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REVIEW

Progress in the application of ablative fractional lasers in chronic wounds

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Abstract
This literature review aims to explore the application of ablative fractional laser in chronic wound healing, focusing on its clinical efficacy and mechanisms of action. Additionally, it summarizes the various lasers and parameters utilized by the authors in their studies. A comprehensive literature search was conducted for studies published between 2008 and 2025 in the Google Scholar, Web of Science, Medline, and PubMed databases, using the keywords: Fractional, Laser, Chronic Wounds, Ulcers, Healing. A substantial body of evidence suggests that carbon dioxide (CO_2) and erbium: yttrium aluminum garnet (Er: YAG) lasers can significantly accelerate the healing of chronic wounds. However, treatment protocols vary considerably across studies, particularly in terms of treatment frequency, power output, and energy density. This lack of standardization makes it challenging to compare outcomes directly and to determine optimal treatment parameters. The majority of studies conclude that CO_2 and Er: YAG laser therapies effectively promote the repair of chronic wounds. Proposed mechanisms include precise debridement, reduction of bacterial burden, improved local perfusion, enhanced transdermal drug delivery, and activation of key signaling pathways, such as Transforming growth factor-β/smad(TGF-β/Smad). Further research is needed to establish standardized treatment protocols and identify the most effective laser parameters for clinical use.

Clinical trial number
Not applicable.

Keywords Fractional · Laser · Chronic wounds · Ulcers · Healing

Abbreviations

AF	Ablative fractional
CO2	Carbon dioxide
Er:YAG	Erbium: yttrium aluminum garnet
TGF-β/Smad	Transforming growth factor-β/smad
SP	Selective photothermolysis
FP	Fractional Photothermolysis
MTZ	Microscopic treatment zones
RDEB	Recessive Dystrophic Epidermolysis Bullosa
PRP	Platelet-rich plasma
NPWT	Endoscopic negative pressure wound therapy
PDT	Photodynamic therapy
HSPs	Heat shock proteins

Introduction

Chronic wounds are wounds that, despite standardized systemic treatment, fails to achieve complete structural and functional repair within the expected timeframe. Clinically, they are commonly defined as wounds that do not shrink by 10–15% per week or fail to reduce by 30% within one month, irrespective of the underlying cause [1]. A key pathological feature of chronic wounds is poor local perfusion,

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Table 1 Summary of published applications of ablative fractional lasers in chronic wounds

Laser type	Age(years)	Causes of wounds	Description of the wound	Wound duration	Device information	Laser settings	Total number of treatments, treatment intervals	Recovery time after laser treatment (adverse effects)	author
CO_2	26	The explosion resulted in bilateral supra-knee amputation and right supraelbow amputation	Multiple unhealed erosions and ulcers on the right amputated stump with fragile skin and limited mobility	5 months	Deep FX(UltraPulse Encore; Lumenis, Ltd)	50 mJ	2 times, 8 weeks apart	All wounds healed almost completely within 2 months	Shumaker et al.(2012) [15]
	28	The explosion resulted in bilateral above-knee amputation	There is a persistent erosion at the right amputated stump with contractile erythematous skin	6 months	Deep FX (UltraPulse Encore; Lumenis, Ltd)	30 mJ	2 times, 8 weeks apart	Complete healing in 6 days	Shumaker et al.(2012) [15]
	39	The blast injuries resulted in amputation of the right arm and distal hand and burns to 30% of the body surface area	Persistent ulceration and scar contraction on the outside of the right elbow and distal forearm	60 months	Deep FX(UltraPulse Encore; Lumenis, Ltd)	50 mJ and 30 mJ	3 times, 6 weeks apart	With treatment, the ulcer gradually heals and the skin elasticity and range of motion improve significantly	Shumaker et al.(2012) [15]
CO_2	70	The car accident resulted in a wound on the back of the left foot	There was an ulcer of 3.0 × 1.7 cm on the instep of the left foot	3 months	Deep FX(Lumenis Ltd)	30 mJ at the base of the wound and 50 mJ from the surrounding skin, 5% density	1 time	Complete healing in 6 weeks	Phillips et al.,(2015) [16]
	70	After surgery for basal cell carcinoma of the right lower leg	The wound is 1.5 × 1.5 cm	11 weeks	Deep FX(Lumenis Ltd)	30 mJ at the base of the wound and 50 mJ from the surrounding skin, 5% density	1 time	Complete healing in 3 weeks	Phillips et al.(2015) [16]
	90	Squamous cell carcinoma of the right lower leg after surgery	The wound size is 2.2 × 1.7 cm	7 weeks	Deep FX(Lumenis Ltd)	30 mJ at the base of the wound and 50 mJ from the surrounding skin, 5% density	1 time	Complete healing in 3 weeks	Phillips et al.(2015) [16]

Table 1 (continued)

Laser type	Age(years)	Causes of wounds	Description of the wound	Wound duration	Device information	Laser settings	Total number of treatments, treatment intervals	Recovery time after laser treatment (adverse effects)	author
CO 2	8	Scar contracture after burns and chemical burns	There is an unhealed wound with a diameter of 1.2 cm in the scar contracture area of the left forearm	8 months	Deep FX(UltraPulse® Lumenis)	50 mJ (ablation depth of about 1.5 mm), 5% density	2 times, 2 months apart	The wound is almost completely epithelialized at 2 months and the wound is completely healed at 4 months	Krakowski et al.(2016) [17]
	17	Cryotherapy of warts with liquid nitrogen causes the wound to not heal	Two unhealed wounds on the distal end of the left tibia, the smaller one is 1.5 cm in diameter and the larger one is 2 cm in diameter, with a maximum depth of 2.2 mm	6 months	Deep FX(UltraPulse® Lumenis)	50 mJ at 5% density	2 times, 1 month apart	The wound healed completely in 2 months	Krakowski et al.(2016) [17]
CO 2	22	Dystrophic epidermolysis bullosa	There is a non-inflammatory ulcer about 7 cm in diameter in the left upper back	9 months	Deep FX(UltraPulse® Lumenis)	30 mJ, 5% density	2 times, 4 weeks apart	At 8 weeks, the wound is almost completely epithelialized	Krakowski et al.(2016) [18]
CO 2	74.8 ± 8.2	Nerve ischemic ulcer	Ulcers that expose bone tissue	CO2 laser alone treatment group: 3.6 ± 3.5 months, CO2 laser combined with PRP treatment group: 12.2 ± 4.4 months	SmartXide2 C80(DEKA, Florence, Italy)	4 J, 80 W, 9 spot/cm²	Up to 6 sessions, 1 week apart	CO2 laser treatment alone: 4 patients healed completely within 3 months, and 1 patient formed granulation tissue covering the entire bone surface within 3 months Two patients in the CO2 laser combined with PRP treatment group had complete healing within 3 months, and two patients had formed granulation tissue covering the entire bone surface within 3 months. No serious adverse effects were reported in both groups.	Matteo Monami et al.(2017) [19]

Table 1 (continued)

Laser type	Age(years)	Causes of wounds	Description of the wound	Wound duration	Device information	Laser settings	Total number of treatments, treatment intervals	Recovery time after laser treatment (adverse effects)	author
CO 2	18–75	Chronic trauma (20 cases of infectious wounds, 2 venous ulcers, 1 diabetic ulcer).	The wound area is 2～20 cm², and there are edema, granulation tissue hyperplasia and necrotic tissue	>30 days	ML-2030CI (Wuhan Miracle Laser Technology Co., Ltd.)	60–140 mJ	Treatment should be performed 1 to 4 days apart until complete epithelialization of the wound has stopped	The healing rate after treatment was significantly higher than that in the traditional surgical debridement group	Bo Jiang et al. (2020) [20]
	18–75	Chronic trauma (various etiologies)	Wounds with an area of 2 to 20 cm² involving full-thickness skin damage	>6 weeks	ML-2030CI (Wuhan Miracle Laser Technology Co., Ltd.)	60–140 mJ	Once a day (for the first 3 days), Do it every 1–4 days (after 3 days).	The healing time was significantly shorter in the laser treatment group compared to the usual care group	Bo Jiang et al. (2021) [21]
CO 2	52–58	Chronic trauma (various etiologies)	There were different degrees of necrotic tissue and aging granulation tissue on the wound surface, and the wound area was ±2 cm²	±2 months	SmartXide2 C80 (DEKA)	15 W, 100 Hz, 3～5 pinholes/cm density (adjusted according to the wound condition).	repeatedly	The healing time was significantly shorter compared to the standard treatment group	Guan et al.(2022) [22]
	53	Pressure ulcers caused by long-term wheelchair use	Sinus tract wound, the sinus wall is pale, edematous, fibrotic, 0.5 cm × 0.5 cm in the external orifice, and about 3.5 cm in depth	Not explicitly mentioned	SmartXide2 CO_2 laser (DEKA)	8 W and 5 W	3 times	Heals within 35 days	Tang et al.(2022) [23]
	50–76	Chronic trauma (10 venous, 9 traumatic, 8 diabetic, 5 compressive)	The wound is located in the calf, thigh, lumbosacral region, foot, etc., and the wound area is 2 × 2～5 × 5 cm	N/A (meeting diagnostic criteria for chronic wounds).	N/A	180 mJ, Dot spacing 1.2 mm	1 time a week until the wound is completely healed	On the 7th, 14th and 21st days of treatment, the wound healing rate was significantly higher than that of the control group	LIU Yifeng & LIU Pinghong (2024) [24]

Table 1 (continued)

Laser type	Age(years)	Causes of wounds	Description of the wound	Wound duration	Device information	Laser settings	Total number of treatments, treatment intervals	Recovery time after laser treatment (adverse effects)	author
CO_2	18–85	Diabetic foot, acute trauma, refractory wounds, deep burns, etc.	Some wounds have bone tissue exposed, and the wound area is 2 ~ 18 cm^2	At least 1 month	ML-2030CI (Wuhan Miracle Laser Technology Co., Ltd.)	25 mJ, 25 W, Dot spacing 2 ~ 5 mm	Multiple treatments	On days 4, 8, 12, 16 and 20, the wound healing rate was significantly higher with laser treatment than without laser treatment	Jiang et al.(2024) [25]
	16 ~ 66	Chronic wounds	The wound area is 3 ~ 12 cm2	4 weeks and above	ML-2030CI (Wuhan Miracle Laser Technology Co., Ltd.)	60 ~ 140 mJ (adjusted according to the wound condition).	Several laser treatments until fresh tissue appears	Compared with the standard treatment group, the healing time was significantly shorter (adverse reactions: burns in one case, redness and swelling in one case).	YU Peng & YU Peng(2024) [26]
CO_2	45.82 ± 8.49 in the conventional group and 47.38 ± 7.41 in the improved group	Acute wounds become chronic, chronic wounds of specific etiology (e.g., diabetic foot ulcers, etc.), chronic wounds caused by constant external pressure or friction	Not explicitly mentioned	More than 1 month	N/A	30 mJ, 30w, 50% density, spot size: 1 mm (conventional group), 2 mm (modified group)	1 time per week, 3 times as a course of treatment	The CO_2 fractional laser with 2 mm spot was better than 1 mm spot in the treatment of refractory wounds (adverse reactions: 1 case of pain and 2 cases of rash in the conventional group. In the modified group, there were 2 cases of pain, 1 case of itching, and 1 case of rash).	Mengxiao WANG & Mengxiao WANG(2025) [27]
Er: YAG	56–78	Chronic wounds	N/A	At least 3 months	Smart2940Dplus(DEKA)	300 mJ, 10 Hz frequency, Spot diameter 3 mm, pulse duration, 350 µsec	N/A	90% of patients had complete wound healing after an average of 2.5 months of treatment	Mezzana et al.(2008) [30]

Table 1 (continued)

Laser type	Age(years)	Causes of wounds	Description of the wound	Wound duration	Device information	Laser settings	Total number of treatments, treatment intervals	Recovery time after laser treatment (adverse effects)	author
Er: YAG	18–89	Diabetic foot ulcers	Full-thickness lesions of the skin, with an average wound area of 6.94 square centimeters	At least 4 weeks	Joule ProFractional 2940 nm	22% density Spot size430µm, debridement time30s	1 time per week	After 4 weeks of treatment, the wound area was reduced by 63.5%, and at 12 weeks, 50% of the wounds were completely healed	Johnson et al.(2019) [32]
	69	Traumatic scar with non-healing ulcers	Multiple chronic, non-healing ulcers in the abdomen with surrounding scarring	2 years	Sciton Profractional, Palo Alto, CA	162.5–187.5 J/cm², 5.5% density	4 times, 6~8 weeks apart	Complete healing after the 4th treatment (no adverse effects observed).	Mehrabi & Kelly(2020) [33]
	The average age is 68	Chronic wounds (7 cases with venous disease, 2 cases with diabetes mellitus, 3 cases with other types)	Chronic, non-healing ulcers with surrounding scarring	Less than 50% reduction in wound surface area over a 4-week period	JOULE®(Sciton, Inc.,Palo Alto, CA)	50 J/cm², 50% spot overlap, Dot spacing 4 mm, pattern repeat 0.5s	1 time	The average wound size decreases at week 2	Hajhosseini et al.(2020) [34]
Er: YAG	43	Arterial lesions of the lower extremities	Recalcitrant foot ulcers	3 months	XR Dynamis(Fotona, Ljubljana, Slovenia)	8–10 J/cm², 100µsec pulse width, 10 Hz frequency(Second treatment: 22 J/cm2, 300µsec pulse width)	4 times, 2 weeks apart	At the 9th week of treatment, the size of the ulcer decreased significantly	Botsali et al.(2021) [35]
	40–90	Arterial ulcer (13 cases) Immune ulcer (9 cases) Venous ulcer (8 cases) Diabetic ulcer (8 cases Mechanical ulcer (5 cases)	N/A	2-240 months	Fotona Dynamis XS	1,500 ms pulse width	2–12 times	79% of lesions achieved complete epithelialization 1 year after treatment	Caliskan & Botsali(2022) [36]

characterized by insufficient blood supply, impaired neovascularization, and persistent inflammatory stimulation of surrounding tissues. These factors contribute to fibrotic tissue proliferation, scar formation, and progressive atrophy or thinning of the skin and subcutaneous layers [2, 3]. Current clinical treatments for chronic wounds fall into two primary categories: surgical and conservative approaches. Surgical intervention is often effective in removing necrotic tissue and promoting wound closure but is associated with significant trauma and elevated risks, particularly when autologous tissue are required. In contrast, conservative management emphasizes the treatment of complex conditions using minimally invasive approaches, making it a more suitable choice when surgical options are restricted or economically impractical. Common conservative therapies include negative pressure wound therapy [4], growth factor-based treatments such as fibroblast growth factor (FGF) and epidermal growth factor (EGF), synthetic polymer-based dressings [5], and biologically active strategies involving platelet-rich plasma, stem cells, and gene therapies. These modalities promote healing by enhancing local blood circulation and reducing the risk of infection. However, prolonged conservative treatment may lead to complications such as nutritional depletion, secondary infections, and increased caregiving burdens, while complex procedures can intensify the workload of healthcare providers [6]. Collectively, these challenges highlight the urgent need for safer, more efficient, and clinically practical strategies to improve chronic wound management [7, 8].

Lasers are widely regarded as one of the most significant technological innovations of the 20th century [9]. In 1960, Maiman successfully validated Einstein's theoretical prediction of stimulated emission and light amplification by using a flashlamp to irradiate a ruby crystal, thereby marking the birth of the modern laser [10]. The foundational mechanism underlying therapeutic laser applications is selective photothermolysis (SP), a concept proposed by Anderson and Parrish in 1983. SP enables precise targeting of pathological tissues while preserving surrounding healthy structures by optimizing parameters such as wavelength, pulse duration, and energy density, thus ensuring both treatment efficacy and safety [11]. In 2004, Manstein and colleagues introduced fractional photothermolysis (FP), a major advancement in laser technology [12]. Unlike conventional lasers, FP delivers light energy in a pixelated pattern that forms microscopic treatment zones (MTZs), consisting of controlled thermal damage interspersed with preserved viable tissue. This spatial distribution not only accelerates post-treatment recovery by leveraging the regenerative capacity of the untreated skin but also enhances treatment flexibility across a wide range of dermatologic conditions. FP is particularly notable for its application in resurfacing photoaged skin and managing burn scars [13]. Among FP devices, carbon dioxide (CO_2) and erbium: yttrium-aluminum-garnet (Er: YAG) lasers have demonstrated substantial clinical success in skin rejuvenation and scar remodeling [14]. Interestingly, emerging studies have revealed their potential in promoting the healing of chronic ulcers—a domain previously unassociated with laser therapy. This article provides a systematic overview of the recent progress in fractional laser applications for chronic wound treatment, In addition, it also summarized the various lasers and parameters utilized by researchers over the past 18 years(Table 1).

Materials and methods

A comprehensive literature search was conducted for studies published between 2008 and 2025 in the Google Scholar, Web of Science, Medline, and PubMed databases, using the keywords: Fractional, Laser, Chronic wounds, Ulcers, and Healing.

Application of CO2 fractional laser in the treatment of chronic wounds

Shumaker et al. [15] from the Naval Medical Center in San Diego were the first to report the application of ablative fractional (AF) CO_2 laser resurfacing in the treatment of chronic wounds associated with traumatic scarring. Their retrospective review included three patients with multiple scars and non-healing wounds resulting from blast injuries. Remarkably, wound healing accelerated significantly following AF laser treatment. In one illustrative case, a 26-year-old patient exhibited visible healing within one week of treatment, with nearly complete epithelialization observed by the second month. The wound continued to improve throughout an eight-month follow-up period.

The intervention employed a 10,600 nm ablative CO_2 laser system (DeepFX and UltraPulse Encore systems), with treatment parameters customized based on the depth and thickness of scar tissue. Pulse energy ranged from 30 to 50 millijoules, and the treatment density was set at 5%.

Subsequently, Phillips et al. [16] evaluated three elderly patients with chronic traumatic lower limb ulcers treated using fractional CO_2 laser. The results showed that within three weeks of treatment, more.

than 60% of the wound area had healed, with complete epithelialization achieved in under six weeks. Notably, all three patients were in generally good health and did not present with complicating factors such as vascular insufficiency, uncontrolled diabetes, or other conditions known to impair wound healing.

Krakowski et al. [17] assessed the safety and effectiveness of AF CO_2 laser therapy for non-scar chronic wounds in pediatric patients. The study included two children with chronic wounds—one receiving a single session of AF laser treatment, and the other undergoing two sessions spaced one month apart. Both patients experienced complete wound healing within 2 to 4 months following treatment, with no recurrence observed during follow-up. These findings suggest that AF CO_2 laser therapy may serve as a promising adjunctive approach in the management of chronic pediatric wounds.

Recessive dystrophic epidermolysis bullosa (RDEB) is a severe genetic skin disorder characterized by extreme skin fragility, recurrent blistering, and contractile scarring. Patients with RDEB frequently suffer from chronic wounds that are highly susceptible to infection and malignant transformation, often leading to premature mortality. Krakowski et al. [18] reported a case involving a 22-year-old RDEB patient with a chronic ulcer, 7 cm in diameter, located on the upper left back and persisting for nine months. The wound was colonized by methicillin-sensitive Staphylococcus aureus, Group B Streptococcus, and Pseudomonas aeruginosa. The patient also exhibited severe allergic reactions to both vancomycin and penicillin, limiting systemic antibiotic options.Treatment with a 10,600 nm AF CO_2 laser (Ultrapulse Encore DeepFX) over four weeks led to a substantial reduction in wound diameter—from 7 cm to 2 cm,—with a 92% decrease in wound area. Following a second session, the wound was nearly fully epithelialized within four weeks. The patient reported no pain and expressed high satisfaction with the therapeutic outcome.

Matteo Monami et al. [19] investigated the effects of CO2 laser treatment on ulcers with exposed bone tissue in diabetic feet. This observational study involved 14 patients with type 2 diabetes, some of whom presented with radiological signs of osteomyelitis. Over a period of 3 months, the researchers created intermittent points on the periosteum of the exposed bone tissue using the CO2 laser until bleeding was observed. In the last 5 patients, platelet-rich plasma (PRP) was administered alongside the laser treatment. Among the 9 patients who received only CO2 laser therapy, 4 achieved complete healing within the 3-month period, while 1 patient developed granulation tissue that covered the entire bone surface. In contrast, among the 5 patients treated with both CO2 laser and PRP, 2 achieved complete healing within 3 months, and 2 patients also developed granulation tissue covering the entire bone surface. The study concludes that CO2 laser treatment demonstrates efficacy in diabetic foot ulcers, particularly those with exposed bone tissue, by facilitating the healing process through the creation of intermittent points on the periosteum.

Jiang Bo et al. [20] compared conventional surgical debridement with laser-assisted debridement using an ultrapulse AF CO_2 laser in a cohort of 18 patients with chronic wounds.Their results indicated that the laser debridement group achieved superior outcomes in terms of promoting wound healing, reducing bacterial colonization, alleviating pain, and improving the overall wound appearance.

In a subsequent study, Jiang Bo et al. [21] further explored the therapeutic mechanisms of ultrapulse CO_2 laser debridement. A total of 54 chronic wounds were randomized into two groups: the routine surgical debridement group (RT group, 28 wounds) and the laser debridement group (LT group, 26 wounds). The LT group received treatment with the ML-2030CI laser system (Wuhan Miracle Laser Technology Co., Ltd.), using energy levels ranging from 60 to 140 millijoules, tailored to individual wound characteristics. A defocused continuous mode was applied, enabling rapid scanning of the wound area within 4–6 s per session. Post-treatment assessment via laser speckle imaging revealed a significant and immediate increase in local blood flow perfusion following laser debridement, which may represent a key physiological mechanism underlying the observed enhancement in wound healing.

Haonan Guan et al. [22] conducted the largest clinical study to date comparing full ablative CO_2 laser debridement with conventional surgical debridement for chronic wound management. The study enrolled 164 patients with chronic skin wounds and utilized the DEKA SmartXide^2 C80 CO_2 laser system, while the control group underwent traditional surgical debridement using scalpels, scissors, or curettes. Results demonstrated that CO_2 laser debridement significantly outperformed surgical methods in improving wound conditions, reducing wound area, and accelerating healing time. Notably, no adverse events were reported throughout the course of treatment.

In a separate case report, JiaJun Tang et al. [23] described the successful treatment of a deep ischial tuberosity sinus tract using a combination of CO_2 laser debridement and endoscopic negative pressure wound therapy (NPWT). The patient, a 53-year-old man with paraplegia and a chronic sinus wound due to prolonged wheelchair use, underwent laser-guided removal of fibrotic tissue from the sinus wall using the DEKA SmartXide^2 CO_2 laser system. Under endoscopic visualization, debridement was performed until fresh red granulation tissue was exposed. As the sinus cavity gradually decreased in depth, the NPWT material was repositioned accordingly. After three laser sessions, the sinus tract closed completely, followed by successful skin grafting. No recurrence was observed during one year of follow-up.

Liu Yifeng et al. [24] conducted a comparative study evaluating the efficacy of AF CO_2 laser therapy combined with standard external dressings versus conventional dressing treatment alone in patients with chronic wounds. The results showed no significant difference in wound edema between the two groups on days 1, 3, and 7. However, by days 7, 14, and 21, the experimental group demonstrated superior granulation tissue formation and faster wound healing rates compared to the control group. These findings suggest that AF CO_2 laser therapy can enhance granulation tissue development and accelerate the healing process in chronic wounds without exacerbating local edema.

Jiang Bo et al. [25] further investigated the application of ultra-pulse CO_2 laser in managing chronic refractory ulcers with bone exposure. The study employed laser drilling techniques to stimulate cortical bone regeneration. Ultrapulse CO_2 laser energy was applied repeatedly to the exposed bone surface until healthy, viable bone tissue appeared. Patients treated with laser therapy showed significantly higher wound healing rates on days 4, 8, 12, 16, and 20 post-treatment compared to those who did not receive laser intervention. Additionally, the laser group experienced reduced treatment costs and lower pain scores.

Yu Peng et al. [26] investigated the clinical outcomes of fractional CO_2 laser therapy in individuals suffering from chronic wounds. Ninety patients were enrolled and divided into two groups: the control group received topical recombinant human basic fibroblast growth factor (rh-bFGF) alone, while the experimental group received additional fractional CO_2 laser treatment. The experimental group demonstrated significantly better clinical outcomes, including enhanced granulation tissue formation and lower pain scores. The study concluded that fractional CO_2 laser therapy has a clear therapeutic benefit for chronic wounds, effectively promoting healing without elevating the risk of complications, and thus holds strong potential for clinical application.

Wang Mengxiao et al. [27] conducted a comparative study involving 122 patients with refractory wounds to assess the therapeutic efficacy of conventional versus modified fractional CO_2 laser therapy when combined with photodynamic therapy (PDT). The findings revealed that the modified CO_2 laser, when used in conjunction with PDT, enhanced the secretion of growth factors in wound exudates, suppressed bacterial proliferation, and mitigated the local inflammatory response. Importantly, this revised protocol not only enhanced wound healing rates but also did not lead to an increased occurrence of adverse events, demonstrating both improved efficacy and sustained safety.

Application of Er: YAG laser in the treatment of chronic wounds

While most existing studies focus on the use of CO_2 lasers for ulcer treatment, Er: YAG lasers also exert therapeutic effects through photothermal mechanisms. By transferring laser energy to water-rich tissues, Er: YAG lasers induce rapid evaporation of intracellular water, resulting in precise tissue ablation and cutting. Actually, this mechanism suggests potential utility in the management of chronic ulcers [28, 29].

Paolo Mezzana et al. [30] investigated the application of Er: YAG laser for debridement in chronic wounds unresponsive to conventional therapy. The study included 30 patients with wound durations exceeding three months, all of whom had failed to improve with advanced topical treatments, including oxidized regenerated cellulose and collagen-based dressings. Debridement was performed using the Smart2940Dplus Er: YAG laser until pinpoint bleeding was observed, followed by wound coverage with a advanced drugs of oxidized regenerated cellulose and collagen matrix. Seven days post-treatment, most wounds had entered the active healing phase, marked by epithelial edge migration and increased granulation tissue formation. Notably, 90% of patients achieved complete wound closure within an average treatment period of 2.5 months. The authors concluded that Er: YAG laser-assisted debridement offers a painless and efficient alternative for optimizing the wound healing process in chronic ulcers.

Diabetic foot ulcers are among the most challenging chronic wounds to manage, with reported healing rates ranging from 18 to 62% even under tightly controlled clinical trial conditions [31]. Matthew et al. [32] investigated the use of Er: YAG laser therapy in treating 22 diabetic foot ulcers across 18 patients. All ulcers had shown minimal or no healing following at least four weeks of standard wound care. Patients were subsequently treated with the Joule ProFractional 2940 nm Er: YAG laser (Sciton, Palo Alto, CA) under standardized laser parameters. The therapeutic response was assessed using the percentage of wound area reduction over a 4-week period.Results showed that 72.7% of the ulcers demonstrated more than a 50% reduction in wound area after 4 weeks of treatment. By week 12, 50% of all ulcers had achieved complete healing. Notably, all ulcers that failed to reach a 50% reduction by week 4 remained unhealed at week 12. Despite the use of a low-frequency treatment protocol (once per week), the Er: YAG laser demonstrated significant clinical efficacy in this patient population.

Joseph N. Mehrabi et al. [33] reported the case of a 69-year-old obese and hypertensive woman with multiple chronic abdominal ulcers that had persisted for over two years. Comprehensive diagnostic testing ruled out malignancy, fungal infections, and vasculitis. Following the failure of multiple standard therapies, the patient received Er: YAG laser treatment, resulting in complete wound closure without any adverse effects or complications. In addition to clinical observations, Mehrabi also reported preclinical findings from diabetic mouse models: In laser-treated animals with acute wounds, Er: YAG therapy led to significantly faster wound contraction compared to natural healing. Molecular analysis revealed upregulated mRNA expression of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF), alongside a downregulation of TGF-β. These results suggest a potential mechanistic pathway through which Er: YAG laser promotes tissue regeneration.

Babak Hajhosseini et al. [34] conducted a crossover clinical study to compare Er: YAG laser debridement with traditional sharp debridement in the management of chronic wounds, focusing on their effects on pain perception and bacterial load. A total of 22 patients with chronic wounds were randomly divided into two groups: one group initially received Er: YAG laser debridement using a 2940 nm device, while the other underwent sharp debridement using a scalpel and/or curette. After one week, the treatment modalities were switched between the groups. The results demonstrated that Er: YAG laser debridement was significantly more effective than sharp debridement in reducing patient-reported pain and lowering bacterial burden at the wound site. Moreover, patients expressed a clear preference for laser-based treatment, likely due to reduced discomfort and tissue trauma.

Aysenur Botsal et al. [35] reported a case highlighting the therapeutic potential of Er: YAG laser in managing ulcers secondary to lower extremity arterial disease. The patient, a 43-year-old man, presented with a persistent foot ulcer unresponsive to 30 sessions hyperbaric oxygen therapy. The treatment protocol included full-field Er: YAG laser ablation to remove ectopic bone tissue within the ulcer, followed by fractional Er: YAG laser therapy to stimulate wound healing.By the ninth week of laser treatment, the ulcer size had significantly decreased, and complete epithelialization was achieved within the first year of follow-up, with no recurrence observed. Despite the presence of underlying arterial hypoperfusion, fractional Er: YAG laser therapy facilitated significant wound healing. The authors also noted that, compared to traditional sharp debridement, Er: YAG laser treatment eliminates the need for consumable tools in repeated procedures and minimizes collateral tissue damage, making it a more sustainable and patient-friendly option.

Ercan Caliskan et al. [36] conducted a retrospective analysis evaluating the efficacy of Er: YAG laser therapy in treating difficult-to-heal chronic wounds. The study included 23 patients and a total of 43 treatment sites, with Er: YAG laser applied using a spot energy density ranging from 6 to 22 J/cm². After one year of treatment, 79% of the lesions achieved complete epithelialization. Among the nine lesions that failed to fully epithelialize, 44.4% had wound areas larger than 50 cm², another 44.4% were arterial ulcers, and 11.1% of patients died from diabetes-related complications. The research indicated that Er: YAG laser therapy demonstrated significant efficacy in treating venous and diabetic ulcers, consistent with previous findings[32,34]. These results support its use as a second-line treatment option for these ulcer types. Mechanical ulcers demonstrated relatively rapid healing, achieving complete epithelialization within an average of four months. In contrast, immunological and arterial ulcers were the most treatment-resistant, highlighting the need for further therapeutic innovation in these subtypes.

Hypothesized mechanisms of action

With the increasing application of AF lasers across various clinical wound-healing scenarios and the expansion of their treatment modalities, several potential mechanisms have been proposed to explain their therapeutic benefits in chronic wound management.

Debridement and scab removal

AF CO_2 laser technology enables highly precise wound bed preparation, which serves as a critical foundation for subsequent tissue regeneration [37]. Through the controlled delivery of thermal energy and the use of fractional ablation, the laser selectively vaporizes necrotic tissue, bacterial biofilms, and senescent epidermal layers. This process preserves adjacent viable tissue essential for re-epithelialization and granulation [14].

Improvement of local blood supply

The laser's localized photothermal effect and photobiomodulation capabilities can induce vasodilation, enhance cutaneous microcirculation, and thereby increase oxygen and nutrient delivery to the wound site [21]. Studies have reported significantly elevated wound exudate scores on days 7, 14, and 28 following laser treatment compared to conventional debridement [21]. These findings suggest that the transient exudative response induced by AF lasers may act as an autologous nutrient-rich medium, supporting the proliferation, differentiation, and migration of reparative cells.Moreover, the deeper microthermal zones generated by CO_2 fractional lasers can directly stimulate dermal tissue remodeling from the basal layers outward. This vertical regeneration gradient not only accelerates wound closure but also promotes organized tissue architecture and functional recovery [38].

Reduction of skin tension around the wound

When the CO_2 fractional laser scanning range is extended to approximately 1-2-cm beyond the wound margin [15], the laser-induced epithelial activation in the peripheral zone stimulates keratinocyte proliferation and migration from the wound edge, thereby accelerating re-epithelialization. Additionally, the fractional ablation of surrounding skin tissue results in a partial relaxation of mechanical tension around the wound. This reduction in peripheral skin tension can decrease wound edge contracture and the risk of recurrence, ultimately promoting more stable and durable [39].

Enhancement of topical drug delivery

Fractional laser perforation creates uniform micropores across the wound surface, significantly increasing the contact area for topical agents, antimicrobial peptides, and growth factors. These microchannels allow therapeutic molecules to penetrate more evenly and deeply into the underlying tissue layers, including those beneath scab formations [40]. This enhanced transdermal delivery pathway improves cellular responsiveness to treatment and stimulates localized regenerative activity.

Reduction of bacterial load

Persistent bacterial colonization is a major contributor to delayed wound healing. AF laser debridement has been shown to significantly reduce bacterial load and inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), primarily through its physical antimicrobial effects [41]. The laser disrupts microbial cell walls and biofilms that are often resistant to traditional therapies [42]. Moreover, AF laser treatment promotes the recruitment of local immune cells [43], thereby creating a microenvironment that is less conducive to bacterial proliferation and more favorable to the transition from chronic inflammation to active tissue repair.

Molecular level changes

The micro-thermal energy generated by CO_2 laser treatment induces the expression of heat shock proteins (HSPs) at the cellular level. As molecular chaperones, HSPs play a critical role in protecting cells from thermal stress while also regulating key processes such as apoptosis and cell proliferation, thus providing cellular protection and supporting the subsequent stages of wound healing [44]. Laser-induced micro-injury activates several crucial signaling pathways, including the transforming growth factor-β/smad(TGF-β/Smad) pathway, which governs the proliferation and differentiation of fibroblasts [45]. This signaling cascade also stimulates the synthesis and remodeling of collagen and other extracellular matrix proteins, facilitating wound structure remodeling and functional recovery [46]. At the molecular level, laser treatment further modulates the secretion of inflammatory mediators. It reduces the production of pro-inflammatory cytokines, such as IL-1 and tumor necrosis factor-alpha(TNF-α), while promoting the release of anti-inflammatory factors like IL-10 [47, 48]. This balance in inflammatory responses ensures a controlled inflammatory environment that supports optimal wound healing. Additionally, the regulation of matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs) by the laser promotes the appropriate degradation and remodeling of the extracellular matrix, thereby preventing excessive scar formation [48].

Conclusion

Fractional laser therapy has become a widely utilized modality in clinical wound healing, demonstrating significant efficacy, particularly in the management of complex wounds, diabetic foot ulcers, and RDEB. However, the precise mechanisms underlying its therapeutic effects remain incompletely understood. Whether using AF CO2 lasers or Er: YAG lasers, most authors emphasize the necessity of adjusting treatment based on the wound's condition. In cases with high skin integrity, significant necrotic tissue, and a high degree of fibrosis, there is a tendency to utilize higher laser treatment energy or more frequent treatment sessions[16,20–22,22–24,26,33,35,36]. However, due to limitations in available cases, extensive research on the safety of fractional laser applications in chronic wounds has not been conducted. Only two studies have reported adverse reactions, such as rashes, itching, and burns [26, 27]. This highlights the need for caution, as although the safety range of fractional lasers is wide, they should still be used judiciously. Additionally, adjusting laser parameters based on the patient's skin type is an important consideration [49]. It is crucial to note that not every non-healing ulcer is suitable for laser treatment; malignant tumors and specific infections must be appropriately ruled out using techniques such as biopsy and culture [18, 33].Moreover, the clinical application of laser therapy is highly variable, with differences in product manufacturers, power settings, dosages, application modes, and treatment frequencies. The diversity of treatment protocols—ranging in power, treatment density, and interval lengths—complicates the comparison of results and the optimal selection of treatment parameters. Therefore, further research is essential to establish standardized treatment protocols and to elucidate the mechanisms of action, thereby enhancing the clinical application of fractional lasers in wound management.

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Declarations

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