available at *www.jstage.jst.go.jp/browse/islsm* **ORIGINAL ARTICLES**

Treatment of Chronic Lower Extremity Ulcers with A New Er:Yag Laser Technology

Alcolea JM [1,7], Hernández E [2], Martínez-Carpio PA [3,7],
Vélez M [4,7], Khomchenko V [5], Sola A [6], Trelles MA [7*]

1: Clínica Alcolea, Barcelona, Spain.
2: Vascular Surgery Service, Hospital Viamed Monegal, Tarragona, Spain
3: Investilaser, Sabadell (Barcelona), Spain
4: Dermatology Service, Hospital del Mar, Barcelona, Spain.
5: Linline Research Department, Minsk, Belarus.
6: Computer Engineering Department, University of Malaga, Spain
7: Instituto Médico Vilafortuny, Cambrils (Tarragona), Spain

Chronic lower extremity ulcers (CLEUs) have a high prevalence and are difficult to treat due to their various aetiologies. The aim of this study is to evaluate the results achieved in treating CLEUs using an Erbium: YAG (Er:YAG) laser with RecoSMA technology. This laser emits thousands of microbeams of energy causing superficial epidermal ablation and a separation of dermal fibres due to a mechanical-acoustic and resonance effect. The evaluation of the results achieved was carried out by questionnaires completed by 18 patients enrolled in the study. Histological studies and photographs taken before each session (16 sessions in total) were analysed to visually monitor the clinical progress. The analyses were carried out with the help of computer software. The results after 16 treatment sessions showed the complete healing of ulcers or a decrease in their initial area of at least 55% in over 65% of the patients treated. The Student's t-test and Fisher's exact test were used for statistical analysis. The Er:YAG laser and RecoSMA technology ablates few epidermal cell layers, producing a mechanical-acoustic effect with resonance action leading to tissue regeneration mechanisms. This technology offers an effective and safe alternative for treating CLEUs.

Keywords: Ulcers · Chronic lower extremity ulcers · Er:YAG · laser · RecoSMA technology · mechanical-acoustic effect.

Introduction

Chronic lower extremity ulcers (CLEUs) represent a challenge for treatment, due to the slow tissue deterioration, high rate of recurrence and accompanying infections [1], as well as their high prevalence [2]. The aetiology is variable, although it is accepted that 90% are of venous origin, 6% ischaemic, 3% mixed (arterial and venous), and the remaining 1% is attributed to other causes (lymphatic issues and/or vasculitis) [3, 4]. The consensus for treating CLEUs prioritises the treatment of the original disease while providing local treatment at the same time. Understanding the aetiology plays a significant role in the choice of treatment. Local therapies use well-known pharmacological products, although the use of antibiotics is not recommended unless there is a well-documented infection [5]. New clinical trials are also being carried out with topical treatments, using extracts of aloe vera/olive oil or *Calendula officinalis* [6 – 8]. Laser therapy for CLEUs has been practised for over 35 years. Low-power density lasers were first used due to tissue photobiomodulation effects and capillary – arterial vasodilation effects [9]. Later, CO_2 and Er:YAG lasers were used in sub-ablative mode and the fractionated energy delivered varying results [10].

The objective of this prospective study was to analyse the response of CLEUs to an Er:YAG 2940 nm laser equipped with a new optical system for energy

Addressee for Correspondence:
Mario A. Trelles, MD, PhD
Av. Vilafortuny, 31. CAMBRILS 43850 (Tarragona), Spain
imv@laser-spain.com

Received date: May 20th, 2017
Accepted date: June 26th, 2017

deposition in tissues. RecoSMA technology is based on a sophisticated optical technology which produces shallow ablation of the epidermis and a resonance effect in the dermis. A combined mechanical and acoustic double-action effect stimulates the regeneration mechanism of the ulcerated tissue. To follow up, the progress of CLEUs treated with Er:YAG plus RecoSMA technology was analysed after a number of pre-established sessions focusing on various factors which play a notable role in the healing process.

Material and Methods

Sample of patients

Eighteen (18) patients signed up for the study and 16 completed it. The gender distribution was as follows: 16 women and 2 men with an average age of 66.3 ± 7.7 years (r=51 – 78). Patients presented 12 venous ulcers, 4 mixed ulcers and 2 lymphatic ulcers. Patients had various pathologies considered as cardiovascular risk factors: 5 had type II diabetes (33%), 9 had high blood pressure (50%), 7 had dyslipidaemia (39%), and 4 were smokers (22%). Additionally, 7 patients had more than one of the aforementioned risk factors **(Table I)**. All patients had previously received multiple topical treatments without success. All the ulcers had lasted for at least 14 months.

Patient inclusion and exclusion criteria

The treatment protocol was approved by the Ethics Committee of the Viamed Monegal Hospital (Tarragona, Spain), and was in accordance with the Declaration of Helsinki. The following criteria were considered for the patient inclusion:

- The informed consent form signed after being explained in detail about the nature of the study, the protocol and the purpose of the treatment. The progress of the CLEUs was monitored until achieving a reduction in size or complete closure, or when the ulcer was in a suitable condition for treatment with skin grafts.
- Ulcers could be of venous origin, mixed (arterial and venous) and/or lymphatic aetiologies, with a

Table I: Demographic data, characteristics of the ulcers and the pathology associated with each patient.

N	Age	Progress (months)	Aetiology	Location (lower extremities)	Previous infection	Associated pathology
1	64	16	CVI	Left	No	DM II
2	73	21	CVI	Left	No	HBP, DL
3	59	19	CVI	Right	Yes	DM II, S
4	71	15	CVI	Left	No	DL
5	66	17	Mixed	Right	Yes	HBP
6	64	14	CVI	Left	No	DL
7	51	16	Mixed	Left	No	DM II
8	72	23	CVI	Bilateral	No	HBP, DL
9	61	16	CVI	Right	No	DM II
10	57	20	CVI	Left	Yes	S
11	68	19	Lymphatic	Right	No	HBP, S
12	55	17	CVI	Left	No	DL
13	76	22	CVI	Right	Yes	HBP, DL
14	74	24	Mixed	Right	No	HBP
15	78	17	CVI	Bilateral	Yes	HBP, DL
16	73	18	CVI	Left	No	HBP
17	62	19	Mixed	Right	No	DM II, S
18	69	14	Lymphatic	Left	No	HBP
Average	66.3	18.2				
SD	7.7	3.0				

(CVI: Chronic venous insufficiency; DM II: Type II Diabetes mellitus; HBP: High blood pressure; DL: Dyslipidaemia; S: Smoker; SD: Standard deviation)

Table II: Measurements and characteristics of the ulcers studied.

N	Age	Progress (months)	Initial area (cm2)	Final area (cm2)	Higher diameter	Initial pain	Final pain	Initial bleeding	Final bleeding
1	64	16	10	3	6	4	2	2	6
2	73	21	16	10	7	3	0	2	5
3	59	19	9	2	5	2	1	1	7
4	71	15	18	12	7	3	2	6	8
5	66	17	13	7	7	8	5	3	6
6	64	14	8	1	5	5	3	1	7
7	51	16	4	0	3	6	3	2	5
8	72	23	21	16	9	4	0	4	6
9	61	16	11		6	3		2	
10	57	20	14	8	8	3	2	3	4
11	68	19	12	7	7	4	3	2	5
12	55	17	7	0	4	5	3	4	7
13	76	22	36	27	12	4	1	4	9
14	74	24	28	21	9	5	3	5	6
15	78	17	23		7	4		2	
16	73	18	27	11	8	3	2	5	8
17	62	19	14	0	5	7	4	4	6
18	69	14	11	2	5	6	2	3	5
Average	66.3	18.2	15.7	7.8	6.7	4.4	2.3	3.1	6.3
SD	7.7	3	8.4	7.5	2.1	1.6	1.3	1.4	1.3

(SD: Standard deviation)

Table III: Predictive factors in the progress of the ulcers

	REDUCTION	N	Average	*p*
AGE	YES	10	65.10	0.024
	NO	7	76	
PROGRESS TIME (MONTHS)	YES	10	7.50	0.005
	NO	7	15.14	

	REDUCTION		*p*
HBP	Less than 50%	Greater than 50%	0.25
NO	1	3	
YES	6	7	

	REDUCTION		*p*
DM	Less than 50%	Greater than 50%	0.15
NO	2	4	
YES	5	6	

period of development of more than 14 months.

- Ulcers were refractory to conventional treatments carried out for at least 4 months without any positive progress, did not have any concomitant infections, and the patients were not taking antibiotics.
- There must not be any infections in the ulcerated area. Serial cultures of the exudate were carried out for this purpose. Patients with a positive culture were treated with antibiotics. Patients with a negative culture had to wait a month in order to observe if the ulcers improved after antibiotic therapy. If there was no improvement, these patients were admitted in the study.

The following patients were excluded from the study:

- Carriers of active infections observable in the cultures in which a notable improvement in the ulcer was observed after starting antibiotic therapy.
- Patients who did not respect the study protocol.
- Patients with intercurrent diseases, apart from the pathologies mentioned above.
- Patients undergoing complex pharmacological treatment that could interfere with and/or alter the healing of the ulcer.

Treatment

All patients were assessed using a Doppler ultrasound study (Esaote™ MyLab™ Fivecon linear probe LA Appleprobe, Esaote S.p.A., Genoa, Italy), in order to determine the aetiology of the ulcers and assess their limb-peripheral blood circulation.

The treatment programme consisted of one session of irradiating the ulcer site and its surrounding areas until forming a rectangle that exceeded each of the edges of the ulcer by 5 cm **(Figure 1)**. The treatment was carried out using the Er:YAG laser with RecoSMA technology. The RecoSMA is attached to the hand piece in the laser beam exit window **(Figure 2)**. When keratin was present in the ulcer, with the skin displaying a dry appearance, the outside edges of the ulcer were peeled using Er:YAG laser without the RecoSMA hand piece in order to achieve a consistent ablative effect by removing the tissue formed by the accumulation of keratin, dead cells and detritus.

In each treatment session a dose of 3.2 J/cm^2 was used with a frequency of 3 Hz. Three passes of the laser were made with a superposition of pulses of approximately 30%, covering the ulcer and the surrounding tissue. One session was carried out each week until completing 16 laser irradiation treatments. The decision to provide treatment for 4 months was agreed upon in order to standardise the protocol: The goal was to achieve the closure or reduction of the wound, or to reach a condition that would be suitable for the patient to receive a skin graft. Two of the patients did not complete the study, withdrawing from the study after the first treatment session. No other withdrawals were observed as signs of improvement started being detected after the third session, particularly in the tissue vitality characteristics.

Laser system and RecoSMA technology

The Er:YAG 2940 nm wavelength laser beam is efficiently absorbed by water. RecoSMA technology, based on a sophisticated optical system, converts the main laser beam into thousands of microbeams. The energy emitted in pulses, when interacting with the tissue modulates spatially which means that the energy affects not only the skin's surface, but also penetrates towards the inside of the dermis. The surface absorption of the laser energy causes a fine ablation and powerful acoustic resonance waves which are transmitted into the tissue. Consequently, collagen fibres undergo separation and microtraumas due to a pushing force. The tissue repair process leads to the formation of new collagen.

The laser radiation area of 1 cm^2 is covered by microbeams with a diameter of 50 μm. The multiple laser beams in the impact area of the skin are separated from each other by a distance of 50 μm. The 250 μs duration of the laser pulse is shorter than the skin's thermal relaxation time [5].

The adjustment of the 3.2 J/cm^2 energy dose value, together with the laser pulse time, makes it possible to achieve a very superficial microablation sufficient to remove a few epidermis cell layers, without exceeding the thickness of this cutaneous layer. The laser energy propagates through the displacement of mechanical-acoustic waves which collide with each other while penetrating the skin, causing a gelification phenomenon of the dermis. The observed histological image is due to the lack of definition of dermic fibres, known as hyalinisation. As the acoustic waves move towards the interior of the dermis, the pushing force decreases to safe levels and then disappears, thereby preserving the tissue's viability.

The density of thousands of ablated microareas on the skin surface achieves individual ablative impacts within an area of 1 cm^2. In the dermis, the mechanical-acoustic effect acts as a series of microexplosions. However, the capacity of each of the waves generated would not be enough to damage the fibres and cells in the dermis, although the intercrossing of the wave interference amplifies the resonance phenomenon, increasing the power acting on the tissue. This is able to cause damage to the cellular membranes, the cytoplasm and/or the nucleus through a mechanical action.

The microlesions, reaching up to 6 mm in depth, produce microtraumas responsible for stimulating tissue repair, but without generating fibrotic tissue thanks to the absence of thermal damage **(Figure 3)**.

Objective and subjective assessment of results

The aspect and characteristics of the ulcers were examined at the beginning and at the end of treatments, 3 months later. The patients' pain and the reduction of the ulcer area were examined at the end of the treatment cycle. For the subjective assessment, questionnaires were used: patients estimated their pain and bleeding and gave their personal opinion concerning the ulcer in terms of its size and progress during the treatments. Visual analogue scales between 1 and 10 were used to score this, with 1 as the minimum, 5 as a medium level and 10 as the maximum level. The same scale was used to define the degree of pain, determine the degree of bleeding and the reduction of the ulcer area.

Once each treatment was carried out, patients were instructed not to apply any kind of product on the ulcer. The lesion was covered only with a polyurethane film and a non-compressive bandage [6].

The ulcers were photographed at a constant distance of 30 cm under the same lighting conditions, using a digital camera (Canon EOS 400D, Tokina ATX Pro 100 f 2.8 with a macro lens, Sea & Sea flash Macro DRF 14; Canon, Tokyo, Japan). Photographs were taken before the first laser session, and then weekly before each treatment. The final photograph was taken before completing the last treatment. This last photograph was taken 3 months after the first laser session. A visual analysis of all the photographs was carried out by an independent doctor, an expert in treating ulcers. The same photographs were used for the objective assessment, which was carried out via a digital analysis of the image.

The predictive factors that play a role in the reduction of ulcers were also assessed: age, gender, cardiovascular risks such as high blood pressure, type II diabetes, dyslipidaemia and smoking. The aetiology of the ulcers, the progress time and its initial area were also checked in the assessment. Finally the treatment was considered to be effective when the ulcer presented a reduction of more than 50% of its initial area.

Assessment by computer

The ulcers were analysed by examining the photographs using a computer program [7]. The "before" images and the images 3 months after finishing laser sessions were compared. The data from each patient were stored in their corresponding files, including all the photographs of the ulcers. The software automatically standardised the size of the lesions, depending on the number of pixels per ulcer area. Generic techniques were used in software analysis, such as segmentation of the lesion edges and changes in ulcer size. To overcome the problem of false interpretations, the program processes images by filtering the signals using morphometric descriptors, which are commonly used in image processing. This technique made it possible to carry out completely independent and customised analyses, with the optimisation of the contrast and brightness parameters, highlighting the elements of interest [8]. Because the analysis process is automatic it was possible to examine the areas of interest with precision, according to the progress of the changes that had occurred in the lesion [9].

The photographs were converted into graphics using the same computer program, to compare the ulcer size at different stages of treatment **(Figure 4)**. Afterwards, the results detected with comparative measurements were taken indicating the percentage, progress and effectiveness of the laser treatment with RecoSMA **(Figure 5)**.

Histological studies

Ten (10) patients in the study were randomly selected for biopsies before beginning the first treatment at 6 weeks, before the sixth session, and before the twelfth session. Lidocaine without epinephrine (Lidocaine Normon 1% injectable solution, EFG) and a punch of 2 mm in diameter were used to take tissue samples which were processed in a standard manner, and were stained with haematoxylin/eosin (HE/EO). The analysis of samples was carried out by the Pathology Service of the Viamed Monegal Hospital (Tarragona, Spain).

Statistical analysis

SPSS® v. 22 software for Windows was implemented for the statistical analysis, using the Student's t-test for quantitative variables. Fisher's exact test was used for qualitative variables, as the study involved a small number of patients. A value of $p < 0.05$ was considered to be statistically significant.

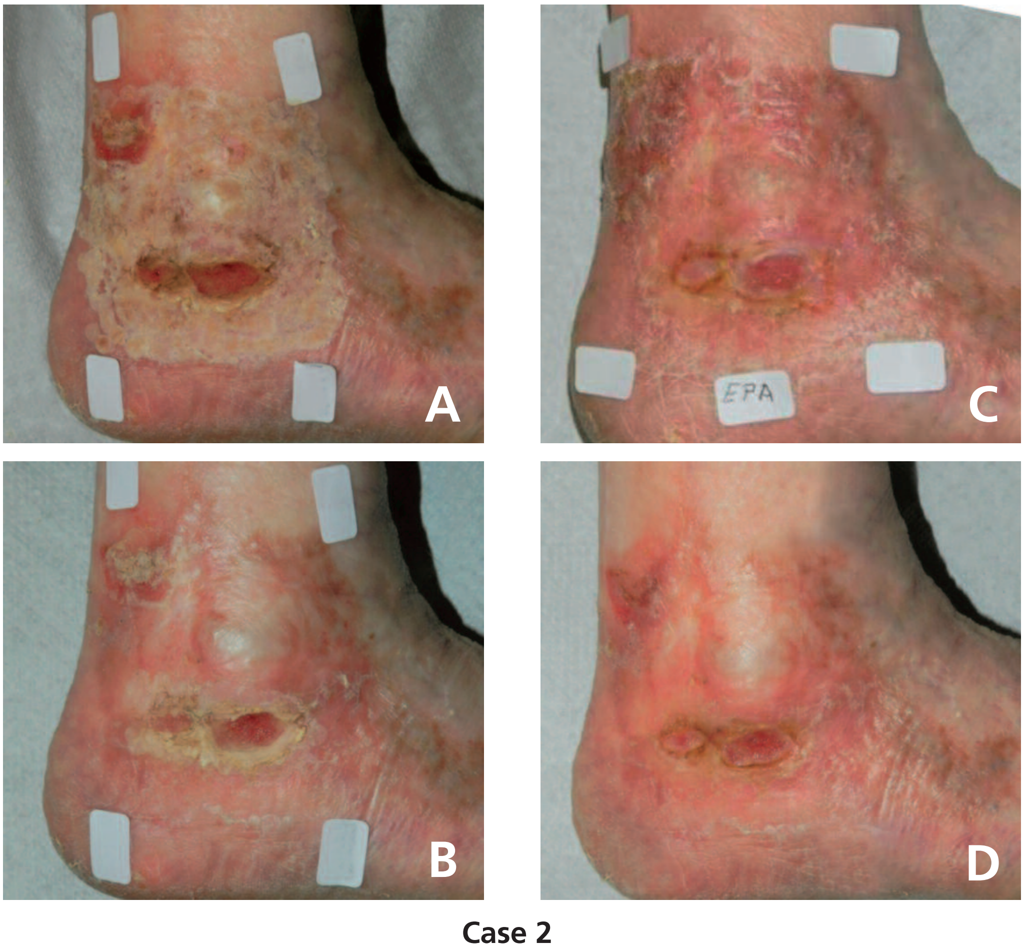
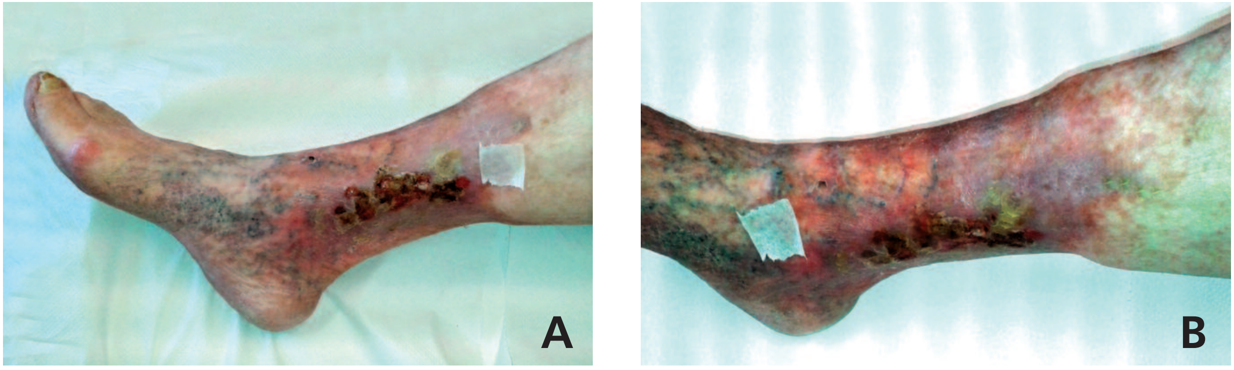


Fig. 1: 73-year-old male, case patient No. 2 of the study. Ulcers have been present for 4 years. **A)** Observe the treated area which surpasses the ulcer. The white labels allow the software to recognise the colour in order to match the tone from the photographs, and to help to define the size of the lesion. **B)**, **C)** and **D)** Are related to the various treatments carried out. The progressive improvement of the ulcer until its closure can be observed.

Fig. 2: The RecoSMA® system has several lenses that allow the laser beam to be divided into 10,000 microbeams/cm^2, with each one of them retaining high power. RecoSMA® is attached to the hand piece of the Er:YAG laser.



Case 9

Fig. 3: A 61-year-old female, patient No. 9 of the study shows multiple ulcers with a slow progress of more than 8 years. **A)**, **B)** and **C)** show the progressive improvement relating to the various treatments.

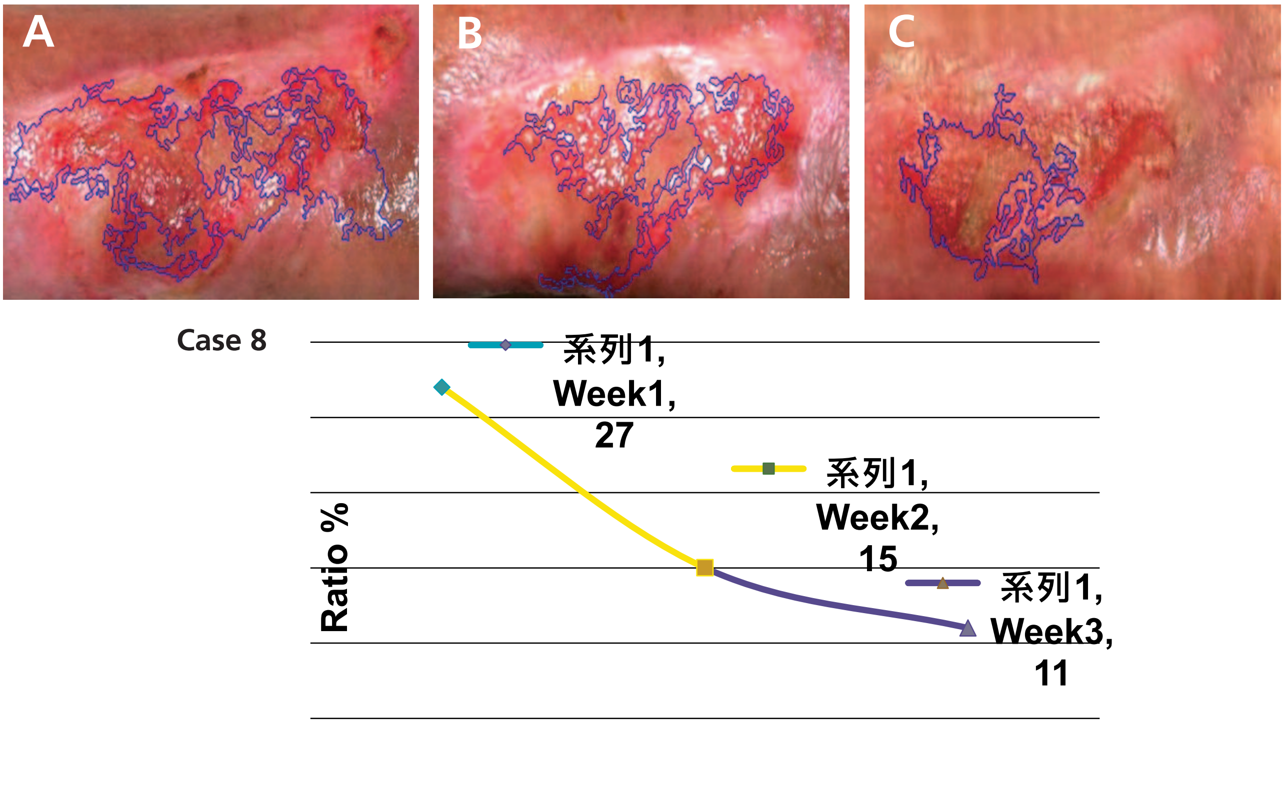


Fig. 4: 72-year-old male, patient No. 8 of the study. **A)** and **B)** show the progress of the ulcer until its final condition **C)** at the end of the scheduled series of treatments. The closure of the ulcer was not achieved, but its condition was improved, preparing the patient to receive a skin graft. The graphic below quantifies the reduction of the ulcer according to calculations made by the software.

Results

The results are expressed as the mean plus standard deviation, taking into account that 2 patients did not complete the study. The average length of the ulcers along the main axis was 6.7 ± 2.1 cm before beginning the treatment, with an initial average area of 15,7 ± 8.4 cm^2 (r=4 – 36). On the scale from 1 to 10 (1 no pain, 10 maximum pain), at the beginning of treatment patients reported an average of 4.4± 1.6 points (r=2 – 8). At the end of treatment patients reported their pain more than 2 points lower on the scale, with an average of 2.3 ± 1.3 points (r=0 – 5).

Regarding the bleeding, measured on the scale from 1 to 10, an increase in the signs of bleeding was observed matching the progress of the number of laser sessions. At the beginning of the treatment, patients presented bleeding of 3.1 ± 1.4 on average (r=1 – 6) and the result at the end of treatment was 6.3 ± 1.3 (r=4 – 9).

Concerning the reduction of the ulcer area at the end of the treatment, 3 patients (18.75%) presented a reduction of under 25%; 4 patients (25%) had a reduction between 25-50%; 2 patients (12.5%) presented a reduction in the ulcer area between 50-75%; 4 patients (25%) presented a reduction greater than 75%, and 3 patients (18.75%) had a complete closure of the ulcer **(Fig. 5-11)**. The final area of the ulcer was reduced to 7.8 ± 7.5 cm^2 in the 13 patients who did not achieve a complete reduction of the lesion. The treatment managed to reduce pain as well as the ulcer area, while the bleeding increased. These parameters were statistically significant (p=0.05), on the Student's t-test for the comparison of averages.

Upon determining the predictive factors indicative of the development of ulcers at the end of the treatment, a reduction was considered to be effective when there was a decrease of more than 50% of the

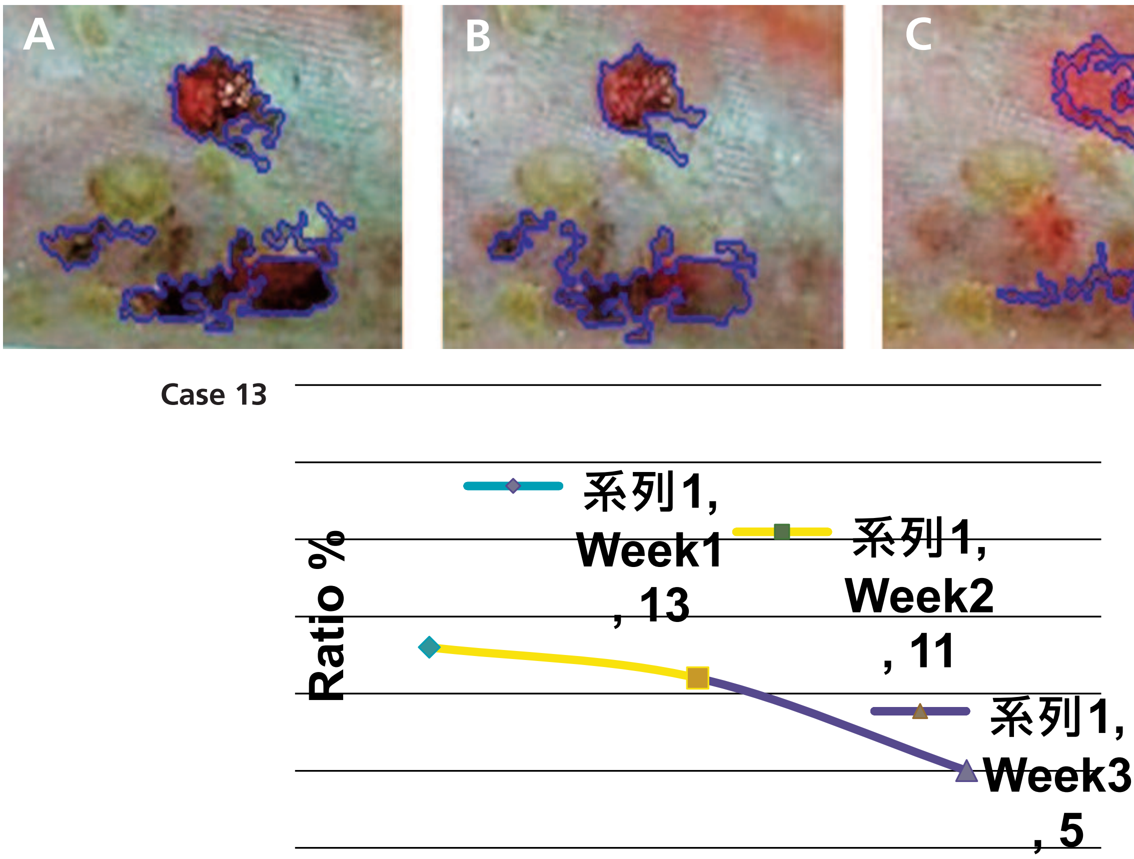


Fig. 5: 76-year-old female, patient No. 13 of the study. **A)** and **B)** represent various conditions until the final healing of the ulcer in **C)**. The graphic below shows the significant progress of the ulcer as quantified by the software.

initial lesion area. The factors that played a statistically significant role in the progress were: age (p = 0.024) and the ulcer progress period (p = 0.005). Other risk factors, such as type II diabetes, high blood pressure, dyslipidaemia and smoking were not observed to be statistically significant under the laser treatment. The Mann-Whitney U test was used for this purpose.

Assessment by computer

When analysing the images using the computer program, a general trend in reducing the ulcer area was noticed in 100% of the patients who completed the study. The treatment achieved complete ulcer closure in 3 patients (18.75%). Regarding the other patients, 3 did not show any significant improvement during the analysed sequence, displaying improvement at insignificant levels (less than 25%). In general, the analysis of the images closely matched the visual examination analysis.

Histological Studies

The samples taken from the centre of the ulcers before beginning the treatment presented a lack of epidermis and a loss of the usual dermal structure. There was practically no papillary layer in the dermis and the collagen fibres were unstructured. No cutaneous annexes were observed. Vascularisation was poor and presence of images of pseudofibrosis was noticed, with fibres encrusted in the reticular dermis. The interfibrilar spaces were wide, and there was a moderate presence of inflammatory cells. The surface of the tissue presented isolated necrotic material, formed by detritus, keratin and cellular remains, with the appearance of dehydrated tissue.

In samples taken after six weeks, an appreciable disappearance of surface detritus and of keratin lumps was noticed. There was an abundance of anti-inflammatory infiltrate with multiple polymorphonuclear cells, basophil cells and a clear neoformation of new capillaries.

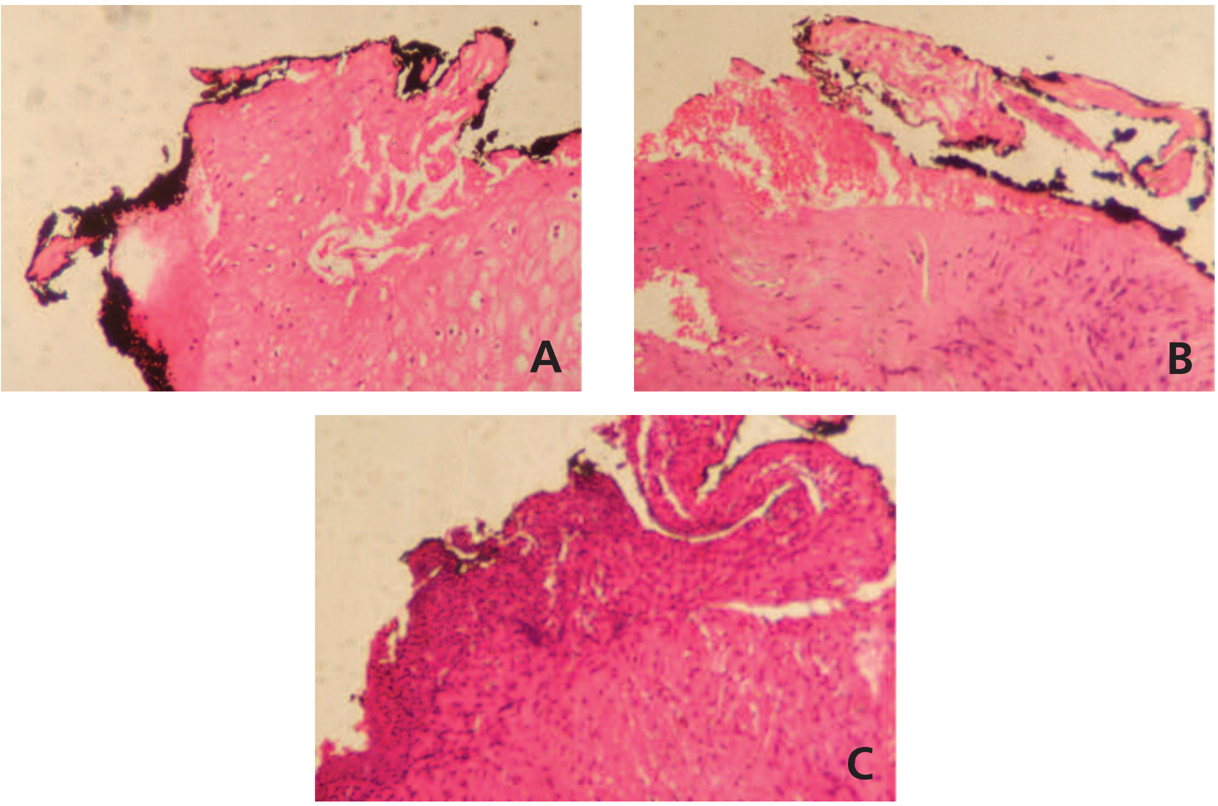


Fig. 6: Histology samples corresponding to **A)** before starting the treatment sessions; **B)** six weeks after, and **C)** three months after beginning the treatment.

In samples three months after beginning the treatment, before the twelfth session, a moderate presence of granulation tissue was observed in 6 of the samples from the 10 patients who had been randomly selected for biopsies. In general, tissue presented a dermis rich in vascularisation, with an abundant presence of microarteries. During examination, epithelial cells were observed which were indicative of an attempt to close the ulcer, due to the formation of an isolated thin, immature epidermis. The formation of new fibres with a vertical and parallel display was noted in the superficial dermis, but they still retained noticeable interfibrilar spaces, without signs of collagen compaction **(Figure 6)**.

Discussion

Chronic ulcers suffer from a phenomenon of stagnation in the standard healing mechanism. In these cases, external manipulation through various therapies is essential to reactivate tissue repair, as the inflammatory phase in this case is significantly inhibited, and the wound healing factors and cytokines do not interact appropriately [10].

After a loss of tissue substance, a series of complex mechanisms is triggered, which are only partially known; these include the phases of haemostasis, inflammation, proliferation and maturation [11, 12]. The first of these phases lasts approximately 72 hours, and its purpose is to cover the lesion (through the formation of a clot) and to keep it clean. Platelets and various inflammatory cells participate in this phase, mainly mast cells and white blood cells, along with soluble mediators (cytokines) that trigger the healing process. The inflammatory phase that should occur immediately afterwards, with local vasodilation and endothelial permeability, to facilitate the arrival of neutrophils and macrophages is blocked. In the case of chronic venous ulcers, the release of proteases to the lesion, especially metalloprotein 1, is compromised [13].

Treatment with the Er:YAG laser and RecoSMA technology produces a microtraumatic mechanical-acoustic "pushing effect" that causes the inflammatory phase to be re-triggered, against the stagnant metabolism in the ulcerated tissue. This assumption is supported by clinical observations and the histological analysis of this study as well as a previous publication [6]. Treatment is also conducted outside the ulcer in order to help the neighbouring tissue to aid the repair activity in the ulcer.

Repair phases following the blocked healing process in chronic ulcers hinder the proliferation of reparative cells whose fundamental aim is to increase collagen and angiogenesis and to build granulation tissue [10]. The maturation phase is not completed in chronic ulcers, "becoming endless" due to the absence of the proliferation of keratinocytes that have to migrate both from the edges of the lesion and from the basal layer [14]. The altered healing mechanisms show an increase in metalloprotein levels; this means an increase in proteolytic activity, preventing the growth factors required for healing from being triggered, as well as causing the degradation of the recently formed extracellular matrix [10]. The inflammatory phase is essential, due to the high activity of resident cells (epithelial cells, fibroblast cells and dendritic cells) for the production of mediators that attract platelets, neutrophils, lymphocytes and macrophages. All these cell phenomena facilitate angiogenesis and the production of granulation tissue [13].

New collagen is essential in the wound closure mechanism. In the best-case scenario, tissue replacement reaches between 70% - 80% of its previous state. The imbalance between the synthesis and degradation of collagen has an effect on repairing the wounds. In diabetic patients, collagen synthesis is altered, which is reflected in the wound closure mechanism. This detail must be emphasised, as the tissue repair mechanisms occur when laser light is used to stimulate new collagen formation [15].

Furthermore, the active vascular neoformation process is always present in the repair mechanism that follows laser treatments [16]. This tissue response has been particularly observed when using low-power density laser doses which, without any thermal action during the treatment, trigger the formation of capillaries. This occurs in the case of chronic ulcers in this study, where a residual thermal effect was not observed in the tissue after laser treatment with the RecoSMA technology [17, 18].

"The stimulatory mechanism of tissue repair by means of the RecoSMA technology, implementing the Er:YAG laser energy, was first noticed on various clinical trials. Promotion of more rapid and active healing of chronic damage tissue was confirmed latter on experiments which were carried out on liver of rats presenting with cirrhosis" It was possible to confirm that the liver parenchyma reacted with the RecoSMA-laser treatment, leading to the formation of regenerative and repaired tissue [5].

Other types of laser have been used as coadjuvant treatments for other therapeutic measures on chronic ulcers with varying results. Helium-Neon 636.2 nm lasers, diode, KTP and carbon dioxide lasers have been used in attempts to improve these lesions. The wavelengths used have varied between 590 and 10,600 nm. In the literature there are references to the complete closure of neuropathic diabetic ulcers within a period of 4 weeks using a 670 nm diode laser [19]. However, other reports do not find any significant differences with respect to standard treatments. In a publication by the Cochrane Foundation in 2000 [20], no benefit was found with low-power density laser treatment when compared with other therapies or with incoherent light. Only one study, with a small selection of cases, states that the combination of laser and infrared light can encourage the healing of ulcers in the lower extremities. However, the use of low-power density laser irradiation does appear to be useful in the reduction of pain. Good results were not observed using a 940 nm diode laser, even though there was an increase in prostaglandin I2 (PGI_2), which promotes the triggering of the repair process for chronic ulcers [21]. Therefore, it can be stated that although lasers are not effective as a monotherapy, they do appear useful when employed as a complement to other treatments.

Nevertheless, it should be remembered that this study follows the path of a new mechanical-acoustic and microablative effect for surface ulcers, which is not comparable with the standard treatment of chronic ulcers, although the tissue regeneration response with the Er:YAG-RecoSMA has been observed in other clinical indications [22–24].

The resonance waves are responsible for patients not experiencing a burning feeling during the treatment; therefore the treatment is carried out without anaesthesia. The stinging or burning feeling usually appears at the end of the treatment and would be a consequence of the increased blood flow and the subsequent rise of temperature in the treated area. The stimulating reaction observed is a consequence of the microcirculatory activation and the triggering of the metabolic processes. With the blood flow activation, the ulcer presents a shiny, hyperaemic appearance, meaning that patients experience a hot, stinging sensation, but this is well tolerated.

The histology research data concerning the interaction between the resonance waves produced by the laser confirm that the depth of the effect reaches up to 6 mm in soft tissue [22]. The presence of wide interfibrilar spaces may be a consequence of the mechanical thrust created by the resonance waves and the oedema reaction following the treatment. The absence of thermal images in the samples analysed avoids the risk of adverse reactions such as post-inflammatory hyperpigmentation.

In the first sessions, particular changes are not observed in the conditions of the CLEUs. This would be justified by the latency period that is required until the formation of new capillaries. Increased phagocyte and polymorphonuclear cell activity is synonymous with the active reparative inflammatory phase activated by the laser energy.

It is likely that if more treatment sessions had been carried out in this study, a higher number of closed ulcers would have been achieved. It therefore remains to be determined why some of the ulcers did not undergo significant changes with the treatment. The following step in this study, already in development, would define the treatment protocol, laser parameters and number of sessions required to achieve a more effective outcome. This would also indicate the treatment prognosis according to the characteristics of the ulcer.

Conclusion

An effective and safe alternative has been observed for refractory CLEUs when using the Er:YAG laser with the RecoSMA technology. Chronic ulcers either closed completely with this treatment or the ulcer area was reduced by over 50% in more than 50% of patients in this study. According to the protocol used, CLEUs were left able to be grafted or underwent total recovery through closure. Although it is not part of this study, the RecoSMA treatment has a direct influence on healthcare costs, because it offers an effective alternative solution. This fast and safe treatment improves, relieves and closes a pathology which is difficult to resolve. Laser treatment is simple to carry out and there is no risk of morbidity, given that no complications were observed during the entire time of this study.

References

1: Gloviczki ML, Kalsi H, Gloviczki P, Gibson M, Cha S, Heit JA. Validity of International Classifications of Diseases, Ninth Revision, Clinical Modification codes for estimating the prevalence of venous ulcer. J Vasc Surg Venous Lymphat Disord. 2014; 2(4):362-7.
2: Lal BK. Venous ulcers of the lower extremity: Definition, epidemiology, and economic and social burdens. Semin Vasc Surg. 2015; 28(1):3-5.
3: Alavi A, Sibbald RG, Phillips TJ, et al. What's new: Management of venous leg ulcers: Approach to venous leg ulcers. J Am Acad Dermatol. 2016; 74(4):627-40.
4: Martínez Carpio PA, Trelles MA. El láser y la fotónica en la Cirugía Plástica española e iberoamericana. Antecedentes históricos, aplicaciones actuales y proyectos de desarrollo inmediato. Cir Plást Iberolatinoam. 2010; 36(1):59-78.
5: Komchenko V. Treatment of Non-healing Wounds with Erbium Lasers. Actual Surgical Questions. The 15th Congress of Surgeons of the Republic of Belarus. Congress Material Extracts, Brest Ed, "Alternative". 2014; 44-5.
6: Hernández-Osma E, Komchenko V, Sola A, Pikirenia II, Alcolea JM, Trelles MA. Tratamiento de las úlceras crónicas de las piernas con láser de Er:YAG y tecnología RecoSMA. Cir Plast Iberolatinoam. 2015; 41(3):271-82.
7: Martín-Vázquez MJ. Trelles MA. Sola A. Calderhead RG. Trelles O. A new user-friendly software platform for systematic classification of skin lesions to aid in their diagnostics and prognosis. Lasers Med Sci. 2006; 21(1):54-60.
8: Trelles MA, Levy JL, Alvarez X. Efficacy of nonablative laser treatment for rhytids: a controlled study with objective evaluation via clinical, profilometric, and computer assessment. Aesth Surg J. 2006; 26(2):136-52.
9: Sadick NS, Trelles MA. A clinical, histological, and computer-based assessment of the Polaris LV, combination diode, and radiofrequency system for leg vein treatment. Lasers Med Surg. 2005; 36(2):98-104.
10: Lal BK, Saito S, Pappas PJ, et al. Altered proliferative responses of dermal fibroblasts to TGF-betta 1 may contribute to chronic venous stasis ulcer. J Vasc Surg. 2003; 37(6):1285-93.
11: Haque NS, Fallon JT, Pan JJ, Taubman MB, Harpel PC. Chemokine receptor-8 (CCR-8) mediates human vascular smooth muscle cell chemotaxis and metalloproteinase-2 secretion. Blood. 2004; 103(4):1296-304.
12: Hashimoto K. Regulation of keratinocyte function by growth factors. J Dermatol Sci. 2000; 24 Suppl 1: S46-S50.
13: Franks PJ, Barker J, Collier M, et al. Management of Patients with Venous Leg Ulcers: Challenges and Current Best Practise. J Wound Care. 2016; 25 Suppl 6 :S1-S67.
14: Rafetto JD. Pathophysiology of wound healing and alterations an in venous leg ulcers-review. Phebology. 2016; 31(1 Suppl):68-73.
15: Trelles MA, Trelles K, Allones I. Láser de CO_2 y Er:YAG en Dermocosmética. In: Cisneros JL, Camacho FM, Trelles MA. Láser en Dermatología y Dermocosmética. Madrid: Aula Médica, 2008; 123-32.
16: Trelles MA, Mester A, Rigau J, et al. Clinical use of He-Ne laser for wound healing. J Bloodless Med Surg. 1989 (b); 7:3-7.
17: Pikirenia II, Zemlyanik AN, Khomchenko VV. Possibilities of liver regeneration with induced cirrhosis at exposure of spatially modulated erbium laser radiation in experimental animals. Novosti Khirurgii. 2015; 23(2):131-7.
18: Pikirenia II, Zemlyanik AN, Khomchenko VV. The ability to regenerate the liver in experimental animals with induced cirrhosis under the influence of the spatially modulated erbium laser. http://www.surgery.by/list.php? PHPSESSID =ae63a86a87a25b6810bda4f37c38a28d&lang=en&year2015 &issue=2.
19: Dinh T, Pham H, Veves A. Emerging treatments in diabetic wound care. Wounds. 2002; 14:2-10.
20: Flemming K, Cullum N. Laser therapy for venous leg ulcers. Cochrane Database Syst Rev. 2000; (2):CD001182.
21: Tam G. Low power laser therapy and analgesic action. J Clin Laser Med Surg. 1999; 17(1):29-33.
22: Trelles MA. A novel platform for multiple laser systems for medical applications. http://www.linline-ms.com/?p=213, 2009, The Linline web page.
23: Trelles MA, Komchenko V, Alcolea JM, Martínez-Carpio PA. A novel method of facial rejuvenation using a 2940-nm erbium:YAG laser with spatially modulated ablation: a pilot study. Lasers Med Sci. 2016; 31(7):1465-71.
24: Volkova NV, Glazkova NK, Khomchenko VV, Sadick NS. Novel method for facial rejuvenation using Er:YAG laser equipped with a spatially modulated ablation module: an open prospective uncontrolled cohort study. J Cosmet Laser Ther. 2017; 19(1): 25-9.221