

## Review

## Systematic Review and Meta-Analysis of the Effect of Various Laser Wavelengths in the Treatment of Peri-Implantitis

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**Background:** The primary aim of this systematic review is to address the following focused question: Is laser therapy, as a monotherapy or as an adjunctive therapy, an efficacious treatment modality for patients with peri-implantitis?

**Methods:** The PubMed database of the U.S. National Library of Medicine and the Cochrane Central Register of Controlled Trials were electronically searched, complemented by manual searches up to June 2013.

**Results:** The search yielded 137 titles and abstracts. After initial screening, 15 of 137 publications were scrutinized during the second phase of the review. In the second phase, nine articles were excluded from the analysis and six controlled, clinical studies were selected. Narrative synthesis of the results revealed that non-surgical laser treatment with a single application of either an erbium: yttrium-aluminum-garnet (Er:YAG) (2,940-nm) laser or a diode (660-nm) laser in combination with a phenothiazine chloride dye is efficient in controlling inflammation around treated implants for at least 6 months following intervention, whereas it has only a mild effect on reduction in probing depth (PD) and gain in clinical attachment level (CAL). There is limited information regarding the clinical application of the CO<sub>2</sub> (10.6-μm) laser in the surgical treatment of peri-implantitis; however, its use may be promising. A meta-analysis could be performed only for the efficacy of Er:YAG laser due to the heterogeneity of the studies and the limited amount of data available. Meta-analysis did not reveal statistically significant evidence for treatment effects in reducing PD and CAL levels in comparison to controls.

**Conclusions:** Based on the limited information currently available, any superiority of laser treatment in comparison to conventional treatment of peri-implantitis could not be identified. Considering the high heterogeneity and the low number of included studies, the authors cautiously conclude that non-surgical laser therapy may be investigated as phase I therapy for the treatment of peri-implantitis. Future research should emphasize detailed description of the specific laser characteristics and power settings in clinical studies. *J Periodontol* 2014;85:1203-1213.

### KEY WORDS

Laser therapy; lasers; lasers, solid-state meta-analysis; peri-implantitis; review, systematic.

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Even though dental implants are a successful treatment modality, failures may occur.<sup>1,2</sup> Peri-implantitis is the most common reason for a late failure and can occur even after years of successful osseointegration.<sup>3,4</sup>

Despite the structural differences between periodontal and peri-implant tissues,<sup>5</sup> there are many similarities in the microbiota responsible for the development of periodontal and peri-implant diseases.<sup>6,7</sup> Peri-implantitis is defined as an inflammatory disease that is characterized by loss of supporting bone around a functioning implant.<sup>8,9</sup> Micro-organisms residing on the implant surface are considered to be the primary etiologic factor of peri-implantitis.<sup>10,11</sup> The role of microbial plaque accumulation in the development of peri-implantitis has been well documented.<sup>10-14</sup> On the other hand, the ideal method of implant surface decontamination to re-establish the health of peri-implant tissue remains to be determined.<sup>15</sup>

Removal of bacterial deposits is essential in the treatment of peri-implant infections, and various therapeutic approaches have been described in the literature, including mechanical debridement, disinfection with chemotherapeutic agents, and laser therapy.<sup>16,17</sup> Recently, there has been a plenitude of scientific data regarding the use of laser irradiation to achieve titanium surface decontamination; thus, research is focusing on lasers' potential use in the treatment of peri-implantitis.<sup>18-20</sup> Results from an in vitro study have shown that erbium:yttrium-aluminum-garnet (Er:YAG), CO<sub>2</sub>, and diode lasers can achieve a high percentage or even complete elimination of surface bacteria on contaminated titanium surfaces.<sup>18</sup> In vitro data have shown that CO<sub>2</sub> and diode lasers do not cause any surface alterations following irradiation.<sup>19,20</sup> Er:YAG lasers can also be used for implant treatment without harming the titanium surface if proper settings are applied.<sup>19,20</sup>

Despite the amount of published data reporting on the treatment of peri-implantitis using different laser wavelengths, there has been no systematic assessment of their efficacy. Therefore, the aim of this review is to address the question, "Is laser therapy, as a monotherapy or as an adjunctive therapy, an efficacious treatment modality for patients with peri-implantitis?"

## MATERIALS AND METHODS

### Search Strategy

The PubMed database of the U.S. National Library of Medicine, the EMBASE database, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched for available data. The search included articles published from January 1990 up to and including June 2013. Articles available online

in electronic form ahead of print were considered eligible for inclusion. For the purposes of the present study, the definition of peri-implantitis described in the First European Workshop on Periodontology and reviewed at the Sixth Workshop is used.<sup>8,21</sup> Based on this definition, peri-implantitis is defined as the presence of inflammation of the mucosa and loss of supporting bone around an implant in function.<sup>8,21</sup>

The first phase of the evaluation of the literature included an electronic search using the following combinations of terms and key words: ("peri-implantitis" OR "periimplantitis") OR ("peri-implant" OR "peri-implant") AND "laser."

Two reviewers (GK and IK) performed the screening independently after reviewing the title and the abstract of each potentially relevant article for inclusion according to specific inclusion criteria. The full texts of all articles considered as potentially relevant by at least one reviewer were obtained for eligibility evaluation against the predetermined inclusion criteria.

**Inclusion Criteria.** During the initial selection, titles and abstracts were reviewed for eligible articles. Inclusion of an article was based on the following criteria: 1) English language; 2) human studies; 3) prospective, controlled clinical studies reporting data from  $\geq 10$  patients; 4) use of laser therapy as monotherapy or as an adjunct in the treatment of peri-implantitis; 5) report of clinical indexes (or report of data allowing the calculation of clinical indexes) of peri-implant disease, including clinical attachment level (CAL) and probing depth (PD); and 6) follow-up of  $\geq 6$  months following treatment.

The electronic search was complemented by manual search of the following journals from January 1990 to June 2013: *Clinical Implant Dentistry and Related Research*, *Clinical Oral Implants Research*, *Journal of Clinical Periodontology*, *Journal of Dental Research*, *Journal of Periodontology*, *Lasers in Medical Science*, *Lasers in Surgery and Medicine*, *Photomedicine and Laser Surgery* (previously, *Journal of Clinical Laser Medicine & Surgery*), *The International Journal of Oral & Maxillofacial Implants*, and *International Journal of Periodontics and Restorative Dentistry*.

Last, the reference list of each of the selected full-text articles was reviewed for article titles suggesting treatment of peri-implantitis with the use of laser as adjunct or monotherapy. If required, an attempt was made to contact the corresponding authors to obtain missing, unclear, or unpublished data.

### Outcome Variables

The primary outcome variables assessed are CAL gain and reduction in PD.

### Selection of Studies and Data Extraction

For the final phase of selection, the full-text articles of all potentially relevant studies were acquired and evaluated independently by the two reviewers. If >1 article corresponded to the same clinical study, only the most recent article was considered for inclusion.

Any disagreement between the reviewers regarding final inclusion of an article was resolved by discussion. In case of a disagreement that was not resolved, the opinion of a third experienced reviewer (IK) would be asked for and would be considered final. If the disagreement persisted, it would be reported and analyzed in the results of this study. Cohen  $\kappa$  coefficient scores were used to determine the level of agreement between the two reviewers.<sup>22</sup>

The two reviewers, using a standardized process and specially designed data-extraction forms, individually conducted data extraction from the selected studies according to the approach reported in a previous systematic review.<sup>23</sup> Briefly, the main characteristics of each study (study design, number of patients/implants included, treatment approach, laser characteristics, adjunctive treatment, type of intervention, and outcome measures) and clinical outcomes of studies were reported. Any data related to adverse events were recorded. Again, any disagreement between the reviewers would be resolved by discussion.

### Quality Assessment of Included Studies

A specific protocol was used independently by the two reviewers for the qualitative assessment of the screened articles. The clinical studies included in this study were assessed using criteria from the revised Consolidated Standards of Reporting Trials (CONSORT) statement for evaluation of randomized controlled trials<sup>24</sup> according to the protocol described in a systematic review by Schwarz et al.<sup>25</sup>

The aim of the quality assessment was to review randomization, masking, follow-up, statistical analysis, and report of outcomes for the selected studies. A cumulative score was formed for each study following quality assessment, and an overall estimation of risk of bias was assigned to each included randomized clinical trial. Studies in which all of the criteria were met were assigned a low risk of bias.<sup>25</sup> A moderate risk was considered when  $\geq 1$  of the criteria was partially met, and a high risk of bias was estimated when  $\geq 1$  of the criteria were not met<sup>25</sup> (see Supplementary Fig. 1 in online *Journal of Periodontology*).

### Statistical Analyses

Meta-analyses were conducted separately for each of the two primary outcomes, CAL and PD. Subgroup effects were studied using metaregression comparing

surgical and non-surgical groups. Heterogeneity among the studies for each outcome were assessed using the  $\chi^2$  test and  $I^2$  statistic.<sup>26</sup> Outcome measures were combined with a fixed-effects model in the absence of heterogeneity or with a random-effects model in the presence of heterogeneity, with a  $P$  value <0.05.<sup>27</sup> Forest plots were produced, reporting weighted average of outcomes with 95% confidence interval (95% CI) and overall treatment effects and subgroup effects at a significance level of 0.05. All statistical analyses were carried out by use of statistical software.<sup>||</sup> Regression tests for funnel plot asymmetry were conducted to explore potential publication bias.<sup>28</sup>

### RESULTS

A total of 136 titles and abstracts were identified following electronic search using the specific combination of terms and key words. The manual search of the journals mentioned above added one potentially relevant article to the search, for a total of 137 titles.<sup>29</sup> After the first phase of selection, 122 articles were excluded based on the title and the abstract. Interexaminer agreement was high (Cohen  $\kappa$  statistic for interreviewer agreement = 0.91).

For the second phase, the complete full-text articles of all studies selected in the first phase ( $n = 15$ ) were scrutinized.<sup>29-43</sup> Throughout this procedure, the full texts of these studies were reviewed independently and twice by two reviewers (GK and IK), and selection was based on the predetermined inclusion criteria.

A total of nine publications were excluded during this stage of selection ( $\kappa = 0.88$ )<sup>29-37</sup> (Table 1). Reference checking of relevant reviews and included studies revealed no additional papers. Six publications (describing six studies) fulfilled the inclusion criteria and were included in this systematic review<sup>38-43</sup> (Fig. 1, Table 2).

### Results of Quality Assessment

One of the six studies was a controlled clinical study,<sup>38</sup> and five were randomized, controlled clinical studies.<sup>39-43</sup> Three studies were assessed as having a high risk of bias,<sup>38,41,42</sup> one as having a moderate risk of bias,<sup>43</sup> and two as having low risk of bias.<sup>39,40</sup>

### Subdivision of Included Studies

Data were subdivided into three categories based on the type of laser investigated in each study (see supplementary Table 1 in online *Journal of Periodontology*).

**Er:YAG laser treatment.** Four publications reported on results of Er:YAG laser treatment using a 2,940-nm wavelength.<sup>39-42</sup> In three of the four

|| Review Manager (RevMan), v.5.2, Cochrane Collaboration, Copenhagen, The Netherlands.

**Table 1.**  
**Studies Excluded in the Second Phase of Selection and Reasons for Exclusion**

Excluded Studies	Reason for Exclusion
Deppe et al. <sup>29</sup>	Non-English language
Romanos and Nentwig <sup>30</sup>	Insufficient clinical data reported
Bach et al. <sup>31</sup>	Insufficient clinical data reported
Schwarz et al. <sup>32</sup>	Non-English language
Schwarz et al. <sup>33</sup>	Uncontrolled study
Sennhenn-Kirchner et al. <sup>34</sup>	Ex vivo study design
Romanos and Nentwig <sup>35</sup>	Different definition of peri-implant disease
Persson et al. <sup>36</sup>	Same study population as Renvert et al. <sup>40</sup>
Schwarz et al. <sup>37</sup>	Same study population as Schwarz et al. <sup>39</sup>

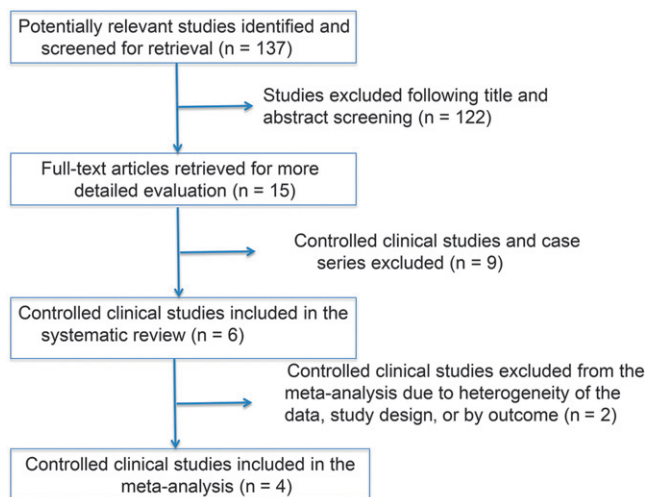
significant difference in both groups at 12 months, but only the control group demonstrated a significant effect in PD reduction at the 24-month interval. Connective tissue attachment loss (AL) and bleeding on probing (BOP) values were significantly reduced in both groups at 12 months, whereas only the BOP values remained statistically significantly reduced at 24 months.

Renvert et al.<sup>40</sup> performed decontamination with an air-abrasive as a control to compare the efficacy of Er:YAG laser as a monotherapy in the non-surgical treatment of peri-implantitis in 100 sites. At 6 months post-treatment, they could not find any significant intergroup or intragroup reduction in peri-implant PD measurements but found a significant decrease

in BOP around implants allocated in both groups.

Two studies evaluated the same treatment approach using Er:YAG laser for the non-surgical treatment of peri-implantitis.<sup>41,42</sup> Mechanical debridement with plastic curets and administration of a chemotherapeutic agent (0.2% chlorhexidine) was used in the control group. Findings from the studies suggest that a significant reduction in PD and AL can be expected following this type of treatment of peri-implantitis at 6 months post-intervention, but this reduction is not maintained at the 12-month interval. The mean reduction in PD and AL was <1 mm in both studies.<sup>41,42</sup> No difference between the test and control groups was noted. Reduction in BOP was significant in comparison to baseline in both studies and was significantly higher with the application of Er:YAG laser treatment.<sup>41,42</sup>

**CO<sub>2</sub> laser treatment.** One prospective study reported on the use of CO<sub>2</sub> laser treatment.<sup>38</sup> Deppe et al.<sup>38</sup> reported the outcomes of CO<sub>2</sub> laser treatment on 29 implants in the test group that were followed for at least 6 months at the observation endpoint. The treatment approach in the test subgroups included disinfection using CO<sub>2</sub> laser irradiation with a 10.6- $\mu$ m wavelength. Implants in the control group (n = 25) were treated with conventional decontamination. Each group was further divided in two subgroups receiving either adjunctive soft tissue resection or guided bone regeneration. At the post-treatment evaluation, all treatment approaches were significantly effective in reducing PD in comparison to baseline. However, CALs were substantially reduced only in the bone augmentation subgroups of each group and not in the soft tissue resection subgroups. In the soft tissue resection/conventional



**Figure 1.**

Process through the stages of the systematic review and meta-analysis modified from the Quality of Reporting of Meta-analyses (QUOROM) statement flowchart.<sup>6</sup>

publications, the same laser system was used for implant surface decontamination.<sup>40-42</sup> The remaining study used a different Er:YAG laser system with the same wavelength and similar power settings.<sup>39</sup> This was the only study in which access flap surgery was used as a treatment approach; in all other studies, Er:YAG irradiation was performed in a non-surgical manner.

In Schwarz et al.,<sup>39</sup> the researchers assessed the effect of Er:YAG laser application in comparison to mechanical cleaning with plastic curets and application of cotton pellets moistened with sterile saline. Evaluation of reduction in PD revealed a statistically

**Table 2.**  
**Presentation of Main Characteristics for Included Studies**

Study	Study Design	Treatment Approach	Intervention	Adjuvant Intervention	Number of Patients/Implants at Baseline	Number of Dropouts	Follow-Up Period (months)
Schär et al. <sup>43</sup>	RCT	Non-surgical	Test group PDT (HELBO®)  Control group Local delivery of minocycline microspheres	Mechanical debridement with titanium curets and glycine-based powder air polishing and irrigation with 3% hydrogen peroxide  Same as test group	20/20  20/20	0	6
Schwarz et al. <sup>39</sup>	RCT	Surgical	Test group Er:YAG laser  Control group Plastic curets and cotton pellets soaked with sterile saline	Implantoplasty at the supracrestally exposed implant threads  Same as test group	15/19  15/16	1  5	24
Renvert et al. <sup>40</sup>	RCT	Non-surgical	Test group Er:YAG laser Control group Air abrasive	No  No	21/55 21/45	0	6
Deppe et al. <sup>38</sup>	Prospective clinical study	Surgical	Test group CO <sub>2</sub> laser application with soft tissue resection or bone augmentation Control group Conventional decontamination with soft-tissue resection or bone augmentation	Air-powder abrasive application supracrestally  Same as test group	19/39  13/34	0	5 to 59
Schwarz et al. <sup>41</sup>	RCT	Non-surgical	Test group Er:YAG laser Control group Mechanical debridement with plastic curets and 0.2% chlorhexidine	No  No	10/20 10/20	0	12
Schwarz et al. <sup>42</sup>	RCT	Non-surgical	Test group Er: YAG laser Control group Mechanical debridement with plastic curets and 0.2% chlorhexidine	No  No	10/16 10/16	0 2	6

treatment subgroup, the CALs remained unchanged, whereas there was a 0.8-mm gain in the soft-tissue resection/laser treatment subgroup. The intersubgroup variation in CAL was diminished between conventional treatment and laser treatment in the bone augmentation subgroups. CO<sub>2</sub> laser treatment was successful in halting the progression of AL in all cases of surgical treatment, but it was significantly more successful than conventional decontamination only when combined with soft-tissue resection.

**Photodynamic therapy.** One randomized clinical trial reported on the use of photodynamic therapy (PDT).<sup>43</sup> In this study the efficiency of a combination of a diode laser with a wavelength of 660 nm and power density of 100 mW with a phenothiazine chloride dye, namely PDT, in non-surgical treatment of peri-implantitis was investigated. The dual application of PDT with a 1-week interval was compared to a single application of minocycline hydrochloride microspheres in the peri-implant sulci. A total of 20 implants per group with a diagnosis of early peri-implantitis was evaluated in this study. All implants had PDs in the range of 4 to 6 mm with active BOP and radiographic signs of bone loss. Pockets in both test groups were irrigated with 3% hydrogen peroxide in addition to the randomly allocated treatment modality. No statistically significant reduction was noted for either of the groups in regard to CALs in comparison to baseline as well as between the two groups. Both treatment modalities resulted in similar and statistically significant reductions in PD at 6 months even though the magnitude of reduction was not clinically significant (PDT group, 0.36 mm). Complete resolution of inflammation as determined by the presence of BOP was unpredictable with either of the two treatment approaches.

#### Adverse Events

Adverse events associated with laser treatment were reported in only one study.<sup>38</sup> Four implants that were treated with CO<sub>2</sub> irradiation and bone augmentation were eventually lost due to chronic infection<sup>38</sup> (Table 3).

#### Meta-Analyses

The heterogeneity among the types of intervention used in each study (laser wavelength) allowed for only one meta-analysis. Because of the adequate number of studies with the use of Er:YAG laser using relatively homogeneous inclusion/exclusion criteria, a meta-analysis could be conducted for the results of Er:YAG laser treatment at the 6-month post-intervention observation interval (Fig. 1). Regression tests for funnel plot asymmetry suggested no evidence of publication bias for CAL and PD ( $P = 0.49$  and  $0.812$ , respectively).

Figures 2 and 3 present the forest plots and summary estimates for weighted mean difference of CAL and PD between the treatment and control groups. For CAL and PD outcomes, three studies were included in the meta-analysis as non-surgical<sup>40-42</sup> and one study was included as surgical.<sup>39</sup> Tests for overall heterogeneity returned to be non-significant for CAL and PD ( $P = 0.12$  and  $0.31$ ). Thus, the fixed-effects models were applied for CAL and PD outcomes.<sup>26</sup> The pooled effect sizes in AL after 6 months for the non-surgical group, for the surgical group, and for all studies were found to be non-significant ( $P = 0.90$ ,  $0.14$ , and  $0.86$ , respectively). No statistically significant evidence for treatment effects in reducing PD level was found for the non-surgical group, surgical group, and all studies ( $P = 0.97$ ,  $0.16$ , and  $0.7$ , respectively). There was no evidence for subgroup difference between surgical and non-surgical treatments in AL and PD reduction ( $P = 0.12$  and  $0.17$ , respectively).

#### DISCUSSION

The present systematic review included six clinical studies that reported on outcomes of laser therapy in the treatment of peri-implantitis.<sup>38-43</sup> The predefined criteria set for selection of relevant studies allowed only for the inclusion of prospective, controlled clinical studies with adequate number of participants and follow-up time to maintain a high level of evidence.<sup>44</sup> Narrative synthesis of the results revealed that all included studies reported improvement in the peri-implant condition of implants treated with the various laser wavelengths. Because of the lack of longitudinal data on implant survival in most of the included studies, CAL and PD were used as relevant surrogates.

The magnitude of reduction in PD and AL varied among studies based on the type of intervention (surgical versus non-surgical).<sup>38-43</sup> In four of six studies, a non-surgical approach was used.<sup>40-43</sup> Non-surgical interventions revealed decreases in AL and PD that were generally <1 mm.<sup>40-43</sup> Results showed that the use of either Er:YAG laser (2,940 nm) or PDT with a diode laser (660 nm) in a non-surgical manner was potent in reducing mucosal inflammation and to some extent the PD around implants diagnosed with peri-implantitis.<sup>40-43</sup> This reduction was significant up to 6 months post-treatment but waned after 12 months had elapsed.<sup>41</sup> Because a limited effect of non-surgical laser therapy exists in PD and AL reduction while its potency in reducing peri-implant inflammation is significant, there may be merit in the investigation of non-surgical laser treatment as phase I peri-implantitis therapy.

In the remaining two studies that used a surgical approach, the reduction in clinical parameters was

**Table 3.**  
**Outcomes Assessment of Included Studies**

Study	Intervention	PD (mm) (mean ± SD)			CAL (mm) (mean ± SD)			Adverse Events
		Baseline	Outcome	Difference	Baseline	Outcome	Difference	
Schär et al. <sup>43</sup>	Test group	4.19 ± 0.55	3.83 ± 0.58	NR*	2.66 ± 0.73	2.50 ± 0.77	NR	None related to laser treatment
	Control group	4.39 ± 0.77	3.90 ± 0.78	NR	2.72 ± 0.72	2.53 ± 0.65	NR	
Schwarz et al. <sup>39</sup>	Test group	5.1 ± 1.6	3.4 ± 0.6	1.7 ± 1.4	6.4 ± 2.0	4.9 ± 1.1	1.5 ± 1.4	None related to laser treatment
	Control group	5.5 ± 1.8	3.1 ± 0.6	2.4 ± 1.5	6.7 ± 2.2	4.5 ± 1.4	2.2 ± 1.4	
Renvert et al. <sup>40</sup>	Test group	5.9 ± 1.7	5.1 ± 1.5	0.8 ± 0.5	NR	NR	NR	None related to laser treatment
	Control group	6.3 ± 2.0	5.4 ± 1.8	0.9 ± 0.9	NR	NR	NR	
Deppe et al. <sup>38</sup>	Test group	5.7 ± 1.4	3.5 ± 1.5	NR	7.2 ± 1.3	5.1 ± 1.1	NR	Chronic infection remained in a site treated with CO <sub>2</sub> laser and bone augmentation; all four implants at the site were eventually lost
	Control group	5.7 ± 1.8	3.4 ± 1.2	NR	7.1 ± 1.3	5.4 ± 6.7	NR	

**Table 3. (continued)**  
**Outcomes Assessment of Included Studies**

Study	Intervention	PD (mm) (mean ± SD)			CAL (mm) (mean ± SD)			Adverse Events
		Baseline	Outcome	Difference	Baseline	Outcome	Difference	
Schwarz et al. <sup>41</sup>	Test group	5.25 ± 1.02†	4.52 ± 0.79†	0.73 ± 0.9	5.88 ± 0.8†	5.4 ± 0.8†	0.4 ± 0.81	None related to laser treatment
	Control group	5.21 ± 0.91†	4.81 ± 0.79†	0.4 ± 0.9	5.82 ± 1.1†	5.54 ± 0.9†	0.28 ± 0.96	
Schwarz et al. <sup>42</sup>	Test group	5.4 ± 1.2	4.6 ± 1.1	0.8 ± 1.15†	5.8 ± 0.9	5.1 ± 0.9	0.7 ± 0.9†	None related to laser treatment
	Control group	5.5 ± 1.5	4.8 ± 1.4	0.7 ± 1.45†	6.2 ± 1.5	5.6 ± 1.4	0.6 ± 1.5†	

\* NR = not reported.

† Reported after contact with the original author.

‡ Calculated by the current authors.

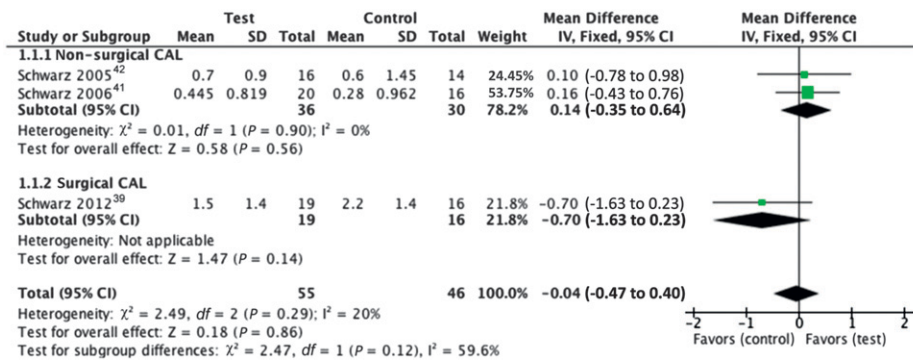
at least two-fold compared to studies that used a non-surgical treatment approach.<sup>38,39</sup> This observation is consistent with the conclusions of other reviews that have compared the effect of type of intervention on peri-implantitis treatment outcome.<sup>45,46</sup> There seems to be a consensus among researchers that non-surgical treatment has limited efficacy in yielding clinically significant improvement in the treatment of peri-implantitis; thus, surgical treatment should be considered the preferred approach.<sup>47</sup>

As previously mentioned, the benefit of laser treatment should be investigated as a prequel to surgical treatment. The reduction of the microbial load in the peri-implant pocket during initial laser therapy with a non-surgical approach could potentially further increase the efficiency of surgical treatment applied in an environment with halted inflammation. Alternatively, as Persson et al.<sup>36</sup> have previously suggested, based on the significant short-term effect of non-surgical laser treatment, a repetition of the laser application may be advantageous. Findings from this review showed that non-surgical therapy is efficient at controlling peri-implant inflammation for at least 6 months post-intervention.<sup>40-43</sup> Based on this knowledge, a relevant research question would be to identify the ideal repetition intervals for application of laser therapy on the contaminated implant surface until a state of health is re-established and can be maintained.

A limitation of the present systematic review and meta-analysis is that the heterogeneity of data relevant to laser wavelengths, energy settings, and laser application techniques did not allow for a quantitative synthesis of data from all the included studies. The all-inclusive use of the term “laser therapy” has to be revisited in future studies. Each laser wavelength and its specific pulse energy at the tip are parameters that define a singular treatment modality. It is not scientifically accurate to compare the efficacy of different laser wavelengths under the generic term laser treatment because this may lead to misleading conclusions. In general, most of the studies underreported the mode of laser-beam application, peak laser power, and contact time. As previously stressed, information on laser wavelength is necessary but not sufficient to convey enough information on how treatment was rendered, and additional data regarding the pulse energy transmitted at the fiber tip are pivotal to treatment outcome. As an example, the safe application of the same laser wavelength (2.94 μm) may become unsafe by causing cracks and decrease in the roughness of an implant with just a 200-mJ increase in its energy.<sup>19</sup>

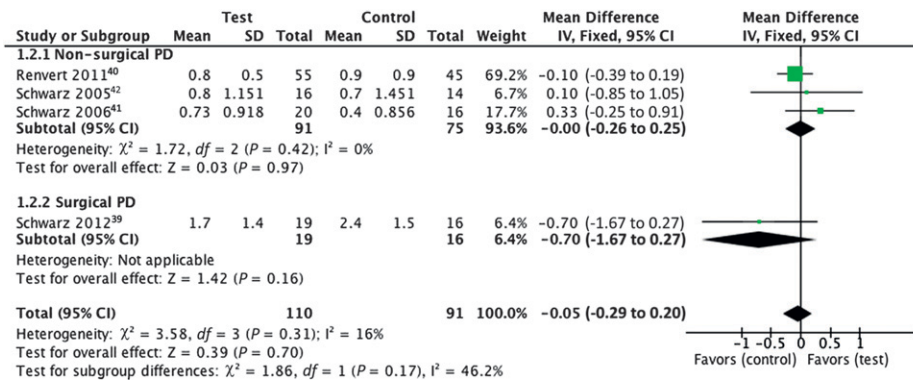
It seems that identification of appropriate parameters for laser application in the treatment of peri-implantitis must precede controlled studies comparing





**Figure 2.**

Forest plot for selected studies reporting CAL changes after 6 months of treatment. Weighted mean differences were estimated by a fixed-effects model. Mean difference >0 indicates better treatment effect in the laser group than the control group. df = degrees of freedom.



**Figure 3.**

Forest plot for selected studies reporting PD changes after 6 months of treatment. Weighted mean differences were estimated by a fixed-effects model. Mean difference >0 indicates better treatment effect in the laser group than the control group. df = degrees of freedom.

the efficacy of laser therapy to conventional implant treatment modalities. Variables such as wave mode, diameter of optic fiber, pulse energy, and pulse duration, among others, may significantly modify the thermal events associated with laser treatment and lead to titanium surface alterations.<sup>19</sup> Subsequently, modified surface structure may alter host tissue response to the treated titanium surface, thus masking the decontamination effect that laser therapy has to offer.<sup>18,48</sup> Therefore, study design of future clinical trials should include identification of the ideal parameter settings that yield the best efficiency-to-toxicity ratio for the specific laser wavelength used as determined by proof-of-principle or pilot studies. It is obvious that an explicit report of power settings and mode of application is of paramount importance in clinical studies assessing the efficacy of laser treatment.

Another factor that may exert significant influence on host response to treatment and was underreported in the included studies is smoking.<sup>49</sup> It has been previously shown that smoking has a dose-dependent

deleterious effect on response to peri-implantitis treatment.<sup>50</sup> Available information regarding the impact of smoking on the outcomes of laser therapy in the treatment of peri-implantitis is missing from the literature. Previous studies on periodontal treatment have shown that laser therapy may provide additional benefits for smokers, even though results are equivocal.<sup>51-53</sup>

A further limitation of this review is that a number of included studies used confounding factors such as hydrogen peroxide, chlorhexidine, or plastic curets in combination with laser treatment. It has been previously reported that these interventions may negatively interfere with the biocompatibility of titanium surfaces.<sup>54-56</sup> Thus, future research studies should be designed to assess the efficiency of a specific laser wavelength by ruling out other confounding variables that may interfere with the outcome, such as chemotherapeutic or mechanical agents. Additionally, the use of such confounding factors in the treatment of patients in each control group warrants cautious interpretation of the meta-analysis

results. Researchers should attempt to use the simplest and most universally accepted treatment modality, such as the use of sterile saline for disinfection, as a control intervention when attempting to assess laser treatment efficacy.<sup>55</sup>

### CONCLUSIONS

The authors conclude that based on the limited information currently available, any superiority of laser treatment in comparison to conventional treatment of peri-implantitis could not be identified. Considering the high heterogeneity and the low number of included studies, the authors cautiously conclude that non-surgical laser therapy may be investigated as phase I therapy for the treatment of peri-implantitis. Future research should emphasize detailed description of the specific laser characteristics and power settings in clinical studies.

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