17TH INTERNATIONAL CONFERENCE OF THE RESEARCH INSTITUTE OF OPHTHALMOLOGY

RIO 2025

Anterior Segment Eye Diseases
Current Status & Future Directions

Photobiomodulation

By
Dr. M.Mohamed-Aly Ibrahim
MD, FRCS,
Ass.prof of ophthalmology
Al Azhar University -Cairo

WHAT IS Photobiomodulation?

- ✓ It is conversion of light energy to metabolic energy, with a corresponding change of cell's biological functions
- ✓ Also known as low-level laser therapy, and far-red to near-infrared (FR/NIR) light therapy.
- ✓ It consists of series of brief illumination with FR/NIR light (600-1000 nm) from a laser or a light emitting diode (LED).

History

- ✓ At the end of the 18th century Finsen (the "father of phototherapy“) had cured skin disorders such as
  - Small blisters using red light
  - lupus vulgaris using UV light.
- ✓ He won the 1903 Nobel Prize in Medicine and Physiology "in recognition of his contribution to the treatment of these diseases.
- ✓ Medical usefulness of FR/NIR light had been "re-discovered" for a second time upon the invention of the laser in the 1960s.

History 2

- ✓It happened due to unexpected research outcome where Mester attempted to use laser-derived 694 nm light to induce skin cancer in mice.
- He shaved the mouse fur covering the location where the light would be applied.
- Light caused the fur to re-grow faster in treated mice compared with untreated control (instead of inducing cancer).

Clinical applications

- ✓ Over the years, PBM was used in several conditions, with the majority having been explored in both animal models and human patients with a spectrum of:
- ✓ *Wound healing*: including diabetic ulcers.
- ✓ *Pain control:* for neurologic neck pain, and pain from chronic joint disorders.
- ✓ *Promotion of the regeneration and functional recovery of tissues with poor healing potential* such as:
  - injured peripheral and optical nerves.
  - recovery following stroke and other central nervous system damage such as traumatic brain injury.

Clinical application

- ✓PBM offers non-invasive therapeutic approach to challenging sight-threatening retinal conditions.
- ✓ **Potential targets include:**
  - Age-related macular degeneration (AMD),
  - Retinopathy of prematurity (ROP),
  - Diabetic retinopathy (DR)
  - Leber's hereditary optic neuropathy
  - Methanol-induced retinal damage
  - Amblyopia.
  - Glaucoma and possibly others.

RIO 2025

Mechanism of action

- ✓ Different wavelengths of light have different degrees of *absorption*, *scattering*, and *reflection* by biological media and tissues.
- ✓ Generally, biological tissues contain a range of chromophores such as:
  - *Water molecules* (significantly absorb light energy at wavelengths greater than 970 nm)
  - *Oxyhemoglobin (HbO2), deoxyhemoglobin (Hb), myoglobin, melanin, and flavins.* (absorb wavelengths shorter than 600 nm).
- ✓ For these reasons, there is an optical window for PBM therapy in the range of the red to NIR spectrum
  - *Cytochrome c oxidase in mitochondria*
  - *Light gated ion channels and opsins*

Mechanism of action 2

- ✓ In conventional laser medicine ***heating and burning*** are the prevailing mechanisms of action.
- ✓ PBM uses the photochemical conversion potential of low-intensity FR/NIR (630-1000 nm) light
- ✓ Studies in the late 1980s and 1990s that implicated mitochondria as the subcellular targets of FR/NIR. It was proposed by that cytochrome C oxidase inside

Cytochrome c oxidase in mitochondria

- ✓ Cytochrome C oxidase is the enzyme that catalyzes the transfer of electrons from cytochrome C to molecular oxygen-the final step in the mitochondrial respiratory chain and essential for the sustained availability of energy inside cells.
- ✓ *Nitric oxide (NO):*
  - Increasing the bioavailability of nitric oxide (vasodilator) by prompting its release from intracellular stores such as heme-containing proteins.

Cytochrome c oxidase in mitochondria

- ✓ 670 nm light completely reverses the ability of tetrodotoxin, (a sodium channel blocker capable of indirect down-regulation of cytochrome C oxidase)
- ✓ *PBM competed with potassium cyanide* (an irreversible inhibitor of cytochrome C oxidase)
- ✓ *NIR light reverses the inhibitory and toxic effect of formic acid* (the active metabolite in methanol intoxication), on mitochondrial cytochrome C oxidase in rat retinas, resulting in improved vision outcomes

Continue (neuroprotection)..

✓ *Direct effect of PBM on the gene expression and metabolism of photoreceptor cells:*

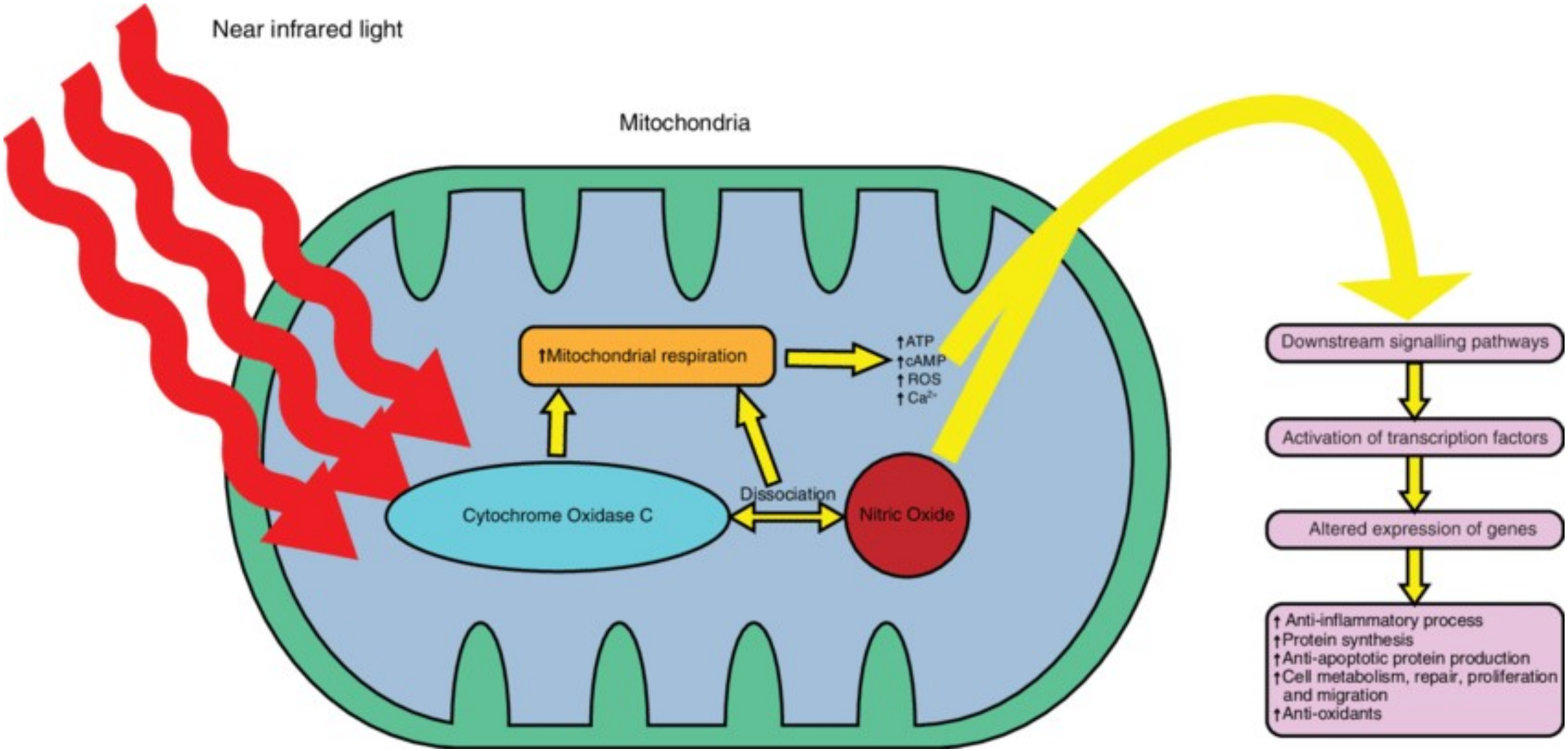
- Upregulation in the proteins that involve the mitochondrial respiratory chain and anti-oxidant genes
- Downregulation of genes implicated in apoptosis and the stress response.

✓ *PBM effect on susceptible stem cells, progenitor cells:*

- It has a potential in enhancing differentiation, which in turn improves the healing rate of tissues.

Mechanism of action Sum(PBM).

- increase ATP (energy) ,reduces oxidative
- Improves blood flow (vasodilatation)
- (stimulates neurogenesis & protect cells from
- Anti inflammatory effect


Near infrared light
Mitochondria
↑Mitochondrial respiration
↑ATP
↑cAMP
↑ROS
↑Ca2+
Cytochrome Oxidase C
Dissociation
Nitric Oxide
Downstream signalling pathways
Activation of transcription factors
Altered expression of genes
↑ Anti-inflammatory process
↑Protein synthesis
↑Anti-apoptotic protein production
↑Cell metabolism, repair, proliferation and migration
↑Anti-oxidants

Role of Photobiomodulation in the Retina-AMD

- ✓ Cones in the aging human retina (mostly at the fovea), progressively accumulate mitochondrial DNA deletions and become more cytochrome C oxidase-deficient over time
- ✓ It is well known that inflammation, complement activation, is associated with the pathogenesis of AMD
- ✓ Since both mitochondria's health and the inflammatory state are influenced by PBM, it obvious that FR/NIR light could treat AMD
- ✓ Evidence for the application of PBM to treat AMD in humans became available in 2008 from a study where Ivandic and Ivandic demonstrated improvement in visual acuity (VA) in patients with the dry and wet forms of AMD.

(Ivandic BT, Ivandic T. Low-level laser therapy improves vision in patients with age-related macular degeneration. *Photomed Laser Surg.* 2008;26(3):241–245.)

RIO 2025

Diabetic retinopathy

- ✓ laser photocoagulation, performed with conventional continuous wave (cw) laser systems cause damage to the neural retinal microstructures by thermal spread from the RPE.
- ✓ PBM reverse the diabetes-induced inflammatory state of the retina by reduction in leukostasis (the adherence of white blood cells to the retinal vascular walls) and in the expression of the intercellular adhesion molecule (ICAM).
- ✓ PBM also led to inhibition of the diabetes-induced production of the oxidative-stress molecule superoxide and reversed the decrease in the anti-oxidant enzyme.

Retinopathy of prematurity

- ✓ The mechanism involves the generation of reactive oxygen species which lead to inflammation and oxidative damage to DNA, including mitochondrial DNA, as well as damage to intracellular proteins and lipids
- ✓ Pre-treatment with 670 nm light reduces neovascularization, vaso-obliteration, retinal hemorrhages, and photoreceptor cell death.

Methanol toxicity in the retina

- ✓ The toxic metabolite in methanol intoxication is formic acid, (a mitochondrial toxin known to inhibit the essential mitochondrial enzyme, cytochrome oxidase) leading to decline of mitochondrial function.
- ✓ treatment with 670 nm light for 2.5min at 5, 25, and 50h after methanol poisoning was able

a rat

Therapeutic photobiomodulation for methanol-induced retinal toxicity

J. T. Eells*†, M. M. Henry*, P. Summerfelt‡, M. T. T. Wong-Riley‡, E. V. Buchmann§, M. Kane§, N. T. Whelan§, and H. T. Whelan§

Retinitis pigmentosa

- ✓ The evidence for this is currently scarce and consists of a single case reports.
- ✓ Treatment with transconjunctival illumination of the whole retina with 780 nm light, generated by a continuous-wave laser diode, for 40s for a total of 0.4 J/cm2 per [illegible] for 2wk reported to improve condition.

Ivandic BT, Ivandic T. Low-level laser therapy improves vision in a patient with retinitis pigmentosa. *Photomed Laser Surg.* 2014;32(3):181–184. Ivandic BT, Ivandic T. Low-level laser therapy improves vision in a patient with retinitis pigmentosa. Photomed Laser Surg. 2014;32(3):181–184.

Amblyopia in adolescents and adults

- ✓ Amblyopia becomes untreatable after the "critical period“ (after the first-decade of life).
- ✓ Evidence that amblyopia in older patients could benefit from PBM was demonstrated by Ivandic and Ivandic
- ✓ No therapy-related ocular or systemic side effects reported.
- ✓ Authors speculated that the mechanism through olyopic eyes, might be similar to those in other retinal conditions

Ivandic BT, Ivandic T. Low-level laser therapy improves visual acuity in adolescent and adult patients with amblyopia. Photomed Laser Surg. 2012;30(3):167

Slowing axial myopia in children

AMERICAN ACADEMY OF OPHTHALMOLOGY

Effect of Repeated Low-Level Red-Light Therapy for Myopia Control in Children

A Multicenter Randomized Controlled Trial

Yu Jiang, MD,[1,*] Zhuoting Zhu, MD, PhD,[2,*] Xingping Tan, MD,[3,*] Xiangbin Kong, MD, PhD,[4,*] Hui Zhong, PhD,[5,*] Jian Zhang, MD,[1] Ruilin Xiong, MD,[1] Yixiong Yuan, MD,[1] Junwen Zeng, MD, PhD,[1] Ian G. Morgan, PhD,[6] Mingguang He, MD, PhD[7,8,9]

Purpose: To assess the efficacy and safety of repeated low-level red-light (RLRL) therapy in myopia control in children.

Design: Multicenter, randomized, parallel-group, single-blind clinical trial.

Participants: Two hundred sixty-four eligible children 8 to 13 years of age with myopia of cycloplegic spherical equivalent refraction (SER) of −1.00 to −5.00 diopters (D), astigmatism of 2.50 D or less, anisometropia of 1.50 D or less, and best-corrected visual acuity (BCVA) of 0.0 logarithm of the minimum angle of resolution or more were enrolled in July and August 2019. Follow-up was completed in September 2020.

Methods: Children were assigned randomly to the intervention group (RLRL treatment plus single-vision spectacle [SVS]) and the control group (SVS). The RLRL treatment was provided by a desktop light therapy device that emits red light of 650-nm wavelength at an illuminance level of approximately 1600 lux and a power of

- ✓ Home based device
- ✓ Tx for 3minutes, 2 times daily
- ✓ 5 days / week
- ✓ Minimum of 4 hours

Axial Shortening in Myopic Children after Repeated Low-Level Red-Light Therapy: Post Hoc Analysis of a Randomized Trial

Wei Wang [*1], Yu Jiang [*1], Zhuoting Zhu [*1,2], Shiran Zhang [*1], Meng Xuan [1], Xingping Tan [3], Xiangbin Kong [4], Hui Zhong [5], Gabriella Bulloch [2,6], Ruilin Xiong [1], Yixiong Yuan [1], Yanping Chen [1], Jian Zhang [1], Junwen Zeng [1], Ian G Morgan [7], Mingguang He [8,9,10]

Affiliations + expand

PMID: 36790672 PMCID: PMC10011250 DOI: 10.1007/s40123-023-00671-7

Abstract

Introduction: Axial length (AL) elongation in myopia is considered irreversible. We aimed to systemically report unexpected AL shortening observed in a randomized clinical trial (RCT) after repeated low-level red-light (RLRL) therapy.

Methods: This is a post hoc analysis of a multicenter, single-masked RCT. Two hundred sixty-four

RIO 2025

Meibomian gland dysfunction

ORIGINAL ARTICLE

Treatment of dry eye disease due to meibomian gland dysfunction using intense pulsed light and low-level light therapy

Khalifa, Ali A.; Ibrahim, Mohamed M.A.; Abdelrahman, Mahmoud S.A.

Author Information

Delta Journal of Ophthalmology 22(2):p 91-96, Apr–Jun 2021. | **DOI:** 10.4103/djo.djo_68_20

- ✓Many of the previous studies were done on animal models
- ✓Through closed eye lids
- ✓Whole body or whole retinal illumination
- ✓Some requires overnight stay at hospitals or home therapy

What is new??

- ✓Now we can benefit from PBM utilizing micropulse diode laser as a SOURCE OF LIGHT
- ✓Can be done using slit-lamp delivery system
- ✓Through the pupil

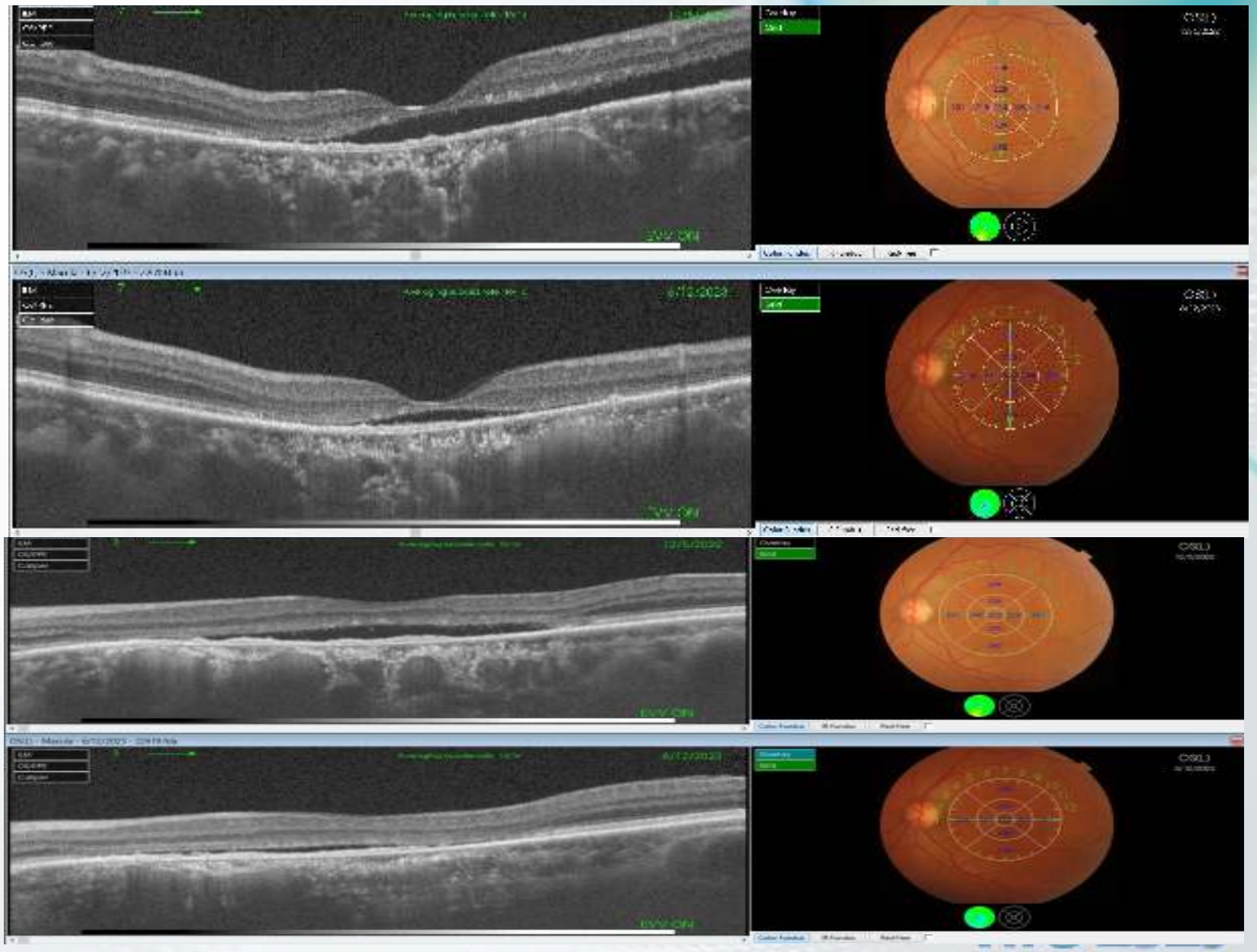
Why micropulse ??

- Reduced risk of thermal damage
- Enhanced cellular response
- Potential for deeper tissue penetration
- Less painful with minimal side effects

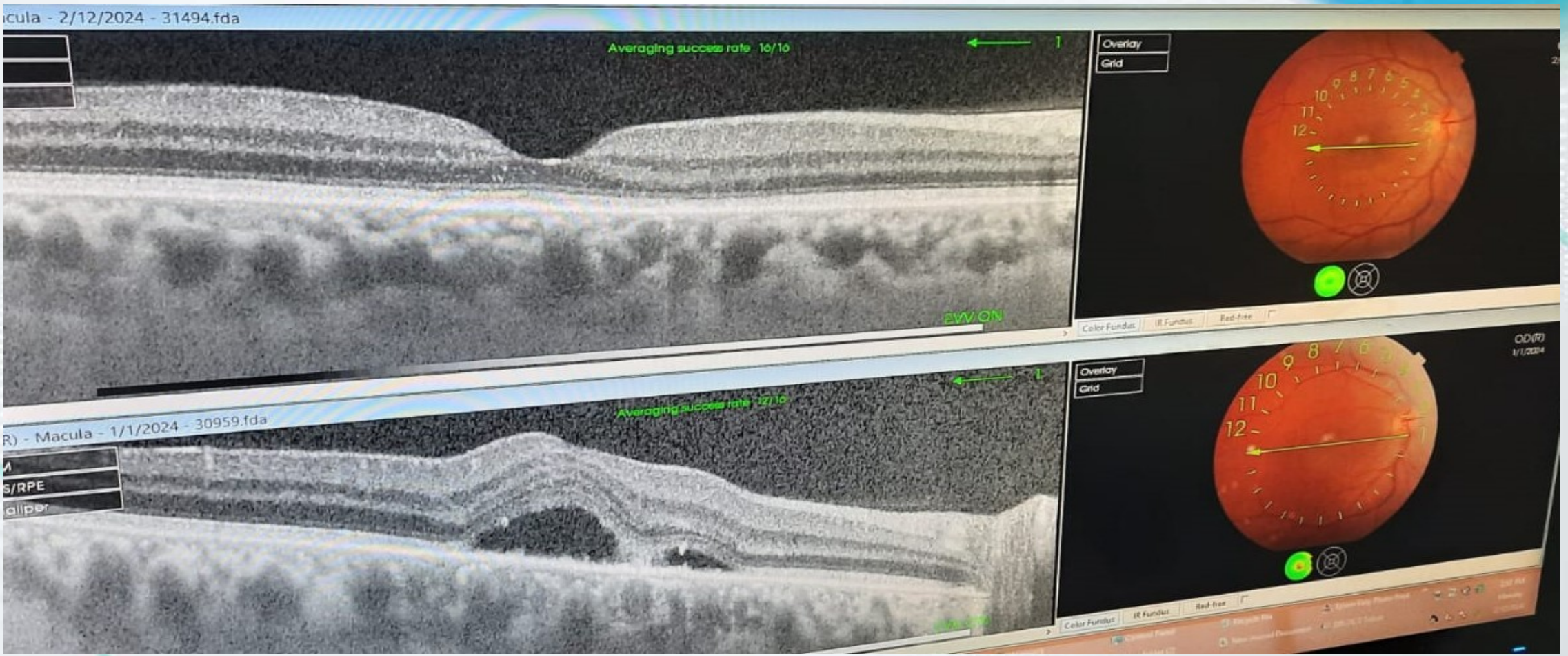
Utilizing PBM principles-MPL team Al-Azhar UN hosp.

Chronic CSR-MPL team Al-Azhar UN hosp.

- ✓ 6m not responding to medical tx
- ✓ Transpupillary MPL
- ✓ Treatment of healthy peripheral retina.

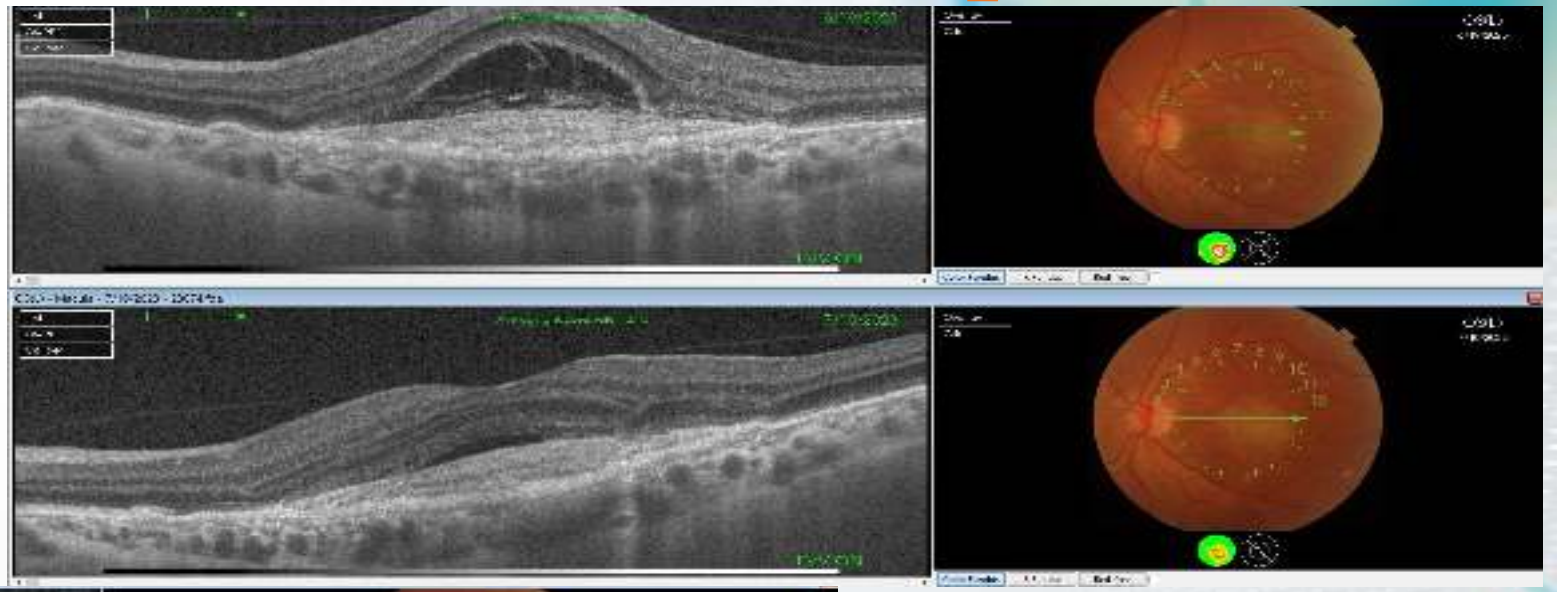


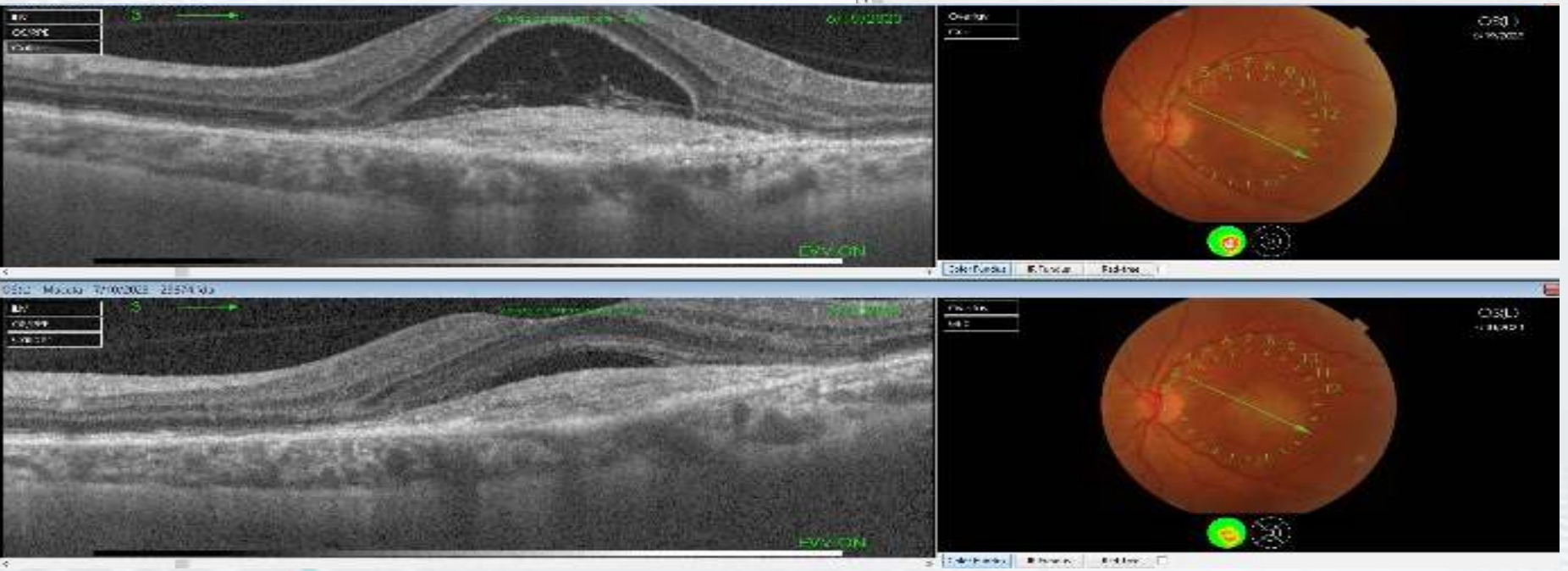
Chronic CSR -MPL team Al-Azhar UN hosp.



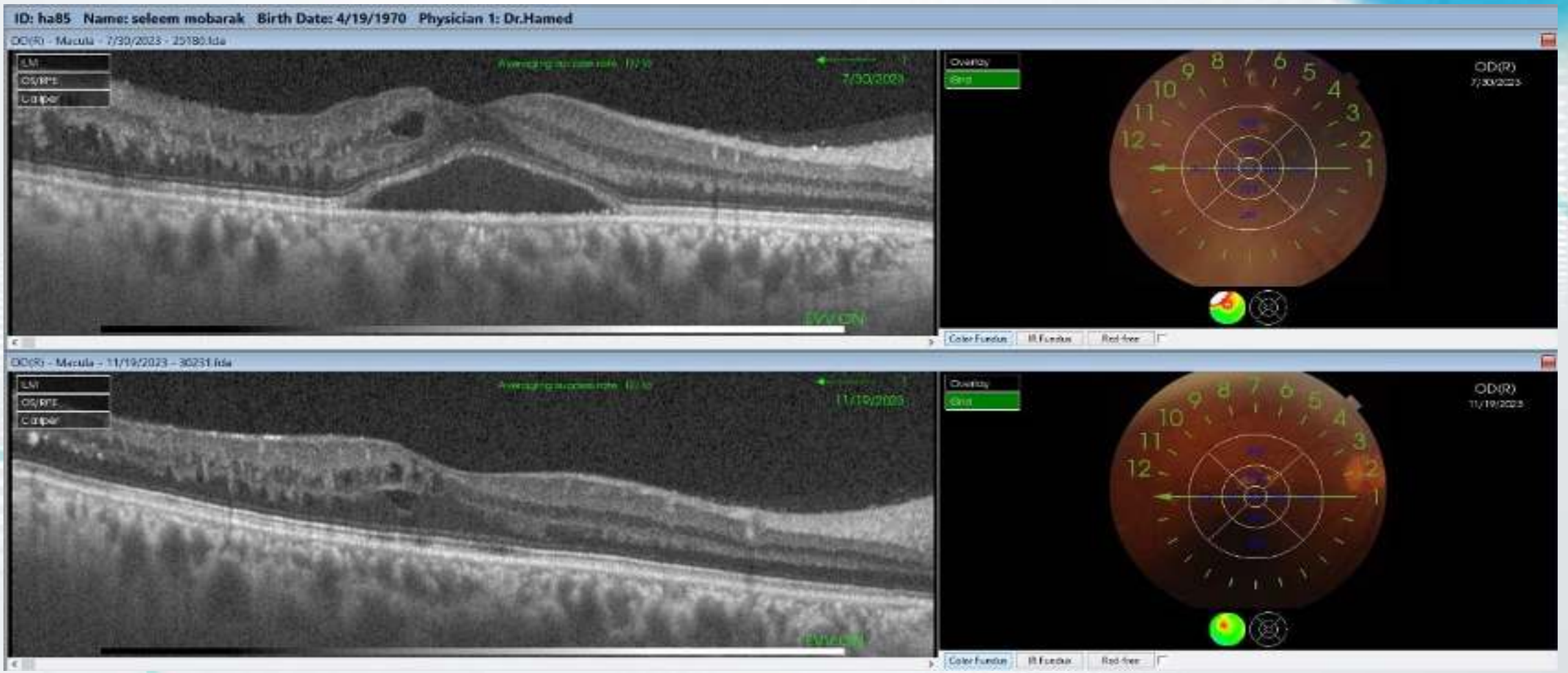
CNV-MPL team Al-Azhar UN hosp.

- ✓ CNV comp. best disease
- ✓ Treatment of the macula & healthy peripheral retina.

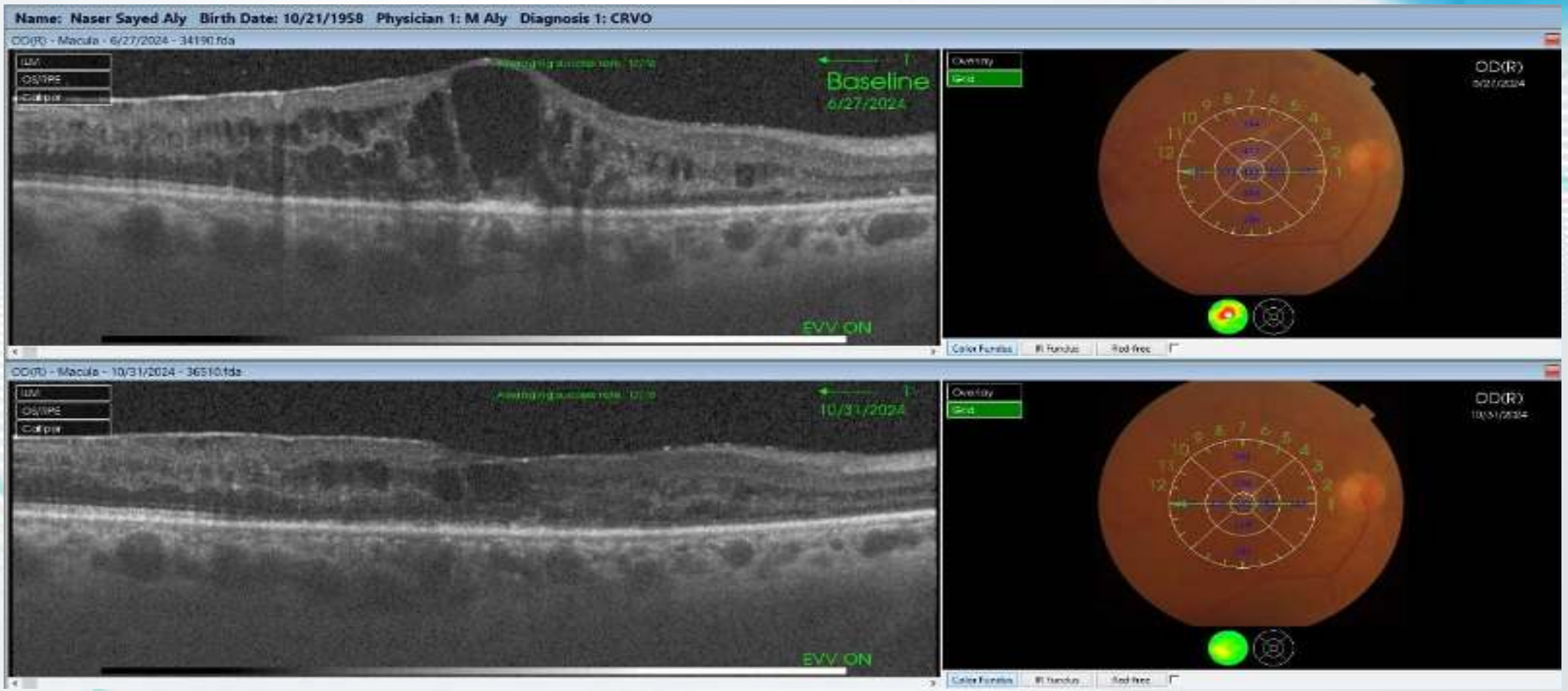




Vien occlusion , trans-scleral MPL



Vien occlusion , trans-scleral MPL



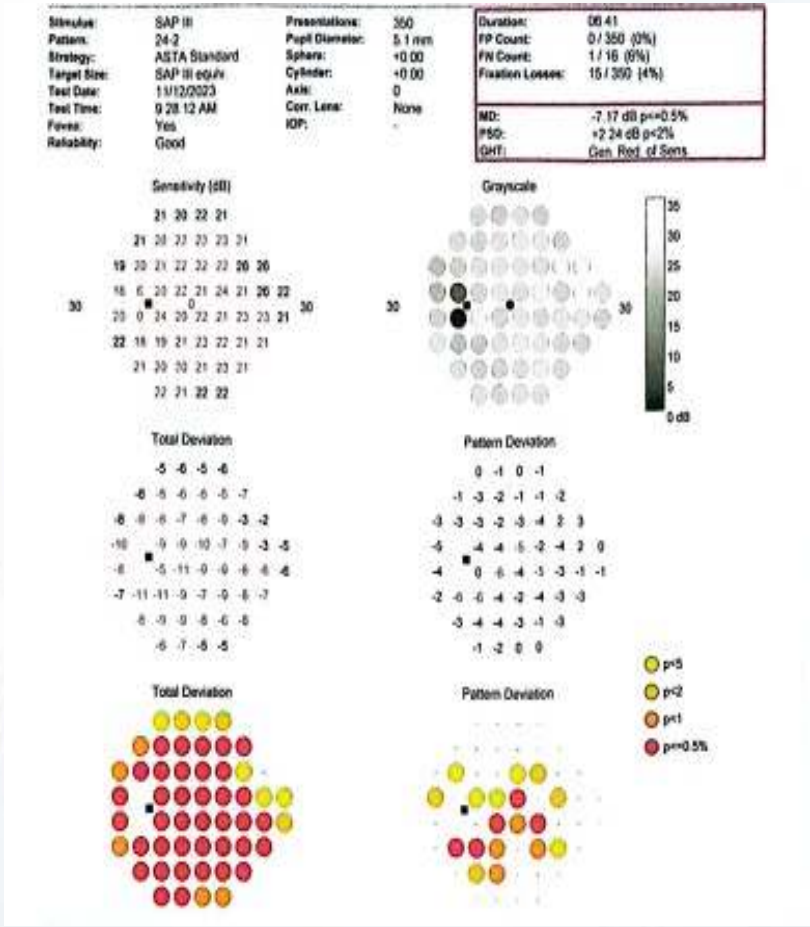
OA Glaucoma-PBM.

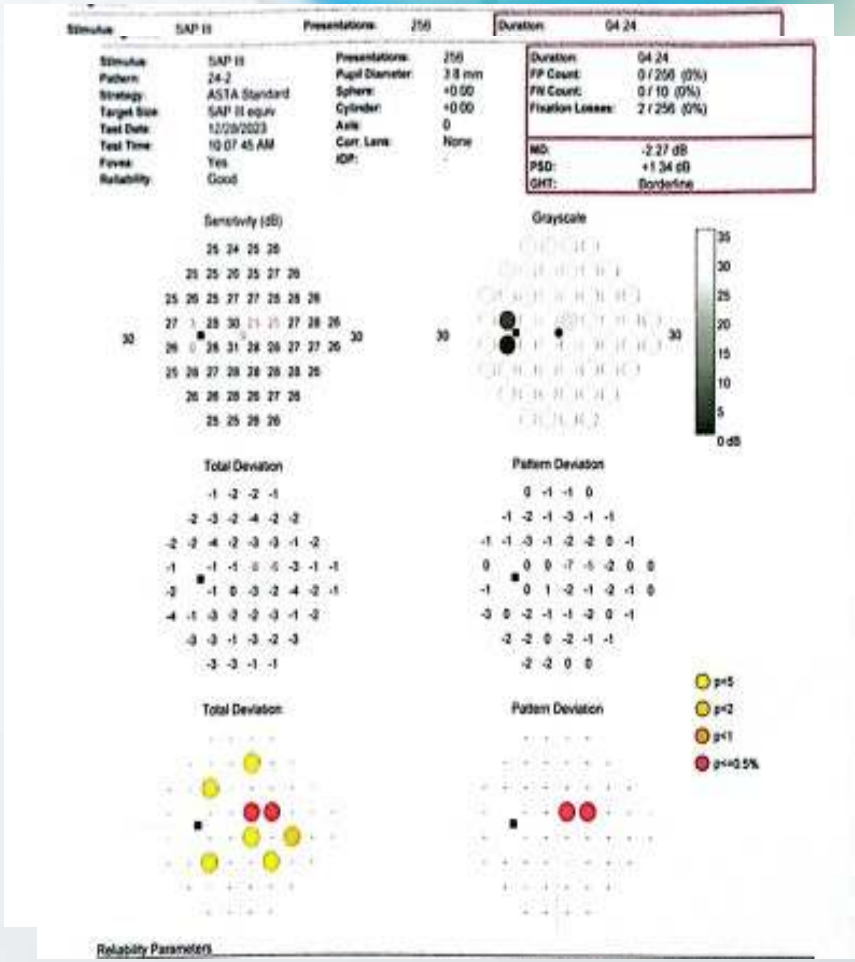
- ✓Transconjunctival peripheral-retinal Diode 810 nm (800 - 900 mw, 10% DC, 0.2 exp. time & 400 SZ)
- ✓1 session / wk for 1m then once monthly for 6 months
- ✓IOP reduction probably due to increased uveo-scleral outflow
- ✓There were also improvements in BCVA & VF .. This needs further F/U studies.
- ✓Though VF was repeated many times before and after tx, patient learning curve should be considered.

RIO 2025

OA Glaucoma-PBM.

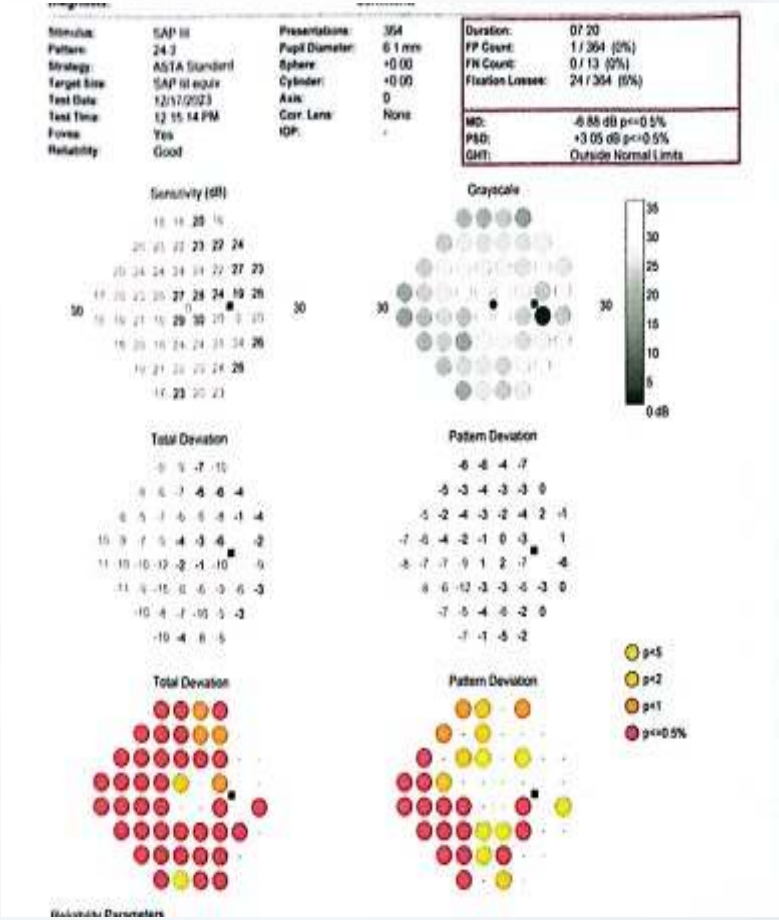
- ✓ Lt eye F.pt.
- ✓ 63 yrs
- ✓ C/D 0.6
- ✓ On BB/acetazolamide & alpha agonist ED
- ✓ BCVA improved from 6/24 to 6/12
- ✓ IOP decreased from 20 to 12 mmhg

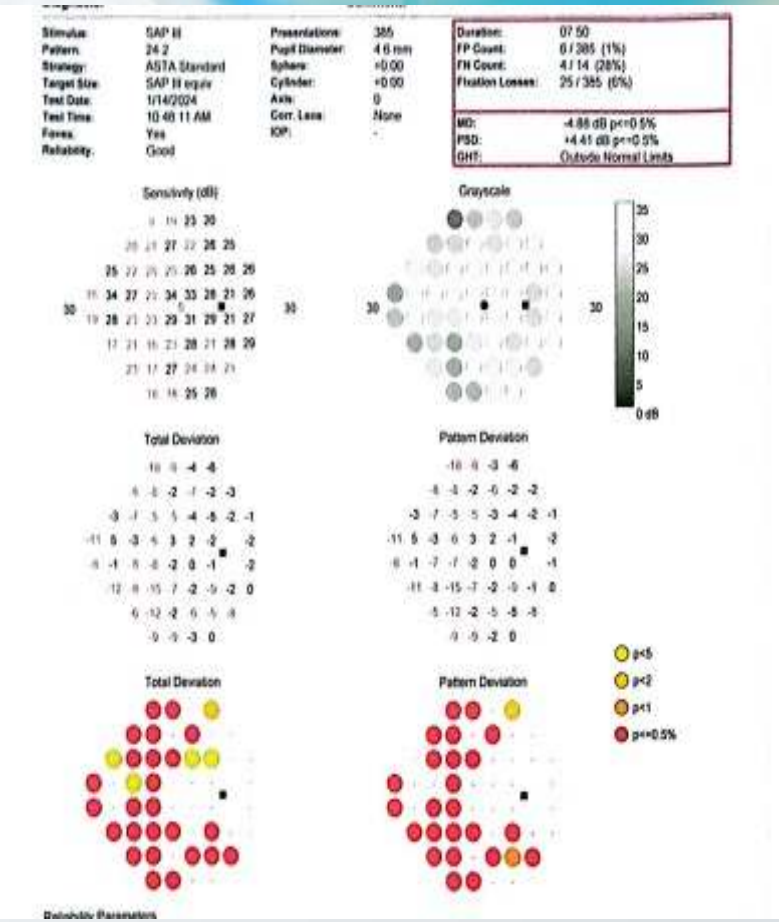




OA Glaucoma-PBM.

- ✓ Rt eye F.pt.
- ✓ 62yrs
- ✓ C/D 0.7
- ✓ On BB/acetazolamide ED
- ✓ BCVA improved from 6/24 to 6/18
- ✓ IOP decreased from 19 to 14 mmhg





Mechanism of PBM in Glaucoma.

- Reduces inflammation
- Improves blood flow (ON, Uveo-scleral outflow ..)
- Neuroprotective effect (stimulates neurogenesis & protect RGC from apoptosis)
- Studies showed reduced IOP, improved visual function & neuroprotective effect

Advantages of PBM

- Non-invasive : minimal risk of infection
- Minimal side effects
- Wide range of applications
- Complementary to other therapies

Disadvantages of PBM

Limited research needed to optimize parameters

Inconsistent results

Cost : PBM devices can be expensive

Take home message

- PBM involves conversion of light energy to metabolic energy → improving cell respiration & energy production.
- It consists of series of brief illumination with FR/NIR light (600-1000 nm) from a laser or a light emitting diode (LED).
- It has many systemic & ocular applications
- Its safer, less destructive & less invasive than other treatments (argon laser, IVI ..etc)
- PBM can be useful in Promotion of the regeneration and functional recovery of tissues with poor healing potential like neurological tissues(can be considered in regenerative medicine)


Thank You!