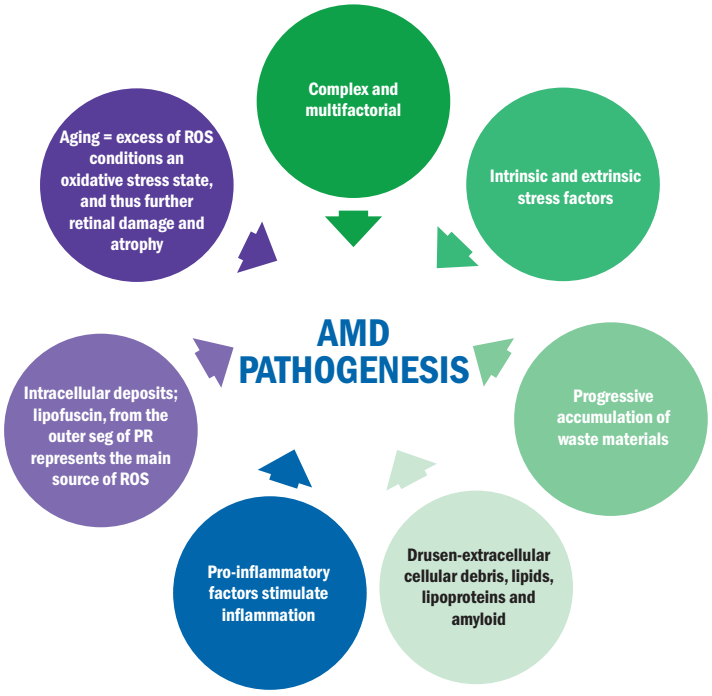
Let there be light therapy

Sarah Farrant discusses low level light therapy and its gamechanging applications in the field of clinical eye care

Only a few times in my career have I stumbled across something so revolutionary and new that it has excited me to my core. And while I know I can get a little over-excited and passionate sometimes, I yet again find myself gazing into the face (or mask) of another gamechanger in the world of optometry and ophthalmology. In this article I will delve into the science behind low level light therapy (LLLT) and its varied clinical implications in eye care.

Natural light affects our biology, from how well we sleep, to our brain function and immune response. Light is the primary signal that synchronises our circadian rhythms, we have specialised retinal cells that detect light and send signals to the suprachiasmatic nucleus in the brain, regulating hormone production and suppressing melatonin during daylight. Vitamin D synthesis occurs due to exposure to UVB in the skin, and natural light exposure has long been associated with higher levels of serotonin (neurotransmitter that helps regulate mood). The advent of light therapy as a means to treat and heal is not a new one. The ancient Egyptians were the first recorded civilisation to recognise the use of light as a healing agent, using solar radiation to heal chronic wounds and ulcers as far back as 5000BCE. This makes light therapy one of the oldest therapeutic methods used by humans.

FIGURE 1 **The pathogenesis of dAMD is complex and associated with inflammation and ageing. ROS (reactive oxygen species)**



LLLT, also referred to as photobiomodulation (PBM), was first reported on in the late 1960s[1] when shaved mice's hair grew back quicker when exposed to LLLT in what was, as is so often the case in epic discoveries, a happy accident looking into carcinogenicity. Nasa also investigated LLLT for plant growing experiments in space and, in subsequent experiments, found enhanced cellular proliferation and wound healing with the potential use realised for reducing tissue atrophy and photo-rejuvenation in astronauts.[2]

PBM involves the application of non-thermal, low-intensity light in the visible to near-infrared (NIR) spectrum to stimulate cellular function and promote tissue repair. The mechanism of action is thought to be mediated primarily through the absorption of light by mitochondrial chromophores, particularly cytochrome c oxidase (COX)[3], which plays a crucial role in the electron transport chain and ATP production. By enhancing mitochondrial function, LLLT has been shown to reduce oxidative stress, increase cellular energy production, and modulate inflammatory pathways[4] – all of which are implicated commonly in the pathophysiology of ageing and disease including both dry eye disease (DED) and dry age-related macular degeneration (AMD). With this in mind, LLLT has been used very successfully in managing DED (particularly related to meibomian gland dysfunction) for a number of years and has indeed been postulated in studies to be even more effective when directly compared to intense pulsed light (IPL) therapy.[5]

AMD is a leading cause of irreversible vision loss in individuals over the age of 50, with the dry (non-exudative) form accounting for approximately 85-90% of cases.[6] The prevalence rate of AMD in Europeans has been shown to be 12.33%, in Asians 7.38%, and Africans 7.53%.[7] Despite the prevalence of dry AMD, treatment options have remained limited, primarily focusing on lifestyle modifications, nutritional supplementation and patient education. Complement factor inhibitors have been explored since 2023 as a potential therapeutic option to help inhibit the rate of geographic atrophy progression.

Ageing, disease or injury can result in mitochondria producing too much nitric oxide, which in turn results in:

- Inhibited electron transport in mitochondria and reduced membrane potential
- Competitive displacement of oxygen from COX, which shuts down the production of ATP
- Displaced oxygen causes oxidative stress by an overproduction of reactive oxygen species (ROS)

The retina is one of the highest oxygen consuming tissues in the →

FIGURE 2 Advantages of LLLT. From Rola, P; Włodarczak, S; Lesiak, M; Doroszko, A and Włodarczak, A. Changes in Cell Biology under the Influence of Low-Level Laser Therapy. *Photonics*, 2022, 9, 502

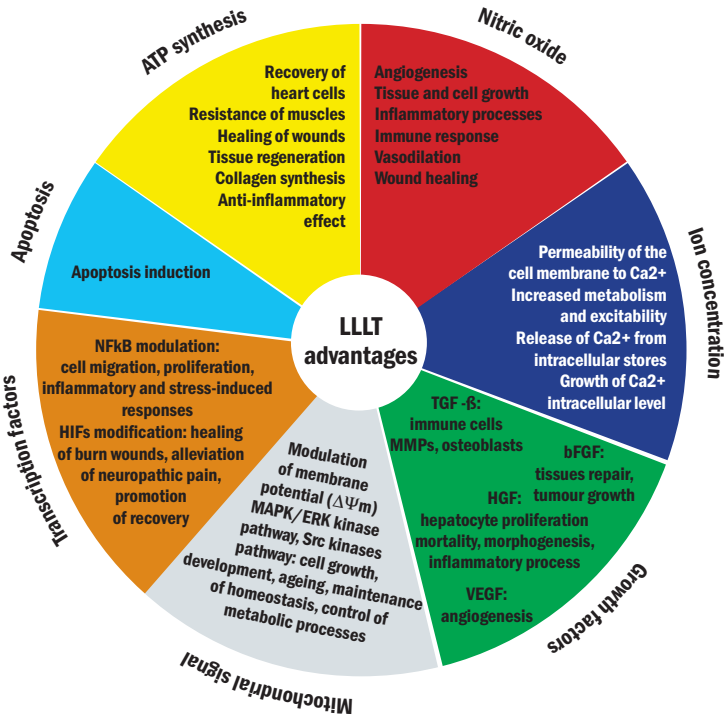


FIGURE 3 Eye-light device with an anterior segment mask (white shell) and a dAMD mask (dark shell)

body by weight, using more oxygen than the brain, with its most basic function being the conversion of light into vision. These processes require a lot of energy, gained via cellular metabolism pathways and respiration, but these processes generate a variety of ROS – the usual by-products of oxidative metabolism. Problems only tend to occur when generation of ROS exceeds the capacity of antioxidant systems to overcome them but abnormal cellular respiration processes can ultimately cause decreased metabolism and premature cell death.

Looking at the overall AMD pathogenesis, inflammation covers a primary role for the onset and progression both of wet and dry forms. Inflammation is a swift and intense response to potential threats, triggered by various factors such as heightened toxicity, proinflammatory mediators and intracellular components released into the extracellular space due to cellular degeneration.

The retina is susceptible to oxidative damage due to the significant amount of ROS production linked with the following:

- RPE exposed to high ambient oxygen partial pressure
- RPE is the outer blood-retinal barrier
- Photoceptor outer segments phagocytosed in RPE
- Vit A metabolism
- Photo-oxidative stress caused by light exposure and absorption at macula
- Short wavelengths (UV and blue) can induce ROS formation in retina and RPE

It has also been hypothesised that photooxidative stress may damage lipids, proteins and DNA and be responsible for most cytotoxicity.

In recent years, low-level light therapy (LLLT) has emerged as a promising therapeutic intervention for mitigating disease progression (see figure 2) and improving visual function.[8] As optometrists increasingly encounter patients with dry AMD, understanding the role of LLLT in clinical practice and how this can extend beyond dry eye disease treatment is essential. By enhancing mitochondrial function, LLLT has been shown to reduce oxidative stress, increase cellular energy production and modulate inflammatory pathways – all of which are implicated in the pathophysiology of dry AMD.

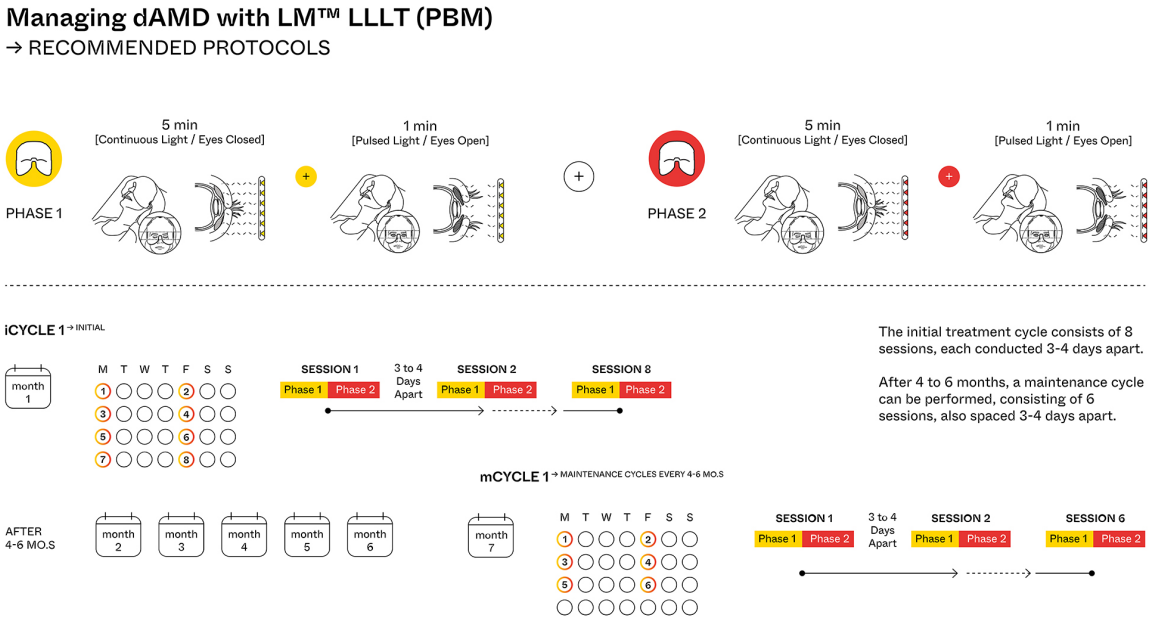
Studies suggest that, in relation to dry AMD, LLLT can:

- Reduce oxidative stress and inflammation in the retina
- Improve mitochondrial function and ATP synthesis in retinal cells
- Enhance retinal cell survival and function
- Improve visual acuity and contrast sensitivity[9]
- Induce remodelling of choriocapillaris[10]

Given these potential benefits, LLLT has garnered significant interest as a non-invasive therapeutic option for dry AMD, particularly in cases where conventional management strategies are insufficient. Its primary indications are for patients falling into the AREDS 2 and AREDS 3 categories (early and intermediate dry AMD).

Several clinical studies have investigated the efficacy of LLLT in patients with dry AMD, with promising results. One of the most well-known studies is the Lightsite I trial,[11] which demonstrated significant improvements in visual acuity, contrast sensitivity and patient-reported outcomes following PBM treatment. The study reported sustained visual improvements over several months, suggesting that LLLT may have lasting therapeutic effects. Subsequent trials, including Lightsite II and III,[12] have continued to explore the benefits of LLLT in a larger patient population, reinforcing its potential role. Existing research suggests LLLT is well-tolerated, with minimal adverse effects, making it an

FIGURE 4 Protocols for dry AMD treatment cycles in clinic, the initial cycle consists of eight sessions and maintenance cycles are six each time (approximately every four to six months)



attractive option for patients seeking non-invasive treatments.[13]

The Eye-light device is a neat unit, which can be table mounted or sit on its own wheeled unit. It consists of the main body, into which different reusable attachments can be selected from IPL, anterior segment LLLT masks (red, blue and yellow) and dry AMD LLLT masks (yellow and red). In dry AMD the red light exposure is directly associated with a significant increase in ATP. The wavelength is chosen based on its known interaction with the photo acceptors in COX, which leads to restoration of mitochondria function and an increase in metabolic activity as well as an inhibition in inflammatory events and cell death. The yellow light naturally inhibits expression of the signalling protein vascular endothelial growth factor (VEGF) that contributes to the development of wet AMD.[14]

The masks must be disinfected between each use using mediwipes in the clinic. Each mask comes pre-loaded with a set number of treatments. The system is very simple, such that a trained technician can easily conduct the LLLT treatments (not IPL) for patients. The protocols for dry AMD (see figure 4) are set according to research and are laid out as a specific guide to allow maximum benefit to patients undergoing treatment. There are two different masks with differing wavelengths – yellow and red. The contraindications include:

- Pregnancy
- Presence of active cancer in treatment area
- Hyper-photosensitivity to light or with history of light-induced nervous system disorders (eg epilepsy, migraines)
- Presence of non-removable piercings in treatment area
- Individuals with *herpes simplex* keratitis or a history within last three months

In our practice, we use a separate light therapy treatment room with a reclining chair to accommodate the system (figure 5). This allows consulting room chair time to be freed up, and only needed for periodic patient reviews and scans. The actual light treatment sessions are organised and carried out by well trained staff members running and overseeing the treatment clinics.

The treatment cycles for dry AMD are involved, with long term four to six monthly ongoing sessions required as maintenance schedules for as long as the patient wishes to continue receiving the treatment. The patient journey within the practice needs to be developed accordingly to incorporate the patient cycles as well as ongoing scans and acuity assessments, etc, in the clinics. Optometrists should establish standardised measures for assessing treatment outcomes, including best-corrected visual acuity (BCVA), contrast sensitivity, fundus imaging and patient-reported quality of life improvements. Objective measurements such as optical coherence tomography and fundus autofluorescence may help monitor retinal changes over time.

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CASE STUDY FOR DRY AMD TREATED WITH LIGHT THERAPY

A 77-year-old male with dry AMD (AREDS category 3) and baseline BCVA of 52 ETDRS (diabetic retinopathy test) letters. Put through the standardised protocol treatment sessions.

Three months after the end of the first treatment session, BCVA showed an improvement: from 52 to 56 (+4). Additionally, a complete resolution of some soft drusen was observed. OCT scan shows a marked reduction in the drusen volume within the macula (see figure 7)

LLLT represents an exciting and innovative approach to managing dry AMD, offering a non-invasive option for enhancing retinal function and improving visual outcomes. As the field advances, optometrists will play a pivotal role in translating research findings into clinical practice, ensuring patients with dry AMD have access to the latest evidence-based interventions.

As clinical evidence continues to accumulate, optometrists have an opportunity to incorporate LLLT into their practice, providing patients with additional therapeutic options beyond traditional management strategies. Using advances in technology like the Eye-light from Espansione Group, enables multimodal tools to treat a variety of common clinical issues with the joy of the footprint and cost of only one machine. By staying informed about emerging research and technological advancements, optometrists can contribute to the evolving landscape of dry AMD treatment and help improve the quality of life for those affected by this progressive condition.

FIGURE 6 A patient wearing the mask undergoing therapy

FIGURE 5 The light therapy room in our clinic doubles up as a dry eye and dry AMD light therapy treatment room

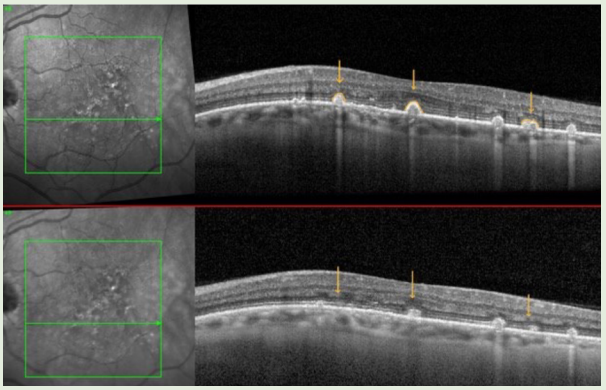

FIGURE 7 OCT scans depicting the marked change in drusen volume between baseline (top image) and four months after treatment (bottom image)

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