



THE SCIENCE OF RED LIGHT THERAPY

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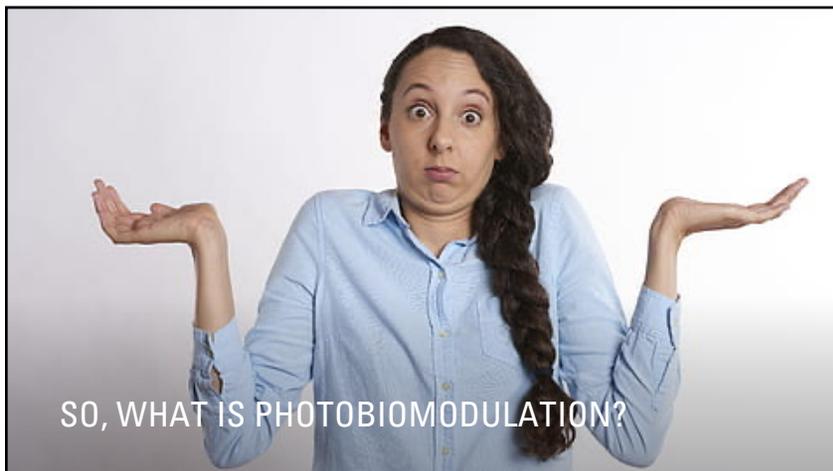
CECELIA KOETTING FINANCIAL DISCLOSURES

"All relevant relationships have been mitigated."

• Horizon-C	• Glaukos-C	• Oyster Point/Viatrix-C,R
• Ivantis-C	• B +L -C, S, R	• Allergan/Abbvie -C, S, R
• Orasis-C, S, R	• Iveric Bio-C	• Alcon-C, S, R
• Trukera (B+L) -C	• Azura-C	• Harrow-C, S
• LENZ-C	• Aldeyra-C	• Thea-C,R
• PRN-C,S	• Dome-C,S,R	• Bruder-C
• Kala-R	• Myze- C	• Blinkjoy-C
• Tarsus-C,S,R	• MOVU- C	• SCOPE-C
• Topcon-C	• Vital Tears- C	• Brill- C




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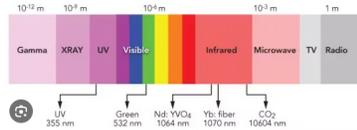


SO, WHAT IS PHOTOBIMODULATION?

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PHOTOBIMODULATION (PBMT)

- Photobiology
 - Scientific discipline that studies the effects of light on living organisms and their biologic process
 - Phototherapy utilizes light waves lengths between 390-1100nm
 - May be pulsed or continuous waves
- Utilizing exposure of nonthermal red and infrared light for therapeutic benefits and functions by stimulating, healing, regenerating and protecting organizations at risk of injury degradation or death.
- Last 2 decades gained recognitions and increased use
 - Non-invasive physical therapy method
 - Pain relief
 - Anti-inflammatory response
 - Tissue regeneration



Mirkouli, M., Chandramohan, N., & Papat, E. B. (2021). Photobiomodulation (low-level light therapy) and dry eye disease. *Clinical and Experimental Ophthalmology*, 104(5), 561-566. <https://doi.org/10.1093/cio/ciaa026>.
 Park, Y., Kim, H., Kim, S., Cho, K. I. Effect of low-level light therapy in patients with dry eye: a prospective, randomized, observer-masked trial. *Sci Rep*. 2022 Mar 4;12(1):3575. doi: 10.1038/s41598-022-07427-6. PMID: 3524656; PMCID: PMC8897482.

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LOW LEVEL LIGHT THERAPY

- LLLT is a type of photobiomodulation
- Low level nonthermal laser irradiation at the red or near infrared end of the spectrum
- 1960's Murine model incidentally found hair regrowth and accelerated wound healing
- Used in neurology, psychiatry, aesthetics, myopia control, MGD among many other applications

Glass GE. Photobiomodulation: A review of the molecular evidence for low level light therapy. J Plast Reconstr Aesthet Surg. 2021 May;74(5):1050-1060. doi: 10.1016/j.bjps.2020.12.059. Epub 2020 Dec 27. PMID: 33436333.

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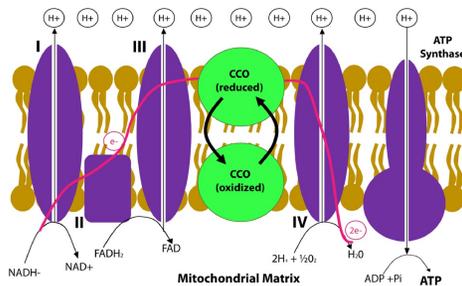
IT'S THE WILD WEST!

Lack of regulatory standards makes it difficult to draw clear conclusions about efficacy and safety but it is crucial that we understand the theoretical basis for PBM



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PROPOSED MOA'S OF LLLT: MITOCHONDRIAL ACTIVITY

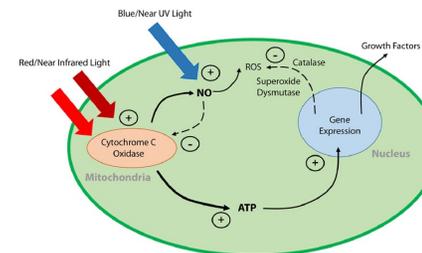


- Excitation of cytochrome c oxidase by light irradiation at the correct wavelength is thought to enhance electron transfer and thus ATP synthesis.
- Irradiation with a diode laser at 904 nanometers (nm) enhanced mitochondrial ATP synthesis in a lymphocyte cell line relative to nonirradiated controls.
- Cytochrome c oxidase is a crucial enzyme in the mitochondrial electron transport chain synthesizing ATP

Low level light therapy activates both reduced and oxidized versions of cytochrome c oxidase (CCO), enhancing adenosine triphosphate (ATP) synthesis. H⁺: protons; e⁻: electrons; NAD: nicotinamide adenine dinucleotide; and FAD: Flavin adenine dinucleotide

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PROPOSED MOA'S OF LLLT: OXIDATIVE STRESS



- Relationship depend on preexisting stressors on the cell
- LLLT increased reactive oxygen species (ROS) in physiologically resting neurons but protected oxidatively stressed neurons from cell death by reducing the levels of reactive oxygen species

The influence of red and blue light on cellular physiology. Simplified diagram of downstream intracellular physiology in response to red and blue light. ATP: adenosine triphosphate; NO: nitric oxide; and ROS: reactive oxygen species

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PROPOSED MOA'S OF LLLT: CELL SIGNALING, GENE EXPRESSION, GROWTH FACTOR RELEASE

Cell Signaling

- Light-induced redox changes influence signaling proteins (e.g., mitochondrial superoxide).
- Activation of Ca^{2+} ATPase, Na^+/H^+ antiport, $\text{Na}^+/\text{Ca}^{2+}$ exchange pathways.
- Modulation of $\text{NF-}\kappa\text{B}$ → alters inflammation and immunity.
- Upregulates MAPK and PDGF pathways → supports proliferation and repair.

Growth Factor Release

- Increases expression of:
 - VEGF, PDGF, FGF-2, NGE, TGF- β
- Enhances angiogenesis, fibroblast migration, and ECM remodeling.
- Reduces ROS and supports endothelial proliferation via ERK/MAPK.

Gene Expression

- Upregulates genes for:
 - Cell proliferation
 - Oxidative stress protection
 - DNA synthesis & repair
 - ECM proteins (collagen I, fibronectin)
- Downregulates:
 - Apoptotic & inflammatory genes (e.g., IL-1, IL-10)
- Wavelength- and dose-dependent effects.

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PROPOSED MOA'S OF LLLT: INFLAMMATORY MODULATION AND MICROVASCULAR CIRCULATION

Inflammatory Modulation

- **COX Pathway Regulation**
 - LLLT reduces PGE2 by downregulating COX-2 expression (e.g., gingival fibroblasts, synoviocytes, macrophages).
 - Mechanism involves ROS dissociation rather than enzyme inhibition (unlike NSAIDs).
- **Cytokine Expression**
 - ↓ Pro-inflammatory cytokines: TNF- α , IL-1 β , IL-6, iNOS, MCP-1 in various in vitro and in vivo models (e.g., tendinitis, lung injury, periodontitis).
 - ↓ IL-10 and SOD expression in some injury models, suggesting antioxidative benefits.
- **NF- κ B Pathway**
 - Effects appear downstream of NF- κ B, which remains unaltered, implying selective transcriptional modulation.

Microvascular Circulation

- **Vasodilation via Nitric Oxide (NO)**
 - Red/NIR light stimulates NO synthesis → local vasodilation, reduced ischemic damage.
 - Blue/UV light also triggers NO release from keratinocytes → enhanced microcirculation and melanogenesis.
- **Clinical Relevance**
 - Improved circulation may enhance tissue oxygenation and nutrient delivery, supporting healing and inflammation resolution.

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LLLT WITH LIGHT EMITTING DIODES (LED)

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CONTRAINDICATIONS

- **Pregnancy:** LLLT should be avoided during pregnancy.
- **Epilepsy or history of light-activated neurological disorders:** Caution should be exercised in patients with epilepsy or other conditions where light can trigger seizures.
- **Photosensitivity:** Individuals with known photosensitivity to red or yellow light should avoid LLLT.
- **Herpetic disease:** LLLT is not recommended for individuals with active herpetic disease.
- **Recent refractive surgery (e.g., LASIK):** LLLT should not be performed for 12 months after refractive surgery.
- **Metallic piercings:** If you have metallic piercings near the treatment area, they should be removed.
- **Certain medications:** Patients taking photosensitizing drugs or dermatologically prescribed medications (like Roaccutane) should inform their practitioner.
- **Use of other cosmetic therapies:** If you are undergoing other skin cosmetic treatments, it's best to inform your practitioner.

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OCULAR SURFACE DISEASE APPLICATION

Tear hyperosmolarity, disruption of the ocular surface, and tear film instability induce dry eye syndrome

- Changed tear composition and decreased tear production result in damage to the ocular surface, inflammation, and apoptosis of epithelial cells

OSD Applications:

- Meibomian gland dysfunction
- Blepharitis
- Chalazion
- Hordeolum
- Demodex → LLLT does not kill (AAOPT 2022 Periman data)

Combination with IPL (Intense Pulsed Light)

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TECHNOLOGY

The best therapeutic outcome appears to come from a combination of both light therapies, IPL and LLLT. At least 5 studies have shown this combined benefit.

- In a 2021 study of 31 patients with MGD who were treated with both IPL and LLLT, the lipid layer thickness improved 6 months after treatment and the mean Ocular Surface Disease Index (OSDI) score improved from severe to normal 6 months after treatment.¹⁰
- In 2019, a retrospective chart review study of 230 patients with MGD who had a combination of IPL and LLLT showed a significant improvement in OSDI score, improvement in MGD grading, and improvement in TBUT.¹¹
- Another retrospective study from 2021 with 11 MGD patients using IPL and LLLT found a significant improvement in OSDI score, MGD grading, TBUT, and corneal fluorescein staining score.¹²
- A 2022 prospective study involving 47 patients with MGD who had IPL and LLLT showed significant improvement in OSDI scores, TBUT, and meibomian gland expressibility 3 months after treatment.¹³ These effects were sustained 6 months after treatment as well.¹³ This study also demonstrated a significant reduction in inflammatory markers such as MMP9 in the treated eyes.¹³
- A study from 2021 involving 20 Sjogren patients who were treated with IPL and LLLT demonstrated an improvement in TBUT 1 month after treatment and an even more statistically significant improvement 3 months after treatment.¹⁴

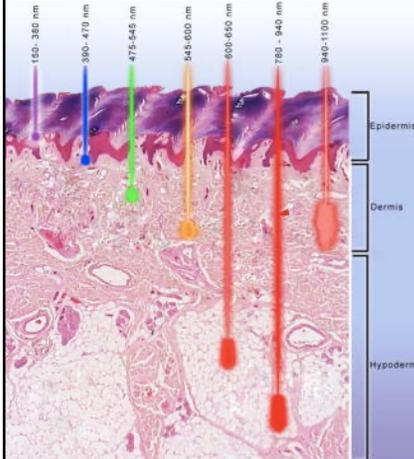


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DEVICES FOR LLLT/RED LIGHT THERAPY

- Well, go back to the Wild Wild West slide. . . . But here are a few things to give direction
- What are we looking for:
 - Good quality LEDs are quasimonochromatic with 98% of photons at the rated wavelength
 - Ensures all photons are travelling in approximately the same direction
- In Office
 - Marco Equinox LLLT
 - Essilor epi-c plus OPE IPL and LM LLLT
 - BioPhotas Celluma LLLT
 - Beware: Click fees for devices
- At Home devices
 - So many.

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DIFFERENT COLORS, DIFFERENT TREATMENTS

- Most common color options, more studies
 - Red light exposure:** pain relief, inflammation
 - Blue light exposure:** acne fighting
- More controversial, few studies
 - Amber light exposure:** improved skin hydration, increased lymphatic drainage, reduced erythema, increased collagen production, decreased MMP9s
 - Green Light:** May help to even out skin tone and reduce hyperpigmentation.
 - Yellow Light:** Can improve skin texture and reduce redness, making it beneficial for those with sensitive skin or rosacea.
 - Purple Light:** May help regenerate skin cells, treat rosacea, and reduce inflammation.

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INTENSE PULSED LIGHT

- Flashes of high powered, filtered polychromatic light to heat target tissues.
 - Filters enables chromophore selectivity
- Photothermolysis is one of the proposed mechanisms of action of IPL for dry eye.
 - Wavelengths selectively destroy blood vessels by targeting chromophores within the blood vessels.
 - Destruction of telangiectasias along the eyelid inhibits access of inflammatory mediators to the meibomian glands.
- Other MOA
 - Mild local warming effect to allow better expression of meibum
 - Destruction of bacteria that cause inflammation at the level of the meibomian glands



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IPL IS NOT AN LLLT, BUT IS A TYPE OF PHOTOBIO-MODULATION

- IPL flashlamp polychromatic high intensity light
- IPL generates heat and targets blood vessels and skin layers
- IPL versatile for many things including targeting surface level tissues
- LLLT uses laser or LED to emit low-energy monochromatic light
- LLLT is non-thermal and focuses on cellular repair
- LLLT is often used for sensitive tissue care, rejuvenation and deeper tissue healing

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INTENSE PULSED LIGHT

- Indications
 - Vascular lesions, pigmented dark spots, skin tightening
 - Dry eye disease and meibomian gland dysfunction
 - Telangiectasias in lid margin and inflammation decrease
 - Heat created makes impacted meibum more mobile
 - Decrease bacterial load on skin
 - Ocular and facial rosacea
 - Blepharitis
- Contraindications
 - Active infections
 - Dysplastic nevi
 - Active cold sore
 - Open laceration or abrasion
- Medications?
 - Accutane
 - Tetracyclines
 - Retinoid
 - Chemotherapy
 - Anticoagulants



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PEER-REVIEWED LITERATURE ON IPL FOR MGD/DED

Authors	Year	P/R	Publication	N	Key Findings
Seo KY et al	2018	P	<i>Cont Lens Anterior Eye</i> , 41(5):430-435.	17	OSDI, TBUT, NIBUT, staining, LM vascularity, meibum quality, meibomian expressibility
Arita R et al	2018	P	<i>Cornea</i> , 37(12):1566-1571.	31	SPEED, TBUT, NIBUT, interferometric pattern, meibum grade, lid margin abnormality score, CFS
Yue Y et al	2018	P	<i>Curr Eye Res</i> , 43(3):308-313.	35	OSDI, TBUT, MGE, MG morphology (confocal)
Rong B et al	2017	P	<i>Zhonghua Yan Ke Za Zhi</i> , 53(9):673-681.	44	MGYSS, SPEED, TBUT, staining, meibography
Liu R et al	2017	P	<i>Am J Ophthalmol</i> , 183:81-90.	44	IL-17A, IL-6, PGE2, MGYCS (clear secretions)
Dell SJ	2017	P	<i>Clin Ophthalmol</i> , 11:1167-1173.	40	TBUT, SPEED, osmolarity, staining, MG score
Albietz JM et al	2017	P	<i>Clin Exp Optom</i> , 101(1):23-33.	26	OSDI, Ocular Comfort Index, AFT use, TBUT, staining
Gupta PK et al	2016	R	<i>Can J Ophthalmol</i> , 51(4):249-253.	100	Lid margins, MG flow, meibum quality, TBUT, OSDI, eyelids
Vegunta S et al	2016	R	<i>Cornea</i> , 35(3):318-322.	35	SPEED2, MGE (liquid secretions)
Jiang X et al	2016	P	<i>J Ophthalmol</i> , 2016:1910694.	40	TBUT, TMH, staining, lid margin, MGA, meibography
Toyos R et al	2016	P	<i>J Clin Exp Ophthalmol</i> , 7(6):619.	16	Tear film osmolarity

Slide Courtesy of Selina McGee, OD, FFAO

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Authors	Year	P/R	Publication	N	Key Findings
Craig JP et al.	2015	P	<i>Invest Ophthalmol Vis Sci.</i> 56(3):1965-1970.	28	Lipid layer grade, NIBUT, tear evap. rate, TMH, VAS, SPEED
Vora GK et al.	2015	R	<i>Curr Opin Ophthalmol.</i> 26(4):314-318.	37	TBUT, lid margins, eyelids, MG oil flow, meibum quality, OSDI
Toyos R et al.	2015	R	<i>Photomed Laser Surg.</i> 33(1):41-46.	78	TBUT, patient satisfaction, meibum quality, lid margin
Vegunta S et al.	2014	R	ARVO, published in <i>Invest Ophthalmol Vis Sci.</i> 55:2018	43	SPEED2, MGE
Shen L et al.	2015	R	ARVO PN 4441/PBN A0067	9	SPEED2, OSDI, MGE, Schirmer test, staining, TBUT, lipid tear film analysis, TMH, meibography
Kim et al.	2015	R	ARVO PN 6193/PBN C0264	53	OSDI
Craig et al.	2015	P	ARVO PN 6193/PBN C0265	28	Lipid layer grade, NIBUT
Shen JF	2014	R	ARVO, published in <i>Invest Ophthalmol Vis Sci.</i> 55:2017	5	SPEED2, OSDI, MGE, Schirmer test, staining, TBUT, lipid tear film analysis, TMH, meibography
Gupta	2014	R	ASCRS	37	Lid margin edema & vascularity, facial telangiectasia, meibum quality, OSDI, TBUT, oil flow score
Toyos R	2013	R	ARVO, published in <i>Invest Ophthalmol Vis Sci.</i> 54:966	91	TBUT, self-satisfaction, physician-judged improvement

PEER-REVIEWED LITERATURE ON IPL FOR MGD/DED

Slide Courtesy of Selina McGee, OD, FAAO

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IPL DEVICE OPTIONS

- OptiLIGHT from Lumenis is the first and only FDA approved for the treatment of MGD and dry eye.
 - But not the only one that works
- Others not FDA approved for DED/MGD
 - Lumibird C.STIM
 - Rohr
 - iLight IPL Pro
 - Many others
- Combination devices with RF or LLLT

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WAVELENGTHS

- Chromophores absorb light most effectively at certain wavelengths
- Light scattering decreases with increased wavelength
- Ranges from about 400-1200nm for IPL depending on your system
- Some wavelengths are then filtered out using a filter
- 2 types of wavelength filters
 - Cut-off filters
 - Most common
 - Block all wavelengths below that filter number
 - Typical cut-off filters: 515, 560, 590, 615, 640, 695 and 755
 - Cut-in filters
 - Block all wavelengths except a small range right around that filter number

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BEFORE YOU TREAT

THE FITZPATRICK SCALE

	TYPE I	TYPE II	TYPE III	TYPE IV	TYPE V	TYPE VI
BEFORE TREAT	Ivory	Fair or pale	Fair to beige, with golden undertones	Olive or light brown	Dark brown	Deeply pigmented dark brown to darkest brown
AFTER TREAT	Always freckles, always burns/freckles, never tans	Usually freckles, often burns/freckles, rarely tans	Might freckle, burns on occasion, sometimes tans	Doesn't really freckle, rarely burns, often tans	Rarely freckles, almost never burns, always tans	Never freckles, never burns, always tans

- The highest absorption of melanin is at lower wavelengths, therefore higher-wavelength filters - which are less absorbed by melanin - offer protection for darker skin types
- Certain wavelengths and filters are used to treat specific skin and eyelid conditions based on the patient's skin type and the desired depth of the treatment
- The patient's skin type is determined by using the Fitzpatrick skin type scale
- IPL works best on patients with skin types I to IV

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IPL COMPLICATIONS AND PREP

- Treated areas should be closely shaven if applicable
- Cleanse face
 - Yes everyone, use something without fragrance or oils
- Apply ultrasound jelly
 - DON'T BE STINGY!
- Hair net to avoid hairline
- Patient Eye protection
 - Laser grade stickers
 - IPL goggles
 - Laser grade corneal shields
- Examiner and anyone else in the room eye protection
 - Green goggles
- Complications
 - Pain
 - Erythema
 - Edema
 - Hyper/hypopigmentation
 - Retinal protection

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DON'T FORGET TO ASK

- Ask about recent sun exposure each treatment, not just the first treatment when skin typing
- Does the patient get cold sores?
 - Prophylactic antivirals
- Facial tattoos? Tattoo eyeliner?
- Keloid scar tissue former?
 - Some studies suggest IPL is actually helpful and not a contraindication
- Are they being treated for facial skin cancer?
- Other recent facial treatments?
- Radiation therapy?
- Seizures or epilepsy?

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TOYOS PROTOCOL

- Toyos Protocol – Only FDA approved Protocol
- Two Pass Method – Tragus to Tragus – With Expression each time
- External Shields not Internal Shields
- 2 to 4 weeks apart – 4 treatments minimum
- Toyos specified parameters – Each IPL system is unique
- Upper Lids were not performed in the FDA study – Upper Lids are performed based on Toyos Published Upper Lid Study
- Variations on the Toyos Protocol should be studied and published (perfect example – failure of a popular protocol)

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TOYOS DARWIN IPL PROTOCOL

IPL Settings for Treatment Within the Orbital Rim

Skin Type	Treatment	Fluence (J/cm ²)	Filter (nm)	Pulse Structure	Pulse Duration (ms)	Delay (ms)	Chiller	Tip Temperature
I	Toyos Dry Eye	12	585	Triple	6	80-100	On	4-5 C°
II		11						
III		10						
IV		10						
V		10						

Upper Lid all Skin Types all the same parameters – 10J/cm² at 100ms Thermal Relaxation Time
 Full Face – Complete Toyos DED Protocol and add 2 J/cm² and complete two passes to rest of face excluding the upper lip and below the jawbone

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KOETTINGS' AMENDED PROTOCOL

- Skin Type I-IV
 - 3 baseline treatments 4-6 weeks apart with expression and blepharoxfoliation
 - 2 passes → sometimes 3 if using different filter
 - 2nd appointment will use an air activated disposable heat mask after treatment for 10-15minutes followed by expression.
 - Maintenance treatments every 4-12 months depending on underlying etiology
 - Rosacea and Demodex Blepharitis patients will be every 4 months
 - Skin Type V (based on Janelle Davison OD protocol)
 - 3-4 treatments 4-6 weeks apart
 - Tragus to tragus ONLY
 - MUST TEST SPOT!
 - 650nm
 - 100 cooling, Long delay
 - LOW joules, around 6-9mj
 - Set expectations
-

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CHALAZIA (DR. LAURA PERIMAN)

- Full face 560nm rosacea treatment, single pass
 - Tragus to tragus 590nm Toyos settings for DED, double pass
 - Toyos setting for DED on eyelids with protective barrier, double pass
 - Stack 3 extra Toyos pulses on top of chalazia
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QUESTIONS?



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THANK YOU!

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