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Current status of Er:YAG laser in periodontal surgery☆

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A B S T R A C T

Lasers have numerous advantageous tissue interactions such as ablation or vaporization, hemostasis, bacterial killing, as well as biological effects, which induce various beneficial therapeutic effects and biological responses in the tissues. Thus, lasers are considered an effective and suitable device for treating a variety of inflammatory and infectious conditions of periodontal disease. Among various laser systems, the Er:YAG laser, which can be effectively and safely used in both soft and hard tissues with minimal thermal side effects, has been attracting much attention in periodontal therapy. This laser can effectively and precisely debride the diseased root surface including calculus removal, ablate diseased connective tissues within the bone defects, and stimulate the irradiated surrounding periodontal tissues during surgery, resulting in favorable wound healing as well as regeneration of periodontal tissues. The safe and effective performance of Er:YAG laser-assisted periodontal surgery has been reported with comparable and occasionally superior clinical outcomes compared to conventional surgery. This article explains the characteristics of the Er:YAG laser and introduces its applications in periodontal surgery including conventional flap surgery, regenerative surgery, and flapless surgery, based on scientific evidence from currently available basic and clinical studies as well as cases reports.

1. Introduction

Mechanical therapy has been the gold standard of treatment for plaque-induced periodontal diseases. However, it has been gradually understood that complete bacterial eradication and/or ideal wound healing may not necessarily be achieved through conventional mechanical therapy using hand and power scalers alone. In particular, periodontal pathogens invade surrounding periodontal tissues and even the cells [1]. Therefore, antimicrobial agents have been added as complimentary adjuncts to mechanical therapy, and mechano-chemotherapy has generally been employed for the treatment of advanced periodontitis [2,3].

Meanwhile, laser application in oral soft tissue surgery began nearly 40 years ago [4–6]. Since then, owing to advantageous physical and biological characteristics, laser applications in dental treatment have been advancing steadily [7,8]. Recently, lasers have often been employed in periodontal treatment [6] due to various beneficial effects including tissue ablation and bacterial killing; and currently, several laser systems are employed in the management of periodontal and peri-implant diseases [6,9–12] (Table 1). Thus, with the use of lasers and light-emitting diodes (LEDs), in recent years mechano-chemo-phototherapy has become available in periodontal therapy [6].

This article explains the physical and biological effects of Er:YAG laser and introduces its applications in periodontal surgery including conventional flap surgery (open flap debridement), regenerative surgery, and flapless surgery, based on scientific evidence from currently available basic and clinical studies as well as cases reports. Also, the limitations and potential drawbacks of Er:YAG laser application for periodontal surgery are discussed.

☆ Scientific field of dental Science: Periodontology

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Table 1
U.S. FDA Marketing Clearances for Er:YAG laser in the field of periodontal therapy.

Intraoral Soft Tissue Surgery (Ablating, Incising, Excising, Coagulating)
Aphthous Ulcer Treatment
Sulcular Debridement
Cutting, Shaving, Contouring, and Resection of Oral Osseous Tissue (Bone)
Osteotomy, Osseous Crown Lengthening, Osteoplasty
Removal of Subgingival Calculus in Periodontal Pockets

2. Effects of lasers

Lasers exhibit numerous tissue interactions including ablation or vaporization, hemostasis, microbial inhibition and destruction, as well as biological effects (biostimulation), which induce various beneficial therapeutic effects and biological responses during and after treatment [11]. Therefore, laser application is considered effective and suitable for treating various inflammatory and infectious conditions in the oral cavity, such as periodontal and peri-implant diseases [6,10,13,14]. Also, laser therapy may provide less-stressful treatment for patients by alleviating physical and mental stress during treatment as well as intraoperative and postoperative pain [15].

2.1. Characteristics of Er:YAG laser

In dentistry, four different types of lasers are available in the clinic. Generally, the degree of absorption, i.e., the depth of penetration of a laser in biological tissue, is dependent on its wavelength. In particular, absorption is strongly influenced by the absorption coefficient in water for each wavelength [16,17]. Thus, lasers are roughly classified into two types depending on their wavelength: 1) a deeply penetrating type, where the laser light penetrates and scatters into the tissue more deeply, such as the Nd:YAG and diode lasers, and 2) a superficially absorbed type (shallowly penetrating type), where the laser light is absorbed in the superficial layer and does not penetrate or scatter deeply, such as the CO_2, Er:YAG, and Er,Cr:YSGG lasers [10,18].

The Er:YAG laser is a solid-state laser that generates a light with a wavelength of 2940 nm. Of all lasers emitting in the near- and mid-infrared spectral range, absorption of the Er:YAG laser in water is the greatest because the wavelength coincides with the large absorption band for water. Theoretically, the Er:YAG laser has a 10, and 15,000–20,000 times higher absorption coefficient of water than the CO_2 and the Nd:YAG lasers, respectively [16,19]. Since the Er:YAG laser is well absorbed by all biological tissues that contain water molecules, this laser can be applied not only for soft tissues but also for hard tissues [6,9], while the Nd:YAG, diode, and CO_2 lasers are basically used for only soft tissue treatment.

As to ablation mechanisms, in soft tissue, the Er:YAG laser causes thermal evaporation (vaporization). In contrast, in hard tissue, it exerts water-mediated explosive ablation by photomechanical or photothermal effects without producing carbonization and cracking [6]. This gives the Er:YAG laser a broad range of applicability in periodontal therapy, including gingival tissue, tooth roots, calculus, bone tissue, as well as titanium implant surfaces.

Regarding thermal influences on irradiated tissues, the high absorption of the Er:YAG laser into water minimizes thermal influences on the surrounding tissues during irradiation. When the Er:YAG laser was used for an incision of porcine gingiva in a contact mode, the formation of a coagulated layer was extremely thin, approximately 18 and 38 μm in thickness with and without water spray, respectively, compared to 138 μm for Nd:YAG and diode lasers and 163 μm for CO_2 laser [20]. Thus, compared to the Nd:YAG, diode, and CO_2 lasers, the hemostatic effect of the Er:YAG laser is lower but resultant weaker hemostasis is, conversely, an advantage in periodontal and peri-implant therapy because it does not interfere with the wound healing of soft tissue and bone tissue following irradiation.

In hard tissue ablation, some degree of heat generation is inevitable with the Er:YAG laser since hard tissue contains very low amounts of water. However, the use of water coolant minimizes heat generation by cooling the irradiated area and absorbing excessive laser energy [21–23]. Er:YAG laser ablation with water irrigation produces an altered layer of 10–20 μm width on cementum and dentin surfaces [24–27] and approximately 22 μm width on bone surface [28].

The Er,Cr:YSGG laser with 2780 nm wavelength, which is more highly absorbed by OH ions than water molecules [29], also exhibits performance similar to that of the Er:YAG laser. However, the Er:YAG laser shows more efficient soft tissue ablation than Er:YSGG laser (2790 nm) [30] and produces less thermal effect on soft tissue (18 μm thick coagulation with water spray), compared to the Er,Cr:YSGG laser (33 μm with water spray) [20]. On root cementum, in terms of thermal influence during irradiation, previous studies showed only slightly charred appearance was produced by Er:YAG laser without water coolant [31], whereas obvious carbonization was observed with Er,Cr:YSGG laser without water coolant [32]. Accordingly, the Er:YAG laser produces less thermogenesis and may be less invasive to the surrounding tissues compared to the Er,Cr:YSGG laser with respect to thermal influences.

During periodontal treatment, the Er:YAG laser has potential to achieve a more comprehensive and extensive decontamination and detoxification of periodontal pockets [11,12,33] through its effectiveness in calculus ablation [34], bacterial elimination [35], lipopolysaccharide ablation [36], and degranulation [12] induced by its photo-thermal and photo-mechanical ablation effects. Thus, the Er:YAG laser exhibits properties highly suitable for periodontal treatment due to its various excellent physical abilities with both periodontal soft and hard tissues [6,10,11].

Recently, in the endodontic field, a novel efficient irrigation technique for root canals using erbium lasers has been developed [37]. The erbium laser-activated irrigation is induced by high streaming of fluids in canals, caused by the collapse of the laser-induced bubble, which may also be effective for decontamination within pocket debridement using erbium lasers.

2.2. Biological effects of Er:YAG laser

Another interesting and characteristic property of lasers is the biostimulation (photobiomodulation) of tissues and cells subsequent to irradiation, a completely unique effect not seen with mechanical therapy [38–42]. It is speculated that during tissue ablation with high-level laser therapy (HLLT), a reduced or markedly reduced amount of energy simultaneously penetrates or scatters into the surrounding tissues, resulting in the induction of biological effects (stimulation/activation) on tissues/cells (low-level laser therapy: LLLT) [11,40]. Furthermore, the photo-thermal effect generated by HLLT may have a positive influence on wound healing as one of its biostimulation effects [40]. Currently, HLLT is performed for ablation of diseased tissues, with concurrent biostimulation in the adjacent tissues, as a desired additional effect [14,33].

During pocket and bone defect debridement in periodontal surgery, the Er:YAG laser induces stimulation/activation of the proximate gingival and bone tissues/cells (Fig. 1) [42]. In vitro studies showed that low-level Er:YAG laser irradiation induces increased cell proliferation of gingival fibroblasts [43–45], periodontal ligament fibroblasts [46], and osteoblasts [47], as well as calcification of primary osteoblast-like cells [48].

Regarding gingival fibroblasts, Pourzarandian et al. [43] first reported that low-level Er:YAG laser irradiation at a fluence of 3.4 J/cm^2 stimulates the proliferation of cultured human gingival fibroblasts (HGFs), and exert its stimulative action on gingival fibroblast proliferation through the production of prostaglandin E_2 via the expression of cyclooxygenase-2 [49]. Ogita et al. [44] performed proteomic analysis and reported that low-level Er:YAG laser irradiation at 2.1 J/cm^2 can induce a significant change in protein expression in HGFs and that the

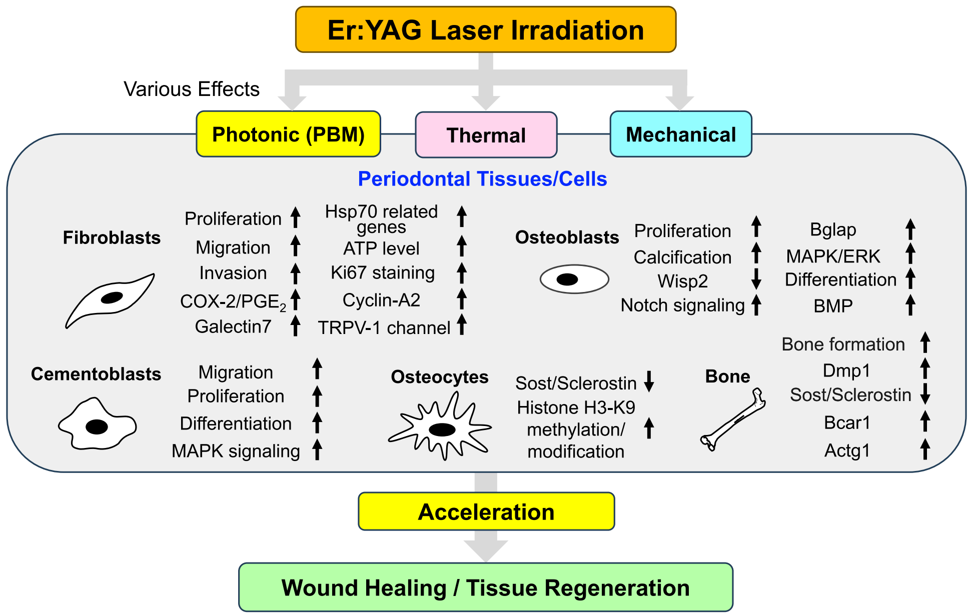

Fig. 1. Biological effects of Er:YAG laser. photonic, thermal, and mechanical stimuli induced by Er:YAG laser produce various advantageous biological effects on periodontal cells/tissues.

upregulation of galectin-7 expression may partly contribute to the increase in cell proliferation.

Kong et al. [45] demonstrated that a moderate-level of Er:YAG laser irradiation at 6.3 J/cm^2 significantly elevated ATP level, Ki67 staining, and cyclin-A2 mRNA expression in HGFs following irradiation. They confirmed that the irradiation affected the cell cycle, increased cell proliferation, and upregulated the mRNA expression of heat shock protein 70 family with the cell surface temperature elevated up to 40.9 °C (14.2 °C increase). The laser-induced proliferation was suppressed by inhibition of thermosensory transient receptor potential channels including transient receptor potential vanilloid 1 (TRPV-1) channel [50]. Despite causing transient cellular alteration in mitochondria and ribosomal endoplasmic reticulum, Er:YAG laser irradiation at 6.3 J/cm^2 strongly potentiated HGF proliferation via photothermal stress, suggesting potential wound-healing benefits. In addition, Lin et al. [46] reported that Er:YAG laser irradiation at 4.2 J/cm^2 on human periodontal ligament fibrobrasts (hPDLFs) promoted cell proliferation, migration, and invasion abilities, and revealed that the silencing of galectin-7 abrogated the Er:YAG laser-induced effects, suggesting that the Er:YAG laser promoted these effects through the induction of galectin-7.

As for the cells related to osteogenesis and calcification, Aleksic et al. [47] reported that low-level Er:YAG laser irradiation at 1.0–4.3 J/cm^2 significantly increased mouse osteoblast (MC3T3-E1) proliferation, mainly by activating extracellular signal-regulated protein kinase (MAPK/ERK), which plays a central role in the control of cell proliferation [51]. Niimi et al. [48] reported that Er:YAG laser irradiation at 3.3 J/cm^2 significantly enhanced calcification of primary osteoblast-like cells from rat calvaria, possibly via enhanced *Bglap* expression, without major thermal effects (3.4 °C increase). Microarray analysis showed that the irradiation caused an upregulation of inflammation-related genes, and downregulation of *Wisp2*, which plays an important role in the differentiation and mineralization of osteoblasts [52]. Gene set enrichment analysis clarified that Er:YAG laser irradiation enriched Notch signaling, which plays a critical role in various cellular functions including the promotion of osteogenic differentiation of osteoblasts in synergy with BMP [53]. Recently, Yong et al. [54] reported that low-level Er:YAG laser irradiation at 2.0 J/cm^2 induces mouse cementoblast (OCCM-30) migration, proliferation and differentiation, and activates the MAPK (ERK1/2, P38 and JNK) signaling pathway.

Ohsugi et al. [55] compared bone ablation with Er:YAG laser and bur drilling in rat calvaria and demonstrated significantly higher bone repair ratios following laser ablation compared to bur drilling. Interestingly, in the laser-treated bone tissue, the irradiation increased *Dmp1* expression, and suppressed *Sost* expression, the gene of Sclerostin that inhibits caronical wnt signaling pathway and suppresses new bone formation. They [56] also confirmed using primary rat osteogenic cells (osteocytes-like cells from osteoblast-like cells differentiation) that Er:YAG laser irradiation at 1.5 and 3.1 J/cm^2 decreased *Sost* expression in the cells and Sclerostin expression in the cultured supernatant, suggesting that Er:YAG laser irradiation may promote bone formation via the suppression of Sost expression.

Regarding the photomechanical effect of Er:YAG laser, Shimohira et al. [57] reported in an in-vivo study that Er:YAG laser irradiation on bone tissue upregulated expression of *Bcar1* and *Actg1*, the main regulators of mechanotransduction in the bone tissue, suggesting the conversion of photonic energy into mechanical stimulation. The laser influenced the expression of genes associated with bone formation immediately after irradiation. Thus, mechanical stress and the biological effects caused by Er:YAG laser irradiation may potentially contribute to bone healing following irradiation. They [58] also reported, using primary rat osteogenic cells, that Er:YAG laser irradiation at 3.1 J/cm^2 showed positive effect on the expression of genes related to bone formation, without major thermal effects (3.1 °C increase), and also that the low level Er:YAG laser irradiation at 3.1 J/cm^2 induced significant enrichment of histone H3-K9 methylation and modification gene sets. These findings may represent critical mechanisms of early bone formation after Er:YAG laser irradiation.

Thus, photonic, thermal, and mechanical stimuli induced by Er:YAG laser produce various advantageous biological effects, which potentially accelerate wound healing and tissue regeneration in the irradiated periodontal tissues.

3. Applications of Er:YAG laser in periodontal surgery

3.1. Effects of Er:YAG laser in conventional flap surgery

In periodontal therapy, surgical procedures are often required in moderate to advanced cases. Since it is difficult to completely remove calculus and plaque non-surgically and blindly from deep periodontal pockets, open flap debridement is often indicated after initial treatment for the successful management of severe periodontitis [3].

Due to the excellent performance characteristics of the Er:YAG laser, this laser had been expected to be useful during surgery. Mizutani et al. [59] histologically investigated the effects of Er:YAG laser application in experimentally-induced periodontitis with furcation involvement in dogs (Fig. 2). During open flap debridement, Er:YAG laser irradiation with water spray effectively removed inflammatory connective tissue (granulation tissue) from bone defects and debrided the root surfaces without visible thermal damage, such as carbonization and coagulation. Compared with conventional instrumentation using Gracey curettes, the required time for de-granulation and root surface debridement was significantly shorter in the laser group. This may be due to laser irradiation facilitating root surface and bone defect debridement in the anatomically complex furcation involvements. Postoperatively, clinically favorable wound healing was observed in both groups. Histological examinations three months post-surgery revealed no anomalous structures such as bone or pulp necrosis, and connective tissue attachment and cementum formation were observed equally for both the laser- and curette-treated sites, suggesting that the lased root surface is biocompatible and does not inhibit periodontal tissue attachment.

Interestingly, new bone formation was significantly more pronounced in the laser sites than in the curette sites. Regarding this improved bone regeneration, there are various potential healing-promoting mechanisms in Er:YAG laser therapy, including high bactericidal [35,60] and detoxification [36] effects, and the microstructural topography of bone and root surfaces following laser irradiation [25,61] which enhances blood clot retention [62–64]. In this study, the authors considered that particularly pronounced bleeding from the bone surface [59,65] during thorough granulation tissue removal from bone defects, as observed in decortication procedure, may have been a more important contributing factor toward the increased new bone formation. In particular, the Er:YAG laser enables thorough removal of granulation tissue even from the microcavities of the bone surface [66]. The biostimulation effects of the laser might have also contributed to promoting bone regeneration.

This study demonstrated that the Er:YAG laser is safe and effective for root surface and bone defect debridement, with results either equal to or even superior to those of conventional mechanical methods, and it further demonstrated that the Er:YAG laser is a favorable preparatory device in periodontal flap surgery.

3.2. Conventional flap surgery using Er:YAG laser

The most important procedure during surgical approaches is the debridement of subgingival calculus and granulation tissue from root and bone surfaces. However, mechanical instruments are difficult to access the complex anatomies of molar root bifurcations and narrow intrabony defects. In such sites, the Er:YAG laser is a suitable debridement device and its fine contact tips easily reach the sites allowing efficient and complete debridement of root surfaces and bone defects. Moreover, the Er:YAG laser is able to assist gingival incision and flap reflection performed with conventional instruments, facilitating the procedures and minimizing the unfavorable trauma of gingival flaps.

In previous clinical studies, Sculean et al. [67] compared the healing of intrabony periodontal defects following conventional access flap surgery using the Er:YAG laser or hand/ultrasonic scalers for degranulation and root debridement in a randomized controlled trial (RCT).

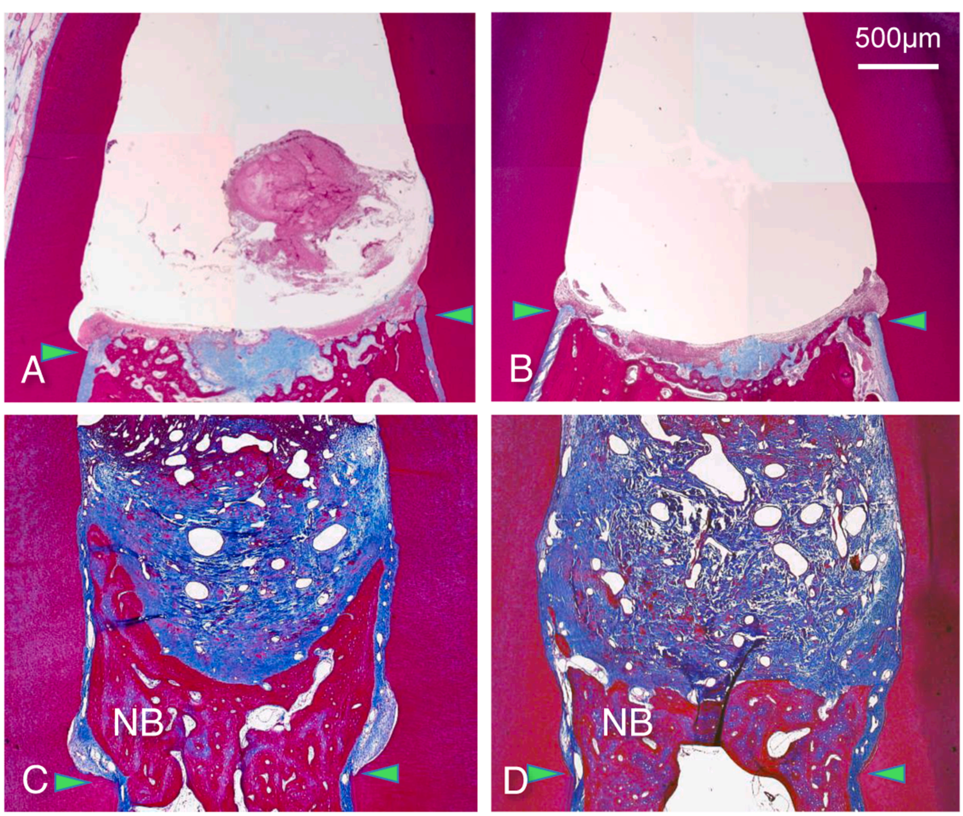

Fig. 2. Application of Er:YAG laser in periodontal flap surgery in dog. Histological photomicrographs of mesio-distal sections of furcation immediately (A, B) and 12 weeks after surgery (C, D). The debridement was performed above the notch (arrow heads) using a hand curette (A) or Er:YAG laser (B). After 12 weeks, in both laser (C) and curette (D) sites, periodontal tissue attachment with bone formation was observed. The newly-formed bone (NB) extended along the dental root surface (D) in the defect. Note the greater new bone formation in the laser-treated site than the curette-treated site (Azan stain).
[Modified pictures and legend from Aoki A et al., Periodontol 2000 68(1): 217–69, 2015 [11]; with permission. © copyright (2015) John Wiley & Sons A/S; and from Mizutani K et al., Lasers Surg Med 38:314–324, 2006 [59]; with permission. © copyright (2006) John Wiley & Sons A/S].

They reported that the application of the Er:YAG laser was equally effective and safe with significant clinical improvements at 6 months post-surgery. The laser group displayed a higher tendency for clinical attachment level (CAL) gain, although the tendency was not statistically significant. They concluded that the Er:YAG laser may represent a suitable alternative for root surface and bone defect debridement in conjunction with periodontal surgery. Gaspirc & Skaleric [68] also compared Er:YAG laser–assisted periodontal flap surgery versus conventional treatment with the modified Widman flap procedure in a RCT study with a split-mouth design. The Er:YAG laser was used to debride the bone defects, scale the root surfaces, and trim the periodontal flaps. The mean probing pocket depth (PPD) reduction and CAL gain were significantly greater at the laser sites up to 3 years postoperatively. This 5-year observational study demonstrated the effectiveness of Er:YAG laser application in periodontal flap procedures and the long-term stability of the postoperative period [68]. Yung [69] reported in a case series that periodontal surgery can be performed safely with the Er:YAG laser with no collateral thermal damage, and that the weaker coagulation produced by the Er:YAG laser compared to that of other lasers may be preferable for better wound healing. Our group also confirmed in a RCT study that applying the Er:YAG laser in open flap debridement for intraosseous defects is equally or more effective than the conventional method regarding mean pocket reduction and attachment gain (unpublished) (Fig. 3).

In these clinical studies, the Er:YAG laser did not adversely affect healing, and has been suggested as a possible alternative to conventional debridement methods [67–69]. Based on this clinical evidence, using the Er:YAG laser in periodontal surgery is recognized as a safe and effective therapeutic approach. Although evidence is still limited, the postoperative wound healing following Er:YAG laser application in surgical debridement may be comparable or occasionally superior to that of conventional mechanical treatment. The Er:YAG laser not only

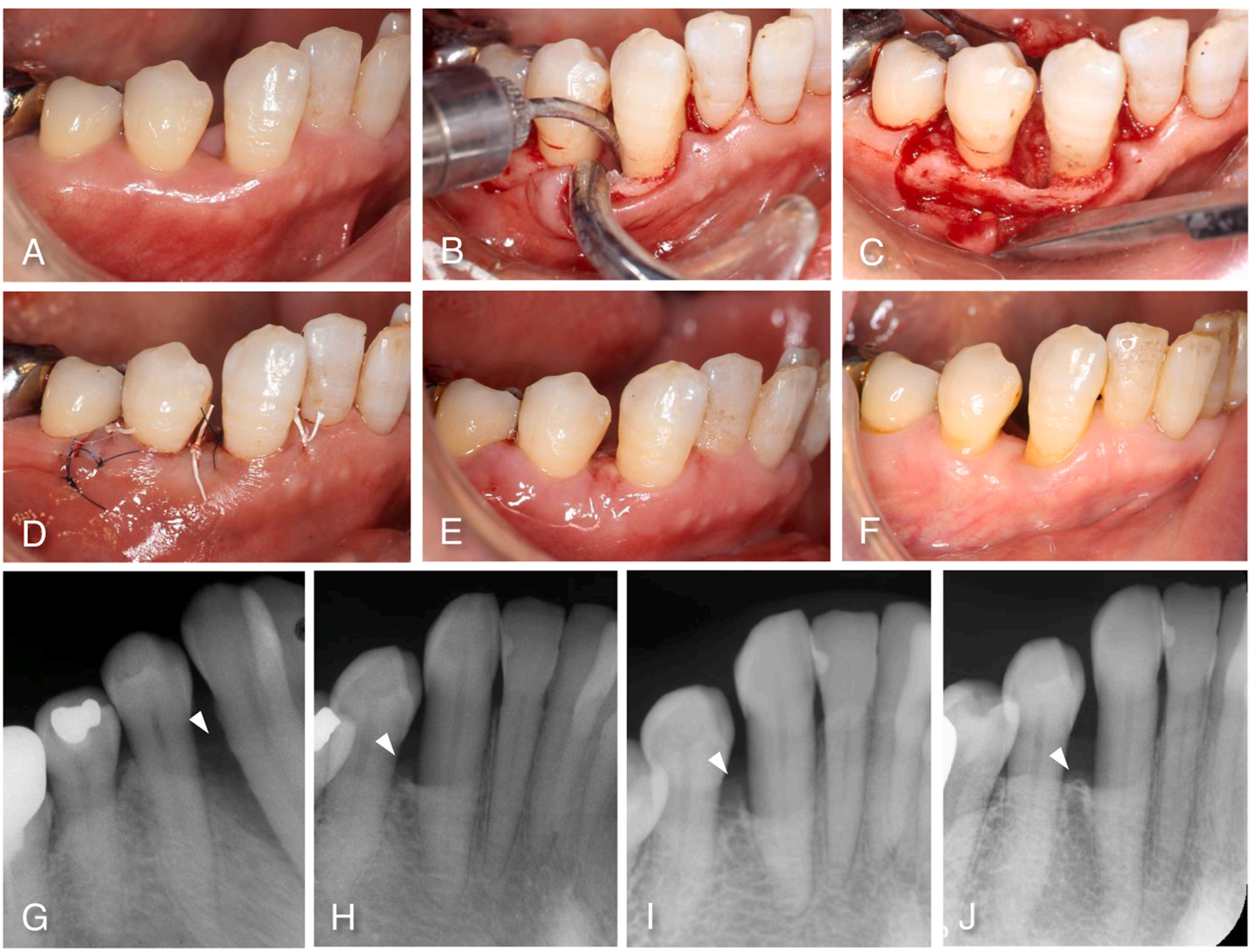

Fig. 3. Periodontal flap surgery (open flap debridement) using Er:YAG laser. A 63-year-old female. Before surgery (A), a 9-mm deep PPD with bleeding on probing remained at the distal site of the mandibular right canine after initial treatment. Granulation tissue removal and root surface debridement were effectively and safely achieved by Er:YAG laser alone at 30 Hz and 80 mJ/pulse (panel setting) using an 80° curved and 600 μm diameter tip in contact mode under saline water spray (B). After complete degranulation, a three–wall, large and deep vertical bone defect with a 7-mm depth was observed and no visible major thermal damage such as carbonization on the laser treated root and bone surfaces was detected. The inner surface of flaps was also ablated with the Er:YAG laser at 30 Hz and 40 mJ/pulse to decontaminate the surface with diseased granulation tissue and stimulate the gingival flap tissue (C). After suturing (D). Wound healing was uneventful without any clinical complications at 1 week (E). Although gingival recession was observed, finally the probing pocket depth decreased to 2 mm without BOP at 14 years following surgery. A 7 mm of pocket reduction and 5 mm of clinical attachment gain were obtained (F). On radiographs, the vertical bone defect (arrow head) on the distal site observed at the first visit (G) was successfully repaired by apparent bone regeneration at 1 (H) and 8 (I), and 17 years (J). No adverse side effects were observed in the irradiated bone tissue (case by A. A.).
[Modified pictures and legend from Aoki A et al., Periodontol 2000 68(1): 217–69, 2015 [11]; with permission. © copyright (2015) John Wiley & Sons A/S].

facilitates the debridement procedure in flap surgery, but it might also be advantageous for tissue repair and regeneration. In addition, a recent review article of Mikami et al. [15] demonstrated by meta-analysis that surgery using erbium lasers significantly reduced patient-reported pain immediately after treatment.

3.3. Regenerative therapy using Er:YAG laser

Recently, periodontal tissue regenerative therapy has been widely performed in dental practice. The regenerative therapy is indicated in treating intrabony defects [70], and various biomaterials are currently applicable.

As a periodontal regenerative therapy using the Er:YAG laser, Schwarz et al. [71] compared the combination therapy of deep intrabony periodontal defects using an Er:YAG laser and enamel matrix protein derivative (EMD) with scaling and root planning (SRP) + ethylenediaminetetraacetic acid (EDTA) + EMD. Consequently, the Er:YAG + EMD group produced regenerative effects comparable to the SRP + EDTA + EMD group. The clinical parameters of PPD and CAL were not significantly different between the groups.

In periodontal regenerative therapy, the suitable treatment methods generally depend on the remaining bone walls [72]. Narrow three-wall intrabony defects can be regenerated using open flap debridement (OFD) and OFD with biologically active regeneration agents (BARAs) such as enamel matrix derivative (EMD), PDGF, or FGF-2 and/or bone graft substitutes (BGSs). In contrast, wide one-wall and two-wall bone defects, and horizontal bone defects, are difficult to regenerate even using BARAs and BGSs. In such cases, with non-containing bone defects, guided tissue regeneration (GTR) techniques, using barrier membranes in combination with BARAs and BGS, are required to regenerate periodontal tissue [73]. However, GTR is technically demanding and presents risks, such as flap dehiscence, infection of membrane and BGSs, and oral vestibule narrowing caused by releasing incisions for tension free suturing [74,75].

In order to avoid these problems, Taniguchi et al. [66,76] developed a novel application of Er:YAG laser in periodontal regenerative therapy [Er:YAG laser-assisted bone regenerative therapy (Er-LBRT)] without using a membrane (Fig. 4). The Er-LBRT procedure employs Er:YAG laser not only to debride root surfaces and bone defects, but also to enhance blood coagulation on the grafted bone surface. With this technique, after incision and flap reflection, remaining subgingival calculus and granulation tissue are debrided using hand instruments and Er:YAG laser (Fig. 4a-c). EMD is applied to the decontaminated root surface and then blood mixed autogenous bone or BGS is filled into the bone defect (Fig. 4d,e), and low-level Er:YAG laser is irradiated on the surface of the grafted bone to physically strengthen and stabilize the grafted bone cluster shape by superficial blood coagulation while simultaneously promoting wound healing of the bone defect via the bio-stimulation effect of the laser (Fig. 4f). After blood clot formation, minimal releasing incisions are performed, and the wound is closed by simple sutures.

The results of the Er-LBRT case series [66] demonstrated excellent treatment outcomes (Fig. 5). In the study, nine bone defects in six patients were treated with EMD and autogenous bone graft using Er-LBRT. At 12 months post-surgery, mean PPD significantly improved from 6.2 mm (before surgery) to 2.0 mm, with a PPD reduction of 4.2 mm,

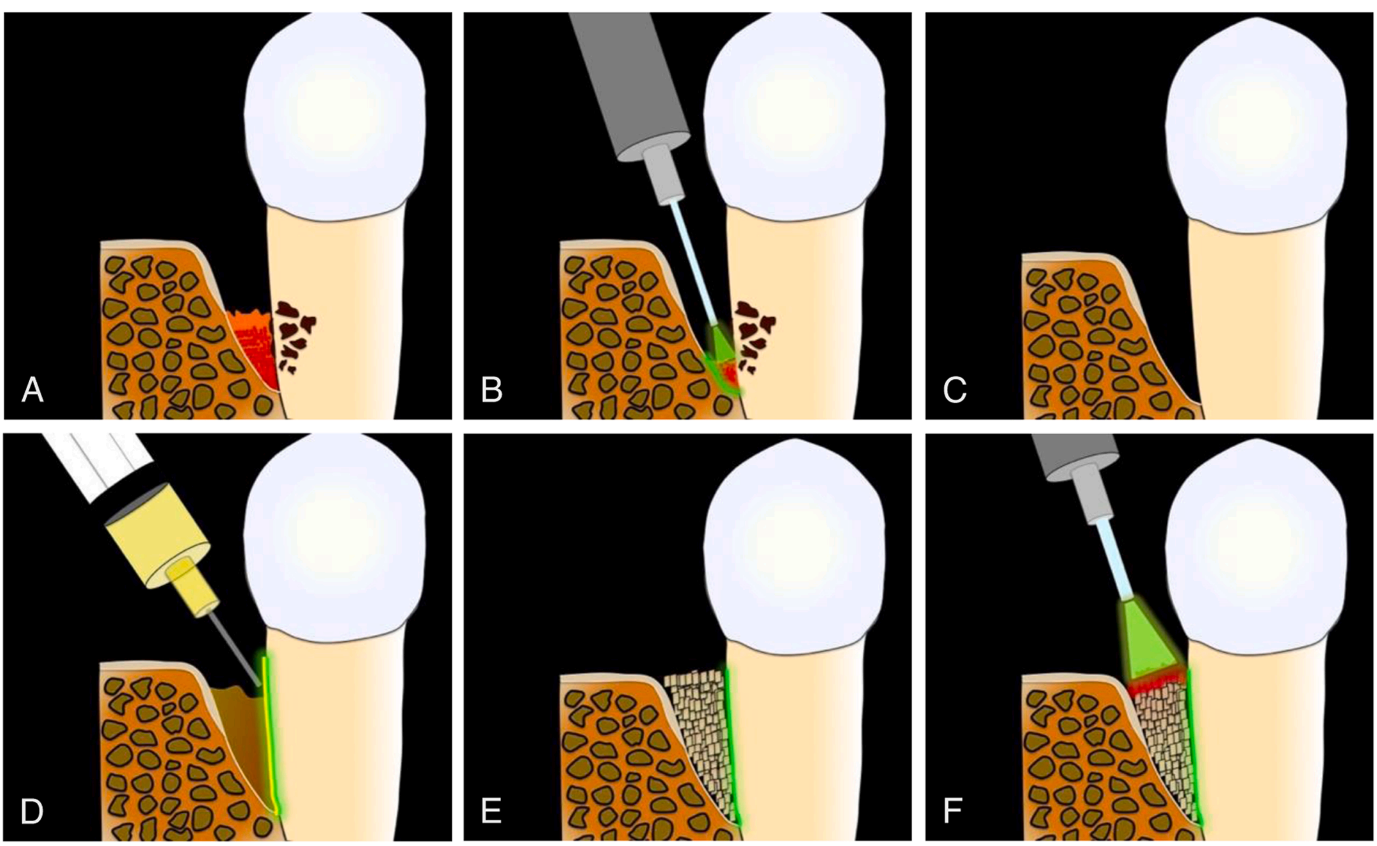

Fig. 4. Schematic Illustration of the procedures of Er:YAG laser-assisted bone regenerative therapy (Er-LBRT). Before surgery (A). After conventional mechanical debridement, thorough debridement of the root surface and the bone defect was performed by applying Er:YAG laser with saline spray in the contact mode (B). Completion of debridement of root surfaces and bone defects (C). Application of enamel matrix derivative (D). After bone grafting into the defect (E), the grafted bone surface was irradiated without saline spray in a defocused mode to form a blood clot on the grafted bone surface.
[Modified pictures and legend from Taniguchi Y et al., Int J Periodontics Restorative Dent, 36: 507–515, 2016 [66]; with permission. © copyright (2016) Quintessence Publishing Co. Inc].

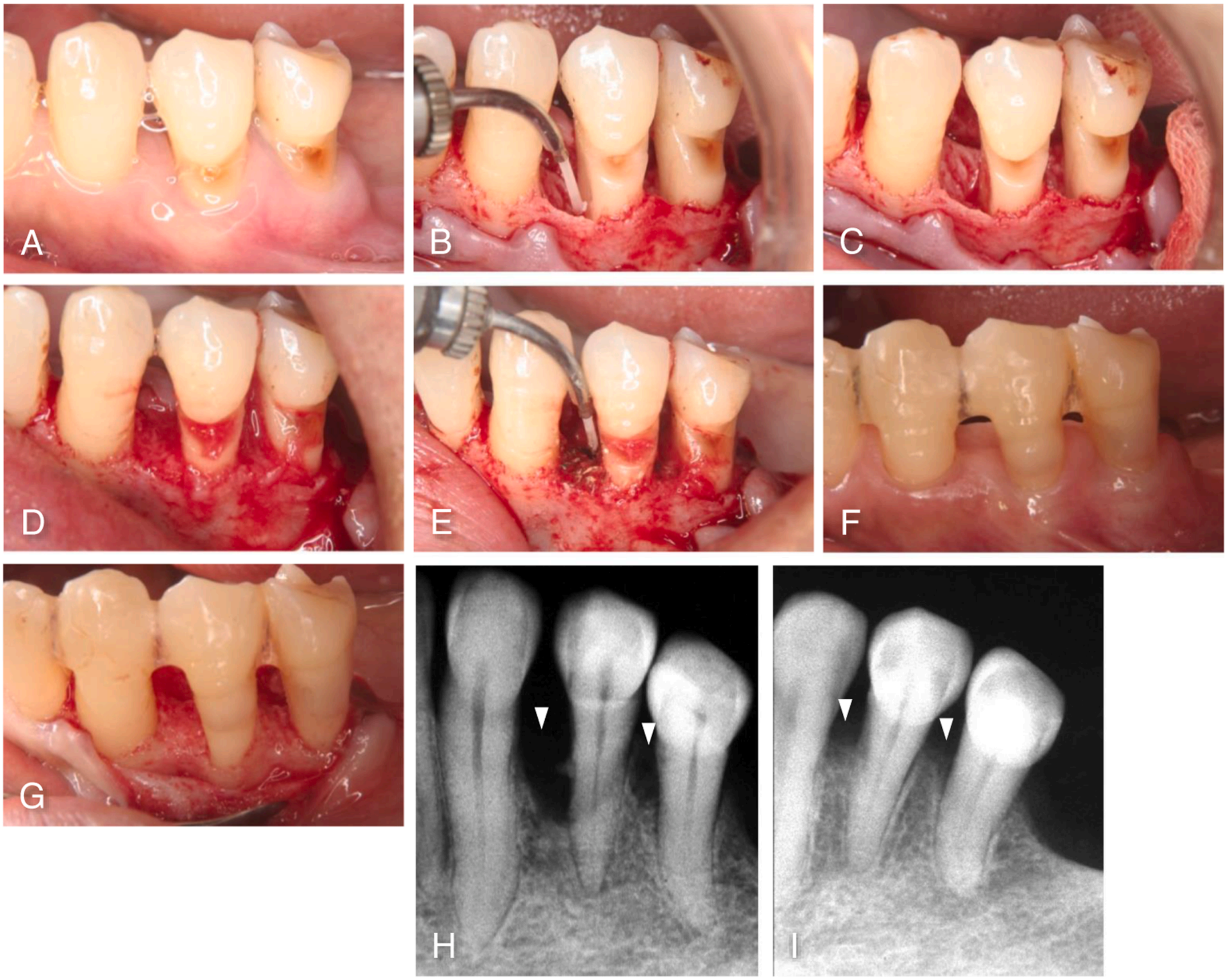

Fig. 5. Er:YAG laser-assisted bone regenerative therapy. A 46-year-old female. Before surgery. The mesial PPD 5–6 mm (CAL 9 mm) for the first premolar and mesial PPD 6–7 mm (CAL 9 mm) for the second premolar (A). After debridement with a curette of the coronal area of the bone defects, remaining granulation tissue and calculus were thoroughly removed using Er:YAG laser at 20 Hz and 70 mJ/pulse (panel setting) with water spray (B). After debridement, a three-wall angular bone defect in the apical area and a one-wall angular bone defect in the coronal area were observed in the mesial region of the first premolar. Granulation tissue in microconcavities on the inner surface of the bone defects had been removed, and more bleeding was observed than is caused by conventional mechanical debridement (C). The root surface was treated with ethylene-diamenetetraacetic acid and irrigated with saline, followed by EMD application to the root surface and autogenous bone graft placement into the bone defect (D). Er:YAG laser defocused irradiation without saline was applied to the grafted bone surface to enhance blood clot formation (E). At 12 months after surgery, the papilla and marginal gingiva were slightly recessed, but no interdental concavity or flap dehiscence had occurred during the healing process. Significant pocket reduction was observed: the mesial PPD 2 mm (CAL 3–4 mm) for the first premolar and mesial PPD 2–3 mm (CAL 3 mm) for the second premolar (F). At reentry surgery after periodontal regenerative treatment, dramatic bone regeneration included even the one-wall component of the defect in the interdental alveolar bone (G). A radiograph before surgery. Deep angular bone defects (arrow head) were noted in the mesial regions of the first and second premolars on preoperative radiographs (H). A radiograph taken 12 months after surgery showed that alveolar bone regeneration had reached the alveolar crest, including the one-wall defect region (I). (case by Y. T.)
[Modified pictures and legend from Taniguchi Y et al., Int J Periodontics Restrative Dent 36(4): 507-15, 2016 [66]; with permission.].

and mean CAL significantly improved from 7.5 mm to 3.4 mm, resulting in a CAL gain of 4.1 mm. Radiographs showed an increase in favorable opacity of the bone defect in all cases, and mean intrabony bone defect depth significantly improved from 6.4 mm (before surgery) to 1.1 mm at 12 months, achieving a 5.2-mm reduction. This novel procedure applying the Er:YAG laser for multiple purposes, including thorough decontamination of root surface and bone defect during debridement, as well as blood coagulation following autogenous bone grafting, induced sufficient bone regeneration and favorable and stable clinical outcomes in angular bone defects, including deep one-wall defects and areas of buccal bone dehiscence.

During Er-LBRT, the extent of required releasing incisions is much less compared to GTR, and thus post-operative swelling and pain, and oral vestibule narrowing tend to be reduced. Also, the risk of post-operative infection is reduced since the primary closure of flaps is easily achieved without major complications. Recently, during Er-LBRT, BGSs such as bovine bone mineral and carbonated apatite have also been employed instead of autogenous bone in clinical practice and favorable results have been obtained [77]. Lin et al. [78] treated a grade III furcation involvement using Er-LBRT with freeze dry bone allograft.

Although complete closure was not achieved, significant bone regeneration was observed in the furcation involvement bone defect.

Thus, the Er-LBRT procedure demonstrates sufficient bone regeneration in various types of severe bone defects [66]. Currently, Er-LBRT is also being applied to implant treatment, such as for ridge preservation, ridge augmentation, and peri-implantitis treatment, and favorable treatment outcomes were reported [77–81].

3.4. Minimally invasive approach using Er:YAG laser

In recent years, several techniques have been established in periodontal surgical treatment as "minimally invasive surgery" (MIS) involving the use of glasses with magnification and operating microscopes [73]. MISs have been developed to enhance wound healing and tissue regeneration following flap surgery. Trombelli et al. [82] reported

Fig. 6. Periodontal surgical procedure with a modified minimally invasive surgical technique using the Er:YAG laser. A 57-year-old female. After non-surgical periodontal treatment, a PPD of 5 mm mesio-buccal and 6 mm mesio-palatal remained on the maxillary right premolar (A). To minimize surgical invasion, only the buccal gingiva was elevated without elevating the interdental papillae following a modified minimally invasive surgical technique (M-MIST) design. The Er:YAG laser was used to perform gingival incision, removal of granulation tissue, and debridement of the root surface at 20 Hz and 80 mJ/pulse (panel setting) under water spray (B). Subsequently, defocused irradiation without water spray was performed on the surface of the clots (C, D). The flap was repositioned and sutured (E). At re-evaluation, 11 months postoperatively, A PPD of 2 mm and CAL gain of 4 mm were observed (F). A 2-mm PPD has been maintained for seven years postoperatively (G). On radiological examination, preoperatively, a deep intrabony defect (arrow head) was found at the mesial site of the first premolar (H). At 11 months postoperatively, radiopacity had increased from the bottom of the defect (I), and after three years, the defect was observed to appear to be filled with bony tissue (J). The newly formed tissue appearance was maintained after seven years (K). (case by K. M.)
[Modified pictures and legend from Mizutani K et al., Jpn J Conserv Dent, 63: 96–104, 2020 [89]; with permission. © copyright (2020) J Conserv Dent].

the single flap approach for intrabony defects, whose basic principle is the unilateral elevation of a limited mucoperiosteal flap facilitating wound stabilization and optimizing wound closure for primary intention healing. Cortellini et al. proposed the minimally invasive surgical technique (MIST) [83] and modified MIST (M-MIST) [84] as novel regenerative therapy for localized periodontal intrabony defects. They reported excellent clinical results by securing blood clot stability in the bone defects. Clinical studies have reported that the favorable healing associated with minimally invasive techniques has a beneficial influence on the outcome of regenerative therapy [83–85]. A recent systematic review has demonstrated that MISs are associated with superior periodontal tissue regeneration and less gingival recession than surgeries employing conventional flap designs [86].

Compared to mechanical therapy, Er:YAG laser debridement is advantageous in narrow and deep bone defects during MISs due to the high accessibility afforded by the laser's fine contact tips. In general, critical factors in wound healing of periodontal tissues involve stability of blood clots, migration and adhesion of cells to the root surface, and cell proliferation and differentiation. The Er:YAG laser-irradiated root [87] and bone surfaces [55] have better biocompatibility for blood clot adherence compared to the mechanically-treated surfaces, and coagulation of the clot surfaces with defocused irradiation can be stabilizing. The irradiated surrounding tissues may also be activated by the biostimulation effects of the laser.

Dyer and Sung [88] performed MIST combined with Er,Cr:YSGG laser for the treatment of periodontal pockets remaining following SRP and showed excellent treatment outcomes. They observed that with 7–9 mm initital PPD, the mean PPD and CAL improved from 7.5 ± 0.6 and 7.6 ± 0.6 mm at baseline to 3.7 ± 1.2 and 3.6 ± 1.2 mm at 2 years, respectively. We have also demonstrated favorable outcomes in the performance of M-MIST, using the Er:YAG laser, for intrabony defects [89] (Fig. 6). Thus, the Er:YAG laser may also be an effective and efficient adjunct in MISs in order to facilitate the procedures and obtain enhanced healing and regeneration.

3.5. Flapless surgery using Er:YAG laser

When considering postoperative wound healing, minimized flap elevation techniques like MIST and M-MIST would be advantageous, and these techniques suggest an important direction for regenerative therapy in localized small defects. Further, a systematic review and meta-analysis by Liu et al. [90] reported that there were no significant differences in treatment of intra-bony defects between the MIS with biomaterials group and the MIS alone group, and they discussed that there need to be in-depth investigations towards the induction of intrinsic postoperative tissue healing with MIS. Accordingly, when complete debridement is achieved during flapless surgery to the same degree as in the case of flap surgery, less invasive regenerative procedures with more favorable outcomes would be expected, compared to conventional MISs, as a minimally-invasive flapless regenerative surgery.

With blinded procedures, detection of subgingival calculus and granulation tissue, its debridement, and the subsequent confirmation of its removal are very important procedures. Regarding detection and confirmation of diseased soft tissue and calculus, further development of endoscopy may be ideally required in the future [91]. In terms of debridement methods, the use of conventional mechanical miniaturized devices/instruments is essential, and the complementary use of lasers would be effective in debriding the diseased tissue more precisely and completely, while inducing additional advantageous biostimulation effects in the surrounding tissues. In blinded conditions during flapless surgery, without the benefits (and disadvantages) of definitive open flap access, the effective treatment of pockets with thorough debridement of all internal pocket aspects would still need to be performed as well as, or better than, that achieved with direct surgical access.

In order to achieve this end, Aoki et al. [11,12] developed a novel treatment modality of flapless surgery implementing a combination of SRP and Er:YAG laser to perform comprehensive pocket management (Er:YAG laser-assisted comprehensive periodontal pocket therapy: Er-LCPT) of moderate to advanced periodontal pockets (Fig. 7).

Regarding the non-surgical use of the Er:YAG laser within pockets, a number of clinical studies have been published so far. Schwarz et al. [92, 93], Crespi et al. [94], and others reported positive results for Er:YAG laser pocket therapy. Sufficient consensus, however, has not yet been reached regarding its clinical effects. A recent American Academy of Periodontology consensus statement reported that laser therapy's benefits may be limited, but that, although not conclusive, some evidence suggests that adjunctive use of Er:YAG or Nd:YAG lasers is superior to conventional periodontal therapy alone in the case of deep periodontal pockets [95].

The authors consider that most previous results have lacked an intentional strategy for effective Er:YAG laser use in non-surgical treatment of periodontal pockets. Therefore, in the development of a new laser-assisted pocket therapy, we considered the specific purposes and manners in which the laser facilitates the achievement of the clinically demanding procedures involved with pocket treatment [33,96, 97].

The Er-LCPT procedure is fundamentally achieved with thorough debridement and decontamination as well as with increased bleeding arising from debrided bone surfaces to facilitate healing/regeneration, not as a non-surgical therapy, but rather as a flapless surgery [11,12] (Fig. 7). Simultaneously, intra-pocket irradiation induces stimulation/activation, including photobiomodulation (PBM), of the proximate gingival and bone tissues/cells [43–45,47,48,55,57,58]. Additionally, ablation of inflamed external gingival surfaces approximating periodontal pockets may be helpful for accelerated wound healing. The deepithelization of the external gingival surface allows delayed migration of epithelial tissue into the pocket during healing [98, 99]; while the ablated, rough gingival surface may be advantageous toward stabilizing the blood clot established at the pocket entrance. Final defocused irradiation enhances blood coagulation [100,101] at the pocket entrance, thereby facilitating the activation and further stabilization of clot formation, assuring its stable sealing of the pocket. This external epithelial removal and blood coagulation process may also activate the gingival tissue [43–45] and the blood clot [100,102](Fig. 8). Thus, LCPT intends to facilitate periodontal tissue attachment and regeneration by comprehensive pocket management [97]. LCPT is also effectively used for the treatment of initial and moderate peri-implantitis [12].

The method was invented originally for the treatment of residual pockets, because residual pockets are less responsive to conventional SRP and a comprehensive and extensive debridement is required to induce bleeding from surrounding tissues and thereby to obtain augmented wound healing potential, which may be necessary for inducing reorganization of periodontal tissues. The authors conducted a retrospective study using Er-LCPT for residual pocket treatment with PPD ≥ 5 mm from 2006 to 2009 and confirmed the safety and effectiveness of this procedure [96]. After 1 year, PPD significantly decreased from 6.4 ± 1.4 mm to 3.5 ± 1.3 mm (n = 40; 3.0 mm reduction), and CAL significantly decreased from 7.5 ± 1.6 mm to 5.2 ± 1.9 mm (n = 40; 2.3 mm gain). Furthermore, regarding single rooted teeth, 70.0% of the treated pockets showed pocket healing with PD ≤ 3 mm and BOP (-) after 12-month post-treatment.

Subsequently, we conducted an RCT study to assess the clinical effectiveness of Er-LCPT as compared to SRP only, using a split-mouth design, for the treatment of residual pockets with PPD ≥ 5 mm in 18 patients [97]. 12 months postoperatively, Er-LCPT demonstrated significantly higher PPD reduction, compared to SRP alone (Er-LCPT 2.78 mm vs. SRP 1.89 mm) with a 0.89 mm superior difference, as well as significantly higher CAL gain compared to SRP alone (Er-LCPT 1.67 mm vs. SRP 1.06 mm) with 0.61 mm superior difference. Later, by applying Er-LCPT in various cases, as shown in Fig. 8 as well, we found

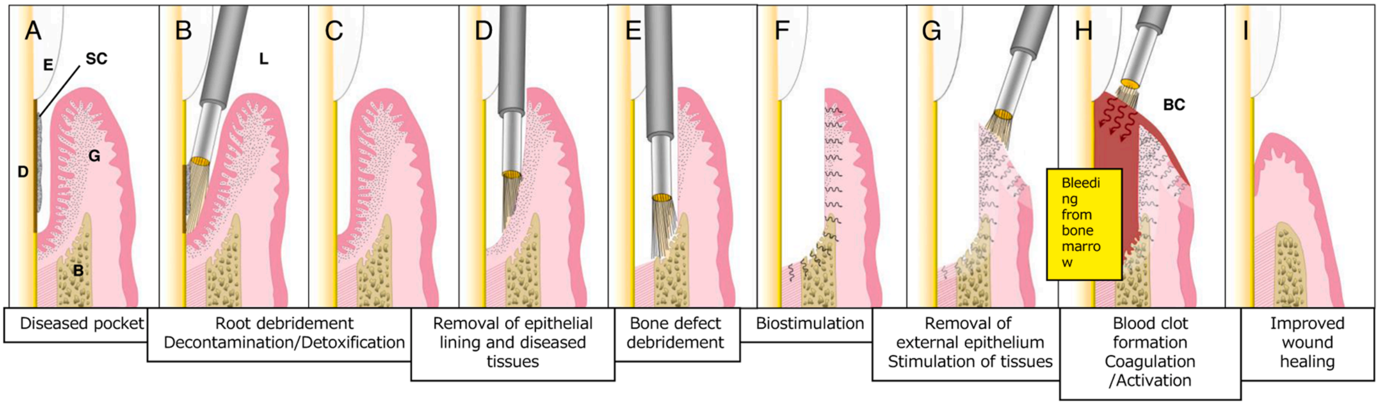

Fig. 7. Schematic illustration of the procedures of Er:YAG laser-assisted comprehensive periodontal pocket therapy (Er-LCPT). Advanced periodontal pocket showing a deep periodontal pocket with vertical bone resorption (A). Laser-assisted debridement following mechanical instrumentation of the diseased root surface for removal of subgingival calculus deposits and decontamination/detoxification of the root surface (B, C). Ablation of lining epithelium and diseased connective tissue on the inner surface of the gingival tissue as well as diseased connective tissue in the vertical bone defect during pocket irradiation for comprehensive treatment in combination with mini-curettes and Er:YAG laser. This aims to thoroughly decontaminate the whole pocket and induce increased bleeding in the bone defect from the bone surface (which may be advantageous for tissue regeneration) (D, E). Expected simultaneous thermal and photobiomodulation (PBM) effects activating the surrounding gingival and bone tissues by low-level laser penetration during high-level laser irradiation within the pocket (F). Laser ablation of the inflamed epithelial tissue on the external gingival surface. Depending on the case, the underlying connective tissue is also ablated to some extent helping in pocket depth reduction. Removal of epithelial tissue also helps prevent down-growth of epithelial tissue due to the immediate collapse of the epithelial end at the pocket entrance into the hollow space of the debrided pocket. Exposure of connective tissue delays epithelial tissue migration from the external surface into the pocket, and production of an ablated, rough soft tissue surface enhances retention of the blood clot formed at the pocket entrance, thereby assuring sealing of the pocket entrance. At the same time, stimulation of the surrounding gingival tissue from the external surface is expected by simultaneous PBM effect. It is acceptable to perform removal of external epithelial tissue as well as connective tissue before debriding the inside of the pocket (G). Blood clot (BC) coagulation at the pocket entrance by defocused irradiation without water spray to stabilize the BC formation and seal the pocket entrance. Use of diode or Nd:YAG lasers may be more advantageous for blood coagulation at deeper sites. It also intends to activate the blood clot and surrounding gingival tissue via the external surface (H). Favorable pocket healing with gingival tissue attachment and bone tissue regeneration (I). E: enamel of tooth crown, D: dentin of tooth root, SC: subgingival calculus, B: alveolar bone, G: gingival tissue, L: laser tip.
[Modified pictures and legend from Aoki A et al., Periodontol 2000 68(1): 217–69, 2015 [11]; with permission. © copyright (2015) John Wiley & Sons A/S].

that Er-LCPT can induce bone regeneration in moderate to advanced cases and may also be useful during initial active therapy before the surgical phase [11,12,96,97,103]. Depending on the circumstances, BARAs and BGSs may also be applied during the flapless surgery in order to minimize gingival recession and shrinkage by maintaining the original tissue volume and enhancing the regeneration as well. Also, a procedure similar to Er-LCPT, but using the Er,Cr:YSGG laser, has been advocated as the REPAIR™ protocols using the Er,Cr:YSGG laser by Biolase Inc [104].

Regarding the application of the Er,Cr:YSGG laser in minimally invasive and flapless surgeries, Al-Falaki et al. [105] conducted minimally invasive closed flap surgery, employing the Er,Cr:YSGG laser to treat periodontal pockets with intrabony defects, and reported that mean PPD diminished from 8.1 $\pm$ 1.9 mm initially to 2.4 $\pm$ 0.9 mm 5–8 months postoperatively, with a significant 5.7 mm reduction in intrabony defect depth. Clem et al. [104] performed a multi-center randomized trial showing that non-surgical (flapless surgical) procedures with Er,Cr:YSGG laser (REPAIR™ protocol) were comparable to MIST [104], and that laser therapy was superior in patient-reported outcomes such as anxiety, pain, and satisfaction.

Thus, it is suggested that the supplemental benefits of laser use for periodontal surgery may be applied to sites with smaller surgical fields, i.e., approximating non-surgical procedures, and that minimally invasive flapless surgery using erbium lasers is an effective treatment modality showing significant clinical improvement for moderate to advanced periodontal pockets.

4. Limitations and potential drawbacks in the application of Er:YAG laser for periodontal surgery

Er:YAG and Er,Cr:YSGG lasers have been increasingly applied in periodontal surgery; however, there exist several limitations for the use of erbium lasers in surgical procedures. The precise physical ablation effects without major thermal influences on the surrounding tissues are very useful regarding debriding root surfaces and bone defects during surgery, and promising aspects of erbium lasers for wound healing and bone regeneration have been reported [6,10–12]; however, available clinical studies are limited and their positive effects have not yet been scientifically and sufficiently clarified [11]. The degree to which they contribute to the promotion of wound healing and tissue regeneration, due to their high decontamination and biological stimulation effects, has not been clearly demonstrated in the clinic. The benefits, usefulness, and effectiveness, of erbium lasers over conventional instruments in open flap surgery or MIS needs to be investigated by further clinical RCT studies, including large-scale multi-center studies and multifaceted assessments of the efficacy of laser-assisted surgical therapy. The outcomes of bone regeneration with Er-LCPT during initial therapy, as well as that with Er-LBRT, need to be further evaluated. Even though the positive effects from the use of erbium lasers may not appear clinically robust, it is necessary to establish a timely consensus based on an accumulation of further clinical studies allowing a meaningful systematic review including meta-analysis.

From a clinical perspective in actual use, careless and/or excessive irradiation procedures may risk inducing defect formation on root surfaces and thermal damage of periodontal tissues, resulting in impairment of wound healing [8]. Furthermore, attention to details such as maintaining proper irradiation technique and irradiation parameters, as well as wearing goggles for eye protection, is necessary to prevent unfavorable wound healing and accidents [8] In particular, flapless surgery is fundamentally a technically demanding procedure requiring long-term clinical experiences in order to acquire the requisite diagnostic and technical skills in precise non-surgical and surgical periodontal modalities. In addition, erbium laser devices are very expensive necessitating a thorough cost–benefit analysis.

As for the biostimulation effects including PBM, basic research has, as of yet, only clarified a small part of the mechanisms, and most of the

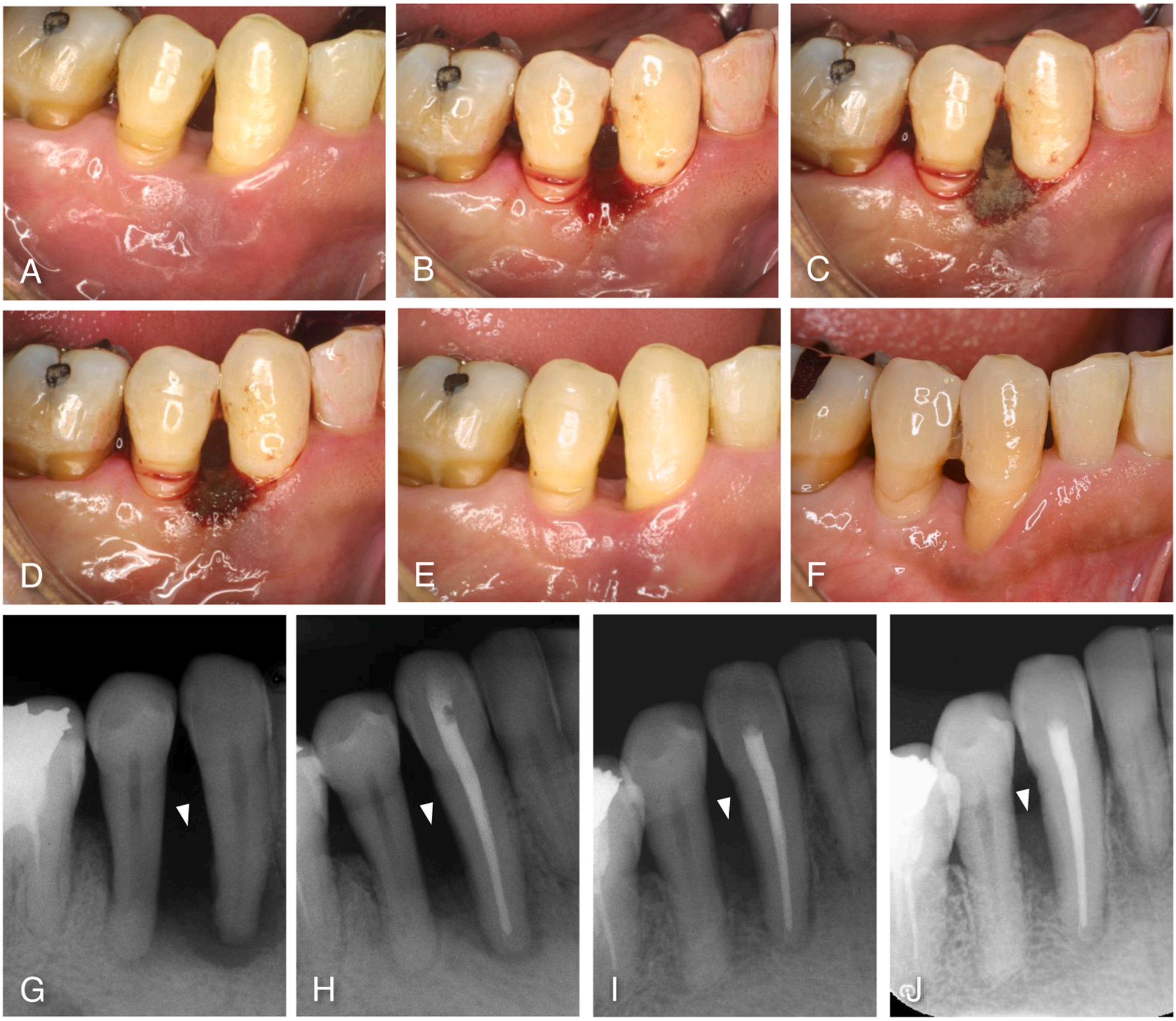

Fig. 8. Er:YAG laser-assisted comprehensive periodontal pocket therapy (Er-LCPT). A 58-year-old male. Before treatment (A), a 13-mm deep PPD (CAL 15 mm) with bleeding on probing (BOP) was detected at the distal site of the mandibular right canine. First, endodontic treatment was performed due to the presence of a perio-endo lesion. Initial periodontal therapy using an Er:YAG laser was performed prior to the planned regenerative surgery. The root surface was debrided by curette, ultrasonic scaler, and Er:YAG laser, and the inner surface of the gingival wall and bone defect was debrided by curette, micro-bone curette, and Er:YAG laser. Granulation tissue removal, root surface and bone defect debridement, and epithelial tissue removal were effectively and safely performed by Er:YAG laser at 30 Hz and 60–80 mJ/pulse (panel setting) in contact mode under water spray with 80° curved contact tips of diameter 400 and 600 μm. The buccal view immediately after pocket treatment as well as removal of external epithelial tissue shows bleeding without major thermal changes (B). Then, the pocket entrance as well as the surrounding gingival tissue were irradiated in non-contact, defocused mode without water spray and the blood was coagulated and slightly carbonized (C). The coagulated blood was stable after mouth rinsing and the pocket entrance was effectively sealed (D). After 1 week (E), wound healing was favorable and epithelialization was completed. Then, wound healing progressed uneventfully without any clinical complications. At five months, the gingival recession progressed slightly and the 6-mm PPD (CAL 8 mm) with BOP still remained; however, around 9 months the PPD was reduced to 3 mm (CAL 6 mm) without BOP and regenerative surgical therapy was postponed. Supportive therapy was initiated. Resin splinting was performed after 2 years. After 14 years (F), the condition was still maintained and finally the PPD reduced to 2 mm (CAL 6 mm) without BOP. A 11-mm PPD reduction and 9 mm CAL gain were obtained. Dental radiographs show that the original bone resorption (arrow head) at the first visit was severe and horizontal (G). After 8 months (H), 5 years (I), and 14 years (J). Bone regeneration gradually progressed and the bone defect was successfully repaired to some extent but the vertical increase was limited; however, no adverse side effects are observed in the irradiated bone tissue (case by A. A.).
[Modified pictures and legend from Aoki A et al., Periodontol 2000 68(1): 217–69, 2015 [11]; with permission. © copyright (2015) John Wiley & Sons A/S].

studies are still limited to in vitro experiments [42]. Blood coagulation procedures have been performed in the clinic, based on the clinical experiences of the operators, and the blood coagulation technique has shown clinically promising results for bone regeneration [66,77,78]. However, basic evidence of the promotion of granulation tissue formation with activated periodontal cells and platelets as well as enhanced angiogenesis, resulting in increased bone formation, has not yet been obtained in vivo. Further in vitro and in vivo studies are required to clarify those positive effects.

As a future strategy, since the PBM effects of erbium lasers are basically weak and delicate [11], the combination of erbium laser therapy with supplemental deeply penetrating lasers, such as diode or Nd:YAG, may allow basic and clinical enhancement of wound healing and tissue regeneration, by the strengthening of blood coagulation and PBM effects owing to the deeper tissue penetration provided by these supplemental lasers [11].

5. Conclusions and future directions

Currently, lasers are being increasingly integrated into conventional mechanical therapy, and favorable wound healing has been demonstrated following laser therapy for the treatment of periodontal disease. Based on the review of the literature, the erbium lasers are the most effective and efficient laser devices for tissue ablation during periodontal flap surgery as an alternative or adjunctive therapy to conventional mechanical treatment modalities.

At present, the available clinical evidence for the promotion of periodontal wound healing/tissue regeneration by erbium lasers is still limited and insufficient [106]. However, the erbium lasers offer a novel, effective technical approach during periodontal surgery, in particular, minimally invasive or flapless surgery. Lasers are completely different from mechanical devices and instruments and have several beneficial effects including biostimulation, allowing them to potentially play more important roles in the future.

Further basic and well-designed clinical studies are required to determine the technical equivalence or superiority of erbium laser application and its potential to improve the outcomes of periodontal surgical procedures. With a better understanding of the characteristics of laser/light as well as the development of laser/LED devices, the role of photonic energy in periodontal surgery is expected to expand in the future. Notwithstanding the above, further studies are required on the promotion of wound healing/tissue regeneration using photo-mediated periodontal tissue engineering with various sources of light energy.

Conflict of Interest

none.

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