Lasers in Orthodontics

Ali Borzabadi-Farahani and Mark Cronshaw

D.J. Coluzzi, S. Parker (eds.), *Lasers in Dentistry—Current Concepts*, Textbooks in Contemporary Dentistry,
DOI 10.1007/978-3-319-51944-9_12

12.1 Applications of Lasers in Orthodontics for Soft Tissue Procedures and Photobiomodulation

Core Message

Scientific literature reports an exponential growth in the number and variety of laser applications in orthodontics. This paper reviews the available laser wavelengths and will discuss some adjunct application of diode lasers for soft tissue procedures. These include photobiomodulation, laser gingivectomy to improve oral hygiene or bracket positioning, aesthetic laser gingival recontouring and laser exposure of the superficially impacted teeth. Selected treated cases will be presented throughout.

Ali Borzabadi-Farahani

12.1.1 Soft Tissue Procedures Introduction

The healthy gingival margin is located 1–2 mm coronal to the cemento–enamel junction [1]. However, this gingival architecture does not always present smile aesthetics during or after orthodontic treatment. Mucogingival surgery on the other hand, is a periodontal treatment to correct the defects in the morphology, position and/or amount of soft tissue and underlying bone support around teeth and implants. Laser incision/excision definitely has a place in modern mucogingival surgery [2]. Compared with a scalpel, a laser beam or the initiated fiberoptic tip of laser device can more easily cut, ablate and reshape the oral soft tissues in the oral cavity, with no or reduced bleeding and less pain, as well as with no or less need for suturing [2]. This represents a range of tissue interactions, such as tissue warming, welding, coagulation, protein denaturation, drying and finally vaporisation (ablation) and carbonisation, where soft tissues are evaporated or incised [2–7]. This process also provides haemostasis, microbial inhibition and destruction and photobiomodulation (PBM) [2–7]. In particular, there is increasing evidence that the appropriate use of lasers is associated with reduced intraoperative and post-operative pain and enhanced wound healing or tissue regeneration, compared to conventional use of scalpel or electrosurgery [2–4]. Electrosurgery can be used for incising soft tissues with good haemostasis [2–4], but comes with a risk of delayed wound healing due to unwanted thermal damage [2, 6] and necrosis of the underlying periosteum and alveolar bone.

12.1.2 Advantages of Laser Excision vs. Scalpel Surgery

Dental lasers have been widely used for soft tissue procedures, such as gingivectomy, gingivoplasty and frenectomy, and, in particular, for aesthetic gingival procedures, such as recontouring or reshaping of gingiva, crown lengthening and depigmentation [2]. For instance, compared to conventional scalpel surgery, the diode laser cut is more precise and more visible due to the laser ability to seal off blood vessels and lymphatics, leaving a clear dry field [2, 7]. The laser also contributes to significant pathogen reduction as it cuts; and residual bacteria are evaporated, destroyed or denatured by laser irradiation [2]. Laser incision with high-level laser therapy (HLLT) excises (ablates) the diseased tissues, with simultaneous provision of low-level laser therapy (LLLT) that penetrates or scatters into the surrounding tissues during high-level laser treatment and stimulates tissues and cells without producing irreversible changes (Fig. 12.1).

LLLT promotes periodontal wound healing of the adjacent tissues as a desired effect [2, 8, 9], a process known as photobiomodulation (PBM) of tissues and cells following laser irradiation [2]. LLLT generates an array of extremely transient biochemical intermediates that result in cascading biological reactions in favour of tissue healing [10–12]. This process works by altering the cellular redox state [10] and production of reactive oxygen species (ROS) in mitochondria, such as superoxide ($O_2^{\bullet -}$) and hydrogen peroxide (H_2O_2), which mainly affect and stimulate cells in a low redox state [12]. Cells in a low redox state are acidic, but after laser irradiation, the cells become more alkaline and are able to perform optimally, inducing the activation of numerous intracellular signalling pathways [12]. Photoabsorption by mitochondrial chromophores, in particular *cytochrome c oxidase*, leads to dissociation of the binding between *nitric oxide* (NO) and *cytochrome c oxidase*, allowing mitochondria to increase ATP production and *nitric oxide* (NO) release [10–12]. The produced ATP modulates a wide range of biological responses, including activation or synthesis of DNA, RNA, enzymes and other cellular components necessary for optimal performance and repair/regeneration of tissues [11]. The LLLT-mediated NO release leads to vasodilatation, involving cGMP-mediated activation of Ca-sensitive K (Kc) channels [11], as well as promotes keratinocyte and tenocyte proliferation, endothelial migration and lumenisation, macrophage function, angiogenesis in ischemic limb injuries and stem cell differentiation [11]. Overall, PTM positively affects each of the four phases of wound healing [11, 13] (Table 12.1).

Within the progressive stages of wound stabilisation and healing, the many cellular and biochemical pathways are potential recipients of sub-ablative (low-level) laser photonic energy between approximately 600 and 1,400 nm wavelength. Outside this range, similar induced effects may be attributable to low thermal rise and consequent tissue stimulation.

PBM can promote changes at the cell level and expression of cytokines that can collectively promote wound healing, by increasing collagen production, reduction of inflammation and pain relief [2, 10–53]. LLLT has been effective in pain reduction [15, 18], wound healing [19–24], bone repair and remodelling [25–33], nerve repair [34–39], angiogenesis [40, 41], as well as increased cell proliferation and biomodulation

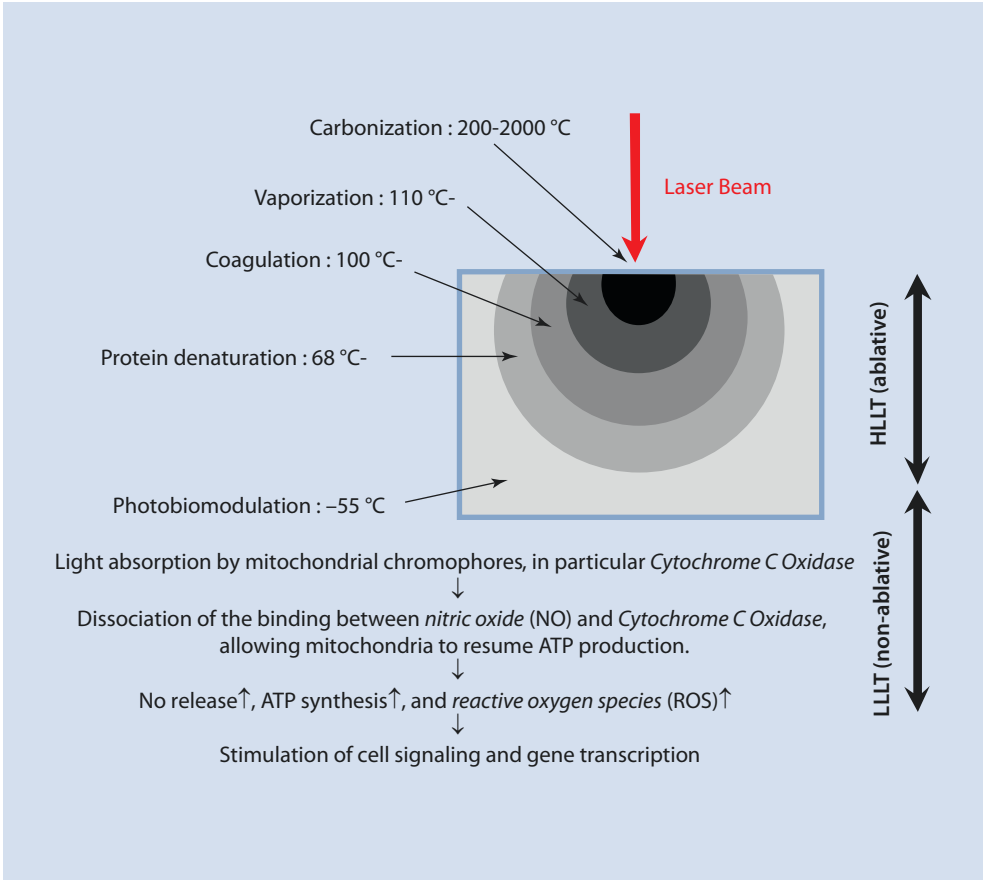

Fig. 12.1 Diagram showing the simultaneous work of high-level laser therapy (*HLLT*) and low-level laser therapy (*LLLT*). HLLT initiates various thermal effects on tissues, such as carbonisation, vaporisation, coagulation and ablation of soft tissue, as well as sometimes removal of the hard tissue (erbium lasers). Simultaneously, a low level of energy (*LLLT*) penetrates or scatters into the surrounding tissues during high-level laser treatment, which stimulates tissues and cells without producing irreversible thermal changes in the tissues, resulting in activation or stimulation (photobiomodulation, PTM) of wound healing in the surrounding tissues (Partially adopted from Aoki et al. [2])

Table 12.1 Effects of photobiomodulation (PTM) on four phases of wound healing [11, 13]

Four phases of wound healing	Effects of PTM on wound healing
Haemostatic phase	Promotes platelet aggregation and activation
Inflammatory phase	Promotes proliferation and degranulation of mast cells
Proliferative phase	Promotes proliferation of fibroblasts, keratinocytes, osteoblasts and chondrocytes as well as induces matrix synthesis
Maturation phase	Improves reorganisation and remodelling of wounds, aids improved tensile strength and restoring functional architecture of the repaired tissues

for cell lines such as fibroblasts [20, 42], keratinocytes [43, 44] and osteoblasts [45]. LLLT predominantly stimulates macrophages and fibroblasts [46–48] and collectively modulates secretion of vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF) and tumour necrosis factor alpha (TNF-α) by macrophages, neutrophils, endothelial cells and fibroblasts, stimulating cell proliferation, cell differentiation and neoangiogenesis, as well as synthesis of extracellular matrix components such as types I and III collagen fibres [46–53]. Less wound contraction and oedema also occur during mucosal healing; scars tend not to develop as less damage occurs to adjacent tissues, and there is rarely a need for periodontal dressing [7, 54]. This phenomenon can be attributed to the low-power (PBM) zones that surround the high-power surgical laser site [11].

These qualities allow faster or more favourable wound healing, needing less pain medication, as well as less postoperative discomfort, compared to usual scalpel surgery [2]. This can lead to reduction in the orthodontic treatment time, when there is a need for soft tissue procedures that otherwise need referral to other specialties such as periodontist or oral surgeon, in particular for fee-paying patients who demand optimal results with minimal effort as quickly as possible [55].

12.1.3 Overview of Lasers Used for Soft Tissue Procedures

Various laser systems have been used for soft tissue procedures, which work by ablating, incising and excising the soft tissue, as well as providing the much-needed coagulating effect. The frequently used soft tissue lasers include the carbon dioxide laser (10,600 nm), erbium lasers [erbium-doped yttrium-aluminium-garnet (Er:YAG) laser (2,940 nm) and

erbium chromium-doped yttrium-scandium-gallium-garnet (Er,Cr:YSGG) laser (2,780 nm)], neodymium-doped yttrium-aluminium-garnet (Nd:YAG) laser (1,064 nm), the diode group of lasers (800–980 nm) and, the potassium, titanium and phosphate ($KTiOPO_4$, KTP) laser (532 nm) [2, 3].

12.1.4 The Shallow or Deeply Penetrating Lasers and Haemostasis

The soft tissue lasers can be categorised into two broadly acting types: the deeply penetrating-type lasers (visible and near-infrared spectrum, 532–1,100 nm) that are essentially transmitted through water, showing a lower absorption coefficient in water [56] such as KTP green laser. This explains their deep penetration into healthy soft tissue, such as Nd:YAG and diode lasers, in which the laser light penetrates and scatters deeply into tissue [56]. However, they are selectively absorbed in areas of inflammation by blood components and tissue pigment [56]. There is also minimal to no interaction of Nd:YAG and diode lasers with healthy (not covered by calculus) dental hard tissue, which makes them suitable for soft tissue procedures [56]. The Nd:YAG laser is often used in free-running pulsed mode, with very-short-duration pulses and an emission cycle (ratio of "on" time to total treatment time) of <1% and very high peak power per pulse (100–1,000 W) [56]. The Nd:YAG laser is a deeply penetrating type of laser and produces a relatively thick coagulation layer on the lased soft tissue surface, exhibiting strong haemostasis. Therefore, the Nd:YAG laser is effective for ablation of potentially haemorrhagic soft tissue. Diode lasers represent a shallower penetration depth compared to Nd:YAG lasers and are less likely to cause pulpal damage after use [55]. The diode lasers can be used in a continuous-wave or gated-CW mode [7] and are the ideal choice for the use in orthodontic set-up because of the smaller size ("footprint") of the laser device and relatively lower cost involved [57] .

The second category highlights the superficially absorbed lasers (CO_2, Er:YAG and Er,Cr:YSGG lasers), in which the laser beam is absorbed in the superficial layer and does not penetrate or scatter deeply [2, 58, 59]. These lasers have higher absorption coefficient in water, and due to the high water content of oral mucosa (>90%), they are very effective soft tissue lasers [55]. However, what make them unattractive for the orthodontic set-up are the relatively high cost and the portability and movement issues [55]. Soft tissue penetration depth for CO_2 laser is approximately 0.2 mm [56, 60] and for erbium lasers (Er:YAG and Er,Cr:YSGG lasers) can be as shallow as 5 μm [56, 58]. CO_2 lasers have the highest absorption in hydroxyapatite and calcium phosphate and must be used with care during soft tissue procedures to avoid direct contact with hard tissue [56]. The CO_2 laser beam is absorbed at the tissue surface with very little scatter or penetration [2] and is associated with relatively thin layer of coagulation around the ablated site. The ablation for CO_2 laser is basically caused by heat generation (carbonisation) [2]. Erbium lasers have the highest absorption into water and target molecular water or the hydroxide ion as primary targets and mineral as a secondary target and therefore are used for ablation of both hard and soft tissues [56]. Erbium lasers provide the most rapid, favourable and uneventful wound healing due to their precise ablation with minimal thermal effects as well as low inflammatory response [60]. However, haemostasis is less effective with the erbium lasers because of the minimal tissue denaturation, which guarantees subsequent sufficient bleeding and blood clot formation in the ablated defects and thereby induces favourable wound healing [6]. Overall, erbium lasers provide the highest absorption into water, minimizing the thermal effects on the surrounding tissues during irradiation, but the cost, laser portability and movement and less clear-cut incision morphology compared to CO_2 and diode lasers [60] are the potential drawbacks in orthodontic practice.

12.1.5 Tissue Ablation: Non-contact or Contact Cutting Mode

As has been seen elsewhere (▶ Chap. 3), laser-tissue interaction is the result of electromagnetic (photonic) energy being absorbed and converted into other (predominately thermal) energy. Three forms of energy transfer can be observed:

Radiation
Where the photon stream is delivered through a short air space with no contact between delivery tip and target tissue. This may be commonly referred to a "non-contact mode".

Conduction
Where enhancement of the energy conversion can be achieved through direct contact between the delivery tip and the tissue. This may be commonly referred to a "contact mode".

Convection
Transfer of energy within the body of the tissue through fluid movement or circulation. This may occur regardless of either contact or non-contact modes.

Most surgical lasers produce a photothermal effect on soft tissue, evaporating soft tissues through rapid thermal rise. The non-contact lasers such as CO_2 or erbium lasers (Er:YAG and Er,Cr:YSGG) directly and easily evaporate soft tissues by photothermal effects that vaporise interstitial water. However, the non-contact mode is associated with less precise cut and lack of proprioceptive feedback compared to contact mode lasers.

When lasers are used in contact mode to make an incision or excise soft tissue, they often need "initiation" of the laser tip end. In this process, part of the emitting light in the

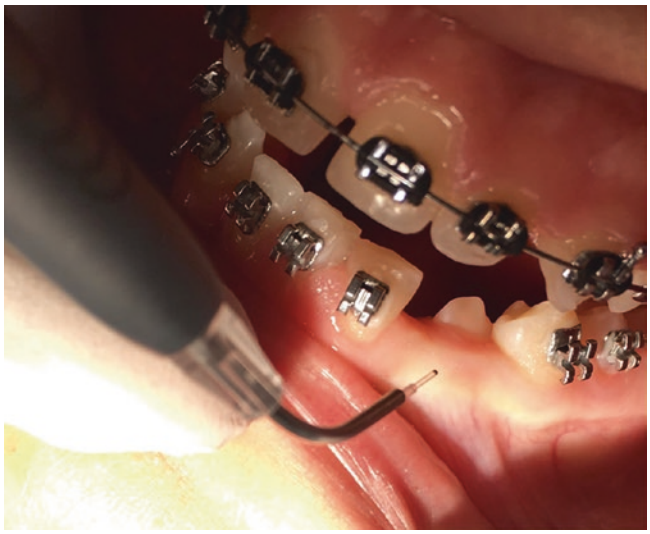

Fig. 12.2 A typical initiated fibre-optic laser tip will be used for laser excision

Nd:YAG and diode lasers is converted into heat by refraction or diffused reflection at the tip end, or in simple terms the laser tip end gets initiated, creating a condition called "hot tip". This initiation produces secondary thermal effects at the heated tip end that can cut or incise soft tissue as well as offer coagulation of the tissue as a result of contact with the overheated tip rather than by the laser energy itself [2, 3]. Figure 12.2 shows an initiated fibre-optic tip prior to laser exposure of an ectopic lower left canine. Diode and Nd:YAG lasers produce a relatively thicker coagulation layer on the treated surface than superficially absorbed lasers [4]. Diode lasers are considered to be ideal for daily practice of orthodontic soft tissue procedures owing to sufficient haemostasis and precise incision margins [61, 62]. For the purpose of this paper, the use of diode lasers for soft tissue procedures will be discussed in more detail due to their ease of use in orthodontics and lower operating cost.

12.1.6 Soft Tissue Diode Lasers

Since their introduction in 1962 [63, 64], the diode laser family has grown considerably and diode lasers with wavelengths in the range of 445-2200 nm have been used for treatment of various medical conditions [55, 57, 65–67]. However, reports on the use of the 810–830 nm, 940 nm, 980 nm and 1,064 nm wavelengths are more frequent in the literature [55, 57, 69]. They have high absorption coefficients in water and haemoglobin and particularly in oxyhaemoglobin, therefore rendering different soft tissue effects. However, diode laser light is poorly absorbed by the hydroxyapatite and enamel [54, 55], and therefore, it is an excellent soft tissue surgical laser for incising, excising and coagulating gingiva and mucosa. The active media of semiconductor (diode) lasers are varied and can include aluminium (Al), gallium arsenide (GaAs) and, occasionally, indium (In) [55, 68, 69]. Examples are gallium-aluminium-arsenic (Ga-Al-As), arsenic-gallium (As-Ga) and indium-gallium-aluminium-phosphorus (In-Ga-Al-P) lasers. The diode lasers are portable (<5 kg), small, relatively inexpensive and simple to use [68]. There is also a stable power output, long lifetime and low installation and maintenance costs [68].

12.1.7 Fibre-Optic Tip Size, Power Output and Continuous/Gated-CW Mode for Diode Lasers

The soft tissue diode lasers usually work in a 'contact mode' and the laser beam is delivered by a fine glass optic fibre, with a fibre system tip that can be angled, so that the dentist holds it in a pencil-like holder for accurate manipulation of the areas that are difficult to handle [68]. For surgical incisions and excision, a 400-μm diameter fibre-optic tip is recommended, as smaller diameter fibres tend to be more friable and liable to fracture [69]. The fibre-optic tip needs initiation prior to performing surgical excision, often by tapping the initiated tip on a thick blue articulating paper and use of black ink, a solid colour in a magazine page or a piece of cork – each with varying degrees of success [55, 70]. Diode lasers with power outputs of <500 mW are used in *low-level laser therapy* (LLLT) to provide photobiomodulation (PBM) and associated wound repair and pain relief [55]. However, for excision there is often a need for a continuous power output of 1.0–1.5 W [70], depending on the fibrotic nature of the tissue. In order to decrease the carbonisation and thermal damage and allow for thermal recovery of the tissue, a gated-CW mode (with repetitive "on–off" cycles of varying length and frequency depending on the make of the laser) has been suggested and implemented in many contemporary diode laser units [69, 71].

12.1.8 Provision of Anaesthesia and Basic Soft Tissue Guidelines

Lower pain sensation and less need for analgesia have been reported when diode laser with superpulsed mode [72] or with gated-CW of one millisecond pulse duration (on/off cycle of 50/50) [73] was used for soft tissue surgery, as compared to continuous wave diode laser. Diode laser soft tissue surgery is often performed using local infiltration (e.g. 2% lidocaine) approximately 5 min before procedure, but literature also reports using topical lignocaine anaesthetic gel, applied for 3 min, particularly with the gated-CW mode [69, 74], or compound topical anaesthetics such as TAC Alternate for 3 min (20% lidocaine, 4% tetracaine and 2% phenylephrine) [69, 70, 75]. Given enough time, topical anaesthetics often provide enough analgesia for laser exposure of buccally superficially impacted teeth; if enough analgesia is not

achieved, additional topical dosage can be applied [69]. Palatal mucosa; however, is thicker and local infiltration is often necessary [69]. In order to confirm adequate anaesthesia prior to laser soft tissue surgery, gently probing the soft tissue will confirm that the patient feels pressure only or feels anything sharp that indicates the need for added dose of local anaesthesia.

During laser ablation, vaporised tissue, water, bacteria and organic chemical residues are liberated; this is known as the "laser plume", and the use of a high-speed suction is recommended to remove this plume and objectionable charred odour, as well as provide a degree of safety against inhalation by patient and attending clinicians [69, 70]. Following the surgical excision, the soft tissue margins can appear dark and charred (carbonised), and the remnants of carbonised tissue at the surgical margins can be removed using sterile gauze dampened with saline [74] or a micro-applicator brush soaked in 3% hydrogen peroxide solution [70].

Various manufacturers present different arrangements for diode laser with respect to output power, diameter of fibre and wavelength. Although these parameters may influence collateral tissue damage, there is currently lack of standardisation in setting the best operating parameters of diode laser for orthodontic soft tissue procedures, which needs to be investigated in future studies [76].

Diode lasers are useful in recontouring the gingiva to gain access to the clinical crown, where there is gingival overgrowth or in case of partially erupted teeth, which prevent the proper positioning of a bracket. When planning laser soft tissue procedures, the general guideline is to leave at least 1.0 mm of pocket depth and to preserve at least 2.0 mm of keratinised tissue to avoid further soft tissue complications such as gingival recession [55]. The aforementioned guidelines are based on the "biologic width" concept, as measured from the free gingival margin to the crestal bone, which is approximately 3 mm, consisting of, on average, 1 mm of junctional epithelium, 1 mm of connective tissue attachment, as well as a gingival sulcus depth of approximately 1 mm [55, 69]. In order to decide between the conventional flap approach and laser gingivectomy, the gingivectomy location should be probed, and the amount of attached gingiva, the location of the crest of bone and the desired amount of crown lengthening should be looked into based on the limitations of the biologic width. In general, an average of 3 mm of soft tissue will rebound (regrow) coronal to the alveolar crest in about 3 months [77].

12.1.9 Laser Gingivectomy to Improve Oral Hygiene or Bracket Positioning

Difficulties in cleaning approximal tooth surfaces and reduction in aerobe/anaerobe ratio of sub- and supra-gingival flora [78, 79] may contribute to the gingival hyperplasia and pseudo-pocketing. This is common following fixed orthodontic therapy and can be seen in about 10% of orthodontic patients [76, 80]. Gingival enlargement often impedes the maintenance of oral hygiene, causing aesthetic and functional problems, and has been reported to compromise orthodontic tooth movement [76, 81, 82]. Conventional treatment for gingival enlargement often includes oral hygiene instruction, scaling, root planing and prophylaxis, but extensive and often fibrotic gingival enlargement compromises the self-care and may necessitate gingivectomy to maintain oral health [76, 83]. The adjunct use of diode laser gingivectomy can produce a greater and faster improvement in gingival health of patient with gingival enlargement [76].

In addition, laser gingivectomy can be performed to remove excess soft tissue and expose the crown of the partially erupted teeth, allowing brackets to be placed properly, ideally in the centre of the teeth, allowing maintenance of an improved level of hygiene during treatment [55, 84].

12.1.10 Aesthetic Laser Gingival Recontouring

Following active orthodontic treatment, it is not unusual to "debond" – remove – adherent orthodontic brackets and come across unsightly gingival margins not conforming to the principles of smile aesthetics, presenting with short or uneven crown heights, disproportionate tooth proportionality ratios and unaesthetic enlarged and fibrotic interdental papillae and gingival margins [7]. Aesthetic procedures such as aesthetic crown lengthening or papilla flattening can be technically demanding tasks in that the gingival margins sometimes need very minor recontouring that needs a higher degree of precision than that achieved with a scalpel blade, regardless of the operator's skill level [85]. Diode lasers offer the precise incision control because of less bleeding and a clear dry field during surgery. Figures 12.3a–c show a patient who has undergone gingival recontouring of the maxillary left central incisor and lateral incisor.

12.1.11 Laser Exposure of the Superficially Impacted Teeth

One of the most interesting applications of diode laser is for exposure of superficially impacted teeth, in particular for maxillary permanent canines, which are the most frequently impacted teeth after third molars (0.92–4.3%) [86, 87]. The conventional approach is to wait for the tooth to erupt, which could delay treatment for months and affect treatment efficacy adversely, or to refer for the placement of an apically positioned flap or mucoperiosteal flap [70]. The flap procedures are relatively aggressive in nature. Accurate

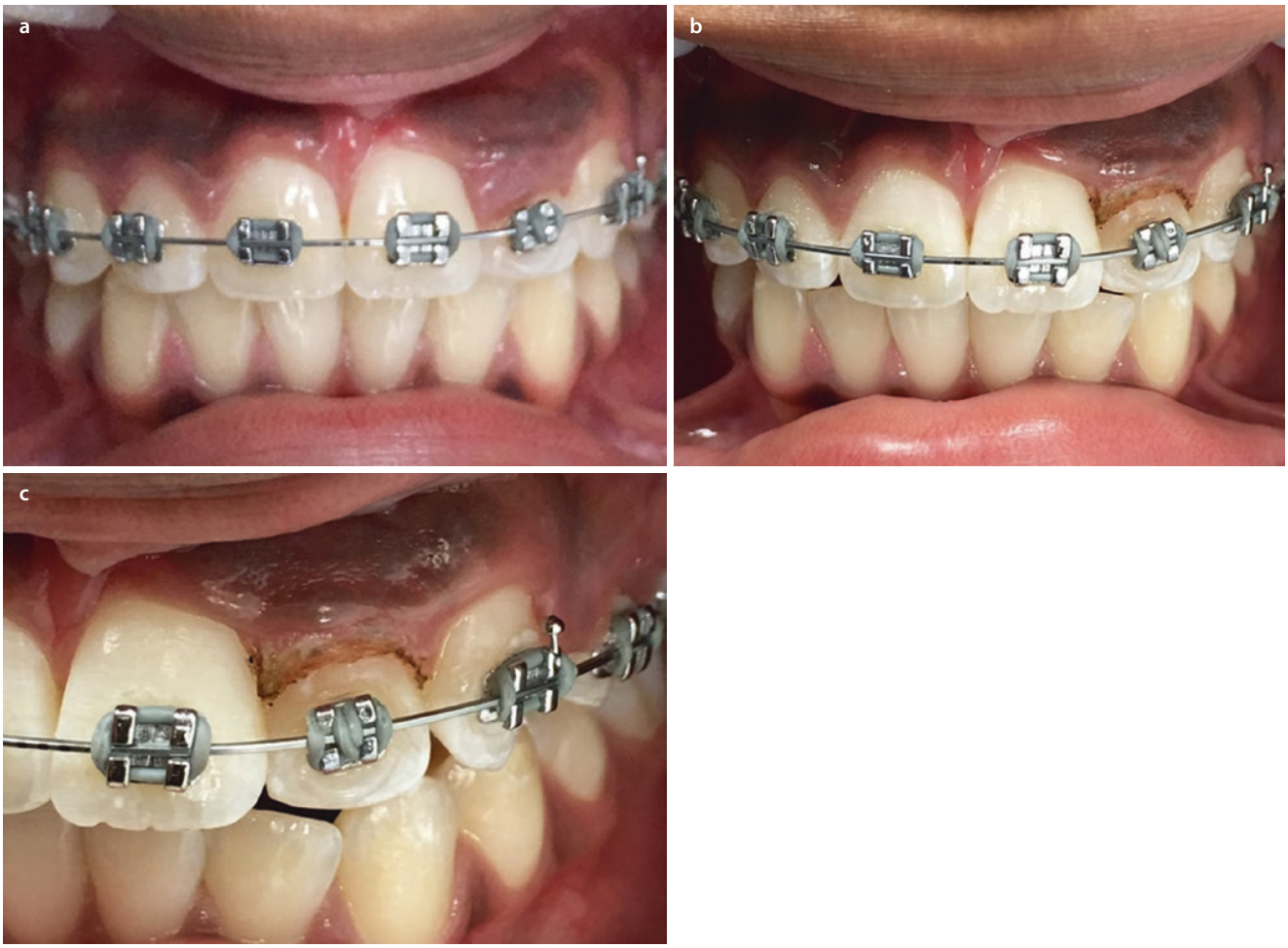

Fig. 12.3 (**a**) A preoperative image of a patient with gingival hyperplasia at the maxillary left lateral incisor (UL2) region. (**b**) Immediate post-operative appearance following local infiltration (2% lidocaine). Laser operating parameters used were the continuous-wave 940 nm diode (InGaAsP) laser (Epic 10, Biolase, Irvine, CA), with a 400-μm diameter fibre-optic tip, in a contact mode after initiation (power output = 1 W). Some carbonisation is evident at the laser gingivectomy site. (**c**) Immediate post-operative close-up view after gingivectomy

localisation of the impacted tooth prior to laser exposure is vital to establish if the impacted tooth is positioned superficially and not covered completely by bone, or needs referral to an oral surgeon or periodontist for surgical exposure. The presence of a labial bulge does not guarantee access to crown after soft tissue exposure as clinical crown might be fully covered by alveolar bone. The localisation should be based on both clinical (blanching of tissue with finger pressure) and, if in doubt, by radiographic examination [88]. Approximately, 85% of canine impactions occur palatally and 15% buccally [88–90].

Diode laser exposure is not applicable in cases of full impaction of teeth covered by cortical bone. In such cases, a conventional full-thickness mucoperiosteal flap (palatal impaction) or an apically positioned flap (buccal impaction) and removal of cortical bone until the crown portion of the retained tooth is exposed are recommended. When superficially impacted teeth are present, it is recommended to create sufficient space before the surgical laser exposure to facilitate bonding an eyelet or bracket and apply orthodontic forces right after laser exposure.

Figures 12.4a–c demonstrate a male patient with a buccally impacted maxillary right canine, which has undergone laser exposure right after exposure and at 24 h follow-up. Note that the amount of post-operative inflammation is minimal.

Figure 12.5a shows a buccally impacted maxillary left canine, right after laser exposure (Fig. 12.5b), bonding (Fig. 12.5c) and applying orthodontic force (Fig. 12.5d) as well as at 2 weeks (Fig. 12.5e) and 11 months follow up (Fig. 12.5f).

Figures 12.6a–d illustrate the remarkable healing process in a male patient with a palatally impacted maxillary right canine, after palatal laser exposure.

Figures 12.7a–j show another patient with a buccally impacted maxillary right canine and a partially erupted maxillary left canine. The gated-CW mode and pulse duration of 1m second was used, which led to minimum post-operative discomfort and excellent healing at

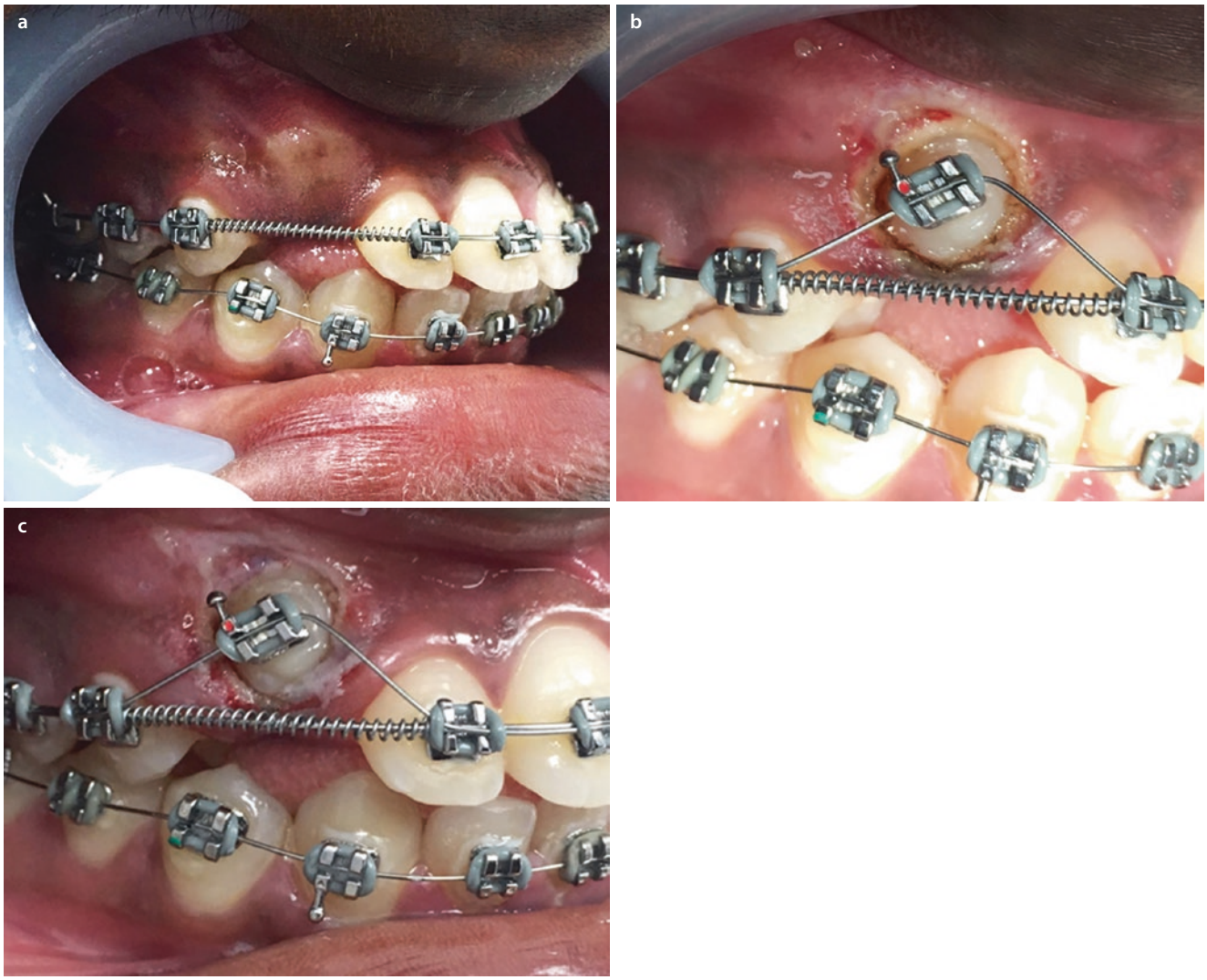

Fig. 12.4 (**a**) A male patient with a buccally impacted maxillary right canine. (**b**) Immediate post-operative view of laser-assisted exposure through soft tissue ablation. The bloodless field facilitates the bonding process and placement of orthodontic brackets. Laser operating parameters were the 940 nm diode laser (Epic 10, Biolase, Irvine, CA), with an initiated 400-μm diameter fibre-optic tip, in a contact mode (gated-CW mode, average power output = 1 W, pulse duration = 1 ms, time on/time off = 50%). Time spent for the laser exposure was approximately 10 mins. (**c**) Appearance at 24 h follow-up. Note that the amount of inflammation is minimal. The patient reported very minimal pain and discomfort during the first 24 h

subsequent follow-ups. The diode laser in this case clearly provided bloodless site that allowed immediate orthodontic bonding of the maxillary canines and reducing the treatment time.

Compared to laser tooth exposure, a patient with a similar superficially palatally impacted canine usually is usually referred for full-thickness mucoperiosteal flap, which can be very aggressive and often needs placement of a protective dressing (pack) over the surgical site whilst it heals [91]. The use of scalpel usually involves suturing with stitches during surgical procedure that need to be removed 1–2 weeks post-operatively. [92] All demonstrated cases were performed using the 940 nm diode (InGaAsP) laser (maximum power output = 10 W, Epic 10, Biolase, Irvine, CA), using a 400-μm diameter fibre-optic tip, in a contact mode and after initiation.

12.1.12 Other Applications of the Laser Soft Tissue Procedures in Orthodontics

Diode lasers have been used to uncover temporary anchorage devices (TADs), in frenectomy where highly attached frenum impedes tooth movement in diastema cases, in removal of operculum on mandibular second molars that prevents banding, or to improve healing of minor aphthous ulceration following placement of fixed orthodontic braces [7, 55, 70].

12.1.13 Post-op Instruction

Literature review indicates suggestions such as keeping the area clean, using soft-bristle toothbrush (or cotton swab), rinsing the

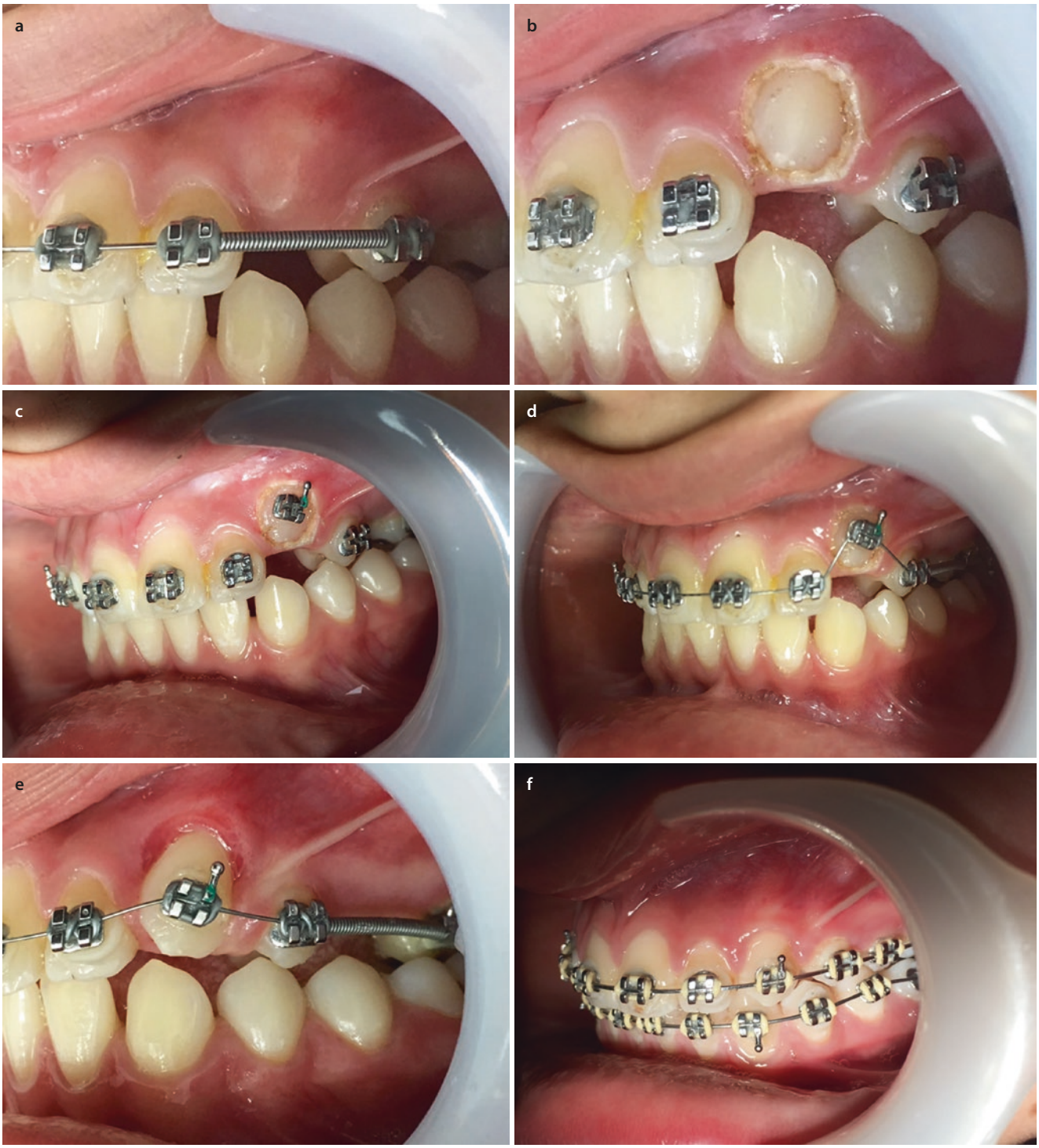

Fig. 12.5 (**a**) A female patient with a buccally impacted maxillary left canine. (**b**) Immediately after laser-assisted exposure. A 940 nm diode laser (Epic 10, Biolase, Irvine, CA) with an initiated 400-μm diameter fibre-optic tip, in a contact mode, was used (gated-CW mode, average power output = 1 W, pulse duration = 1 ms, time on/time off = 50%). Time spent for the laser exposure was approximately 10 min. (**c**) After bonding the bracket, please note that the bloodless exposure site facilitates immediate placement of orthodontic bracket. (**d**) Applying orthodontic force immediately after exposure reduces the treatment time. (**e**) At 2 weeks follow-up. (**f**) at 11 month follow-up, note the adequate amount of keratinised tissue at the maxillary left canine buccal aspects

mouth with salt water three or four times daily for several days and removing any remaining tissue with a wet cotton swab [7, 55], rubbing vitamin E gel over the healing area (to aid in healing and keeping the treated area moist), as well as taking over-the-counter analgesics such as acetaminophen (500-mg tablet qid prn 3 3/7) that have been suggested for pain control [55, 76].

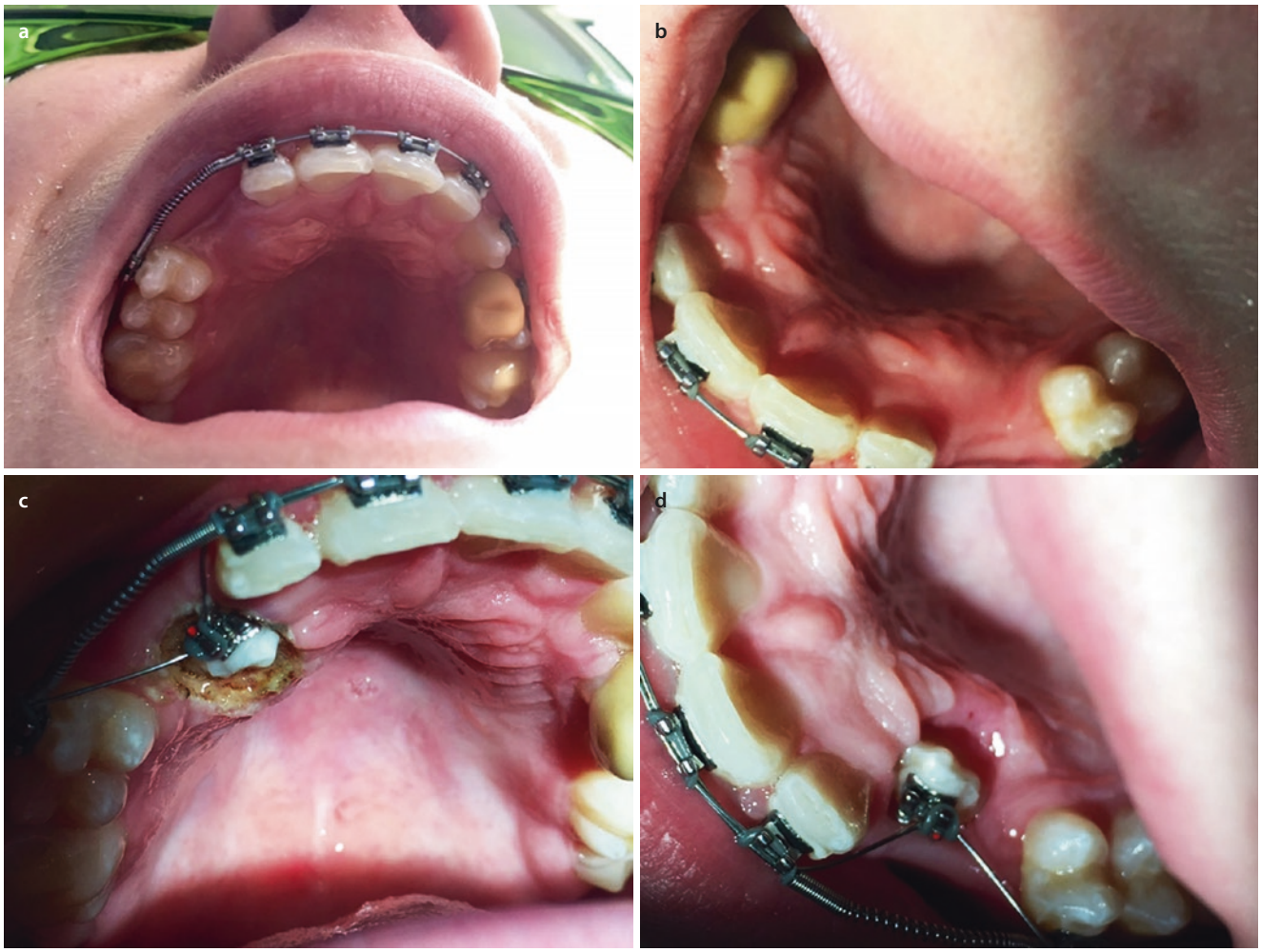

Fig. 12.6 (**a**) Preoperative appearance with the patient wearing the safety protective glasses. The palatal canine bulge is clinically evident. (**b**) Palatal view. (**c**) Immediately after palatal laser exposure. Laser operating parameters were the 940 nm diode laser (Epic 10, Biolase, Irvine, CA), with an initiated 400-μm diameter fibre-optic tip, in a contact mode (gated-CW mode, average power output = 1 W, pulse duration = 1 ms, time on/time off = 50%). Time spent for the laser exposure was approximately 15 min. An aggressive conventional full-thickness mucoperiosteal flap often needs placement of a protective dressing (pack) over the surgical site whilst it heals and is associated with significant bleeding in the exposure site that can compromise the bonding process. (**d**) At 2 weeks follow-up. Please note the excellent healing without signs of inflammation

12.1.14 Laser Photobiomodulation in Orthodontics

As previously mentioned, lasers with power outputs of <500 mW are used in *low-level laser therapy* (LLLT) to provide biomodulation, wound repair and pain relief [55]. This application involves two main uses including the acceleration of orthodontic tooth movement and the reduction of orthodontic pain.

12.1.15 Lasers for Orthodontic Pain Reduction

There is body of evidence confirming that placement of orthodontic separators and initial aligning archwires induce pain that reaches peak intensity at approximately 24 h [91, 93, 94–97]. This pain caused by orthodontic treatment can affect patient's compliance and even force them to terminate treatments prematurely [98].

Two recent systematic reviews that included meta-analysis of the previous randomised controlled trials (RCTs) investigated the effects of diode LLLT on orthodontic pain [99, 100]. One stated that the comparison of laser versus placebo demonstrated that LLLT reduced the pain score significantly compared with placebo groups *($P < 0.00001$)* [99]. Furthermore, a trend of earlier pain termination in laser versus control and placebo groups was detected, but without statistical significance *($P > 0.05$)* [99]. The other study revealed that diode LLLT significantly reduced orthodontic pain by 39% in comparison with placebo groups *($P = 0.02$)* [91]. Diode LLLT was shown to significantly reduce the maximum pain intensity amongst parallel-design studies (*$P = 0.003$* versus *placebo groups*; *$P = 0.000$* versus *control*

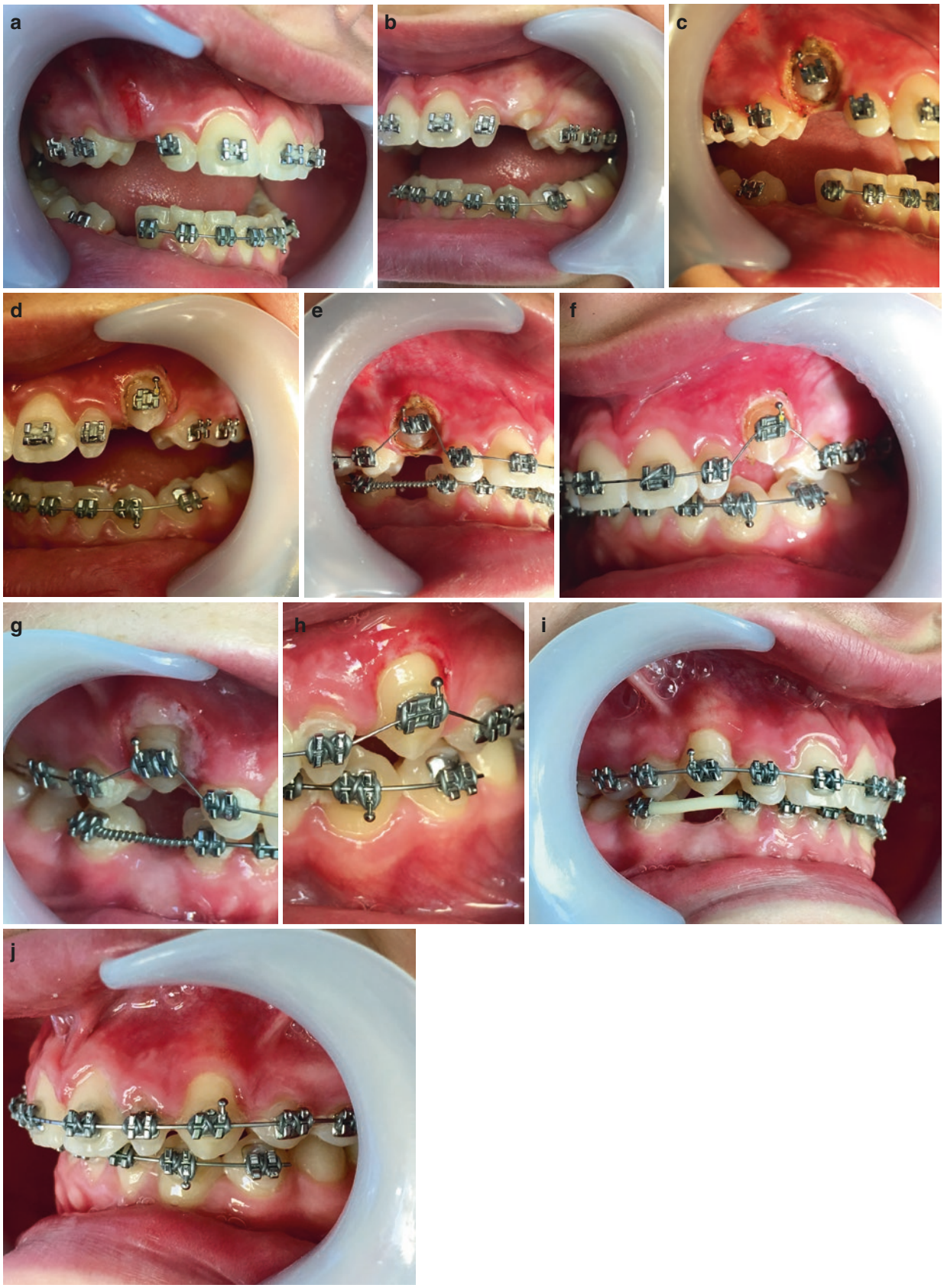

Fig. 12.7 (**a**, **b**) A male patient with a buccally impacted maxillary right canine and a partially erupted maxillary left canine (**c**–**f**) Immediate postoperative view after laser-assisted exposure and bonding and following placement of orthodontic wire. Laser operating parameters were the 940 nm diode laser (Epic 10, Biolase, Irvine, CA), with an initiated 400-μm diameter fiber-optic tip, in a contact mode (gated-CW mode, average power output = 1 W, pulse duration = 1 ms, time on/time off = 50%). Time spent for the laser exposure was approximately 15 mins. Appearance at one week (**g**, **h**) and at 4 month (**i**, **j**) follow- up

groups) [100]. Authors of both systemic reviews concluded that the use of diode LLLT for orthodontic pain appears promising. However, due to methodological weaknesses, there was insufficient evidence to support or refute LLLT's effectiveness [99, 100]. Therefore, RCTs with better designs and appropriate sample power are required to provide stronger evidence for diode LLLT's clinical applications and identify the appropriate laser parameters such as irradiation dose, power output, fluency and continuous/pulsed mode.

12.1.16 Lasers for Acceleration of Orthodontic Tooth Movement

This area of investigation is quite recent, and new studies are emerging. Receptor activator of nuclear factor kappa-B ligand (RANKL) and its receptor RANK are members of the tumour necrosis factor (TNF) and TNF receptor superfamilies and present a regulatory function in bone homoeostasis [101]. The available limited evidence suggest that LLLT increases the expression of RANK and RANKL [102] and may have a rule in accelerating orthodontic tooth movement [103–109]; however, identifying the ideal parameters of the LLLT needs more investigations, such as the most effective laser wavelength, power output, energy density, irradiation dose and ideal time interval between them, as well as the method of delivery.

Acknowledgment: The author (Ali Borzabadi-Farahani) is grateful to AEGIS Communications for granting permission to reprint excerpts from previously published material (Compendium of Continuing Education in Dentistry 2017;38 (eBook 5):e18–e31).

Summary

The use of diode lasers for soft tissue procedures and photobiomodulation introduced alternative adjuncts for gingivectomy, to improve oral hygiene or bracket positioning and gingival recontouring, to enhance gingival aesthetics, and for laser exposure of the superficially impacted teeth, to reduce the treatment time as well as for reducing the orthodontic pain or potentially decreasing orthodontic treatment time. The diode laser incision/excision is usually performed in a contact mode, and the use of a 400-μm diameter fibre-optic tip is recommended. Compared to scalpel surgery, diode lasers offer a clean and bloodless surgical site, with an added benefit of photobiomodulation that enhances the wound healing and reduces the patient discomfort. There is obviously a strong argument for laser safety that can be addressed with proper training. However, there is paucity of data regarding the most effective wavelength (810, 940 or 980 nm) for performing diode laser gingivectomy or tooth exposure, as well as other laser parameters such as continuous or pulsed/gated mode of delivery, and the optimum power output that requires further research.

12.2 Photobiomodulation Concepts Within Orthodontics

Mark Cronshaw

Lasers and LED phototherapy appliances have been the subject of many scientific in vitro, in vivo animal and more recently clinical studies for a variety of non-surgical effects. The possibility of applying photonic energy as a treatment modality to biomodulate cellular, humoral, vascular and neuronal tissue behaviour has been subject to many studies over the past 45 years. The potential applications of lasers and LED phototherapy for orthodontics include pain relief as well as the possibility of shortening treatment time by accelerating the rate of orthodontic tooth movement. Pain associated with standard orthodontic treatment is a common problem, and along with protracted treatment times, these issues represent a significant problem reducing patient compliance and acceptance of treatment. Initial investigations studied the observable effects of laser devices to influence pain and discomfort experienced by patients associated with the forces applied to teeth to achieve movement. The mechanisms underlying orthodontic pain are discussed here along with a discussion of the problem and an analysis of the current literature.

12.2.1 Background

At present the consensus opinion is that further studies are required to strengthen the evidence base and define the optimum methodology; however, the published studies to date are encouraging and indicate some positive clinical benefits. In respect of the acceleration of orthodontic tooth movement, there has been considerable interest as reflected in the volume of published studies attempting to use both in surgery laser devices and more recently the use of patient home-use LED phototherapy appliances to shorten treatment time. A description and discussion of the various animal and clinical studies are presented here. Due to the highly heterogeneous nature of the various studies, there is at present no consensus on appropriate treatment strategies, although this is clearly an area worthy of continued investigation. The current evidence base is inadequate. However, there are some interesting animal and clinical studies which support this topic as worthy of further in-depth evaluation. The most recent clinical trials use a patient home-LED therapy device which could potentially represent an entirely new approach to shorten treatment time and overcome a major obstacle to the uptake of orthodontics.

A variety of light sources have been investigated for possible therapeutic gain in orthodontics for a range of non-surgical applications. Of the optical sources investigated, a variety have been applied, the majority of which are diode semiconductor lasers or LED lights in the waveband range of 650–980 nm A variety of clinical applications have been proposed, for instance, as an adjunct to the possibility of reducing the frequency of incidence, duration and intensity of pain associated with standard orthodontic therapies. Also, researchers have evaluated the potential of phototherapy to accelerate orthodontic tooth movement (OTM) or conversely enhance anchorage. Many of the published studies have used in-surgery laser equipment, although more recently home application devices for patient self-administration of home-based phototherapy have been developed using transdermal or intra-oral LED devices [110–112].

The potential clinical gain to treat orthodontic patients taking advantage of the known physiological properties of light is an intriguing area. There are many in vitro, in vivo animal studies and some clinical trials and reports in the current scientific literature. As a product of over 40 years of research, quite a lot is known about how light can interact with biological tissues which can result in a variety of possible beneficial effects. More bone, enhanced repairs, reduced inflammation, vasodilatation and analgesia are amongst a long list of possible effects [113, 114].

At the time of writing, there have been, within the past 3 years, over 10 systematic and narrative reviews on various aspects of orthodontic phototherapy, assessing animal and clinical studies that have been published during the preceding 20 years. This high level of recent activity is indicative of the considerable interest surrounding the claims of proficiency in the literature. This is an area shrouded in confusion, and notwithstanding the volume of publications, this is still a subject with a developing scientific evidence base. It is the intention here to offer an overview of the subject along with a critical analysis and description of some of the various suggested treatment strategies [110, 111, 115–122].

It is worthy of note to examine the reasons for the current level of clinical interest and scientific endeavour. Every year, many millions of children and adults worldwide receive orthodontic treatment with a trend towards the increasing uptake of this type of therapy by adults. A typical course of orthodontic treatment can take between 12 and 24 months to complete with a variable amount of post-treatment time for retention with appliances or fixed splints. Orthodontic treatment can frequently be associated with a variety of side effects, including variable degrees of pain and discomfort, alveolar bone resorption, root resorption, caries and a variety of periodontal issues. Due to the protracted nature of orthodontic treatment and the various possible associated complications, there can be a loss of patient motivation. Also, extended treatment results in increased costs, due to time away from school, work, extracurricular and recreational activities. Particularly for adults the commitment to time is a prime deterrent to patients to commit to this type of therapy. All of these issues result in a reduction in treatment uptake as well as failures in treatment compliance. Any assistance that can improve patient comfort and shorten treatment length consequent to the acceleration of the rate of OTM can help to alleviate these risk and challenges [123–130].

12.2.2 Pain Studies

It is accepted that orthodontic tooth movement involves a complex cascade of processes consequent upon the creation of tensile and compressive areas in the periodontium. An inflammatory response is essential in the remodelling of alveolar bone and periodontal ligament during orthodontic tooth movement. As a response to the acute inflammation, there is increased osteoclastogenesis and an upregulation of matrix metalloproteinases associated with tissue remodelling [131].

In response to the application of load, there is mechanical stimulation as well as some damage of cells and tissues and associated changes in blood flow. This is a trigger to a complex pro-inflammatory cascade of cytokines including histamine, bradykinin and prostaglandins amongst others. The nervous system contributes to the physiology of the resultant peripheral inflammation mediated via neuropeptides such as substance P, neurokinin A and calcitonin gene-related peptide. These potent mediators induce vasodilatation, increased vascular permeability and the activation of nuclear factor kappa B. The overall resulting biological response is to produce so-called aseptic inflammation which results in the stimulation of C-nerve and A-delta nerve fibres producing pain symptoms. These symptoms can vary in intensity and duration and are most normally seen during the first hours after the application of forces. Pain usually reaches a peak after around 18–36 h with a gradual decline over the following week. This pain/discomfort experience is commonly associated with fixed and removable appliances, separator and band placement, bracket debonding and wire displacement. The consequent deterioration in patient comfort can in prevalence affect the majority of patients and is recognised as a key barrier to the completion of orthodontic treatment [128–131].

Strategies to manage orthodontic pain have been proposed, including the application of transcutaneous electrical nerve stimulation, vibratory appliances and other methods such as chewing gum or plastic wafers. The most common option has been to prescribe non-steroidal anti-inflammatory drugs (NSAIDS). These are effective in pain relief; however they are associated with the hindering of osteoclastic activity due to the inhibition of the production of prostaglandins via COX2 suppression. Also, NSAIDs can be associated with serious adverse effects such as gastric bleeding, ulcers and allergy. Studies in experimental animals have demonstrated a reduction in the rate of OTM in conditions where inflammation has been suppressed, and it is apparent that induced acute inflammation is a necessary component associated with OTM bone remodelling [115, 117, 118, 132–137].

Laser phototherapy has been applied for the management of acute and chronic pain for a wide variety of conditions, including various arthropathies and neuropathies, as well as to ameliorate the pain and discomfort associated with cancer chemotherapy- and radiotherapy-induced oral mucositis. The precise mode of operation of laser-induced analgesia is still the subject of continued investigation. It is thought to operate on a variety of local and systemic pathways including the inhibition of axonal depolarisation; the selective reduction of acute inflammatory mediators such as prostaglandins, IL1-B, IL-6 and TNF-α; vasodilatation and improved lymphatic drainage; as well as systemic effects mediated through humeral and peripheral neural pathways [138–144].

A variety of laser wavelengths have been found to be useful in producing analgesia including the helium-neon laser, the diode laser, the Nd:YAG laser, the Er:YAG and ErCr:YSGG lasers as well as the CO_2 [114, 121, 138–140, 143, 145] (see also Table 12.2). Due to the potential for deep tissue penetration, consequent upon the low absorption of the incident photonic energy by tissue chromophores such as water, the wavelengths that may be best suited for this purpose are the diode lasers as well as the Nd:YAG. Lasers differ from broader spectrum light sources such as LEDs by virtue of narrow waveband in comparison to the LEDs, as well as by being a coherent light source, whereby all the photons are in the same phase and space. This physical phenomenon can result in the generation of areas of interference and amplification; in turn, this can result in laser sources having deeper penetration into tissues, compared to a noncoherent light source – hence facilitating the delivery of an adequate dose. In addition, a free-running pulsed laser such as the Nd:YAG can have very high peak power (albeit for a very short pulse duration) which could, in principle, cumulatively permit sufficient energy to reach deeper tissue layers to precipitate the photochemical and photophysical changes associated with analgesia. The choice of wavelength and type of laser applied, however, has not been subject to a meta-analysis, and at this stage, it is premature to make an evidence-based determination [114, 138, 159].

In respect of the orthodontic literature, two types of diode laser have been used most frequently: the InGaAlAs laser (λ 630–700 nm) and the GaAlAs laser (λ 780–890 nm).

A recent review by Ren et al. [121] included a total of 14 eligible studies. It was noted that the output power and energy delivered varied greatly between studies (0.18–9 J per treatment point). There were marked differences in the methodology of application as some studies used a single-point method, whereas others used multiple points of application along the root in contact with the mucosa. There was also a range of application frequency from a single time through to multiple additional irradiation within 1 week of orthodontic treatment. Although the majority of studies included supported the beneficial effects of laser irradiation, it was a highly heterogeneous set of studies. Also, regrettably, there was incomplete reporting of the parameters as important information concerning beam size and energy density was missing in some of the studies. In consequence, it was not possible for the authors to draw conclusions as to the merits of diode laser therapy for orthodontic pain control. It was, however, noted that in respect of the prevalence of pain that of a synthesis of two studies [150, 151] by meta-analysis, the pain was reduced by 39% at a significant level compared with the placebo. The time course of pain was investigated in two studies which revealed that pain subsided significantly earlier in the laser-treated group compared to the placebo. Also, this interesting review paper noted that in the parallel-type studies, there was a marked reduction in pain severity, whereas in the split-mouth studies, this was only slightly reduced. This may be explained by the possibility of cross-over effects and photo-contamination of the test sites as well as the proposal that laser-induced analgesia may, in part, be mediated systemically, hence the different outcomes between the two types of study.

A more recent systematic review by Sonesson et al. [110] reported that of the 13 studies included, all reported a significant reduction in pain amongst the treated patients. This outcome was consistent with two previous systematic reviews. Sonesson's group applied strict measures for inclusion and a high level of assessment to score the clinical trials following the guidelines of The Swedish Council on Technology Assessment in Health Care [160]. Sonesson et al. identified inconsistencies in design of the studies, reporting and different outcome parameters (acute pain as opposed to delayed pain). The overall quality of the evidence was regarded as poor, largely consequent upon inconsistencies in study design and conformity of laser method applied. The fact remains, however, that notwithstanding strict guidelines, it was accepted that this is an evidence-based approach; the significance of the level of pain reduction compared to the placebo/control group was questioned.

There is the need to further develop the scientific understanding of the mechanisms underlying laser-induced analgesia which has been found clinically useful in restorative dentistry as well as in a variety of unrelated pain studies. The orthodontic modulation of pain by laser is clearly an emerging area which shows some promise, and perhaps as the evidence base further matures, this may in time turn into a useful management approach for a highly significant clinical problem.

12.2.3 Acceleration of Orthodontic Tooth Movement

Many methods to accelerate tooth movement have been attempted, including surgical corticotomy, pulsed electromagnetic fields, ultrasound, electrical stimulation and the use of a variety of drug injections. For example, increased rates of OTM have been reported following the administration by

Table 12.2 Summary of data from recent clinical studies on acute pain [146–158]

Study	Subjects	Study design (laser/placebo/control)	Pain measure	Wavelength	Power	Time	Frequency	Result
Lim [146] (1995)	39/39	Double-blind placebo RCT (split mouth)	VAS	830 nm GaAsAl	30 mW	15 s–5 min	1/d 5d	Null
Harazaki [147] (1997)	20/20/44	Single-blind RCT	NRS (1–5)	632.8 nm He-Ne	6 mW	30 s–24 min	1	↓Onset
Harazaki [148] (1998)	20/20	Single-blind CCT	NRS (1–5)	632.8 He-Ne	6 mW	30 s–5 min	1	Pain 48.4%↓
Fujiyama [149] (2008)	60/60/30	Single-blind CCT (split mouth)	VAS	10,600 CO2	2000 mW	30s–1 min	One	Pain 40%↓
Tortamano [150] (2009)	20/20/20	Double-blind RCT	NRS (1–5)	830 nm GaAsAl	30 mW	16 s–37min	One	↑Resolution
Doshi-Mehta [151] (2012)	20/20	Single-blind RCT	VAS	800 nm AlGaAs	0.7 mW	30 s–∞	Day 0/3/7/14	↓25% d3 ↓38% d30
Kim [152] (2012)	28/30/30	Single-blind RCT	VAS	635 nm AlGaInP	6 mW	30 s–28 min	2×/d 1wk	↓45% av
Artés-Ribas [153] (2012)	20/20	Single-blind RCT (split mouth)	VAS	830 nm GaAlAs	100 mW	20–300 s	One	↓45%
Domínguez [154] (2013)	60/60	Single-blind RCT (split mouth)	VAS	830 nm GaAlAs	100 mW	22–44 s	One	↓52%
Eslamían [155] (2013)	37/37	Single-blind RCT (split mouth)	VAS	810 nm AlGaAs	100 mW	20–300 s	Two	↓VAS d3 ↓22%
Nóbrega [156] (2013)	30/30	Double-blind RCT	VAS	830 nm AlGaAs	40.6 mW	25–125 s	One	↓88%
Abtahi [157] (2013)	29/29	Single-blind RCT (split mouth)	VAS	904 nm GaAs	200 mW	7.5–30 s	1×/d, 5d	↓40%
Heravi [158] (2014)	20/20	Single-blind CCT (split mouth)	???	810 nm GaAlAs	200 mW	30–240 s	Day: 4/7/11/15/28 32/35/39/43/56	Null

Adapted from Sonesson et al. [110]
The majority of studies demonstrated a reduction in pain following orthodontic procedural visits

local injection of biomodulators such as prostaglandins, vitamin D, corticosteroids, osteocalcin or parathyroid hormone. However, these agents are rapidly flushed from the tissues, and daily injections are required for the delivery of some of the pharmacological agents, such as corticosteroids. Although these methods may confer advantages in shortening treatment time, they also have some drawbacks as they may call for the use of specialist apparatus. The application of chemicals can have negative effects on bone metabolism or contribute to root resorption, and surgery in the form of corticotomy can be an unpleasant experience for the patient. Surgical approaches are by nature invasive requiring some

surgical skill, or the administration of frequent painful injections may be required with drug injections which may reduce patient acceptance.

By contrast, phototherapy is not associated with any negative side effects. Other than the need for good optical protection whilst applying intense light sources, there are no common complications or safety concerns in relation to phototherapy. Indeed, should in future the technique become an evidence-based standard, there is the possibility of supplying the patient with an appropriate home therapy appliance which, if proven effective, could significantly reduce the burden on resources and improve patient compliance [117, 122, 132–136].

Orthodontic treatment consists of directed tooth movement and an associated cycle of bone apposition and resorption. Forces applied to teeth produce areas of compression and tensile pressure in the periodontal apparatus, which results in a change in osteoblast and osteoclast activity. An extended duration of orthodontic treatment is associated with an increased risk of root resorption, periodontal disease and caries [122, 161].

On the application of an orthodontic force, a rapid acute inflammatory tissue response is elicited. The subsequent application of phototherapy apparently optimises the cellular response permitting an increase in bone metabolism. It is recognised, however, that higher doses of phototherapy can have an inhibitory effect on cellular metabolism. However this will not result in tissue damage, providing the applied energy is kept below the level required to significantly heat the tissues to the point of protein degradation [114, 162].

As OTM requires the trigger to bone remodelling of acute inflammation, it would appear counterproductive to apply lasers which have been found to have selective anti-inflammatory properties. Cytokines associated with the acute inflammatory response such as TNF-α, IL-1 and IL-6 are known to be downregulated by red to near-infrared phototherapy. Also, PGE2 is selectively downregulated along with NFKB, and there is evidence of the selective apoptosis of pro-inflammatory cells. However, there are many animal studies demonstrating an increase in bone resorption and apposition associated with the application of laser or LED phototherapy. It is known that cellular physiology is significantly affected by phototherapy, and depending on dose, a variety of effects can be seen. For example, there is a change in the redox status of the cells such that there is a strong increase in the manufacture of ATP by mitochondria. In addition, there is the release and increased production of nitric oxide which is a potent vasodilator. There is a small but significant increase in the production of reactive oxygen species (ROS) which are recognised as being a potent trigger for mitosis at low levels, whereas at higher levels ROS can be associated with the activation of the heat stress protein (HSP) cascade which can slow cellular metabolism. At even higher levels, ROS can trigger cellular toxicity and apoptosis [162–165].

Downstream effects of phototherapy include signs of increased cellular activity such as increased motility, migration, differentiation and phagocytosis plus there is a considerable increase in the rate of cell division (mitosis). Studies in bone metabolism have found a sustained increase post irradiation in alkaline phosphatase, which is a key enzyme involved in bone deposition as well as an increase in platelet-derived growth factor (PDGF) [166, 167].

Studies conducted in animal models using rats, dogs and rabbits have shown promise that laser and LED phototherapy can improve OTM. Measures applied in the animal studies have included histology assessing bone density and volume, the proliferation of osteoclasts and osteoblasts, the number of capillaries and changes in the number of inflammatory cells. By using monoclonal antibodies, there have been immunohistochemical measures for important cytokines involved in bone remodelling, such as osteoprotegerin (OPG) and the receptor activator of nuclear factor kappa-B ligand (RANKL). Animal studies have used metrics on movement of the adult first molar in rats and dogs, although perhaps controversially a few of the studies used movement of the rat incisor as the experimental model. There are studies looking at the effects on the mid-maxillary suture in rapid maxillary expansion augmented with laser or LED phototherapy. Animal studies showed that the application of lasers in the wavelengths of 650–940 nm increased the rate of tooth movement 2–3x compared to control groups. In addition, this outcome was supported by histological evidence of increased cellular activity and significant signs of an increase in bone remodelling compared to control [168–176].

In a recent animal study by Suzuki et al. [177], laser phototherapy was found to increase the number of osteoclasts present on the pressure side, whilst there was a corresponding increase in the number of osteoblasts on the tension side. Aside from the histomorphometric analysis, this interesting study applied an immunohistochemistry analysis of RANKL/OPG and tartrate-resistant acid phosphatase (TRAP) activity. This further correlated the histological findings of increased osteoclast activity in the test group on the pressure side (elevated levels of RANKL and TRAP) and increased bone apposition and osteoblast activity on the tension side (an increase in OPG). Furthermore, the rate of OTM was found to be increased by around 40% compared to the control.

Animal studies represent a substantial body of evidence-based research [111]; however, there is no agreement on laser or LED wavelength, duration of treatment, frequency of treatment, energy density applied or total dose (fluence). Faced with a heterogeneous set of experimental studies based on a variety of animal models ranging from rats, to dogs, to rabbits, it is not possible to extrapolate the results to human subjects. The animal studies are, however, highly supportive of a possible future role for photobiomodulation as an effective tool in accelerated bone metabolism in relation to OTM.

12.2.4 Clinical Trials

In respect of clinical trials, there are published anecdotal case reports, case series, pilot studies and at present a relatively few well-constructed randomised controlled trials.

The table below (Table 12.3) summarises the clinical trials that have been included amongst the many recent reviews and systematic reviews on phototherapy and OTM.

As can be seen from the table of clinical studies [151, 158, 178–182], there is no agreement in respect of choice of wavelength, parameters or frequency of application. It is, however, apparent that in the studies with a positive outcome, there is a trend towards a dose in the range of 2–8 J/cm^2 and that frequent applications of phototherapy are required. Also studies which used high doses returned a null result (Herravi, Limpanichkul [158, 179]). The issue of standardised therapy delivery is a key problem yet to be properly overcome as effective phototherapy requires the administration of photonic energy within a narrow range. Too little energy results in a zero response as does an excessive dose, perhaps consequent to photobioinhibition, as higher doses are associated with cellular stasis rather than stimulation of cellular metabolism [162].

Conventional wisdom suggests that the therapeutic target for the beneficial effects of photobiostimulation falls in a therapeutic dose delivered at tissue level of around 2–8 J/cm^2 [183]. There are, however, many compounding factors which may affect tissue penetration, not least of which is the depth at which the target rests. Incident visible red to near-infrared wavelength photonic energy is absorbed by a variety of tissue chromophores including protein, haemoglobin and melanin. At a target depth of 5–10 mm from the surface of the tissues, the amount of light that penetrates can range from 2 to 10% depending on the wavelength chosen as well as local tissue characteristics, such as the presence of pigments or dense layers of highly keratinised epithelium. Further complicating factors that can make accurate dosimetry difficult include beam divergence (distance from the surface), beam profile (typically it is Gaussian in distribution) and spot size at the tissue surface (which may have a marked effect on energy density). As the very many laser and LED devices are not the same, it is not at present possible to make anything but highly tentative proposals on treatment and management practices [113, 114](Fig. 12.8).

Amongst the significant drawbacks to the use of laser phototherapy for accelerated OTM is that the equipment is expensive to purchase and training is required to develop the necessary clinical skills. There are also safety implications as, due to the potential for serious optical damage, appropriate eye protection is required. A further problem is that the treatment strategies adopted to date require frequent re-care attendance by patients, which has important implications for the logistics of the availability of appropriately trained personnel.

12.2.5 Current Trends

More recently, clinical studies have tested the use of LED phototherapy as an alternative to lasers to modulate the rate of OTM [184–187]. LED devices are relatively inexpensive compared to laser equipment. In addition, the output power and the absence of optical coherence which is inherent to lasers reduce the potential optical hazards. Finally, in a departure from previous surgery-based equipment, devices have become available which are intended for self-administration at home. This has important advantages over office-based systems, as it can reasonably be anticipated to improve patient access to treatment. Potentially this may have an impact on compliance whilst reducing the need for repeated visits to the operatory over a period of many months. The use of a handheld laser by a skilled operator is time-consuming and requires frequent applications.

The first of this type of appliance was a transdermal device which used a near-infrared wavelength of 850 nm. The initial reports on a retrospective cohort study by Kau, Kantarci and Shaughnessy et al. [184] assessed a treatment time of 20 or 30 min on a daily basis or a single 60 min treatment (Fig. 12.9), once a week by the patients at home. The surface of the cheek was irradiated at a power density of 60 mW/cm^2, and the 73 test subjects were compared to a control group treated by another centre without the intervention. Tooth movement was assessed by Little's Irregularity Index (LII) which is a quantitative measure of five contact points. The technique involves measurement directly from the mandibular cast with a calliper (calibrated to at least tenths of a millimetre), held parallel to the occlusal plane. The linear displacement of the adjacent anatomic contact points of the mandibular incisors is determined, the sum of the five measurements representing the Irregularity Index value of the case. Assessments were conducted at baseline, then every 2 weeks for a 6-week period and then every 4 weeks until alignment was achieved. The average results appeared to demonstrate that the mean rate of change in LII was 0.49 and 1.12 mm/week for the control and test groups implying an increase in the rate of OTM by two- to threefold. There are, however, issues related to the design of this groundbreaking study, as the intervention was not a randomised controlled or blinded trial. In addition, different operators were involved in placing the fixed appliances which may have used different bracket systems. The test group is noted by the authors to have at the outset a higher LII, and the authors acknowledge that there was the need for a larger and longer clinical trial to assess the long-term stability of the outcome. The study was sponsored by the manufacturer of the appliance, and this study can at best be viewed indicative of the need for further independent and better designed studies.

The same appliance was subsequently subject to an independent hospital-based controlled clinical trial by Chung et al. [185]. This was a split-mouth randomised controlled

Table 12.3 Summary of clinical trials included in recent systematic reviews

No	First author (publication year)	*N*	Laser					Application			Result velocity
			Laser type	Wave-length	Power, time	Dose (J/cm [2])	Total energy (j)	Irradiation interval	Applied tooth	Force (g)	
70	Cruz [178] (2004)	11	Diode laser	780 nm	20 mW, 10 s 0.04 cm^2	5/point 50/ session	0.2/point 2.0/session	4 days of each month	Canine	150	Increase 34% (2 months)
71	Limpanichkul [179] (2006)	12	Diode laser	860 nm	100 mW, 23 s 0.09 cm^2	25/point 200/ session	2.3/point 18.4/ session	First 3 days of each month	Canine	150	No effect (3 months)
72	Youssef [180] (2008)	15	Diode laser	809 nm	100 mW, 10/20/10s	No information	8.0/session	0,3,7, 14 days	Canine	150	2 × Increase (6 months)
73	Sousa [181] (2011)	13	Diode laser	780 nm	20 mW, 10s 0.04 cm^2	5/point 50/ session	0.2/point 2.0/session	0,3,7 days of each month	Canine	150	2 × Increase (4 months)
74	Genc [182] (2013)	20	Diode laser	808 nm	20 mW, 10s 0.28 cm^2	0.71/ point 7.1/ session	0.2/point 2.0/session	0,3,7,14, 21,28 days	Upper lateral incisors	80	20–40% increase (1 month)
44	Doshi-Mehta [151] (2012)	20	Diode laser	800 nm	0.25 mW, 10s 0.04 cm^2	8 J 10/ session	2.5 mJ/ point 8.0 J/ session	0,3,7,14, 29,44 days	Canine	150	Increase 30%
51	Herravi [158] (2014)	20	Diode laser	810 nm	200 mW, 30s 0.28 cm^2	21.4 J 10/ session	6 J/point 60 J	0,4,7,11, 15,28, 32, 35,39,43, 56 days	Canine	150	No effect

Adapted from Kim et al. [110]
High-dose regimes were not beneficial, whereas low doses of 2–8 J/cm [2] increased movement by 20–40%

clinical trial, which assessed closure of single tooth extraction sites. LED phototherapy was applied to one side for 21 min/day, and the LED array was inactive on the contralateral side which acted as the control. The output power was set by the manufacturer at 150 mW/cm^2 (from private correspondence to the authors) resulting in a sum total of 189 J/cm^2 delivered daily. Measurements from casts were taken by two independent and blinded assessors on a sum total of 17 dental arches from 11 orthodontic participants – all of whom required bilateral symmetrical extraction of premolars. Three measurements were taken at the outset (T0), at 3–7 weeks after the initiation of space closure (T1) and again at a further 3–7 weeks (T3) after T1. Compliance of home use was measured by the device as well as a record maintained by the participants. The results were that there was no discernible difference in outcome between the test and control sites. It is worthy of note that the rate of compliance by the subjects was reported at around 80% over the study period. This well designed and conducted study followed the CONSORT statement guidelines, and there were no declared conflicts of interest. The authors recognise that there was the potential for photo leakage to the contralateral side. In private correspondence, the authors stated that they sought in their analysis to detect any indication of either stimulation in either or both the control and test sites. However, both sites were found to be the same and also that the outcome was comparable to patients treated with conventional fixed appliance therapy.

The transdermal LED appliance required high output power, to compensate for the high absorption and scatter of the incoming photonic energy. It is debatable whether a meaningful dose can be reliably delivered at depth to

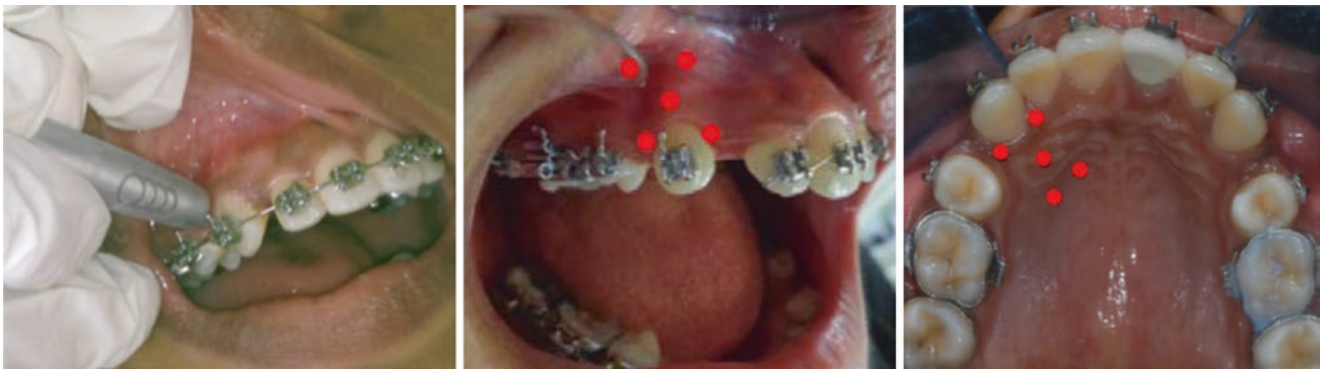

Fig. 12.8 Images illustrating points of application using in this case a 940 nm diode laser in contact with the mucosa at 5 points buccal and palatal to the canine undergoing retraction (Courtesy of Dr Premila Suganthan)

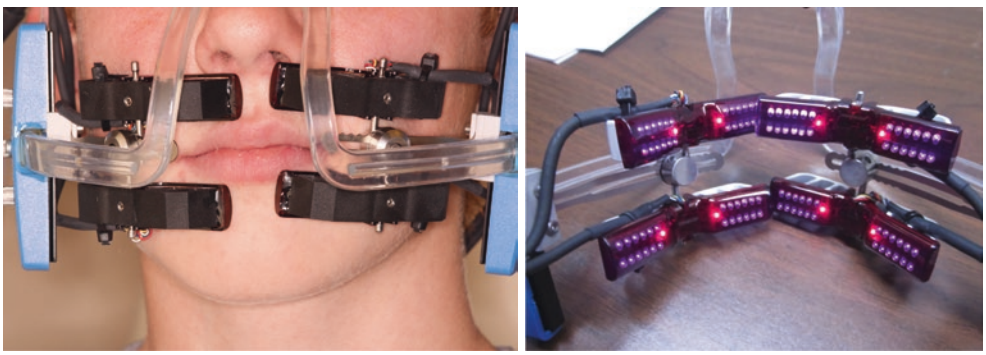

Fig. 12.9 An initial model of the LED extra-oral transmucosal phototherapy appliance for patient home use. Reproduced with permission from Biolux Research Ltd.

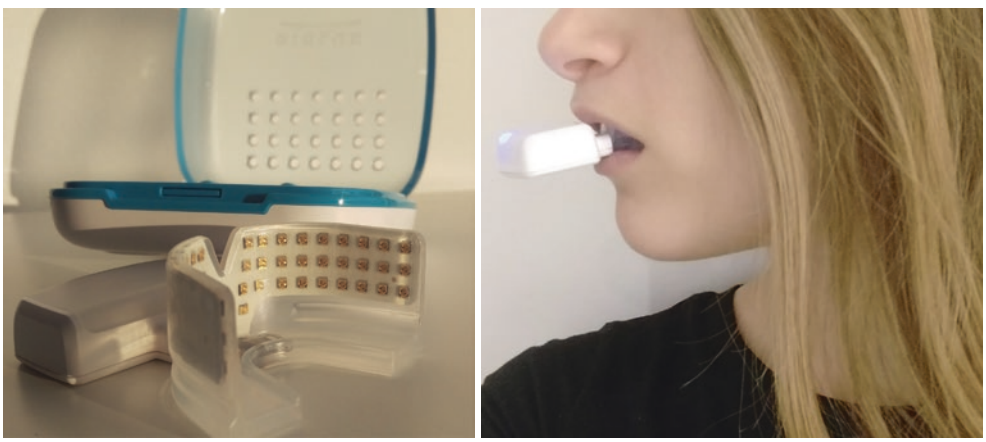

Fig. 12.10 The latest version of the patient home-use LED phototherapy device uses an intra-oral tray lined with arrays of 850 nm LEDs. This appliance is intended for daily home use, and it meters frequency and duration of use. Images reproduced by permission of Biolux Research Ltd.

the target tissues, as the administered light had to cross three layers of highly keratinised epithelium to reach the target tissues. Anatomical variations in cheek thickness between individuals and issues, such as superficial skin pigmentation, effectively prohibit a reliable and reproducible protocol.

In a recent pilot clinical trial conducted by Shaughnessy, Kantarci and Kau et al. [112], a further design of LED home-use appliance was tested (Fig. 12.10). This time, the device was placed intra-orally, and the 850 nm LED arrays are built into an intra-oral applicator tray with a declared output power density of 42 mW/cm^2, used for 3.8 min/day for each arch treated. Nineteen patients were conscripted into the study with the first eight patients being enrolled as the control group of ten arches (three upper and seven lower). The next 11 patients were the test group who provided a total of 18 test arches (ten upper and three lower arches). As in the previous study, the unit of measurement was Little's Irregularity Index, and measurements were taken from casts by a blinded technician. Measures were taken from casts at

the outset (T0) and at a second point at which by visual assessment supported by photographs, LII was estimated to have reached ≤1 mm. The outcome reported was that the average period to achieve alignment was 48 and 104 days for the test and control groups.

The authors recognise some limitations to the study as there was no sham device used. The sample size was small, and there were some inconsistencies in the type of bracket applied. Again, this was a company-sponsored study, and it is noteworthy that the control group had a preponderance of lower arches compared to the test group. In addition, as recognised by Chung et al., there can be differences in parallel-type studies between participants; there can be variation in jaw and tooth positions and growth patterns between individuals, which can make comparisons between test and control unreliable especially in small study group sizes. Shaughnessy et al. conclude that overall treatment time in the test groups was significantly reduced, although the authors recognise the need for a larger randomised sham-control clinical trial to further assess the effects of daily patient-administered intra-oral phototherapy.

Most recently, Shaughnessy et al. [186] have published anecdotal clinical reports appearing to support the value of LED intra-oral phototherapy. There is a remarkable case report from Ojima et al. which describes a patient treated with the LED intra-oral appliance, Invisalign clear aligners for upper and lower anterior crowding, an anterior open bite and a lateral incisor crossbite with a v-shaped maxillary arch. Usually a patient would require a new pair of upper and lower aligners once every 2 weeks over a period forecast, in this case to be 21 months. The device was used by the patient for 5 min for each arch daily. Ojima et al. [187] report that following the adjunctive daily use of the LED intra-oral device, the aligners were changed every 3 days and that the whole course of treatment was completed in 6 months.

However, clinical reports and poorly controlled non-randomised case series, in the absence of adequate blinding, are at the lowest level of evidence base and can at best only be viewed as indicative of the need for further well-designed assessments by controlled randomised clinical trials. It can only be concluded that there is at present no adequate scientific base to support the integration of this highly innovative technique of patient self-administered therapy.

Conclusion

Based on in vitro, in vivo animal studies and a limited scientific clinical evidence base, the prospects for the use of clinical phototherapy in orthodontic case management look promising. However, there is much that is still not known about the dosimetry of phototherapy and the consistent delivery of photonic energy to the correct target tissue depth. Significant efforts are needed to standardise the clinical dosing and delivery protocols of phototherapy, to ensure the maximal efficacy to achieve analgesia and manipulate the cellular and molecular processes associated with bone remodelling. In addition, as in many other areas of clinical practice, more high-quality research is required, prior to general acceptance of this method as an evidence-based approach.

References

1. Zucchelli G, Mounssif I. Periodontal plastic surgery. Periodontol 2000. 2015;68(1):333–68.
2. Aoki A, Mizutani K, Schwarz F, et al. Periodontal and peri-implant wound healing following laser therapy. Periodontol 2000. 2015;68:217–69.
3. Pang P, Andreana S, Aoki A, Coluzzi D, Obeidi A, Olivi G, Parker S, Rechmann P, Sulewski J, Sweeney C, Swick M, Yung F. Laser energy in oral soft tissue applications. J Laser Dent. 2010;18:123–31.
4. Aoki A, Sasaki K, Watanabe H, Ishikawa I. Lasers in non-surgical periodontal therapy. Periodontol 2000. 2004;36:59–97.
5. Takei HH, Carranza FA. Gingival surgical techniques. In: Newman MG, Takei HH, Klokkevold PR, Carranza FA, editors. Carranza's clinical periodontology. 10th ed. St. Louis: Elsevier; 2006. p. 915.
6. 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.
7. Sarver DM, Yanosky M. Principles of cosmetic dentistry in orthodontics: part 2. Soft tissue laser technology and cosmetic gingival contouring. Am J Orthod Dentofacial Orthop. 2005;127:85–90.
8. Aoki A, Takasaki A, Pourzarandian A, Mizutani K, Ruwanpura S, Iwasaki K, Noguchi K, Oda S, Watanabe H, Ishikawa I, Izumi Y. Photo-bio-modulation laser strategies in periodontal therapy. Proceedings of light-activated tissue regeneration and therapy II, New York Springer 2008:181–90.
9. Izumi Y, Aoki A, Yamada Y, Kobayashi H, Iwata T, Akizuki T, Suda T, Nakamura S, Wara-Aswapati N, Ueda M, Ishikawa I. Current and future periodontal tissue engineering. Periodontol 2000. 2011;56:166–87.
10. Avci P, Gupta A, Sadasivam M, et al. Low-level laser (light) therapy (LLLT) in skin: stimulating, healing, restoring. Semin Cutan Med Surg. 2013;32:41–52.
11. Khan I, Arany P. Biophysical approaches for oral wound healing: emphasis on photobiomodulation. Adv Wound Care (New Rochelle). 2015;4:724–37.
12. Tunér J, Beck-Kristensen PH, Ross G, Ross A. Photobiomodulation in dentistry. In: Convissar RA, editor. Principles and practice of laser dentistry. 2nd ed. St. Louis: Elsevier; 2016. p. 251–74.
13. AlGhamdi KM, Kumar A, Moussa NA. Low-level laser therapy: a useful technique for enhancing the proliferation of various cultured cells. Lasers Med Sci. 2012;27:237–49.
14. Mester E, Spiry T, Szende B, Tota JG. Effect of laser rays on wound healing. Am J Surg. 1971;122:532–5.
15. Enwemeka CS, Parker JC, Dowdy DS, Harkness EE, Sanford LE, Woodruff LD. The efficacy of low-power lasers in tissue repair and pain control: a meta-analysis study. Photomed Laser Surg. 2004;22:323–9.
16. Woodruff LD, Bounkeo JM, Brannon WM, Dawes KS, Barham CD, Waddell DL, Enwemeka CS. The efficacy of laser therapy in wound repair: a meta-analysis of the literature. Photomed Laser Surg. 2004;22:241–7.
17. Albertini R, Villaverde AB, Aimbire F, Salgado MA, Bjordal JM, Alves LP, Munin E, Costa MS. Anti-inflammatory effects of low-level laser therapy (LLLT) with two different red wavelengths (660 nm and 684 nm) in carrageenan-induced rat paw edema. J Photochem Photobiol B. 2007;89:50–5.
18. Bjordal JM, Johnson MI, Iversen V, Aimbire F, Lopes-Martins RA. Low-level laser therapy in acute pain: a systematic review of possible

mechanisms of action and clinical effects in randomized placebo-controlled trials. Photomed Laser Surg. 2006;24:158–68.
19. Isman E, Aras MH, Cengiz B, Bayraktar R, Yolcu U, Topcuoglu T, Usumez A, Demir T. Effects of laser irradiation at different wavelengths (660, 810, 980, and 1064 nm) on transient receptor potential melastatin channels in an animal model of wound healing. Lasers Med Sci. 2015;30:1489–95.
20. Ogita M, Tsuchida S, Aoki A, Satoh M, Kado S, Sawabe M, Nanbara H, Kobayashi H, Takeuchi Y, Mizutani K, Sasaki Y, Nomura F, Izumi Y. 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.
21. Dias SB, Fonseca MV, Dos Santos NC, Mathias IF, Martinho FC, Junior MS, Jardini MA, Santamaria MP. Effect of GaAlAs low-level laser therapy on the healing of human palate mucosa after connective tissue graft harvesting: randomized clinical trial. Lasers Med Sci. 2015;30:1695–702.
22. de Melo Rambo CS, Silva JA Jr, Serra AJ, Ligeiro AP, de Paula VR, Albertini R, Leal-Junior EC, de Tarso Camillo de Carvalho P. Comparative analysis of low-level laser therapy (660 nm) on inflammatory biomarker expression during the skin wound-repair process in young and aged rats. Lasers Med Sci. 2014;29:1723–33.
23. Liao X, Xie GH, Liu HW, Cheng B, Li SH, Xie S, Xiao LL, Fu XB. Helium-neon laser irradiation promotes the proliferation and migration of human epidermal stem cells in vitro: proposed mechanism for enhanced wound re-epithelialization. Photomed Laser Surg. 2014;32:219–25.
24. Fujimura T, Mitani A, Fukuda M, Mogi M, Osawa K, Takahashi S, Aino M, Iwamura Y, Miyajima S, Yamamoto H, Noguchi T. Irradiation with a low-level diode laser induces the developmental endothelial locus-1 gene and reduces proinflammatory cytokines in epithelial cells. Lasers Med Sci. 2014;29:987–94.
25. Batista JD, Sargenti-Neto S, Dechichi P, Rocha FS, Pagnoncelli RM. Low-level laser therapy on bone repair: is there any effect outside the irradiated field? Lasers Med Sci. 2015;30:1569–74.
26. Pinheiro AL, Aciole GT, Ramos TA, Gonzalez TA, da Silva LN, Soares LG, Aciole JM, dos Santos JN. The efficacy of the use of IR laser phototherapy associated to biphasic ceramic graft and guided bone regeneration on surgical fractures treated with miniplates: a histological and histomorphometric study on rabbits. Lasers Med Sci. 2014;29:279–88.
27. de Vasconcellos LM, Barbara MA, Deco CP, Junqueira JC, do Prado RF, Anbinder AL, de Vasconcellos LG, Cairo CA, Carvalho YR. Healing of normal and osteopenic bone with titanium implant and low-level laser therapy (GaAlAs): a histomorphometric study in rats. Lasers Med Sci. 2014;29:575–80.
28. Tim CR, Pinto KN, Rossi BR, Fernandes K, Matsumoto MA, Parizotto NA, Rennó AC. Low-level laser therapy enhances the expression of osteogenic factors during bone repair in rats. Lasers Med Sci. 2014;29:147–56.
29. Pagin MT, de Oliveira FA, Oliveira RC, Sant'Ana AC, de Rezende ML, Greghi SL, Damante CA. Laser and light-emitting diode effects on pre-osteoblast growth and differentiation. Lasers Med Sci. 2014;29:55–9.
30. Peccin MS, de Oliveira F, Muniz Renno AC, Pacheco de Jesus GP, Pozzi R, Gomes de Moura CF, Giusti PR, Ribeiro DA. Helium-neon laser improves bone repair in rabbits: comparison at two anatomic sites. Lasers Med Sci. 2013;28:1125–30.
31. Boldrini C, de Almeida JM, Fernandes LA, Ribeiro FS, Garcia VG, Theodoro LH, Pontes AE. Biomechanical effect of one session of low-level laser on the bone-titanium implant interface. Lasers Med Sci. 2013;28:349–52.
32. Pinheiro AL, Soares LG, Barbosa AF, Ramalho LM, dos Santos JN. Does LED phototherapy influence the repair of bone defects grafted with MTA, bone morphogenetic proteins, and guided bone regeneration? A description of the repair process on rodents. Lasers Med Sci. 2012;27:1013–24.
33. Rosa AP, de Sousa LG, Regalo SC, Issa JP, Barbosa AP, Pitol DL, de Oliveira RH, de Vasconcelos PB, Dias FJ, Chimello DT, Siéssere S. Effects of the combination of low-level laser irradiation and recombinant human bone morphogenetic protein-2 in bone repair. Lasers Med Sci. 2012;27:971–7.
34. Anders JJ, Moges H, Wu X, Erbele ID, Alberico SL, Saidu EK, Smith JT, Pryor BA. In vitro and in vivo optimization of infrared laser treatment for injured peripheral nerves. Lasers Surg Med. 2014;46:34–45.
35. Takhtfooladi MA, Jahanbakhsh F, Takhtfooladi HA, Yousefi K, Allahverdi A. Effect of low-level laser therapy (685 nm, 3 J/cm(2)) on functional recovery of the sciatic nerve in rats following crushing lesion. Lasers Med Sci. 2015;30:1047–52.
36. Masoumipoor M, Jameie SB, Janzadeh A, Nasirinezhad F, Soleimani M, Kerdary M. Effects of 660- and 980-nm low-level laser therapy on neuropathic pain relief following chronic constriction injury in rat sciatic nerve. Lasers Med Sci. 2014;29:1593–8.
37. Gasperini G, de Siqueira IC, Costa LR. Lower-level laser therapy improves neurosensory disorders resulting from bilateral mandibular sagittal split osteotomy: a randomized crossover clinical trial. J Craniomaxillofac Surg. 2014;42:e130–3.
38. Akgul T, Gulsoy M, Gulcur HO. Effects of early and delayed laser application on nerve regeneration. Lasers Med Sci. 2014;29:351–7.
39. Lazovic M, Ilic-Stojanovic O, Kocic M, Zivkovic V, Hrkovic M, Radosavljevic N. Placebo-controlled investigation of low-level laser therapy to treat carpal tunnel syndrome. Photomed Laser Surg. 2014;32:336–44.
40. de Sousa AP, Silveira NT, de Souza J, Cangussú MC, dos Santos JN, Pinheiro AL. Laser and LED phototherapies on angiogenesis. Lasers Med Sci. 2013;28:981–7.
41. Góralczyk K, Szymańska J, Łukowicz M, Drela E, Kotzbach R, Dubiel M, Michalska M, Góralczyk B, Zając A, Rość D. Effect of LLLT on endothelial cells culture. Lasers Med Sci. 2015;30:273–8.
42. Esmaeelinejad M, Bayat M, Darbandi H, Bayat M, Mosaffa N. The effects of low-level laser irradiation on cellular viability and proliferation of human skin fibroblasts cultured in high glucose mediums. Lasers Med Sci. 2014;29:121–9.
43. Pellicioli AC, Martins MD, Dillenburg CS, Marques MM, Squarize CH, Castilho RM. Laser phototherapy accelerates oral keratinocyte migration through the modulation of the mammalian target of rapamycin signaling pathway. J Biomed Opt. 2014;19:028002.
44. Basso FG, Oliveira CF, Kurachi C, Hebling J, Costa CA. Biostimulatory effect of low-level laser therapy on keratinocytes in vitro. Lasers Med Sci. 2013;28:367–74.
45. Fujihara NA, Hiraki KR, Marques MM. Irradiation at 780 nm increases proliferation rate of osteoblasts independently of dexamethasone presence. Lasers Surg Med. 2006;38:332–6.
46. Gonçalves RV, Novaes RD, Matta SLP, Benevides GP, Faria FR, Pinto MVM. Comparative study of the effects of gallium-aluminum-arsenide laser photobiomodulation and healing oil on skin wounds in Wistar rats: a histomorphometric study. Photomed Laser Surg. 2010;28:597–602.
47. Xavier M, David DR, Souza RA, et al. Anti-inflammatory effects of low-level light emitting diode therapy on achilles tendinitis in rats. Lasers Surg Med. 2010;42:553–8.
48. Novaes RD, Gonçalves RV, Cupertino MC, et al. The energy density of laser light differentially modulates the skin morphological reorganization in a murine model of healing by secondary intention. Int J Exp Pathol. 2014;95:138–46.
49. Posten W, Wrone DA, Dover JS, Silapunt S, Alam M. Low-level laser therapy for wound healing: mechanism and efficacy. Dermatol Surg. 2005;31:334–40.
50. Houreld NN, Sekhejane PR, Abrahamse H. Irradiation at 830 nm stimulates nitric oxide production and inhibits pro-inflammatory cytokines in diabetic wounded fibroblast cells. Lasers Surg Med. 2010;42:494–502.

51. Pogrel MA, Chen JW, Zhang K. Effects of low-energy gallium-aluminum-arsenide laser irradiation on cultured fibroblasts and keratinocytes. Lasers Surg Med. 1997;20:426–32.
52. Martignago CC, Oliveira RF, Pires-Oliveira DA, Oliveira PD, Pacheco Soares C, Monzani PS, Poli-Frederico RC. Effect of low-level laser therapy on the gene expression of collagen and vascular endothelial growth factor in a culture of fibroblast cells in mice. Lasers Med Sci. 2015;30:203–8.
53. Gonçalves RV, Mezêncio JMS, Benevides GP, et al. Effect of gallium-arsenide laser, gallium-aluminum-arsenide laser and healing ointment on cutaneous wound healing in Wistar rats. Braz J Med Biol Res. 2010;43:350–5.
54. Kang Y, Rabie AB, Wong RW. A review of laser applications in orthodontics. Int J Orthod Milwaukee. 2014;25:47–56.
55. Chmura LG, Convissar RA. Lasers in orthodontics. In: Convissar RA, editor. Principles and practice of laser dentistry. 2nd ed. St. Louis: Elsevier; 2016. p. 203–19.
56. Mizutani K, Aoki A, Coluzzi D, Yukna R, Wang CY, Pavlic V, Izumi Y. Lasers in minimally invasive periodontal and peri-implant therapy. Periodontol 2000. 2016;71:185–212.
57. Migliorati EKJ, de Almeida Rosa DS. Regenerative laser periodontal therapy. In: Convissar RA, editor. Principles and practice of laser dentistry. 2nd ed. St. Louis: Elsevier; 2016. p. 67–88.
58. Ishikawa I, Aoki A, Takasaki AA, Mizutani K, Sasaki KM, Izumi Y. Application of lasers in periodontics: true innovation or myth? Periodontol 2000. 2009;50:90–126.
59. Pang P, Andreana S, Aoki A, Coluzzi D, Obeidi A, Olivi G, Parker S, Rechmann P, Sulewski J, Sweeney C, Swick M, Yung F. Laser energy in oral soft tissue applications. J Laser Dent. 2011;18:123–31.
60. Merigo E, Clini F, Fornaini C, Oppici A, Paties C, Zangrandi A, Fontana M, Rocca JP, Meleti M, Manfredi M, Cella L, Vescovi P. Laser-assisted surgery with different wavelengths: a preliminary ex vivo study on thermal increase and histological evaluation. Lasers Med Sci. 2013;28:497–504.
61. Goharkhay K, Moritz A, Wilder-Smith P, Schoop U, Kluger W, Jakolitsch S, Sperr W. Effects on oral soft tissue produced by a diode laser in vitro. Lasers Surg Med. 1999;25:401–6.
62. Jin JY, Lee SH, Yoon HJ. A comparative study of wound healing following incision with a scalpel, diode laser or Er,Cr:YSGG laser in guinea pig oral mucosa: a histological and immunohistochemical analysis. Acta Odontol Scand. 2010;68:232–8.
63. Hall RN, Fenner GE, Kingsley JD, Soltys TJ, Carlson RO. Coherent light emission from GaAs junctions. Physical Review Letters. 1962;9(9): 366–368.
64. Nathan MI, Dumke WP, Burns G, Dill FH, Lasher G. Stimulated emission of radiation from GaAs pn junctions. Applied Physics Letters. 1962;1(3):62–64.
65. Nasim H, Jamil Y. Diode lasers: From laboratory to industry. Optics & Laser Technology. 2014;56:211–222.
66. Fornaini C, Merigo E, Rocca JP, Lagori G, Raybaud H, Selleri S, Cucinotta A.450 nm Blue Laser and Oral Surgery: Preliminary ex vivo Study. J Contemp Dent Pract. 2016;17(10):795–800.
67. Braun A, Berthold M, Frankenberger R. The 445-nm semiconductor laser in dentistry – introduction of a new wavelength. Quintessenz 2015;66(2):205–211.
68. Arroyo HH, Neri L, Fussuma CY, Imamura R. Diode laser for laryngeal surgery: a systematic review. Int Arch Otorhinolaryngol. 2016;20:172–9.
69. Borzabadi-Farahani A. The adjunctive soft-tissue diode laser in orthodontics. Compend Contin Educ Dent. 2017;38(eBook 5):e18–e31.
70. Kravitz ND. The application of lasers in orthodontics. In: Krishnan V, Davidovitch Z, editors. Integrated clinical orthodontics. 1st ed. West Sussex: Wiley; 2012. p. 422–43.
71. Colluzzi DJ. Fundamentals of dental lasers: Science and instruments. Dent Clin N Am. 2004;48:751–70.
72. Borchers R. Comparison of diode lasers in soft-tissue surgery using CW-and superpulsed mode: an in vivo study. Int J Laser Dent. 2001;1:17–27.
73. Al-Khatib AA, Al-Azzawi AS. Comparative study of diode laser 940 nm in performing frenectomy in both: Continuous and pulsed modes: An in vivo study. J Dent Lasers. 2015;9:50–68.
74. Prabhu M, Ramesh A, Thomas B. Treatment of orthodontically induced gingival hyperplasia by diode laser – case report. Nitte Univ J Health Sci. 2015;5:66–8.
75. Kravitz ND, Graham JW, Nicozisis JL, Gill J. Compunded topical anesthetics in orthodontics. J Clin Orthod. 2015;49:371–7.
76. To TN, Rabie AB, Wong RW, McGrath CP. The adjunct effectiveness of diode laser gingivectomy in maintaining periodontal health during orthodontic treatment. Angle Orthod. 2013;83:43–7.
77. Hempton TJ, Dominici JT. Contemporary crown-lengthening therapy: a review. J Am Dent Assoc. 2010;141:647–55.
78. van Gastel J, Quirynen M, Teughels W, Coucke W, Carels C. Longitudinal changes in microbiology and clinical periodontal variables after placement of fixed orthodontic appliances. J Periodontol. 2008;79(11):2078–86.
79. Yáñez-Vico RM, Iglesias-Linares A, Ballesta-Mudarra S, Ortiz-Ariza E, Solano-Reina E, Perea EJ. Short-term effect of removal of fixed orthodontic appliances on gingival health and subgingival microbiota: a prospective cohort study. Acta Odontol Scand. 2015;73(7): 496–502.
80. Kloehn JS, Pfeifer JS. The effect of orthodontic treatment on the periodontium. Angle Orthod. 1974;44:127–34.
81. Palomo L, Palomo JM, Bissada NF. Salient periodontal issues for the modern biologic orthodontist. Semin Orthod. 2008;14:229–45.
82. Camargo PM, Melnick PR, Pirih FQ, Lagos R, Takei HH. Treatment of drug-induced gingival enlargement: aesthetic and functional considerations. Periodontol 2000. 2001;27:131–8.
83. De Oliveira Guaré R, Costa SC, Baeder F, De Souza Merli LA, Dos Santos MT. Drug-induced gingival enlargement: biofilm control and surgical therapy with gallium–aluminum–arsenide (GaAlAs) diode laser-A 2-year follow-up. Spec Care Dentist. 2010;30:46–52.
84. Sarver DM, Yanosky M. Principles of cosmetic dentistry in orthodontics: part 3. Laser treatments for tooth eruption and soft tissue problems. Am J Orthod Dentofacial Orthop. 2005;127:262–4.
85. Lee EA. Laser-assisted gingival tissue procedures in esthetic dentistry. Pract Proced Aesthet Dent. 2006;18(suppl):2–6.
86. Ericson S, Kurol J. Radiographic assessment of maxillary canine eruption in children with clinical signs of eruption disturbance. Eur J Orthod. 1986;8:133–40.
87. Pini-Prato G, Mancini EA, Papini O, Crescini A. Mucogingival approaches in young orthodontic patients: combined strategies for success. Semin Orthod. 2014;20:150–69.
88. Wriedt S, Jaklin J, Al-Nawas B, Wehrbein H. Impacted upper canines: examination and treatment proposal based on 3D versus 2D diagnosis. J Orofac Orthop. 2011;73:28–40.
89. Hitchen AD. The impacted maxillary canine. Br Dent J. 1956;100:1–14.
90. Counihan K, Al-Awadhi EA, Butler J. Guidelines for the assessment of the impacted maxillary canine. Dent Update. 2013; 40(770–2):775–7.
91. Firestone AR, Scheurer PA, Bürgin WB. Patients' anticipation of pain and pain-related side effects, and their perception of pain as a result of orthodontic treatment with fixed appliances. Eur J Orthod. 1999;21:387–96.
92. Parkin N, Benson PE, Thind B, Shah A. Open versus closed surgical exposure of canine teeth that are displaced in the roof of the mouth. Cochrane Database Syst Rev. 2008;4:CD006966.
93. Scheurer PA, Firestone AR, Burgin WB. Perception of pain as a result of orthodontic treatment with fixed appliances. Eur J Orthod. 1996;18:349–57.
94. Bondemark L, Fredriksson K, Ilros S. Separation effect and perception of pain and discomfort from two types of orthodontic separators. World J Orthod. 2004;5:172–6.
95. Sandhu SS, Sandhu J. Effect of physical activity level on orthodontic pain perception and analgesic consumption in adolescents. Am J Orthod Dentofacial Orthop. 2015;148:618–27.

96. Sandhu SS, Sandhu J. A randomized clinical trial investigating pain associated with superelastic nickel-titanium and multistranded stainless steel archwires during the initial leveling and aligning phase of orthodontic treatment. J Orthod. 2013;40:276–85.
97. Sandhu SS, Cheema MS, Khehra HS. Comparative effectiveness of pharmacologic and nonpharmacologic interventions for orthodontic pain relief at peak pain intensity: a Bayesian network meta-analysis. Am J Orthod Dentofacial Orthop. 2016;150:13–32.
98. Shi Q, Yang S, Jia F, Xu J. Does low level laser therapy relieve the pain caused by the placement of the orthodontic separators?–A meta-analysis. Head Face Med. 2015;11:28.
99. Li FJ, Zhang JY, Zeng XT, Guo Y. Low-level laser therapy for orthodontic pain: a systematic review. Lasers Med Sci. 2015;30:1789–803.
100. Ren C, McGrath C, Yang Y. The effectiveness of low-level diode laser therapy on orthodontic pain management: a systematic review and meta-analysis. Lasers Med Sci. 2015;30:1881–93.
101. Walsh MC, Choi Y. Biology of the RANKL-RANK-OPG System in Immunity, Bone, and Beyond. Front Immunol. 2014;5:511.
102. Fujita S, Yamaguchi M, Utsunomiya T, Yamamoto H, Kasai K. Low-energy laser stimulates tooth movement velocity via expression of RANK and RANKL. Orthod Craniofac Res. 2008;11:143–55.
103. Cruz DR, Kohara EK, Ribeiro MS, Wetter NU. Effects of low-intensity laser therapy on the orthodontic movement velocity of human teeth: a preliminary study. Lasers Surg Med. 2004;35:117–20.
104. Limpanichkul W, Godfrey K, Srisuk N, Rattanayatikul C. Effects of low-level laser therapy on the rate of orthodontic tooth movement. Orthod Craniofac Res. 2006;9:38–43.
105. Youssef M, Ashkar S, Hamade E, Gutknecht N, Lampert F, Mir M. The effect of low-level laser therapy during orthodontic movement: a preliminary study. Lasers Med Sci. 2008;23:27–33.
106. Sousa MV, Scanavini MA, Sannomiya EK, Velasco LG, Angelieri F. Influence of low-level laser on the speed of orthodontic movement. Photomed Laser Surg. 2011;29:191–6.
107. Doshi-Mehta G, Bhad-Patil WA. Efficacy of low-intensity laser therapy in reducing treatment time and orthodontic pain: a clinical investigation. Am J Orthod Dentofacial Orthop. 2012;141:289–97.
108. Gkantidis N, Mistakidis I, Kouskoura T, Pandis N. Effectiveness of non-conventional methods for accelerated orthodontic tooth movement: a systematic review and meta-analysis. J Dent. 2014;42:1300–19.
109. Kalemaj Z, Debernardl CL, Buti J. Efficacy of surgical and non-surgical interventions on accelerating orthodontic tooth movement: a systematic review. Eur J Oral Implantol. 2015;8:9–24.

Photobiomodulation Concepts within Orthodontics

110. Sonesson M, et al. Efficacy of low-level laser therapy in accelerating tooth movement, preventing relapse and managing acute pain during orthodontic treatment in humans: a systematic review. BMC Oral Health. 2017;17:11. doi:10.1186/s12903-016-0242-8.
111. Torri S, Weber JBB. Influence of low level laser therapy on the rate of orthodontic tooth movement: a literature review. Photomed Laser Surg. 2013;31(9):411–21.
112. Shaughnessy T, et al. Intraoral photobiomodulation-induced orthodontic tooth alignment: a preliminary study. BMC Oral Health. 2016;16:3. doi:10.1186/s12903-015-0159-7.
113. Huang YY. The handbook of photomedicine. Boca Raton: CRC Press; 2014. ISBN 978-1-4398-8469-0
114. Hode L, Tuner J. Laser phototherapy: clinical and scientific background. Grängesberg: Prima Books; 2014. ISBN 978-91-976478-5-4
115. Andrade I, Sousa AB, da Silva GC. New therapeutic modalities to modulate orthodontic tooth movement. J Orthod. 2014;19(6):123–33.
116. Ge MK, He WL, Chen J, et al. Efficacy of low level laser therapy for accelerating tooth movement during orthodontic treatment: a systematic review. Lasers Med Sci. 2015;30(5):1609–18.
117. Kalemaj Z, Debarnardi C, Buti J. Efficacy of surgical and non-surgical interventions on accelerating orthodontic tooth movement. Eur J Oral Implantol. 2015;8(1):9–24.
118. Kim SJ, et al. Effect of low level laser therapy on the rate of tooth movement. Semin Orthod. 2015;21(3):210–8.
119. Long H, Zhou Y, Xue J, et al. The effectiveness of low-level laser therapy in accelerating orthodontic tooth movement: a meta-analysis. Lasers Med Sci. 2015;30:1161–70.
120. Li FJ, Zhang Y, Zeng XT, et al. Low level laser therapy for orthodontic pain: a systematic review. Lasers Med Sci. 2015;30(6):1789–803.
121. Ren C, McGrath C, Yang Y. The effectiveness of low level diode laser therapy on orthodontic pain management: a systematic review and meta-analysis. Lasers Med Sci. 2015;30:1881–93.
122. Long H, Pyakurel U, Wang Y, et al. Interventions for accelerating orthodontic tooth movement: a systematic review. Angle Orthod. 2013;83(1):164–71.
123. Fink DF, Smith RJ. The duration of orthodontic treatment. Am J Orthod Dentofacial Orthop. 1992;102:42–51.
124. Geiger AM, Gorelick L, Gwinnett AJ, et al. Reducing white spot lesions in orthodontic populations with fluoride rinsing. Am J Orthod Dentofacial Orthop. 1992;101:403–7.
125. Royko A, Denes Z, Razouk G. The relationship between the length of orthodontic treatment and patient compliance. Fogorz Sz. 1999;92:79–86.
126. Pandis N, Nasika M, Polychronopoulou A, et al. External root resorption in patients treated with conventional and self-ligating brackets. Am J Orthod Dentofacial Orthop. 2008;134:646–51.
127. Mizrahi E. Risk management in clinical practice Part 7. Dentolegal aspects of orthodontic practice. Br Dent J. 2010;209:381–90.
128. Polat O. Pain and discomfort after orthodontic appointments. Semin Orthod. 2007;13(4):292–300.
129. Ngan P, Kess B, Wilson S. Perception of discomfort by patients undergoing orthodontic treatment. Am J Orthod Dentofacial Orthop. 1989;96(1):47–53.
130. Zhang M, McGrath C, Hagg U. Changes in oral health related quality of life during orthodontic appliance therapy. Am J Orthod Dentofacial Orthop. 2008;133(1):25–9.
131. Yamaguchi M, Garlet G. The role of inflammation in defining the type and pattern of tissue response in orthodontic tooth movement. In: Krishna V, Davidovich Z, editors. Biological mechanisms of tooth movement. Chichester/Ames: Wiley; 2015. Ch. 9. ISBN: 978-1-118-68887-8.
132. Roth PM, Thrash WJ. Effect of transcutaneous electrical nerve stimulation for controlling pain associated with orthodontic tooth movement. Am J Orthod Dentofacial Orthop. 1986;90(2):132–8.
133. Marie SS, Powers M, Sheridan J. Vibratory stimulation as a method of reducing pain after orthodontic appliance adjustment. J Clin Orthod. 2003;37(4):205–8.
134. Mohri Y, Fumoto M, Sato-Suzuki I, et al. Prolonged rhythmic gum chewing suppresses nociceptive response via serotegenic decending inhibitory pathway in humans. Pain. 2005;118(1):35–42.
135. Polat O, Karaman AI, Durmus E. Effects of pre-operative ibuprofen and naproxen sodium on orthodontic pain. Angle Orthod. 2005;75(5):791–6.
136. Bird SE, Williams K, Kula K. Pre-operative acetaminophen vs ibuprofen for control of pain after orthodontic separator placement. Am J Orthod Dentofacial Orthop. 2007;132(4):504–10.
137. Walker JB, Buring SM. NSAID impairment of orthodontic tooth movement. Ann Pharmacother. 2001;35(1):113–5.
138. Bjordal JM, Johnson MI, Iversen V, et al. Low level laser therapy in acute pain: a systematic review of possible mechanisms of action and clinical effects in randomised placebo controlled trials. Photomed Laser Surg. 2006;24(2):158–68.
139. Bjordal JM, Couppe C, Chow RT, et al. A systematic review of low level laser therapy with location specific doses for pain from chronic joint disorders. Aus J Physiother. 2003;49:107–16.

140. Gigo-Benato D, Geuna S, Rochkind S. Phototherapy for enhancing peripheral nerve repair: a review of the literature. Muscle Nerve. 2005;31:694–701.
141. Bensadoun RJ, Nair RG. Low level laser therapy in the prevention and treatment of cancer therapy induced mucositis. Curr Opin Oncol. 2012;24:363–70.
142. Lalla J, Bowen J, et al. MASCC = ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. Cancer. 2014; doi:10.1002/cncr.28592.
143. Chow R, Armati P, Laakso EL, et al. Inhibitory effects of laser irradiation on peripheral mammalian nerves and relevance to analgesic effects: a systematic review. Photomed Laser Surg. 2011;29(6):365–81.
144. Chung H, Dai T, Sharma SK, et al. The nuts and bolts of low level laser therapy. Ann Biomed Eng. 2012;40:516–33.
145. Poli R, Parker S. Achieving dental analgesia with the erbium chromium yttrium scandium gallium garnet laser (2780 nm): a protocol for painless conservative treatment. Photomed Laser Surg. 2015;33(7):1–8.
146. Lim HM, Lew KK, Tay DK. A clinical investigation of the efficacy of low level laser therapy in reducing orthodontic postadjustment pain. Am J Orthod Dentofacial Orthop. 1995;108:614–22.
147. Harazaki M, Isshiki Y. Soft laser irradiation effects on pain reduction in orthodontic treatment. Bull Tokyo Dent Coll. 1997;38:291–5.
148. Harazaki M, Takahashi H, Ito A, Isshiki Y. Soft laser irradiation induced pain reduction in orthodontic treatment. Bull Tokyo Dent Coll. 1998;39:95–101.
149. Fujiyama K, Deguchi T, Murakami T, Fujii A, Kushima K, Takano-Yamamoto T. Clinical effect of CO2 laser in reducing pain in orthodontics. Angle Orthod. 2008;78:299–303.
150. Tortamano A, Lenzi DC, Haddad AC, Bottino MC, Dominguez GC, Vigorito JW. Low-level laser therapy for pain caused by placement of the first orthodontic archwire: a randomized clinical trial. Am J Orthod Dentofacial Orthop. 2009;136:662–7.
151. Doshi-Mehta G, Bhad-Patil WA. Efficacy of low-intensity laser therapy in reducing treatment time and orthodontic pain: a clinical investigation. Am J Orthod Dentofacial Orthop. 2012;141:289–97.
152. Kim WT, Bayome M, Park JB, Park JH, Baek SH, Kook YA. Effect of frequent laser irradiation on orthodontic pain. A single-blind randomized clinical trial. Angle Orthod. 2013;83:611–6.
153. Artes-Ribas M, Arnabat-Dominguez J, Puigdollers A. Analgesic effect of a low-level laser therapy (830 nm) in early orthodontic treatment. Lasers Med Sci. 2013;28:335–41.
154. Dominguez A, Velasquez SA. Effect of low-level laser therapy on pain following activation of orthodontic final archwires: a randomized controlled clinical trial. Photomed Laser Surg. 2013;31:36–40.
155. Eslamian L, Borzabadi-Farahani A, Hassanzadeh-Azhiri A, Badiee MR, Fekrazad R. The effect of 810-nm low-level laser therapy on pain caused by orthodontic elastomeric separators. Lasers Med Sci. 2013;29:559–64.
156. Nobrega C, da Silva EM, de Macedo CR. Low-level laser therapy for treatment of pain associated with orthodontic elastomeric separator placement: a placebo-controlled randomized double-blind clinical trial. Photomed Laser Surg. 2013;31:10–6.
157. Abtahi SM, Mousavi SA, Shafaee H, Tanbakuchi B. Effect of low-level laser therapy on dental pain induced by separator force in orthodontic treatment. J Dent Res. 2013;10:647–51.
158. Herravi F, Moradi A, Ahrari F. The effect of low level laser therapy on the rate of tooth movement and pain perception during canine retraction. Oral Health Dent Manag. 2014;13:183–8.
159. Niemz M. Laser tissue interactions. 3rd ed. Heidelberg: Springer-Verlag; 2007. ISBN: 978-3-540-72191-8
160. Goodman CS. Report from the Swedish council on technology assessment in health care (SBU). literature searching and evidence interpretation for assessing health care practices. Int J Technol Assess Health Care. 1994;10:714–5.
161. Krishnan V, Davidovich Z. Mechanisms of tooth movement. Wiley; 2015; ISBN: 978–1–118-68887-8.
162. Huang YY, Sharma S, Carroll J, et al. Biphasic dose response in low level laser therapy. Dose Response. 2011;9:602–18.
163. Bakthisaran R, Tangirala R, Rao M. Small heat shock proteins: role in cellular function and pathology. Biochim Biophys Acta. 1854;2015:291–319.
164. Richter K, Haslbeck M, Buchner J. The heat shock response: life on the verge of death. Mol Cell. 2010;40:253–66.
165. Agrawal T, Gupta G, Rai V, et al. Pre-conditioning with low level laser (light) therapy: light before the storm. Dose Response. 2014;12:619–49.
166. Haxsen V, Schikora D, Sommer U, et al. Relevance of laser irradiance threshold in the induction of alkaline phosphatase in human osteoblast culture. Lasers Med Sci. 2008;23:381–4.
167. Kesler G, et al. Platelet derived growth factor secretion and bone healing after Er:YAG laser bone irradiation. J Oral Implantol. 2011;37:195–204.
168. Pagin M, et al. Laser and light emitting diode effects on pre-osteoblast growth and differentiation. Lasers Med Sci. 2014;29:55–9.
169. Choi EJ, et al. Biological effects of a semi-conductor diode laser on human periodontal ligament fibroblasts. J Periodontal Implant Sci. 2010;40(3):105–10.
170. Altan A, Sokucu O, Ozkut M, et al. Metrical and histological effects of low level laser therapy on orthodontic tooth movement. Lasers Med Sci. 2012;27(1):131–40.
171. Rosa CB, Habib FA, de Araujo TM, et al. Effect of the laser and light emitting diode (LED) phototherapy on mid palatal suture bone formation after rapid maxillary expansion: a Raman spectroscopy analysis. Lasers Med Sci. 2014;29(3):859–67.
172. Shirazi M, Akhoundi A, Javadi E, et al. The effects of diode laser (660 nm) on the rate of tooth movement an animal study. Lasers Med Sci. 2015;30(2):713–8.
173. Cossetin E, Janson G, de Carvalho MG, et al. Influence of low level laser on bone remodelling during induced tooth movement in rats. Angle Orthod. 2013;83(6):1015–21.
174. Ekizer A, Uysal T, Yuksel Y. Light emitting diode photobiomodulation: effect on bone formation in orthopedically expanded suture in rats – early bone changes. Lasers Med Sci. 2013;28:1263–70.
175. Ekizer A, Uysal T, Guray E, et al. Effect of LED mediated photobiomodulation therapy on orthodontic tooth movement and root resorption in rats. Lasers Med Sci. 2015;30:779–85.
176. Fonseca P, de Lima FM, Higashi DT, et al. Effects of light emitting diode (LED) therapy at 940 nm on inflammatory root resorption in rats. Lasers Med Sci. 2013;28(1):49–55.
177. Suzuki SS, Garcez AS, Suzuki H, et al. Low level laser therapy stimulates bone metabolism and inhibits root resorption during tooth movement in a rodent model. J Biophotonics. 2016; doi:10.1002/jbio.201600016.
178. Cruz D, Kohara E, Ribeiro M, et al. Effects of low intensity laser therapy on the orthodontic movement velocity of human teeth: a preliminary study. Lasers Surg Med. 2004;35:117–20.
179. Limpanichkul W, Godfrey K, Srisuk N, et al. Effects of low level laser therapy on the rate of orthodontic tooth movement. Orthod Craniofac Res. 2006;9:38–43.
180. Youssef M, Ashkar S, Hamade E, et al. The effect of low level laser therapy during orthodontic movement: a preliminary study. Lasers Med Sci. 2008;23:27–33.
181. Sousa MV, Scanavini MA, Sannomiya EK, et al. Influence of low level laser therapy on the speed of orthodontic movement. Photomed Laser Surg. 2011;29:191–6.
182. Genc G, Kocadereli I, Tasar F, et al. Effect of low level laser therapy (LLLT) on orthodontic tooth movement. Lasers Med Sci. 2013;28:41–7.

183. http://waltza.co.za/wp-content/uploads/2012/08/Dose_table_780-860nm_for_Low_Level_Laser_Therapy_WALT-2010.pdf.
184. Kau CH, Kantarci A, Shaugnessy T, et al. Photobiomodulation accelerates orthodontic tooth alignment in the early phase of treatment. Prog Orthod. 2013;14:30–9.
185. Chung SE, Tompson B, Gong S-G. The effect of light emitting diode phototherapy on rate of orthodontic tooth movement: a split mouth controlled clinical trial. J Orthod. 2015;42(4):274–83.
186. Shaughnessy TG. Long distance orthodontic treatment with adjunctive light therapy. J Clin Orthod. 2015;49(12):757–69.
187. Ojima K, Dan C, Kumagai Y, et al. Invisalign treatment accelerated by photobiomodulation. J Clin Orthod. 2016;50(5):309–17.