Original Research Article

Comprehensive Formulas for Volume Efficacy for Accommodative Gain in Presbyopic Eye using a new procedure of Laser Scleral Softening (LSS)

ABSTRACT

Purpose: To derive and provide, for the first time, comprehensive analytic formulas for scleral softening volume efficacy (SVE) for accommodative gain (AG) via the increased space between ciliary body and lens (SCL) and mobility of the posterior vitreous zonules (PVZ).
Study Design: To increase the AG of presbyopic eye by a new procedure, laser scleral softening (LSS).
Place and Duration of Study: New Taipei City, Taiwan, between May 2022 and July 2022.
Methodology: The SVE is calculated based on the time and spatial integral of the scleral temperature profiles, $T(z,t)$, solutions of a heat diffusion equation. Analytic formulas for SVE is derived based on the covered area given by a triangle area. The SVE of a 3-D model is governed by the "volume" covered by the laser beam, or its spot size area, the effective penetration depth (z''), which is an increasing function of laser dose, but a decreasing function of the absorption coefficient (A), due to the Beer's law of laser intensity, $I(z)=I_0\exp(-Az)$. The efficacy depth-range (dZ) and time-ranges (dT) are defined for efficient softening with $T(z,t)>T^*$, where T^* is the scleral softening threshold temperature.
Results: The accommodative gain is proportional to the 3-D SVE given by: SEV(3D) = SEV(1D) x laser beam spot (2-D area) x total number of spots (N) acting on the sclera, in which SVE is proportional to the efficacy ranges dZ and dT, in which dZ is an increasing of laser irradiation time; in comparison, dT is a decreasing function of depth. Softening of the scleral tissue after a thermal laser leading to the increase of PVZ mobility and SCL. However, the actual relation of SVE and the PVZ and SCL changes require measured data.
Conclusion: Safety and efficacy of scleral softening for presbyopia treatment depend upon the laser parameters (intensity, dose, spot size, wavelength) and the effective depths. The SVE is proportional to the efficacy depth-range (dZ) and time-range (dT), in which dZ is an increasing of laser irradiation time and dT is a decreasing function of depth. The AG is proportional to the SVE(in 3-D).

1. INTRODUCTION

Presbyopia correction using laser scleral tissue ablation (LSA) via IR laser of Er: YAG (at 2.94 µm) and UV laser (at 266 nm) was proposed by Lin [1-7]. These prior arts using laser scleral ablation suffer the drawbacks of being invasive, surgical bleeding, complex and slow procedure, having major postsurgical regression [4,6].

Comparing to the prior arts of laser scleral ablation (LSA) [1-7], a new method (US patent pending by JT Lin) called laser scleral softening (LSS) was proposed and offer the advantages of: being noninvasive, non-surgical, no scleral bleeding, less pain, fast recovery and less (expected) post treatment regression [8].

The author recently presented the theory for accommodation gain (AG) for presbyopic eyes via lens reshaping and lens anterior shift. This AG is also proportional to the increase of the space between

the ciliary body and lens (SCL) and mobility of the posterior vitreous zonules (PVZ) [9,10]. However, the relation between AG and the temperature rise or softening efficacy of the scleral tissue after a thermal laser leading to these PVZ and SCL changes is not yet explored. We note taht the CPV

We have recently developed a thermal modeling for corneal collagen shrinkage for a new 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 [10,11]. The above thermal model was also extended for the calculation of scleral softening efficacy which depends on a rate equation for thermal heated tissue, and a rate coefficient given by an Arrhenius formula defined by the temperature rise $T(z,t)$ of the treated tissue [8]. However, the laser heating area for CPV is on the cornea, whereas it is on the scleral tissue behind the limbus for the LSS procedure.

The objective of the present article is, for the first time, to further calculate the scleral softening "volume" efficacy (SVE) for the accommodative gain of presbyopic eyes. The SVE given by a double integral of $T(z,t)$ over time (t) and depth (z), is governed by the key parameters of the threshold temperature for a given conversion depth, the tissue absorption coefficient, light intensity and dose (or irradiation time). We will demonstrate that SVE is proportional to the efficacy-range of depth (dZ) and time (dT), in which dZ is an increasing of laser irradiation time; in comparison, dT is a decreasing function of depth. Comprehensive formulas for SVE(3-D) are developed as the guidance of further clinical studies and the optimal protocol.

2. METHODS AND MODELING SYSTEMS

2.1 Temperature Rise

The temperature change of the scleral tissue due to laser heating can be described by a heat diffusion equation [13,14]

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

where the laser volume heating source term, $S(z)$ is given by $S(z,t)=(A/K)I_0\exp(-Bz)$, with I_0 being the laser intensity on the surface (at z=0). 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, $[dT/dz]$(at z=0)=$(h/K)[T(t,0)-T_0]$, where h is the heat transport coefficient due to the air convection or heat sink cooling window of the scleral surface.

2.2 The Softening Efficacy

As reported that the accommodation gain (AG) after the scleral softening is due to the increase of the space between the ciliary body and lens (SCL) and mobility of the posterior vitreous zonules (PVZ) [16,17]. For example, the PVZ length was reduced from 4.6 mm for a un-accommodative state to 3.6 mm (and 4.45 mm) in an accommodation state for a non-presbyopia (and presbyopia) eye. Furthermore, SCL is about 0.68 mm and 0.35 mm for non-presbyopia and presbyopia eye, respectively. We expect that the AG is proportional to the softening efficacy (Seff) of the scleral tissue after a thermal laser leading to the increase of PVZ mobility and SCL. However, the actual relation of Seff and the PVZ and SCL changes require measured data.

The scleral softening efficacy (Seff) is defined by [15]

Seff $=1 - M(z,t)/M_0$ (2)

2

where M_0 is the amount of initial scleral tissue prior to the laser irradiation, and M(t) is the amount of modified or softened scleral tissue after the laser heating, given by the solution of [8,15]

$$\frac{dM(z,t)}{dt} = -k(z,t)M(z,t) \qquad (3.a)$$

$$k(z,t) = A_0 \exp\left(-E_a/[R(T + 273)]\right) \qquad (3.b)$$

where k(z,t) is the rate coefficient given by an Arrhenius formula , Eq. (2.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 Seff=1-exp(-S'), with S' is the time integral of k(z,t).

The 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. Therefore, a scleral softening "volume" efficacy (SVE) 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 for the accommodative gain of presbyopia eyes. The SVE can be defined by two methods: (i) integral of Seff(z,t) over z, based on the rate equation, Eq. (3); or (ii) double integral of T(z,t) over time (t) and depth (z), based on the solution of heat diffusion equation Eq. (1), as follows.

Method (i):

$$SVE= \int_0^z [1 - exp(-S')\,]dz \qquad (4)$$

with S' is the time integral of k(z,t), the rate coefficient given by an Arrhenius formula, Eq. (3.a), which also defines the activation energy

Method(ii):

$$SVE= \int_{t'}^{t''} \int_{z'}^{z''} T(z,t)\,dzdt \qquad (5)$$

with the range of dz is z' to z", as shown in Fig. 1; and dt is t' to t", as shown in Fig. 2, and defined by a scleral softening threshold temperature (T*). Greater details are shown in the next section 3.

3. RESULTS AND DISCUSSION

3.1 Softening "volume" efficacy (SVE)

Both Eq. (3) and (4) need numerical solutions of Eq. (1) and the numerical integrals. For comprehensive formulas, we use the approximated temperature profile given by

$$T(z,t)= T_0+F(t)G(z) \qquad (6)$$

As shown by Fig. 1, (left figure), the efficacy depth range dZ=(z"-z'), show by blue bars, defined by when the temperature is above the softening threshold temperature (T*), about 65 to 70 ^{0}C. As shown by Fig. 1 (A,B,C), this dZ increases from 0, to about 0.3 mm for laser irradiation time increase from 50 ms to 200 ms. For analytic formulas, the G(z) profile is approximated by linear function of G'(z)= a'z (for z'<z<zp), and G(t)=a' zp- Az (for zp<z<z"), with a' and b' are the fit parameters. Let T(z' or z", t)=T*, we found z'=dT'/(a'F); and z"=(a'zp - dT'/F]/b, with dT'= (T*-T_0), where T* is the scleral softening threshold temperature, about 65 to 70 ^{0}C. The maximum temperature (at z=zp) requires numerical calculation. For comprehensive formulas, we consider the case of small z'<<z", and ignore the thin layer due to surface cooling effects (or z'=zp=0). We also approximated G(z)= 1-Az, for small Az.

As shown by Fig. 2, the T(z,t) profile is approximated by linear function of F(t) = at (for t'<t<tp), and F(t) = F'(t)=a tp- bt (for tp<t<t"), with a and b are the fit parameters (proportional to the light intensity and

A), and tp is the laser irradiation time. The time range t' and t" are given by when T(z,t' or t")=T*. We obtain t'=(T*- T_0)/(aG); and t"=[a tp - (T*-T_0)/G)]/b, with G(z)= 1-Az. We note that the efficacy range dT=(t"-t')= (a/b)tp - (1/a+1/b)dT'/G, is an increasing function of G(z), or decreasing function of z. That is deeper depth has smaller efficacy range, leading to a smaller SVE. SVE is proportional to the efficacy depth-range dZ=(z"-z') and efficacy time-range dT=(t"-t'), in which dZ is an increasing of laser irradiation time; in comparison, dT is a decreasing function of depth.
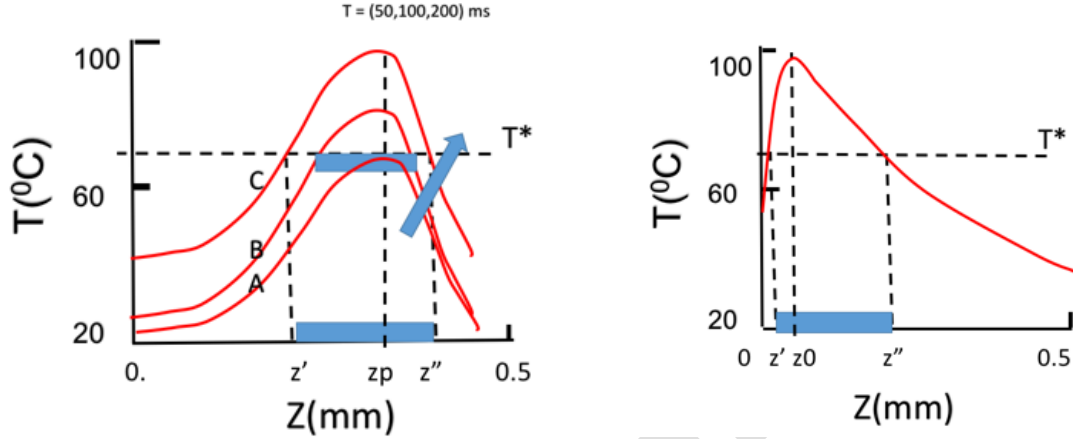

Fig. 1. Scheme of temperature spatial profile T(z,t') at a given laser irradiation time (t'), and z' and z" are the depth range for efficient softening with T(z,t')>T*. the threshold scleral softening temperature. Left (and right) figure for strong (and weak) surface cooling. Fig. 1 left figure, curve (A,B,C) are for laser irradiation time of (50,100,200) ms.
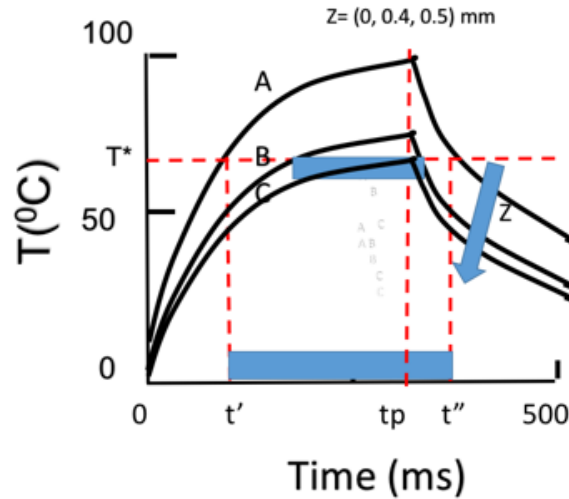

Fig. 2 Scheme of temperature temporal profiles T (z',t), at a given depth z, with laser irradiation (on-time) tp; t' and t" are the time range for efficient softening with T(z,t)>T*. Curve (A,B,C) are for sclera depth of z=(0, 04, 0.6) mm.

By approximating (within 10% errors), the areas of Fig. 1 and Fig. 2 by triangles, such that its area of softening is given by H(t)=0.5z"F(t) for the spatial profile of Fig.1.
Therefore, the z-integral of T(z,t) leads to

$$\text{SVE}= \int_{t'}^{tp} H(t)dt + \int_{tp}^{t"} H'(t)dt \qquad (7)$$

4

with analytic form of $H(t)= 0.5atz"$, and $H'(t)= 0.5z"(a\,tp- bt)$; noting that $z"(t)$ is a function of t, given by $z"=[1-(T^*-T_0)/F(t)]/A$.

Again, the temporal integral of Eq. (6) can be approximated by the area of a triangle given by profile of Fig. 2, without integral of Eq. (6), which becomes the area covered by a triangle having a base length of $(t"-t')$ and height defined by $T(z, t=tp)$. We obtain,

$$SVE=0.5 (t"-t') [(aG)tp - dT] \qquad (8)$$

with $t'=dT/(aG)$; and $t"=[(a/b) tp - dT/(bG)]$, and $dT=(T^*-T_0)$,
We note that $(t"-t')= (a/b)tp - (1/a+1/b)dT/G$, therefore, SVE is proportional to $(a\,tp)^2G/b$, but it is a decreasing function of $dT=(T^*-T_0)$. However, SVE is still function of $G(z)=1- Az$, which can be taken as an averaged over z, or mean $G=G'=1- 0.5A\,z"$, becomes z independent. Our new method of LSS require $z"$ to be about 450 to 600 um for efficient increase of SCL and mobility of PVZ.

3.2 Efficacy 3-D model and effect of laser spot size

The SVE discussed above is still based on a 1-D model with depth (z) and integral over time. In actual laser heating, the SVE needs a 3-D model. We note that the laser acting area is a cone-shape having wider area at the top than the bottom. This can be mathematically seen by the efficacy range $(t"-t')= (a/b)tp - (1/a+1/b)dT/G$, is a decreasing function of z. That is deeper depth has smaller efficacy range, leading to a smaller SVE.

As shown in Fig. 3, a laser beam (with a spot diameter R, for a round beam) penetrates through the scleral surface layer (in blue) to its stroma having a temperature profile shown in the left figure. As defined by the softening threshold temperature (T*), only up to the depth of $z"$ has enough temperature rise for efficient scleral softening, and this depth is also an increasing function of the laser dose (intensity x irradiation time), given by $z"=[1-(T^*-T_0)/F(t)]/A$, in which the laser heating cone-volume is given by the "volume" covered by the laser beam, or its spot size area, $3.14 (R/2)^2$, x effective penetration defined by $z"$, which is an increasing function of laser dose, or integral of F(t), but a decreasing function of the absorption coefficient (A), due to the G-function, $G(z)=\exp(-Az)$.

Therefore, the SVE in our 1-D model, given by Eq. (4), (7), is revised for a 3-D model as: $SEV(3D)= SVE(1D)$ x Volume = $SEV(1D)$ x laser beam spot (2-D area) x total number of spots (N) acting on the sclera, that is

$$SVE(3D)= 3.14(R/2)^2 N SVE(1D) \qquad (9)$$

where SVE(1D) is given by Eq. (3), (4) or (8).
However, to minimize the invasive and pains, and potential fracture of the eye, we propose laser round-spot diameter (R) is about 0.2 to 0.6 mm and N is about 4 to 16.

We also note that $z"=[1-(T^*-T_0)/F(t)]/A$, is a deceasing function of T* and the absorption coefficient (A), but an increasing function of the temperature temporal profile, $F(t) = at$ (for $t'<t<tp$), and $F(t) = F'(t)=a\,tp- bt$ (for $tp<t<t"$), with a is proportional to the light intensity, or $a=(AI_0)$, and tp is the laser irradiation time. Therefore, $z"$ has a maximum at $t=tp$, or $z" (max)= [1 - dT/(AE)]/A$, where E= laser dose=$I_0 tp$; $z"$ (max) is proportional to laser dose (E), but a decreasing function of A. We further note that $z"$ can be fine tuned by irradiation time and/or light intensity, or dose (E), for a given absorption coefficient (A).
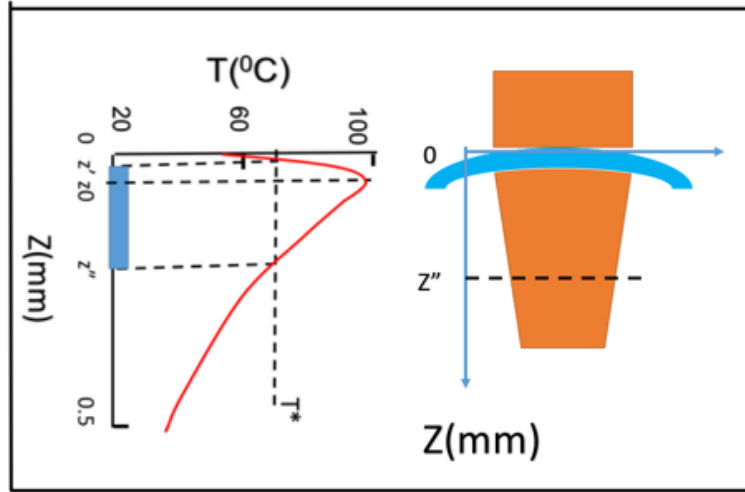
5

Fig. 3 Scheme of temperature spatial profiles T(z) inside the scleral stroma, in which the laser penetration volume is given by the cone-volume (in orange color) in 3-D model.

3.3 Softening Efficacy vs. Accommodative Gain (AG)

As discussed earlier that the AG after the scleral softening is due to the increase of SCL and mobility of PVZ [8-10]. We expect that the AG is proportional to the SVE (3D). However, the relation of SVE, AG and the amount of PVZ and SCL increase require clinically measured human eye data, or animal model. For sufficient AG (>2.0 diopter), the old LAS method using Er:YAG requires the ablation depth >90% of the scleral thickness. Similarly, in our new method of LSS, we also require z" to be about 450 to 600 um for efficient increase of SCL and PVZ mobility, or enough AG to correct presbyopic eyes.

The mechanisms of LSA (ablation) and LSS (softening) are similar. Both lead to the restored mechanical efficiency of the accommodative mechanism, and the Improved biomechanical mobility of ciliary body and/or PVZ to achieve accommodative power. These mechanical and biomechanical efficacy depend not only on the total tissue volume (N x area x depth) treated, but also locations of the treated spots. We proposed that laser treated areas are between 1.0 to 6 mm (most preferred of 2.0 to 4.0 mm) behind the corneal iimbus for the increase of SCL and PVZ mobility. However, the actual relations of AG and SVE, temperature rise (dT), laser dose, beam spot size, conversion depth (z") and total number of spots (N) and locations acting on the sclera, per Eq. (8), require further clinical studies. We also note that both LSS and LSA result to the decrease of local rigidity, aqueous outflow blockage, zonular slack, therefore, their applications include the treatment for presbyopia and glaucoma.

3.4 Effective Depths and Optimal Wavelength

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 20^0C. 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 65 to 90 ^{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 this Z_C is our earlier definition of z" given by the threshold temperature (T*), which is the threshold conversion temperature (T2), in (ii).

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.

To calculate the volume efficacy, one requires the temperature spatial (Fig. 4) and temporal (Fig. 5) 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. 4 and Fig. 5 provide us comprehensive features as 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. We should note that the effective depths can be fine tuned by irradiation time and/or light intensity for a given absorption coefficient. We note that Fig. 5 (for the role of A on the efficacy range has an opposite trend comparing to that of Fig. 2 (for the role of z), since A and z are competing factor.

(ii) As shown by Fig. 5, for efficient conversion, large A, shown by Curve-A, is needed such that (t2-t1) is maximum for maximum volume Seff, which is proportional to the time integral of k(z,t) or T(z,t), over t1 to t2. The Seff (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 to 35 cm^{-1}, t about 100 to 600 ms, for a spot diameter of about 0.2 to 0.6 mm (or intensity is about 100 to 300 W/cm^2), and laser dose about 100 to 150 mJ/cm^2 are required.

(iii) In the LAS method using Er:YAG, ablation depth about 90% of the scleral thickness is required for efficient AG. Similarly, in our new method of LSS, we also require z" (or Z_C) to be about 450 to 600 um for efficient increase of the space between the ciliary body and lens (SCL) and mobility of the posterior vitreal zonules (PVZ). These theoretically predicted, proposed parameters, however, need further confirmation by clinical data.
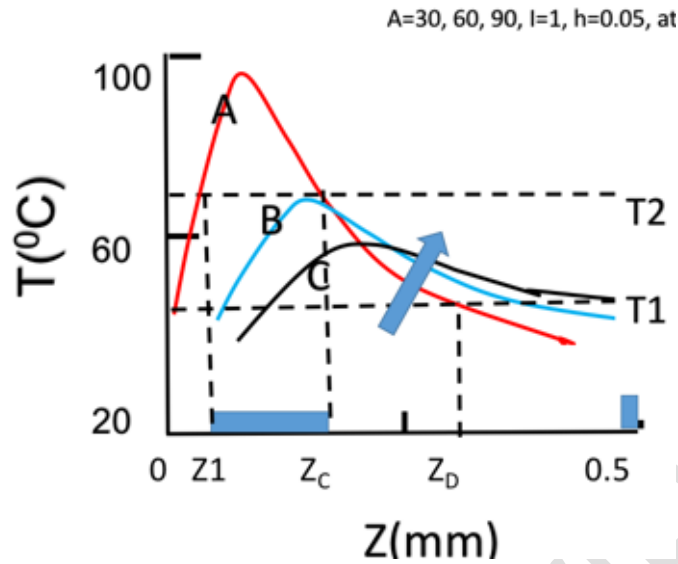
A=30, 60, 90, I=1, h=0.05, at

Fig. 4 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 [8]
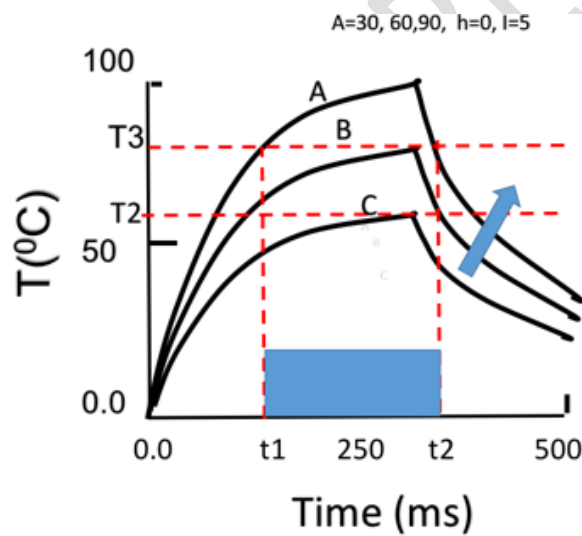
A=30, 60,90, h=0, I=5

Fig. 5. 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 [8].

3.5 The Proposed Protocol
Inclusion:
　　Reading add +1.50 D or more;
　　Reduced DCNVA @ 40cm; ≥20/50 (logMAR 0.40)；
　　UNVA 20/50 or worse；
　　Age 48+，Less than 1.0 D Astigmatism; MRSE +/- 0.50 D
Exclusion:
　　Cataract, dry eye, previous ocular surgery (other than LSS),
　　and any ocular disease.

3.6 Summary of Safety and Efficacy

_____

Based on our analytic formulas, Eq. (8), (9), and Figs. 1 to 5, the key factors and issues for the safety and efficacy of LSS for the treatment of presbyopia are summarized as follows.

(i)   laser parameters (intensity, dose, spot size, wavelength, or absorption coefficient);
(ii)   scleral response: the tissue damage depth (Z_D), temperature penetration depth (Z_T), conversion depth (Z_C or z").
(iii)   the softening efficacy: in 1-D model, the SVE (1-D) depends on the temperature rise, the conversion depth (z" or Z_C) and the time integral of a rate coefficient, $k(z,t)$, or temperature profile, $T(z,t)$;
(iv)   SVE is proportional to the efficacy depth-range $dZ=(z"-z')$ and efficacy time-range $dT=(t"-t')$, in which dZ is an increasing of laser irradiation time; in comparison, dT is a decreasing function of depth.
(v)   In 3-D model, the SVE is given by Eq. (8) for various parameters of N (no. of laser treated spots), R (laser spot size) and laser dose etc. Our new method of LSS also require z" to be about 450 to 600 um for efficient increase of SCL and mobility of the posterior vitreal zonules (PVZ).
(vi)   measured data of AG for presbyopia eye vs. analytic formulas of SVE,
(vii)   clinical protocol (laser irradiation time, treatment locations and spot size)
(viii)   mechanisms of action for accommodation gain, which also define the rate coefficient, $k(z,t)$;
(ix)   long-term effects, including evolution of accommodation gain, and post-operation regressions (if any), comparing to the old method of laser scleral ablation (LSA) by Er:YAG laser.

Comparing to the existing method using laser scleral ablation (LSA), using Er:YAG laser (US patented in 2002 by Lin [1-3]), the present new method (US patent pending) using diode laser scleral tissue softening, (LSS) offers the "predicted" advantages of: non-ablative, no bleeding, less pains, less redness and a much faster procedure (one minute vs 10 minutes in Er:YAG). However, these "predicted" advantages are based on the basic science [8-11]. The pig's eye model [8] and the proposed protocol, however, requires further clinical studies.

4. 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, $k(z,t)$, or temperature, $T(z,t)$, Eq. (3), (4). An effective conversion depth (z") and time ranges (t' and t") are defined for efficient softening with $T(z",t)>T^*$ and $T(z, t_j) > T^*$, with $t'<t_j<t"$, where T^* is the scleral softening threshold temperature. SVE is proportional to the efficacy depth-range $dZ=(z"-z')$ and efficacy time-range $dT=(t"-t')$, in which dZ is an increasing of laser irradiation time; in comparison, dT is a decreasing function of depth. The AG is proportional to the SVE(3D), given by Eq. (8), where the sclera softening efficacy after a thermal laser leading to the increase of PVZ mobility and SCL. However, the actual relation of SVE and the PVZ and SCL changes require measured data.

REFERENCES
1.   Lin JT. Apparatus and methods for the treatment of presbyopia using fiber-coupled-lasers. US Pat. No 6824540; 2000.
2.   Lin JT. Methods and apparatus for presbyopia treatment using a scanning laser system. US Pat. No 6745775; 2004.
3.   Lin JT. Refractive surgery and presbyopia correction using infrared and ultraviolet lasers. US Pat. No. RE40184; 2008.
4.   Lin JT, Mallo O. Treatment of presbyopia by infrared laser radial sclerectomy. J Refract Surg. 2003;19:465-7.
5.   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; 2002.
6.   Hipsley A, Ma DH, Sun CC, et al. Visual outcomes 24 months after LaserACE. Eye Vis (Lond). 2017;4:15.

7. Hipsley A, Hall B, Rocha KM. Long-term visual outcomes of laser anterior ciliary excision. Am J Ophthalmol Case Rep. 2018;10:38-47.

8. Lin JT. Efficacy Theory and Proposed Protocol for Presbyopia Correction using New, Non-invasive Scleral Softening by Infrared Diode Lasers. Ophthalmology Research, International Journal; 2022, 17, (in press).

9. 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.

10. 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.

11. 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, 16, 37-48; Article no. OR.88521.

12. 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.

13. Lin JT. Design of clinical procedures using diode lasers operated in continuous wave and pulsed modes. Medical Device Diagn Eng. 2016;1: 29-35.

14. 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.

15. Lin JT, Cheng, DC. Modeling the efficacy profiles of UV-light activated corneal collagen crosslinking. PloS One. 2017;12:e0175002.

_____