

device technology

Photobiomodulation shows the power of light

Study results demonstrate effectiveness in treating dry age-related macular degeneration

By Roberto Pinelli, MD; Special to Ophthalmology Times®

Age-related macular degeneration (AMD) is an eye disease that leads to vision loss and can cause blindness. The dry form affects 80% of individuals with AMD; it tends to progress more slowly than the wet type and results in a subsequent loss of visual acuity.¹

At present, there is no approved treatment or cure for the dry form. In dry AMD, drusen form beneath the macula, causing a progressive loss of central vision over time.

However, several studies with strong and moderate evidence in the past 5 years have shown encouraging results in treating eye diseases, such as AMD,^{1,12} retinopathy of prematurity, and diabetic macular edema, with a technique known as photobiomodulation (PBM).⁷⁻¹⁰

PBM has also been used in the last 20 years for musculoskeletal pain, injury, dysfunction, and wound healing; to improve acute muscle performance and reduce muscle damage after exercise;⁷ and for neuropathic pain, lymphedema, and oral mucositis.^{1,3-15} PBM, or low-level light therapy, is the application of monochromatic light to a part of the body with the aim of repairing tissues and reducing inflammation, edema, and pain.⁷

The process is not a heat therapy, but is more akin to photosynthesis in plants. Light, in the far red and near-infrared spectral range, can stimulate the cells, which leads to a cascade of photochemical reactions. The low-powered light is absorbed locally by the cytochrome c oxidase; mitochondrial energy is then produced by releasing oxygen, which results in increased adenosine triphosphate concentration and reduced oxidative stress. This photochemical reaction then activates enzymes and second messengers, leading to a cellular and, indirectly, systemic response by tissues that have not absorbed photons.^{1,16,17}

PBM can be used in acute and chronic eye diseases such as dry AMD, as mitochondrial dysfunction and oxidative stress play a key role in many macular diseases.^{1,7,11} The technique does not worsen the disease, has no side effects, and is completely noninvasive.^{1,18} The protocol we use provides a combination of 9 PBM therapies.

PBM is performed through a medical device which applies light-emitting diodes (LEDs) to stimulate cel-

lular function and improve energy production. Each cycle of therapy delivers wavelengths between 590 nm and 850 nm for 4 minutes per eye. The PBM cycles are completed in approximately 1 month.

Clinical outcomes are determined using an optical coherence tomography (OCT) test; an Amsler grid, to detect wavy, broken, or distorted lines; a Pelli-Robson chart, for assessment of contrast sensitivity; a Snellen chart, for far visual acuity (VA); and a Jaeger chart, for near VA. The outcomes are measured at the end of the PBM procedure, after 3 months and after 6 months.

The clinical results of a case after PBM are shown in **Figure 1**. Nine PBM cycles were administered to a patient over 1 month. After 1 month and 6 months, the OCT scan showed reduced drusen. The patient obtained

subjectively improved vision, less eye strain, more color contrast, higher definition, and better far and near uncorrected VA. Contrast sensitivity improved from 1.8 to 2.0. Outcomes remained stable at the 6-month follow-up.

This case demonstrates a successful noninvasive treatment with improved quality of vision in dry AMD. Irradiation could, therefore, offer a new, noninvasive, adverse effect-free means of stimulating retinal stem cells to regenerate.

PBM is a treatment whereby quality of vision is improved and not worsened in some patients suffering from dry AMD, leading to better VA and contrast sensitivity and a less damaged macular profile. Overall, these results are encouraging and indicate how protocols could be consolidated in the future.

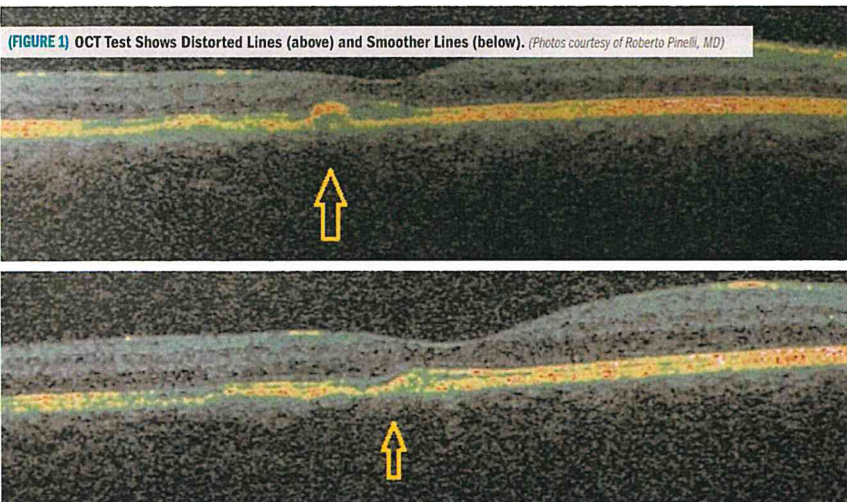
Promoting cellular regeneration by using light waves represents a challenge in ophthalmology. To date, there are no approved theories for many retinal diseases. Intriguingly, this protocol seems to offer an extremely promising approach to prevent VA from worsening and to promote tissue repair in the dry form of AMD. Moreover, the approach has the enormous advantage of being entirely noninvasive.

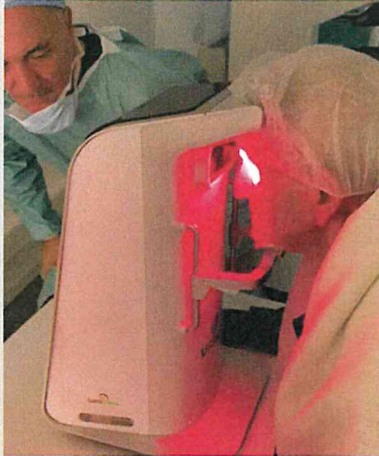
According to this hypothesis, at certain wavelengths, irradiation could regenerate retinal cells.

Thus, modulated light can offer a novel, valid

TAKE-HOME

► **Modulated light can offer a novel valid therapeutic approach for dry AMD, which may facilitate the repair of damaged tissues in the retina and promote the survival and function of epithelial cells within the retinal pigmented epithelium.**

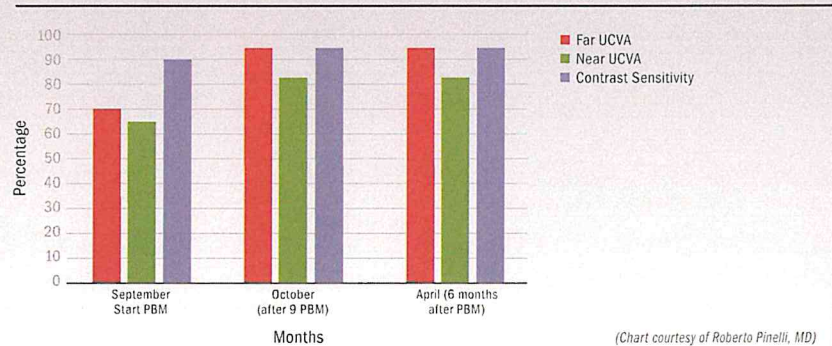




Ophthalmologists can use photobiomodulation to treat chronic eye diseases, such as dry AMD. The technique does not worsen the disease, has no side effects and is non-invasive.

(Photos courtesy of Roberto Pinelli, MD)

Figure 3. Far Uncorrected Visual Acuity, Near Uncorrected Visual Acuity, and Contrast Sensitivity Progression Before and 6 Months After Treatment



(Chart courtesy of Roberto Pinelli, MD)

therapeutic approach for dry AMD, which may facilitate the repair of damaged tissues in the retina and promote the survival and function of epithelial cells within the retinal pigmented epithelium.¹⁹ ■

Miorica Bertelli, OD, and Elena Scaffidi, MS, contributed to this report.

REFERENCES

1. Markowitz SN, Devenyi RG, Munk MR, et al. A double-masked, randomized, sham-controlled, single-center study with photobiomodulation for the treatment of dry age-related macular degeneration. *Retina*. Published online August 9, 2019. doi:10.1097/IAE.0000000000002632
2. Forte R, Cennamo G, Finelli ML, Bonavolontà P, de Crecchio G, Greco GM. Combination of flavonoids with Centella asiatica and Melilotus for diabetic cystoid macular edema without macular thickening. *J Ocul Pharmacol Ther*. 2011;27(2):109-113. doi:10.1089/jop.2010.0159
3. Khoo HE, Ng HS, Yap WS, Goh HJH, Yim HS. Nutrients for prevention of macular degeneration and eye-related diseases. *Antioxidants (Basel)*. 2019;8(4):85. doi:10.3390/antiox8040085
4. Pawlowska E, Szczepanska J, Koskela A, Kaarimirta K, Blasiak J. Dietary polyphenols in age-related macular degeneration: protection against oxidative stress and beyond. *Oxid Med Cell Longev*. 2019;2019:9682318. doi:10.1155/2019/9682318
5. Riva A, Togni S, Franceschi F, et al. The effect of a natural, standardized bilberry extract (Mirtoselect) in dry eye: a randomized, double blinded, placebo-controlled trial. *Eur Rev Med Pharmacol Sci*. 2017;21(10):2518-2525.
6. Tao Y, Chen T, Yang GQ, Peng GH, Yan ZJ, Huang YF. Anthocyanin can arrest the cone photoreceptor degeneration and act as a novel treatment for retinitis pigmentosa. *Int J Ophthalmol*. 2016;9(1):153-158. doi:10.18240/ijo.2016.01.25
7. Hamblin MR. Photobiomodulation or low-level laser therapy. *J Biophotonics*. 2016;9(11-12):1122-1124. doi:10.1002/jbio.201670113
8. Merry G, Devenyi R, Dotson R, Markowitz SN, Reyes SV. Treatment of dry age-related macular degeneration with photobiomodulation. Paper presented at: Association for Research and Vision in Ophthalmology 2012; May 7, 2012; Fort Lauderdale, FL.
9. Natoli R, Valler K, Barbosa M, et al. 670nm photobiomodulation as a novel protection against retinopathy of prematurity: evidence from oxygen induced retinopathy models. *PLoS One*. 2013;8(8):e72135. doi:10.1371/journal.pone.0072135
10. Tang J, Herda AA, Kern TS. Photobiomodulation in the treatment of patients with non-center-involving diabetic macular oedema. *Br J Ophthalmol*. 2014;98(8):1013-1015. doi:10.1136/bjophthalmol-2013-304477
11. Ferraresi C, Kaipert B, Avci P, et al. Low-level laser (light) therapy increases mitochondrial membrane potential and ATP synthesis in C2C12 myotubes with a peak response at 3-6 H. *Photochem Photobiol*. 2015;91(2):411-416. doi:10.1111/php.12397
12. Koev K, Avramov L, Borissova E. Clinical results from low-level laser therapy in patients with autosomal dominant cone-rod dystrophy. *J Phys: Conf Ser*. 2018;992:012060. https://iopscience.iop.org/article/10.1088/1742-6596/992/1/012060
13. Holanda VM, Chavantes MC, Wu X, Anders JJ. The mechanistic basis for photobiomodulation therapy of neuropathic pain by near infrared laser light. *Lasers Surg Med*. 2017;49(5):516-524. doi:10.1002/lsm.22628
14. Baxter GD, Liu L, Petrich S, et al. Low level laser therapy (photobiomodulation therapy) for breast cancer-related lymphedema: a systematic review. *BMC Cancer*. 2017; 17(1):833. doi:10.1186/s12885-017-3852-x
15. Zadik Y, Arany PR, Fregnani ER, et al. Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/ International Society of Oral Oncology (MASCC/ISOO). Systematic review of photobiomodulation for the management of oral mucositis in cancer patients and clinical practice guidelines. *Support Care Cancer*. 2019;27(10):3969-3983. doi:10.1007/s00520-019-04890-2
16. Natoli R, Zhu Y, Valler K, Bisti S, Eells J, Stone J. Gene and noncoding RNA regulation underlying photoreceptor protection: microarray study of dietary antioxidant saffron and photobiomodulation in rat retina. *Mol Vis*. 2010;16:1801-1822.
17. Gkotsi D, Begum R, Salt T, et al. Recharging mitochondrial batteries in old eyes. Near infra-red increases ATP. *Exp Eye Res*. 2014;122:50-53. doi:10.1016/j.exer.2014.02.023
18. Huang YY, Chen ACH, Carroll JD, Hamblin MR. Biphasic dose response in low level light therapy. *Dose Response*. 2009;7(4):358-383. doi:10.2203/dose-response.09-027.Hamblin
19. Saini JS, Temple S, Stern JH. Human retinal pigment epithelium stem cell (RPESC). *Adv Exp Med Biol*. 2016;854:557-562. doi:10.1007/978-3-319-17121-0_74

ROBERTO PINELLI, MD

E: pinelli@seri-lugano.ch

Roberto Pinelli, MD, is founder of the Switzerland Eye Research Institute in Lugano.