

New Horizons in Posterior Segment Care

LM[®] LLLT (PBM) for dAMD and Beyond





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Blocco 27, Via Degli Orefici 152 Centergross, Funo (BO) 40050, Italy

VAT NUMBER: IT 00707821203 TAX CODE: 00874760408 -WHY WE'RE HERE

Helping people, through science. That's the privilege we take pride in.

We have the ambition to establish new paradigms in ophthalmology, driven by our desire to provide our customers and their patients with the best, certified medical technologies.

The resonance of our tech has been incredible, with new scientific research building up at an impressive pace on known and new applications.

> POSTERIOR SEGMENT

dAMD



Scientific Papers

CSC



Scientific Paper

-WHERE WE ARE



 12^{+}

55+

Scientific Papers

Technology Patents

Countries

> ANTERIOR SEGMENT

> DED (MGD, CLD, ...)



4+

Scientific

Papers

Scientific Papers + Articles Scientific Articles

MICROBIOME STABILIZATION

& DEMODEX BLEPHARITIS

CHALAZION

Scientific Paper

SJÖGREN'S

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BLEPHARITIS

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Scientific Papers

CATARACT & REFRACTIVE SURGERY

5+

Scientific Paper

Enabling progress through science for the betterment of all isn't an easy purpose to work towards—yet it's our north star, the guiding principle of all our actions.

That's what guided us for over four decades. That's what moved us to become the one and only company to develop, patent and certify Light Modulation[®] LLLT, a unique photobiomodulation (PBM), technology.

With a strong focus on anterior segment care, we challenge the status quo in ophthalmology, innovate with care and ingenuity, and believe in the power of our people. We aspire to extend our leadership beyond ocular surface conditions into the posterior segment field, leveraging our decades-long expertise in photobiomodulation (PBM) technology.

Our goal is to redefine the management of posterior segment pathologies through the most optimized and disruptive light-based solutions.

We have always delivered the highest standard in the industry—pushed on by expert craftsmanship and family-owned values coupled with a global mindset and aspiration. Every day, we invest heavily in researching and developing the Espansione Ecosystem of technologies and solutions to achieve our ambition.

4



ESPANSIONE ECOSYSTEM > eye-light®





eye-light®

From the front to the back of the eye, an all-in-one powerhouse for eye care.

The Espansione Ecosystem offers a comprehensive range of certified medical devices, ensuring safety and reliability while meeting patient and operator needs.

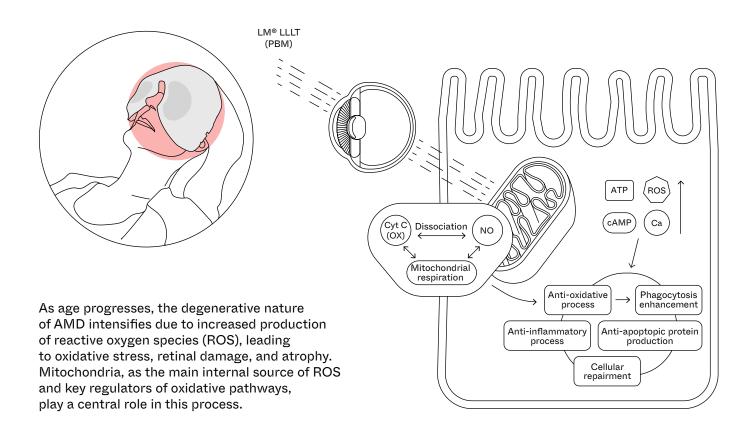
eye-light[®], our core solution, integrates our groundbreaking patented technology: Light Modulation[®] Low Level Light Therapy.

LM[®] LLLT already providing highly effective, non-invasive treatment for various ocular surface conditions, from Dry Eye Disease (DED) to Sjogren's Syndrome, is now venturing into posterior segment management starting with dAMD and CSC.

Discover LM[®] LLLT/PBM

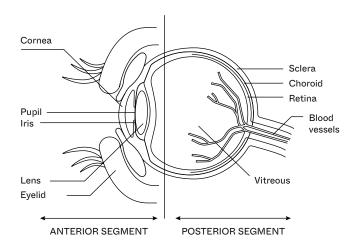
At the heart of our ecosystem lies Light Modulation[®] LLLT, our innovative, patented **photobiomodulation (PBM)** technology.

Utilizing powerful LEDs, LM[®] LLLT stimulates ATP production in cells, promoting healing and regeneration at the biological level. Enabled by LM[®] LLLT (PBM), photobiostimulation therapy is a unique kind of near-infrared light therapy (NILT) completely painless for the patient—yet extremely effective in managing a vast number of eye conditions, from the front to the back of the eye.



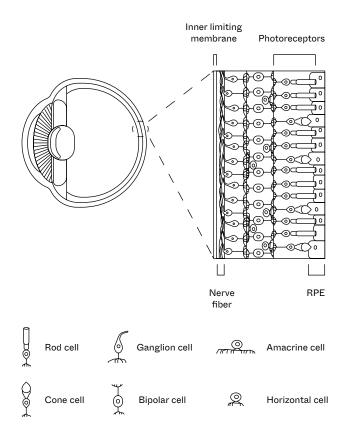
Photobiomodulation targets these mitochondrial dysfunctions effectively by stimulating ATP production and reducing oxidative stress, thus reducing the progression of AMD and supporting retinal health. **POSTERIOR SEGMENT > ABOUT RETINA**

The Posterior Segment of the eye comprises crucial structures like the retina, optic nerve, and vitreous body, and it plays a vital role in processing visual information.



Retina, operating as a camera's film, captures incoming light, transforms it into neural signals, and transmits these signals via the optic nerve to the brain, facilitating vision.

Each retina's component plays a role in maintaining the retina's ability to process visual information efficiently and accurately.



Photoreceptors, primarily rods and cones in the retina, are key for vision by converting light into neural signals.

Rods, sensitive to low light, enable night vision, while **cones**, located in the central macula, handle sharp, detailed vision and color perception under higher light levels.

Behind these, the retinal **pigment epithelium (RPE)** supports visual processing and retinal health through nutrient transport, light absorption, and oxidative stress protection.

Damage to photoreceptors and the RPE, as seen in conditions like age-related macular degeneration, can significantly impair vision.

AMD—leading cause of irreversible blindness in the developed world



NORMAL VISION



MACULAR DEGENERATION

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in the developed world, that predominantly affects individuals aged 60 and above.

Estimates suggest that nearly 50 million people worldwide are affected by AMD.

AMD is a progressive retinal disease that irreversibly impairs vision by damaging the macula, primarily affecting photoreceptors and the retinal pigment epithelium (RPE).

SOURCE: SCHULTZ NM, ET AL. "GLOBAL BURDEN OF DRY AGE-RELATED MACULAR DEGENERATION: A TARGETED LITERATURE REVIEW." CLIN THER. 2021;43(10):1792-1818.

-RISK FACTORS

















AGE

CIGARETTE SMOKING

GENETIC SUSCEPTIBILITY

IC HY BILITY

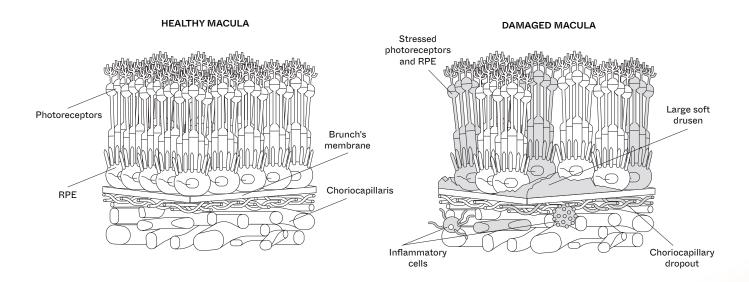
HYPERTENSION

FAMILY HISTORY

HYPERCHOLESTROLEMIA

NUTRITION

AMD > PATHOGENESIS & CLASSIFICATION



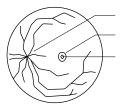
Age-related macular degeneration (AMD) involves complex factors including drusen formation, which significantly contributes to the disease's progression.

Drusen, accumulations of lipids, proteins, and debris between the retinal pigment epithelium (RPE) and Bruch's membrane, are not adequately cleared by RPE cells.

Their presence is a key risk factor for advancing to severe stages of AMD.

There are two main forms of AMD and they affect the eye in different ways:

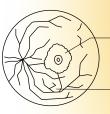
> Dry (Atrophic)> Wet (Exudative)



Optic Disc Macula Fovea Centralis



Drusen deposit buildup



Leaked blood and fluid

Abnormal blood vessels

NORMAL RETINA

DRY (ATROPHIC)

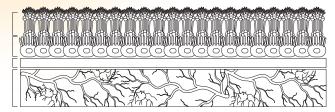
WET (EXUDATIVE)

AMD > DEFINITION & CLASSIFICATION

Dry AMD, which is also known as the atrophic or nonexudative form, represents the majority of AMD cases, accounting for about 90% of diagnoses.

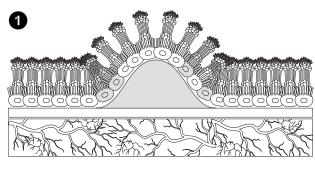
Photoreceptors RPE Bruch's Membrane

Choroid

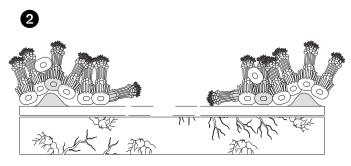


MACULA

It is characterized by the gradual accumulation of drusen [①]—tiny yellow or white deposits under the retina. As the RPE degenerates, it fails to support the photoreceptors effectively, leading to their gradual dysfunction and death.

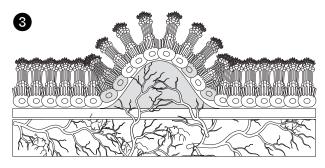


Drusen Formation in Dry AMD



Late AMD (Geographic Atrophy)

Geographic Atrophy (GA) [②] is the advanced stage of dry Age-related Macular Degeneration (AMD). It involves irreversible damage to the macula, characterized by the loss of retinal pigment epithelium (RPE) cells, photoreceptors, and the underlying choriocapillaris. The degenerated areas where the RPE has atrophied form "geographic" patches with map-like outlines.



CNV in Wet AMD

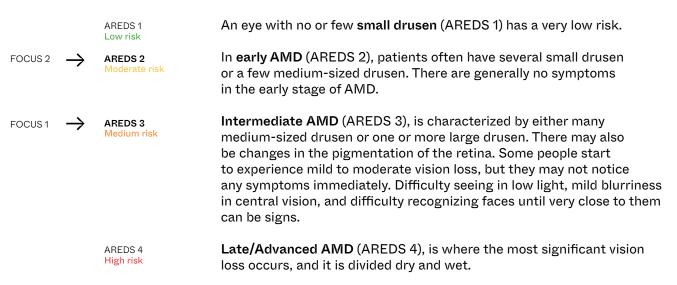
Wet AMD [③], also known as exudative AMD, is less common than dry AMD but progresses more rapidly to severe vision loss.

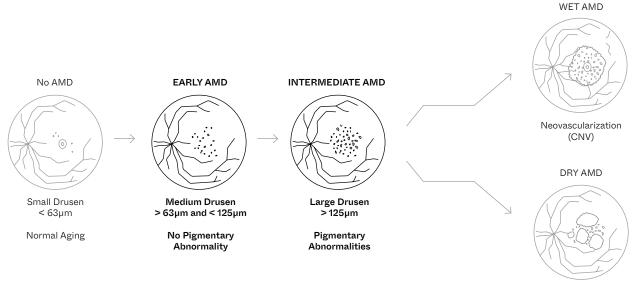
It is marked by the growth of fragile, abnormal blood vessels from the choroid behind the retina, a condition known as choroidal neovascularization (CNV). These vessels often leak fluid and blood, causing significant damage.

The leakage can elevate the macula, leading to pigment epithelial detachment (PED), distorting vision and causing rapid central vision loss. AMD > CLASSIFICATION

Age-related macular degeneration (AMD) is commonly classified based on its clinical presentation into early, intermediate, and late stages. The Age-Related Eye Disease Study (AREDS) provided a detailed classification system that is widely used in research and clinical practice.

Here's an overview of the classification:





Geographic Atrophy (GA) DRY AGE-RELATED MACULAR DEGENERATION > THE STATUS QUO

So far, no treatments have been proven to effectively prevent the onset of GA or to halt lesion enlargement and/or retard vision loss.^[1]

> Management focuses on risk factor reduction and use of dietary supplements. The approaches being investigated to reduce the rate of disease progression include:

1. Drugs with antioxidative properties

2. Inhibitors of the complement

3. Neuroprotective agents

4. Visual cycle inhibitors

- 5. Gene therapy
- 6. Cell-based therapies

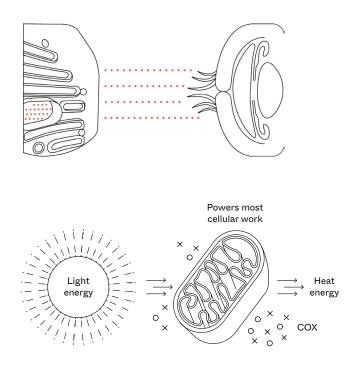
UNMET CLINICAL NEEDS...UNTIL NOW

For unmet clinical needs in dry AMD, the solution is Photobiomodulation (PBM).

This groundbreaking technology uses light therapy to promote cellular repair and regeneration, providing a promising new guideline for treating dry AMD, particularly for AREDS 3 and lower classifications. PBM addresses current management gaps, offering a scientifically backed method to potentially slow disease progression, preserve vision, and improve the quality of life for patients.

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LIGHT SCIENCE > THE POWER OF PBM



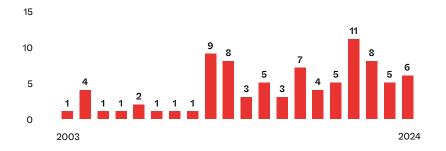
LM[®] LLLT, our patented photobiomodulation (PBM), involves targeted use of selected wavelengths of visible light to near-infrared light (500-1000 nm) produced by a laser or a noncoherent light source such as light-emitting diodes.

The primary effect of LM[®] LLLT is a localized transient stimulus of the absorbing chromophore based on electric or light oscillations.

Beneficial effects of LM[®] LLLT on the eye have been found in a wide array of ocular surface conditions, from **MGD** to **Sjögren's Syndrome**, from **Chalazia** all the way to the prevention of **Cataract** and **Refractive Surgery-induced latrogenic DED**.

Recent clinical research has highlighted increasing interest in PBM as a potential treatment for dAMD. Studies show that PBM improves visual acuity and decrease drusen volume.

These findings emphasize the effectiveness of PBM as a treatment and reflect the scientific community's dedication to broadening therapeutic approaches for dAMD.

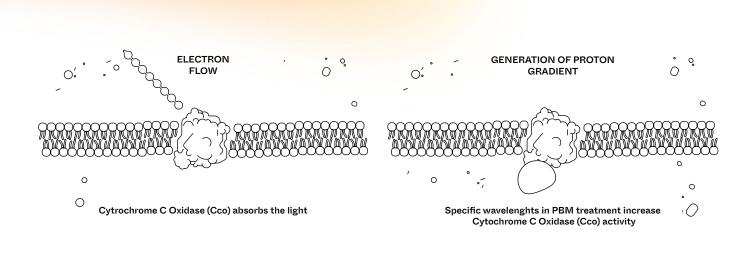




→ GO TO PUBMED WEBSITE

Read the Updates

PUBMED TIMELINE RESULTS BY YEAR / SEARCH QUERY: PHOTOBIOMODULATION AND AGE RELATED MACULAR DEGENERATION, MAY 2024

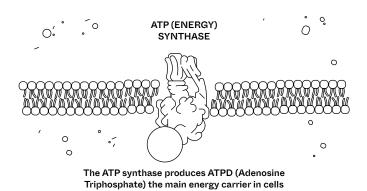


DRY AGE-RELATED MACULAR DEGENERATION > THE STATUS QUO

1

The initial photon absorption event occurs in the cellular mitochondria, and the principal molecule that absorbs the light is an enzyme called **Cytochrome C Oxidase (CCO)**. 2

When cells are damaged by disease or aging, the mitochondria within the cells produce excess nitric oxide (NO), which inhibits electron transport within mitochondria and decrease mitochondrial membrane potential.





Cellular respiration and methabolism are improved through increased ATP production

3

Light absorption triggers the photodissociation of NO from cytochrome c oxidase (CCO), facilitating its release. Given that NO plays a role in inhibiting electron transport, PBM's action leads to an increase in mitochondrial membrane potential, oxygen consumption, and the proton gradient, culminating in boosted ATP production. 4

PBM also reduces oxidative stress and **inflammation** and modulates cell signaling and gene expression.

PBM FOR AMD > MECHANISM OF ACTION

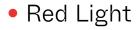


The Yellow light (590 nm wavelength) **naturally inhibits expression of vascular endothelial growth factor (VEGF)**, a signaling protein that stimulates the formation of blood vessels that contributes to the development of the wet-form of AMD.

It also increases the signaling protein, nitric oxide which reduces oxidative stress-mediated injury in the cell and increases local O2 delivery. Light absorption leads to NO dissociation from CCO, restoring mitochondrial function and increasing ATP production.

> Oxydative Stress Reduction> VEGF Inhibition> Oedema Reduction & Drainage





The Red (630 nm) light exposure is directly associated with a significant **increase in ATP**. The 630 nm wavelength is chosen based on its known interaction with cellular photo acceptors in CCO.

The 630 nm wavelength promote electron transfer and oxygen binding, respectively, in CCO leading to restoration of mitochondria function and increases in metabolic activity (i.e. energy production) and inhibition in inflammatory events and cells death.

> HIF-1α Factor Stimulus
> Inflammatory Biomarkers Reduction
> ATP Stimulus





PBM FOR dAMD > MECHANISM OF ACTION

A technology Like no other.

Operators and patients can enjoy the unique benefits of LM[®] LLLT technology.



- i. it's fast—a treatment lasts 12'
- ii. it's painless
- iii. it's easy and safe
- iv. it's plug&play—requires minimal training

De

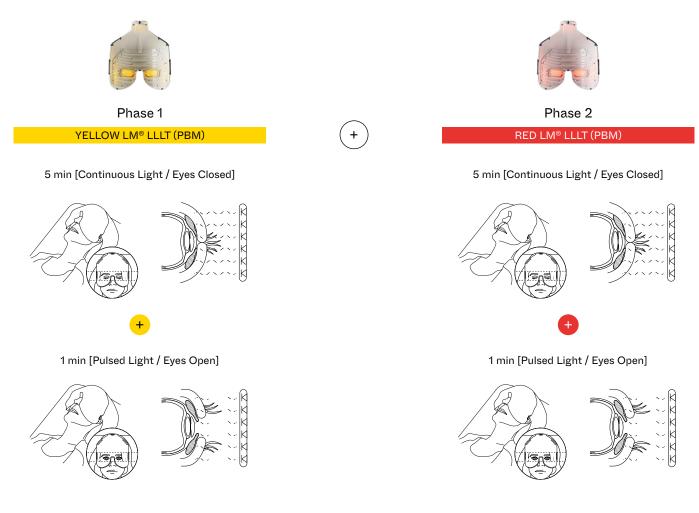
dAMD > RECOMMENDED PROTOCOL

LM[®] LLLT (PBM)



> IN-DEPTH SESSION SEQUENCE

In each session, there are two phases: Phase 1 involves wearing the LM[®] LLLT yellow mask for 6 minutes, during which the patient experiences 5 minutes of continuous light exposure with their eyes closed, followed by 1 minute of pulsed light with their eyes open. Phase 2 entails wearing a red mask for 6 minutes, with the same pattern of light exposure: 5 minutes continuous with eyes closed, and 1 minute pulsed with eyes open.



≥e

dAMD > RECOMMENDED PROTOCOL

LM[®] LLLT (PBM)



↓ FOCUS

The initial treatment cycle consists of 8 sessions, each conducted 3-4 days apart. After 4 to 6 months, a maintenance cycle can be performed, consisting of 6 sessions, also spaced 3-4 days apart.

iCYCLE 1 → INITIAL MTWTFSS 3 to 4 SESSION 1 SESSION 2 **SESSION 8** Days month Phase 1 Phase 2 Phase 1 Phase 2 Phase 1 Phase 2 Apart 1 300400 $(5) \bigcirc \bigcirc (6) \bigcirc \bigcirc$ (7) () () (8) ()AFTER month month month month month 4-6 MO.S 2 3 4 5 6 mCYCLE 1 → MAINTENANCE CYCLES EVERY 6-9 MO.S MTWTFSS 3 to 4 SESSION 1 SESSION 2 **SESSION 6** Days month Phase 1 Phase 2 Phase 1 Phase 2 Phase 1 Phase 2 Apart 7 $(3) \bigcirc \bigcirc (4) \bigcirc \bigcirc$ $5 \bigcirc \bigcirc \bigcirc 6 \bigcirc \bigcirc$



DOWNLOAD↓ LIGHTWAVE I CASE REPORT PRESS RELEASE LightWave I

LightWave I: First Dry AMD Multi-centric Study

A female subject, aged 68, diagnosed with Age-Related Macular Degeneration (AMD) classified under the Age-Related Eye Disease Study (AREDS) Category 3, was incorporated into the multicentric, randomized controlled investigation termed LightWave I.

At baseline, the subject's best-corrected visual acuity was quantified at 50 letters on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart. The subject underwent a regimen of photobiomodulation (PBM) employing Light Modulation® Low-Level Light Therapy (LM® LLLT) via the eye-light® system. The treatment protocol entailed bi-weekly sessions spanning a four-week duration.

Subsequent to a one-month interlude post the culmination of the therapy, a reevaluation of the subject's best-corrected visual acuity manifested an enhancement to 55 ETDRS letters. Additionally, a complete resolution of certain soft drusen was observed.

> CASE REPORT #1

[WOMAN, 68 Y/O, AREDS 3] CASE #1—Describes a 68-year-old female patient with AMD (AREDS Category 3) witnessed an improvement in visual acuity from 50 to 55 ETDRS letters post-treatment.



Figures 1, 2, and 3, which are retinal images of the identical eye, depict a marked decrement in the volume of drusen within the macular region, corroborating the therapeutic efficacy of the intervention.

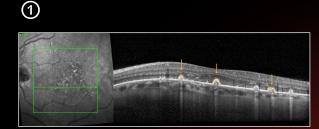
RESEARCH > LIGHTWAVE I > CASE REPORT #2

A female subject, aged 72, diagnosed with Age-Related Macular Degeneration (AMD) classified under the Age-Related Eye Disease Study (AREDS) Category 3, was included in the multicentric randomized controlled investigation termed LightWave I.

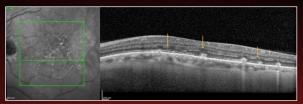
At baseline, the subject's best-corrected visual acuity was quantified at 52 letters on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart. The subject underwent a regimen of photobiomodulation (PBM) employing Light Modulation[®] Low-Level Light Therapy (LM[®] LLLT) via the eye-light[®] system. The treatment protocol entailed bi-weekly sessions spanning a four-week duration.

Subsequent to a one-month interlude post the culmination of the therapy, a reevaluation of the subject's best-corrected visual acuity manifested anenhancement to 56 ETDRS letters. Additionally, a marked decrement in the volume of certain soft drusen was observed.

[WOMAN, 72 Y/O, AREDS 3] CASE #2—Describes a 72-year-old female patient with AMD (AREDS Category 3) witnessed an improvement in visual acuity from 52 to 56 ETDRS letters post-treatment.







Figures 1 and 2, showing retinal images of the same eye, illustrate a significant reduction in drusen volume, confirming the effectiveness of the treatment.

RESEARCH > LIGHTWAVE I > CASE REPORT #3

A male participant, aged 55, was recruited with a diagnosis of n**on-neovascular age-related macular degeneration**.

The participant underwent a therapeutic regimen of Light Modulation[®] Low-Level Light Therapy (LM[®] LLLT) through the **eye-light**[®] solution.

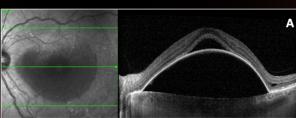
At baseline, the participant's best-corrected visual acuity was ascertained to be 25 letters on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart, and Spectral-Domain Optical Coherence Tomography (SD-OCT) revealed a substantial pigment epithelial detachment (PED) accompanied by subretinal fluid at its apex. The therapeutic protocol encompassed **one session per week for a duration of four weeks**, followed by one session **bi-weekly for an additional two months**.

At a one-month follow-up subsequent to the final treatment, there was a **complete reabsorption** of the subretinal fluid and a collapse of the pigment epithelial detachment, with no residual retinal atrophy. The best-corrected visual acuity was recorded at 60 ETDRS letters.

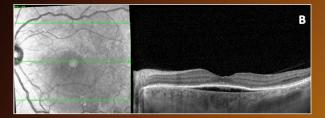
[MAN, 55 Y/O, NON-NEOVASCULAR AMD]

CASE #3—Describes a 55-year-old male patient diagnosed with non-neovascular AMD observed a staggering rise in visual acuity from 25 to 60 ETDRS letters, accompanied by pronounced therapeutic effects at the cellular level.

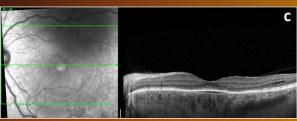




The picture delineates the SD-OCT images at **baseline** [①] which exhibit a pronounced pigment epithelial detachment (**PED**) with **subretinal fluid**. The SD-OCT image at the **one-month follow-up** [②] reveals a flattening of the PED with the persistence of flat PED accompanied by hyper/hyporeflective material. The SD-OCT image at the three-month follow-up [③] demonstrates further flattening of the PED. 2







RESEARCH > LIGHTWAVE I > CASE REPORT #3

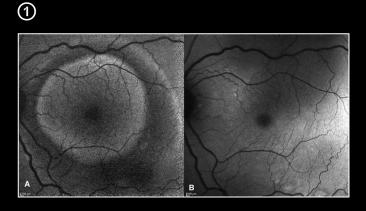


FIGURE 1

The exhibit portrays the baseline fundus autofluorescence (FAF) which exhibits a hyperautofluorescent ring at the periphery of the PED.

The three-month follow-up image reveals isoautofluorescence in the macular region without any legacy of retinal pigment epithelial atrophy. (2)

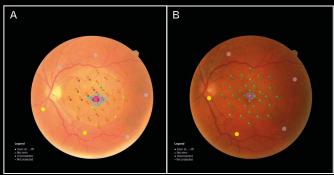


FIGURE 2

Illustrates the **microperimetry at baseline [A]** which shows a reduction in retinal sensitivity in the macular area with a mean value of 7.4 dB.

The microperimetry at the three-month follow-up [B] exhibits a significant enhancement in retinal sensitivity in the macular area with a mean value of 26.5 dB.

KEY BENEFITS IN dAMD TREATMENT

What are the benefits?

LM[®] LLLT delivers wavelengths of 590 nm and 630 nm in continuous and pulsed mode addressing independent cellular mechanisms that are important in age-related macular degeneration (AMD). Below are the key benefits offered:

 Visual Acuity Improvement

- ② Contrast Sensitivity Improvement
- ③ Central Drusen Volume Reduction
- Completely Painless Therapy
- ▲ dAMD remains a degenerative condition with no cure, but PBM potentially offers:
 - > Painless & Safe Therapy
 - > Drusen Volume Reduction w/ No Atrophy
 - > BCVA Improvement
 - > Contrast Sensitivity Improvement



LightWave II Seeing Beyond

We're **pioneering** what's next in retinal care through a second wave of **large-scale**, **global**, **multi-centric** research studies.



APPLY & JOIN LIGHTWAVE II CLINICAL TRIALS LightWave II





Not all solutions and use cases available in all countries. Every piece of information shown ought to be consideredas fact-based evidence deriving from publicly available literature, for the sole purpose of scientific exchange.

SCIENTIFIC COMMUNITY > KOLS



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A growing and heterogeneous community of prominent thought leaders actively support us in developing new applications and elevating posterior segment care.

Become Part of our Global Scientific Community!

Throughout the years, valued members of the scientific community have contributed to the resonance of Espansione technologies by publishing a vast array of research and scientific, peer-reviewed papers applications.



Explore the cutting-edge advancements with Espansione Group's Scientific Community.

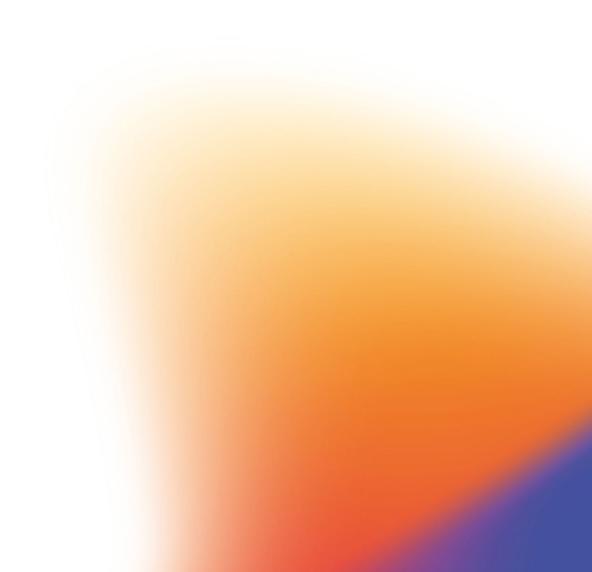
Join us for exclusive resources, expert-led webinars, and invaluable insights from global leaders in LM[®] LLLT and OPE[®] IPL technologies.



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Visit our Scientific Community to connect and grow with fellow innovators.

LM[®] LLLT —Our Journey



OUR JOURNEY

Founded with a strong focus on anterior segment care, Espansione Group has been a pioneer in ophthalmology, developing and patenting the innovative Light Modulation® LLLT technology.

Science told us. It just works.



Numerous clinical studies validate the effectiveness of LM[®] LLLT (PBM) in ophthalmology for a wide array of ocular surface conditions, from MGD to Sjögren's Syndrome, from Chalazia all the way to the prevention of Cataract and Refractive Surgery-induced latrogenic DED.

However, **the potential of ocular surface conditions extends beyond** direct treatment of ocular surface conditions, making the Espansione Ecosystem the optimal choice for enhancing your practice.

We have consistently been at the forefront of treating ocular surface conditions such as MGD, DED, and blepharitis, and we are now expanding our expertise to include posterior segment management.

Join us as we continue to challenge the status quo and innovate for the betterment of ocular health.

Discover the Science behind LM[®] LLLT

No pain, Extreme gains.

Photobiostimulation therapy enabled by LM[®] LLLT is a unique kind of near-infrared light therapy (NILT) that's completely painless for the patient —yet extremely effective in managing a vast number of Conditions.

Different wavelengths (Red, Blue, Yellow) are available for various applications, making it a versatile solution for both anterior and posterior segment conditions.

CERTIFIED FOR MEDICAL USE



Se



ON AMD

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Blocco 27, Via Degli Orefici 152 Centergross, Funo (BO) 40050, Italy

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