Transcatheter ablation: comparison between laser photoablation and electrode shock ablation in the dog

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ABSTRACT To characterize and compare the effects of transcatheter laser and electrical energy on endocardium, 35 laser pulses were delivered to the endocardial surfaces of isolated canine hearts, and 33 endocardial lesions were produced by the transarterial delivery of either transcatheter laser irradiation or electrical shock in closed-chest anesthetized dogs. Laser-induced lesion dimensions in vitro and in vivo increased with increased total dose of energy; however, the lesions produced in vivo were different in morphology and were significantly larger than lesions produced by equivalent doses of energy delivered in vitro (p < .05). Endocardial lesions produced in vivo by laser at 40 and 80 J (7.9 x 5.4 x 6.6 and 7.9 x 5.1 x 7.5 mm) were comparable in gross morphology and size to those produced by electrical shock at 100 and 200 J (8.5 x 6.6 x 6.6 and 10.0 x 8.5 x 8.2 mm, respectively; p = NS), but transcatheter electrode shock produced significantly more ventricular tachycardia (p < .003), premature ventricular beats in the 7 min after energy discharge (p < .05), and wall motion abnormality (p < .005). Transcatheter laser photoablation can create controlled endocardial lesions with less energy and fewer deleterious effects than transcatheter electrode shock.


RECURRENT sustained ventricular tachycardia continues to be a difficult problem in patients with ischemic heart disease, and it has been estimated that only 41% of such patients referred for electrophysiologic testing respond to standard medical antiarrhythmic drug regimens.1 Despite disappointing results with conventional drug treatment, important advances have been made in the development of alternative treatment modalities, including encircling ventriculotomy,2 endocardial resection,3 and, most recently, transcatheter shock ablation.4 The therapeutic goals of these procedures are the surgical isolation or interruption of reentrant circuits and the excision or ablation of endocardial arrhythmogenic foci either surgically or via catheter-mediated destruction of tissue.

Laser radiation is monochromatic, coherent, and can be delivered by flexible optical fibers; thus, it has potential utility in the selective ablation of ventricular endocardial sites. Although the interaction of laser and various isolated tissues has been studied,5-7 little is known about the interactions of laser energy with the beating heart in vivo.

The purpose of this study was to characterize the short-term functional, electrocardiographic, and morphologic sequelae of laser discharge on ventricular endocardium in vitro and in vivo, and to compare these effects to those of electrical discharge.

Methods

Twenty-six mongrel dogs weighing approximately 15 to 20 kg each were studied. Laser energy was supplied by a Nd:YAG (neodymium, yttrium, aluminum, garnet) laser (Moletron Medical Model 8000) coupled to a 0.9 mm diameter quartz core fiber (Moletron Medical Model 8200). For transcatheter laser photoablation studies, the quartz fiber was housed within the lumen of a No. 8F flexible catheter, with the tip of the fiber protruding 1 mm from the end of the catheter. In transcatheter electric shock studies, unipolar direct-current shock was delivered from the distal pole of a No. 7F bipolar electrode catheter (United States Catheter and Instruments Co.), positioned against the left ventricular endocardium, to an external left chest paddle. The proximal pole was used only for recording endocardial electrograms. Electrical energy was supplied by a standard
external defibrillator (Physio-Control Life Pak 4) coupled to the distal pole of the catheter (cathodal output) and the external chest paddle (anodal sink) by a modified defibrillator input unit (R2 Corporation Model 170).

Initial experiments were performed with the laser beam focused on the endocardial surface of the isolated canine heart to characterize the dose-response relationship for the Nd:YAG laser. After pentobarbital anesthesia (30 mg/kg), hearts from two mongrel dogs were removed and the left ventricular endocardial surfaces were exposed via an incision through the free wall of the left ventricle. The beating hearts were immediately washed free of blood and moistened with normal saline. With the tip of the quartz fiber in contact with the endocardial surface, 35 laser pulses were delivered with power and pulse durations ranging from 20 W over 1 sec (20 J) to 100 W over 1 sec (100 J).

The laser discharges were distributed as follows: 20 W × 1 sec, n = 5; 20 W × 2 sec, n = 5; 30 W × 1 sec, n = 6; 40 W × 1 sec, n = 5; 80 W × 0.5 sec, n = 4; 80 W × 1 sec, n = 5; 100 W × 1 sec, n = 5. The hearts were examined for gross lesion morphology and fixed in formalin and the largest dimensions (length, width, and depth) of the lesions were measured with a micrometer. For lesion measurements, myocardial slices were made through the area of visible injury at 1 mm intervals.

Transcatheter laser photoablation and electrode shock ablation in vivo were performed in intact anesthetized mongrel dogs. After pentobarbital anesthesia, each dog was intubated and ventilated (Harvard Model 607 respirator) and the right femoral artery was catheterized by a sterile technique. For transcatheter electrode shock studies, the bipolar electrode catheter was advanced under fluoroscopic guidance and positioned against the left ventricular endocardial surface. In several dogs, the apposition of the catheter tip to the endocardial surface was confirmed additionally by electrocardiographic ST elevation recorded from the distal electrode. Synchronized electric shocks of 100, 200, and 300 watt-seconds (100, 200, and 300 J) were delivered to selected endocardial sites using a maximum of two discharges per dog as follows: 100 J, n = 5; 200 J, n = 5; 300 J, n = 2. These energy doses were chosen based on energy doses of electrical shock used clinically.

For transcatheter laser photoablation studies, a luminal No. 8F flexible plain or quadripolar electrode catheter housing the quartz fiber was advanced in a similar manner from the right femoral artery to the left ventricular cavity and positioned fluoroscopically with the tip pointing toward and touching the left ventricular endocardial surface. This position was additionally confirmed in half of the laser discharge experiments by observing electrocardiographic ST elevation recorded from the distal, but not proximal, electrode of the luminal electrode catheter housing the laser fiber. Laser energies of 20, 40, and 80 W were delivered over 1 sec each (20, 40, and 80 J) to selected endocardial sites. A maximum of two discharges were used per dog as follows: 20 J, n = 3; 40 J, n = 13; 80 J, n = 5. Before each electric shock or laser discharge, the position of the catheter tip was verified by fluoroscopy and two-dimensional echocardiography, and efforts made to maximize the distances between discharge sites. For both methods, attempts were made to position the catheters at the level of the papillary muscle tips, either toward the anterior septum or posterior free wall. When a second discharge was given, it was separated from the first by approximately 20 min. The electrocardiogram was continuously monitored throughout each experiment.

Two-dimensional echocardiographic studies were performed on anesthetized dogs that were in the right lateral decubitus position with the use of a commercially available ultrasonoscope (Diasonic 3400R or Varian 3000) coupled to a 3.5 or 2.25 MHz transducer. Two-dimensional long- and short-axis images were recorded at multiple levels before and after each laser or electrical discharge, with care taken to record the short-axis image at the level of catheter apposition to the myocardium. Echocardiographic studies were recorded on ¼ inch videotape for subsequent review in real-time, slow-motion, or stop-action modes.

Left ventricular cross-sectional areas were computed at end-diastole and end-systole with a sound digitizer connected to a dedicated microcomputer (Digisonics). The percent change in fractional area (FAC) was calculated as the end-diastolic area minus the end-systolic area divided by the end-diastolic area.

For analysis of regional wall motion abnormality, the crosssectional views of the left ventricle were displayed on a video monitor in slow motion and real time. Wall motion was categorized as normal, hypokinetic, akinetic, or dyskinetic by two independent observers. Interobserver disagreements were resolved by mutual consensus. All echocardiographic measurements were made in dogs in normal sinus rhythm. To examine the effects of perfusing the coronary circulation with microcaviations, two-dimensional echocardiograms were performed during laser discharge with the laser tip in the aortic root. Laser power of 10 W and durations of 1 to 10 sec were used.

Nineteen dogs were killed immediately after these experiments and their hearts were inspected for acute morphologic damage. Tissues were subsequently fixed in formalin for gross measurements and histologic examination. Gross measurements were made of the largest length, width, and depth in millimeters of the acute lesions, as previously described. Samples of left ventricular tissue were taken from the morphologically damaged areas as well as from the surrounding visibly normal tissue. These tissues were embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Five dogs (two receiving electric shock and three receiving laser ablation) were allowed to recover for 3 weeks before they were killed so that the healed lesions could be characterized. These dogs were given a lethal dose of intravenous anesthetic and their hearts were excised through an incision in the fourth left intercostal space. The hearts were examined grossly and histologically as described above.

**Statistical methods.** Results are expressed as mean ± SD. The Student t test was used to compare lesion dimensions and echocardiographic percent FAC after laser and electrical discharge. The Fisher's exact test was used to compare the different proportions of wall motion abnormalities resulting from laser vs electrical discharge. Statistical significance was assumed at p < .05.

**Results**

*Studies in vitro.* At all energy levels and pulse durations tested, the gross morphologic lesions produced by the Nd:YAG laser in the isolated canine heart consisted of a central vaporized crater surrounded by a rim of necrotic tissue (figure 1). Lesion size, expressed as length, width, and depth, increased as a function of total energy delivered, as shown by the dose-response curve (figure 2). The total duration of delivery of laser energy was a more important determinant of lesion size than the absolute amount of energy delivered. When energy levels equivalent to 40 J were used, lesions produced by 20 W delivered over 2 sec and those produced by 40 W over 1 sec were both significantly larger than those produced by 80 W over 0.5 sec (figure 3; p < .01).
Studies in vivo. The dimensions of the acute lesions produced by transcatheter laser energy in anesthetized closed-chest dogs are shown in figure 4, right. Unlike laser-induced lesions in the isolated heart, most lesions seen in the heart in situ did not have a vaporized crater or rim of necrosis, and consisted instead of an irregular area of darkened endocardium (figure 5, A). Only at higher energy levels (80 J) were occasional craters as well as shallow intramyocardial linear lesions seen. On cut section, the characteristic lesions were oval-shaped, visibly hemorrhagic areas that extended into the myocardium to the depths indicated in figure 4. Faint finger-like projections of hemorrhage 1 to 2 mm in length and distant to the primary lesion were seen in several of the earlier specimens, but were not found in any of the lesions produced with the laser core housed within the electrode catheter and guided by electrocardiographic ST elevation.

Microscopically, the primary lesions consisted of areas of hemorrhage with myocellular swelling (figure 5, B); the cytoplasm of the affected myocytes had either a homogeneous appearance or contained numerous vacuoles and few contraction bands. In some instances, focal deposits of fibrin and platelets were found on the endocardial surface.

Lesion size increased as a function of energy delivered; however, the increments in lesion size were smaller than those seen in isolated hearts. Lesion length, width, and depth in the closed-chest dog heart were 2 to 3.5 times larger than those produced by an equivalent amount of energy in the isolated heart (figure 4; p < .005).

Acute endocardial lesions produced by transcatheter electrode shock were morphologically similar to those produced by laser, consisting of a smooth oval dark-
Transcatheter electric laser tachycardia was shown within 1 only laser discharge. A) The dimensions of laser-induced lesions in isolated hearts were significantly larger than those produced in situ (p < .005).

FIGURE 4. Comparison between dimensions of laser-induced lesions in vitro and in vivo. At all energy levels, lesions produced in situ were significantly larger than those produced in vitro (p < .005).

The dimensions of the electrically induced lesions also increased as a function of energy delivered. As shown in figure 6, the lesions produced by 100 to 200 watt-seconds (100 to 200 J) of electric shock were comparable in size to those produced by 40 to 80 W of laser energy delivered over 1 sec (40 to 80 J; p = NS).

Electrocardiographic observations. Although the gross lesions produced by 40 to 80 J of laser energy and by 100 to 200 J of electrical energy were comparable in size, their arrhythmogenic potential was markedly dissimilar. Figure 7 illustrates representative tracings of arrhythmias occurring immediately after 80 W of laser discharge over 1 sec and after 100 watt-seconds of electric shock. At all energy levels tested, electric shock caused sustained ventricular tachycardia, whereas laser discharge caused ventricular tachycardia only within 1 sec of lasing. In two instances, however, a single 80 watt-second laser discharge and 300 watt-second electrical discharge caused immediate ventricular fibrillation. The disparate effects of laser and electrical energy on arrhythmia formation are graphically shown in figure 8, in which the number of beats of ventricular tachycardia immediately after laser or electrical discharge (figure 8, A) and the number of ventricular ectopic beats per minute for the first 4 min after laser or electrical discharge (figure 8, B) are plotted. Transcatheter electric shock caused significant ventricular irritability, with an average of 39 beats of ventricular tachycardia following a single 200 watt-second discharge. Frequent ventricular ectopic beats and runs of ventricular tachycardia continued for up to 7 min after electrical shock. In contrast, laser energy of 20, 40, or 80 W over 1 sec caused an average of 2, 6, and 6 beats of ventricular tachycardia, respectively, immediately after laser discharge (p < .003). Ventricular ec- tomy after laser discharge was dramatically less frequent than that after electric shock, with only occasional premature ventricular beats lasting for up to 2 min following laser discharge (p < .05). There were no differences in complexity or frequency of arrhythmias between the first and second discharges, be they laser or electrical.

Two-dimensional echocardiography. Two-dimensional echocardiography was performed in 22 dogs immediately before and after laser or electrical discharge. Echocardiograms obtained during electrical discharge showed microcavitation formation in the left ventricular cavity immediately after all shocks. Wall motion abnormalities developed at the level of the catheter tip immediately after electrical discharge in all dogs and were dose dependent. At energy levels of 100 and 200 J, two of seven electrical discharges (29%) resulted in hypokinetic segments and five of seven (71%) resulted in akinetic or dysskinetic segments. Also, within several minutes of delivery of electrical shock, transmural echo densities formed within the myocardial wall at the site of the electrical discharge in five of seven dogs (71%). While these echo densities were initially thought to represent intramural hematoma, gross anatomic examination did not reveal hematoma; however, microscopic examination showed variable degrees of edema, hypercontraction of myocytes, and focal extravasation of red blood cells. Although these echo densities appeared more frequently at higher energy doses, they also occurred after doses of 100 J. On two occasions, an intracavitary density appeared after electrical discharge and was found to be an organized mural thrombus at necropsy 3 weeks later.

Two-dimensional echocardiograms were also obtained during laser discharge. The appearance of some evidence of intracavitary microcavitation occurred during 10 of 15 laser discharges (66%), regardless of the amount of energy or type of catheter used, and most likely represented the effects of laser energy on the adjacent blood pool that resulted from intermittent incomplete apposition of the fiber tip to the endocardial surface. With the use of slow-motion and stop-frame playback, microcavitations were observed to begin at the fiber tip and to progress to complete...
FIGURE 5. Comparison of the gross and histologic morphologic characteristics of the endocardial lesions induced by laser (A to C), and electric shock (D to F). A, Endocardial surface in the area of the anteromedial papillary muscle showing two areas (outlined by dots) of hemorrhage at sites of laser discharge. B, Histologic section of an acute lesion, similar to that in A, showing extravasation of red blood cells along myocardial cleavage planes. Hematoxylin and eosin stain; original magnification x150. C, Histologic section of laser-induced lesion after 3 weeks of healing, showing replacement fibrosis. Masson trichrome stain. D, Endocardial surface in the area of electric shock appears as a dark spot. E, Histologic section of an acute lesion similar to that in D shows hemorrhage and interstitial edema. Contraction bands are demonstrated in the inset at the lower right. Hematoxylin and eosin stain; original magnification x150; inset, x400. F, Shock-induced lesion after 3 weeks of healing shows interstitial fibrosis. Hematoxylin and eosin stain; original magnification x150.

FIGURE 6. A comparison between lesion dimensions produced in vivo by transcatheter-delivered laser energy on the left, and electrical energy on the right. There are no significant differences between dimensions of lesions produced by laser energy of 40 and 80 J and those of lesions produced by electric shock of 100 and 200 J.

opacification of the left ventricular blood pool. With ventricular emptying and subsequent clearing of ventricular blood pool opacification, progressive echocardiographic opacification of the left ventricular myocardium was seen. This effect was likely the result of perfusion of the coronary arteries with microcavitations since it was reproduced when low-power, long-duration laser energy was directed at the blood pool within the aortic root. Although blood pool microcavitations were detected echocardiographically with as little as 10 W delivered over 1 sec at the aortic root, myocardial opacification was adequately seen only after 7 to 10 sec of continuous laser discharge.

At energy levels of 40 to 80 W over 1 sec, five of 15 laser discharges (33%) produced no wall motion abnormalities, a significant difference compared with the 100% incidence of wall motion abnormalities...
after electrical shock (p < .05). Four of 15 laser discharges (26%) resulted in minimally hypokinetic segments immediately after discharge, while one of 15 (6%) resulted in akinetic segments, and this at an energy level of 80 J. There were no differences in percent FAC after either laser (−2.0% ± 10.6) or electrical (−8.7% ± 9.8) discharges (p = NS), and neither segmental wall motion nor global left ventricular function were affected by myocardial opacification with microcavitations. Focal transmural echodensities at the level of the catheter tip similar to those seen after electric shock occurred during four of 15 laser discharges (26%), and these only at an energy level of 80 J. No intracavitary opacifications representing mural thrombus appeared over the short term and there were no organized mural thrombi found on gross examination in any of the dogs. However, a healed lesion in one dog that had received a 40 watt-second laser discharge showed microscopic evidence of organized mural thrombus. The sequence of discharge had no effect on the resulting wall motion pattern.

The small number of specimens in which lesion edges could be accurately defined 3 weeks after either electric shock or laser discharge precluded meaningful analysis of lesion dimensions. Histologic examination of the 3-week-old lesions showed replacement and interstitial fibrosis in both laser-induced (figure 5, C), and electrically induced lesions (figure 5, F). The fibrosis appeared to involve the endocardial and subendocardial regions to a similar extent in both laser- and electrically induced lesions.

Discussion

The results of this study show that transcatheter photoablation of endocardial sites in the beating heart in situ can be produced in a controlled fashion with the Nd:YAG laser. Endocardial lesions produced by the Nd:YAG laser demonstrated a dose-response relationship, with lesion size increasing with increasing amount of delivered energy. The duration of delivery of laser energy appeared to be a more important determinant of lesion size and depth than total amount of energy delivered. At a given dose of laser energy, lesions produced by lower power and longer laser pulse durations were larger and deeper than those produced at higher power and shorter pulse durations. This may be of practical importance in attempts at photoablation, since short, repetitive laser bursts may produce a lesion that is shallower and wider in surface dimensions, and will therefore cover a larger endocardial area while lessening the risk of perforation of the ventricular wall.

Although the morphologic and histologic effects of the argon laser on isolated bovine myocardium have been previously described, we performed our studies with the Nd:YAG laser in the dog to compare the effects of laser energy in vitro with those seen in the beating heart in situ. Of practical importance is the finding that the lesions produced by the Nd:YAG laser in the beating hearts in vivo were larger, and of different morphology, than those produced in the isolated heart. These differences are likely the result of the different refractive, absorptive, and conductive characteristics of laser energy in a blood medium, and to the effects of cardiac motion on the relatively long laser discharge durations used in this study. Similar enhancement of Nd:YAG laser energy within a blood medium was observed by Abela et al., who observed that laser-induced lesions in coronary atherosclerotic plaques were larger and deeper when the coronary...
Transcatheter laser photoablation produced lesions comparable in size to those produced by transcatheter electrode shock at less than half the energy of the electrical doses. However, transcatheter electrode shock caused significantly more frequent ventricular tachycardia and ventricular ectopic activity compared with laser-delivered energy. The doses of electrical energy used in this study were chosen on the basis of those used clinically.\(^8,9\) The frequent ventricular tachyarrhythmias seen after transcatheter electric shock in this study may have been the result of the large energy dose/body weight ratio, the deleterious effects of electrical energy beyond the cathodal catheter tip, or may have been peculiar to the canine preparation. Recently, however, others have also observed the markedly arrhythmogenic effects of electrical discharge in the dog heart at energy levels as low as 50 J.\(^{14-16}\)

Presumably because of the greater far-field effects of electrical injury caused by the transmission of transcatheter electrode shock from an endocardial electrode to an external chest paddle, greater deleterious effects were seen not only electrically but also mechanically. After every electrical discharge, significant regional wall motion abnormalities occurred at the site of the electrode catheter tip, regardless of the energy levels used. In contrast, wall motion abnormalities greater than very minimal hypokinesis were seen after laser discharge only in one dog at an energy level of 80 J. In addition, left ventricular mural thrombi formed in two dogs soon after electrical discharge and were detected by two-dimensional echocardiography. These thrombi were well organized when the hearts were excised 3 weeks later. In contrast, laser discharge did not produce echocardiographic evidence of mural thrombi; however, microscopic evidence of an organized mural thrombus was detected overlying a 3-week-old healed lesion in one dog.

Microcavitations occurred in approximately half of laser discharges at energy levels exceeding 20 W/sec and caused progressive opacification of the ventricular blood pool at higher energy levels. This finding most likely reflects incomplete apposition of the fiber tip to the ventricular endocardial surface during the relatively long period of laser discharge and probably represents gas formation resulting from laser irradiation of

FIGURE 8. A, Histogram plotting the number of consecutive beats of ventricular tachycardia after laser and electrical energy discharge. Electrical shock caused significantly more ventricular tachycardia than did laser photoablation immediately, during, and after energy discharge (\(p < .003\)). B, Histogram plotting the number of premature ventricular complexes (PVCs) per minute in the first 4 min after laser photoablation and electric shock. Electrical shock caused significantly more PVCs/min than did laser photoablation (\(p < .05\)).

arteries were perfused with blood rather than with saline. They hypothesized that hemoglobin pigment released from laser-damaged red blood cells may have adhered to the vessel wall causing preferential absorption of laser energy, and demonstrated a similar increase in absorption of laser energy when tissue was treated with dyes such as Sudan Black.

Transcatheter-delivered laser energy is capable of creating discrete areas of endocardial damage. While small finger-like projections of hemorrhage remote to the primary lesion were seen in several dogs after laser discharge via a plain catheter, these were not noted when the laser fiber was housed within a luminal electrode catheter and guided by electrocardiographic ST elevation in addition to echocardiographic and fluoroscopic guidance. This was a likely consequence of the better positioning of the laser fiber tip allowed by this method. Histologic examination of the acute laser lesions showed hemorrhage and interstitial edema that extended from the endocardial surface several millimeters into the myocardium. After 3 weeks of healing, the lesions consisted of endocardial and subendocardial fibrosis. These lesions should be of sufficient depth to disrupt, destroy, or modify reentrant circuits or arrhythmogenic foci.\(^13\)

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blood pool elements. Washout of blood pool opacification was followed by progressive opacification of the left ventricular myocardium, most likely due to perfusion of the coronary circulation with microcavitations. An interesting future application for this finding may be the evaluation of coronary perfusion after laser recanalization. Deleterious effects of microcavitation formation on left ventricular function were not apparent.

In conclusion, transcatheter laser photoablation of endocardial arrhythmogenic foci may have the potential for becoming a useful modality in the management of intractable ventricular tachycardia since it has the capacity for creating discrete endocardial lesions with less energy than transcatheter electrode shock ablation and produces fewer arrhythmias and wall motion abnormalities. However, further work will be necessary to delineate the long-term effects of laser energy on myocardium, the optimal method of delivery of laser energy to the myocardium, and the efficacy of laser ablation in the prevention of ventricular tachycardia in a preparation of inducible arrhythmias. Since patients in whom this technique is likely to be used have preexisting coronary artery disease and left ventricular dysfunction, in contrast to the normal dogs used in this study, caution must be taken in extrapolating our data to the clinical setting.

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