50th Anniversary
UB Oral Biology Graduate Program

Buffalo Niagara Dental Meeting

University at Buffalo
Dental Alumni Association
School of Dental Medicine

11/04/2022,
Buffalo

# Lasers in Dentistry

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University at Buffalo
School of Dental Medicine

# Current Disclosures *(Nov 2022)*

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|---|---|---|---|---|---|---|---|---|
| Vielight | | X | | | | | | |
| NLM / NIH MAHE, PIDC, Shepherd University | | X | | | | | | |
| Harvard University | | | | X | | | | |
| University at Buffalo | | | | X | | | X | |
| Biolase, Summus, Weber, Fotona,Ultradent, LIghtScalpel, Kerber | | | | | | | | X |
| OptiMed Technology, Conjunction LLC | | | | | | X | | |

## Immediate Past President,
**W**orld **A**ssociation for PhotobiomoduL**L**ation **T**herapy

## Immediate Past President,
**N**orth **A**merican **A**ssociation for PhotobiomoduL**L**ation **T**herapy

## Co-Chair, Mechanisms of Photobiomodulation
International Society for Optics and Photonics

## Chair, Senior Fellow, Technical Group on Photobiomodulation
**Optica (prior O**ptical **S**ociety of **A**merica )

## Secretary
**W**ound **H**ealing **S**ociety (**WHS**)

# Purpose of this workshop

- What?

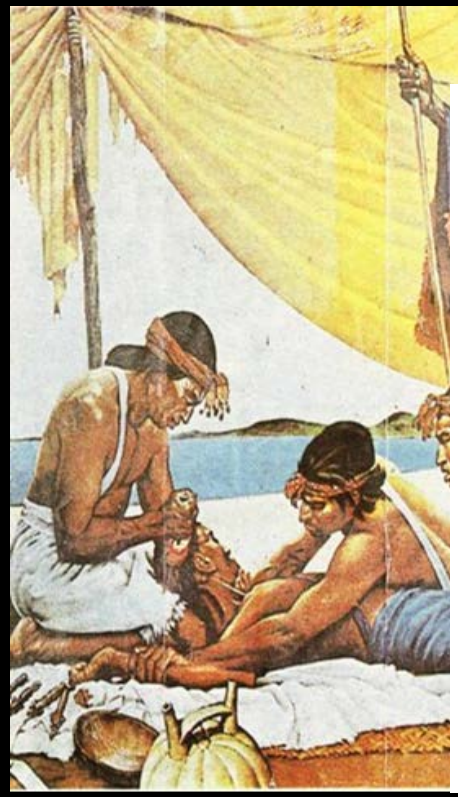
Theoretical foundation for laser applications in dentistry for a sound biological rationale-driven clinical knowledge……

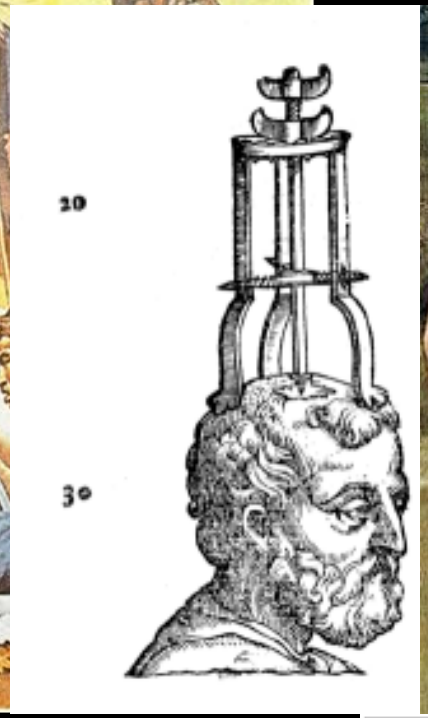
- Why?

Conventionally, no formal education on lasers or biophotonics (even basic physics/optics) in the dental curriculum…
*Exception* - D4s UB SDM & 17 schools in US-Canada & Boards!

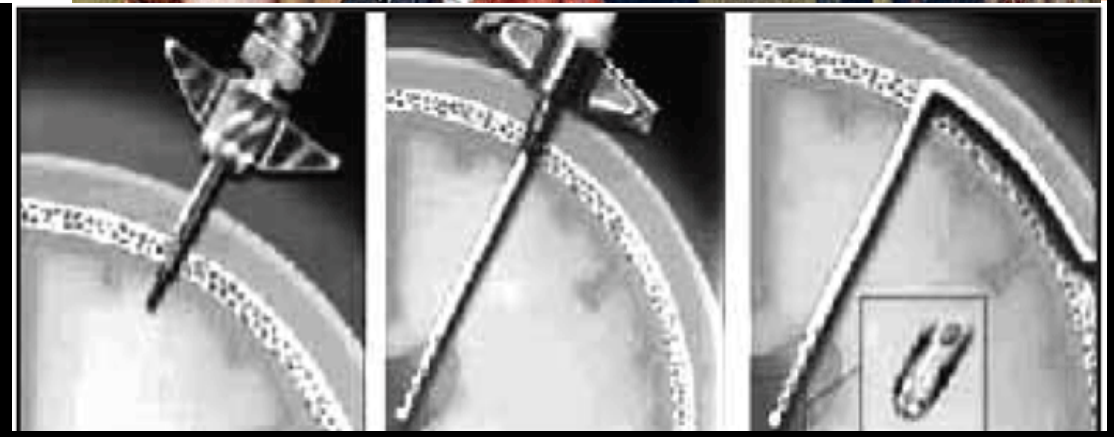
# Introduction

# HISTORY OF MEDICINE






## Trephining



☞ relieve intracranial pressure

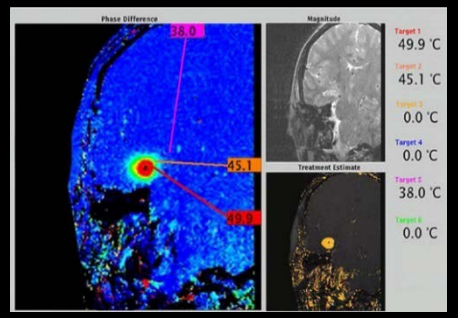
# HISTORY OF MEDICINE

## Blood-letting

☞ Transfusion, Dialyses

## Lobotomy

☞ Relieves seizures




## Stretching

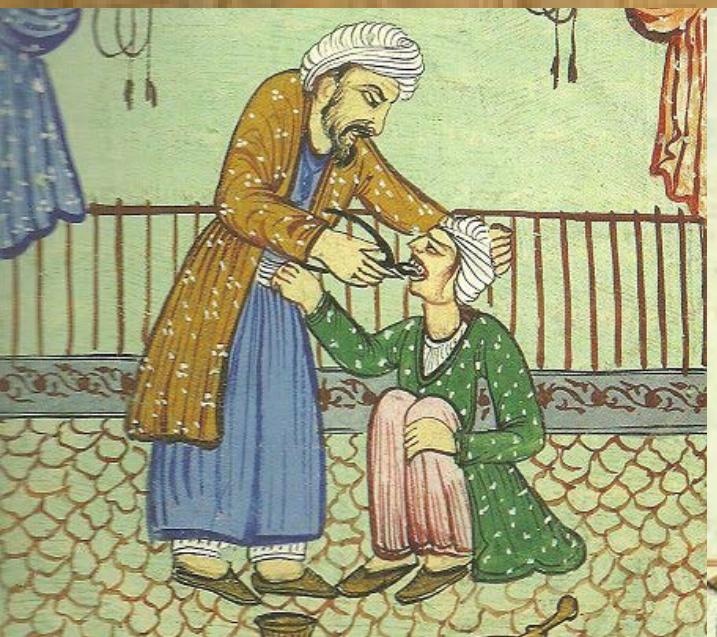
☞ Move teeth, Heal fractures, Physical therapy

# *BRIEF* HISTORY OF DENTISTRY

ADEA | THE VOICE OF DENTAL EDUCATION

Dentistry is one of the oldest medical professions, dating back to **7000 B.C.** with the Indus Valley Civilization.

However, it wasn't until **5000 B.C**. that descriptions related to dentistry and tooth decay were available. At the time, a *Sumerian* text described tooth worms as causing dental decay, an idea that wasn't proven false until the 1700s!



# A BRIEF HISTORY OF DENTISTRY

*By Tim Lambert*
http://www.localhistories.org/dentistry.html

## Early Dentistry

In the Middle Ages some people cleaned their teeth by *chewing twigs*. Others made toothpaste from things like *crushed eggshells*.

The Chinese invented the toothbrush in 1498 and introduced into England in the mid 17th century.

In the Early Middle Ages **monks** acted as doctors, surgeons and dentists.

However in the early 12th century the Church forbade clergy to and a new type of craftsman called ……

a ***Barber-Surgeon*** emerged.

Furthermore during the 17th century some barber-surgeons began to *specialize in dentistry* and gradually dentistry became separated from surgery.

http://www.ada.org


M. MACHOIRE DENTIST
DU GRAND MOGOL

# Modern Dentistry

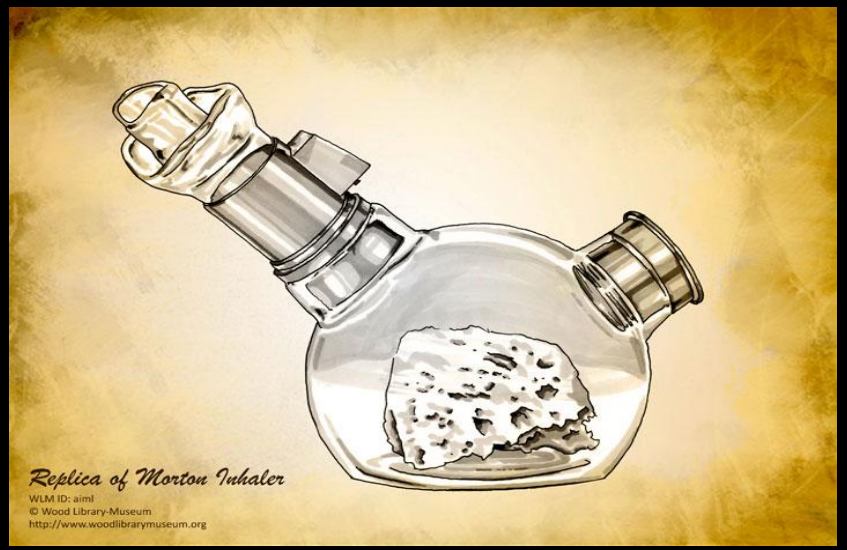
In the 18th century dentistry became more scientific.

In 1723, **Pierre Fauchard,** a French surgeon credited as the Father of Modern Dentistry, published his influential book, ***The Surgeon Dentist, a Treatise on Teeth***, introduced the *idea of dental fillings and the use of dental prosthesis, and he identified that acids from sugar led to tooth decay.*

In 1771 an Englishman called John Hunter published a book called The ***Natural History of the Human Teeth***.

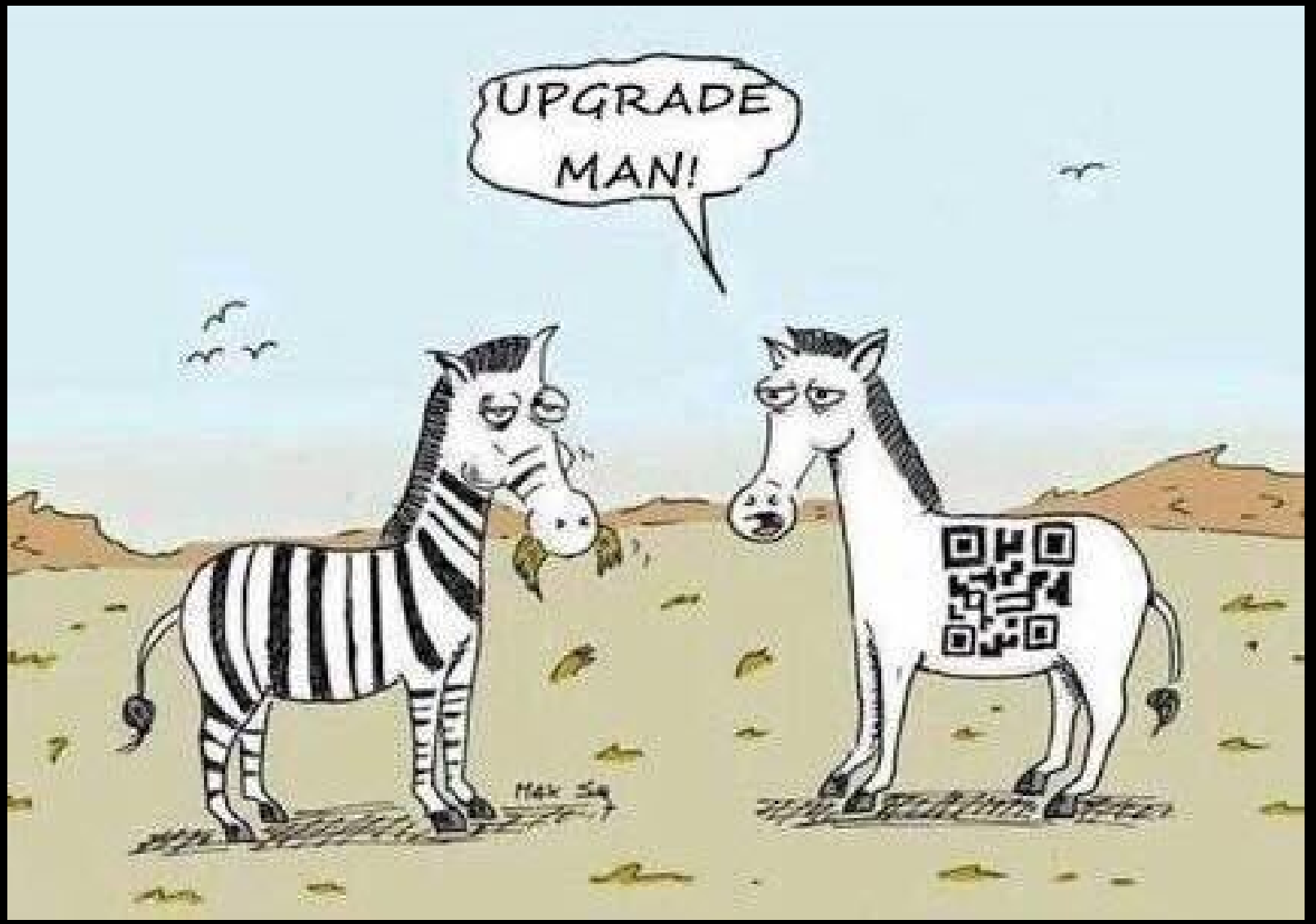
Dentistry took huge leaps in the late 18th century and the 19th century.

- 1770 - Porcelain false teeth were invented
- 1790 - Josiah Flagg invented the dentists chair.
- 1832 - James Snell invented a reclining chair.
- 1877 - Basil Manly Wilkerson invented a hydraulic chair.
- 1840 - the first dental college (Baltimore College of Dental Surgery)
- 1841 - Alabama led the way by enacting the first dental practice act
- 1846 - Henry Morton demonstrated the use of ether as an anesthetic in dentistry.
- 1860 - The department of Oral Biology, first in the country, started in 1960 http://www.youtube.com/watch?v=svawJm2CbZw&feature=youtu.be
- 1861 – American Dental Association (ADA) formed
- 1864 - George Fellows invented a clockwork dental drill.
- 1868 - University of Buffalo School of Dental Medicine
- 1875 - Green invented an electric dental drill.
- 1957 - Air turbine dental drill (using compressed air) was introduced

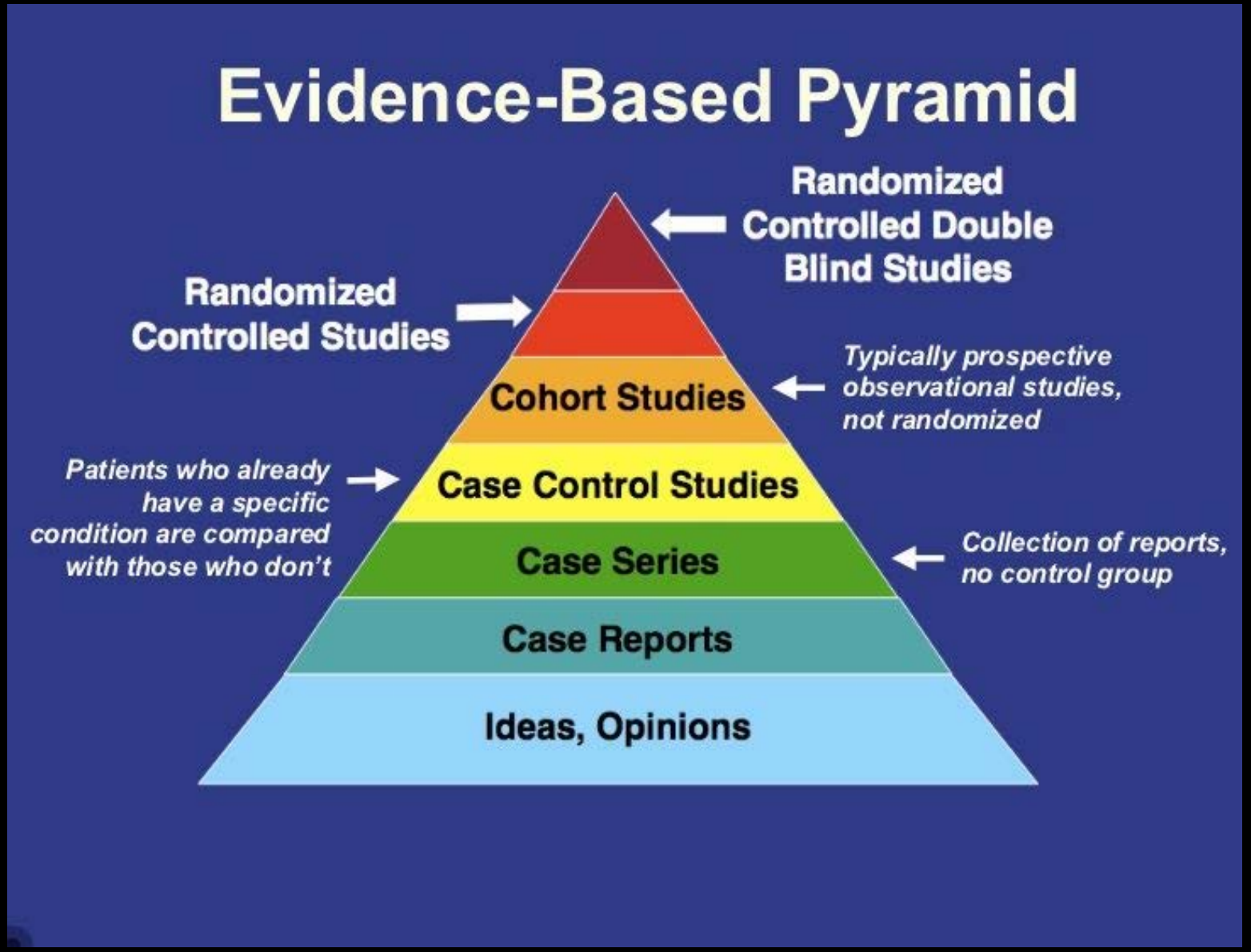



Ether Done, MGH, Boston

# Changing faces of Dental Education…



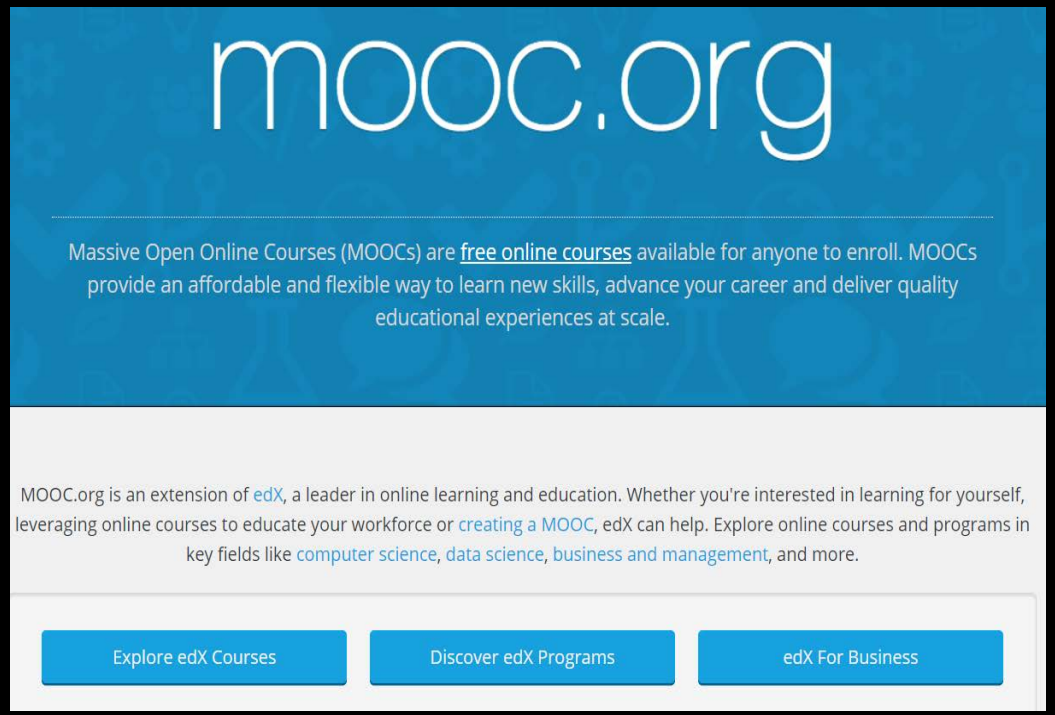
# Evidences to Clinical Practice…



*Old...*

New!

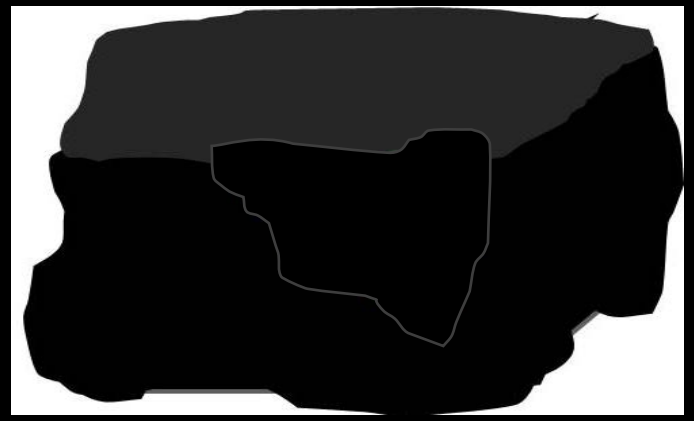
- Wikipedia *
- YouTube
- Facebook
- Instagram
- Pinterest




# Precision Medicine

**Clinical Observation** → **Molecular Mechanisms** *Research* → **Clinical Practice**

Clinical *Translational* Studies



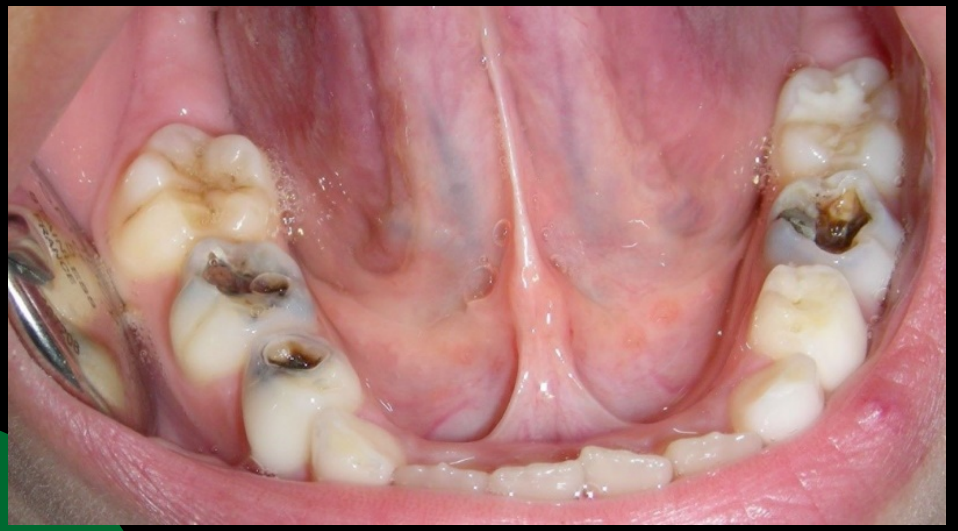
*Mechanism*

***Understanding*** **Biological Regulation**

***Control*** **Clinical Outcomes**

Arany PR **J Dent Res** 2016, 95, 9, 977

# Clinical Dentistry

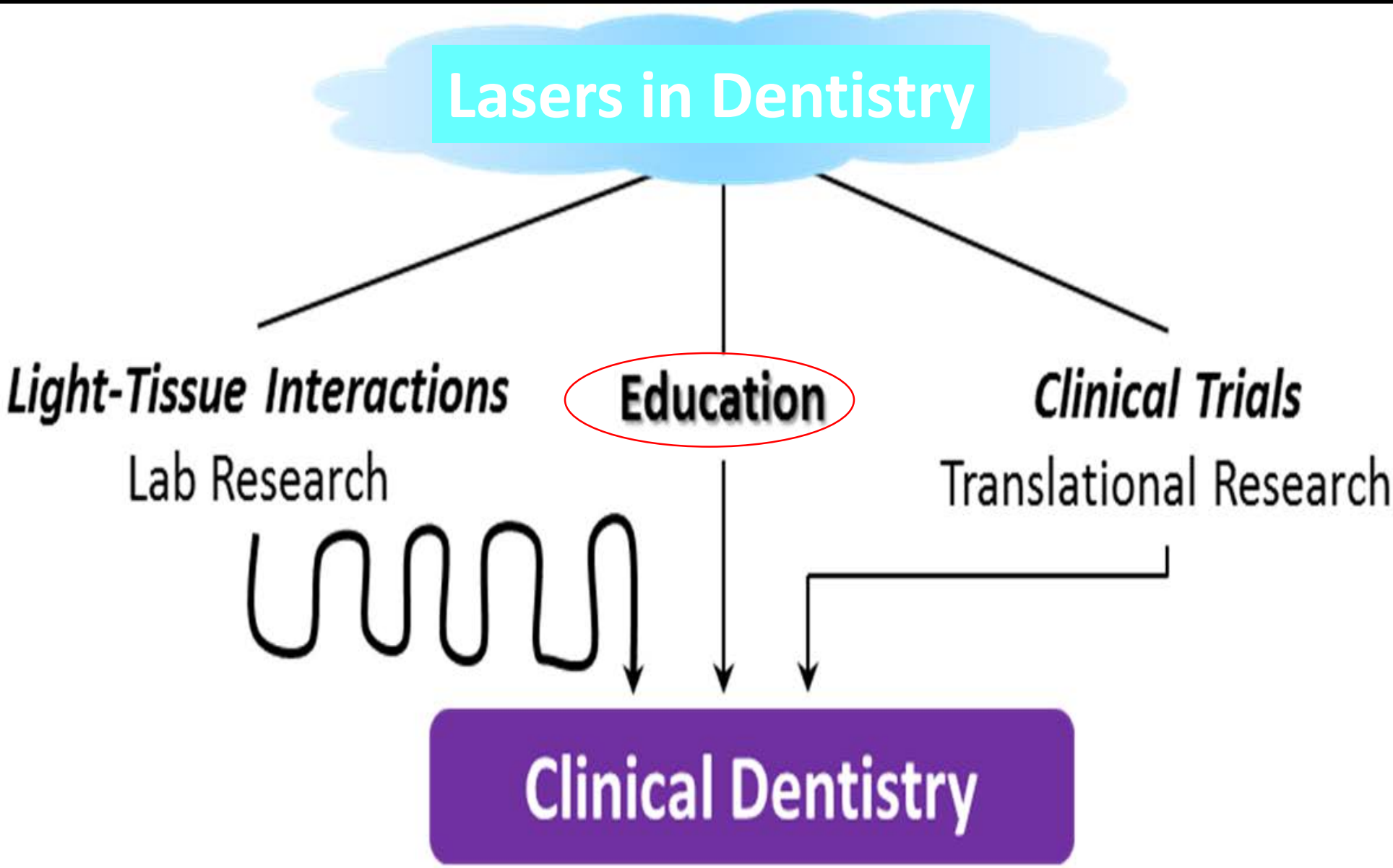
Remove
Noxious / Damage

Healing &
Regeneration

Disinfection

# Dent ers





Lasers in Dentistry
Light-Tissue Interactions
Lab Research
Education
Clinical Trials
Translational Research
Clinical Dentistry

# Laser in Dentistry: Core Curriculum Guidelines (ADEA-ALD)

**DIDACTICS**

1. **Fundamentals of light and Lasers**

   Dual nature of light, Electromagnetic spectrum, Stimulated emission (LASER) and its characteristics, laser device components, classifications of lasers (wavelength, source, power), laser device characteristics

2. **Light-tissue interactions**

   Physical (Reflection, scattering, transmission, absorption), Thermal (variable, effects, applications), Mechanical (photoacoustic), Chemical (reactive intermediates).

3. **Light-biological interactions and clinical applications**

   Surgical: Destroy or disrupt tissues via vaporization, coagulation, disruption
   Non-Surgical: Diagnose (optical imaging) or treat (Photodynamic therapy, PDT or Photobiomodulation PBM)

4. **Laser safety**

   Regulatory agencies and guidelines, required training, essential safety practices and practice guidelines, designated personnel, adverse event reporting, clinical dentistry specific safety hazards (flammable gases, plume hazards, laser sterilization).

5. **Laser practice management**

   Clinical diagnoses and case selection, Applications and limitations of lasers, complications and follow up care, objective documentation, financial and insurance considerations, jurisprudence, ethics and malpractice consideration, current knowledge resource and access strategy.

HANDS ON: ***Either*** of the following hands on demonstration of safe clinical utilization of a laser device could be acceptable for basic competency.

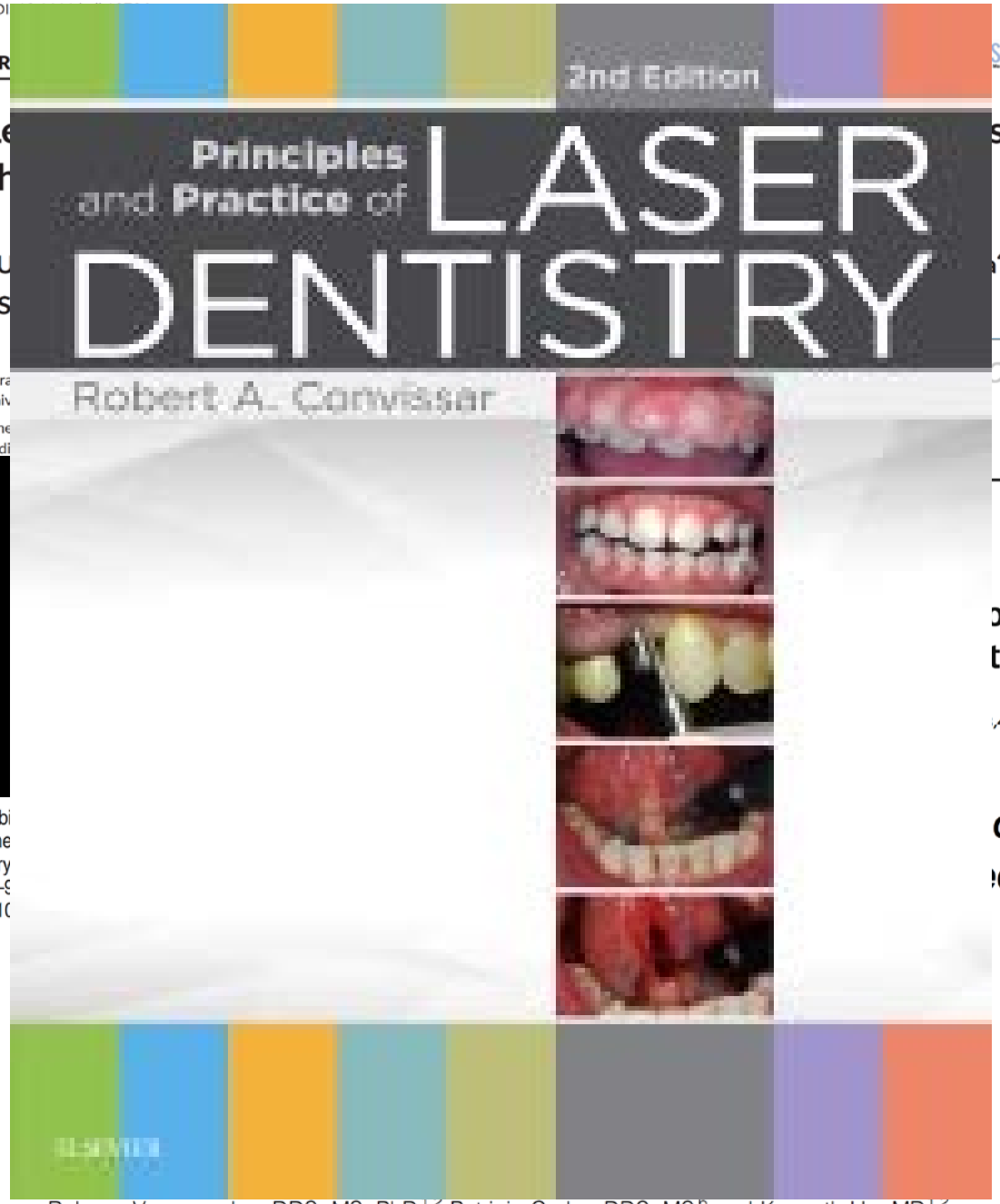
**1. Wavelength or Clinical procedural-specific competency**

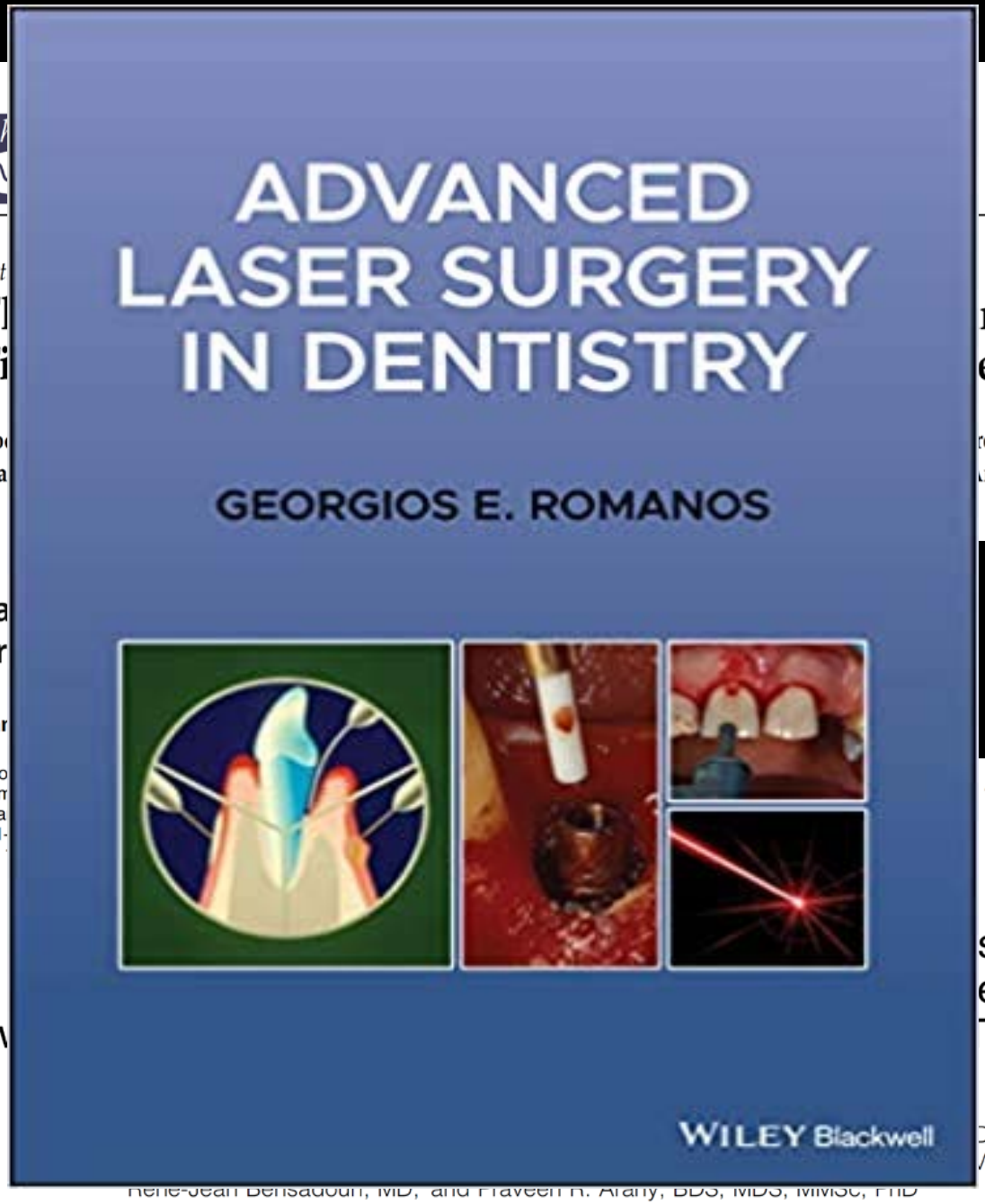
The operator must demonstrate basic safety and appropriate use of the device for a routinely used clinical procedure. Some examples are a $CO_2$ laser for soft tissue incision, troughing with a Nd:YAG; cavity preparation with a Er:YAG, pain or inflammation alleviation with a diode unit; etc.

**2. Device-specific competency**

Alternatively, should the operator (school) have access to specific (FDA approved) laser device, they may demonstrate safe and effective use of this unit for its clinical procedures as per the manufacturer's recommendation. Some examples are the Waterlase, Lightwalker or Solea units for cavity preparation, Epic or Picasso for photobiomodulation, etc.

Received: 1 October 2017 | Revised: 6 October 2017 | Accepted: 9 October 2017

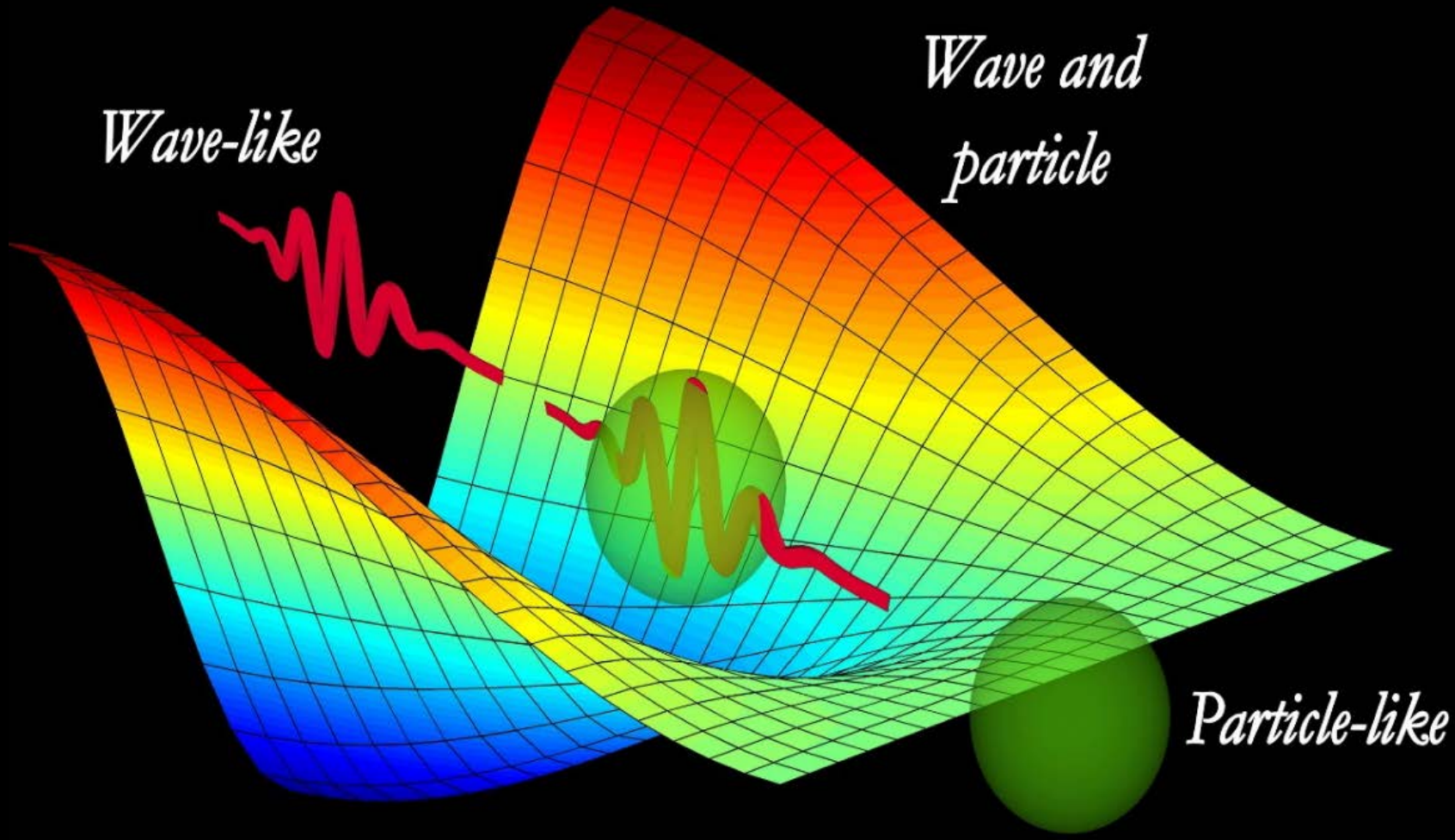



Rebeca Vasconcelos, DDS, MS, PhD,[1,2] Patricia Corby, DDS, MS,[6] and Kenneth Hu, MD[1,2]

Renie-Jean Bensadoun, MD, and Praveen R. Arany, BDS, MDS, MMSc, PhD

# Light

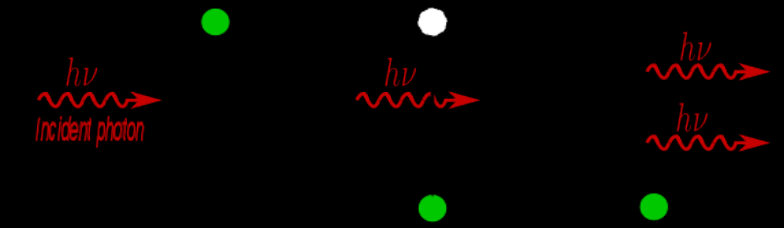


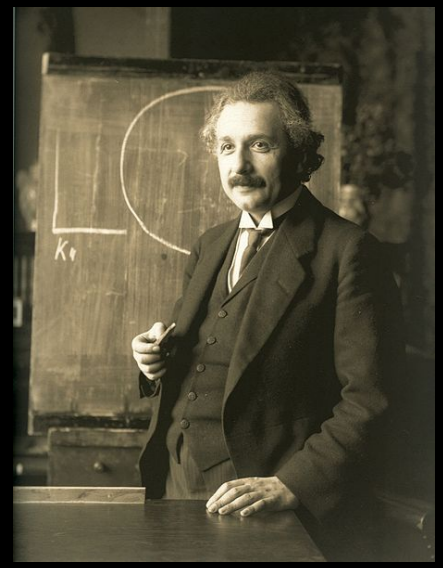

https://www.livescience.com/24509-light-wave-particle-duality-experiment.html

Arany PR *J Dent Res* 2016

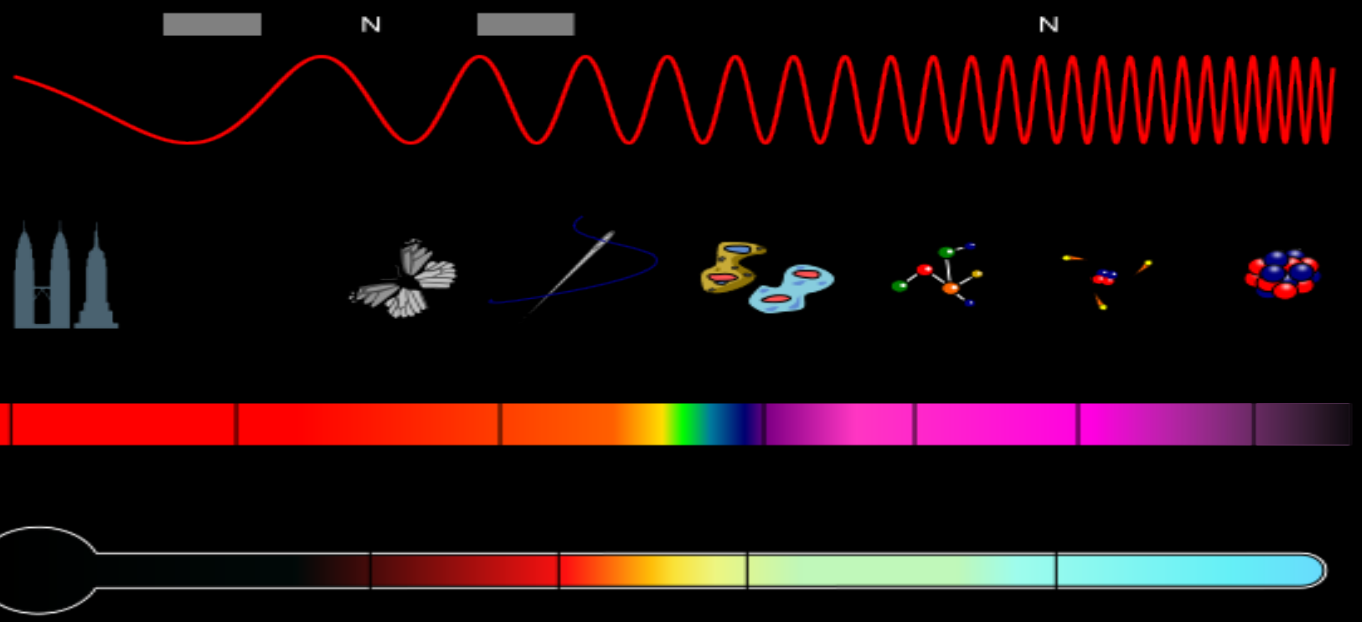
# LASER is an acronym for

Light
Amplification by
Stimulated
Emission of
Radiation



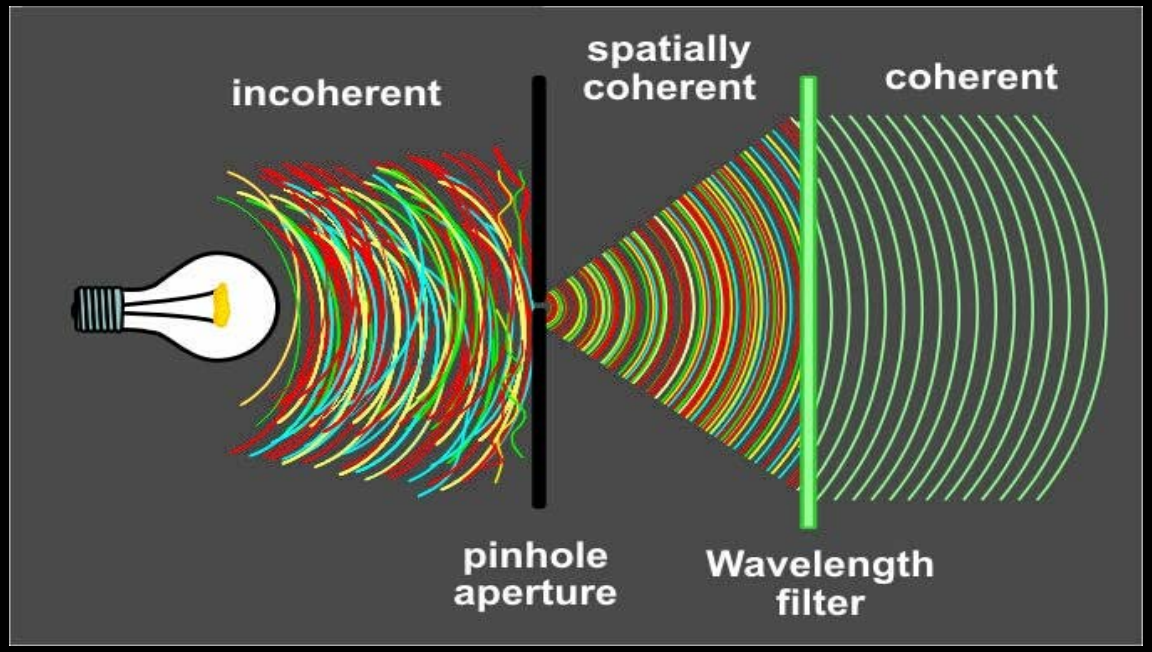



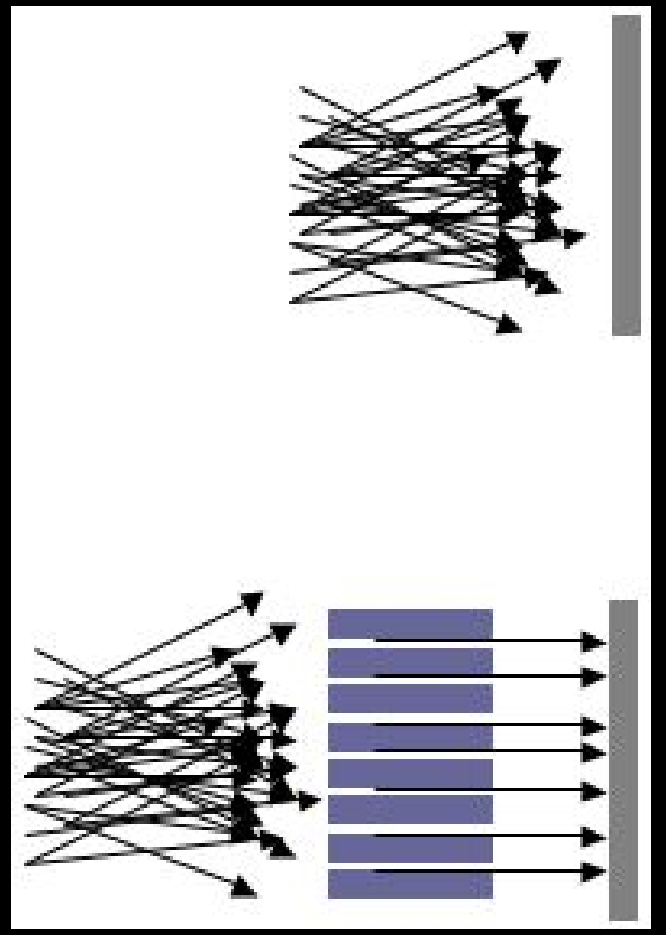
Einstein 1917



# Characteristics of *Laser*

- Collimated (particle/phase)
- Coherent (Wave)



# Types

http://cultureshock.scripts.mit.edu/fa2011/img/pop-culture-is-the-worlds-culture.png

# Types of Lasers: Source

| Laser type | | Wave length | Indication (periodontology) |
|---|---|---|---|
| Diode lasers | InGaAsP<br>Indium-gallium-arsenide-phosphorus | 655 nm | Photodynamic therapy |
| | GaAs<br>Gallium, Arsenide | 685 nm | Photodynamic therapy |
| | GaAlAs<br>Gallium, Aluminium, Arsenide | 810 nm | Soft tissue vaporaziton, koagulation<br>Biofilm removal |
| | InGaAs<br>Indium, Gallium, Arsenide | 980 nm | Soft tissue vaporaziton, koagulation<br>Biofilm removal |
| Gas laser | $CO_2$ | 10 600 nm | Soft tissue vaporaziton, de-epithelization |
| Solid state laser | Nd:YAG<br>Neodymium-doped Yttrium,Aluminium,Garnet | 2780 nm | Soft curette, cutting |
| | Er:YAG<br>Erbium-doped Yttrium, Aluminium, Garnet | 2940 nm | Calculus, biofilm removal |

http://www.tankonyvtar.hu/en/tartalom/tamop412A/2011-0032_angol/ch05s02.html

# Types of Lasers: Manner of Use

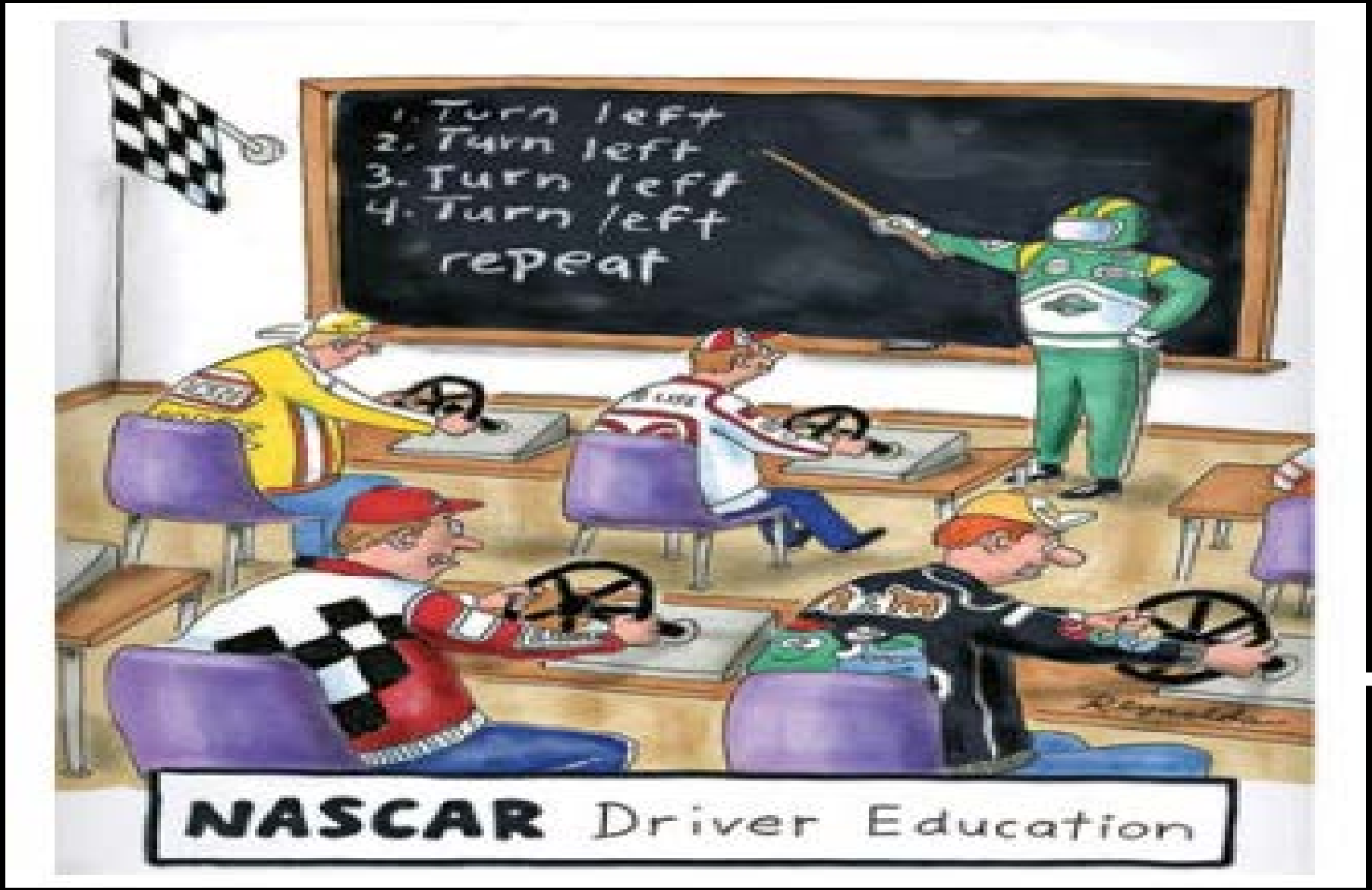
Contact
(Diodes)

Non-Contact
($CO_2$, YAG, YSGG)

# Types of Lasers: FDA Safety (power output)

Class 1
Class 2
Class 3
Class 4

# Safety Considerations




Slides courtesy Drs. Ross, True, Patthoff and Benjamin (NAALT & ALD)

# Laser Device Classifications

**Class 1** Safe, but should not be viewed with optical instruments such as magnifying glass

Eg: CD, DVD player, scanner

**Class 2** Generally considered safe, has *potential* to cause eye damage, do not stare into beam, do not use magnifying instruments

Eg: Classroom laser pointers

Eg; some laser pointers are class 3R

**Class 3R** Use caution, avoid direct exposure to eyes, can cause damage to eyes

**Class 3B** Warning, Eye hazard, can heat skin, can burn material

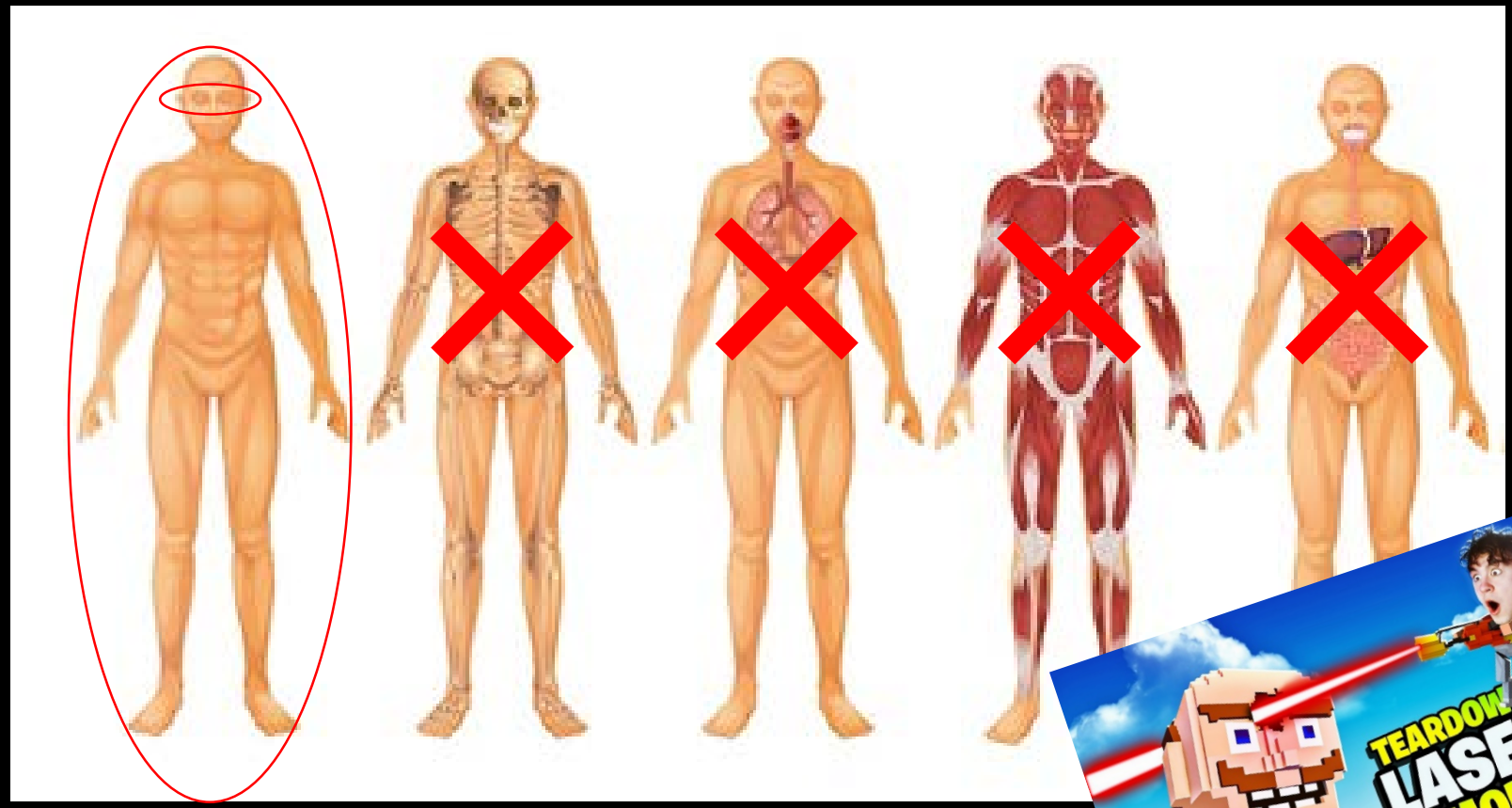
Eg: Spectrometry, Laser light shows

**Class 4** Dangerous, avoid exposure to eye, skin or direct/scattered radiation, severe eye hazard from direct or reflected beam, can instantly burn skin and materials

Eg: Surgical lasers, Research lasers, Drilling, Cutting, Welding, Micromachining

# Laser Damage / Injury

Eye



Skin

# Effects on the Eye

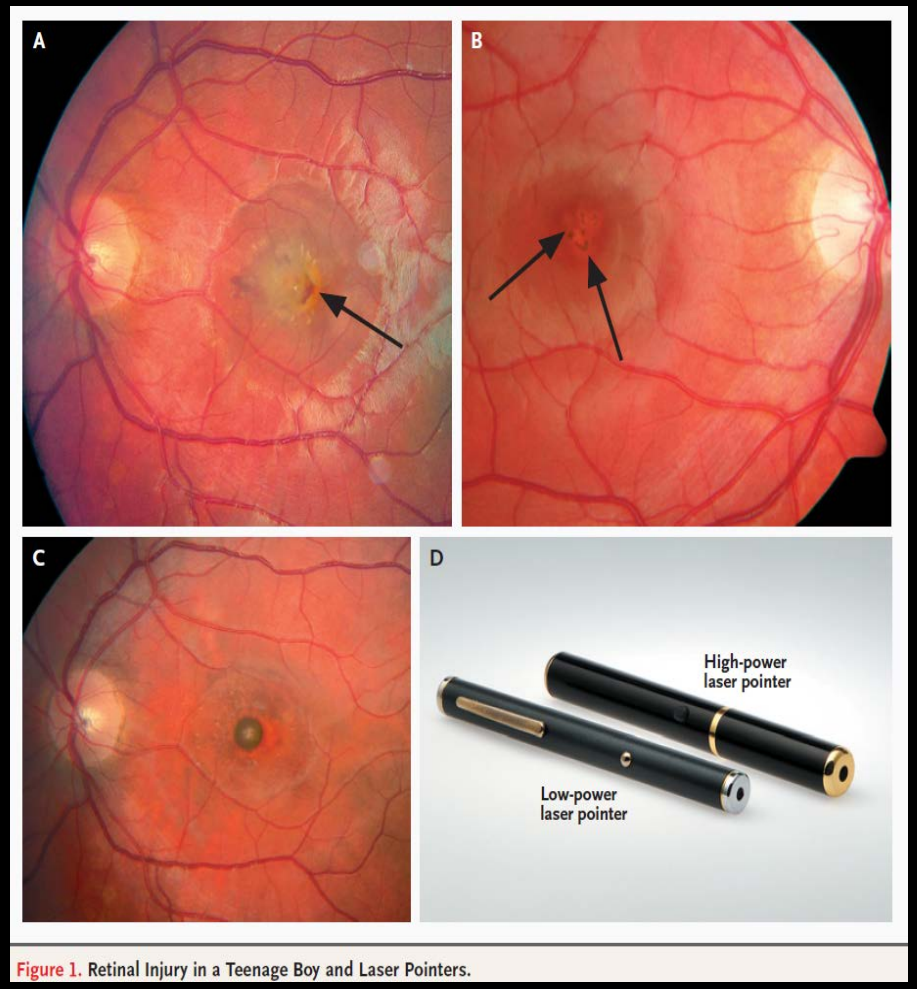
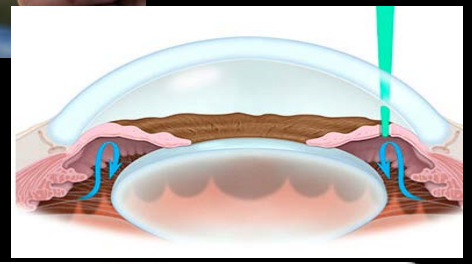
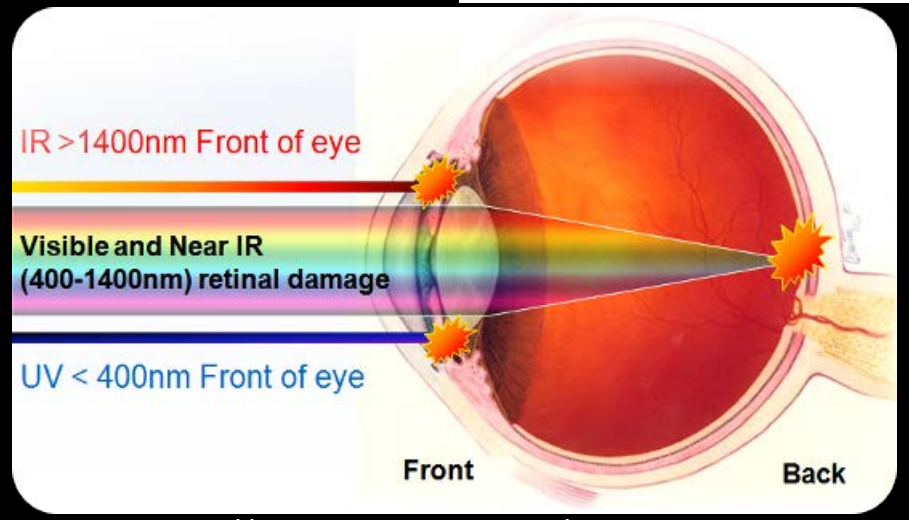



Figure 1. Retinal Injury in a Teenage Boy and Laser Pointers.

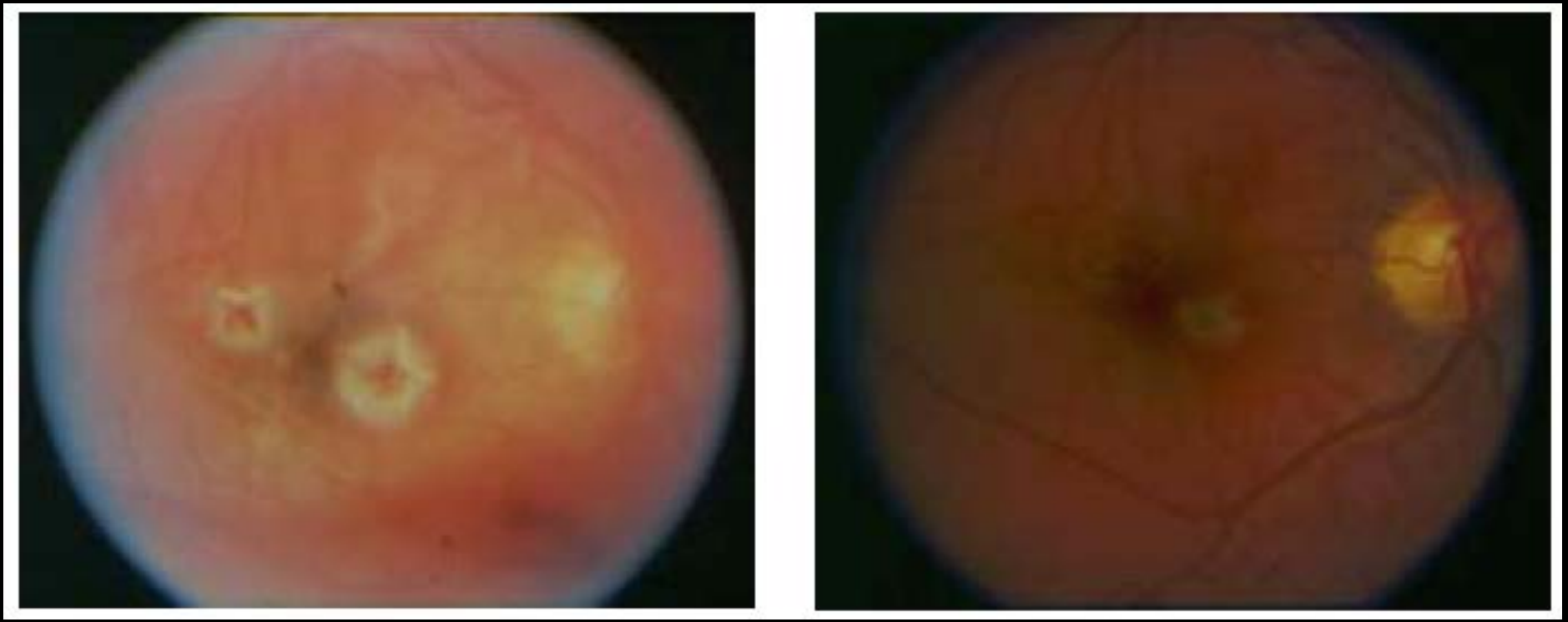
NEJM 2010, 363; 11






https://www.lasersafe.co.uk/laseradvice3.php

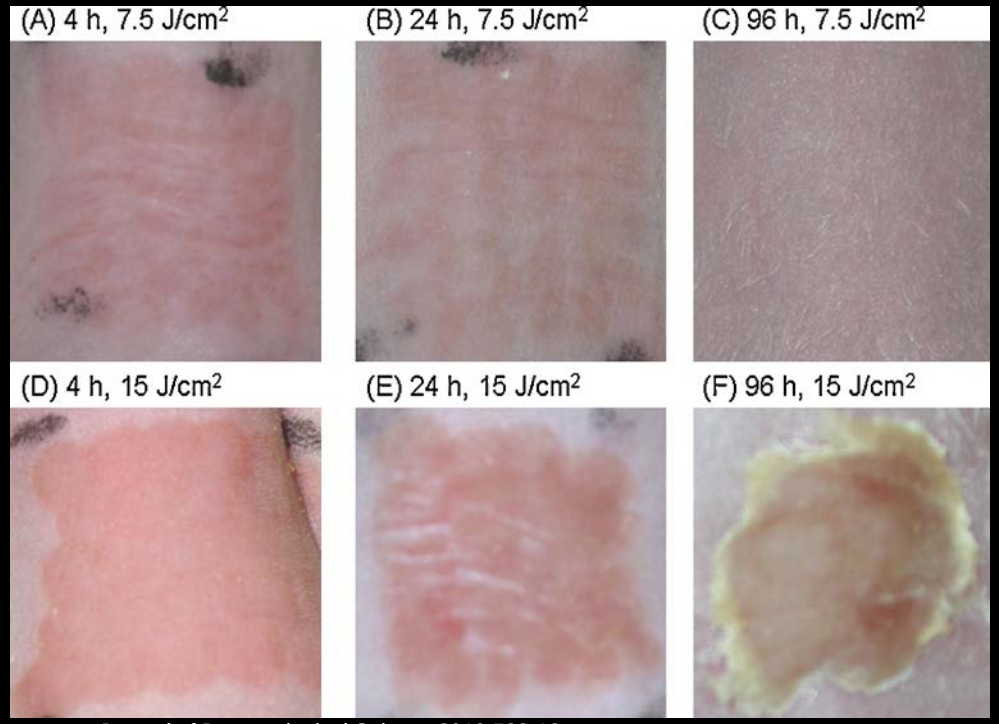
# Eye Injury from Laser Exposure



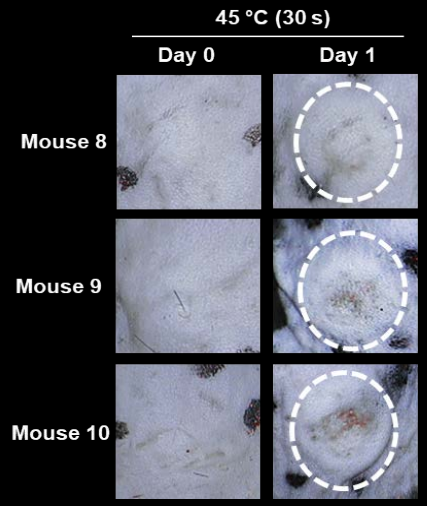
a. Retinal burns from Nd:YAG laser 1064nm rangefinder.
b. Several weeks later visual acuity 20/200

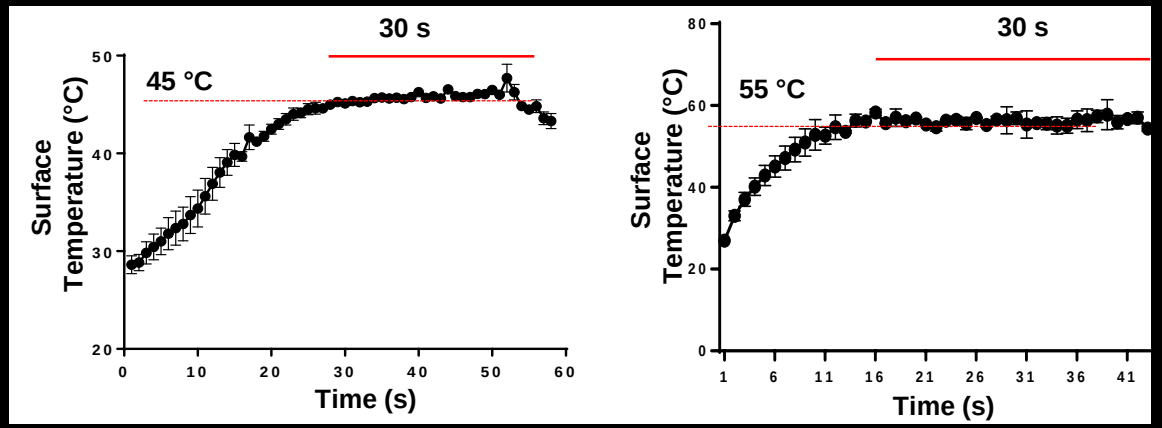
Walter Reed Army Institute - Ocular Laser Injuries

# Effects on the Skin




*Journal of Dermatological Science* 2010 588-18




Khan I *et al* **Sci Reports** 2015 , 1, 510581

# Laser Safety Measures

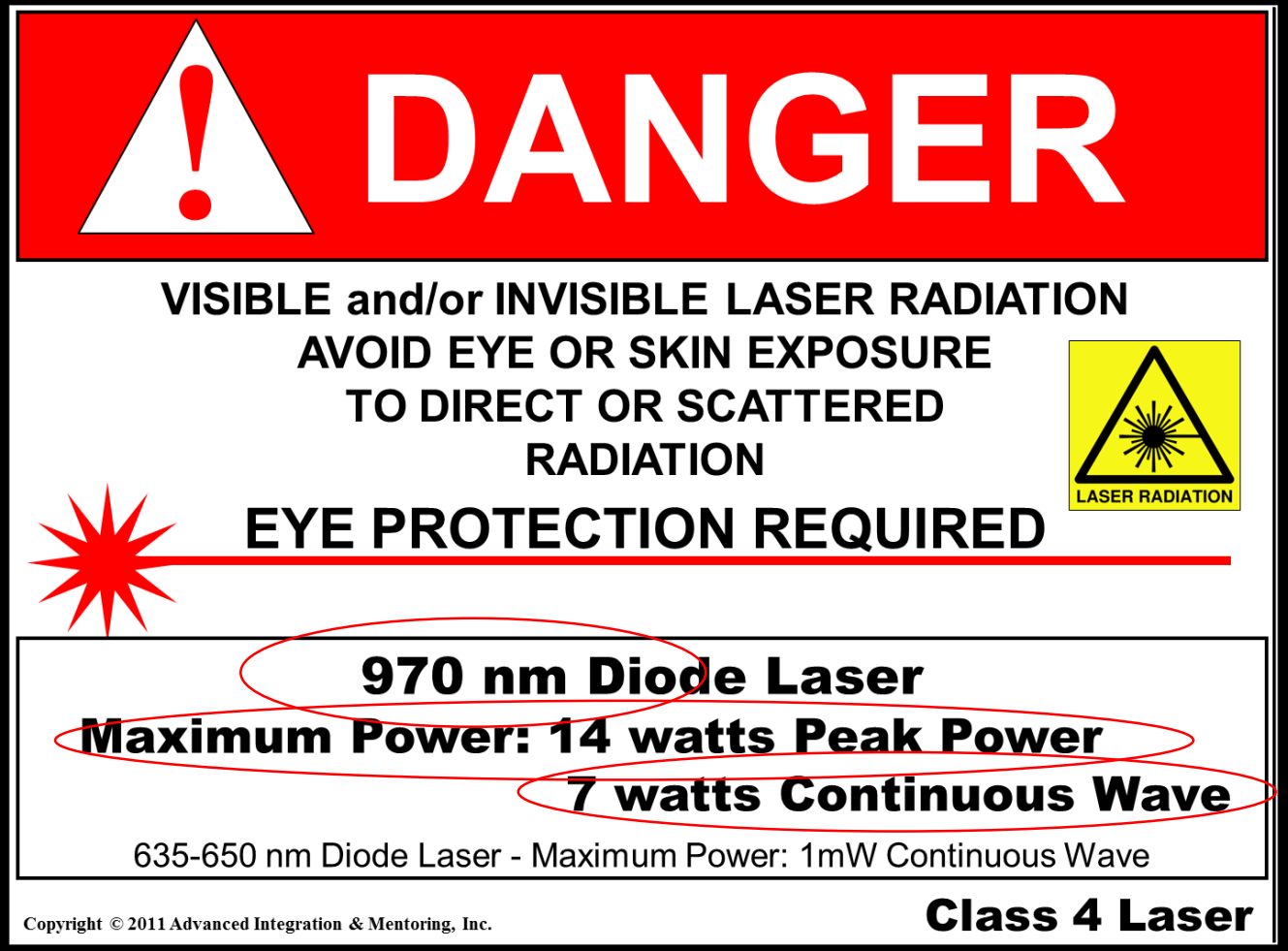
I. Access Controls
II. Engineering Controls
III. Process Controls


# I. Access Controls

- Door signs
- Nominal Hazard Zone

# Warning Signs

- Must be placed at every entrance into the NHZ (Nominal Hazard Zone / Operatory)
- Must identify needed eyewear (Wavelength and maximum power)



# Nominal Hazard Zone

*(Controlled Area)*

- The NHZ must be designated with appropriate ***signage***.
- **NHZ (operatory)** should be ***restricted*** to patient and only necessary personnel
- All personnel in the NHZ (operatory) ***must*** **wear appropriate** ***eye protection!***

- Reasonably *minimize* the amount of reflective surfaces within the NHZ.

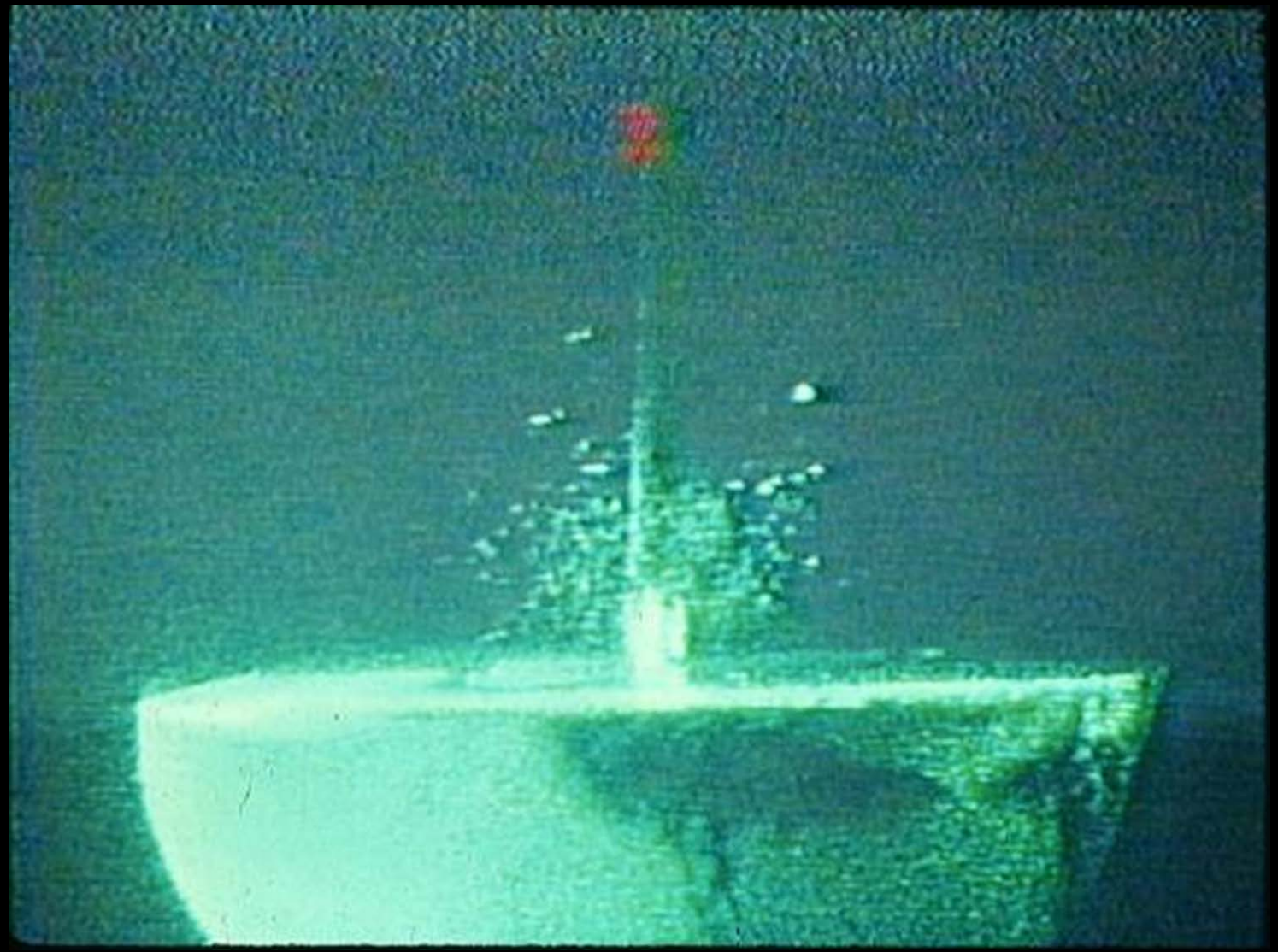
# II. Engineering Controls

- Device safety
- Eye wear
- Fire safety
- Electrical safety
- Respiratory safety
- Compressed gases

# Device Safety Mechanisms

- Keys
- Password access
- Emergency Shut-Off Switch
- Software self-check at start up
- Automatic Sleep Mode
- Guarded activation Switch
  - Foot Control "Safety" Cover
  - Recessed Finger Switch
- Fiber / Containment Case Interlock Switch


# Eye protection

Slide Courtesy: Dr. Thomas Mang

# Respiratory Hazards

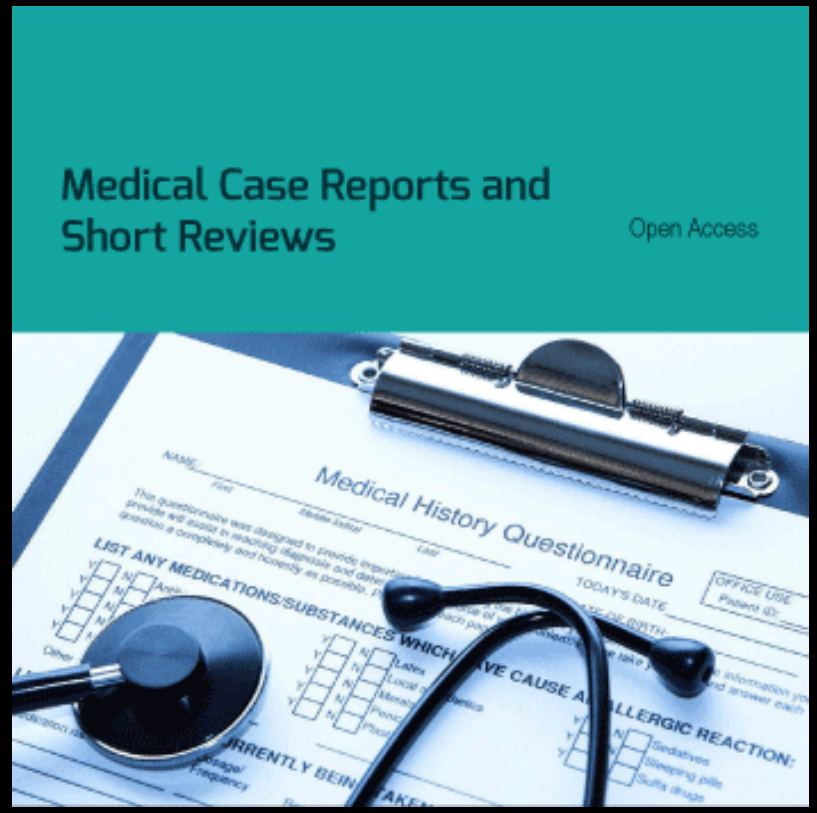
- Ablative lasers - MUST high volume evacuation
  - Laser plume is a biological hazard of gas fumes created when tissue is ablated (vaporized), also referred to as Laser Generated Airborne Contaminants (LGAC).
  - Laser plume can contain vital strains of the Human Papilloma Virus (HPV) and other organisms.
- Nonetheless, additional surgical masks are recommended

# III. Process Controls

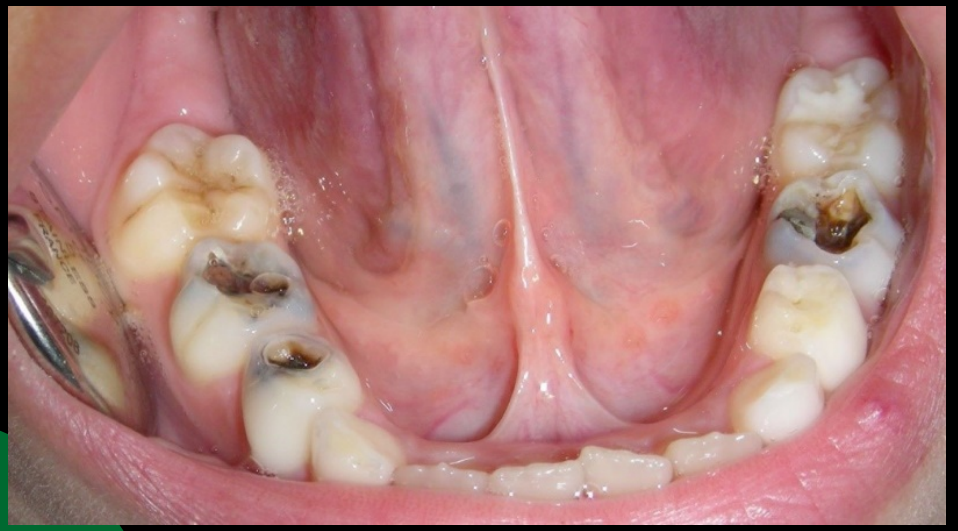
- Training-Certification
- Guidelines
- Documentation

LIA™
LASER INSTITUTE OF AMERICA

- Important laser procedure details documented
  1. Clinical presentation
  2. Device parameters
     - Wavelength
     - CW or pulsing (Hz)
     - Treatment Surface Irradiance (mW/cm$^2$)
       *or* power (W/mW) and distance (cms)
  3. Manner of use
     - Treatment time (sec)
     - Repetitions (sessions per week)
     - Scanning or stationary



# Clinical Dentistry

Remove
Noxious / Damage

Healing &
Regeneration

Disinfection

# Surgical Lasers

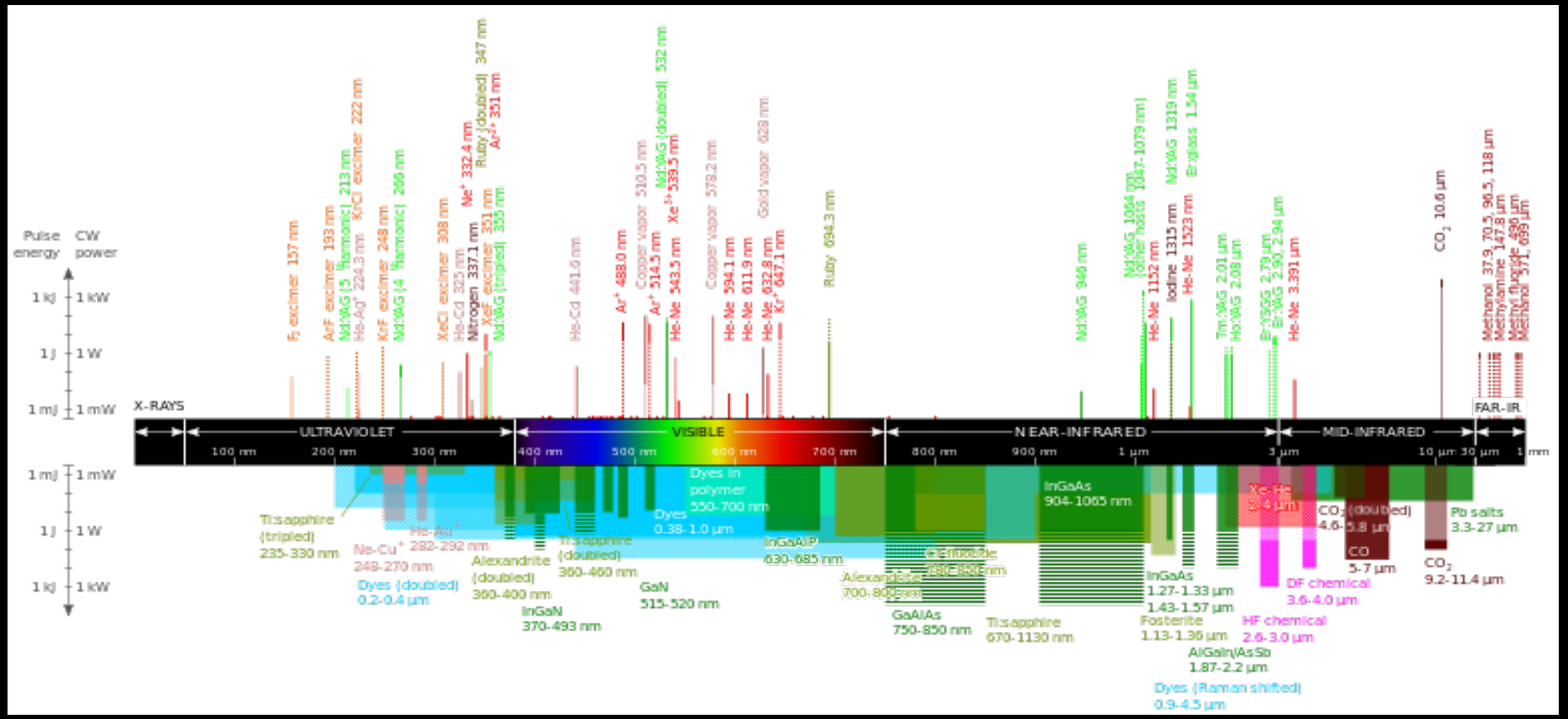
## Incision, Excision, Curettage & Disinfection

PRIMARY GOAL: Tissue or Biofilm *Removal*

(*Thermal*)

# Laser and LED Devices

## Visible or invisible light




En.Wikipedia.org

# *High Power* Laser Applications

Hard tissue procedures: Excavation, Bleaching, Prevent demineralization, Dentin desensitization, Bracket bonding / debonding, Photon-Induced Photoacoustic Streaming (PIPS)

Soft tissue procedures:

Excisions, Photocoagulation, Field ablation, Recontouring (Esthetics, Snoring, Halitosis), Depigmentation, Curettage

# Soft tissue surgery

No Bleeding during surgery



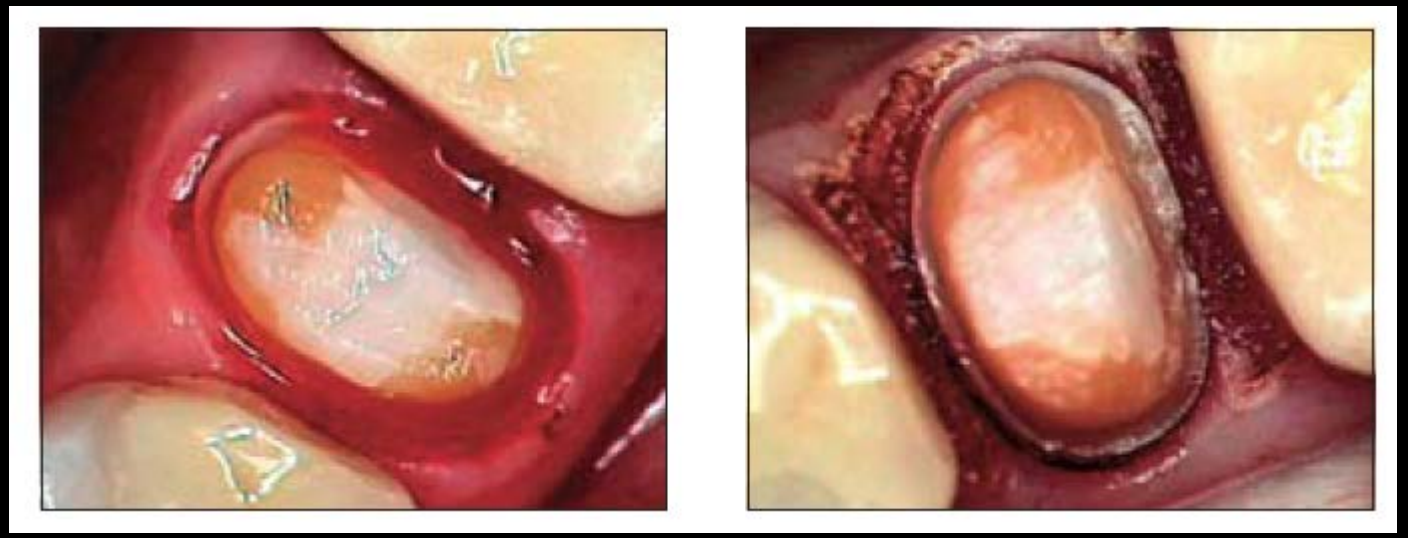


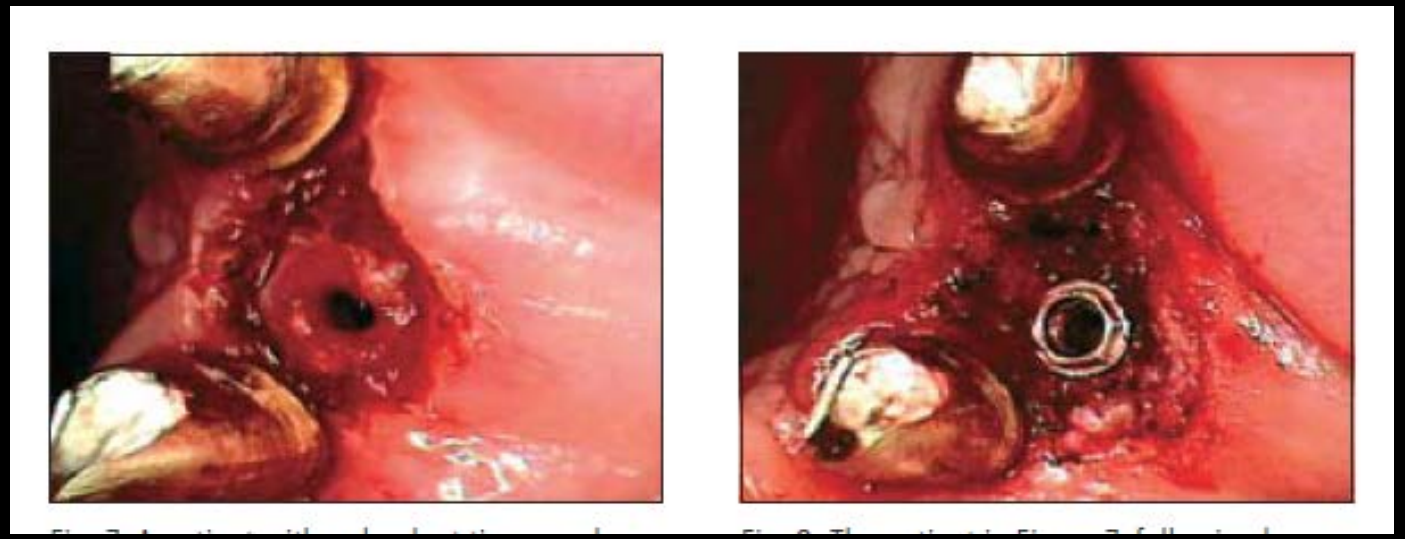
*Minimal* scaring,
Excellent healing (regeneration)

Arany PR J Invest Derm 2019

# Crown Lengthening

(‘*Trough*’ing)





Lomke M General Dentistry 2009, Jan-Feb, 47-59

# Excisions

**Irritation Fibroma**

**Pericoronitis**

Lomke M General Dentistry 2009, Jan-Feb, 47-59

# Frenectomy

**Lingual Frenum**

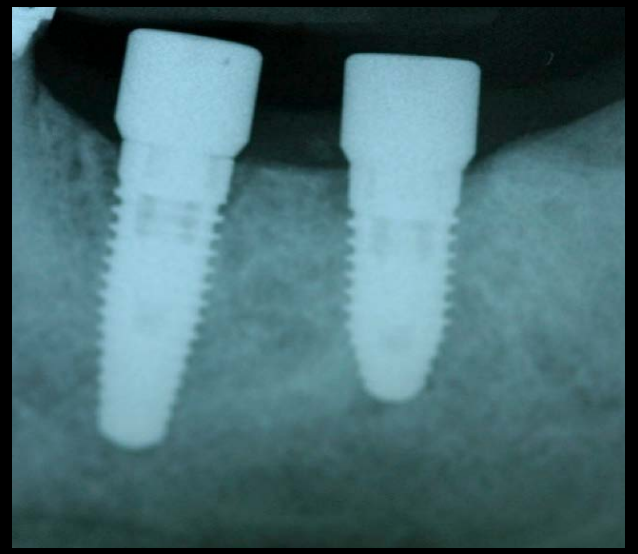
**Buccal Frenum**

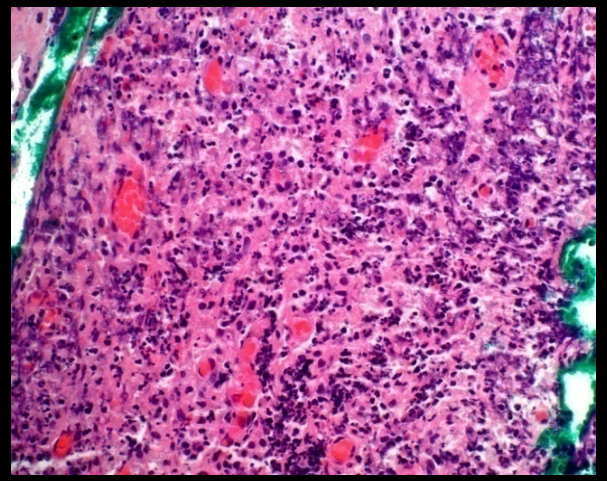


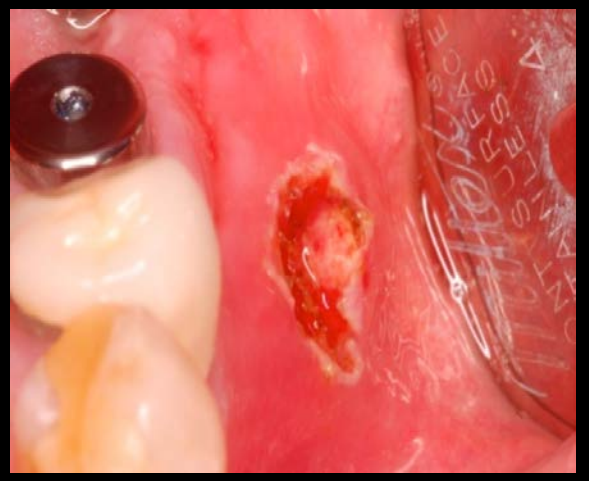
Lomke M General Dentistry 2009, Jan-Feb, 47-59

# Surgical Lasers

## Curettage & Disinfection







3 weeks post op

**Gingival abscess removal using a soft-tissue laser**
**Prasad, Andreana, Monaco 2011 AADR**

# High-Power Surgical Lasers in Dentistry

- Soft tissue surgery: *well-established*
- Hard tissues: *increasingly popular*

☞ Advantages:

- Precision (size & depth)
- Blood-less field
- Better healing*

☞ Limitations:

- Training (non-tactile, rate movement)
- Specialized, *expensive* equipment
- Safety

Myth – *widely held false belief*

Fallacy – *mistaken belief based unsound reasoning*

A single laser unit can have multiple applications

TRUE

# A laser can have multiple applications

Sure it can! Just as a smart phone can:

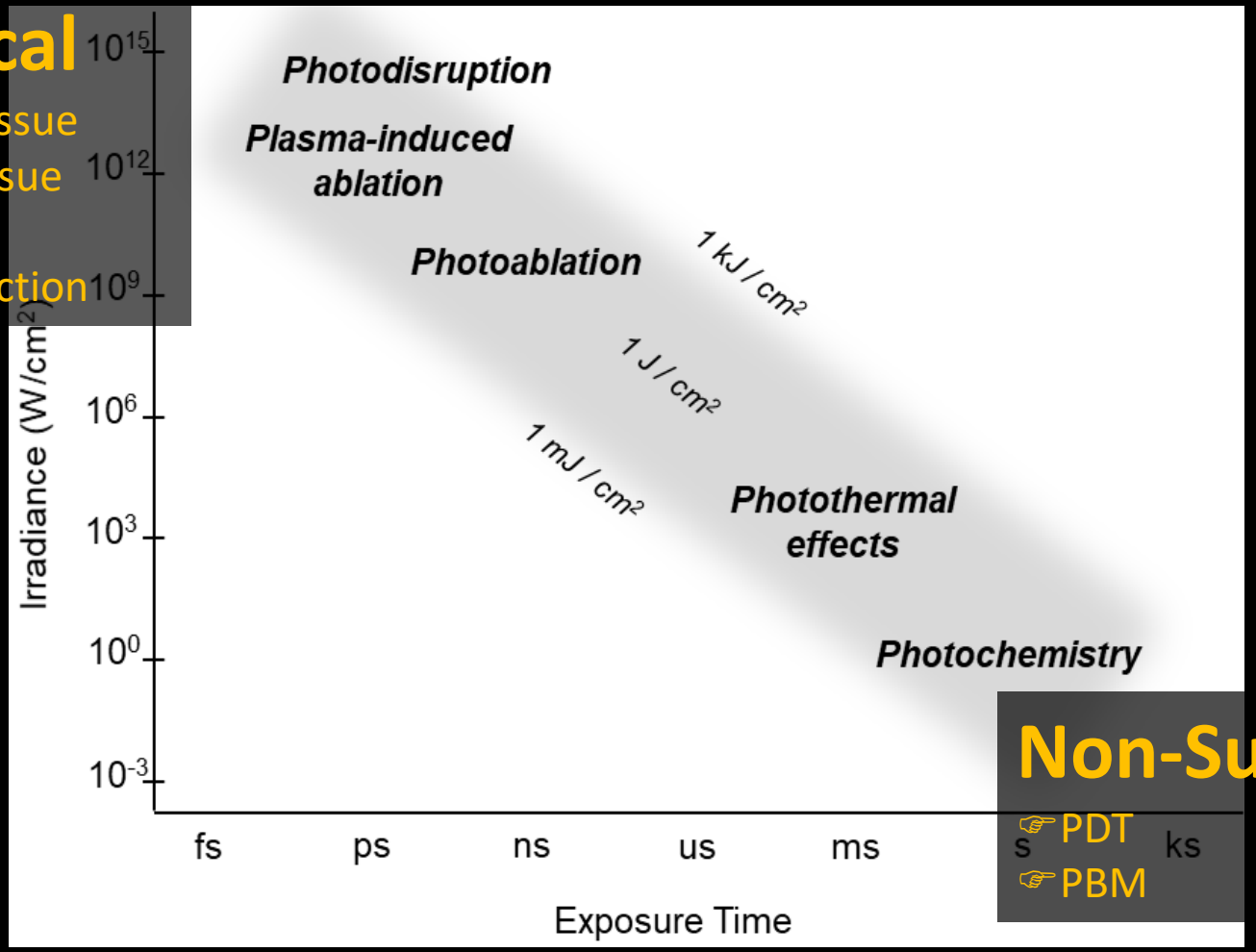
- *Voice*
- *WiFi*
- *Bluetooth*
- *NFC*


*The laser is a 'tool'…*
*need to understand context and purpose!*

# Light-Biological Tissue Interactions

## Surgical

- Hard tissue
- Soft tissue
- Disinfection

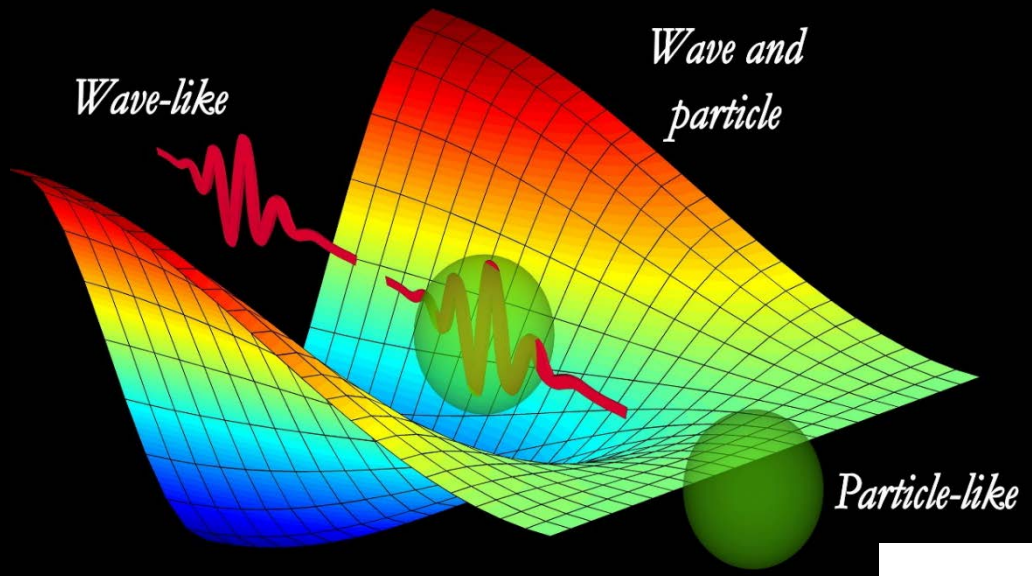



## Non-Surgical

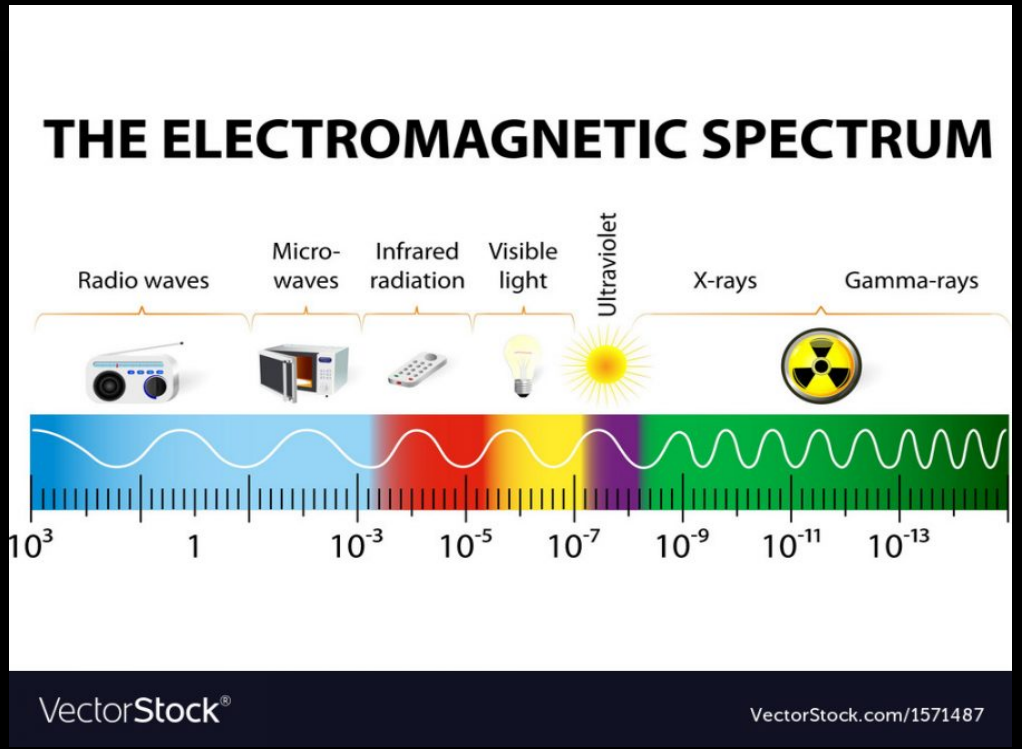
- PDT
- PBM


Fallacy

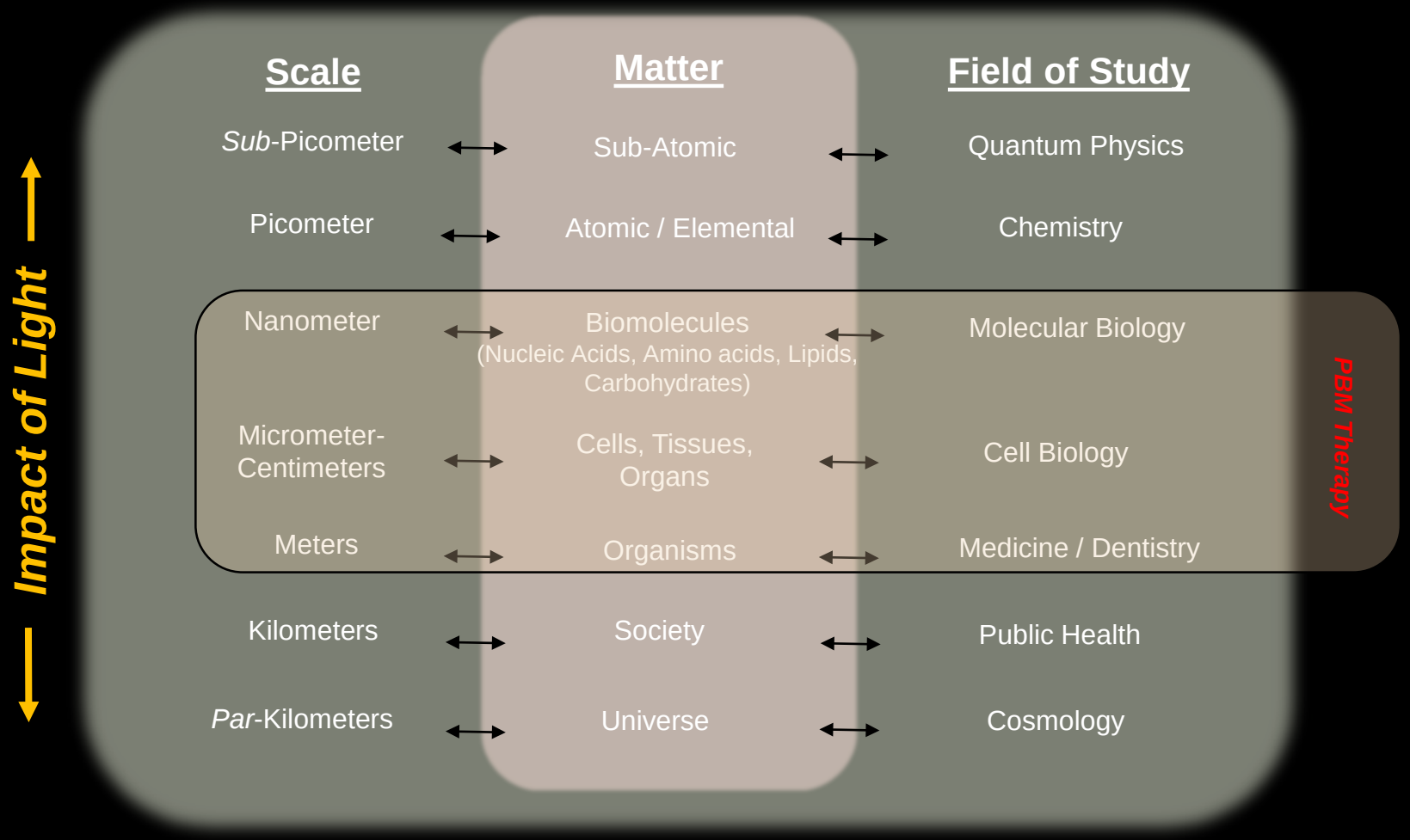
# Light is a physical form of Energy




https://www.livescience.com/24509-light-wave-particle-duality-experiment.html



# Light

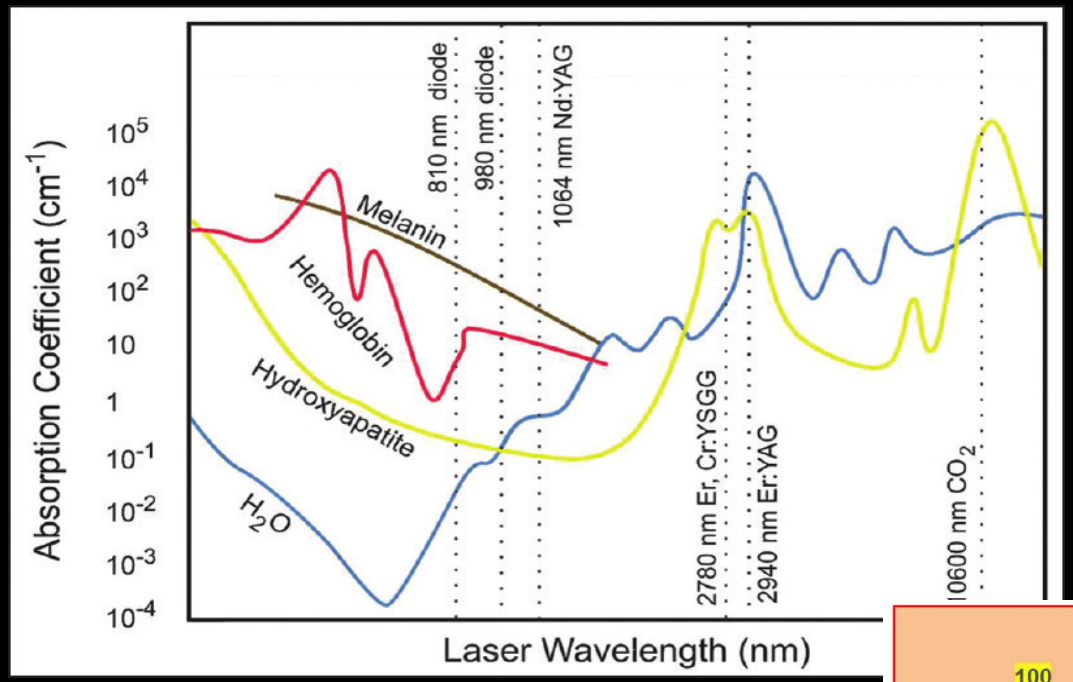



Arany PR *J Dent Res* 2016

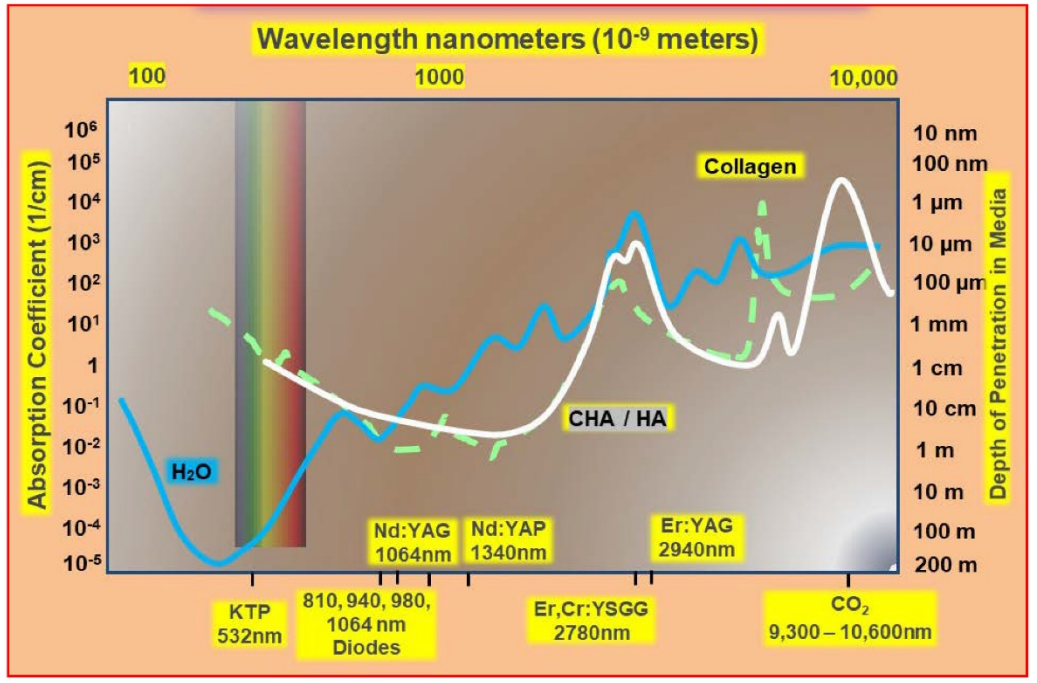
More laser power provides better clinical outcomes?

Myth

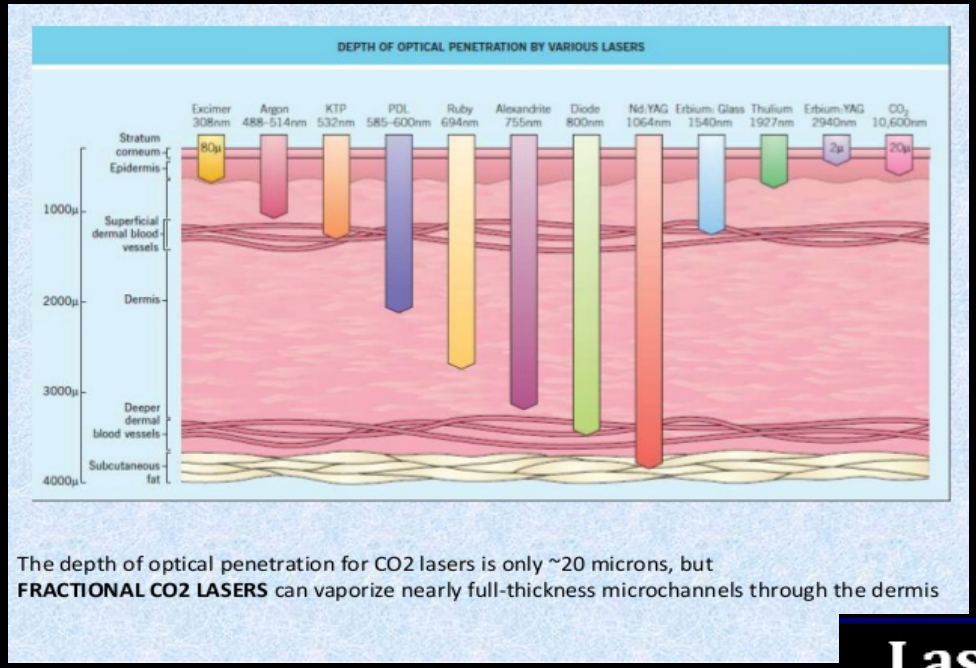
# Laser Biological Effects




*Absorption* ➔ *'Attenuation' Efficiency!*

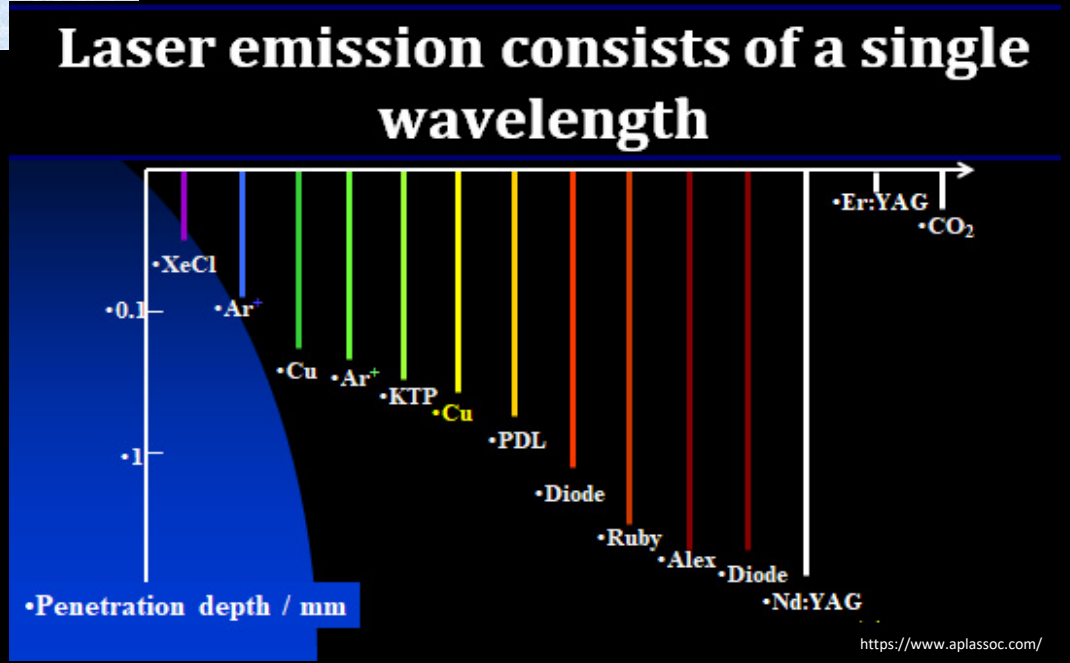


# Laser Biological Effects




The depth of optical penetration for CO2 lasers is only ~20 microns, but **FRACTIONAL CO2 LASERS** can vaporize nearly full-thickness microchannels through the dermis

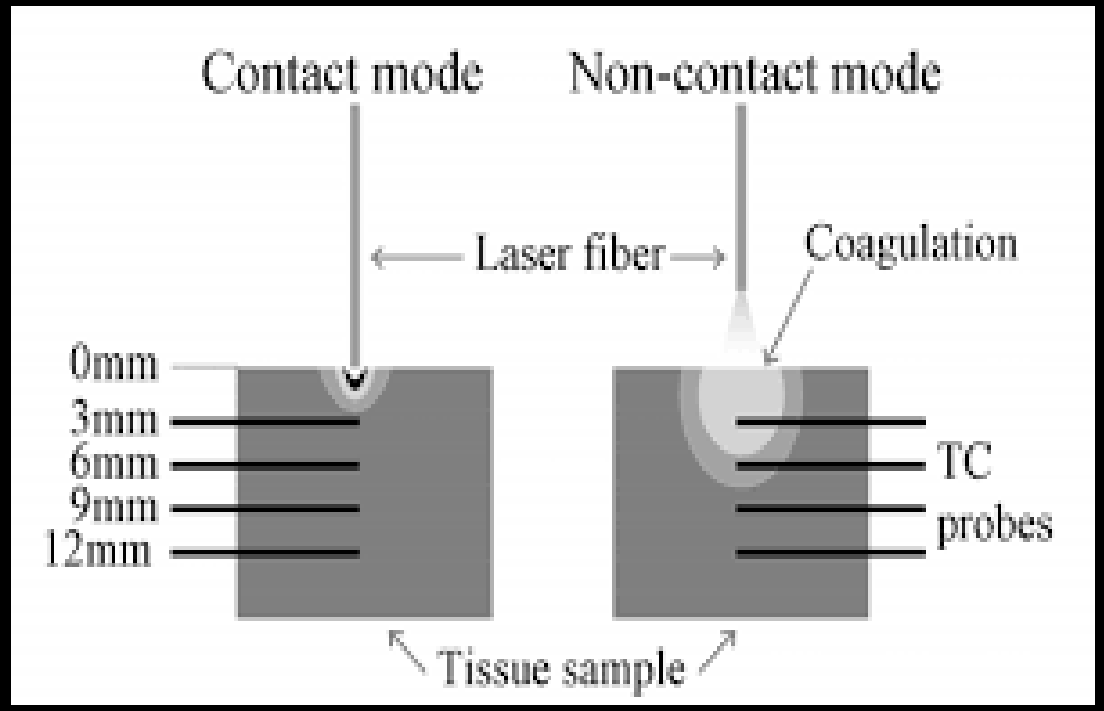
*Energy ➔ NOT equal to 'Penetration'*

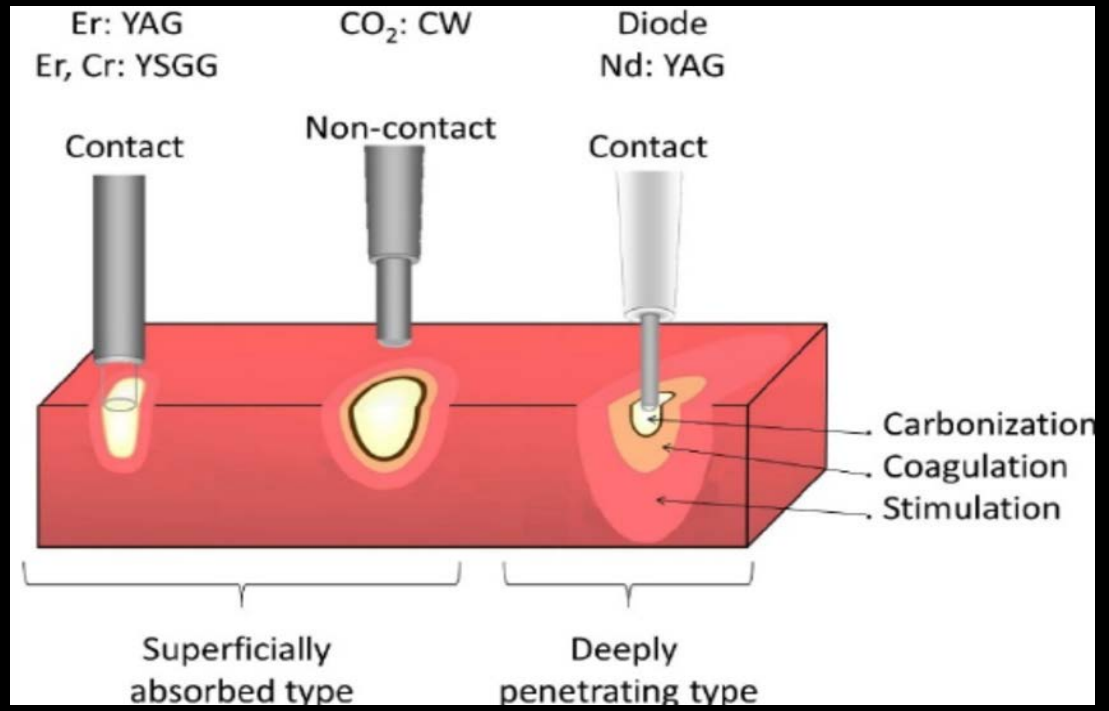


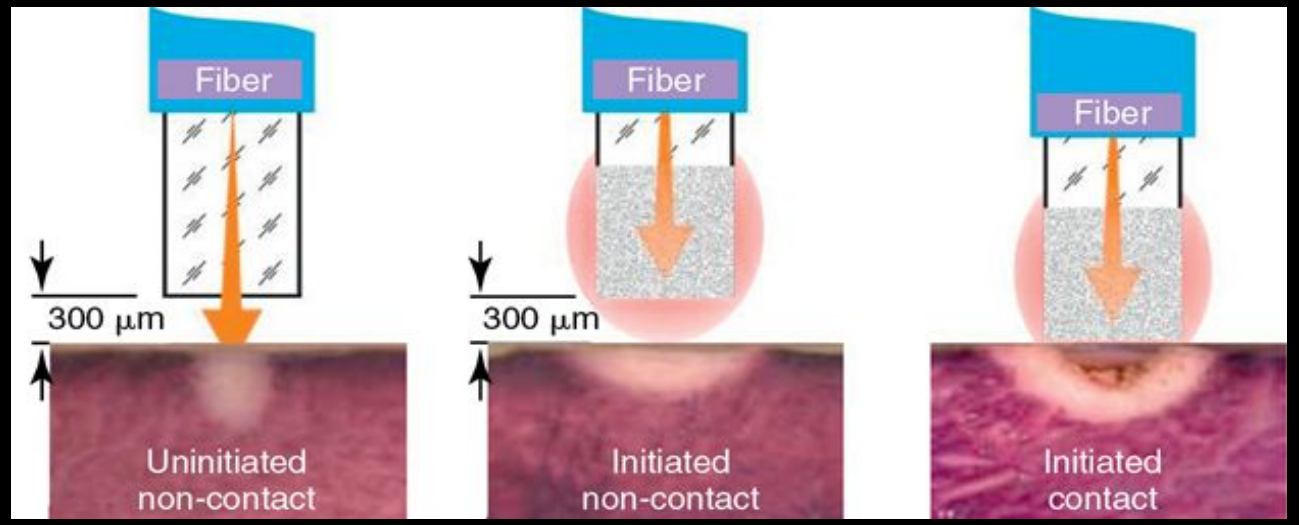
Larger laser spot / fiber size is more important than wavelength for deeper ablation?

Fallacy

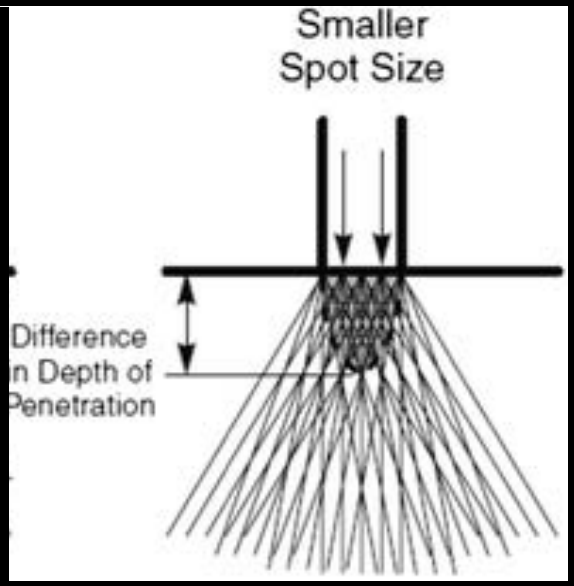
# Manner of Laser Use - Important!



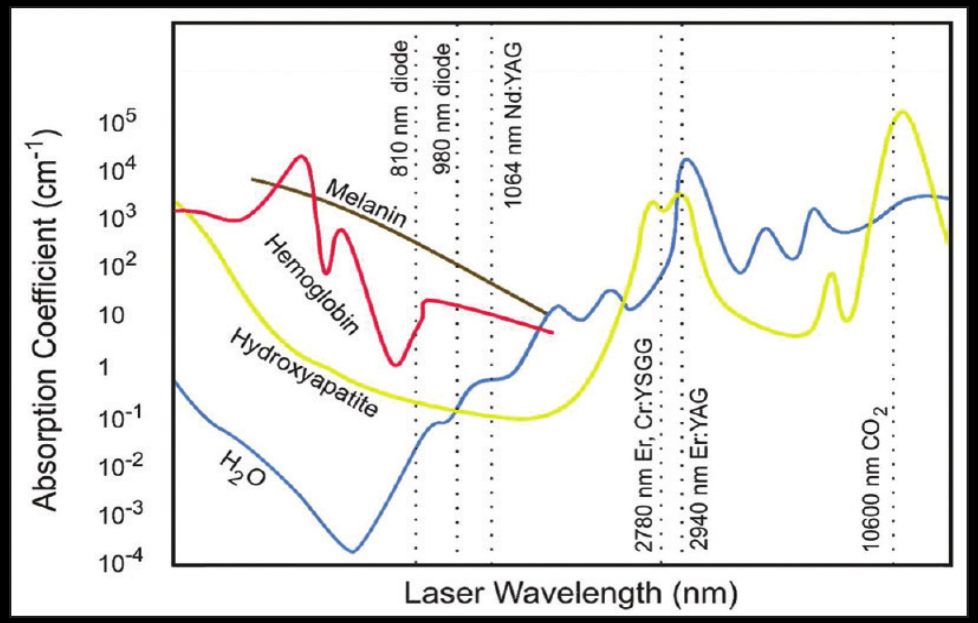
# Effect of Spot / Fiber Sizes



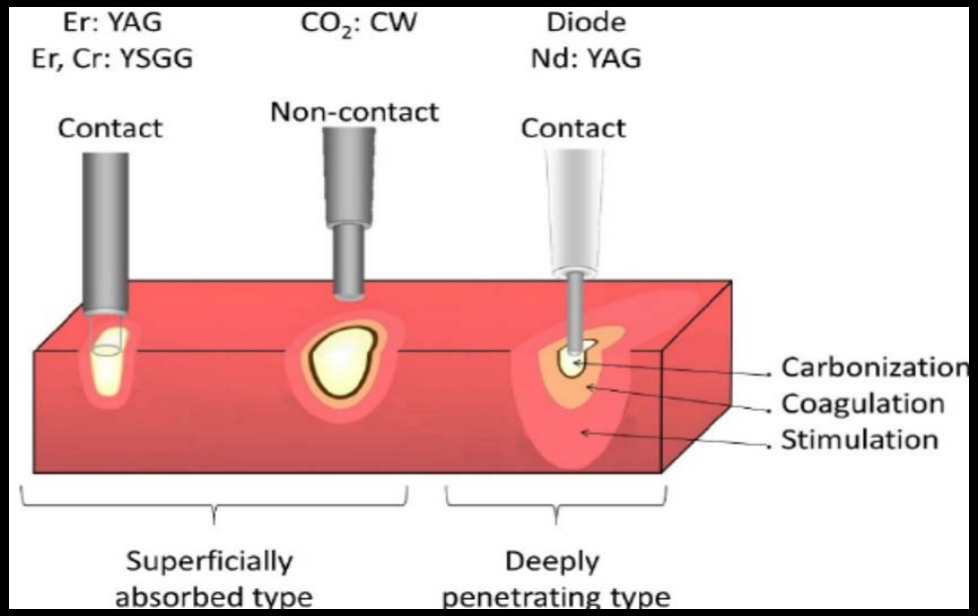
Laser procedures have a poor clinical finish, hence poor outcome

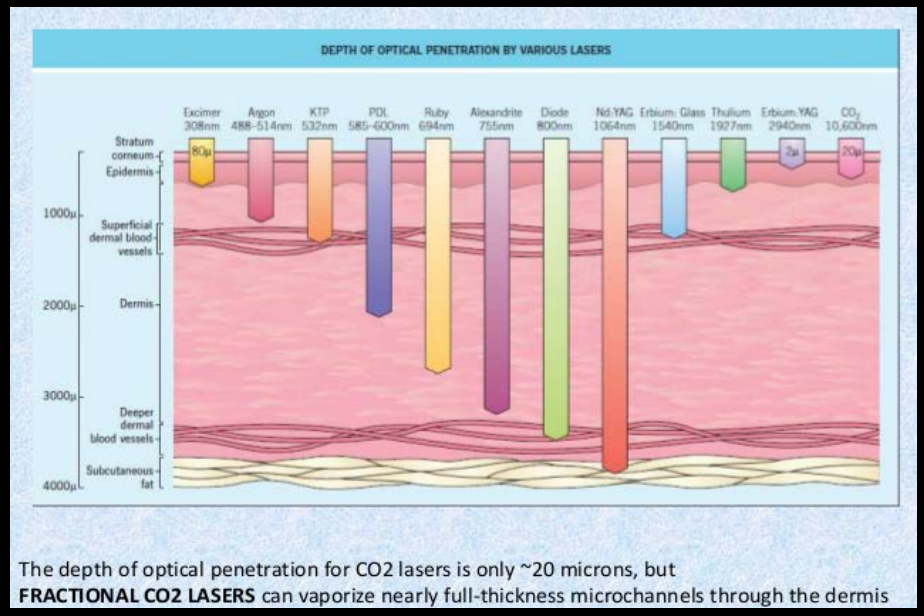
Myth

# Laser Biological Effects




*Absorption* → *'Attenuation' Efficiency!*




The depth of optical penetration for CO2 lasers is only ~20 microns, but **FRACTIONAL CO2 LASERS** can vaporize nearly full-thickness microchannels through the dermis

# Fundamental Laser Surgical Parameters in Clinical Dentistry

- Device Variables: Laser settings from device pre-sets and prior study;
- Operator variables: hand speed and optimal pressure (*light*)
- Subject variables: hydration (absorption & cooling), pigmentation

Nicole Walawander
Undergrad-D3

Asad Tanveer
Undergrad-D1


Figure 11: Example of varying parameters (power, pulsing, hand speed) for an apple incision. The second row of incisions has minimal charring and great precision, which represents ideal parameters. By Oleg Borisiuk

# Results: Apple (low water, high pigment)

**Navigator**

Non-Ideal:

Pulsed - 1.0W

CW- 4.0W

Pulsed - 5.0W

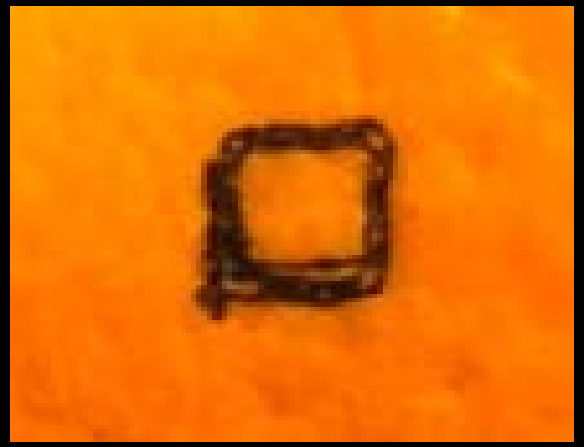
| | Hydration | Pigmentation |
|---|---|---|
| **Apple** | Low | High |
| **Orange** | Medium | High |
| **Egg Shell** | Low | Low |
| **Ham** | Medium | Low |
| **Steak** | High | High |

# Results: Orange (medium water, high pigment)

**$CO_2$ Luxar**

Non-Ideal:

P-2.0W



CW-2.0W

P-6.0W

| | Hydration | Pigmentation |
|---|---|---|
| **Apple** | Low | High |
| **Orange** | Medium | High |
| **Egg Shell** | Low | Low |
| **Ham** | Medium | Low |
| **Steak** | High | High |

# Results: Ham (medium water, low pigment)

**Gemini**

Non-Ideal:

Pulsed - 0.5W
810nm

Pulsed - 1.0W
980nm

Pulsed - 1.5W
810nm

| | Hydration | Pigmentation |
|---|---|---|
| **Apple** | Low | High |
| **Orange** | Medium | High |
| **Egg Shell** | Low | Low |
| **Ham** | Medium | Low |
| **Steak** | High | High |

# Analyses of Quality of Laser Surgical Procedure

- Quantify the tissue separation and amount of charring with Image J

**Effective tissue separation ?**

**←→**

**Charring ?**

# Robotics & AI to increase Surgical Laser Precision

Aaron Gorsline
Undergrad-Masters

*Manuscript in preparation*

# Preventive Laser Hard Tissue

Caries (& Periodontitis) is the most human diseases. It is also COMPLETELY preventable!

A *lifetime caries risk* can be gauged by the incidence of pediatric /adolescent caries indices……..

Newly erupted teeth are MOST prone to caries due to…

1. Deep fissures and pits
2. Limited manual dexterity
3. Diet/habits

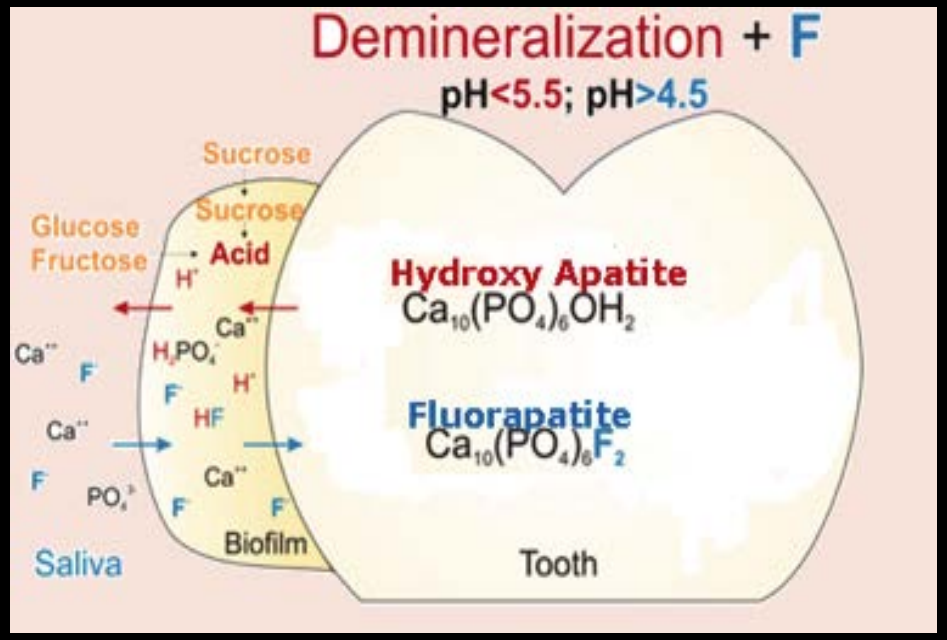
# Laser (non-ablative) Adjunct



Diode


$CO_2$

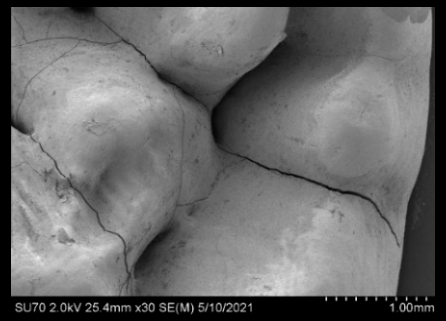

Er:Cr;YSGG

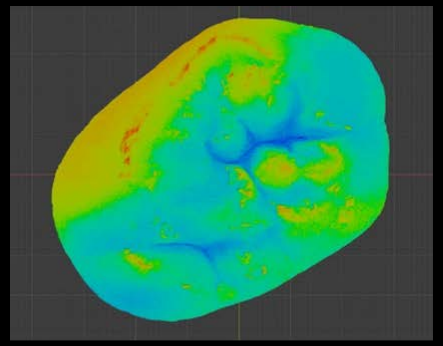



$Ca^{2+} + PO_4 + F \rightarrow Ca_{10}(PO_4)_{10}F_2$

# Laser Odontoplasty

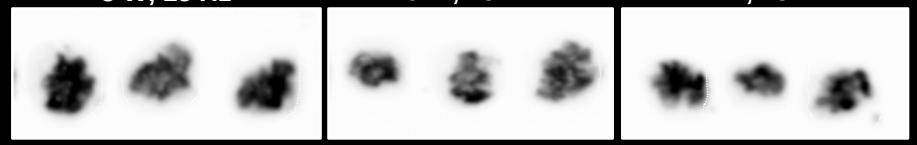
Pre-Laser



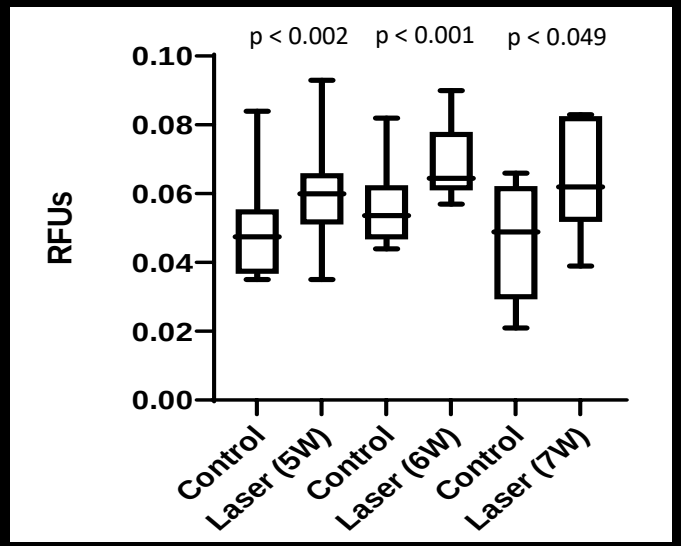
Control
(Before toothbrushing)

5 W, 15 Hz | 6 W, 15 Hz | 7 W, 15 Hz



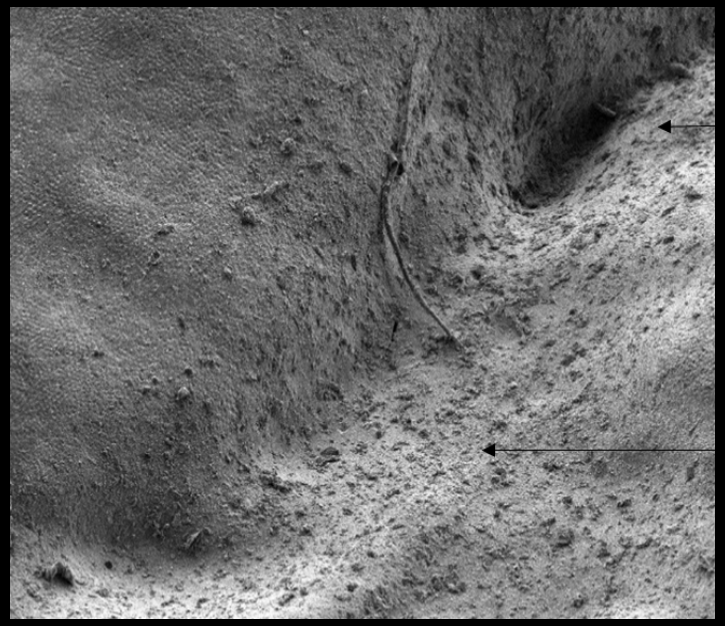
Erica Lavere
Pedo Resident / Practice

Oleg Borisiuk
Undergrad / D2 Penn

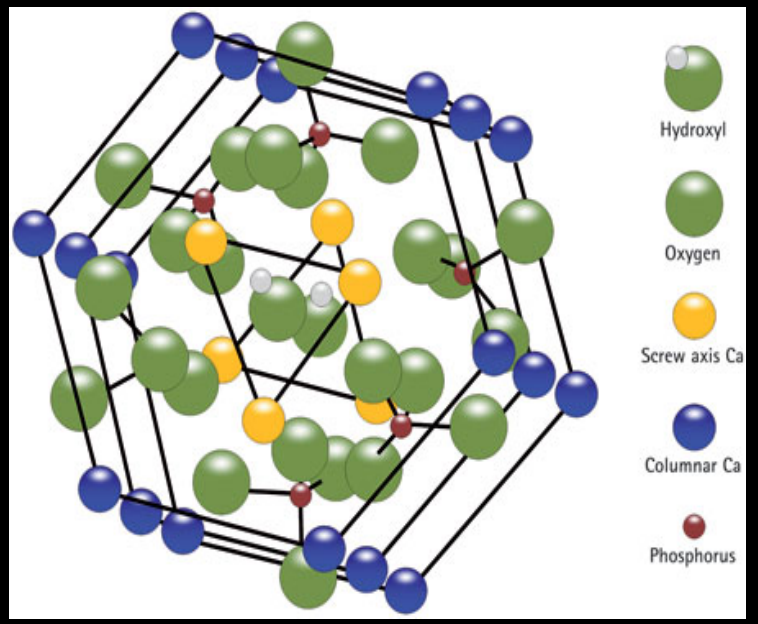



*Manuscript submitted*

# Buffalo Fluoride Laser Odontoplasty
## (B.F.L.O.)



Laser Recontouring – remove retentive areas

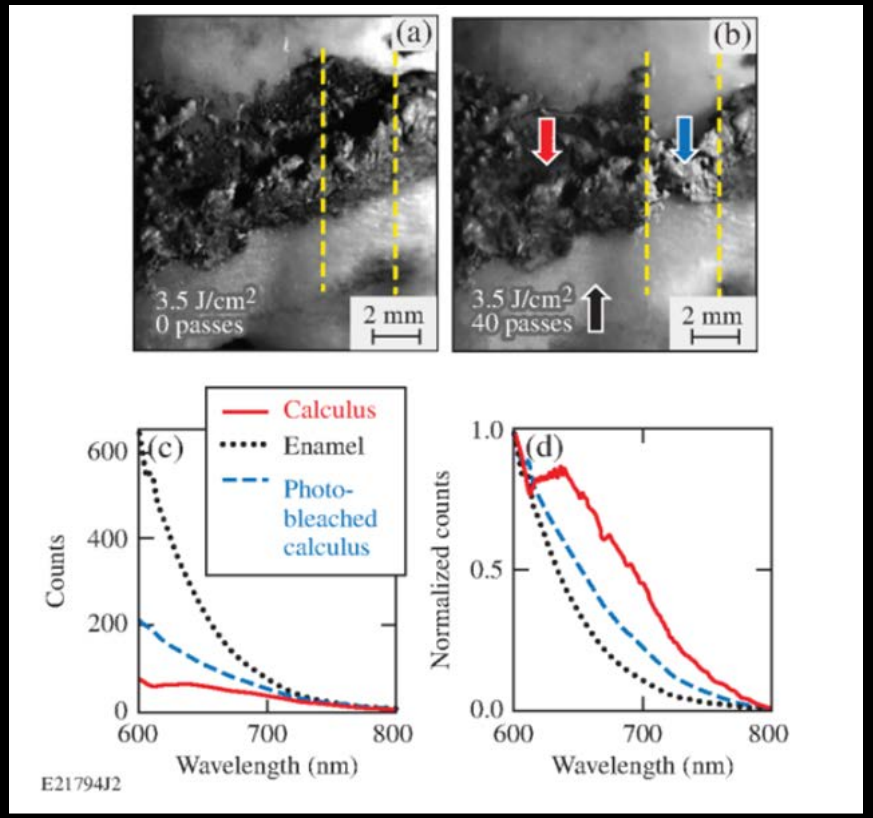



Laser Fluoride – increase acid resistance

*Manuscript under preparation*

# Laser SRP for Calculus Removal

- Various wavelengths have been used eg; NdYAG, ErYAG, ErCr YSGG, Ti:Sapphire
- Several studies have shown comparable efficacy between laser and mechanical SRP
- Calculus has water within structure and pores.
- Hard tissue (mid and far-infrared) lasers are absorbed by water and cause microexplosions termed *photomechanical* or *thermomechanical ablation*
- Other benefits of laser SRP
  - precision of lasers
  - concurrent photocoagulation /cautery
  - non-surgical benefits (aPDT & PBM)




**Safety Guidelines for the Laser Removal of Dental Calculus**

www.jstage.jst.go.jp/browse/islsm

Japanese Society for Laser Dentistry

# L.A.N.A.P.

## Histologic Evaluation of an Nd:YAG Laser–Assisted New Attachment Procedure in Humans

*Raymond A. Yukna, DMD, MS**
*Ronald L. Carr, DDS***
*Gerald H. Evans, DDS**

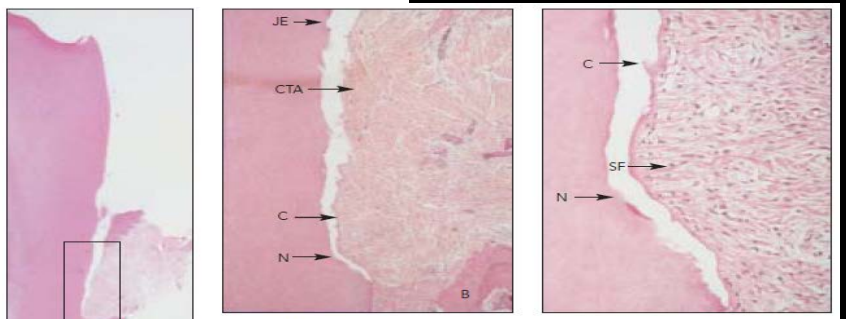



**Fig 3** *LANAP-treated mandibular left second premolar of a 48-year-old man with an infrabony defect (hematoxylin & eosin). (left) Low-power view (×1) outlining the area of interest. (center and right) Medium-power (×16) and high-power (×63) views showing the calculus notch (N), thin layer of new cementum (C) in and coronal to the base of the notch, junctional epithelium (JE) at the coronal level, new CTA with Sharpey fibers (SF), and new bone (B) adjacent to the notch. (Cementum is artificially separated from tooth.)*

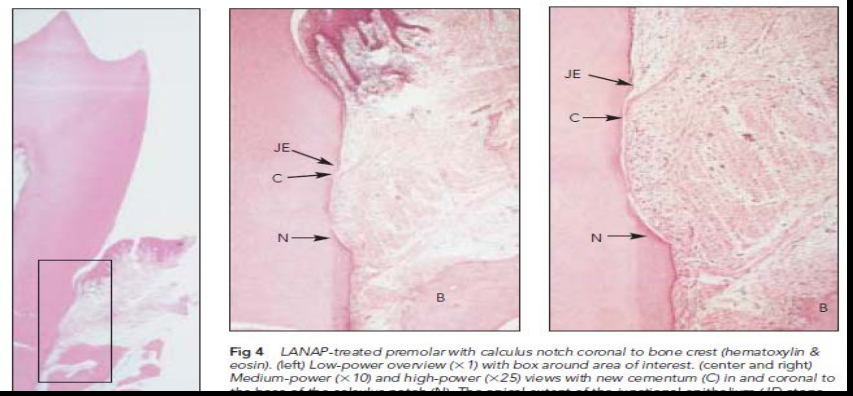
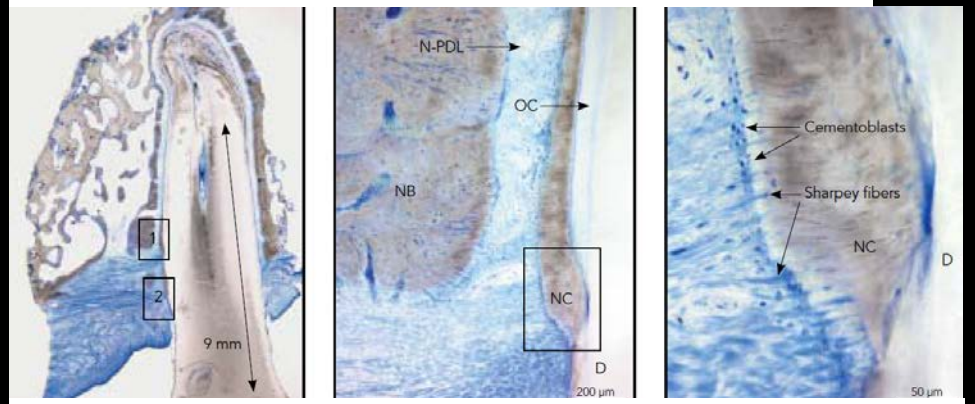



**Fig 4** *LANAP-treated premolar with calculus notch coronal to bone crest (hematoxylin & eosin). (left) Low-power overview (×1) with box around area of interest. (center and right) Medium-power (×10) and high-power (×25) views with new cementum (C) in and coronal to*

(Int J Periodontics Restorative Dent 2007;27:577–587.)

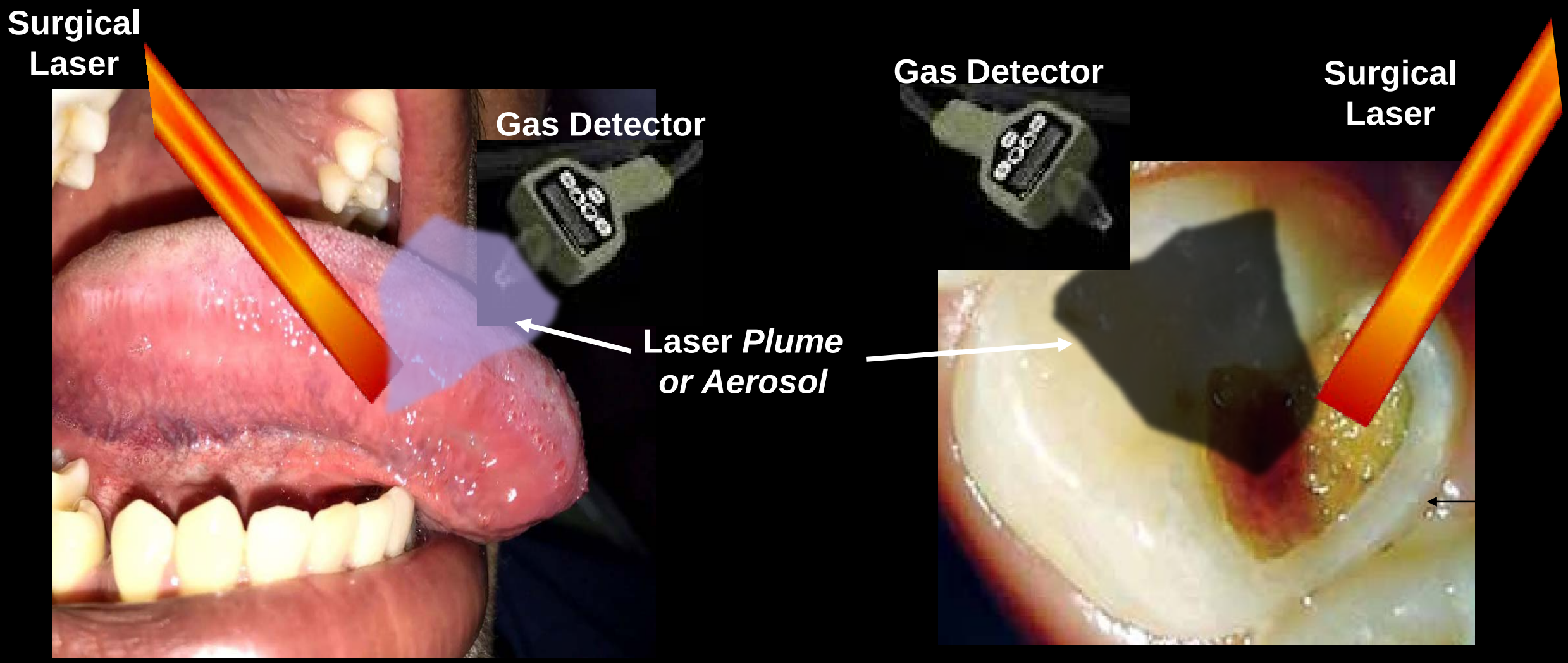
## Human Clinical and Histologic Evaluation of Laser-Assisted New Attachment Procedure

*Marc L. Nevins, DMD, MMSc[1]/Marcelo Camelo, DDS[2]*
*Peter Schupbach, PhD[3]/Soo-Woo Kim, DMD, MS[4]*
*David M. Kim, DDS, DMSc[5]/Myron Nevins, DDS[6]*




(Int J Periodontics Restorative Dent 2012;32:497–507.)

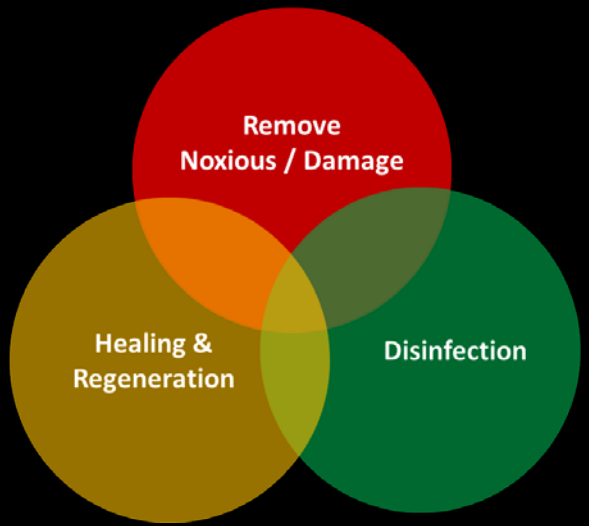
# Theranostics - *Realtime* therapy coupled to diagnostics




Yan R et al. Proc SPIE Int Soc Opt Eng. 2015,24; 9306: 93060

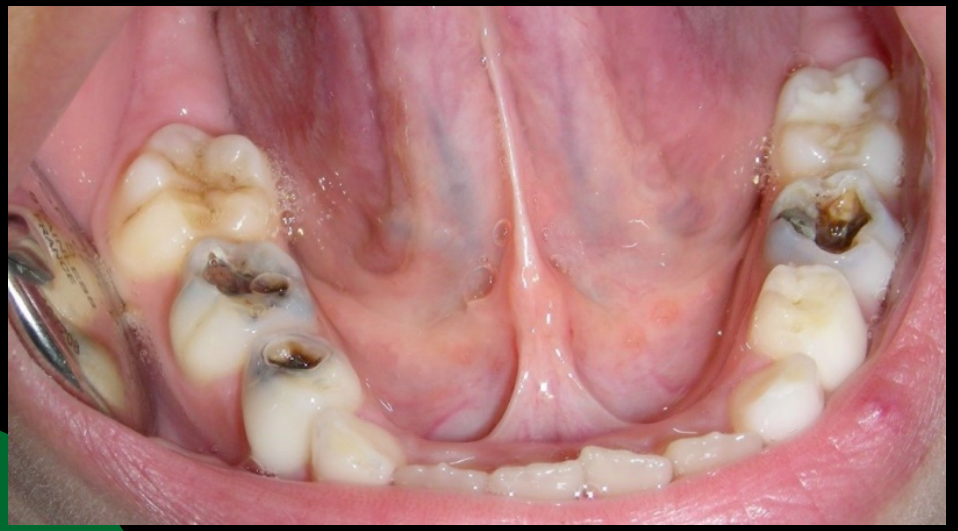
# Questions?


## Clinical Dentistry




prarany@buffalo.edu

# Clinical Dentistry

Remove
Noxious / Damage

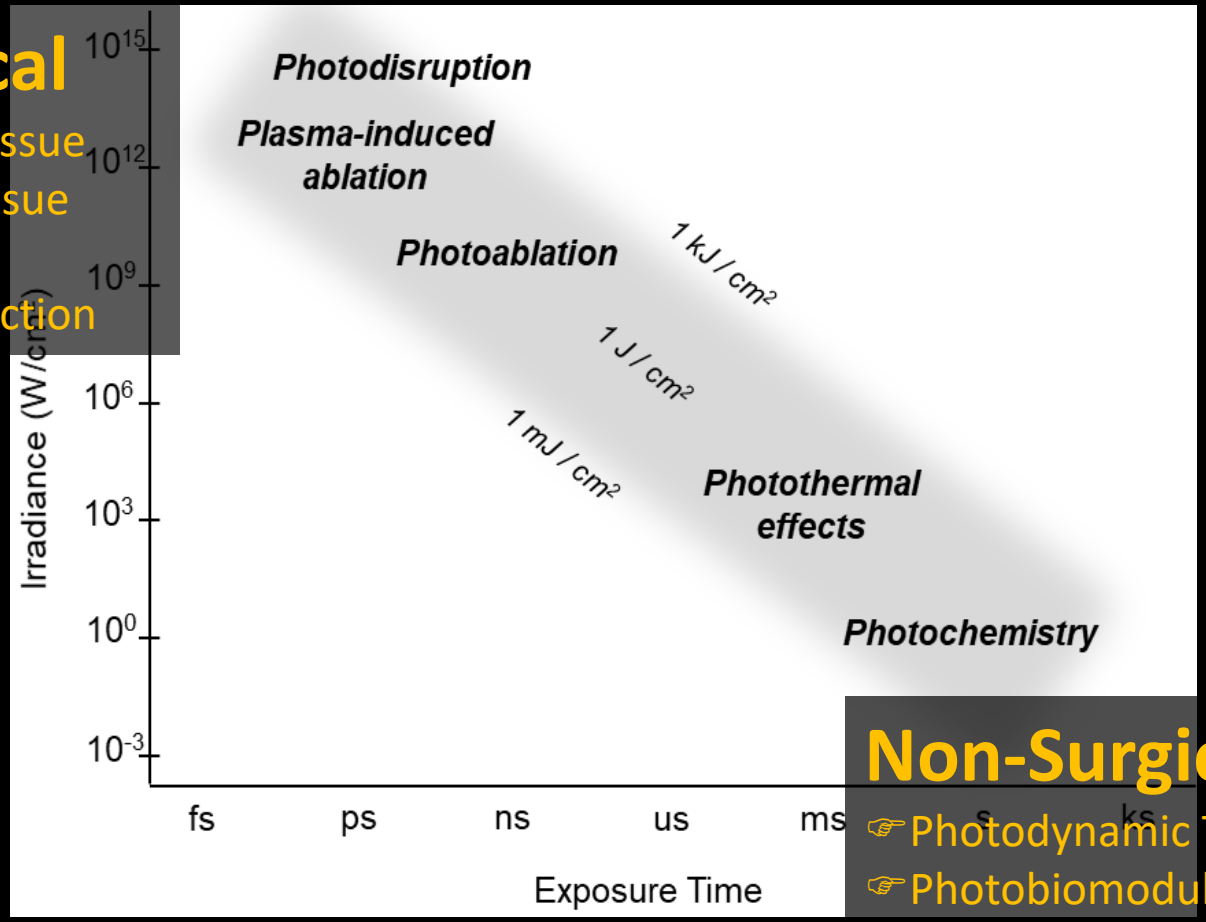
Healing &
Regeneration

Disinfection

# Light-Biological Tissue Interactions

## Surgical

- Hard tissue
- Soft tissue
- Disinfection




## Non-Surgical

- Photodynamic Therapy (PDT)
- Photobiomodulation Therapy (PBM)

# Non-Surgical Lasers

## Photodynamic Therapy

Antitumor & Antimicrobial

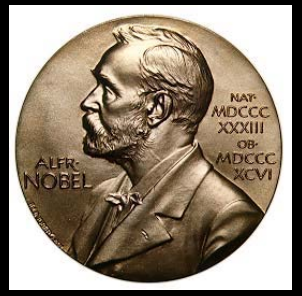
PRIMARY GOAL: DISINFECTION

(*Non-Thermal:* ROS)

# Therapeutic uses of *Light*

Niels Ryberg Finsen

Nobel Prize 1903



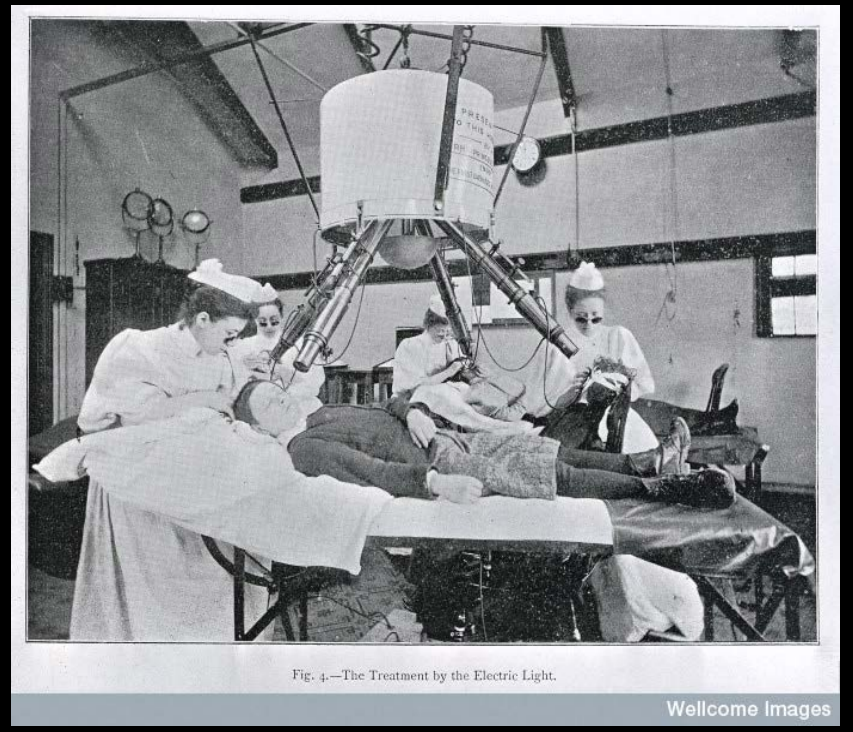



Fig. 4.—The Treatment by the Electric Light.

Wellcome Images


JNCI JOURNAL of the NATIONAL CANCER INSTITUTE

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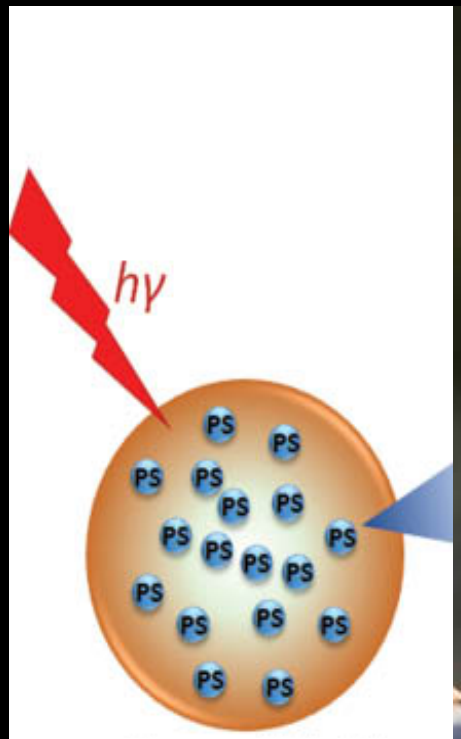
## Activated Dyes as Antitumor Agents

Thomas J. Dougherty Author Notes

*JNCI: Journal of the National Cancer Institute*, Volume 52, Issue 4, April 1974, Pages 1333–1336, https://doi.org/10.1093/jnci/52.4.1333

**Published:** 01 April 1974 **Article history** ▾

# Photodynamic Therapy

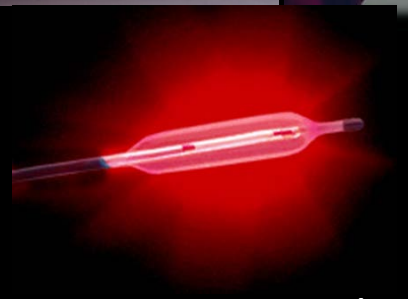



**Hamblin MR et al** Nanotechnology Reviews. 2015, 4, 359–372

# Light Delivery systems


Pinnacle/Diomed 630 PDT

Modulight

bioLitec Ceramoptic

Images courtesy Dr. Thomas Mang, UB

# Photosensitizers for PDT

## Natural

Hematoporphyrin (Heme)
Chlorines (Chorophyll)
Porphycenes (Porphyrins)

## Synthetic

- Chlorin E6 (Red 660 nm)
- Indocyaninegreen liposomal (Infrared 810 nm)
- Hypericin (Yellow 589 nm)
- Curcumin (Blue 447 nm)
- Riboflavin (Blue 447 nm)

# Systematic review and meta-analysis on the nonsurgical treatment of chronic periodontitis by means of scaling and root planing with or without adjuncts

Christopher J. Smiley, DDS; Sharon L. Tracy, PhD; Elliot Abt, DDS, MSc, MS; Bryan S. Michalowicz, DDS; Mike T. John, Dr med dent, PhD, MPH; John Gunsolley, DDS, MS; Charles M. Cobb, DDS, PhD; Jeffrey Rossmann, DDS, MS; Stephen K. Harrel, DDS; Jane L. Forrest, EdD; Philippe P. Hujoel, DDS, MSD, MS, PhD; Kirk W. Noraian, DDS, MS, MBA; Henry Greenwell, DMD, MSD; Julie Frantsve-Hawley, PhD; Cameron Estrich, MPH; Nicholas Hanson, MPH

JADA 2015:146(7):508-524

**Evidence profile summary: scaling and root planing with adjuncts versus scaling and root planing alone.**

| THERAPY | LEVEL OF CERTAINTY ASSESSMENT CRITERIA | | | | | | | LEVEL OF CERTAINTY | BENEFIT,‡ MILLIMETERS |
|---|---|---|---|---|---|---|---|---|---|
| | Quantity of Evidence | | Risk of Bias | Consistency | Applicability† | Precision | Publication Bias | | |
| | No. of RCTs* | No. of participants | | | | | | | |
| SRP and Diode Laser (PDT§) | 10 | 306 | Low | Inconsistent | Yes | Serious imprecision | None detected ($P = 0.679$)¶ | Moderate | 0.53 (0.06-1.00) |
| SRP and Diode Laser (non-PDT) | 4 | 98 | Unclear | Substantial inconsistency | Yes | Serious imprecision | Too few studies to assess | Low | 0.21 (−0.23 to 0.64) |
| SRP and Nd:YAG** Laser | 3 | 82 | Unclear | Moderate inconsistency | Yes | Serious imprecision | Too few studies to assess | Low | 0.41 (−0.12 to 0.94) |
| SRP and Erbium Laser | 3 | 82 | Low | Inconsistent | Yes | Serious imprecision | Too few studies to assess | Low | 0.18 (−0.63 to 0.98) |

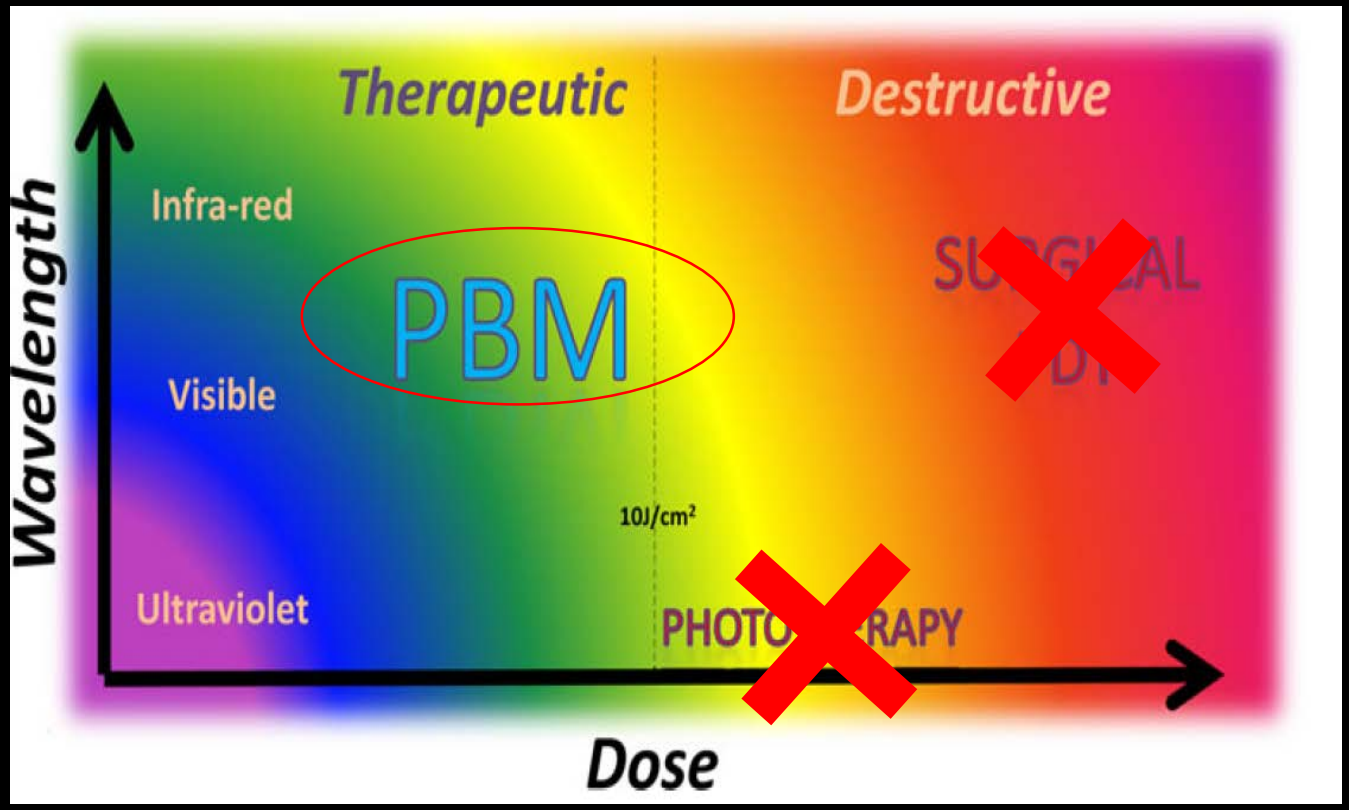
# Non-Surgical Lasers

## Photobiomodulation Therapy

PRIMARY GOALS:
Inhibition (Pain or Inflammation) or Stimulation (Healing / Regeneration)
(*Non-Thermal:* ROS)

# Photo ‘Helio’ Therapy

- **Photodynamic therapy** (PDT) – Dye/chromophore + light
- Psoralen UV-A  (PUVA) for Psoriasis
- NB UV-B Rx: Neonatal jaundice, Vitligo, Eczema, Atopic Dermatitis, Cutaneous T Cell Leukemia, Lichen Planus,
- Psychosomatic – Seasonal and non-seasonal disorders, depression, circadian rhythm sleep disorder.




Arany PR **Photmed Las Surg** 2012, 30, 9, 1

# Differences between PDT and PBM

| | Photobiomodulation (PBM) Therapy | Photodynamic Therapy (PDT) |
|---|---|---|
| ***Common*** | ☞ Low-dose light treatments<br>☞ Non-thermal effects<br>☞ Therapeutic benefits | |
| ***Differences*** | | |
| | Endogenous | Endogenous and Exogenous |
| | Low | Higher |
| | Modulation (Stimulation / Inhibition) | Destruction |

# NAALT-WALT Nomenclature workshop 2014

## Arlington, VA

# Applications of Photobiomodulation Therapy

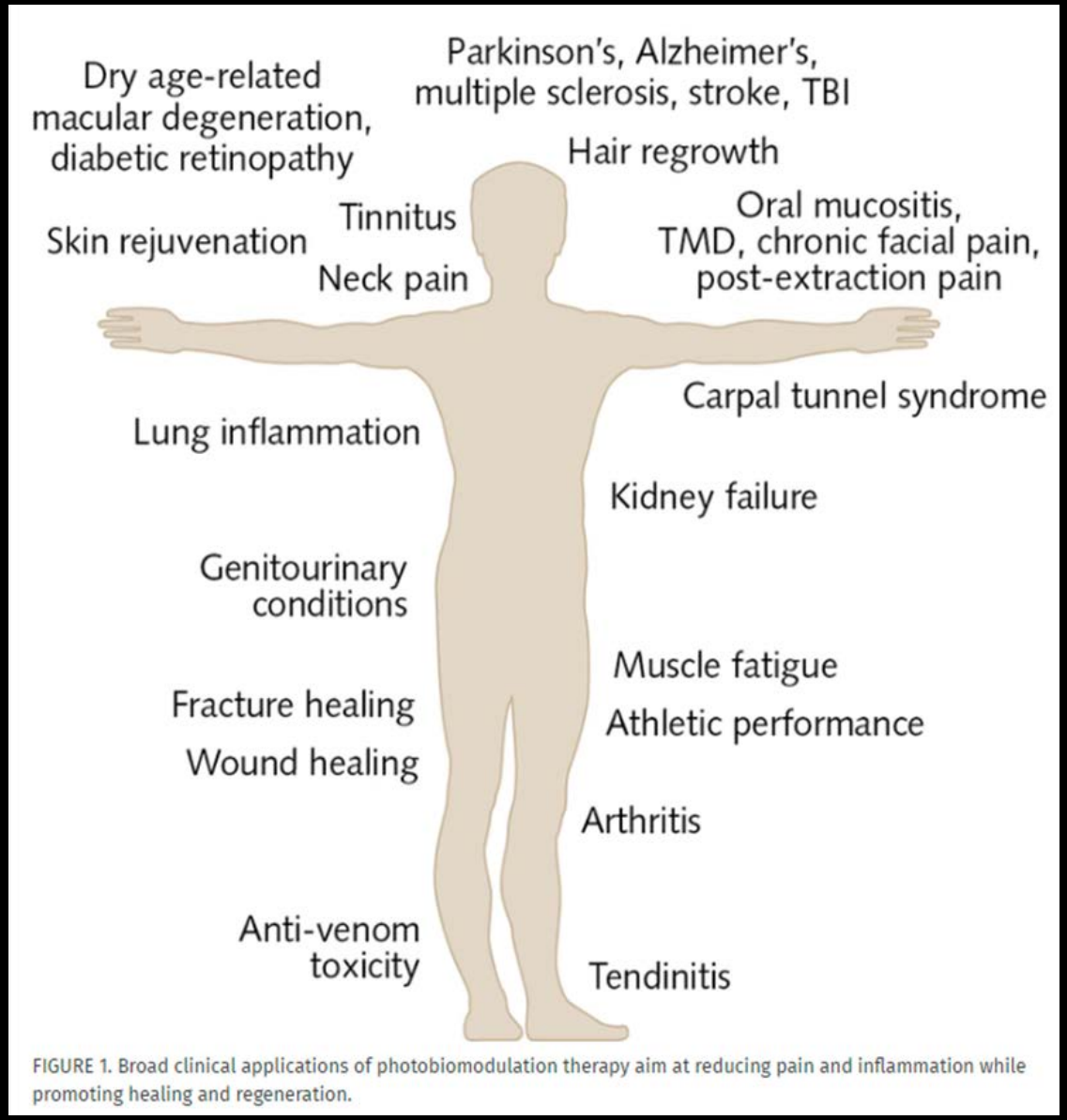



FIGURE 1. Broad clinical applications of photobiomodulation therapy aim at reducing pain and inflammation while promoting healing and regeneration.

https://www.laserfocusworld.com/lasers-sources/article/14037967/photobiomodulation-therapyeasy-to-do-but-difficult-to-get-right

# Photobiomodulation therapy units



Dental


Ophthalmology

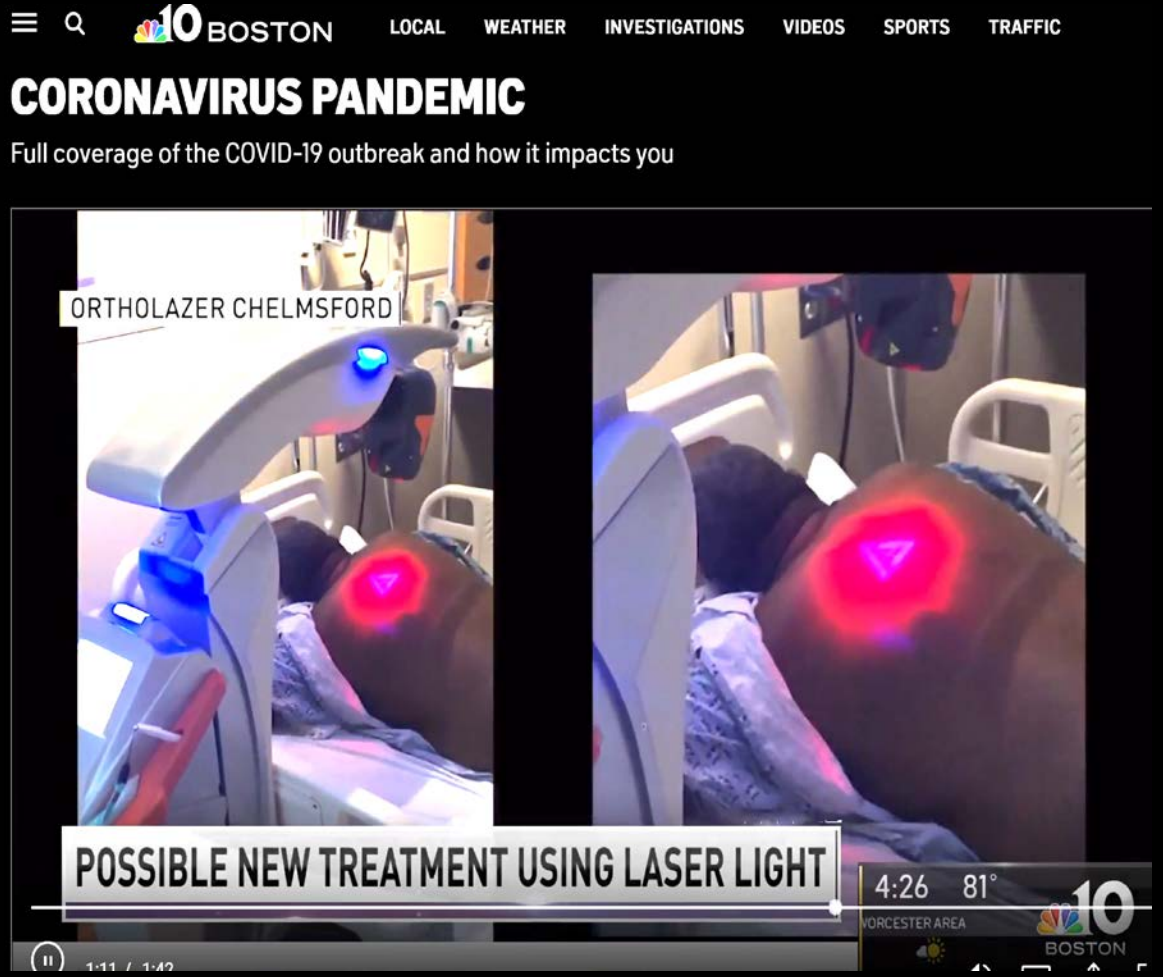

Neurorehabilitation


Whole-body treatments

Is there evidence for this treatment?

# Non-UV / Non-viral targeting Light Therapy!

## Improves host resilience




https://www.nbcboston.com/news/coronavirus/doctor-uses-laser-light-therapy-to-treat-lung-inflammation/2185828/


https://www.nbcchicago.com/top-videos-home/company-says-red-light-treatment-could-be-used-to-fight-coronavirus/2266443/

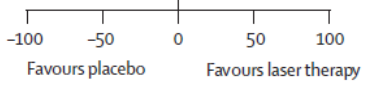
# PBM and Neck Pain

## Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials

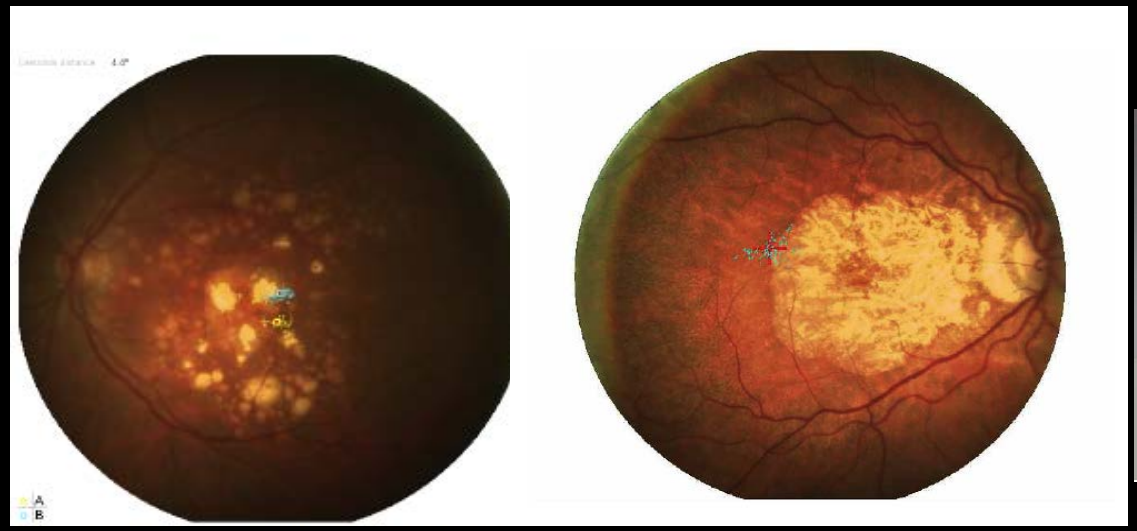
Roberta T Chow, Mark I Johnson, Rodrigo A B Lopes-Martins, Jan M Bjordal

Lancet 2009; 374: 1897–908

| | N | Laser therapy mean (SD) | N | Placebo mean (SD) | WMD (95% CI) | Weight (%) | WMD (95% CI) |
|---|---|---|---|---|---|---|---|
| **Method quality 3/5 or above** | | | | | | | |
| Ceccherelli et al (1989)[43] | 13 | 37·20 (27·80) | 14 | −6·30 (16·50) | | 6·76% | 43·50 (26·09 to 60·91) |
| Flöter et al (1990)[45] | 60 | 15·60 (25·50) | 60 | 4·30 (25·50) | | 7·99% | 11·30 (2·18 to 20·42) |
| Laakso et al (1997)[49] (high IR) | 7 | 30·00 (15·00) | 5 | 16·00 (18·00) | | 6·45% | 14·00 (−5·30 to 33·30) |
| Laakso et al (1997)[49] (low IR) | 8 | 21·00 (19·00) | 4 | 16·00 (21·00) | | 5·61% | 5·00 (−19·43 to 29·43) |
| Seidel et al (2002)[51] (30 mW) | 13 | 10·20 (23·40) | 13 | 8·90 (27·80) | | 6·37% | 1·30 (−18·45 to 21·05) |
| Seidel et al (2002)[51] (7 mW) | 12 | 20·90 (18·70) | 13 | 8·90 (27·80) | | 6·59% | 12·00 (−6·45 to 30·45) |
| Özdemir et al (2001)[50] | 30 | 53·00 (18·40) | 30 | 5·00 (14·30) | | 8·09% | 48·00 (39·66 to 56·34) |
| Gur et al (2004)[46] | 30 | 42·80 (32·30) | 30 | 10·80 (36·80) | | 6·74% | 32·00 (14·48 to 49·52) |
| Hakgüder et al (2003)[47] | 30 | 41·30 (22·80) | 30 | 12·10 (22·40) | | 7·69% | 29·20 (17·76 to 40·64) |
| Chow et al (2004)[42] | 10 | 27·00 (19·00) | 10 | 7·00 (15·80) | | 7·10% | 20·00 (4·68 to 35·32) |
| Altan et al (2005)[41] | 23 | 27·20 (6·90) | 25 | 23·20 (5·30) | | 8·49% | 4·00 (0·50 to 7·50) |
| Chow et al (2006)[13] | 45 | 27·00 (21·00) | 45 | −3·00 (21·00) | | 8·05% | 30·00 (21·32 to 38·68) |
| Dundar et al (2006)[44] | 32 | 9·00 (31·40) | 32 | 10·00 (31·80) | | 7·08% | −1·00 (−16·48 to 14·48) |
| **Subtotal** | **313** | | **311** | | | **93·00%** | **19·65 (9·27 to 30·03)** |
| Test for heterogeneity: $\chi^2$=136·76, df=12 (p<0·00001), $I^2$=91·2% | | | | | | | |
| Test for overall effect: Z=3·71 (p=0·0002) | | | | | | | |
| **Methodological quality below 3** | | | | | | | |
| Ilbuldu et al (2004)[48] | 20 | 43·50 (24·00) | 20 | 21·00 (27·40) | | 7·00% | 22·50 (6·54 to 38·46) |
| **Subtotal** | **20** | | **20** | | | **7·00%** | **22·50 (6·54 to 38·46)** |
| Test for overall effect: Z=2·76 (p=006) | | | | | | | |
| **Total** | **333** | | **331** | | | **100·00%** | **19·86 (10·04 to 29·68)** |
| Test for heterogeneity: $\chi^2$=137·76, df=13 (p<0·0001), $I^2$=90·6% | | | | | | | |
| Test for overall effect: Z=3·96 (p<0·0001) | | | | | | | |



# PBM for Dry Age-Related Macular Degeneration

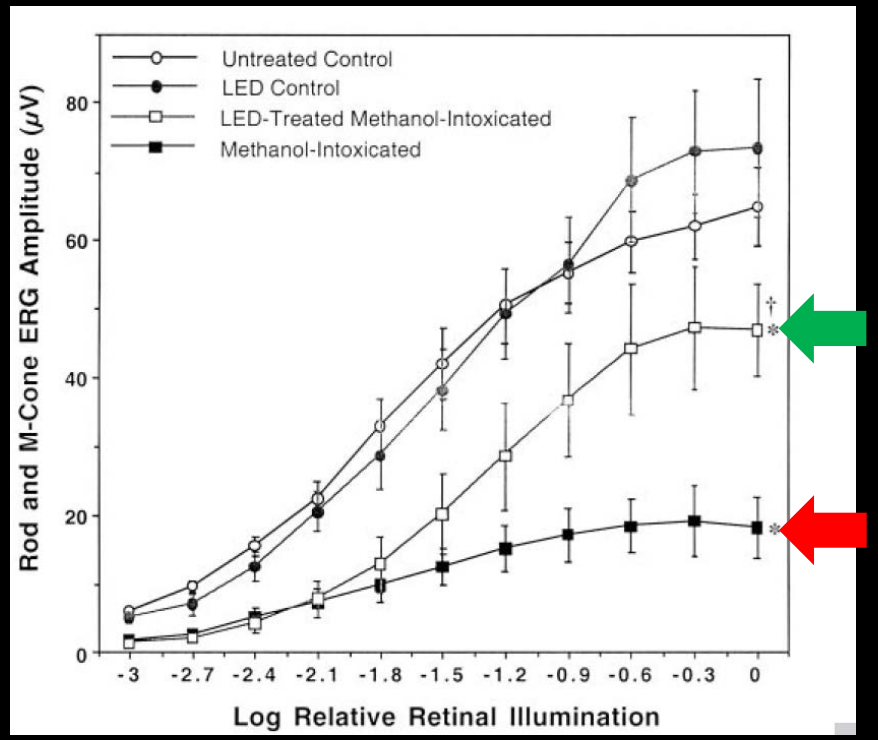


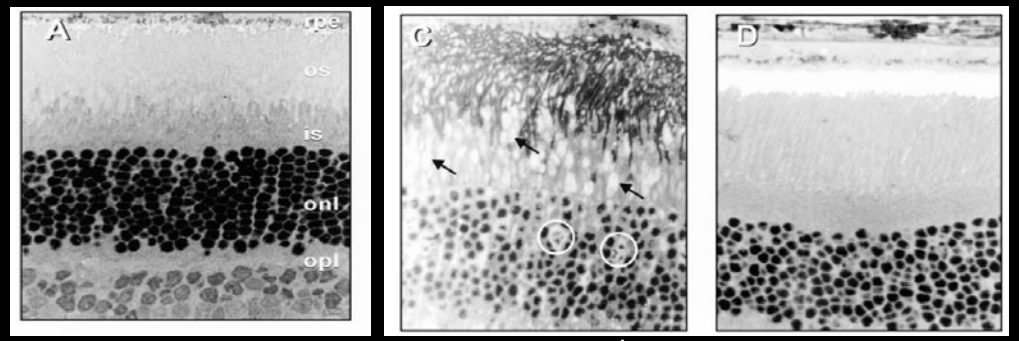

## Treatment of dry Age-related Macular Degeneration with Photobiomodulation

Graham Merry MBBS, LMCC[1], Robert Devenyi MD, MBA, FRCSC, FACS, DABO[2], Robert Dotson MD, FAAO[3], Samuel N. Markowitz, MD, FRCSC[4], Sophia V. Reyes, MD[4],

Presented at ARVO, Fort Lauderdale, May 7, 2012

# PBM in Methanol Toxicity



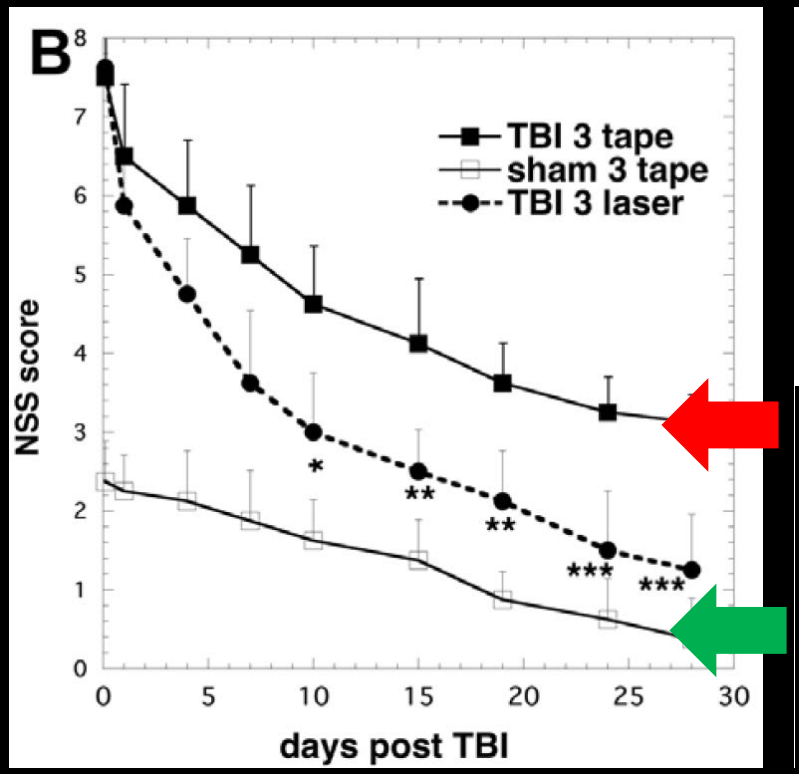



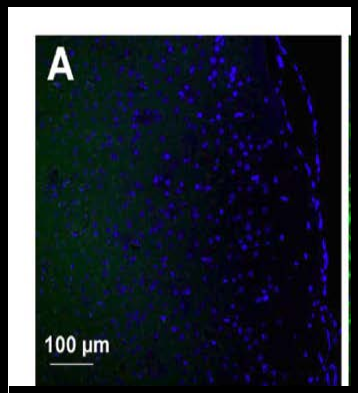

Normal Untreated PBM

Methanol-Toxicity

Eells J et al PNAS 2003, 100, 6, 3439

# PBM in Traumatic Brain Injury



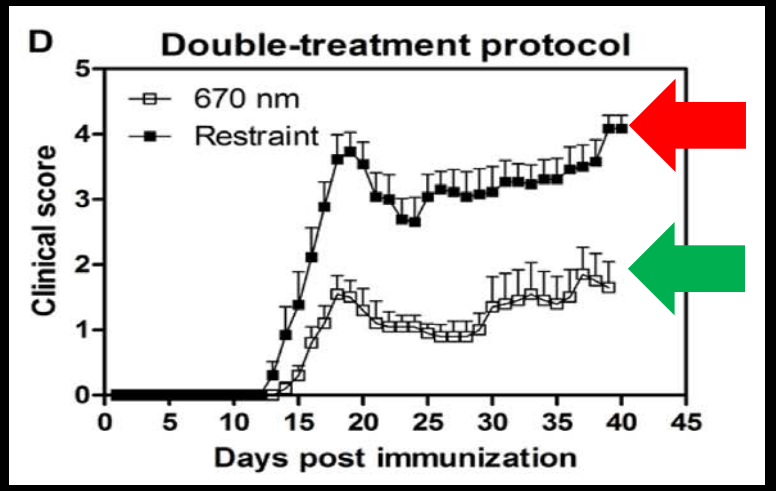

OPEN ACCESS Freely available online

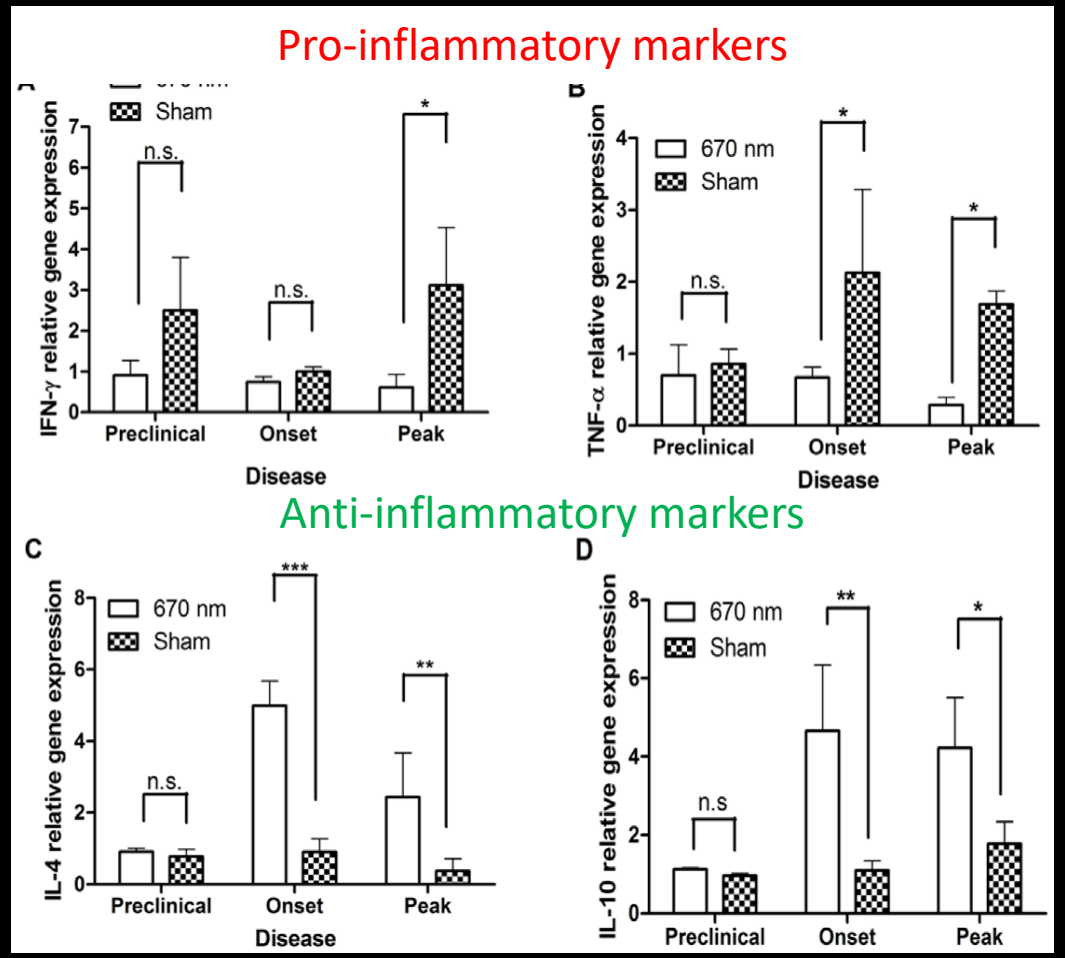
PLoS one

## Comparison of Therapeutic Effects between Pulsed and Continuous Wave 810-nm Wavelength Laser Irradiation for Traumatic Brain Injury in Mice

Takahiro Ando[1,2], Weijun Xuan[1,3,4], Tao Xu[1,3,5], Tianhong Dai[1,3], Sulbha K. Sharma[1], Gitika B. Kharkwal[1,3], Ying-Ying Huang[1,3,6], Qiuhe Wu[1,3,7], Michael J. Whalen[8], Shunichi Sato[9], Minoru Obara[2], Michael R. Hamblin[1,3,10]*

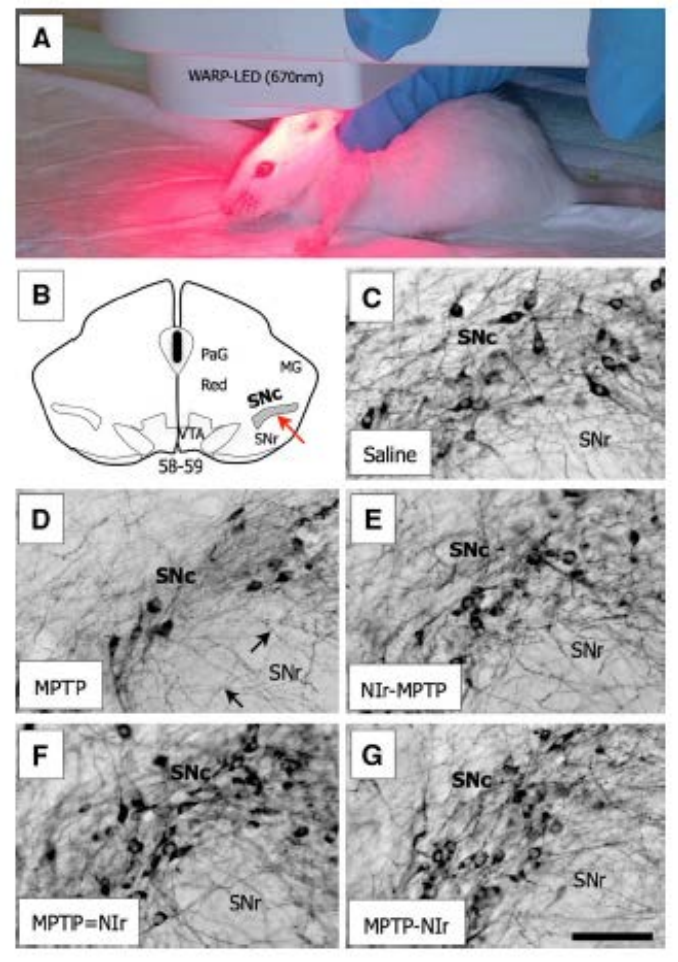
# PBM in Multiple Sclerosis (EAE)

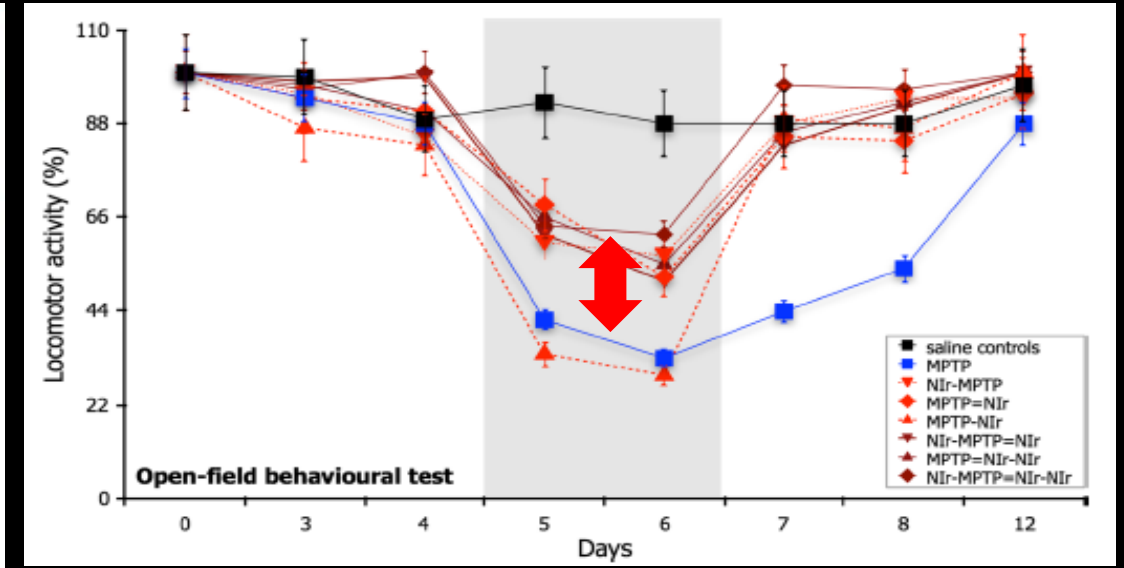



Muili K et al PLoS One 2012, 7, 1, e30655

# PBM in Parkinsons Disease



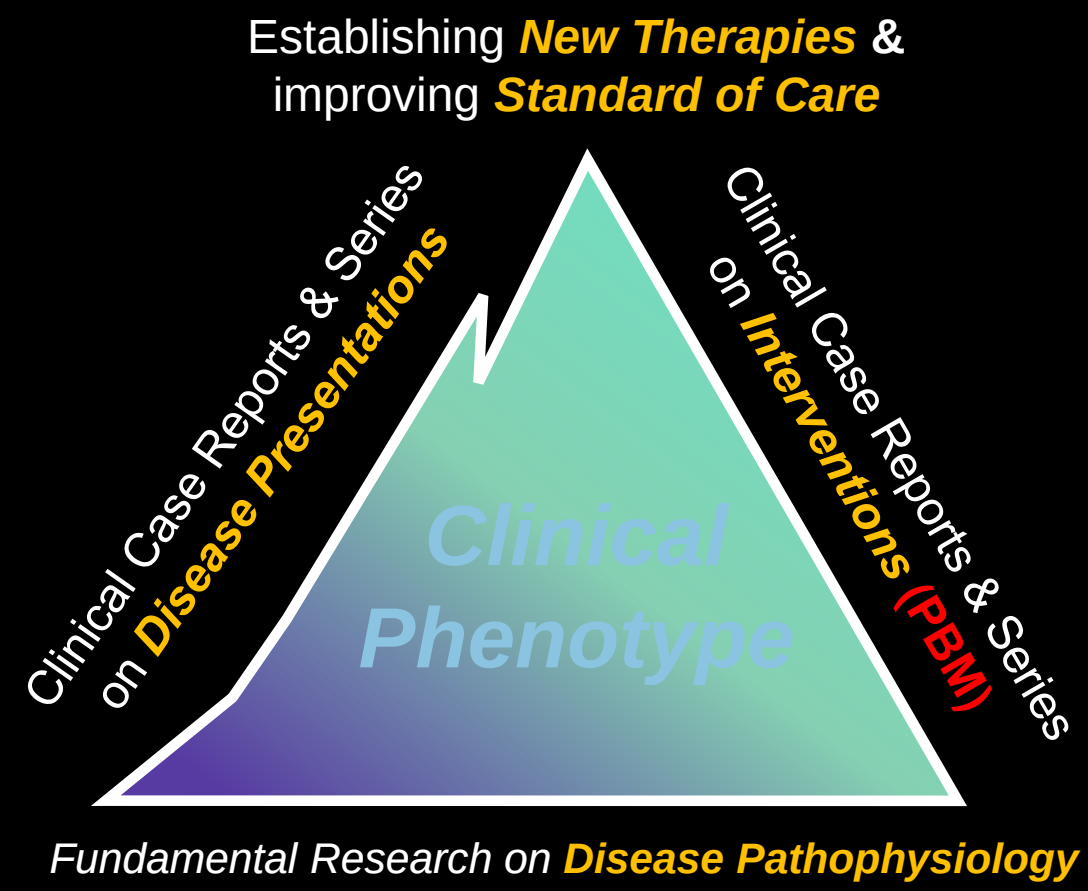

Exp Brain Res
DOI 10.1007/s00221-016-4578-8

RESEARCH ARTICLE

## Near-infrared light (670 nm) reduces MPTP-induced parkinsonism within a broad therapeutic time window

Florian Reinhart[1] · Nabil El Massri[2] · Daniel M. Johnstone[3] · Jonathan Stone[3] · John Mitrofanis[2] · Alim-Louis Benabid[1] · Cécile Moro[1]

# Clinical Translation of PBM…




Email: prarany@buffalo.edu

Rahman S et *al* **Oral Dis** 2018, 24, 1, 261

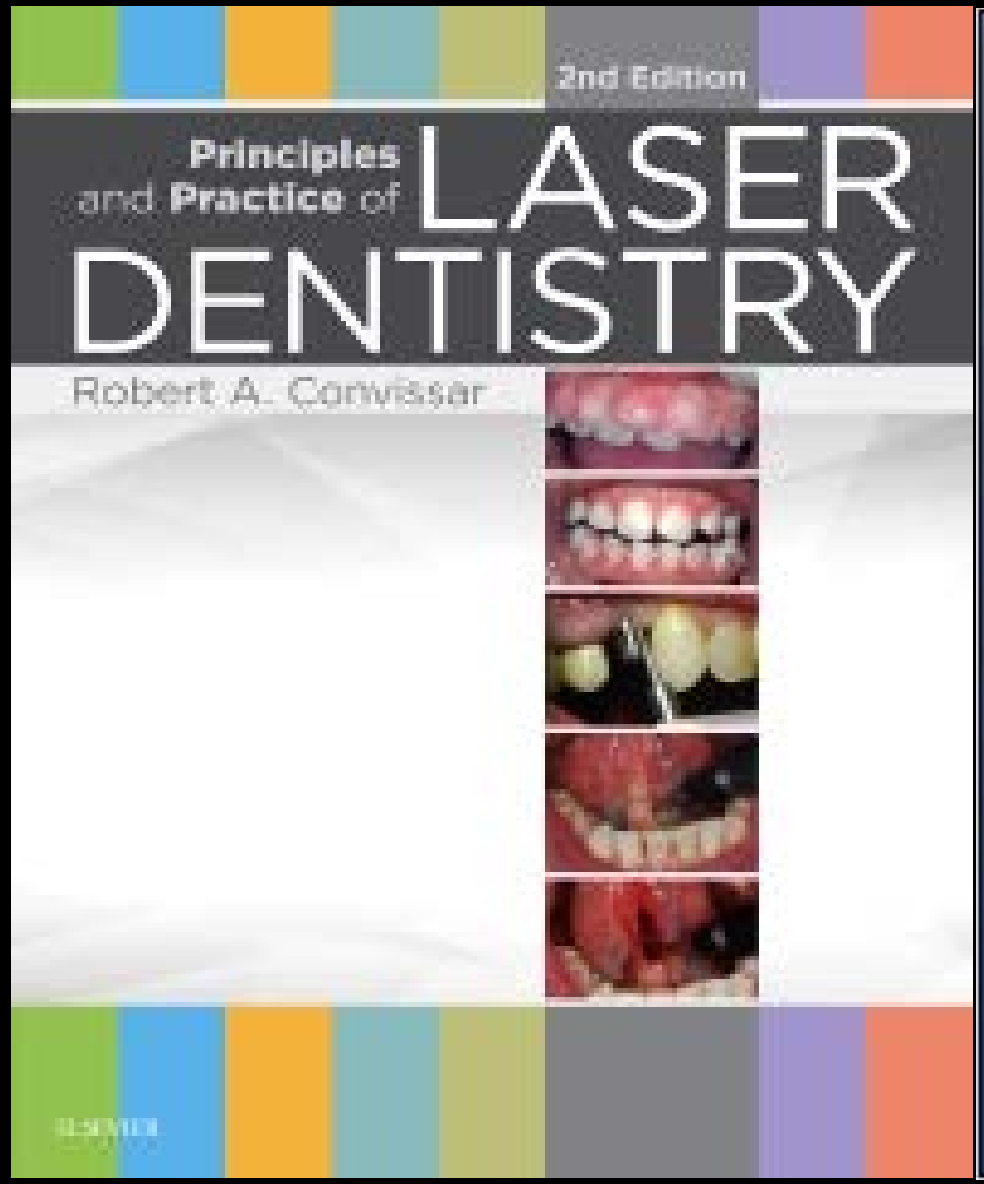
| Oral specialty | Application | LLLT effect |
|---|---|---|
| Endodontics | Dentinal hypersensitivity | Reduced tactile and thermal sensitivity |
| | Pulp | Improved dentin formation in the dental pulp |
| | | Promotion of HDP cell mineralization |
| Maxillofacial | Bisphosphonate related osteonecrosis of the jaw | Reduced pain, reduced edema, pus and fistulas, improved healing |
| | Mandibular distraction | Improved bone trabeculation and ossification |
| | Mandibular advancement | Improved bone formation in condylar region |
| | | Improved osteogenesis |
| | Temporo-mandibular joint disorder | Reduced pain |
| | | Improved range of mandibular movement |
| | Trauma to the mandibular | Improved bone healing |
| Oral pathology | Burning mouth syndrome | Reduced symptoms, reduced pain |
| | HSV | Improved healing and reduced reoccurrence |
| | Lichen planus | Reduced lesion size, less pain |
| | | As effective as corticosteroids |
| | Oral mucositis | Reduced incidence, duration and severity |
| | Xerostomia/dryness | Regeneration of salivary duct epithelial cells |
| | | Improved salivary flow, improved antimicrobial characteristics |
| Oral surgery | Healing | Improved healing after gingivectomy, reduced gingival Inflammation |
| | Paresthesia/alveolar nerve | Improved mechanical sensory perception |
| | Third molar extraction | Reduced pain, reduced swelling, improved trismus |
| Orthodontics | Orthodontic pain | Reduced pain |
| | | Faster remodeling |
| | Titanium implants | Improved healing |
| | | Improved attachment |
| | | Improved osseointegration |
| | Tooth movement | Accelerated tooth movement |
| | | Improved osteoblast/osteoclast activity |
| | | Improved collagen deposition |
| Pediatric | Cavity preparation | Reduced pain |
| | Mandibular distraction | Faster healing |
| | Gingivitis | |
| Periodontics | Chronic gingivitis | Reduced inflammation |
| | | Improved healing |
| | Periodontal ligament | Increased early hyalinization |
| | Periodontitis | Improved pocket depth |
| | | Less inflammation |
| Prosthodontics | Denture stomatitis | Reduced yeast colonies |
| | | Reduced palatal inflammation |
| | Implants | Faster bone formation |
| | | Improved bone–implant interface strength |
| | | Improved osseointegration |

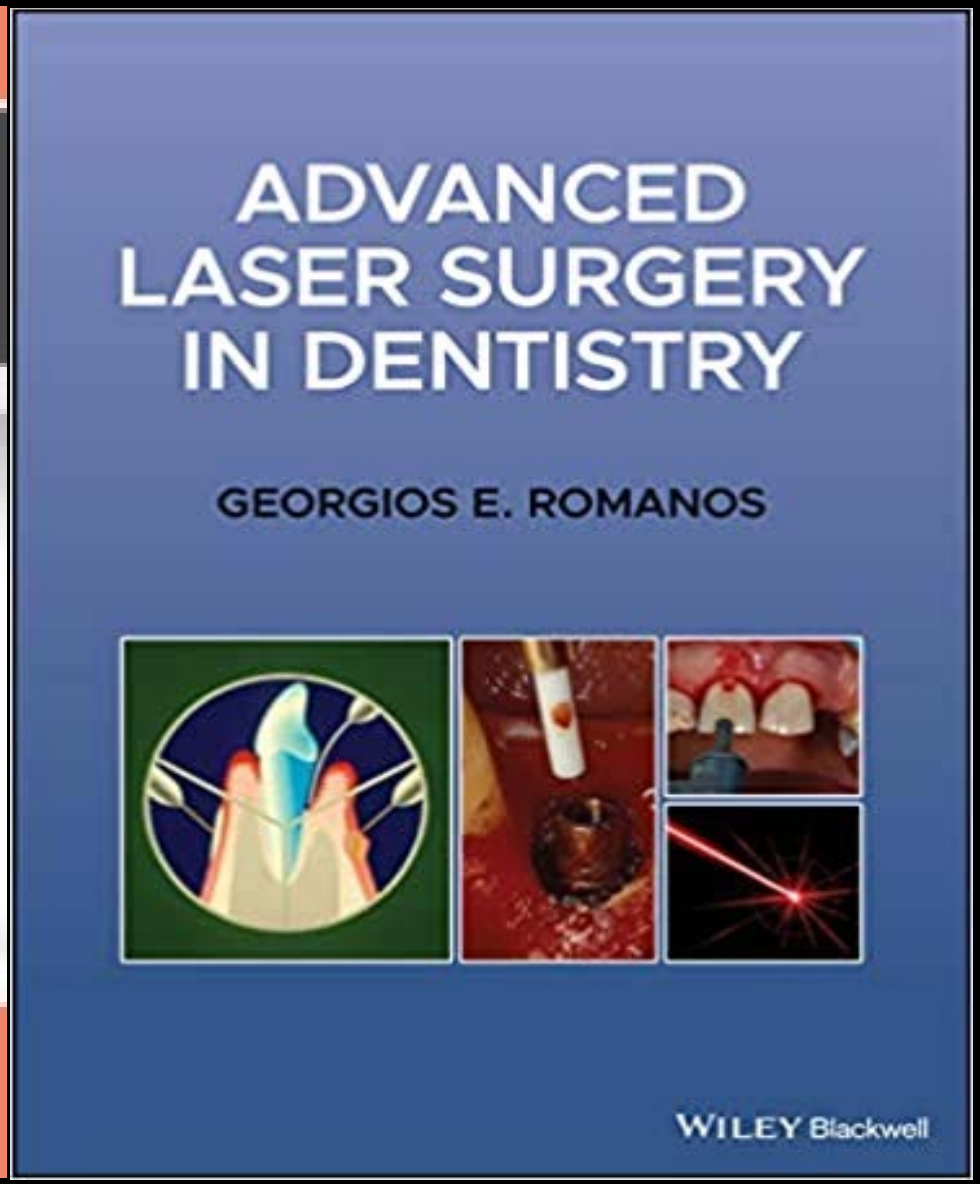
Orthopulse

*Biolux*

LANAP/LAPIP/LAR

*Millennium*


2nd Edition
Principles and Practice of LASER DENTISTRY
Robert A. Convissar
ELSEVIER

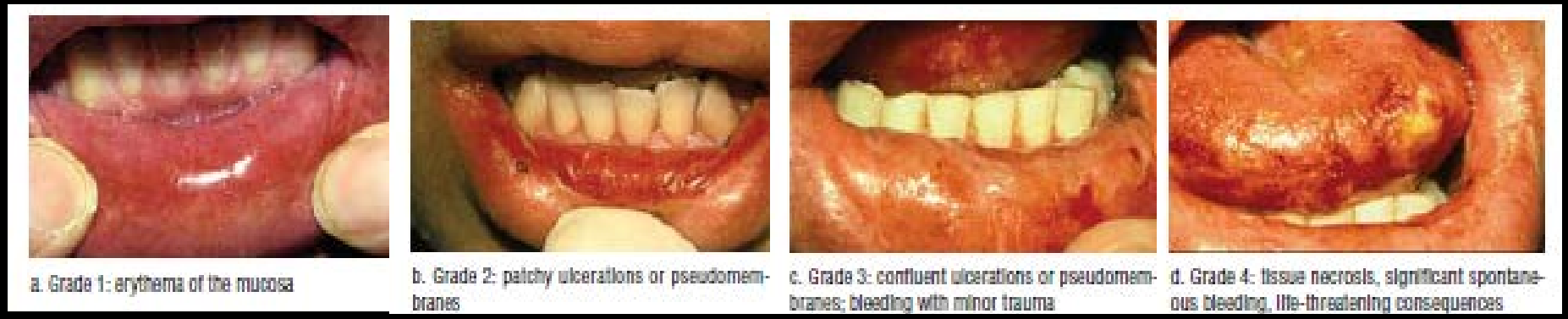

ADVANCED LASER SURGERY IN DENTISTRY
GEORGIOS E. ROMANOS
WILEY Blackwell

# PBM for Oral Mucositis

# Clinical Need: *Oral Mucositis*

- Seen in Post-chemo (5-40% with 5FU, Methotrexate, Doxorubicin)
  Post-radiation (80% Head & Neck)
  Post-BMT (60-80%)
- Causes significant morbidity (difficulty eating, swallowing, nutrition) & extreme cases could delay oncotherapy (mortality)

Pain | Inflammation | Immune | Wound Healing



a. Grade 1: erythema of the mucosa

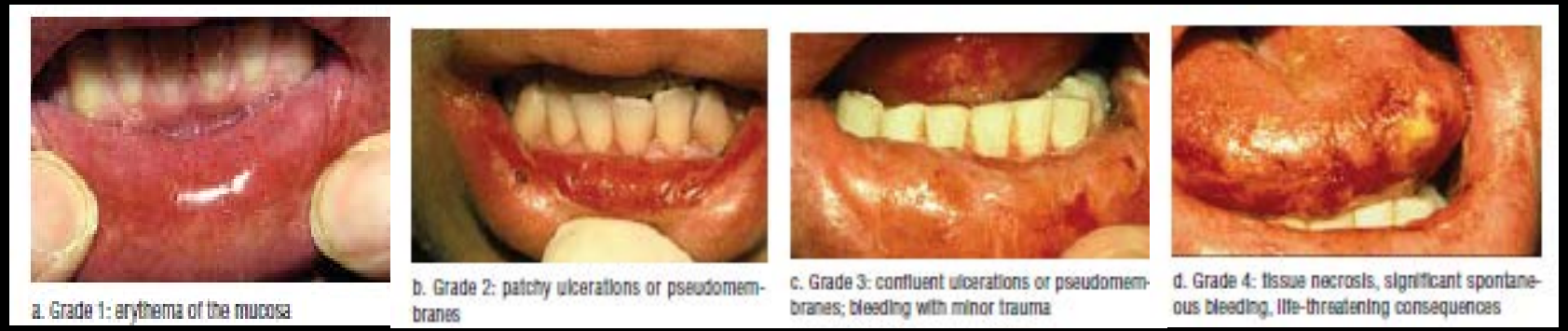
b. Grade 2: patchy ulcerations or pseudomembranes

c. Grade 3: confluent ulcerations or pseudomembranes; bleeding with minor trauma

d. Grade 4: tissue necrosis, significant spontaneous bleeding, life-threatening consequences

Cawley & Bensen **Clin J Onco Nur** 2005, 9, 5, 584

# PBM is now recommended as *Standard of Care* for Oral Mucositis



a. Grade 1: erythema of the mucosa

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c. Grade 3: confluent ulcerations or pseudomembranes; bleeding with minor trauma

d. Grade 4: tissue necrosis, significant spontaneous bleeding, life-threatening consequences

Cawley & Bensen **Clin J Onco Nur** 2005, 9, 5, 584

Supportive Care in Cancer
https://doi.org/10.1007/s00520-019-04890-2

SPECIAL ARTICLE

Check for updates

## Systematic review of photobiomodulation for the management of oral mucositis in cancer patients and clinical practice guidelines

Yehuda Zadik[1,2] · Praveen R. Arany[3] · Eduardo Rodrigues Fregnani[4] · Paolo Bossi[5] · Hélíton Spindola Antunes[6] · René-Jean Bensadoun[7] · Luiz Alcino Gueiros[8] · Alessandra Majorana[9] · Raj G. Nair[10] · Vinisha Ranna[11] · Wim J. E. Tissing[12] · Anusha Vaddi[13] · Rachel Lubart[14] · Cesar Augusto Migliorati[15] · Rajesh V. Lalla[16] · Karis Kin Fong Cheng[17] · Sharon Elad[13] · On behalf of The Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO)

Received: 31 January 2019 / Accepted: 22 May 2019


**Abstract**

**Purpose** To systematically review the literature and update the evidence-based clinical practice guidelines for the use of photobiomodulation (PBM), such as laser and other light therapies, for the prevention and/or treatment of oral mucositis (OM).

**Methods** A systematic review was conducted by the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society for Oral Oncology (MASCC/ISOO) using PubMed and Web of Science. We followed the MASCC methods for systematic review and guidelines development. The rigorously evaluated evidence for each intervention, in each cancer treatment setting, was assigned a level-of-evidence (LoE). Based on the LoE, one of the following guidelines was determined: Recommendation, Suggestion, or No Guideline Possible.

**Results** Recommendations are made for the prevention of OM and related pain with PBM therapy in cancer patients treated with one of the following modalities: hematopoietic stem cell transplantation, head and neck (H&N) radiotherapy (without chemotherapy), and H&N radiotherapy with chemotherapy. For each of these modalities, we recommend 1–2 clinically effective protocols; the clinician should adhere to all parameters of the protocol selected. Due to inadequate evidence, currently, No Guideline Possible for treatment of established OM or for management of chemotherapy-related OM. The reported clinical settings were extremely variable, limiting data integration.

**Conclusions** The evidence supports the use of specific settings of PBM therapy for the prevention of OM in specific patient populations. Under these circumstances, PBM is recommended for the prevention of OM. The guidelines are subject to continuous update based on new published data.

Zadik et *al.* Supp Car Ca 2019, 24, 6, 2793

Supportive Care in Cancer
https://doi.org/10.1007/s00520-020-05803-4

ORIGINAL ARTICLE

Check for updates

## MASCC/ISOO clinical practice guidelines for the management of mucositis: sub-analysis of current interventions for the management of oral mucositis in pediatric cancer patients

Wanessa Miranda-Silva[1] · Wagner Gomes-Silva[2,3] · Yehuda Zadik[4,5] · Noam Yarom[6,7] · Abdul Rahman Al-Azri[8,9] · Catherine H. L. Hong[10] · Anura Ariyawardana[11,12] · Deborah P. Saunders[13] · M. Elvira Correa[14] · Praveen R. Arany[15] · Joanne Bowen[16] · Karis Kin Fong Cheng[17] · Wim J. E. Tissing[18] · Paolo Bossi[19] · Sharon Elad[20] · On behalf of the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer / International Society for Oral Oncology (MASCC/ISOO)

Received: 12 July 2020 / Accepted: 24 September 2020


**Abstract**

**Objective** The aim of this sub-analysis was to highlight the MASCC/ISOO clinical practice guidelines for the management of oral mucositis (OM) in pediatric patients and to present unique considerations in this patient population.

**Methods** This sub-analysis of the pediatric patient population is based on the systematic review conducted by the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISSO) published in 2019/2020. Studies were scored and assigned a level of evidence based on previously published criteria. Data regarding adverse effects and

Miranda-Silva et *al.* Supp Car Ca 2021, 29, 3539

frontiers | Frontiers in Oncology

TYPE Systematic Review
PUBLISHED 30 August 2022
DOI 10.3389/fonc.2022.927685

Check for updates

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SPECIALTY SECTION
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Robijns J, Nair RG, Lodewijckx J, Arany P, Barasch A, Bjordal JM, Bossi P, Chilles A, Corby PM, Epstein JB, Elad S, Fekrazad R, Fregnani ER, Genot M-T, Ibarra AMC, Hamblin MR, Heiskanen V, Hu K, Klastersky J, Lalla R, Latifian S, Maiya A, Mebis J, Migliorati CA, Milstein DMJ, Murphy B, Raber-Durlacher JE, Roseboom HJ, Sonis S, Treister N, Zadik Y, Bensadoun R-J and "Cancer Supportive Care" WALT Working

## Photobiomodulation therapy in management of cancer therapy-induced side effects: WALT position paper 2022

Jolien Robijns[1], Raj G. Nair[2], Joy Lodewijckx[1], Praveen Arany[3], Andrei Barasch[4], Jan M. Bjordal[5], Paolo Bossi[6], Anne Chilles[7], Patricia M. Corby[8], Joel B. Epstein[9], Sharon Elad[10], Reza Fekrazad[11], Eduardo Rodrigues Fregnani[12], Marie-Thérèse Genot[13], Ana M. C. Ibarra[14], Michael R. Hamblin[15], Vladimir Heiskanen[16], Ken Hu[17], Jean Klastersky[18], Rajesh Lalla[19], Sofia Latifian[20], Arun Maiya[21], Jeroen Mebis[1], Cesar A. Migliorati[22], Dan M. J. Milstein[23], Barbara Murphy[24], Judith E. Raber-Durlacher[25], Hendrik J. Roseboom[25], Stephen Sonis[26], Nathaniel Treister[26], Yehuda Zadik[27], René-Jean Bensadoun[28]* and "Cancer Supportive Care" WALT Working Group

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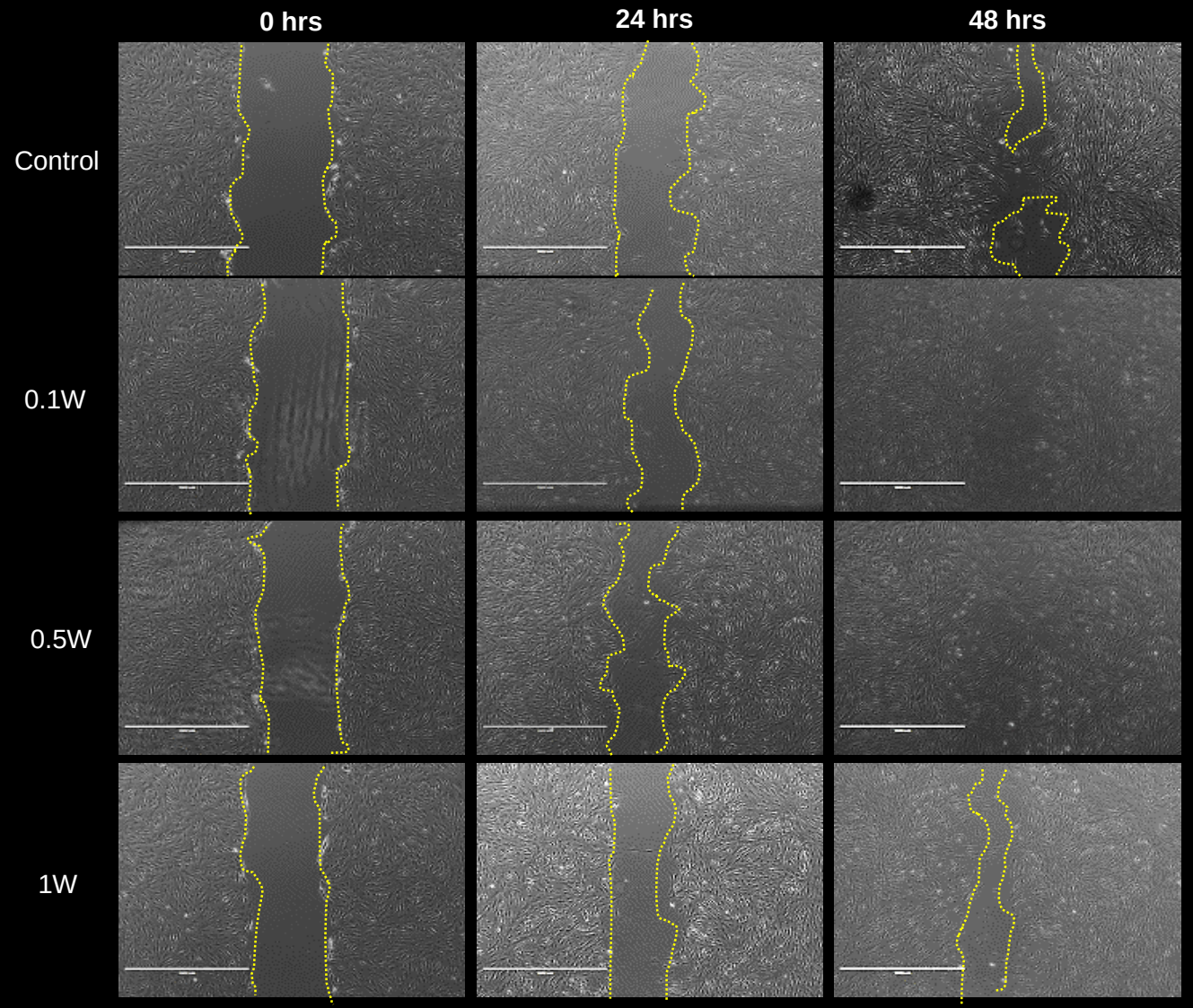
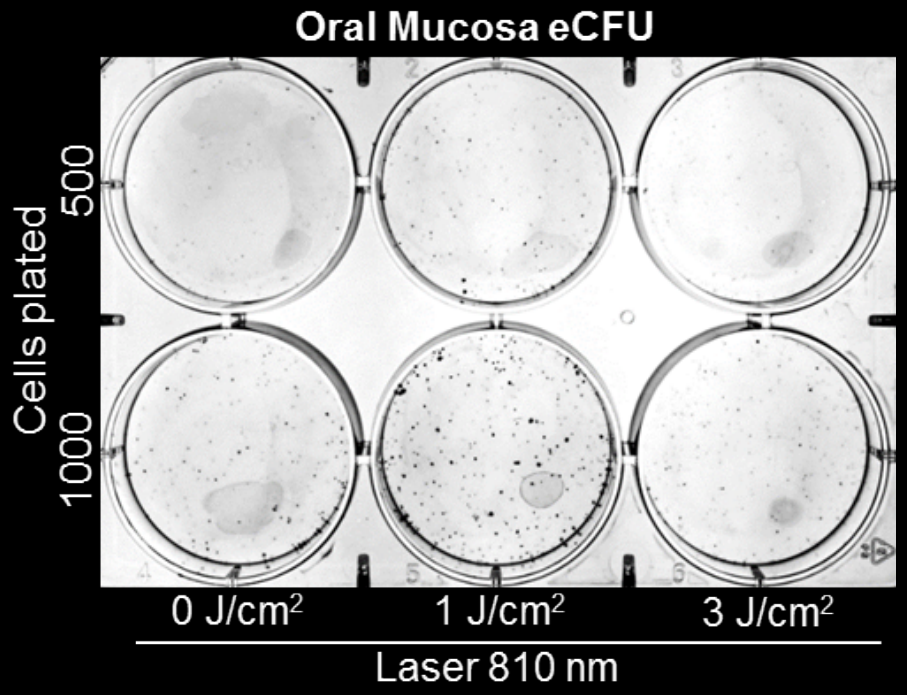
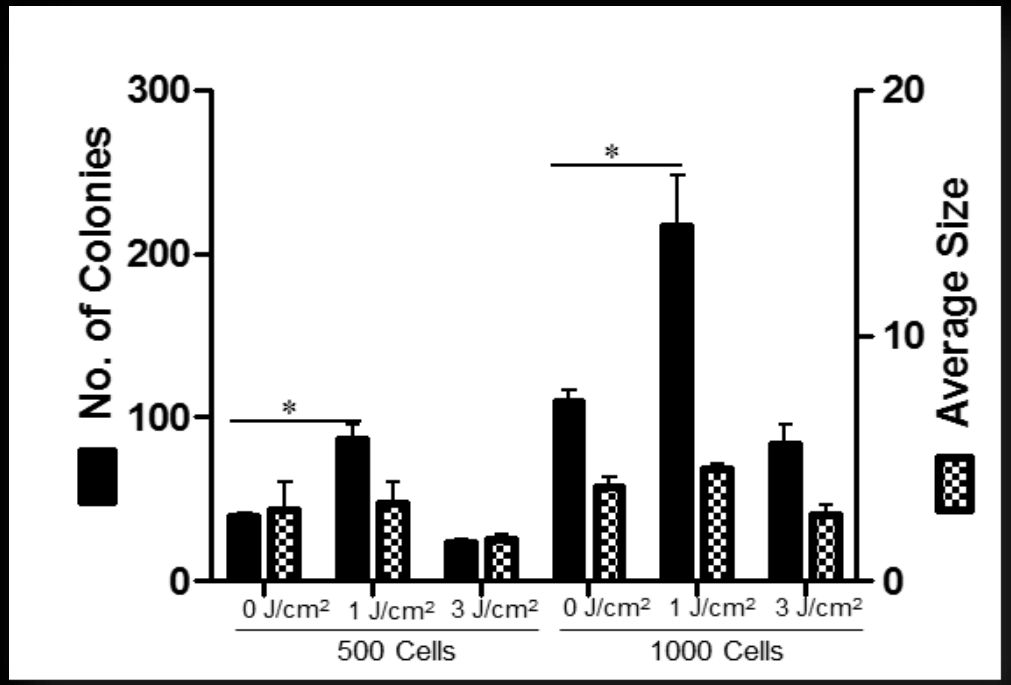
# PBM promotes Keratinocyte migration




Khan et al *in preparation*

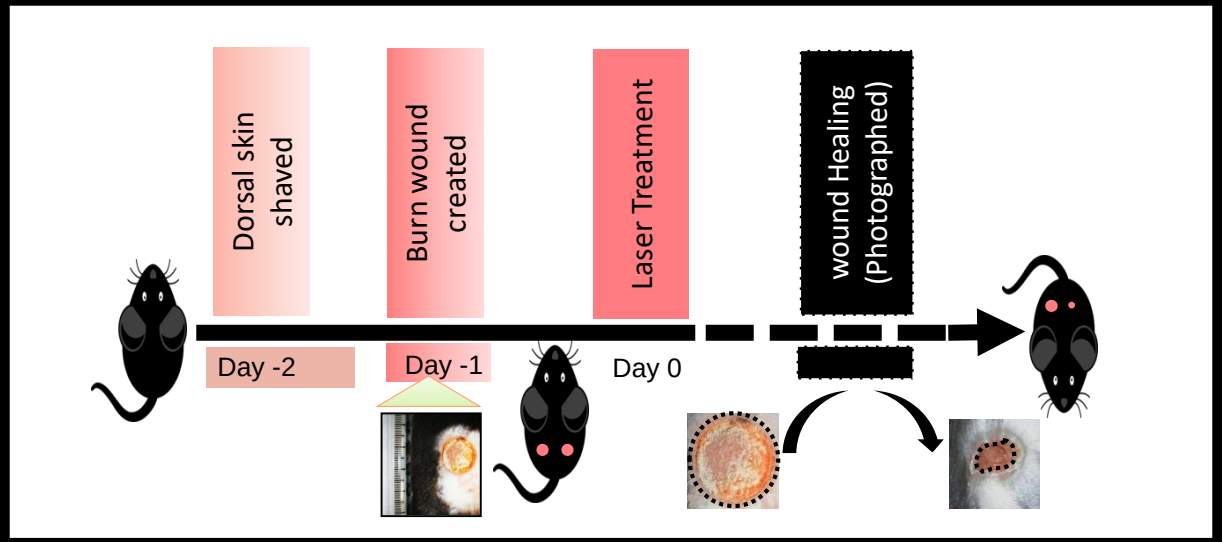
# PBM increases eCFUs

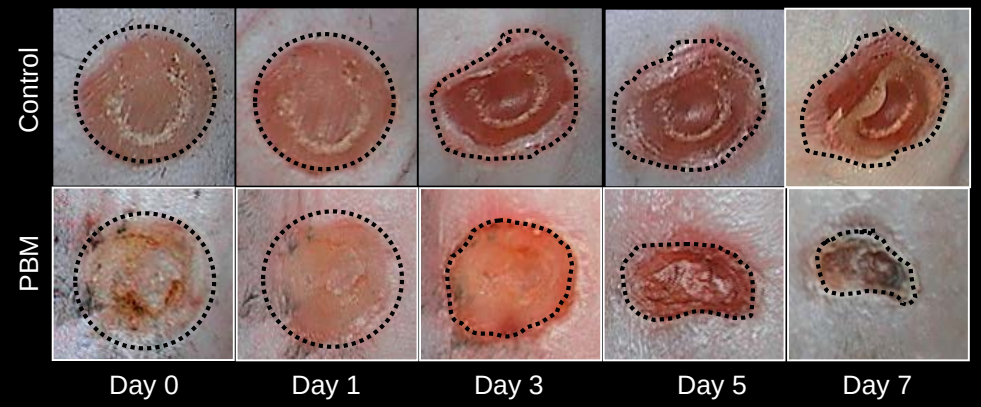


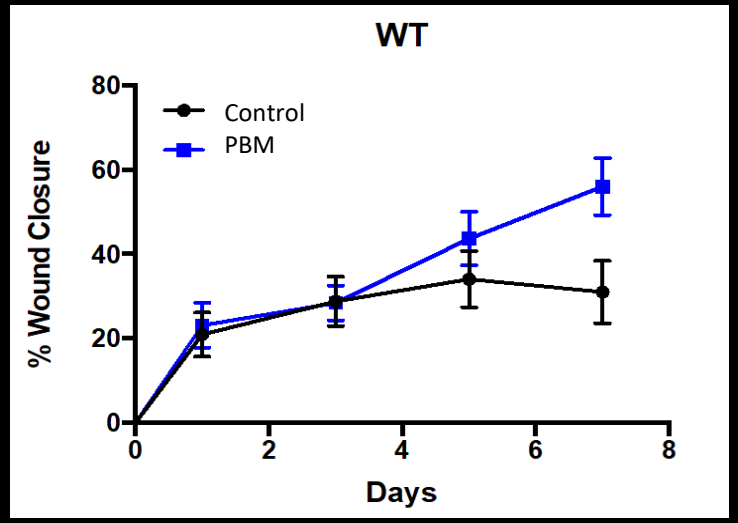




Khan and Arany Photomed Laser Surg 2016

# PBM promotes Burn Wound Healing

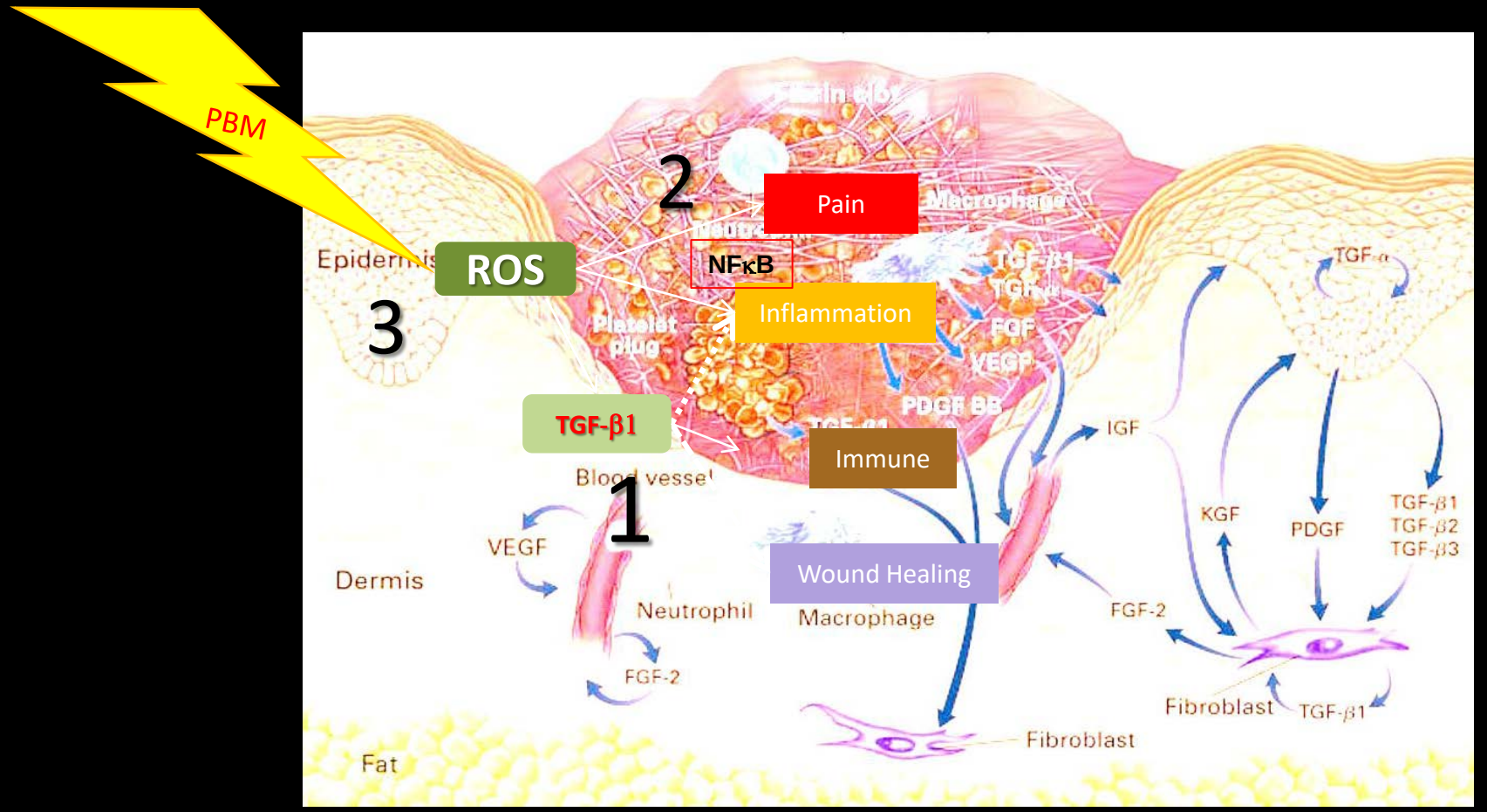



Khan et al *in preparation*

# Rationale: Photobiomodulation in Oral Mucositis




1. Arany *et al* **WRR** 2007 2. Chen*, Arany* *et al* **PLoS One** 2012 3. Arany *et al* **PMLS** 2016

# Photobiomodulation therapy



# Applications of PBM Therapy

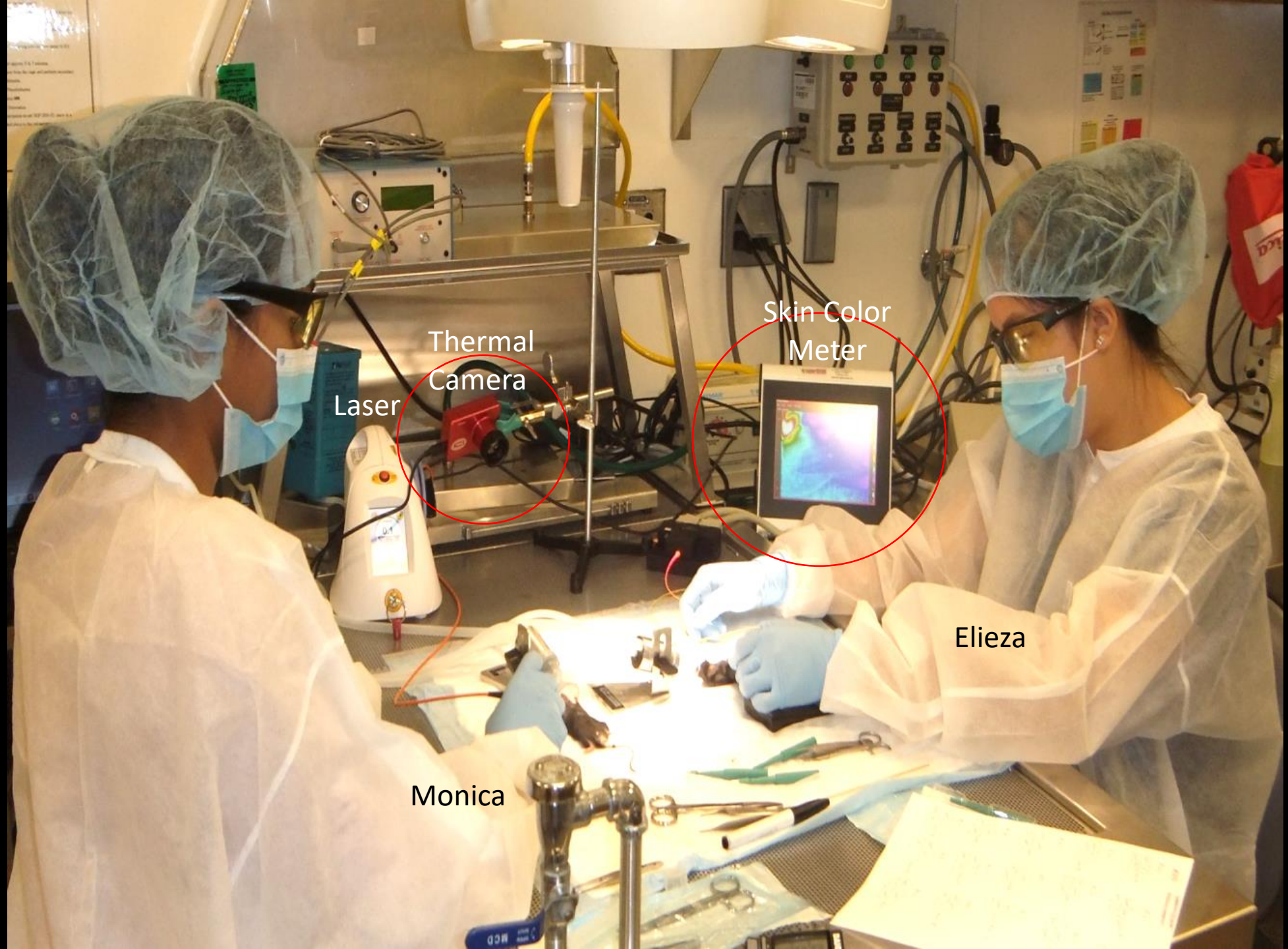
## Low-level laser therapy/photobiomodulation in the management of side effects of chemoradiation therapy in head and neck cancer: part 2: proposed applications and treatment protocols

Judith A. E. M. Zecha[1] · Judith E. Raber-Durlacher[1,2] · Raj G. Nair[3] · Joel B. Epstein[4,5] · Sharon Elad[6] · Michael R. Hamblin[7,8,9] · Andrei Barasch[10] · Cesar A. Migliorati[11] · Dan M. J. Milstein[1] · Marie-Thérèse Genot[12] · Liset Lansaat[13] · Ron van der Brink[5] · Josep Arnabat-Dominguez[15] · Lisette van der Molen[13] · Irene Jacobi[13] · Judi van Diessen[14] · Jan de Lange[1] · Ludi E. Smeele[1,13] · Mark M. Schubert[16] · René-Jean Bensadoun[17]

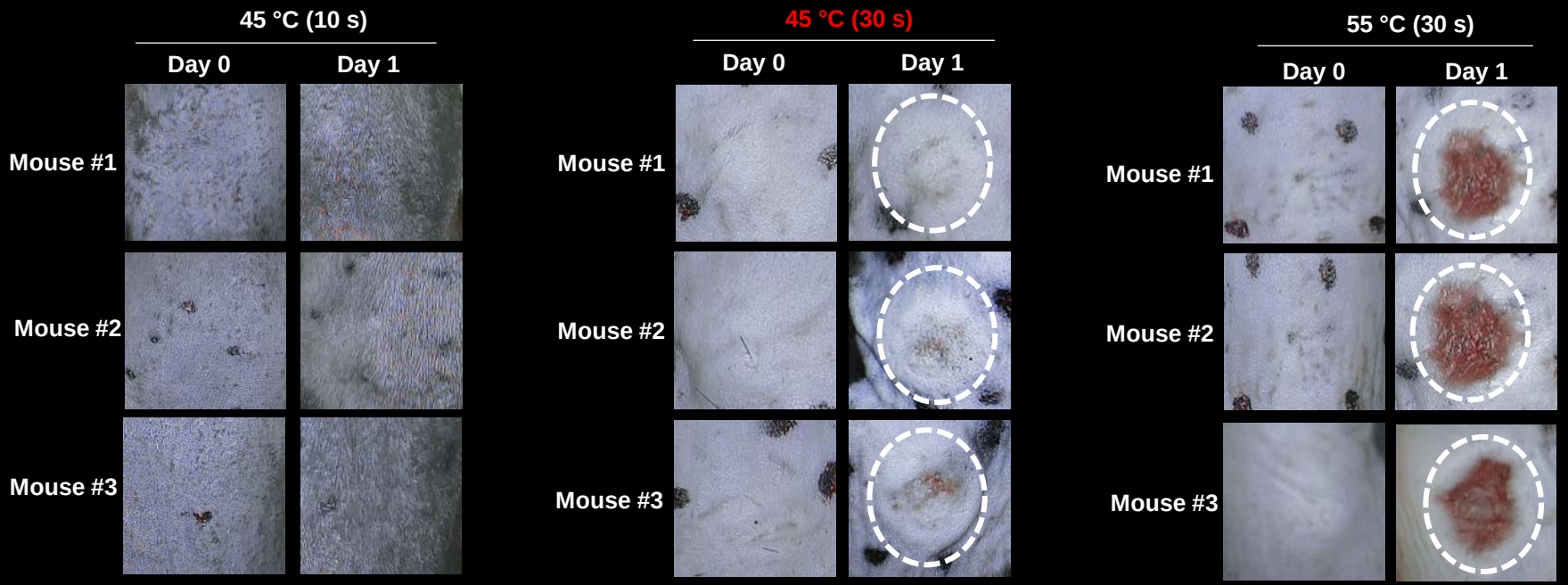
Support Care Cancer 2016
DOI 10.1007/s00520-016-3153-y

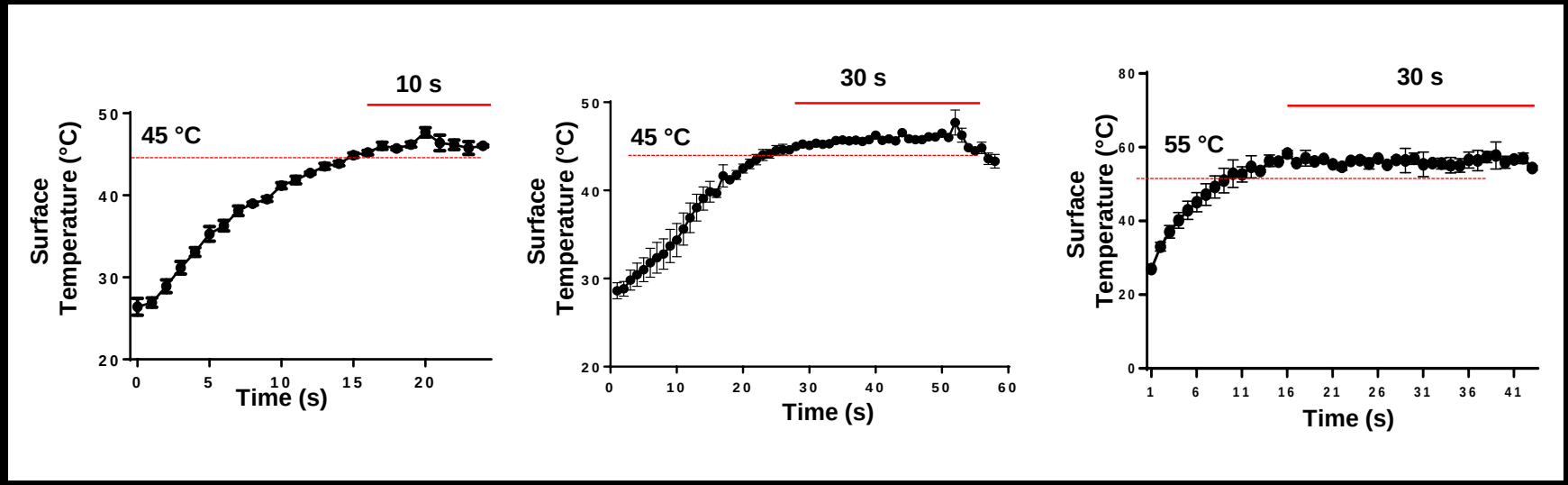
| Complication | Treatment protocol** | Treatment area | PBM Device Characteristics and application | Therapeutic PBM Dose | Optional target tissues |
|---|---|---|---|---|---|
| Oral Mucositis | *Prophylactic*:<br>*Chemotherapy*: Protocols vary. Start PBM treatment at first day of CT or prior to therapy and continue during all courses of chemotherapy<br><br>*Radiotherapy*: start PBM treatment the first day of RT or prior to RT and continue during all days of RT (no requirement regarding the timing of PBM sessions, before of after RT session)<br><br>*Therapeutic*:<br>Continue treatment at least 3 times a week until symptoms improve<br>Daily treatment is recommended in case of severe mucositis |  | *Extra-oral*:<br>Infrared (IR) LED cluster<br>or<br>Mixed Red and IR LED cluster 20mW/cm$^2$ - 80mW/cm$^2$<br><br>*Intra-oral:*<br>630 - 830nm<br>20mW - 80mW | *Extra-oral*:<br>3 J/cm$^2$ IR LED cluster<br><br>*Intra-oral*:<br>*Prophylactic*: 2 J per point<br>*Therapeutic*: 4 J per point until the whole area involved is covered<br>(2 J for prophylactic use) | *Extra-oral*:<br>Lips, cutaneous surface corresponding to the buccal mucosae, bilateral cervical lymphatic chain*<br><br>*Intra-oral*:<br>*Prophylactic*: treat each of the at risk mucosal surfaces *<br>*Therapeutic*: sites vary, depending upon the site of mucositis |

# Cancer risk?


Skin Color
Meter
Thermal
Camera
Laser
Elieza
Monica

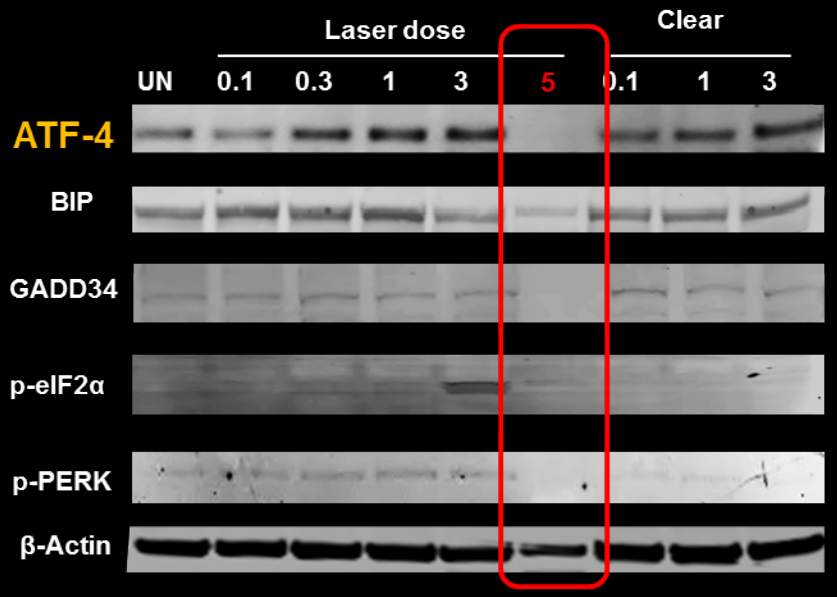
# Dose escalation studies for Laser Phototoxicity

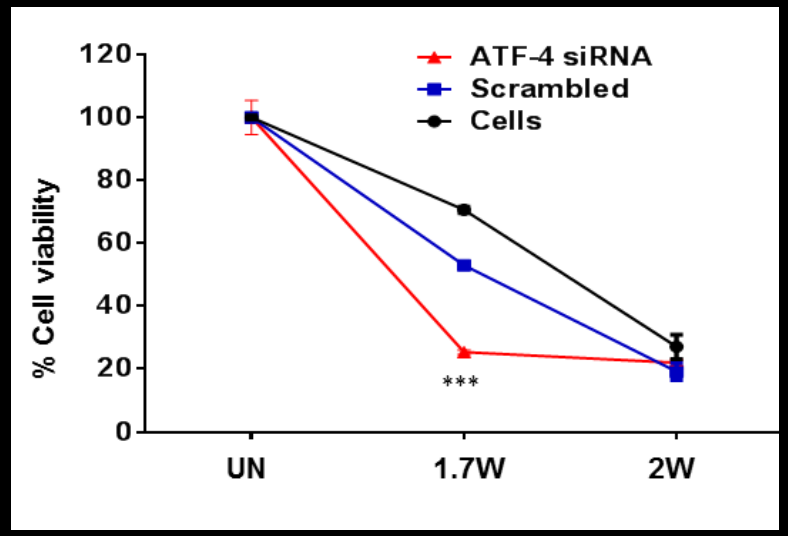


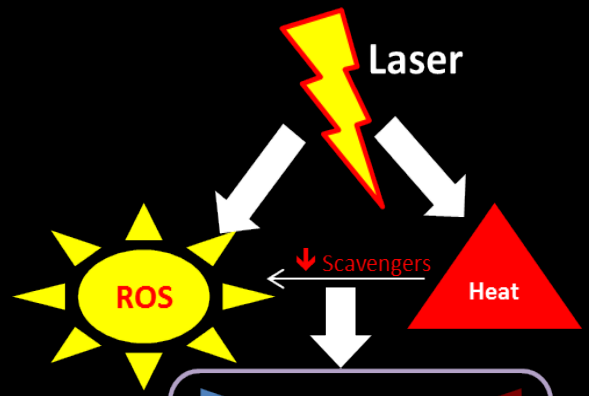



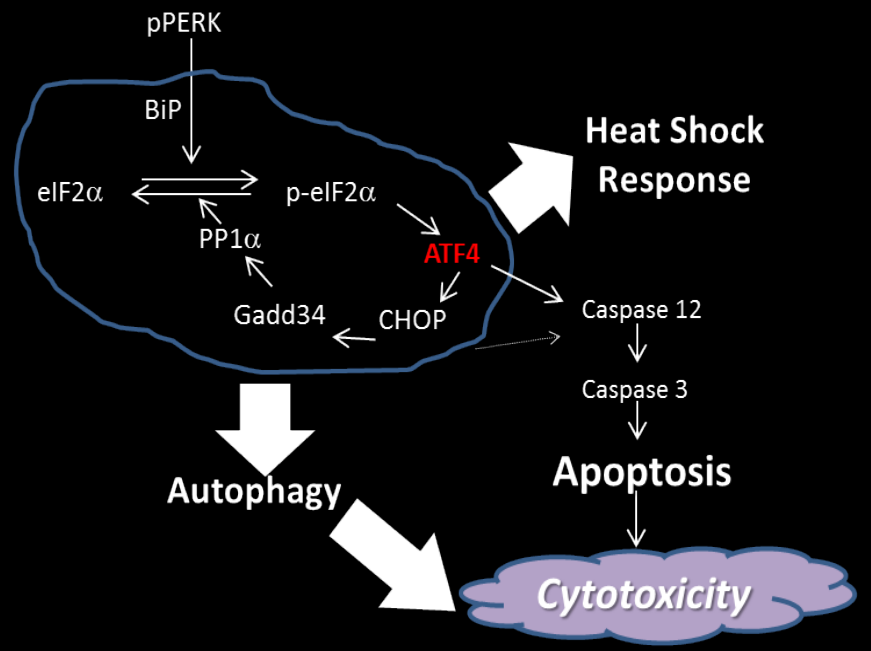

Khan et al Sci Reports 2015

# PBM Phototoxicity



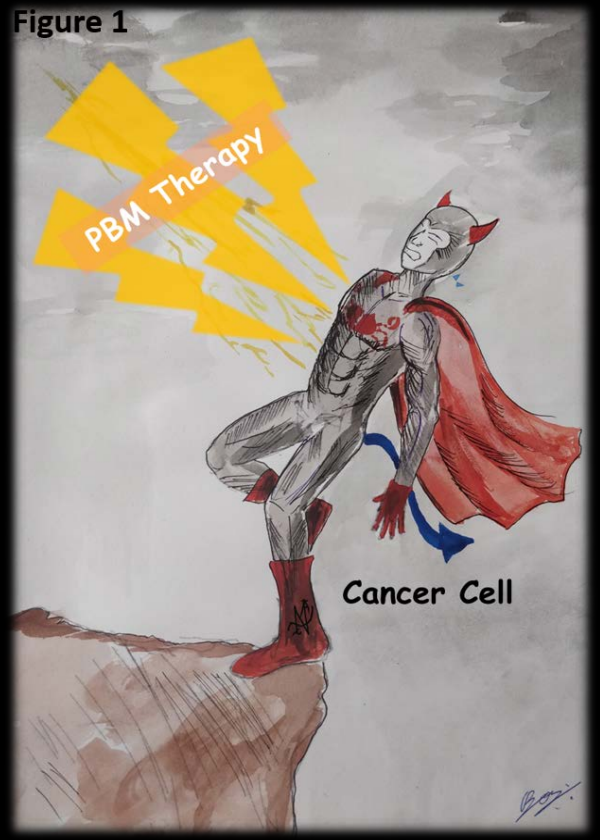

Khan I *et al* Sci Reports 2015 , 1, 510581
Khan & Arany Arch Trans Med 2016

# Is PBM '*photostimulation*' going to be detrimental for cancer cells?

*Healing* Tumors with Light: Science Fiction or *the* Future of Medicine?

Praveen R. Arany, DDS, PhD

Figure 1




**Direct effects** on tumor cells:

- Redox
- Metabolic / Bioenergetics
- Adhesion
- Proliferation
- Differentiation
- Migration
- Senescence

Figure 2


Indirect effects of anti-tumor host responses:

- Immune surveillance
- Vascular supply
- Lymphatic drainage

Arany PR **Photmed Las Surg** 2016, 35, 5,227

# PBM for Trismus
## (Radiation Fibroses)

Photomedicine and Laser Surgery
Volume XX, Number XX, 2017

Pp. 1–8
DOI: 10.1089/pho.2017.4297

**Case Report**

# Photobiomodulation Therapy Alleviates Tissue Fibroses Associated with Chronic Graft-Versus-Host Disease: Two Case Reports and Putative Anti-Fibrotic Roles of TGF-$\beta$

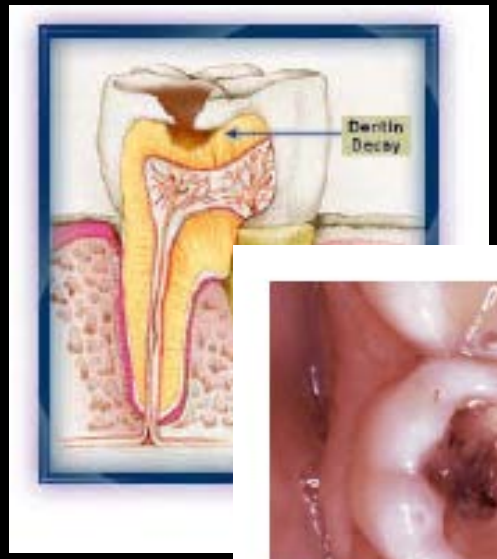
Joel B. Epstein, DMD, MSD, FRCD(C), FDS RCS(E),[1,2] Judith E. Raber-Durlacher, DDS, PhD,[3,4] Marie-Charlotte Huysmans, DDS, PhD,[5] Maria C.E. Schoordijk, RN, MANP,[6] Jerry E. Cheng, MD,[2,7] Rene-Jean Bensadoun, MD,[8] and Praveen R. Arany, BDS, MDS, MMSc, PhD[9]

5min 50mW/cm$^2$ for 3 min
IO+EO

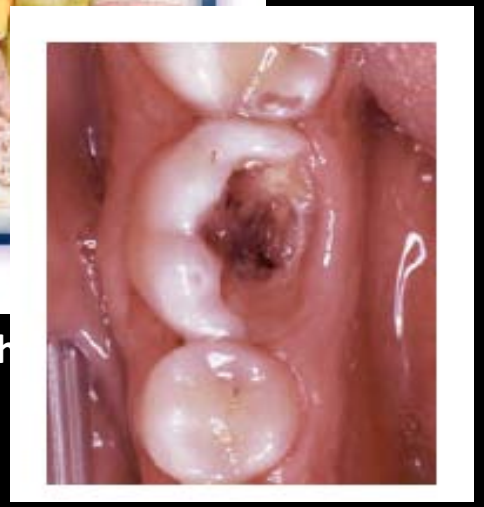
3 Weeks,
Once weekly

# PBM for Dentin Regeneration

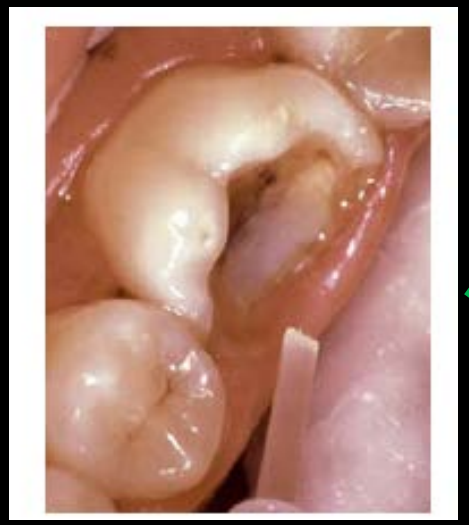
# PBM TGF-β1 Dentinogenesis: Pulp Capping




Tooth



Excavation of decayed Tooth

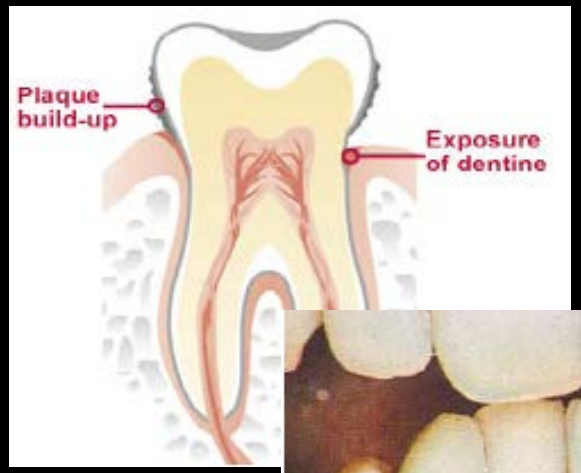


**Conventional:** Pulp Capping with Calcium Hydroxide / MTA

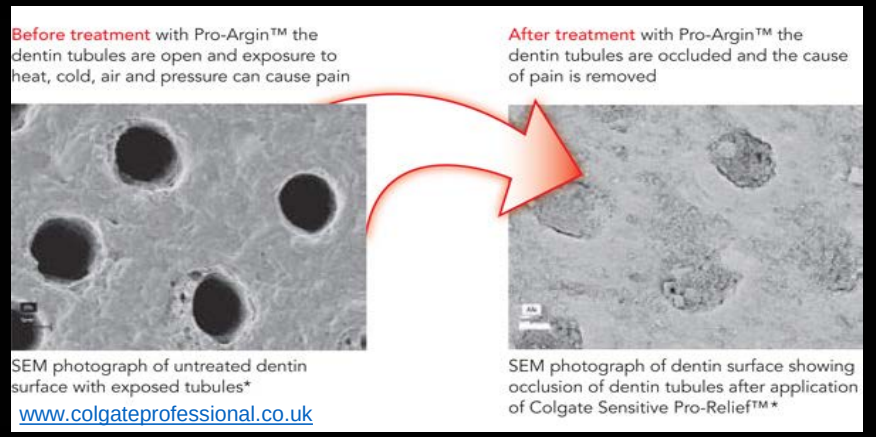

**New:** Laser Treatment

Filling

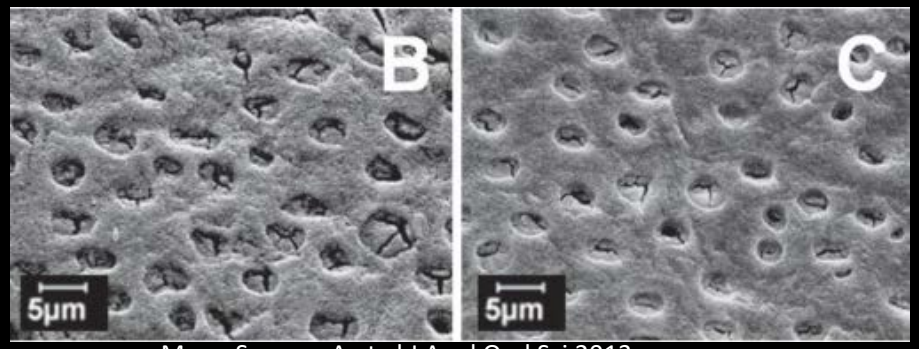
# PBM TGF-β1 Dentinogenesis: Desensitization




**Gingival Recession**



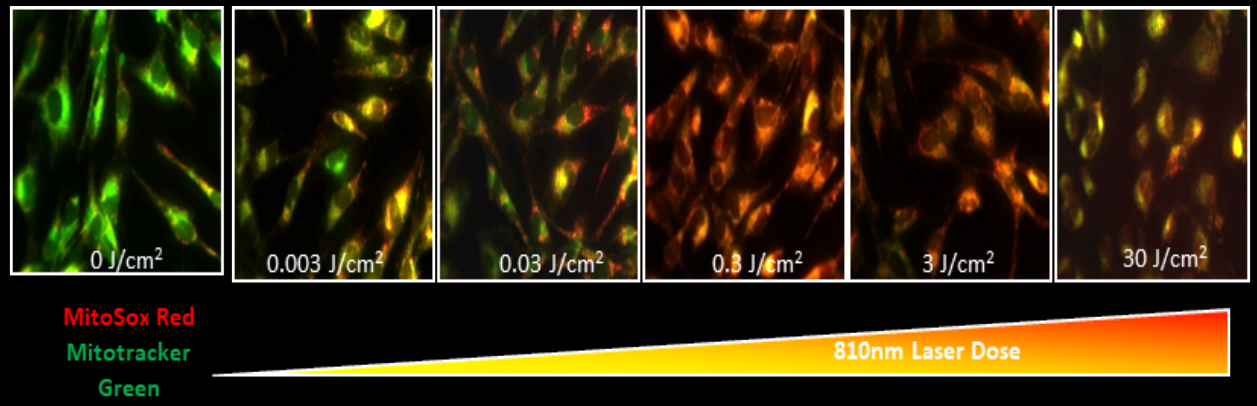

**Conventional:**
**Desensitization Toothpastes**

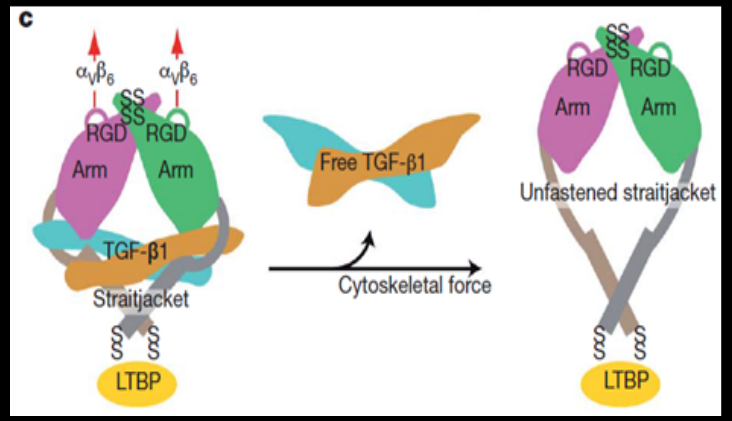


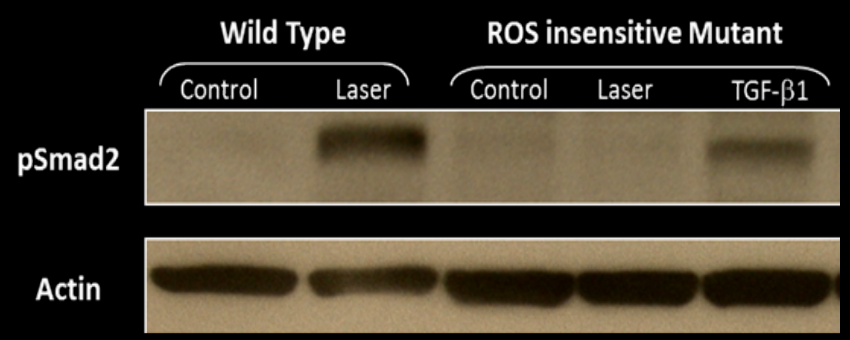

Mena-Serrano A et al J Appl Oral Sci 2013


**New: Laser Desensitization**

# PBM activates TGF-β1



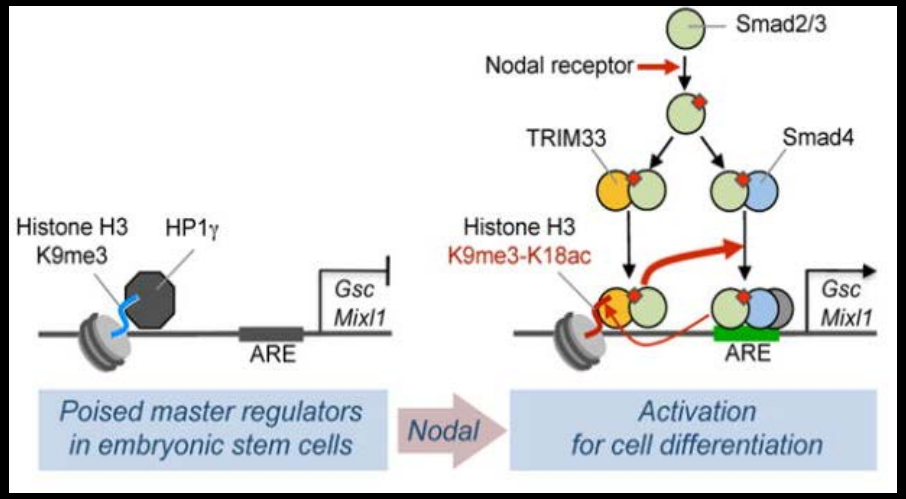

**Laser** → **ROS** → **TGF-β1**

Physical → Biochemical → Biological

Michael Hamblin, MGH
Mary-Helen Barcellos Hoff, NYU

Arany PR *et al* **Sci Transl Med** 2014, 6, 238, 1

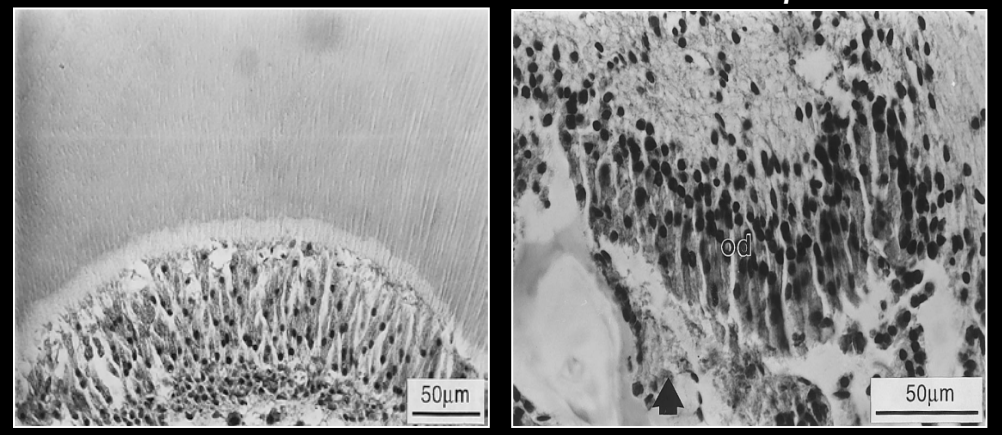
# Dental Application: PBM activated TGF-β1?




Mullen AC et al Cell 2011, 147, 565 Xi Q et al Cell 2011, 147, 1524

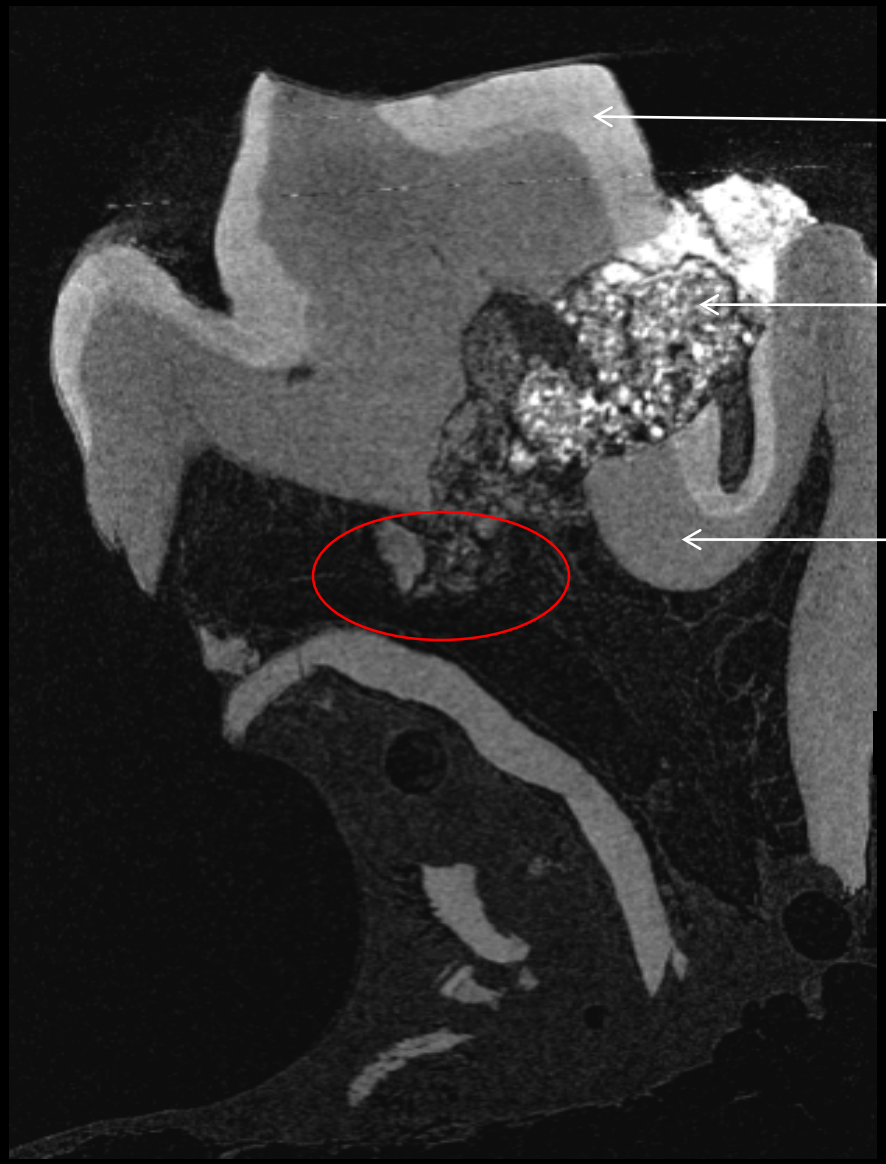
TGF-β1 is a central player in **stem cell fate**

TGF-β1 has a key role in **Dentin homeostasis**



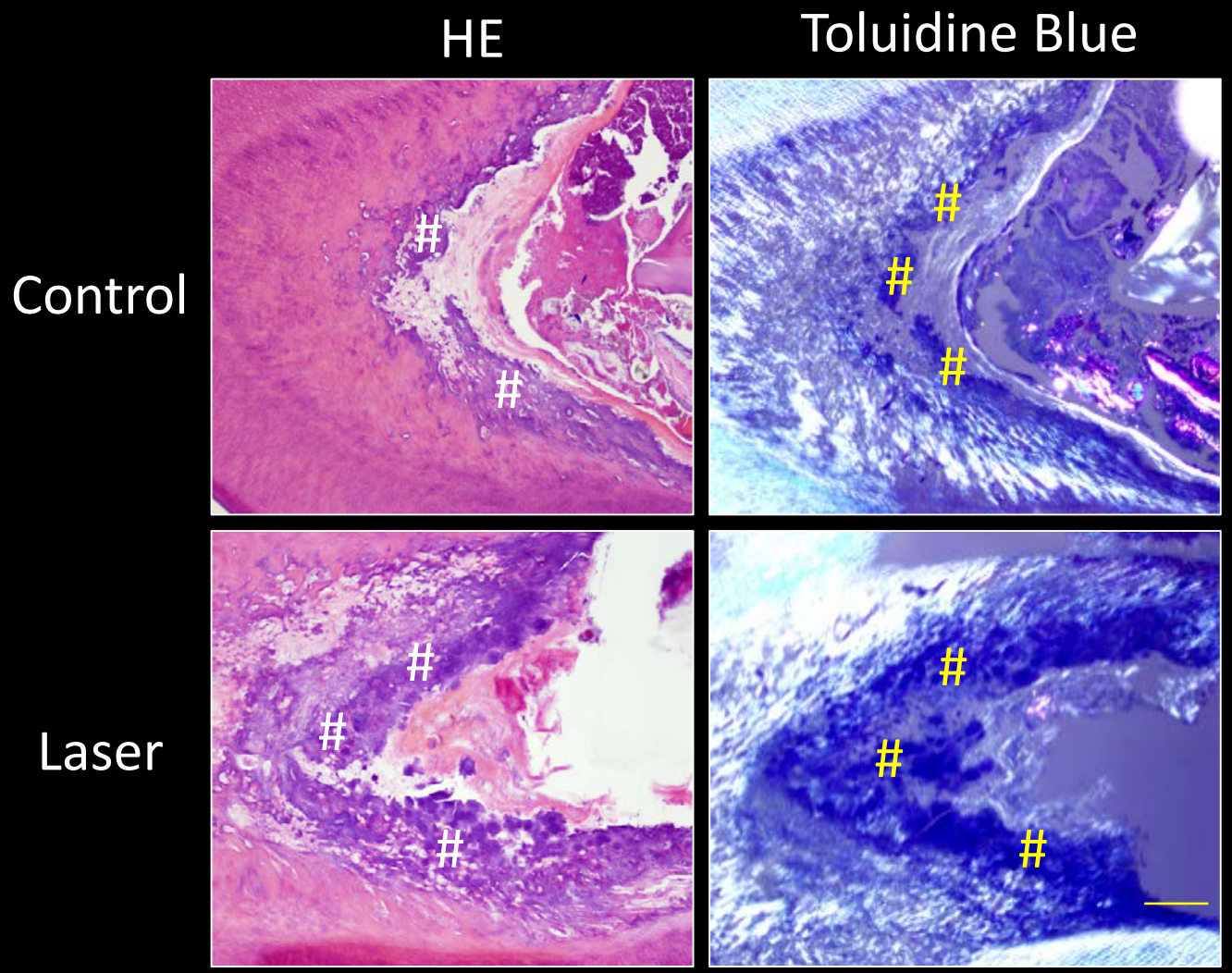

Sloan AJ and Smith AJ **Arch Oral Bio** 1999, 44, 149
D'Souza, RN et al **Eur J Oral Sci** 1998, 106 , 1, 185

# PBM therapy induces Dentin *in vivo*




12 weeks Post-Op

# PBM-induced mineralized tissue is Dentin



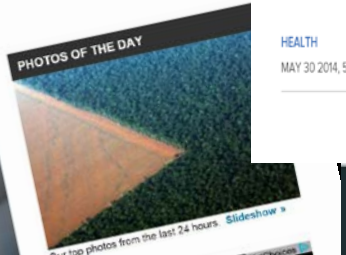
REUTERS

Don't let your opportunities be a hacker's opportunities.
Cisco Security

# A nice, bright smile: Scientists use lasers to regrow teeth

WASHINGTON | BY WILL DUNHAM

PHOTOS OF THE DAY



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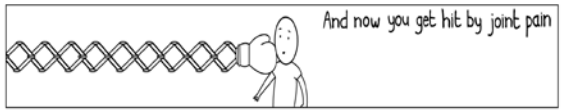


HEALTH > HEALTH NEWS

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HEALTH

MAY 30 2014, 5:24 PM ET

# Bright Idea: Scientists Use Laser Lights to Regrow Teeth

FOX NEWS

This could be our last water shortage.
The unveiling of a new solution.

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CAVITIES

# Goodbye root canals? Researchers use lasers to regrow parts of teeth

By Loren Grush · Published May 28, 2014 · FoxNews.com

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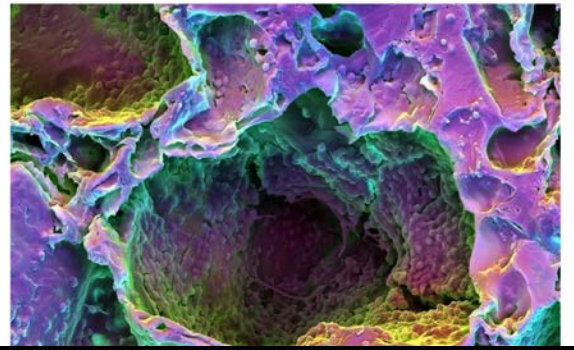
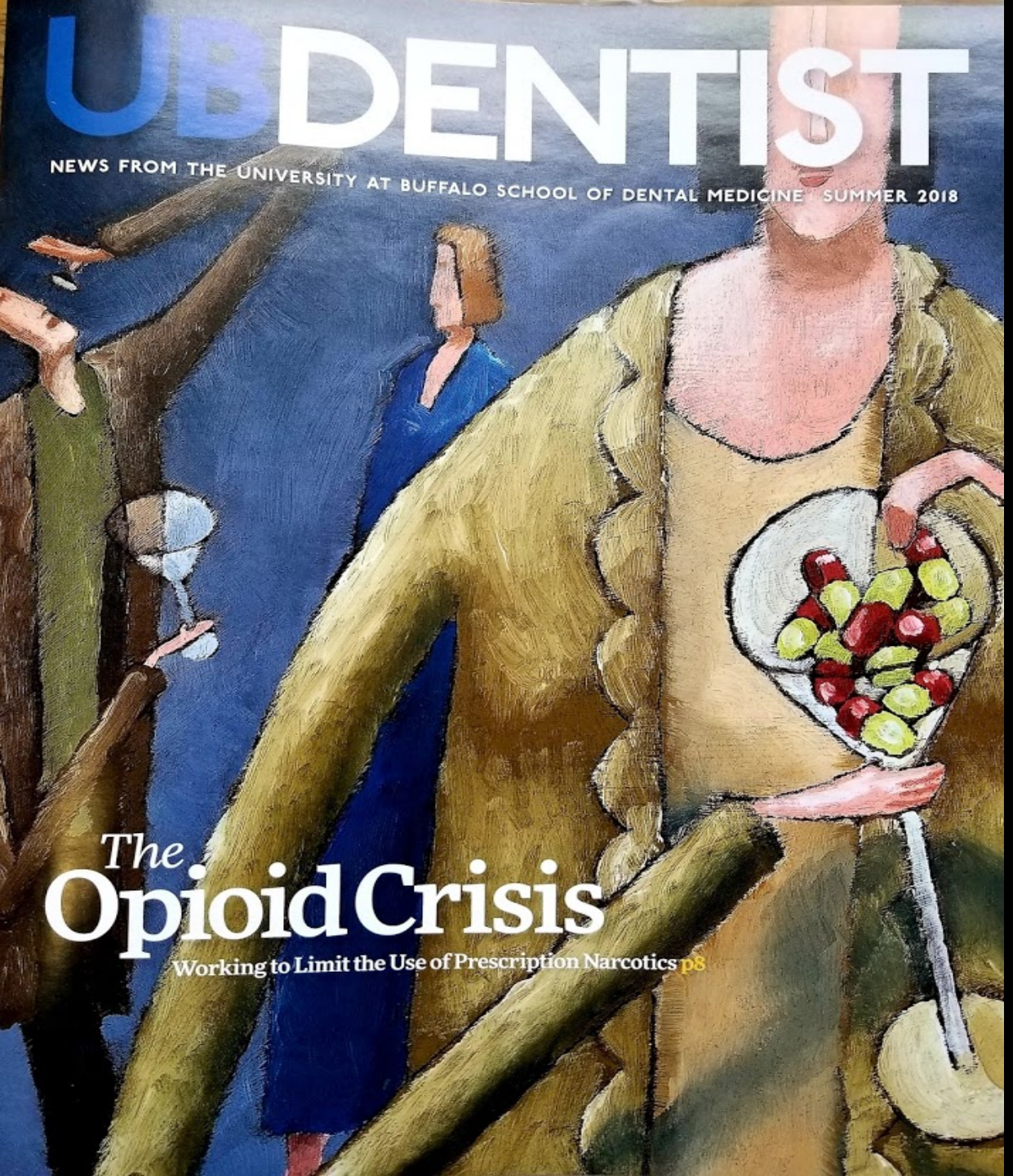
DAILY NEWS 29 May 2014

# Forget the dentist's drill, use lasers to heal teeth



# PBM for Pain




# *Are dentists to blame?*

- ☞ *Expose adolescents to opioids (extractions)*
- ☞ *Indiscriminate use*

Lasers in Dental Science
https://doi.org/10.1007/s41547-019-00075-6

ORIGINAL ARTICLE

# Photobiomodulation therapy for management of inferior alveolar nerve injury post-extraction of impacted lower third molars

Wei Qi[1,3,4,5] · Yuguang Wang[2,3,4,5,7] · Ying-Ying Huang[7,8] · Yuxi Jiang[2,3,4,5] · Lintian Yuan[2,3,4,5] · Peijun Lyu[2,3,4,5] · Praveen R Arany[6] · Michael R. Hamblin[7,8,9]

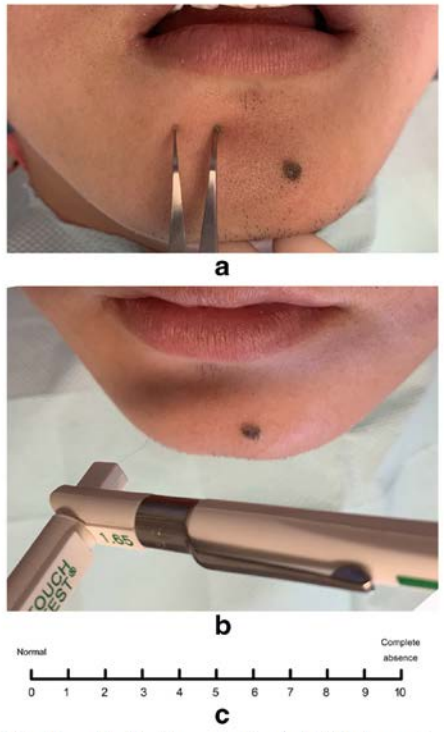
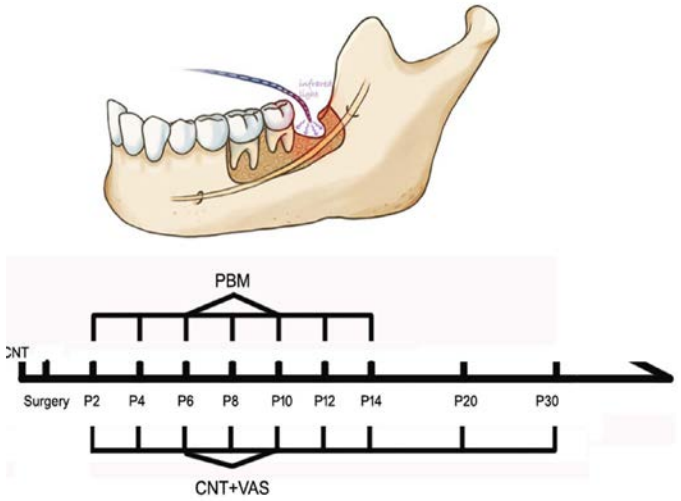



Fig. 1 Objective and subjective evaluation for IAN injury. **a** Two-points discrimination test with a Boley gauge with blunt points; **b** light touch test with Semmes-Weinstein monofilaments; **c** table for VAS test



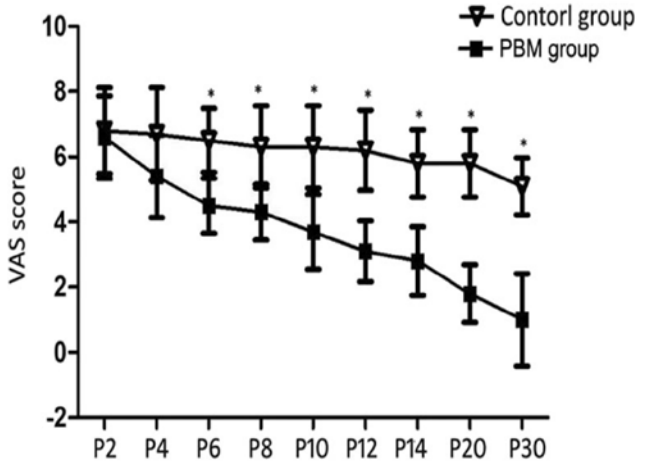
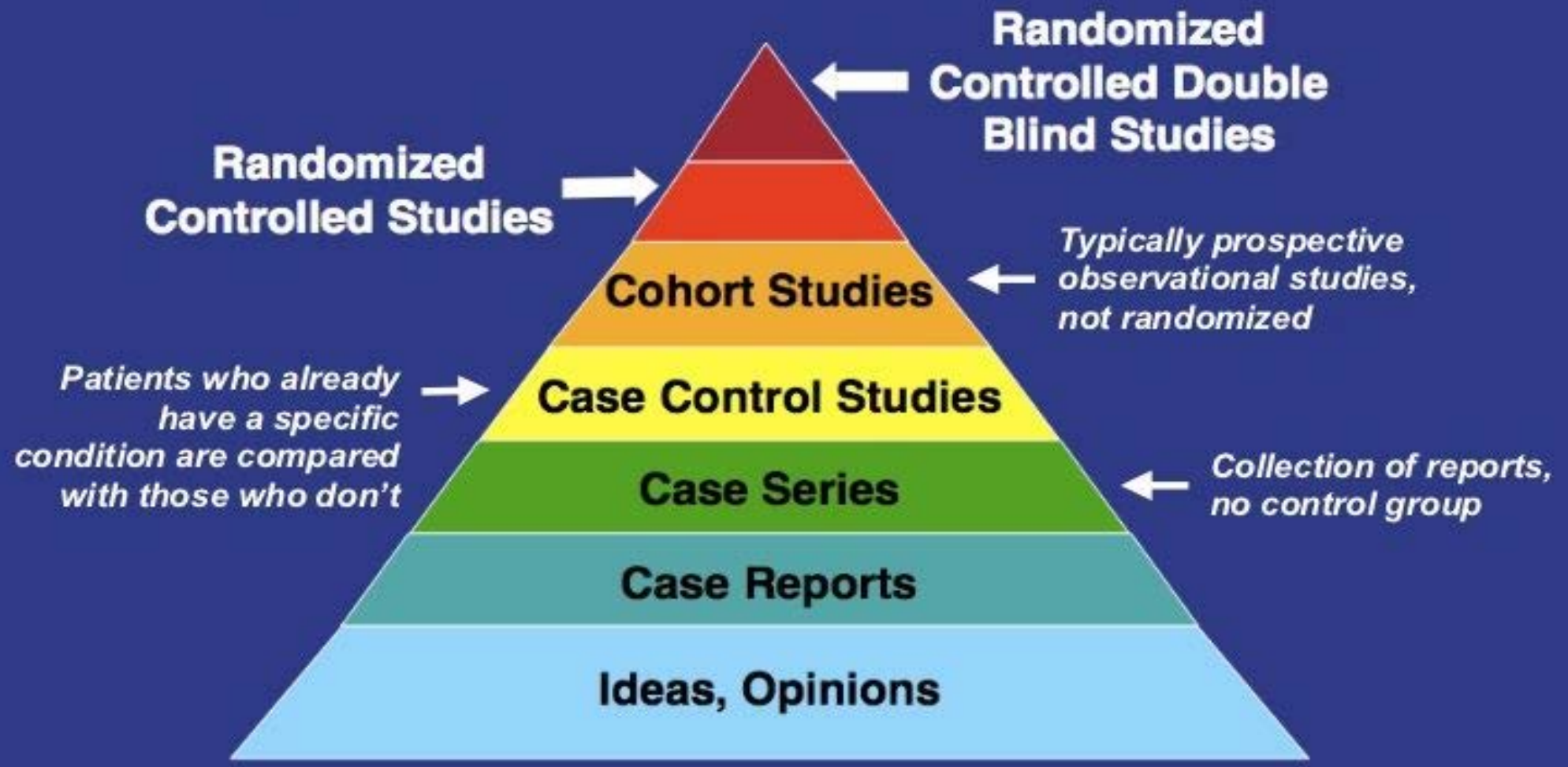




**Table 3** Results of TPD and LT before and after PBM treatment in each group

| | IAN injury[1] | | | |
|---|---|---|---|---|
| | TPD[2] | | LT△3 | |
| | P2 | P30 | P2 | P30 |
| Control<br>Mecobalamine group | 7/10 | 6/10 | 5/10 | 5/10 |
| Treatment<br>PBM group | 7/10 | 3/10 | 4/10 | 1/10 |
| *p* value | 1 | 0.37 | 1 | 0.14 |

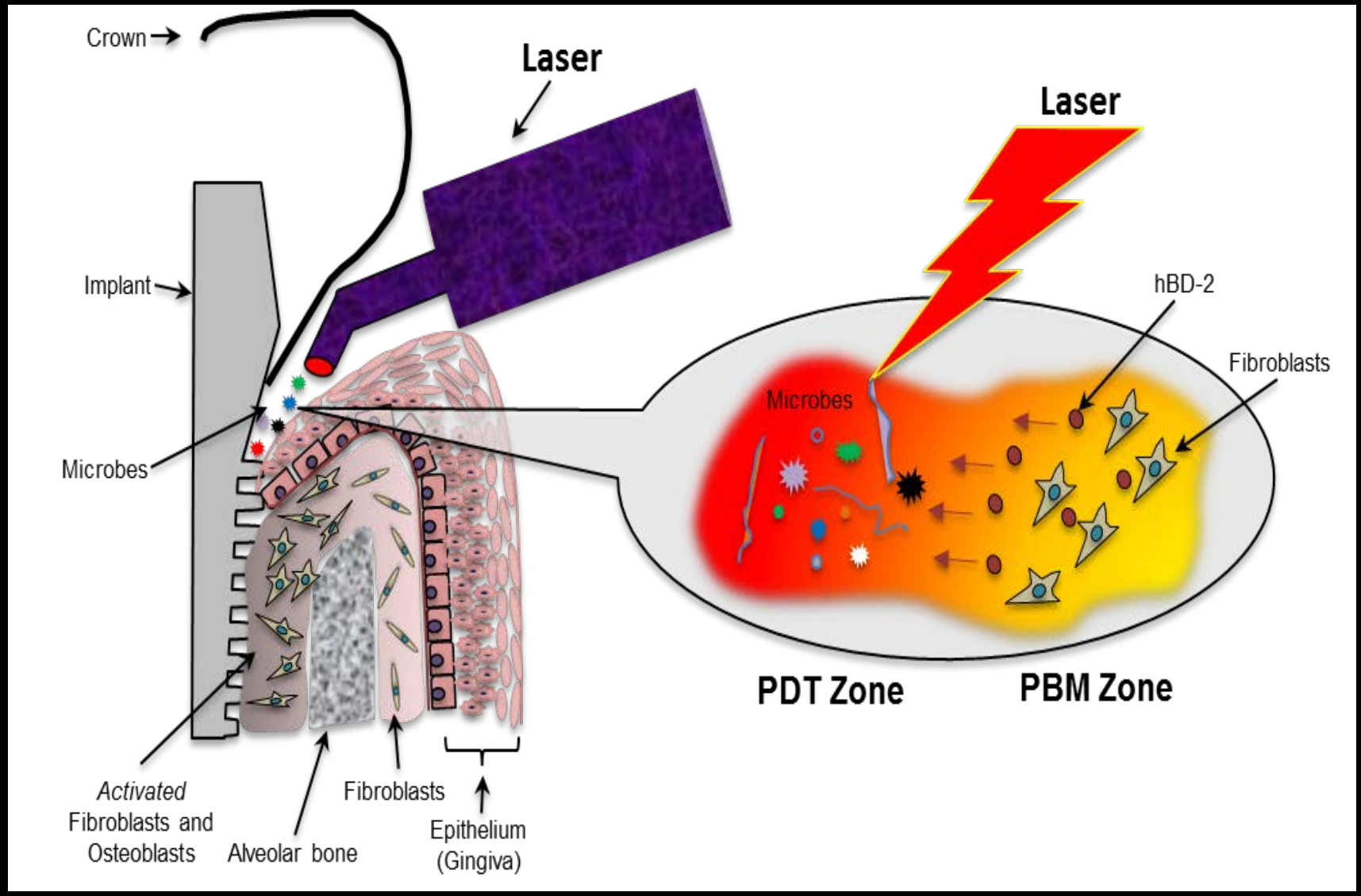
# Problem

# Evidence-Based Pyramid



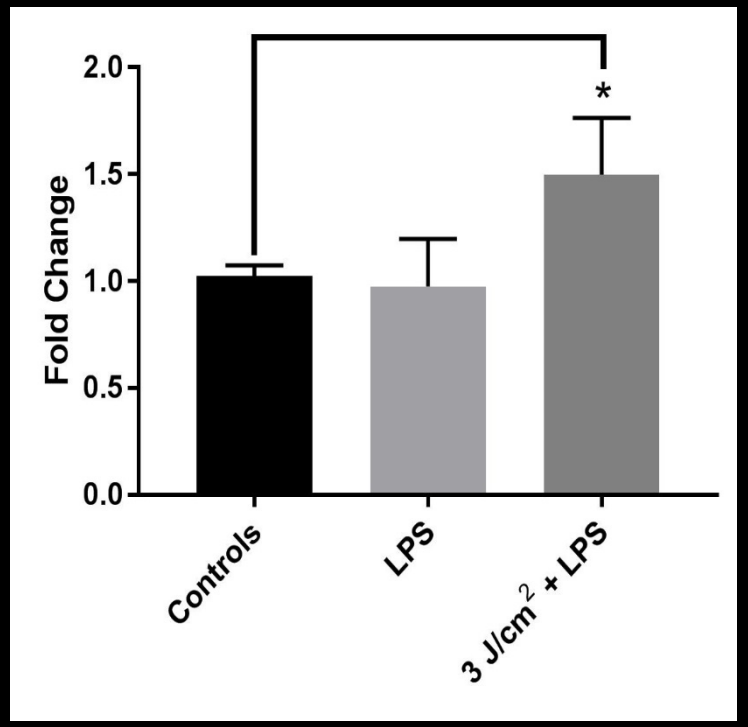
# PBM therapy for Peri-implantitis

# Laser Periodontitis / Peri-implant Therapy

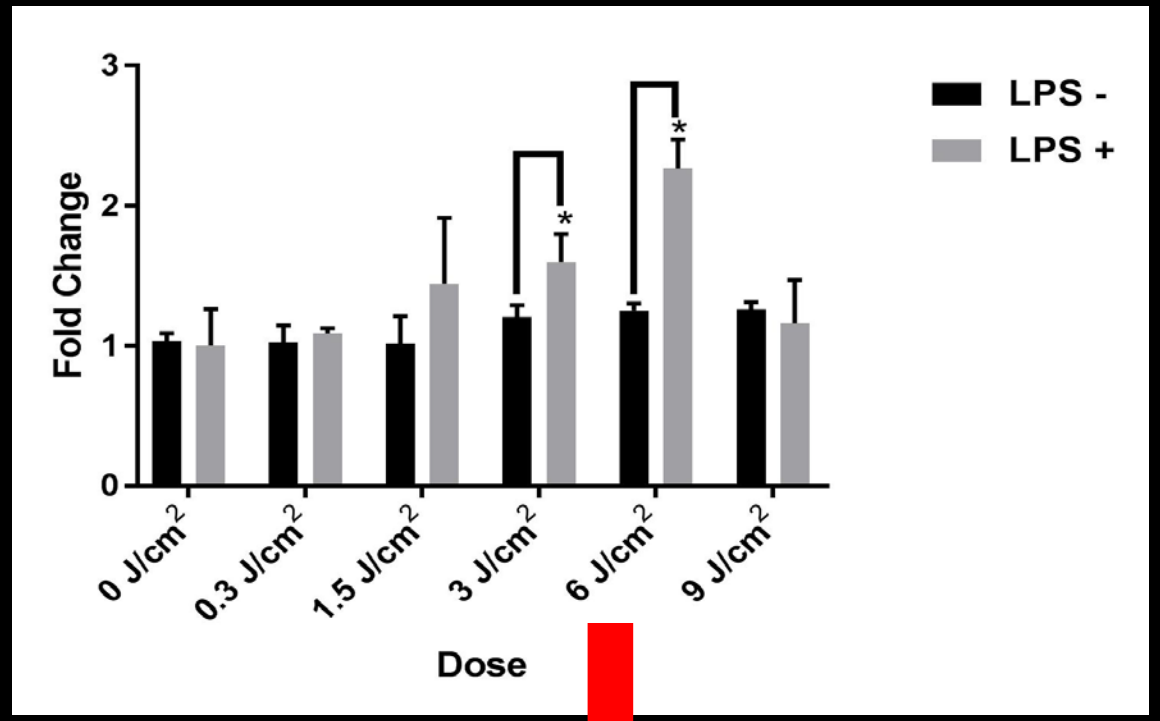


# Results

- PBM therapy induces HBD-2 in *P. gingivalis* LPS-stimulated human oral fibroblasts.




1 way ANOVA p<0.05




2 way ANOVA p<0.05

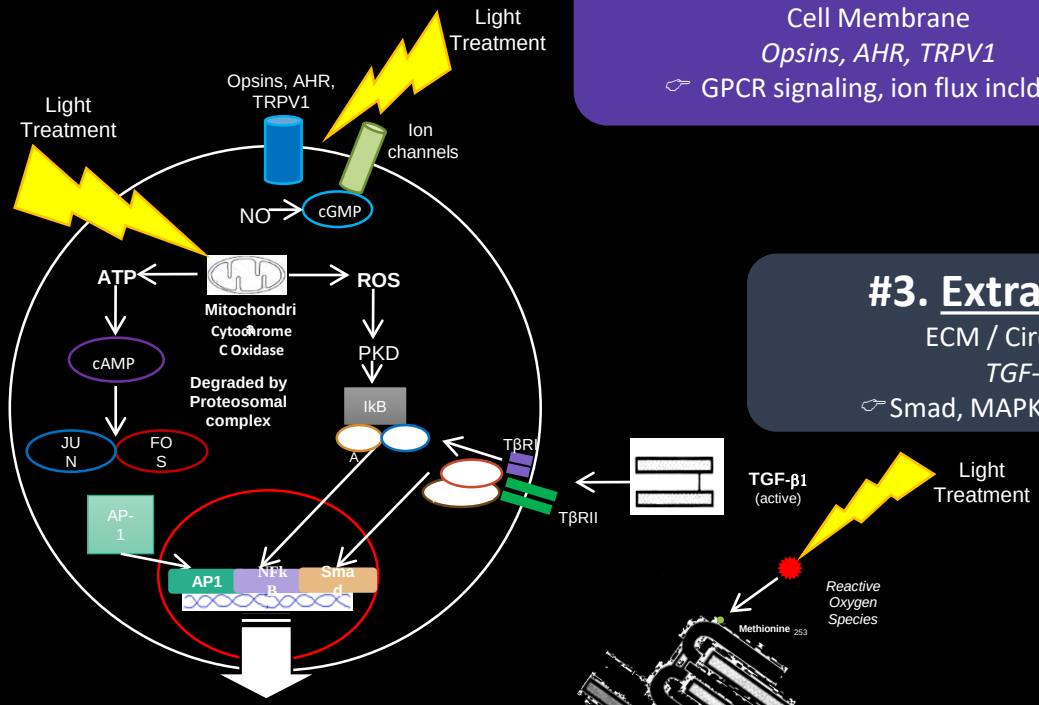
10mW/cm$^2$ and 600 sec (10 min)!

# PBM Mechanisms

**#1. Intracellular**
Mitochondria
*Cytochrome C Oxidase*
☞ ATP, ROS incld NO

**#2. Photoreceptors**
Cell Membrane
*Opsins, AHR, TRPV1*
☞ GPCR signaling, ion flux incld $Ca^{2+}$

**#3. Extracellular**
ECM / Circulating
*TGF-β1*
☞ Smad, MAPK, NFkB, ATF-4







Modified from Khan I and Arany *Adv Wound Care 2015*

# PBM mechanism 1: Intracellular

ELSEVIER

J. Photochem. Photobiol. B: Biol. 49 (1999) 1–17

Journal of Photochemistry and Photobiology B:Biology

Invited Review

## Primary and secondary mechanisms of action of visible to near-IR radiation on cells

Tiina Karu *

*Laser Technology Research Center of Russian Academy of Sciences, 142092 Troitsk, Moscow Region, Russia*

Received 17 March 1998; accepted 9 November 1998

Lasers in Surgery and Medicine 36:307–314 (2005)

## Cellular Effects of Low Power Laser Therapy Can be Mediated by Nitric Oxide

Tiina I. Karu, PhD,[1]* Ludmila V. Pyatibrat, MS,[1] and Natalia I. Afanasyeva, PhD[2]

[1]*Institute of Laser and Information Technologies of the Russian Academy of Sciences, 142190 Troitsk, Moscow, Russia*

[2]*Spectrooptical Sensing, Inc., Portland, Oregon 97205*

NEUROCHEMISTRY NEUROREPORT

## Light-emitting diode treatment reverses the effect of TTX on cytochrome oxidase in neurons

Margaret T. T. Wong-Riley,[CA] Xuetao Bai, Ellen Buchmann[1] and Harry T. Whelan[1]

Departments of Cell Biology, Neurobiology and Anatomy, and [1]Neurology, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA

[CA]Corresponding Author

Received 10 July 2001; accepted 24 July 2001

*AIMS Biophys.* 2017 ; 4(3): 337–361. doi:10.3934/biophy.2017.3.337.

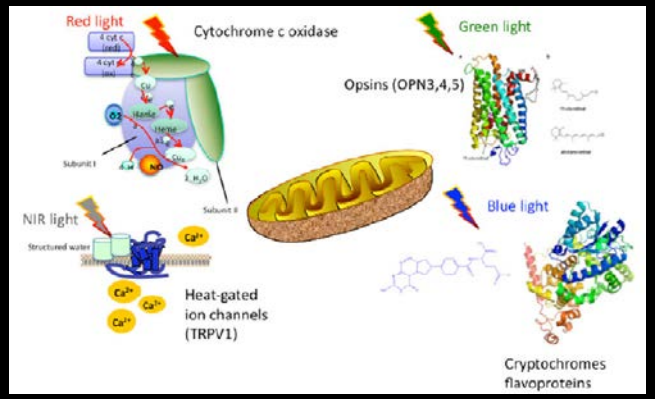
## Mechanisms and applications of the anti-inflammatory effects of photobiomodulation

**Michael R Hamblin**[1,2,3,*]

[1]Wellman Center for Photomedicine, Massachusetts General Hospital, BAR414, 40 Blossom Street, Boston, MA 02114, USA

[2]Department of Dermatology, Harvard Medical School, Boston, MA 02115, USA

[3]Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA 02139, USA



# PBM mechanism 2: Cell Membrane

SCIENTIFIC REPORTS

OPEN

## Red (660 nm) or near-infrared (810 nm) photobiomodulation stimulates, while blue (415 nm), green (540 nm) light inhibits proliferation in human adipose-derived stem cells

Received: 12 January 2017
Accepted: 29 June 2017
Published online: 10 August 2017

Yuguang Wang[1,2,3,4], Ying-Ying Huang[3,4], Yong Wang[1,2], Peijun Lyu[1,2] & Michael R. Hamblin[3,4,5]

SCIENTIFIC REPORTS

OPEN

## Gene expression profiling reveals aryl hydrocarbon receptor as a possible target for photobiomodulation when using blue light

Received: 10 June 2016
Accepted: 01 September 2016
Published: 27 September 2016

Anja Becker[1], Anna Klapczynski[1], Natalia Kuch[1], Fabiola Arpino[1], Katja Simon-Keller[1], Carolina De La Torre[1], Carsten Sticht[1], Frank A. van Abeelen[2], Gerrit Oversluizen[2] & Norbert Gretz[1]

PNAS

## Melanopsin mediates light-dependent relaxation in blood vessels

Gautam Sikka[a], G. Patrick Hussmann[b], Deepesh Pandey[a], Suyi Cao[a], Daijiro Hori[c], Jong Taek Park[a], Jochen Steppan[a], Jae Hyung Kim[a], Viachaslau Barodka[a], Allen C. Myers[d], Lakshmi Santhanam[a,e], Daniel Nyhan[a], Marc K. Halushka[f], Raymond C. Koehler[a], Solomon H. Snyder[f,1], Larissa A. Shimoda[g], and Dan E. Berkowitz[a,e,1]

[a]Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University, Baltimore, MD 21287; [b]Department of Neuroscience, Johns Hopkins University, Baltimore, MD 21205; [c]Department of Surgery, Johns Hopkins University, Baltimore, MD 21287; [d]Department of Allergy and Immunology, Johns Hopkins University, Baltimore, MD 21224; [e]Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD 21205; [f]Department of Pathology, Johns Hopkins University, Baltimore, MD 21287; and [g]Division of Pulmonary Medicine, Johns Hopkins University, Baltimore, MD 21224

Contributed by Solomon H. Snyder, October 24, 2014 (sent for review June 22, 2014)

Lasers in Surgery and Medicine 49:705–718 (2017)

## A New Path in Defining Light Parameters for Hair Growth: Discovery and Modulation of Photoreceptors in Human Hair Follicle

Serena Buscone, BSc,[1,2] Andrei N. Mardaryev, MD, PhD,[1] Bianca Raafs, BSc,[2] Jan W. Bikker,[3] Carsten Sticht, PhD,[4] Norbert Gretz, MD, PhD,[4] Nilofer Farjo, MD,[5] Natallia E. Uzunbajakava, PhD,[2**] and Natalia V. Botchkareva, MD, PhD[1*]

[1]*Faculty of Life Sciences, University of Bradford, Centre for Skin Sciences, Bradford, West Yorkshire BD7 1DP, United Kingdom*
[2]*Philips Research, High Tech Campus 34, Eindhoven 5656 AE, The Netherlands*
[3]*Consultants in Quantitative Methods BV, Eindhoven, The Netherlands*
[4]*Faculty Mannheim, University of Heidelberg, Center of Medical Research, Heidelberg, Germany*
[5]*Farjo Hair Institute, Manchester, United Kingdom*

*Am J Physiol Lung Cell Mol Physiol* 314: L93–L106, 2018.
First published September 7, 2017; doi:10.1152/ajplung.00091.2017.

RESEARCH ARTICLE

## Opsin 3 and 4 mediate light-induced pulmonary vasorelaxation that is potentiated by G protein-coupled receptor kinase 2 inhibition

Sebastian Barreto Ortiz,[1*] Daijiro Hori,[1,2*] Yohei Nomura,[1,2] Xin Yun,[3] Haiyang Jiang,[3] Hwanmee Yong,[4] James Chen,[5] Sam Paek,[4] Deepesh Pandey,[1] Gautam Sikka,[1] Anil Bhatta,[1] Andrew Gillard,[1] Jochen Steppan,[1] Jae Hyung Kim,[1] Hideo Adachi,[6] Viachaslau M. Barodka,[1] Lewis Romer,[1,5,7] Steven S. An,[4] Larissa A. Shimoda,[3] Lakshmi Santhanam,[1,5] and Dan E. Berkowitz[1,5]

[1]*Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University, Baltimore, Maryland;* [2]*Division of Cardiac Surgery, Johns Hopkins University, Baltimore, Maryland;* [3]*Division of Pulmonary and Critical Care Medicine, Johns Hopkins Asthma and Allergy Center, Johns Hopkins University, Baltimore, Maryland;* [4]*Department of Environmental Health and Engineering, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland;* [5]*Department of Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland;* [6]*Department of Cardiovascular Surgery, Saitama Medical Center, Jichi Medical University, Shimotsuke, Japan; and* [7]*Departments of Cell Biology, Pediatrics, and the Center for Cell Dynamics, Johns Hopkins University, Baltimore, Maryland*

Submitted 28 February 2017; accepted in final form 1 September 2017

# PBM mechanism 3: Extracellular

RESEARCH ARTICLE

REGENERATIVE MEDICINE

## Photoactivation of Endogenous Latent Transforming Growth Factor–β1 Directs Dental Stem Cell Differentiation for Regeneration

Praveen R. Arany,[1,2,3,4,5] Andrew Cho,[5] Tristan D. Hunt,[1] Gursimran Sidhu,[1] Kyungsup Shin,[1,3] Eason Hahm,[1] George X. Huang,[1] James Weaver,[2] Aaron Chih-Hao Chen,[6] Bonnie L. Padwa,[7] Michael R. Hamblin,[6,8,9] Mary Helen Barcellos-Hoff,[10] Ashok B. Kulkarni,[5] David J. Mooney[1,2]*

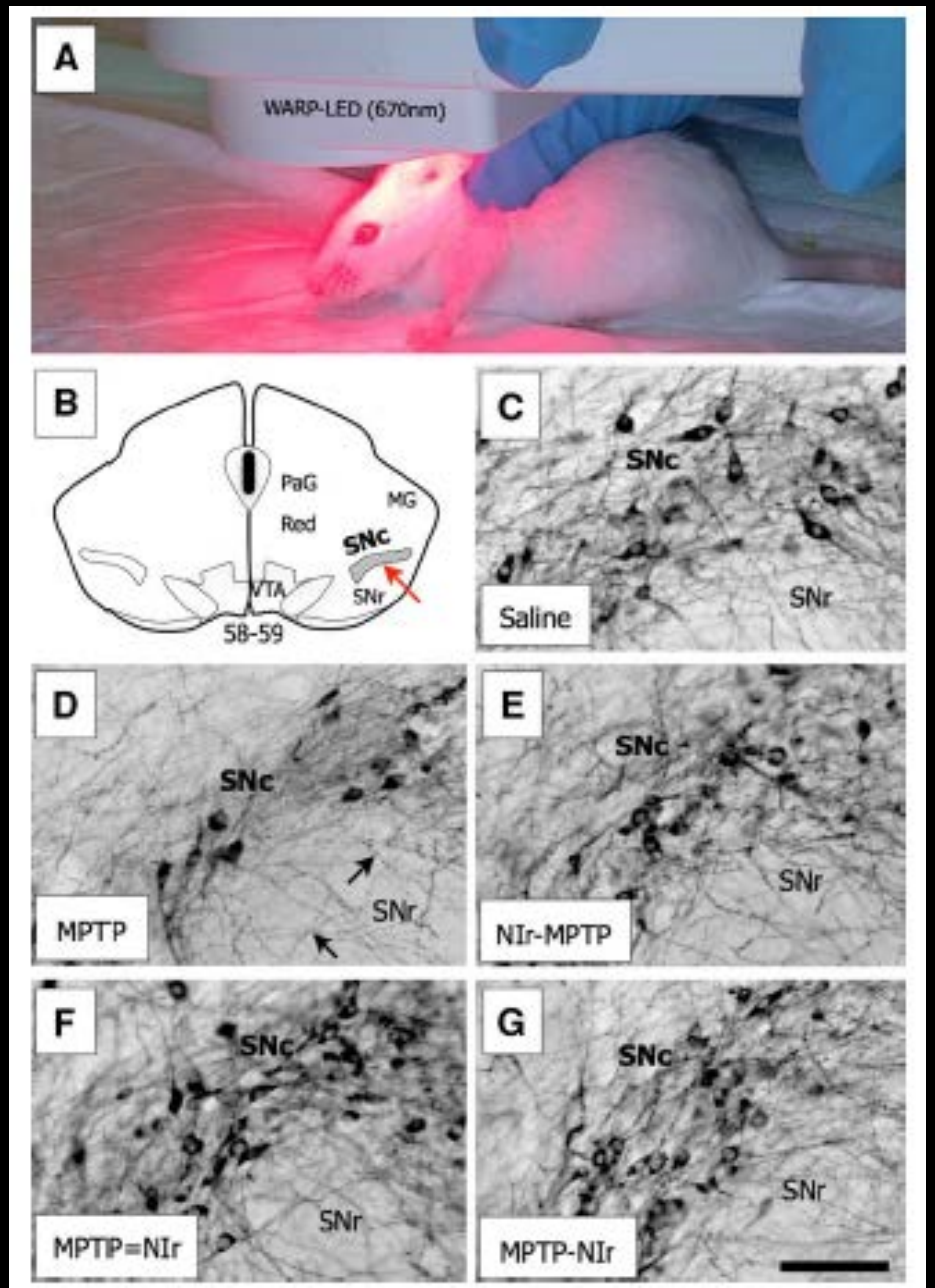
Rapid advancements in the field of stem cell biology have led to many current efforts to exploit stem cells as therapeutic agents in regenerative medicine. However, current ex vivo cell manipulations common to most regenerative approaches create a variety of technical and regulatory hurdles to their clinical translation, and even simpler approaches that use exogenous factors to differentiate tissue-resident stem cells carry significant off-target side effects. We show that non-ionizing, low-power laser (LPL) treatment can instead be used as a minimally invasive tool to activate an endogenous latent growth factor complex, transforming growth factor–β1 (TGF-β1), that subsequently differentiates host stem cells to promote tissue regeneration. LPL treatment induced reactive oxygen species (ROS) in a dose-dependent manner, which, in turn, activated latent TGF-β1 (LTGF-β1) via a specific methionine residue (at position 253 on LAP). Laser-activated TGF-β1 was capable of differentiating human dental stem cells in vitro. Further, an in vivo pulp capping model in rat teeth demonstrated significant increase in dentin regeneration after LPL treatment. These in vivo effects were abrogated in TGF-β receptor II (*TGF-βRII*) conditional knockout (*DSPP*$^{Cre}$*TGF-βRII*$^{fl/fl}$) mice or when wild-type mice were given a TGF-βRI inhibitor. These findings indicate a pivotal role for TGF-β in mediating LPL-induced dental tissue regeneration. More broadly, this work outlines a mechanistic basis for harnessing resident stem cells with a light-activated endogenous cue for clinical regenerative applications.

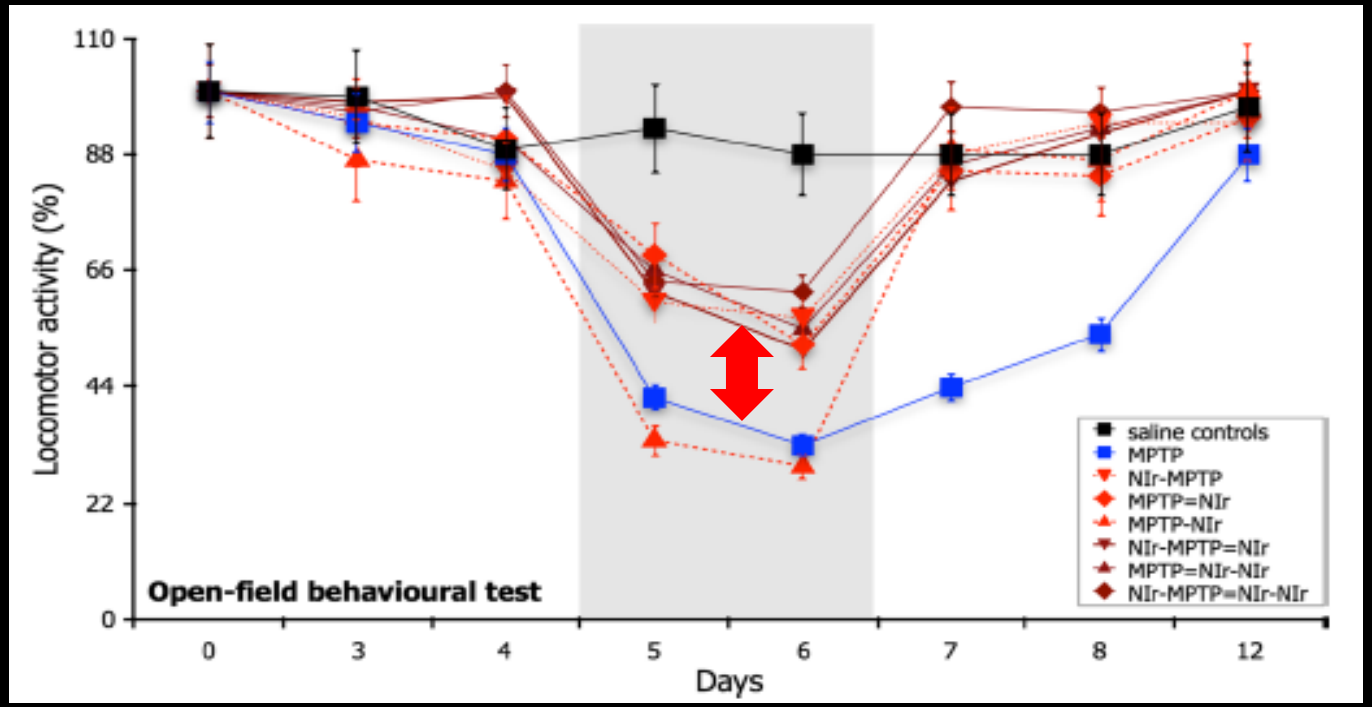
Michael Hamblin, MGH
Mary-Helen Barcellos Hoff, NYU

Arany PR *et al* **Sci Transl Med** 2014, 6, 238, 1
Jobling MF *et al* **Rad Res** 2008, 166, 839

# How can we use PBM therapy - Safely and Effectively?

# PBM in Parkinson's Disease




Exp Brain Res
DOI 10.1007/s00221-016-4578-8

RESEARCH ARTICLE

## Near-infrared light (670 nm) reduces MPTP-induced parkinsonism within a broad therapeutic time window

Florian Reinhart[1] · Nabil El Massri[2] · Daniel M. Johnstone[3] · Jonathan Stone[3] · John Mitrofanis[2] · Alim-Louis Benabid[1] · Cécile Moro[1]

Photobiomodulation, Photomedicine, and Laser Surgery
Volume XX, Number XX, 2019

Pp. 1–8
DOI: 10.1089/photob.2019.4663



# The "Buckets": Early Observations on the Use of Red and Infrared Light Helmets in Parkinson's Disease Patients

Catherine L. Hamilton, MBBS, MPH,[1] Hala El Khoury, BSc,[1] David Hamilton, BSc,[1]
Frank Nicklason, MBBS, FRACP,[1,2] and John Mitrofanis, PhD[1]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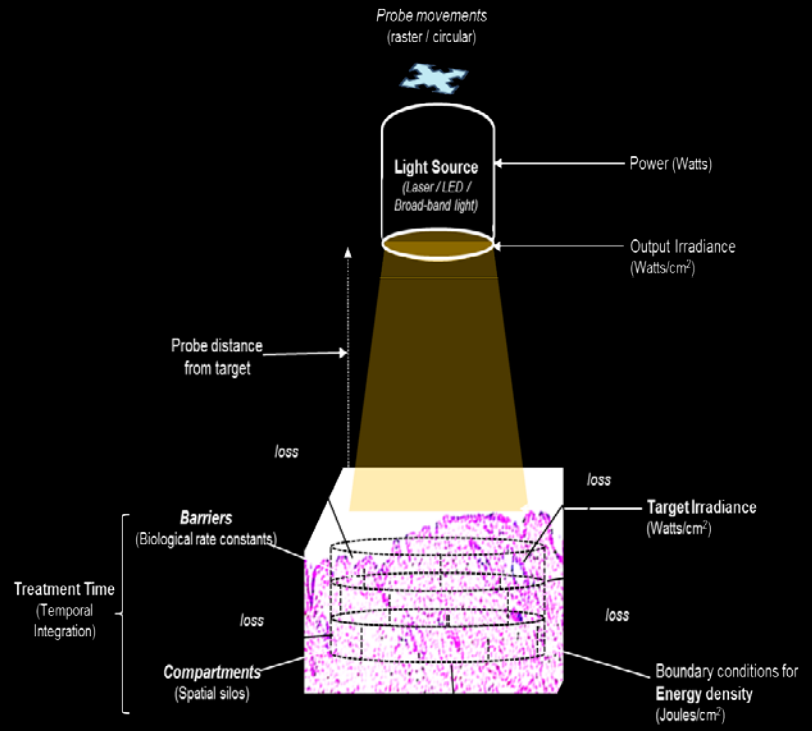
# Phototherapy: Photobiomodulation therapy—easy to do, but difficult to get right

When non-ionizing, non-thermal light treatment called photobiomodulation (PBM) therapy is used in the right dose and clinical context, this treatment can reduce pain and alleviate inflammation while stimulating tissue healing and regeneration.

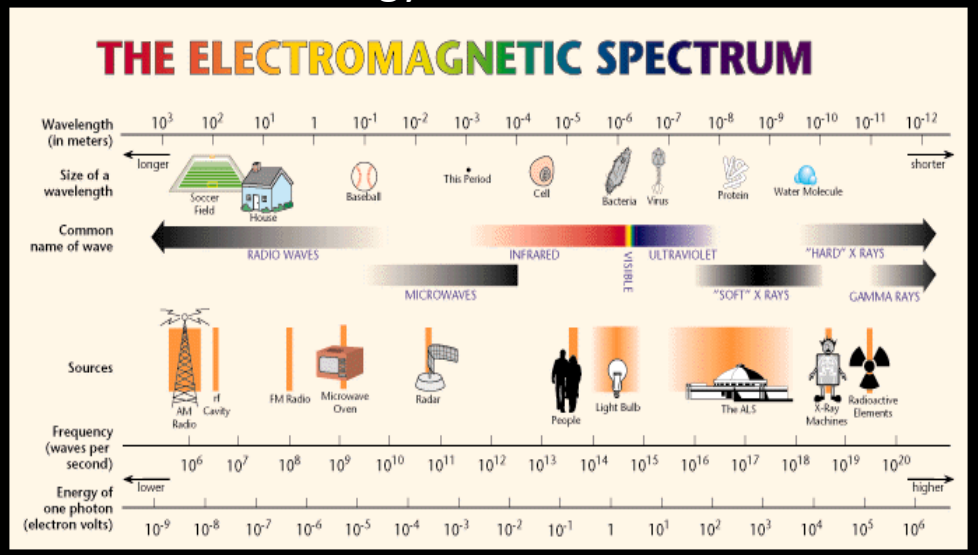
https://www.laserfocusworld.com/lasers-sources/article/14037967/photobiomodulation-therapyeasy-to-do-but-difficult-to-get-right



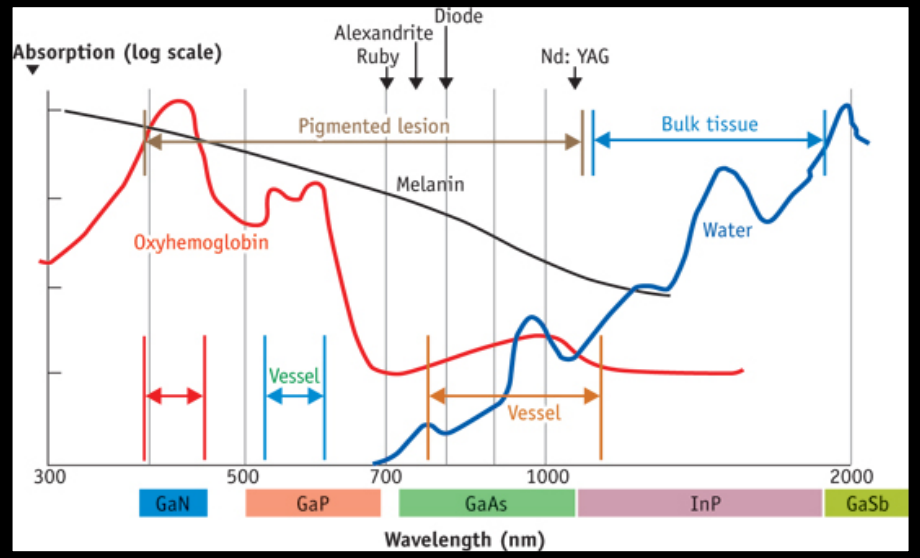

Arany PR *J Dent Res* 2016

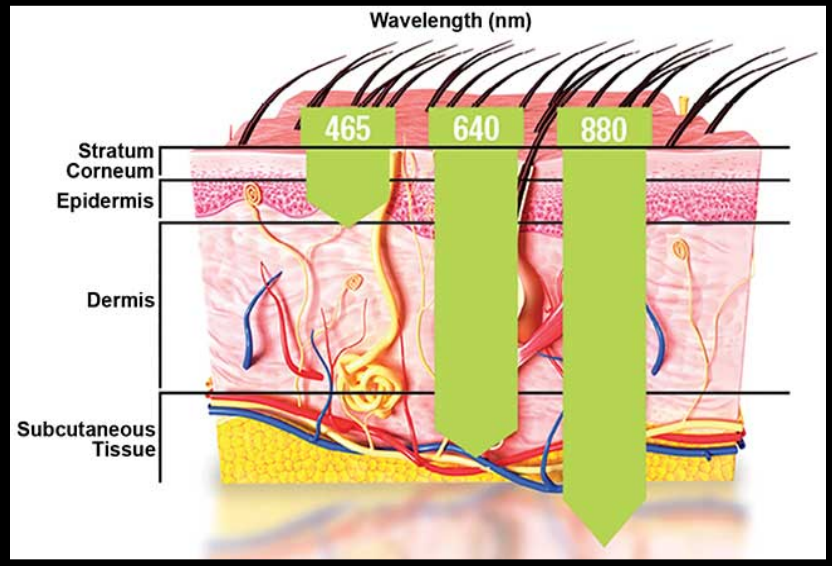
# Wavelength and Treatment zone: *NOT INTUITIVE!*

Energy ➔ 'Penetration'




Absorption ➔ 'Attenuation'

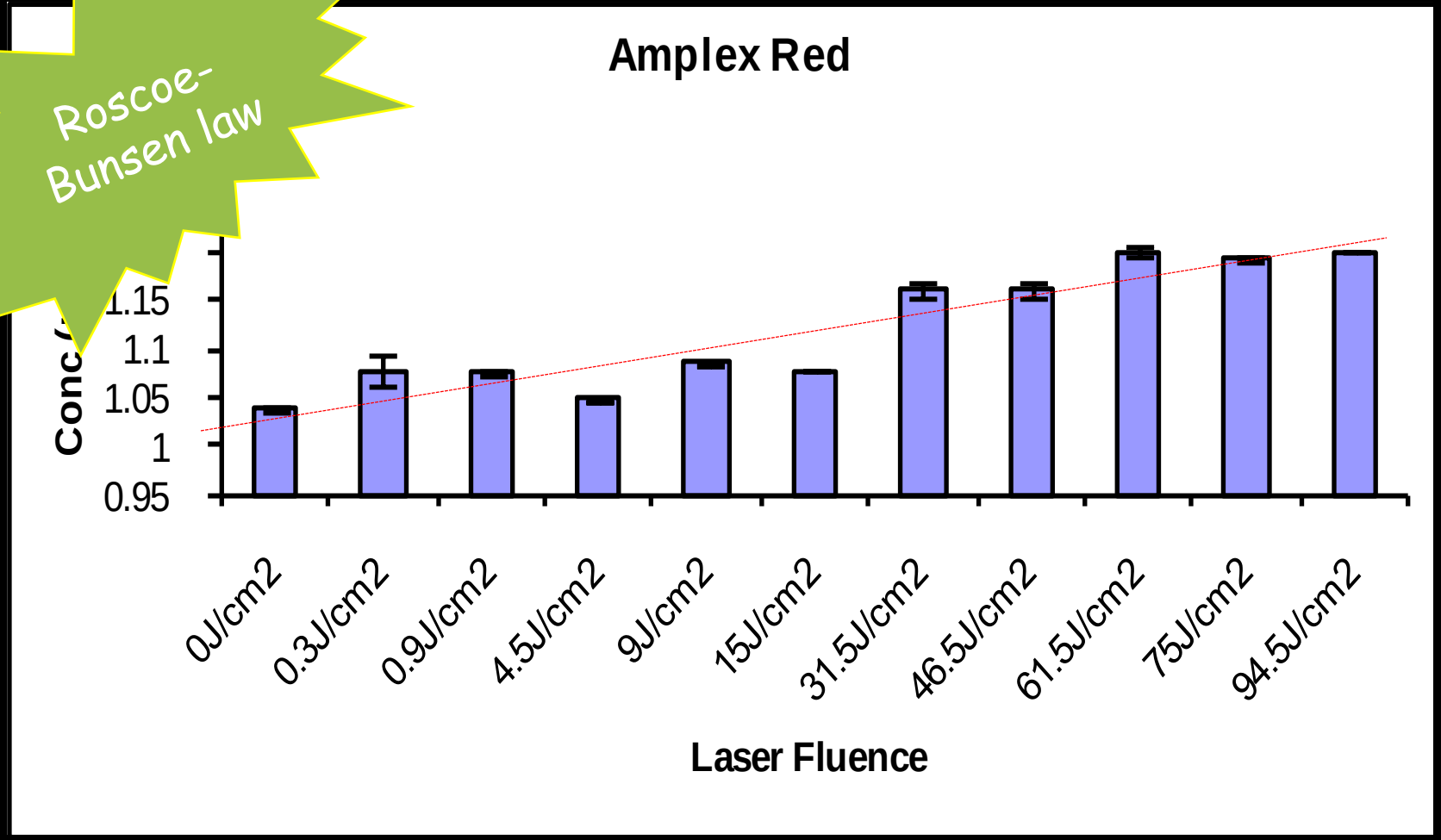



☞ PBM treatment wavelengths can be chosen based on *specific* target chromophore and / or treatment zone

# Laser Biochemical effects - Linear

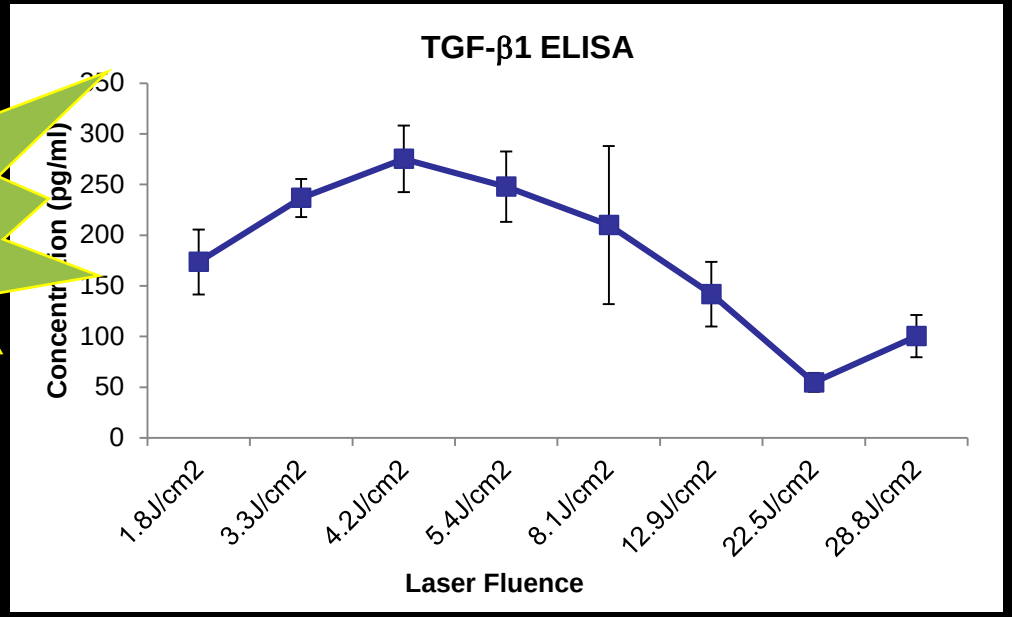
Roscoe-Bunsen law

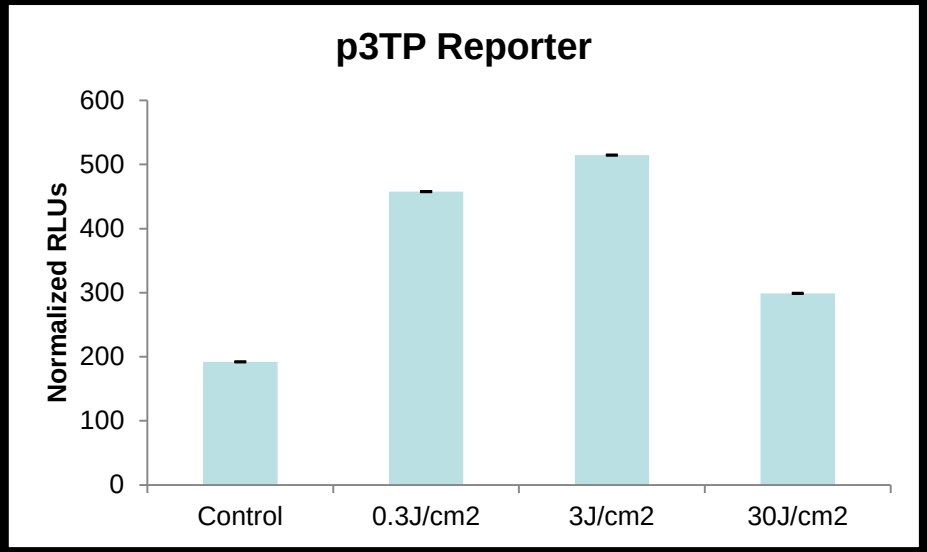


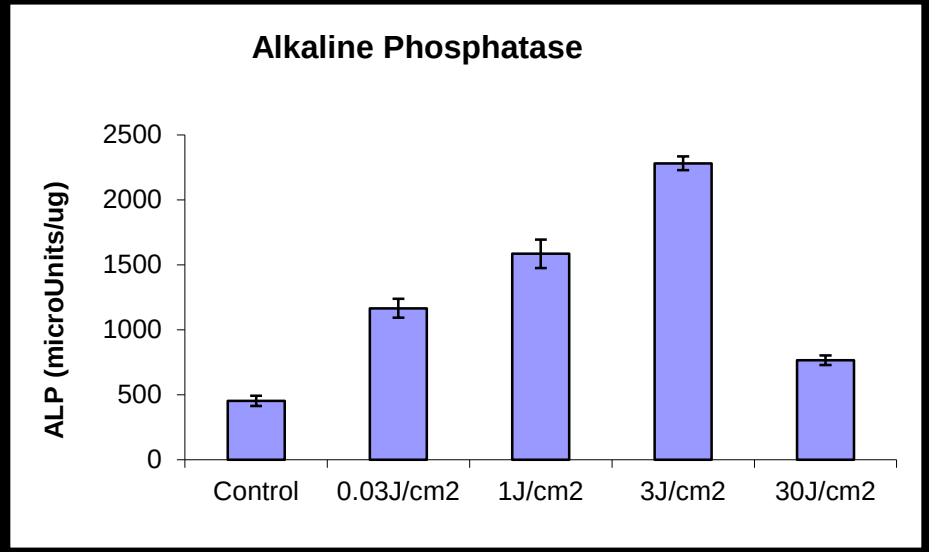

**Grothus-Draper Law** ☞ Absorption = response

# Laser Biological effects: Non-linear

Arndt Schultz law



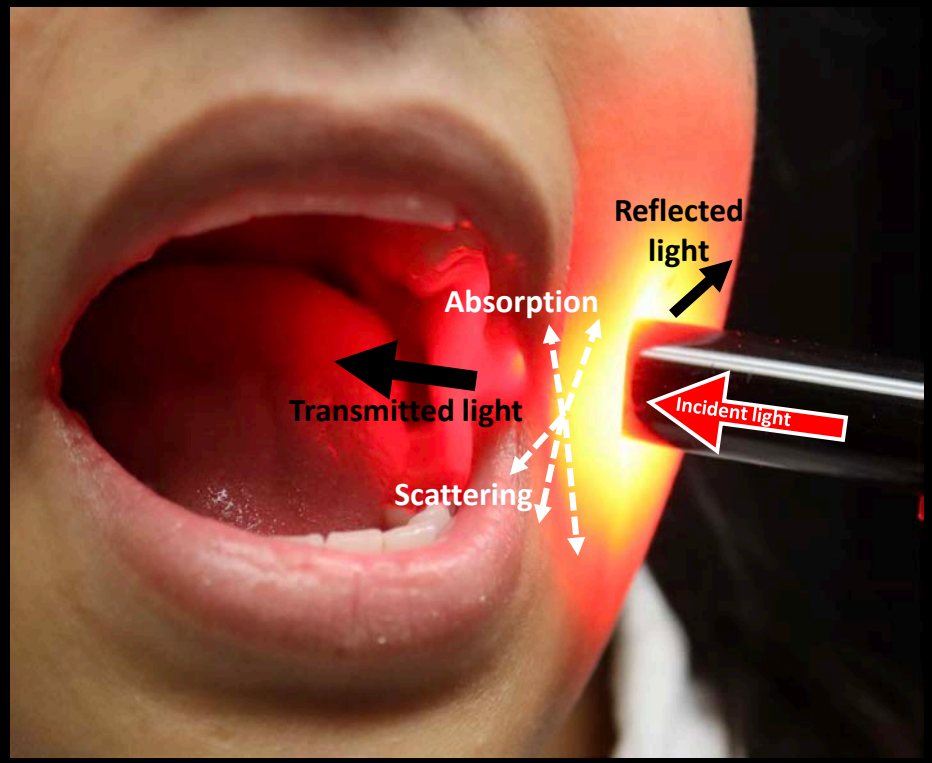




Arany PR **Photomed Las Surg** 2012, 30, 9, 507

# A novel Dose Concept:

## *PBM as an Energy Transfer Phenomenon…*



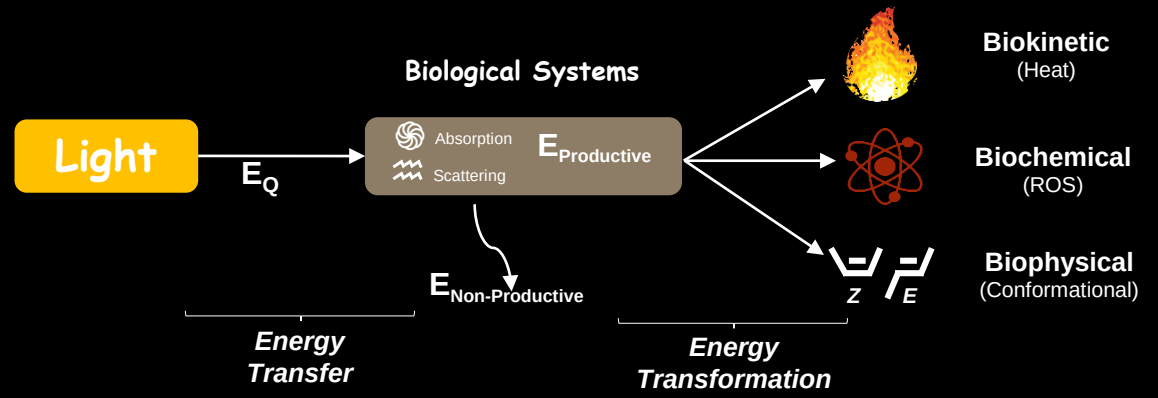

***Total Energy***

$$E_Q = \underbrace{EA + Esi}_{E_P} + \underbrace{Ese + E_T + ER}_{E_{NP}}$$

***Photonic Energy Transfer (PET)***

$$EP = EQ - E_{NP}$$

| | | |
|---|---|---|
| $E_Q$ | = Total quantum energy | *(per wavelength photon)* |
| $E_p$ | = Productive energy | (transfer) |
| $E_A$ | = Absorption | (transfer) |
| $E_{si}$ | = Scattering, inelastic | (transfer) |
| $E_{NP}$ | = Non-productive | (non-transfer) |
| $E_R$ | = Reflection | (non-transfer) |
| $E_{se}$ | = Scattering, elastic | (non-transfer) |
| $E_T$ | = Transmission | (non-transfer) |




Young et *al 2022 JBiophot*

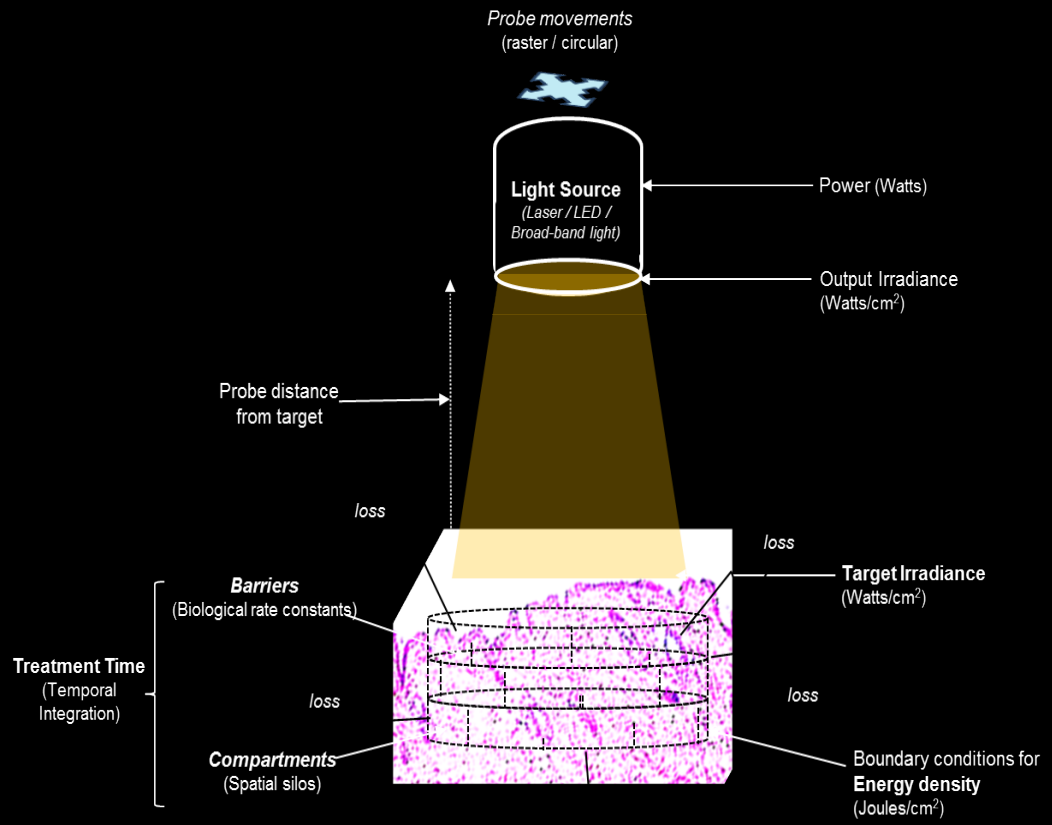
# Summary: Evolution of PBM Dose Models in the Arany Lab

**Fluence** : J/cm²
**Irradiance** : W/cm²
**Time** : sec

## FIT

*Model* ☞ 'Modular-Leaky-Balanced Bucket'
*Concepts* ☞ ***Threshold dose concept***

Arany PR **J Clin Las Dent** 2011, 19, 2, 231





## Wound Healing

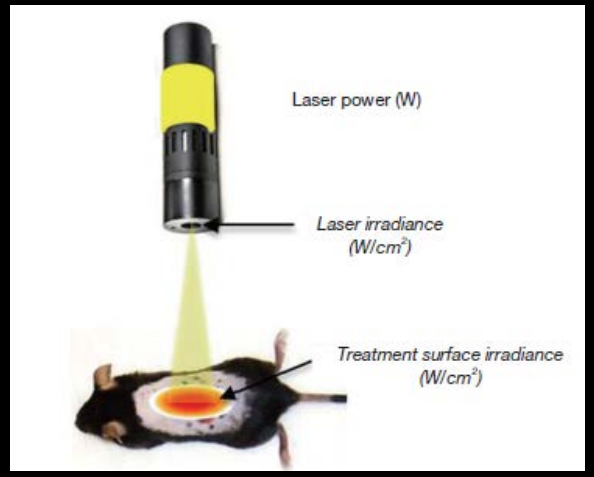
*Model* ☞ *'Context'* **cFIT**
*Concept* ☞ *Pathophysiological state*

Hahm E et al **Phot Las Med** 2012, 30, 9, 507

*Concepts* ☞ *Cumulative dose concept, non-absorption (inelastic Scattering), physical and kinetic barriers*

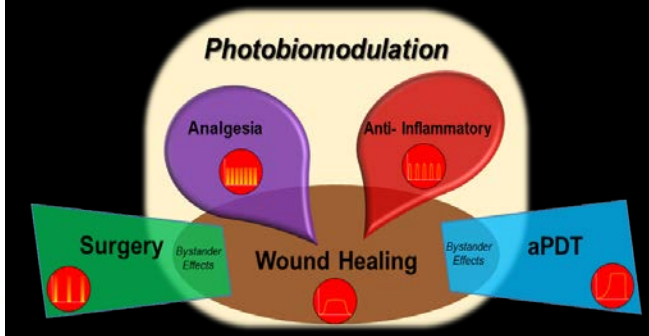
Arany PR **J Dent Res** 2016, 95, 9, 977-984.

# Summary: Evolution of PBM Dose & Delivery protocols in Arany lab

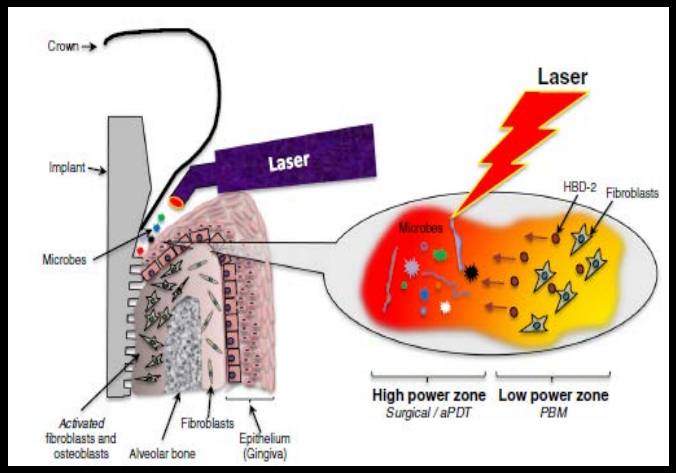



Khan I and Arany PR **Arch Transl Med** 2016, 4, 10, 208.

*Concepts ☞ Target Surface Irradiance*

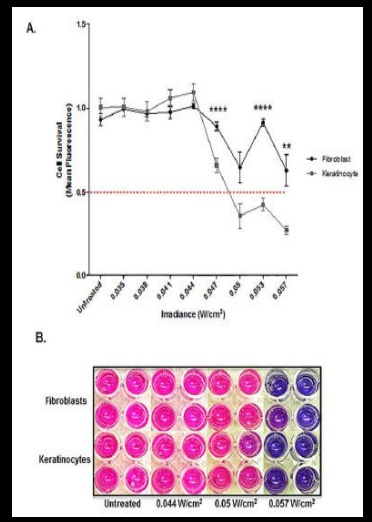


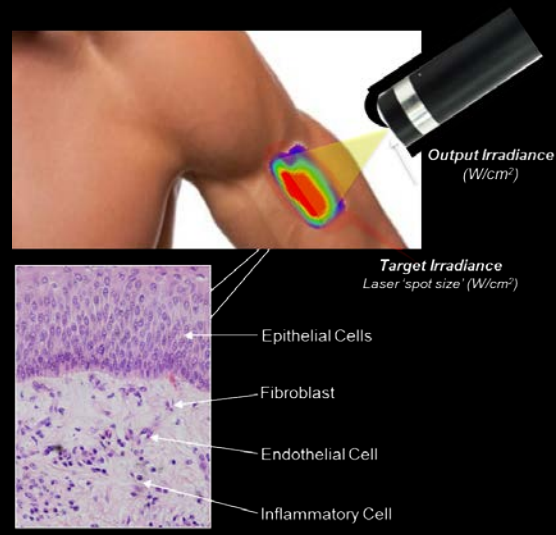

Arany PR **J Dent Res** 2016, 95, 9, 977-984




Tang E et al **J Perio** 2016, 52(3):360-367

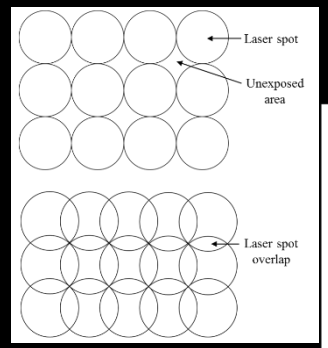
*Concepts ☞ Bystander / episcopal effects*

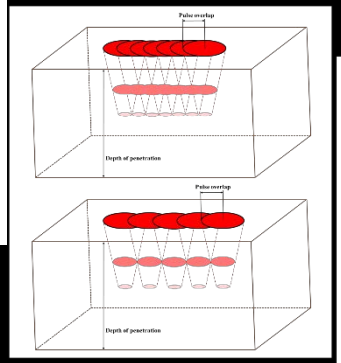


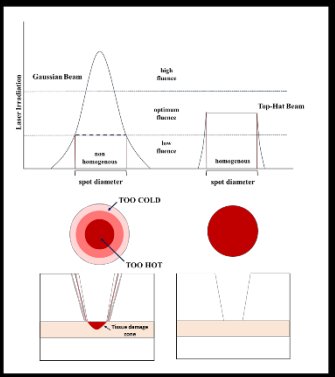




Engel K et al **J Biophot** 2016, 1-9.

*Concepts ☞ Cell lineage specificity*






Rahman SU et al **Oral DisRes** 2018, 24, 1, 261-276

*Concepts ☞ Delivery scanning patterns = 'Biological' pulsing*

# The way we think of PBM *dose*….

$$\frac{\partial TGF}{\partial t} = D_{TGF}\nabla^2(TGF) + f_{TGF}(t) - r_{TGF}(TGF) - k_{on,TGF}(TGF)(abTGF) + k_{off,TGF}(TGFcomplex)$$

$$\frac{\partial abTGF}{\partial t} = D_{abTGF}\nabla^2(abTGF) + f_{abTGF}(t) - r_{abTGF}(abTGF) - k_{on,abTGF}(TGF)(abTGF) + k_{off,abTGF}(TGFcomplex)$$

$$\frac{\partial (TGFcomplex)}{\partial t} = D_{TGFcomplex}\nabla^2(TGFcomplex) - r_{TGFcomplex}(TGFcomplex) + k_{on,TGFcomplex}(TGF)(abTGF) - k_{off,TGFcomplex}(TGFcomplex)$$

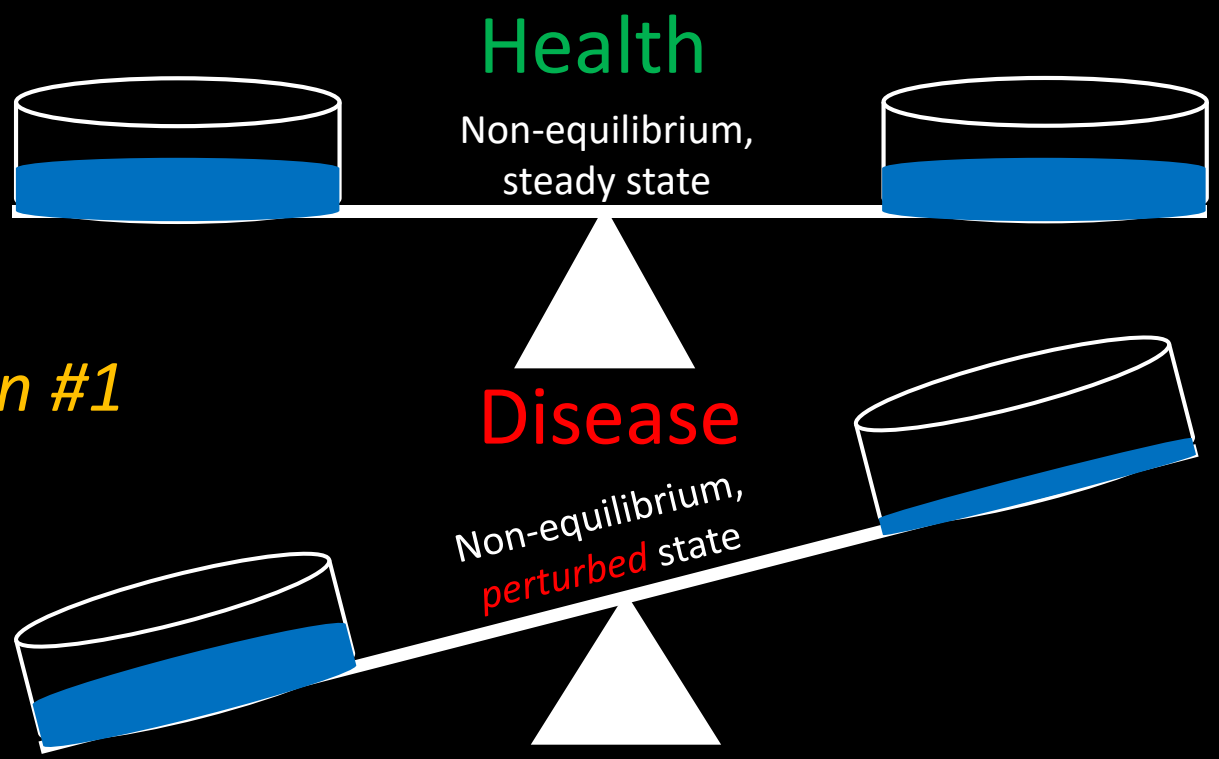
$$\frac{\partial BMP}{\partial t} = D_{BMP}\nabla^2(BMP) + f_{BMP}(t) - r_{BMP}(BMP) - k_{on,BMP}(BMP)(abBMP) + k_{off,BMP}(BMPcomplex)$$

Mathematical approach……

Illustrative approach……

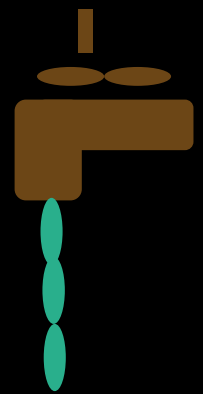
# PBM DOSE MODELS:

*Is PBM dosing a simple energy transfer problem?*




*Assumption #1*

*Assumption #2*



Water ☛ Energy

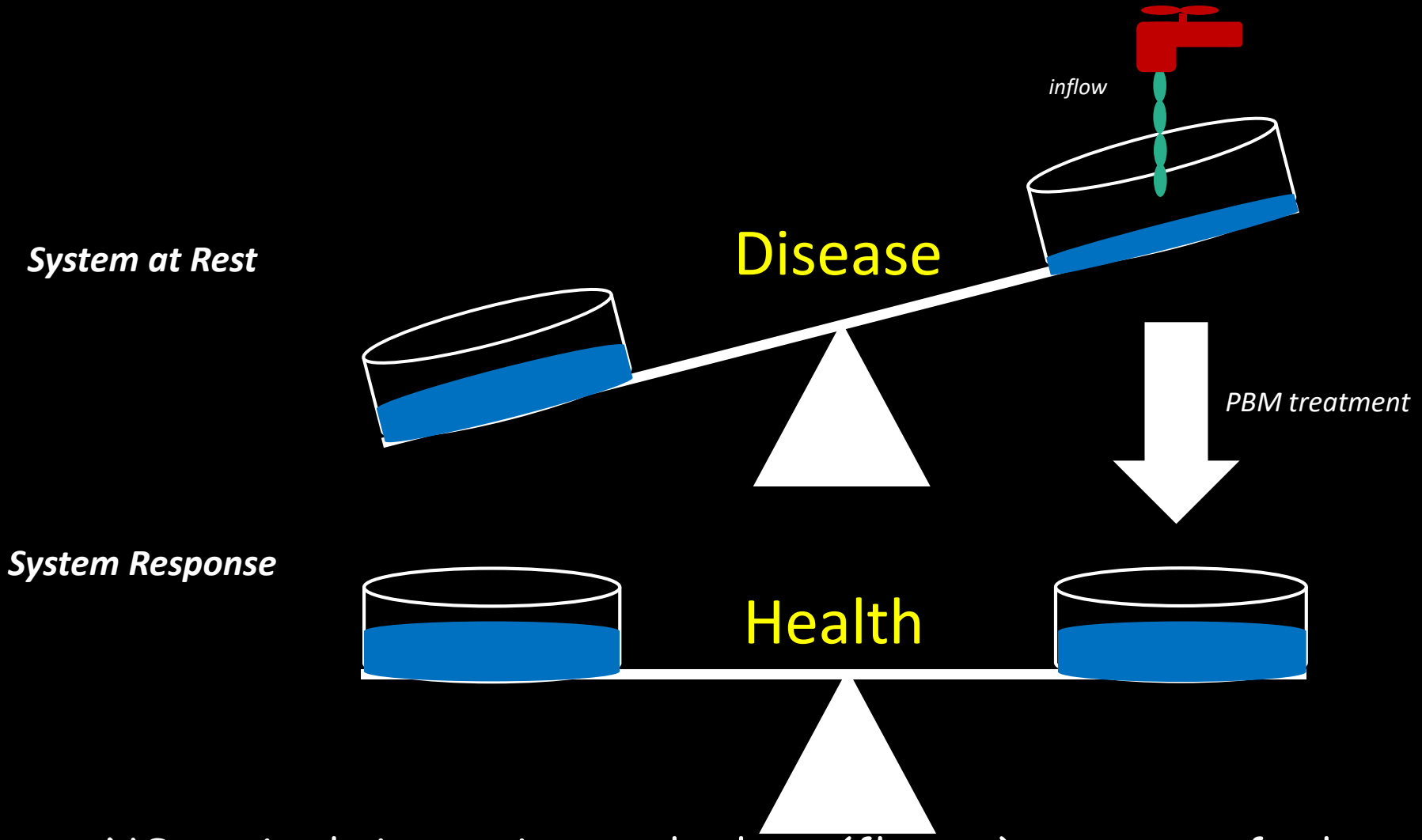
Rate = Irradiance ($W/cm^2$)

Amount = Fluence ($J/cm^2$)

Arany PR **J Dent Res 2016,** 95, 9, 977-984

# #1. Balanced Bucket Model

## Is Fluence (J/cm$^2$) sufficient to predict PBM outcome?



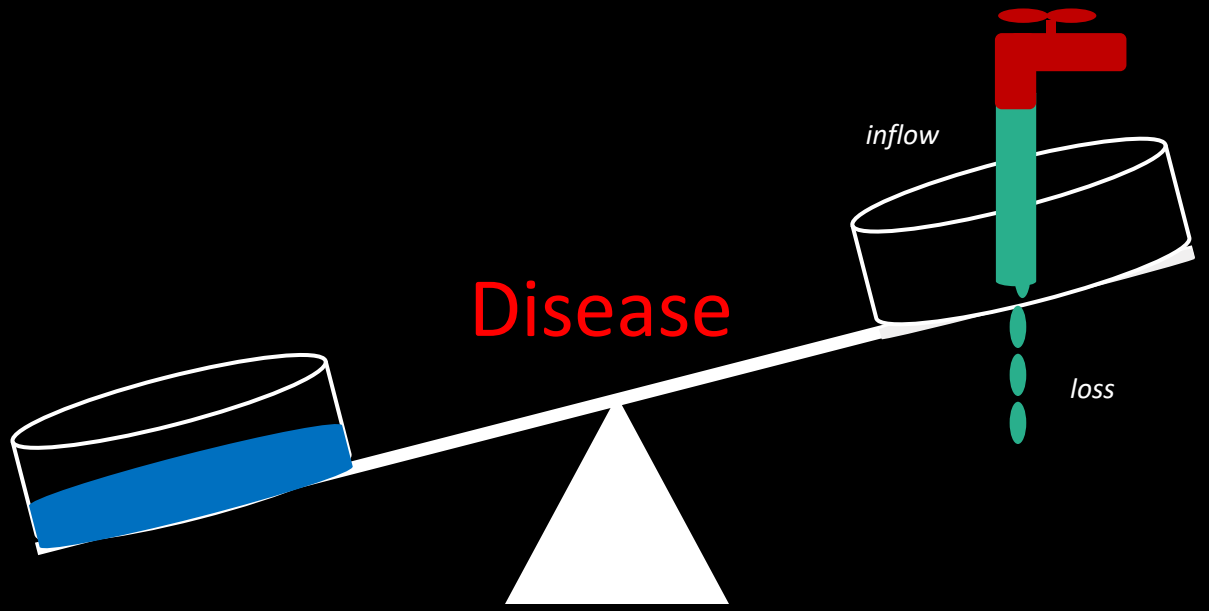

NO as simply increasing total volume (fluence) to account for loss does not reliably predict treatment response due to 'leakiness'.

Arany PR **J Dent Res 2016,** 95, 9, 977-984

# #2. *Leaky* Balanced Bucket Model?

## *Threshold Dose model* - Both Fluence (J/cm$^2$) & Irradiance (W/cm$^2$)

*'Treatments based on fluence & irradiance '*




Increasing rate of flow (irradiance) to account for 'loss' in system does still NOT predictably result in consistent, reproducible PBM treatment responses.

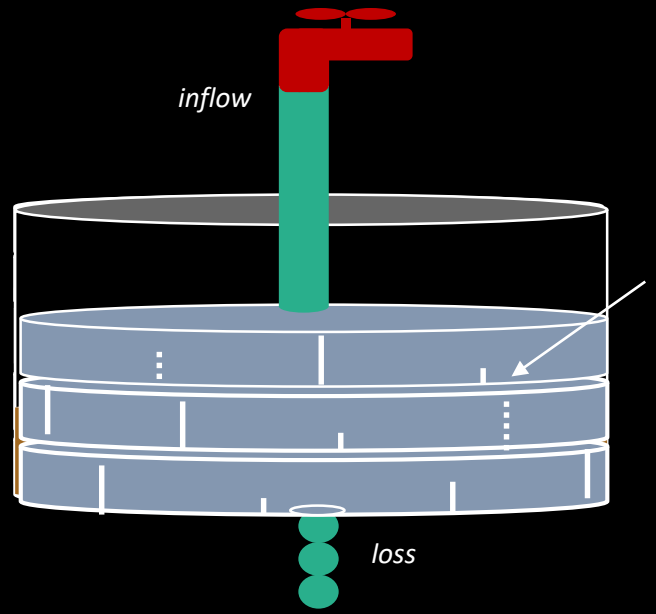
In this approach, we noted increased potential for thermal damage.

Arany PR **J Dent Res 2016,** 95, 9, 977-984

# #3. Modular-Leaky-Balanced Bucket Model

***Cumulative Dose* - Fluence** J/cm$^2$ **+ Irradiance** W/cm$^2$ **+ Time** *Sec*

***+ Time***




*Modularity:*
*due to anatomical compartments, reaction constants, diffusion barriers, presence of promoter (catalysts) or inhibitors*

Adequate time of treatment allows to overcome internal 'barriers / constraints' that can be both anatomical (spatial) and kinetic (biochemical or diffusion limited).

While an optimal maximal treatment time is not yet defined, a minimum of 30sec treatments in specific contexts has been identified.

We have observed that accounting for all three parameters appear to be critical to evoke consistent, reproducible treatment response.

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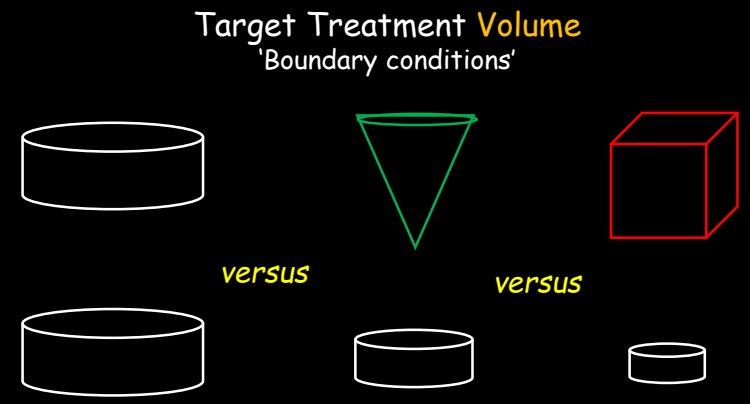
# But also, the Clinical Context…

These clinical conditions will require specific dose adjustments.

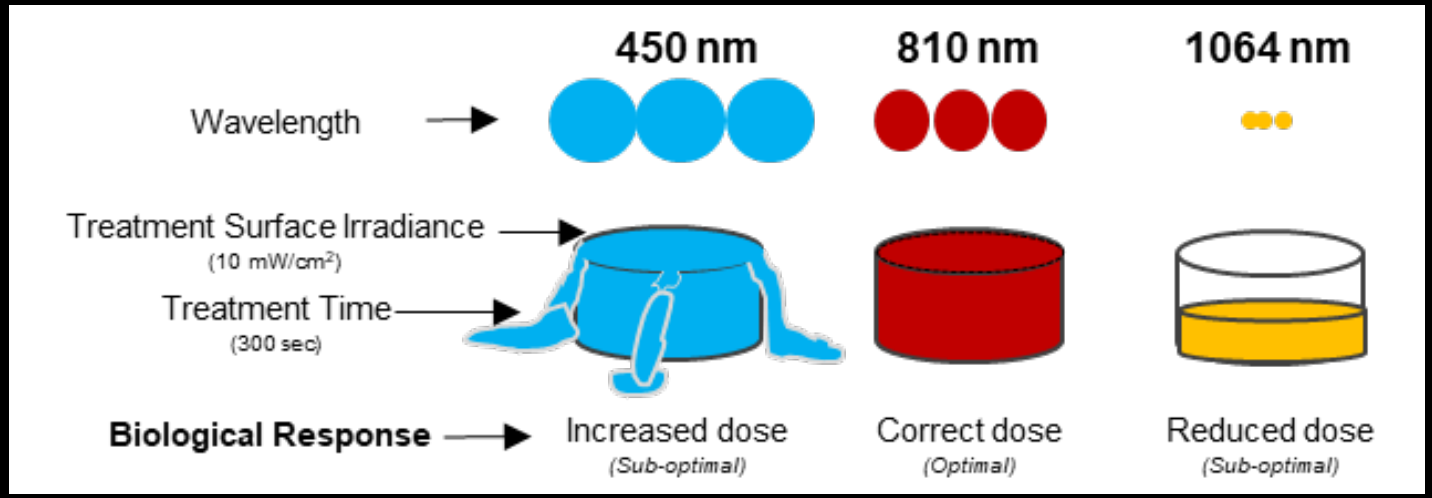




| LASER / LIGHT | ABSORPTION |
|---|---|
| RED | ☞ LOW |
| BLUE | ☞ HIGH |
| NEAR-INFRARED | ☞ LOW* |

* Lower absorbance at surface, target layer


☞ *Variable affecting PBM dose must focus on 'productive' interactions and 'boundary' conditions*

# E  uence q..  cm$^2$




| Wavelength (nm) | | q Factor | Adjustment |
|---|---|---|---|
| **Blue** | **(400-499 nm)** | **1.8** | *80% less* |
| **Green** | **(500-599 nm)** | **1.5** | *50% less* |
| **Yellow** | **(600-699 nm)** | **1.3** | *30 % less* |
| **Red** | **(700-799 nm)** | **1.1** | *10% less* |
| **Near Infrared** | (800-899 nm) | **1** | ***Einstein*** |
| **Near Infrared** | (900-999 nm) | **0.9** | *10% more** |
| **Near Infrared** | (1000-1100 nm) | **0.8** | *20% more** |
| **Near Infrared** | (1100-1200 nm) | **0.7** | *30% more** |

** Must not increase surface temperature above 45 °C*

Arany *2022* under review

Arany, Bensadoun, WALT *2022* in preparation

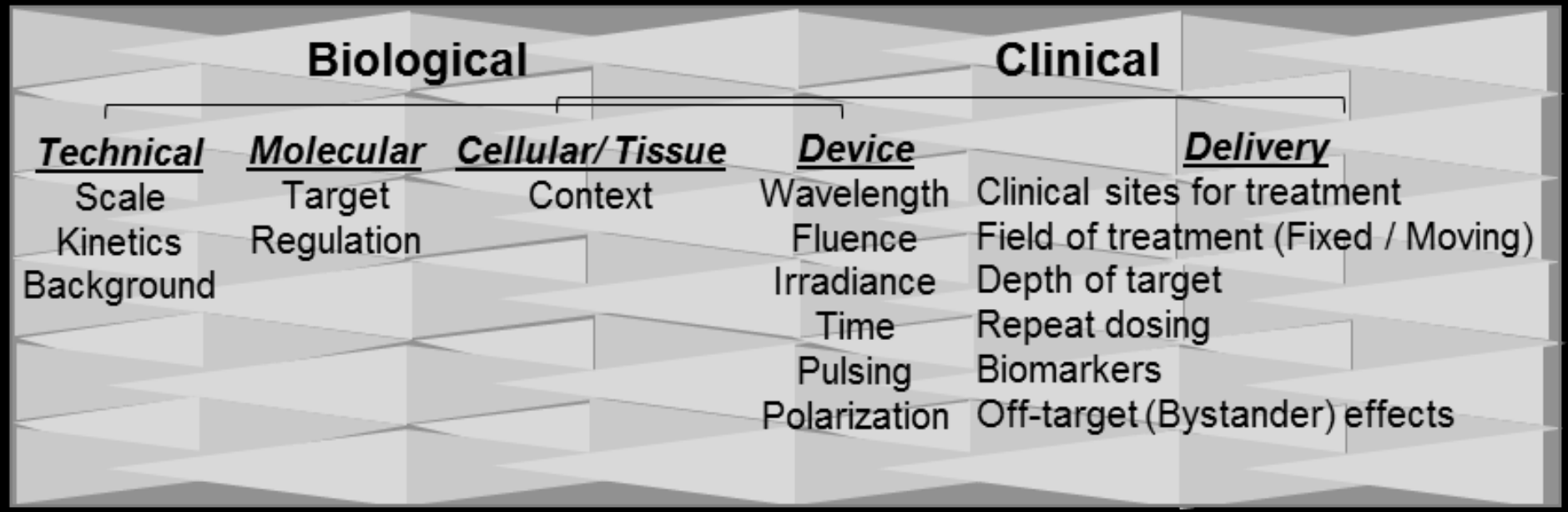
Young et *al 2022 JBiophot*

# Can light be a drug?

## Yes, A *photoceutical* approach for PBM Therapy

*Photokinetics* *(Pharmacokinetics)*
'What body does to the light (drug)'

*Photodynamics* *(Pharmacodynamics)*
'What light (drug) does to the body'




Arany PR *J Dent Res* 2016

COMMITTEE ON
# SCIENCE, SPACE, & TECHNOLOGY
Lamar Smith, Chairman

Oct 11th 2018,
Washington DC


**HR6, Public Law 115-271** that mandates examination of current evidences (clinical practice guidelines, insurance), further research and funding on ***alternative pain treatments***……

# MULTI RADIANCE MEDICAL THERAPEUTIC LASER RECEIVES FDA CLEARANCE FOR THE TREATMENT OF PAIN ASSOCIATED WITH FIBROMYALGIA

Solon, OHIO – Multi Radiance Medical (MRM) has become the first laser therapy manufacturer to receive FDA clearance to treat pain associated with fibromyalgia.

The American College of Rheumatology defines fibromyalgia as chronic widespread pain and tenderness in specific tender points characterized by muscular tenderness, pain, fatigue, and cognitive difficulties. With no known cause or cure, fibromyalgia is usually treated with prescription medications; however, they only provide relief for approximately 10% of patients who use them.

Through a photoceutical approach to care, the new patent pending MRM FibroLux therapy laser represents a breakthrough in pain management options, offering patients a non-pharmacological, non-invasive, and side effect-free treatment for fibromyalgia that is now cleared by the FDA. Like pharmaceuticals, photoceutical devices are validated through clinical studies and deliver optimal doses of light energy using a combination of curated wavelengths, administered at the correct dose (time and power), and the ideal dosage (frequency of application) resulting in consistent, reproducible outcomes.

# Questions?

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