TITLE: OPAL A for the treatment of chronic ulcers: A prospective study

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ABSTRACT

The aim of this prospective study was to examine the clinical effectiveness of OPAL A, an alkalised and filtered product extracted from the inner flesh of paw paw, for treating chronic ulcers. Patients with chronic ulcers were invited to participate in the study. OPAL A was applied to gauze, which was placed on the wound bed. Dressings were changed daily from Monday to Friday. Compression therapy was provided where indicated. Follow-up assessments were performed at Weeks 4, 8, and 10. There were nine patients; four had venous ulcers, three had pressure injuries, and two had mixed aetiology ulcers. All patients had their ulcers for ≥ 6 months before the study. Ulcers were located on lower limbs in eight patients and on the spine in one patient. Three patients withdrew at different weeks due to maceration, cognitive decline, and wound infection, respectively. During treatment, seven patients exhibited wound bed improvement, three had a reduction in wound bed size, three reported reduced pain, and all except one had reduced wound exudate. Overall, seven patients reported that the OPAL A dressing was comfortable. These findings suggest that OPAL A, when used as a primary dressing, may help promote healing of chronic wounds.

INTRODUCTION

Chronic wounds are a common condition, affecting approximately 270,000 Australians at any one time[1], that can have a number of negative consequences and associated costs, including reduced quality of life, loss of mobility and independence, and disturbed sleep[2, 3]. People with chronic wounds may also experience social isolation, withdrawal, and depression[3, 4]. In addition to these personal costs, treating and caring for patients with chronic wounds are associated with a significant financial burden[3, 4]. Clearly, optimising wound management strategies and expediting wound healing is of paramount importance.

Wound dressing remains an important part of wound management. Indeed, appropriate wound dressing is not only essential to keep the wound bed clean, but also to promote wound healing[5]. Currently, there are thousands of dressing products available for use in wound management. These include various interactive dressings, which aim to manipulate the wound environment (for example, by exerting antimicrobial effects) to optimise healing[5]. However, there is a lack of data from high-quality studies and conflicting evidence as to whether such dressings are effective[5].

OPAL A, an alkalised and filtered product extracted from *Carica papaya* (paw paw fruit), is under investigation as a treatment for chronic wounds. Of note, a number of previous reports have suggested that OPAL A may help promote healing of chronic wounds[6-9]. Specifically, daily topical treatment with OPAL A filtrate and cream was associated with wound healing in nine quadriplegics with difficult-to-heal chronic pressure injuries[7]. Likewise, treatment with OPAL A filtrate and cream was associated with evidence of wound healing in a paraplegic with a chronic sacral pressure injury for which previous treatments had been unsuccessful[8],

and in a series of patients with pressure, diabetic foot, or venous ulcers[9]. Further prospective information on the effectiveness of OPAL A for treating chronic wounds is clearly needed.

The aim of this prospective study was to obtain further information on the clinical effectiveness of OPAL A, administered as a primary wound dressing, for the treatment chronic ulcers of varying aetiology.

PATIENTS AND METHODS

Patients

All patients with chronic ulcers attending the Outpatient Wound Clinic at Royal Hobart Hospital (Tasmania, Australia) were invited to participate in the study, regardless of wound aetiology or the stage of wound healing. For patients who had multiple ulcers, only the largest (index) ulcer was studied. Patients with reduced cognitive function who were unable to make informed decisions were excluded from the study.

Patients were provided with written information about OPAL A (including a summary of the findings from previous studies) and the purpose and design of the study. All patients provided written informed consent before the start of the study.

This study was approved by the Tasmanian Health and Medical Human Research Ethics Committee.

Study Design

The single-arm prospective study was conducted over a 10-week period. All patients were followed up at the Outpatient Wound Clinic on Weeks 1, 4, 8, and 10.

At Week 1, each patient's age, demographics, mobility status, medical history, and wound characteristics were noted.

Treatment

During the study period, patients were required to have their dressings changed once daily from Monday to Friday. OPAL A (Health Focus Products Australia, Sandy Bay, Tasmania,

Australia) was originally planned to be applied directly on the wound bed using a nonadherent dressing to keep the treatment in situ. However, the low viscosity of OPAL A made direct application difficult. Therefore, OPAL A was applied to six to eight layers of gauze until soaked through, cut to size, and placed in the wound bed. The gauze was soaked before removal and changed once daily as already described. The skin immediately surrounding each patient's wound was dressed with OptiDerma® Moisturising Skin Support cream (Health Focus Products Australia).

Patients who required compression therapy had their bandaging replaced with Tubular-Form Shaped Support Bandages (TF SSB) that provided a pressure of 18 to 22 mmHg. Individual ankle and calf measurements were taken to ensure that TF SSBs were correctly sized. The ankle brachial pressure index was calculated to exclude arterial insufficiency according to the Australian and New Zealand Clinical Practice Guideline for Prevention and Management of Venous Leg Ulcers[10].

When possible, the same nurse at the Outpatient Wound Clinic attended to the same patient at each follow-up visit. All other dressings and weekly documentation were completed by trained nursing staff, employed as Community Nurses or in General Practice.

Study Outcomes

Outcomes assessed throughout the study included the following: tissue type of the wound bed (ie, percentage granulation, slough, etc); size of the wound bed as determined by photography and direct measurement; amount, colour, and odour of wound exudate; condition of the skin surrounding the wound; ease of application and removal of the dressings; and pain (rated by patients as 0 = no pain through to 10 = worst pain imaginable).

RESULTS

Nine patients were enrolled in the study, whereas 20 eligible patients declined to enrol because of various reasons, including inconvenience of daily dressing changes, fear of exacerbation of pain, and possible deterioration of the existing ulcer. Of the nine patients enrolled, six completed the 10-week treatment regimen.

Of the nine patients, four had chronic venous ulcers (Table 1), three had chronic pressure injuries (Table 2), and two had chronic ulcers of mixed aetiology (Table 3). All patients had their ulcers for at least six months. All but one patient (patient 7) had ulcers located on lower limbs. Of the patients enrolled, two withdrew at Week 4 due to cognitive decline / inability to make informed decisions and maceration, respectively, whereas one withdrew at Week 6 due to wound infection. The patient who withdrew due to maceration did not complete any follow-up assessments and was not included in the analyses.

Overall, wound bed tissue showed improvement in seven patients, although wound bed size decreased in only three patients. The most noticeable improvement in wound bed occurred in patients with chronic venous ulcers (Table 1). Reduction in pain was reported by three patients. Wound exudate was decreased in seven patients, with no evidence of maceration or dehydration around the wound edges or surrounding skin. All except one patient reported that the OPAL A dressing was comfortable. One patient reported experiencing pain when the dressing dried out over the weekend.

Nurses' reports concerning the practical use of OPAL A were generally favourable; however, all reported that the viscosity of OPAL A was low. All nurses reported that the dressing was easy to apply and that there were no untoward effects when the dressing was removed.

Patient Case Details

Chronic Venous Ulcers

Patient 1 was a 44-year-old obese man who had a spontaneously occurring venous ulcer on his medial malleolus for six months. He had a history of previous leg ulcers, varicose veins, deep vein thrombosis, hypertension, and peripheral vascular disease. He was mobile, capable of performing activities of daily living (ADL), and had a job that required him to stand for long periods of time. He was fitted with two layers of TF SSB for compression. At Week 1, the patient's wound bed had 100% healthy granulation tissue, whereas, by Week 10, the wound bed had 95% epithelialisation with a progressive reduction in size and exudate. The patient's pain increased from Week 0 to Week 4, but thereafter gradually decreased as wound healing progressed. By the end of Week 10, he had no pain. Shortly after completing the study, the patient's ulcer was completely healed and has (at the time of this report) remained healed.

Patient 2 was a 29-year-old obese woman who had a venous ulcer on the pretibial aspect of her lower leg for nine months that occurred following a suspected spider bite with associated cellulitis. She had a history of varicose veins. She was mobile, capable of performing ADL, and had a full-time job that required her to stand for long periods of time. She was fitted with two layers of TF SSB for compression; however, the shape of her leg would not support this compression for long periods of time. Therefore, the TF SSB was replaced with double Tubigrip™ (Mölnlycke Health Care, Frenchs Forrest, Australia). At Week 1, the patient's wound bed had 90% slough, whereas by Week 10, this had changed to 90% healthy granulation tissue. The patient's wound bed decreased in size during the study, as did the

amount of exudate. Pain decreased from 8 out of 10 before the study to 3 out of 10 at Week 10. One year after completing the study, the patient's ulcer remains unhealed.

Patient 3 was an 82-year-old obese woman who had a spontaneously occurring venous ulcer on her medial malleolus for five years. She had a history of previous leg ulcers, arthritis, peripheral vascular disease, peripheral oedema, pulmonary embolism, and a knee replacement. The patient was mobile, but required assistance with ADL. She was fitted with one layer of TF SSB as she could not tolerate two layers for high compression. At Week 1, the patient's wound bed had 100% granulation tissue. At Week 4, maceration and oedema were evident, presumably because of subtherapeutic compression and the development of cellulitis. The patient withdrew from the study during Week 4 and was eventually recommenced on four-layer compression bandages. Her ulcer subsequently healed and has (at the time of this report) remained healed.

Patient 9 was a 59-year-old man who had a venous ulcer on his medial malleolus for > 14 months following trauma. He had a history of diabetes. The patient was non-ambulant, required a wheelchair for mobility, and required assistance with ADL. He was fitted with one layer of TF SSB for compression. At the end of Week 4, the patient was excluded from the study because he exhibited cognitive decline and was unable to make informed decisions.

Chronic Pressure Injuries

Patient 6 was a 76-year-old woman who had a pressure injury on her lateral malleolus for two years, secondary to inappropriate footwear. She had a history of diabetes, varicose veins, peripheral vascular disease, cerebral vascular accident, atrial fibrillation, and arthritis. The patient was non-ambulant, required a motorised scooter for mobility, and required assistance

with ADL. She was fitted with two layers of TF SSB for compression. The wound bed had 100% slough at Week 1, whereas by Week 10, the wound bed was covered with 100% healthy granulation tissue. Her wound bed size remained unchanged, but the amount of exudate increased at Week 6. Pain was 7 out of 10 before the study and gradually decreased thereafter. By Week 10, she was pain free. Two weeks after completing the study, her pressure injury had completely healed and has (at the time of this report) remained healed.

Patient 7 was a 61-year-old woman who had a pressure injury on her spine for more than two years, secondary to scoliosis. She had a history of heart disease, scleroderma, Raynaud's phenomenon, arthritis, kidney disease, severe malnutrition, and metastatic cancer of the spine requiring radiation therapy. The patient was mobile, but required assistance with ADL. At Week 1, the patient's wound bed had 95% granulation tissue. She failed to attend the Week 10 follow-up visit, but was followed up at Week 13, at which time a large necrotic blister was noted over the wound bed. After unroofing of the blister, healthy granulation tissue was observed. Her wound decreased in size at Week 4, but remained unchanged at Week 13. There was an increase in the amount of exudate during the study. Pain remained at 0 out of 10 throughout the study. After the study, the patient's cardiac function deteriorated, leading to three hospital admissions. Her pressure injury did not respond to management thereafter, and she has since died.

Patient 8 was a 42-year-old obese woman who had a pressure injury on her heel for six months, secondary to footwear and an inability to independently change position. She was a paraplegic due to spina bifida and had a history of arthritis. The patient was non-ambulant, required a motorised scooter for mobility, and required assistance with ADL. At Week 1, her wound bed had 100% slough, whereas by Week 4, this was replaced with 90% healthy

granulation tissue. At Week 6, the patient's general practitioner noticed an increase in the amount of exudate, diagnosed a wound infection, and commenced antibiotic treatment; she consequently withdrew from the study. Her pressure injury subsequently healed and has (at the time of this report) remained healed.

Chronic Mixed Aetiology Ulcers

Patient 4 was an 85-year-old woman who had two ulcers of mixed aetiology on her medial malleolus for two years. She had a history of previous leg ulcers, deep vein thrombosis, failed skin grafting at the site of the present ulcer, and peripheral vascular disease. The patient was mobile and capable of performing ADL. She was fitted with one layer of TF SSB for compression. At Weeks 1, 4, and 10, the patient's wound bed remained stagnant, and had 80% slough. Her wound bed increased in size, as did the amount of exudate, and her two wounds became one. Pain increased from 0 out of 10 before the study to 5 out of 10 during the study. Findings from clinical investigation confirmed increased arterial insufficiency due to arterial stenosis. After the study, the patient received hyperbaric treatment and continued with very low grade compression, both of which were unsuccessful in healing her ulcer.

Patient 5 was a 60-year-old obese woman who had a mixed aetiology ulcer on her lateral malleolus for 11 months. She had a history of diabetes, previous leg ulcers, arthritis, deep vein thrombosis, and skin grafting. The patient became immobile and no longer capable of performing ADL during the study (details ensue). She was fitted with one layer of TF SSB for compression. At Week 1, the patient's wound bed had 80% slough, which was reduced to 50% slough at Week 10. The patient's wound increased in size. During Week 4, the patient sustained a fracture to the medial aspect of her ankle (the same ankle on which the ulcer was located). As a result, she was hospitalised for six weeks and her dressings were changed by

hospital nursing staff. She was non-ambulant for three weeks while her fracture healed and did not regain full strength or mobility after discharge. Her respiratory function also decreased markedly. After the study, the condition of the patient's ulcer deteriorated, as did her respiratory function. She died six months after completing the study.

DISCUSSION

In this prospective study carried out at the Royal Hobart Hospital, nine patients with chronic venous, pressure, or mixed aetiology ulcers were treated with OPAL A as a primary wound dressing. Improvements in several parameters of wound healing and reductions in pain were observed following treatment. These findings are consistent with those reported previously[7-9], and suggest that OPAL A may be effective in the treatment of chronic wounds.

Of note, we found that seven patients had an overall improvement in wound bed appearance and that three of these patients had a reduction in wound bed size after treatment with OPAL A. These changes are consistent with a shift in the wound bed from the inflammatory phase of healing to the proliferative phase of healing[11-13]. This shift usually occurs when non-viable tissue, which causes chronic inflammation due to a high bacterial load, is removed from the wound bed by debridement[12]. OPAL A treatment may have helped debridement of the wound bed and thereby promoted the normal healing process.

Pain scores were reduced in three patients after treatment with OPAL A. As patients did not receive any additional pain medications or other methods of pain reduction during the course of the study, OPAL A treatment may have contributed to the reduction in pain.

Nursing staff involved in this study reported that the low viscosity of the OPAL A formulation used prevented direct application of the formulation to the wound. However, other factors, aside from application of OPAL A, must also be considered when managing chronic wounds. Indeed, wound management requires a multifaceted approach and should address patients' comorbidities, lifestyle, and underlying wound aetiology to maximise treatment outcomes.

The mechanism of action of OPAL A is not completely understood. However, several mechanisms have been proposed[6] and some evidence of anti-inflammatory and vasodilatory effects has been published[14, 15]. Evidence for OPAL A exerting an anti-inflammatory effect comes from a study of human isolated neutrophils, in which the investigators found that OPAL A inhibited 5-lipoxygenase activity and, consequently, production of the pro-inflammatory mediator leukotriene B_4[14]. Evidence for OPAL A exerting a vasodilatory effect comes from a study of isolated preconstricted segments of human blood vessels, in which the investigators found that OPAL A exerted a nitric oxide-dependent vasodilatory effect[6, 15]. Such vasodilation may increase blood flow to the site and promote healing. Indeed, nitric oxide has been reported to promote angiogenesis, exert a bactericidal effect, and promote epithelialisation in wounds[16].

This study is limited by the small number of patients who had different ulcer aetiologies and comorbidities. Indeed, the diversity of aetiologies and comorbidities among patients with chronic wounds is a well-recognised problem in studies of wound healing, including large, randomised controlled trials[17].

In conclusion, the results from this prospective study lend some support to the notion that OPAL A may be an effective treatment for chronic wounds. Larger scale, randomised controlled clinical trials are needed to further evaluate the effectiveness of OPAL A as a treatment for chronic wounds.

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Belinda Free designed the study, was involved in the collection of data, and analysed the data. Both authors participated in the interpretation of study results, and in the drafting, critical revision, and approval of the final version of the manuscript.

The authors have no conflicts of interest to declare.

REFERENCES

1. Independence Australia. What's happening in wound care across Australia. Available from: http://www.independenceaustralia.com/uploads/HS%20Content/Wound_Care_Help/Whats%20Happening%20in%20Wound%20Care%20Across%20Australia.pdf, accessed 9 September 2013.

2. Guo S & Dipietro LA. Factors affecting wound healing. J Dent Res 2010; 89(3): 219-29.

3. Herber OR, Schnepp W & Rieger MA. A systematic review on the impact of leg ulceration on patients' quality of life. Health Qual Life Outcomes 2007; 5(44.

4. Jones J, Barr W, Robinson J & Carlisle C. Depression in patients with chronic venous ulceration. Br J Nurs 2006; 15(11): S17-23.

5. Morin RJ & Tomaselli NL. Interactive dressings and topical agents. Clin Plast Surg 2007; 34(4): 643-58.

6. McDonald K. Healing touch of pawpaw. Aust Life Sci 2013; 7(4): 30-3.

7. Graves N & Ashby AE. The use of OPAL001 filtrate and cream in the treatment of chronic pressure ulcers. Wound Practice Res 2008; 16(2): 22-9.

8. Baldwin C & Bonham S. Treatment of a sacral pressure ulcer and extensive hyperkeratosis with OPAL A filtrate and cream: A case study. Wound Practice Res 2011; 19(4): 196-9.

9. Mitchell GK. Clinical observations supporting a vasodilatory effect of the modified papaya extract OPAL001. Wound Practice Res 2011; 19(4): 189-95.

10. Australian Wound Management Association & New Zealand Wound Care Society. Australian and New Zealand Clinical Practice Guideline for Prevention and Management of Venous Leg Ulcers. 2012. Available from: www.awma.com.au/publications/2011_awma_vlug.pdf, accessed 7 August 2013

11. Falanga V, Brem H, Ennis WJ, Wolcott R, Gould LJ & Ayello EA. Maintenance debridement in the treatment of difficult-to-heal chronic wounds. Recommendations of an expert panel. Ostomy Wound Manage 2008; Suppl(2-13; quiz 4-5.

12. Schultz GS, Sibbald RG, Falanga V, Ayello EA, Dowsett C, Harding K, Romanelli M, Stacey MC, Teot L & Vanscheidt W. Wound bed preparation: a systematic approach to wound management. Wound Repair Regen 2003; 11 Suppl 1(S1-28.

13. Percival SL, Thomas JG & Williams DW. Biofilms and bacterial imbalances in chronic wounds: anti-Koch. Int Wound J 2010; 7(3): 169-75.

14. Russell FD, Windegger T, Hamilton KD & Cheetham NWH. Effect of the novel wound healing agent, OPAL A on leukotriene B4 production in human neutrophils and 5-lipoxygenase activity. Wound Practice Res 2011; 19(4): 200-3.

15. Mitchell GK, Windeggar T & Russell FD. Clinical observations and physiological data supporting a vascular response as a mechanism of the novel wound-healing agent, OPAL A. Wound Repair Regen 2010; 18(A65 (meeting abstract).

16. Luk PP, Sinha SN & Lord R. Upregulation of inducible nitric oxide synthase (iNOS) expression in faster-healing chronic leg ulcers. J Wound Care 2005; 14(8): 373-5, 8-81.

17. Gottrup F, Apelqvist J, Price P & European Wound Management Association Patient Outcome G. Outcomes in controlled and comparative studies on non-healing wounds:

recommendations to improve the quality of evidence in wound management. J Wound Care 2010; 19(6): 237-68.

TABLES

Table 1. Characteristics and changes in wound-related variables for patients with chronic venous ulcers who received OPAL A treatment

	Patient Number			
Characteristic / Variable	1	2	3	9
Age, years	44	29	82	59
Sex	Man	Woman	Woman	Man
Ambulant status	Independent	Independent	Dependent	Dependent
Mobility aid used	None	None	Walking stick	Wheelchair
Location of ulcer	Medial malleolus	Pretibial	Medial malleolus	Medial malleolus
Time ulcer had existed	6 months	9 months	5 years	> 14 months
Tissue type				
Before study	100% granulation	10% granulation, 90% slough	100% granulation	80% granulation, 20% slough
Week 4	100% granulation	30% granulation, 70% slough	Maceration (no percentage documented)	50% granulation, 50% slough
Week 10	95% epithelialisation, 5% granulation	90% granulation, 10% slough	NA[a]	NA[b]
Wound size				
Before study	3.0 x 4.0 cm (satellite area)	11.0 x 5.7 cm	1.4 x 2.4 cm	6.0 x 1.0 cm
Week 4	Not recorded	10.5 x 4.5cm	NA[a]	6.0 x 1.1 cm
Week 10	3 mm crust	10.0 x 5.0 cm	NA[a]	NA[b]
Bandage before study	TF SSB x 2 layers	Retention as compression slipped	Compression x 3 layers	Compression x 3 layers
Bandage during study	TF SSB x 2 layers	Double graduated Tubigrip as TF SSB slipped	TF SSB x 1 layer as unable to tolerate 2 layers	TF SSB x 1 layer
Dressing class before study	Silicone/foam with border	Non-adhesive and pad	Foam	Hydrofibre
Pain rating				
Before study	0/10	4-8/10	5/10	2/10
Week 4	8-10/10	2-8/10	NA[a]	Not determined
Week 10	0/10	3/10	NA[a]	NA[b]
Exudate				

	Patient Number			
Characteristic / Variable	1	2	3	9
Before study	Moderate, non-offensive	Heavy, non-offensive	Minimal, non-offensive	Minimal, non-offensive
Week 4	Moderate, non-offensive	Heavy, non-offensive	Moderate, malodourous	Moderate
Week 10	Minimal, non-offensive	Minimal, non-offensive	NA[a]	NA[b]
Pre-existing factors affecting wound healing potential	Hypertension, ulcers, varicose veins, DVT, PVD, obesity	Obesity, varicose veins	Leg ulcers, arthritis, PVD, obesity, peripheral oedema, PE, TKR	T2DM, ex-smoker, reduced mobility

Abbreviations: DVT, deep vein thrombosis; NA, not applicable; PE, pulmonary embolism; PVD, peripheral vascular disease; T2DM, type 2 diabetes mellitus; TF SSB, Tubular-Form Shaped Support Bandage; TKR, total knee replacement.

[a] Patient withdrew due to maceration at Week 4 and was not included in the analyses.

[b] Patient was withdrawn at the end of Week 4 because he exhibited cognitive decline and an inability to make informed decisions.

Table 2. Characteristics and changes in wound-related variables for patients with chronic pressure injuries who received OPAL A treatment

	Patient Number		
Characteristic / Variable	6	7	8
Age, years	76	61	42
Sex	Female	Female	Female
Ambulant status	Dependent	Independent	Dependent
Mobility aid used	Motorised scooter	None	Motorised scooter
Location of injury	Lateral malleolus	Spinal process	Heel
Time injury had existed	2 years	> 2 years	6 months
Tissue type			
Before study	100% slough	95% granulation, 5% slough	100% slough
Week 4	100% granulation	70% granulation, 30% slough	90% granulation, 10% slough
Week 10	100% granulation	Hypergranulation (at Week 13)	NA[a]
Wound size			
Before study	0.7 x 0.8 cm	6.5 x 2.2 cm (1 cm undermining depth)	1.0 x 1.0 cm (1 cm undermining depth)
Week 4	1.2 x 1.8 cm	Proximal 2.0 x 1.4 cm	1.0 x 1.0 cm (1 cm undermining depth)
Week 10	0.7 x 0.8 cm	Not assessed[b]	NA[a]
Bandage before study	Compression x 3 layers	None	None
Bandage during study	TF SSB x 2 layers	None	None
Dressing class before study	Antimicrobial and padding	Antimicrobial and padding	Alginate and foam
Pain rating			
Before study	7/10	0/10	0/10 (no sensation)
Week 4	6/10	0/10	0/10 (no sensation)
Week 10	0/10	Not assessed[b]	NA[a]
Exudate			
Before study	Minimal, non-offensive	Minimal, non-offensive	Minimal, offensive
Week 4	Minimal, non-offensive	Heavy, non-offensive	Minimal, non-offensive

	Patient Number		
Characteristic / Variable	6	7	8
Week 10	Moderate, non-offensive	Not assessed[b]	NA[a]
Pre-existing factors affecting wound healing potential	Diabetes, arthritis, AF, CVA, PVD, varicose veins, osteoporosis, reduced mobility	Heart disease, renal disease, arthritis, radiation therapy, scleroderma, Raynaud's phenomenon, severe malnutrition, metastatic cancer of the spine requiring radiation therapy	Spina bifida, paraplegia, obesity, arthritis

Abbreviations: AF, atrial fibrillation; CVA, cerebrovascular accident; NA, not applicable; PVD, peripheral vascular disease; TF SSB, Tubular-Form Shaped Support Bandage.

[a] Patient withdrew from the study at Week 6 due to wound infection on the recommendation of her general practitioner.

[b] Patient was followed up after completion of the study at Week 13.

Table 3. Characteristics and changes in wound-related variables for patients with chronic ulcers of mixed aetiology who received OPAL A treatment

	Patient Number	
Characteristic / Variable	4	5
Age, years	85	60
Sex	Female	Female
Ambulant status	Independent	Independent
Mobility aid used	None	None
Location of ulcer	Medial malleolus	Lateral malleolus
Time ulcer had existed	2 years	11 months
Tissue type		
Before study	20% granulation, 80% slough	20% granulation, 80% slough
Week 4	20% granulation, 80% slough	50% granulation, 50% slough
Week 10	20% granulation, 80% slough	50% granulation, 50% slough
Wound size		
Before study	2.5 x 1.5 cm	2.3 x 4.5cm
Week 4	Not documented	2.3 x 4.7cm
Week 10	4.5 x 4.1cm	3.3 x 4.5cm
Bandage before study	Compression x 3 layers	Retention
Bandage during study	TF SSB x 1 layer	TF SSB x 1 layer for 1 week and then retention for remainder of study
Dressing class before study	Zinc bandage x 4 layers and pad	Pad
Pain rating		
Before study	0/10	9/10
Week 4	5/10	0/10
Week 10	3- 4/10	0/10
Exudate		
Before study	Moderate, non-offensive	Moderate, non-offensive
Week 4	Moderate, offensive	Heavy, non-offensive
Week 10	Heavy, non-offensive	Moderate, non-offensive
Pre-existing factors affecting wound healing potential	PVD, DVT, previous leg ulcer, skin graft	Diabetes, previous leg ulcer, previous skin graft site, anticoagulant therapy, steroid therapy, arthritis, deep vein thrombosis, obesity

Abbreviations: DVT, deep vein thrombosis; PVD, peripheral vascular disease; TF SSB, Tubular-Form Shaped Support Bandage.