, laser endarterectomy surface and laser angioplasty surface. A fresh wood applicator stick was applied to the blood-surface inter-

face every 15 sec and clotting times were determined as the time at which a reproducible strand of fibrin attached to the applicator stick and pulled away from the surface. Each applicator was used only once. Six donor rabbits were used. A total of 2.0 ml of blood was withdrawn from each donor rabbit so that progressive exsanguination and subsequent changes in the coagulability of the donor rabbit blood did not occur. Prior to use as a donor, a 0.05 ml sample of blood was applied to a glass slide to assure that the donor blood had not been activated. None of the donors were found to be hypercoagulable by this method. There were 12 experiments performed on normal intima (control), 26 experiments performed on atheromas, conventional endarterectomy surfaces, and laser endarterectomy surfaces, and 8 experiments on laser angioplasty surfaces.

Following the determination of surface clotting time, the aortas were harvested from the rabbits and the rabbits were sacrificed (barbiturate injection). The aortas were examined under a dissecting microscope. No perforations were seen. The laser endarterectomy and laser angioplasty sites were measured to determine the surface area irradiated. Energy fluence (J/cm^2) was calculated from the energy necessary to perform each laser procedure and the surface area of each laser procedure. Surface thrombogenicity was calculated as the ratio of the clotting time of the atheroma, conventional endarterectomy, laser endarterectomy, or laser angioplasty surface to normal intima. The values of surface thrombogenicity were eval-

uated by the F statistic for a single factor analysis of variance [21] and the Kruskal-Wallis test for equality of means [14]. Differences amounting to a value of $P < 0.05$ were considered significant.

RESULTS

The results are reported as the mean $\pm$ SD for the rabbits in each group (Table 1). Atheromatous plaque was found to have a clotting time of 247 ± 35 sec for a surface thrombogenicity of 0.58 ± 0.06 . This was highly significant ($P < 0.001$) from control clotting time, 425 ± 51 sec. The clotting times of the conventional and laser endarterectomy surfaces were 193 ± 40 and 192 ± 36 sec, respectively, for identical surface thrombogenicity values of 0.46 ± 0.08 ($P < 0.001$ from atheroma). The laser angioplasty surface achieved a clotting time of 117 ± 13 sec for a surface thrombogenicity value of 0.27 ± 0.03 ($P < 0.001$ from endarterectomy). The laser endarterectomy required an average energy density of $112 \pm 12 \text{ J}/\text{cm}^2$ and the laser angioplasty required an average energy density of $92 \pm 30 \text{ J}/\text{cm}^2$.

DISCUSSION

The purpose of intraluminal angioplasty is recanalization of a stenotic or occluded arteriosclerotic artery. The procedure does not remove atheromas or reconstruct a diseased artery. Open laser endarterectomy is a reconstructive procedure for the removal of atheromatous plaques like a conventional surgical endarterectomy. Since arterioscle-

TABLE I
SURFACE CLOTTING TIME AND THROMBOGENICITY^a

Surface	Number of rabbits	Clotting time (sec)	Surface thrombogenicity
Normal intima	6	425 ± 51	1.0 ± 0.03
Atheroma	12	247 ± 35	0.58 ± 0.06
Conventional endarterectomy	12	193 ± 40	0.46 ± 0.08
Laser endarterectomy	12	192 ± 36	0.46 ± 0.08
Laser angioplasty	3	117 ± 13	0.27 ± 0.03

^a All values are means $\pm$ SD.

rotic plaques have a fibrous cap, the laser angioplasty procedure will remove the cap and leave an exposed atheroma. Lyford *et al.* [16] have homogenized atheromas to create atheromatous gruel and demonstrated that this atheromatous gruel is a highly thrombogenic substance. When atheromatous gruel was injected into rats, thrombocytopenia, intravascular coagulation, and thromboembolic phenomena ensued. The exposed atheroma following intraluminal laser angioplasty, therefore, may be highly thrombogenic.

Our data support this hypothesis. The laser angioplasty surface, denuded of its fibrous cap, had the fastest clotting time of the surfaces studied and the surface thrombogenicity of laser angioplasty was significantly greater than the surface thrombogenicity of laser endarterectomy. The endarterectomy clotting times (laser versus conventional) were nearly identical. This is not unexpected because both procedures remove the atheroma from beneath the internal elastic lamina. The surfaces were significantly more thrombogenic than normal intima or undisturbed atheroma but this occurs because endarterectomy leaves exposed collagen fibers and eliminates the fibrinolytic system of the intact vascular endothelium [2, 10, 11]. In the present study, atheromas were also found to be thrombogenic. This is in agreement with previous studies that have shown that atheromas are preferential sites for platelet adhesion and thrombus formation [17, 18].

Grundfest and associates have questioned the quality of the argon ion laser angioplasty surface because of carbonization and cellular vacuolization [9]. They have proposed the excimer laser (308 nm) for laser angioplasty because the excimer laser angioplasty surface appears free of carbon and "blast" injury. Since it may be the exposed atheroma rather than the carbonization that is responsible for thrombosis following photoradiation, the excimer laser surface may be just as thrombogenic as the argon ion laser surface. Certainly if the argon ion effects alone were responsible

for increased thrombogenicity, the laser endarterectomy surface should be more thrombogenic than the conventional endarterectomy surface. Our data do not support this. The only other study of the thrombotic potential of a photoradiated arterial surface was performed by Van Stiegmans *et al.* [22]. They photoradiated segments of normal porcine carotid arteries with a Nd-YAG laser (1.06 μm) and implanted these segments in an aortic window. They reported a lack of thrombus formation in these segments, but they qualified their results by noting that the experiments were not analogous to laser radiation of arteriosclerotic arterial segments. They performed chronic experiments, however, as opposed to our acute experiments. We could not perform chronic endarterectomy experiments in the arteriosclerotic rabbits. By the time the lesions were advanced enough for study, the rabbits were too ill to routinely survive thoracoabdominal exploration. They had coronary artery disease as well as peripheral vascular disease. They also had fatty infiltration of the liver and approximately 20% had lipid ascites. If chronic investigations of thrombogenicity following laser treatment of arteriosclerosis are to be performed, a different animal model must be used.

Thrombosis is one of the major complications of intraluminal laser use [1, 8, 13]. Ginsburg and co-workers have shown that thrombotic complications increase as the amount of argon ion laser energy delivered increases [8]. Of course, the patients with the most severe disease would probably require the highest levels of energy for recanalization, so their results may be a reflection of the severity of disease rather than increased thrombotic potential due to laser energy. In the present study, comparable energy fluence was used to perform both laser endarterectomy and laser angioplasty. Since laser light was delivered in perpendicular and tangential directions for laser endarterectomy and in a coaxial direction for laser angioplasty, the laser endarterectomy surface probably received more direct laser energy than the

laser angioplasty surface. Hence, the greater thrombotic potential of laser angioplasty cannot be attributed to greater energy fluence. Livesay has recommended the liberal use of anticoagulants and antiplatelet medications following carbon dioxide laser (10.6 μm) radiation of coronary artery arteriosclerosis [15]. Lyford *et al.* showed that blood from patients receiving heparin retained its anticoagulant properties when exposed to atheromatous gruel whereas blood from patients receiving coumadin did not [16]. He did not study the effect of antiplatelet medications on the coagulant response to atheromatous gruel, however. Since we have shown that laser-irradiated atheromas are highly thrombogenic, we agree with Livesay's recommendation for anticoagulation following laser recanalization.

The surface clotting time measures the thrombogenicity of a blood flow surface. Although it is a static measurement which does not reflect the fibrinolytic capability of high velocity blood flow or the coagulant effects of neointima formation, it does provide a reliable measure of the relative thrombogenicity of arterial surfaces [19, 23]. Various arterial prostheses have been evaluated by this technique and subsequent clinical results have confirmed the experimental results. Based upon the surface thrombogenicity, we would expect better patency following laser endarterectomy than laser angioplasty. Since it may be the exposed atheroma rather than the laser-atheroma interaction which is responsible for increased thrombogenic potential, the laser angioplasty surface may be highly thrombogenic no matter which laser is used.

ACKNOWLEDGMENTS

The authors thank Jeffrey J. Andrews, B.A., Regina Reyes, and Shannon Smith for technical assistance in this work. The authors thank Arline Nakanishi, B.S., and Howard G. Tucker, Ph.D., for statistical consultation. R. L. Maxwell prepared the manuscript.

REFERENCES

1. Abela, G. S., Normann, S. J., Cohen, D. M., Franzini, D., Feldman, R. L., Crea, F., Fenech, A., Pine, C. J., and Conti, C. R. Laser recanalization of occluded atherosclerotic arteries in vivo and in vitro. *Circulation* **71**: 403, 1985.
2. Benditt, E. P. Implications of the monoclonal character of human atherosclerotic plaques. *Amer. J. Pathol.* **86**: 693, 1977.
3. Constantinides, P. Plaque fissures in human coronary thrombosis. *J. Atheroscler. Res.* **6**: 1, 1966.
4. Eugene, J., McColgan, S. J., Hammer-Wilson, M., and Berns, M. W. Laser endarterectomy. *Lasers Surg. Med.* **5**: 265, 1985.
5. Eugene, J., McColgan, S. J., Hammer-Wilson, M., Moore-Jeffries, E. W., and Berns, M. W. Laser applications to arteriosclerosis: Angioplasty, angiography, and open endarterectomy. *Lasers Surg. Med.* **5**: 309, 1985.
6. Eugene, J., McColgan, S. J., Pollock, M. E., Hammer-Wilson, M., Moore-Jeffries, E. W., and Berns, M. W. Experimental arteriosclerosis treated by conventional and laser endarterectomy. *J. Surg. Res.* **39**: 31, 1985.
7. Eugene, J., McColgan, S. J., Pollock, M. E., Hammer-Wilson, M., Moore-Jeffries, E. W., and Berns, M. W. Experimental arteriosclerosis treated by argon ion and neodymium-YAG laser endarterectomy. *Circulation* **72**(Suppl. II): 200, 1985.
8. Ginsburg, R., Wexler, L., Mitchell, R. S., and Proffitt, O. Percutaneous transluminal laser angioplasty for treatment of peripheral vascular disease: Clinical experience with 16 patients. *Radiology* **156**: 619, 1985.
9. Grundfest, W. S., Litvack, I. F., Goldenberg, T., Sherman, T., Morgenstern, L., Carroll, R., Fishbein, M., Forrester, J., Morgitan, J., McDermid, S., Pacala, T. J., Rider, D. M., and Laundenslager, J. B. Pulsed ultraviolet lasers and the potential for safe laser angioplasty. *Amer. J. Surg.* **150**: 220, 1985.
10. Huttner, I., and Gabbiani, G. Vascular endothelium: recent advances and unanswered questions. *J. Lab. Invest.* **47**: 409, 1982.
11. Jaffe, E. A. (Ed.) *Biology of Endothelial Cells*. Boston: Martinus' Nijhoff, 1984.
12. Lee, G., Ikeda, R., Herman, I., Dwyer, R. M., Bass, M., Hussein, H., Kozina, J., and Mason, D. T. The qualitative effects of laser irradiation on human arteriosclerotic disease. *Amer. Heart. J.* **105**: 885, 1983.
13. Lee, G., Ikeda, R. M., Theis, J. H., Chan, M. C., Stobbe, D., Ogata, C., Kumagi, A., and Mason, D. T. Acute and chronic complications of laser angioplasty: Vascular wall damage and formation of aneurysms in the atherosclerotic rabbit. *Amer. J. Cardiol.* **53**: 290, 1984.
14. Lehman, E. L. *Nonparametrics: Statistical Methods Based on Ranks*. San Francisco: Holden-Day, 1975. P. 202.
15. Livesay, J. J., personal communication.
16. Lyford, C. L., Connor, W. E., Hoak, J. C., and

- Warner, E. D. The coagulant and thrombogenic properties of human atheroma. *Circulation* **36**: 284, 1967.
17. Prentice, C. R. M., McNichol, G. P., and Douglas, A. S. Effect of normal and atheromatous aortic tissue on platelet aggregation in vitro. *J. Clin. Pathol.* **19**: 343, 1966.
18. Powers, W., Mathias, C. J., Welch, M. J., Sherman, L. A., Siegel, B. A., and Clarkson, T. B. Scintigraphic detection of platelet deposition in atherosclerotic macaques: A new technique for investigation of antithrombic drugs. *Thromb. Res.* **25**: 137, 1982.
19. Roon, A. J., Moore, W. S., Goldstone, J., Towan, H., and Campagna, G. Comparative surface thrombogenicity of implanted vascular grafts. *J. Surg. Res.* **22**: 165, 1977.
20. Stoney, R. J. The technique of thromboendarterectomy. In R. B. Rutherford (Ed.), *Vascular Surgery*, 2nd ed. Philadelphia: Saunders, 1984. P. 357.
21. Tucker, H. G. *An Introduction to Probability and Mathematical Statistics*. New York: Academic Press, 1962. P. 200.
22. Van Stiegmann, G., Kahn, D., Rose, A. G., Bornman, P. C., and Terblanche, J. Endoscopic laser endarterectomy. *Surg. Gynecol. Obstet.* **158**: 529, 1984.
23. Yates, S. G., Nakagawa, Y., Berger, K., and Sauvage, L. R. Surface thrombogenicity of arterial prostheses. *Surg. Gynecol. Obstet.* **136**: 12, 1973.