Letters to the Editor

International Retinal Laser Society Guidelines For Subthreshold Laser Treatment

The recent advent of new laser approaches has revolutionized the laser treatment techniques for retinal diseases. In particular, the goal of modern subthreshold laser (STL) treatment is now retinal preservation and normalization, rather than destruction.[1–8] Despite the proven effectiveness of STL, lack of standardization has limited its clinical application and usefulness.[2–8] The International Retinal Laser Society (LIGHT) would like to provide simple evidence-based treatment guidelines to optimize STL application for all users.[9]

The Target

The target of treatment is the retinal pigment epithelium (RPE). The therapeutic effects of retinal laser are the result of RPE cell hyperthermia caused by laser absorption in RPE melanosomes.[1–6]

Low-Intensity Treatment

All therapeutic effects of STL arise from RPE cells affected, but not killed, by laser exposure, through thermal activation and enhanced function of intra-RPE heat-shock proteins (HSPs).[3–6,10] As an enzymatic threshold phenomenon, the response at the cellular level is switch-like; "on/off," all-or-nothing, rather than graduated.[10] Treatment intensities exceeding the HSP activation threshold increase the risk of retinal damage but do not improve therapeutic effects. Designed to respond to acute existential threats, HSP activation is catalytic; initiating reparative cascades within the cell, locally, and systemically to normalize function.[3–6,11] The therapeutic range (TR) is the zone wherein treatment is therapeutically effective and safe, sublethal to the retina. The breadth of the TR, and thus likelihood of clinical treatment safety, varies markedly depending on laser mode and parameters.[4,5] The TR is broadened and safety maximized by use of longer wavelengths, longer pulse durations, and low-frequency pulse trains[4,5,10] (Table).

High-density Treatment

Normalization of RPE function at the cellular level requires amplification to achieve and maximize therapeutic clinical effects. This is accomplished by confluent treatment of broad areas of dysfunctional retina to recruit and normalize the RPE en masse. The most common error with modern retinal laser therapy is undertreatment; characterized by too few spot applications, of insufficient density, over too small areas [2–6]

Titration?

Titration of laser treatment intensity is an idea rooted in the photocoagulation era, which used immediately visible physical, rather than invisible physiologic, endpoints. Titration is discouraged by LIGHT because it increases the likelihood of unintended retinal damage.[4,5] Instead, LIGHT recommends use of published "fixed" laser parameters (identical settings in all eyes) shown to be reliably safe and effective (Table).

Technique

Bearing in mind the action of STL is mediated through the RPE, an extensive RPE area must be treated to maximize clinical outcomes.[4] Thus traditional targeted focal and local treatment is discouraged. For most applications, we consider panmacular treatment the optimal approach.[6] In panmacular treatment, the entire retina between the vascular arcades is "painted" with confluent laser spots, several times over in a single treatment session, to ensure complete coverage and avoid undertreatment. The number of laser spots required depends on the spot size. For example, panmacular treatment with a 125-μm spot may require 2000 shots, whereas a 500-μm spot requires only 400 to 450. STL can be used like a drug to treat the entire retina, repeated as necessary, and used in conjunction

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Table. Example Treatment Parameters for Various Laser Modes and Settings and Effects on Therapeutic (Clinical Safety) Ranges

Laser Mode	Wavelength (nm)	Retinal Spot (um)	Power (Watts)	Duty Cycle (%)	Spot Duration (Seconds)	Therapeutic Range[g] (Watts)
Nano[a]	532	400	~24(mJ)[d]	CW	3×10^{-9}	0
Micro[b]	532	100	~ 0.117[d]	CW	0.00002	0.010
MP[8] [c,e]	577	105	0.250	5	0.20	0.29
MP[6] [c,e]	810	210	1.4	5	0.15	4[h]
MP [c,e,f]	810	525	1.7	5	0.30	15[h]

[a]Nanosecond continuous wave (CW).
[b]Microsecond CW.
[c]Micropulsed.
[d]Estimate, by titration.
[e]Fixed, published.
[f]Fixed, currently preferred; used in over 20,000 consecutive panmacular treatments (Luttrull, unpublished data 2020).
[g]Calculated difference between the laser power at given laser parameters required for reaching the activation threshold of 1.0 for the Arrhenius integrals of the therapeutic reset effect (lower limit of TR) and the 50/50 risk of thermal cell death (upper limit of TR).
[h]Note that the TR of these 810nm laser parameters exceed the maximum available power of current retinal lasers allowing use in all eyes of all patients for all indications, safely and effectively.

with surgery or drugs to maximize management options and treatment outcomes.

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