The Retinal Effects of Copper Vapor Laser Exposure

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Lasers in ophthalmology are used mainly for retinal coagulation, iridectomy and lens capsulotomy. Argon laser is now widely in use as a retinal photocoagulator,1,2 as it is well-transmitted by the ocular media3 and well-absorbed by the retinal pigment epithelium (RPE) and hemoglobin.4 Since coagulation is the final result of a thermal effect,5 a continuous wave (CW) laser, such as the argon laser, is a suitable light source for coagulation. Capsulotomy and membrane cutting can be done only by a pulsed laser characterized by a high peak power, inducing mechanical effects.6–8

The question is whether one laser system can perform all the above mentioned ocular treatments successfully. A CW laser which is effective for retinal coagulation cannot be suitable for capsulotomy, where there is a need for very high irradiance. On the other hand, a pulsed laser which fits the capsulotomy requirements may cause undesired retinal damage by mechanical effects. The answer should therefore be a variably high repetition rate pulsed laser, which inherently has the characteristics of a pulsed laser, but can at the same time act as a quasi-CW laser, depending on the pulse energy, the time interval between the pulses and the reaction time constant. Such a laser system is the copper vapor laser (CVL). This laser is a high repetition rate pulsed laser9 which can operate at a repetition rate range between 1 kHz and above 20 kHz, delivering two wavelengths: 510.6 nm and 578.2 nm.10 The pulse peak power can be increased by decreasing the repetition rate, while the average power has an optimal level at intermediate repetition rate. As irradiance is a function of the laser focal spot size, the mechanical effects of the CVL can be increased by decreasing the focal spot size to 50 μm. Therefore, it is hoped that the CVL will be suitable for iridectomy as well as capsulotomy, a fact which will have to be proven in future experiments. By increasing the repetition rate and the spot size, the pulse characteristics are changed toward CW mode, which is suitable for retinal coagulation without any undesired mechanical damage.

Retinal coagulation is caused by a thermal effect,5 which depends on the temperature rise in the tissue. The temperature rise depends not only on the energy absorbed by the RPE but also on the exposure time. The CVL pulse width is only 15 nsec; therefore, in such a short time, the volume of absorbing tissue can be regarded as an isolated volume from which the heat diffusion is negligible. Hence, exposure of the retina to the CVL beam can instantaneously elevate the tissue temperature to a higher degree than can a CW laser, while delivering the same energy.10,11

Moreover, since the retina was exposed to a burst of several hundreds of pulses, the net result depends on the combination between the single pulse energy and the total exposing energy.11,12 This total energy can be equally delivered either by a high pulse energy combined with a low repetition rate or by a low pulse energy combined with a high repetition rate.

As the CVL is inherently a pulsed laser with a variably high peak power, we decided to study its retinal coagulation ability first in order to look for any undesired mechanical side effects. In this work, we examined the interaction between the copper vapor laser beam and the rabbit retina, in order to learn the safest range of peak power, pulse repetition rate and...
Materials and Methods

Copper Vapor Laser

The copper vapor laser used in our experiments is an air-cooled laser which was designed and constructed by Laser-On (affiliate of Rotem Industries, Nuclear Research Center, Beer Sheva, Israel). This is a self-terminating pulsed laser, the emission of which is simultaneously composed of two wavelengths, 510.6 nm (green) and 578.2 nm (yellow). This laser emits up to 8 W average power at 4 kHz repetition rate, at a ratio of 2:1 between green and yellow, respectively. The laser pulse width is about 15 nsec and the beam diameter is 30 mm. An unstable resonator was constructed to decrease the beam divergence in order to achieve a small focused spot size. The pulse repetition rate can be varied between 2 kHz and 20 kHz. The two laser wavelengths are well-transmitted by the ocular media and well-absorbed by the RPE and hemoglobin, but not absorbed by the xanthophyll. Therefore, this laser can be safely used at the macular region. Moreover, the yellow wavelength which is suggested to be the ideal wavelength for retinal photocoagulation gives this laser an advantage over other lasers currently in use. Finally, a compact copper vapor laser of about 8 W average power has low installation requirements of about 2.5 kW electrical power (single phase) and 2 liter per minute tap water cooling or even air cooling. The latter characteristics make it convenient for installation even in small eye clinics.

Delivery System

The diagram illustrated in Figure 1 presents all the system components which govern the laser power, exposure time and beam spot size. The laser beam is delivered from the laser cavity (1-3) towards the rabbit eye, passing through an attenuator (4), which controls the output power, then meets a narrowing telescope (5, 6) and falls upon a shutter (7). The shutter reflects more than 99% of the light to a power meter (8), which sends a signal to a microprocessor that presents the laser power measured at the power meter (or the calibrated power at the cornea). The remaining power is used as an aiming beam, which passes through dual polarizing sheets to control the aiming beam intensity. Opening the shutter for the desired exposure time enables full power delivery to the retina. The beam then passes through an articulated arm (9) connected to a Haag Streit (Bern, Switzerland) Universal Slit Lamp, model BM 900 (12). A movable focussing lens (10) is placed in such a way that in its backward position the laser beam focusing plane coincides with the slit lamp illumination focusing plane. In this position, the laser spot on retina is minimal. Increasing the laser spot on the retina can be achieved by shifting the lens toward the slit lamp. The beam is then reflected by a prism (11) along the slit lamp axis, then passes through the slit lamp output lens (13) and finally is reflected again by a mirror (14) towards the retina. The stereo biomicroscope (15) is used to fix the slit lamp focal plane on the retina. The filter (16) is positioned in front of the biomicroscope, prior to full power laser exposure, in order to prevent damage to the physician’s eyes by a scattered laser light.

All the optical components of the system are achromates, in order to focus the two wavelengths (green and yellow) to one small focal point on the retina. The laser control system consists of a microprocessor which automatically controls the laser operation, governs the treatment parameters and takes care of the safety requirements during the exposure process.
Methods

All our experiments were performed on pigmented rabbits which were anesthetized by chlorpromazine, 5 mg/kg, together with ketalar, 50 mg/kg, given intramuscularly. A series of 10 to 15 lesions were made in three different areas in the retina of rabbit eye, surrounded by four intense demarcation spots. Each treatment retinal area was devoted to different laser parameters. The location of each treatment area was marked on a corresponding diagram of the rabbit eye fundus. The laser beam was focused to a spot diameter of 200 μm on the retina, which remained constant during all the experiments. The other laser parameters, such as pulse energy (or peak power), pulse repetition rate and exposure time were changed to fit the experimental program. The rabbits were sacrificed and their eyes enucleated 10 to 12 hr following the last laser exposure. The enucleated eyes were slit along the limbus and fixed in 2.5% buffered glutaraldehyde for 10 min. Thereafter, gradual removal of the cornea and iris was performed, accompanied by refixation in the same fixative. Finally, the whole ciliary body and lens were removed and the rest of the eye was fixed in the buffered glutaraldehyde for another 24 hr. The three treated areas were subsequently identified and cut from each eye. Each piece of tissue was serially sectioned, Epon-embedded following osmic acid (1%) fixation and then cut thin (less than 1 μm) as for transmission electron microscopy and finally stained by methylene blue stain.

Two major groups of experiments were performed, one in repetition rate of 4 kHz, where the peak power range was 400-4000 W, and the other in 18 kHz where the peak power range was 50-300 W.

These experiments adhered to the ARVO Resolution on the Use of Animals in Research.

Results

The histological analysis of the lesion performed by 4 kHz repetition rate with pulse energy greater than 20 μJ, showed undesired side effects, such as exudative choroidal, pigment epithelial and retinal detachment, disruption of the photoreceptor outer segments and RPE cells together with vacuolar changes in the latter, which can be related to mechanical (nonthermal) effects. Mild choroidal hemorrhage was also noted in the area of the burns. The severity of the tissue damage decreased gradually as the pulse energy...
Fig. 5. Severe damage to the photoreceptor nuclei (karyorrhexis and karyopyknosis) with outer segments disruption. The RPE cells show vacuolization and displacement from Bruch's membrane. Methylene blue, original magnification ×400. Laser parameters: 0.1 W, 0.1 sec, 4 kHz.

was lowered. Figures 2 to 5 present the histological appearance of the typical lesion caused by 4 kHz repetition rate, while the representative parameters are 25 μJ pulse energy (1600 W peak power or irradiance of 5 MW/cm²) and total exposure energy of 10 mJ. The striking finding is severe disruption of the photoreceptor outer segments and the RPE cells in the center of the lesion (Figs. 2, 3), and the accumulation of intraretinal and subretinal fluid (Fig. 4). Figure 2 also shows evidence of mild choroidal hemorrhage. In addition, severe vacuolar degeneration, swelling and displacement of the RPE cells are also seen together with piknosis and karyorrhexis of the photoreceptor nuclei (Fig. 5). Extensive RPE and choroidal detachment were also noted (Figs. 3, 4). In order to reduce the retinal disruption and the other mechanical effects, we gradually decreased the pulse peak power by neutral density filters down to 200 W. While decreasing the peak power down to 400 W, it was found that the lower the peak power the less the disruption effect (see Fig. 6). Below 400 W we have not seen any sign of disruption nor coagulation.

At this point, we concluded that 400 W peak power is the upper limit of "nondisruption range," while using the same spot size of 200 μm. As no coagulation was seen, it was realized that the total exposing energy (in a relevant exposure time) had to be increased. This was achieved by increasing the repetition rate to 18 kHz, following which the peak power was decreased by 80%, as compared with the 4 kHz mode, while the average power remained almost the same.

The histological finding of the lesions formed by 18 kHz repetition rate are presented in Figures 7 to 10. A nice coagulation effect was found when the laser pulse energy was changed between 2 μJ and 5 μJ (40 mW and 100 mW average power), while the maximal exposure time was limited to 100 msec. In Figure 7, it...
Fig. 8. Coagulation of the photoreceptor outer segments and RPE cells. A thermal damage is also noticed in the photoreceptor nuclei with some internal displacement of this layer and the other inner retinal layers (arrow). Methylene blue, original magnification X400. Laser parameters: 100 mW, 0.1 sec, 18 kHz.

Fig. 10. Disruptive changes are seen in the RPE together with displacement of RPE cells from Bruch's membrane. Additionally, a thermal damage is noticed in the photoreceptor outer segments and nuclei (arrow). Methylene blue, original magnification X400. Laser parameters: 150 mW, 0.1 sec, 18 kHz.

can be seen that the photocoagulation effect is localized only in the photoreceptor outer segments and RPE, while the photoreceptor nuclei and the inner segments seem to be intact. The laser parameters in this experiment were 3.5 μJ per pulse (70 mW average power) and 100 msec exposure time. At 6 μJ per pulse (100 mW average power) and 100 msec exposure, the photocoagulation effect was noticed also in the outer nuclear layer (Fig. 8). Above 6 μJ per pulse (120 mW average power), a mild thermal damage was found in the inner retinal layers in addition to mild disruption of the RPE, as can be seen in Figures 9 and 10, respectively. In the latter experiment the pulse energy was 7.5 μJ (average power of 150 mW) and the exposure time was 100 msec. It should be noted that below 2 μJ per pulse (40 mW average power), in a relevant exposure time, no sign of coagulation was found either by direct visualization during the experiment or histologically.

Discussion

Several studies have been published on the effect of pulsed laser exposure on the retina16-19 that present the same histological results as we have found in our experiments done with 4 kHz pulse repetition rate. Geeraets16 found that Q-switch YAG laser caused displacement of the RPE layer and bulging of the photoreceptor outer nuclear layer. Frisch17 reported on the findings of severe irregularities in the RPE layer associated with vacuolization of the photoreceptors and at times subretinal hemorrhages, following exposure to Q-switch ruby laser. Marshall18 found disruption and vacuolization of the RPE cells in addition to photoreceptor inner and outer segment damage while using the same laser. Birngruber19 is of the opinion that any pulsed laser which has a pulse width of less than 1 μsec causes a mechanical effect including disruption and displacement of several retinal layers. These results are in contrast to the thermal effect of the CW argon laser, causing coagulation of the outer retinal cells, which remain adherent to each other in their original layers.20 It should be stressed that all the above-mentioned experiments16-19 were performed while using a single pulse YAG or ruby Q-switched laser.

Mosier et al12 are the only researchers to report on experiments done with high repetition pulse of a frequency-doubled YAG laser (532 nm) exposure on the retina which can be compared with our experimental parameters. These authors12 point out that the use of a focal spot size between 50 and 100 μm aggravates the mechanical effects on the retina due to irradiance...
problems. They therefore recommend the use of a larger spot size (200 μm or more), as was done in our CVL experiments. Their histological findings, following retinal exposure to a single pulse or to a burst which consists of a first high peak power pulse, were disruption and tearing of the retina and subretinal and vitreal hemorrhages with dispersion of the melanin granules between the red blood cells. The latter findings are similar to ours at 4 kHz pulse repetition rate, with the exception that we have not found vitreal and subretinal hemorrhages but only choroidal hemorrhages associated with exudative detachment of the RPE, choroid and retina. Mosier et al. report that the lesion caused by a uniform pulse train of 10 kHz repetition rate of the frequency-doubled YAG laser showed a definite zone of coagulation extending from the RPE through the photoreceptors. The primary site of damage was the RPE, where he found gross disruption of the cells with melanin pigment dispersion. The RPE cells that remained intact were highly vacuolated. The lamellar membranes of the photoreceptor outer segments were fused together or disintegrated. No damage was noticed in Bruch’s membrane or choroid, and there was some cellular disintegration near the retinal surface. The latter findings are very similar to our histological results described for retinal exposure to 18 kHz repetition rate, with the exception that no vacuolization was noticed in the RPE cells, and that with the pulse energy of 3.6 μJ (70 mW average power) and exposure time of 0.1 second, only pure coagulation effect limited to the outermost retinal layers was seen, without any signs of cellular disruption. This desired coagulation damage is very similar to that described by Apple et al. using a CW argon laser with 200 mW power and exposure time of 0.2 second. It should be added that other authors have described a wide range of retinal lesions produced by the CW argon laser, such as severe damage to all retinal layers associated with subretinal exudation and hemorrhage, vacuolation of the RPE cells and photoreceptors and even thermal damage to the inner retinal layers.

It is our conclusion that the high repetition rate copper vapor laser is suitable for retinal photoa- gulation in the range of 40 to 120 mW average power with 200 μm spot size and in relevant exposure time (around 0.1 sec). It is hoped that future modification of this device will make it useful both as a retinal coagulator as well as a photodisruptor laser for the treatment of anterior segment pathology.

Key words: copper vapor laser, high repetition rate pulsed laser, variable peak power, photodisruption, quasi-CW laser

References