Effects of Laser Physical Parameters on Lesion Size in Retinal Photocoagulation Surgery: Clinical OCT and Experimental Study

Soleimani A.[1,2], Rasta S. H.[3,4,5]*, Banaei T.[6], Asgharsharghi Bonab A.[7]

ABSTRACT

Introduction: The aim of the present study was to determine burn intensity in retinal laser photocoagulation based on laser parameters; wavelength, power, beam size and pulse duration, using Optical Coherence Tomography (OCT), fundus camera, physical eye model and computer simulation in a clinical study.

Materials and Methods: Participants were 10 adult patients between 50-80 years with proliferative diabetic retinopathy. A multicolor-photo coagulator with 532 nm green and 672 nm red for retina photocoagulation in diabetic retinopathy was used to investigate the participants. Lesion size was measured for spot sizes 50 and 100 µm, with 100 and 150 mW laser power, and pulse duration 50 and 100 ms by OCT. Artificial eye and Zemax-optical design software were used with the same laser parameters.

Results: Appearance of OCT and fundus images showed direct relationship between retina burn size and lesion intensity with exposure time and power and also reverse relationship with laser spot size. Compared to red wavelength, burn size and lesion intensity increased in green wavelength. On the other hand, results from physical eye model were the same as clinical examination shown. Laser spot size in retina with Zemax simulation demonstrated that red wavelength was greater than green one.

Conclusion: This study showed shorter pulses provide decrease in duration of laser surgery with significantly reduced pain. Results and calculations described in this article can help clinicians adjusting the required total coagulated area, the number of lesions and pattern density.

Keywords
Retinal Laser Surgery, Photocoagulation, Diabetic Retinopathy, Lesion Size, Optical Coherence Tomography, Laser Parameters of surgery

Introduction

Retinal laser photocoagulation was introduced in Early Treatment Diabetic Retinopathy Study (ETDRS) as an effective treatment for many retinal diseases such as proliferative and non-proliferative diabetic retinopathy and macula edema [1]. However, contrast sensitivity, color visual loss, seizure and acute pain are common problems of laser photocoagulations [2, 3]. In order to reduce side-effects and increase success level in treatment, understanding the lesion intensity and retina burn diameter seem to be necessary.

Laser photocoagulation depends on both physical factors i.e. power,

[1]Department of Medical Physics, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Medical Physics Department, Reza Radiotherapy Oncology Centre, Mashhad, Iran
[3]Stem Cell Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran
[4]Department of Medical Bioengineering, Faculty of Advanced Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran
[5]School of Biomedical Sciences, University of Aberdeen, Aberdeen, AB25 2ZD, UK
[6]Retina Research Center, Mashhad University of Medical Science, Mashhad, Iran
[7]Research Unit, Sensory Biology & Organogenesis (SBO), Helmholtz Zentrum München, 85764 Neuherberg – Munich, Germany

*Corresponding author: S. H. Rasta, Department of Medical Bioengineering and Stem Cell Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran
E-mail: s.h.rasta@abdn.ac.uk

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spot size, exposure time and wavelength and tissue characteristics (kind of pigmentation and amount of water) [4, 5]. Various investigations were carried out for laser parameters effect on burn size [6-9]. In one investigation, Jain et al. examined the effect of pulse duration on the size and character of the lesion in retinal photocoagulation in rabbits. In this study, 532 nm Nd: YAG laser was applied [7]. In another study, Palanker et al. confirmed time duration effect on burn intensity in patients undergoing pan retinal photocoagulation for proliferative, diabetic retinopathy by reduction in the width of 20 ms burns by 35% compared with 100-msexposures [8]. Moreover, Negapal et al. stated that multi-spot laser compared to single spot lasers for diabetic retinopathy allows less damaging and more efficient treatment delivery [9]. The present study is a follow-up of previous studies on retina burn diameter and burn intensity of laser spot size in retina by comparing clinical and computer models. In terms of clinical examination, we used Optical Coherence Tomography (OCT) and fundus images capable of detecting measured laser burn [10- 12]. For the first time, in this study to compare laser burn size and lesion intensity in human retina and artificial eye and to approve clinical data from OCT and fundus, we used physical eye model.

The knowledge of laser beam path in the eye makes us capable of predicting powerful laser effects in treating procedures of retina tissue. This helps to predict the treatment side effects and achieve good results. There are wide ranges of optical simulation software with specific applications such as ZEMAX (trademark of ZEMAX Development Corporation) that is widely used to simulate the optical elements of the eye and provides a chance to analyze complicated systems performance [13, 14]. This modelling will provide useful information about eye and its performance [15]. In the current study, the effects of different wavelengths of laser beam size in retina Zemax were selected. This detailed information is beneficial in designing experimental setup for the sake of real eye optometry, eye surgery, etc.

Material and Methods

Clinical Examination

Ten eyes of those diabetic patients undergoing photocoagulation for severe non-proliferative or proliferative diabetic retinopathies were included. Study protocol and informed consent forms were confirmed by the Ethic Committee, Tabriz University of Medical Sciences, Iran. Exclusion criteria were the presence of media opacity due to cataract or vitreous hemorrhage and the existence of significant refractive error (more than an absolute spherical equivalent to 3 Diopters). One eye from each patient was recruited. If both eyes were eligible, then the eye which was treated by laser last was included. To perform laser photocoagulation, the pupils were dilated with 3 drops of Tropicamide 1%. Then, eyes were anesthetized for the procedure with Tetracaine 0.5% drops, and the formerly scheduled laser therapy was done. To ensure spot size in slit lamp (ELLEX-Integre-PRO) delivery system before laser exposure, a spot check paper scaled for 50, 100, 200, 500-micron size was used. Figure 1 shows 200-micron laser beam selected in slit lamp that is fixed in 200-micron spot in paper check. Then, laser burns with solid state diode for the purpose of study were placed with Volk Area Central with laser beam

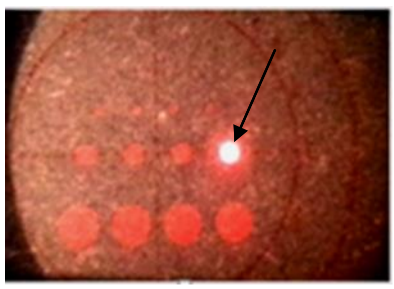

Figure 1: The spot check paper used to verify slit lamp laser beam size. 200 μm laser beam punched 200 μm circle spot showed a precise spot size.

magnification factor of 0.94 at the margin of posterior pole of the retina, in an area which was devoid of edema by a retinal specialist. Aerial beam sizes of 50 and 100 μms were applied. With each of mentioned sizes, laser was then shot with powers of 100 and 150 mW, and durations of 0.05 and 0.1 seconds (Table 1). Separately, this procedure was performed to each wavelength of laser. Immediately after the placement of laser spots, patients were sent for fundus photography and OCT. Fourty five-degree fundus photographs (TRC- 50 EX camera, Topcon) were then taken. OCTB scans were taken with Spectral-Doman OCT (Heidelberg Engineering, Germany). The OCT scans were taken as 6 mm with 25 compactness and with spacing of 30μms between scans. Fundus photograph was applied as a template to find the burns in OCT scans. After identification of each study burn, the scan with the widest width of burn was then selected and the caliper of the Spectralis SD OCT software was then applied to measure the diameter of the burn at the level of the ellipsoid zone. Three measurements were carried out for each burn cross section and the mean level was recorded. Figure 2 provides OCT images taken after laser surgery.

Computer Simulation

In the present study, we used Zemax (EE-2005) software to simulate eye optical elements and analyze laser beam size in retina. Liou & Brennan (L&B, 1997) eye model has been chosen having many factors similar to authentic eye such as aspheric surfaces, a Crystalline lens with two different gradient-index sections, an off-axis object and a curved retina surface [16]. Still, new models are in progress which get closer to real eye. In this simulation, a bunch of rays was passing through the eye and producing the spot image of the object infinitely. It should be mentioned that eye could be considered as an optical instrument that has lenses, apertures; different media with different refraction index; therefore, imaged

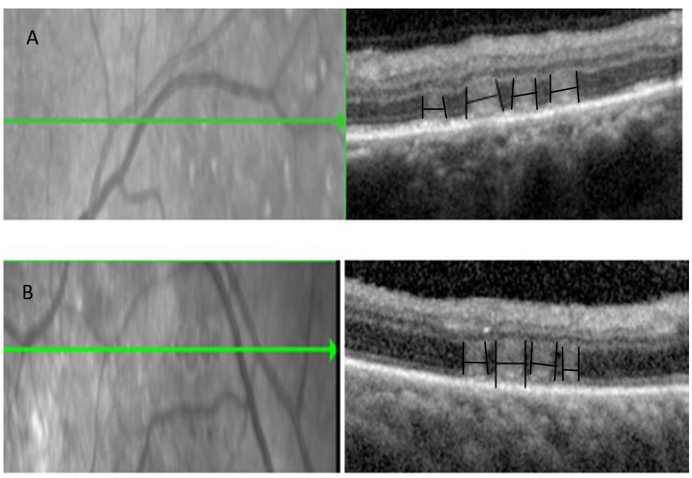

Figure 2: Optical coherence tomography (OCT) images ;(A) OCT image of red laser burn in photoreceptor layer. (B) OCT image of green laser burn in photoreceptor layer.

Table 1: Laser study parameters

Power (mW)	100				150			
Spot Size (μm)	50		100		50		100	
Time Duration (Sec)	0.1	0.05	0.1	0.05	0.1	0.05	0.1	0.05

spot over the retina would not be as perfect and small as airy disk of those ideal optical imaging instruments. But the most interesting part goes back to the size of the spot in different wavelengths. If we take a look at the size of the spot on the retina at different wavelengths, we could discover the relationship between light wavelengths and spot size that is very crucial in surgery. We choose visible wavelengths of green (532 nm) and red (672 nm) that we used in our clinical examination.

By the way, spot diagrams were used in the analysis of tools to measure the spot size of laser beam in retina. Spot diagram can depict RMS radius and GEO radius in micron scale.

Physical Eye Model

The physical eye model was designed and then made according to previous experience and research. Standard values of eye physical parameters were derived from existing literature and applied in eye model [17, 18]. The model eye which was used in this project differs from previous design in two ways; first, it was designed so that samples of reflecting material representing the fundus can be precisely positioned inside the model. Making such simple to perform adjustments is important as the model eye is filled with water, representing the aqueous and vitreous fluid. Secondly, the adjustable holder for the fundus material is given the same curvature as that of the real fundus.

The general structure of the model consisted of two chambers; the anterior chamber included a black aperture that simulated the iris in front of the anti-reflection lens. The lens was bounded to posterior position by the aperture, which had the same diameter as the general structure of the model consisting of two chambers. The anterior chamber included a black aperture that simulated the iris in front of the anti-reflection lens. The lens was bounded to posterior position by the aperture, which had the same diameter as the lens. The posterior chamber lies behind the lens and included the reflecting "fundus" with the same curvature as that of the eye's fundus. The posterior and anterior chambers were sequential through the middle media when contained water was used to simulate vitreous humor. The water chamber contained a movable fundus holder that provided additional accurate movement to focus onto the fundus. This avoided the need to vary the focus of the lens when different materials were used as the fundus. The specifications of model eye were; a black aperture whose size could be selected as either =5, 6 or 8 mm, a symmetric convex lens (f= 18 mm, d= 13 mm, thickness= 4.4 mm, design wavelength= 546.1 nm, index= 1.5187) with antireflection coating, a waterproofed box (internal dimensions= 50×50×30 mm) made from transparent material Perspex/acrylic sheet, a moveable curved holder (d= 25 mm) and adjustable post and post holder (h= 150 mm) with a collar to fix the height.

Water was used as a coupling media inside the model eye, the reflections from having an interface of two different media, air and sample were removed by the application of water. In this study, physical eye model was placed in slit lamp and the same laser parameter that used in clinical examination was chased for laser exposure. Lasers with green (532 nm) and red (672 nm) were used. Previously, laser burn in the retina physical eye model in different power, pulse duration and spot size was shown (Table 1). The burn size was measured with stereo-microscope. Also, in Figure 3 it was shown that laser burn appears after laser exposure in retinal physical eye model in its upper row by green (532 nm) and lower row by red (672 nm). The burn was produced in 0.1 pulse duration and with various powers and spot size setting.

Image Tool

OCT images are generally used for morphology of laser burns and measuring laser lesion size. In this study, we introduced a method to measure burn size using fundus images and

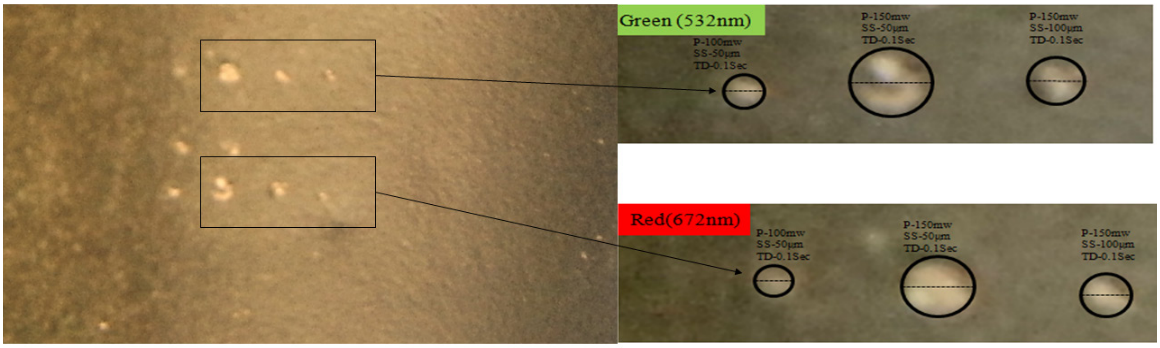

Figure 3: The burn size measured in retinal physical eye model.

applying calibration curve, which was obtained from OCT measurements in scale of micrometer and diameter of burn size with respect to the number of pixels in fundus images. For this, we measured burn diameter and pixel size in fundus images taken after laser photocoagulation using IT software, UTHSCSA 2002. Length of burn diameter was shown in pixels on fundus image and in micrometer scale in OCT image.

Results

Experimental Results

Results from clinical examination and from OCT scan are summarized in Tables 2 and 3. Data points for 0.05 second laser exposures and 100 mW at red wavelength are not shown because clinically visible lesions could not be produced in these settings.

The impressive parameter was power that as it raised, burn size increased significantly. Increased power induced visible clinical burn and greater lesion size compared to lower power. For example, with 50 μm spot size and 0.1 sec time duration, decreased power from

Table 2: Ratio of the lesion width to the retinal beam size for various pulse durations and power at green wavelength

Beam in Cornea (μm)	Beam in Retina (μm)	Power (mW) – Duration (Sec)			
		150-0.1	150-0.05	100-0.1	100-0.05
100	(×0.94)[a] 94	3.02	2.1	2.4	1.7
50	(×0.94)[a] 94	6.1	5.1	5.7	4.2

a: Volk Area Centralis contact lens (magnification×0.94)

Table 3: Ratio of the lesion width to the retinal beam size for various pulse durations and power at red wavelength

Beam in Cornea (μm)	Beam in Retina (μm)	Power (mW) – Duration (Sec)			
		150-0.1	150-0.05	100-0.1	100-0.05
100	(×0.94)[a] 94	2.2	1.9	2	---
50	(×0.94)[a] 94	5.9	4.1	4.7	---

a: Volk Area Centralis contact lens (magnification×0.94)

150 mW to 100 mW reduced lesion size from 291 to 220 µm. The increase in lesion size opposed the increasing laser beam diameter. Thermal spread of the lesion had an important relative effect on smaller spots. In fixed power and pulse duration, increased beam size decreased burn diameter.

At fixed power, the increase of the lesion size with pulse duration could be approximated by a linear function. As an example, for a 100µm laser spot and 150 mW powers the retinal lesion size increased from 220 to 280 µm as the exposure time increased from 0.05 to 0.1 second. At shorter pulse durations, the width and axial extents of the retinal lesions are smaller than longer ones. Figure 4 shows the clinical size of retinal lesion as a function of laser power and spot size. Figure 5 shows that 50 µm beam diameter in both 100 mW and 150 mW had larger lesion compared to 100µm beam area in similar power.

In this examination, we compared both green (532 nm) and red (672 nm) wavelengths in identical parameters such as spot size, power and pulse duration. In the same slit lamp setting, laser spot size in retina which used shorter wavelength was greater than longer wavelength. The reason behind this was that shorter wavelengths have more scattering effects in comparison with longer wavelength.

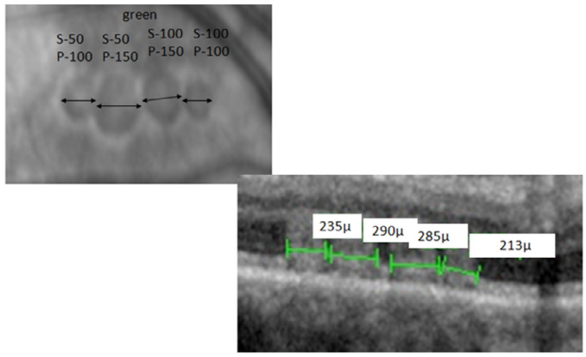

Figure 5: Fundus image (left)-OCT image (right). Burn size diameter compared in different laser beam and two power setup

Thermal damage spreads in a large area of retina in a green wave in comparison with red wave (672 nm), but red wave on the other hand had deeper penetrate versus that of green (532 nm). Figure 6 shows fundus and SD-OCT appearance of the retinal lesions produced with the same laser setting at green and red wavelengths.

Calibration Curve for Lesion Size

Calibration curve is shown in Figure 7. By application of calibration curve, we obtained different measurements such as laser lesion burn, optic disc, eye vessels, etc.

Lesion Size in Physical Eye Model

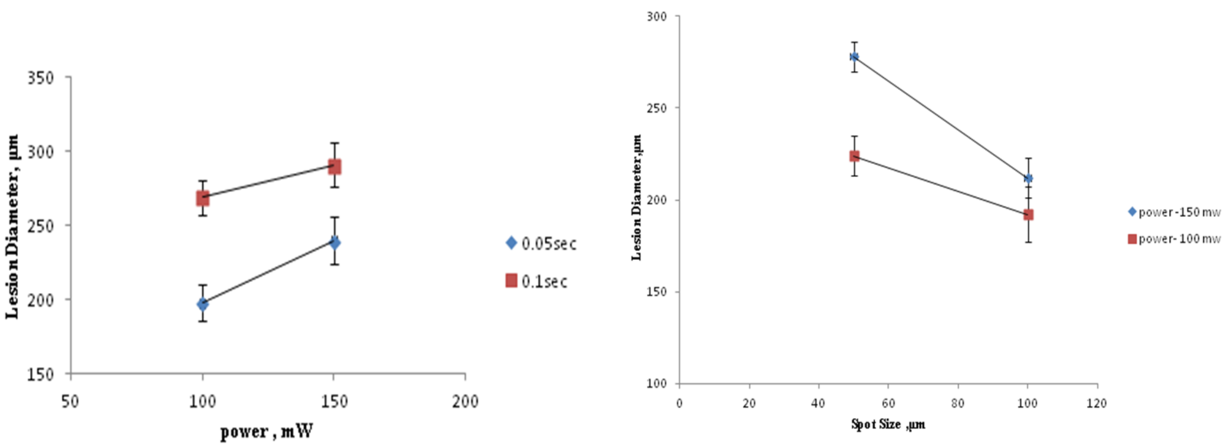

Figure 4: (A) Clinical size of the retinal lesion as a function of laser power for pulse durations ranging from 0.05 to 0.1seconds with a laser beam size of 50µm, (B) Laser lesion size affected with spot size in two different power and Constance exposure time (0.05 sec)

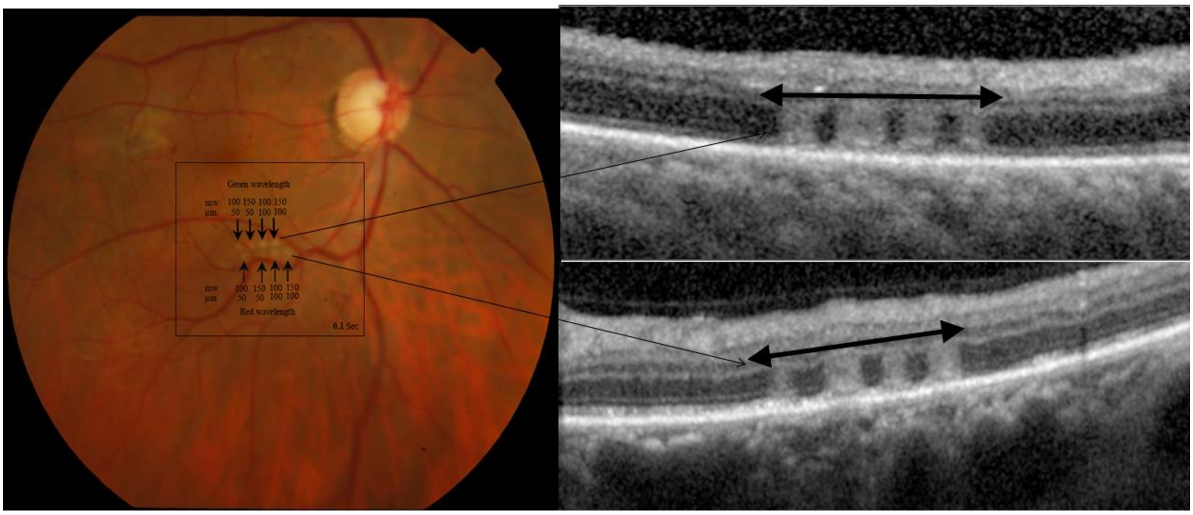

Figure 6: Fundus color and OCT images of a study area. (A) Show color fundus images immediately after treatment. 2 rows indicate the position of each lesion. Green wavelength placed at upper row and red wavelength placed at lower row. From left to right, powers and spot sizes was chosen 100 mW, 50 µm; 150 mW, 50 µm; 100 mW, 100 µm; 150 mW, 100 µm in constant (0.1Sec) time. (B-C) shows an SD-OCT image of the corresponding fundus.

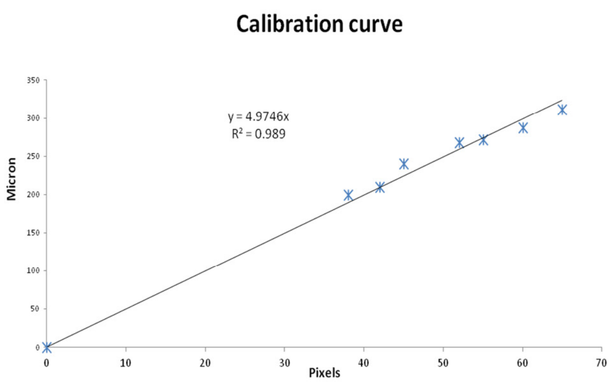

Figure 7: Calibration curve

Lesion size and the grade of laser burn visibility were derived from physical eye model. Similarly, clinical examination demonstrated that laser power and exposure time had direct effected on clinical grade size, lesion diameter and reverse influence on spot size. Tables 4 and 5 summarize the results of burn size.

Computer Model

After laser passed through the eye model, spot size in retina was calculated with Spot Diagram in Analysis tool bar in Zemax. In 100 µm laser beam GEO radius was 9.7 µm for green (532 nm) and GEO radius was 10 µm for red (672 nm). In green wavelength with 50µm laser beam diameter GEO radius was 4.85 µm and in red wavelength 5.01 µm was computed (Figure 8).

Discussion

This study demonstrated physical parameters of laser such as power density, beam size, time duration and wavelength affecting the final size of burn and lesion intensity in retinal photocoagulation. Presented results in Tables 2 and 3 show that although burn size on retina was directly changed with power and time duration, the spot size of laser changed burn size reversely. On the other hand, the effect of laser wavelengths showed bigger burn size for green compared to red laser. These results are in agreement with other studies on human retina [7-9]. Result reveal small spot size produces larger lesion diameters due to thermal spread effect. 50µm spot size in all various laser setting induces wide lesion areas. Palanker et al. in their study demonstrated

Table 4: Burn size produced at green wavelength in physical eye model

Wavelength (nm)	Green							
Power (mW)	100				150			
Spot Size (µm)	50		100		50		100	
Time Duration (Sec)	0.1	0.05	0.1	0.05	0.1	0.05	0.1	0.05
Burn Size (µm)	270±4	220±9	230±4	200±6	410±11	270±5	300±9	225±5

Table 5: Burn size produced at red wavelength in physical eye model

Wavelength (nm)	Red							
Power (mW)	100				150			
Spot Size (µm)	50		100		50		100	
Time Duration (Sec)	0.1	0.05	0.1	0.05	0.1	0.05	0.1	0.05
Burn Size (µm)	265±8	210±4	225±9	195±11	350±9	235±9	285±9	220±5

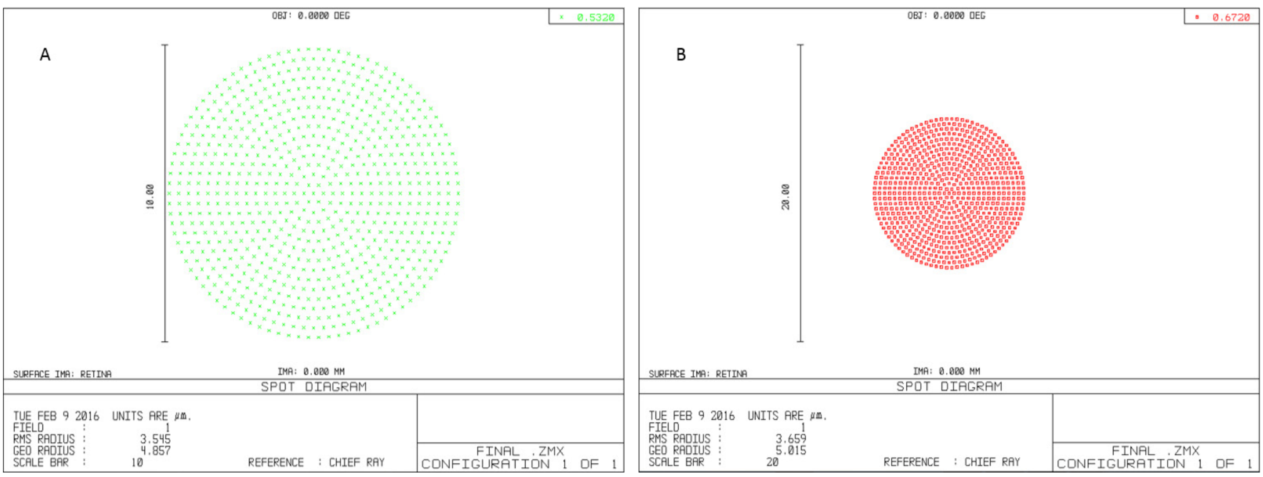

Figure 8: Laser spot size in retina human eye model with 50µm beam diameter; (A) green wavelength, (B) red wavelength. Spot size at red wavelength was greater than the green one

heat/temperature spread using smaller spot laser [8]. We compared the effect of two different wavelengths in retina burn sizes, using similar power, spot size and exposure time setting. Images of SD-OCT scan, fundus photo and physical eye model presented that shorter wavelengths have a greater lesion diameter compared to longer wavelengths. Due to inverse relation between scattering coefficient (αs) and wavelength (λ), green wave tends to cause more collateral damage as compared to red wavelength (Figure 6). In contrast, red wavelength with less scattering light needed higher energy levels with longer exposure to achieve visible burn. Results from red wavelength threshold laser demonstrate that moderate burn happen at least 0.1 sec. time duration with 100mw (Table 3). Results derived from simulation method showed that laser beam diameter in retina human eye model depended on wavelength. Outcome from Zemax presented that beam size at red wavelength was greater than green one which accommodates with physical equation: $d=2.44f\lambda/D$:

in which d is spot size, λ represents wavelength of the laser and D is the diameter of beam and f represents focal length of the lens. It seems that laser spot in retina at green wavelength becomes smaller than the red but scattering effect with laser interaction to retina tissue causes lesion size at shorter wavelength becoming greater than longer one. Moreover, increasing laser power from 100 to 150 mW releases the ratio of the lesion size to laser beam from 5 to 6 times in fixed time duration (0.1 sec) and spot size (50 µm). Because the amount of heat generated in the pigmented layers increases with absorption coefficient and laser power, variations in pigmentation will affect lesion characteristics, as do variations of laser power. Thus, retinal lesions in the areas with variable pigmentation are expected to have more uniform sizes in shorter pulse durations than conventional longer durations. Results show that change of exposure time also affects the retina lesion size. When diode laser continues, mode increases exposure two times greater than the cause of size of the retinal lesion exceeding. This effect is related to energy density and time of exposure. This research can estimate burn size and lesion intensity before selecting laser parameter for photocoagulation. Moreover, the results of our study demonstrated that not only the laser beam size but also pulse duration and power can strongly affect the final size of the retinal lesion intensity. In brief, final lesion sizes for 50 to 100 ms pulses exceed the retinal beam size by a factor of 3 or more. Because the amount of generated heat increases with laser power, variations in pigmentation will affect laser power. The safe range of retinal coagulation, the range of power sufficient for coagulation but not exceeding the threshold of retinal rupture, is expected to decrease with decreasing pulse durations. For the first physical eye model was used to investigate the effects of laser parameter on retina burn size and lesion intensity. Obtained result from physical eye model approved that final retinal burn size and lesion intensity are affected by various laser parameters. The result derived from this study shows maximum burn size produced by increase in power and exposure time and decrease in laser spot size at shorter wavelengths.

In summary, our data suggest that conventional laser photocoagulation duration with regard to the predictability of the lesion size reduces collateral injury through reduced axial and lateral spread of heat, and ability to pattern scan during the eye fixation time.

Conclusion

This study demonstrated that shorter pulses provide decrease in the duration of laser surgery with significantly reduced pain. For lighter lesions, the thermal damage is better confined to the photoreceptor layer, resulting in better healing of the lesions and reduced scarring. Regarding the therapeutic benefits and complications of lighter lesions versus the standard ones in various clinical conditions, further clinical trials are required. Results and calculations described in this article can help adjust the required total coagulated area, the number of lesions and the pattern density.

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Conflict of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper

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