Diode laser thermokeratoplasty: Application strategy and dosimetry

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ABSTRACT

Purpose: To investigate suitable application parameters for efficient hyperopic correction by laser thermokeratoplasty (LTK) using mid-infrared laser diodes.

Setting: Medical Laser Center Lübeck, Lübeck, Germany.

Method: A tunable continuous-wave laser diode in the spectral range between 1.845 and 1.871 µm was used. Transmitted by waveguides, the laser energy was used to induce coagulations on freshly enucleated porcine eyes to increase corneal curvature. The coagulations were equidistantly applied by a fiber–cornea contact and a noncontact focusing device that were adjusted on a ring concentric to the corneal apex. Different laser parameters and application geometries were evaluated. Refractive changes were measured by computer-assisted corneal topography before and after treatment. Polarisation light microscopy and temperature calculations were used to analyse the coagulations.

Results: Because of the tunability of the laser diode, the influence of the corneal absorption coefficient (between 0.9 and 1.6 mm⁻¹) on the refractive change could be measured. A laser power between 125 and 200 mW was adequate to achieve refractive changes up to 10.0 diopters. In the preferred focusing device, the refractive change increased almost logarithmically with the irradiation time up to 15 seconds. The number of coagulations on a fixed application ring showed no significant influence on refractive change; however, it showed an almost linear decrease with increasing ring diameter from 5.0 to 10.0 mm. Histological analysis revealed 3 stages of thermal damage.

Conclusion: Diode LTK provided defined and uniform coagulations when using a well-adapted focusing device, resulting in sufficient refractive change. The results indicate that diode LTK is superior to pulsed holmium LTK. J Cataract Refract Surg 1998; 24:1185–1207.

Refractive surgery by laser irradiation now complements the classic tools of vision correction. Hyperopia affects about one third of the world's population.1 Excimer laser photorefractive keratectomy (PRK) for hyperopia does not offer satisfactory results. Another method to steepen the central corneal curvature is laser thermokeratoplasty (LTK), which uses heat-induced corneal collagen contraction to change the biomechanical stress distribution within the cornea. For hyperopic correction, coagulations are equidistantly applied on a ring concentric to the corneal apex in the periphery (Figure 1).
A review of the literature indicates that pulsed laser sources with a certain fixed wavelength are not the best candidates for use in LTK. Clinically, refractive changes achieved with different holmium laser systems initially yield around 3.0 diopters (D), regressing to about only 1.0 to 2.0 D after 1 year. A broad wound-healing response and collagen replacement have been observed after Ho:YAG laser LTK.

From the physicist's viewpoint, high peak temperatures, which inevitably occur in pulsed LTK with pulse durations below 1 ms, lead to high temperature gradients followed by large temperature fluctuations in time and space. Moreover, in vitro studies using pulsed holmium lasers in a noncontact focusing mode showed that high but short-lasting peak temperatures do not significantly contribute to refractive changes, unlike longer lasting base temperatures achieved by pulse trains applied with a high pulse repetition rate. In addition, experimental studies on collagen denaturation kinetics showed that temperature and time have a dramatic influence on coagulation, which is especially significant in the second time domain as the typical irradiation time in LTK.

The most suitable LTK system should provide continuous heating and thus uniform collagen contraction from the anterior to the posterior stroma without adversely affecting the endothelium and underlying structures in the anterior chamber. Although cw sources such as the cw holmium laser and cobalt:magnesium

![Figure 1.](image1.png)  
Figure 1. (Brinkmann) With a suction ring mask, 8 coagulations were equidistantly applied on a ring concentrically adjusted to the corneal apex. Application: focused mode—focal depth 500 μm; laser power 150 mW; irradiation time 10 seconds; wavelength 1850 nm with a corresponding absorption of 0.96 mm⁻¹.

In 1889, Lans reported that corneal power can be changed by localized heat exposure. Almost a century later, penetrating hot wire probes were used to treat keratoconus. However, the procedure led to major complications and had limited predictability.

In 1980, modern laser procedures for deliberately altering corneal refractive power were introduced in which the continuous-wave (cw) carbon dioxide laser was used to heat and shrink corneal collagen. However, the superficial penetration depth of the 10.6 μm radiation produced only small, transient curvature changes. In the 1980s, laser radiation with moderate absorption in corneas was reported. The first method used a pulsed erbium:glass laser at a wavelength of 1.54 μm with high single-pulse energies; although the technique produced refractive changes, it damaged the iris. In 1990, Soller and coauthors reported using a repetitively pulsed holmium:YAG (Ho:YAG) laser for LTK. Its wavelength of 2.06 μm yields a penetration depth almost matching the thickness of the cornea, with a sufficient safety range to protect the intraocular tissue beneath.

Suppose that only deep stromal coagulations effect refractive changes and to avoid surface ablation, radiation is focused into the stroma. An overview of the wavelength window useful for LTK is shown in Figure 2. Several laser systems have been investigated for LTK, but only holmium-based pulsed lasers were used in commercially available systems.

![Figure 2.](image2.png)  
Figure 2. (Brinkmann) Useful wavelength range for LTK. Upper curve: Absorption of water. Lower curve: Absorption of cornea (rhesus monkey). The window is defined by the absorption coefficient of the cornea. Too much absorption leads to superficial coagulations with the risk of ablation, while too little absorption damages the sublying intraocular tissue.
fluoride (Co: MgF2) laser have been used for in vitro LTK studies, they are complicated and were not used in clinical trials. High-power tunable cw laser diodes with wavelengths between 1.75 and 2.05 μm are available; these diodes have been proposed as the ideal laser source for LTK. Their capability was demonstrated in the first in vitro trial. Selecting a diode emitting a wavelength of around 1.87 μm, the system can be tuned over the entire useful wavelength range for LTK (Figure 2) by changing the working temperature of the diode, which allows users to match the wavelength with the desired corneal absorption.

Our study sought to determine the suitability of mid-infrared laser diodes for LTK and investigate the range of useful parameters (diode wavelength, laser power, and time of irradiation). On the application side, handheld fiber–cornea contact applicators and noncontact focusing devices applied via suction ring masks have been studied. Both provide equidistant coagulation patterns, with the contact applicators being the most simple technically. Properly focusing the radiation into the stroma has an advantage because power losses caused by corneal absorption may be compensated by decreasing the beam diameter toward the posterior cornea, providing uniform temperature distribution and thus homogeneous collagen shrinkage within most of the irradiated volume. Other parameters evaluated were ring diameter and the number of coagulations on a ring.

As a model for this study, we chose freshly enucleated porcine eyes and measured the refractive power before and after LTK. To analyze the coagulations in view of refractive changes and extent of thermal damage, Sirius-red stained histologies were evaluated by polarization light microscopy. Sirius red is an elongated molecule that enhances the natural birefringence of collagen by its preferred binding parallel to collagen molecules. It is thus a suitable dye for differentiating the various stages of damage in thermally altered collagen. To analyze the histological findings, temperature calculations were performed.

**Materials and Methods**

*Laser System*

A cw infrared laser diode (SDL 6432-P1, Spectra Diode Labs) emitting a maximum power of 500 mW was used for the study. A standard laser diode driver (SDL 820, Spectra Diode Labs) with current and temperature stabilization allowed the use of diode temperatures from −10 to 30°C, with the corresponding wavelengths between 1.845 and 1.871 μm, respectively. The laser radiation was coupled to different optical multimode fibers.

*Model and Experimental Setup*

Porcine eyes without major observable corneal pathology were enucleated immediately postmortem, stored in physiological saline solution (sodium chloride 0.9%) at 10°C, and used for experimental LTK within 4 hours postmortem. During the experimental LTK, the eyes were kept at a room temperature of 20°C; an intraocular pressure of 20 mm Hg was maintained with an infusion drip. Before and immediately after LTK, keratometry was performed with a computerized videokeratoscope (Akco EH 270, Visiometrics/Adatomed) using a tear film substitute polyvidone (Vidisept N®) to increase epithelial reflexion. Measurements were repeated 3 times in all eyes.

Spherical refraction was calculated by taking the mean of the simulated keratometry values (the mean of the 2 main axes in the 3.0 mm zone) before and after LTK. The spherical refractive change plotted in the graphics is the difference of the spherical refractions before and after LTK. Only eyes with astigmatism less than 2.5 D were used in the experiments.

Induced astigmatism was calculated as the astigmatism after LTK minus the astigmatism before LTK. For each refractive data point in vitro, 10 eyes were coagulated and the refractive change and standard deviation noted. Regressions calculated through the data points in Figures 4 to 8 are linear or simple exponential or logarithmic functions. For light microscopy and histomorphometry, selected eyes were fixed in formalin, embedded in paraffin, and stained with Sirius red F3BA.

*Application Device*

Two types of application devices were used to measure refractive changes:

1. In the contact mode application, a bare 300 μm core diameter fiber with a numerical aperture of 0.4 (PCS, Ceram Optec) was fixed in a pencil-like applicator. Before irradiation, the cornea was marked with a
radial keratotomy marker (F9011, Storz). During treatment, the applicator was held by hand perpendicular to the cornea.

2. In the focused mode application (Figure 3), the distal end of a 400 μm core diameter fiber with a numerical aperture of 0.2 (WF 400/440, Ceram Optec) was mounted in an applicator containing a planoconvex lens with a focal length of 2.0 mm to focus the laser radiation tightly into the stromal tissue, as shown in Figure 3. The focal depth within the cornea could be adjusted by varying the distance between the lens and the epithelium. The eye globe was fixed by a custom-built suction ring mask that was placed on the epithelium, centered on the corneal apex, and fixed by low pressure (~700 mbar). An exchangeable mask, containing 8 bores equidistantly arranged perpendicular to the epithelium on various ring diameters, was applied to the suction ring system. For LTK, the applicator was inserted successively and cross-wise into the bores of the mask.

Absorption Coefficients of Water and Cornea; Temperature Calculations

Water absorption was measured for the different laser diode temperatures with a 1.0 mm thick cuvette filled with distilled water at different temperatures. Laser power was measured in front and the transmitted power behind the cuvette using a calorimetric power meter (380101, Scientech, Inc.). The attenuation of laser radiation through corneal tissue was measured by inserting a 600 μm core diameter fiber (WF 600/680, Ceram Optec) into the anterior chamber of the eye in soft contact perpendicular to the central endothelium. The laser power was measured directly in front of the fiber tip before insertion and in front of the epithelium after insertion while the diode was operated far below the coagulation threshold. Using Beer's law, the absorption coefficient was calculated by considering the corneal thickness, which was determined using a confocal laser tomographic scanner (LTS, Heidelberg Instruments) before each measurement.¹⁹

In this paper, the term absorption coefficient is used instead of diode temperature or wavelength when discussing the refractive changes achieved because it is the most important parameter regarding the interaction of laser radiation with the stromal tissue. Due to absorption, the laser energy is converted into heat. Moreover, the stress and thus the refractive effect achieved depend only on the temperature profile within the heated stromal volume and on the time duration at which high temperatures are present. As temperature cannot accurately be measured within the stromal volume during heating, the equation of heat diffusion was numerically solved to correlate the thermal damage ranges shown in the histology with the corresponding temperatures. Details and limitations of the model have been pub-
Table 1. Measured absorption coefficients of water and cornea and corresponding wavelengths at selected diode temperatures.

<table>
<thead>
<tr>
<th>Diode Temp (°C)</th>
<th>Absorption Coefficient (mm⁻¹)</th>
<th>Diode Wavelength (nm)</th>
</tr>
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<td>Porcine Cornea</td>
<td>Water</td>
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<td>−10</td>
<td>0.91</td>
<td>1.16</td>
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<td>NM</td>
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<tr>
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</tr>
<tr>
<td>30</td>
<td>2.04</td>
<td>NM</td>
</tr>
</tbody>
</table>

Temp = temperature; NM = data not measured

listed, and the constants used are found in the literature.

Results

Absorption Coefficients of Water and Cornea

The absorption coefficients of water at 30 and 80°C and of porcine cornea at 20°C are shown in Table 1 for selected laser diode temperatures between −10 and +30°C. A review of accurate spectral water absorption tables allows calculation of the corresponding wavelengths. At laser diode temperatures between −10 and +25°C, the peak emission of the diode was at wavelengths of 1845 and 1868 nm, respectively. However, the spectral bandwidth of the diodes is about 10 nm full width at half maximum. The absorption coefficients increased with increasing wavelength and rose linearly toward higher temperatures. The absorption coefficient of the cornea increased from 0.91 mm⁻¹ at a diode temperature of −10°C to 2.04 mm⁻¹ at a diode temperature of 30°C. The penetration depth (1/µ) of the radiation into corneal tissue ranged from 1.10 to 0.49 mm. The mean thickness of eyes treated was 857 µm ± 59 (SD).

Refractive Changes In Vivo

Figure 4 shows the refractive changes as a function of applied laser power by the application of 8 coagulations on a 6.0 mm ring using low absorption in the focused mode. Refractive changes started rather sharply at a laser power of about 150 mW and rose almost linearly up to 6.6 D at a power of 200 mW. Further increasing the laser power led to near saturation. A standard deviation in the order of 1.0 D increasing to 2.0 D at higher laser powers was found.

Figure 5 shows refractive changes as a function of irradiation time for both application modalities using the same low absorption of 0.91 mm⁻¹ and 8 coagulations on a 6.0 mm ring. Both curves show an increase in refractive effect with irradiation time. In the contact mode, saturation was found beyond 10 seconds, with the parameters used at 2.8 D. In the focused mode, the refractive change increased up to 15 seconds with a refractive change of nearly 8.0 D. However, high standard deviations (up to 50%) were calculated for the experiments.

![Figure 4](https://example.com/fig4.png)

Figure 4. (Brinkmann) Refractive changes as a function of laser power. Application: focused mode—focal depth 700 µm; irradiation time 10 seconds; absorption 0.91 mm⁻¹.

![Figure 5](https://example.com/fig5.png)

Figure 5. (Brinkmann) Refractive changes as a function of irradiation time. Application: contact mode—laser power 150 mW; absorption = 0.91 mm⁻¹; focused mode—focal depth 700 µm; laser power 200 mW; absorption 0.91 mm⁻¹.
The geometry of the application had a major influence on refractive outcome. Figure 7 shows the refractive change when different numbers of coagulations are applied to the cornea on a single ring in the contact mode using low absorption. The average refractive change within a range of 1.0 D was nearly independent of the number of coagulations on the ring, while its diameter ranged between 5.0 and 7.0 mm. A strong influence on the refractive change could be observed when varying the ring diameter, as seen in Figure 8, which shows 8 coagulations applied equidistantly on different ring diameters. An almost linear decrease of the refractive change was observed when the ring diameter was increased. At a 5.0 mm diameter, 3.8 D were found on the average, decreasing to 0.5 D for an 8.0 mm ring. At a ring diameter of 10.0 mm, even a slight myopic correction was measured.

Examples of the induced astigmatism using 8 coagulations on a 6.0 mm ring are 1.1 ± 0.6 D for the hand-held fiber contact application at 150 mW (Figures 7 and 8) and 1.0 ± 0.6 D for the focused application at 170 mW (Figure 4).

**Histology**

The histologies in Figure 9 show central sections through a coagulation in the contact mode at a laser power of 150 mW and irradiation time of 15 seconds for different absorptions. Figure 9, A shows the depth of a thermal lesion about 550 μm (65%) into the corneal stroma, approximately the thickness of the
human cornea. Tuning the wavelength of the diode toward a higher absorption (Figure 9, B) resulted in maximal axial thermal damage of about 71% and a slight crater at the surface. The damaged diameter at the surface was 1.15 mm. Severe damage (dark zones) of 850 μm in diameter were seen.

The histologies (Figures 9 and 10) show different zones of thermal damage: a transition zone of high
birefringence (bright yellow zone), where collagen lamellae become visible by standing out against their interwoven state of unaltered stroma, are swollen in thickness and contracted in axial length (compare with Figure 9, C); an intermediate zone distinguished by reduced birefringence (light brown area) and a beginning reduction in lamellar thickness (compare with Figure 9, C); a central zone showing little birefringence and few substructures (Figure 9, B, central parts in the anterior stroma), with thin stromal lamellae that became invisible (Figure 9, B, dark area). The tissue seems to become homogenized and gelatin like.

Figure 9, C is a magnification of a posterior segment of the coagulation shown in Figure 9, A and depicts the transition of single lamellae from the interwoven unaltered stroma into the transition zone of increased birefringence and further into the intermediate zone, the second stage of thermal damage.

Figure 10 shows a histology in the focused mode using low absorption (0.91 mm⁻¹) but high laser power (200 mW), yielding a refractive change of 6.6 D (Figure 4). The central denatured area in Figure 10 shows a remaining but decreased birefringence; collagen lamellae are clearly visible in the central area as is typical in the intermediate zone (compare with Figure 9). The intermediate zone penetrated the stroma to about 80% and the transition zone, to about 95% in depth. A central zone of thermal damage was not observed.

Temperature Calculations

Temperature calculations performed for the 3 histologies showed that the boundary line between the 3 zones of thermal damage best correlated to the isothersms with the following temperatures: unaltered stroma to transition zone, 75°C (Figure 9, A and B) and 85°C (Figure 10); transition zone to intermediate zone, 85°C (Figure 9, A and B) and 105°C (Figure 10); intermediate zone to central zone, 110°C (Figure 9, B). The temperatures reveal isothersms calculated for the end of the irradiation time of 15 seconds (Figure 9) and 10 seconds (Figure 10). All temperatures are lower estimations because the increase of the absorption coefficient with increasing temperature during heating was neglected. After starting the irradiation, the temperature rose exponentially, the time after which 67% (1/e decay) of the final equilibrium temperature increase was obtained was 1.2 seconds in the center of the coagulation.

Discussion

This in vitro study shows promising results for LTK with cw mid-infrared diode lasers. Absorption measurements revealed that diodes emitting on the extremely steep slope of water absorption between 1.85 and 1.9 µm can be tuned by their working temperature over the entire window useful for LTK. With the diode used in this study, the wavelength could be tuned over 26 nm; thus, the radiation shows that a corneal absorption between 0.91 and 2.04 mm⁻¹ can be chosen. Refractive changes achieved in the porcine cornea model are significantly larger than those achieved with even high-repetition-rate holmium lasers.¹² Surface ablation has not been observed when working with low absorption coefficients because of the lack of peak pulse intensities and subsequent temperature spikes.

Refractive Changes as a Function of Corneal Absorption and Laser Power

In the fiber contact mode using a small 300 µm diameter fiber and applying 8 coagulations on a 6.0 mm diameter ring, a refractive change up to 5.0 D was
achieved by using laser powers as low as 125 mW for 15 seconds (absorption 1.13 to 1.60 mm$^{-1}$). Using a lower absorption (0.91 mm$^{-1}$), the applied power must be increased to achieve comparable refractive changes. Applying 150 mW, corrections of 2.4 D have been measured; however, no surface ablation was found. Thus, higher absorption, even with slightly reduced laser power, seems to be more effective than working at low absorptions. However, applying 150 mW at a higher absorption (1.13 mm$^{-1}$), produced a small crater in the corneal surface. This probably indicates desiccation and evaporation of stromal water resulting from temperatures exceeding 100°C at the epithelium. Thus, the cooling effect of the quartz fiber in contact with the surface, which has already been described with cw holmium LTK, is not sufficient.

The threshold power for surface ablation decreases as the absorption coefficient increases, while the temperature gradient in the axial direction increases. Thus, at high absorption coefficients, the ablation threshold is reached at the epithelium, while in the posterior cornea, temperatures are too low to induce sufficient stress. This leads to more superficial coagulations that penetrate only the anterior stroma, which does not result in stable long-time refractive changes. In terms of an optimized LTK, it might be more efficient to use lower absorptions compensated for by higher laser power to induce collagen contraction also in the posterior part of the cornea while avoiding surface ablation.

The reasons for higher efficiency with increasing laser power or absorption are the higher temperatures and the subsequent higher stresses achieved from collagen contraction within and around the application volume. The temperature increases proportionally to the laser power and with an increasing absorption coefficient. In the latter case, this leads to a different heat distribution within the irradiated volume, resulting in higher anterior but lower posterior corneal temperatures. In all cases, however, heat diffusion plays a major role. Especially in the fiber contact modes, the highest temperatures are achieved about 100 μm below the epithelium due to heat flow into the surrounding tissue, aqueous humor, and fiber; the latter reduces the surface temperature. However, high temperatures and stress are achieved within the anterior stroma in the fiber-contact mode, producing moderate refractive changes.

In the focused mode, we found a relatively steep gradient of refractive change as a function of laser power, which agrees with the results of studies of pulsed holmium lasers. Between a power of 140 and 170 mW, the refractive change increased from 0 to 3.2 D. Further increasing the power resulted in a saturation around 6.5 D at 200 mW but no surface ablation. Most remarkable, a steep increase of the refractive change was produced by slightly increasing the absorption coefficient from 0.91 mm$^{-1}$ (1.1 D) to 1.13 mm$^{-1}$ (10.5 D) at a laser power of 150 mW.

A steep increase in refractive change with increasing laser power or absorption can be expected. With temperature-matched focusing, achieved by focusing the radiation into the stroma so that the temperature achieved in the heated volume is nearly uniform and constant over a large stromal volume, the threshold of collagen contraction is exceeded simultaneously within most of the irradiated volume. Since the contracted volume is large, the refractive change is steep. This is supported by the observation that the histology, although achieved with a power as high as 200 mW, shows a substantially large volume of denatured stroma in the transition and intermediate zones, but does not show the central, homogenized zone of collagen denaturation. Increasing the laser power above 200 mW caused further lateral broadening of the coagulation but also homogenization in its center, resulting in saturation of refractive changes. This means that the stress was maintained in a basket-like fashion; that is, only the rim of the coagulation bore all residual forces, which might negatively influence a long time stable refractive change.

The desired uniform but moderate heating and stress distribution achieved by proper focusing are likely keys to inducing and maintaining high amounts of stress. With an absorption of 0.95 mm$^{-1}$, a refractive change of 5.1 D is achieved with a power of 150 mW (Figure 8). Applying the same laser parameters with a bare 400 μm fiber held 0.5 mm from the epithelium (not shown in this article), only half of this value (2.4 D) is found, although the anterior stromal temperatures achieved are much higher.

Geometry and Application Pattern

With regard to suitable nomograms for LTK for hyperopia, the most important finding is the linear
decrease in refractive power with increasing ring diameter, achieved by keeping the irradiation parameters constant. This result has also been described for the application of pulsed holmium laser radiation\(^7\) and is supported by finite element models that predict this behavior.\(^2,3,24\) The theoretical results show that the geometry of the corneal shell, but less the contracted volume, is responsible for this effect.\(^24\) During the clinical learning curve on blind mice, a corresponding diagram for the irradiation parameters chosen should be applicable by applying the spots on small and large ring diameters and interpolating the remaining data.

Furthermore, the number of coagulations on a certain ring do not significantly influence mean refractive change. Only a slight increase with an increasing number of coagulations is found up to 12 spots on 1 ring. This agrees with studies of holmium lasers, which found refractive saturation with more than 8 coagulations.\(^22\) However, another study\(^22\) found increased hyperopic corrections when the number of spots was increased from 8 to 16 on human cadaver eyes. However, it can be assumed that at least 8 coagulations per ring should be applied to achieve a uniform change in curvature of the entire corneal shell. We found that suction ring application with exchangeable masks gives a more regular application pattern and is easier to handle than hand-held devices. The induced astigmatism of about 1.0 D is much less than expected because of the hand-held application and less spherical porcine pupil compared with the human pupil; this helps center the marker or the mask concentrically to the corneal apex.

**Effect of Tissue Temperature and Irradiation Time on Collagen Denaturation**

Besides the beam profile, laser power, and absorption coefficient, the thermal properties of the tissue determine the temperature profile within the corneal stroma. However, for the denaturation of biological tissue, the time of irradiation is also a major parameter because the kinetics of denaturation always depend on temperature and the time the temperature is present. In LTK, with preferable exposure times of several seconds, a strong time dependence of the threshold temperatures for corneal collagen denaturation was found.\(^12\) Earlier studies found that the onset of denaturation in the second time domain could be described with the theory of Arrhenius.\(^12\) As a function of temperature and time, collagen undergoes different phase transitions.

Stress measurements on corneal stripes as a function of temperature showed the onset of stress at about 60°C and a maximal shrinkage rate at about 80°C by heating in the minute time range.\(^24\) In view of LTK, collagen contraction was experimentally investigated for heating periods of 10 seconds.\(^13\) The threshold of collagen shrinkage and the onset of stress occur at 80°C. This agrees with the calculated temperatures performed for the histologies in our study. With regard to maximum residual stress, temperatures of about 95°C were measured to be optimal. Temperatures above 100°C lead to strong relaxation. Generally, increasing the irradiation time reduced the phase transition temperatures and vice versa. This shift was obvious when comparing the temperatures of the histologies with coagulation times of 10 and 15 seconds.

When the heating time was further reduced, the threshold temperatures decreased. Using a pulsed holmium laser at a repetition rate of 10 Hz, an onset of stress was measured after 800 ms at a calculated temperature of 95°C.\(^12\)

It is therefore not surprising that radiation time influenced the refractive effect. In all focused applications, we found a nearly logarithmic increase in refractive power up to irradiation times of 30 seconds. Even on this large time scale, the border of the coagulation grew laterally as a result of the time/temperature dependence of denaturation, although the temperature equilibrium was achieved much earlier. However, at least 5 to 10 seconds are needed to achieve sufficient refractive changes.

Regarding contractile forces, comparable refractive changes can be achieved with low temperatures (low laser power) applied for a longer time or by much higher temperatures (high laser power) applied for shorter times.\(^13\) However, the degrees of thermal damage may be different. Although the optimal LTK parameters (temperature versus time) with regard to regression are still unknown, it is likely that lower temperatures and long irradiation times lead to a large but mild denatured stromal volume,\(^13\) keeping the collagen fibril and lamellae structure almost intact and preventing homogenization. Irradiation times below 5 seconds require temperatures far exceeding 100°C with the subsequent steep temperature gradient. This results in different zones of thermal damage and stress and boiling of intrastromal water.
Analysis of Histologies with Respect to Thermal Damage

Regarding the thermal damage, histologies were done for 2 application modalities and absorption coefficients. Sirius red, used for staining, is a strongly elongated anisotropic molecule that is preferably bound parallel to the collagen molecules and thus enhances their natural birefringence. A detailed discussion on the background and physics of the observed effects in polarization light microscopy is found in the literature.13

The uptake of the dye showed no differences across the whole coagulation when the sections were observed with unpolarized light; however, 3 stages of thermal damage were identified when using polarization light microscopy.

1. The transition zone has increased birefringence (compared with unaltered stroma). In this zone collagen lamellae can be resolved and increase in thickness toward the central coagulation. Because of the unraveling of the collagen triple helix, the collagen molecules and therefore the fibrils and lamellae contract in an axial direction, a preferred direction compared with the wavy structure in the unaltered stroma. The strong birefringence most likely resulted from this molecular alignment.

2. The intermediate zone of damage shows reduced birefringence and therefore indicates the beginning disintegration of the collagen fibrillar structure. As a consequence, the thickness of the swollen lamellae decreases; however, their path through the damaged volume can still be observed.

3. The central zone, characterized by a nearly total loss of birefringence, was only visible in the anterior stroma. This zone experienced the highest temperatures, and few lamellae remained in this area. The tissue was largely homogenized, which is supported by light scattering in the visible and the near-infrared. It shows almost no remaining scattering compared with that in the intermediate zone.14,27

It can be postulated that with regard to efficient LTK, these centrally overcoagulated zones should be avoided because they do not maintain the required stress needed for refractive changes. Denaturation should only be performed up to the intermediate zone. Maintaining corneal lamellae across the heated area is probably necessary in maintaining the induced stress. The histology in Figure 10 showed less severe thermal damage than with the contact mode; however, the refractive change was 2.6 times higher than that in Figure 9. Moreover, it can be assumed that collagen being totally disintegrated and homogenized will induce a pronounced healing response and collagen replacement in these areas.

Comparing the extension of the thermal damage of both contact mode histologies in Figure 9 shows that the axial and lateral extent of the coagulations increase with increasing absorption; thus, they increase with reduced penetration depth of the laser energy. The reason is the total energy absorbed: Following Beer’s law of absorption and assuming a corneal depth of 850 μm, the cornea absorbed a total energy of 61.7% of the incident energy at an absorption of 1.13 mm⁻¹ but only 53.5% at 0.91 mm⁻¹. With higher absorption, relatively more energy is absorbed and converted into heat in the anterior stroma, showing that heat diffusion is responsible for the larger lateral broadening.

Conclusion

Our study shows that refractive changes can be achieved with mid-infrared cw diode lasers within the entire LTK window independent of the special application system and wavelength used. Compared with the commonly used pulsed holmium lasers, the diodes have these advantages: cw emission, which avoids peak temperatures and ablation and allows uniform heating when the radiation is properly focused into the stroma; tunability, allowing one to choose the ideal wavelength and thus absorption for LTK; low cost and high reliability.

The ophthalmologist wanting to perform LTK with this diode should carefully analyze the system and method he or she is going to use. Although the ideal set of LTK parameters are not yet identified, we believe the user should consider the following points:

1. Focusing devices, properly matched to the absorption coefficient, are preferable to pure fiber contact or noncontact devices.

2. Suction ring mask systems seem more convenient than hand-held devices in terms of regularity of the corneal coagulations.

3. We agree with others7,10,16,23 that individual refractive correction should be performed by altering the application ring diameter using the same laser parameters in all cases.
4. Eight coagulations on a ring is sufficient, and the use of double rings seems to stabilize the refractive change.25,28

5. The parameters to be used should induce mild coagulation over the whole irradiated volume while strictly avoiding overcoagulation.

6. Axial penetration depth should be about 90% of corneal thickness.

7. Irradiation time should be at least 5 to 10 seconds, and extremely high absorption coefficients should be avoided to induce sufficient stress in the posterior stroma without causing surface ablation.

8. We recommend using a higher corneal absorption coefficient (1.5 to 2.0 mm⁻¹) than reported here because the porcine cornea is about 50% thicker than the human cornea. Thus, for irradiation of comparable volumes as discussed here, a laser power between 100 and 130 mW should be sufficient.

To observe and control the extent of the coagulations and the degree of thermal damage, optical coherence tomography has proved to be an excellent tool to use directly after LTK and in the clinical follow-up period. Current26,28,30 and future clinical trials must verify the potential of diode LTK in correcting hyperopia and astigmatism. However, all results should be carefully analyzed in terms of regression and endothelial cell damage31 and correlated to the application parameter set.

References


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