

PHOTOBIO-MODULATION: INNOVATION ON THE HORIZON FOR DRY AMD

A novel, noninvasive therapeutic approach may stave off vision loss.

By Richard B. Rosen, MD



Photobiomodulation (PBM) is a photostimulation therapy delivered using light-emitting diodes at targeted wavelengths to enhance cellular function. In the setting of disease, normal metabolic processes may be interrupted or corrupted and may benefit from additional energetic support to encourage restoration of function. PBM is a minimally invasive method of stimulating mitochondrial energy production to help restore cellular processes and produce observable clinical benefits.

PBM therapy has been studied for decades in many models of biological stress and injury and has shown positive benefits for a variety of musculoskeletal, neurological, inflammatory, and painful indications and, more recently, in ophthalmic disease.¹⁻³ Over the past decade, more than 30 published studies have explored

the value of PBM for ocular conditions. Here, I share the mechanisms of action and recent clinical trial findings that demonstrated the positive effects of multiwavelength PBM in ophthalmology.

PBM MECHANISMS OF ACTION

The primary mechanism of action for PBM appears to affect bioenergetic output, although other functions may also be affected. Mitochondria are the organelles in the cell that are critical for energy production, maintaining cellular function, and controlling cell survival. The retina is one of the most energy-demanding organs in the body, with energy requirements that exceed those of the brain. Retinal cells—including the retinal pigment epithelium (RPE), retinal ganglion cells, and photoreceptors—have high concentrations of mitochondria, and considering their

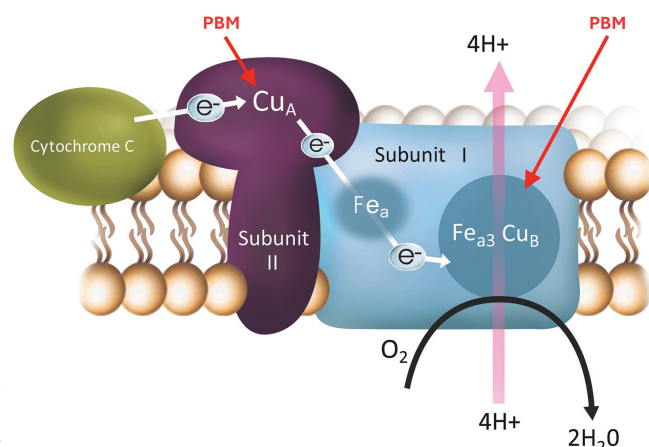


Image courtesy of Lumithera

Figure 1. Photobiomodulation therapy targets photo-acceptors in the mitochondria to improve bioenergetic output.

AT A GLANCE

- ▶ Photobiomodulation (PBM) is a promising new therapeutic approach for the treatment of dry AMD and other ocular diseases.
- ▶ PBM interacts with subcellular processes to boost the energy output through mitochondrial pathways, which helps to restore normal metabolic function.
- ▶ A randomized clinical trial evaluated multiwavelength PBM in patients with dry AMD and achieved statistically significant improvement in visual acuity gain through 24 months.

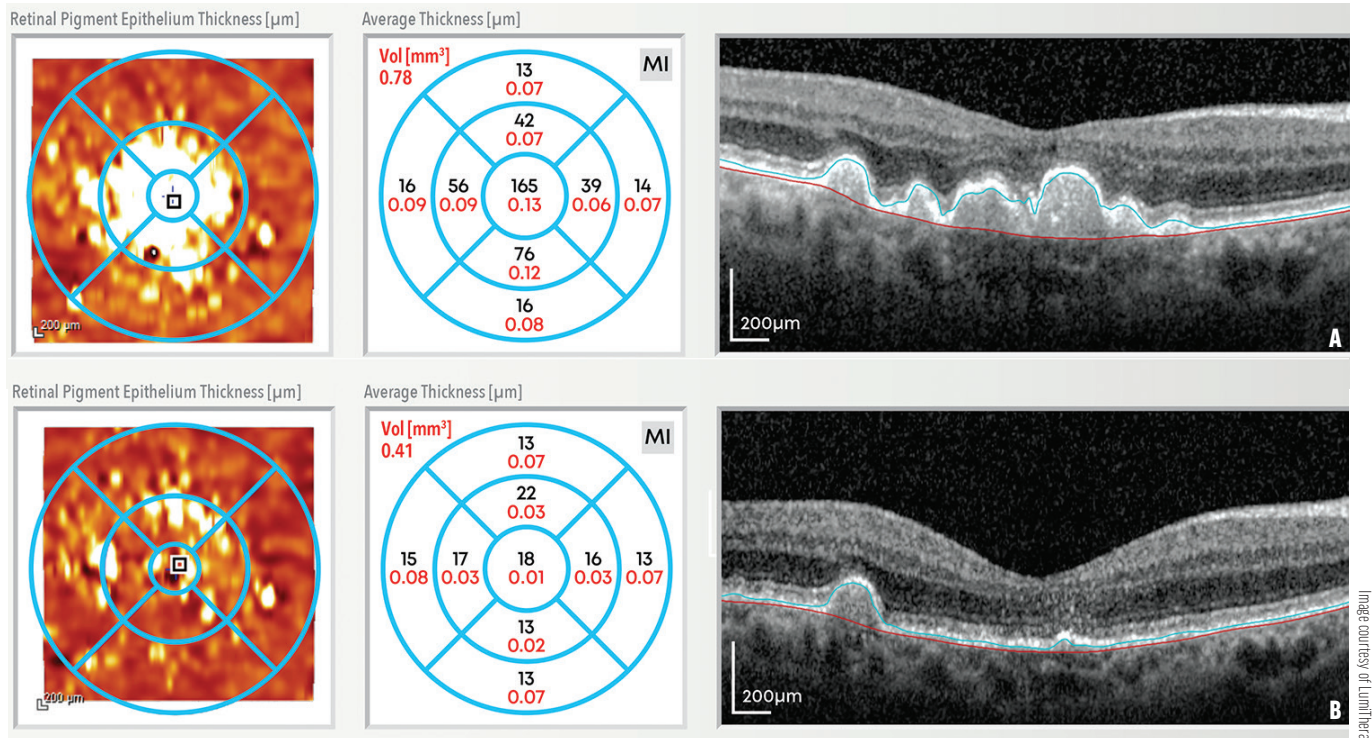


Figure 2. This patient, who participated in the LIGHTSIGHT study, experienced a reduction in drusen from baseline (A) over 12 months following PBM treatment (B).

intense energy demand, mitochondrial dysfunction can have immediate and devastating effects on retinal health.⁴

As we age, retinal cells show a functional decline in mitochondrial energy output, which contributes to cellular waste buildup, hampering function.⁴ PBM is absorbed by mitochondrial cytochrome c oxidase in the electron transport chain, thus stimulating energy production in the cell. Increased energy availability promotes intrinsic cell functions that aid in cellular repair processes and reduce potential further cell dysfunction and damage.⁵⁻⁷

Mechanistically, the ability of PBM to directly influence energy generation and subsequent bioenergetic output of the cell is hypothesized to underlie improved clinical and anatomical outcomes in degenerative disease states, such as AMD (Figure 1). The unique and direct activity of PBM at the mitochondrial level provides an appealing interventional strategy to potentially improve mitochondrial dysfunction at early signs of disease.

While some ocular PBM studies have targeted ocular conditions using single wavelength approaches, others, such as those investigating the Valeda Light Delivery System (LumiThera), employ yellow (590 nm), red (660 nm), and near-infrared (850 nm) wavelengths. This multiwavelength approach targets several enzyme sites to stimulate mitochondrial output and modify degenerative processes. This combination offers multiple opportunities for engagement in the cellular system, improving the odds of enhancing cellular outcomes and subsequent clinical benefits.^{8,9}

THE CLINICAL TRIAL

The LIGHTSITE III clinical trial evaluated the long-term safety and efficacy of multiwavelength PBM treatments in patients with early and intermediate dry AMD (Figure 2). In this 24-month, double-masked, prospective study, participants were randomly assigned to PBM or sham treatment groups (2:1) and received one series of treatment (nine sessions delivered three times a week over 3 to 5 weeks) every 4 months.

The study met the primary visual acuity efficacy endpoint at month 13 (after four series of PBM treatment) with a statistically significant difference between the PBM and sham treatment groups ($P = .02$) and a gain of 5.4 letters in the PBM group, which was further increased to 5.9 letters at month 24 ($P < .0001$). Participants showed improvements in quality of life and anatomical outcomes following PBM treatment.

A reduction in the progression of AMD to later stages of the disease was observed, as well as a favorable safety profile with no signs of phototoxicity.^{10,11}

POTENTIAL CLINICAL IMPLICATIONS

PBM is not a cure for AMD, and retreatment is necessary to maintain the benefits and potentially further enhance the effects over time. While most patients saw beneficial effects after one series of treatment, clinical benefits in visual acuity were more pronounced at 24 months after six series of treatments. The extension study currently

THE AMD TREATMENT LANDSCAPE

underway will add additional long-term data on the effect of PBM over time.

The positive findings from the LIGHTSITE III trial in AMD align with published reports showing the benefit of PBM in other ocular indications, such as diabetic macular edema, retinitis pigmentosa, Stargardt disease, myopia, and retinopathy of prematurity.¹²⁻²⁰ With the growing evidence supporting PBM therapy in ophthalmology, further research is underway to develop diagnostics that can rapidly detect response and help clinicians tailor treatment regimens for individual patients. ■

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