



Management of Physiological Gingival Melanosis by Diode Laser Depigmentation versus Surgical Scalpel: A Systematic Review

Francesco Inchingolo^{a,1,*}, Alessio Danilo Inchingolo^{a,1}, Irene Palumbo^a, Mariafrancesca Guglielmo^a, Liviana Balestriere^a, Lucia Casamassima^a, Danilo Ciccicarese^a, Pierluigi Marotti^a, Antonio Mancini^a, Andrea Palermo^b, Angelo Michele Inchingolo^{a,1}, Gianna Dipalma^{a,1}

^a Department of Interdisciplinary Medicine, University of Bari "Aldo Moro", Bari 70124, Italy

^b College of Medicine and Dentistry, Birmingham B4 6BN, UK

ARTICLE INFO

Keywords:

Gingival melanosis
Oral hyperpigmentation
Diode laser
Surgical blade
Surgical scalpel
Melanin hyperpigmentation

ABSTRACT

Introduction: Pigmented lesions in the oral cavity mucosa, primarily found in African, Asian, and Mediterranean populations, are caused by increased melanin granule production or melanocyte abundance. These lesions typically appear in childhood and increase with age. This study aimed to evaluate, based on the evidence in the literature, the efficacy of diode laser in the treatment of physiological gingival melanosis in terms of clinical and aesthetic variables, based on the patient, compared to conventional surgical therapy such as the scalpel technique.

Materials and methods: Electronic databases (PubMed, Web of Science and Scopus) were examined in March 2024, in the last 10 years. We performed a manual screening of the reference lists of potential studies. The risk of bias was measured with the ROBINS tool.

Results: The search found 840 publications, but 40 of them were duplicates and were therefore excluded. Titles and abstracts of 800 articles were accessed and 646 were excluded. After applying the inclusion and exclusion criteria, we included 12 studies out of the remaining 154. Data were collected from the selected articles and organized into tables for comparison and study.

Conclusions: The diode laser obtained better results in terms of intraoperative bleeding and perception of pain for the patient. However, there were no differences in depigmentation and wound healing intensity. Due to the small research samples and the heterogeneity of the data provided, more studies with a high degree of scientific relevance and with a clear research protocol are needed.

1. Introduction

In the mucosa of the oral cavity, a wide range of pigmented lesions can be found with colors ranging from blue to brown to gray [1–4]. These lesions may be the expression of changes in the normal anatomy of the mucosa (Fig. 1), lesions caused by exogenous and endogenous substances, or even lesions concomitant with systemic diseases [5–10]. Exogenous pigmentation is usually caused by the presence of a foreign material while endogenous pigmentation is usually produced by

melanin, hemoglobin, hemosiderin, and/or carotene [11–14]. The mucosal epithelium of the oral cavity is composed of keratinocytes and melanocytes [15–19]. The latter cells are present in the basal layer with cytoplasmic extensions and are responsible for the production of melanin granules [20–23]. Thus, pigmented lesions may be the expression of an increased production of melanin granules or a greater number of melanocytes within the epithelium of the oral cavity [24–27].

These occur most frequently in populations with cutaneous hyperpigmentation such as African, Asian and Mediterranean populations

Abbreviations: DOPI, Dummatt-Gupta oral pigmentation index; LASER, light amplification by stimulated emission of radiation; RCTs, randomized controlled trial; VAS, visual analog scale.

* Corresponding author.

E-mail address: francesco.inchingolo@uniba.it (F. Inchingolo).

¹ These authors contributed equally to this work.

<https://doi.org/10.1016/j.dentre.2024.100146>

Received 7 May 2024; Received in revised form 6 July 2024; Accepted 19 July 2024

Available online 21 July 2024

2772-5596/© 2024 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

[28]. They are usually already present in childhood and tend to increase with age [28,29].

The physiological pigmentations usually affect the adhered gums, bilaterally and delimited, mainly on the vestibular aspect, lips and tongue [30–33]. One aspect peculiar to this type of condition is that the free gingival margin is usually not involved not even in cases of diffuse pigmentation [32,34–37].

Although gingival melanosis is a benign hyperpigmentation of the gums (Fig. 2) that does not represent a health problem, those who suffer from it seek a remedy for reasons that are not the same purely aesthetic [38–43].

Currently, there are several surgical techniques for this purpose: chemical methods, such as alcohols, phenols, and ascorbic acid surgical procedures such as gingival abrasion, epithelial excision using scalpel, laser, electrosurgery, cryosurgery and radiosurgery [4,44–47].

1.1. Laser

The laser was introduced in 1960 in the specialty of dermatology and was first used in dentistry in the hope of overcoming some drawbacks arising from conventional methods of dental treatments [9,48–50]. The word LASER currently stands for "Light Amplification by Stimulated Emission of Radiation" [8,51–55]. Laser technology is developing very rapidly giving a diversification of lasers in the field of dentistry [56]. This therapy is based on the biological response through energy transfer [57]. The emitted wavelength devices determine the effective depth of penetration [58]. The effects of the laser depend on the type of laser used, as well as the type of tissue, as it can transmit, absorb, scatter or reflect laser light [59–61].

In the oral cavity, the energy of laser photons is absorbed by chromophores, groups of atoms capable of coloring a substance, made up of melanin, hemoglobin, pigmented proteins, hydroxyapatite and water [62–63]. When the energy is absorbed by the water in the cells, the temperature rises and the boiling point is reached, producing water-induced ablation, while when the energy of the laser photons is absorbed by the melanin or chromophores of hemoglobin, cleavage and coagulation occur [19,20,64,65].

1.1.1. Diode laser

The diode laser is a high-power semiconductor laser that emits energy at a wavelength between 800 and 1000 nm and can cut the soft tissues with surgical precision, creating zones of thermal necrosis of less than 1 mm and hemostasis of the affected mucosa [48,66,67]. It is also able to reduce the bacterial load of periodontal pockets. To etch or vaporize soft tissues, the light of this laser is emitted through synthetic sapphire tips in contact mode, transmitted thanks to optical fibers [68,68] (Fig. 3).

Diode lasers have revolutionized various aspects of dentistry, offering precise and minimally invasive solutions for a wide range of dental procedures [69–72]. These compact, portable devices emit light at specific wavelengths that are absorbed by pigmented tissues, making them particularly effective for soft tissue surgeries, periodontal treatments, and cosmetic procedures [73–77].

In periodontics, diode lasers are commonly used for procedures such as gingivectomy, gingivoplasty, and crown lengthening [78–82]. They enable the dentist to precisely remove excess gum tissue, reshape the gums, and expose more tooth structure for restorative purposes, all with minimal bleeding and discomfort for the patient [67,63,83–85].

Moreover, diode lasers are invaluable tools in endodontics for disinfecting root canals and promoting healing in cases of periapical lesions [1,36,48]. Their bactericidal properties help eliminate bacteria and reduce the risk of post-operative infections, leading to improved treatment outcomes [86–89].

In cosmetic dentistry, diode lasers are utilized for procedures like teeth whitening and gum depigmentation [67,88]. The controlled application of laser energy allows for the efficient removal of stains from enamel surfaces and the reduction of melanin pigmentation in the gums, enhancing the patient's smile aesthetics [90–92].

Overall, the usage of diode lasers in dentistry offers numerous benefits, including enhanced precision, reduced discomfort, faster healing times, and improved patient satisfaction [16,93–95]. As technology continues to advance, diode lasers are poised to play an increasingly integral role in modern dental practice [96–98].

1.2. Surgical scalpel

The surgical scalpel technique is a surgical procedure that involves scraping off the hyperpigmented gingival epithelium and secondary healing of the exposed connective tissue [62,99]. It's simple, cost-effective, and easy to carry out with minimal time and effort [69]. Although surgical removal of the gum has a lower cost and a lower probability of recurrence, it is related to pain, postoperative discomfort, intra- and postoperative bleeding, and the need for a periodontal dressing [100,74].

This procedure is contraindicated in patients with a thinner gingival biotype and narrow papillary areas [60].

The surgical removal of gingival melanosis typically involves the use of a surgical scalpel [101]. This procedure, known as gingivectomy, aims to excise the pigmented tissue from the gums, resulting in a more uniform and lighter appearance [28,102–104].

Before the procedure, the dentist or oral surgeon will thoroughly examine the affected area to determine the extent of pigmentation and plan the surgical approach [47,105]. Local anesthesia is usually administered to ensure the patient's comfort throughout the procedure



Fig. 1. Example of physiological gingival melanosis.



Fig. 2. Benign hyperpigmentation of the gums.



Fig. 3. Diodo Laser that emits energy.

[106–109].

Once the area is numb, the surgeon carefully uses a surgical scalpel to make precise incisions along the gum line, removing the excess pigmented tissue [54]. Special care is taken to avoid damaging the surrounding healthy tissue and to achieve a symmetrical and aesthetically pleasing outcome [50,110,111].

After the excess tissue is removed, the surgical site is thoroughly irrigated to remove any debris and ensure proper healing [100,112,113]. Depending on the extent of the procedure and the patient's healing response, sutures may be placed to close the incisions and facilitate optimal healing [100,113].

Following the surgery, patients are typically provided with post-operative instructions to promote healing and minimize discomfort [33]. This may include instructions on oral hygiene practices, dietary restrictions, and the use of prescribed medications [42,114,115,70].

This systematic review aims to evaluate the efficacy of diode laser in the treatment of physiological gingival melanosis in terms of clinical and aesthetic variables, comparing them to conventional surgical therapy

using a scalpel [116,117,71].

The Variables considered in this systematic review are the intensity of repigmentation, the perception of the pain about treatment received, intraoperative bleeding, and wound healing.

2. Materials and methods

2.1. Search processing

The current systematic review followed the PRISMA and International Prospective Register of Systematic Review Registry procedures (full ID: CRD – 541,390) [118,119]. The following databases: PubMed, Web of Science and Scopus, were examined from 12 March 2024 to 25 March 2024, to search articles of the last 10 years. The search strategy was created by combining terms relevant to the study's purpose.

The following Boolean keywords were applied: (((Gingival Melanosis) OR (Oral pigmentation)) OR (oral melanin)) OR (Oral Hyperpigmentation)) OR (Pigmentation disorder)) OR (Melanotic macula)) OR (Gingival melanin pigmentation)) OR (Pigmented lesion)) OR (Physiological gingival pigmentation)) OR (Physiological pigmentation)) OR (Black gums)) OR (oral mucosa pigmentation)) OR (Melanotic lesion)) OR (pigmentation disease)) AND (Diode Laser)) OR (Laser semiconductor)) OR (semiconductor)) OR (laser therapy)) OR (Laser oral depigmentation)) AND (Surgical blade)) OR (abrasion therapy)) OR (Abrasion depigmentation)) OR (bur abrasion)) OR (mucoabrasion therapy)) AND (melanin depigmentation)) OR (Melanosis depigmentation)) OR (Depigmentation oral)) OR (Gingiva depigmentation).

2.2. Inclusion and exclusion criteria

The reviewers worked in group to assess all relevant studies that analyzed or compared the effects of diode laser or surgical removal by blade on gingival physiologic melanosis, according to the following inclusion criteria:

- Studies that did the research “in vivo” or in “humans”;
- Case-controls studies, cohort studies, RCTs;
- Studies that were published in the last 10 years;

Studies that fulfill at least one of the following exclusion criteria were excluded: reviews, case reports and series, letters to the authors; animal models; in vitro studies and research done in patients with pathologic gingival melanosis.

PICO Question

The PICO question addressed was:

“Will the use of diode laser provide more additional clinical and aesthetic benefits in the treatment of gingival melanosis than conventional surgical therapy such as the scalpel technique?”

- I. Population: Patients with physiologic gingival melanosis;
- II. Intervention: Diode laser as a treatment for pigmented lesion;
- III. Comparison: Scalpel technique as a treatment for pigmented lesions;
- IV. Outcome: Which treatment has the greatest clinical and aesthetic benefits;

2.3. Data processing

Four independent reviewers (P.M., L.C., D.C., L.B., I.P. and M.G.) assessed the quality of the included studies using specified criteria such as selection criteria, methods of outcome evaluation, and data analysis.

This enhanced ‘risk of bias’ tool additionally includes quality standards for selection, performance, detection, reporting, and other biases. Any differences were settled through conversation or collaboration with other researchers (A.D.I., A.M., A.P., A.M.I., G.D.). The reviewers screened the records according to the inclusion and exclusion criteria. Doubts have been resolved by consulting the senior reviewer (F.I.). The selected articles were downloaded into Mendeley (Tables 1–6).

3. Results

3.1. Characteristics of included articles

Fig. 4 shows the flow diagram of a systematic review carried out using the PRISMA reporting criteria. The diagram describes the search strategy, inclusion and exclusion of publications at each stage of detection.

A total of 840 publications were identified in three databases, including PubMed (511), Web of Science (152), and Scopus (177),

obtaining 800 records after the duplicates were deleted (40). The title and abstract analysis resulted in the exclusion of 646 articles because they were off-topic. The remaining 154 records were read deleting 142 articles that did not fill the inclusion criteria. The evaluation includes a total of 12 publications for qualitative analysis.

3.2. Study of the variables

Table 3, 4, 5, 6.

3.3. Quality assessment and risk of bias of included articles

The risk of bias in the included studies is reported in Fig. 5. Regarding bias due to confounding, most studies have a medium risk. The bias resulting from measurement is a parameter with low risk of bias. Many studies have a low risk of bias due to participant selection. Post-exposure bias is low in most studies. Bias due to missing data is medium in many studies. The bias resulting from the outcome measurement cannot be calculated due to heterogeneity. The selection bias of the reported results is low in half of the studies and medium in the other half. The final results show that 2 studies have a low risk of bias, 7 have a medium risk of bias, and 2 have a high risk of bias.

4. Discussion

The systematic review undertook a comprehensive synthesis, meticulously amalgamating evidence culled from a diverse array of clinical studies. Through this rigorous process, it illuminated the intricate nuances surrounding the comparative effectiveness of surgical methods *vis-à-vis* diode lasers in the eradication of gingival melanosis. This analytical endeavor not only sheds light on the efficacy of these treatment modalities but also furnishes invaluable insights crucial for informed decision-making in clinical practice.

4.1. Bleeding

Variations in intraoperative bleeding were noticed during the one-month follow-up. Bakutra et al., Chandra et al., Hamzah B., El Shenawy et al. evaluated intraoperative bleeding [101,120,123,129].

The immediate coagulation capabilities of the laser caused

Table 1
Methodology, characteristics of the studies.

AUTHORS AND YEARS	TYPE OF STUDY	STUDY SAMPLE (N°PATIENTS)	GENDER PROPORTION (M:F)	FOLLOW UP (MONTHS)	AGE OF SAMPLE (years)	VARIABLES
Suragimath G. et al. 2016 [17]	Randomized Comparative Clinical Study	12	7:5	12 months	NA	Intensity of repigmentation, pain,
Bakutra G. et al. 2017 [120]	Clinical study	20	12:8	12 months	NA	pain, bleeding, wound healing
Grover H. et Al. 2014 [121]	Clinical study	20	11:9	3 months	NA	pain
Chandra G. et al. 2020 [101]	Randomized comparative clinical study	20	NA	9 months	NA	pain, bleeding, wound healing
Mahajan G. et al. 2017 [122]	Randomized comparative clinical study	10	NA	9 months	NA	Intensity of repigmentation
Hamzah BF et al. 2022 [123]	Randomized comparative clinical study	20	9:11	4 weeks, 3 years	16–29	Bleeding
Mikhail F. et al. 2023 [124]	Randomized comparative clinical study	24	NA	12 h	>18	Wound healing Pain
Jagannathan R. et al. 2020 [125]	Prospective study	30	15:15	14 months	24–38	Pain
Shah N. et al. 2023 [126]	Clinical Study	64	NA	3 and 6 months.	18 –50	Pain
Mojahedi S. et al. 2023 [127]	Clinical study	21	NA	6 months	25–30	Pain
Mojahedi S. et al. 2023 [128]	Clinical study	19	5:14	3 mouths	25–26	Intensity of repigmentation
El Shenawy HM. et al. 2015 [129]	Cohort study	15	7:8	1 week 1 month 3 months	15–45	Bleeding

Table 2
Diode laser characteristics.

Author and year	Diode laser brand	Wave lenght (nm)	Type of wave	Power (W)	Energy (mJ)
Suragimath G. et al.2016 [17]	Photon Plus; Zolar Tech Technology	980 nm	Continous	0,5 W	12mJ
Bakutra G. et al. 2017 [120]	Piccaso 810 nm Diode Unit, AMD Lasers, Indianápolis, USA	810 nm	Continous	3 W	–
Grover et al. 2014 [121]	FONA, Diode, LaserTM, Sirona, Germay	800–980 nm	Pulsed	2,5 W	–
Chandra G. et al. 2020 [101]	–	810 nm	Continous	1,5 W	–
Mahajan G. et al. 2017 [122]	EPIC	940 nm	Continous	1 W	–
Hamzah BF. et al. 2022 [123]	Diode Epic, BioLaser	940 nm	Continous and Pulsed	1 W	–
Mikhail F. et al. 2023 [124]	Doctor Smile Diode Laser, LAMPDA, Italy	980 nm	Continous	1 W	–
Jagannathan R. et al.2020 [125]	Biolaser	940nm	Pulsed	1W	–
Shah N. et al. 2023 [126]	Diode laser	810 nm	Continuos	1W	–
Mojahedi S. et al. 2023 [127]	Diodo lasers from ARC Company (Laser GmbH; Nuremberg, Germany)	445 nm - 810 nm	Continuos	1W	–
Mojahedi S. et al. 2023 [128]	Dr Smile diode laser Model: LA5D0001.1; Italy	810 nm	Continuos	1W	–
El Shenawy HM. et al. 2015 [129]	Quanta laser system made in Italy class 4 laser	980 nm	Contact mode	4W	–

Table 3
Intensity of repigmentation.

Authors	Technique	Pre- operative	Follow-up
Suragimath G. et al. 2016 [17]	Scalpel Diode Laser	$M = 2.58$ severe	$M = 0.3$ slight
Mahajan G. et al.2017 [122]	Scalpel Diode Laser	$M = 1.84$ moderate	$M = 0.648$ slight
Mojahedi S. et al. 2023 [128]	Scalpel Diode laser	$M = 2.4$ severe	$M = 0.52$ slight

M (mean); slight, moderate,severe (DOPI* values, repigmentation intensity).
*Dummet-Gupta Oral Pigmentation Index (DOPI):.
1. 0: There is no clinical pigmentation of the gums.
2. 0.031–0.97: Slight clinical pigmentation.
3. 1.0–1.9: Moderate clinical pigmentation.
4. 2.0–3.0: Severe clinical pigmentation.

statistically different findings for the two study groups. At most, patients treated with the diode laser had minor bleeding; in many cases, as the one reported by Hamzah et al., there was no bleeding at all [123]. As a result, the patient had less trauma throughout the treatment and the operator had an easier time. However, some patients—especially in the Bakutra et al. study—experienced severe bleeding after receiving surgical scalpel treatment [120]. Diode laser treatment demonstrated

Table 4
Wound healing.

Authors	Technique	1 day	1 week	1 month
Bakutra G. et al.2017 [120]	Laser Scalpel	8 (40 %) = partial 12(60 %) = ulcers 4(20 %) = parcial	16 (80 %) = complete 4 (20 %) = parcial 16 (80 %) = complete	20(100 %) = complete 20(100 %) = complete
Chandra G. et al.2020 [101]	Laser Scalpel	- -	13(65 %) = complete 7(35 %) = parcial 11(55 %) = complete 9(45 %) = parcial	20(100 %) = complete 20 (100 %) = complete
Mikhail F. et al.2023 [124]	Laser Scalpel	- -	7(87 %) = complete 1(13 %) = parcial 6(75 %) = complete 2(25 %) = parcial	- -

A: Complete epithelialization; B: Partial epithelialization; C: Ulcer; D: Necrosis.

Table 5
Bleeding.

Authors	Technique	Bleeding
Bakutra G. et al. 2017 [120]	Scalpel Laser	4(20 %) = slight 12(60 %) = moderate 4 (20 %) = severe 18(90 %) = slight 2 (10 %) = moderate
Chandra G. et al. 2020 [101]	Scalpel Laser	11 (55 %) = slight 9 (45 %) = moderate 20 (100 %) = no bleeding
Hamzah BF. et al. 2022 [123]	Laser (CW mode) Laser (Pulsed mode)	7 (70 %) = no bleeding 3 (30 %) = slight 10 (100 %) = no bleeding
El Shenawy HM. et al. 2015 [129]	Laser	3 (20 %) = slight bleeding 12 (80 %) = no bleeding

A: No bleed; B: Slight bleeding; C: Moderate bleed; D: Severe hemorrhage.

immediate coagulation capability, leading to minimal to moderate bleeding or even absence of bleeding in some cases. This not only facilitated smoother surgical procedures but also contributed to a less traumatic experience for patients [101,120,123,129].

4.2. Pain

Studies used the VAS Scale to compare postoperative pain between surgical and laser treatments for depigmentation. Pain perception one day and one week following the operation was taken into consideration in all articles on both the Diode Laser approach and surgical procedures [17,101,120,121,124–127]. There were discrepancies between the diode laser and scalpel procedures on the first post-operative day. The laser group’s patients typically reported lower pain thresholds, with light pain being the most common. The scalpel group, on the other hand, had mild pain at its worst. The authors of publications on surgical scalpels, Hanaa M. El Shenawy et al., Bakutra, Mojahedi et al., and Faten Fawzy Mikhail et al., reported no pain seven days after surgery [51,120,124,127,129]. However, Suragimath et al., Bakutra et al., Chandra et al. 2020, Jagannathan et al. 2020, and Shah et al. 2023 reported mild pain after 7 days [17,120,125,126].

Table 6
Pain.

Authors	Tecnique	1 day	7 days
Suragimath G. et al. 2016 [17]	Scalpel	M = 3.5	M = 0,4167
	Laser	M = 1.5	M = 0,0833
Bakutra G. et al. 2017 [120]	Scalpel	M = 3.8	0
	Laser	M = 1,8	0
Chandra G. et al. 2020 [101]	Scalpel	14 (70 %): mild pain	17 (85 %): no pain
	Laser	6 (30 %): moderate pain	3 (15 %): mild pain
		8 (40 %): no pain	20 (100 %): no pain
		12 (60 %): mild pain	
Jagannathanet R. et al. 2020 [125]	Scalpel	M = 2,7	M = 0,8
	Laser	M = 0,8	M = 0,2
Shah N. et al. 2023 [126]	Scalpel	M = 3.5	M = 1
	Laser	M = 1.5	M = 0
Mojahedi S. et al. 2023 [127]	Scalpel	15(70 %): mild pain	18 (85 %): no pain
	Laser	6 (30 %): moderate pain	3 (15 %): mild pain
		8 (40 %):no pain	21 (100 %): no pain
		13 (60 %): mild pain	
Mikhail F. et al. 2023 [124]	Surgical scalpel	M = 3.5 moderate pain	M = 0 no pain
	Diode laser	M = 1,5 mild pain	M = 0 no pain
El Shenawy HM. et al. 2015 [129]	Diode Laser	12 (80 %): no pain	15 (100 %): no pain
		3 (20 %): mild pain	0 (0 %): mild pain

*M(medium);%(intergroupal); no pain, mild pain, moderate pain, severe pain, (Visual Analogue scale, VAS).
The “Visual Analog Scale” (VAS), Visual Analog Scale is used to evaluate the subjective pain that the patient reports[120]. The VAS consists of a 10 cm (100 mm) horizontal line, on one end it says “no pain” and on the other “severe pain.” The patient is asked to mark the intensity of the pain. The distance of this point, in centimeters, from the left end of the scale was recorded and used as the VAS score.:
0: no pain.
1–3: mild pain.
3.1–6: moderate pain.
6.1–10: severe pain.

4.3. Wound healing

Analysis of wound healing outcomes unveiled intriguing subtleties between the contrasting treatment modalities. These investigations meticulously scrutinized the progression of wound healing at diverse intervals post-surgery. Both Bakutra et al. and Chandra et al. delved into wound recovery after a month, discerning no discernible disparities within the designated time spans [101,120]. Furthermore, Chandra et al.’s exploration revealed uniform healing at one week; however, the immediate post-operative healing status was not evaluated [101]. Bakutra et al. noted that following laser intervention, a remarkable 80 % of patients showcased complete wound closure merely a week post-treatment, whereas 20 % exhibited partial healing [120]. Conversely, employing the traditional scalpel method, 80 % of cases displayed partial healing, with the remaining 20 % demonstrating complete wound closure [124]. These findings underscore the intricate interplay between treatment strategies and wound healing dynamics, warranting further exploration to optimize patient outcomes and refine clinical practices.

4.4. Repigmentation

Despite the meticulous examination of various study designs and the inclusion of diverse patient popula-tions, a strikingly consistent finding emerged: regardless of the modality employed—be it the traditional surgical scalpel or the more contemporary diode laser techniques—there

ensued a discernible occurrence of minor repigmentation subsequent to treatment [128]. Remarkably, this phenomenon manifested with such uniformity that no significant differences in repigmentation intensity were discerned during the meticu-lous follow-up period [122]. Such findings underscore a pivotal revelation: both surgical approaches, despite their methodological disparities, exhibit comparably efficacious outcomes in achieving depigmentation goals, thus transcending the initial severity of pigmentation as a determinant of success [17].In summary, the thorough examination carried out in this systematic review offers solid proof of the relative efficacy of diode laser and surgical scalpel methods for gingival depigmentation. When follow-up photos are taken, both groups show slight repigmentation, suggesting that both methods are equally effective in producing depigmentation results [17, 122,128]. Although the two treatments seem to have similar wound healing outcomes, the diode laser presents unique benefits in terms of reducing intraoperative bleeding and maybe lowering postoperative pain levels. These results highlight the significance of taking intra-operative and postoperative parameters into account in addition to depigmentation efficacy when choosing the best strategy for gingival depigmentation treatments.

4.5. Clinical implications and aesthetic considerations

It is impossible to overestimate the influence of gingival melanosis on dentofacial aesthetics, which makes efficient treatment choices essential for patients looking to improve their appearance. Techniques using diode lasers and surgical scalpels both provide workable answers with long-term cosmetic advantages. However, several considerations, such as patient preference, postoperative pain, intraoperative bleeding, and effectiveness, should be taken into account while choosing between these procedures. In order to customize the strategy and maximize treatment outcomes, physicians should also evaluate the unique characteristics of each patient as well as their goals for the course of treatment.

4.6. Limitations and future directions

It is important to recognize a few limitations in spite of the system-atic review’s insightful findings. The presence of heterogeneity in study design, sample size, follow-up protocols, and treatment characteristics among studies impedes the direct comparability of results and restricts their generalizability. Moreover, variations in data analysis techniques and variations in the application of diode lasers complicate attempts to reach firm findings [58,131–133]. Furthermore, some research small sample sizes raise the possibility of bias and highlight the necessity of conducting bigger, better-designed clinical trials. Standardized proced-ures and cooperative efforts among scientists are necessary to overcome these constraints and progress our knowledge of the relative merits of diode lasers and surgical techniques in the management of gingival melanosis [102,84,134].

In summary, although diode laser and surgical scalpel methods provide good treatment choices for gingival melanosis, the subtle vari-ations in results and the noted drawbacks underscore the clinical complexity of this field. Through acknowledging these constraints and adopting a cooperative research methodology, medical professionals and scholars can strive to improve treatment procedures, maximize patient results, and ultimately elevate the standard of care in cosmetic dentistry.

The more we learn about the implications of treating gingival melanosis, the more clear it is that thorough study is essential to improving our comprehension and strategy. While the systematic review offered here provides a strong starting point, more research is necessary to fully realize the promise of treatment modalities. One avenue of exploration could involve longitudinal studies tracking patients over extended periods to assess the longevity of treatment outcomes.

Furthermore, examining the psychological effects of gingival

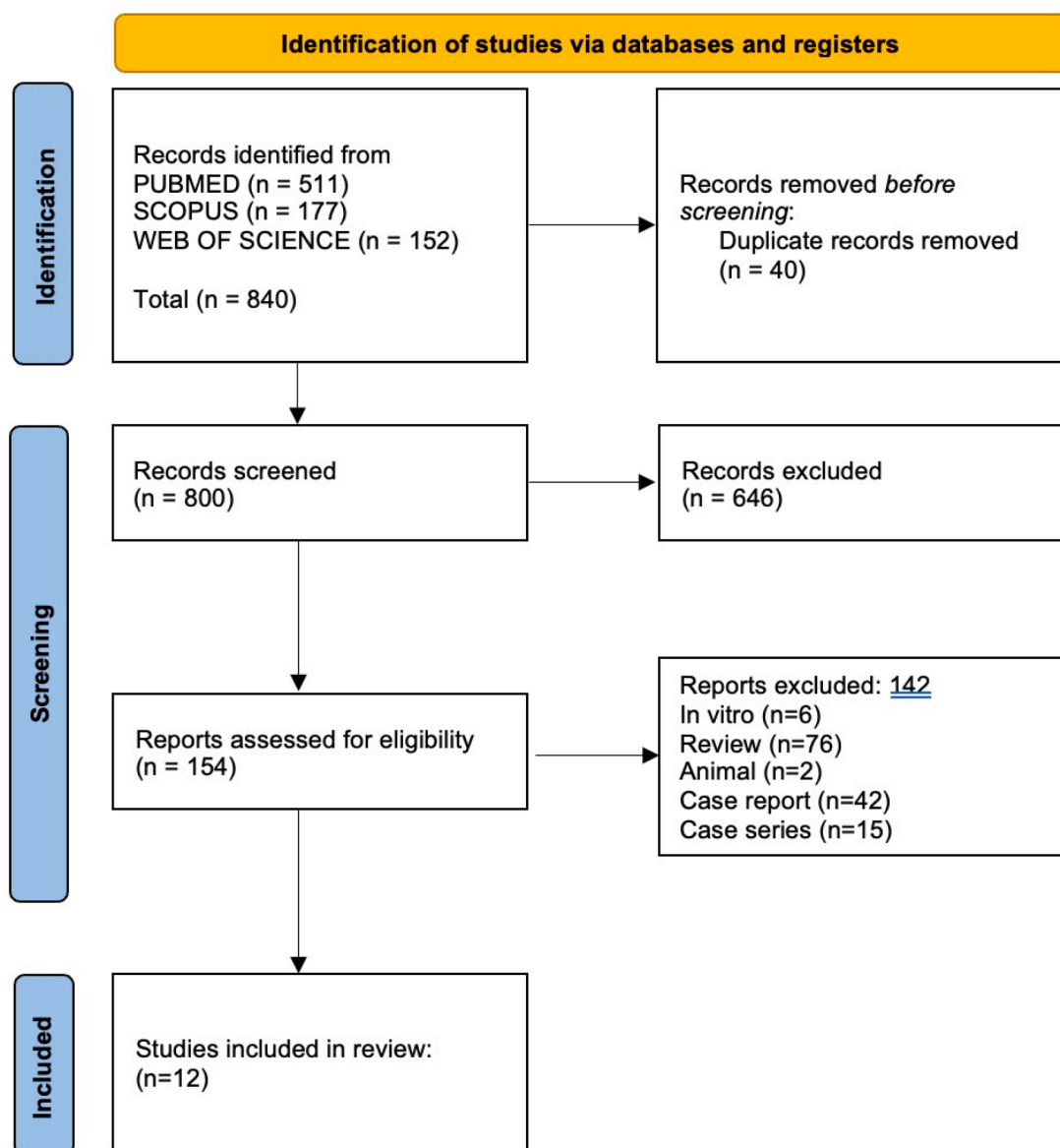


Fig. 4. Literature search Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram and database search indicators [118,130].

melanosis and its management on patients' quality of life may yield insightful information. Additionally, investigating new technologies and incorporating them into treatment plans has the potential to completely transform the industry by providing more effective and patient-centered methods. Essentially, the search for the best course of care for gingival melanosis is still underway, and the secret to realizing its full potential will be sustained cooperation and innovation.

5. Conclusions

In analyzing the outcomes of this systematic review, several key observations emerge regarding the comparison between surgical scalpel and diode laser techniques in gingival depigmentation:

- 1) Regarding the intensity of repigmentation, there were no differences between the surgical scalpel and diode laser techniques. Both presented slight repigmentation at follow-up.
- 2) In wound healing, it has not been possible to establish which of the two techniques provided a better postoperative period because both of the techniques showed similar results in the follow up.

- 3) Intraoperative bleeding was consistently lower with the diode laser in all studies.
- 4) In terms of pain, gingival depigmentation is not a very painful procedure, but most studies showed that the laser presented less pain compared to the use of a surgical scalpel.

In essence, while both methods demonstrate comparable outcomes in certain aspects such as repigmentation and wound healing, the diode laser exhibits advantages in terms of intraoperative bleeding and pain management, suggesting its potential as a preferred approach in gingival depigmentation procedures.

Funding

This research received no external funding.

Informed consent statement

Not applicable.

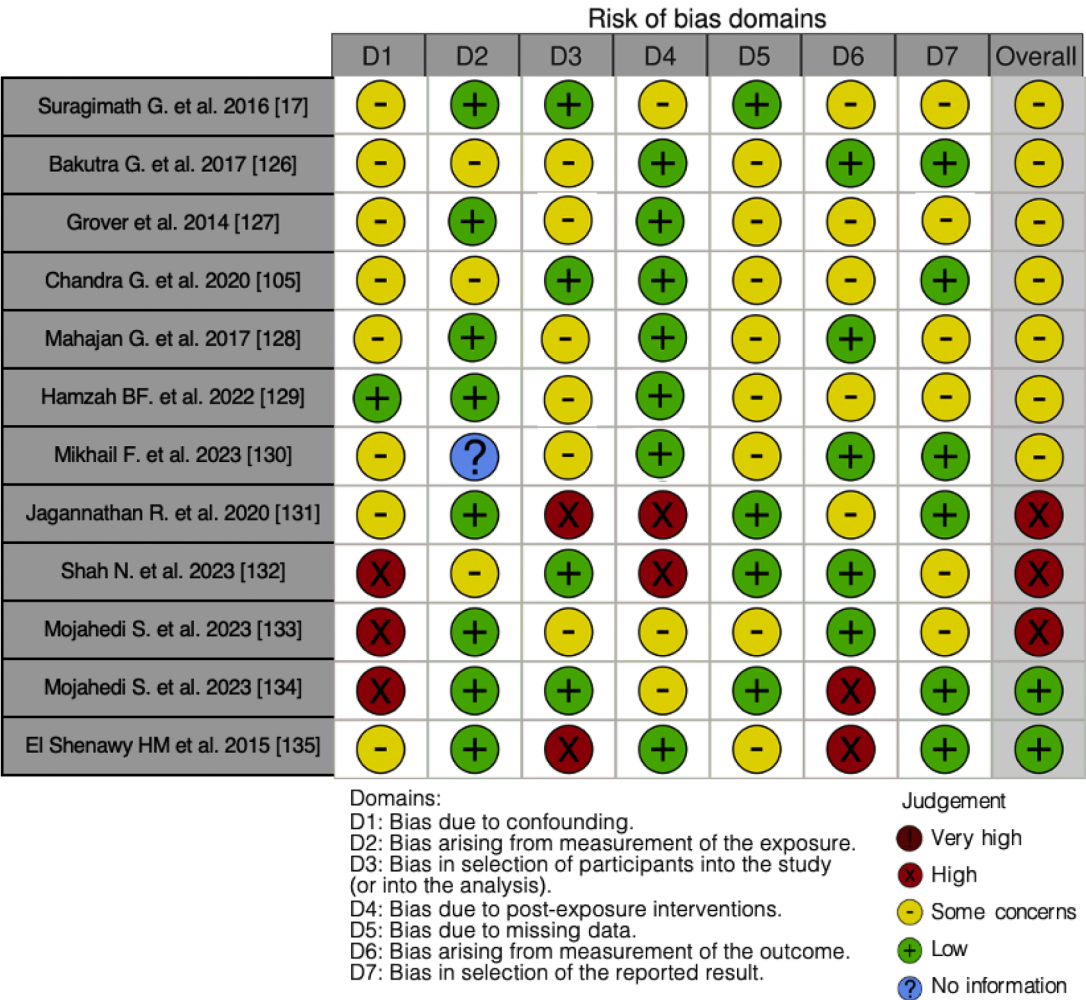


Fig. 5. Bias assessment.

CRediT authorship contribution statement

Francesco Inchingolo: Conceptualization, Methodology, Validation, Formal analysis, Data curation, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration. **Alessio Danilo Inchingolo:** Conceptualization, Methodology, Software, Validation, Formal analysis, Resources, Data curation, Writing – original draft, Writing – review & editing, Supervision, Project administration. **Irene Palumbo:** Conceptualization, Resources, Data curation, Writing – review & editing, Supervision. **Mariafrancesca Guglielmo:** Conceptualization, Resources, Writing – review & editing, Supervision. **Liviana Balestriere:** Conceptualization, Methodology, Data curation, Writing – original draft, Writing – review & editing, Supervision. **Lucia Casamassima:** Conceptualization, Methodology, Resources, Writing – original draft, Writing – review & editing, Supervision. **Danilo Ciccarrese:** Conceptualization, Formal analysis, Data curation, Writing – original draft, Visualization. **Pierluigi Marotti:** Conceptualization, Formal analysis, Data curation, Writing – original draft, Visualization. **Antonio Mancini:** Methodology, Formal analysis, Writing – review & editing. **Andrea Palermo:** Conceptualization, Methodology, Software, Formal analysis, Resources, Writing – review & editing, Visualization, Supervision. **Angelo Michele Inchingolo:** Conceptualization, Methodology, Validation, Formal analysis, Resources, Data curation, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration. **Gianna Dipalma:** Conceptualization, Methodology, Software, Validation, Formal analysis, Resources, Data curation, Writing – original draft, Writing – review & editing, Visualization, Supervision,

Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Gupta G. Management of gingival hyperpigmentation by semiconductor diode laser. *J Cutan Aesthet Surg* 2011;4:208. <https://doi.org/10.4103/0974-2077.91256>.

[2] Sridharan S, Ganiger K, Satyanarayana A, Rahul A, Shetty S. Effect of environmental tobacco smoke from smoker parents on gingival pigmentation in children and young adults: a cross-sectional study. *J Periodontol* 2011;82: 956–62. <https://doi.org/10.1902/jop.2010.100479>.

[3] Inchingolo F, Tatullo M, Abenavoli FM, Marrelli M, Inchingolo AD, Inchingolo AM, et al. Comparison between traditional surgery, CO2 and Nd:Yag laser treatment for generalized gingival hyperplasia in Sturge-Weber syndrome: a retrospective study. *J Investig Clin Dent* 2010;1:85–9. <https://doi.org/10.1111/j.2041-1626.2010.00020.x>.

[4] Minetti E, Palermo A, Inchingolo AD, Patano A, Viapiano F, Ciocia AM, et al. Autologous tooth for bone regeneration: dimensional examination of Tooth Transformer® granules. *Eur Rev Med Pharmacol Sci* 2023;27:5421–30. <https://doi.org/10.26355/eurrev.202306.32777>.

[5] Gondak RO, da Silva-Jorge R, Jorge J, Lopes MA, Vargas PA. Oral pigmented lesions: clinicopathologic features and review of the literature. *Med Oral Patol Oral Cir Bucal* 2012;e919–24. <https://doi.org/10.4317/medoral.17679>.

[6] Akram Z, Al-Shareef SAA, Daoud U, Asiri FY, Shah AH, AlQahtani MA, et al. Bactericidal efficacy of photodynamic therapy against periodontal pathogens in

- periodontal disease: a systematic review. *Photomed Laser Surg* 2016;34:137–49. <https://doi.org/10.1089/pho.2015.4076>.
- [7] Abduljabbar T, Vohra F, Javed F, Akram Z. Antimicrobial photodynamic therapy adjuvant to non-surgical periodontal therapy in patients with diabetes mellitus: a meta-analysis. *Photodiagnosis Photodyn Ther* 2017;17:138–46. <https://doi.org/10.1016/j.pdpdt.2016.11.008>.
 - [8] Tarullo A, Laino L, Tarullo A, Inchingolo F, Flace P, Inchingolo AM, et al. Use of a diode laser in an excisional biopsy of two spoonlike neoformations on the tongue tip. *Acta Biomed* 2011;82:63–8.
 - [9] Patano A, Malcangi G, Sardano R, Mastrodonato A, Garofoli G, Mancini A, et al. White spots: prevention in orthodontics-systematic review of the literature. *Int J Environ Res Public Health* 2023;20. <https://doi.org/10.3390/ijerph20085608>.
 - [10] Inchingolo F, Hazbala D, Inchingolo AD, Malcangi G, Marinelli G, Mancini A, et al. Innovative concepts and recent breakthrough for engineered graft and constructs for bone regeneration: a literature systematic review. *Materials (Basel)* 2022;15. <https://doi.org/10.3390/ma15031120>.
 - [11] Vohra F, Akram Z, Saffi SH, Vaithilingam RD, Ghanem A, Sergis K, et al. Role of antimicrobial photodynamic therapy in the treatment of aggressive periodontitis: a systematic review. *Photodiagn Photodyn Ther* 2016;13:139–47. <https://doi.org/10.1016/j.pdpdt.2015.06.010>.
 - [12] Akram Z, Abduljabbar T, Sauro S, Daoud U. Effect of photodynamic therapy and laser alone as adjunct to scaling and root planing on gingival crevicular fluid inflammatory proteins in periodontal disease: a systematic review. *Photodiagn Photodyn Ther* 2016;16:142–53. <https://doi.org/10.1016/j.pdpdt.2016.09.004>.
 - [13] Abduljabbar T, Javed F, Shah A, Samer MS, Vohra F, Akram Z. Role of lasers as an adjunct to scaling and root planing in patients with type 2 diabetes mellitus: a systematic review. *Lasers Med Sci* 2017;32:449–59. <https://doi.org/10.1007/s10103-016-2086-5>.
 - [14] Fasbinder DJ. Dental laser technology. *Compend Contin Educ Dent* 2008;29:456. 452–4458–9; quiz 460, 462.
 - [15] Peeran SW, Ramalingam K, Peeran SA, Altaf OB, Alsaid FM, Mugerab MH. Gingival pigmentation index proposal of a new index with a brief review of current indices. *Eur J Dent* 2014;08:287–90. <https://doi.org/10.4103/1305-7456.130640>.
 - [16] Abduljabbar T, Vohra F, Akram Z, Ghani SMA, Al-Hamoudi N, Javed F. Efficacy of surgical laser therapy in the management of oral pigmented lesions: a systematic review. *J Photochem Photobiol B* 2017;173:353–9. <https://doi.org/10.1016/j.jphotobiol.2017.06.016>.
 - [17] Suragimath G, Lohana MH, Varma S. A split mouth randomized clinical comparative study to evaluate the efficacy of gingival depigmentation procedure using conventional scalpel technique or diode laser. *J Lasers Med Sci* 2016;7: 227–32. <https://doi.org/10.15171/jlms.2016.40>.
 - [18] Minervini G, Franco R, Marrapodi MM, Ronsivale V, Shapira I, Cicciù M. Prevalence of temporomandibular disorders in subjects affected by Parkinson disease: a systematic review and metanalysis. *J Oral Rehabil* 2023;50:877–85. <https://doi.org/10.1111/joor.13496>.
 - [19] Donnarumma G, De Gregorio V, Fusco A, Farina E, Baroni A, Esposito V, et al. Inhibition of HSV-1 replication by laser diode-irradiation: possible mechanism of action. *Int J Immunopathol Pharmacol* 2010;23:1167–76. <https://doi.org/10.1177/039463201002300420>.
 - [20] Biagi R. Laser-assisted treatment of dentinal hypersensitivity: a literature review. *Ann Stomatol (Roma)* 2015. <https://doi.org/10.11138/ads/2015.6.3.075>.
 - [21] Polizzi A, Antonocito S, Patini R, Quinzi V, Mummolo S, Leonardi R, et al. Oral alterations in heritable epidermolysis bullosa: a clinical study and literature review. *Biomed Res Int* 2022;2022:1–8. <https://doi.org/10.1155/2022/6493156>.
 - [22] Memè L, Sartini D, Pozzi V, Emanuelli M, Strappa EM, Bittarello P, et al. Epithelial biological response to machined titanium vs. PVD zirconium-coated titanium: an in vitro study. *Materials (Basel)* 2022;15:7250. <https://doi.org/10.3390/ma15207250>.
 - [23] Mummolo S, Sapio S, Falco A, Vittorini OL, Quinzi V. Management of pedodontic patients in moderate sedation in clinical dentistry: evaluation of behaviour before and after treatment. *J Biol Regul Homeost Agents* 2020;34:55–62. DENTAL SUPPLEMENT.
 - [24] Alasmari DS. An insight into gingival depigmentation techniques: the pros and cons. *Int J Health Sci (Qassim)* 2018;12:84–9.
 - [25] Araki S, Murata K, Ushio K, Sakai R. Dose-response relationship between tobacco consumption and melanin pigmentation in the attached gingiva. *Arch Environ Health Int J* 1983;38:375–8. <https://doi.org/10.1080/00039896.1983.10545823>.
 - [26] Ballini A, Cantore S, Signorini L, Saini R, Scacco S, Gnoni A, et al. Efficacy of sea salt-based mouthwash and xylitol in improving oral hygiene among adolescent population: a pilot study. *Int J Environ Res Public Health* 2020;18. <https://doi.org/10.3390/ijerph18010044>.
 - [27] Becker SW. Melanin pigmentation through the Ages1. *J Invest Dermatol* 1946;7: 381–99. <https://doi.org/10.1038/jid.1946.45>.
 - [28] Bergamaschi O, Kon S, Doine AI, Ruben MP. Melanin repigmentation after gingivectomy: a 5-year clinical and transmission electron microscopic study in humans. *Int J Periodontics Restorative Dent* 1993;13:85–92.
 - [29] Cobb CM. Lasers in periodontics: a review of the literature. *J Periodontol* 2006; 77:545–64. <https://doi.org/10.1902/jop.2006.050417>.
 - [30] De Benedittis M, Petrucci M, Pastore L, Inchingolo F, Serpico R. Nd:YAG laser for gingivectomy in Sturge-Weber syndrome. *J Oral Maxillofac Surg* 2007;65:314–6. <https://doi.org/10.1016/j.joms.2006.05.011>.
 - [31] De Falco D, Di Venere D, Maiorano E. An overview of diode laser-assisted oral surgery. *Cureus* 2020. <https://doi.org/10.7759/cureus.9297>.
 - [32] DUMMETT CO. Physiologic pigmentation of the oral and cutaneous tissues in the Negro. *J Dent Res* 1946;25:421–32. <https://doi.org/10.1177/0022345460250060201>.
 - [33] Dummett CO. Systemic significance of oral pigmentation and discoloration. *Postgrad Med* 1971;49:78–82. <https://doi.org/10.1080/00325481.1971.11696473>.
 - [34] Dummett CO, Barends G. Oromucosal pigmentation: an updated literary review. *J Periodontol* 1971;42:726–36. <https://doi.org/10.1902/jop.1971.42.11.726>.
 - [35] Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1978;32:377–84. <https://doi.org/10.1136/jech.52.6.377>.
 - [36] Esen E, Haytac MC, Oz IA, Erdoğan O, Karsli ED. Gingival melanin pigmentation and its treatment with the CO2 laser. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004;98:522–7. <https://doi.org/10.1016/j.tripleo.2004.02.059>.
 - [37] Fitzpatrick RE, Goldman MP, Ruiz-Esparza J. Laser treatment of benign pigmented epidermal lesions using a 300 nsecond pulse and 510 nm wavelength. *J Dermatol Surg Oncol* 1993;19:341–7. <https://doi.org/10.1111/j.1524-4725.1993.tb00355.x>.
 - [38] Fujimoto K, Kiyosaki T, Mitsui N, Mayahara K, Omasa S, Suzuki N, et al. Low-intensity laser irradiation stimulates mineralization via increased BMPs in MC3T3-E1 cells. *Lasers Surg Med* 2010;42:519–26. <https://doi.org/10.1002/lsm.20880>.
 - [39] Friedmann PS, Gilchrist BA. Ultraviolet radiation directly induces pigment production by cultured human melanocytes. *J Cell Physiol* 1987;133:88–94. <https://doi.org/10.1002/jcp.1041330111>.
 - [40] Fukuhara E, Goto T, Matayoshi T, Kobayashi S, Takahashi T. Optimal low-energy laser irradiation causes temporal G2/M arrest on rat calvarial osteoblasts. *Calcif Tissue Int* 2006;79:443–50. <https://doi.org/10.1007/s00223-006-0072-9>.
 - [41] Isacco CG, Ballini A, De Vito D, Nguyen KCD, Cantore S, Bottalico L, et al. Rebalancing the oral microbiota as an efficient tool in endocrine, metabolic and immune disorders. *Endocr Metab Immune Disord Drug Targets* 2021;21:777–84. <https://doi.org/10.2174/1871530320666200729142504>.
 - [42] Malcangi G, Patano A, Inchingolo AD, Ciocia AM, Piras F, Latini G, et al. Efficacy of carbamide and hydrogen peroxide tooth bleaching techniques in orthodontic and restorative dentistry patients: a scoping review. *Applied Sciences* 2023;13: 7089. <https://doi.org/10.3390/app13127089>.
 - [43] Kumar S, Bhat GS, Bhat KM. Comparative evaluation of gingival depigmentation using tetrafluoroethane cryosurgery and gingival abrasion technique: two years follow up. *J Clin Diagn Res* 2013;7:389–94. <https://doi.org/10.7860/JCDR/2013/4454.2779>.
 - [44] Meleti M, Vescovi P, Mooi WJ, van der Waal I. Pigmented lesions of the oral mucosa and perioral tissues: a flow-chart for the diagnosis and some recommendations for the management. *Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol* 2008;105:606–16. <https://doi.org/10.1016/j.tripleo.2007.07.047>.
 - [45] Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c869. <https://doi.org/10.1136/bmj.c869>.
 - [46] Müller S. Melanin-associated pigmented lesions of the oral mucosa: presentation, differential diagnosis, and treatment. *Dermatol Ther* 2010;23:220–9. <https://doi.org/10.1111/j.1529-8019.2010.01319.x>.
 - [47] Nakamura Y, Hossain M, Hirayama K, Matsumoto K. A clinical study on the removal of gingival melanin pigmentation with the CO(2) laser. *Lasers Surg Med* 1999;25:140–7. [https://doi.org/10.1002/\(sici\)1096-9101\(1999\)25:2<140::aid-lsm7>3.0.co;2-7](https://doi.org/10.1002/(sici)1096-9101(1999)25:2<140::aid-lsm7>3.0.co;2-7).
 - [48] Ozbayrak S, Dumlu A, Ercalik-Yalcinkaya S. Treatment of melanin-pigmented gingiva and oral mucosa by CO2 laser. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;90:14–5. <https://doi.org/10.1067/moe.2000.106396>.
 - [49] Patano A, Malcangi G, De Santis M, Morolla R, Settanni V, Piras F, et al. Conservative treatment of dental non-carious cervical lesions: a scoping review. *Biomedicine* 2023;11:1530. <https://doi.org/10.3390/biomedicine11061530>.
 - [50] Scarano A, Lorusso F, Inchingolo F, Postiglione F, Petrini M. The effects of erbium-doped yttrium aluminum garnet Laser (Er: YAG) irradiation on Sandblasted and Acid-Etched (SLA) titanium, an in vitro study. *Materials (Basel)* 2020;13. <https://doi.org/10.3390/ma13184174>.
 - [51] Soliman MM, Al Thomali Y, Al Shammrani A, El Gazeerly H. The use of soft tissue diode laser in the treatment of oral hyper pigmentation. *Int J Health Sci (Qassim)* 2014;8:133–40. <https://doi.org/10.12816/0006079>.
 - [52] Tal H, Oegieser D, Tal M. Gingival depigmentation by erbium:YAG laser: clinical observations and patient responses. *J Periodontol* 2003;74:1660–7. <https://doi.org/10.1902/jop.2003.74.11.1660>.
 - [53] Talebi M, Farmanbar N, Abolfazli S, Sarraf Shirazi A. Management of physiological hyperpigmentation of oral mucosa by cryosurgical treatment: a case report. *J Dent Res Dent Clin Dent Prospects* 2012;6:148–51. <https://doi.org/10.5681/jodd.2012.030>.
 - [54] Tamizi M, Taheri M. Treatment of severe physiologic gingival pigmentation with free gingival autograft. *Quintessence Int* 1996;27:555–8.
 - [55] Tsatmali M, Ancans J, Thody AJ. Melanocyte function and its control by melanocortin peptides. *J Histochem Cytochem* 2002;50:125–33. <https://doi.org/10.1177/002215540205000201>.
 - [56] Wheeland RG. History of lasers in dermatology. *Clin Dermatol* 1995;13:3–10. [https://doi.org/10.1016/0738-081x\(94\)00021-s](https://doi.org/10.1016/0738-081x(94)00021-s).
 - [57] Coletan S. Lasers in surgical periodontics and oral medicine. *Dent Clin North Am* 2004;48:937–62. <https://doi.org/10.1016/j.cden.2004.05.008>.

- [58] Bakhshi M, Rahmani S, Rahmani A. Lasers in esthetic treatment of gingival melanin hyperpigmentation: a review article. *Lasers Med Sci* 2015;30:2195–203. <https://doi.org/10.1007/s10103-015-1797-3>.
- [59] Esen E, Haytac MC, Öz İA, Erdoğan Ö, Karşlı ED. Gingival melanin pigmentation and its treatment with the CO2 laser. *Oral Surg Oral Med Oral Pathol Oral Radiol Endodontology* 2004;98:522–7. <https://doi.org/10.1016/j.tripleo.2004.02.059>.
- [60] Mahesh H, Harish M, Shashikumar B, Ramya K. Gingival pigmentation reduction: a novel therapeutic modality. *J Cutan Aesthet Surg* 2012;5:137. <https://doi.org/10.4103/0974-2077.99458>.
- [61] Dummett CO, Gupta OP. Estimating the epidemiology of oral pigmentation. *J Natl Med Assoc* 1964;56:419–20.
- [62] Murthy Mb, Kaur J, Das R. Treatment of gingival hyperpigmentation with rotary abrasive, scalpel, and laser techniques: a case series. *J Indian Soc Periodontol* 2012;16:614. <https://doi.org/10.4103/0972-124X.106933>.
- [63] Kawashima Y, Aoki A, Ishii S, Watanabe H, Ishikawa I. Er:YAG laser treatment of gingival melanin pigmentation. *Int Congr Ser* 2003;1248:245–8. [https://doi.org/10.1016/S0531-5131\(02\)01298-0](https://doi.org/10.1016/S0531-5131(02)01298-0).
- [64] Farronato D, Mangano F, Briguglio F, Iorio-Siciliano V, Riccietello F, Guarnieri R. Influence of laser-look surface on immediate functional loading of implants in single-tooth replacement: a 2-year prospective clinical study. *Int J Periodontics Restorative Dent* 2014;34:79–89. <https://doi.org/10.11607/prd.1747>.
- [65] Contaldo M, Lauritano D, Carinci F, Romano A, Di Stasio D, Lajolo C, et al. Intraoral confocal microscopy of suspicious oral lesions: a prospective case series. *Int J Dermatol* 2020;59:82–90. <https://doi.org/10.1111/ijd.14574>.
- [66] Şimşek Kaya G, Yapıcı Yavuz G, Sümbüllü MA, Dayı E. A comparison of diode laser and Er:YAG lasers in the treatment of gingival melanin pigmentation. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2012;113:293–9. <https://doi.org/10.1016/j.tripleo.2011.03.005>.
- [67] Pavlic V, Brkic Z, Marin S, Cicmil S, Gojkovic-Vukelic M, Aoki A. Gingival melanin depigmentation by Er:YAG laser: a literature review. *J Cosm Laser Therapy* 2018; 20:85–90. <https://doi.org/10.1080/14764172.2017.1376092>.
- [68] Hegde R, Padhye A, Sumanth S, Jain AS, Thukral N. Comparison of surgical stripping; Erbium-doped:yttrium, aluminum, and garnet laser; and carbon dioxide laser techniques for gingival depigmentation: a clinical and histologic study. *J Periodontol* 2013;84:738–48. <https://doi.org/10.1902/jop.2012.120094>.
- [69] Zeredo JL, Sasaki KM, Yozgatian JH, Okada Y, Toda K. Comparison of jaw-opening reflexes evoked by Er:YAG laser versus scalpel incisions in rats. *Oral Surg Oral Med Oral Pathol Oral Radiol Endodontology* 2005;100:31–5. <https://doi.org/10.1016/j.tripleo.2004.11.012>.
- [70] Kishore A, Kathariya R, Deshmukh V, Vaze S, Khaliya N, Dandgaval R. Effectiveness of Er:YAG and CO2 lasers in the management of gingival melanin hyperpigmentation. *Oral Health Dent Manag* 2014;13:486–91.
- [71] 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;85:554–61. <https://doi.org/10.1902/jop.2013.130219>.
- [72] Azzeah MM. Treatment of gingival hyperpigmentation by Erbium-Doped:yttrium, Aluminum, and Garnet Laser for Esthetic Purposes. *J Periodontol* 2007;78: 177–84. <https://doi.org/10.1902/jop.2007.060167>.
- [73] Pourazarandian A, Watanabe H, Ruwanpura SMPM, Aoki A, Ishikawa I. Effect of low-level Er:YAG laser irradiation on cultured human gingival fibroblasts. *J Periodontol* 2005;76:187–93. <https://doi.org/10.1902/jop.2005.76.2.187>.
- [74] Aleksic V, Aoki A, Iwasaki K, Takasaki AA, Wang C-Y, Abiko Y, et al. Low-level Er:YAG laser irradiation enhances osteoblast proliferation through activation of MAPK/ERK. *Lasers Med Sci* 2010;25:559–69. <https://doi.org/10.1007/s10103-010-0761-5>.
- [75] Ogita M, Tsuchida S, Aoki A, Satoh M, Kado S, Sawabe M, et al. Increased cell proliferation and differential protein expression induced by low-level Er:YAG laser irradiation in human gingival fibroblasts: proteomic analysis. *Lasers Med Sci* 2015;30:1855–66. <https://doi.org/10.1007/s10103-014-1691-4>.
- [76] Giannelli M, Bani D, Viti C, Tani A, Lorenzini L, Zecchi-Orlandini S, et al. Comparative evaluation of the effects of different photoablative laser irradiation protocols on the gingiva of periodontopathic patients. *Photomed Laser Surg* 2012; 30:222–30. <https://doi.org/10.1089/pho.2011.3172>.
- [77] Gokhale SR, Padhye AM, Byakod G, Jain SA, Padbidri V, Shivaswamy S. A comparative evaluation of the efficacy of diode laser as an adjunct to mechanical debridement versus conventional mechanical debridement in periodontal flap surgery: a clinical and microbiological study. *Photomed Laser Surg* 2012;30:598–603. <https://doi.org/10.1089/pho.2012.3252>.
- [78] Goharkhay K, Moritz A, Wilder-Smith P, Schoop U, Kluger W, Jakolitsch S, et al. Effects on oral soft tissue produced by a diode laser in vitro. *Lasers Surg Med* 1999;25:401–6. [https://doi.org/10.1002/\(sici\)1096-9101\(1999\)25:5<401::aid-lsm6>3.0.co;2-u](https://doi.org/10.1002/(sici)1096-9101(1999)25:5<401::aid-lsm6>3.0.co;2-u).
- [79] Giannini R, Vassalli M, Chellini F, Polidori L, Dei R, Giannelli M. Neodymium: yttrium aluminum garnet laser irradiation with low pulse energy: a potential tool for the treatment of peri-implant disease. *Clin Oral Implants Res* 2006;17:638–43. <https://doi.org/10.1111/j.1600-0501.2006.01278.x>.
- [80] Goldoni R, Dolci C, Boccari E, Inchingolo F, Paghi A, Strambini L, et al. Salivary biomarkers of neurodegenerative and demyelinating diseases and biosensors for their detection. *Ageing Res Rev* 2022;76:101587. <https://doi.org/10.1016/j.arr.2022.101587>.
- [81] Gómez C, Domínguez A, García-Kass AI, García-Núñez JA. Adjunctive Nd:YAG laser application in chronic periodontitis: clinical, immunological, and microbiological aspects. *Lasers Med Sci* 2011;26:453–63. <https://doi.org/10.1007/s10103-010-0795-8>.
- [82] Goultchin J, Gazit D, Bichacho N, Bab I. Changes in teeth and gingiva of dogs following laser surgery: a block surface light microscope study. *Lasers Surg Med* 1988;8:402–8. <https://doi.org/10.1002/lsm.1900080411>.
- [83] 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. *Journal of Cosmetic and Laser Therapy* 2019;21:209–12. <https://doi.org/10.1080/14764172.2018.1511912>.
- [84] Ishikawa I, Aoki A, Takasaki AA. Potential applications of Erbium:YAG laser in periodontics. *J Periodontol Res* 2004;39:275–85. <https://doi.org/10.1111/j.1600-0765.2004.00738.x>.
- [85] Tal H, Oegieser D, Tal M. Gingival depigmentation by Erbium: YAG laser: clinical observations and patient responses. *J Periodontol* 2003;74:1660–7. <https://doi.org/10.1902/jop.2003.74.11.1660>.
- [86] Giannelli M, Formigli L, Lorenzini L, Bani D. Combined photoablative and photodynamic diode laser therapy as an adjunct to non-surgical periodontal treatment: a randomized split-mouth clinical trial. *J Clin Periodontol* 2012;39: 962–70. <https://doi.org/10.1111/j.1600-051X.2012.01925.x>.
- [87] Inchingolo AD, Patano A, Coloccia G, Ceci S, Inchingolo AM, Marinelli G, et al. The efficacy of a new AMCOP® elastodontic protocol for orthodontic interceptive treatment: a case series and literature overview. *Int J Environ Res Public Health* 2022;19:988. <https://doi.org/10.3390/ijerph19020988>.
- [88] Inchingolo F, Tarullo A, Cagiano R, Resta G, Dipalma G, Inchingolo AM, et al. Successful use of a topical mixture with ozonolipole in the treatment of actinic ulcers. *Clin Cosmet Investig Dermatol* 2015;8:147–50. <https://doi.org/10.2147/CCID.S67826>.
- [89] Rosa DSA, Aranha ACC, de Paula Eduardo C, Aoki A. Esthetic treatment of gingival melanin hyperpigmentation with Er:YAG laser: short-term clinical observations and patient follow-up. *J Periodontol* 2007;78:2018–25. <https://doi.org/10.1902/jop.2007.070041>.
- [90] Şimşek Kaya G, Yapıcı Yavuz G, Sümbüllü MA, Dayı E. A comparison of diode laser and Er:YAG lasers in the treatment of gingival melanin pigmentation. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2012;113:293–9. <https://doi.org/10.1016/j.tripleo.2011.03.005>.
- [91] Hanioka T, Tanaka K, Ojima M, Yuuki K. Association of melanin pigmentation in the gingiva of children with parents who smoke. *Pediatrics* 2005;116:e186–90. <https://doi.org/10.1542/peds.2004-2628>.
- [92] Pontes AEF, Pontes CC, Souza SLS, Novaes AB, Grisi MFM, Taba M. Evaluation of the efficacy of the acellular dermal matrix allograft with partial thickness flap in the elimination of gingival melanin pigmentation. A comparative clinical study with 12 months of follow-up. *J Esthet Restor Dent* 2006;18:135–43. https://doi.org/10.1111/j.1708-8240.2006.00004_1.x. discussion 143.
- [93] Gregg RH, McCarthy DK. Laser ENAP for periodontal bone regeneration. *Dent Today* 1998;17:88–91.
- [94] Grzech-Leśniak K, Nowicka J, Pajczkowska M, Matys J, Szymonowicz M, Kurokpa P, et al. Effects of Nd:YAG laser irradiation on the growth of *Candida albicans* and *Streptococcus mutans*: in vitro study. *Lasers Med Sci* 2019;34: 129–37. <https://doi.org/10.1007/s10103-018-2622-6>.
- [95] Halaban R, Cheng E, Svedine S, Aron R, Hebert DN. Proper folding and endoplasmic reticulum to golgi transport of tyrosinase are induced by its substrates, DOPA and tyrosine. *Journal of Biological Chemistry* 2001;276: 11933–8. <https://doi.org/10.1074/jbc.M008703200>.
- [96] Ribeiro FV, Cavaller CP, Casarin RC V, Casati MZ, Cirano FR, Dutra-Corrêa M, et al. Esthetic treatment of gingival hyperpigmentation with Nd:YAG laser or scalpel technique: a 6-month RCT of patient and professional assessment. *Lasers Med Sci* 2014;29:537–44. <https://doi.org/10.1007/s10103-012-1254-5>.
- [97] Sterne JA, Hernán MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;i4919. <https://doi.org/10.1136/bmj.i4919>.
- [98] Ferrazzano GF, Cantile T, Sangianantonio G, Ingenito A, Rengo S, Alcidi B, et al. Oral health status and Unmet Restorative Treatment Needs (UTN) in disadvantaged migrant and non migrant children in Italy. *Eur J Paediatr Dent* 2019;20:10–4. <https://doi.org/10.23804/ejpd.2019.20.01.02>.
- [99] Ribeiro FV, Cavaller CP, Casarin RC V, Casati MZ, Cirano FR, Dutra-Corrêa M, et al. Esthetic treatment of gingival hyperpigmentation with Nd:YAG laser or scalpel technique: a 6-month RCT of patient and professional assessment. *Lasers Med Sci* 2014;29:537–44. <https://doi.org/10.1007/s10103-012-1254-5>.
- [100] Sawabe M, Aoki A, Komaki M, Iwasaki K, Ogita M, Izumi Y. Gingival tissue healing following Er:YAG laser ablation compared to electrosurgery in rats. *Lasers Med Sci* 2015;30:875–83. <https://doi.org/10.1007/s10103-013-1478-z>.
- [101] Chandra G, Kumar MV, Walavalkar N, Vandana K, Vardhan P. Evaluation of surgical scalpel versus semiconductor diode laser techniques in the management of gingival melanin hyperpigmentation: a split-mouth randomized clinical comparative study. *J Indian Soc Periodontol* 2020;24:47. <https://doi.org/10.4103/jisip.186.19>.
- [102] Iwata T, Yamato M, Zhang Z, Mukobata S, Washio K, Ando T, et al. Validation of human periodontal ligament-derived cells as a reliable source for cytotherapeutic use. *J Clin Periodontol* 2010;37:1088–99. <https://doi.org/10.1111/j.1600-051X.2010.01597.x>.
- [103] Inchingolo AD, Inchingolo AM, Malcangi G, Avantario P, Azzollini D, Buongiorno S, et al. Effects of resveratrol, curcumin and quercetin supplementation on bone metabolism—a systematic review. *Nutrients* 2022;14: 3519. <https://doi.org/10.3390/nu14173519>.
- [104] Inchingolo AM, Malcangi G, Ferrara I, Viapiano F, Netti A, Buongiorno S, et al. Laser surgical approach of upper labial frenulum: a systematic review. *Int J Environ Res Public Health* 2023;20. <https://doi.org/10.3390/ijerph20021302>.

- [105] Wise R, Chen C-Y, Kim D. Treatment of physiologic gingival pigmentation with surgical blade: a 25-year follow-up. *Int J Periodontics Restorative Dent* 2018;38:s45–8. <https://doi.org/10.11607/prd.3701>.
- [106] Hedin CA. Smokers' melanosis. Occurrence and localization in the attached gingiva. *Arch Dermatol* 1977;113:1533–8. <https://doi.org/10.1001/archderm.113.11.1533>.
- [107] Inchingolo AD, Inchingolo AM, Bordea IR, Malcangi G, Xhajanka E, Scarano A, et al. SARS-CoV-2 disease through viral genomic and receptor implications: an overview of diagnostic and immunology breakthroughs. *Microorganisms* 2021;9:793. <https://doi.org/10.3390/microorganisms9040793>.
- [108] Inchingolo AD, Patano A, Coloccia G, Ceci S, Inchingolo AM, Marinelli G, et al. Genetic pattern, orthodontic and surgical management of multiple supplementary impacted teeth in a rare, cleidocranial dysplasia patient: a case report. *Medicina (B Aires)* 2021;57:1350. <https://doi.org/10.3390/medicina57121350>.
- [109] Zuo Y-G, Ma D-L, Jin H-Z, Liu Y-H, Wang H-W, Sun Q-N. Treatment of laugier-hunziker syndrome with the Q-switched alexandrite laser in 22 Chinese patients. *Arch Dermatol Res* 2010;302:125–30. <https://doi.org/10.1007/s00403-009-0930-1>.
- [110] Scarano A, Petrini M, Inchingolo F, Lorusso F, Amuso D. A new technique for the treatment of nasal telangiectasia using atmospheric plasma (voltaic arc dermabrasion): postoperative pain assessment by thermal infrared imaging. *J Cosmet Dermatol* 2020;19:2912–8. <https://doi.org/10.1111/jocd.13414>.
- [111] Raposo G, Marks MS. Melanosomes—dark organelles enlighten endosomal membrane transport. *Nat Rev Mol Cell Biol* 2007;8:786–97. <https://doi.org/10.1038/nrm2258>.
- [112] Guzzardella GA, Fini M, Torricelli P, Giavaresi G, Giardino R. Laser stimulation on bone defect healing: an in vitro study. *Lasers Med Sci* 2002;17:216–20. <https://doi.org/10.1007/s101030200031>.
- [113] Fukuoka H, Daigo Y, Enoki N, Taniguchi K, Sato H. Influence of carbon dioxide laser irradiation on the healing process of extraction sockets. *Acta Odontol Scand* 2011;69:33–40. <https://doi.org/10.3109/00016357.2010.517556>.
- [114] Trylovich DJ, Cobb CM, Pippin DJ, Spencer P, Killoy WJ. The effects of the Nd:YAG laser on in vitro fibroblast attachment to endotoxin-treated root surfaces. *J Periodontol* 1992;63:626–32. <https://doi.org/10.1902/jop.1992.63.7.626>.
- [115] Qadri T, Poddani P, Javed F, Tunér J, Gustafsson A. A short-term evaluation of Nd:YAG laser as an adjunct to scaling and root planing in the treatment of periodontal inflammation. *J Periodontol* 2010;81:1161–6. <https://doi.org/10.1902/jop.2010.090700>.
- [116] Galli C, Macaluso GM, Elezi E, Ravanetti F, Cacchioli A, Gualini G, et al. The effects of Er:YAG laser treatment on titanium surface profile and osteoblastic cell activity: an in vitro study. *J Periodontol* 2011;82:1169–77. <https://doi.org/10.1902/jop.2010.100428>.
- [117] Galioto N, Egeland E. Disorders of the oral cavity. *Fam med. Cham: Springer International Publishing*; 2022. p. 1015–24. https://doi.org/10.1007/978-3-030-54441-6_80.
- [118] Urrútia G, Bonfill X. Declaración PRISMA: una propuesta para mejorar la publicación de revisiones sistemáticas y metaanálisis. *Med Clin (Barc)* 2010;135:507–11. <https://doi.org/10.1016/j.medcli.2010.01.015>.
- [119] Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6:e1000097. <https://doi.org/10.1371/journal.pmed.1000097>.
- [120] Bakutra G, Shankarapillai R, Mathur L, Manohar B. Comparative evaluation of diode laser ablation and surgical stripping technique for gingival depigmentation: a clinical and immunohistochemical study. *Int J Health Sci (Qassim)* 2017;11:51–8.
- [121] Dadlani H, Bhardwaj A, Grover H, Yadav A, Lal S. Evaluation of patient response and recurrence of pigmentation following gingival depigmentation using laser and scalpel technique: a clinical study. *J Indian Soc Periodontol* 2014;18:586. <https://doi.org/10.4103/0972-124X.142450>.
- [122] Mahajan G, Kaur H, Jain S, Kaur N, Sehgal N, Gautam A. To compare the gingival melanin repigmentation after diode laser application and surgical removal. *J Indian Soc Periodontol* 2017;21:112. <https://doi.org/10.4103/jisp.jisp.152.17>.
- [123] Hamzah BF, Alattar AN, Salman TA. Long-term esthetically depigmented gingiva in a short operative duration, using two modes of 940 nm diode lasers—a randomized clinical trial. *Int J Dent* 2022;2022:1–8. <https://doi.org/10.1155/2022/8215348>.
- [124] Mikhail FF, El Menoufy H, El Kilani NS. Assessment of clinical outcomes and patient response to gingival depigmentation using a scalpel, ceramic bur, and diode laser 980 nm. *Clin Oral Investig* 2023;27:6939–50. <https://doi.org/10.1007/s00784-023-05310-w>.
- [125] Jagannathan R, Rajendran S, Balaji TM, Varadarajan S, Sridhar LP. Comparative evaluation of gingival depigmentation by scalpel, electrosurgery, and laser: a 14 months' follow-up study. *J Contemp Dent Pract* 2020;21:1159–64.
- [126] Shah N, Rai J, Shah M, Gupte M. Clinical evaluation and digital photographic analysis: a modern approach to assess gingival depigmentation. *World Journal of Dentistry* 2024;14:1084–90. <https://doi.org/10.5005/jp-journals-10015-2348>.
- [127] Mojahedi Nasab SM, Frentzen M, Mayr A, Rahmani S, Anbari F, Meister J, et al. Comparison of the diode laser wavelengths 445 nm and 810 nm in gingival depigmentation – a clinical evaluation. *J Lasers Med Sci* 2023;14:e63. <https://doi.org/10.34172/jlms.2023.63>.
- [128] Mojahedi SM, Bakhshi M, Babaei S, Mehdipour A, Asayesh H. Effect of 810 nm diode laser on physiologic gingival pigmentation. *Laser Ther* 2018;27:99–104. <https://doi.org/10.5978/islsm.18-OR-08>.
- [129] El Shenawy HM, Nasry SA, Zaky AA, Quriba MA. Treatment of gingival hyperpigmentation by diode laser for esthetical purposes. *Open Access Maced J Med Sci* 2015;3:447–54. <https://doi.org/10.3889/oamjms.2015.071>.
- [130] Higgins JPT, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928. <https://doi.org/10.1136/bmj.d5928>.
- [131] Ferrazzano GF, Scaravilli MS, Ingenito A. Dental and periodontal health status in Campanian children and relation between caries experience and socio-economic behavioural factors. *Eur J Paediatr Dent* 2006;7:174–8.
- [132] Kauzman A, Pavone M, Blanas N, Bradley G. Pigmented lesions of the oral cavity: review, differential diagnosis, and case presentations. *J Can Dent Assoc* 2004;70:682–3.
- [133] Kathariya R, Pradeep AR. Split mouth de-epithelization techniques for gingival depigmentation: a case series and review of literature. *J Indian Soc Periodontol* 2011;15:161–8. <https://doi.org/10.4103/0972-124X.84387>.
- [134] Ishikawa I, Aoki A, Takasaki AA. Clinical application of erbium:YAG laser in periodontology. *J Int Acad Periodontol* 2008;10:22–30.