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Systematic Review of Post-Surgical Laser-Assisted Oral Soft Tissue Outcomes Using Surgical Wavelengths Outside the 650–1350 nm Optical Window

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Abstract

Objective: To explore via systematic review the validation of uneventful post-surgical healing, associated with shorter and longer laser wavelength applications in minor oral surgery procedures.

Methods: From April 28 to May 11, 2020, PubMed, Cochrane Database of Systemic Reviews, and Google Scholar search engines were applied to identify human clinical trials of photobiomodulation (PBM) therapy in clinical dentistry. The searches were carried out with reference to (1) dental laser wavelengths shorter than 650 nm; (2) wavelengths localized within the 2780–2940 nm; and (3) the 9300–10,600 nm range. Selected articles were further assessed by three independent reviewers for strict compliance with PRISMA guidelines and modified Cochrane Risk of Bias to determine eligibility.

Results: Using selection filters of randomized clinical trials, moderate/low risk of bias, and the applied period, and following PRISMA guidelines, 25 articles were selected and examined. A risk of bias was completed, where 11 out of 25 publications were classified as low risk of bias, and 14 out of 25 were classified as medium risk status. In total, 6 out of 13 (46% of) studies comparing the examined laser wavelengths with scalpel-based treatment showed positive results, whereas 6 out of 13 (46%) showed no difference, and only 1 out of 13 (7.7%) presented a negative outcome. In addition, 5 out of 6 (83% of) studies comparing the examined laser wavelengths with other diodes (808–980 nm) showed positive results, whereas 1 out of 6 (17%) had negative outcomes.

Conclusions: A detailed and blinded examination of published studies has been undertaken, applying strict criteria to demonstrate research outcome data, which suggests positive or at worst neutral comparatives when a given laser wavelength system is used against an alternative control therapy. As such, substantiated evidence for laser surgery in delivering uneventful healing and analgesic effects, as an expression of a PBM-like (quasi-PBM) influence, has been shown.

Keywords: laser, oral, soft tissue, healing, photobiomodulation, optical window

Introduction

BY CONVENTION, PHOTOBIMODULATION (PBM) involves the manipulation of cellular behavior by using low-intensity light sources. Originally referred to as Low Level Laser Therapy,¹ this was superseded by the Medical Subject Heading (MeSH) term “PBM” in 2015.² PBM has been developed from a concept to received evidence-based accreditation through considerable research efforts. As a

phenomenon, PBM therapy has been found to be beneficial in its effects toward cellular, local tissue, systemic, and biochemical processes, and it can significantly contribute as an adjunct in the resolution of pain and inflammation, together with the treatment of the pathophysiological processes of disease³; as such, it may be considered an attribute in achieving the delivery of “uneventful healing” that accompanies post-surgical, oral soft tissue laser therapy in clinical dentistry.⁴

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During soft tissue laser surgical therapy, attenuation of the incoming photonic energy at deeper and distant areas may be viewed as a function of the incident wavelength relative to the absorption and scattering coefficients and tissue anisotropy, along with other factors, including the temperature of irradiated tissues.^{5,6} At a distance from the site of tissue ablation, and along a combined thermal and scatter gradient, the reduction in applied laser fluence may deliver sub-ablative photonic energy density; with absorption by tissue components, a modulation process ensues, with examples of enhanced cellular activity, increased local vascular and lymphatic circulation, and analgesic effects that, combined, can promote a positive and advantageous healing process. The latter represents a combination of direct suppression of an inflammatory cascade, in addition to the facilitated optimization of conditions that are conducive to cellular repair and regeneration phenomena.⁷⁻⁹

Through an “assumed” convention, the capacity of a relatively narrow bandwidth of visible and near infra-red (NIR) wavelengths to deliver tissue penetration and photon scatter has been denoted as the “optical window,” with emissions ranging from ~650 to 1350 nm.¹⁰⁻¹³ The NIR optical window may be computed from the absorption coefficient spectrum expressed relative to that of target tissue components.¹⁴ The length of the optical pathway may be viewed as a function of multiple factors, including the refractive index of the tissue medium, the angle of incidence, and the wavelength itself, as well as parameters such as irradiance, surface spot size, and optical beam profile.

Hence, some questions remain regarding accountability for the degree of uneventful healing that may accompany surgical procedures when using laser wavelengths that are outside or remote from this optical window bandwidth.

This systematic review sets out to evaluate published articles related to para-surgical, post-surgical, and healing outcomes of dental laser applications whose emission wavelengths are shorter and longer than the optical window (650–1350 nm) range. Prime criteria applied are randomized controlled human studies during a 10-year period that conform to an acceptable risk of bias, and they also represent post-surgical outcomes that have been independently evaluated by three of the review authors.

Materials and Methods

During the period April 28 to May 11, 2020, an electronic literature search was conducted through the search engines PubMed, Cochrane Database of Systematic Reviews, and Google Scholar. The applied keywords and their combinations were as follows:

(CO₂ OR carbon dioxide OR erbium OR Er:YAG OR Er,Cr:YSGG OR green OR KTP OR blue OR 445 OR 450 OR 532 OR visible) AND laser AND (soft tissue OR oral surgery OR lip OR tongue OR buccal mucosa OR granuloma OR gingivectomy OR biopsy OR leukoplakia OR lichen OR ankyloglossia OR frenectomy OR fibroma OR mucocoele OR ranula OR gingiva hyperpigmentation OR gingiva depigmentation OR implant recovery OR second stage surgery).

In addition, the following MeSH Terms were employed: surgery, oral; lasers; ankyloglossia; gingiva; tongue; granuloma; ranula; mucocoele; mouth mucosa; biopsy; leukoplakia;

gingivectomy; fibroma; oral surgical procedures; erbium; lip; hyperpigmentation; carbon dioxide; lichen; and sub-heading: pathology.

From this, it could be arrived at that 8378 articles were first indicated before limitation to clinical, humans, 10 years, and from peer-reviewed journals in the English language only. After application of these selection criteria, this total number was reduced to 282 articles.

After removal of pilot studies, no clinical trials, *in vitro* studies, other medical fields (e.g., dermatology, general surgery), non-surgical dental fields [e.g., periodontology, endodontics, antimicrobial photodynamic therapy (aPDT)], three independent reviewers further reduced the total to 58 articles. After removal of duplicates, 46 articles remained thereafter.

These articles were subject to full-text evaluation; studies with small sample sizes (<10 patients), no control group, case series, animal studies, and literature reviews were removed. From 31 articles, non-randomized controlled trials were excluded, a process further reducing the final number of eligible articles to 25. Within this final number, 4 articles were related to the use of “blue/green” (445–532 nm), 12 related to a mid-IR group (2780–2940 nm), and 9 articles to a far-IR (9300–10,600 nm) group of wavelengths.

Within this number and range, the following inclusion and exclusion criteria were then strictly represented:

Inclusion criteria:

- laser wavelength outside the “optical window” (650–1350 nm) used as a light source;
- only randomized controlled clinical trials;
- ≥10 samples/participants per group;
- an applicable “control” group.

Exclusion criteria:

- dermal and/or general medical applications;
- duplicates or studies with the same ethical approval number;
- no control group;
- no randomized controlled clinical trials or pilot studies;
- low sample sizes.

In accordance with the PRISMA statement,¹⁵ details of the selection criteria are presented in Fig. 1.

Data extraction

Having reached an agreement regarding the selection of included articles, the three reviewers involved subsequently and independently extracted data regarding:

- Citation (first author and publication year);
- Test/control groups;
- Type of study/number of patients;
- Aim of study;
- Examined parameters;
- Laser parameters;
- Follow-up;
- Outcomes.

Quality assessment

During data extraction, the reliability and validity of the included articles were further evaluated by assessing their risk of bias adhering to the PRISMA statement.¹⁵ The

Identification

Screening

Eligibility

Included

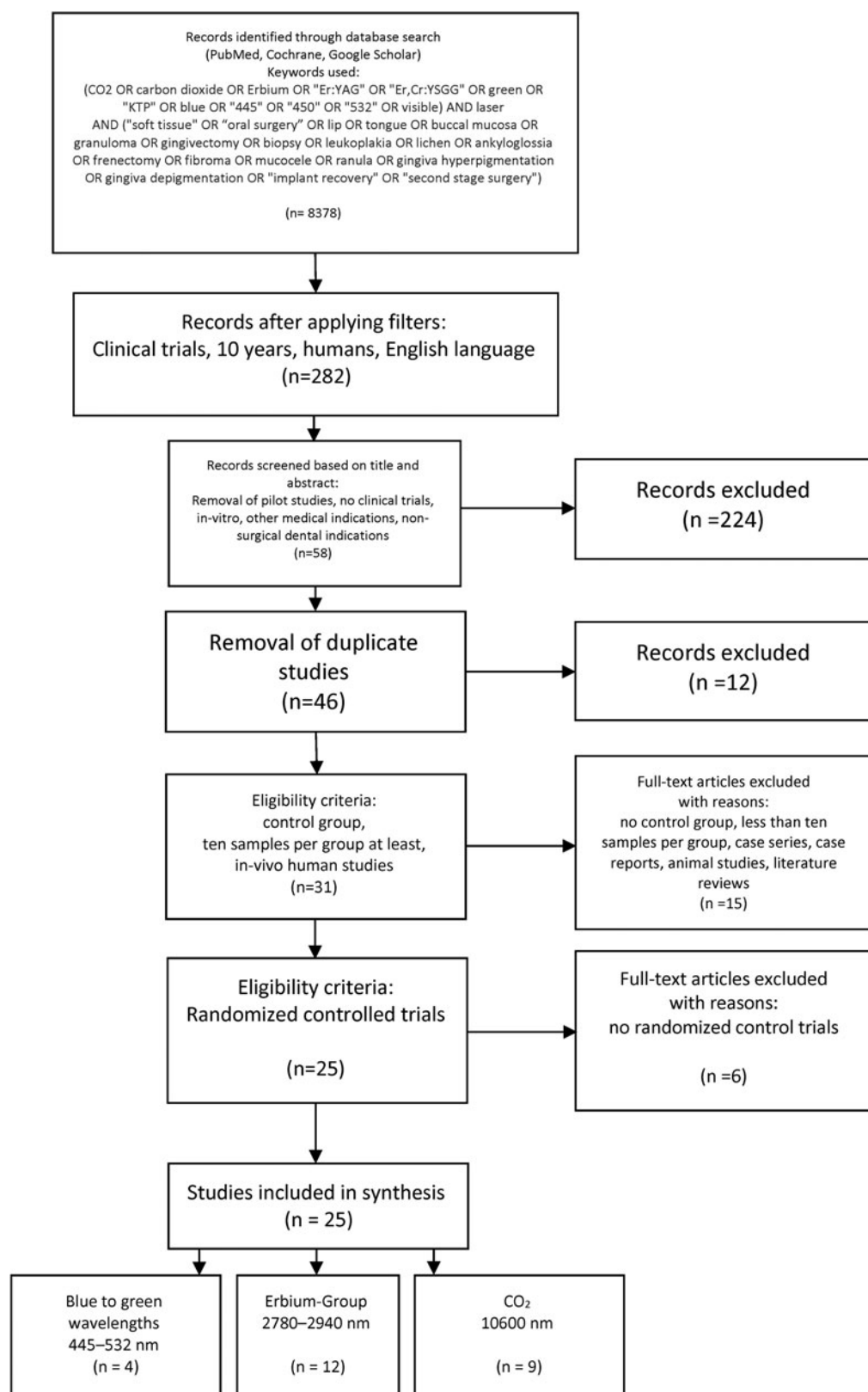


FIG. 1. PRISMA diagram of articles selected.

Cochrane Risk of Bias tool¹⁶ was modified according to the requirements of this systematic review.

The risk of bias was determined according to the number of “yes” or “no” responses to the parameters provided next, which were allocated to each study:

- Sufficient randomization?
- Sample size calculation and required sample numbers included?
- Baseline situation similar to that of the test group?
- Existence of blinding?
- Parameters of laser use described appropriately and correctly?
- Power meter used?
- Numerical results available (statistics)?
- No missing outcome data?
- All samples/patients completed the follow-up evaluation?
- Correct interpretation of data acquired?

The classification was performed according to the total number of “yes” answers to the questions just cited. For the current study, the degree of bias was computed according to the score limits provided next:

High risk: 0–4; moderate risk: 5–7; low risk: 8–10.

Results

Primary outcome

The primary goal of this systematic review was to critically appraise the treatment outcome regarding indices of healing and pain after oral soft tissue surgeries performed by laser wavelengths outside the 650–1350 nm optical window selection criterion.

Data presentation

The results related to combined Blue/Green and CO₂ wavelengths are grouped to recognize the similar inherent continuous wave (CW) emission modes. Details of each study are shown in Tables 1 and 2.

Information acquired related to the erbium chromium YSGG and erbium YAG (free running pulsed [FRP] emission mode) is shown in Tables 3 and 4.

Quality assessment presentation

The risk of bias of the included studies is presented in Table 5. In consideration of the factors determined by the authors to indicate scientific rigor, the risk was valued as high risk: 0–4; moderate risk: 5–7; low risk: 8–10.

In total, 11 out of 25 (44% of) articles showed a low risk of bias with the following gradings:

- 9/10 score—3 articles^{24,24,26} (Ref.²⁴ in Erbium and CO₂ groups)
- 8/10 score—8 articles^{17,21,25,29,30,33,35,36}

Overall, 14 out of 25 (56%) articles, respectively, showed a medium risk of bias with the following gradings:

- 7/10 score—6 articles^{22,23,27,31,34,38}
- 6/10 score—6 articles^{18,19,32,37,39,40}
- 5/10 score—2 articles^{20,28}

As far as the risk factor that gained the most common negative answers, the use of a power meter was recorded in only one of the studies, and only five of them performed sample size calculation and included the required number of participants. Regarding the correct and complete description of the laser protocol applied, 15 out of 25 studies had indicated it appropriately.

Analysis of data

Analysis of the studies was performed to evaluate the treatment outcome per each wavelength, with reference to the respective control group:

- Blue (445 nm) compared with:
Diodes (808 and 970 nm): 2/2 positive^{17,18}
- Green (532 nm) compared with:
Diode 980 nm: 1/1 positive for the first 14 days¹⁹
532 nm+hyaluronic acid compound: 1/1 negative in healing, and no difference in pain²⁰
- Erbium (2940 or 2780 nm) compared with:
Scalpel: 3/7 positive,^{24,26,29} 4/7 no difference^{22,23,27,30}
Diodes (808, 810 and 980 nm): 2/3 positive,^{21,32} 1/3 negative²⁸
CO₂ (10,600 nm): 1/2 positive,²⁴ 1/2 no difference²⁵
- CO₂ (10,600 nm) compared with:
Scalpel: 3/6 positive,^{24,37,38} 2/6 no difference,^{34,39} 1/6 negative³⁵
Low level laser therapy (LLLT) (890 and 633 nm): 1/1 negative⁴⁰
CW versus gated mode: 2/2 no difference^{33,36}

In total, 6 out of 13 (46% of) studies comparing laser wavelengths with scalpel treatment showed positive results, whereas 6 out of 13 (46%) reported no difference and only 1 out of 13 (8%) presented negative outcomes.

In addition, 5 out of 6 (83% of) studies comparing laser wavelengths with other diodes (808–980 nm) showed positive results, whereas 1 out of 6 (17%) had negative outcomes.

Regarding the laser protocol applied, 10 out of 25 (40%) articles reported an incomplete laser parameter description.^{19,20,22,27,28,32,34,37,38,40} The deficiencies concerned the following parameters:

- Average Power delivered: 1/10 articles³⁸
- Tip or spot size: 5/10 articles^{28,34,37,38,40}
- Gated/pulsed frequency: 3/10 articles^{28,34,37}
- Fluence/irradiance (either missing or wrongly calculated): 6/10 articles^{20,28,34,37,38,40}
- Total energy delivered: 8/10 articles^{20,22,28,32,34,37,38,40}
- Tip-to-tissue distance: 7/10 articles^{19,20,27,28,34,38,40}
- Gated/pulse duration: 3/10 articles^{19,20,22}
- Irradiation time: 7/10 articles.^{27,28,32,34,37,38,40}

Discussion

This systematic review has applied strict evaluation and risk-of-bias criteria to identify the quality and quantity of outcomes from laser-assisted oral soft tissue surgery, and to explore those outcomes that might be interpreted as examples of non-ablated tissue PBM effects.

It was noted that the specifics of laser parametry and energy delivered was unclear in many of the articles examined. Similar deficiencies were found in the selected articles

TABLE 1. PUBLISHED ARTICLES IDENTIFIED FROM A REVIEW OF THE LITERATURE REGARDING THE HEALING OUTCOME EFFECTS

Citations	Test/control	Study type/patients per group	Aim of study	Examined parameters	Laser operating parameters applied/"dose"	Follow up	Outcome
Blue-green Gobbo et al. ¹⁷	445 nm (1) 970 nm (2) scalpel (3)	RCT/ 39 patients (1) 27 patients (2) 27 patients (3)	Excisional biopsy of benign oral lesions	Pain (VAS) Bleeding Pain killer consumption Biopsy thermal damage (μm)	PP 2 W, t-on 20 ms and t-off 8 ms, AP 1.4 W, 320 μm fiber	30 days	Group 1 compared with both other groups: Pain: sign.diff. at 7 and 14 days ($p < 0.05$) Bleeding: sign.diff. only at day 0 ($p < 0.05$) Pain killer consumption: sign.diff. only at day 7 ($p < 0.05$) Biopsy thermal damage: sign.diff. ($p < 0.05$) 450 nm results similar to 808 nm with no significant difference between them. Er:YAG only significantly improved immediately after treatment (compared with earlier)
Rocca et al. ¹⁸	450 nm (1) 2940 nm (2) 635 nm (3) 808 nm (4)	RCT/ 15 patients (1) 15 patients (2) 15 patients (3) 15 patients (4)	Aphthae management	Recurrent aphthous stomatitis Pain (VAS)	450 nm: AP 0.5 W CW 300 μm fiber, 2 cm distance, scanning mode on area of 1.5 cm diameter, 60 sec irradiance 0.28 W/cm ² , fluence 17 J/cm ² 2940 nm: 50 mJ, 20 Hz, 80 μs pulse, 1.3 mm tip, scanning mode on area of 1 cm diameter, 60 sec fluence 76.43 J/cm ² no air no water	7 days	
Romeo et al. ¹⁹	532 nm	RCT 18 patients laser-only/ 31 patients laser+hyaluronic aminoacid compound	Role of laser+hyaluronic aminoacid compound in surgical biopsies wound healing	PHI NRS	1.5 W CW, 300 μm tip, Fluence of 2123 J/cm ²	7 days	PHI: laser+compound significantly better $p = 0.0447$ NRS: no significant difference $p = 0.77$
Bargiela-Pérez et al. ²⁰	532 nm (1) 980 nm (2)	RCT 532 nm 10 patients 980 nm 10 patients	Resection of benign hyperplastic lesions of the oral mucosa	NRS (1–5) for pain, scarring, inflammation, and consumption of drugs	532 nm 1.5 W CW, 320 μm fiber. PBM post-op 0.5 W, non-contact	28 days	532 nm: pain significantly worse at day 28 ($p = 0.035$) Inflammation significantly worse at day 28 ($p = 0.023$) Scarring and drug consumption no difference No significant differences between groups in any parameters for days 0, 1, and 14

(continued)

TABLE 1. (CONTINUED)

Citations	Test/control	Study type/patients per group	Aim of study	Examined parameters	Laser operating parameters applied/"dose"	Follow up	Outcome
CO ₂ Suter et al. ³³	10,600 nm CW/ 10,600 nm CF	RCT N=60 patients 30 patients CO ₂ CW 30 patients CO ₂ CF mode. Surgical excision of buccal fibroma lesions	Excisional biopsies of fibrous hyperplasia	Time taken, complications, histopathologic collateral damage zones, pain (VAS), analgesics taken	(i) CW 5 W, 200 μ m at 1–2 mm (ii) "Char Free mode" 4.62 W, 140 Hz, 400 μ s pulse, 33 ml, 200 μ m spot, 1–2 mm distance	Pain VAS 3 days, 7 days. Histopathologic evaluation. Follow-up 2 weeks, 1 month	Post-operative complications: no significant difference (p 0.55). Histopathologic collateral damage zones no significant difference. No statistically significant difference between the VAS values. Analgesic intake (p = 0.23, not significant). No statistically significant correlation between TDZs and post-op VAS scores
Hegde et al. ³⁴	10,600/2780 nm/ scalpel	Split-mouth RCT. N = 35 patients (140 sites: 10,600 nm 35 sites, 2780 nm 35 sites, surgical stripping 70 sites)	Gingival depigmentation	Pain, change in DOPI, Hedin index, and change in area of pigmentation from baseline to 6 months	CO ₂ 2–4 W CW, non-contact, defocused	1-, 3-, 6-month post-op.	Comparison of microscopic evaluation, VAS, and DOPI No significant differences between groups in re-pigmentation, changes in area of pigmentation, and changes in histologic parameters

Blue/green and CO₂.^{17–20,33,34}

AP, average power; CF, char-free mode; CW, continuous wave; DOPI, Dummett oral pigmentation index; NRS, numeric rating scale; PBM, photobiomodulation; PHI, percentage healing index; PP, peak power; RCT, randomized clinical trial; TDZ, thermal damage zone; VAS, visual analogue scale.

TABLE 2. PUBLISHED ARTICLES IDENTIFIED FROM A REVIEW OF THE LITERATURE REGARDING THE HEALING OUTCOME EFFECTS

Citations	Test/control	Study type/patients per group	Aim of study	Examined parameters	Laser operating parameters applied/"dose"	Follow-up	Outcome
CO ₂ Monteiro et al. ³⁵	10,600 nm multi λ lasers, scalpel, electrocauter	RCT. <i>N</i> = 130 patients 27 CO ₂ (6 Gps—electroscalpel, cold scalpel, diode, Nd:YAG, Er:YAG and CO ₂).	Excision of oral fibrous-epithelial lesions	Changes in histological mix of tissue, thermal extension, and degree of carbonization	4.0 W, 50 mJ, 80 Hz 500 μ m spot, focused, Fluence 40.8 J/cm ² power density 2040.8 W/cm ²	Histological study, no follow-up	CO ₂ moderate improvement over scalpel. Most regular incisions among the lasers (<i>p</i> = 0.001)
Suter et al. ³⁶	10,600 nm (CW gated/CF pulsed)	RCT. <i>N</i> = 100 49 patients CO ₂ CW 51 patients CO ₂ CF mode. Surgical excision of buccal fibroma lesions	Excision of oral fibrous hyperplasia	Post-op pain (2 weeks) VAS, analgesics, and post-op compl'n's, max. width of collateral thermal damage (mm) in excised tissue	(i) CW 5 W, 200 μ m at 1–2 mm. (ii) "Char free mode" 4.62 W, 140 Hz, 400 μ s pulse, 33 mJ, 200 μ m spot, 1–2 mm distance	6 months. 78 re-attended 22 FTA	No significant differences between groups in post-operative pain VAS, complications, intraoperative bleeding, or thermal damage. More analgesics intake (<i>p</i> = 0.04) in CW group More scars with CF (<i>p</i> = 0.03).
Suter et al. ²⁴	10,600 nm/erbium YAG/scalpel	RCT <i>n</i> = 75 lesions. CO ₂ 25 patients/2940 nm 25 patients/Scalpel 25 patients. Blinding. Sample size calculation Baseline similar	Excisional biopsies of fibrous hyperplasia	Duration, intra-op bleeding, need for post-op pain, post-op complications, need for analgesics, VAS, and TDZ	"Char Free mode" 4.62 W, 140 Hz, 400 μ s pulse, 33 mJ, 200 μ m spot, 1–2 mm distance	3, 7, 15 days, 6 months	CO ₂ -group: duration significantly less than scalpel control (<i>p</i> < 0.001), bleeding sign less than in scalpel group (<i>p</i> < 0.001). Need for sutures sign lower (<i>p</i> < 0.001). Intra-op bleeding, Post-op pain, post-op complications, need for analgesics VAS: no significant differences TDZ significantly higher in CO ₂ group (<i>p</i> < 0.001) compared with 2940 nm

(continued)

TABLE 2. (CONTINUED)

Citations	Test/control	Study type/patients per group	Aim of study	Examined parameters	Laser operating parameters applied/"dose"	Follow-up	Outcome
López-Jornet et al. ³⁷	10,600 nm cf cold knife	RCT. 10,600 nm (20 patients) cold knife (28 patients)	Excision of oral leukoplakia	VAS for pain VAS for swelling	5–15 W CW, 15 mm distance, defocused, 5–15 sec	7 days	CO ₂ group significant difference in pain and swelling, respectively: 12 h ($p=0.001$, $p<0.001$), 1 days ($p=0.001$, $p=0.008$), 2 days ($p=0.003$, $p=0.007$), 3 days ($p=0.029$, $p=0.019$) 10,600 nm group significantly better in: blood loss and need for bipolar cautery ($p<0.05$) intraoperative margins ($p=0.03$) No difference in operation time 10,600 nm group: less surgery time ($p=0.002$) less bleeding ($p<0.001$) more vestibular depth (medial $p=0.076$ /middle $p=0.018$ /lateral $p=0.005$) less re-epithelialization at day 7 ($p=0.021$), no difference at day 14 ($p=0.18$) edema no difference ($p=0$) 10,600 nm group significantly worse at all time intervals in all examined parameters ($p<0.05$)
Chee et al. ³⁸	10,600 nm cf scalpel	RCT. 10,600 nm (24 procedures) scalpel (23 procedures)	Excision of oral leukoplakia	Time, blood loss, bipolar cautery use, and intraoperative margins needed	10 W CW	Ongoing	
Karimi et al. ³⁹	10,600 nm cf scalpel	RCT split-mouth (19 patients)	Excision of epulis fissuratum	Time, bleeding, vestibular depth, re-epithelialization, and edema	AP 6.2 W, 50 Hz, pulse duration 3 ms, 0.7 mm spot, focused	7, 14 days	
Agha-Hosseini et al. ⁴⁰	10,600 nm cf LLLT (890+633 nm)	RCT 10,600 nm (13 patients with 27 lesions) LLLT (15 patients with 30 lesions)	Treatment of oral lichen planus	Lesion size (scaled tongue blade) Pain (VAS) Clinical sign (Thongprasom)	3 W, defocused	2 weeks, and at 1, 2 and 3 months	

CO₂.^{35–40}

FTA, failed to afford; Gps, groups; LLLT, low level laser therapy.

TABLE 3. PUBLISHED ARTICLES IDENTIFIED FROM A REVIEW OF THE LITERATURE REGARDING THE HEALING OUTCOME EFFECTS OF MID-INFRA-RED SURGICAL LASER USE

Citations	Test/control	Study type/patients per group	Aim of study	Examined parameters	Laser operating parameters applied/"dose"	Follow up	Outcome
Er:Cr:YSGG Er:YAG Giannelli et al. ²¹	2940/810 nm	Split-mouth RCT. <i>n</i> = 21 1 Q 2940 nm/1 Q 810 nm	Gingival depigmentation	Wound healing, bleeding, pain on a scale 0–3 Histology of 13 samples	2940 nm, 100 mJ 10 Hz, 400 μ s pulse width, 1.0 W AP, 800 μ m tip, in contact, 2.5 mm/s, Fluence 50 J/cm ²	7, 30, 180 days	Pain during treatment <i>p</i> < 0.005, on day of treatment <i>p</i> < 0.001, and until day 7 <i>p</i> < 0.001 significantly higher in 2940 nm group. Healing time and bleeding significantly higher in 2940 nm group, <i>p</i> < 0.001
Alhabashneh et al. ²²	2940 nm/scalpel	Split-mouth blinded prospective clinical trial 20 patients	Gingival depigmentation	DOPI, HMI, hemostasis, time, pain (NRS), Wound healing (degree of epithelialization), tx time, level of satisfaction	1.0 W AP, 800 μ m tip, 5 mm distance, brush stroke movement, 50% air/water	1, 2 weeks, 1, 3, and 6 months	DOPI, HMI, tx time, pain, degree of epithelialization, patient preference, and satisfaction with non-significant differences at any timepoint. Bleeding statistically significant higher in scalp group <i>p</i> < 0.001
Ipek et al. ²³	2940 nm/Kirkland knife	Split-mouth RCT 20 patients	Gingival depigmentation	Tissue injury and inflammation by osmotic pressure changes (OP), pain (VAS)	2 W AP, 200 mJ, 10 Hz, 1000 μ s pulse, 1300 μ m tip at 1 mm. Brush technique	2, 8 h, daily until day 7	Test group significantly better in: VAS 2 h (<i>p</i> < 0.001), 8 h (<i>p</i> < 0.001), 1 day (<i>p</i> < 0.05), 2 days (<i>p</i> < 0.05) OP: no statistical differences between groups
Suter et al. ²⁴	2940 nm/CO ₂ /scalpel	RCT <i>n</i> = 75 2940 nm 25 patients/CO ₂ 25 patients/scalpel 25 patients	Excisional biopsies of fibrous hyperplasias	Duration, intra-op bleeding, need for bleeding control, post-op pain, post-op complications, need for analgesics, VAS, TDZ	7 W AP, 200 mJ, 35 Hz, 297 μ s pulse, 400 μ m tip, non-contact, Water 22.5 mL/min	3, 7, 15 days	2940 nm-group. Duration significantly less than scalp control (<i>p</i> = 0.003), need for electrocauter bleeding control significantly higher in 2940 nm-group (<i>p</i> < 0.001). Need for sutures sign lower (<i>p</i> < 0.001). Intra-op bleeding, post-op pain, post-op complications, need for analgesics, VAS: no significant differences. TDZ significantly lower in 2940 nm group (<i>p</i> < 0.001) compared with CO ₂

(continued)

TABLE 3. (CONTINUED)

Citations	Test/control	Study type/patients per group	Aim of study	Examined parameters	Laser operating parameters applied/"dose"	Follow up	Outcome
Suter et al. ²⁵	2940 nm/CO ₂	RCT 31 patients 2940 nm 16/CO ₂ 15	Excisional biopsies of fibrous hyperplasias	Duration, intra-op bleeding, need for bleeding control, post-op pain, post-op complications, need for analgesics, VAS, TDZ	7 W AP, 200 mJ, 35 Hz, 297 μ s pulse, 400 μ m tip, non-contact, water 22.5 mL/min	1, 7, 15 days	Intra-op bleeding significantly higher in 2940 nm group $p=0.007$, need for electrocauterization $p=0.015$, No significant differences in duration of surgery, post-op pain, post-op complications, need for analgesics, VAS. TDZ significantly lower in 2940 nm group ($p<0.0001$)
Broccoletti et al. ²⁶	2940 nm/scalpel	RCT $n=344$ patients 2940 nm 173 lesions/scalpel 221 lesions	Excision of non-dysplastic white oral lesions	Pain (VAS), duration of surgery, QOL test, Oral Health Impact Profile, number of analgesics	1.5 W AP 150 mJ 10 Hz 500 μ s pulse, 900 μ m spot, distance 2 mm	3 days, 1 week	2940 nm significant difference in duration of surgery-shorter ($p<0.001$), VAS lower d3 $p=0.005$ QOL better $p=0.038$ Analgesics in lesions >1 cm $p=0.026$
Arduino et al. ²⁷	2940 nm/scalpel	RCT $n=117$ lesions 2940 nm 59 lesions, scalpel 58 lesions	Excision of non-dysplastic oral leukoplakia	Healing, recurrence	1.5 W AP 150 mJ 10 Hz 500 μ s pulse, 900 μ m spot	Every 6 months for 5 years	No significant difference between groups
Aras et al. ²⁸	2940 nm/diode 808 nm	RCT $n=16$ patients 2940 nm 8 patients/808 nm 8 patients	Lingual frenectomy	Pain level and post-surgical discomfort (5-point Likert-type scale) Requirement for local anesthesia	1.0 W AP, 80% air no water	7 days	2940 nm in the first 3 h significantly higher pain $p=0.005$ No significant difference in any other timepoint Post-surgical discomfort: no significant difference in any other timepoint No statistics for requirement for local anesthesia

References.²¹⁻²⁸

HML, hedon melanin index; OP, osmotic pressure; QOL, quality of life.

within this investigation, such as power meter used, fluence, irradiation, and total energy delivered. In addition, it was challenging to establish accurate values for the outcomes that were examined. Without a risk of bias and consideration of probability values related to statistical significance, a meaningful interpretation of results would have been difficult. An earlier article⁴¹ by the authors in this group highlighted the significant disparity in reported parameters within published articles focused on PBM.

However, it is encouraging from the results that 46% of the post-operative observations were positive in relation to laser versus scalpel treatment, and compared with other diode lasers (808–980 nm), this respective percentage was 83%. It may be possible to explore the reasons for such results in terms of laser-tissue interactions as a function of varying wavelengths applied.

Laser (and other light) therapies are effective, and their benefits are based on the principle of inducing a biological response through energy transfer.⁴² This applies to both surgical (ablative) therapy and sub-ablative PBM therapy. The optimal photonic dose for oral soft tissue surgical management (photothermal ablation/incision) must be the subject of recommended settings and power meter confirmation. In addition, with NIR “hot tip” delivery, sufficient attenuation of the beam must be achieved to not only enable the tip temperature but also allow sufficient wavelength-specific photons to enter the tissue to achieve PBM.⁴³ Through anecdotal investigation, the authors estimate an optimal onward transmission of 15%. Photothermolysis should also represent a measured function of tissue type, laser wavelength relative to chromophore/absorptive tissue bimolecular components, and a deliverance of energy concentration to achieve efficient tissue ablation with minimum risk of collateral thermal damage. Average power, peak power, energy and power densities, exposure time, and, at some distance from the tissue zone of maximum photothermolysis and ablation (along a thermal and scatter gradient), the applied value of fluence will diminish and tissue temperature will reduce to a level where dose parameters for PBM effects may occur;⁴⁴ therapies are usually within the range of 2–10 J/cm² for enhanced qualities of healing, with a higher range of 10–30 J/cm² for laser-induced analgesia.⁴⁵

Within research limited to dental and oral applications, an optical window has been understood to be between 650 and 1350 nm, without doubt founded on important existential phenomena of absorption and scatter effects of these wavelengths within oral soft tissues.⁴⁶ The predominance of investigations into laser-assisted surgical procedures with a generic “diode” laser offers an extremely high number of publications that are referenced in the PRISMA diagram related to the >650 nm wavelength range. Clearly, this fails to offer explanations regarding reported similar healing benefits when using laser wavelengths that are both shorter and longer than those represented by the NIR optical window.

With accepted opinion related to the delivery of PBM effects with near IR wavelengths, a question regarding what mechanisms might pertain in promoting positive uneventful healing phenomena when using shorter and longer wavelengths is therefore posed.

Shorter wavelengths of 400–600 nm have relatively low optical transmission within tissues. This is a consequence of absorption by chromophoric proteins as well as further

colored agents, particularly those containing transition metal ions such as those of iron and copper, and to a lesser extent, manganese. The effects of absorption are dose related and can range from protein denaturation to mild transient hyperthermia.⁴⁷ In surgical mode, a small optical spot size is applied typically in contact with the tissues. The high radiant exposure and localized absorption results in tissue destruction by vaporization and/or coagulation, or at even higher settings carbonization. In the immediate periphery of the zone of destruction, there can be sufficient localized heat to generate collagen contraction, which results in capillary closure. Dependent on operator technique, this can produce a relatively narrow zone of collateral tissue damage with excellent hemostasis. Also, in view of the high localized thermocline, there is an area of disinfection since most bacteria, viruses, and fungi are sensitive to temperatures elevated above 50°C. Consequently, beyond the immediate wound edge, there is an interstitial zone of sterile coagulation that acts as what may be termed a “laser bandage.” Beyond this zone of coagulation, however, the vital tissues respond with a classic tissue damage cascade, and as previously noted, there is an activation of the immune system producing an initiation of the cycle of wound damage mitigation, inflammation, primary wound matrix deposition, healing, and finally wound remodeling to the point of regeneration under optimal conditions.⁴⁸

Longer wavelengths in the mid-IR range of 2780–3000 nm are strongly absorbed by water. Since biological tissues are water rich, these wavelengths permit only a shallow depth of field surgery. If adequate superficial cooling air/water sprays dissipate heat accumulation, the zone of collateral destruction beyond the area of tissue disruption is of the order of up to 50 μ m after explosive ablation and spallation. This type of tissue cutting is a differential affair to that associated with either the short or near IR wavelengths that primarily cut via photothermolysis. This phenomenon arises from the use of FRP laser devices with ultra-short pulse durations, along with exceptionally high peak power with the erbium-type laser sources. Since chemical -O-H functions are highly responsive to photo-excitation at these wavelengths, there is a process of phase transition from water to steam within microseconds of exposure. The consequent rapid volumetric change of the expanded area of superheated vapor within a contained area, therefore, produces an explosive tissue disruption.^{49,50} The fragmented target tissues are removed by exposure to an adjunct water spray and high-volume evacuation. Consequently, there is remarkably little heat diffusion to the deeper layers of the collateral tissues. Subject again to good operator technique and the informed use of appropriate parameters, the area of collateral tissue damage may be minimal; moreover, there can again be a highly localized tissue rim that is disinfected and coagulated again with an associated vasoconstriction to support hemostasis. In addition, there can be a localized rim of tissue that is disinfected and coagulated with an associated vasoconstriction to support hemostasis.

Given the reduced optical penetration of both the shorter and the longer wavelengths of applied photonic energy, it is interesting to consider the multiple processes that may explain the mitigation of post-operative pain and swelling. Further, there is some evidence of an enhanced quality of repair; for example, Kesler et al.⁵¹ in an animal study identified a sustained increase in platelet-derived growth factor in

TABLE 4. PUBLISHED ARTICLES IDENTIFIED FROM A REVIEW OF THE LITERATURE REGARDING THE HEALING OUTCOME EFFECTS OF MID-INFRA-RED SURGICAL LASER USE

Citations	Test/control	Study type/patients per group	Aim of study	Examined parameters	Laser operating parameters applied/ "dose"	Follow-up	Outcome
Er:Cr:YSGG Er:YAG Eroglu et al. ²⁹	2780 nm/scalpel	RCT $n = 44$ cases 2780 nm 22 lesions/scalpel 22 lesions	Excision of epulis fissuratum	Pain (VAS) Total wound surface (Bates-Jensen Wound Assessment Tool), edema, healing erythema, suppuration	Ablation: 2.75 W AP 75 Hz 140 μ s pulse Air 20/water 40. 550 μ m tip. 1 mm spot, slight contact Hemostasis: 1.5 W AP, 50 Hz, 700 μ s pulse, air 20/water 0. 660 μ m tip. 1 mm spot 2780 nm setting 1 4.5 W, 50 Hz, 60 μ s pulse, 80% air. 17 mL/min water, 800 μ m tip in contact, brush strokes 2780 nm setting 2 2.5 W, 50 Hz, 700 μ s pulse, 40% air, 9 mL/min water, 800 μ m tip in contact, brush strokes 1.5 W AP. 20 Hz, 75 mL, pulse width 140 μ s, 12% water and 8% air, spot 0.6 mm, 600 μ m tip, straight handpiece. Fluence 26.54 J/cm ² . Mean irradiation time 77 sec	2, 7, 14, and 30 days	No significant difference between groups in pain, patient satisfaction at any timepoint. Healing laser groups better $p = 0.05$ at day 1, $p = 0.001$ at day 7 30 days no significant difference. Relapse, no significant difference between groups at 12 months No statistical analysis 2780 nm: less hemostatic effect than 10,600 nm., longer time required, healing faster. No relapse for any group after 4 months
Gholami et al. ³⁰	2780 nm two settings/scalpel	RCT $n = 66$ treated sites 2780 nm setting 1 22 sites/ 2780 nm setting 2 22 sites/ Scalpel 22 sites	Gingival depigmentation	Pain (VAS) Patient satisfaction, Gingival wound healing, relapse (DOPI Hedini indices)		VAS 1 days 7 days Patient satisfaction 7 days Wound healing	No significant difference between groups in pain, patient satisfaction at any timepoint. Healing laser groups better $p = 0.05$ at day 1, $p = 0.001$ at day 7 30 days no significant difference. Relapse, no significant difference between groups at 12 months No statistical analysis 2780 nm: less hemostatic effect than 10,600 nm., longer time required, healing faster. No relapse for any group after 4 months
Pié-Sánchez et al. ³¹	2780/10,600 nm	RCT 50 patients 2780 nm 25 patients, 10,600 nm 25 patients	Upper lip frenectomy	Surgical bleeding Time required Healing Relapse		7, 14, and 21 days and 4 months	No statistical analysis 2780 nm: less hemostatic effect than 10,600 nm., longer time required, healing faster. No relapse for any group after 4 months
Tunc et al. ³²	2780/980 nm diode	RCT, X-sectional study, 40 patients 2780 nm 51 implants/ 980 nm 50 implants	Second-stage implant surgery	Surgery time, bleeding, VAS, post-op complications		3 days. Onward restorative treatment	Overall no statistically significant differences in time, bleeding, VAS, and complications. Surgery ($p = 0.7$). VAS ($p = 0.6$), swelling ($p = 1.0$)

References,²⁹⁻³²

TABLE 5. RISK OF BIAS OF ARTICLES SELECTED

Citations	Sample size		Baseline situation similar	Parameters of laser use described appropriately and calculations correct		Power-meter used	Numerical results available (statistics)	No missing outcome data	All samples/patients completed the follow-up	Correct inter-pretation of data	Total score/10
	Randomization	calculation and required number included									
Blue green 4 articles											
Gobbo et al. ¹⁷	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
Rocca et al. ¹⁸	Yes	No	Yes	No	Yes	No	No	Yes	Yes	Yes	6
Romeo et al. ¹⁹	Yes	No	No	No	No	Yes	Yes	Yes	Yes	Yes	6
Bargiela-Pérez al. ²⁰	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	5
Erbium group 12 articles											
Giannelli et al. ²¹	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	8
Alhabashneh et al. ²²	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	7
Ipek et al. ²³	Yes	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	7
Suter et al. ²⁴	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	9
Suter et al. ²⁵	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Broccoletti et al. ²⁶	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	9
Arduino et al. ²⁷	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	7
Aras et al. ²⁸	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	5
Eroglu et al. ²⁹	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
Gholami et al. ³⁰	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
Pié-Sánchez et al. ³¹	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Tunc et al. ³²	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6
CO ₂ group 9 articles											
Suter et al. ³³	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	8
Hegde et al. ³⁴	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	7
Monteiro et al. ³⁵	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
Suter et al. ³⁶	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
Suter et al. ²⁴	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	9
López-Jornet et al. ³⁷	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Chee et al. ³⁸	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	7
Karimi et al. ³⁹	Yes	No	Yes	No	Yes	No	Yes	Yes	Yes	No	6
Agha-Hosseini et al. ⁴⁰	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6

osseous tissues exposed to an erbium laser wavelength of 2940 nm, and Pourzarandian et al.⁵² reported that COX-2 gene expression and PGE-2 concentration increased in an output-dependent manner by irradiating human fibroblasts (*in vitro*) with an Er:YAG laser system. In addition, a report by Lubart⁵³ claimed that an Er-YAG laser system dissociates water and generates $\bullet\text{OH}$ radicals, possibly via an intermolecular vibrational (V-V) energy transfer in water, which competed with vibrational relaxation and was dependent on the pulse repetition rate and energy density per laser pulse. At low concentrations of such reactive oxygen species (ROS), fibroblast stimulation may cause collagen and extracellular matrix formation. Therefore, ROS formation may be a contributory factor featured in the wound-healing effect of erbium lasers in dentistry.

In consequence, it was the purpose of this review to examine the evidence base to critically evaluate and identify the nature of any added value of clinical laser integration into practice, and also to facilitate the highlighting of any areas worthy of consideration for future research into the mechanisms of PBM. The acronym “q-PBM”—that is, quasi-PBM⁵⁴—has been suggested to possibly explain a post-surgery tissue response that mimics that achieved within the “optical window,” and also to question the cellular and biochemical processes that may be stimulated by these longer and shorter wavelengths involved.

In providing surgery for the treatment of oral soft tissue pathology and cosmetic alterations, the dental professional has an obligation to maintain a positive benefit–risk ratio. The use of laser photonic energy of appropriate applied wavelength, dose, and timing has been shown to offer benefits during surgical procedures, and also to the patient during the early healing period. Indeed, there are considerable published data available to support the effectiveness of incisional hemostasis, and the development of a post-surgical surface coagulum^{55–60} when using a range of surgical laser wavelengths, although a predominance of investigations into “uneventful” healing has centered on the IR wavelengths that fall within the 650–1350 nm optical window. Significantly, PBM is also considered an attribute to the delivery of “uneventful healing” that accompanies post-surgical laser therapy within clinical dentistry.⁴ However, to date, the processes associated with these benefits are not fully understood. As stated earlier, at a distance from the site of tissue ablation, along a combined thermal and scatter gradient, there may be a direct influence of sub-ablative photonic energy density during a modulation process of enhanced cellular activity, increased local vascular and lymphatic circulation, and analgesic effects that, combined, can promote a positive and advantageous healing process. The latter represents a combination of direct suppression of an inflammatory cascade, in addition to the facilitated optimization of conditions that are conducive to cellular repair and regeneration phenomena.^{6–8}

With the development of lasers as adjunctive surgical instruments, the benefits of each wavelength range within the series of commercially available dental lasers available have been summarized to represent one or more of the following:⁶¹

Precision/control of non-linear incisions: relative to width/depth of ablation

Incisional hemostasis: relative to laser wavelength

Selective ablation: relative to tissue composition

Pathogen control: incisional pathogen reduction/wound protection through post-ablation coagulum

Hard/soft tissue treatment harmonization: co-treatment, stage harmonization

Positive healing phenomena

As has been adequately described in the studies evaluated, such terminology is used to describe the para- and post-surgical outcomes of surgical laser-tissue interaction.

Critical to photothermolysis, a thermal threshold exists within the tissue, below which the incident photonic energy values are insufficient to initiate structural disruption, a process resulting in warming, and below a sustained threshold of 45.5°C, tissues are not irreparably harmed,^{62,63} with the potential for beneficial positive changes in cellular structures and biochemical processes.⁶⁴ In addition, with the use of red visible and NIR laser wavelengths, photon attenuation with a distance from the site of application will result in diminished irradiance to a point below that required to achieve the ablation threshold of the tissue, yet it also allows the absorption of energy by cellular structures, resulting in collateral PBM remote from the zone of tissular ablation.⁶⁵

With all incident wavelengths, laser-assisted soft tissue surgery (tissue injury) prompts a succession of responses and reactions in the host tissue that may be summarized as the wounding, inflammation, proliferation, and remodeling phases. The primary wound and bleeding prompt the trigger of a coagulation cascade, and activation of the complement system and the kinin cascade.^{66,67} The cellular response after wounding begins early, showing considerable changes already at 12–24 h post-surgery, and from a clinical viewpoint, healing during the first post-operative days is crucial for the maintenance of wound stability and subsequent successful treatment outcomes.⁶⁸

Conclusions

A detailed and blinded examination of published studies has been undertaken, applying strict criteria to demonstrate result data that suggest positive, or at worst neutral comparatives when a given laser wavelength is used against an alternative control therapy. With reference to the number of published articles examined, a significant improvement in addressing risk of bias and in reporting laser operating parameters would enable a wider range of published data to be examined within the strict criteria of this systematic review. As such, a substantiated evidence of laser surgery in delivering uneventful healing and analgesic effects, as an expression of PBM-like (quasi-PBM) influence, has been shown. From this series of investigations, a greater understanding of molecular, cellular, and regional tissue responses to applied energy at these wider wavelength ranges is sought. A summation of investigations of currently commercially available laser wavelengths in dentistry may then allow a more-inclusive meld of PBM effects within the current optical window, together with an adoption of a descriptive q-PBM to explain similar outcome effects of wider laser wavelength use in oral surgery. In this way, a desired outcome of understanding of soft tissue laser-tissue interaction, across the current therapeutic electromagnetic spectrum, may evolve.

This systematic review supports a belief that through multiple biophysical and host cellular and biochemical responses, oral soft tissues are positively modulated through laser use.

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References

- Smith K. The photobiological basis of low level laser radiation therapy. *Laser Therapy* 1991;3:6.
- Medical Subject Heading (MeSH). U.S. National Library of Medicine 2015. Available at: www.nlm.nih.gov (Last accessed 2020).
- Hamblin MR. Mechanisms and applications of the anti-inflammatory effects of photobiomodulation. *AIMS Biophys* 2017;4:337–361.
- Parker S. Lasers and soft tissue: loose soft tissue surgery. *Br Dent J* 2007;202:185–191.
- Steiner R. Laser-tissue interactions. In: Raulin C, Karsai S. *Laser and IPL Technology in Dermatology and Aesthetic Medicine*. New York: Springer, 2011; Ch.2 pp. 23–36.
- Tuchin VV. *Tissue Optics: Light Scattering Methods and Instruments for Medical Diagnosis*. Bellingham, WA: SPIE 2015. ISBN: 9781628415162.
- Karu T. Mechanisms of interaction of monochromatic visible light with cells. In: *Proceedings of SPIE 2639*. Bellingham, WA: SPIE—The International Society for Optical Engineering, 1996;pp. 2–9.
- Parrish JA, Deutsch TF. Laser photomedicine. *IEEE J Quantum Electron* 1984;QE-20:1386–1396.
- Kudoh Ch, Inomata K, Okajima K, Motegi M, Ohshiro T. Effects of 830 nm gallium aluminium arsenide diode laser radiation on rat saphenous nerve sodium-potassium-adenosine triphosphate activity: a pain attenuation mechanism examined. *Laser Ther* 1989;1:63–67.
- Sordillo LA, Pu Y, Pratavieira S, Budansky Y, Alfano R. Deep optical imaging of tissue using the second and third near-infrared spectral windows. *J Biomed Opt* 2014;19:056004.
- Huang YY, Hamblin M. Biphasic dose response in low level light therapy. *Dose Response* 2009;7:358–383.
- Anderson R, Parrish J. The optics of human skin. *J Invest Dermatol* 1981;77:13–19.
- Curcio J, Petty C. The near infrared spectrum of liquid water. *J Opt Soc Am* 1951;41:302–304.
- Wang LV, Wu H. Ch. 1.3 Absorption and its biological origins. In: *Biomedical optics, Principles and Imaging*. Hoboken, NJ: Wiley, 2007. p. 5.
- Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement (reprinted from *annals of internal medicine*). *PLOS Med* 2009;6:e1000097.
- Higgins J, Altman D, Gøtzsche P, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials *BMJ* 2011;343:d5928.
- Gobbo M, Bussani R, Perinetti G, et al. Blue diode laser versus traditional infrared diode laser and quantic molecular resonance scalpel: clinical and histological findings after excisional biopsy of benign oral lesions. *J Biomed Opt* 2017;22:121602.
- Rocca JP, Zhaoa M, Fornaini C, Tanc L, Zhaoa Z, Merigo E. Effect of laser irradiation on aphthae pain management: a four different wavelengths comparison. *J Photochem Photobiol B* 2018;189:1–4.
- Romeo U, Libotte F, Palaia G, et al. Oral soft tissue wound healing after laser surgery with or without a pool of amino acids and sodium hyaluronate: a randomized clinical study. *Photomed Laser Surg* 2014;32:10–16.
- Bargiela-Pérez P, González-Merchan J, Díaz-Sánchez R, et al. Prospective study of the 532 nm laser (KTP) versus diode laser 980 nm in the resection of hyperplastic lesions of the oral cavity. *Med Oral Patol Oral Cir Bucal* 2018;23:e78–e85.
- Giannelli M, Formigli L, Bani D. Comparative evaluation of photoablative efficacy of erbium: yttrium-aluminium-garnet and diode laser for the treatment of gingival hyperpigmentation. A randomized split-mouth clinical trial. *J Periodontol* 2014;85:554–561.
- Alhabashneh R, Darawi O, Khader YS, Ashour L. Gingival depigmentation using Er:YAG laser and scalpel technique: a six-month prospective clinical study. *Quintessence Int* 2018;49:113–122.
- Ipek H, Kirtiloglu T, Diraman E, Acikgoz G. A comparison of gingival depigmentation by Er:YAG laser and Kirkland knife: osmotic pressure and visual analog scale. *J Cosmet Laser Ther* 2019;21:209–212.
- Suter V, Altermatt H, Bornstein M. A randomized controlled trial comparing surgical excisional biopsies using CO2 laser, Er:YAG laser and scalpel. *Int J Oral Maxillofac Surg* 2020;49:99–106.
- Suter V, Altermatt H, Bornstein M. A randomized controlled clinical and histopathological trial comparing excisional biopsies of oral fibrous hyperplasias using CO2 and Er:YAG laser. *Lasers Med Sci* 2017;32:573–581.
- Broccoletti R, Cafaro A, Gambino A, Romagnoli E, Arduino PG. Er:YAG laser versus cold knife excision in the treatment of nondysplastic oral lesions: a randomized comparative study for the postoperative period. *Photomed Laser Surg* 2015;33:604–609.
- Arduino PG, Cafaro A, Cabras M, Gambino A, Broccoletti R. Treatment outcome of oral leukoplakia with Er:YAG laser: a 5-year follow-up prospective comparative study. *Photomed Laser Surg* 2018;36:631–633.
- Aras MH, Göregen M, Güngörmüş M, Akgül HM. Comparison of diode laser and Er:YAG lasers in the treatment of ankyloglossia. *Photomed Laser Surg* 2010;28:173–177.
- Eroglu CN, Tunç SK, Elasan S. Removal of epulis fissuratum by Er,Cr:YSGG laser in comparison with the conventional method. *Photomed Laser Surg* 2015;33:533–539.
- Gholami L, Moghaddam SA, Rigi Ladiz MA, et al. Comparison of gingival depigmentation with Er,Cr:YSGG laser and surgical stripping, a 12-month follow-up. *Lasers Med Sci* 2018;33:1647–1656.
- Pié-Sánchez J, España-Tost AJ, Arnabat-Domínguez J, Gay-Escoda C. Comparative study of upper lip frenectomy with the CO2 laser versus the Er, Cr:YSGG laser. *Med Oral Patol Oral Cir Bucal* 2012;17:e228–e232.
- Tunc SK, Yayli NZ, Talmac AC, Feslihan E, Akbal D. Clinical comparison of the use of ER,Cr:YSGG and diode lasers in second stage implants surgery. *Saudi Med J* 2019;40:490–498.
- Suter V, Altermatt H, Dietrich T, Reichart P, Bornstein M. Does a pulsed mode offer advantages over a continuous wave mode for excisional biopsies performed using a carbon dioxide laser? *J Oral Maxillofac Surg* 2012;70:1781–1788.
- Hegde R, Padhye A, Sumanth S, Jain AS, Thukral N. Comparison of surgical stripping; erbium-doped:yttrium, aluminium, and garnet laser; and carbon dioxide laser techniques for gingival depigmentation: a clinical and histologic study. *J Periodontol* 2013;84:738–748.

35. Monteiro L, Delgado M, Garcês F, et al. A histological evaluation of the surgical margins from human oral fibrous-epithelial lesions excised with CO₂ laser, diode laser, Er:YAG laser, Nd:YAG laser, electrosurgical scalpel and cold scalpel. *Med Oral Patol Oral Cir Bucal* 2019;24:e271–e280.
36. Suter V, Altermatt H, Dietrich T, Warnakulasuriya S, Bornstein M. Pulsed versus continuous wave CO₂ laser excisions of 100 oral fibrous hyperplasias: a randomized controlled clinical and histopathological study. *Lasers Surg Med* 2014;46:396–404.
37. López-Jornet P, Camacho-Alonso F. Comparison of pain and swelling after removal of oral leukoplakia with CO₂ laser and cold knife: a randomized clinical trial. *Med Oral Patol Oral Cir Bucal* 2013;18:e38–e44.
38. Chee M, Sasaki C. Carbon dioxide laser fiber for the excision of oral leukoplakia. *Ann Otol Rhinol Laryngol* 2013;122:547–549.
39. Karimi A, Sobouti F, Torabi S, et al. Comparison of carbon dioxide laser with surgical blade for removal of epulis fissuratum. A randomized clinical trial. *J Lasers Med Sci* 2016;7:201–204.
40. Agha-Hosseini F, Moslemi E, Mirzaii-Dizgah I. Comparative evaluation of low level laser and CO₂ laser in treatment of patients with oral lichen planus. *Int J Oral Maxillofac Surg* 2012;41:1265–1269.
41. Parker S, Cronshaw M, Anagnostaki E, Lynch E. Parameters for photobiomodulation therapy in clinical dentistry: a systematic review. *Photobiomodul Photomed Laser Surg* 2019;37:784–797.
42. Hamblin M, Ferraresi C, Huang Y, Freitas L, Carroll J. Chapter 1: Photobiomodulation. In: *Low-Level Light Therapy*, 1st ed. Bellingham, WA: SPIE Press, 2018, p. 1.
43. Romanos GE, Sacks D, Montanaro N, Delgado-Ruiz R, Calvo-Guirado JL, Javed F. Effect of initiators on thermal changes in soft tissues using a diode laser. *Photomed Laser Surg* 2018;36:386–390.
44. Wehner M, Betz P, Aden M. Influence of laser wavelength and beam profile on the coagulation depth in a soft tissue phantom model. *Lasers Med Sci* 2019;34:335–341.
45. Cronshaw M, Parker S, Arany P. Feeling the heat: evolutionary and microbial basis for the analgesic mechanisms of photobiomodulation therapy. *J Photobiomodul Photomed Laser Surg* 2019;37:517–526.
46. Sordillo D, Sordillo L, Sordillo P, Shi L, Alfano R. Short wavelength infrared optical windows for evaluation of benign and malignant tissues. *J Biomed Opt* 2017;22:045002.
47. Serrage H, Heiskanen V, Palin W, et al. Under the spotlight: mechanisms of photobiomodulation concentrating on blue and green light. *Photochem Photobiol Sci* 2019;18:1877–1909.
48. Chung H, Dai T, Sharma SK, et al. The nuts and bolts of low level laser therapy. *Ann Biomed Eng* 2012;40:516–533.
49. Rizioiu I, Eversole L, Kimmel A. Effects of an erbium, chromium: yttrium, scandium, gallium, garnet laser on mucocutaneous soft tissues. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;82:386–395.
50. Palmieri B, Capone S, Rottigni V. Er:YAG laser: tissue interaction and histomorphological characterization. *Clin Ter* 2011;162:473–486.
51. Kesler G, Shvero DK, Tov YS, Romanos G. Platelet derived growth factor secretion and bone healing after Er:YAG laser bone irradiation. *J Oral Implantol* 2011;37 Spec No:195–204.
52. Pourzarandian A, Watanabe H, Ruwanpura SM, Aoki A, Noguchi K, Ishikawa I. Er:YAG laser irradiation increases prostaglandin E production via the induction of cyclooxygenase-2 mRNA in human gingival fibroblasts. *J Periodontol Res* 2005;40:182–186.
53. Lubart R, Kesler G, Lavie R, Friedmann H. Er:YAG laser promotes gingival wound repair by photo-dissociating water molecules. *Photomed Laser Surg* 2005;23:369–372.
54. Q-PBM Trademark No. UK00003419626 2019. UK Patent (Intellectual Property) Office. Available at: www.gov.ukipo (Last accessed 2020).
55. Shang J, Gong K, Xu D, Sun L, Qu W. The Nd:YAG laser or combined with Er:YAG laser therapy for oral venous lakes. *Photobiomodul Photomed Laser Surg* 2020;38:244–248.
56. Protásio A, Galvão E, Falci S. Laser techniques or scalpel incision for labial frenectomy: a meta-analysis. *J Maxillofac Oral Surg* 2019;18:490–499.
57. Uraz A, Çetiner FD, Cula S, Guler B, Oztoprak S. Patient perceptions and clinical efficacy of labial frenectomies using diode laser versus conventional techniques. *J Stomatol Oral Maxillofac Surg* 2018;119:182–186.
58. Tenore G, Palaia G, Mohsen A, et al. Could the super-pulsed CO₂ laser be used for oral excisional biopsies? *Adv Clin Exp Med* 2019;28:1513–1517.
59. Andreadis D, Lazaridi I, Anagnostou E, Pouloupoulos A, Panta P, Patil S. Diode laser assisted excision of a gingival pyogenic granuloma: a case report. *Clin Pract* 2019;9:1179.
60. Fekrazad R, Nokhbatolfoghahaei H, Khoei F, Kalhori K. Pyogenic granuloma: surgical treatment with Er:YAG laser. *J Lasers Med Sci* 2014;5:199–205.
61. Parker S. Laser–tissue interaction and its application in clinical dentistry. *Int J Laser Dent* 2011;1:1–8.
62. Letokhov V. Effects of transient local heating of spatially and spectrally heterogeneous biotissue by short laser pulses. *Nuovo Cimento* 1991;13D:939–948.
63. Lepock J. Cellular effects of hyperthermia: relevance to the minimum dose for thermal damage. *Int J Hyperthermia* 2000;19:252–266.
64. Chen L, Arbueva Z, Guo S, Marucha P, Mustoe T, DiPietro L. Positional differences in the wound transcriptome of skin and oral mucosa. *BMC Genom* 2010;11:471.
65. Karu T. Primary and secondary mechanisms of action of visible to near-IR radiation on cells. *J Photochem Photobiol B* 1999;49:1–17.
66. Nagarajan VK, Yu B. Monitoring of tissue optical properties during thermal coagulation of ex vivo tissues. *Lasers Surg Med* 2016;48:686–694.
67. Wong M, Hollinger J, Pinero G. Integrated processes responsible for soft tissue healing. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;82:475–492.
68. Ausprunk D, Folkman J. Migration and proliferation of endothelial cells in preformed and newly formed blood vessels during tumor angiogenesis. *Microvasc Res* 1977;14:53–65.

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