Treatment of symptomatic abnormal skin scars with electrical stimulation

• **Objective:** To evaluate the effect of non-invasive biofeedback electrical stimulation on symptomatic abnormal skin scars.

• **Method:** Thirty patients with over 140 scars with long-term pain and itch were recruited into the study. Patients monitored the intensity of symptoms (pain and itching) on a numerical rating scale. In addition, a modified Manchester scar scale was used to objectively assess digital photographs of each scar in terms of colour, contour, distortion and texture, while a non-invasive spectrophotometric intracutaneous analysis was used to monitor the scars' physical characteristics.

• **Results:** The electrical stimulation device resulted in a clinically and statistically significant ($p<0.05$) reduction of symptoms and scar scores.

• **Conclusion:** These results give a preliminary indication of the potential role of non-invasive biofeedback electrical stimulation in the management of chronic scar pain and itch. However, further large scale controlled studies are warranted to elucidate its overall efficacy and mechanistic action.

• **Conflict of interest:** Funding was provided from Eumedics Ltd for this study.

itch; pain; sensitive scars; pruritus; abnormal skin scarring

All cutaneous scarring has the potential to affect quality of life.[1,2] With nearly 100 million people acquiring skin scars every year in the developed world alone,[3–5] finding an effective treatment poses a significant challenge. Current management options are often unacceptable to the patient, and minimally invasive procedures, such as steroid injections, or radical interventions, such as scar excision, can cause further pain. A promising area of development in the management of problematic soft tissue conditions is electrical stimulation.

Undamaged human skin has an endogenous electrical potential and a transcutaneous current potential (10–60mV),[6] generated by the inward movement of sodium ions through Na^+/K^+ ATPase pumps in the epidermis.[7] When an injury affects epidermal integrity, an overall flow of current through the wound pathway generates a lateral electrical field, both within and beneath the epidermis; this is known as the 'current of injury' or the 'skin battery' effect.[8] As the wound heals, the current of injury returns to its baseline level.[9] Therefore, the current of injury is thought to be significant in triggering biological repair; indeed, it is absent in some chronic wounds.[8,10,11]

In the past few years, there has been greater recognition of the role played by electrical fields in cellular behaviour and motility.[12,13] Studies have demonstrated that electrical stimulation can enhance tissue healing by promoting the migration of keratinocytes and macrophages,[14] encouraging angiogenesis,[15] stimulating fibroblasts, and increasing adenosine triphosphate and protein synthesis.[16] Further evidence suggests it may have antimicrobial effects.[17]

In 2009, Poltawski and Watson reviewed the evidence on microcurrent therapy, which applies electrical current levels similar to those produced by the body during normal tissue repair, and concluded that it can promote healing in skin lesions and may have a potential role to play in wound care.[18]

More recently, a novel *in vitro* model for testing the effects of precisely defined types of electrical stimulation on collagen expression in normal and keloid human skin fibroblasts was developed at the senior author's (AB) laboratory.[19] Both cell types were electrically stimulated with alternating current, direct current or degenerate waves (the wave form generated by the biofeedback electrical stimulation device investigated in this paper). Following 12 hours of exposure to degenerate waves, keloid fibroblasts (which show excessive collagen production) were found to have a statistically significant decrease in collagen I expression. This indicates that electrical currents, in particular degenerate waves, are a promising, novel therapeutic strategy for suppressing excessive collagen I formation in keloid disease.

Meanwhile, there is growing acknowledgement of the link between the skin's electrical impedance patterns (surface readings of electrical field gradients[20,21]) and underlying clinical conditions, such as asthma.[22,23] It is thought these electrical impedence

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patterns represent a modification of cell behaviour which may also be represented at the central nervous system level. Interactions between the central nervous system and the skin involve neuropeptides, cytokines, hormones and other effector molecules.[24] It has been proposed that there is an interrelationship between the skin, endocrine, immune and central nervous systems, which has been termed the neuro-immuno-cutaneous-endocrine model. According to this theory, electrical stimuli at the skin surface can influence all of these systems at both a local and central level.[25] For example, transcutaneous electrical nerve stimulation activates opioid receptors in the central nervous system, as demonstrated in basic science studies using both high and low frequencies.[26,27] In mild asthma, electrical stimulation appears to facilitate neurological adjustment of mast cell sensitivity.[28]

The Fenzian treatment system

An emerging adjuvant therapy is the Fenzian biofeedback electrostimulation treatment system (Eumedic, UK, Fig 1), which delivers a low-intensity transcutaneous electrostimulation current to specific skin areas. It follows the theory that the electrical potential of skin forms a global electrical network, and that any changes in skin impedance reflect underlying neurological activity.[29] The mechanism by which this body-wide electrical network might stimulate a healing response is not yet fully understood. However, the disruption to these body-wide potential patterns during injury is a likely trigger for tissue repair, in addition to the release of hormones and numerous chemical medicators.[30,31]

The Fenzian system detects the skin's electrical impedance using a microcurrent generator. The outgoing transformer signal is measured across a concentric electrode, and a biofeedback impulse is applied (this comprises a sequence of electrical impulses, the sizes of which depend on alterations in skin response).[32] The user is guided to optimal biofeedback sites by a numerical depiction of the outgoing signal characteristics. When this shows that biofeedback is complete (by reaching an unchanging electrical state), an audible bell sounds and the device is then moved to another site, or the treatment may be complete (depending on the protocol).

Fenzian is applied to a patient's skin by a specially trained medical practitioner (a doctor, nurse or physiotherapist) in a protocol that depends on the individual patient. Patients are treated while sitting or (very occasionally) lying down. This microcurrent electrical stimulation uses currents that are in the microampere range, which are a thousand times lower than transcutaneous electrical nerve stimulation (TENS). Pulse widths are also different (average 0.5 seconds), typically 2,500 times longer than a TENS unit, and often below the sensation threshold.[33] The device has a 45 x 22mm electrode, which is brushed or physically held in contact with the skin for the duration of treatment. Impulses are of short duration (~10µs) and of relatively high amplitude (80V).

Fig 1. The Fenzian treatment system

Table I. Basic demographics (n=19)

Sex (male/female)	3/16
Age (years)	
• ≤25	7
• 26–35	3
• 36–45	4
• ≤46 & over	5
Ethnicity: Caucasian/other	14/5
Fitzpatrick skin scale	
• I–III	14
• IV–VI	5
Positive abnormal family scar history	2
Positive previous history of abnormal scarring	4
Past medical history conditions	
• Respiratory	3
• Dermatological	4
• Other	5

Background to the evaluation

Many scars have a chronic inflammatory component, either with erythematous colouration[34] or as a result of acute sensitisation of nociceptors and/or activation of puriceptors,[35] although the exact underlying mechanism is not fully understood.[36]

Previous retrospective case note reviews[32] and controlled pilot studies[28] of the Fenzian system have demonstrated a persistent pattern of improved symptoms across a wide range of conditions, including asthma and traumatic cutaneous injuries.

We conducted an open-label observational study to assess the subjective benefits and objective changes in symptomatic, raised, dermal scars treated with the Fenzian system. This is the first study to formally evaluate its use in cutaneous scars. Problematic scarring was chosen because of the extent of

pain and pruritic symptoms endured by some patients, and the poor range of non-invasive management options currently available.

Materials and method

Patients attending the specialist scar service clinic at the University Hospital of South Manchester (UHSM) NHS Foundation Trust between January 2009 and June 2009 were eligible for recruitment. Inclusion criteria were:

- Patients with one or more cutaneous scars that had not responded to previous treatment, such as steroid injections, surgical excision and silicone gel therapy (based on unsatisfactory scar appearance and/or symptoms), or for which the patient had requested further non-invasive management
- Patients with any problematic scar type, such as keloid, hypertrophic, or history of scarring such as trauma, surgery, acne.

Exclusion criteria were:

- Patients taking medication that reduce electrical activity of the skin, such as antibiotics and steroids)[37]
- Patients with implanted electrical devices, such as pacemakers and cochlear implants
- For cautionary reasons, patients who were pregnant or planning to conceive

There were no exclusion criteria relating to sex, age or past medical history.

The intervention

The biofeedback electrical stimulation therapy was administered by a single therapist as part of the patient's routine care. The battery-operated Fenzian system is both CE approved and US FDA 510(k) registered, and it passed the UHSM Trust Medical Engineering requirements for clinical usage.

As the device was used as indicated by its CE mark, ethics committee approval was not required. However, all patients gave written informed consent for the image/photographic monitoring of their scars.

Treatment was administered according to standardised local (scar location) or global (whole body) protocols, depending on the anatomical site affected and the physiological systems linked with the individual's scar history (for instance, targeting lower abdominal hormonal sites in relation to acne scarring).

Treatment times were dictated by the device via its biofeedback electrical mechanism (average 20 minutes in duration) and administered by a single clinician. For the first 3–4 weeks, treatments were administered twice weekly. Further treatments and review appointments continued for up to 6 months, on a monthly basis.

Patients did not receive any other forms of scar therapy during the course of bioelectrical stimulation treatment.

Assessment

Subjective and objective outcome measures were recorded by a single unblinded therapist (first author, DP) and then evaluated by the senior author (AB).

- At every visit, we recorded the patient's subjective rating of perceived pain and intensity of itch over the past 24 hours, using the validated 11-point numerical rating scale (NRS, where 0 = no pain/itch, 10 = worst possible pain/itch). We also noted whether the symptom was constant or intermittent
- Digital photographs were taken and the scar sites were clinically evaluated at all treatment visits using a modified Manchester Scar Score (mMSS).[38] This includes assessment of scar colour, contour, distortion and texture. Each parameter is scored on a linear scale of 1–4, with increasing scar severity scoring more highly. This also records each scar's matte or shiny appearance, with 1 = matte and 2 = shiny. Scores are totalled and range from 5 (clinically well-healed scar) to 18 (clinically poor scar).[38]
- At multiple time points throughout treatment and on consistently selected scar site areas, objective spectrophotometric intracutaneous analysis (SIA) or

Table 2. Presenting abnormal scar data

Scar details		No.
Location	Sternum/breast	8
	Shoulder girdle	4
	Other	7
Scar cause	Surgery	13
	Trauma	2
	Acne/spots	4
Scar age	<1 week	1
	1 week to 11 months	8
	1–3 years	5
	>3 years	5
Scar type	Keloid	11
	Hypertrophic scar	5
	Other	2
	New wound (previous hypertrophic/keloid)	1
Lesion history	Primary	11
	Recurring	8
Symptoms	No symptoms	5
	Pain only	3
	Itch only	5
	Pain and Itch	6
Modified Manchester scar score (5–18)*		14 (8–17)
NRS Pain (0–10)*		0 (0–9)
NRS Itch (0–10)*		5 (0–9)

Results are presented as median (range)

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Table 3. Symptomatic response to treatment

	Pain	Itch
	No.	No.
Initial symptom		
0	10	8
1–3	0	1
4–6	4	5
7–10	5	5
Response at 1 week (with score ≥1 at baseline)		
Increased	2	2
Decreased	4	6
Same	3	3
Overall response to biofeedback electrical stimulation by 2 months (with score ≥1 at baseline)		
Increased	0	0
Decreased but continued symptom	4	4
Same	0	0
Symptom resolved	5	7

SIAscopy (Siascope, Astron Clinica Ltd, Cambridge, UK) was performed. Using a non-invasive light-based technology probe, the quantities of light remitted by the skin at different wavelengths are determined,[39] providing a photographic pigmentary status and quantitative numerical values for the constitutional elements of the first 2mm of skin (melanin, haemoglobin and collagen).[40]

Additionally, basic demographic data were collected from the patient notes for cross analysis purposes. If patients presented with more than one scar, the most problematic scars were selected for objective monitoring. Patients were also monitored for any adverse reactions.

Statistical analysis

Descriptive statistics were used to document trends between demographic characteristics and variables where group size prevented inferential statistical testing. Only one scar per subject (defined by the highest pain, itch and scar scores) was selected for inclusion in the statistical analysis. Non-parametric Wilcoxon signed rank tests were applied to assess differences in pain, itch, scar score and chromophores between time points. The statistical package SPSS version 15.0 was used, and all analyses were carried out using the conventional 5% significance level.

Results

Demographics

Thirty patients with more than 140 (52 evaluated) scars were treated with the biofeedback electrical stimulation system (the test treatment). Patient demographic details are given in Table 1. Eleven participants were excluded from the basic statistical analysis due to either failing to complete a basic course of treatment (minimum five sessions) or because they started medication known to reduce the therapeutic effects of the test treatment. This resulted in an observational case series sample of 19 patients with 31 monitored scars, of which 19 were included in the statistical analysis.

Patients had a mean age of 37 years (range 15–85), a modal Fitzpatrick skin classification of type II (fair skin, burns easily and tans poorly) and 84% were female. Co-existing dermatological conditions were common, and included eczema, psoriasis and acne.

Presenting complaint

The 19 individuals included presented with a range of abnormal skin scars (Table 2), primarily due to surgery. Acne keloid scarring or a strong propensity for keloid disease accounted for the majority of self-defined 'problematic' scars. Most scarring was keloid in nature, affecting the sternum/breast, and was over 3 years in duration (median 2 years, range one week to 30 years).

On entry into the study, most individuals had a primary abnormal scar lesion (not previously excised). However, one new wound also received treatment, following repeat debulking surgery.

At the start of treatment, five patients had no pain or itch, five complained of itch only, three of pain only, and six of itch and pain together. At baseline, the median NRS pain score was 0 (range 0–9) and the median NRS itch score was 5 (range 0–9). In general, a high proportion of scars were rated 'clinically poor' using the mMSS (median 14, range 8–17).

Therapeutic outcomes

The 19 patients received a median of nine (range 5–16) treatments over a median 70-day period (range 27–138).

Outcome data were selected and grouped into specific one-week, and one, two and three-month time point ranges for simplification. The latter time point was omitted from statistical analysis as only 11 patients had follow-up data at this time.

Symptomatic outcome

Patient-perceived symptomatic outcomes are displayed in Table 3. Of the nine patients with pain at

baseline, four (44%) reported decreased pain at one week. Symptoms more frequently decreased in itch sufferers, with six (55%) of the 11 with itch at baseline reporting improvement. In all, four scars had an initial exacerbation of symptoms (three by one NRS point and one by two NRS points). For those patients in whom pain and itch improved, median reductions of four (range 2–6) and 2.5 (range 1–7) NRS points were observed for pain and itch respectively, following initial treatment.

By one month, of the nine patients with pain at baseline, three had no pain and the remaining six had reduced pain. Of these six patients, two had no pain by 2 months. Therefore, resolution of pain was achieved by 2 months for five (56%) of the nine patients with pain at baseline, after a median of six treatments (range: 5–8). Of the four patients with continuing pain, pain scores had reduced by a median of 2.5 (range: 1–6).

Of the 11 patients with itch at baseline. Five had no itch by one month, and the remaining six had reduced symptoms. By 2 months, resolution of itch was achieved in a total of seven (64%) patients after a median of six treatments (range: 5–14). Of the remaining four patients, itch scores had reduced by a median of 3.5 (range: 2–6).

Median scores and ranges are displayed in Table 4, together with Wilcoxon test results, which show that statistically significant changes from baseline occurred at one and 2 months for both pain and itch scores.

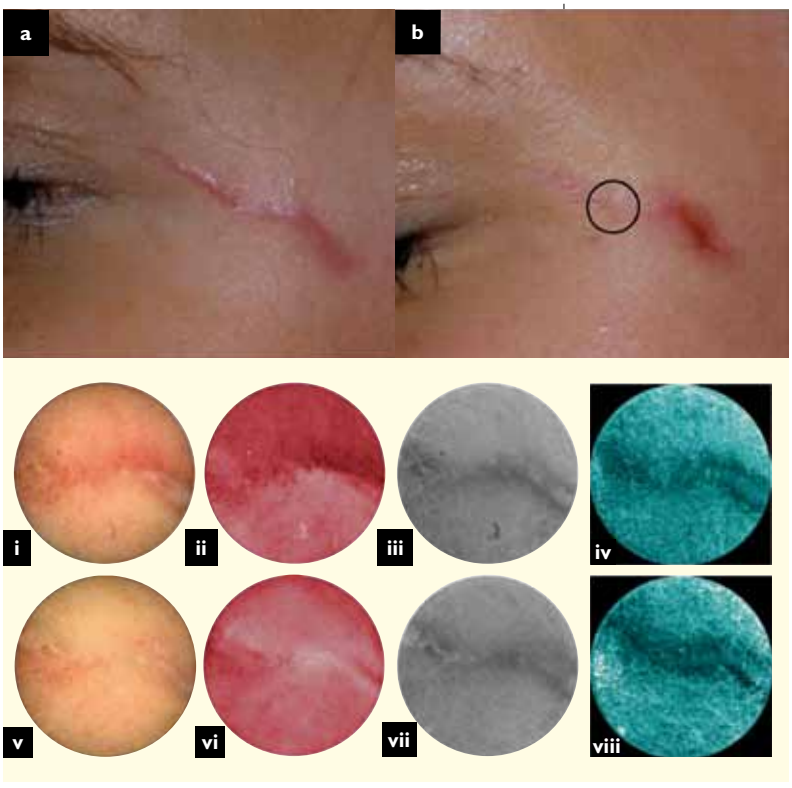

Fig 2. Four month old raised facial scar before treatment (a) and 6 weeks' post-initial treatment (b). SIAmetrics chromophore images (ordered plain photograph, haemoglobin, melanin and collagen) taken from the scar region highlighted depict changes before (i–iv) and after (v–viii).

Observed scar score outcomes

A positive response was observed in 24 of the 31 scars affecting the 19 patients. Only two patients had no observed alteration in their scar characteristics during adjuvant therapy.

Overall, the mMSS had reduced by a median of three (range: 0–5) at two months. We observed statistically significant reductions in total scar scores at one week, one month and two months (see Table 4).

Scar score reductions recorded using the mMSS were largely due to objective reduced scores in the 'colour' and 'texture' categories, but also in the 'matte/shiny' appearance. Figs 2–4 display example plain photographs and colour, haemoglobin, melanin and collagen SIAmetric images of three scars before initial Fenzian application and after treatment.

Objective melanin, haemoglobin and collagen chromophore analysis

No known widespread normative quantitative values of melanin, haemoglobin and collagen chromophores exist in new wounds or abnormal scarring. Hence, data were examined for cumulative and significant patterns within individuals. No statistically significant changes in haemoglobin levels, collagen and melanin were observed (see Table 4).

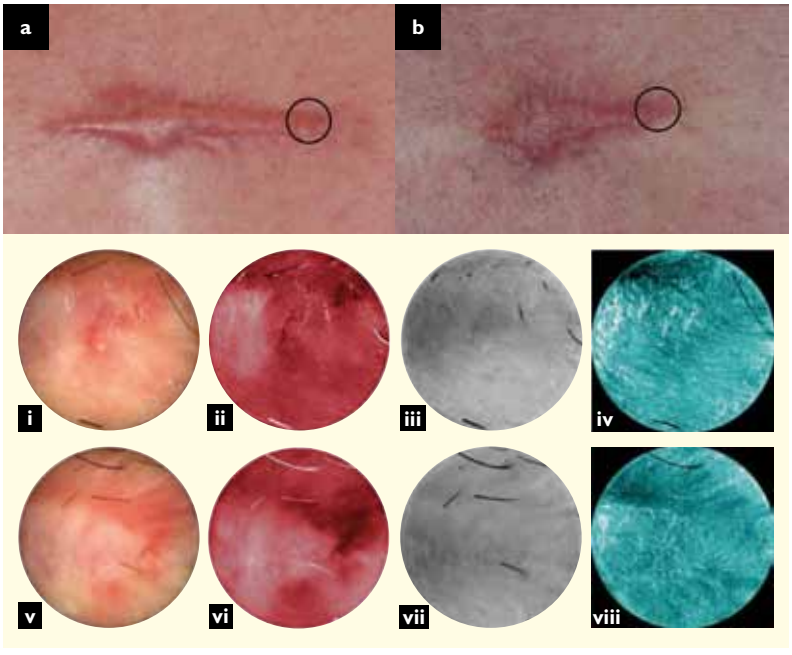

Fig 3. Eight month old recurring keloid sternal scar before treatment (a) and 2 months post-initial treatment (b). SIAmetrics chromophore images (ordered plain photograph, haemoglobin, melanin and collagen) taken from the scar region highlighted depict changes before (i–iv) and after (v–viii).

Table 4. Symptomatic outcomes scores

Variable	Baseline	1 week	1 month	2 months
Pain (n=9)	7 (4–9)	5 (0–9)	3 (0–8)**	0 (0–7)**
Itch (n=11)	6 (3–9)	4 (0–8)	2 (0–6)**	0 (0–4)**
Scar score (n=19)	14 (8–17)	13 (8–17)*	12 (6–17)**	11 (6–17)**
Haemoglobin (n=19)	191 (16–224)	196 (14–244)	190 (14–244)	184 (9–236)
Collagen (n=19)	192 (129–226)	190 (135–293)	200 (132–301)	195 (146–233)
Melanin (n=19)	216 (117–842)	202 (139–842)	212 (103–842)	228 (120–842)

Scores are presented as median (range)
*p<0.05, **p<0.01
For pain and itch scores, only patients with non-zero scores at baseline are included

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Other effects

A number of additional 'side-effects', not formally evaluated, were observed during the treatment process. Three individuals with increased skin oil production and scars caused by acne/spots[41] appeared to have a reduction in symptoms in the upper trunk region following 1–6 treatments. Three participants described a non-painful tingling sensation at the treatment site for approximately 2 hours post-therapy. Furthermore, two patients with high-intensity scar pain noted immediate (within 12–24 hours) relief of symptoms for 4 and 7 days post-initial treatment. In one patient this was maintained with further treatment to eradicate pain, while the other individual's pain persisted, but at a lower intensity. No adverse events were reported.

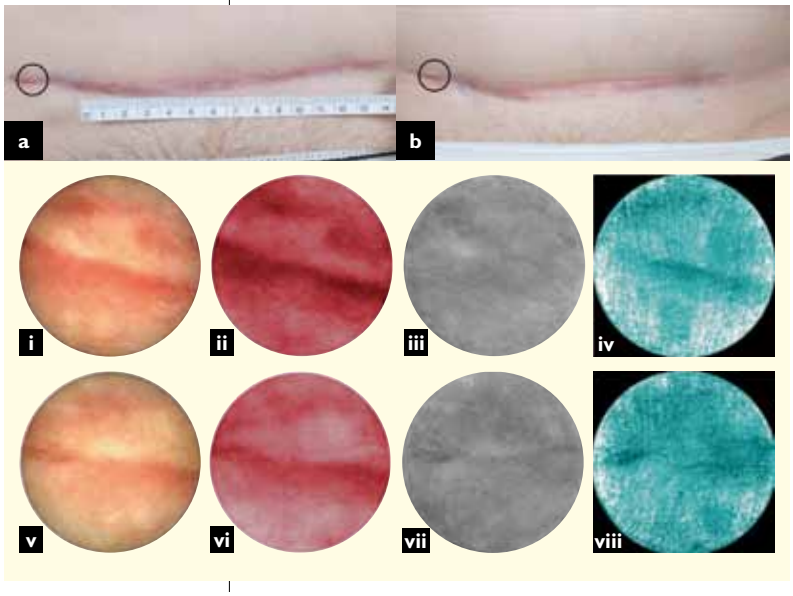

Fig 4. Eighteen-month-old red and partially raised caesarean section scar before treatment (a) and post-3 months after initial treatment (b). SIAmetrics chromophore images (ordered plain photograph, haemoglobin, melanin and collagen) taken from the scar region highlighted depict changes before (i–iv) and after (v–viii)

Discussion

A positive effect was observed with the biofeedback stimulation adjuvant therapy, in terms of both symptoms and the objective scar parameters monitored during treatment. Pain and itch were significantly reduced ($p<0.05$) in all participants at the three monthly intervals recorded, and the majority of patients' symptoms resolved completely during the study period. These results are clinically significant, as illustrated by the reduction of two NRS points, a requirement for a clinically important difference to be proven.[42]

Despite their similarly matched baseline NRSs, greater pain relief was observed in keloid scars and greater itch relief was observed in hypertrophic scars. Mast cells, which are involved in the healing process, contain many itch mediators (including histamine and substance P).[43] Raised scars have been shown to have higher substance P nerve fibre densities, greater substance P quantities and an increased number of mast cells.[44] Substance P is also thought to mediate pain via small, unmylinated C fibres.[45] In raised scars, it may contribute to an exuberant neuroinflammatory response due to a reduction in its regulatory enzyme, endopeptidase.[46] Inflamed scars are often typically red and raised. The post-treatment reduction in scar score (by objective parameters), as well as reduction in pain and itch, indicated a decreased inflammatory state. However, this would have to be verified histologically.

Significant reductions in scar scores were noted at all time points, and the clearest reductions were observed in hypertrophic and surgical scars. Given that scar score reductions recorded using the mMSS were most frequently associated with a lessening of colouration, and that problematic hypertrophic scars are often persistently erythematous,[34] it makes sense that this group had lower scores following therapy. It has been suggested that neurogenic inflammation stimulates abnormal scarring,[47] so normalisation of this response may enhance abnormal scar resolution.

We examined the chromophore levels of constitu-

al elements in the epidermis (melanin, haemoglobin and collagen) for general pattern changes, as no current literature exists to suggest the extent and specificity of cellular changes following biofeedback electrical stimulation treatment. An electro-therapeutic, pro-inflammatory response can be observed initially, as haemoglobin increases, and it has been suggested that this may stimulate chronically inflamed tissue to progress to resolution.[28,31] Previous data suggest that low frequency electrical stimulation increases blood flow, causing vasodilation by the release of neuropeptides from the terminal endings of excited axons through C fibres.[48] Hence, we postulate a mechanistic path for altered scar symptoms with biofeedback electrical stimulation.

At 3 months, greater improvements were noted in symptoms and scar scores, perhaps signalling resolution of the acute inflammatory response. No scars grew larger in response to the treatment.[49] Fluctuations in the scar collagen levels recorded may account for the raised collagen levels in these individuals.

Overall, a chromophore's trend response to the treatment can only be postulated, due to the lack of published scar data and questions of the suitability of the instrument used in this preliminary study. Additionally, the proposed body-wide mechanism of action of this treatment prevents determination of the extent of any changes, as there is no opportunity for a subject to act as his or her own control.

Skin, endocrine and immune system interactions involve a number of neuropeptides, cytokines, hormones and other effector molecules.[24] Therefore, stimuli at the skin's surface have influence both locally and centrally. A growing body of evidence suggests that interaction between the skin and nervous system contributes greatly to wound healing.[50] The nervous system can modulate locally induced inflammatory responses in the skin through the release of neuropeptides.[25]

This was a small, open label observational case series study designed to gather preliminary data to help guide future applications of this modality. Obvious study limitations exist. These include the limited follow-up period, due to the new therapeutic service studied in this case series, and the possible placebo effect in certain cases. Hence, in order to establish evidence of any long-term, symptomatic and objective benefits, future standard follow-up assessments should be completed using a larger sample group, and a RCT or a prospective comparative cohort study be performed.

A number of different measurement tools were used in this study. Although the NRS has no intrinsic meaning, it is easy for patients to understand, quick to apply and clinically valid. Hence, the NRS presents a useful research tool in gauging the main focus of symptomatic change. For additional objective monitoring, the Manchester Scar Score is the only currently available valid and reliable clinician-rated instrument for use with all scar types. However, some of its rating categories can prove ambiguous in practice, especially the 'contour' category, for which 'keloid' has the maximum ranking. This categorical rating lacks clinical significance, as some keloid lesions may be morphologically flat and widespread in contrast to extensively raised hypertrophic scars, which would in practice achieve lower scores.

The current study would have benefited from independent evaluation and scar scoring of the images taken at treatment appointments, to reduce possible bias. This was not attempted, as our treatment facilities were changed part way through the case series, which dramatically affected the lighting of photos and could have led to the interpretation of variances. All treatments and objective data collections were completed by the same individual, so we assume that any errors were standardised throughout the study, negating their impact. Given the risk of bias with an unblinded assessor, we used objective scar measurement tools and independent statistical analysis methods.

Our sample group consisted largely of individuals with long histories of problematic scarring and symptomatic distress, in whom previous routine treatments had either 'failed' or achieved inadequate results. Therefore, initial symptom scores were high. Post-surgical scars represented the largest aetiological group, including scars from both primary surgery and previous scar revision. Due to the nature of keloids, these secondary lesions have a high risk of recurrence. It is possible that the relatively high representation of these scars in our sample group skewed the statistical analysis. The relatively low representation of some other groups restricts other analysis possibilities. For instance, a cross analysis of treatment outcome against propensity for scarring (considering family history, or personal scarring history) was not possible. Analysis was further restricted by the strict statistical analysis methods employed, as only one scar could be included from each patient.

Conclusion

All patients with symptomatic scars had a positive outcome. Individuals with keloid scars showed the greatest pain relief, those with hypertrophic scars had the best improved itch symptoms, while scar score reduction was better achieved in hypertrophic and surgical scar cases. Our results suggest that patient age and the number of problematic scars present affects response to biofeedback electrical stimulation. Further controlled studies are warranted. The current study provides encouraging early evidence of the use of biofeedback electrical stimulaton in the successful management of symptomatic abnormal skin scarring. ■

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