

Application potential of therapeutic ultrasound in oral diseases

FANG WANG, PHD & DONG-DONG ZHANG, BED

ABSTRACT: Purpose: To review the literature on the application potential of ultrasound in the treatment of various oral and dental diseases. **Methods:** Two reviewers carried out a computer-based literature search using PubMed and Web of Science to identify papers published up to February 2025. The keywords used in the investigation were “therapeutic ultrasound”, “low-intensity pulsed ultrasound”, and various words related to oral and dental disease (oral submucosal fibrosis, burning mouth syndrome, periodontitis, orthodontic tooth movement, and tooth trauma or caries). **Results:** Therapeutic ultrasound, particularly low-intensity pulsed ultrasound (LIPUS), showed beneficial effects in interfering with pathological fibrosis, suppressing inflammatory responses, promoting periodontal tissue regeneration, and facilitating the repair of dentin-pulp complex injuries in oral and dental diseases. (*Am J Dent* 2025;38:263-266).

CLINICAL SIGNIFICANCE: Therapeutic ultrasound, particularly low-intensity pulsed ultrasound (LIPUS), showed beneficial effects in interfering with oral and dental diseases and may become an important adjunctive treatment modality in oral and dental medicine in the future.

✉: Dr. Fang Wang, Center for Cariology, Endodontics and Periodontics, School & Hospital of Stomatology, Wuhan University, Wuhan, China. E-mail: wangfang-nm@whu.edu.cn

Introduction

Oral and dental health are crucial components of the overall human well-being. Oral diseases affect many people worldwide, causing discomfort, pain, and functional impairments. Traditional treatment methods often have limitations in restoring oral tissue function and structure. Therefore, the exploration of novel therapeutic approaches is essential. Ultrasound has been widely applied in the clinical treatment of fractures and soft-tissue injuries.¹ It provides a safe and non-invasive mechanical stimulus. Initially, research focused on its thermal effects, but recently, the non-thermal effects, including cavitation and acoustic microstreaming, have attracted increasing attention.² These effects can trigger a series of biochemical reactions in target tissues, showing potential in promoting tissue regeneration, reducing inflammation, and modulating neural function.² This review comprehensively assessed the application potential of ultrasound in the treatment of various oral and dental diseases.

Oral submucosal fibrosis

Oral submucosal fibrosis (OSF) is a chronic, progressive, and potentially malignant disorder mainly caused by the habitual chewing of areca nuts. It is characterized by extensive submucosal fibrosis, a leathery texture of the oral mucosa, and restricted mouth opening.³ The pathogenesis of OSF involves abnormal excessive collagen deposition and reduced collagen degradation, leading to fibrosis.⁴ Additionally, there are significant changes in the immune microenvironment, with the activation of inflammatory mediators and growth factors.⁵

Clinical studies showed that ultrasound improved mouth opening in OSF patients when combined with conventional treatments. For example, Shil et al⁶ conducted a comparative study, equally dividing OSF patients into three groups: Group 1 received oral colchicine + intralesional hyaluronidase; Group 2, oral colchicine + intralesional hyaluronidase + therapeutic ultrasound; and Group 3, intralesional dexamethasone + hyaluronidase. For the group receiving therapeutic ultrasound, a MEDGEARS Therapeutic Ultrasound Machine (MG-68) was

used. The treatment parameters were set as follows: frequency of 3 MHz, pulsed mode with a 1:1 duty cycle, and intensity ranging from 1 to 2.5 Watt/cm². The therapy was administered for 10 minutes per session, over a 15-day period, with 1 allowable rest day per week. At 2nd-, 3rd-, and 6th-month follow-ups, the ultrasound group had significantly greater maximum mouth opening (P = 0.009, P = 0.001, P = 0.000), and tongue protrusion (P = 0.000, P = 0.000, P = 0.000). Dani & Patel⁷ reported that OSF patients who received ultrasound treatment at an intensity of 0.7 Watt/cm² for 7 minutes with a frequency of 3 MHz, combined with jaw-opening exercises, had a greater improvement in mouth opening (0.22 cm more) compared to the control group that only performed jaw-opening exercises. Raj et al⁸ treated OSF patients with three interventions: standalone ultrasound therapy, standalone active physiotherapy, or their combination. Therapeutic ultrasound (Physiotrack machine) used parameters: 1.5 Watt/cm² intensity, continuous mode, 3 MHz frequency, and 6 minutes per session. The combined therapy group showed the most substantial improvements in mouth opening (baseline: 22.63 ± 4.47 mm; 2 months: 24.39 ± 4.65 mm; P = 0.001) and cheek flexibility (baseline: 5.25 ± 2.36; 2 months: 6.85 ± 2.20; P = 0.001). Above all, the thermal effect of continuous-mode ultrasound plays a role in improving mouth opening. It can increase the temperature of the oral mucosa, separate collagen fibers, loosen and soften fibrous tissues, and reduce the stiffness of the oral mucosa.

Low-intensity pulsed ultrasound (LIPUS), with frequencies of 1-3 MHz and output in pulsed mode at intensities of 0.02-1 Watt/cm², had minimal thermal effects.¹ It mainly induces non-thermal physical effects such as cavitation and acoustic microstreaming, which can modulate signal-transduction pathways related to inflammation and fibrosis.¹ For instance, in vitro studies^{9,10} showed that LIPUS inhibited the gene expression of fibrosis-related factors (e.g., CTGF) and inflammatory mediators (e.g., IL-6, TNF- α). In animal models of fibrosis,¹¹⁻¹³ LIPUS suppressed the activation of the TGF- β 1 signaling pathway and the transformation of fibroblasts into myofibroblasts. These findings suggest that LIPUS may be effective in

attenuating the fibrotic process of OSF. However, more in-depth clinical studies are needed to confirm their long-term efficacy and safety.

Burning mouth syndrome

Burning mouth syndrome (BMS) is a chronic oral pain syndrome characterized by idiopathic orofacial pain and intraoral burning or dysesthesia. Its etiology is complex, involving peripheral and central neuropathies.¹⁴ Peripheral neuropathology is associated with a lower density of epithelial and subepithelial nerve fibers and the upregulation of certain ion channels in surviving nerve fibers.^{14,15} Trigeminal neuropathy is also considered a possible cause, with the hyperactivity of somatosensory fibers in the trigeminal nerve hypothesized to result from damage to taste fibers.^{14,16}

The treatment of BMS remains challenging, and current therapies, including topical and systemic drugs and non-pharmacological treatments, often yield variable and unsatisfactory results.¹⁷ Therapeutic ultrasound has shown potential in reducing pain. Savernini et al¹⁸ demonstrated in an experimental rat model of trigeminal neuropathic pain that three pulsed ultrasound applications with a 2-hour interval between each significantly reduced ipsilateral thermal hyperalgesia. The maximal effect occurred 24 hours after the first application, and the thermoneocceptive threshold returned to the initial level 48 hours after the third application. The device parameters used were a frequency of 1 MHz, a pulse frequency of 100 Hz, a pulse 1/5, and intensities of 0.3 and 0.4 Watt/cm² for 2 minutes; a stronger wave intensity led to a greater effect. Chen et al¹⁹ applied therapeutic ultrasound at a frequency of 1 MHz and intensities of 0.25, 0.5, or 1 Watt/cm² (100% on-off cycle) to a peripheral mono-neuropathic model for 5 minutes a day for 22 days. They found that neuropathic pain was attenuated only at the highest intensity, along with the inhibition of the expression of neurokinin-1 receptor, substance P, TNF- α , and IL-6 at the affected site. The analgesic effect of therapeutic ultrasound is thought to be related to its ability to suppress the expression of pro-inflammatory cytokines and neurotransmitter or neuro-modulator factors involved in pain.¹⁸⁻²⁰ However, the application of ultrasound in BMS treatment is still in the experimental stage, and more clinical trials are required to determine its optimal treatment parameters and efficacy.

Periodontal tissue reconstruction - Periodontitis

Periodontitis is a common oral disease characterized by the progressive inflammation and destruction of periodontal tissues, including the gingiva, alveolar bone, and periodontal ligament, which can ultimately lead to tooth loss.² The global burden of periodontitis has been increasing, with a prevalence reaching up to 99% from 1990 to 2019.²¹

Bone remodeling is a continuous process that requires appropriate biochemical and mechanical stimulations.² In periodontitis, the chronic inflammation disrupts the balance between bone formation and bone resorption in the alveolar bone.²² Guided tissue regeneration (GTR) technology is commonly used to treat periodontitis-related bone loss, but its clinical outcomes are limited by factors such as oral hygiene and the operator's skills.²³ LIPUS has shown potential in the treatment of periodontitis. Wang et al²⁴ conducted experiments on beagle

dogs with buccal alveolar bone defects. The results showed that the combined application of LIPUS (using parameters recommended by the FDA: a pulse frequency of 1.5 MHz, a pulse width of 200 μ s, a repetition of 1 kHz, an intensity of 30 mWatt/cm², 20 minutes a day) and GTR led to higher regenerated bone volume, bone surface, trabecular number, and trabecular thickness compared to GTR alone or no treatment. In another study²⁵ on periodontal disease models with Class II furcation involvement, LIPUS also showed a synergistic effect with GTR or periodontal flap surgery.

The regenerative potential of periodontal bone tissue comes from periodontal ligament cells (PDLs), which contain osteogenic progenitor cells and mesenchymal stem cells (MSCs), and gingival mesenchymal stem cells (GMSCs), a subset of gingival fibroblasts (GFs).² In vitro studies^{2,26} revealed that different intensities of LIPUS can regulate the behaviors of PDLs and periodontal ligament stem cells (PDLSCs) through various signaling pathways. Wang et al²⁷ found that LIPUS treatment promoted the homing of PDLSCs by upregulating the expression of TWIST1 and SDF-1. TWIST1 may act as a mechanical stress sensor during LIPUS-induced mechanotransduction. Human PDLs can perceive mechanical signals from LIPUS and translate them into signaling molecules that regulate osteogenic differentiation, such as MAPK pathway, FOXO1, and BMP pathway.²⁸⁻³¹ LIPUS-exposed GFs can also undergo osteogenic differentiation and contribute to periodontal bone regeneration.³² In addition, LIPUS can inhibit the expression of LPS-induced inflammatory cytokines in macrophages, protect alveolar bone from oxidative stress and endoplasmic reticulum stress, and regulate the anti-inflammatory mechanism of autophagy in PDLs.³³⁻³⁶ These effects create a favorable microenvironment for periodontal regeneration. However, further large-scale clinical trials are needed to optimize the treatment protocol and evaluate the long-term stability of the treatment effect.

Tooth movement and root resorption during orthodontic treatment

Orthodontic tooth movement (OTM) involves the remodeling of alveolar bone and periodontal ligament in response to applied forces.³⁷ LIPUS has the potential to modulate the outcomes of orthodontic force application and accelerate OTM. A retrospective clinical study³⁸ showed that the use of a LIPUS device (with FDA-recommended parameters) significantly reduced the number of days per tray worn and the overall treatment duration compared to appliance treatment alone. The mean rate of tooth movement in the LIPUS-treated side was also significantly higher than that in the control side in a prospective randomized controlled trial.³⁸ However, a split-mouth study³⁹ applying LIPUS at 3-week intervals found no significant difference in the rate of tooth movement between the experimental and placebo groups. The regulatory mechanisms of LIPUS for accelerating OTM have been explored. In an ex-vivo mandible slice organ culture model,⁴⁰ LIPUS treatment improved bone remodeling and enhanced the reparative ability of the cementum. Arai et al⁴¹ reported that LIPUS exposure increased the intermolar width and compensatory bone formation in a rat OTM model. Xue et al⁴² found that LIPUS significantly increased the OTM distance by stimulating the

HGF/Runx2/BMP-2 signaling pathway and RANKL expression in an orthodontic rat model.

Orthodontically-induced inflammatory root resorption (OIIRR) is a common complication during OTM, with a prevalence of 73%-80%.⁴³ LIPUS reduced OIIRR by altering OPG/RANKL ratio.^{44,45} Al-Dboush et al⁴⁶ reported that patients using clear aligner therapy and LIPUS had less volumetric root loss in teeth compared to those using clear aligner therapy alone. Other studies⁴⁷⁻⁴⁹ also found that LIPUS-exposed teeth had decreased resorption areas and resorption lacunae counts, with histologic evidence of hypercementosis on the resorbed root surface. These results suggest that LIPUS can optimize orthodontic treatment outcomes. However, the optimal application frequency and duration of LIPUS in orthodontic treatment still need to be further studied.

Tooth repair

The dentin-pulp complex has an endogenous repair mechanism. When it is damaged by severe tooth trauma or decay, the tertiary dentin is formed to protect the dental pulp.^{50,51} The formation of tertiary dentin involves the activation and recruitment of MSCs in the dental pulp, which then differentiate into odontoblast-like cells to regulate dentin production and mineralization.⁵⁰ Bioactive growth factors such as TGF- β 1 and VEGF play important roles in this process.^{50,52} Studies using in vitro⁵¹ and in vivo⁵² models showed that LIPUS can promote dentin formation. Exposure of the dentin-pulp complex to LIPUS upregulates the expression of TGF- β 1 and calcium ion transport-related proteins, which are involved in stimulating the secretion of extracellular matrix by odontoblasts and dentin mineralization. However, the long-term effects of LIPUS on the structure and function of the repaired dentin-pulp complex need to be further investigated.

Discussion

There are some limitations with LIPUS. The existing research on the application of ultrasound in oral diseases is relatively limited, and most of the evidence comes from in vitro and animal studies. The number of large-scale, high-quality randomized double-blinded clinical trials is insufficient, which makes it difficult to accurately evaluate the long-term efficacy and safety of ultrasound treatment. Moreover, the study designs and parameters used in different studies vary greatly, leading to inconsistent results. For example, in the study of orthodontic tooth movement, different application frequencies and intensities of LIPUS resulted in different effects on tooth movement and root resorption. The lack of a unified standard for ultrasound application parameters also makes it difficult to compare and generalize the research results.

Future research directions should address these limitations; they should also focus on conducting more large-scale, randomized double-blind clinical trials. These trials should be designed to compare the efficacy of ultrasound treatment with traditional treatment methods and to determine the optimal treatment parameters for different oral and dental diseases. In addition, more in-depth basic research is needed to further clarify the biophysical mechanisms underlying the effects of ultrasound on oral tissues. Comparative studies can be carried out to explore the differences in the responses of different cell

types and tissues to ultrasound, which will help to optimize the treatment protocol and improve the treatment effect.

In conclusion, therapeutic ultrasound, particularly LIPUS, has shown beneficial effects in interfering with pathological fibrosis, suppressing inflammatory responses, promoting periodontal tissue regeneration, and facilitating the repair of dentin-pulp complex injuries in oral and dental diseases. However, its clinical application in these fields is still in the initial stage. To fully use ultrasound in oral and dental treatments, more high-quality research is required. This includes well-designed clinical trials to provide solid evidence-based support and in-depth basic research to understand the underlying mechanisms better. By addressing the current limitations, ultrasound may become an important adjunctive treatment modality in oral and dental medicine in the future.

Disclosure statement: The authors declared no conflict of interest. This work was supported by a grant from the National Natural Science Foundation of China (No. 82201067).

Dr. Fang is a Research Fellow, State Key Laboratory of Oral & Maxillofacial Reconstruction and Regeneration, Key Laboratory of Oral Biomedicine Ministry of Education, Hubei Key Laboratory of Stomatology, School & Hospital of Stomatology, Wuhan University, China and Associate Chief Physician, Center for Cariology, Endodontics and Periodontics, Optical Valley Branch, School & Hospital of Stomatology, Wuhan University, China. Mr. Zhang is Technologist-in-Charge, Department of Neurological Rehabilitation, Zhongnan Hospital of Wuhan University, Wuhan University, China.

References

- Jiang X, Savchenko O, Li Y, Qi S, Yang T, Zhang W, Chen J. A review of low-intensity pulsed ultrasound for therapeutic applications. *IEEE Trans Bio-Med Med Eng* 2019;66:2704-2718.
- Aimajiang M, Liu Y, Zhang Z, Qin Q, Liu M, Abulikemu P, Liu L, Zhou Y. LIPUS as a potential strategy for periodontitis treatment: A review of the mechanisms. *Front Bioeng Biotechnol* 2023;11:1018012.
- Warnakulasuriya S, Kujan O, Aguirre-Urizar JM, Bagan JV, González-Moles M, Kerr AR, Lodi G, Mello FW, Monteiro L, Ogden GR, Sloan P, Johnson NW. Oral potentially malignant disorders: A consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer. *Oral Dis* 2021;27:1862-1880.
- Shetty SS, Sharma M, Kabekkodu SP, Kumar NA, Satyamoorthy K, Radhakrishnan R. Understanding the molecular mechanism associated with reversal of oral submucous fibrosis targeting hydroxylysine aldehyde-derived collagen cross-links. *J Carcinog* 2021;20:9.
- Wang L, Tang Z. Immunopathogenesis of oral submucous fibrosis by chewing the areca nut. *J Leukoc Biol* 2022;111:469-476.
- Shil M, Goswami P, Gaikwad TV, Jadaun G, Sridhar T, Bandyopadhyay B, Surana P. Efficacy of oral colchicine and intralesional hyaluronidase with and without ultrasound therapy in the management of oral submucous fibrosis - A comparative study. *J Pharm Bioallied Sci* 2024;16:S586-S588.
- Dani VB, Patel SH. The effectiveness of therapeutic ultrasound in patients with oral submucosal fibrosis. *Indian J Cancer* 2018;55:248-250.
- Raj A, M Bhambal A, Choudhary P, D Sathe R, Upadhyay K, Mishra P. Echoes of healing: Evaluating therapeutic ultrasound in oral submucous fibrosis - An experimental study. *Bioinformation*. 2025;21:467-470.
- Kitagawa T, Kawahata H, Aoki M, Kudo S. Inhibitory effect of low-intensity pulsed ultrasound on the fibrosis of the infrapatellar fat pad through the regulation of HIF-1 α in a carrageenan-induced knee osteoarthritis rat model. *Biomed Rep* 2022;17:79.
- Itaya N, Yabe Y, Hagiwara Y, Kanazawa K, Koide M, Sekiguchi T, Yoshida S, Sogi Y, Yano T, Tsuchiya M, Saijo Y, Itoi E. Effects of low-intensity pulsed ultrasound for preventing joint stiffness in immobilized knee model in rats. *Ultrasound Med Biol* 2018;44:1244-1256.
- Aibara Y, Nakashima A, Kawano K, Yusoff F, Mizuki F, Kishimoto S, Kajikawa M, Maruhashi T, Higashi Y. Daily low-intensity pulsed ultrasound ameliorates renal fibrosis and inflammation in experimental hypertensive and diabetic nephropathy. *Hypertension* 2020;76:1906-1914.
- Liao B, Guan M, Tan Q, Wang G, Zhang R, Huang J, Liu M, Chen H, Li K, Bai D, Zhu Y. Low-intensity pulsed ultrasound inhibits fibroblast-like syno-

- viocyte proliferation and reduces synovial fibrosis by regulating Wnt/ β -catenin signaling. *J Orthop Translat* 2021;30:41-50.
13. Zhao K, Zhang J, Xu T, Yang C, Weng L, Wu T, Wu X, Miao J, Guo X, Tu J, Zhang D, Zhou B, Sun W, Kong X. Low-intensity pulsed ultrasound ameliorates angiotensin II-induced cardiac fibrosis by alleviating inflammation via a caveolin-1-dependent pathway. *J Zhejiang Univ Sci B* 2021;22:818-838.
 14. Russo M, Crafa P, Guglielmetti S, Franzoni L, Fiore W, Di Mario F. Burning mouth syndrome etiology: A narrative review. *J Gastrointest Liver Dis* 2022;31:223-228.
 15. Teruel A, Patel S. Burning mouth syndrome: A review of etiology, diagnosis, and management. *Gen Dent* 2019;67:24-29.
 16. Feller L, Fourie J, Bouckaert M, Khammissa RAG, Ballyram R, Lemmer J. Burning mouth syndrome: Aetiopathogenesis and principles of management. *Pain Res Manag* 2017;2017:1926269.
 17. Nosratzahi T. Burning mouth syndrome: A review of therapeutic approach. *J Complement Integr Med* 2021;19:83-90.
 18. Savernini Á, Savernini N, de Amaral FA, Romero TR, Duarte ID, de Castro MS. Assay of therapeutic ultrasound induced-antinociception in experimental trigeminal neuropathic pain. *J Neurosci Res* 2012;90:1639-1645.
 19. Chen YW, Tzeng JI, Huang PC, Hung CH, Shao DZ, Wang JJ. Therapeutic ultrasound suppresses neuropathic pain and upregulation of substance P and neurokinin-1 receptor in rats after peripheral nerve injury. *Ultrasound Med Biol* 2015;41:143-150.
 20. Huang PC, Tsai KL, Chen YW, Lin HT, Hung CH. Exercise combined with ultrasound attenuates neuropathic pain in rats associated with downregulation of IL-6 and TNF- α , but with upregulation of IL-10. *Anesth Analg* 2017;124:2038-2044.
 21. Wu L, Zhang SQ, Zhao L, Ren ZH, Hu CY. Global, regional, and national burden of periodontitis from 1990 to 2019: Results from the Global Burden of Disease study 2019. *J Periodontol* 2022;93:1445-1454.
 22. Usui M, Onizuka S, Sato T, Kokabu S, Ariyoshi W, Nakashima K. Mechanism of alveolar bone destruction in periodontitis - Periodontal bacteria and inflammation. *Jpn Dent Sci Rev* 2021;57:201-208.
 23. Vaquette C, Pilipchuk SP, Bartold PM, Huttmacher DW, Giannobile WV, Ivanovski S. Tissue engineered constructs for periodontal regeneration: Current status and future perspectives. *Adv Healthc Mater* 2018;7:e1800457.
 24. Wang Y, Qiu Y, Li J, Zhao C, Song J. Low-intensity pulsed ultrasound promotes alveolar bone regeneration in a periodontal injury model. *Ultrasonics* 2018;90:166-172.
 25. Wang Y, Chai Z, Zhang Y, Deng F, Wang Z, Song J. Influence of low-intensity pulsed ultrasound on osteogenic tissue regeneration in a periodontal injury model: X-ray image alterations assessed by micro-computed tomography. *Ultrasonics* 2014. 54: 1581-1584.
 26. Tanaka E, Kuroda S, Horiuchi S, Tabata A, El-Bialy T. Low-intensity pulsed ultrasound in dentofacial tissue engineering. *Ann Biomed Eng* 2015;43:871-886.
 27. Wang Y, Li J, Qiu Y, Hu B, Chen J, Fu T, Zhou P, Song J. Low-intensity pulsed ultrasound promotes periodontal ligament stem cell migration through TWIST1-mediated SDF-1 expression. *Int J Mol Med* 2018;42:322-330.
 28. Zhang N, Chow SK, Leung KS, Cheung WH. Ultrasound as a stimulus for musculoskeletal disorders. *J Orthop Translat* 2017;9:52-59.
 29. Ren L, Yang Z, Song J, Wang Z, Deng F, Li W. Involvement of p38 MAPK pathway in low intensity pulsed ultrasound induced osteogenic differentiation of human periodontal ligament cells. *Ultrasonics* 2013;53:686-690.
 30. Chen D, Xiang M, Gong Y, Xu L, Zhang T, He Y, Zhou M, Xin L, Li J, Song J. LIPUS promotes FOXO1 accumulation by downregulating miR-182 to enhance osteogenic differentiation in hPDLCS. *Biochimie* 2019;165:219-228.
 31. Yang Z, Ren L, Deng F, Wang Z, Song J. Low-intensity pulsed ultrasound induces osteogenic differentiation of human periodontal ligament cells through activation of bone morphogenetic protein-smad signaling. *J Ultrasound Med* 2014;33:865-873.
 32. Mostafa NZ, Uludağ H, Varkey M, Dederich DN, Doschak MR, El-Bialy TH. In vitro osteogenic induction of human gingival fibroblasts for bone regeneration. *Open Dent J* 2011;5:139-145.
 33. Zhang X, Hu B, Sun J, Li J, Liu S, Song J. Inhibitory effect of low-intensity pulsed ultrasound on the expression of lipopolysaccharide-induced inflammatory factors in U937 cells. *J Ultrasound Med* 2017;36:2419-2429.
 34. Ying S, Tan M, Feng G, Kuang Y, Chen D, Li J, Song J. Low-intensity pulsed ultrasound regulates alveolar bone homeostasis in experimental periodontitis by diminishing oxidative stress. *Theranostics* 2020;10:9789-9807.
 35. Li H, Deng Y, Tan M, Feng G, Kuang Y, Li J, Song J. Low-intensity pulsed ultrasound upregulates osteogenesis under inflammatory conditions in periodontal ligament stem cells through unfolded protein response. *Stem Cell Res Ther* 2020;11:215.
 36. Li Y, Sun C, Feng G, He Y, Li J, Song J. Low-intensity pulsed ultrasound activates autophagy in periodontal ligament cells in the presence or absence of lipopolysaccharide. *Arch Oral Biol* 2020;117:104769.
 37. Li Y, Zhan Q, Bao M, Yi J, Li Y. Biomechanical and biological responses of periodontium in orthodontic tooth movement: Up-date in a new decade. *Int J Oral Sci* 2021;13:20.
 38. Kaur H, El-Bialy T. Shortening of overall orthodontic treatment duration with low-intensity pulsed ultrasound (LIPUS). *J Clin Med* 2020;9:1303.
 39. Qamruddin I, Alam MK, Mahroof V, Karim M, Fida M, Khamis MF, Husein A. Biostimulatory effects of low-intensity pulsed ultrasound on rate of orthodontic tooth movement and associated pain, applied at 3-week intervals: A split-mouth study. *Pain Res Manag* 2021;2021:6624723.
 40. Alshihah N, Alhadlaq A, El-Bialy T, Aldahmash A, Bello IO. The effect of low intensity pulsed ultrasound on dentoalveolar structures during orthodontic force application in diabetic ex-vivo model. *Arch Oral Biol* 2020;119:104883.
 41. Arai C, Kawai N, Nomura Y, Tsuge A, Nakamura Y, Tanaka E. Low-intensity pulsed ultrasound enhances the rate of lateral tooth movement and compensatory bone formation in rats. *Am J Orthod Dentofacial Orthop* 2020;157:59-66.
 42. Xue H, Zheng J, Cui Z, Bai X, Li G, Zhang C, He S, Li W, Lajud SA, Duan Y, Zhou H. Low-intensity pulsed ultrasound accelerates tooth movement via activation of the BMP-2 signaling pathway. *PLoS One* 2013;8:e68926.
 43. El-Bialy T, Farouk K, Carlyle TD, Wiltshire W, Drummond R, Dumore T, Knowlton K, Tompson B. Effect of low intensity pulsed ultrasound (LIPUS) on tooth movement and root resorption: A prospective multicenter randomized controlled trial. *J Clin Med* 2020;9:804.
 44. Liu Z, Xu J, E L, Wang D. Ultrasound enhances the healing of orthodontically induced root resorption in rats. *Angle Orthod* 2012;82:48-55.
 45. Gul Amuk N, Kurt G, Guray E. Effects of photobiomodulation and ultrasound applications on orthodontically induced inflammatory root resorption; transcriptional alterations in OPG, RANKL, Cox-2: An experimental study in rats. *Photomed Laser Surg* 2018;36:653-659.
 46. Al-Dboush R, Rossi A, El-Bialy T. Impact of low intensity pulsed ultrasound on volumetric root resorption of maxillary incisors in patients treated with clear aligner therapy: A retrospective study. *Dental Press J Orthod* 2023;28:e2321252.
 47. El-Bialy T, El-Shamy I, Graber TM. Repair of orthodontically induced root resorption by ultrasound in humans. *Am J Orthod Dentofacial Orthop* 2004;126:186-193.
 48. Raza H, Major P, Dederich D, El-Bialy T. Effect of low-intensity pulsed ultrasound on orthodontically induced root resorption caused by torque: A prospective, double-blind, controlled clinical trial. *Angle Orthod* 2016;86:550-557.
 49. Al-Daghreer S, Doschak M, Sloan AJ, Major PW, Heo G, Scurtescu C, Tsui YY, El-Bialy T. Effect of low-intensity pulsed ultrasound on orthodontically induced root resorption in beagle dogs. *Ultrasound Med Biol* 2014;40:1187-1196.
 50. Scheven BA, Shelton RM, Cooper PR, Walmsley AD, Smith AJ. Therapeutic ultrasound for dental tissue repair. *Med Hypotheses* 2009;73:591-593.
 51. Zuo J, Zhen J, Wang F, Li Y, Zhou Z. Effect of low-intensity pulsed ultrasound on the expression of calcium ion transport-related proteins during tertiary dentin formation. *Ultrasound Med Biol* 2018;44:223-233.
 52. Wang F, Li Y, Yang Z, Lu K, Zuo J, Zhou Z. Effect of low-intensity pulsed ultrasound on a rat model of dentin-dental pulp injury and repair. *Ultrasound Med Biol* 2017;43:163-175.