Spatially modulated erbium YAG laser as a treatment for diabetic ulcer

Objective: Diabetic ulcers are a significant healthcare challenge, capable of diminishing quality of life, lengthening hospitalisation stay, and incurring substantial costs for patients and healthcare systems. Erbium-doped yttrium-aluminum-garnet (Er-YAG) laser has been evolving as a prospective intervention for addressing wounds of various aetiologies. Despite this, the literature remains limited in appraising the effectiveness of laser therapy specifically in diabetic wounds. This study investigates the impact of employing a spatially modulated Er-YAG laser as a therapeutic approach for treating diabetic ulcers.
Method: In a single-arm study conducted from November 2017 to April 2023, patients with hard-to-heal ulcers were treated in a two-step approach of wound debridement using Er-YAG laser for ablation and biostimulation through deep tissue resonance using RecoSMA (Multiline laser system, LINLINE MS, Latvia) laser technology. Ulcers received weekly laser treatment, together with routine care until healing occurred and were then followed up to observe any recurrence. The primary outcome measure was wound closure; the secondary outcome measures were time to closure, and the number of laser treatments required. Data related to sociodemographic details, size and number of diabetic ulcers, and number of sessions related to laser treatment were collected using a predesigned, pretested questionnaire before initiating the treatment.
Results: A total of 59 patients attending the clinic during the study period with diabetic ulcers were included in the study. The mean wound surface area at baseline was 25.7cm² (median: 12cm²). The average number of sessions of laser treatment required was 4.41, ranging from 1–11. The size of the ulcer reduced with each session of laser treatment. The diabetic ulcers healed completely at the end of the treatment, indicating the effectiveness of the Er-YAG/RecoSMA two-step approach.
Conclusion: Spatially modulated erbium YAG laser is effective as a therapeutic approach for treating diabetic ulcers.
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diabetic foot ulcer • diabetic ulcer • diabetic wound • erbium YAG • hard-to-heal wounds • laser • RecoSMA technology • wound • wound care • wound dressing • wound healing

Diabetes is a major public health issue that is characterised as a global pandemic. According to the International Diabetes Federation, 463 million people are diagnosed with diabetes globally, estimated to increase by 50% in the next 30 years.[1]

Diabetic foot ulcer (DFU) is one of the most significant and devastating complications of diabetes, and is defined as a foot affected by ulceration associated with neuropathy and/or peripheral arterial disease of the lower limb.[2]

Infection is a frequent complication of DFUs, with up to 58% of ulcers presenting with infection at a diabetic foot clinic, rising to 82% in patients hospitalised with a DFU. These infections are correlated with poor clinical consequences for the patient and considerable expense for both the patient and the health care system.[3] A person with diabetes is 15 times more likely to undergo lower extremity amputation than those who do not have diabetes.[4] DFU management involves a multidisciplinary approach.[2] Several surgical and medical conservative therapeutic options are available for treating DFUs.

Laser technology has been used in various medicinal fields. The erbium-doped yttrium-aluminum-garnet (Er-YAG) laser with wavelength of 2940nm has been widely used for scar revision, skin resurfacing, wound healing and periodontal disease.[5,6]

The pulsed Er-YAG laser emits light within the mid-infrared portion of the electromagnetic spectrum with a wavelength of 2940nm, corresponding to the water absorption peak.

Each pass of the high-power erbium laser heats tissue to >300°C. As a result, water in the tissue is rapidly expanded to eject the charred debris from the wound surface without leaving behind a necrotic eschar.[7]

Absorption of a short laser pulse creates mechanical stress waves that propagate out of the laser-irradiated site into the surrounding tissue.

Using a particular RecoSMA module (Multiline laser system, LINLINE MS, Latvia), the Erbium laser radiation is divided into many microbeams, which together

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create a periodic structure of the stress wave epicentres on the surface of the irradiated tissue. Er-YAG laser with RecoSMA technology produces microablation on the wound surface and epidermis, and the resonance effect on deeper tissues underneath the ulcer stimulates the regeneration mechanism of wound healing.[8]

The study's objective is to assess the efficiency of Er-YAG and RecoSMA laser technology for the treatment of diabetic ulcers.

Method

The study was conducted in the Department of Plastic Surgery at Elrevo Clinic, Aurangabad, India. The study period ran from November 2017 to April 2023. Patients with diabetic wounds visiting inpatient and outpatient departments were assessed, and information was provided to them about the study. Those patients who provided written consent for publication of data and photographs were enrolled in the study. The ethics committee of Ishwar institute of healthcare provided approval for the study.

Inclusion and exclusion criteria

The inclusion criteria for enrolling the patients for the study were patients with ulcers who were ready to follow treatment until complete healing occurred. The exclusion criteria were lack of consent, missing follow-up appointments and patients who opted for or were indicated for secondary surgical procedures to achieve complete healing.

Sample size

The ulcers were classified as per Wagner's grading system.[9] Sample size was calculated using Cochrane's formula, taking the prevalence of diabetes as 8.8% and prevalence of diabetic ulcers[10] as 2.2%, the allowable error as 4% and 10% non-responders. The sample size was therefore calculated as 59.

Use of Er-YAG laser for wound healing

The use of the Er-YAG laser for wound healing was specified in the official user manual of the laser device, registered and approved by the European Union notified body, relying on clinical studies conducted during the CE-Mark certification process. A prestructured and pretested questionnaire was used to collect patient sociodemographic data and details about their condition.

Prior to the laser treatment, the vascular assessment was performed by manually palpating the dorsalis pedis artery and posterior tibial artery in dorsum of the foot and posterior to medial malleolus, respectively. Both pulsations were palpable in all patients included in the study.

The technique

After removing the dressing, the wound was cleaned with saline solution. Wound measurements were taken using a transparent calibrated grid marking placed on the wound. The two-step protocol was applied to every patient included in the study.

Step 1: Short pulse high-power Er-YAG laser ablation

The Er-YAG laser emitter was connected to the laser device and the ablation mode was selected. The 4mm Er-YAG laser tip was then attached to the laser handpiece, and the other parameters of frequency of 3Hz and energy of 15.9J/cm² were selected. The laser tip was brought close to the surface of the ulcer avoiding direct contact with it. It was advised to keep the laser tip at a minimum of 5cm away from the surface of the wound while performing the laser procedure. The handpiece should be held in such a way that the laser beam is delivered at right angles to the wound surface. The smoke evacuator was used to remove the fumes during the laser procedure. The laser beam was delivered to the surface and the edge of the ulcer. It was delivered as a single pass in a continuous pattern with minimal overlap. More passes of ablation were used whenever necrotic tissue was observed on the wound surface in order to reach the viable tissue. The capillary bleeding on the ulcer surface indicated adequacy of the laser ablation.

Step 2: Biostimulation with RecoSMA Laser

The Er-YAG handpiece was connected to the multiline laser machine and the RecoSMA laser mode was selected. The spatially modulated ablation (SMA) module was connected to the Er-YAG laser emitter, and the frequency of 3Hz and energy of 2.30J/cm² were selected. The RecoSMA laser tip was kept in contact with the wound surface while firing the laser. The tip should be at a right angle to the wound's surface while delivering the laser beam. The wound surface, edge of the wound and 3cm periphery of the wound were treated. The laser spots made a continuous pattern with some overlap. The smoke evacuator removed the smoke generated while performing the laser procedure.

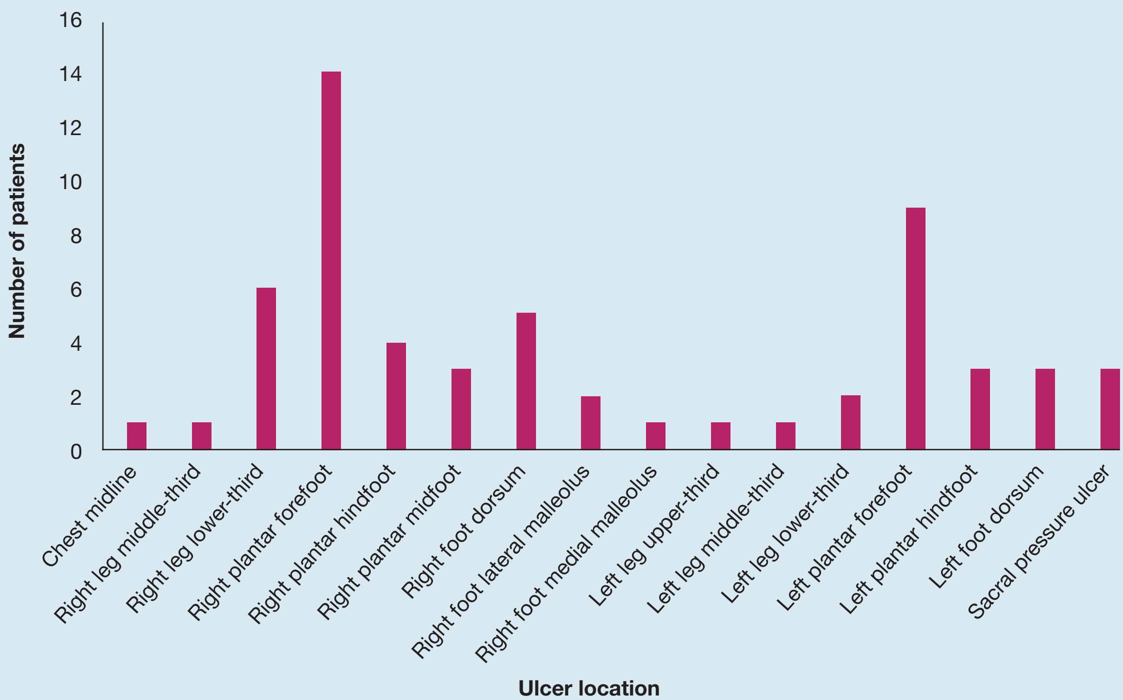
RecoSMA technology is a highly specialised optical technology that spatially modulates the Er-YAG laser ablation to perform the highly selective mechanical microdestruction of deeper tissues. It accelerates new collagen synthesis, enhances revascularisation and supports the healing process of wounds.

A dry gauze dressing was applied on the wound surface after the laser treatment, and patients were advised to change the dressing every alternate day, as well as apply topical antiseptic ointments and take oral medications whenever indicated as standard care. The sessions took place until the ulcer healed.

Clinical photographs of wounds were taken during each session of laser treatment to compare the progress of healing.

Patients were advised to avoid direct pressure on the wounds when following routine activities, and avoid excessive or strenuous working patterns. The patients with plantar ulcers were instructed to avoid direct pressure on the ulcer area until it healed completely. Removable cast walkers were advised as offloading

Fig 1. Distribution of study patients based on location of ulcer



footwear to avoid recurrence in patients with plantar ulceration. Adherence to wearing the offloading devices was not uniform in all patients; however, they were advised and encouraged to use it during each follow-up visit in outpatient care. The importance of its use to prevent ulcer recurrence in future was explained.

Data collection

The data were collected, compiled and entered into an Excel worksheet (Microsoft Corp., US). It was analysed using the Statistical Package for Social Sciences trial version (IBM Corp., US). Descriptive statistics were calculated, and the Chi-squared test was applied. A p-value of <0.05 was considered as statistically significant.

Results

Of the 274 patients with diabetic wounds attending ~~the~~ clinic during the study period, 59 patients who met the inclusion criteria were included in the study.

Table 1 shows the clinico-socio-demographic characteristics of patients, of which 47 (79.7%) were male and 12 (20.3%) were female. The majority (20, 33.9%) of patients belonged to the 61–70 years' age group, and only one (1.69%) patient belonged to the 81–90 years' age group. Of the patients, 23 (39.0%) had systemic hypertension and only one (1.69%) participant had varicose vein. Moreover, 48 (81.4%) patients had diabetes, with duration ranging from 1–10 years. Mean blood glucose level was 236.56mg/dl (range: 168–318mg/dl).

Table 1. Clinico-socio-demographic profile of study patients

Parameters		n (%)
Age, years	31–40	3 (5.1)
	41–50	11 (18.6)
	51–60	12 (20.3)
	61–70	20 (33.9)
	71–80	12 (20.3)
	81–90	1 (1.7)
Sex	Male	47 (79.7)
	Female	12(20.3)
Associated comorbidities	Hypertension	23 (39)
	Varicose Vein	1 (1.7)
Duration of diabetes, years	<1	2 (3.4)
	1–10	48 (81.4)
	11–20	6 (10.2)
	>20	3 (5.1)
Blood glucose* levels, mg/dl	101–200	15 (25.42)
	201–300	40 (67.80)
	>300	4 (6.78)

Table 2. Details of wound and laser treatment

Parameters		n (%)
Duration of ulcer, weeks	≤34	37 (62.7)
	>34	22 (37.3)
Initial surface area of ulcer, cm²	≤25	41 (69.5)
	>25	18 (30.5)
Oedema	Present	21 (35.6)
Number of laser treatment sessions	1–5	41 (69.5)
	6–10	17 (28.8)
	>10	1 (1.7)
Aftercare of ulcer	Alternate day dressing	59 (100.0)
	Antibiotics	37 (62.7)
	Enzyme	21 (35.6)

The average ulcer duration was 34 weeks. In 37 (62.7%) patients, ulcer duration was ≤34 weeks. Fig 1 shows the distribution of patients based on ulcer site. The most common site was right plantar forefoot (27.1%). Average initial surface area of ulcers were 25cm². For 41 (69.5%) patients, the initial surface area of the ulcer was ≤25cm², and for 18 (30.5%) patients, the initial surface area of the ulcer was >25cm². The majority of patients (41, 69.5%) received ≤5 rounds of laser treatment (Table 2). Figs 2–6 show the results of laser treatment in three patients who participated in the study.

Of the patients, 37 (62.7%) and 21 (35.6%) received aftercare in the form of oral antibiotics and enzyme preparation, respectively, in this study. Alternate day dressings were undertaken in all patients until complete healing.

The average number of sessions of laser treatment required for complete healing was 4.41 (range: 1–11; median: 4). Associated hypertension (p=0.027), initial surface area of ulcer (p=0.001) and presence of oedema (p=0.007) were significantly associated with number of laster sessions (Table 3). Follow-up visits were arranged for all patients after complete healing of the ulcer (range: 4–70 months, average: 22.95 months). No recurrence of ulcer was found at the same site.

Table 3. Distribution of study patients according to number of sessions of laser treatment to wound closure

Parameters		n (%)	Number of sessions of laser treatment to wound closure 1–4	>4	p-value
Duration of diabetes, years	<10	50 (100)**	32 (64)	18 (36)	0.268
	≥10	9 (100)	4 (44)	5 (56)	
Duration of ulcer, weeks	≤34	37 (100)	25 (68)	12 (32)	0.181
	>34	22 (100)	11(50)	11 (50)	
Associated hypertension (HTN)	HTN +	23 (100)	10 (43.5)	13 (56.5)	0.027*
	HTN –	36 (100)	26 (72)	10 (28)	
Initial surface area of ulcer, cm²	</=25	41 (100)	31 (75.6)	10 (24.4)	<0.001*
	>25	18 (100)	5 (27.8)	13 (72.2)	
Oedema	Present	21 (100)	8 (38)	13 (62)	0.007*

*Significant; **Figures in parenthesis are row-wise percentages

Discussion

DFUs are a major health concern for people with diabetes. The occurrence of a DFU significantly affects the patient's quality of life. For hard-to-heal ulcers that are not showing signs of improvement, a specialist's opinion on DFU care is warranted. Clinical assessment and investigations are required to identify the reasons for the slow progression of healing and to formulate a treatment plan.

Traditional wound care methods involve various ointments, topical applications and dressing materials. Depending on the condition of the wound, surgical interventions, ranging from simple debridement to amputation, and major wound reconstruction involving microsurgery, may be planned. Surgical debridement is a standard of care for treating hard-to-heal DFUs as it transitions the hard-to-heal wound into the active healing stage.[12,13] Amputation leads to major psychosocial concerns for the patient.

Effective treatment expedites wound healing and saves patients from prolonged morbidity and increased mortality risk. Newer technologies, such as the Er-YAG laser, promote healing or prepare the wound for reconstructive procedures, such as skin grafting and flap surgeries. Infection and biofilm on the wound surface are one of the causes of stalled healing in DFUs, inhibiting the progression of re-epithelialisation from the edge of the wound.[14] The presence of biofilm also leads to poor granulation tissue formation and necrosis of the surface layer of the wound.[15] Wound debridement was traditionally achieved through chemical means and surgery. In recent years, the Er-YAG laser has been used to perform laser debridement of wound surfaces. It effectively transitions the hard-to-heal wound to an active stage of healing. The pain experienced with laser debridement is reduced and it can be carried out at the outpatient clinic, whereas sharp surgical debridement requires the use of the operating theatre.[16]

In this study, Er-YAG laser was used to debride the wound surface through superficial ablation. In this phase of laser irradiation, the tissues attain vaporisation temperature within a short time, which is quicker than the time required to transfer heat to the surrounding non-irradiated area.[17] There is no damage to the tissue which is not being laser-ablated. The healing commences with new collagen synthesis from surrounding non-damaged tissue and does not lead to fibrosis formation. The rapid attainment of the vaporisation temperature also leads to the destruction of microorganisms as well as necrotic tissue, thus serving the purpose of cleaning the biofilm from the surface of the wound.[17] Laser ablation with Er-YAG laser is not a painful procedure and so there is no need for local anaesthesia or hospitalisation. The procedure takes a few minutes to complete and can be performed in the outpatient clinic. The patient can immediately leave the hospital and continue with their daily routine.

Wound healing involves four significant steps: haemostasis, inflammation, proliferation and remodelling. The first three steps are essential for wound closure. The last step of remodelling is related to scar maturation. Er-YAG laser with a wavelength of 2940nm improves or promotes wound healing by laser ablation which is a type of debridement. It cleans the wound surface and thereby accelerates the healing process through the production of heat shock proteins, and delivery of a low concentration of reactive oxygen species.[16] Both mechanisms promote fibroblast proliferation, resulting in the stimulation of collagen and extracellular matrix formation.[16] The Er-YAG laser in this present study uses laser ablation for wound surface debridement, as mentioned earlier in Step 1 of the laser treatment.

In Step 2, RecoSMA creates the optimal conditions for wound healing by spatially modulated ablation. In this step, the Er-YAG laser beam is divided into thousands of microbeams by a sophisticated optical system. When these beams hit the surface of the ulcer, they cause an ablation as well as a resonance effect, creating progressive acoustic waves moving deeper below the surface of the ulcer. While progressing through the deeper tissue, these expanding waves collide with each other, creating the mechanical destruction of tissue, also known as a

Fig 2. A 70-year-old male patient diagnosed with a right diabetic foot ulcer on dorsum with tendon exposed. Duration: 8 weeks. Initial area: 60 cm². Sessions: 8. Time to wound closure: 9 weeks. Follow up: 6 months

Fig 3. A 76-year-old female patient diagnosed with a right leg lower-third ulcer. Duration: 60 weeks. Initial area: 108 cm². Sessions: 8. Time to wound closure: 9 weeks. Follow up: 14 months

Fig 4. A 48-year-old female patient diagnosed with a right plantar hindfoot ulcer. Duration: 3 weeks. Initial area: 42 cm^2. Sessions: 6. Time to wound closure: 7 weeks. Follow up: 62 months

cavitation effect.[17] This mechanical destruction in the deeper tissue retriggers the inflammatory phase of wound healing. The inflammatory phase is crucial as it represents the high activity level of epithelial cells, fibroblast cells and dendritic cells, producing the inflammatory mediators to attract platelets, neutrophils, lymphocytes and macrophages. It leads to neoangiogenesis and the production of granulation tissue.[18] The imbalance of collagen synthesis and degradation results in delayed or stalled wound closure,[19] as has been observed in clinical and histological examination.[2] In this way, the RecoSMA laser stimulates the body's own healing mechanism without any external chemical agent; hence, it is referred to as laser biostimulation of the healing mechanism. The Er-YAG laser in this study provided a holistic solution to wound healing by cleaning the wound by laser ablation and the inflammatory phase was stimulated by the RecoSMA laser technique.

Wound healing occurs through re-epithelialisation from the wound edges and granulation from the depth of the wound bed. Re-epithelialisation reduces the dimensions of the wound, while granulation fills the wound. Both processes are important in wound healing. The speed of healing also depends on many variables, such as age, blood glucose level, blood circulation, etc. The endpoint of healing is the complete coverage of the wound, either by re-epithelialisation or reconstruction by a skin graft or flap cover. Healing through re-epithelialisation benefits the patient by avoiding hospitalisation, surgical procedures and associated expenses. There are no clear guidelines on which size of wound should be healed through primary or secondary intention, i.e., re-epithelialisation or reconstruction. In a study by Alcolea at al.,[8] 16 patients were treated with Er-YAG laser for wound healing in the lower extremity.

Fig 5. A 48-year-old male patient diagnosed with a left leg lower-third ulcer. Duration: 28 weeks. Initial area: 22cm^2. Sessions: 9. Time to wound closure: 10 weeks. Follow up: 12 months

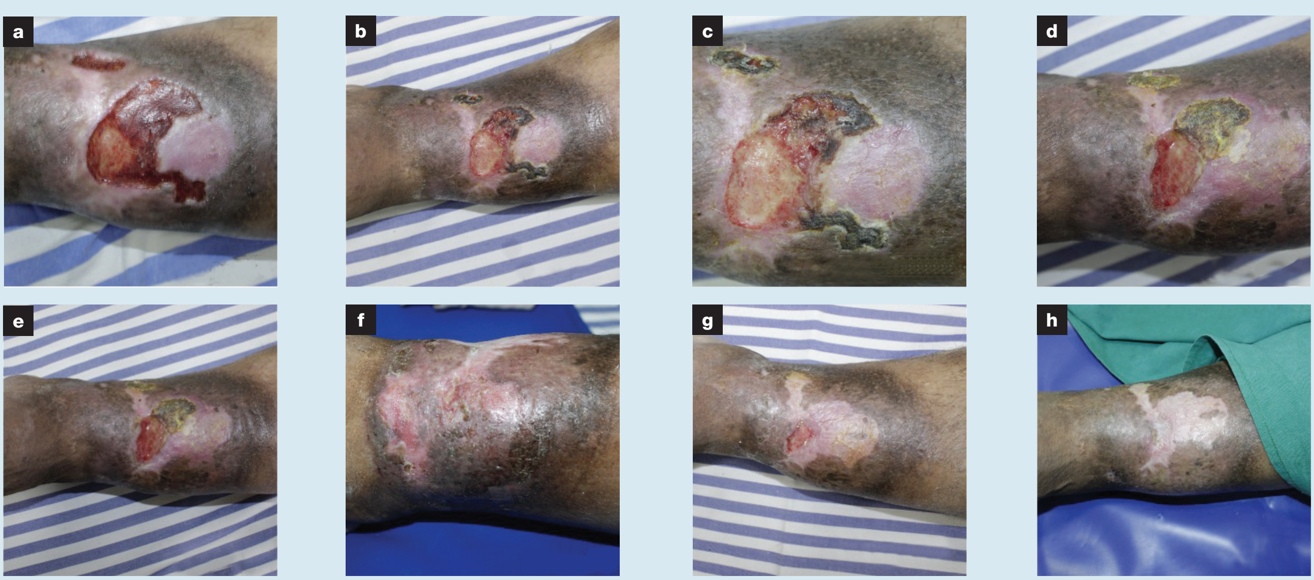


Fig 6. A 71-year-old male patient diagnosed with a right leg lower-third ulcer. Duration: 68 weeks. Initial area: 36 cm². Sessions: 6. Time to wound closure: 7 weeks. Follow up: 5 months

Of the patients, three (18.75%) achieved complete healing without the need for surgical intervention. The initial average area of the wound was 15.7cm². In the present study, we included 59 patients with an initial average wound area of 25cm² and achieved complete healing without surgical intervention in all patients included in the study. Based on these observations, we propose that the Er-YAG laser treatment could be offered with assurance as a tool for the complete healing of diabetic ulcers of up to 25cm² without the need for surgical intervention.

Our selection of diabetic ulcers exclusively for this study was due to the focus on the increasing incidence of patients with a diabetic ulcer. Amputations of the extremities are common in patients with diabetes, leading to psychosocial disturbances and mortality. Due to associated comorbidities and financial concerns, patients become reluctant to take up treatment at a hospital. Often, such patients arrive in an advanced stage of infection and consequently experience a high rate of amputations. Er-YAG laser with RecoSMA technology provided a convenient, cost-effective and efficient solution to diabetic ulcer healing of any grade and stage.

Limitations

The study had a number of limitations including a small population size due to some patients being lost the follow-up, and so is not representative of the wider population. Therefore, results of this study can not be generalised to other patient populations.

Use of a different wound healing treatment method or technique in this present study could have provided a comparison to the laser treatment.

The patients had varying comorbidities which might have had different implications for healing, and so results can not truly represent all patients with diabetes.

The measurement of ulcers using a calibrated grid could have subjective variations in calculations, and undertaking histological analysis of healed ulcers could have produced specific data on regenerated tissue.

Conclusion

Er-YAG lasers achieved wound closure in all 59 hard-to-heal diabetic ulcers with a mean of 4.41 treatments. The debridement and biostimulation of the patients' own inflammatory mechanism resulted in complete healing. The treatment was convenient for the patients as it could be performed on an outpatient basis. Further multicentre studies with diverse patient populations, for example by dividing patients into groups based on on associated comorbidities, such as varicose vein, hypertension, peripheral vascular disease or autoimmune vasculitis to obtain more precise data for treatment planning and help to formulate a protocol-based treatment. Software-based applications for wound measurement could also provide more precise calculation of the ulcer's surface area. Further studies can be conducted to evaluate the results in the wounds of different aetiologies. JWC

Reflective questions

- From a patient perspective, what are the potential benefits and challenges of undergoing laser therapy for diabetic foot ulcers (DFUs), considering factors such as pain, convenience and recovery time?
- How might sociodemographic factors, such as age, sex, duration of diabetes and comorbidities, influence the response to laser treatment, and what implications could this have for tailoring treatment plans for patients with diabetes?
- What additional research or clinical studies would you recommend to further evaluate and validate the effectiveness of Erbium YAG laser combined with RecoSMA technology for treating DFUs, and how might this impact future treatment guidelines?

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