Original Research Article

Efficacy Analysis for presbyopia correction using noninvasive scleral softening by infrared diode lasers

ABSTRACT

Purpose: To derive and provide analytic formulas for an accommodative gain of presbyopia eyes. via scleral softening for decreased posterior vitreal zonules length and increased space between the ciliary body and lens lens.
Study Design: To increase the accommodation of presbyopia by scleral heating.
Place and Duration of Study: New Taipei City, Taiwan, between April 2022 and June 2022.
Purpose: To analyze the safety and efficacy of presbyopia treatment via scleral softening.
Methodology: The scleral softening efficacy is calculated based on the rate equation of the scleral tissue with a rate coefficient given by an Arrhenius formula, The temperature spatial and temporal profiles are given by the numerical solutions of a heat diffusion equation with a volume heating source. Various effective depths including the tissue damage depth, temperature penetration depth and conversion depth, governed by the tissue absorption coefficient, light intensity and dose (or irradiation time), and the related threshold values, are introduced in replacing the conventional penetration depth based on a Beer's law.
Results: Given the the temperature spatial and temporal profiles, the scleral softening efficacy can be calculated. Scleral surface damage can be prevented by cooling window. The suggested protocol for scleral softening treatments include: a diode laser at about 1.47 µm wavelength (with absorption coefficient about 20 to 25 cm^{-1}). The laser power is about 0.2 to 0.4 W per spot, having a total of 4 to 16 spots, and irradiation time of 250 to 500 ms
Conclusion: The safety and efficacy of scleral softening treatment depend upon: laser parameters (intensity, spot size, wavelength), and the effective depths. By choosing the laser treated areas, a dual function treatment using scleral softening or presbyopia and using cornea stroma shrinkage for hyperopia is proposed.

Keywords: presbyopia; scleral softening; diode laser heating; efficacy; accommodation gain.

1. **INTRODUCTION**

The principles of presbyopia were given by the classical hypothesis of von Helmholtz [4] and Schachar [5-7] and the modern theory of Lin [8-12]. Non-traditional methods [5-14] for presbyopia correction, including Schachar using scleral band expansion [5-7] and scleral tissue ablation via IR laser of Er: YAG (at 2.94 µm) and UV laser (at 266 nm) [8-14]. The prior art of US patent, Lin and Martin [15], proposed a non-invasive method using a gonio lens guided infrared laser to heat the zonules fiber of the eye for the treatment of presbyopia.

We have recently presented accommodation gains for presbyopia eyes using Laser ablation (or shrinkage) of sclera via lens reshaping and lens anterior shift due to the decease of the posterior vitreal zonules (PVZ) length and increase of the space between the ciliary body and lens (SCL) [16,17]. However, the softening efficacy (Seff) of of the scleral tissue after a thermal laser leading to these PVZ and SCL changes is not yet explored. The scleral tissue can be heated to a temperature within a range from about 70 ^{0}C to about 90 ^{0}C in order to weaken (soften) the tissue. The softened portion can include four softened portions of four locations away from muscles of the eye including inferior muscles, superior muscles, nasal muscles, and temporal muscles in order to inhibit damage to the muscles. The heat sink or cooling air or window is required to inhibit damage to the conjunctiva of the eye.

We have recently developed a thermal modeling [18] for corneal collagen shrinkage for a new corneal procedure called corneal photovitrification (CPV) for vision improvement of age-related macular degeneration (AMD) eyes, by reduced hydration and increase modulus of the treated corneal stroma [19]. The Seff may be calculated based on the rate equation thermal heated scleral tissue, and a rate coefficient given by an Arrhenius formula defined by the temperature rise of the sclera [18].

The temperature spatial and temporal profiles are given by the numerical solutions of a heat diffusion equation with a volume heating source. Various effective depths including the tissue damage depth, temperature penetration depth and conversion depth, governed by the tissue absorption coefficient, light intensity and dose (or irradiation time), and the related threshold values, are introduced. By choosing the laser treated areas, we are able to propose a dual function treatment using scleral softening for for presbyopia, and using cornea stroma shrinkage for hyperopia.

2 Methods and Modeling Systems

2.1. Temperature rise

The temperature change of the scleral tissue (stroma) due to light heating can be described by a generalized heat diffusion equation [20,21]

$$\nabla^2 T(z,t) - \frac{1}{k'}\frac{\partial T(z,t)}{\partial t} = -S(z) \qquad (1.a)$$

where the laser heating source term, S(z) is given by

$$S(z,t) = \frac{A(t)I(z,t)}{K}\, e^{-Bz} \qquad (1.b)$$

k' and K are, respectively, the thermal conductivity and diffusivity of the tumor. B is the extinction coefficient of the sclera (at a specific laser wavelength), which consists of two components: B=[A (A+2b)]1/2, with A and b are the absorption and scattering coefficients, respectively. In this study, we will focus on the role of the absorption term (A), with b<<A, such that B=A in our calculations.

The above heat diffusion equation may be solved numerically under the initial condition: $T(z,0)=T_0$, and under the boundary condition (at z=0) [20]

$$\left[\frac{\partial T(z,t)}{\partial z}\right]_{z=0} = \frac{h}{K}[T(t,z=0) - T_0] \qquad (2)$$

where h is the heat transport coefficient due to the air convection or heat sink cooling window of the scleral surface.

In a cw (or long pulse) laser operation, the laser-heated solution will reach a steady-state when the irradiation time is much longer than the thermal relaxation time and the steady state solution, for dT/dt=0, is given by [21]:

$$T(z) = I_0\,(1 - e^{-Az})/(AK) - (I_0/K + G)z \qquad (3.a)$$

$$G = \frac{h}{K}[T_0 - T(t,z=0)] \qquad (3.b)$$

We note that the slope of T(z) is given by Eq, (2), which has an optimal z* given by when dT/dz (z=z*)=0, or z*=(1/A) ln [$1/(1+KG/I_0)$]. When a sapphire window is contacted to the scleral surface, it has a room temperature T (t,z=0) =20° C, the heat flows from the warmer cornea (at initial T_0 approximately 35° C) to the sapphire window such that G>0, initially and becomes G<0 later.

2.2. The Softening efficacy

The scleral softening efficacy (Ceff) is defined by Ceff =1 − $M(z,t)/M_0$ =1-exp(-S'), where M_0 is the amount of initial scleral tissue prior to the light irradiation, and M(t) is the amount of modified scleral tissue after the laser heating, given by the solution of [22]

$$\frac{dM(z,t)}{dt} = -k(z,t)M(z,t) \qquad (4.a)$$

$$k(z,t) = A_0 \exp(-E_a/[R(T+273)]) \qquad (4.b)$$

where k(z,t) is the rate coefficient given by an Arrhenius formula , Eq. (4.b), in which Ea (in J/mole) is the activation energy (for softening to occur) and R [in J/(Kmole ^{0}C)] is the gas constant R=8.314(in J/mole/^{0}C, and T(t,z) is the temperature in ^{0}C. Therefore Ceff=1-exp(-S'), with S' is the time integral of k(z,t).

The Ceff, In general, is both time (t) and depth (z) dependent due the light intensity penetration depth in the tissues which is inverse proportional to the tissue absorption coefficient. Therefore, a "volume" efficacy is required to define an actual conversion within the volume (area x depth) of light acting soft tissues. This is a new concept proposed in the present article. More details will be discussed later.

3. Results and discussions

We have previously published the numerical results for a anti-cancer lasers system [21,23] using nanogold as the absorber, in which a diode laser at 808 nm was used having laser irradiation time is about few minutes due to the rather low absorption coefficient of nanogold at about A= 3 to 5 cm^{-1} and a penetration depth at about Z_P=1/A=0.2 to 0.33 cm. A temperature increase of about 10 to 15 ^{0}C is required to kill the cancer cells. In comparison, in an eye system with scleral stroma under laser thermal effects, much higher A= 20 to 25 cm^{-1} and Z_P= 0.4 to 0.5 mm are involved and therefore a shorter irradiation time of about 250 to 500 ms is required for a temperature increase of about 40 to 60 ^{0}C (from the initial sclera tissue of about 35 ^{0}C). The numerical solutions of Eq. (1) and (4) require all the related parameters and properties of the heated soft tissues (corneal stroma or sclera). The present article will focus on the simplified and/or limiting cases such that analytic formulas are available for key features of scleral tissue softening. The numerical data of anti-cancer system will be scaled (in time and depth) proportionally to present the trends/features of an eye systems without repeating the complex numerical simulations (which will be shown elsewhere). The scaling process is based on the steady-state formula of Eq. (3.c), in which the T(z) is a decreasing function of I_0z/K. Greater details are shown as follows.

3.1 Temperature profiles

Fig. 1 shows the calculated surface temperature profiles T(t, z=0). For a fixed absorption coefficient (left figure), the temperature profiles has faster rising curve for higher laser intensity. Similarly, for a fixed I, it is a faster rising curve for higher A (right figure).

Fig. 2 shows the calculated temperature spatial profiles T(z) at a given laser irradiation time of 500 ms for various A=(15, 30,60) cm^{-1}, with a fixed I_0=100 W/cm^2. It shows that higher A leads to a higher peak temperature, but a smaller penetration depth, which is also demonstrated by Eq. (3).

Fig. 3 shows the calculated scleral surface temperature T(z=0,t') vs. laser intensity, for A=(15, 30,60) cm^{-1} (curves low to top) at a given laser irradiation time (t'=0.5 s). It shows that T(0,t) is an increasing function of A and I_0. Therefore, to reach a desired temperature for a given irradiation time (t'), one may adjust laser intensity for a given A (or laser wavelength); or choose a laser wavelength (from 1.4 to 2.2 um) for a fixed laser intensity.

Fig. 4 shows the irradiation time needed (t') for T(0,t') to reach a temperature of 60 ^{0}C, for various A=(30,40,90) cm^{-1}. It shows that t' is a decreasing function of A and I_0. Therefore, to reach a desired temperature, one may adjust the irradiation time (from 0.1 to 0.5 s) for a fixed laser intensity; or adjusted the intensity (from 100 to 200 W/cm^2) for a fixed A (or laser wavelength).

We note that the information provided by Figs. 1 to 4 provides the guidance to choose an appropriate laser wavelength (which also defines A), such that the desired surface (and volume) temperature could be reached by adjusting the combined parameters of (I_0, t'), with I_0= (50 to 200) W/cm^2, and t'=(0.1 to 1.0 s). However, to protect the scleral surface layer, the appropriate laser wavelength must be in the range of 1.42 to about 2.2 um, having A= 15 to 100 cm^{-1}, such that the penetration depth (approximately given by 1/A) is in the range of 100 to 650 um.

Besides the use of cooling window, a pulsed (on-off) laser with various off-time and a fixed on time could be used [21]. It shows that T(t,z) is a decreasing function of the off-time due to the heat transport during the off-period. This controlled pulsed laser method can be tailored to optimize the efficacy and avoid surface damage,

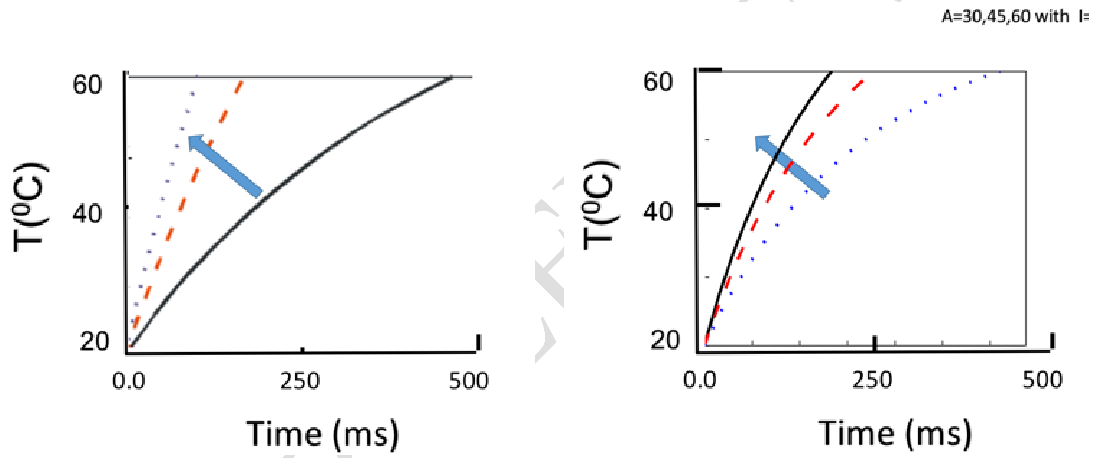

Fig. 1 Calculated surface temperature profiles T(z=0) (Left) for the effects of laser intensity, I_0=(50,100,200) W/cm^2, for curves right to left, for a fixed A=60 cm^{-1}. (Right) temperature profiles for a fixed I_0=100 W/cm^2, but for various A=(30,45,60) cm^{-1}, for curves right to left.

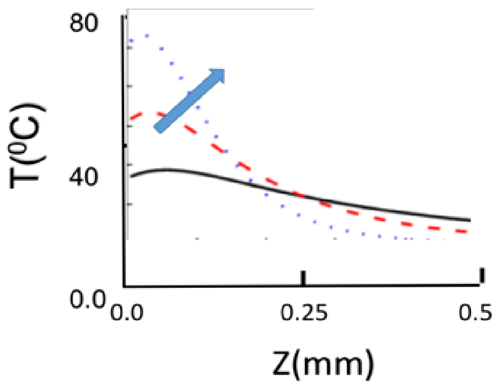

Fig. 2 Calculated temperature spatial profiles T(z) at a given laser irradiation time (t=500 ms) for A=(15, 30,60) cm^{-1}, for curves low to top, with a fixed I_0=200 W/cm^2, and heat transport coefficient range of G= 0.5 WC/cm^2.

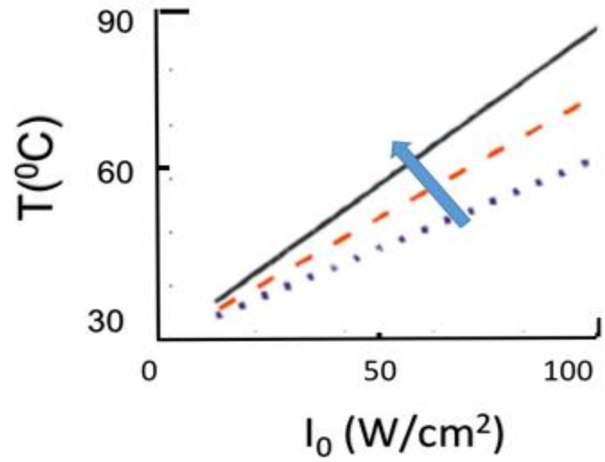

Fig. 3 Calculated surface temperature vs. laser intensity, for A=(15, 30,60) cm^{-1} (curves low to top) at a given laser irradiation time (t=0.5 s).

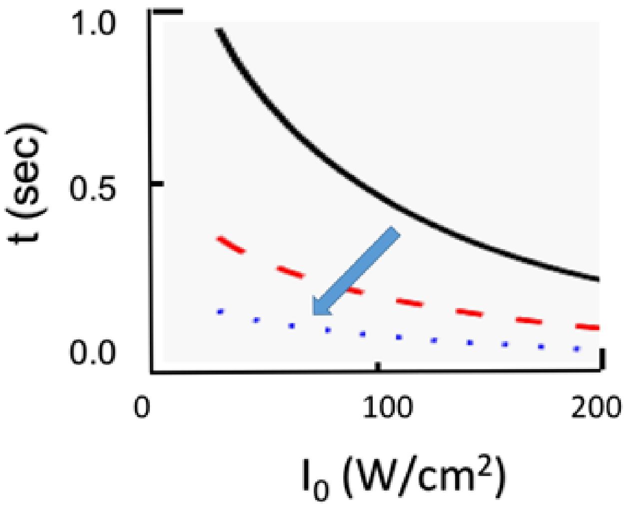

Fig. 4 The calculated irradiation time needed (t) to reach a surface temperature of 60 ^{0}C, for various A=(30,40,90) cm^{-1}, for curves from top to low, for an irradiation time of 0.5 s.

3.2 Effective depths

The conventional definition of light penetration depth (z') is based on the Beer's law exp(-Az), when Az=1, or z'=1/A, which is an inverse function of the absorption coefficient (A). However, this simple definition can not describe the complete features of measured parameters such as the tissue damage depth (Z_D), temperature penetration depth (Z_T), and conversion depth (Z_C), which are governed by the parameters of light intensity and light dose (or irradiation time), and the related threshold values, besides the absorption coefficient (A). We propose the more rigorous definitions for Z_D, Z_T and Z_C as follows.

As shown in Fig. 4, the temperature spatial profiles for various absorption coefficient (A), at a given irradiation time and under a cooling window for an initial surface temperature about 20 ^{0}C. Fig. 4 shows the following features:

(i) Larger A (shown by Curve-A) leads to a higher peak temperature, but a smaller temperature penetration depth (Z_T) defined by T(z=Z_T) =T(peak), which is approximately given by 1/A.

(ii) The tissue damage depth (Z_D) is defined by a threshold damage temperature (T1 about 50 ^{0}C), therefore, large A (Curve-A) with a small Z_D has a better protection of the posterior layer (at about 500 um) than that of small A (Curve-B and C), but it damages the anterior layer (Z1, about 70 um). In contrast, Curve-C (with the smallest A) protects the anterior layer, but not the posterior layer. Curve-B having an optimal A protects both anterior and posterior layers.

(iii) The conversion depth (Z_C) is defined by threshold conversion temperature (T2, about 70 ^{0}C) such that the rate constant, k(t,z=Z_C) is high enough to achieve a threshold efficacy and at depth Z_C.

We note that the above discussed depths are all inverse proportional to A, but the exact relationship requires numerical calculation of T(z,t), and they are also function of the light intensity and irradiation time (or light dose) having a nonlinear power. For example, the irradiation time must be sufficiently short to prevent overheating of anterior and posterior layers and localize the temperature rise within the corneal stroma (or T1<T<T2 for z<Z_D), but long enough to achieve the conversion threshold depth (Z_C) for a given optimal A. More details of Z_C will be discussed later.

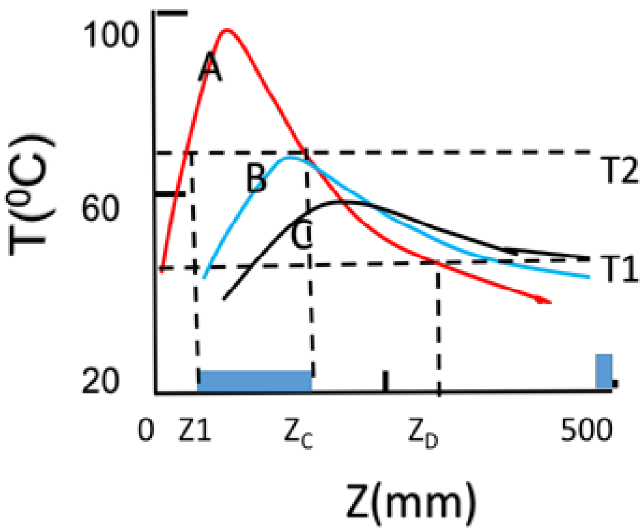

Fig. 5 Calculated temperature spatial profiles (at irradiation time t=500 ms) for various A=(30,60,90) cm^{-1}, for Curve-C, -B, -A; and a fixed I_0=100 W/cm^2.

3.3 Softening efficacy

To calculate the volume efficacy, one requires the temperature spatial (Fig. 5) and temporal (Fig. 6) profiles and the related temperatures T1, T2, and T3; and the depths of Z1, Z_C and Z_D. The volume efficacy is given by the double integral of k(z,t), for time integral of t=t1 to t2 (shown by Fig. 5) and the spatial integral of z=Z1 to Z_C (as shown by Fig. 4). As defined earlier (referred to Fig. 4) that the conversion depth (Z_C) is defined by threshold conversion temperature (T2) such that the rate constant, k(t,z=Z_C) is high enough to achieve a threshold efficacy and at depth Z_C. Numerical integration of k(z,t) is needed, even when the analytic solution of T(z,t) is given, and it will be presented elsewhere. However, Fig. 5 and Fig. 6 provide us comprehensive features s follows:

(i) For efficient conversion (with Ceff >0.6), as shown by Fig. 5, large A (Curve-A) leads to a small Z_D has a better protection of the posterior layer (at about 500 µm) than that of small A, but it also leads to a smaller volume Ceff. Therefore optimal A is required for deep z>Z_C, with T (at z=Z_C) >T2, for maximum Ceff, but small z<Z_D with T (at z=Z_D)<T1 to avoid posterior damage.

(ii) As shown by Fig. 6, for efficient conversion, large A, shown by Curve-A, is needed such that (t2-t1) is maximum for maximum volume Ceff, which is proportional to the time integral of k(z,t) over t1 to t2. The Ceff (z,t) also increasing function of the light irradiation time, which should be long enough (for large t2 and T>T2), but short enough (with T<T1 at $z=Z_D$) to avoid the posterior damage. For example, if a conversion scleral stroma depth of 500 um is desired, parameters of A about 20 cm^{-1}, t abut 500 ms, for a spot diameter of 0.4 mm (or intensity is about 200 W/cm^2), and laser dose about 100 mJ/cm^2 are required. In comparison, for the case of CPV with shallow corneal depth (about 150 µm), parameters of A about 80 cm^{-1}, t about 250 ms, and I_0 about 200 W/cm^2 are required. These theoretically predicted/proposed parameters, however, need further confirmation by measure data.

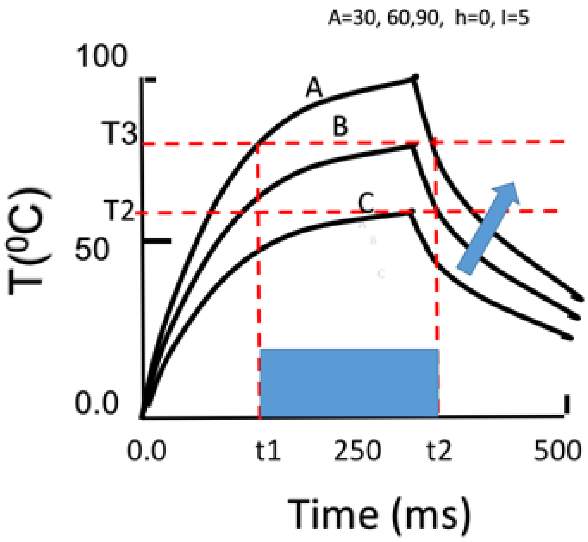

Fig. 6 Calculated surface temperature (at z=0) profiles for various A=(30,60,90) cm^{-1} for Curve-C, -B, -A , and a fixed I_0=200 W/cm^2, where T2 (t1) and T3 (t2) define the temperature range of efficient scleral softening.

3.4 Surface damage and cooling

Besides the use of pulse mode to reduce the scleral surface temperature and avoid the surface damage, a pulsed-train technique was also proposed by Lin for increased volume temperature without over heating the tissue surface [21].

The heat sink cooling process may be passive such as the use of dynamic cooling performed pre-laser and/or intra-laser irradiation [21]. Sapphire or other material(s) may be used for this heat sink application in the transparent window. Based on the thermal properties of sapphire and cornea, we found that during light irradiation of the cornea (about 500 ms), the "thermal depth" could be approximately 80 µm for the cornea and approximately 760 µm for sapphire. Since thermal diffusion is more rapid in sapphire compared to the cornea, heat transfer is "rate-limited" by thermal diffusion through the cornea.

When a sapphire window (at room temperature T_0=approximately 20° C) contacts the cornea (at physiological temperature T_p=approximately 35° C., although this varies as a function of age, room temperature, and so on), heat flows from the warmer cornea into the cooler heat sink. This heat transfer case is similar to the case of a semi-infinite solid (the cornea and the rest of the body behind it) bounded at its anterior surface (z=0, the tear film/anterior epithelium) by a heat sink kept at a fixed temperature T_0. As shown by Fig. 4, the temperature rise spatial profiles (at a given light irradiation time about 500 ms) having a lower temperature near the surface (for z<Z1), and a peak value at $z=Z_C$. for bare sclera and for sclera in contact with a sapphire window.

For light wavelength in the range of 1.9 to 2.0 μm (with A is about 80 to 120 cm^{-1}), the posterior layer can be protected when temperature reaches about 70 ^{0}C, where the light penetration is limited to about 150 μm depth and it is desired for applications require a shallow penetration such as corneal heating for CPV procedure. However, for applications require deeper penetration of 500 to 600 μm (such as sclera softening), light wavelength with a smaller absorption coefficient (with A <30 cm^{-1}), is desired, such as in the range of 1.45 to 1.48 μm or 2.05 to 2.15 μm, which however has less posterior protection.

4. Clinical aspects and analysis

We will now analyze the clinical aspect based on our mathematical model and the numerical analysis of temperature rise and various effective depths described in Section 3.2: the tissue damage depth (Z_D), temperature penetration depth (Z_T), and conversion depth (Z_C). These depths are governed by the parameters of light intensity and light dose (or irradiation time), and the related threshold values, besides the absorption coefficient (A).

As discussed earlier the scleral softening efficacy, Seff, is given by the solution of Eq. (4) or the time integral of a rate coefficient, k(z,t), which is related to the temperature by an an Arrhenius formula. Seff, In general, is both time (t) and depth (z) dependent due the light intensity penetration depth in the tissues which is inverse proportional to the tissue absorption coefficient. Our modeling system having numerical data shown by Figs. 1 to 3, provide quantitative guidance and/or predictions for the following clinical aspects:

Scleral softening for the treatment of presbyopia, the safety and efficacy issues are summarized as follows.

(i) laser parameters (intensity, dose, spot size, wavelength);
(ii) scleral response: the tissue damage depth (Z_D), temperature penetration depth (Z_T);
(iii) the efficacy: depends on the temperature rise, the conversion depth (Z_C) and the time integral of a rate coefficient, k(z,t);
(iv) clinical protocol (laser irradiation time, treatment area and spot size)
(v) mechanisms of action for accommodation gain, which also define the rate coefficient, k(z,t);
(vi) long-term effects, including evolution of accommodation gain.

4.1 Safety and Efficacy

For safety, the scleral treatment should not produce serious adverse events (SAEs) or complications, including discomfort, SAEs include scleral perforation, scleral scarring and persistent scleral epithelial defect. The safety issue is discussed by the tissue damage depth (Z_D) which is further defined by a threshold damage temperature (T1); and a large A (Curve-A) leads to a small Z_D has a better protection of the posterior but it damages the anterior layer (about 70 μm). To overcome the surface layer damage under a laser having a large A (about 60 to 90 cm^{-1}), a sapphire window (at about 20°C) was used as a heat sink to protect the sclera surface (having an initial physiological temperature about 35°C), such that the tear film/anterior epithelium by a heat sink kept at a fixed temperature T_0, having a lower temperature near the surface (for z<Z1), and a peak value at $z=Z_C$, as demonstrated by Fig. 5.

For efficacy, the treatment should produce maximum vision improvement as rapidly as possible after treatment and the accommodation gain should have a long duration of effect (at least few years). The short term efficacy is given by Ceff (z,t) = 1 - $M(z,t)/M_0$, and M(z,t) is given by the solution of the rate eq. (4). The "volume" efficacy is proportional to the heated effective zone volume (or area x depth).

4.2 Suggested protocols

Clinical observations are required to to determine the maximum laser dose (intensity x irradiation time) that retains an undamaged scleral surface layer. Our current softening treatments use a diode laser at a wavelength of about 1.47 µm or about 1.86 µm , or about 2.15 µm, such that A is about 20 to 25 cm^{-1}, where an1-to-4 fiber splitter with fiber core of 200 to 400 µm, and the sapphire window with one mm thickness were used. The laser dose is calculated to be about 100 to 250 J/cm^2/spot, for a laser power of 0.2 to 0.4 W with spot diameter of 0.2 to 0.4 mm (or intensity is about 100 to 200 W/cm^2), and irradiation time of 250-500 ms. We note that the damage threshold is defined by the dose, or energy per unit area (and depends on the spot size), rather than the energy or power (which is independent to the spot size).

We also propose a total of 4 to 16 laser spots with 1 to 4 spots for each quarter portion of the eye, as shown by Fig. 7, where the treated areas are defined by area between two circles having a diameters of about 12 mm (inner circle) and 18 mm (outer circle), and the treated patterns could be dots, lines, curves etc. The use of fiber splitters (1 to 2, or 1 to 4) could speed up the procedure. We note that all the treated areas (except Fig. 7.D) are outside the limbus of the eye such that the cornea shape remain intact leading to unchanged of far and near vision, except the increase of accommodation. This is a distinct difference between the scleral and corneal heating. We further note that hyperopia correction can be simultaneously treated with the presbyopia using a smaller inner circle of about 6 to 8 mm, which causes a corneal reshaping due to laser thermal shrinkage (see Fig. 7.D).

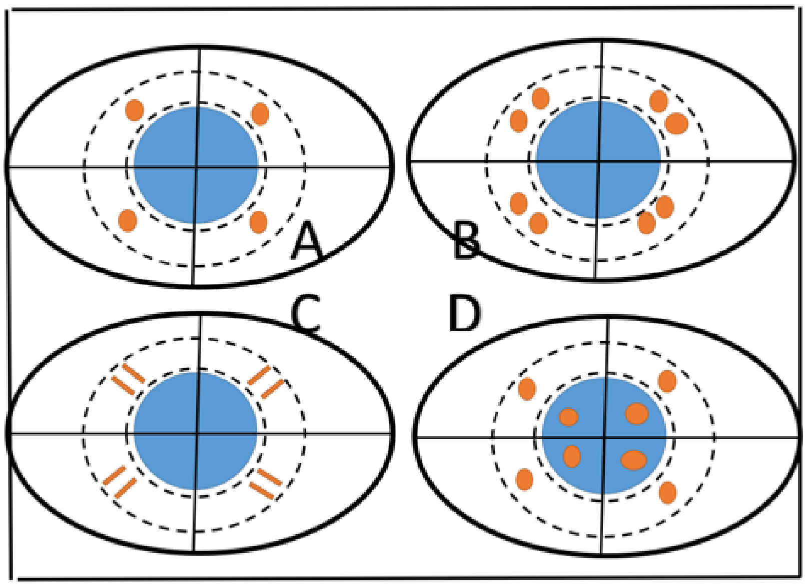

Fig. 7 The treated sclera/cornea locations and patterns for presbyopia corrections (figures A,B and C), and for hyperopia-and-presbyopia dual function treatment (figure D).

5. CONCLUSION

The safety and efficacy of scleral softening treatment depend upon: laser parameters (intensity, spot size, wavelength), the tissue damage depth (Z_D), temperature penetration depth (Z_T), the conversion depth (Z_C), and the time (t) and depth (z) integral of a rate coefficient, k(z,t), given by an Arrhenius formula. The suggested protocol for our current scleral softening treatments include: a diode laser at a wavelength of about 1.47 µm, or about 1.86 µm or about 2.15 µm (with A about 20 to 25 cm^{-1}), laser power of 0.2 to 0.4 W, and irradiation time of 250 to 500 ms. By choosing the laser treated areas, a dual function treatment using scleral softening or presbyopia and using cornea stroma shrinkage for hyperopia is proposed.

REFERENCES

1. Agrawal S (ed.). Presbyopia: A Surgical Textbook. Thorofare, NJ: SLACK; 2002.
2. Pallikaris I, Planis S, Charman WN, ed. Presbyopia, origins, effects, and Treatment, Thorofare, NJ: SLACK; 2002.
3. Garg A, Lin JT et al (ed.). Mastering the Presbyopic Surgical Lens and Phakic IOLs. Jaypee Brother (New Delhi, 2002).
4. von Helmholtz, H. Uber die Akkommodation des Auges. Arch. Ophthalmol. 1985, 1, 1–74.
5. Schachar, R.A., 1992. Cause and treatment of presbyopia with a method for increasing the amplitude of accommodation. Ann. Ophthalmol. 24, 445–452.
6. Schachar, R.A., Abolmaali, A., Le, T., 2006. Insights into the age-related decline in the amplitude of accommodation of the human lens using a non-linear finite element model. Br. J. Ophthalmol. 90, 1304–1309.
7. Schachar RA, Chan RW, Fu M. Viscoelastic properties of fresh human lenses under 40 years of age: implications for the etiology of presbyopia. Br. J. Ophthalmol. 2011, 95, 1010–1013.
8. Lin JT. Apparatus and methods for the treatment of presbyopia using fiber-coupled-lasers. US Pat. No 6824540 (2000).
9. Lin JT. Methods and apparatus for presbyopia treatment using a scanning laser system. US Pat. No 6745775 (2004).
10. Lin JT. Refractive surgery and presbyopia correction using infrared and ultraviolet lasers. US Pat. No. RE40184 (2008).
11. Lin JT. Presbyopia corrections: Laser vs. Nonlaser. In: Mastering the Presbyopic Surgical Lens and Phakic IOLs, Ed. Garg A, Lin JT et al., Jaypee Brother (New Delhi, 2002), page 219-234.
12. Lin JT, Kadambi V. The new mechanism of laser presbyopia reversal and accommodation. In Agrawal S (ed.). Presbyopia: A Surgical Textbook. Thorofare, NJ:SLACK; 2002; Chapt. 6 and Chapt 13.
13. Hipsley A, Ma DH, Sun CC, et al. Visual outcomes 24 months after LaserACE. Eye Vis (Lond) 2017;4:15.
14. Hipsley A, Hall B, Rocha KM. Long-term visual outcomes of laser anterior ciliary excision. Am J Ophthalmol Case Rep 2018;10:38-47.
15. Lin JT and Martin H. U.S. Pat. No. 6,491,688,
16. Lin JT. Principles of Accommodation and Technology update of Presbyopia Correction using IR and UV lasers. Ophthalmology Research, International Journal. 2021; 14:17-28; DOI: 10.9734/OR/2021/v14i430199.
17. Lin JT. Analysis of Accommodation Gain of Presbyopia Eye after Laser Ablation (or Shrinkage) of Sclera via Lens Reshaping and Lens Anterior Shift. Ophthalmology Research, International Journal. 2021; 15:13-22; Article no.OR.72586.
18. Lin JT, Berry M. Efficacy Analysis of corneal photo-vitrification (CPV) for Improved vision of age-related macular degeneration (AMD) eyes. Ophthalmology Research, International Journal. 2022,
19. Deveenyl R, Markowitz SN, Berry II M. et al. Corneal laser procedure for vision improvement in patients with neovascular age-related macular degeneration and other retinal disorders involving central vision loss: a retrospective cohort study F1000Research, 2022, 11:316.
20. Carsiaw HS and Jaeger JC. Conduction of Heat Solids. 2a Edition (Oxford University Press, London, 1959).
21. Lin JT. Design of clinical procedures using diode lasers operated in continuous wave and pulsed modes. Medical Device Diagn Eng. 2016;1: 29-35.
22. Lin JT, Cheng, DC. Modeling the efficacy profiles of UV-light activated corneal collagen

crosslinking. PloS One. 2017;12:e0175002.
23. Lin JT, Chiang S, Lin GH, Liu HW. In vitro photothermal destruction of cancer cells using gold nanorods and pulsed-train near-infrared lase. J. Nanomaterials. 2012; article ID 861385.