Original paper

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Usefulness of high-frequency ultrasound to assess the healing progress of shin ulcers

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Keywords

ulcer, healing, monitoring, high-frequency ultrasound, laser biostimulation

Abstract

Introduction: As the average lifespan becomes longer, the number of cases of chronic shin ulcers is rising, which is slowly becoming a societal problem. Currently, there no methods for objective evaluation of ulcer healing process. **Aim of the study:** The aim of the study was to assess the use of high-frequency ultrasound to monitor the healing of shin ulcers subjected to laser biostimulation. **Material and methods:** The study included 8 patients (4 men and 4 women) aged from 46 to 81 years with 9 shin ulcers in whom the healing process did not progress within 8 weeks despite effective causal treatment. The ulcers were subjected to laser biostimulation. The induced changes were monitored using high-frequency ultrasound and photographic records. Ultrasound examination was used to assess the depth of ulceration and the thickness of granulation tissue, migrating epidermis, subepidermal low-echogenic band (SLEB) and epidermis in the immediate vicinity. The wound severity index and ulcer vascularity were also assessed. **Results:** As a result of laser therapy, in 7 out of 9 cases the ulcers healed completely and in the remaining 2 cases ulcer size was reduced. During the ulcer healing process induced by laser therapy, ultrasound examination revealed decreasing ulcer depth, wound severity index and SLEB thickness. Granulation tissue increased in thickness and there was an epidermal formation effect (newly formed epidermis was much thicker than the one surrounding the wound and became thicker as a result of laser therapy sessions). During the healing of ulcers induced by laser therapy no significant changes were observed in ulcer vascularity and thickness of the surrounding epidermis. **Conclusions:** High-frequency ultrasound is a useful technique for the imaging of leg ulcers. It allows one to monitor their healing process induced by laser biostimulation. Further research on the subject needs to be pursued.

Introduction

Chronic shin ulcer is a chronic wound with complete skin loss which does not heal within 6–8 weeks or its surface does not decrease to a significant extent (by 20–40%) within 2–4 weeks. The prevalence of shin ulcers increases with age; they are found in 0.6–3% of patients aged over 60 and in 5% of patients aged over 80[(1)]. As the average lifespan becomes longer, the number of chronic shin ulcers is rising, which is slowly becoming a societal problem.

The most common causes of ulcers include chronic venous insufficiency (CVI), peripheral artery disease (PAD) and diabetes mellitus (DM)[(2)]. One should also bear in mind less frequent causes which include local skin infections, skin cancer, Buerger's disease, Raynaud's disease, impaired lymphatic drainage, connective tissue diseases, anaemia, polycythemia and dysproteinemia[1,3,4]. However, the most common cause of shin ulcers, which accounts for 70% of cases, is CVI, which is usually caused by reflux or post-thrombotic lesions in the lower extremity venous system.

The current therapy of shin ulcers involves both causal and local treatment. Causal treatment should include elimination or significant reduction of reflux in the lower extremity venous system, arterial revascularization, blood glucose level regulation and appropriate therapy for less common conditions. It is very important to perform concomitant local treatment that includes wound cleaning and stimulation of epithelialization. Local treatment methods include various, often technologically advanced dressings, vacuum-assisted closure (VAC), hyperbaric oxygen therapy, local administration of growth factors and laser therapy[1,2,5]. During both causal and local treatment, it is very important to monitor progress. To this end, various scales are used that are based on visual, subjective assessment of ulcers, such as Leg Ulcer Measurement Tool (LUMT), Sussman Wound Healing Tool (SWHT), Wound Healing Scale (WHS) and others[6]. However, the assessment of healing progress using these scales is time consuming and has a low level of objectivity due to their imperfection: most importantly, they are examiner-dependent.

In recent years, high-frequency ultrasound has become increasingly common and is widely used in dermatology. It is primarily used to differentiate between skin marks and to monitor the course of chronic diseases, e.g. scleroderma, atopic dermatitis, psoriasis and similar conditions[7]. Single reports focus on skin assessment in CVI; however, they do not include a thorough analysis of venous ulcer morphology[8].

High-frequency ultrasound transducers make it possible to assess both the epidermis and dermis[9]. This allows one to monitor ulcers during the healing process based on ulcer depth, granulation tissue thickness, the presence and thickness of newly formed epidermis, the thickness of epidermis in the immediate vicinity of the wound and the thickness of subepidermal low-echogenic band (SLEB). SLEB is histopathologically consistent with the papillary layer of the dermis. In addition, colour Doppler ultrasound makes it possible to assess the vascularity of the lesions. Due to the fact that high-frequency ultrasound is an increasingly common, non-invasive and relatively inexpensive diagnostic method, it seems that it can be widely used to monitor ulcer healing process.

In this study, the present authors attempted to assess the usefulness of high-frequency ultrasound to monitor the healing process of ulcers subjected to laser biostimulation therapy.

Aim of the study

The aim of the study was to assess the use of high-frequency ultrasound to monitor the healing of shin ulcers subjected to laser biostimulation.

Material and methods

The study was conducted from 2016 to 2018 and included 8 patients (4 men and 4 women) aged from 46 to 81 years (mean 70.2 ± 11.6) with shin ulcers. In the study, 9 shin ulcers were examined, with one patient having bilateral lesions. All ulcers were venous ulcers; in addition, two individuals had diabetes. The study included patients with shin ulcers in whom ulcer healing did not progress within 8 weeks despite effective causal treatment (elimination of reflux in the superficial venous system of the legs, regulation of blood glucose levels). Before the start of the study, the patients were informed of the nature of the study and provided their informed consent to participate in it.

Before the start of laser therapy, histopathological examination of the ulcer margin was performed to exclude skin cancer. Every patient also had a microbiological culture test performed on a sample from the surface of the ulcer; however, due to the lack of clinical signs of infection, antibiotic therapy was not administered. The patients underwent local therapy using a Polish laser biostimulation device called SMARTs (Lasotronix, Piaseczno, Poland) with a maximum power of 400 mW and wavelength of 635 nm (Fig. 1). Biostimulation sessions were conducted twice a week; a dose of 400 mW was applied on every 1 cm^2 for 10 seconds. In one patient, laser biostimulation was used before intermediate-thickness skin graft and it was continued during the period of graft integration.

Photographic images were taken and ultrasound scans were performed of ulcers in all patients before, during and after laser biostimulation therapy. Photographic images of ulcers were taken using the Canon EOS 5D Mark III camera with the same equipment settings and lighting arrangement. The photographs were used to assess the size of the ulcer surface and to compare the visual changes in the wounds with ultrasound images. A classic Philips EPIQ 5 ultrasound machine equipped with an L18-5 broadband linear transducer was used for ultrasound examination. On ultrasound, the ulcers were examined at the border between healthy skin and the wound. The most advanced sites of ulceration were selected for analysis. All scans were performed at constant values of time gain compensation (TGC) with the device set to the highest resolution, but small penetration depth. The same settings were used for all scans.

The following were determined in the collected material:

- **ulcer depth and wound severity index (WSI)**: in order to determine the depth of ulceration the authors partly used the mathematical model of wound healing and remodelling proposed by Lemo *et al*.[10] This model was originally developed for small-surface wounds; therefore, it required modification for the purpose of this study. Due to large surfaces of the ulcers, their depth was assessed indirectly. The distance was measured between reflection from the epidermis and deep fascia

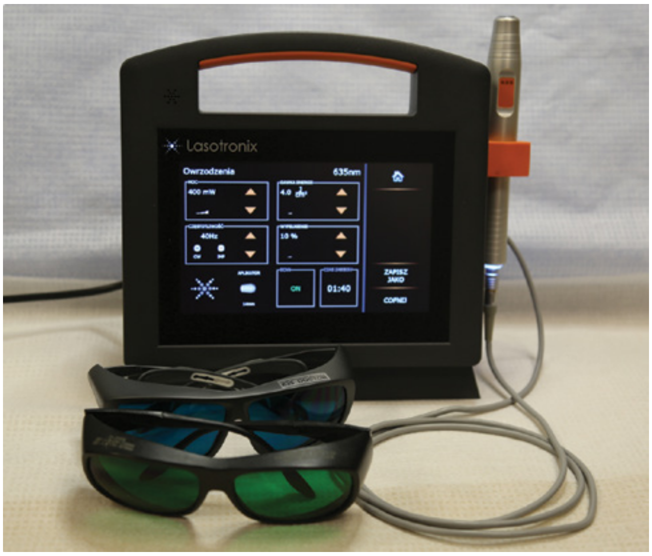

Fig. 1. *SMARTs laser biostimulation device (Lasotronix, Piaseczno, Poland)*

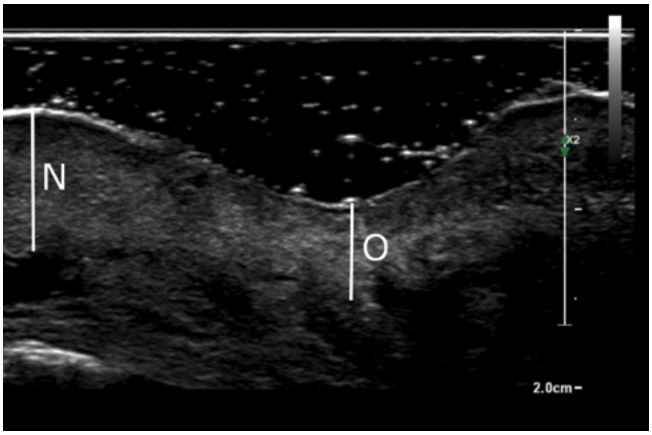

Fig. 2. *Figure showing measurements necessary to determine ulceration depth (N – distance between reflection from the epidermis and deep fascia; O – distance between the external surface of the ulcer base and deep fascia)*

separating subcutaneous tissue from the muscle layer in the ulcer vicinity (N) and between the external surface of the ulcer base and deep fascia separating subcutaneous tissue from the muscle layer (O). Based on this, ulcer depth was determined using the following formula (G for depth): G = N – O. In addition, using Lemo *et al*. findings, wound severity index was calculated: WSI = (N – O)/N (Fig. 2);

- **granulation tissue thickness** measured at the ulcer base. The measurements were taken from the reflection occurring between the gel echo and the surface of hypoechoic granulation tissue up to the border between the end of hypoechoic granulation tissue and dermis echo (Fig. 3);
- **migration of newly formed epidermis**: its presence or lack, and its thickness. The thickness of the newly formed epidermis was the thickness of hyperechoic linear reflection occurring below the gel echo, on the surface of the dermis (Fig. 4);

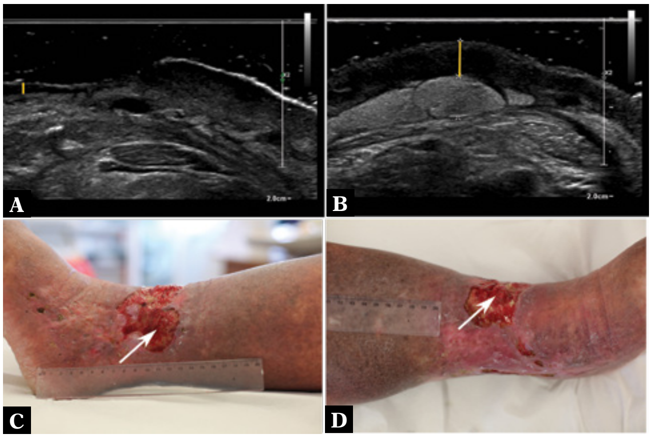

Fig. 3. *Example measurement of granulation tissue thickness.* **A.** *Ultrasound examination of the ulcer before laser therapy with granulation tissue thickness measurement.* **B.** *Ultrasound examination of the ulcer during laser therapy with an evident increase in the amount of granulation tissue and its measurement.* **C.** *Photographic image before laser therapy (the arrow marks the granulation tissue).* **D.** *Photographic image during laser therapy (the arrow marks the granulation tissue)*

- **epidermis and SLEB thickness** in the vicinity of the ulcer. The thickness of the epidermis was the thickness of hyperechoic linear reflection occurring below the gel echo, on the surface of the dermis. SLEB thickness was the thickness of the hypoechoic band parallel to the surface of the skin, located directly below the epidermis[8,9] (Fig. 4);
- **degree of vascularity of the ulcer base and the surrounding tissues** imaged on CD. The degree of ulcer vascularity was rated as: 1 – low, 2 – moderate, 3 – high (Fig. 5).

The assessment was performed before, during and after laser biostimulation therapy. In order to minimize measurement errors, all measurements were performed three times; subsequently an arithmetic mean value was calculated. The data obtained were analysed.

Results

In the study group, the ulcer surface was between 2 and 102 cm^2 (mean 24.1 ± 31.9); the duration of ulcer presence was between 7 and 360 months (mean 92.6 ± 117.2). The ulcer healed completely in 6 patients (7 ulcers), and in 2 other patients the ulcer surface was reduced by over 30 and 40%. The ulcers are described in Tab. 1.

During laser therapy sessions the depth of all ulcers was reduced: before laser therapy it ranged between –1.33 and 4.53 mm and during the sessions it was between –1.33 and 3.07 mm. In 8 individuals wound severity index (WSI) was also reduced; in addition, in a patient with ulcer overgrowth above the surface of the surrounding skin the overgrowth decreased (Tab. 2). Fig. 6 and Fig. 7 show example ulcers and their ultrasound

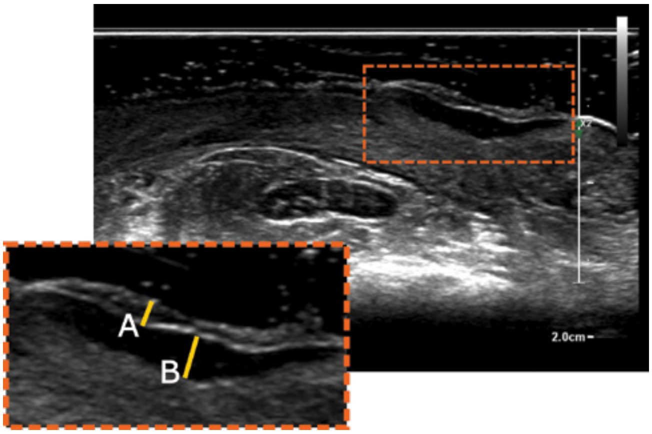

Fig. 4. *Figure showing measurements of migrating epidermis and SLEB thickness. A – epidermal thickness, B – SLEB thickness*

images before and after laser therapy. The maximum depth of granulation tissue before laser therapy ranged between 0.9 and 6.13 mm (mean 2.66 mm ± 1.41 mm) and it was 2.03–4.17 mm (mean 2.97 mm ± 0.7 mm) during treatment (Tab. 2).

Ultrasound examination of ulcers also made it possible to determine the thickness of epidermis in the vicinity of the wound and observe newly formed epidermis and determine its thickness. The process of epidermis formation was evident in 5/9 ulcer cases before laser therapy. During therapy, it was observed in all wounds. The mean thickness of newly formed epidermis was 0.92 mm ± 0.23 mm and 1.09 mm ± 0.26 mm before and during laser therapy, respectively. However, the thickness of the surrounding epidermis did not change significantly during laser therapy. The maximum SLEB values in the immediate vicinity of the wound were determined; in the majority of the individuals (7/9) they were observed to decrease: 0.13–1.13 mm (mean 0.78 mm ± 0.3 mm) and 0.13–1.43 mm (mean 0.57 mm ± 0.37 mm) before and during laser therapy, respectively. No relationships regarding vascularity were observed before, during and after laser therapy (Tab. 3).

After the laser biostimulation therapy was completed, in 7 out of 9 cases ulceration was cured completely, while in 2 patients the ulcer size was reduced by 30% and 40%. After the completion of laser therapy, the assessment of the majority of parameters mentioned above was purposeful in only 2 patients in whom ulceration did not heal completely. In those

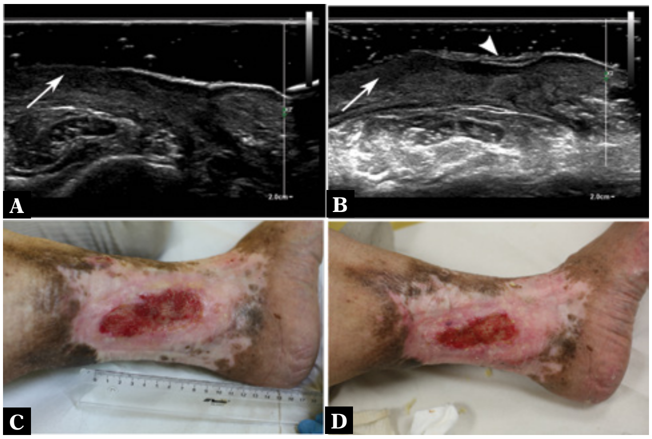

Fig. 6. *Example ulceration in an 81-year-old female patient before and after laser therapy in whom ulcer size was reduced by over 30%.* **A.** *Ultrasound examination of the ulcer before laser therapy [migrating epidermis was not visualized, but granulation tissue is evident (arrow)].* **B.** *Ultrasound examination of the ulcer after laser therapy [granulation tissue (arrow) and migrating epidermis (arrow head) were visualized].* **C.** *Photographic image before laser therapy.* **D.** *Photographic image after laser therapy*

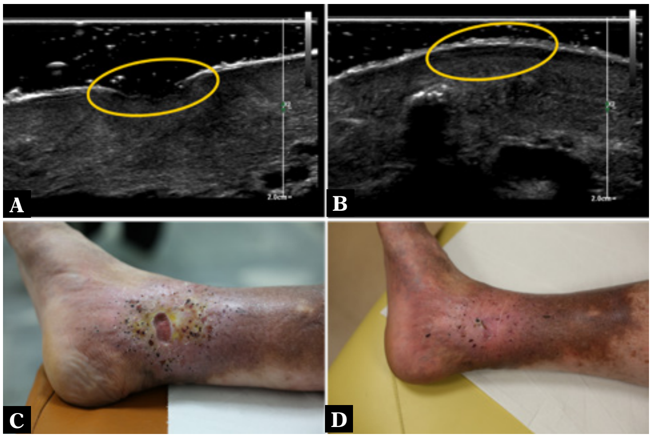

Fig. 7. *Example ulceration in a 46-year-old male patient before and after laser therapy in whom the ulcer healed completely.* **A.** *Ultrasound examination of the ulcer before laser therapy which shows epidermal loss and partial dermal loss (ellipse).* **B.** *Ultrasound examination of the ulcer after laser therapy with evident reconstruction of the epidermis and dermis on the previous ulcer site (ellipse).* **C.** *Photographic image before laser therapy.* **D.** *Photographic image after laser therapy*

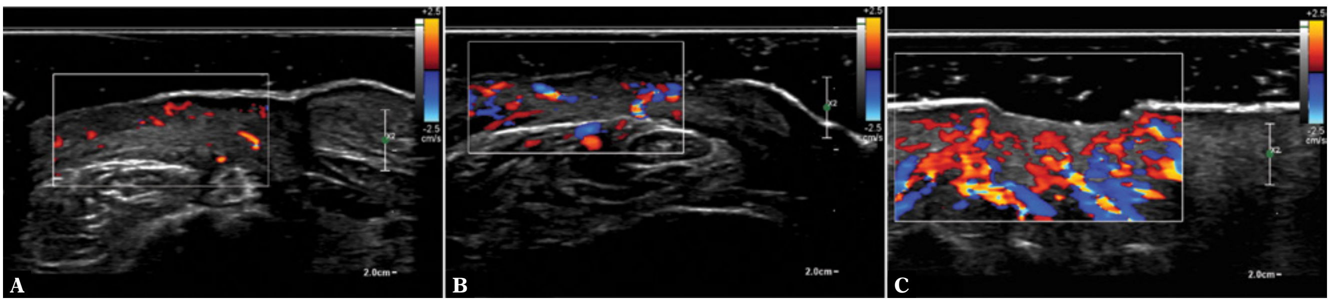

Fig. 5. *Degree of ulcer vascularity* **A.** *Low.* **B.** *Moderate.* **C.** *High*

Tab. 1. *Description of ulcers and laser therapy duration*

No.	Sex	Age	Side	Ulcer aetiology	Duration [months]	Ulcer surface [cm²]	Duration of laser therapy [weeks]	Ulcer status after treatment
1	M	78	P	CVI	120	6	12	healed
2	M	71	P	CVI	15	7	4	healed
3	K	77	P	CVI	96	102	6	healed after transplant
4	K	75	P	CVI	360	11	5	reduction by 40%
5	K	81	P	CVI/DM	180	24	7,5	reduction by 30%
6	M	60	P	CVI/DM	7	12	24	healed
7	M	60	L	CVI/DM	8	45	14	healed
8	K	74	P	CVI	30	8	15,5	healed
9	M	46	P	CVI	18	2	19	healed
CVI – chronic venous insufficiency; DM – diabetes mellitus								

Tab. 2. *Data on ulcer depth and granulation tissue amount before and during treatment*

No.	Duration of laser therapy [weeks]	Ulcer depth [mm]	WSI	Granulation tissue thickness [mm]	Time of examination from laser therapy start [weeks]	Ulcer depth [mm]	WSI	Granulation tissue thickness [mm]
		Before biostimulation				**During** biostimulation		
1	12	4.53	0.54	1.43	8	3.07	0.39	2.9
2	4	1.03	0.23	2.5	*	*	*	*
3	6	3.43	0.53	0.9	2	1.93	0.32	2.03
4	5	2.67	0.38	2.57	2	1.73	0.31	2.6
5	7.5	2.1	0.22	2	2	1.57	0.19	2.57
6	24	3.63	0.28	2.27	3	3.5	0.28	2.3
7	14	2.37	0.25	2.7	3	–1.33	–0.18	3.83
8	15.5	–1.33	–0.23	3.4	10	–1.07	–0.12	3.3
9	19	2.9	0.21	6.13	2	1.4	0.11	4.17
* Ulceration was cured before follow-up examination; negative values refer to raised ulcers.								

Tab. 3. *Data on epidermal and SLEB thickness before and during treatment*

No.	Migrating epidermis thickness [mm]	Thickness of epidermis surrounding the ulcer [mm]	SLEB [mm]	Vascularity	Time of examination from laser therapy start [weeks]	Migrating epidermis thickness [mm]	Thickness of epidermis surrounding the ulcer [mm]	SLEB [mm]	Vascularity
	Before biostimulation					**During** biostimulation			
1	**	0.47	1.13	3	8	1	0.47	0.67	3
2	0.90	0.43	0.7	3	*	*	*	*	*
3	**	0.77	1.03	1	2	1.1	0.43	0.53	2
4	1.00	0.5	1.1	1	2	1.6	0.57	1.43	2
5	**	0.47	0.9	3	2	0.7	0.37	0.7	2
6	1.00	0.43	0.13	2	3	1.1	0.47	0.13	2
7	0.50	0.5	0.67	2	3	1	0.33	0.23	2
8	1.20	0.53	0.83	3	10	1.3	0.4	0.37	3
9	**	0.4	0.53	3	2	0.8	0.47	0.57	3
* Ulceration healed before follow-up examination. ** No newly formed epidermis.									

patients, the trend observed on a previous follow-up examination continued: the wound depth and WSI decreased and the thickness of the granulation tissue was slightly higher than previously: 2.83 mm and 2.65 mm (previously 2.6 mm and 2.57 mm, respectively). In both patients, epithelialization was observed; the thickness of newly formed epidermis was 1.3 mm and 0.8 mm, respectively (previously 1.6 mm and 0.7 mm). The thickness of the surrounding epidermis and SLEB was similar to that observed on a previous follow-up examination. In the patients whose ulcers healed completely, the processes of granulation, epithelialization, and epidermal and dermal loss were not observed. On the site of the healed ulcer epidermal thickening was observed (mean 0.95 mm ± 0.17 mm), while the thickness of SLEB was comparable to the values recorded during laser therapy (mean 0.57 mm ± 0.3 mm).

Discussion

Shin ulcers are a difficult clinical problem usually affecting elderly individuals[1,11]. Currently, there are no available methods allowing one to make a precise and objective assessment of extensive wound healing. Usually photographic images are used to monitor this process; attempts are also being made to use 3D spatial models for assessment[12]. However, these methods do not make it possible to examine internal structures, i.e. the skin and subcutaneous tissue and observe changes occurring in them. The present authors attempted to perform ultrasound assessment of ulcers in patients with CVI. They found few papers on similar topics in the literature.

Histologically, ulceration is described as loss of the epidermis and part of the dermis which rarely extends to subcutaneous tissue[13]. Ultrasound examination made it possible to assess these layers and visualize the tissue loss described above in a non-invasive way. Ultrasound was also used for quantitative assessment of ulcer depth before and during healing. It demonstrated that laser biostimulation therapy is useful in reducing ulcer depth.

The typical presentation of chronic wound and ulcer healing is healing by granulation with slow approximation of wound margins and gradual migration of newly formed epidermis[6,14]. The present authors attempted to assess both processes during the study. Granulation tissue amount turned out to be a relatively easy parameter to control since it was characterized by lower echogenicity in comparison with the surrounding dermis and was well-defined against it[15]. In some cases, the selection of the site for the measurement of granulation tissue thickness was difficult, which was due to a large ulceration area and uneven distribution of newly formed granulation tissue. As a result, it was necessary to measure this parameter a few times and calculate the mean. It was relatively easy to notice newly formed epidermis. It was characterized by heterogeneous reflection of hyperechoic echo and was much thicker from the epidermis in the immediate vicinity of the wound. This appearance is confirmed by histopathology reports[16]. Based on the present authors' experience, ultrasound is not a good tool to determine the quantity of newly formed epidermis. This is primarily due to its uneven migration and a large ulceration surface area. However, it is possible to assess this process precisely using other imaging techniques, such as, for example, a confocal microscope[17]. Nevertheless, ultrasound examination can be useful in confirming the onset of new epidermis formation, whose visual assessment is not possible. In the current study, laser biostimulation therapy was demonstrated to have a positive effect in terms of the amount of both newly formed granulation tissue and newly formed epidermis on the ulcer site. These results are consistent with the findings of Solmaz *et al*. regarding the effect of laser biostimulation treatment on wound healing rate[18].

Another interesting parameter that was assessed was SLEB thickness. According to literature data, SLEB thickness is a variable parameter which depends on the patient's age and UV radiation exposure, among other factors, thus being a possible marker of skin ageing[19]. Some authors emphasize the fact that SLEB thickness does not only reflect structural changes, but can also be a marker of water retention in the papillary layer of the skin[19,20]. In the study material, the present authors observed significant thickening of SLEB before treatment and reduction in its thickness in the course of laser therapy. They believe this may have been due to decreasing oedema of the papillary layer of the skin during the treatment. However, further research is necessary to confirm this presumption.

It is also surprising to find that the degree of vascularity was not significant in this study on the effect of laser therapy on the healing process. This may be due to the small patient sample size; therefore, further research on the topic is warranted.

Conclusions

The results of the present study show that high-frequency ultrasound is a useful technique for the imaging of leg ulcers. It allows one to monitor their healing process induced by laser biostimulation. Due to the fact that there are no publications on the subject, further research is necessary.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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