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percutaneous experiments, respectively (Figure 1). The distal end of each fiber had been modified by attachment of a 5-mm “diffusing element” and a 4-mm sharpened (bare fiber) tip. Titanium dioxide particles uniformly embedded in the diffusing element scatter photons when struck by laser light (Figure 2), increasing the volume and slowing the rate of heating. A dielectric mirror between the diffusing element and sharpened tip reflects photons internally and prevents the direct heating of tissue ahead of the fiber. In pilot studies, large lesions least likely to damage either myocardial surface were induced once the distal 1 cm (including the sharpened tip and diffusing element) had penetrated the tissue at 90°.

A diode laser (Diomed Ltd) operating at 805 nm was used in all experiments. Light transmission through the optical fibers was measured at baseline and before each exposure with an integrating sphere to ensure stable power delivery. Fibers were discarded if output was diminished by charring or fracture of the fiber tip.

Experimental Protocol
Approval was obtained from the Institutional Review Board and Animal Care and Use Committee of the University of Texas Medical Branch at Galveston.

Open-Chest Experiments
Normal mongrel dogs weighing 15 to 25 kg were intubated after receiving butorphenol 0.1 mg/kg, acepromazine maleate 0.05 mg/kg, and atropine 0.02 mg/kg. Anesthesia was induced with intravenous thiopental sodium 20 mg/kg and maintained with 1% to 2% thiopental sodium and atropine 0.02 mg/kg. Anesthesia was induced with intravenous saline was infused at room temperature by a Harvard pump (10 mL/min) for epicardial cooling. Before irradiation, the distal electrode pairs before, during, and after each laser application. After this, the fiber was again retracted into the guiding catheter, and both the catheter and fiber were removed.

Dosing
Pilot lesions were made to determine “acceptable” doses, ie, doses ranging in 30-second and 0.5-W increments from the lowest that first caused visible coagulation to the highest that did not extensively char or vaporize the lesion. This range was 3 to 4.5 W and 30 to 120 seconds in the open-chest model. In the percutaneous experiments, 2, 2.5, and 3 W were delivered over 60 seconds, and 2.5 W was delivered over 90 seconds. Because 2.5 W over 90 seconds and 3.0 W over 60 seconds induced lesions of similar size, the former was not used for dosimetry analysis.

Lesion Measurement and Pathology
Lesions were bisected in a plane perpendicular to the epicardial or, in the percutaneous experiments, endocardial surface. The maximum lesion width (short axis) and length (long axis) were measured with a micrometer before tissue fixation in 10% neutral-buffered formalin. A “maximum depth” was determined for percutaneously induced lesions, because distal margin depth often exceeded lesion length. Lesion volume was calculated as $\frac{4}{3}\pi r^3$, the volume of an ellipse rotated about its long axis (or prolate spheroid). Fixed lesions were sectioned parallel to the original bisection plane and processed for standard histopathological analysis.

Statistics
In open-chest experiments, a 2-way ANOVA determined the effects of exposure time (30, 60, 90, and 120 seconds) and power (3.0, 3.5, 4.0, and 4.5 W), and their interaction, on the continuous outcome variables of lesion depth, width, and volume. Data are analyzed with the caveat that the highest and lowest doses were not used: 3.0 and 3.5 W×30 seconds produced no visible lesions, and 4.5 W×120 seconds charred tissue. Differences among levels of time and power and of their interaction were evaluated with Bonferroni-adjusted t tests, using an experiment-wise error rate of 0.05. For example, for width, which demonstrated a time×power interaction, the alpha level of significance was 0.0006 for pairwise t tests (or 0.05/120, where 120 was the number of possible comparisons). The GLM procedure in the statistical software SAS with option LSMEANS/PDIFF was used for all analyses.27 Means are given with their ±SD. All t tests mentioned in the Results section are Bonferroni-adjusted.

In percutaneous experiments, lesion dimensions at power levels of 2.0, 2.5, and 3.0 W delivered over 60 seconds were evaluated with 1-way ANOVA followed by Bonferroni-adjusted t tests. The sensitivity and specificity that electrogram changes had for lesion induction were determined at each fluoroscopic position, using gross coagulation at the matching site found postmortem as the “gold-standard,” comparative test.28 Only well-defined ST-segment depression and T-wave peaking, as illustrated in Figure 4, were analyzed.

Results
Open-Chest Experiments
Nine animals underwent thoracotomy and 88 laser applications (5 to 15 lesions per heart; mean, 10±1 per heart). Of...
these, 80 could be measured accurately. Fiber insertion caused occasional premature ventricular contractions and brief runs of nonsustained VT. Ventricular fibrillation (VF) occurred in 2 animals during the 10th and in another during the 4th lesion. After defibrillation, this third animal underwent 8 additional lesions without incident. All 9 dogs survived the protocol, including the 1-hour observation period.

Combining all 13 doses (Table 1), mean lesion width was 7.24 ± 1.5 mm (range, 4.8 to 10.8 mm). Mean depth (10.4 ± 1.6 mm; range, 6.3 to 14.7 mm) approximated tip length. Mean lesion volume was 2460.9 ± 1307 mm$^3$ (range, 837.8 to 6316 mm$^3$).

Examining the effects of power and time on width showed a significant power×time interaction ($P=0.02$). Thus, to understand how width relates to exposure time, one must consider the power level, and vice versa. This interaction permits lesion widths to be compared as in Table 1, yielding a general pattern of increasing width with increasing time and power. The 30-second level was an exception, producing narrow lesions across all powers. The entire range of widths could be induced by varying either time (30 to 120 seconds) against 4Wo r power (3.0 to 4.5 W) against 60 seconds. Grouped as such, widths increased linearly with time but nonlinearly with increasing power (Figure 3).

Most photons diffuse laterally$^{23}$; however, with longer exposures, lesion depth increased significantly ($P<0.01$). No power×time interaction ($P=0.48$) affected depth. The $t$ tests showed that levels of 90 seconds (10.77±1.23 mm) and 120 seconds (10.73±1.8 mm) differed from 30 seconds (8.96±1.24 mm), but there were no significant pairwise differences between power levels.

Likewise, there was no power×time interaction on volume ($P=0.10$), but significant effects of power and time were present (both $P<0.0001$). For power, $t$ tests showed significant pairwise differences comparing levels of 3.5 W (2548±1162 mm$^3$), 4.0 W (2366±1104 mm$^3$), and 4.5 W (3193±1778 mm$^3$) with 3.0 W (1606±445 mm$^3$), but the higher levels did not differ from each other. For time, levels of 60 seconds (2361±1419 mm$^3$), 90 seconds (2722±1209 mm$^3$), and 120 seconds (2805±1347 mm$^3$) differed from 30 seconds (1256±479 mm$^3$) but not from each other.

**Percutaneous Experiments**

Eleven dogs underwent 48 laser applications (2 to 7 per heart). Twenty-eight lesions were found (#5 per heart). Higher and lower doses were identified equally well, suggesting that lesions were missing because of unsuccessful fiber

<table>
<thead>
<tr>
<th>Dose</th>
<th>W×s</th>
<th>n</th>
<th>Width</th>
<th>Relation to Other Doses*</th>
<th>Depth, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.0×60</td>
<td>6</td>
<td>5.8±0.50</td>
<td>&lt;6, 9, 10, 12, 13</td>
<td>9.54±1.1</td>
</tr>
<tr>
<td>2</td>
<td>3.0×90</td>
<td>8</td>
<td>6.6±0.42</td>
<td>&lt;6, 10, 12, 13</td>
<td>10.41±1.0</td>
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<tr>
<td>3</td>
<td>3.0×120</td>
<td>7</td>
<td>6.4±0.68</td>
<td>&lt;6, 10, 12, 13</td>
<td>10.2±1.74</td>
</tr>
<tr>
<td>4</td>
<td>3.5×60</td>
<td>6</td>
<td>6.0±0.88</td>
<td>&lt;9, 10, 12, 13</td>
<td>10.55±1.56</td>
</tr>
<tr>
<td>5</td>
<td>3.5×90</td>
<td>7</td>
<td>7.4±0.76</td>
<td>...</td>
<td>10.78±1.13</td>
</tr>
<tr>
<td>6</td>
<td>3.5×120</td>
<td>6</td>
<td>8.5±1.30</td>
<td>&gt;7, 11</td>
<td>11.5±1.84</td>
</tr>
<tr>
<td>7</td>
<td>4.0×30</td>
<td>5</td>
<td>5.9±0.89</td>
<td>&lt;9, 10, 12, 13</td>
<td>9.1±1.7</td>
</tr>
<tr>
<td>8</td>
<td>4.0×60</td>
<td>7</td>
<td>7.3±0.87</td>
<td>...</td>
<td>9.82±1.45</td>
</tr>
<tr>
<td>9</td>
<td>4.0×90</td>
<td>6</td>
<td>8.0±0.82</td>
<td>&gt;11</td>
<td>9.75±1.1</td>
</tr>
<tr>
<td>10</td>
<td>4.0×120</td>
<td>3</td>
<td>9.1±0.84</td>
<td>&gt;11</td>
<td>10.5±1.85</td>
</tr>
<tr>
<td>11</td>
<td>4.5×30</td>
<td>5</td>
<td>5.7±0.77</td>
<td>&lt;12, 13</td>
<td>8.84±0.71</td>
</tr>
<tr>
<td>12</td>
<td>4.5×60</td>
<td>7</td>
<td>8.9±1.30</td>
<td>...</td>
<td>11.23±2.23</td>
</tr>
<tr>
<td>13</td>
<td>4.5×90</td>
<td>7</td>
<td>8.8±1.30</td>
<td>...</td>
<td>11.76±1.0</td>
</tr>
</tbody>
</table>

*Significant differences in width ($P<0.05$), according to 2-way ANOVA followed by Bonferroni-adjusted $t$ tests.

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**Figure 3.** Dosimetry from open-chest experiments. With a single power (4 W) or time (60 seconds), width changed linearly (A) or exponentially (B) within ranges of time and power used.
tip penetration. Successful deployments caused ventricular ectopy but no ST-T changes in the endocardial electrogram. Brief, well-tolerated, nonsustained VT occurred rarely during heating. A brief idioventricular rhythm was seen in 1 animal 5 minutes after catheter removal. Sustained VT or VF did not occur, and arterial pressure remained stable in the 6 animals monitored.

With the 400-μm fiber, a smaller and lower-power range induced “acceptable” lesions similar to the open-chest experiments. As before, width increased nonlinearly with power (Table 2), ranging from 4 to 10 mm (6.3±1.4 mm); the mean of maximum depths (10.2±1.8 mm; range, 7.3 to 13.3 mm) approximated tip length and generally exceeded lesion length (8.3±1.2 mm; range, 6 to 11.4 mm). Occasional lesions were centered within the LV wall (Figure 6).

One-way ANOVA followed by Bonferroni-adjusted t tests detected significant pairwise differences when comparing widths for 2.5 and 3.0 W with 2.0 W and when comparing 2.5 with 3.0 W. Increasing power caused a trend but no significant change in lesion length or maximum depth. Volumes at 3 W differed significantly from those at 2.5 and 2.0 W. The greatest widths and volumes were generated by 3 W over 60 seconds.

### Table 2. Lesion Dimensions of Percutaneous Experiments

<table>
<thead>
<tr>
<th>Dose</th>
<th>n</th>
<th>Width, mm</th>
<th>Length, mm</th>
<th>Maximum Depth, mm</th>
<th>Volume, mm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 W×60 s</td>
<td>6</td>
<td>5.5±0.48</td>
<td>7.8±0.7</td>
<td>8.7±1.4</td>
<td>1005.9±245.3</td>
</tr>
<tr>
<td>2.5 W×60 s</td>
<td>8</td>
<td>6.1±1.2</td>
<td>7.7±1.3</td>
<td>8.7±1.5</td>
<td>1280.2±731.0</td>
</tr>
<tr>
<td>3 W×60 s</td>
<td>8</td>
<td>7.9±1.1*</td>
<td>9.0±1.2</td>
<td>10.5±2.0</td>
<td>2470.9±934*</td>
</tr>
</tbody>
</table>

*Significant (P≤0.05) vs each of the 2 lower doses, according to 1-way ANOVA followed by Bonferroni-adjusted t tests. Length and maximum depth are defined in the text.

Endocardial Electrograms

ST and T waves did not change with endocardial penetration. Epicardial penetration did not occur; thus, possible ST-T changes accompanying this event are unknown. However, heat-induced ST depression with T-wave peaking (by 0.5 to 2.0 and 0.5 to 3.0 mV, respectively) were specific for gross intramyocardial lesion induction (Figure 4 and Table 3), but T-wave peaking alone was not. Marked T-wave peaking and ST depression were unusual when proximal lesion margins were deep. RR and QTc intervals did not change nor did R-waves regularly decrease with coagulation.

Pathology

The epicardium and endocardium were remarkably free of gross tissue damage in both open-chest and percutaneous experiments; in the latter, lesion sites were not apparent on inspection of the endocardium, and transmural perforation, pericardial tamponade, and epicardial coronary artery damage did not occur.

In cross section, lesions ranged from elliptical to spherical and were well outlined grossly by a line of congested blood vessels (Figures 5 and 6). Microscopically, coagulated tissue abruptly bordered viable tissue (Figure 7A). Necrotic tissue was characterized by extensive, homogeneous contraction bands. No evidence of vascular thrombi or hemorrhage was seen (Figure 7B). Focal subendocardial cell necrosis was noted within a 1- to 2-mm radius from the insertion point, but this was not associated with platelet or fibrin adherence to the endocardial surface (Figure 7C).

Discussion

This unique optical fiber diffuses light for slow, intramural heating and large, deep, well-circumscribed lesions that do not disrupt either endocardium or epicardium. It therefore appears well suited for the treatment of postinfarction VT.

Thermal conduction through tissue is directly proportional to the temperature gradient across the medium and to the time allowed for conduction to occur; however, a steep gradient that chars, boils, or increases tissue reflectance will reduce

### Table 3. Sensitivity and Specificity That Electrogram Changes Had for Coagulation

<table>
<thead>
<tr>
<th>T-Wave Peaking, 0.5–3.5 mV*</th>
<th>ST-Segment Depression, 0.5–2.0 mV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, %</td>
<td>81</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>75</td>
</tr>
</tbody>
</table>

*Deviation (range) that occurred with heating.
heat transfer\textsuperscript{7,21} and, if it involves the endocardium, may promote mural thrombi.\textsuperscript{10–14} Surface cooling increases lesion size but transfers high temperatures into the midmyocardium,\textsuperscript{15,30} where tissue vaporization and explosion may cause pericardial tamponade.\textsuperscript{15} By heating tissue more slowly, this fiber both reduces risk and generates deep, large-volume lesions.

Once deployed, the entire diffusing element is intramycocardial, and the opposing tissue surface is not directly irradiated. The endocardium is not disrupted but remains free of adherent platelets and fibrin. Well-defined margins reduce the arrhythmogenic potential of the lesions.\textsuperscript{31,32} Most photons diffuse laterally,\textsuperscript{23} and within certain dose ranges, lesion width changes linearly or nonlinearly with increases in time and power, respectively. Mean depths approximated the tip length inserted (here 10 mm); thus, a tip shorter than the target tissue is thick should not damage the epicardium. However, the wide range of depths suggests that tip length is not the sole determinant of this parameter. In the open-chest experiments, longer exposure times (90 and 120 seconds) increased lesion depth significantly compared with 30 seconds. In the percutaneous experiments, the highest powers (\(\geq 4.5\) W) delivered over 120 seconds seriously carbonized the tissue. Widths gradually approached a maximum with increasing exposure time (Figure 3, top). As power increased over a fixed time, lesions widened more abruptly (Figure 3, bottom), implying rapid heat deposition and an increased risk of carbonization. Finally, lesion length increased significantly only with the longest exposure times, because this is not the primary direction of heat conduction.

Coagulation could be identified in only 58\% of all lesions attempted percutaneously. We suspect that the optical fiber had not penetrated the tissue, a problem that should be solved with device improvement. Alternatively, adequate tempera-
Figure 7. Light micrographs of lesions induced percutaneously (Movat's pentachrome stain). A, Well-defined border of necrotic myocardium (at left) demonstrates homogeneous contraction-band necrosis, in contrast to adjacent viable tissue. Magnification \( \times 150 \). B, Interstitial edema and coagulation necrosis are present at center of lesion. Vessels appear congested, but no evidence of acute thrombi is seen here or elsewhere. Magnification \( \times 150 \). C, Higher-power view of endocardium within 1 to 2 mm of optical fiber insertion site shows a normal endocardial surface free of platelet aggregation and thrombus (left ventricular cavity is at top; internal elastic lamina is darkly stained). A few scattered, superficial subendocardial myocytes show acute necrosis with contraction bands (arrows). Viable, lighter-staining adjacent myocytes with intact cross-striations and intercalated disks are at bottom of photomicrograph. Acutely necrotic subendocardial myocytes are the only evidence of endocardial injury. Magnification \( \times 290 \).

Intramyocardial heating caused VF, but its infrequency precludes correlation with lesion number, size, or delivered energy, and its long-term implications are unknown. All episodes were in the open-chest experiments (occurring with lesion 10 in 2 animals and during lesion 4 in a third). Other, nonsustained episodes of ventricular ectopy did not require intervention and had no apparent adverse sequelae.

In summary, this diffusing-tip optical fiber is unique in its ability to induce large intramural lesions without directly heating the endocardium. Volumetric heating that is modified to forestall charring and vaporization reduces the likelihood of transmural perforation and allows thermal energy to conduct to its theoretical maximum. Tip penetration sustains tissue contact; verification of adequate deep tissue coagulation may be confirmed by ST-segment depression recorded from the guiding catheter. Because only low powers are necessary to induce these lesions, diode laser generators capable of VT ablation should remain small and thus feasible for use in electrophysiology laboratories. The technique is limited by the requirement that the guiding catheter remain nearly perpendicular to the endocardium and, at the present time, by difficulty with successful tissue penetration. However, its potential for effective VT therapy is incentive for improvements that could make it a very useful addition to our clinical armamentarium.

Acknowledgments

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References


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