Laser and Light Interaction:
PBM: Healing, Repair and Regeneration

DE MONTFORT UNIVERSITY LEICESTER

Dr Mark Cronshaw
PhD, B.Sc(Hons), BDS, LDS RCS (Eng), M.Sc

Email: Drmarkcronshaw@outlook.com
www.dentallaseracademy.co.uk

Amery House Dental Practice, Cowes, Isle of Wight

All services Including:

- General dentistry
- Implants
- Orthodontics
- Aesthetic dentistry
- Endodontics
- Etc!

Dentistry & Technology: Cad-Cam, Lasers & more!

Clinical Challenges:

Rapid resolution of pain & associated loss of function

Minimal trauma associated with clinical interventions

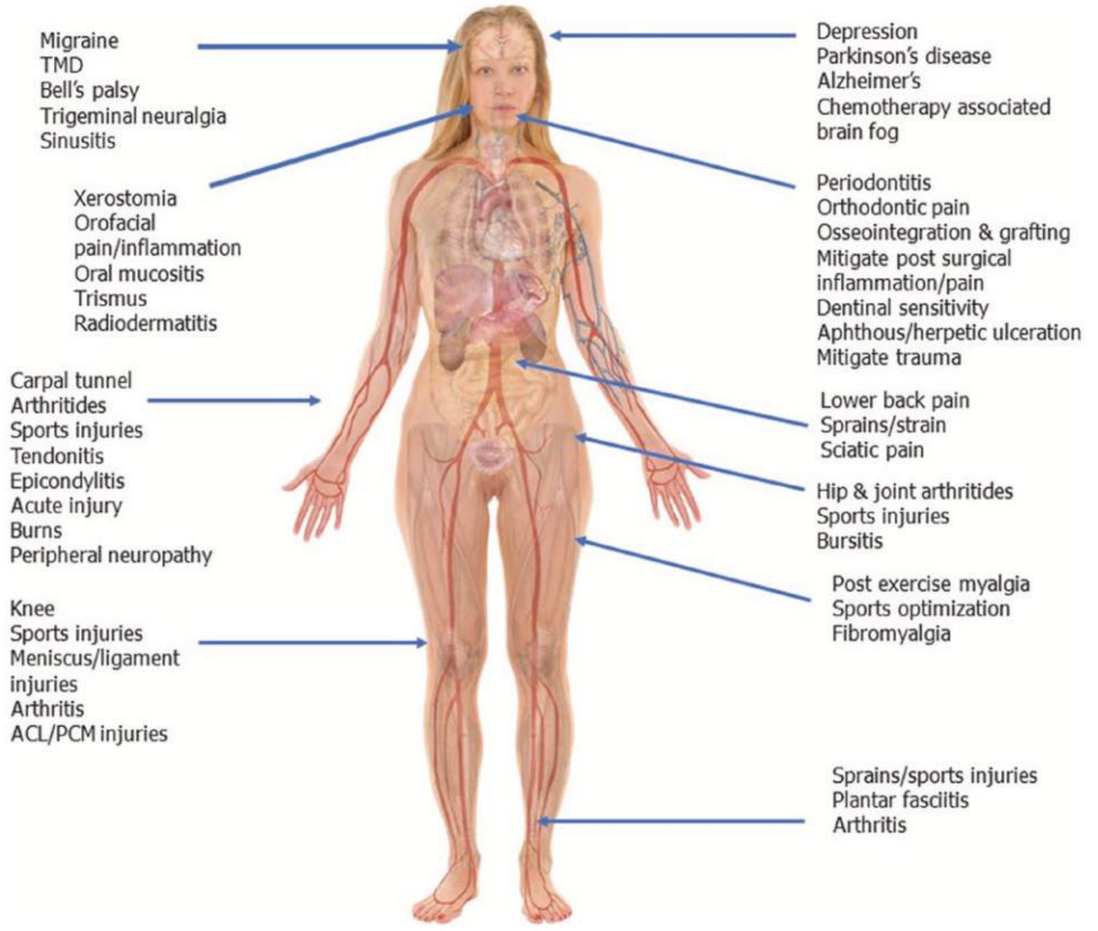
Arrest & reverse effects of disease

Optimise outcome: reliable, simple, durable & inexpensive

Laser & Light Tissue Interaction: What is Photobiomodulation (PBM)?

PBM :

- Targeted application of light for therapeutic purposes
- Source can be a laser, an LED or another light source
- Intensity & accumulated energy below threshold to damage proteins & fatty acids
- Achieves beneficial directed changes in tissue healing, repair & regeneration
- Mediated locally, regionally and systemically
- Promotes mitosis & production of matrix eg. Collagen, bone
- Enhanced vasculature & improve lymphatic drainage
- Reduce & Resolve inflammation
- Relieve pain
- Pre-conditioning: increase cellular resistance to stress eg. radiotherapy, chemotherapy



Images reproduced courtesy © Dr Steven Parker

Cronshaw M, Mylona V. Photobiomodulation Therapy Within Clinical Dentistry: Theoretical and Applied Concepts. In: Lasers in Dentistry Current Concepts 2024 Jan 9 (pp. 173-236). Springer International Publishing.

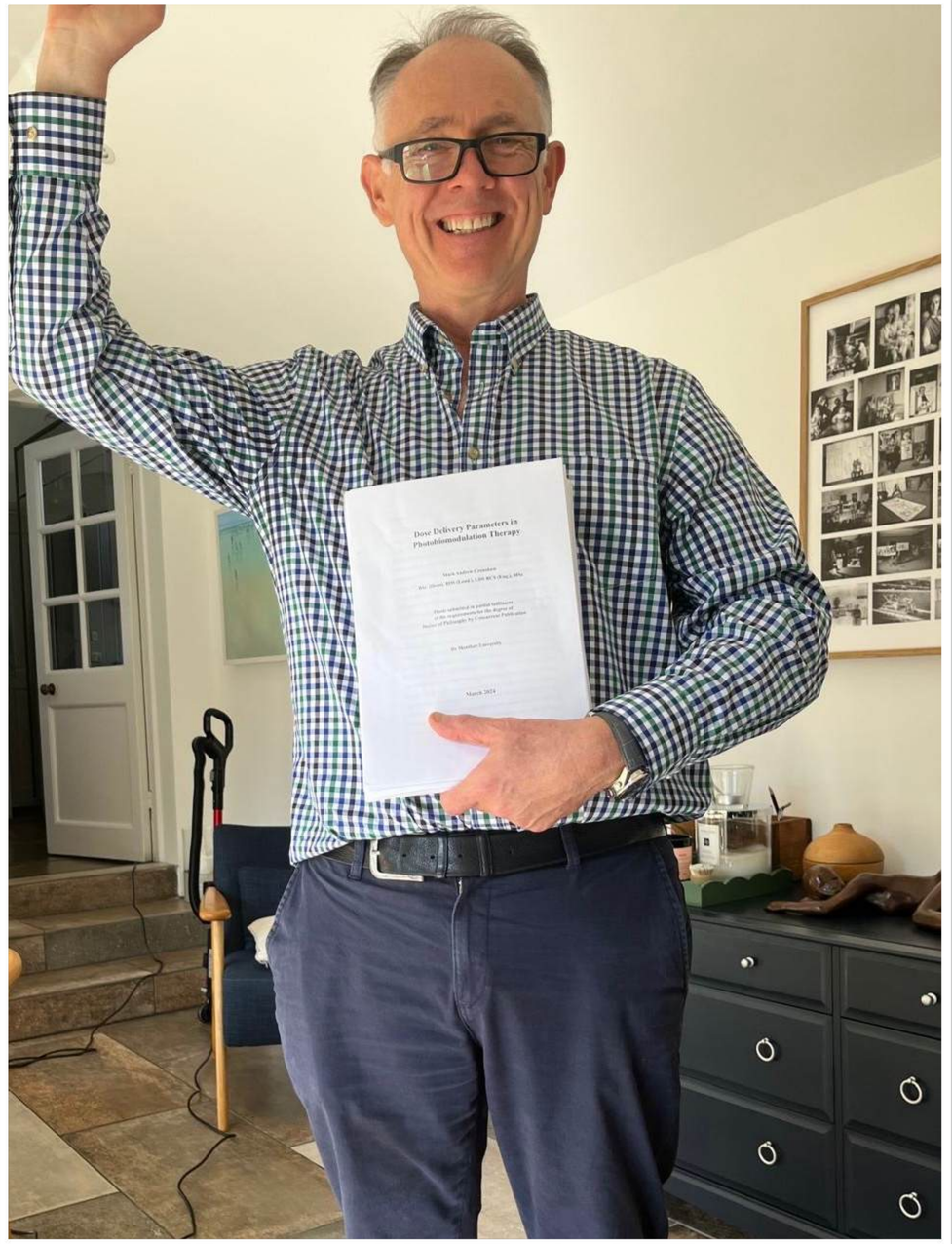
Research Journey:

Expanded reading:

- Accepted published research
- Published literature reviews based on outcome
- Experimental studies: output power & photothermal

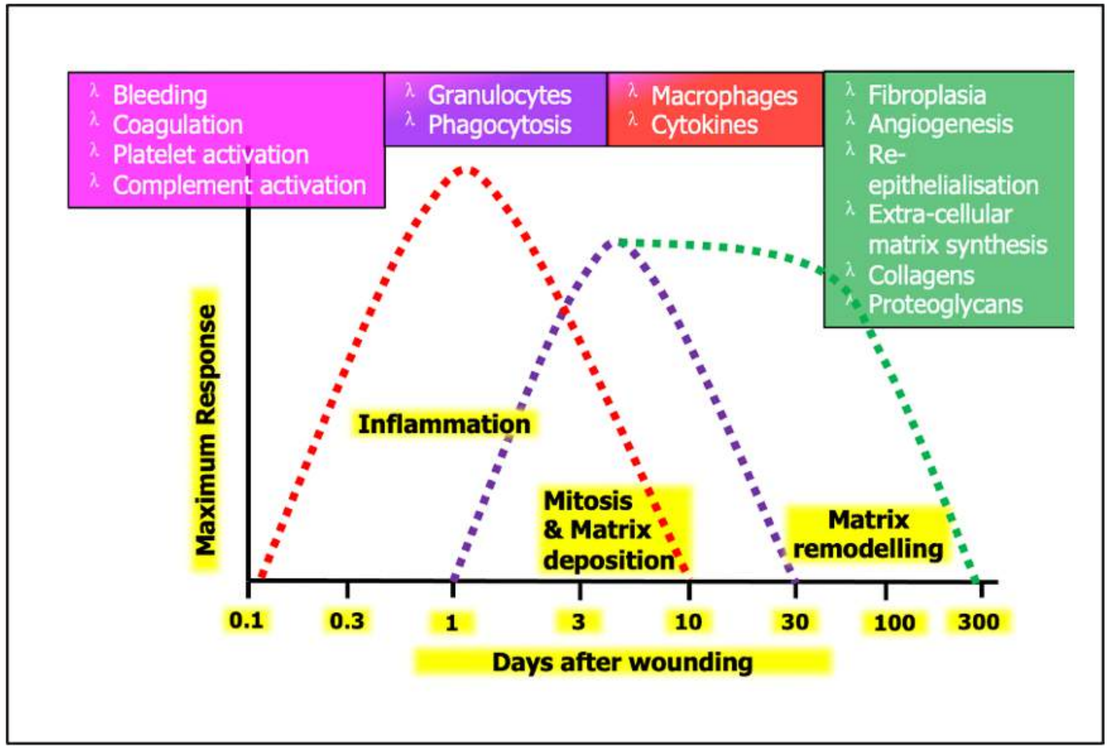
- Evolutionary & microbial basis of analgesia mechanisms in PBM
- Orthodontics: pain control & tooth movement
- Pain, inflammation & PBM
- PBM & Periodontics
- Parameters: Quality Analysis of parameter reportage
- Parameters: Importance of optical spot size & relation to target depth
- Oral mucositis
- Parameters: Power output variation between devices
- Parameters: Expanded analysis of delivery techniques
- LED PBM & aPDT
- Cryotherapy/PBM

- Cronshaw M, Parker S, Arany P. Feeling the heat: evolutionary and microbial basis for the analgesic mechanisms of photobiomodulation therapy.

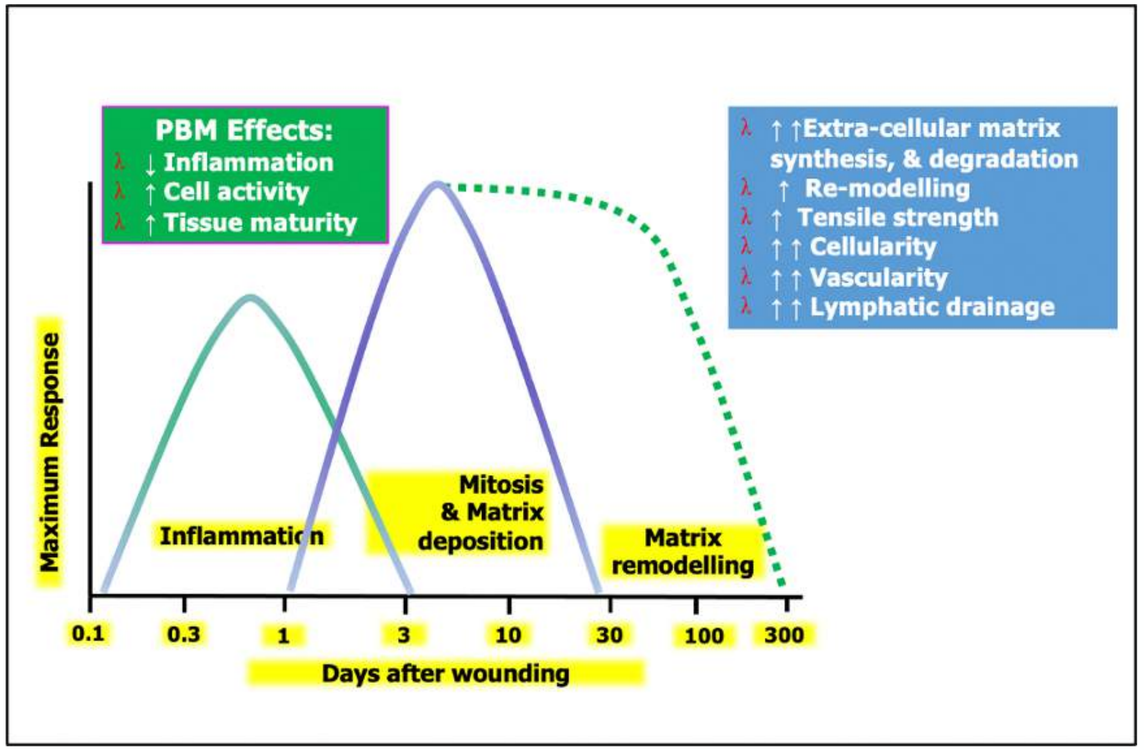


- .Parker S, Grzech-Leśniak K, Cronshaw M, Matys J, Nammour S. Full operating parameter recording as an essential component of the reproducibility of laser-tissue interaction and treatments. Advances in Clinical and Experimental Medicine. 2024;33(6):653-6.

Managed Biological Healing:



Azizi A & Osgouie K "Dermal Wound Healing" IEEE 2010; 2:88-90



Images reproduced courtesy © Dr Steven Parker

Obstacles to healing:

- Infection (biofilm)
- Disrupted/lost blood clot
- Dietary insufficiency eg. vit D, Fe++
- Hypoxia (CVD, COPD, Polycythaemia)
- Systemic disease: diabetes, cancer, general inflammatory disorders eg. rheumatoid arthritis, inflammatory bowel disease
- Obesity (elevated LDL, inc. systemic inflammation)
- Iatrogenic: drugs NSAID's, SSRI's, ACE inhibitors etc!

Haxsen V,et al.. Relevance of laser irradiance threshold in the induction of alkaline phosphatase in human osteoblast cultures. Lasers in medical science. 2008 Oct;23:381-4.
Pagin MT, et al.Laser and light-emitting diode effects on pre-osteoblast growth and differentiation. Lasers in medical science. 2014 Jan;29:55-9.
Choi H, et al.Inflammatory cytokines are suppressed by light-emitting diode irradiation of P. gingivalis LPS-treated human gingival fibroblasts: inflammatory cytokine changes by LED irradiation. Lasers in medical science. 2012 Mar;27:459-67.
Pesevska S, Et al.The effect of low-level diode laser on COX-2 gene expression in chronic periodontitis patients. Lasers in medical science. 2017 Sep;32:1463-8.
Cronshaw M, Parker S, Anaganostaki E, Bordin-Aykroyd S, Lynch E. Photobiomodulation therapy and periodontitis: A discussion paper. EC Dental Sci. 2019;18:1791-7.

- Meta analysis and systematic reviews support the efficacy of PBM in the management of some common orthopaedic conditions eg. tennis elbow

- *Bjordal J, Rodrigo AB et al, BMC Musculoskeletal Disorders 2008;9:75*

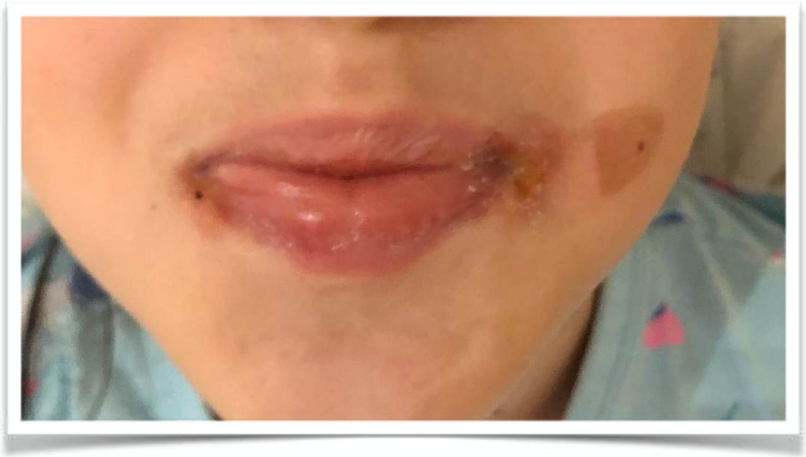
Snake Bite
treatment:
940nm contour handpiece

Initial therapy:
coagulation no tip 1w surgical handpiece with movement
Then PBM
contour handpiece 4W cw 1cm away slow movement 300secs
Repeated two further visits
Outcome at 4 months

Clinicians Wish List:

- Optimise tissue stress resistance
- Increased production of biomatrix
- Eliminate infection
- Minimise trauma
- Mitigate & reduce post Rx pain
- Reduce peak & duration of acute inflammatory stage

Severe burn (hot tap)



72 hours

@ 6 days (Christmas Eve!)

Khan,I et al. Accelerated burn wound healing with photobiomodulation therapy involves activation of endogenous latent TGF-1ℬ
Scientific Reports 2021.11:13371

A 3 year old child was injured by a dog and sutures were placed. PBMT commenced at day 4 through the transparent wound dressing using a 940 nm Diode laser and a 7.1cm^2 area applicator at an output power of 3.5W continuous wave (CW) to two adjacent areas with a scanning movement for a total of 200s/session. Dose: 50 J/cm^2.

Sutures were removed at day 8 and PBMT was repeated on a daily basis whilst acute inflammation resolved up to day 10. After day 10 the treatment protocol was changed to a lower setting at 1.4W CW using a contour handpiece with a surface area of 2.8cm^2 for 24s total to two adjacent areas again with a scanning motion twice weekly. Dose 6 J/cm^2.

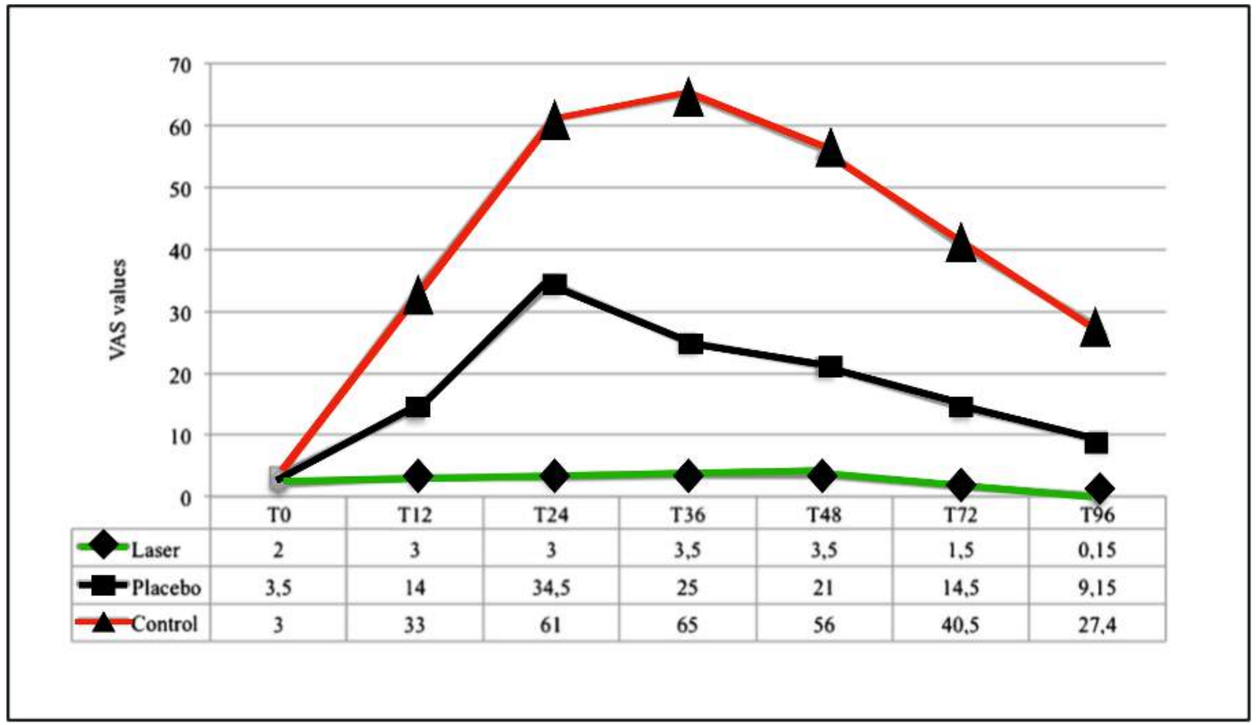
Case: Dr Charlotte Van Belle

Clinical Challenges In Daily Practice:

- Pathogenic biofilms can be difficult to eradicate
- Elderly & medically compromised patients: high needs limited capacity
- Complex multi-disciplinary treatments required
- Patient compliance issues: trust, cost, tolerance & time

Healing& Pain Management: Preconditioning:?

- Prophylaxis vs. Healing/repair?
- Dosimetry for healing vs. Analgesia?
- Placebo effects in analgesia?



	T0	T12	T24	T36	T48	T72	T96
Laser	2	3	3	3,5	3,5	1,5	0,15
Placebo	3,5	14	34,5	25	21	14,5	9,15
Control	3	33	61	65	56	40,5	27,4

Image adapted from: Marini et al.The effect of diode superpulsed low-level laser therapy on experimental orthodontic pain caused by elastomeric separators: a randomized controlled clinical trial. Lasers Med Sci 2015;30:35–41.
M. A Cronshaw PhD Thesis: publication pending.

Borzabadi-Farahani A, Cronshaw M, Lasers in orthodontics. Lasers in dentistry—current concepts. 2017 Sep 22:247-71.

Cronshaw M, Parker S, Anagnostaki E, Lynch E. Systematic review of orthodontic treatment management with photobiomodulation therapy. Photobiomodulation, photomedicine, and laser surgery. 2019 Dec 1;37(12):862-8.

.

Oral Mucositis:

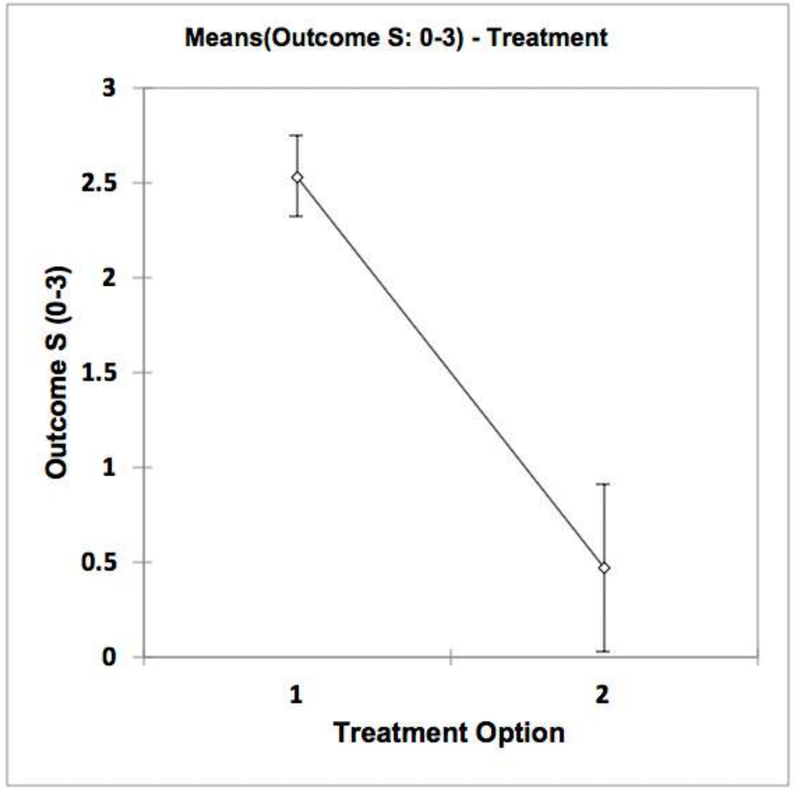
dentistry journal

MDPI

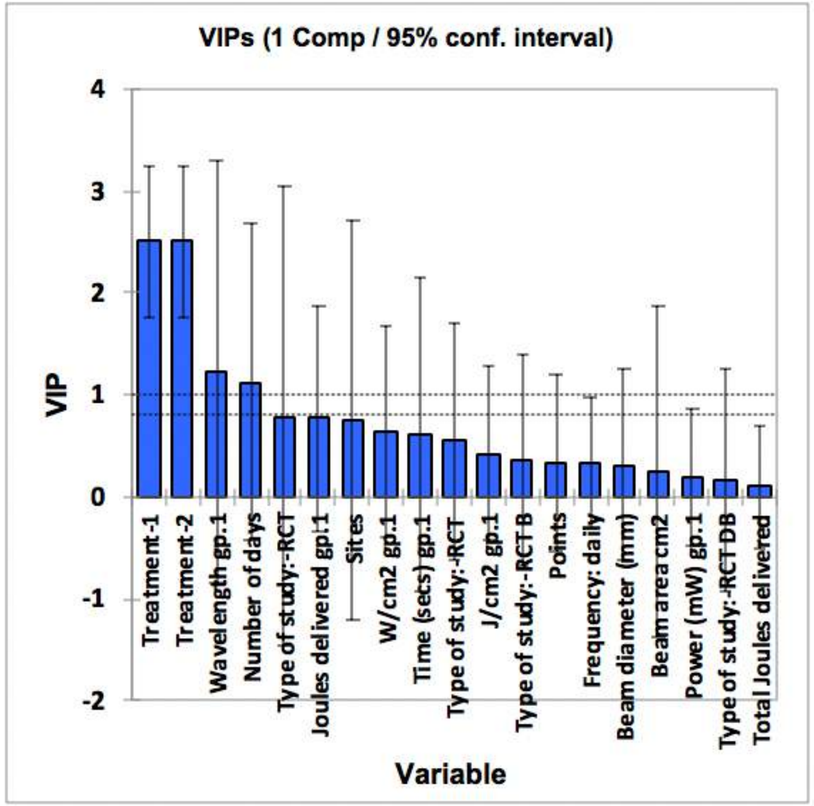
Review

Photobiomodulation and Oral Mucositis: A Systematic Review

Mark Cronshaw [1,2,*], Steven Parker [1], Eugenia Anagnostaki [1], Valina Mylona [1], Edward Lynch [1,3] and Martin Grootveld [1,3]



Univariate ANCOVA :Mean CI values 1= Pre- 2= post Rx



Outcome:

- Clear difference between prevention > therapy
- Large beam area: P< 0.00735
- VAS: positive trend

Multivariate PLS-R analysis (sample size weighted)

dentistry journal

MDPI

Review

Photobiomodulation and Oral Mucositis: A Systematic Review

Mark Cronshaw [1,2,*], Steven Parker [1], Eugenia Anagnostaki [1], Valina Mylona [1], Edward Lynch [1,3] and Martin Grootveld [1,3]

Case: Sanae El hasnaoui (UK)

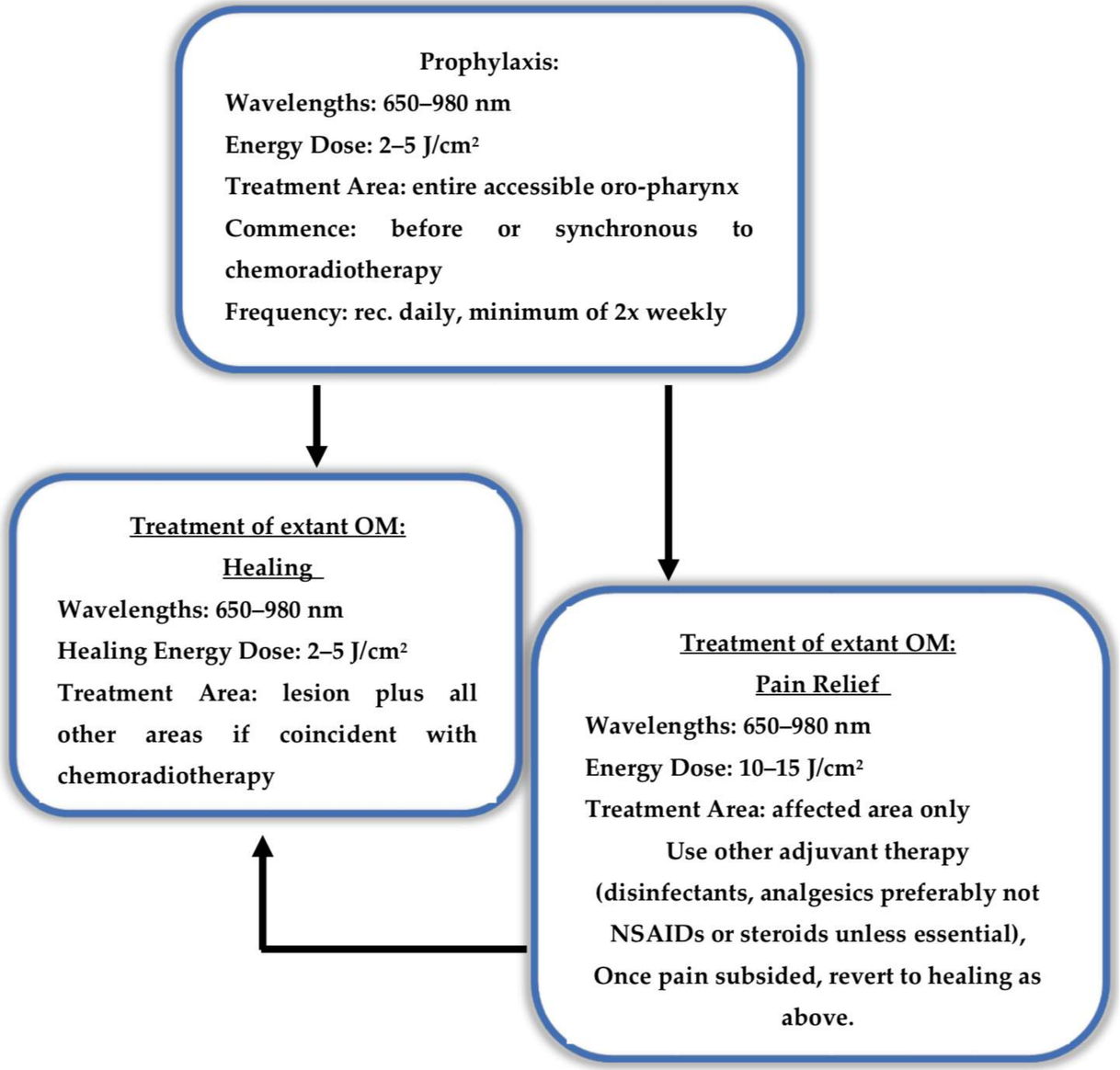
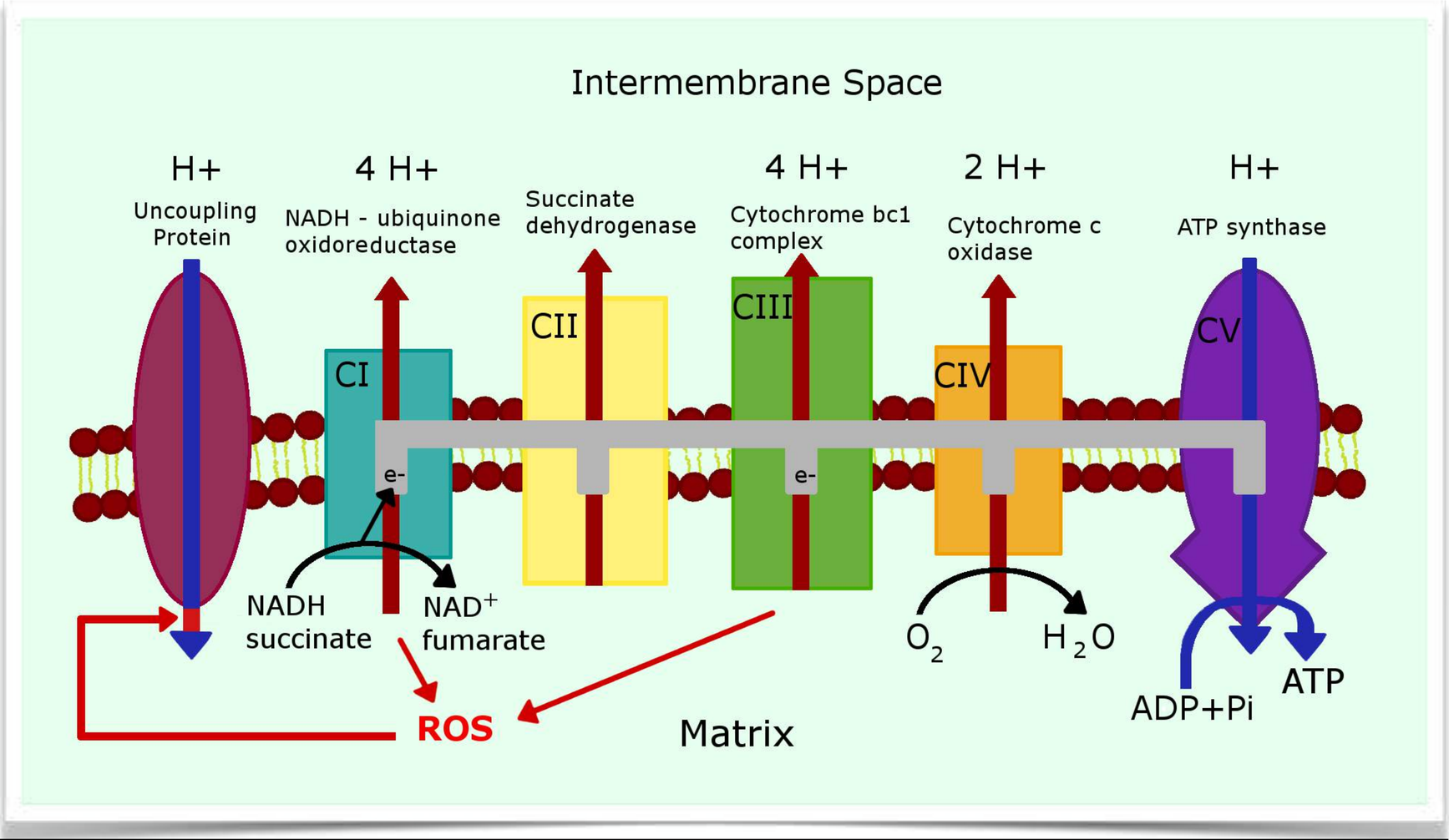


Figure 3. Proposed treatment decision tree—pain or healing? Outline of applied photobiomodulation (PBM) dose parameters to address the needs of pain relief and healing.

Clinicians algorithm

Possible Photon Transduction Pathways:

- Photochemical
- Photothermal
- Photoelectric
- Photofluorescent
- Photomechanical
- Photomagnetic



Jovaisaite V, Mouchiroud L, Auwerx, J. The mitochondrial unfolded protein response, a conserved stress pathway with implications in health and disease. J Exp Biol 2014;217: 137–143.

Parker S, Anagnostaki E, Mylona V, Cronshaw M, Lynch E, Grootveld M. Systematic Review of Post-Surgical Laser-Assisted Oral Soft Tissue Outcomes Using Surgical Wavelengths Outside the 650–1350 nm Optical Window. Photobiomodulation, Photomedicine, and Laser Surgery. 2020 Oct 1;38(10):591-606.

Discussion

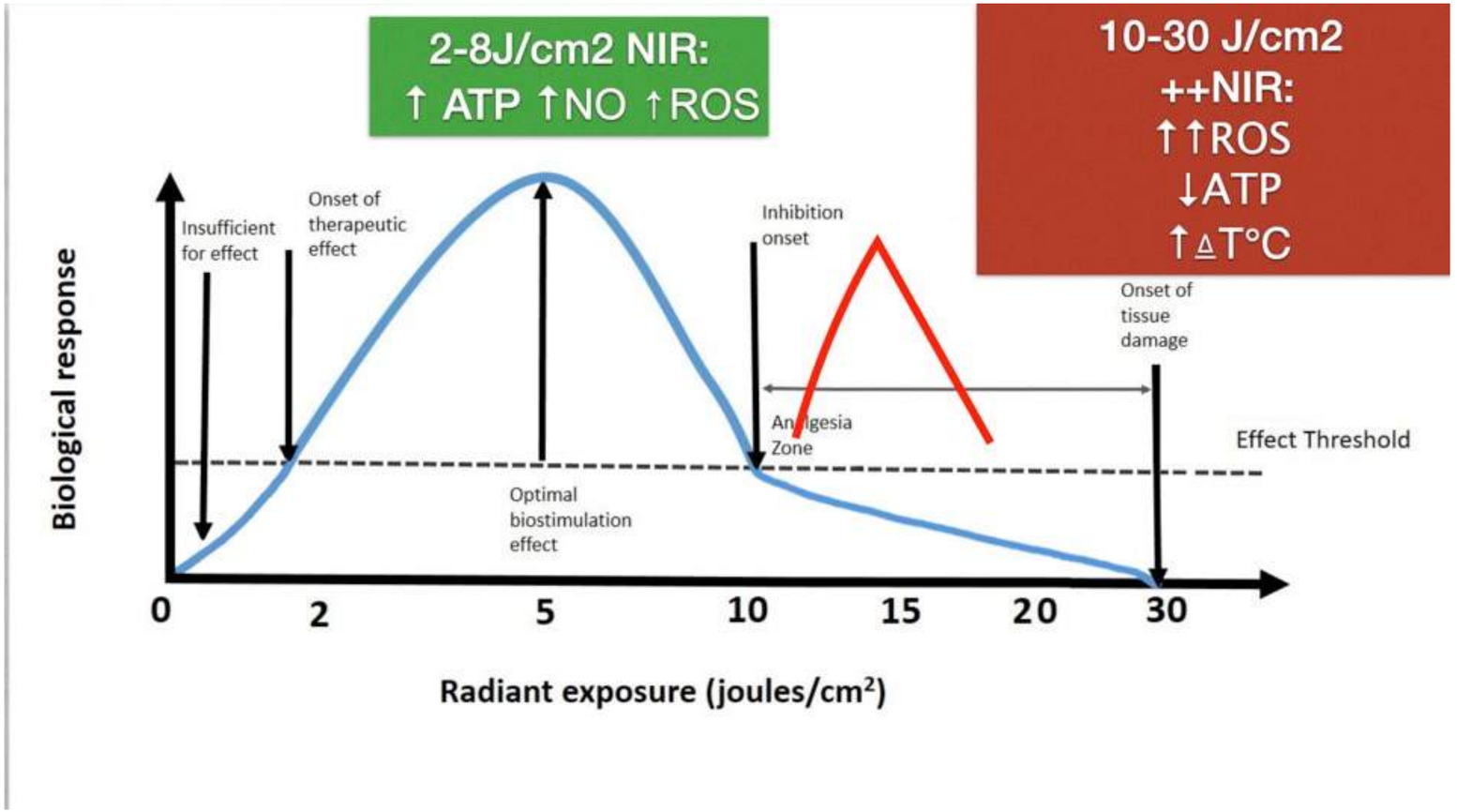
PBM Mechanisms- Stimulation & Inhibition:

Dose Related Response Low Dose:

- Promotes aerobic metabolism
- Reduces apoptosis as ↑cellular resilience
- Reduced complications: ↑activity of immune system
- Better quality healing & repair ↑matrix production

Dose Related Response High Dose:

- Hormetic response to ROS & ↑ ΔT
- Mediated by HSP's, ATF-4 & TRPV's
- Reduces apoptosis as ↑cellular resilience
- ↑HSP's: Protects part formed proteins
- ↓↓↓Cellular activity
- Translocation of mitochondria
- Stabilised axonal membranes
- Axonal varices
- Reduction in pro-inflammatory mediators



Parker S, Cronshaw M, Grootveld M. Photobiomodulation delivery parameters: an evidenced based approach Photobiomodulation, photomedicine, and laser surgery 2022: 40: 42-50

Tissue volume -

Simultaneous Effects:

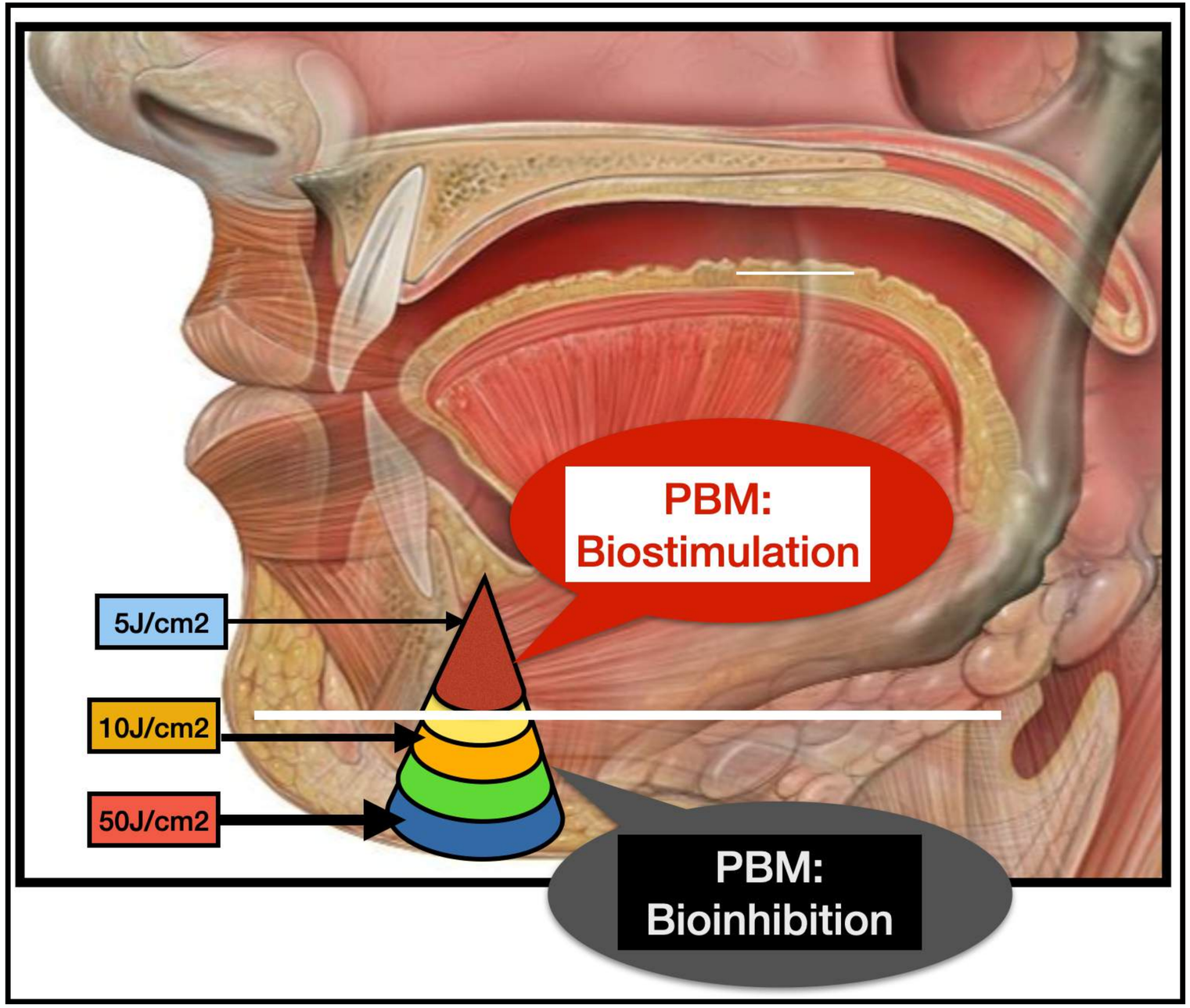
- Surface layers- Inhibition
- Deeper layers- Stimulation

At surface:

- Analgesia
- Disinfection
- Vasodilatation (lymphatics & blood vessels)
- ↓ Apoptosis

At depth:

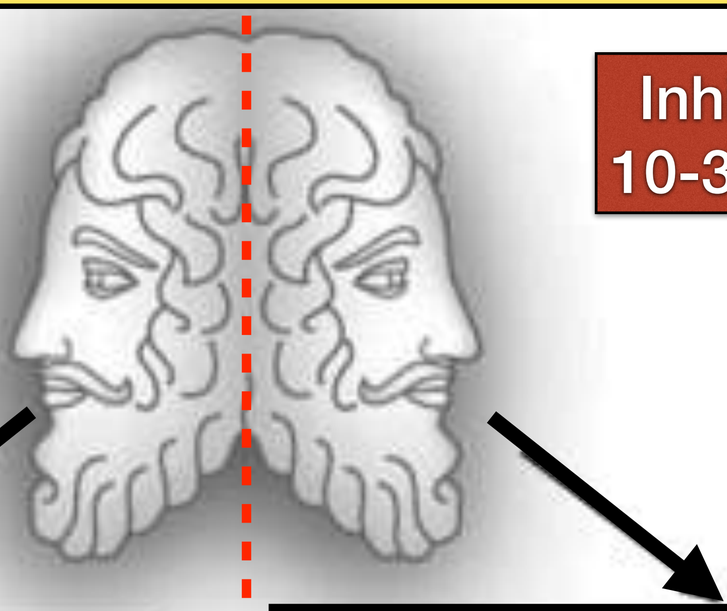
- ↑↑ Mitosis
- ↑↑ Matrix
- ↑↑ VEGF/TGF



M. A Cronshaw PhD Thesis: publication pending.

The Janus Effect:
Two faces of PBM induced conditioning

Stimulation:
2-8J/cm2



Inhibition:
10-30J/cm2

Increased cellular resilience:

↑↑↑ ATP
NO

- Vasodilatation : ↑↑O2
- Anti-inflammatory gene transcription
- ↑↑Immune response
- ↓Apoptosis (ROS/NFkB)

Increased cellular resilience:

↑↑ HSP's
↑↑ ATF-4
↓↓ ATP

- Activation of UCP's: decoupled ETC
- Translocation of mitochondria
- Axonal membrane changes (varices)
- Interference with Na+/K+ pump?
- Gate theory?
- ↓Apoptosis

Image adapted from:
https://www.researchgate.net/figure/Janus-the-two-faced-Roman-God-from-whose-name-Janiceps-derives-Janus-is-the-god-of_fig2_27799030
Courtesy: www.MedFriendly.com

M. A Cronshaw PhD Thesis: publication pending.

LED vs. Lasers?

- Laser >intensity cf. LED
- Laser best for delivery to depth
- Laser: optical hazard > risk
- Cost laser ++££
- LED maybe OK for patient self delivery?

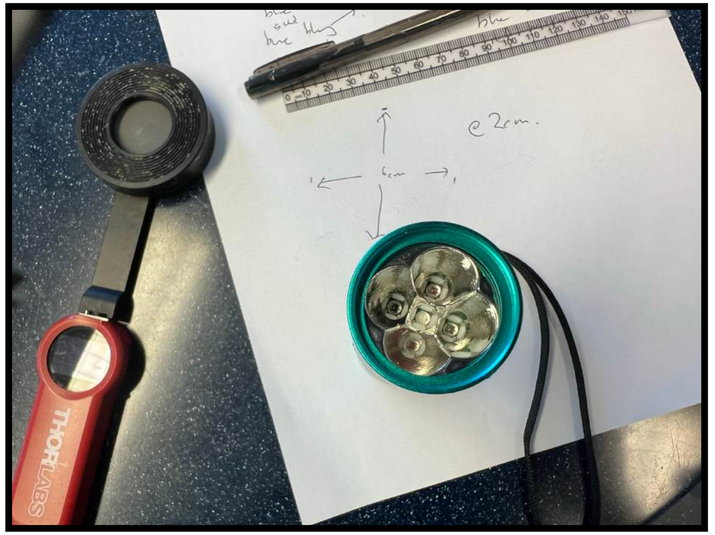
A Pilot Study Of LED Home Use PBMT Devices: Design, Function And Potential

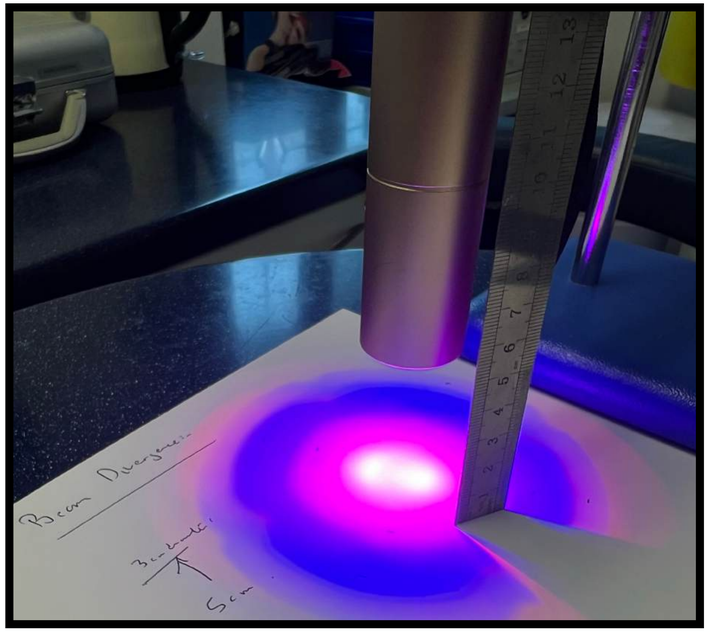
M Cronshaw, S Parker, E Anagnostaki, V Mylona, M Grootveld, E Lynch

De Montfort University

Objective:

- Logistical issues: PBM integration?
- Growing public awareness of the potential benefits of PBMT
- Inc. demand for access to Rx
- Home therapy devices on sale
- No formal scientific assessments





- Design?
- Efficacy?
- Safety?
- Professional applications?

Dr Mark Cronshaw De Montfort University, Leicester, UK.

Optical Penetration: Laser >> LED

Subject	Gender	Age	Skin Type	Anatomy of Right Cheek with Open Mouth Obtained from MRI			Surface Power 399mW/cm2	Measured Transmission, mW/cm^2	Simulated Transmission, mW/cm^2	Measured Percentage Transmission
				Skin, mm	Fat, mm	Muscle, mm				
1	M	25	IV	2	3	7		0.47	0.41	**0.12%**
2	F	57	VI	1	0	5		2.14	2.12	**0.54%**
3	F	25	II	1	2	3		2.38	2.07	**0.54%**
4	M	43	I	2	1	6		0.83	0.82	**0.6%**

LED's:

- Less expensive
- Patient self administer
- Can be effective ??
- Optical penetration?

Henderson TA, Morries LD. Near-infrared photonic energy penetration: can infrared phototherapy effectively reach the human brain?. Neuropsychiatric disease and treatment. 2015 Aug 21:2191-208.

Heiskanen V, Hamblin MR. Photobiomodulation: lasers vs. light emitting diodes?. Photochemical & Photobiological Sciences. 2018;17(8):1003-17.

M. A Cronshaw PhD Thesis: publication pending.

Image adapted from: Yaroslavsky AN, Iorizzo TW, Juliano AF, Adnan A, Carroll JD, Sonis ST, Duncan CN, London WB, Treister NS. Monte Carlo based dosimetry of extraoral photobiomodulation for prevention of oral mucositis. Scientific Reports. 2023 Nov 22;13(1):20425.

LED

LED

LED

LED

LASER

LASER

LASER

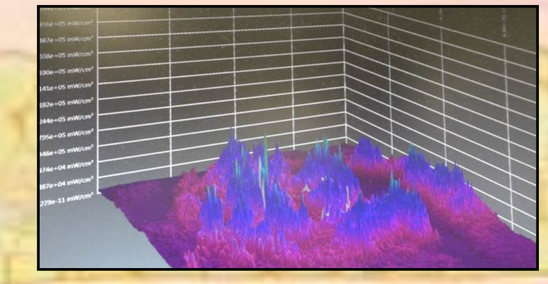
LASER

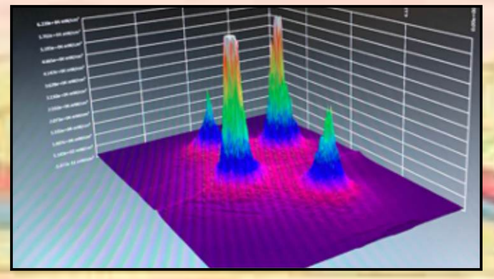
LASER

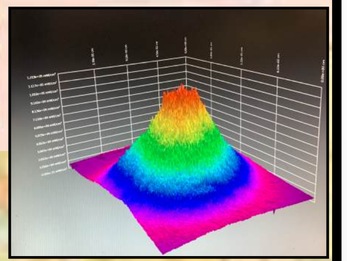
LED Array

Laser Array

Single laser: large source

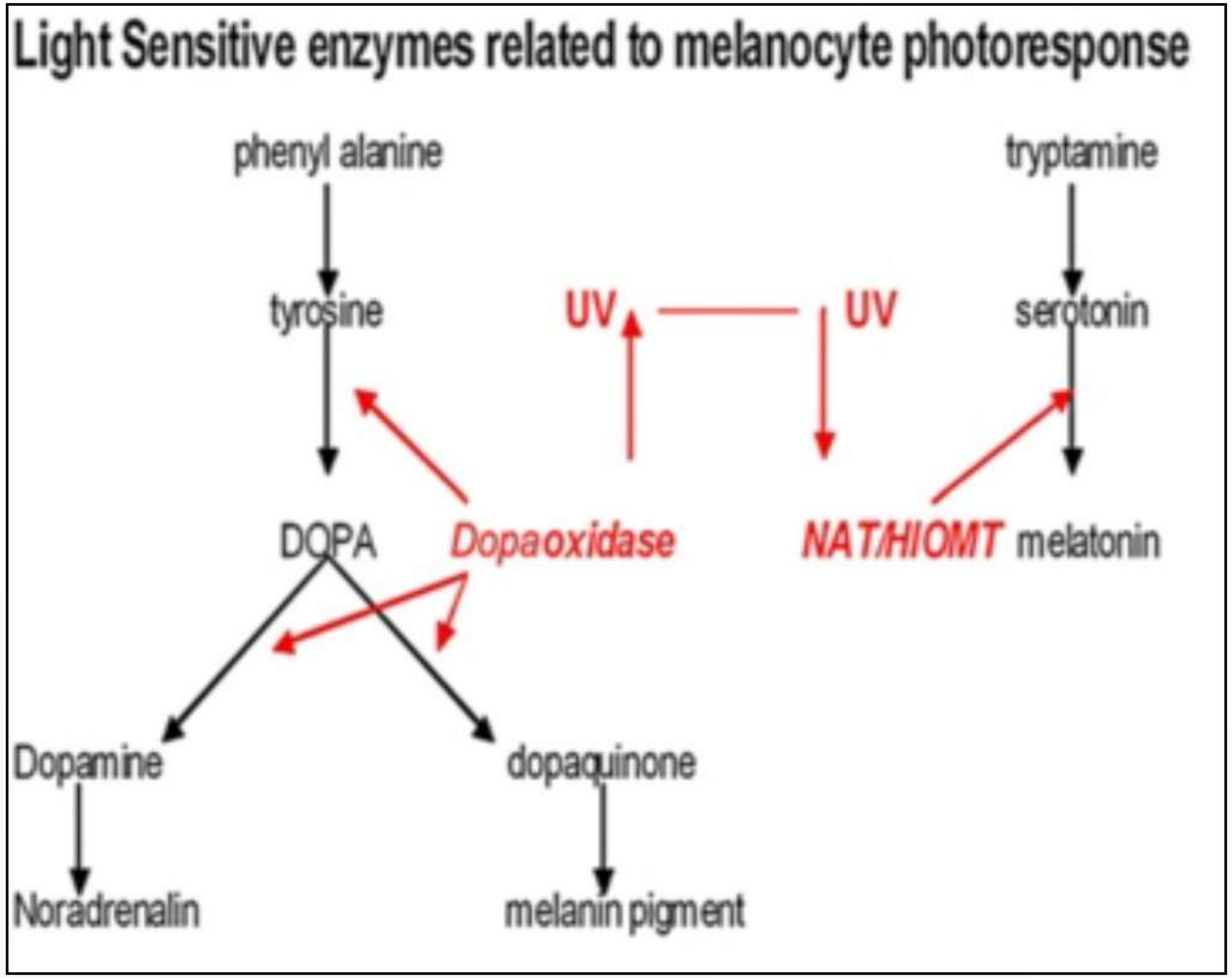






Melanoncytes Are Photoreceptors:

- Serotonin manufacture on photo exposure (SAD)
- Hibernation in winter
- Inc. noradrenaline
- Inc. dopamine
- Inc. HGH, ACTH, PRL :
- + 80-85% @ 2 mins peaks at 3 hours



Iyengar B “The melanocyte photosensory system in the human skin” SpringerPlus 2013, 2:158 http://www.springerplus.com/content/2/1/158

Skin: Interactive network between cutaneous nerves, neuroendocrine axis & immune system:

- **Serotonin:**
  Regulates mood, appetite & sleep.
  Platelet bound (vasoconstriction)
- **Noradrenaline:**
  Fear, fright & flight!
- Inc. HR, BP, glucose & blood to muscle
- **Dopamine:**
  Reward motivated behaviour
- Basis of addiction & psychosis

- **HGH:**
  Stimulates immune system
  ↑ osteoblasts, chondrocytes & muscle

- **ACTH:**
  Stimulates adrenal gland- cortisol release
  ↑ VEGF by osteoblasts

- **Prolactin:**
  milk production, angiogenesis, haematopoiesis & anti apoptotic

Iyengar B "The melanocyte photosensory system in the human skin" SpringerPlus 2013, 2:158 http://www.springerplus.com/content/2/1/158

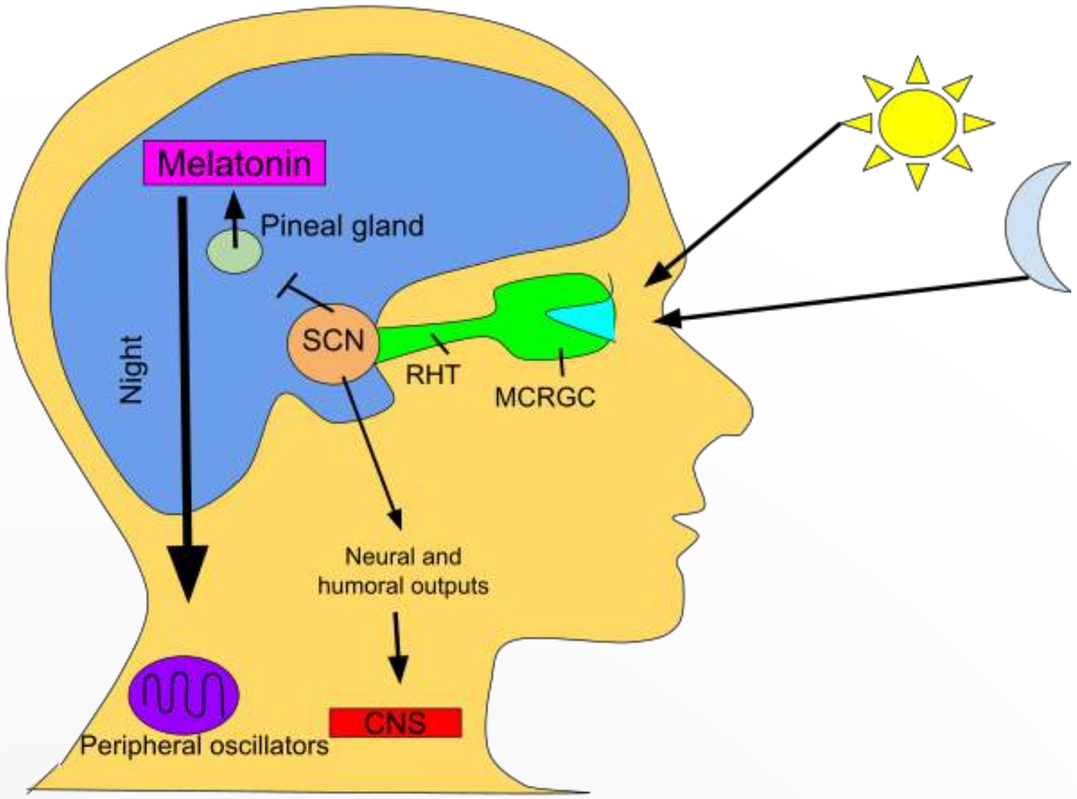
Entrainment, Melatonin & the Circadian Cycle:

Entrainment:

- EM radiation- oscillating source
- Two or more oscillating sources can interact
- Can enhance or negate
- Can synergise: greater amplitude (resonance)
- Can become phase locked & stable (harmony)

Melatonin:

- Synchronises biological clock
- Affects ANS: activates parasympathetic NS
- Promotes sleep
- Powerful ROS scavenger (2x vit E)
- Regulates sex hormones
- Maybe strengthens immune system



Jimenez A, Lu Y, Jambhekar A, Lahav G. Principles, mechanisms and functions of entrainment in biological oscillators. Interface Focus. 2022.12:20210088.

Cavallini C, Olivi E, Tassinari R, Ventura C. Mechanotransduction, cellular biophotonic activity, and signaling patterns for tissue regeneration. Journal of Biological Chemistry. 2024 Sep 30:107847

Entrainment & Photobiomodulation Therapies:

Many light sensitive intracellular targets:

Transition metals in key proteins

- Cytochromes
- Cryptochromes
- Flavins
- Nuclear chromatin
- Inclusion bodies

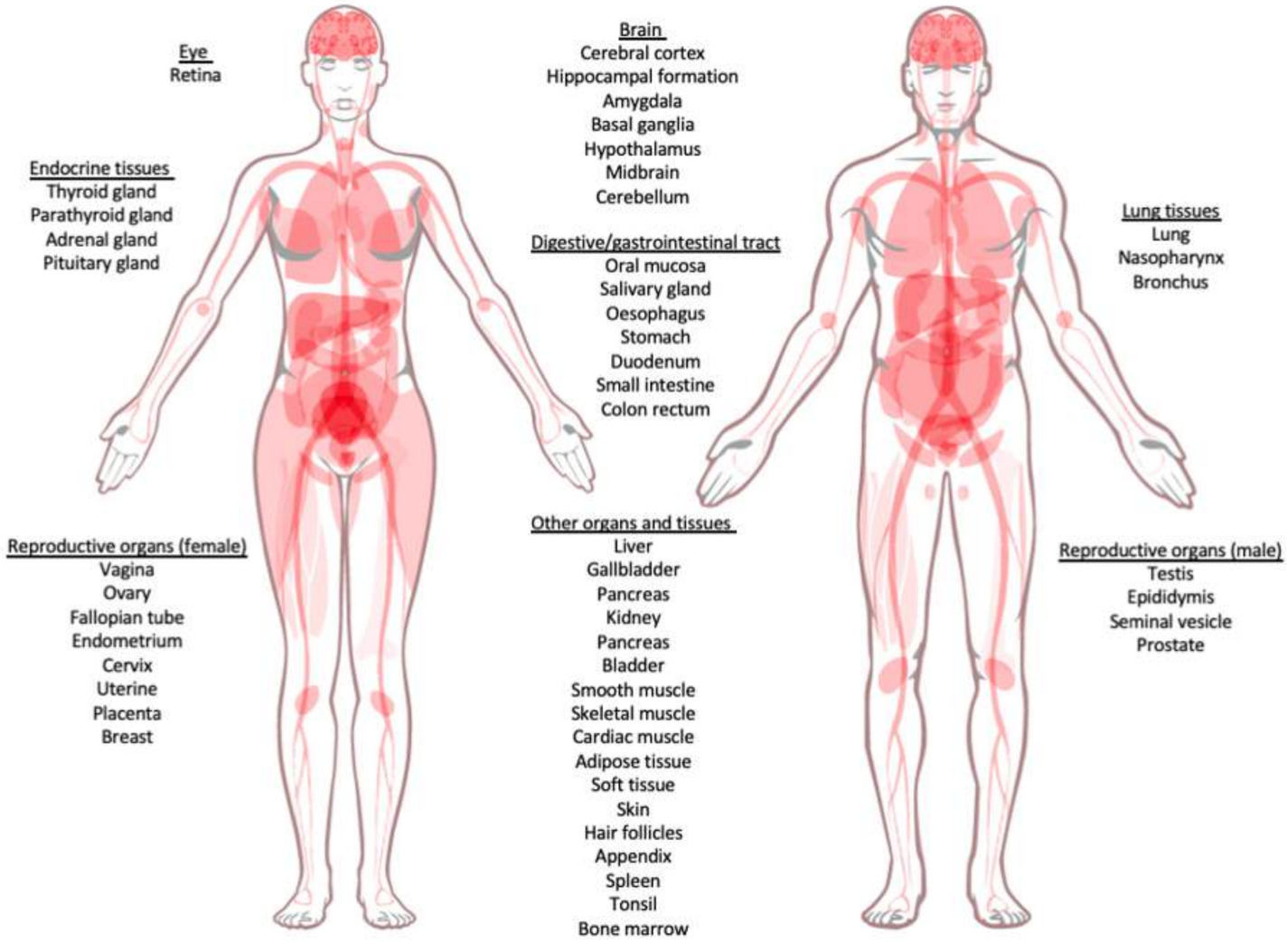
Membrane bound Opsins:

- Ca++ ion channels
- Na+ & K+ ions
- Light sensitive
- Thermal sensitivity
- Touch sensitivity

Myelinated nerve sheaths:

Biophotons

Optic transmission PBM?



Distribution of opsins in the body.

Liebert A et al. A Perspective on the Potential of Opsins as an Integral Mechanism of Photobiomodulation: It's Not Just the Eyes Photobiomodulation, Photomedicine, and Laser Surgery Volume 40, Number 2, 2022

Entrainment & Photobiomodulation Therapies:

Photon transduction & Optic pathways:

- Transmission
- Scattering & absorption
- Epidermal and dermal myelinated axons?
- Hair?

Photo-activated stimulation melanocytes:

Autocrine, paracrine & endocrine effects

Photothermal effects:

Vasodilatation
hormesis (ATF-4, HSP's)
Analgesia?

Opsins: TRPVs

Analgesia

Photofluorescent effects:

Biophotons

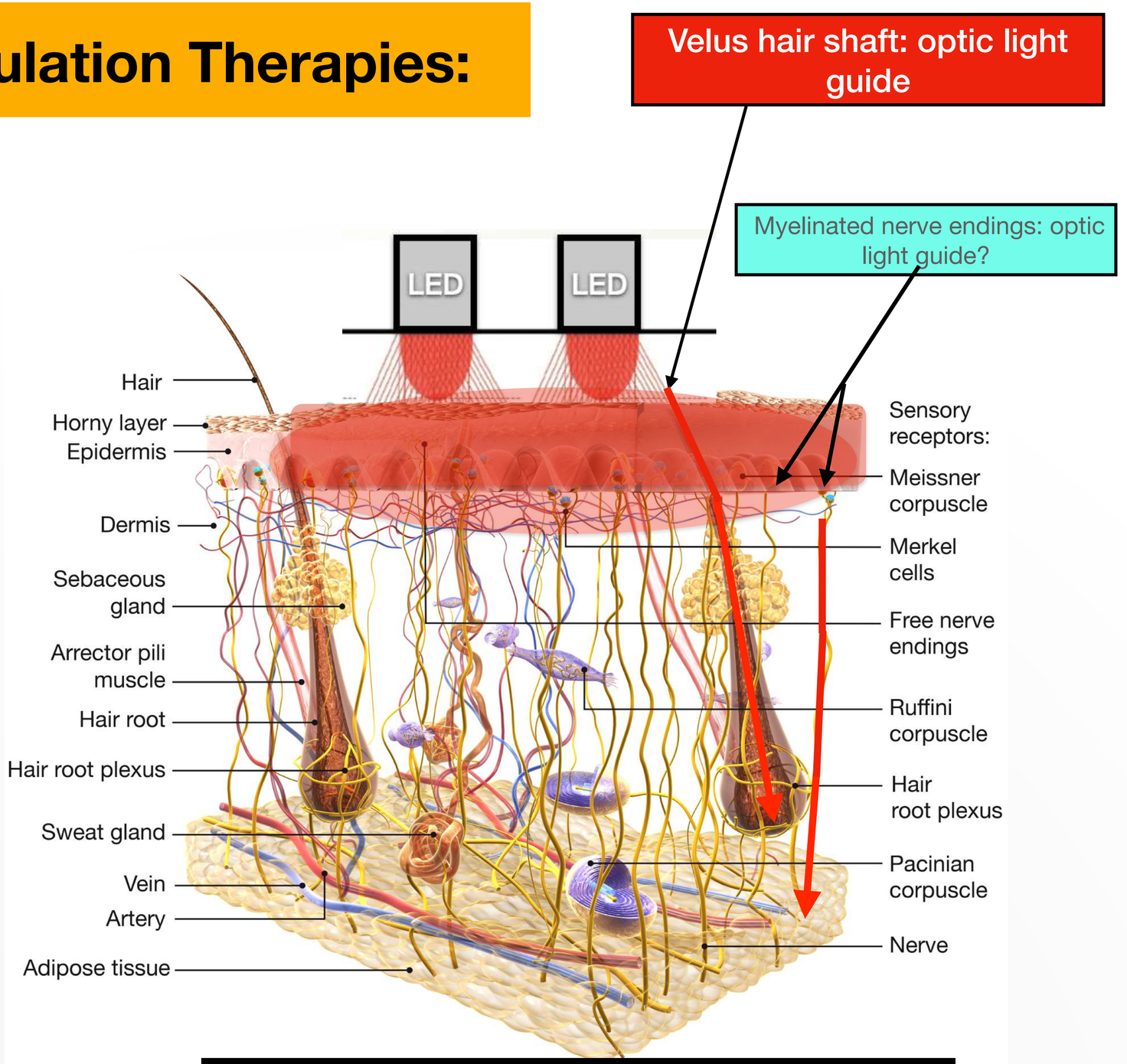
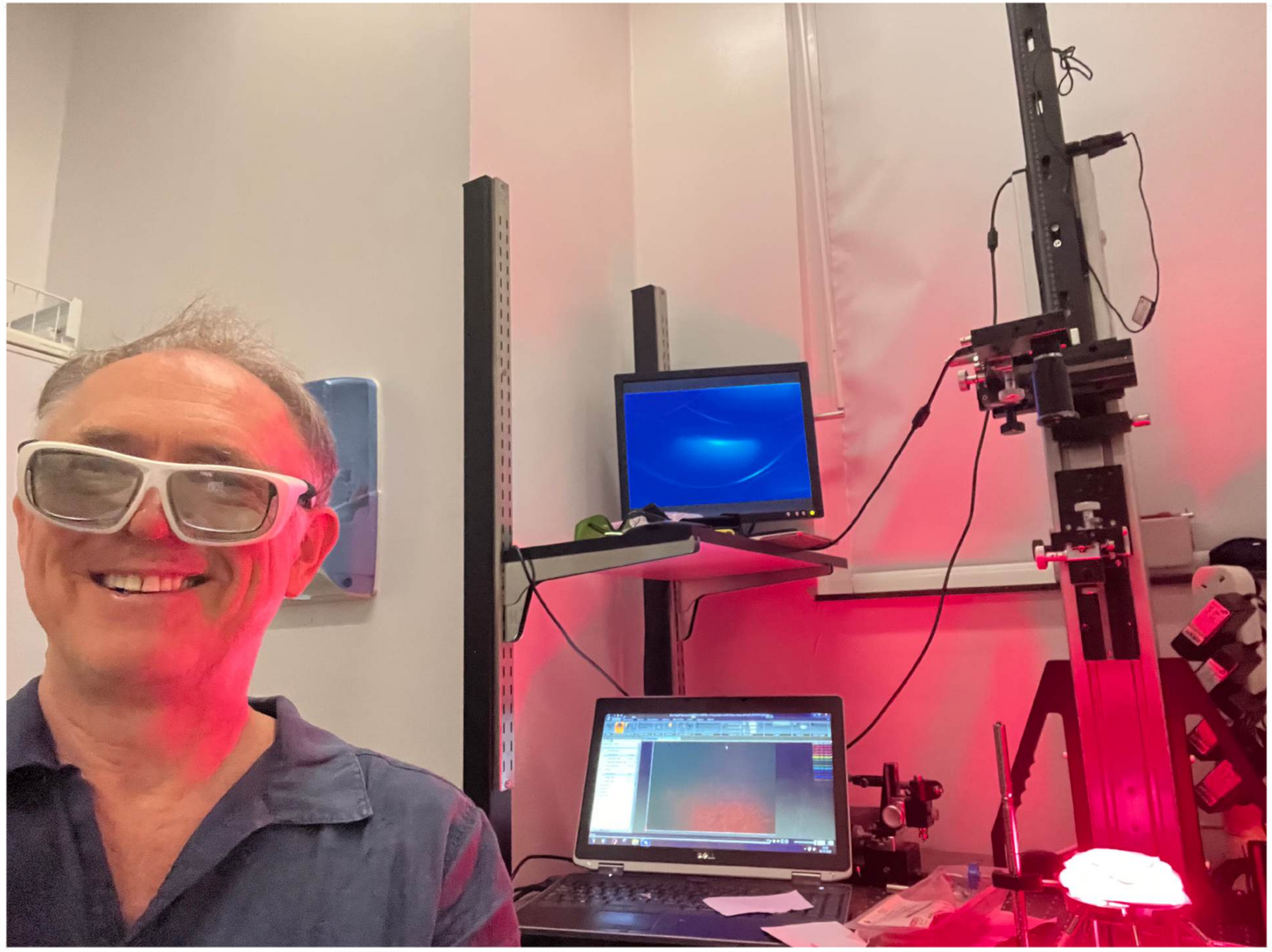


Image adapted - copyright permission: dreamstime_xxl_274989135.jpg



With thanks to my co-workers:
Eugenia Anagnostaki, Valina Mylona, Steven Parker
Special thanks to Prof. R-J Bensadoun
And my PhD supervisors:
Martin Grootveld, Ed Lynch(DMU)

Dr Mark Cronshaw :

Thank you for your kind attention!

Drmarkcronshaw@outlook.com

www.dentallaseracademy.co.uk

DE MONTFORT UNIVERSITY LEICESTER

Dr Mark Cronshaw PhD BSc BDS LDSRCS(Eng) MSc

Faculty of Health and Life Sciences,
De Montfort University,
Leicester, UK.
E: drmarkcronshaw@outlook.com