Low intensity laser therapy for chronic venous leg ulcers

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Ulceration of the lower extremities is one of the most important medicosocial problems (Skobelkin *et al* 1990). In this article, two case studies show that it is the length of time that laser therapy is used that can have a significant impact on ulcer size.

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- Wounds

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Venous disease, as a cause of ulceration, accounts for up to 90 per cent of all chronic wounds of the lower extremity (Baker *et al* 1991). The prevalence of venous ulceration has been well researched and documented. Cornwall *et al* (1986) found an incidence of 1.8/1000. Their management places a considerable financial strain upon the National Health Service. Costing of the management of venous ulceration is speculative, but it is estimated that the annual expenditure is £200 million in the UK alone (Freak *et al* 1995). Furthermore, ulceration of the lower limb is a common cause of morbidity in older people (Goodfield 1997).

While treatment decisions should be made on the grounds of evidence-based practice, where this is lacking the management of venous ulceration has often been pragmatic. The plethora of treatments currently available is not only evidence of this, but also evidence of the lack of the unsurpassed efficacy of any one treatment above the others.

The range of dressings available is vast – enzyme cleaners, foams, hydrocolloids, semipermeables, alginates – and tends to be the mainstay of treatment, alongside compression hosiery and bandaging techniques; the latter being well and quantitatively established (Burton 1993). Recent novel treatments include fibrinolytic therapy (Zeegelaar *et al* 1997), as well as electrotherapeutic and other modalities, such as hyperbaric oxygen, ultrasound and UV light. More aggressive treatments include the application of skin grafting techniques (Kirsner *et al* 1997). Despite the apparent popularity of many of these treatments, their use has failed to improve clinical results significantly (Sugrue *et al* 1990).

Low intensity laser therapy

In an attempt to discover an effective treatment for the acceleration of wound healing, low intensity laser therapy (LILT) has emerged. Despite the recent popularity and enthusiastic advocacy of this treatment (Baxter *et al* 1991), there has been a reluctance to accept this treatment due to a lack of a convincing understanding of underlying mechanisms of action involved (King 1990). The effects of LILT on wound healing have been investigated for over three decades, with Mester's early research conducted at a cellular level (Mester *et al* 1971, Mester and Mester 1989). In general, work conducted on cell function and animal studies has yielded positive observations on the so called photobiostimulatory effects of laser therapy (Shields and O'Kane 1994). Increasing interest has arisen for the application of LILT in the clinical arena in recent years. This has resulted in an improvement in clinical studies which were previously anecdotal and lacking detail, to better controlled and reported work (Basford 1989). Despite this, further clinical studies are still required to establish definitively the efficacy of these devices in the management of wounds. The range of wounds suitable for potential treatment applications using laser has been addressed by Ashford and Baxter (1994).

To date, several clinical studies have been conducted investigating wounds of various aetiologies and employing a range of treatment parameters. Accelerated wound healing using a multisource diode and a dosage of 4.2J/cm^2 has been reported for a chronic neuropathic ulcer (Ashford *et al* 1995). Three additional single-case designs of diabetic ulcers reported were highly in favour of the use of LILT for this type of ulceration (Lagan *et al* 1996). Successful wound closure in chronic diabetic ulcers has been reported elsewhere (Hull 1991, Kleinman *et al* 1996, Lichtenstein and Morag 1994, Robinson and Walters 1991). Patients with diabetes *arteriosclerosis obliterans* have also been studied with successful reports by several authors (Lichtenstein and Morag 1994, Matsumara *et al* 1992).

Clinically, venous ulceration has been extensively researched. Mester (1975) reported positive findings collectively of experimental and clinical work investigating crural leg ulcers. Subsequent studies by several authors have yielded equivocal results on the efficacy of irradiation (Bihari 1984, Malm and Lundeberg 1991, Santoianni *et al* 1984, Soriano 1994, Sugrue *et al* 1990). Findings of a controlled study reported by Santoianni *et al*

Box 1. Case one: relevant past medical history

1959	Venous ulcers, right and left ankles
1963	Venous ulcer, right ankle Bilateral stripping of varicose veins
1982	Bilateral venous ulcers – admitted for four weeks – complete healing not achieved
1983	Bilateral venous ulcers – admitted for eight weeks – complete healing achieved September 1983
1984	Right ankle ulcer broke down – admitted for five weeks
1986	Right ankle ulcer broke down
1990	Diabetes mellitus diagnosed – diet only treatment required
1992	Venous ulcer right leg – admitted for four weeks
1993	Cellulitis associated right ankle ulcer – admitted for ten days
1994	Right venous ulcer – admitted for four weeks Cellulitis left leg – admitted for three weeks
1995	Bilateral venous leg ulcers – admitted for six weeks
1996	Cellulitis left leg – admitted for ten days

Box 2. Case two: relevant past medical history

1983	Exacerbation of chronic obstructive airways disease – admitted to hospital – noted to have significant peripheral vascular disease. Advised to stop smoking, which he did in 1984
1984	Referred to vascular surgery because of unhealed leg ulcer. Angiography showed infra-renal abdominal aortic aneurysm and occlusion of the left superficial femoral artery and severe stenosis of the right superficial femoral artery. Claudication distance fifty yards
1995	Venogram suggested probable previous deep vein thrombosis in the left leg. The vascular surgeons felt that the ulcer on his left leg was predominantly venous in origin, but that there was significant co-existing arterial disease present which was not amenable to surgery because of the state of his chest

(1984) observed that helium-neon laser irradiation had no advantages over conservative treatment at dosages of 1-4J/cm^2. Similarly, Malm and Lundeberg (1991), in a placebo controlled study using a GaAs laser, reported no differences in results between the two groups investigated. In contrast to this, a significant reduction in ulcer size following treatment, as well as a significant increase in granulation tissue formation, capillary density and a decrease in ulcer pain was reported in a pilot study (Sugrue *et al* 1990).

More recent work conducted by Kleinman *et al* (1996) has employed several laser types and reported complete healing (assessed by wound closure) in 85.7 per cent of patients over a mean period of 3.5 months.

Similarly, Lichtenstein and Morag (1994) reported 87 per cent wound closure in patients studied with ankle ulcers associated with venous insufficiency syndrome. Controlled group studies conducted at other centres have also focused on venous ulceration (Clements *et al* 1996, Howard *et al* 1998).

Both authors have conducted controlled work using GaAlAs lasers, 660-950nm, 532mW; 4J/cm^2 and 10.6J/cm^2 respectively. While Clements *et al* (1996), using identical laser parameters to earlier work of Ashford *et al* (1995) reported a reduction in pain levels, but only marginal improvements in wound area, a significant positive treatment effect of ulcer area was observed by Howard *et al* (1998).

On the basis of previous positive clinical findings at set laser parameters (Ashford *et al* 1995, Clements *et al* 1996), this study was undertaken to assess further the potential clinical effects of LILT on venous ulcers; for this, two patients continued to receive treatment following participation in a double blind randomised crossover trial (RCT). Wound surface area measurements and pain levels recorded served as the cardinal clinical effects of monitoring response to LILT.

Method

This case report relates to two patients who were originally entered into a double blind randomised crossover trial (RCT) (Boxes 1 and 2). The recruitment criteria for inclusion in the trial were as follows:

- The leg ulcers were at least 1.5 cm in diameter.
- Ankle brachial index (ABI) >0.5.
- Unsuitable for compression bandaging.

Patients were randomly allocated to two groups. One group received an active cluster head probe containing 41 diodes. The pulsing frequency was set at 5KHz and delivered an average density of 4.2 J/cm^2. Patients were irradiated for a total of 120 seconds twice per week. The other group received sham irradiation. Clinicians were not aware of the status of either probe which were marked A or B and colour coded. Each group received their allocated cluster treatment for a period of six weeks followed by a two week rest period, then six weeks with the other treatment probe.

The leg ulcers were dressed twice weekly with an alginate dressing and light support bandaging throughout the study period and laser therapy was applied immediately before redressing.

The ulcers were traced three times onto an acetate sheet and photographed every two weeks. The mean surface area was quantified by WAND2© software. At the end of each two week period, each patient was asked to score on a 10cm visual analogue scale the level of pain experienced during the previous two weeks.

The patients' general health was also monitored throughout the trial and subjective comments were also sought. At the end of the study period the two patients reported here had demonstrated some improvement in wound appearance and pain reduction during the time that laser B (Tables 1 and 2) was applied. In view of this it was decided to continue to treat them according to the same treatment regime previously described, this time using a known active cluster head.

Table 1. Treatment regime for case one

	START DAY	FINISH DAY
LASER TREATMENT		
Laser A	0	42
Rest	42	56
Laser B	56	98
Active laser	98	232
DRESSINGS		
Alginate	0	232
ANTIBIOTICS		
Erythromycin	63	77
Cephalexin	77	91
Ciprofloxacin	161	172
Cephalexin	217	224

Table 2. Treatment regime for case two

	START DAY	FINISH DAY
LASER TREATMENT		
Laser B	0	42
Rest	42	56
Laser A	56	98
Active laser	98	232
DRESSINGS		
Alginate	0	98
Potassium permanganate	98	154
Antibacterial	154	232
ANTIBIOTICS		
Co-amoxiclav	14	42

Case one

The participant in case one was a 93-year-old woman who had recurrent bilateral leg ulceration since 1959. She had numerous hospital admissions with only limited success in achieving ulcer healing. The ulcer on the lateral part of her right ankle had proved particularly difficult to heal. Before entering this study, the last time her right ankle ulcer had healed was in June 1987, immediately prior to bilateral knee replacement surgery. This ankle broke down in December 1987 and subsequently had proved impossible to heal. She was unsuitable for compression bandaging due to co-existing arterial disease. The ankle brachial index (ABI) was 0.72.

Her medication at the start of the trial was: thyroxine 50mg daily; temazepam 20mg at night; hydroxyzine hydrochloride 10mg tablets; aspirin 75mg daily. To which was added: frusemide 20mg and gliclazide 40mg daily.

Her right ankle ulcer remained unhealed from December 1987 until entry into the trial. The size of her ulcer had increased in association with episodes of infection, but had never been significantly smaller than at entry into the laser study. A previous regime of 1:8,000 potassium permanganate wet dressings was applied for 20 minutes before redressing with an alginate dressing three times per week was carried out. The episodes of infection were treated with antibiotics as appropriate, in an attempt to contain the problem. Healing was never achieved with this regime.

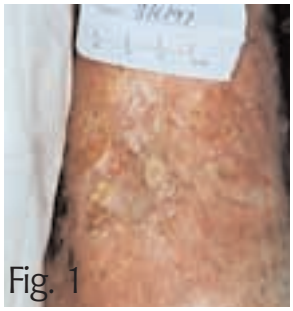


Fig. 1

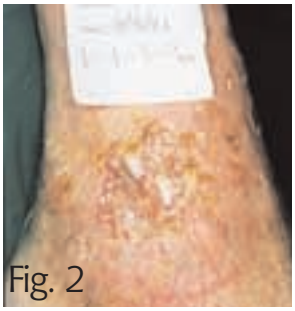


Fig. 2

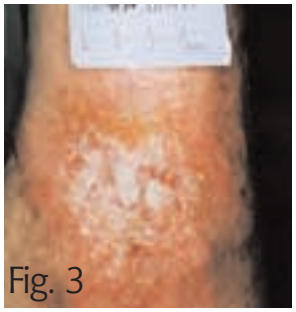


Fig. 3

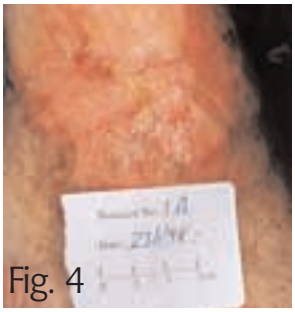


Fig. 4

Fig. 1. Ulcer at entry point into RCT – 160mm²
Fig. 2. Ulcer at end of RCT – 170mm²
Fig. 3. After three months active treatment – 25mm²
Fig. 4. Approximately 20 weeks – ulcer shows almost complete healing

During the course of the study period she developed cellulitis in her left leg at week nine, which required two weeks treatment with erythromycin, followed by two weeks with cephalexin and local application of mupiricin, before the problem was successfully resolved.

In November 1997, she developed a urinary tact infection which was treated with ciprofloxacin for seven days. In January 1998 she developed a chest infection following a viral illness; this caused cardiac failure and a deterioration in her diabetic control. This required treatment with frusemide 80mg daily for three days which was then reduced to 40mg daily for seven days, and she was finally maintained on 20mg daily. Her diabetic control also deteriorated and gliclazide 80mg daily was added to her treatment. The dose was reduced after two weeks to 40mg daily and this had been maintained.

The patient appeared to show improvement during treatment with laser B and, once treatment with a known active laser head was commenced in September 1997, there was a steady improvement in the appearance of her leg ulcer, with reduction in pain and a marked reduction in size.

Result of continuation of active therapy

Figure 1 illustrates the ulcer at the entry point into the RCT. At this point the ulcer measured 160mm². Following the initial trial to completion (14 weeks in total) the graph in Figure 5 shows very little change in the ulcer size over this time frame. Detailed analysis highlights that between the fourth and tenth week there is a steep reduction in ulcer size, followed by a plateauing off and a subsequent increase. Figure 2 illustrates the ulcer at

Fig. 5. Ulcer size against time in RCT and during therapy

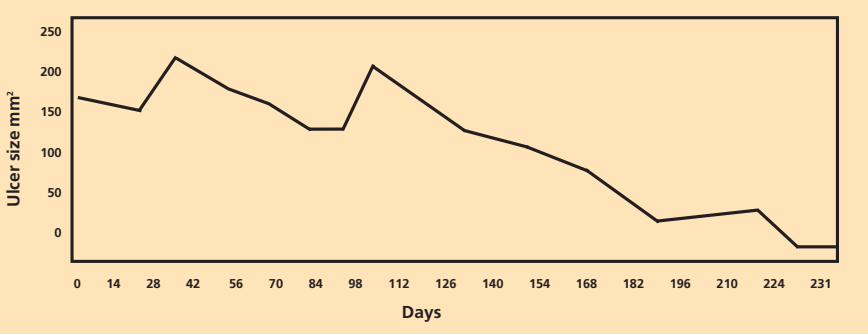
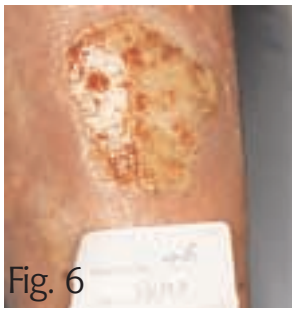
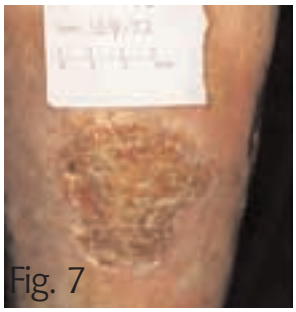
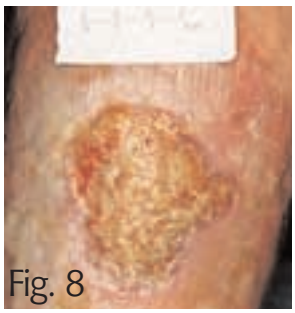
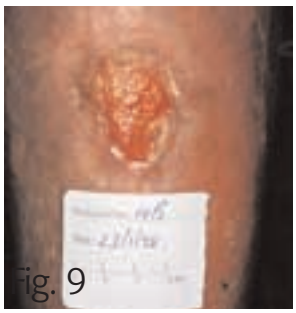


Fig. 6. Recruitment onto trial – day zero
Fig. 7. End of RCT (14 weeks) – no size difference
Fig. 8. One month following treatment – no significant difference to RCT
Fig. 9. At 20 weeks ulcer reduced by 78 per cent compared to day zero









the end of the RCT, at which point no difference was recorded; indeed the ulcer was actually larger. Figure 3 shows the ulcer three months after active treatment to be 84 per cent smaller compared to the original size of the ulcer at the start of RCT recruitment. Figure 4 illustrates the almost complete resolution of this most chronic ulcer after 20 weeks active treatment.

No significant results were recorded from the visual analogue scales, however the patient did comment on reduced pain levels during active therapy.

Case two

The participant in case two was a 64-year-old man who had a chronic ulcer on the anterior/lateral part of his left leg, 10cm below the knee. The ulcer developed following an injury to the left leg in October 1993. This area of trauma became infected with the development of cellulitis and ulceration. His ankle/brachial index was 0.6.

The patient's medication at the start of the trial was: fluticasone propionate via volumatic; salbutamol 5mg via nebuliser; ipratropium 500 microgram; co-amilofruse 5mg:40mg daily; aminophyline 450mg bd; chlordiazepoxide 5mg daily.

Prior to entry into this study his leg ulcer had been dressed, with no evidence of significant improvement, with the following: streptokinase/streptodornase; hydrogel; algimate; polyurethane foam; polymyxin and bacitracin; silver sulphadiazine.

During the course of the study he had an exacerbation of chronic obstructive airways disease requiring treatment with co-amoxiclav 500/250 for three weeks.

At the end of the double blind study, the leg ulcer dressing was changed from an alginate dressing to a 1:8,000 potassium permanganate wet dressing applied for 20 minutes before redressing with an alginate dressing for eight weeks. The dressing was changed at this point to an exudate absorbant-antibacterial which was continued until the end of the study period.

Results of continuation of active therapy

A similar picture appears to that of case one. The only methodological difference can be traced to the RCT episode. During the RCT, the cluster heads were in reverse order (Tables 1 and 2). Again, no significant difference was recorded during the 14 weeks of the RCT (Figs. 6 and 7). One month into active treatment (Fig. 8) no difference, in terms of size, was recorded. Moreover, six weeks into active treatment still no difference in ulcer size was recorded. This is a particularly interesting observation because, at the same point in the RCT (either probe), no difference is noticeable. However, continuation of active treatment after this point gives a 78 per cent reduction in ulcer size compared to the original size after 20 weeks (Fig. 9).

The visual analogue results did not produce a significant decrease in pain levels. This was probably due to the patient's pre-existing perception of his pain level. The patient's comments regarding pain were encouraging, however. He noted how comfortable his ulcer had become throughout the study, particularly during the active therapy.

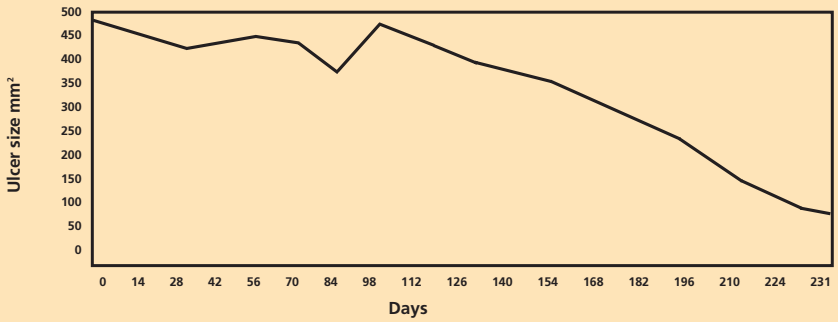
Discussion

These two patients showed a remarkable response to laser treatment. They had been written off as 'will never heal' by the medical centre personnel and the hospital specialists who had seen them.

In case study one, the ulcer did not decrease in size during the 14 weeks of the RCT, but reductions were noted, particularly when laser B (Figure 5) had been used. The size recorded at the start of the RCT was 160mm^2 and 170mm^2 at the finish of the RCT. However, when active treatment was initiated, the ulcer reduced to 15mm^2 – 91 per cent its original size.

In case study two, a similar picture emerges when laser B is considered (Fig. 10) – a reduction in ulcer size is noted between day zero and day 28 in the RCT. This then increases and a reduction

Fig. 10. Ulcer size against time in RCT and during therapy



is also noted at the start of the sham irradiation (laser A). The ulcer returns to its original size at the end of the RCT and systematically demonstrates a reduction in size proportional to the start of the RCT during active therapy (day 98-126). Moreover, the ulcer continues to reduce in size over the active therapy until a 78 per cent reduction is recorded at the end of the 20 weeks of active treatment.

Neither of the case studies showed any significant reduction in pain levels. Other studies have shown pain can be diminished when using laser treatment (Ashford *et al* 1997, Mester and Mester 1987).

The use of LILT in wound management is still rather controversial and has, to date, no substantial clinical research findings to draw on. A number of *in vitro* studies have shown an effect, but in the clinical arena there is an absence of standardised protocols for the treatment of specific conditions. Standardised protocols would give the clinician a clearer understanding of which variables to increase or decrease, to initiate maximum therapeutic effect.

In the case reports presented, standardising the double blind RCT did not have major effects on the patients in question. The time frame of the therapy seems to have been more important. Both ulcers decreased considerably when the active cluster head was used over a much longer time period.

The authors acknowledge the limitations of case study reports. However, with such an overwhelming result, the research team has decided to abort this particular RCT with a view to comparing different time frames using active cluster heads in each. Under such a study, all patients recruited will receive active therapy. Rather than looking at the efficacy of LILT *per se*, the researchers wish to begin to address the other issue of establishing suitable protocols. The only way to establish such protocols is by comparing different aspects of the variables at the clinicians fingertips, for example, time and frequency of treatment.

Finally, the effectiveness of this physical modality must now be extended to other ulcer types. The nursing profession is in a prime position to take this treatment into the hospital and community settings. It is therefore recommended that, to test the efficacy of this treatment, many more trials are required and who better to be driving the research than the profession that would be delivering the therapy?

It must be remembered that LILT is not a panacea for all ulcers, but it could be seen as an adjunct to the existing physical and dressing repertoire

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