# Effectiveness of Intermittent Pneumatic Compression for the Treatment of Venous Ulcers in Subjects with Secondary (Acquired) Lymphedema

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## Abstract

Fifty-two subjects with secondary lymphedema, chronic venous insufficiency, and hard to heal lower leg ulceration (>1year old & >20cm$^2$ surface area) were treated with either intermittent, gradient, pneumatic compression (IPC* n=27) plus standard compression therapy or compression therapy alone (control). Compression therapy consisted of a non-adherent primary wound dressing plus a 4-layer compression bandage (4-LB** n=25). The mean age and size of the ulcers were 1.4 years and 31cm$^2$, respectively, and did not differ significantly between groups. IPC was performed using a 4-chamber pneumatic leg sleeve and gradient, sequential pump. All pumps were calibrated to a pressure setting of 50 mmHg on each subject, and treatments were for 1 hour, twice daily. Evaluations were performed weekly to measure edema, local pain, degree of wound granulation, and wound healing (incidence of complete closure and rate of healing from wound surface area measurements). The median time to wound closure by 9 months was 141 days for the IPC-treated group and 211 days for the control group (P= 0.031). The rate of healing was 0.8±0.4 mm/day for the control group and 2.1±0.8 mm/day for the group treated with IPC (P<0.05). When compared to subject treated with standard care, the group treated with IPC reported less pain at each evaluation point for the first 6 weeks of the trial. At week 2 and 3, the visual analog pain scores were significantly lower for the IPC-treated group (P<0.05). These results suggest that IPC is a valuable adjunct to compression therapy in the management of large or painful venous ulcers. ClinicalTrials. *Gov ID: NCT01079299*

## Introduction

The most common type of lymphedema is secondary lymphedema. It is caused by injury or damage to the lymphatics resulting in obstruction or constriction and leading to inadequate lymphatic drainage. Common causes include morbid obesity, untreated chronic venous insufficiency (CVI), cancer, surgery, trauma, radiation and infections. In the early stages, (intermediate fibrosis) fluid accumulates predominantly in the lymphatic vessels. In the more advanced stages (firm fibrosis), extravasation of lymph fluid occurs causing pooling of lymp between the collagen bundles in the perivascular space. Diagnostic features of secondary

lymphedema include swollen feet, deep creases of the skin, square (shovel) toe, Stemmer's sign, papillomatosis (verruca papillomata), hemosiderosis, bullae and venous ulceration.[2]

As with CVI, the cornerstone of treatment for secondary lymphedema is compression. Compression forces the fluid that has leaked into the perivascular space back into circulation. As with CVI, ideal compression pressures for these patients remain unknown. Complete decongestive therapy (CDT) is the combination of a mild massage called manual lymph drainage (MLD) and serial compression with short stretch bandages. Although proven effective, it has several shortcomings. CDT can only be performed by certified therapists, it must be done daily and its reimbursement is problematic. Intermittent pneumatic compression devices (IPC) have also been proven effective, but compliance and reimbursement (especially for Medicaid patients) are major hurdles. A distinct advantage of IPC therapy is that it can be done by the patient or other family member in the home with little or no training. Compression alone with multi-layer or short stretch bandage systems are helpful but requires application by a skilled (trained) nurse or technician dedicated family member be trained to appropriately apply the multi-layer short stretch bandage system.

Venous ulcers in patients with secondary lymphedema pose a significant challenge as these wounds are one of the most difficult to heal. These patients have significant brawny edema, fibrosis, and very large legs making bandaging difficult as gradient compression pressures are often not achieved. IPC has been shown to accelerate the healing of venous ulcers in several randomized trials. However, it has never been shown to be more effective than standard compression provided with short stretch or multi-layered bandage systems. Our goal was to investigate if intermittent compression (IPC) assisted the healing of venous ulcers in lymphedema patients that were already receiving standard compression with short stretch or multilayered compression therapy.

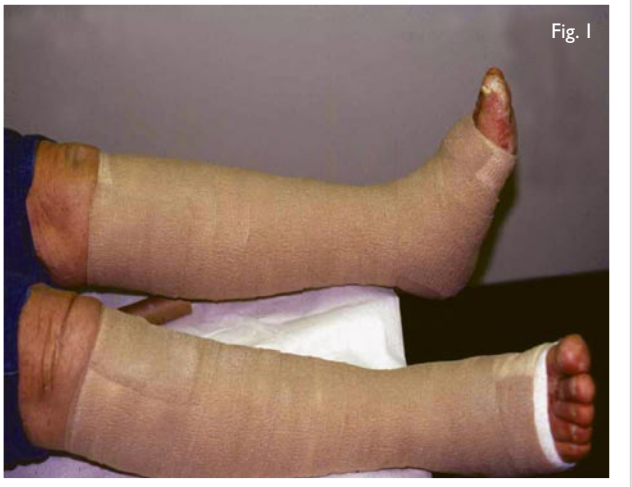
Fig. 1

## Study Design and Study Population

The study was a prospective, randomized, controlled, parallel-group, comparative trial. Eligible subjects aged 18-85 years were randomly assigned to receive either control treatment, consisting of compression bandage therapy alone, or IPC therapy plus compression bandaging. Subjects were followed up to 12 months for analysis of safety and efficacy. Endpoints were prospectively set at 8 months. Subjects were entered into the study after informed consent was obtained. Those who qualified were assigned to either the IPC or control treatment groups according to a computer-generated randomization schedule. A total of 52 subjects were treated with 27 randomized to compression bandage therapy alone (control) and 25 to IPC therapy. The ulcers were secondary to venous insufficiency had to be open for a minimum of 1 year, had to be >20cm$^2$, and the degree of local wound pain had to be >6 on a visual analog scale (VAS) of 0-10. Significant arterial insufficiency had to be excluded by demonstrating an ABI >0.75. Exclusion criteria included: active infection, ulcers of non-venous etiology, current use of systemic corticosteroids, chemo or radiotherapy, confinement to bed or chair, and active participation in another investigational study.[3]

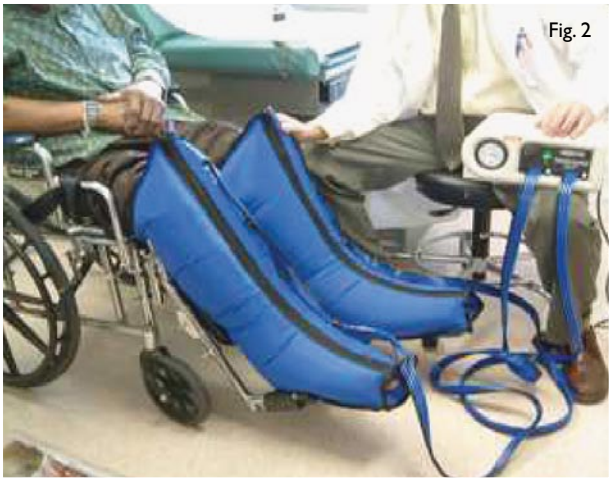
Fig. 2

## Treatment Protocol and Follow Up

The ulcers of the control subjects were dressed and bandaged using the Profore™ 4-layer bandage system (4 LB, Figure 1, Smith and Nephew, Largo FL). In the IPC treatment group, the ulcers were dressed and bandaged using the same 4-layer bandage system described for the control group. In the IPC group, additional compression therapy was provided by a 4-chamber intermittent gradient, sequential, pneumatic compression device (Figure 2, Sequential Circulator Model 2004, BioCompression Inc. Moonachie, NJ). Therapy sessions were performed for 1 hour, twice daily (morning and evening) at 40-50 mmHg while the subject was in a

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reclining or decubitus position. Coression therapy with IPC was performed over the compression bandage. In all cases either the 19- or 31-inch leg sleeves were used. Daily diaries were maintained by the study subjects, and the IPC devices and sleeves were checked every 4 weeks. In-service to the patient and family was provided. All subjects were followed weekly for 96 weeks. At each weekly evaluation visit, the wounds were measured, wound and pain assessments were performed, and adverse events (if any) were recorded. For most patients, bandage changes were performed twice weekly (once at the Wound Center and once by the visiting nurse). Wound measurements were performed using a 3 mega pixel digital camera and photo-digital planimetry software (Pictzar™CDM BioVisual Inc, Elmwood Park, NJ).

Table 1

**Rate of Healing**

| Treatment | Control | IPC | P Value |
|---|---|---|---|
| Rate of Closure mm/day ± SEM | 0.8 ± 0.2 | 1.7 ± 0.5 | 0.041 |
| N | 25 | 27 | |

Table 2

**Leg Edema**
**Ankle and Calf Circumference**

| Group | Baseline Ankle/Calf (cm) | Week - 20 Ankle/Calf (cm) | % Ankle/Calf (cm) |
|---|---|---|---|
| IPC plus 4LB | 46.5/59.3 | 37.6/48.2 | 19.1/18.7 |
| 4LB (Control) | 44.7/56.4 | 39.6/49.2 | 12.0/13.2 |

Fig. 3

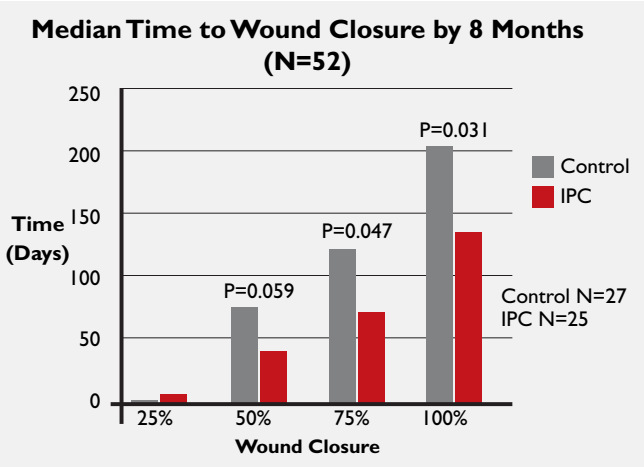
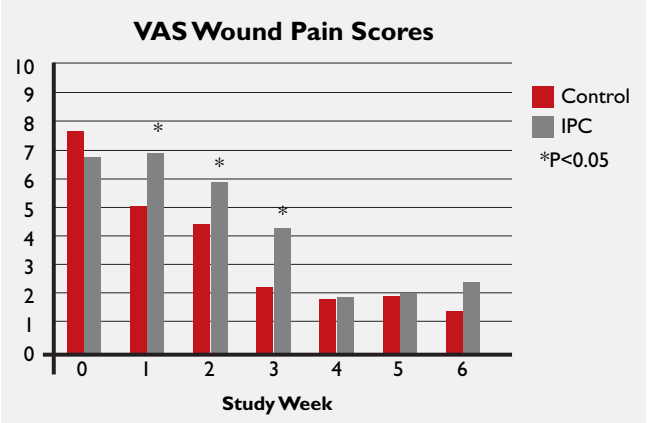



Fig. 4




## Results

There were no significant differences between the control and IPC treatment groups in patient demographics and baseline ulcer size and duration. The median time to wound closure at 8 months is shown in Figure 3. When compared to control treatment at the 8-month time point, IPC therapy reduced by 1.6 fold the median time to complete healing (p=0.031). The rate of healing for both treatment groups is shown in Table 1. The speed of healing in mm/day was more than 2 times greater in the group receiving both standard compression bandages and IPC therapy (p=0.41). The effect of IPC therapy on leg edema is shown in Table 2. After 20 weeks, the percent reduction in ankle and calf circumference was slightly greater favoring the IPC group but this difference was not statistically significant. Local wound VAS pain scores for both treatment groups are shown in Figure 4. Significant (p< 0.05) wound pain relief was reported by study subjects receiving IPC only during the first 3 weeks of treatment. Thereafter, both treatment groups reported less wound pain.

## Conclusions

- The median time to healing by 9 months was 141 days for the IPC-treated group and 211 days for the control group (p=0.031).
- The rate of healing was 1.1 mm/day for the control group and 2.3 mm/day for the group treated with IPC (p<0.05).
- Compared to subjects treated with compression alone, the group treated with IPC reported less pain at each evaluation point for the first 6 weeks.
- The IPC-treated group had greater reduction in leg edema (19% vs 11%), but this difference was not statistically significant.[4]

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