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Photobiomodulation for Dry Age-Related Macular Degeneration

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A leading cause of vision loss in Americans >60 years of age.

Age-Related Macular Degeneration (AMD)

What is needed?

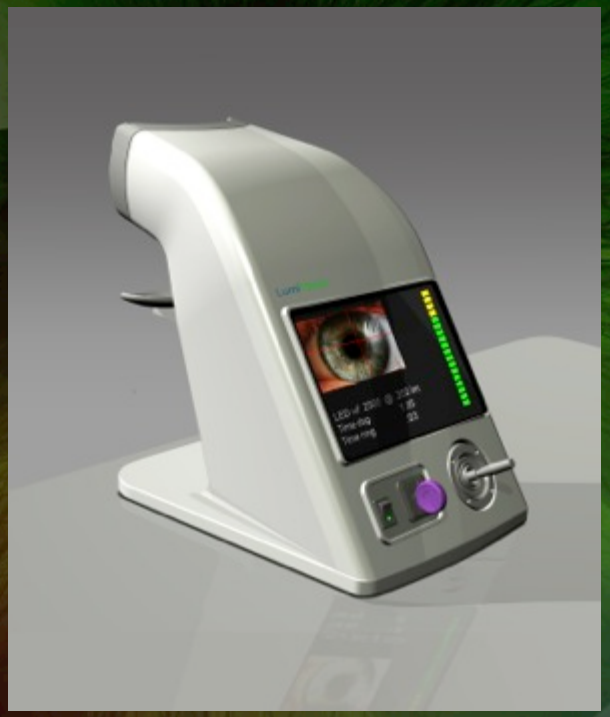
Low cost, regenerative treatment deliverable to millions, globally

Business Overview – Improve Vision in the Elderly

- Medical Device Company Targeting
  Dry - Age Related Macular Degeneration
- Multiple wavelength, LED Instrument Station
- Non-invasive Photobiomodulation (PBM)
- Positive Human Clinical Data with up to 1 year follow-up
- Proprietary Issued Patent and Pending Patent Application(s)

LT-300: Ophthalmologic LED Device

- Light emitting diodes (LED) provide low level, non-coherent light
- Class II Device (510K)
- Noninvasive procedure
- Targets Retina and macula



Commercial Design Prototype Illustration - System is Limited by Federal Law to Investigational Use Only

Age-related Macular Degeneration

Dry Age Related Macular Degeneration

Normal vision

Dry Age Related Macular Degeneration

Blurred vision

Dry Age Related Macular Degeneration

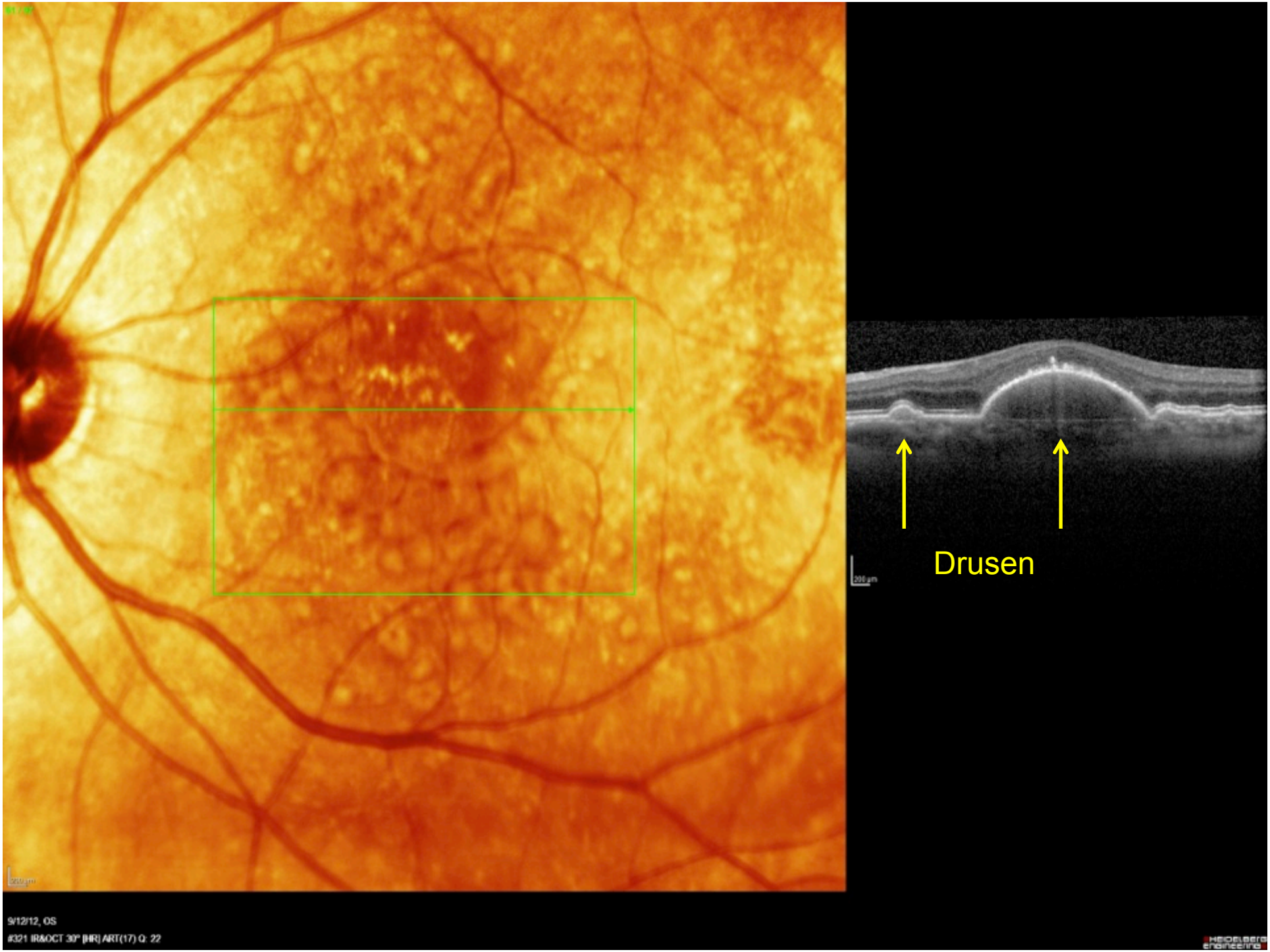
Loss of contrast

Dry Age Related Macular Degeneration

Loss of central vision

Dry Age Related Macular Degeneration

and it gets worse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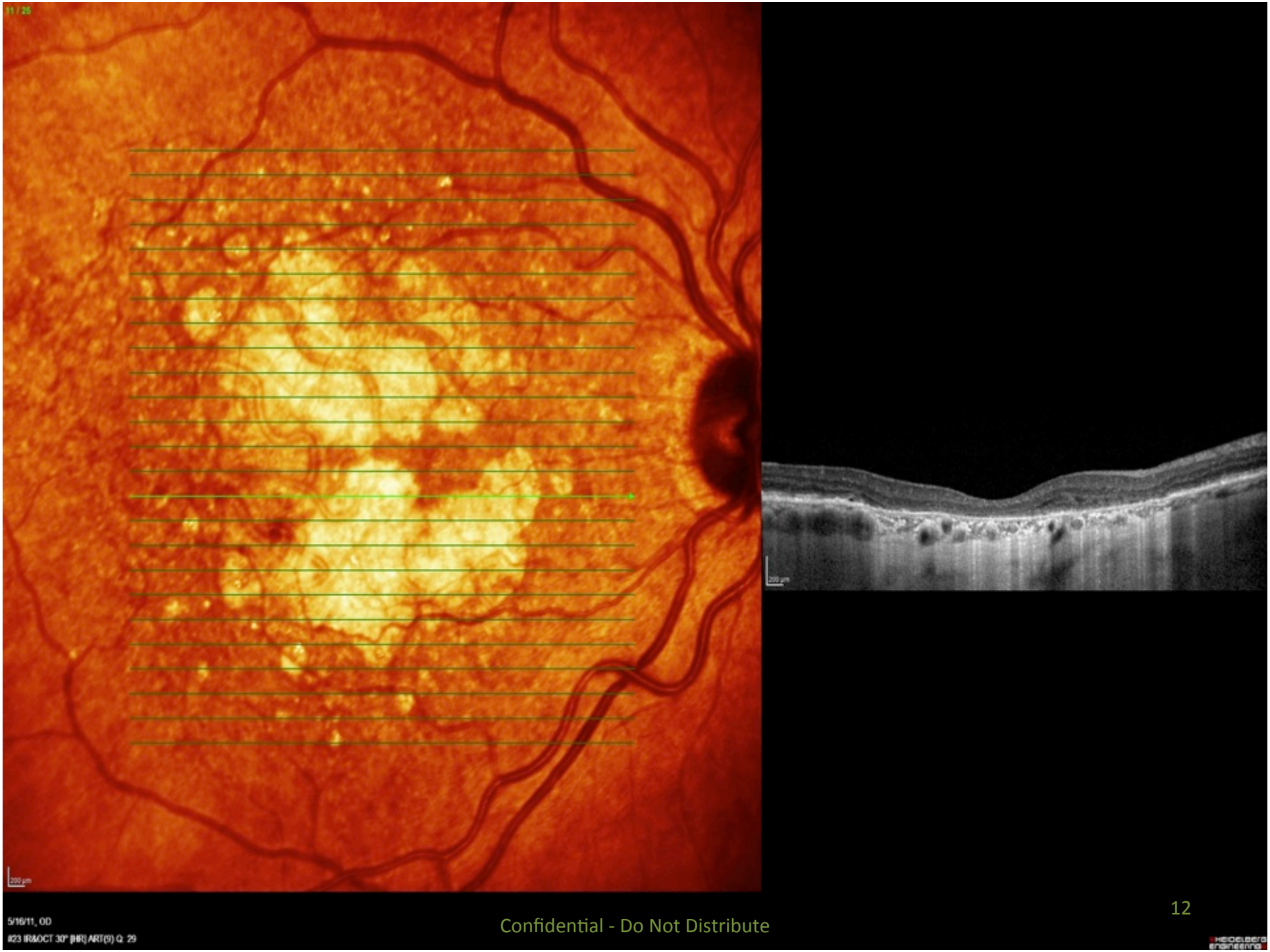

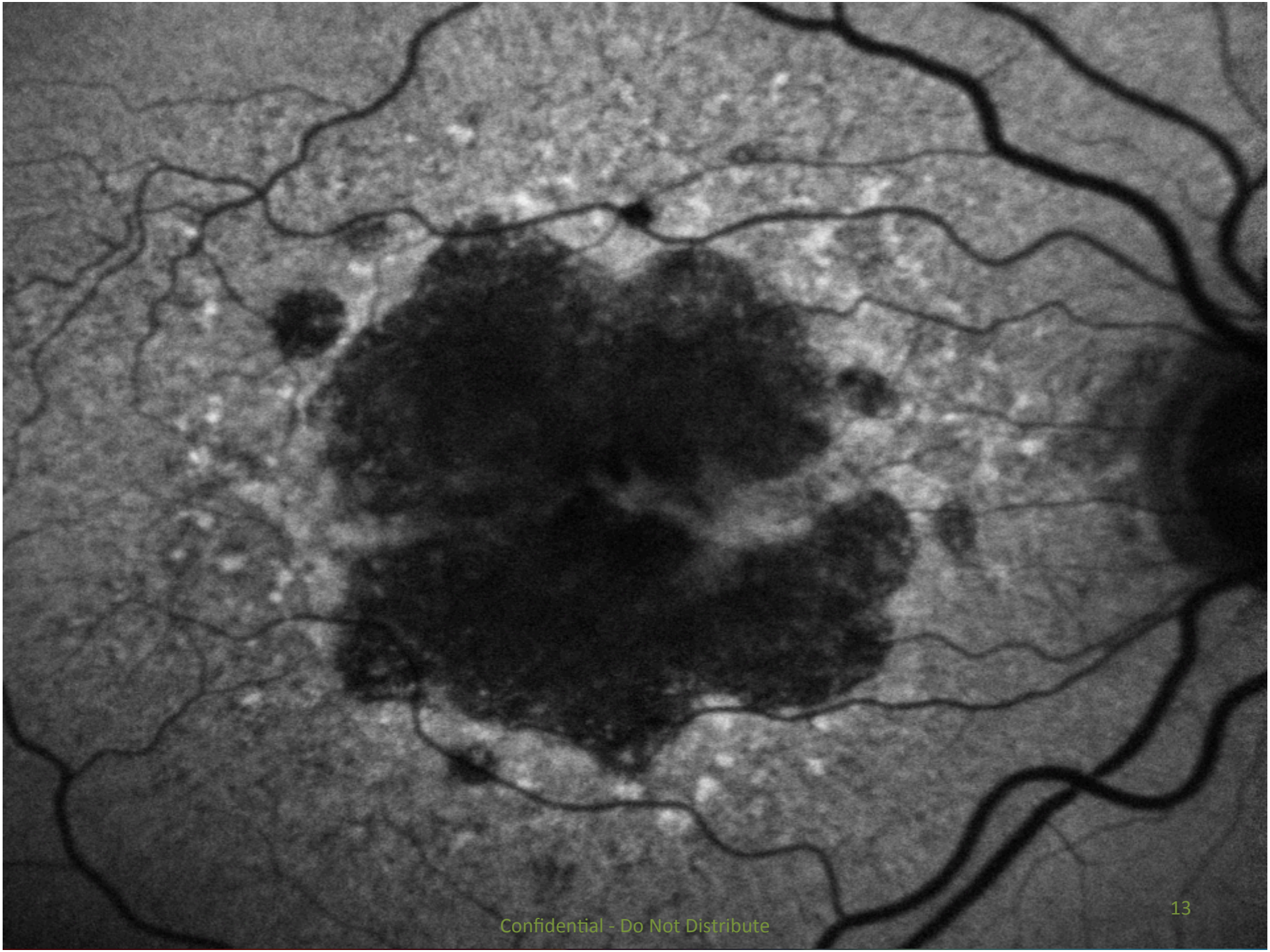

Macular Degeneration (AMD)

Affects ~10 million people in the United States. This number is expected to double to ~22 million by 2020.

Direct health care costs of AMD in the USA and Canada are ~$98 billion.

Two types:

- Wet type, affecting 10%;
- Dry type, affecting 90%.

Wet type: Intra-ocular anti-VEGF drugs.

Dry type: No proven treatments.

Anti-VEGF injection

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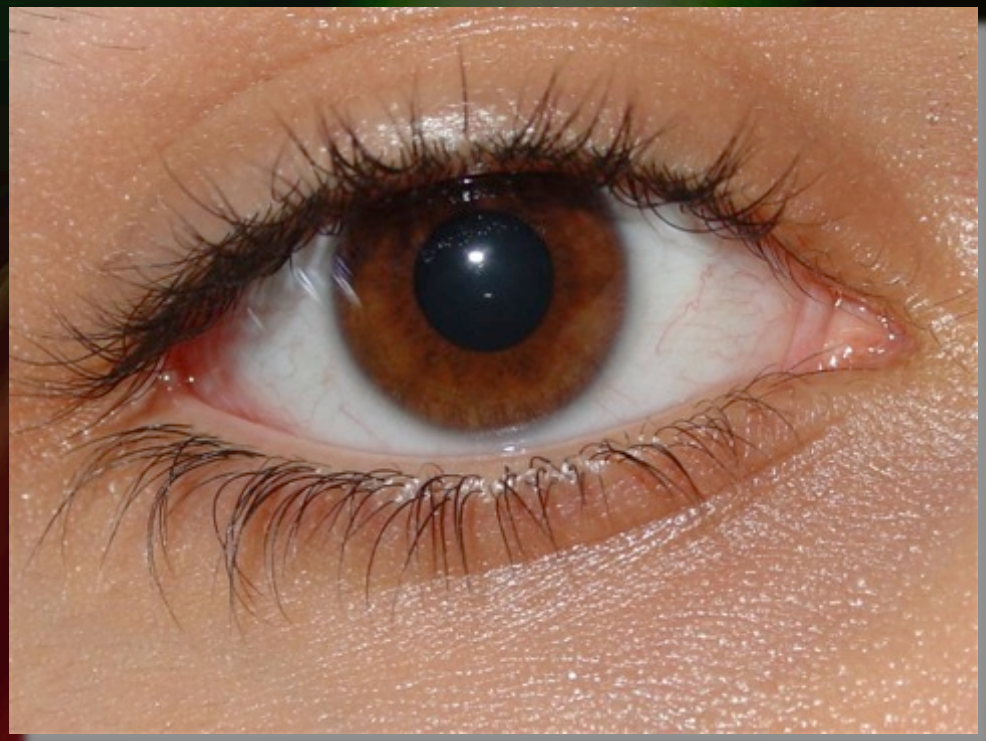
Does PBM Treatment Lend Itself to the Disease?

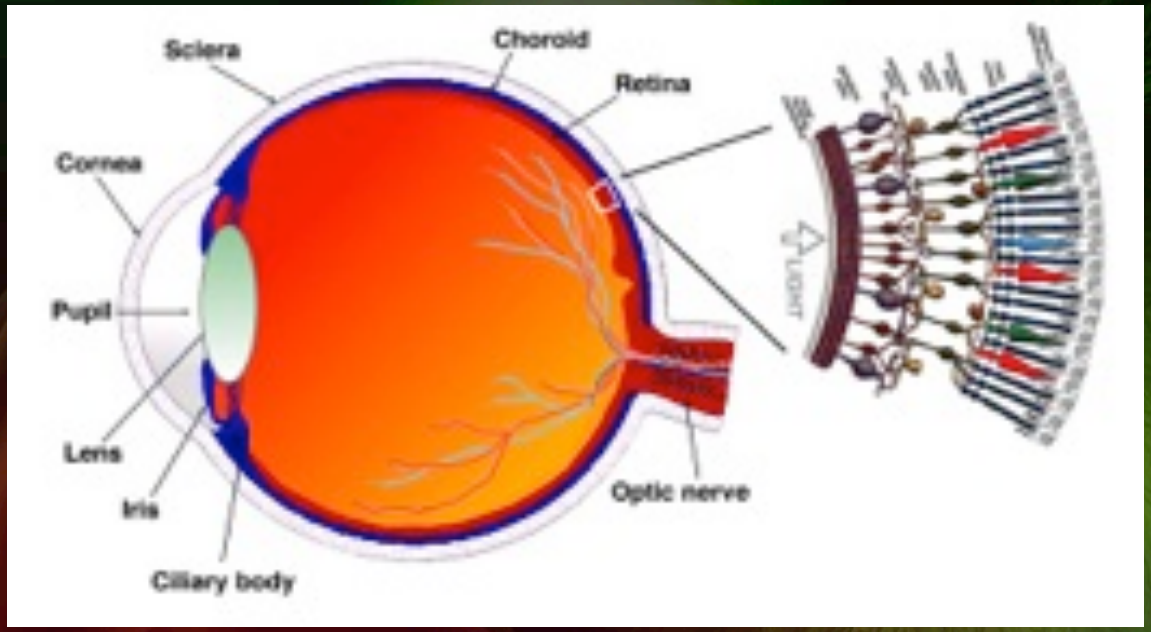
Does PBM Mechanism of Action Fit the Disease?

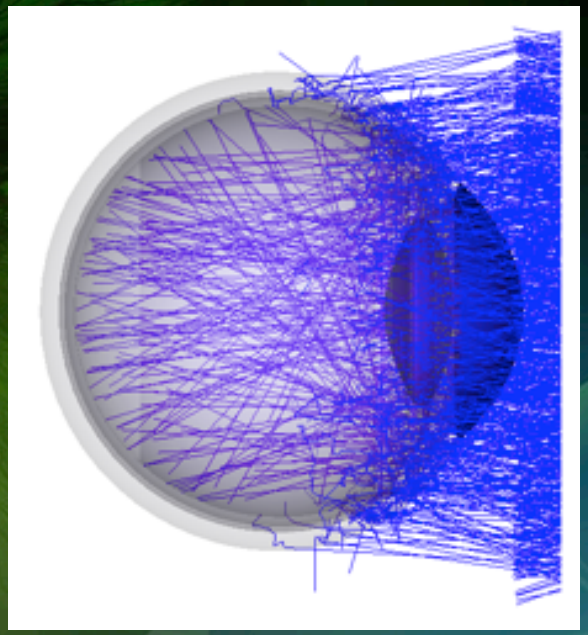
PhotoBioMedicine – Ophthalmic Applications



- The human eye is uniquely accessible to phototherapy...

PhotoBioMedicine – Ophthalmic Applications





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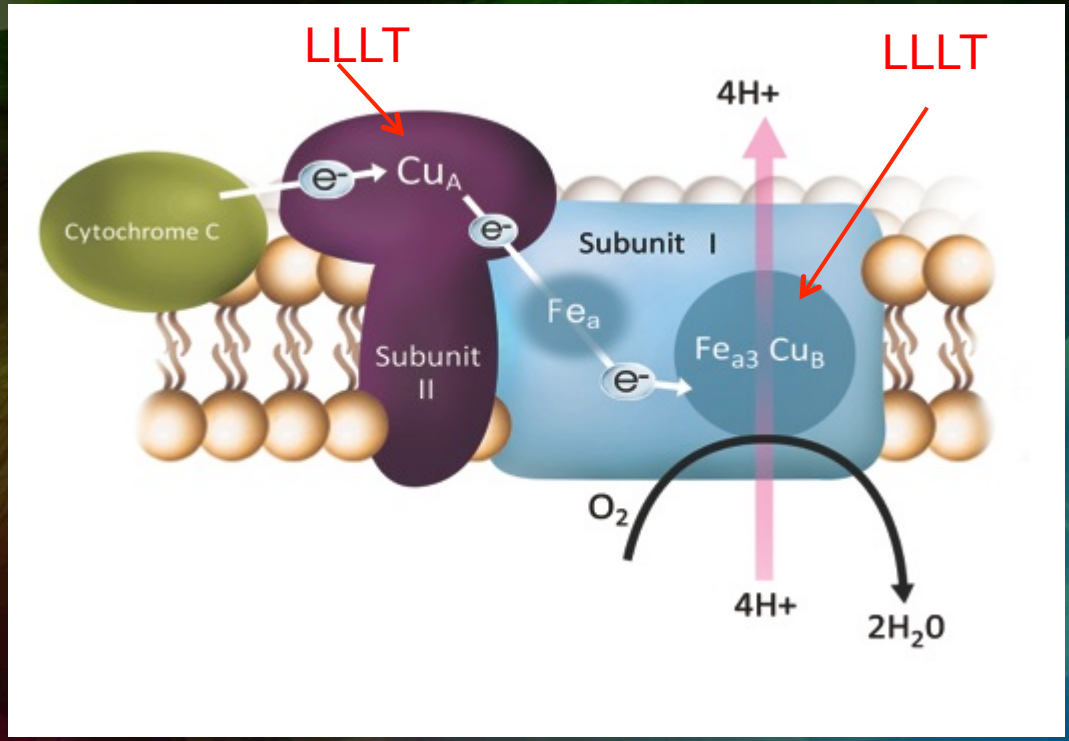
Does PBM treatment lend itself to the Disease?

YES!

Cytochrome C Oxidase is Key Photoacceptor

LLLT Photons Target Cu_A at 810 nm and $Fe_{a3}Cu_B$ at 650 nm

- Improves Blood Flow
- Enhances O_2 binding
- Increases CCO Activity
- Improves ATP Formation
- Reduces Oxidative Stress (NO, ROS)
- Resets Cellular Metabolic Function



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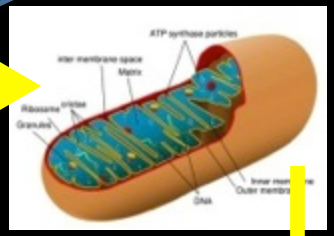
LLLT Therapy

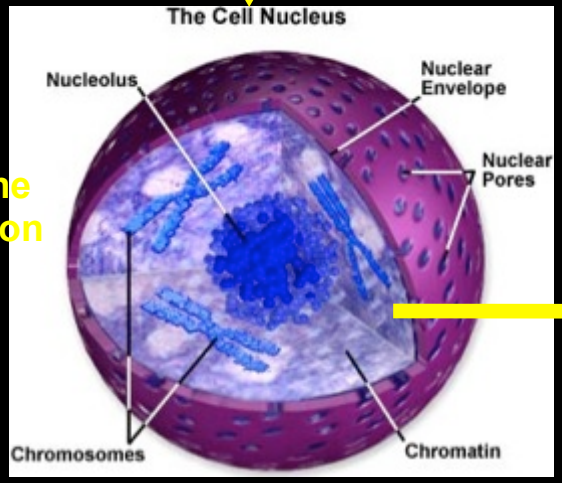


Improves Mitochondrial Function

Activates transcription factors NFkB

CELL SURVIVAL

Creates stable microenvironment



Alters gene transcription

Alters protein synthesis

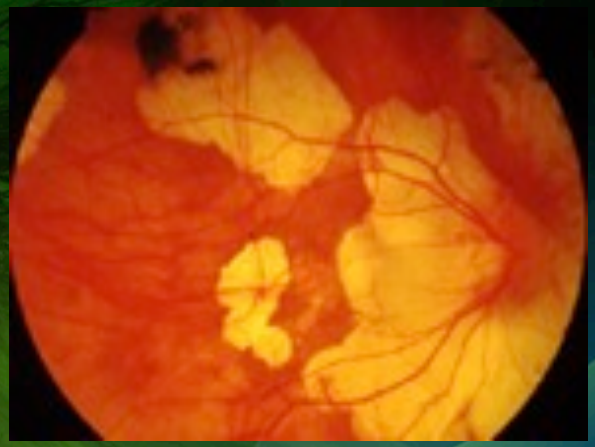
LLLT stimulates Longer-Term Benefits

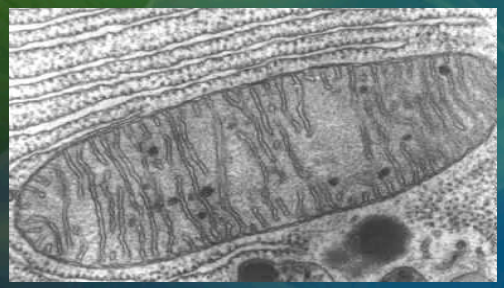
Activation of Multiple Downstream Pathways/Effectors

- Mitochondrial Enzyme Activity - ↑ MTT reduction *(Hamblin, Lo)*
- Apoptosis - ↑ Bcl-2, HSPs (Oron), PI3k/Akt, ↓ Bax, Caspase
- Cytoprotection - ↑ BDNF, BMP, TSP-1*(Lapchak)*
- Protein Processing - α- & β- secretase, Aβ peptide *(Kindy)*
- Inflammation - ↓ IL1β, TNFα, TGFβ, β-secretase, *(Kindy)*

Mitochondrial Dysfunction and Oxidative Stress Play a Key Role in Aging and Degenerative Diseases

- Mitochondrial Disease - LHON
- Degenerative Eye Diseases - Macular Degeneration, Diabetic Retinopathy, Retinitis Pigmentosa, Glaucoma
- Neurodegenerative Diseases - Parkinson's Disease, Alzheimers Disease, Huntington's Disease, Multiple Sclerosis
- Cardiovascular Disease and Stroke
- Metabolic Diseases - Diabetes

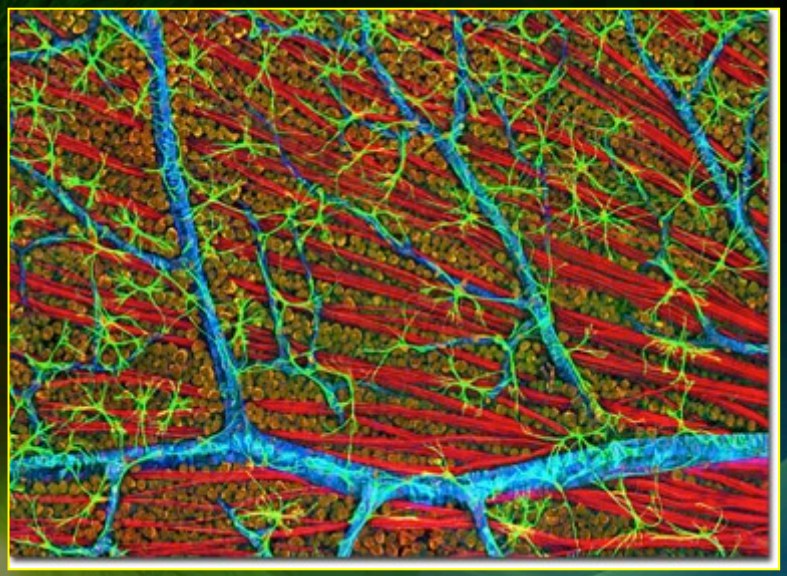




AMD Ophthalmology Therapy Implications

PBM offers non-pharmaceutical, non-surgical way to:

- Suppress VEGF
- Suppress inflammation
- Stimulate retinal cell regeneration/revitalization
- Protect/revitalize optic nerve and retinal cells against toxicity



Mouse retina

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Does PBM Mechanism of Action fit the Disease?

YES!

Is There Animal Model Data to Support the PBM Approach in Ocular Disease?

PBM Animal Studies

- Eells, *et al.,* University of Wisconsin, have demonstrated:
  - Protective effect and enhanced recovery in a Rat Retina model – methanol toxicity
  - LED Tx x3 in first 50 hrs after methanol exposure
  - Significant recovery of rod, M cone and UV cone mediated retinal function (ERG data $P < 0.001$)

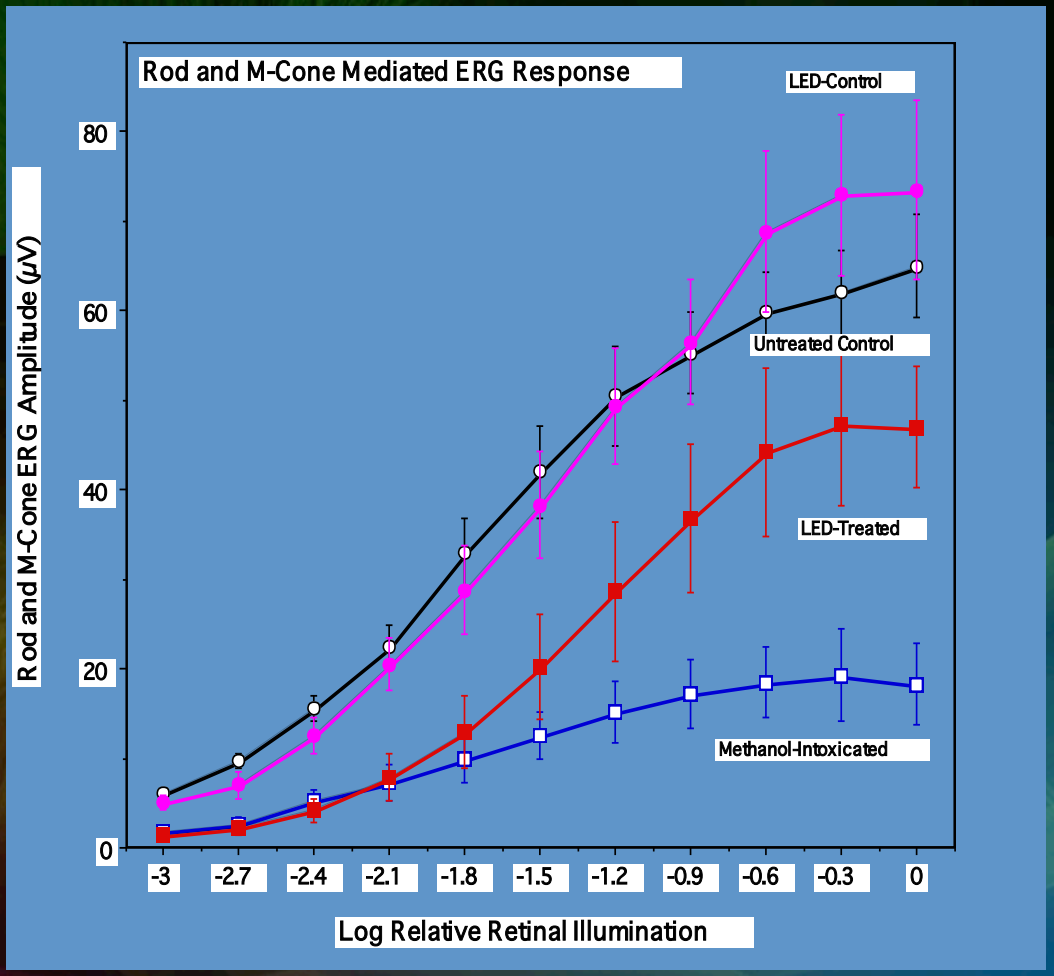
Retinal PBM Animal Studies - *Eells*

670 nm Treatment

At 5 hr, 25hr, 50 hr

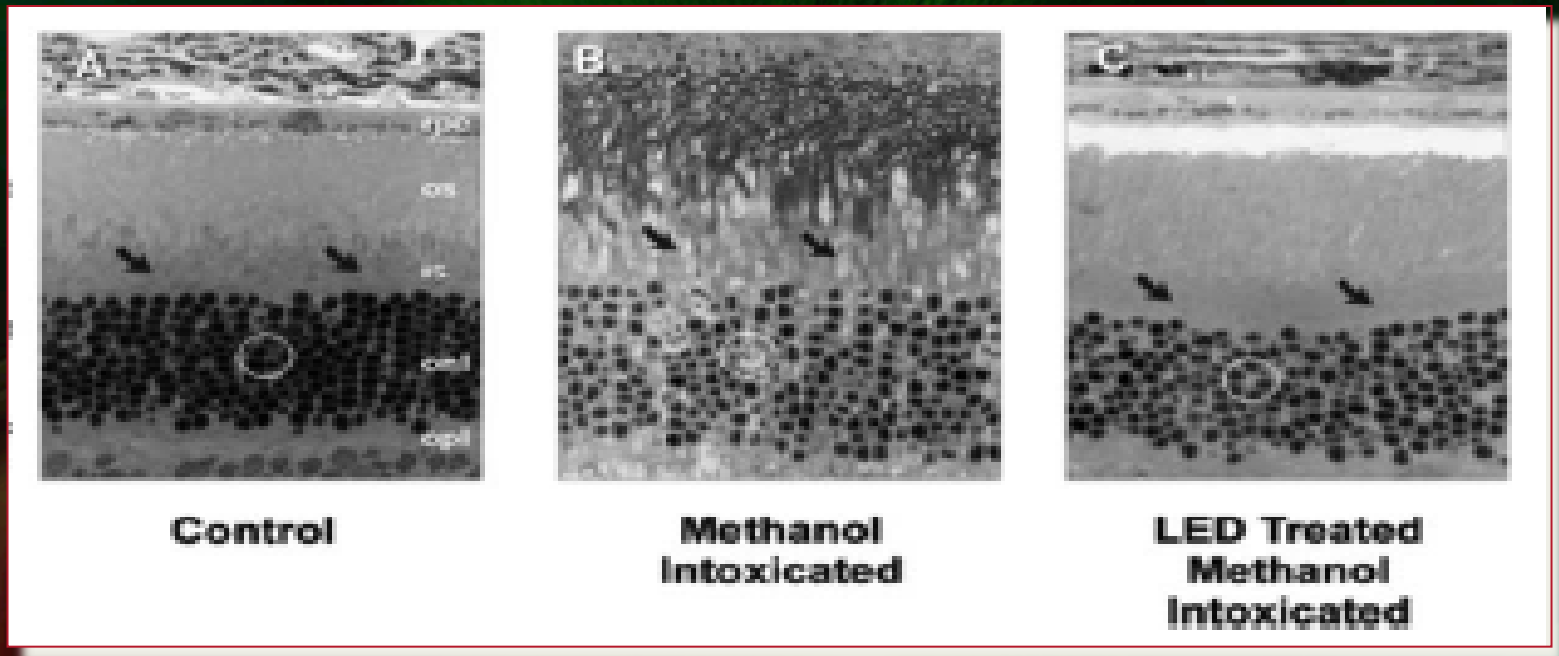
28 mW/cm^2 - 2 min

4 joules/cm^2



Eells, et al., Wisconsin, 2004

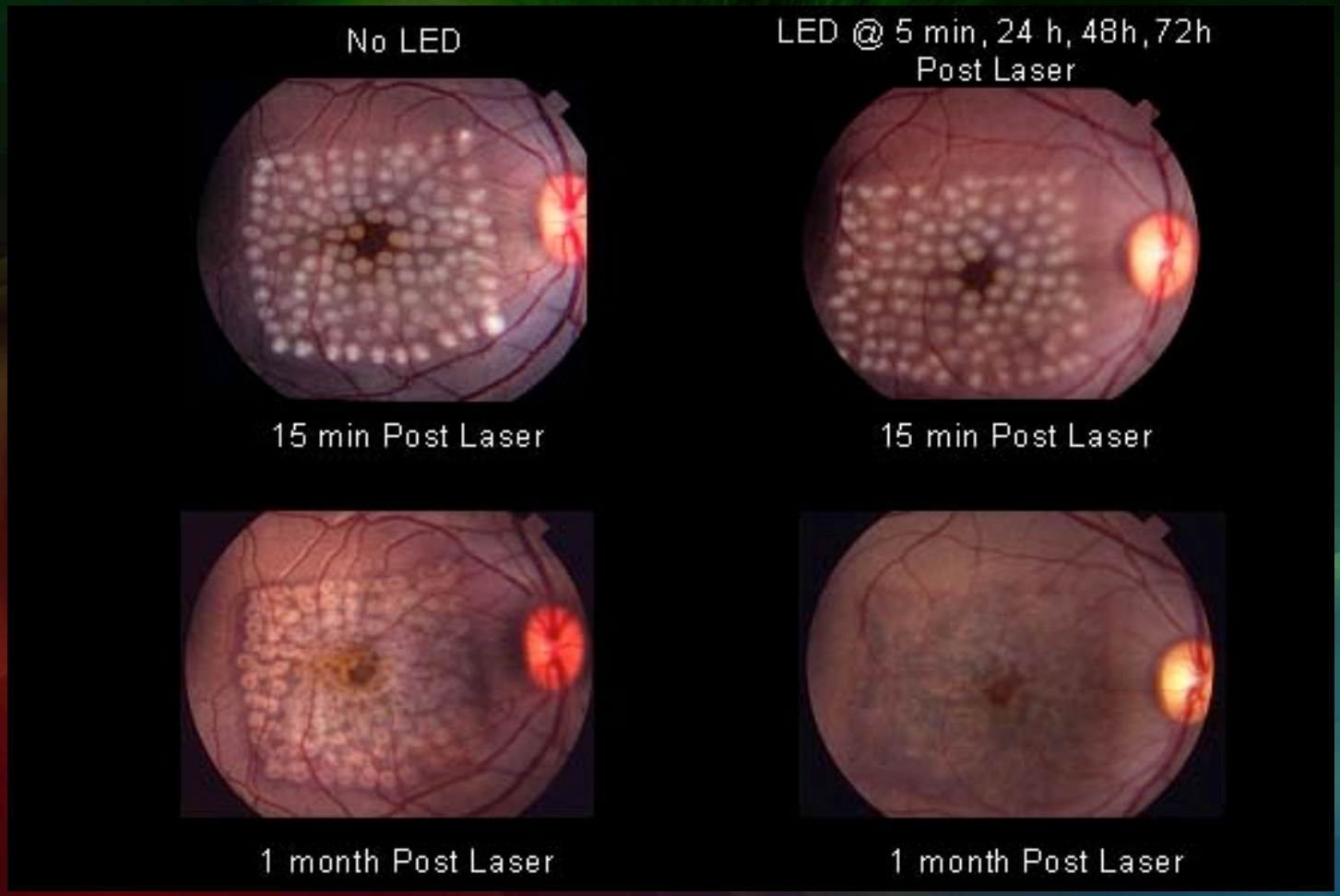
Retinal PBM Animal Studies - *Eells*



- Histopath showed retinal edema, swelling of photoreceptor inner segments & changes in photoreceptor nuclei, but LED treated were indistinguishable from untreated control!

Eells, et al., Wisconsin, 2004

LLLT Reduces Inflammation and Improves Healing in Preclinical Retinal Laser Damage Models - *Eells*



Eells, et al., Wisconsin, 2008

LLLT Reduces Outer Retinal Inflammation in CFH$^{-/-}$ Mice

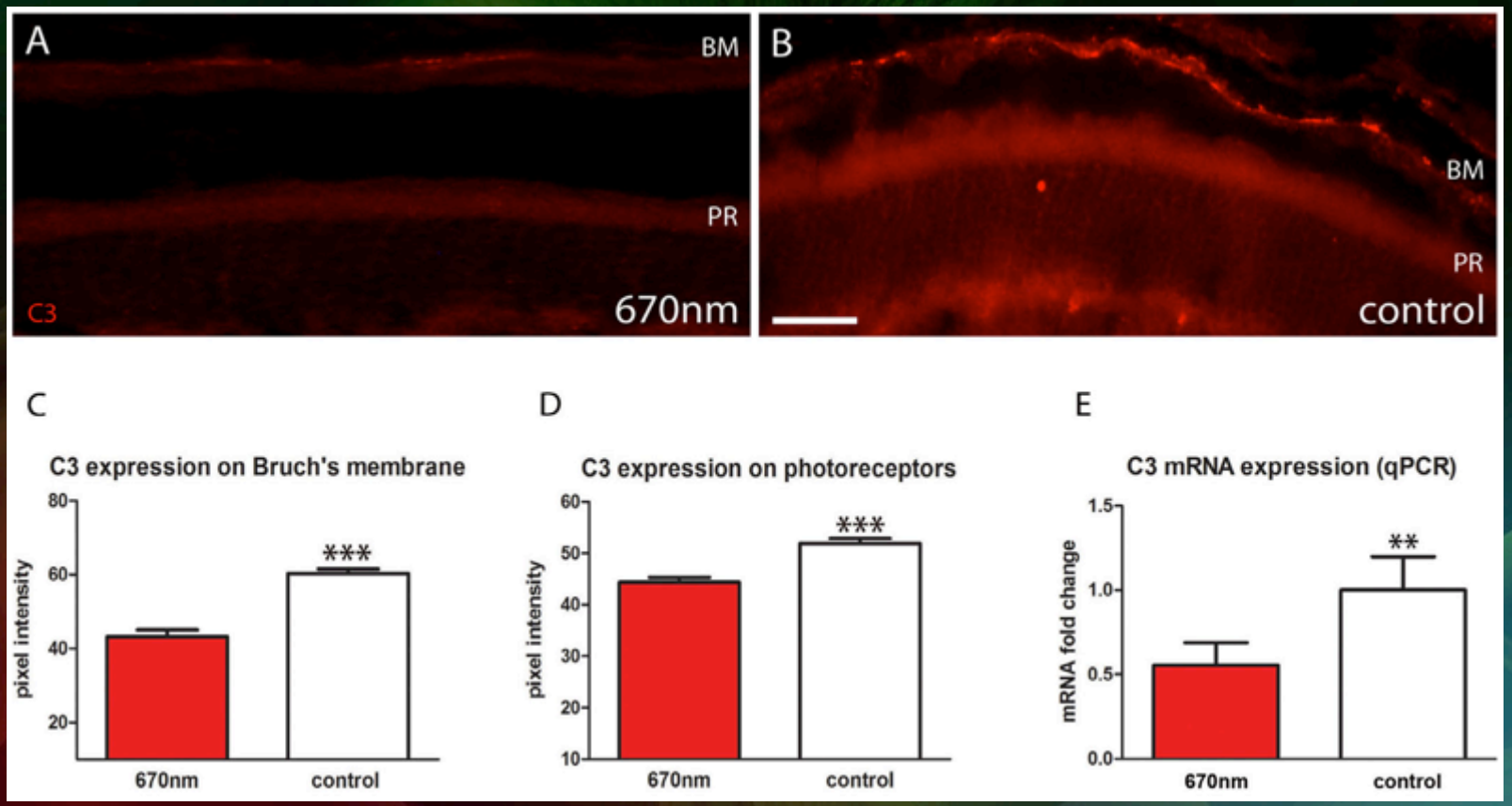


Figure A and B. Retinal sections stained with C3 (red). C3 accumulates on Bruch's membrane and outer segments. Figure C and D Following 670 nm treatment, C3 was significantly reduced on Bruch's membrane and photoreceptor outer segments (p = 0.0001 for each). E. These data were confirmed with qPCR analysis, Abbreviations, Bruch's membrane (BM), photoreceptor (PR), complement component (C3). Scale bars = 40 mm.

Begum, et al., 2013

Is There Clinical Data to Support Use of PBM in Dry Age-related Macular Degeneration?

TORPA (Toronto-Oak Ridge Study for Dry AMD)

Prospective Study

- University of Toronto, Dr. Devenyi – Chief, Retinal Surgical Center

Inclusion Criteria:

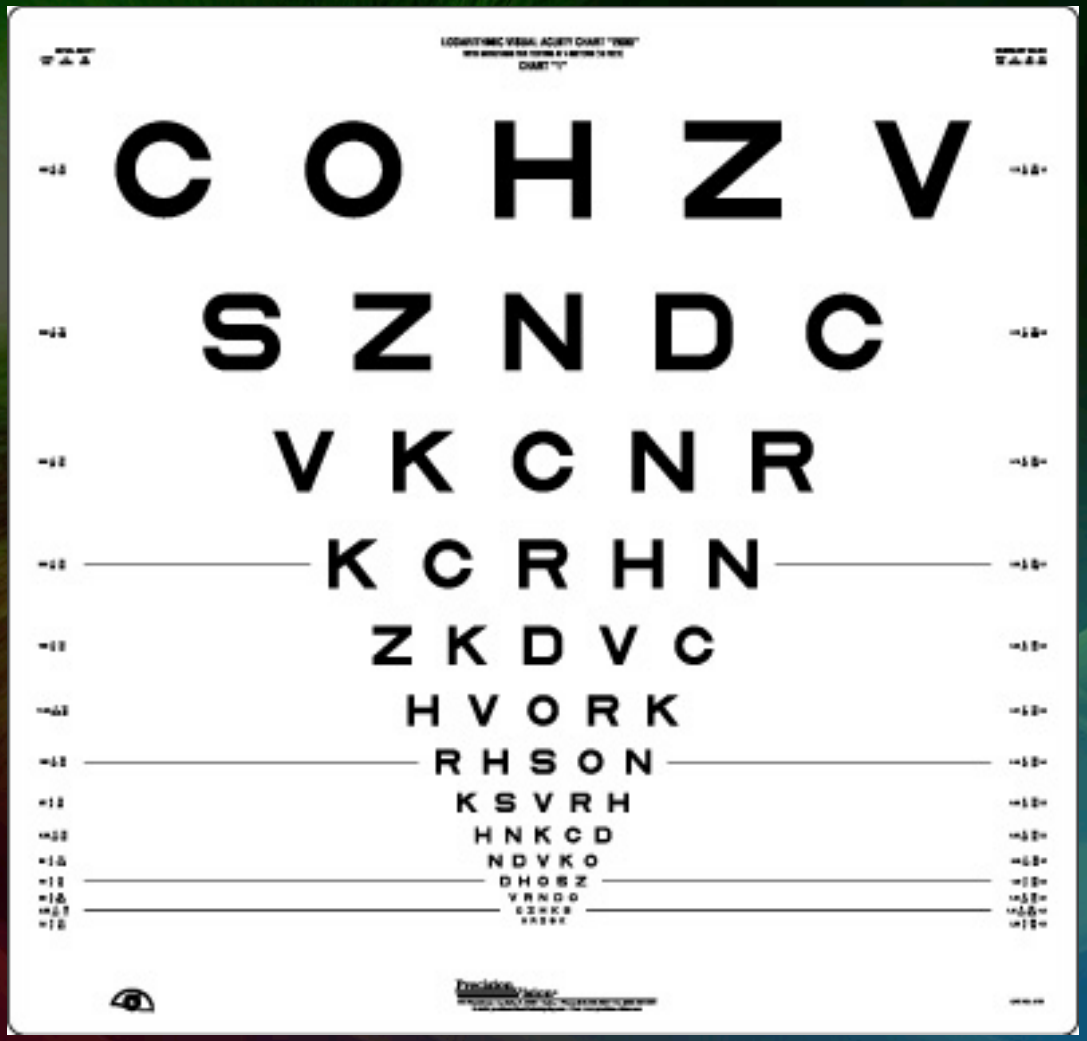
- ≥ 50 years of age.
- Clinically diagnosed Dry ARMD in study eye.
- BCVA between 20/20 and 20/200.

Exclusion Criteria:

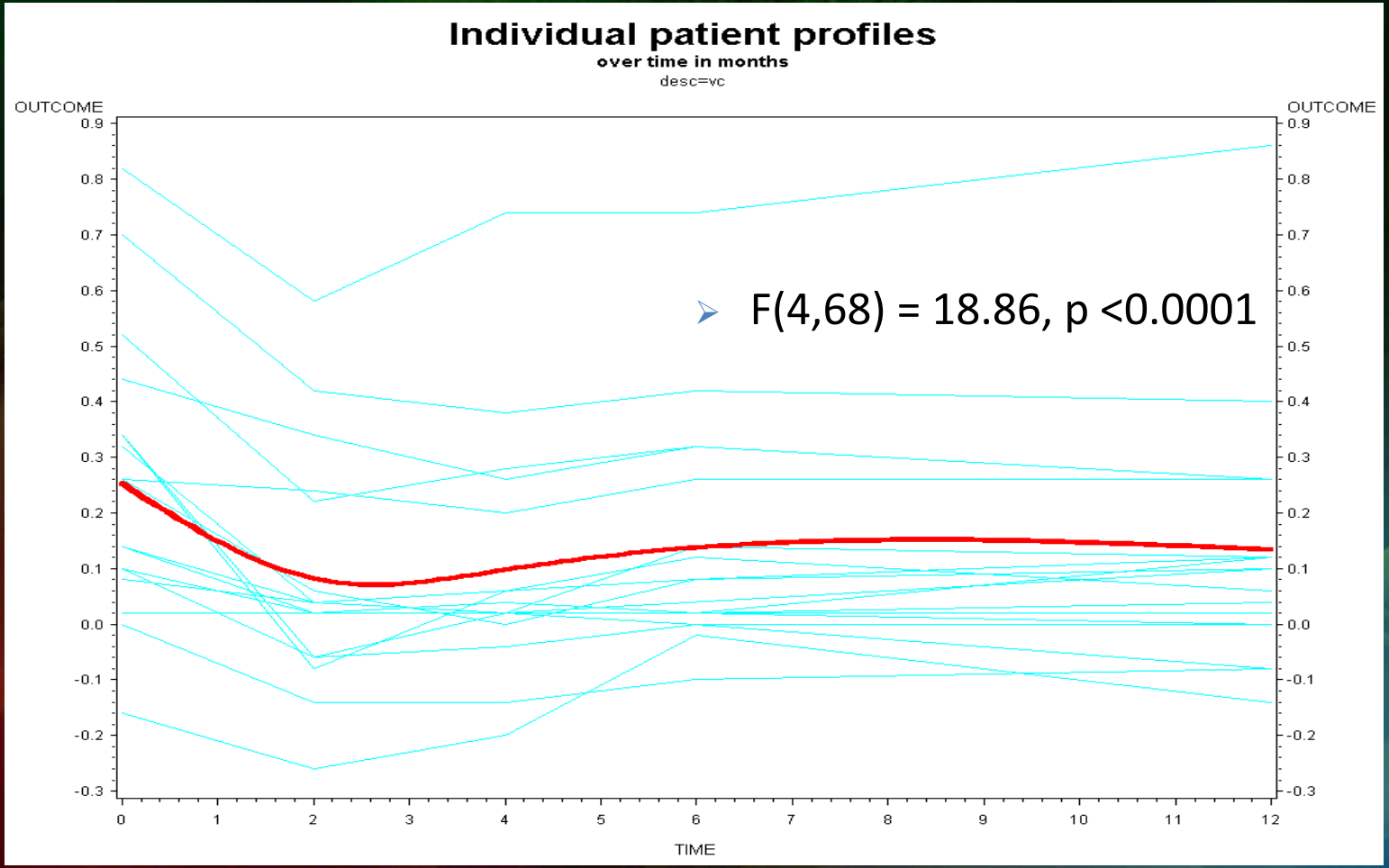
- Visually-significant cataract.
- Visually-significant capsular clouding post-cataract/IOL
- Any visually-significant disease process.

ETDRS Visual Acuity logMAR Test – Validated Clinical Outcomes

- 22 eyes
- 3 x per week for 6 weeks
- ETDRS Visual Acuity statistically significant at 1 year post-treatment
- Contrast Sensitivity also showed statistically significant improvements

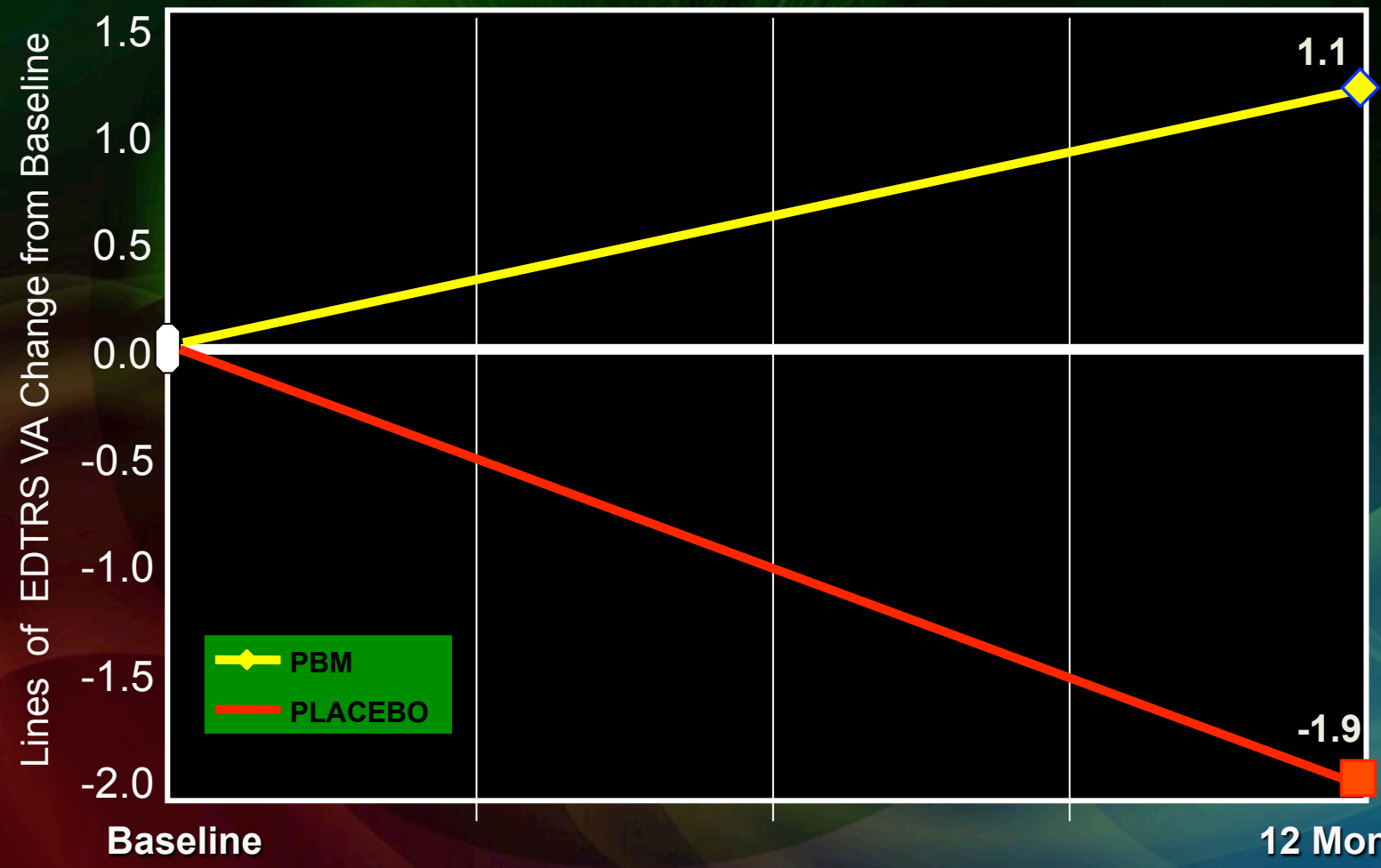


One Year Benefit in ETDRS Visual Acuity logMAR



- F(4,68) = 18.86, p <0.0001

Comparison of TORPA benefits versus Rheopheresis Placebo Arm in Dry AMD patients



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Is There Animal Model Data to Support Use of PBM in Dry Age-related Macular Degeneration?

YES!

Is There Clinical Data to Support Use of PBM in Dry Age-related Macular Degeneration?

YES!

Competition

Medical Device Competition

	ACUITY / SCYFIX	*ELLEX*	*LUMITHERA*
MECHANISM	Electro - microstimulation, Not elucidated	Microbubble damage to RPE cells	Restorative, multi-factorial, PBM is well documented
EASE OF USE	Non invasive – 2x daily	Laser to retina – episodic treatments	Non invasive – episodic treatments
TREATMENT TIME	20 mins x 2	Office procedure	5 min per eye
SIDE EFFECTS	Unknown	Cellular damage at laser site	None recorded
EFFICACY	Approx. 60% response	Drusen area decrease. VA?	> 90% response. VA & CS improvement and Drusen reduction

Competition Summary

LumiThera's approach is a multi-factorial treatment designed to target underlying disease mechanisms

- Photobiomodulation is regenerative and restorative
- Noninvasive and cost-effective
- Pharmaceutical agents are single-target approaches
- Drugs are in early development – Phase I/II
- Devices – unknown mechanisms or disruptive

PBM in dry AMD Summary

- Huge unmet medical need — Yes!
- Safe and effective non-invasive solution — Yes!
- Multiple ocular platforms for expansion — Yes!
- Experienced, dedicated PBM team — Yes!
- Several exit points with favorable ROI — Yes!
- IP and pilot clinical human data established — Yes!
- Significantly improve lives — Yes!

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