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ORIGINAL ARTICLE

Pulpal response following photo-biomodulation with a 904-nm diode laser: a double-blind clinical study

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Abstract The aim of this study was to evaluate pulpal responses in healthy human teeth to photo-biomodulation therapy (PBMT) with 904-nm GaAs diode laser. The study followed a double-blind split mouth design, with a randomly selected maxillary first premolar acting as a sham-irradiated control tooth, and the contralateral tooth receiving active laser treatment. Two coded but otherwise identical laser probes (Irradia™, SpectraMedics Ltd., NC, USA) were used to deliver the sham (placebo) and laser radiation, with both the operator and patient unaware of each probe's identity. The selection of teeth for sham or laser irradiation was randomised for each treatment. Pulpal responses were assessed using electric pulp testing (EPT), 2 min prior to exposure, and immediately after laser irradiation (60 s, 30 mW average power, 25 Hz pulse frequency, 3.6 J/cm^2). Treatment effects were analysed using the Wilcoxon-signed rank test. A total of 30 participants provided written informed consent. Majority of the participants (66.7 %) demonstrated an analgesic effect following PBMT (elevated EPT scores); however, nine participants (30 %) reported the lower EPT scores than the control. Both the treatment effects (stimulation and analgesia) were significant compared to the placebo. In most individuals, PBMT of healthy teeth with a 904-nm GaAs diode laser can induce analgesia, as witnessed by elevated EPT scores. A converse effect can occur in a minority of subjects.

Keywords Diode laser · Analgesia · Pulp testing · Endodontics · Pain

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Introduction

Despite the proven clinical efficacy of injected solutions of local anaesthetics in dentistry, there is significant dental anxiety and fear associated with dental injections [1, 2]. To overcome this concern, alternatives such as topical anaesthetic formulations and needleless pressure injection systems have been developed; however, their efficacy compared to conventional injection techniques has been questioned [3].

Photo-biomodulation therapy (PBMT) with Nd:YAG and Er:YAG pulsed lasers has been reported to induce pulpal analgesia [4–6] and represents a potential alternative to injected local anaesthetics for hard tissue procedures performed on teeth. On the other hand, near-infrared and visible red diode lasers may attenuate nerve conduction in slow myelinated and unmyelinated nerve fibres [7–10]. Since these wavelengths fall within the "optical window", good penetration through tooth structure and into the tissues of the dental pulp can be expected [11]. Despite the positive results seen in previous studies with Nd:YAG lasers in terms of analgesic effects [4, 5], it is unclear whether near-infrared diode lasers which emit at shorter wavelengths can give useful analgesic actions. As diode lasers are considerably more affordable and compact compared to traditional solid-state lasers, they could be better suited for use in everyday clinical dental practice.

The efficacy of 810–830 nm diode lasers in the treatment of dentinal hypersensitivity (DH) lends support to their ability to induce analgesic actions [12–20]. Current research has

reported that PBMT with diode lasers for dentinal hypersensitivity has similar efficacy to existing treatments, including the applications of fluoride varnish [12] or potassium oxalate gels (3 %) [15]. The desensitising effect of diode laser irradiation appears unrelated to the occlusion of dentinal tubules [21], and some studies have reported that direct analgesic effects on the dental pulp may occur [6, 12, 22]. Although it has been suggested by some authors that PBMT can induce an effect in both Aδ and C-fibres found in the dental pulp [8], other studies have reported that only C-fibres are targeted [8].

Since there is a significant variation (Table 1) in the laser parameters utilised in existing studies, it is difficult to ascertain the ideal laser parameters for the treatment of DH and, by extension, the appropriate settings to induce pulpal analgesia. Laser fluences utilised for the treatment of dentinal hypersensitivity vary between 2 [16] and 5 J/cm^2 [13]. Although the work of Marsilio et al. in 2003 [13] did not report significant variations in treatment effect between laser fluences of 3 and 5 J/cm^2, the effects of PBMT are known to be highly dose-dependent [23, 24]. There are disparities in PBMT treatment durations, which range from 25 [16] up to 190 s [15]. From the present literature, it remains unclear if more rapid delivery of laser energy influences the treatment effect.

Other disparities in the methodology used in past studies include the type and duration of stimulus used to induce sensitivity, as well as the subjective scales utilised to quantify pain response. Although most studies of sensitivity have used an air blast from a triplex syringe as a stimulus [12, 13, 15–17], this is a poor indication of pulpal analgesia in healthy teeth without dentine exposure. Furthermore, the duration of the air blast stimulus has not been standardised and varies from as little as 1 s [15] to as much as 5 s [12, 13, 16].

Little is known regarding the efficacy of 904-nm GaAs diode lasers for inducing pulpal analgesia. This laser wavelength is longer than the visible red lasers (655–670 nm) used in most past studies of DH; however, it is closer to the 1064 nm wavelength of the Nd:YAG laser utilised in previous studies of pulpal analgesia [4, 11]. The present study was undertaken to assess changes in pulpal response following PBMT using a 904-nm GaAs diode laser irradiation. The hypothesis of the study was PBMT with a 904-nm GaAs diode laser does produce a significant change in EPT scores in healthy teeth when applied on teeth or gingiva.

Whilst the null hypothesis was that PBMT with a 904-nm GaAs diode laser does not produce a significant change in EPT scores in healthy teeth when applied on teeth and gingiva.

Methods

The Ethics committee, Griffith University, Australia, approved this doubl-blind clinical study (DOH/26/12/HREC). A total of 30 participants provided written informed consent. Details of the subject selection process are presented in Fig. 1. All participants were selected from a cohort of dental students, based on the following selection criteria: age at least 18 years and at least two comparable healthy permanent first premolar teeth free of caries, restorations and other defects. Individuals who suffered from DH, were on analgesic medications or desensitising agents, who had cardiac arrhythmias or

Table 1 Reported treatment of methods for dentinal hypersensitivity with PBMT

Author and year of study	Treatment	Laser parameters	Application of laser	Measurement scale
Corona et al. 2003 [12]	660 nm GaAlAs diode laser	15 mW applied for 30 s total (450 mJ total energy). Power density 4 J cm^{-2}	20 s in the cervical area of tooth + 10 s at the apex of tooth	5 s air blast and the DH scale[a]
Dilsiz et al. 2010 [16]	808 nm diode + potassium chloride desensitising dentrifice	100 mW applied for 25 s (2.5 J total energy). Power density 2 J cm^{-2}	Laser applied in mesio-distal scanning motion on exposed root surface	5 s air blast and 10 cm visual analogue scale
Marsilio et al. 2003 [13]	670 nm diode laser	1.Group A—3 J/cm^2 for 1 min 54 s 2.Group B—5 J/cm^2 for 3 min 10s[b]	Laser applied in buccal cervical area	5 s air blast and 10 cm visual analogue scale
Orhan et al. 2011 [17]	655 nm diode laser	4 J/cm^2 applied over 160 s	Laser applied to exposed dentine surfaces in sweeping motion	Air blast until first response and 10 cm visual analogue scale
Vieira et al. 2009 [15]	660 nm diode laser	4 J/cm^2 applied over 120 s	Laser applied on buccal, lingual and apical areas	Air blast for 1 s + tactile stimulus and 10 cm visual analogue scale

[a] Four point Likert scale developed by Uchida (26)

[b] Total energy dose not report

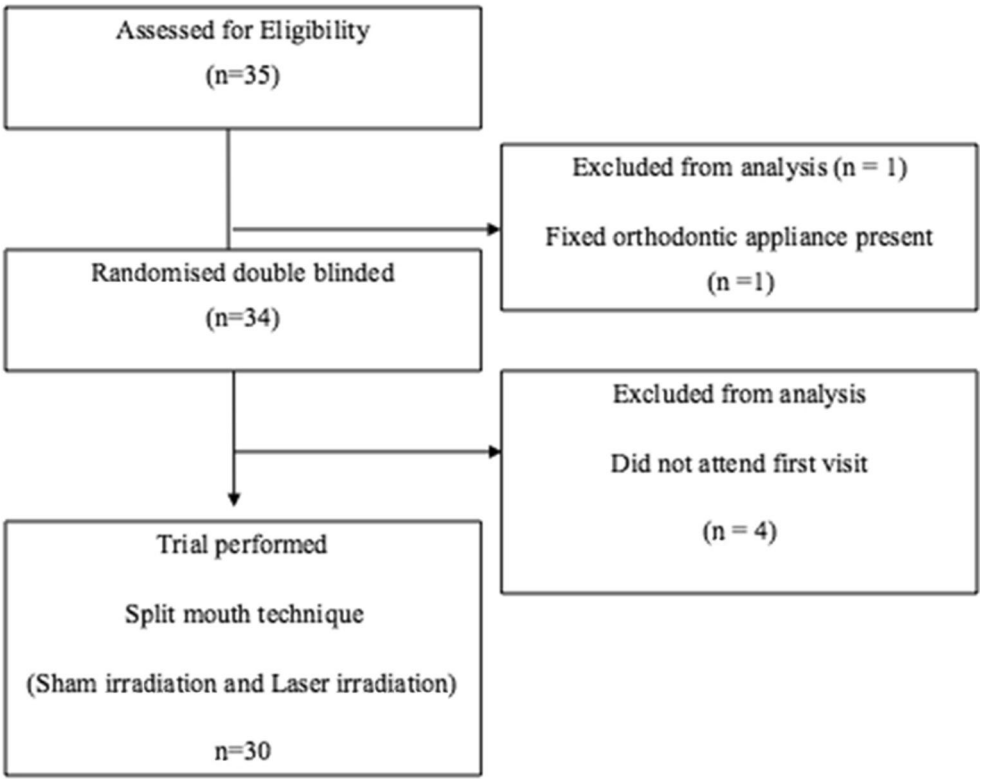

Fig. 1 Sampling methodology

pacemakers, or who were currently undergoing fixed orthodontic treatment were excluded.

Experimental groups

A split mouth design was utilised in this study, with each participant being subjected to both laser and sham (placebo) treatments delivered in a random sequence. Two comparable contralateral teeth were used to assess the laser or sham (placebo) effect. All patients and operators were required to wear appropriate laser protective eyewear.

The 904-nm GaAs diode laser used in the study (Irradia™, SpectraMedics Ltd., Stockholm, Sweden) consisted of a sham (placebo) probe and an active laser treatment probe. These were indistinguishable and were coded so that neither the operator nor patient was aware of their identity. Data for electric pulp test (EPT) readings were decoded following completion of the study.

For each participant, the two maxillary first premolar teeth were assigned randomly by coin toss to receive one or other of the treatment probes. This procedure also ensured that the sequence in which the sham and laser treatments were applied was also randomised, resulting in a robust double-blind control design.

Laser parameters

The laser was operated with an average power of 30 mW and was pulsed at 25 Hz with a duty cycle of 50 %. The laser probes were applied on the buccal surface of the first premolar tooth for 60 s. The total energy dose delivered to the tooth was 3.6 J. As the area of the spot was 1 cm^2, the energy density was 3.6 J/cm^2.

Electric pulp test

The EPT methodology followed that from past studies of pulpal analgesia with the Nd:YAG laser [4, 5]. In brief, the rate at which current was delivered, standardised at 4 EPT units per second. The EPT device (Analytic Endodontics, Sybron Dental Specialties Inc., Orange, CA, USA) utilised in this study has demonstrated a high degree of reliability in previous clinical studies [26]. Each participant was instructed to release their hand off the metal handle of the unit immediately when they perceived a mild or tingling sensation in the tooth, which broke the current flow and stopped the measurement. The EPT readout at the point of termination was then recorded. Prior to laser or sham treatment, EPT was conducted on a non-experimental tooth to familiarise the participant with the sensations experienced during the test. Pulpal responses to EPT were assessed at similar positions on the tooth surface before and after laser treatment. The test was performed in an isolated and dry field three times prior to exposure to treatment procedures to evaluate reliability of EPT response. Following laser treatment, EPT values were recorded again. In accordance with previous studies [4, 5], the effect of the treatment was calculated by subtracting pre-intervention EPT scores from post-intervention EPT scores, with a positive difference

Table 2 Summary of treatment effects

Group	>10 % increase	<10 % change	>10 % decrease	Total
Active	25 (47.2 %)	14 (26.4 %)	14 (26.4 %)	53 (100.0 %)
Placebo	0 (0.0 %)	52 (98.1 %)	1 (1.9 %)	53 (100.0 %)

indicating an analgesic effect, and a negative difference indicating excitation or sensitivity effect.

Assessment of pulpal responses following root exposure

In addition to testing the pulpal response following coronal laser exposures, the pulpal response was also assessed when the laser treatment was applied to the gingiva overlying the root of the tooth. This was performed on a random premolar at a separate visit, at least 1 week from the previous laser exposure and was similarly controlled using sham irradiation on the contralateral side. The laser probe was applied gently on the gingiva directly overlying the target tooth, approximately 10 mm from the gingival margin. EPT scores were measured before and immediately after laser irradiation.

Data analysis

Data was compiled and analysed for normality using the Shapiro-Wilk test. A repeated measure non-parametric analysis (Wilcoxon-signed ranks test) was used, with the level of significance set to $p < 0.05$. Data analysis employed the Statistical Package for Social Sciences (SPSS) software version 22.0 (IBM Corp., Armonk, NY, USA).

The analysis of treatment responses mapped the EPT scores as being elevated by 10 % or more, showing a less than 10 % change, or depressed by 10 % of more. The distribution of responses between the active and placebo (sham irradiated) groups was compared using the chi-squared test for independence. Values for individual sites before and after treatment were assessed for linear correlation using the least squares method. As there were no effects of gender, data for the experimental interventions were combined for male and female subjects.

Results

A total of 35 participants provided informed consent, but five were excluded as one participant had a fixed orthodontic appliance in the maxillary arch, and four subjects failed to attend all sessions, resulting in a final sample size of 30 (Fig. 1). The mean age of the participants was 22 years, with a range of 19–54. There were 18 males and 12 females.

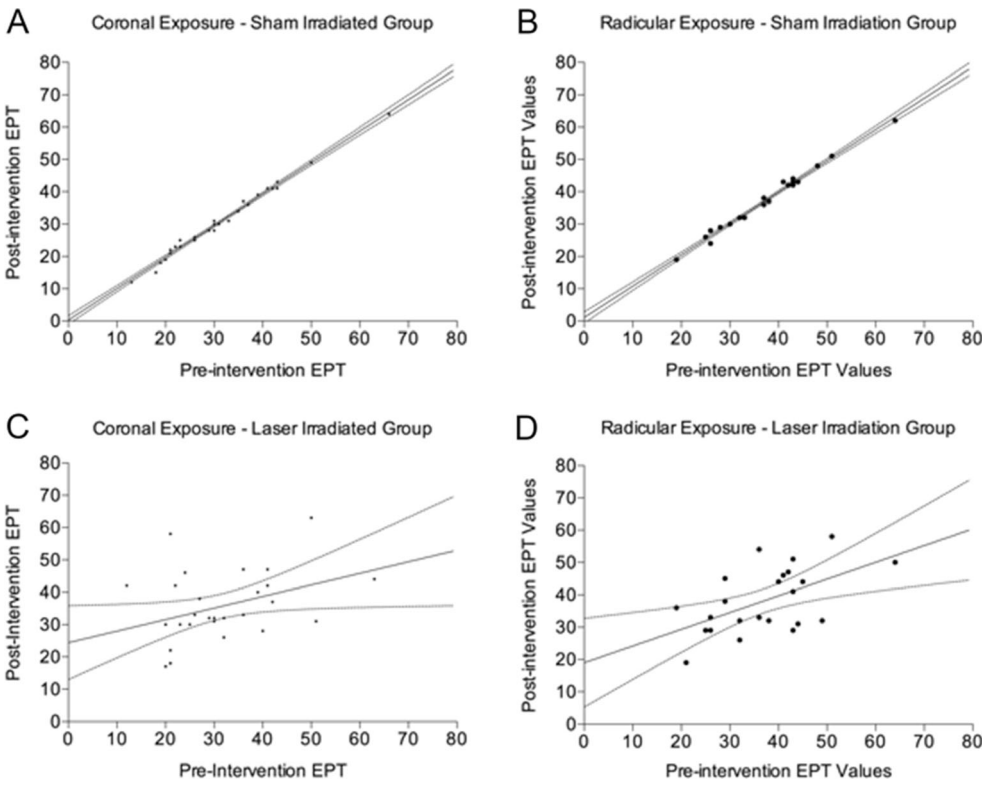

Fig. 2 Comparisons of treatment responses. **a** and **c** show the placebo groups, for tooth and gingival sites, whilst **b** and **d** show the active groups

Table 3 Summary of treatment effects by gender

Group	>10 % increase	<10 % change	>10 % decrease	Total
Male	9 (28.1 %)	13 (40.6 %)	10 (31.3 %)	32 (100.0 %)
Female	5 (23.8 %)	12 (57.1 %)	4 (19.0 %)	21 (100.0 %)

No adverse events from laser treatment were reported or observed. No participants reported any discomfort or any other symptoms during laser irradiation. Furthermore, participants did not experience any lingering pain or sensations following either the EPT or laser irradiation procedures.

The overall assessment of response patterns is shown in Table 2. Some 52 out of 53 paired assessments (98.1 %) of sites treated using sham irradiation gave results that were within 10 % of the baseline value. In contrast, a greater than 10 % change in EPT response was observed in more than half the teeth (52.8 %) at sites treated with the active laser, signifying a significant treatment effect. The difference in response patterns between active and placebo treatments was significant ($\chi^2 = 58.15, p < 0.0001$).

The scatter plot of the data comparing the same sites before and after treatment showed minimal change for the placebo (sham irradiation), with minimal spread and a high positive linear correlation very close to 1.0, indicating no significant effects (Fig. 2a). Both analgesic effects (elevated scores) and stimulation (depressed scores) occurred across the cohort. For the active treatment, there were different effects for tooth and gingival sites, with the greatest proportional changes seen for tooth sites, especially for those with low baseline scores (Fig. 2b–d). This is reflected in the lower slopes for the lines of best fit for the active sites versus the placebo sites. The study did not show any significant difference in the effect of laser (active) irradiation on males versus females (Table 3). Table 4 shows the regression coefficients of pre-intervention EPT values and post-intervention EPT values.

Discussion

The present study indicates that under double-blinded conditions, sham irradiation does not produce a significant effect, whilst PBMT with a 904-nm diode laser alters the response threshold, with the majority of teeth experiencing an elevation in EPT scores, indicative of analgesia, whilst others show a depression of EPT scores, signifying stimulation. These effects were greater for irradiation delivered at the level of the teeth rather than the adjacent gingiva. Although this duality of effects has yet to be reported for laser-induced analgesia, large variations in the treatment effect of PBMT are a common feature seen in previous studies, with both enhancement or suppression of effects seen as doses vary [4, 5]. The magnitude of the effects seen, with EPT elevations of 10 or more, are comparable to those reported by Chan et al. [5], who reported a mean increase of 10.1 EPT units (SD = 12.7) following Nd:YAG laser irradiation.

This variation in treatment effect is potentially related to the dosage of the laser energy reaching the dental pulp, in line with the Arndt-Schulz Law [11]. The specific dose–response mechanisms of PBMT for pulpal analgesia remain unclear from the current literature. Significant analgesic effects following LLLT have been observed in the treatment of DH utilising fluences of approximately 4 J/cm^2 [12, 13, 15, 17]; however, smaller doses (0.3–0.45 J/cm^2) have also been reported to be effective [5]. As the manufacturer recommended, the current study utilised a fluence of 3.6 J/cm^2; however, the variation in pulpal response seen suggests that other factors such as thickness and colour of the dental hard tissues may have influenced the total energy dose delivered in the pulp and hence the resulting pulpal effects. Differences in tooth shade would influence the penetration of laser energy through the teeth. In darker teeth, it is likely that more laser energy may have been absorbed in endogenous pigments in tooth structure, causing stimulation through small increases in temperature. Likewise, this mechanism could explain the lesser effect that PBMT has on pulpal sensibility when applied on the adjacent gingiva rather than on the crown of the tooth itself. The gingival tissue and underlying bone and periodontal ligament through which the laser energy would need to pass before entering the tooth structure could cause both scattering of laser energy and partial attenuation from absorption through water, haemoglobin and other chromophores. Additional studies are needed to examine this aspect.

Despite variations of treatment effect between individual teeth, the present study found no significant differences in the treatment effect of PBMT according to gender. The possible

Table 4 Regression coefficients of pre-intervention EPT values and post-intervention EPT values

	N	Regression coefficient (95 % confidence interval)	R^2	ANOVA F
Coronal exposure–sham irradiation	30	0.98 (0.94 to 1.02)	0.99	2671 ($p < 0.0001$)
Coronal exposure–laser irradiation	30	0.36 (0.02 to 0.70)	0.14	4.53 ($p < 0.05$)
Radicular exposure–sham irradiation	23	0.52 (0.16 to 0.87)	0.31	9.09 ($p < 0.01$)
Radicular exposure–laser irradiation	23	0.97 (0.93 to 1.02)	0.99	1995 ($p < 0.0001$)

influence of gender on the effectiveness of PBMT has not been explored in previous studies [4, 5].

The EPT method was used in this study to assess pulpal responses, and by extension the presence and magnitude of analgesic and stimulatory hyperalgesic effects. Previous work by Whitters et al. in 1995 [4] and by Chan et al. in 2012 [5] also used EPT for assessing pulpal analgesia following Nd:YAG laser treatment. Although EPT is commonly used in clinical dental practice to assess the health of the dental pulp, it has also been used to evaluate the effectiveness of various local anaesthetic agents [25–29], because of its high reproducibility [30]. The utilisation of EPT scores allows for comparisons between PBMT-induced analgesia and traditional local anaesthetic agents.

The factors, which determine pulpal responses following PBMT, remain poorly understood. As PBMT is inherently dose-dependent [23], the laser dose entering the pulp chamber is potentially confounded by individual variations in the colour and thickness of the dental hard tissues [31]. It is hypothesised that these individual variations may have resulted in the duality of treatment effects (analgesia and stimulation) observed in this study; however, further research is required to explore the individual variations in the transmission of laser energy into the pulp.

It is evident that the current laser parameters are not yet optimised for the induction of analgesia. As previous authors have suggested [4, 5], a major future research direction for PBMT is to determine the laser parameters capable of inducing the maximum possible therapeutic benefit.

Conclusions

- In most individuals, PBMT of healthy teeth with a 904-nm GaAs diode laser can induce analgesia, as witnessed by elevated EPT scores.
- A converse effect can occur in a minority of subjects.
- It is important that further research be undertaken to establish the correlations between the absorbed dose and the laser effects (analgesia or stimulation).

Compliance with ethical standards The Ethics committee, Griffith University, Australia, approved this double-blind clinical study (DOH/26/12/HREC). A total of 35 participants provided written informed consent.

References

1. Armfield JM (2010) The extent and nature of dental fear and phobia in Australia. Aust Dent J 55:368–377
2. Armfield JM, Spencer AJ, Stewart JF (2006) Dental fear in Australia: who's afraid of the dentist? Aust Dent J 51:78–85
3. Malamed SF (2013) Handbook of local anesthesia. Elsevier Health Sciences, St Louis, pp 82–382
4. Whitters CJ, Hall A, Creanor SL, Moseley H, Gilmour WH, Strang R, Saunders WP, Orchardson R (1995) A clinical study of pulsed Nd: YAG laser-induced pulpal analgesia. J Dent 23:145–150
5. Chan A, Armati P, Moorthy AP (2012) Pulsed Nd: YAG laser induces pulpal analgesia: a randomized clinical trial. J Dent Res 91:S79–S84
6. Walsh LJ (2008) Laser analgesia with pulsed infrared lasers: theory and practice. J Oral Laser Appl 8:7–16
7. Tsuchiya K, Kawatani M, Takeshige C, Matsumoto I (1994) Laser irradiation abates neuronal responses to nociceptive stimulation of rat-paw skin. Brain Res Bull 34:369–374
8. Wakabayashi H, Hamba M, Matsumoto K, Tachibana H (1993) Effect of irradiation by semiconductor laser on responses evoked in trigeminal caudal neurons by tooth pulp stimulation. Laser Surgery Med 13:605–610
9. Wesselmann U, Kerns JM, Rymer WZ (1994) Laser effects on myelinated and nonmyelinated fibers in the rat peroneal nerve: a quantitative ultrastructural analysis. Exp Neurol 129:257–265
10. Greathouse DG, Currier DP, Gilmore RL (1985) Effects of clinical infrared laser on superficial radial nerve conduction. Phys Ther 65: 1184–1187
11. Hamblin MR, Demidova TN, editors. Mechanisms of low level light therapy. Proc SPIE6140:614001.
12. Corona SA, Nascimento TN, Catirse AB, Lizarelli RF, Dinelli W, Palma-Dibb RG (2003) Clinical evaluation of low-level laser therapy and fluoride varnish for treating cervical dentinal hypersensitivity. J Oral Rehabil 30:1183–1189
13. Marsilio AL, Rodrigues JR, Borges AB (2003) Effect of the clinical application of the GaAlAs laser in the treatment of dentine hypersensitivity. J Clin Laser Med Surg 21:291–296
14. Aranha AC, Pimenta LA, Marchi GM (2009) Clinical evaluation of desensitizing treatments for cervical dentin hypersensitivity. Braz Oral Res 23:333–339
15. Vieira AH, Passos VF, de Assis JS, Mendonça JS, Santiago SL (2009) Clinical evaluation of a 3% potassium oxalate gel and a GaAlAs laser for the treatment of dentinal hypersensitivity. Photomed Laser Surg 27:807–812
16. Dilsiz A, Aydin T, Emrem G (2010) Effects of the combined desensitizing dentifrice and diode laser therapy in the treatment of desensitization of teeth with gingival recession. Photomed Laser Surg 28(Suppl 2):S69–S74
17. Orhan K, Aksoy U, Can-Karabulut DC, Kalender A (2011) Low-level laser therapy of dentin hypersensitivity: a short-term clinical trial. Lasers Med Sci 26:591–598
18. Yilmaz HG, Kurtulmus-Yilmaz S, Cengiz E, Bayindir H, Aykac Y (2011) Clinical evaluation of Er, Cr:YSGG and GaAlAs laser therapy for treating dentine hypersensitivity: a randomized controlled clinical trial. J Dent 39:249–254
19. Kimura Y, Wilder-Smith P, Yonaga K, Matsumoto K (2000) Treatment of dentine hypersensitivity by lasers: a review. J Clin Periodontol 27:715–721
20. Gentile LC, Greghi SLA (2004) Clinical evaluation of dentin hypersensitivity treatment with the low intensity gallium-aluminum-arsenide laser-AsGaAl. J Appl Oral Sci 12:267–272
21. Gholami GA, Fekrazad R, Esmaiel-Nejad A, Kalhori KA (2011) An evaluation of the occluding effects of Er; Cr: YSGG, Nd: YAG, CO2 and diode lasers on dentinal tubules: a scanning electron microscope in vitro study. Photomed Laser Surg 29:115–121
22. Walsh LJ (1997) The current status of low level laser therapy in dentistry. Part 2. Hard tissue applications. Aust Dent J 42:302–306
23. Huang Y-Y, Chen AC-H, Carroll JD, Hamblin MR (2009) Biphasic dose response in low level light therapy. Dose-Response 7:358–383
24. Ohshiro T, Caldenhead RG (1991) Development of low reactive-level laser therapy and its present status. J Clin Laser Med Surg 9: 267–275

25. Agren E, Danielsson K (1981) Conduction block analgesia in the mandible. A comparative investigation of the techniques of Fischer and Gow-Gates. Swed Dent J 5:81–89
26. Kaufman E, Leresche L, Sommers E, Dworkin SF, Truelove EL (1984) Intraligamentary anesthesia: a double-blind comparative study. J Am Dent Assoc 108:175–178
27. Montagnese TA, Reader A, Melfi R (1984) A comparative study of the Gow-Gates technique and a standard technique for mandibular anesthesia. J Endod 10:158–163
28. Vreeland DL, Reader A, Beck M, Meyers W, Weaver J (1989) An evaluation of volumes and concentrations of lidocaine in human inferior alveolar nerve block. J Endod 15:6–12
29. Nist RA, Reader A, Beck M, Meyers WJ (1992) An evaluation of the incisive nerve block and combination inferior alveolar and incisive nerve blocks in mandibular anesthesia. J Endod 18(9):455–459
30. Dal Santo FB, Throckmorton GS, Ellis E III (1992) Reproducibility of data from a hand-held digital pulp tester used on teeth and oral soft tissue. Oral Surg Oral Med Oral Path 73:103–108
31. Fried D, Glena RE, Featherstone JD, Seka W (1995) Nature of light scattering in dental enamel and dentin at visible and near-infrared wavelengths. Appl Opt 34(7):1278–1285