Low-energy, Q-switched ruby laser iridotomies in Macaca mulatta

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Laser iridotomies have been pursued as a means of performing anterior segments surgery as a virtually noninvasive procedure. An ideal single laser pulse technique has been elusive. In this study, iridotomies in rhesus monkeys were produced with a single exposure to a Q-switched ruby laser pulse. The iridotomy formation was accompanied by acoustic wave generation, bubble formation, and explosive tissue disruption, evidence of a nonlinear laser-iris interaction. The average energies at which these iridotomies were produced ranged between 18 and 48 mJ, some of the lowest energies reported for a laser iridotomy. Corneal changes were observed both at the epithelium and at the endothelium in some, but not all, of the eyes exposed. The epithelial changes morphologically resembled nonlinear damage reported for transparent solids. Damage to physical materials has been attributed to stimulated Brillouin scattering, a mechanism that may also play a role at the cornea. Consideration of such phenomena should be a part of the clinical evaluation prior to exposure of a cornea to high-power laser pulses. Although the endothelial change was more difficult to analyze, a shock-wave effect could not be discounted.

Key words: iridotomy, iridectomy, laser, laser surgery, ruby laser, Q-switched laser, glaucoma

Utilization of a light source to produce an iridotomy without surgically opening the eye has long been an attractive idea to ophthalmic surgeons. The first attempt to achieve this end was made with a xenon arc by Meyer-Schwicherath in 1956 and has continued into the present era of lasers. Pulsed laser systems with pulse durations in the millisecond range (10⁻³ sec) have the advantage of producing a photocoagulative effect which does not allow sufficient time for damaging thermal diffusion as occurred with other light sources. As laser pulse duration has been further decreased into the nanosecond range (10⁻⁹ sec) by the technique of Q-switching, the thermal absorption generates physical forces that rupture tissue, in contrast to photocoagulation of tissue.

In this report a single low-energy pulse from a Q-switched ruby laser was used to form iridotomies in rhesus monkeys. Multiple-pulse techniques were evaluated both as a means of preventing closure of iridotomies as well as a method to reopen iridotomies that closed. In addition to the iris effect, corneal effects also were noted. The mechanism of the Q-switched pulse differs from that of the conventional pulsed laser and is discussed in relation to the effects observed.

Methods and materials

The laser system (Fig. 1) was a Korad K-1 ruby laser with a line width per spectral element of 0.1
Fig. 1. Laser assembly. The laser cavity and shutter mechanism, the Pockels cell, are located to the right. The ruby pulse traveled from right to left and was deflected 90 degrees by a mirror at the end of the optical rail. The next mirror in the path of the pulse was on a trip mechanism activated when the laser fired. It pivoted toward the viewer to allow the pulse to pass through the beam splitter and focusing lens. He-Ne laser was used for aligning the iris. This beam was brought into the exposure area by means of the beam splitter. The exposure area was viewed through a Zeiss surgical microscope assembly. The field of view was directed toward the viewer by first the trip mirror and then the mirror below the microscope objective assembly.

Fig. 2. Photomicrograph of an area of exposed radiographic film subjected to a Q-switched ruby laser pulse. This film was at the focal point of the focusing lens (see Fig. 1).

The diameter of the rod was 12 mm. The beam divergence at half-angle and half-power was 4 mrad. The laser system was mounted on an optical rail with the exposure area located 90 degrees to the beam path. The beam was deflected into the exposure area by means of a mirror. After deflection the beam passed through a 100 mm objective lens used to focus the beam. The viewing system incorporated the optics of a Zeiss surgical microscope assembly. A helium-neon (He-Ne) laser was used for aiming and aligning the target area prior to exposure to the ruby pulse. A ballistic thermo-
Fig. 3. Pre-exposure and postexposure energy measurements for each animal are shown. The individual energy values are denoted with a small horizontal bar. The average of the five values is represented by a closed circle for the pre-exposure energies and an open circle for the postexposure energies.

Table I. Pulse parameters in air

<table>
<thead>
<tr>
<th>Animal</th>
<th>Pulse* energy (mj)</th>
<th>Spot size†</th>
<th>Energy density (J/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>205</td>
<td>18.1</td>
<td>0.010</td>
<td>0.079</td>
</tr>
<tr>
<td>48E</td>
<td>38.3</td>
<td>0.012</td>
<td>0.113</td>
</tr>
<tr>
<td>261</td>
<td>41.9</td>
<td>0.023</td>
<td>0.491</td>
</tr>
<tr>
<td>140E</td>
<td>42.2</td>
<td>0.013</td>
<td>0.177</td>
</tr>
<tr>
<td>588E</td>
<td>48.2</td>
<td>0.025</td>
<td>0.030</td>
</tr>
</tbody>
</table>

*Average of 10 readings.
†At the focal point, in air.

Rhesus monkeys (*Macaca mulatta*) were sedated with intramuscular injections of either ketamine HCl or phencyclidine HCl. The eyelids were held open by a wire speculum, and the cornea was kept moist with applications of physiologic normal saline. The iris was positioned perpendicular to the beam, brought into sharp focus, and exposed to the Q-switched ruby laser pulse. In each iris of five monkeys (ten eyes) both a nasal and a temporal site were exposed. All nasal sites received a single pulse; all temporal sites received two pulses 1 min apart. These monkeys received no medications following exposures.

Three of the five animals were re-exposed to a single pulse to the temporal site 1 week following the original iridotomy in order to evaluate the efficacy of reopening iridotomies that had closed.

In a sixth monkey, laser exposures were made every other day on adjacent peripheral sites of the same iris for an 8-day period. During this time this eye was treated with 2% pilocarpine twice daily.

All animals were examined daily with a slit lamp for a period of 5 weeks. The lens and posterior segment were examined at 5 weeks through a dilated pupil with a slit lamp and indirect ophthalmoscope.

Results

Dosimetry. The energy measurements showed variation from pulse to pulse with individual values less than 80 mj (Fig. 3). The 10 energy determinations for each animal experiment were averaged to give a mean figure for the experiment. The averaged values were less than 50 mj. Variations in spot size between experiments were noted (Table I); during any experiment the pulse geometry remained constant.

Immediate effects on the anterior segment.

At the time of the pulse delivery, a sharp, high-frequency sound was heard. Bubbles were seen at the exposure site and in the anterior chamber. The iris was opened from the anterior surface through the pigment epithelium. The iris opening was filled with a blood-tinged, pigmented tissue matrix. A blood-tinged,
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Fig. 4. Photograph immediately after laser exposure. The picture was taken through a surgical microscope equipped with a beam splitter. The temporal exposure site, on the left, is marked by localized suspension of blood and tissue debris released at time of the exposure. The small dark spots over the iris are pigmented fragments of tissue from the exposure site. Note that they are distributed throughout the anterior chamber. Beneath the bright corneal reflection is a cluster of bubbles. Two other bubbles may be noted at approximately 10 o'clock from the reflection. These bubbles were formed in the anterior chamber by the laser pulse.

viscous-appearing material surrounded the site. No active iris hemorrhage was produced. Some pigmented tissue debris was thrown across the face of the iris (Fig. 4). Localized contracture of the dilator muscle sometimes occurred, producing a small transient iris elevation adjacent to the exposure site on the pupillary side of the exposure site. In those sites receiving a second pulse, some additional clearing of the pigmented matrix in the iris opening was effected.

Postexposure iris effects. Of the 10 iris sites receiving a single pulse, nine were found to be iridotomies. In the 10 sites receiving two pulses, all 10 sites were iridotomies. Slit-lamp examinations revealed that the iridotomy closures began 24 to 36 hr after formation and occurred at the level of the pigment epithelium rather than the stroma. At 1 week the iridotomies were closed and appeared as thinned, hyperpigmented sites. Three of these iridotomy closures were readily reopened with a single laser pulse, which produced less tissue debris in the anterior chamber than the initial exposure. Again, a trace of blood was noted in the anterior chamber, but no active hemorrhage occurred. Bubble formation accompanied the reopening. However, in 5 to 7 days, the reopened sites closed.

Iris vessels near the exposure site became engorged 12 hr following exposures and remained prominent for several days thereafter.

Corneal effects. In two eyes a circular corneal area less than 1.0 mm in diameter was immediately denuded of epithelium by a single laser pulse, with an accompanying formation of a central small superficial pit in the underlying corneal stroma (Fig. 5). Be-
Fig. 5. Slit-lamp photograph of corneal epithelial lesion resulting from a Q-switched ruby laser pulse (arrow). The epithelial lesion is shown immediately following exposure. The epithelium has been lost, and there is some pitting of the corneal stroma.

Fig. 6. Endothelial change seen 48 hr following laser exposure. The endothelial ring appeared vacuolated and pigmented.
Fig. 7. Series of five Q-switched ruby laser iridotomies in an eye treated with 2% pilocarpine twice daily. The exposure site on the left is shown immediately following laser exposure. The iridotomy to the immediate right is 48 hr old. There is a fibrin clot in the site. The middle site is 4 days old and is clear of fibrin and hemorrhage. The iris margins are beginning to appear smooth and regular. The fourth and fifth sites are 6 and 8 days after laser exposure, respectively. The sites are clear, and the iris margins are judged to be healed. The asymmetry of the pupil was not present when the induced miosis dissipated. The prominence of the iris vessels represents vascular engorgement following laser exposure.

neath these sites of corneal damage, iris perforations were formed. During the following week these corneal areas healed, and no scar was detected on slit-lamp examination. In another eye uninvolved with the epithelial changes, an endothelial change was noted 48 hr following laser exposure (Fig. 6). The lesion was a circular area of pigmentation at the level of the endothelium. Pigmentation increased over the following 2 days. The periphery of the ring was more heavily pigmented than the center. This pigmented ring was located toward the optical center of the cornea and not in the path of a laser pulse. The lesion did not change during the 5-week follow-up period.

Postexposure effects on anterior chamber, lens, and retina. An aqueous flare was noted minutes after laser exposure. Initially, there were small pieces of pigmented tissue debris within the anterior chamber and on the iris surface. The anterior chambers cleared within 72 hr without treatment. Five weeks after exposure, the lenses and retina were examined through a fully dilated pupil. No lens changes were noted on slit-lamp examination, and no retinal lesions were found with an indirect ophthalmoscope.

Pilocarpine treatment. In the sixth animal treated b.i.d. with 2% pilocarpine, iridotomy closure was prevented. The patency of the initial iridotomy was maintained for 8 days, at which time the iris margins had healed to form a smooth, regular border (Fig. 7).

Discussion

The present study has demonstrated that a single, high-power, ultrashort laser pulse can be used at relatively low energy levels to form iridotomies in the rhesus monkey. The
The experimental use of a single low-energy pulse technique to form iridotomies is a recent accomplishment. The initial laser study by Zaret et al. in 1963 exposed the irises of brown rabbits to a 0.5 msec ruby laser pulse with an energy density of 0.1 J cm⁻². In this study as well as in those conducted over the following decade, single laser pulses were unsuccessful in producing iridotomies in rabbits, although coagulation of iris tissue was marked. Models based on monkeys and cats also were used with similar results. Multiple-pulse exposure techniques, however, were found to successfully penetrate the iris. In 1970 a single laser pulse of 650 mJ applied to a 1.0 mm area of a pigmented rabbit iris for 500 msec was successful in producing an iridotomy.

The initial human trials using a single laser pulse produced iris coagulation similar to that reported in the animal studies. The first laser iridotomies in patients also were achieved through a multiple-exposure technique. In 1973, utilizing the high energy levels of 4.5 to 8.0 J, Beckman and Sugar produced iridotomies in patients with a single pulse from a ruby laser. Similar results were obtained in the same year by Perkins and Brown, who used a 900 mJ ruby pulse with a 650-μsec duration. In a study reported in 1968, Campbell et al. exposed the rabbit iris to a Q-switched ruby laser with maximum energies of 8.3 to 8.5 mJ, over a spot size less than 1.0 mm. Disturbance of the surface of the iris stroma was the only effect observed, leading the author to state that the ultrashort pulse had no application in clinical ophthalmology. However, 2 years later Zweng et al. produced iridotomies in monkeys with a single Q-switched ruby laser pulse with an energy of 1.0 J. The patency of these iris perforations, however, was short-lived, closing 5 days following formation. More recently, a multiple-laser, multiple-exposure technique was used by Krasnov, both experimentally and clinically, to produce iridotomies. In Krasnov's work, argon laser applications coagulated the iris site several days before exposure to a Q-switched ruby pulse. With this pretreatment technique, Q-switched pulses with energies of 100 to 120 mJ could create an iris opening. The energy levels recorded in this study are less than any reported to date for the use of a Q-switched ruby laser and are in close agreement with the 40 mJ values obtained by Wheeler using a dye laser operating at 480 nm focused on the pigmented iris of rabbits for 2 μsec. Variation in the pulse-to-pulse energy content was noted and is inherent in high-power, solid-state laser systems.

In this study, the cross-sectional geometry of the pulse was taken to be circular, and energy density calculations were based on the assumption of a homogeneous energy distribution over a circular area. It is acknowledged that high-power lasers in reality do not produce such homogeneous energy distributions, but such calculations provide a useful approximation of energy density at the focal point. A low energy level offers an obvious margin of safety to surrounding ocular tissues. As the beam diverges from the focal point on the anterior iris surface, the energy density will decrease as the inverse of the radius squared. This exposed the lens and the posterior segment to energy densities that did not show evidence of damage during the 5-week follow-up period.

Analysis of the effects of Q-switched lasers on either physical or biologic material is complex and varies with the nature of the target material and its surface. Two categories of laser interaction have been defined: absorption by opaque surfaces and damage to transparent material. In passage through the cornea to the iris, the Q-switched laser pulse interacts with both types of material. As an opaque surface, the iris may be expected to experience a phase change or vaporization if flux densities of 10⁹ W cm⁻² or greater are attained. Calculations based on the iris exposures reported in this study show that such levels were reached. The dynamics of tissue vaporization have been reported with both theoretical and experimental evidence, demonstrating that energies sufficient to cause vaporization would also result in the formation of acoustic transients.
accompanied by acoustic phenomena, but the converse is not true. Acoustic phenomena may occur without vaporization.\textsuperscript{24, 25} These are nonlinear, power density–dependent mechanisms.

Ham et al.\textsuperscript{23} were the first to recognize that mechanisms other than photocoagulative events were effective in high-power laser irradiation when they studied the effects of Q-switched pulses on the retina. The rapid pulse delivery produces an intense heating of the exposed tissue at a rate much greater than can be dissipated.\textsuperscript{20} The resulting effect is the generation of damaging mechanical stresses. In particular, the generation of acoustic transients and acoustic waves have been reported to have a significantly greater potential for tissue damage or disruption than the thermal or photocoagulative component.\textsuperscript{24–26}

The production of the iridotomies in this study was an immediate event. The iridotomy appeared as though it had been produced by tearing of the iris; the edges were rough and ragged. The audible report and the appearance of bubbles were compatible with a vaporization event. The tissue dispersed into the anterior chamber was heavily pigmented and was judged to be primarily the result of a laser–iris pigment epithelium interaction. However, pigmentation within the iris stroma may also contribute to the opening of the iris. In an iris model proposed by Wheeler,\textsuperscript{29} the pigmentation with the iris stroma would produce qualitatively the same effects as the pigment epithelium. Thus throughout the iris stroma there could be produced hot spots at sites of pigmentation, resulting in a chain of microexplosions and tearing of the iris.

The most frequent complication in this study was the closure of the iridotomies, which occurred at all sites. The delivery of two pulses 1 min apart to the same site was intended to clear the site of tissue fragments and prevent closure. Although additional clearing was achieved, it was not found in this study to be beneficial in preventing closure. Reopening of closed areas a week following the initial application of the laser pulse did not result in a permanent iridotomy. In one animal the use of pilocarpine was found to be effective by maintaining sufficient separation of the iris margins to prevent bridging and closing of the wound.

The appearance of the corneal epithelial defect bears a strong morphological resemblance to laser-induced surface damage to glass and other transparent materials.\textsuperscript{28–30} The transmittance of the cornea at the frequency of the ruby laser has been shown to be greater than 90%.\textsuperscript{31} The difference in the nondestructive passage of light through transparent material and the destructive effects of Q-switched lasers on the same material has been explained on the basis of rate of energy deposition, or power.\textsuperscript{2} One of the complex nonlinear phenomena active when high-power lasers interact with the surface of transparent solids and liquids is that of Brillouin scattering.\textsuperscript{2, 22, 25} From studies of Q-switched laser effects on transparent solids, it has been shown that as these events take place, the effects may be the loss of surface material, vaporization, and violent shattering of the surface.\textsuperscript{30}

The epithelial lesion, however, did not appear with each pulse that passed through the cornea. Several aspects of these exposures may account for the sporadic nature of this cornea-laser interaction. Surface irregularities or structural inhomogeneities of transparent materials have been shown to increase the degree of coupling between the laser pulse and the target material with enhancement of damage.\textsuperscript{32} The corneal epithelial defects could have been the result of inadequate tear film in the sedated animal, with an accompanying corneal irregularity and a concomitant increase in electric field coupling. Obviously, further studies are required to accurately characterize the basis of such changes. However, these observations and considerations should be weighed before exposing corneas with surface irregularities or stromal disease to high-power laser pulses. Such corneas should be considered as a medium in which high-powered lasers may have a destructive effect.

The endothelial ring seen in one eye was
delineated by pigment liberated from the iris that either adhered to or was phagocytized by the endothelium. This was a delayed effect and one that did not appear to be in a path taken by the laser pulse through the cornea to the iris. The finding has been interpreted as secondary to the laser pulse. A morphologically similar but unpigmented endothelial changes have been interpreted as a shock-wave effect common to both cases. This is a highly speculative explanation, but concern has been expressed in other investigations that high-power laser irradiation of the eye might result in the formation of a damaging shock wave.

REFERENCES


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