In this RWC column we will discuss:

- Photobiomodulation for Non-Neovascular AMD;
- High Definition TRD with NGENUITY1.5;
- Retinopathy of Prematurity.

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**HOT TOPIC IN THE WORLD OF RETINA**

# Photobiomodulation for Non-Neovascular AMD

Submitted by: Marion R. Munk, MD, PhD; David Boyer, MD; Eric H. Souied, MD, PhD

A new frontier in treating dry age-related macular degeneration (dry AMD) has emerged with the Food and Drug Administration (FDA) clearance of photobiomodulation (PBM).[1] As this innovative approach begins to take shape, questions linger about its potential impact. Our experts share their insights in navigating the nuances of this developing field.

***Marion R. Munk, MD, PhD:*** The management of dry AMD is an evolving field with recent advancements transforming the treatment landscape. Historically, patients with dry AMD had limited options and were typically advised only to make lifestyle changes and take vitamin supplements. Dry AMD patients were monitored for progression of disease and offered anti-vascular endothelial growth factor (anti-VEGF) injections upon advancement to neovascular AMD (nAMD). The limited treatment landscape has been discouraging to patients and providers alike. In recent years, injectable treatments for advanced dry AMD/geographical atrophy (GA) and PBM treatment for early/intermediate stage dry AMD patients have emerged as new and approved therapies for this patient population.

Photobiomodulation is a noninvasive light-based therapy that utilizes specific wavelengths to induce biological changes in the target cells to improve bioenergetic output. This is important in retinal disease as the retina is the most energy-demanding organ in the body and mitochondrial dysfunction has long been linked to degenerative disease states. Interest in the utility of PBM as a treatment for dry AMD has led to considerable research exploring the potential benefit across case reports, pilot, and randomized controlled trials (RCTs). The most robust data for the use of PBM in dry AMD was collected from the LIGHTSITE series of RCTs using the Valeda® Light Delivery System (Valeda, Lumithera). Valeda delivers multi-wavelength PBM treatment with yellow (590 nm), red (660 nm), and near-infrared (850 nm) wavelengths that act on multiple cellular targets to improve retinal health and vision outcomes. The pivotal 24-month LIGHTSITE III trial evaluated Valeda in intermediate dry AMD patients and showed significant benefit in vision observed with an average vision gain of > 1-line improvement measured via the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart. At month 24, approximately 63.7% of PBM-treated eyes responded with $a \geq 5$ letter gain (mean of 8.8 letters), 18.7% of PBM-treated eyes responded with $a \geq 10$ letter gain (mean of 12.8

**RWC KIRK PACKO VIDEO GALLERY CASE OF THE MONTH**

# High Definition TRD with NGENUITY 1.5

Submitted by: Rohit Agrawal, MBBS, MSOphthal, FVRS; Vitreo-Retina, Uvea and ROP Services, Rohit Eye Hospital and Child Care Center, Indore, India

https://retinaworldcongress.org/surgical/ high-definition-retina-trd-with-ngenuity-1-5/

In this video, the surgical management of a tractional retinal detachment (TRD) in a diabetic patient using the Ngenuity 1.5 digital visualization platform is demonstrated. This video highlights the advantages of the new tissue detail mode, which provides enhanced clarity of fine membranes and retinal layers, allowing safer and more precise dissection. Step-by-step approach to complex TRD surgery including various ways of dissection and peeling the membrane, the practical benefits of high-definition 3D visualization during surgery, and how advanced technology can transform the surgical experience for the surgeon is demonstrated.

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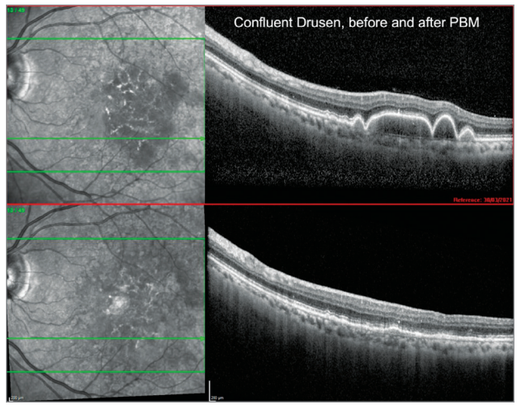


**Figure 1.** Spectral domain optical coherence tomography (OCT) before and after photobiomodulation (PBM). Top panel: OCT image of the left eye of a 64-year-old woman with large confluent drusen, exhibiting visual acuity of 20/40. Bottom panel: Comparative OCT scan 6 months after a single series of PBM treatments. The PBM regimen consisted of nine sessions (three times a week for three consecutive weeks) using the Valeda device. Image courtesy of Eric H. Souied.

letters), and 4.4% of PBM-treated eyes responded with $a \geq 15$ letter gain (mean of 16.3 letters). The trial also showed additional benefits such as a significantly reduced risk to progress from intermediate AMD to GA and an improved quality of life.[2-5]

In 2024, the FDA authorized marketing of Valeda treatment for dry AMD patients to improve vision.[1] Valeda is CE marked in the European Union, UKCA marked in the United Kingdom, and is available in select countries in Latin America. Photobiomodulation represents a new biotechnology and is an important milestone in this field that allows for treatment earlier in the course of disease and represents a unique modality that can improve vision with potential disease-modifying effects.

***David Boyer, MD:*** The LIGHTSITE III trial was a double masked, randomized, sham control multicenter trial that utilized three different wavelengths of light: 590, 660, and 850 nm. These wavelengths have been shown experimentally to improve mitochondria function, boost ATP production, reduce oxidative stress and inflammation, and promote cell survival.

To be included in the study, eyes have to have at least three medium drusen (> 63 µm and ≤ 125 µm in diameter) and/or non-central GA, and vision between 20/32 and 20/100. Exclusion criteria included the presence of a choroidal neovascular membrane or the presence of GA within 1 mm from the center of the fovea. Patients received light therapy 3 times a week for 3 weeks with a resting period of 4 months and retreatment every 4 months utilizing the same criteria. The study included 100 patients that were randomized 2 to 1. The trial met its primary predetermined endpoint of improvement of best-corrected visual acuity (BCVA) at month 21 with a gain of almost 6.2 letters versus sham of 2.4 letters. Best-corrected visual gains, percentage of vision losses, and quality of life measurements all favored the active PBM treated group. Post hoc analysis showed many anatomic improvements, including decreased drusen volume, decreased progression to GA, reduction of progression (iRORA) to complete reticular pseudodrusen-associated with outer retinal atrophy (cRORA), though it is important to remember this was post hoc analysis and the numbers of patients in each group was small. The study showed excellent safety. There were no signs of phototoxicity. There seemed to be a slight increase in conversion to nAMD compared to the sham group, though the conversion rate was similar to other FDA-approved treatments for GA. There are several ongoing studies, including the Eurolight registry, an open-label, retrospective and prospective study with at least 500 patients, as well as the LIGHTSITE 3B study that will provide more longitudinal data to substantiate the efficacy of this noninvasive treatment.[2-5] At present, I am treating patients with 20/40 or less vision, large drusen volume, and patients with iRORA not near the fovea, with light therapy.

***Eric H. Souied, MD, PhD:*** The LIGHTSITE studies demonstrated significant results for regression of large drusen and visual acuity. However, these results raise several questions.

The first question is the reproducibility in independent studies and in real life. To answer this question, we made a study on a series of 20 eyes affected with large confluent drusen. In this prospective single-center pilot study, we evaluated the effectiveness of PBM in 20 eyes with dry AMD featuring large soft drusen and/or drusenoid pigment epithelial detachment (dPED). Patients received 10 PBM sessions (two per week for 5 weeks) using the Valeda light delivery system. At 6 months, BCVA significantly improved by an average of 5.5 letters ($P = 0.007$), and quality of life (QoL) increased by 3.07 Visual Function Questionnaire (VFQ-25) points ($P = 0.05$). Drusen volume and central drusen thickness decreased significantly. Geographic atrophy showed minimal progression (+0.06 mm²), suggesting a potential protective effect. No major adverse events were reported.[6] In real life, we still do not understand why PBM shows remarkable effects in some patients and no or mild effects in others.

Second, in parallel to large drusen, PBM therapy was evaluated in patients with reticular pseudodrusen (RPD). Although visual acuity remained stable, a shift in RPD stages was observed: stage 3 RPD decreased whereas stage 1 increased after 6 months, suggesting potential regression of advanced lesions.[7]

The third issue at hand concerns patient acceptability and their ability to attend multiple treatment sessions per week. Our elderly patients are often dependent on caregivers, and the number of ophthalmology centers currently offering this treatment remains limited.

Expanding the number of centers closer to patients could represent a practical solution. Moreover, alternative treatment protocols—other than the current 3 times per week for 3 weeks schedule—should be evaluated. Finally, to address the variability in therapeutic response, personalized treatment protocols may emerge in the coming years (**Figure 1**).

## REFERENCES

1. FDA Roundup: November 5, 2024. U.S. Food & Drug Administration. Accessed August 12, 2025. https://www.fda.gov/news-events/press-announcements/fda-roundup-november-5-2024
2. Merry GF, Munk MR, Dotson RS, Walker MG, Devenyi RG. Photobiomodulation reduces drusen volume and improves visual acuity and contrast sensitivity in dry age-related macular degeneration. *Acta Ophthalmol.* 2017;95(4):e270-e277. https://doi.org/10.1111/aos.13354 PMID:27989012
3. 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.* 2020;40(8):1471-1482. https://doi.org/10.1097/IAE.0000000000002632
4. Burton B, Parodi MB, Jürgens I, et al. LIGHTSITE II randomized multicenter trial: evaluation of multiwavelength photobiomodulation in non-exudative age-related macular degeneration. *Ophthalmol Ther.* 2023;12(2):953-968. https://doi.org/10.1007/s40123-022-00640-6 PMID:36588113
5. Boyer D, Hu A, Warrow D, et al. LIGHTSITE III: 13-month efficacy and safety evaluation of multiwavelength photobiomodulation in nonexudative (dry) age-related macular degeneration using the Lumithera Valeda light delivery system. *Retina.* 2024;44(3):487-497. https://doi.org/10.1097/IAE.0000000000003980 PMID:37972955
6. Benlahbib M, Cohen SY, Torrell N, Colantuono D, Crincoli E, Amoroso F, Semoun O, Jung C, Souied EH. Photobiomodulation therapy for large soft drusen and drusenoid pigment epithelial detachment in age-related macular degeneration: a single-center prospective pilot study. *Retina.* 2023 1;43(8):1246-1254. https://doi.org/10.1097/IAE.0000000000003805
7. Le HM, Mehanna CJ, De Rosa I, Miere A, Souied E. Effects of photobiomodulation in patients presenting with reticular pseudodrusen: a retrospective observational case series study. *Medicina (Kaunas).* 2022;58(11):1662. https://doi.org/10.3390/medicina58111662 PMID:36422201

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RETINA ROCKS IMAGE GALLERY CASE OF THE MONTH

# Retinopathy of Prematurity

Submitted by: Kanwaljeet Harjot Madan, MS-Ophthalmology, FAICO;
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This 4-year-old girl's parents noticed that her right eye was deviating outwards for several months, along with decreased vision bilaterally. Her mother gave a history of prematurity at 28 weeks gestational age with a low birth weight of 1,175 grams and oxygen exposure. Upom presentation, visual acuity was counting fingers in the right eye and 20/80 in the left eye. There was a large right exotropia.

Fundus photography in her right eye shows a prominent retinal fold extending from the optic disc to the inferotemporal periphery (**Figure 1**). Diffuse chorioretinal scarring is noted surrounding the retinal fold. The left retinal vessels are dragged inferotemporally with marked foveal ectopia.

Retinopathy of prematurity (ROP) is a potentially blinding vasoproliferative disease occurring in premature infants. Although multifactorial, current screening guidelines are based primarily on low birth weight and gestational age.[1] Screening and treatment for these eyes is extremely subspecialized, with treatment options primarily including timely scatter laser photocoagulation and intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections.[2]

Patients with ROP have an increased risk for vision-threatening complications, including vitreous hemorrhage and retinal detachment, throughout their lives.[3] We should therefore monitor these patients regularly.

This case is from the Retina World Congress' Retina Rocks (retinaworldcongress.org/retina-rocks), the world's largest online, open-source image gallery and reference library.

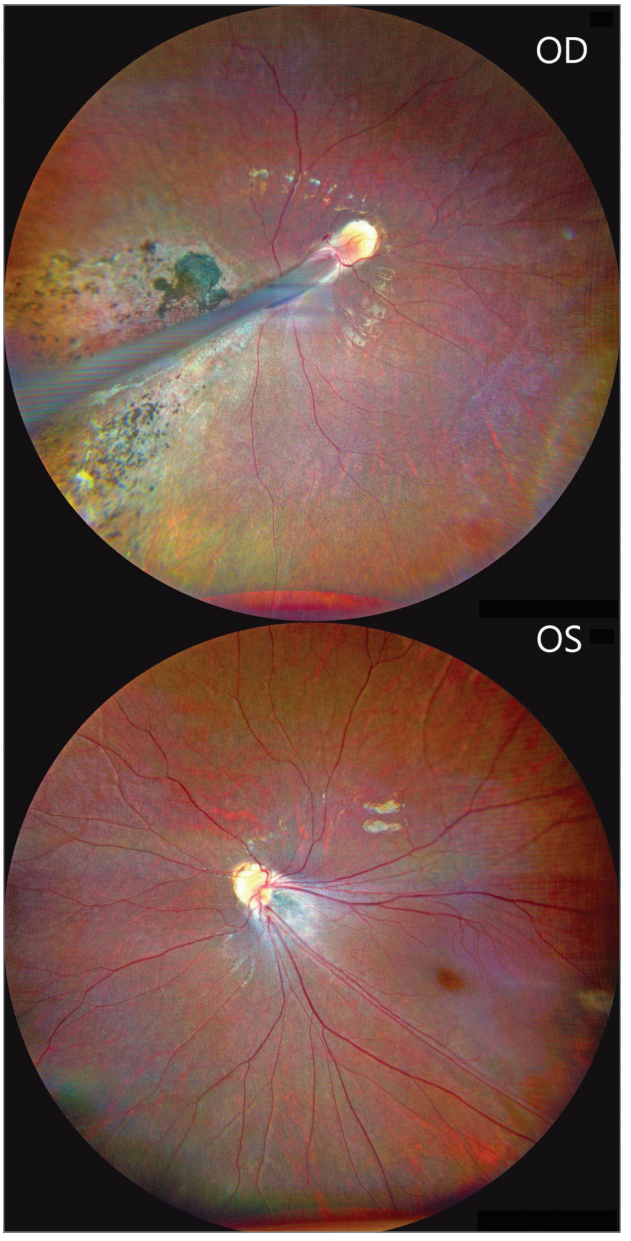


**Figure 1.** Right eye: there is a prominent retinal fold extending from the optic disc to the inferotemporal periphery. Diffuse chorioretinal scarring is noted surrounding the retinal fold. Left eye: the retinal vessels are dragged inferotemporally with marked foveal ectopia.

## REFERENCES

1. Kim SJ, Port AD, Swan R, Campbell JP, Chan RVP, Chiang MF. Retinopathy of prematurity: a review of risk factors and their clinical significance. *Surv Ophthalmol*. 2018;63(5):618-637. https://doi.org/10.1016/j.survophthal.2018.04.002 PMID:29679617
2. Yonekawa Y, Thomas BJ, Thanos A, et al. The cutting edge of retinopathy of prematurity care: expanding the boundaries of diagnosis and treatment. *Retina*. 2017;37(12):2208-2225. https://doi.org/10.1097/IAE.0000000000001719
3. Hsu HT, Yu-Chuan Kang E, Blair MP, et al. Late vitreoretinal complications of regressed retinopathy of prematurity: retinal break, vitreous hemorrhage, and retinal detachment. *Ophthalmol Retina*. 2023;7(1):72-80. https://doi.org/10.1016/j.oret.2022.07.005 PMID:35843486