Variability of Contact Transscleral Neodymium:YAG Cyclophotocoagulation

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Purpose. To study the variability of ciliary body lesions created by contact Nd:YAG cyclophotocoagulation and to evaluate modifications in probe design to reduce this variability.

Methods. Contact transscleral Nd:YAG cyclophotocoagulation was performed on fresh, enucleated porcine eyes in three ways: using a standard, handheld fiber-optic probe (98 eyes); using the same probe with an adjunctive contact lens guide to control for probe pressure, angle, and position (69 eyes); and using a spring-loaded handpiece to control for probe pressure (148 eyes). Four laser lesions were created in each eye and were rated for size and severity of tissue response.

Results. For the three groups of eyes, the mean for size differences (largest lesion minus smallest lesion in millimeters for each eye) was 2.55, 1.65, and 2.36, respectively. The mean for severity differences (most severe lesion minus least severe lesion for each eye, based on a four-part subjective rating) was 1.9, 1.1, and 1.7, respectively. These measures of size difference and severity difference were significantly lower with the lens guide than with the other two systems \( (P = 0.022 \text{ and } P = 0.020, \text{ respectively}) \).

Conclusions. These findings indicate that contact transscleral cyclophotocoagulation can be associated with considerable variation in the size and severity of the ciliary body reaction. This variation has a significant dependence on probe pressure and orientation against the eye and can be reduced by modification in probe design. Invest Ophthalmol Vis Sci. 1995;36:497–502.

Consideration of the optimum form of cyclophotocoagulation, as a treatment option for intractable glaucoma, includes a variety of delivery modes. Although laser energy can be applied to the ciliary processes under direct visualization by either the external transpupillary or the internal pars plana route, the transscleral approach has proven to be the most practical and is currently the standard for this group of operations. Transscleral cyclophotocoagulation can be performed with either a noncontact, slit lamp delivery system or a contact, fiber-optic delivery system. These two approaches have relative advantages and disadvantages and can be performed with available Nd:YAG or semiconductor diode lasers.

Compared to most slit lamp delivery systems, fiber-optic units are more portable and less expensive, and they allow treating the patient in the supine position. One of the disadvantages of the contact systems, however, is that the amount of pressure applied to the eye by the probe may influence the percentage of transscleral transmission of laser energy. The precise anatomic positioning and orientation of the treatment beam may also be less controlled with freehand fiber-optic delivery than with slit lamp delivery. Variability in these parameters increases the variation in ciliary body tissue response.

We report herein a series of experiments designed to evaluate the extent of the variation in tissue response that might be anticipated with a contact, transscleral Nd:YAG cyclophotocoagulation unit, and how this variability might be reduced by two modifications in probe design.

MATERIALS AND METHODS. In each set of experiments to be described, numerous adult porcine eyes were enucleated and chilled in ice water within 1 hour of slaughter for other purposes at a meat packing plant under USDA regulation. Because the three experiments were performed on different days, the number of eyes in each study group was determined by the availability of eyes on that day.

A continuous-wave Nd:YAG laser (Microrupter 3, HS Meridian; Bern, Switzerland) attached to a 600-μm diameter quartz fiber probe with a flat tip was used in all experiments. All laser treatments were performed by one investigator (DAE), using a power setting of 6 watts and a duration of 1 second. Intraocular pressure was maintained at 30 mm Hg in each eye during the laser applications by impaling the posterior pole of each eye on a large-gauge needle connected to a fluid column of appropriate height.

In the first set of experiments, group 1, the center of the handheld laser probe tip (Fig. 1) was placed in contact with the sclera 1.2 mm from the limbus, as determined with calipers. Following the traditional clinical practice for performing contact transscleral cyclophotocoagulation, a subjective effort was made to maintain a gentle, constant pressure against the eye with the probe, and the angle of the probe was

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A hole was drilled through the probe guide to allow passage of the fiber-optic probe system. The hole was oriented 15° from the visual axis and was perpendicular to the top surface of the guide. It emerged on the contact surface with the center 1.2 mm peripheral to the outer diameter of the corneal vault. The hole was 16.75 mm in length and had a diameter of 1.6 mm to allow passage of a 17-gauge protective metal sleeve that enclosed the 600-μ diameter quartz fiber. The fiber extended 4 mm beyond the end of the metal sleeve to keep materials away from the fiber tip that might absorb laser energy and cause excessive heating. The metal sleeve was threaded to accept a nut, which could be adjusted to control the length of the quartz fiber tip that extended beyond the contact surface of the guide, thereby controlling the amount of pressure exerted by the tip against the eye. In this study, the nut was preset to allow the quartz fiber tip to protrude 0.3 mm beyond the contact surface when the probe was fully inserted in the probe guide.

The probe guide was placed against the porcine eye with minimal pressure evenly distributed in all quadrants. The edge of the corneal curve closest to the hole was aligned with the limbus; that is, the center of the hole was placed 1.2 mm posterior to the limbus. The probe was then inserted through the shaft in the guide until the nut contacted the top surface of the guide, allowing the fiber tip to indent the ocular tissue 0.3 mm beyond the scleral surface of the guide. Using the same technique described in the first experiment, one laser application was placed in each quadrant of all eyes in this experiment.

In the third experiment, group 3, a spring-loaded handpiece was used to control for the amount of probe pressure against the eye (Fig. 3). This device has been described by Rol et al.1 A 600-μ diameter quartz fiber, similar to that used in the first two experiments, was connected to the handheld portion of the probe that controlled the pressure exerted by the fiber against the eye through two opposing forces, a linear spring and a pair of magnets. The compression of the fiber-optic contact probe system was used with probe guide (group 2). (bottom) Tip of fiber-optic contact probe used with freehand technique (group 1).

In the remaining two experiments, the only change in procedure involved modifications of the fiber-optic probe system. In the first of these, group 2, a contact lens probe guide was used to control the position, angle, and pressure of the probe (Figs. 1, 2). The probe guide was fabricated from clear optical acrylic, with an index of refraction matching that of the human cornea. The portion of the guide designed for contact with the sclera had a rounded outer edge, a diameter of 20 mm, and a radius of curvature of 12.5 mm. Within the scleral surface was a central portion designed for contact with the human cornea, which had a diameter of 11.75 mm and a radius of curvature of 8.1 mm. A circle was engraved between the corneal and scleral curvatures to facilitate visualization by the surgeon. The corneal and scleral curvatures were designed to fit “flat” enough to allow use without goniosolution and to allow the surgeon to compress and blanch the conjunctiva adjacent to the treatment site. The top of the probe guide had an 8-mm wide band with a diameter of 28 mm to facilitate holding the lens. The top surface had a convex shape with a radius of curvature of 43.5 mm, which provided a magnified view of the anterior ocular tissues.

FIGURE 1. (top) Contact probe with metal sleeve and nut used with probe guide (group 2). (bottom) Tip of fiber-optic contact probe used with freehand technique (group 1).

FIGURE 2. (A) Contact lens probe guide used in group 2. (B) Contact probe with metal sleeve and nut shown inserted through probe guide.
Reports were calibrated with a steel ruler, and measurements were recorded to the nearest 0.1 mm. Severity was estimated for each lesion by using a four-part, subjective grading system as follows: grade 1 = mild blanching without evident tissue shrinkage; grade 2 = moderate blanching with mild tissue shrinkage; grade 3 = marked blanching with moderate tissue shrinkage but no tissue disruption; and grade 4 = marked tissue shrinkage with central tissue disruption (Fig. 4).

In each of the three study groups, the average size and average severity were calculated for the four lesions in each eye. In addition, the difference in size between the largest and the smallest lesions, and the difference in severity between the most severe and the least severe lesions, was determined for the set of four lesions for each eye. For each of the three study groups, the distributions of these four variables (i.e., size average, severity average, size difference, and severity difference) were plotted and calculated for mean, median, mode, standard deviation, and standard error. A one-way analysis of variance was used to compare 95% confidence intervals for each of the four variables between the three study groups, allowing for differences in group size.

RESULTS. The number of porcine eyes available and used in study groups 1 through 3 was 98, 69, and 148, respectively. Tables 1 to 4 summarize the mean, standard deviation, and standard error for the size and severity variables.
TABLE 1. Averages of Lesion Sizes*

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (manual)</th>
<th>Group 2 (probe guide)</th>
<th>Group 3 (spring-loaded)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (eyes)</td>
<td>98</td>
<td>69</td>
<td>148</td>
</tr>
<tr>
<td>Mean</td>
<td>4.67</td>
<td>4.77</td>
<td>4.18</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.96</td>
<td>0.74</td>
<td>0.81</td>
</tr>
<tr>
<td>Standard error</td>
<td>0.10</td>
<td>0.09</td>
<td>0.07</td>
</tr>
<tr>
<td>95% Confidence interval for the mean</td>
<td>4.47-4.9</td>
<td>4.60-4.95</td>
<td>4.10-4.32</td>
</tr>
</tbody>
</table>

* Largest diameter in millimeters of four cyclophotocoagulation lesions in each eye.

standard deviation, standard error, and 95% confidence interval for the mean of the size average, size difference, severity average, and severity difference within each study group.

Group 2 (probe guide) showed the least variation for all four variables. With regard to lesion size, the standard deviation of the mean for size average was 0.73 for group 2, compared to 0.96 mm for group 1 (manual) and 0.81 mm for group 3 (spring-loaded handpiece). The mean and standard deviation for size difference (largest minus smallest in each eye) were 1.65 ± 0.87 mm for group 2, compared to 2.53 ± 1.24 mm for group 1 and 2.36 ± 1.31 mm for group 3. The difference in 95% confidence interval for the means of the two variables was significant between group 2 and the other two study groups (P = .013 for size average and .022 for size difference).

With regard to severity of the lesions, the standard deviation of the mean for severity average was 0.5417 for group 2, compared to 0.7 for group 1 and 0.7 for group 3. The mean and standard deviation for severity difference (most severe minus least severe in each eye) were 1.1 ± 0.8 for group 2, compared to 1.9 ± 0.9 for group 1 and 1.7 ± 1.0 for group 3. The difference in 95% confidence interval for the mean severity difference was significant between group 2 and the other two study groups (P = .020), but it did not reach statistical significance for the mean severity average (P = .288).

DISCUSSION. Two sets of variables influence the degree of tissue response created by transscleral cyclophotocoagulation: those associated with the individual eye and those associated with the treatment parameters and techniques. Among the former, ocular pigmentation is an important variable. Coleman et al showed that human autopsy eyes of black persons require less energy to create similar lesions than autopsy eyes of white persons, presumably because the former had more uveal melanin to absorb the laser energy. Conversely, as noted by Fankhauser et al, increased melanin in the conjunctiva or sclera may reduce the percentage of laser energy reaching the ciliary body. Other variables of the individual eye that may influence cyclophotocoagulation lesions include scleral thickness, uveal blood flow, and preoperative intraocular pressure. Although these variables are difficult to control, it may be possible to compensate for them, if they can be recognized, by altering the treatment parameters or techniques.

Treatement variables that influence the ciliary body response to cyclophotocoagulation include power, duration of exposure, and the wavelength of the laser energy. With regard to contact cyclophotocoagulation, Rol et al have noted that two factors that influence scleral transparency, and hence the percentage of laser energy reaching the ciliary body, are probe pressure against the eye and duration of that pressure. In previous studies using videographic observation of cyclophotocoagulation lesions as they are created in human autopsy eyes, we observed the influence of probe pressure on the extent of laser lesions.

The purpose of the present study was, first, to evaluate the degree to which this relationship between probe pressure and tissue response influences variability in the cyclophotocoagulation lesions, and, second, to explore ways to reduce this variable. If considerable variation is seen within one eye, treated by one investigational Ophthalmology & Visual Science, February 1995, Vol. 36, No. 2

TABLE 2. Differences in Lesion Sizes*

<table>
<thead>
<tr>
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<tr>
<td>n (eyes)</td>
<td>98</td>
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<td>148</td>
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<tr>
<td>Mean</td>
<td>2.53</td>
<td>1.65</td>
<td>2.36</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>1.25</td>
<td>0.87</td>
<td>1.32</td>
</tr>
<tr>
<td>Standard error</td>
<td>0.13</td>
<td>0.11</td>
<td>0.11</td>
</tr>
<tr>
<td>95% Confidence interval for the mean</td>
<td>2.28-2.78</td>
<td>1.44-1.86</td>
<td>2.15-2.58</td>
</tr>
</tbody>
</table>

* Largest minus smallest diameter in millimeters of four cyclophotocoagulation lesions in each eye.
gator, it is reasonable to assume that even greater variation occurs when a surgeon operates on different eyes on different days—especially when the results of different surgeons are compared. The resulting lesion variability most likely influences the surgical outcome in an operation that is well known for unpredictable results.

Several limitations in the present study must be recognized. Porcine eyes, rather than human eyes, were used because the latter were not available in sufficient numbers on a day-to-day basis, and the wide range of freshness and preexisting autolysis might have influenced the observed laser lesions. Freshly enucleated porcine eyes were used to minimize this potential variable and to permit the study in a large series of eyes. One disadvantage of porcine eyes is scleral pigmentation, which reduces the amount of laser light reaching the ciliary body, thereby influencing the variability of laser lesions. Uveal pigmentation, on the other hand, appeared by subjective evaluation to be constant within individual eyes. Because lesions were compared to others in the same eye, variation in uveal pigmentation among eyes would not be expected to influence the observations.

The sample size was different in the three groups, a result of the number of eyes available at the time of each experiment. However, the sample size in each experiment (98, 69, and 148 eyes, respectively) was thought to be large enough to minimize that source of error, and any potential bias was accounted for in the statistical analysis. Furthermore, a larger sample size should have reduced the tendency for variation, whereas the group with the least variation (probe guide) had the smallest sample size. Another potential limitation was that the three treatment systems were performed separately, rather than randomly. However, this was thought to minimize variability for each system because the investigator performed all applications with one system consecutively in a single day before inspecting and grading the tissue response. Finally, the study design was limited by the fact that the two measured outcomes, lesion size and severity, were not obtained in a masked fashion, because the three experiments were performed on separate days and the variable of severity was determined subjectively.

Notwithstanding these limitations, this study strongly suggests that marked variation in the extent of the cyclophotocoagulation lesions occurs when a contact fiber-optic probe is used. When differences in lesion size were calculated by subtracting the smallest from the largest in each eye, the means of these size differences ranged from 1.7 to 2.5 mm with the three different probe systems studied. When variations in severity of tissue response were evaluated by subtracting the least severe from the most severe lesion in each eye, based on a four-part subjective rating scale, the means of the severity differences ranged from 1.1 to 1.9 mm. These findings support the need for measures to minimize variation in probe pressure through modification in probe design, two of which were evaluated in this study.

The spring-loaded handpiece, in which the pressure exerted by the fiber tip against the eye was controlled by the tension of a spring within the hand-
piece, provided variation in size and severity of the cyclophotocoagulation lesions that was not significantly different from that of the standard probe, in which the pressure was manually controlled by the investigator. This is similar to the observations of Fankhauser et al, who also evaluated the spring-loaded handheld probe in porcine eyes and found less variation in lesion severity when the probe pressure was controlled intuitively by an experienced surgeon.

The adjunctive use of a contact lens probe guide was associated with significantly less variation in lesion size and severity compared to the other two systems. This system of a modified probe and contact lens guide controls for three variables: probe orientation (angle to the visual axis); probe position (distance from the limbus); and probe pressure (length of fiber optics allowed to indent the eye). An alternative to the probe guide is to incorporate the features of angle, position, and pressure control into the design of the handheld probe itself. Such a device has been developed for performing transscleral cyclophotocoagulation with a semiconductor diode laser. It may also be that a surgeon who performs this operation with reasonable frequency can learn to control for probe pressure, in addition to controlling for probe angle and position.

The present study does not distinguish between the relative significance of treatment parameters and techniques on the variability of contact transscleral cyclophotocoagulation compared to the influence of biologic characteristics of the individual eye, such as pigmentation, scleral thickness, and position of ciliary processes. Nevertheless, the study does suggest that variability in tissue response is a significant problem and can be minimized through modifications in probe design. Further development and evaluation of such instruments for contact transscleral cyclophotocoagulation is warranted.

Key Words

cyclophotocoagulation, Nd:YAG, lasers, intraocular pressure, intractable glaucoma

References


Crystallin Degradation and Insolubilization in Regions of Young Rat Lens With Calcium Ionophore Cataract

Naoki Iwasaki,* Larry L. David,* and Thomas R. Shearer*

Purpose. To determine if the susceptibility of rat lenses to cataract formation in culture changes with increasing age and to investigate the regional differences in crystallin degradation and insolubilization during the formation of cataracts in cultured lenses.

Methods. Lenses from 4-week-old (young group) and 12-week-old (adult group) rats were divided into four subgroups: noncultured control, cultured control, cultured in calcium ionophore A23187, and cultured in ionophore plus calpain inhibitor E64. Lenses were cultured for 7 days, and the cortex and nucleus were homogenized and separated into water-soluble and water-insoluble fractions. Two-dimensional electrophoresis and N-terminal sequencing were then performed.

Results. Young lenses treated with ionophore produced thin cortical and dense nuclear opacities. Adult lenses treated with ionophore also developed thin cortical opacity, but no nuclear opacity was observed, even though a large increase in the concentration of insoluble protein occurred. Two-dimensional electrophoresis and sequencing suggested that calpain caused protein degradation in the cortex region. However, unlike nuclear opacity, the formation of opacity in the cortex was not inhibited by E64 in young or adult lenses.

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