The Role of the New Generation of Lasers in Retina

BY VICTOR CHONG, MD, FRCS, FRCOPHTH

Through the years, laser has evolved dramatically. Although intravitreal injections have become the first line of treatment of macular pathologies such as diabetic macular edema (DME), laser application within clinical settings continues to prove efficacious in macular conditions.

When introduced more than 50 years ago, macular laser was initially used as a photocoagulator to destroy lesions. Today, the newest lasers can be customized to deliver energy in different ways by varying power settings, shortening duration, and employing a train of pulses to achieve a targeted endpoint. To fully comprehend how new lasers are different from each other, and to ensure its proper clinical use, it is important to examine how and why lasers work, how laser is delivered, and how the target tissue in the retina reacts.

The evolution of the laser treatment of DME illustrates this topic well:

At the very beginning, we simply learned to "shoot the red dots," in order to perform a direct coagulation of the leaking microaneurysms. However, it was not uncommon to miss these microaneurysms and to discover that the treatment remained effective.

We gradually learned that most of the laser energy is absorbed primarily by melanin in the retinal pigment epithelium (RPE) and the choroid. Furthermore, it is believed that the energy induces a change in the RPE cells, changing the microenvironment, which improves the edema instead of directly destroying the microaneurysms. This led to a debate of "light" versus "classic" laser treatment for clinically significant DME. The idea was to reduce power to obtain a barely visible burn but still have microaneurysm absorption. This was considered to be the threshold point separating the power needed to cause a color change in the neurosensory retina during the procedure visible to the surgeon. As some retinal specialists alternatively defined threshold as needing a clearly visible reaction, this inherently led to the question, "If we don't see a reaction, is the treatment effective?"

SUBTHRESHOLD LASERS AVAILABLE ON THE MARKET

	SubLiminal	Endpoint management/ Non-damaging	Nanosecond/Rejuvenation
Duration of laser in each pulse	0.1 ms	10 to 20 ms	0.000003 ms
OCT change after treatment	None visible	Clearly visible	Seen in some cases
AF imaging after treatment	None visible	Clearly visible	No published data but RPE changes visible on color fundus photos
Randomized controlled trials published	Several in DME and CSC	None	Reduced AMD progression (in post-hoc analysis)

Figure 1. Comparison of available subthreshold lasers available on the market.

CONVENTIONAL VERSUS SUBTHRESHOLD LASER PHOTOCOAGULATION

Conventional continuous-wave laser photocoagulation has been used to treat different macular retinal diseases for many years. As an example, the treatment settings for DME were defined by the ETDRS study in 1987.[1] These treatment settings were thermal laser therapy and based on the idea of obtaining a clearly visible reaction while lasering. Reported complications in patients with DME who undergo ETDRS laser include scotoma, visual field defects, and chorioretinal atrophy.[2]

To address these risks, and to implement a process of delivering more energy with minimal damage, less-invasive laser treatments were introduced. This paved the way for subthreshold laser photocoagulation. Subthreshold, using micropulsing, has shown efficacy without any visible changes on the retina.[3] Indeed, if the energy is reduced, the reaction can barely be seen, and we are able to achieve a positive clinical effect with no visible scarring.

Nowadays, three main types of subthreshold retina lasers are available on the market:

Endpoint Management (Topcon) is based on continuous delivery with decreased power levels and duration in an attempt to achieve no visible scarring with positive clinical effect. Though this approach makes sense in theory, it is unclear how this translates in clinical practice. To date, there is only one case series[4] showing clinical success without retinal damage on central serous chorioretinopathy (CSC). There are no controlled trials published in the treatment of DME,

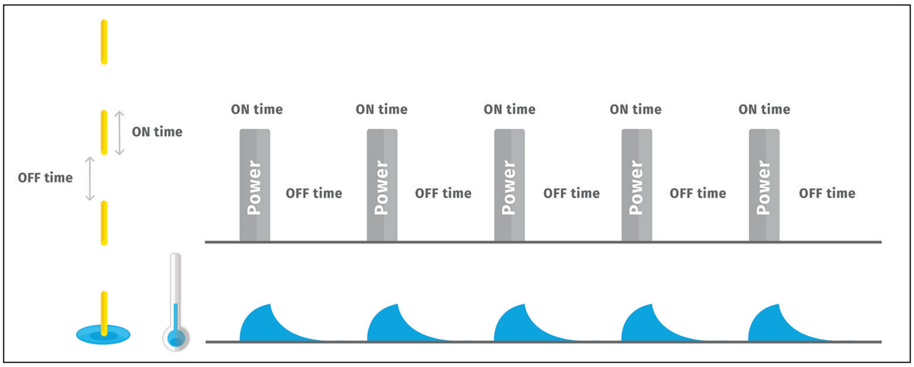

Figure 2. SubLiminal laser therapy treatment: Train pulse.

however, independent investigators have reported scarring and changes to RPE visible by using fundus autofluorescence imaging and OCT.

The 2RT nanosecond laser (Ellex) is using similar specifications to selective laser trabeculoplasty (SLT laser). 2RT treatment energy is based on power testing to a threshold color change and uses short pulse duration (0.000003 ms) and multiple beams delivered at 400-µm spot size (Figure 1). 2RT is thought to cause RPE death without damage to the retina. Nevertheless, it is causing some "RPE changes," which could be considered as scarring.

Its use to stimulate a natural, biological healing response to slow the degenerative process that causes retinal diseases, such as intermediate age-related macular degeneration (iAMD), has recently started to garner some attention. However, a controlled clinical trial (LEAD study[5]) demonstrating the slowing of AMD progression failed to meet its targeted endpoint. Only a post-hoc analysis excluding the reticular pseudodrusen demonstrated a slowing of the pathology, so it remains to be seen how effective 2RT will be.

SubLiminal laser therapy (Quantel Medical) offers laser energy delivery through a series of extremely short (microsecond) laser pulses (Figure 2). SubLiminal laser therapy is based on a stimulation concept, which allows for a cooling period between pulses resulting in no visible scarring (even with fundus autofluorescence imaging and OCT), and no detectable photoreceptor loss. This further results in the improvement of retinal sensitivity in edematous retina and reading speed, while also preventing retinal damage.

The latest SubLiminal laser uses a 577-nm true yellow wavelength that provides peak absorption of oxyhemoglobin, excellent lesion visibility, low intraocular light scattering and pain, and negligible xanthophyll absorption. With these absorption characteristics, the subliminal laser 577-nm yellow wavelength has the versatility of the 532-nm green wavelength yet causes less scatter, uses lower energy levels,[6] and also allows titration as compared with 810-nm infrared laser.

CLINICAL STUDIES SHOWING THE BENEFITS OF SUBLIMINAL LASER

Quantel Medical's technology allows a combination of multispot and SubLiminal delivery modes and features a customizable macular grid allowing the surgeon to customize the treatment area of the edema on the macula. In CSC, studies[7] have demonstrated that SubLiminal laser therapy is a promising alternative treatment strategy. The study concluded that SubLiminal laser is an effective treatment even in patients without sufficient improvement after photodynamic therapy. As I am confident in SubLiminal laser therapy for treating DME and CSC, I wonder what other retinal diseases could be treated? Evidence supports SubLiminal laser therapy can be used to supplement treatment in idiopathic polypoidal choroidal vasculopathy cases with suboptimal response to anti-VEGF treatment. Currently, there are several clinical trials using SubLiminal laser therapy for AMD. The goal is to show that SubLiminal laser therapy could also remove drusen and potentially slow the evolution of AMD without the limits of 2RT.

CONCLUSION

What we know today about SubLiminal laser therapy encourages us to move away from using conventional laser for macular treatment. In addition to the study of SubLiminal laser therapy on AMD, there are other exciting studies taking place right now to examine SubLiminal laser contributions to other retinal diseases, including retinitis pigmentosa, Stargardt disease, and geographic atrophy. I encourage you to monitor future updates, follow industry leaders conducting ongoing studies, and implement the technologies available to you today. ■

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Victor Chong, MD, FRCS, FRCOphth
- Consultant Ophthalmic Surgeon, Optegra Eye Hospital, London, United Kingdom
- victor@eretina.org
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