2022

Does Acupuncture/Dry Needling Improve Pain and Itch in Abnormal Hypertrophic Scars

Catherine Tuckey
The University of Notre Dame Australia

DOES ACUPUNCTURE/DRY NEEDLING IMPROVE PAIN AND ITCH IN ABNORMAL HYPERTROPHIC SCARS?

Catherine R. Tuckey (nee. Smith)

BHSc (Physiotherapy), P.G Cert (Western Acupuncture)

Submitted in the fulfillment of requirements for Masters of Science (Research)

School of Physiotherapy

Fremantle Campus

September 2022

Declaration of Authorship

To the best of the candidate's knowledge, this thesis contains no material previously published by another person, except where due acknowledgement has been made.

This thesis is the candidate's own work and contains no material which has been accepted for the award of any other degree or diploma in any institution.

Human Ethics (For projects involving human participants/tissue, etc) The research presented and reported in this thesis was conducted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007, updated 2018). The proposed research study received human research ethics approval from the University of Notre Dame Australia Human Research Ethics Committee (EC00418), Approval Number #017029F

Signed:

Catherine Tuckey

14/09/2022

Acknowledgments

This research project was supported by an Australian Government Research Training Program (RTP) scholarship.

I would like to acknowledge my two academic supervisors: Associate Professor Dale Edgar and Mrs Susan Kohut for their ongoing support and input into this project.

Finally, I need to thank my husband and family for supporting me and encouraging me throughout this process.

Dissemination Outputs Arising from this Project

Tuckey, C., Kohut, S., & Edgar, D. W. (2019). Efficacy of acupuncture in treating scars following tissue trauma. *Scars, Burns & Healing, 5*. doi:10.1177/2059513118831911

Tuckey, C. R., Kohut, S. H., & Edgar, D. W. (2022). Case study: Pilot testing of a local acupuncture intervention protocol for burn scars. *Scars, Burns & Healing, 8*. doi:10.1177/20595131211058430

Tuckey, C., Kohut, S.H. & Edgar, D.E. (2020) Efficacy of acupuncture in treating scars following tissue trauma: A narrative literature review. *Integrative Medicine Research, 9, Suppl 1, 100577*. doi:10.1016/j.imr.2020.100577 (abstract published)

Poster Presentations

Hypertrophic scars and their management using acupuncture: A narrative review of the literature. Tuckey, C., Kohut, S.H. & Edgar, D.E. World Congress of Physical Therapy, Geneva, Switzerland, 11.05.2019.

Hypertrophic scars and their management using acupuncture: A narrative review of the literature. Tuckey, C., Kohut, S.H. & Edgar, D.E. Acupuncture Association of Chartered Physiotherapists, London, United Kingdom. 18.05.2019.

Efficacy of acupuncture in treating scars following tissue trauma: A narrative literature review. Tuckey, C., Kohut, S.H. & Edgar, D.E. KIOM-SAR 2020 International Research Conference (KIOM - Korea Institute of Oriental Medicine & SAR - Society of Acupuncture Research) - " Bridging East & West from Acupuncture & Traditional Medicine Research to Practice. Seoul, Korea / online conference. 11-13.09.2020.

Conference Presentation

Australia and New Zealand Burn Association Annual Scientific Meeting, October 2021. Case Study: Pilot testing of a local acupuncture intervention protocol for burns scars.

Abstract

This research program investigated the use of acupuncture intervention as an adjunct for hypertrophic scar (HTS) management. Mechanistic evidence from ex vivo and animal studies suggests that acupuncture has the potential to modulate neurogenic inflammation to influence pain and itch associated with HTS. Further, acupuncture may mediate non-neuronal cells involved in the proliferation and remodelling stage of healing to promote scar maturation. Previous studies using acupuncture for scar management demonstrated positive outcomes, however low-quality clinical trials and case studies provide limited evidence for treatment benefit.

A treatment protocol was designed to investigate the effects of locally applied acupuncture compared to distant acupuncture, combined with routine care scar massage therapy. The protocol was tested for feasibility on one participant with scarring post-burn injury and demonstrated reduced pain, and improved scar physical characteristics. Results from expanded testing of the research protocol in participants with surgical or linear scars are presented as a case series. Outcomes from the case series show improvement in scar symptoms for most participants, however no clear difference was seen between local and distant acupuncture outcomes. Finally, data analysis suggested one sub-group of hypersensitive participants (with high initial scores for both pain and itch) responded to acupuncture intervention possibly providing insight into treatment mechanisms and adding weight to recommendations for future research and clinical practice.

Introduction

Health professionals, including physiotherapists, are often involved in patient management and treatment of scar tissue developing because of trauma or surgery (Atiyeh, 2007; Monstrey et al., 2014). Scarring is a normal consequence of tissue damage as a result of a complex wound healing response (Beldon, 2010). Normal healing leaves a flattened 'normotrophic' scar that fades as it matures and has similar properties to normal skin (Beldon, 2010). Scar tissue forms during the proliferative phase of healing and involves the production of collagen fibres to provide structure to the wound region and re-epithelisation or restoration of the skin surface (Beldon, 2010). Uncomplicated scar tissue proliferation can last between seven-ten days in a superficial (epidermal depth) wound or continue for three-six weeks in deeper injuries producing scars due to a greater loss of dermal tissue such as in thermal injury (Beldon, 2010; Wolfram et al., 2009). Once re-epithelisation is complete the remodelling phase of healing commences and can last for 12 months or more in pathological scars (Wolfram et al., 2009).

Common pathological scarring responses following surgical incision or thermal injury include hypertrophic, atrophic and keloid scars (Bordoni & Zanier, 2013; Zhu et al., 2016). Hypertrophic scars (HTS) are raised, red, itchy and may have reduced tissue pliability leading to reduced range of joint motion, pain, and disfigurement (Clark et al., 1996; Clark et al., 1996; Gauglitz et al, 2011; Wolfram et al., 2009; Zhu et al., 2016). These symptoms can lead to physical impairments, psychological issues, and reduced quality of life (Finlay et al., 2017; Gauglitz et al., 2011; Kvannli et al., 2011; Zhu et al., 2016). Hypertrophic scar formation becomes evident within four to eight weeks of injury, has a rapid growth phase that can last up to six months and can persist for several years while gradually resolving (Gauglitz et al., 2011). Atrophic scars form a depression or sunken area with respect to surrounding uninjured skin and may cause the same symptoms as hypertrophic scars such as pain, itch, and movement restriction, however they have a different aetiology and healing timeframes (Bordoni & Zanier, 2013). Keloid scars may form up to several years following minor skin injury and are common in individuals with a family history of keloids (Gauglitz et al., 2011). Unlike HTS or atrophic scars, keloids extend beyond the margins of the original wound and do not spontaneously regress (Gauglitz et al., 2011). Due to differences in

aetiology and histology of different pathological scars and therefore different treatment requirements, this thesis is provided in the context of hypertrophic scars.

For optimal outcomes, scar management should begin as soon as possible after wounding (Atiyeh, 2007). For example, following burn injury, early scar management includes the actions of the acute care team, such as first aid and pre-hospital interventions followed by inpatient medical care, and if necessary, surgical intervention. Scar management aims to promote normal wound healing, prevent pathological scarring, and treat scars that do become pathological during the tissue maturation process (Atiyeh, 2007). Prophylactic scar treatment is commonly used following burn injury and includes surgical intervention (e.g., skin grafting) combined with conservative treatments including compression garments, silicone therapies and scar massage (Monstrey et al., 2014). Surgical scar prophylactic treatment may include taping and silicone therapies (Monstrey et al., 2014). Subsequent to a scar becoming pathological, the same prophylactic treatment interventions may be continued, along with additional therapies depending on the type of pathological scarring response (Atiyeh, 2007).

Incidence of HTS formation has been reported to be as frequent as 32-72% following burn injury (Lawrence et al., 2012) and up to 60% post-surgery (Mahdavian Delavary et al., 2012). In burn injuries, the severity of the trauma, time to heal, infection and prolonged inflammation beyond two weeks are considered factors contributing to the formation of HTS (Butzelaar et al., 2016; Finlay et al., 2017; Zhu et al., 2016). Prolonged inflammation may be the result of excessive nociceptor stimulation resulting in neurogenic inflammation (Akaishi et al., 2008). This process activates fibroblasts which produce collagen and when overstimulated, contribute to fibroproliferative disorders such as hypertrophic scars (Akaishi et al., 2008; Wang et al., 2008). While prolonged inflammation is a risk factor for HTS following burn injury, Butzeelaar et al. (2016) demonstrated that an inadequate early inflammatory response (three hours after wounding) correlated to surgical scars being hypertrophic 12 months after surgery. Normotrophic scars are rarely painful (<2%), however, 30-68% of abnormal scars, such as hypertrophic scars (HTS) generate high intensity pain levels (Bijlard et al., 2017). Chronic pain and itch can have a significant negative impact on quality of life of the individual, hence are a focus of many treatment interventions (Tracy et al.,

2020). An Australian and New Zealand outcomes study found that 12 months following burn injury; 13% of subjects had moderate to severe pain and 27% had itching (Tracy et al., 2020). Chronic pain and/or itch up to one-year post-burn, was associated with lower physical and mental well-being scores as measured by the SF-36 (V2) (Tracy et al., 2020). In that study, patients with moderate to severe bodily pain were less likely to have returned to work at one- and twelve-months post-burn injury compared to patients with low or no pain. In comparison, itch was not associated with any reduction in return-to-work rates, despite impacting quality of life (Tracy et al., 2020). Interventions that target scar thickness may influence itch as severity of itch increased in correlation with scar thickness when scar biopsies were analysed (Choi et al., 2013).

Physiotherapists contribute to the conservative management of scarring as part of a multidisciplinary team (Atiyeh, 2007; Monstrey et al., 2014; Zanier & Bordoni, 2015). A systematic review on conservative, non-invasive treatments for burns scars identified 22 articles with six categories of treatment including massage therapy, pressure therapy, silicone therapy, combined pressure and silicone therapy, hydration therapy and ultrasound therapy (Anthonissen et al., 2016). Massage therapy was shown to have limited evidence to support improvement in scar pliability, pain, and itch. However, due to different treatment protocols and generally low participant numbers, inconsistent results were reported between different trials. Both pressure and silicone therapy were found to provide clinically relevant improvements in scar thickness, redness, and pliability; however, there are inconclusive results regarding efficacy of combined therapy over either treatment option alone (Anthonissen et al., 2016). Hydration therapy (via creams and lotions) had contradictory findings regarding an effect on itching, and ultrasound therapy showed no meaningful effect on range of motion or scar pain (Anthonissen et al., 2016). Other studies were of insufficient quality to support other non-invasive treatments such as splinting, casting, physical activity, exercise, and mobilisations. Therefore, it was concluded that more high-quality studies are needed to further investigate the use and benefits of conservative treatment in scar management.

The investigator, during her early career, sought additional training in acupuncture and became interested in the use of acupuncture for scarring during her studies. The clinic where she worked was contacted to participate in the treatment of

an outpatient with 60% total burn surface area (TBSA) who needed ongoing physiotherapy management. Her studies required her to use a clinical example and discuss the local neurophysiological effects of acupuncture treatment for this condition. Therefore, she researched the use and application of acupuncture for scars and trialled acupuncture treatment with this patient (after gaining consent from his medical team and the patient). Acupuncture treatment was applied on the scar over the dorsum of his hand as this was affecting his ability to grip due to skin tension and pain. Over the course of several treatments, an initial increase in sensitivity and redness was observed, followed by improved pliability, and reduced height of the scar tissue. The investigator later decided to pursue a higher degree by research and continue her investigations into acupuncture needling for the treatment of pathological scars.

This project is based on acupuncture explained using a Western Medical Science framework making it novel in the literature investigating acupuncture effects. Acupuncture treatment using Western Medical reasoning, is applied based on knowledge of the neuromuscular system. Acupuncture needles are often inserted locally or within shared dermatomes or myotomes as the target tissue. This treatment paradigm will be discussed further in Chapter 1. However, many clinical trials for acupuncture operate under a Traditional Chinese Medicine (TCM) paradigm where acupuncture point location is based on meridian theories (Birch et al., 2022). Using TCM reasoning, acupuncture needles are inserted into very specific points on the skin located on meridian channels and are thought to produce specific treatment effects (Birch et al., 2022; Ots et al., 2020). This belief underpins the choice of placebo/sham treatment protocols in clinical research which do not control for shared segmental spinal nerve innervation (Langevin et al., 2006; Langevin et al., 2012). Acupuncture randomised controlled trials have suffered considerable criticism because sham and placebo acupuncture practices have produced similar outcomes to verum acupuncture (Birch et al., 2021; Ots et al., 2020). Hence acupuncture has been labelled by some, as placebo (O'Connell et al., 2009). These placebo/sham treatment protocols include needling at a short distance from the acupuncture point, shallow needle insertion over the acupuncture point or use of a non-penetrating needle or device aiming to mimic the sensation of needle insertion over the acupuncture point (Birch et al., 2021; Birch et al., 2022; Ots et al., 2020). Therefore,

sham controls have stimulated similar neural pathways as the verum treatment, often producing similar results (Birch et al., 2021; Birch et al., 2022). Recent studies (Birch et al., 2021; Ots et al., 2020) reporting on the use of sham interventions in acupuncture trials demonstrate that the difference between sham and verum treatment effect correlates with the amount of shared innervation between points used in treatment. Hence this research program was designed to investigate the use of acupuncture for treating symptomatic scars using a Western Medical framework. The application and effects of acupuncture applied in this manner will be discussed in detail in Chapter 1.

This research program comprised of investigating the mechanisms of acupuncture, how these could particularly be applied to scar management, and testing the proposed intervention protocol in a clinical trial model or context. Information from acupuncture clinical trials, mechanistic and animal studies was extracted and analysed with reference to wound healing and scar management in order to develop a theory for how acupuncture may be a beneficial treatment for symptomatic HTS (Chapter 1). A comprehensive literature review (Tuckey et al., 2019) was published on the current evidence supporting the use of acupuncture in the treatment of symptomatic scars in humans, and is presented in Chapter 2. Chapter 3 presents the clinical trial protocol that was developed from the findings of chapters one and two. After receiving ethical approval, the protocol was tested on a small sample of subjects including an inaugural pilot of the methods in one burn-injured subject, which was published as a separate case study (Tuckey et al., 2022), presented in Chapter 4. Sufficient participant numbers to complete a fully powered clinical trial were not able to be recruited in the research program timeframe due to the COVID19 pandemic and other personal events, hence the available results form a case series and are included and discussed as a feasibility trial in Chapter 5. Finally, Chapter 6 discusses the project as a whole and presents a re-developed version of the acupuncture intervention protocol for use in future research studies.

Research aims:

1. Investigate the effect of application of acupuncture on symptoms of pain and itch in Hypertrophic scars:
2. Develop and test the feasibility of a protocol for acupuncture application for symptomatic hypertrophic scars;
3. Provide a finalised treatment protocol for use in future research projects.

Objectives:

1. Perform a comprehensive literature review to inform the acupuncture treatment protocol (chapters 1-2);
2. Develop a protocol for application of acupuncture for HTS (chapter 3);
3. Determine the feasibility of the acupuncture protocol in a clinical setting (chapter 4);
4. Test the feasibility of the randomised controlled protocol in a research context (chapter 5) and;
5. Provide recommendations for future research based on the findings of this study program (chapter 6).

References

Akaishi, S., Ogawa, R., & Hyakusoku, H. (2008). Keloid and hypertrophic scar: neurogenic inflammation hypothesis. *Medical Hypotheses, 71*, 32-38. https://doi.org/10.1016/j.mehy.2008.01.032/c

Anthonissen, M., Daly, D., Janssens, T., & Van den Kerckhove, E. (2016). The effects of conservative treatments on burn scars: A systematic review. *Burns, 42*(3), 508-518. https://doi.org/10.1016/j.burns.2015.12.006

Atiyeh, B. S. (2007). Nonsurgical management of hypertrophic scars: evidence-based therapies, standard practices, and emerging methods. *Aesthetic Plastic Surgery, 31*(5), 468-492. https://doi.org/10.1007/s00266-006-0253-y

Beldon, P. (2010). Basic science of wound healing. *Surgery (Oxford), 28*(9), 409-412. https://doi.org/10.1016/j.mpsur.2010.05.007

Bijlard, E., Uiterwaal, L., Kouwenberg, C. A. E., Mureau, M. A. M., Hovius, S. E. R., & Huygen, F. J. P. M. (2017). A systematic review on the prevalence, etiology, and pathophysiology of intrinsic pain in dermal scar tissue. *Pain Physician, 20*, 1-13.

Birch, S., Lee, M. S., Kim, T.-H., & Alraek, T. (2021). Historical perspectives on using sham acupuncture in acupuncture clinical trials. *Integrative Medicine Research*. https://doi.org/10.1016/j.imr.2021.100725

Birch, S. J., Lee, M. S., Kim, T.-H., & Alraek, T. (2022). On defining acupuncture research and its techniques: a commentary on the problem of sham. *Integrative Medicine Research, 11*. https://doi.org/10.1016/j.imr.2022.100834

Bordoni, B., & Zanier, E. (2013). Skin, fascias, and scars: symptoms and systemic connections. *Journal of Multidisciplinary Healthcare, 7*, 11-24. https://doi.org/10.2147/JMDH.552870

Butzelaar, L., Schooneman, D. P. M., Soykan, E. A., Talhout, W., Ulrich, M. M. W., van den Broek, L. J., . . . Niessen, F. B. (2016). Inhibited early immunologic response is associated with hypertrophic scarring. *Experimental Dermatology*, xx1-8. https://doi.org/10.1111/exd.13100

Butzelaar, L., Ulrich, M. M., Mink van der Molen, A. B., Niessen, F. B., & Beelen, R. H. (2016). Currently known risk factors for hypertrophic skin scarring: A review. *Journal of Plastic Reconstructive and Aesthetic Surgery, 69*(2), 163-169. https://doi.org/10.1016/j.bjps.2015.11.015

Choi, Y. H., Kim, K. M., Kim, H. O., Jang, Y. C., & Kwak, I. S. (2013). Clinical and histological correlation in post-burn hypertrophic scar for pain and itching sensation. *Annals of Dermatology, 25*(4), 428-433. https://doi.org/10.5021/ad.2013.25.4.428

Clark, J. A., Cheng, J. C. Y., & Leung, K. S. (1996). Mechanical properties of normal skin and hypertrophic scars. *Burns, 22*(6), 443-446.

Clark, J. A., Leung, K. S., Cheng, J. C. Y., & Leung, P. C. (1996). The hypertrophic scar and microcirculation properties. *Burns, 6*(22), 447-450.

Finlay, V., Burrows, S., Burmaz, M., Yawary, H., Lee., J., Edgar, D. W., & Wood, F. M. (2017). Increased burn healing time is associated with higher Vancouver Scar Scale score. *Scars, Burns & Healing, 3*(1), 1-10. https://doi.org/10.1177/2059513117696

Gauglitz, G. G., Korting, H. C., Pavicic, T., Ruzicka, T., & Jeschke, M. G. (2011). Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. *Molecular Medicine, 17*(1-2), 113-125. https://doi.org/10.2119/molmed.2009.00153

Kvannli, L., Finlay, V., Edgar, D. W., Wu, A., & Wood, F. M. (2011, Feb). Using the Burn Specific Health Scale-brief as a measure of quality of life after a burn-what score should clinicians expect? *Burns, 37*(1), 54-60. https://doi.org/10.1016/j.burns.2010.07.010

Langevin, H. M., Hammerschlag, R., Lao, L., Napadow, V., Schnyder, R. N., & Sherman, K. J. (2006). Controversies in acupuncture research: selection of controls and outcome measures in acupuncture clinical trials. *Journal of Alternative and Complementary Medicine, 12*(10), 943-953. https://doi.org/10.1089/acm.2006.12.943

Langevin, H. M., Wayne, P. M., MacPherson, H., Schnyer, R., Milley, R. M., Napadow, V., Lao, L., Park, J., Harris, R. E., Cohen, M., Sherman, K .J., Haramati, A., & Hammerschlag, R. (2011). Paradoxes in acupuncture research: strategies for moving forward. *Evidence-Based Complementary and Alternative Medicine*, 2011, Article 180805. https://doi.org/10.1155/2011/180805

Lawrence, J. W., Mason, S. T., Schomer, K., & Klein, M. B. (2012). Epidemiology and impact of scarring after burn injury: a systematic review of the literature. *Journal of Burn Care and Research, 33*(1), 136-146. https://doi.org/10.1097/BCR.0b013e3182374452

Mahdavian Delavary, B., van der Veer, W. M., Ferreira, J. A., & Niessen, F. B. (2012). Formation of hypertrophic scars: evolution and susceptibility. *Journal*

of Plastic Surgery and Hand Surgery, 46(2), 95-101. https://doi.org/10.3109/2000656X.2012.669184

Monstrey, S., Middelkoop, E., Vranckx, J. J., Bassetto, F., Ziegler, U. E., Meaume, S., & Teot, L. (2014). Updated scar management practical guidelines: non-invasive and invasive measures. *Journal of Plastic Reconstructive and Aesthetic Surgery,* 67(8), 1017-1025. https://doi.org/10.1016/j.bjps.2014.04.011

Ots, T., Kandirian, A., Szilagyi, I., DiGiacomo, S. M., & Sandner-Kiesling, A. (2020). The selection of dermatomes for sham (placebo) acupuncture points is relevant for the outcome of acupuncture studies: a systematic review of sham (placebo) controlled randomized acupuncture trials. *Acupuncture in Medicine, 38*(4), 211-226. https://doi.org/10.1177/0964528419889636

Perreault, T., Flannagan, S. O., Grubb, M. T., & Grubb, R. (2018). Mechanisms and dose parameters of electric needle stimulation: clinical considerations - Part 1. *Acupuncture in Physiotherapy, 30*(2), 17-26.

Perreault, T., Grubb, M. T., Gendron, B. C., Perez-Santiago, J. C., & Flannagan, S. O. (2019). Mechanisms and dose parameters of manual needle stimulation: clinical considerations - Part 2. *Acupuncture in Physiotherapy, 31*(1), 9-23.

Tracy, L. M., Edgar, D. W., Schrale, R., Cleland, H., & Gabbe, B. J. (2020). Predictors of Itch and Pain in the 12 months following burn injury: Results from the Burns Registry of Australia and New Zealand (BRANZ) Long-term Outcomes Project. *Burns and Trauma, 8*. https://doi.org/10.1093/burnst`/tkz004

Tuckey, C., Kohut, S., & Edgar, D. W. (2019). Efficacy of acupuncture in treating scars following tissue trauma. *Scars, Burns and Healing, 5*, 1-12. https://doi.org/10.1177/2059513119831911

Tuckey, C. R., Kohut, S. H., & Edgar, D. W. (2022). Case study: Pilot testing of a local acupuncture intervention protocol for burns scars. *Scars, Burns and Healing, 8*, 1-10. https://doi.org/10.1177/20595131211058430

Wang, J., Dodd, C., Shankowsky, H. A., Scott, P. G., Tredget, E. E., & Wound Healing Research, G. (2008). Deep dermal fibroblasts contribute to hypertrophic scarring. *Laboratory Investigation, 88*(12), 1278-1290. https://doi.org/10.1038/labinvest.2008.101

Wolfram, D., Tzankov, A., Pulzl, P., & Piza-Katzer, H. (2009). Hypertrophic scars and keloids--a review of their pathophysiology, risk factors, and therapeutic management. *Dermatologic Surgery, 35*(2), 171-181. https://doi.org/10.1111/j.1524-4725.2008.34406.x

Zanier, E., & Bordoni, B. (2015). A multidisciplinary approach to scars: a narrative review. *Journal of Multidisciplinary Healthcare, 8*, 359-363. https://doi.org/10.2147/JMDH.S87845

Zhu, Z., Ding, J., & Tredget, E. E. (2016). The molecular basis of hypertrophic scars. *Burns and Trauma, 4*(1). https://doi.org/10.1186/s41038-015-0026-4

Chapter 1 - Acupuncture mechanisms and use in scar management

Confirming the physiological effects of acupuncture needle insertion and stimulation and respecting the physiology of healing and scarring processes has been a vital component of designing and implementing this research program. The author acknowledges the lack of high-quality evidence available for acupuncture mechanisms, which is primarily supported by animal and laboratory studies. A critical review of studies using acupuncture for scars in human subjects will be provided in Chapter 2. This chapter will more closely examine the healing process and how inflammation and mechanical loading contribute to scar hypertrophy. Finally, the physiological effects of acupuncture will be discussed to support its use in conservative scar management.

Clinical trials in both humans and animals use either manual acupuncture (needle is inserted and manually manipulated to elicit deqi (Perreault et al., 2019)) or Electroacupuncture (EA) (after needle insertion, continuous electrical stimulation is applied to the needle(s) controlling the amount of stimulation applied (Perreault et al., 2018)).

Use of acupuncture in the early stages post-injury has been supported by work in human burn subjects by Loskotova and Loskotova (2017). They found that applying acupuncture within 48 hours of burn injury was associated with significantly improved scar quality in a retrospective case series of 1008 patients treated with acupuncture between 1983 and 2015. The authors also compared outcomes for 198 patients (with 0.5-10% TBSA and mid-dermal burn depth) who received acupuncture and 63 who did not, finding all patients who received acupuncture within 48 hours of burn injury healed with no sign of HTS in six weeks. In comparison, 42.9% (n=27) of patients not receiving acupuncture had HTS at six weeks (Loskotova & Loskotova, 2017). Results from this study must be interpreted with caution due to the low level of evidence from retrospective case series and group data used for comparison. However, these outcomes support findings from animal studies which indicate that acupuncture may reduce pain and distress post-wounding and improve healing timeframes.

Animal studies help provide evidence for acupuncture mechanisms and place less focus on the potential treatment effect of the practitioner-patient relationship.

Many animal studies have investigated the effect of acupuncture on wound healing, finding faster wound closure in diabetic rats (Chen et al., 2021) and enhanced angiogenesis with reduced pain in burn-injured rats (Abali et al., 2015; Abali et al., 2022). Abali et al. (2022) sought to investigate the mechanisms of these findings and collected blood and tissue samples, measuring concentration of various cells and mediators including beta-endorphin (an opioid released in response to pain and stress (Abali et al., 2022)) and Interleukin-6 (IL-6)-a pro-inflammatory cytokine associated with inflammatory pain (Abali et al., 2022). Rats who received daily acupuncture had significantly lower IL-6 concentrations and did not require additional pain medication or veterinary care compared to those not receiving acupuncture (Abali et al., 2022). Humoral beta-endorphin levels were similarly low in both groups of burn-injured rats, however the opioid pain medication provided to rats not receiving acupuncture may have inhibited their endogenous opioid (beta-endorphin) release (Abali et al., 2022). Acupuncture accelerated skin regeneration in burn-injured mice (Lee et al., 2011) and increased angiogenesis to hasten wound closure in mice with punch biopsy wounds (Lee et al., 2014). Manual acupuncture increased angiogenesis and enhanced wound closure in burn-injured rats (Ishak et al., 2022). Electroacupuncture attenuated mechanical hyperalgesia in mice with inflammatory pain via down-regulating acid-sensing-ion-channel-3 (ASIC3) in the dorsal root ganglion (Chen et al., 2011). Both EA and manual acupuncture downregulated M1 macrophages and pro-inflammatory cytokines whilst upregulating M2 macrophages and anti-inflammatory cytokines (i.e., IL-10), in inflammatory pain models in mice and rats (da Silva et al., 2015; Zhao et al., 2017). Hence there is mechanistic evidence to support the effect of acupuncture in modulating the tissue and immune response in the early stages of wound healing.

Tissue response to injury – Haemostasis and inflammation

The skin is the largest organ in the body functioning as a barrier between the internal and the external environment, thereby helping to maintain homeostasis within the body (Slominski & Wortsman, 2000). Thus, restoration of structural integrity of the skin is critical and requires rapid response mechanisms in case of injury (Slominski & Wortsman, 2000). Damage to the skin leads to activation of the innate immune system which causes an immediate, robust, non-specific response via mechanisms including

the complement system of plasma and serum proteins (Dunkelberger & Song, 2010). Complement is vital in identifying and responding to invading microorganisms (i.e., bacteria) as well as in responding to tissue damage via regulating inflammatory and cytolytic immune responses (Dunkelberger & Song, 2010). Tissue healing is often divided into four overlapping stages including haemostasis, inflammation, proliferation, and remodelling (Li et al., 2007). This process is tightly regulated by various growth factors and cytokines, which when disrupted can result in prolonged healing responses such as HTS (Li et al., 2007).

Damage to blood vessels from tissue damage causes bleeding and thus via the actions of platelets, leads to clotting (haemostasis) (Li et al., 2007). The secondary action of platelets is to activate a healing cascade by attracting inflammatory cells such as neutrophils, macrophages, and mast cells to the area via release of chemotactic agents (Li et al., 2007; Marieb & Hoehn, 2016). Inflammation, as part of the overall immune response to tissue damage, helps to eliminate any pathogens introduced during wounding and prepare the area for angiogenesis and granulation tissue formation (Li et al., 2021). The inflammatory phase of healing usually lasts from 24-48 hours but may persist up to two weeks (Li et al., 2007). In acute tissue damage both immune mediated and neurogenic inflammation play a protective role in activating immune cells and facilitating wound healing (Chiu et al., 2012). Immune mediated inflammation is triggered by the release of vasoactive cytokines from platelets and mast cells that arrive in the local tissue as part of the haemostatic phase of healing (Beldon, 2010). Neurogenic inflammation occurs as part of the peripheral nervous systems response to tissue injury via activation of nociceptive nerve endings in the proximity of the wound (Akaishi et al., 2008; Chiu et al., 2012; Marieb & Hoehn, 2016).

The sensory nervous system plays an important role in both recognising and responding to tissue damage and is the target of acupuncture treatment. Sensory receptors responding to noxious stimuli (e.g., pressure, heat, pH, acupuncture needle insertion) initiate neural impulses that are transported via sensory nerves to the spinal cord and eventually to higher brain centres including the sensory cortex (Sluka, 2009). Neuropeptides including Substance P (SP), Calcitonin gene-related peptide (CGRP) and Neurokinin A (NKA) are released from the free nerve endings at the injury site and cause a local inflammatory response (neurogenic inflammation) (Brain, 1997; Brain &

Cox, 2006). These neuropeptides cause increased microvascular permeability leading to tissue edema and vasodilation, which increases local blood flow (Brain, 1997). Mast cells, platelets and other immune cells migrate to the area of tissue damage and release chemical mediators that interact with the neuropeptides and free nerve endings (Zhang et al., 2012). The immune response is tightly regulated by the central nervous system in order to prevent excessive and ongoing tissue damage, chronic inflammation and inflammatory diseases (Jin et al., 2019). The inflammatory reflex is described as an immune-regulatory vagus nerve circuit which helps bring the inflammatory phase of healing to an end via inhibition of cytokine production from inflammatory M1 macrophages (Sundman & Olofsson, 2014).

Abnormal inflammatory responses contribute to scars becoming hypertrophic. Butzelaar et al. (2016) compared normal and hypertrophic surgical scars in 120 patients undergoing elective cardiothoracic surgery. Skin biopsies taken immediately and three hours after surgery analysed mRNA, proteins and cells involved in the inflammatory phase of healing. One year post surgery scar quality was assessed and compared to analysis of the skin biopsies in 89 patients (six were deceased and 25 discontinued study involvement). For the 28% of patients (n=25) that had developed hypertrophic scars; the original three-hours post-incision skin biopsies demonstrated inflammatory proteins Interleukin-6 (IL-6), Interleukin-8 (IL-8) and Chemokine Ligand 2 (CCL2) concentrations were up to three times lower than for those who healed normally ($p<0.05$). These inflammatory proteins play important roles in the initiation of inflammation and leucocyte recruitment (Butzelaar et al., 2016). The authors postulated a delayed or insufficient early response to tissue damage may affect the overall healing process and subsequently the quality and amount of scarring that occurs.

Mechanical stimulation during healing such as tissue stretch, scratching an itch or tissue adhesions can lead to further release of neuropeptides such as SP and CGRP from mechanosensitive nociceptors (Akaishi et al., 2008; Rosa & Fantozzi, 2013). Substance P causes mast cells to degranulate and release several mediators including Adenosine Triphosphate (ATP), cytokines, growth factors (such as Neurotrophic Growth Factor (NGF)) and histamine (Rosa & Fantozzi, 2013; Widgerow & Kalaria, 2012; Zhang et al., 2008). Histamine irritates the nerve endings promoting

further release of SP and CGRP (Rosa & Fantozzi, 2013) as well as increasing tissue edema and attracting other inflammatory cells to the area (Widgerow & Kalaria, 2012). Calcitonin gene-related peptide is a potent vasodilator, but in low doses can inhibit inflammation by reduced recruitment of dermal neutrophils (Gherardini et al., 1998). The resulting altered cytokine production causes further mast cell degranulation and subsequent histamine release leading to ongoing lowered threshold nociceptive signalling due to this neural stimulation, with possible peripheral and central sensitisation of the area (Akaishi et al., 2008). Sensitised nerve endings are more responsive to mechanical and chemical stimuli which can lead to self-perpetuating local tissue inflammation (Akaishi et al., 2008). Acupuncture is also a mechanical stimulus with the ability to modulate and down-regulate the activity of pro-inflammatory mediators (Li et al., 2021; Perreault et al., 2019), hence not all mechanical stimulation is detrimental to the healing process.

Persistent inflammation beyond two weeks may lead to an imbalance of extracellular matrix (ECM) deposition and degradation, and consequently a nett increase in collagen fibre production resulting in excessive scar tissue formation (Akaishi et al., 2008; Zhu et al., 2016). Post-burn HTS tissue demonstrated histological changes when compared to normal skin in patients undergoing surgical release and skin graft of scars (Choi et al., 2013). Scar tissue epidermis was thicker with more layers than normal skin ($p<0.001$), and had thinner, yet more densely packed collagen fibres than normal skin ($p<0.05$). Hypertrophic burn scars, demonstrating pain and itch, 12 months or more since injury, were shown to have significantly higher levels ($p<0.001$) of SP and CGRP in the epidermis and dermis than normal skin (Kwak et al., 2014). Thus, neurogenic inflammation may play an important role in contributing to formation of excess scar tissue as well as symptoms such as pain and itch in hypertrophic scars (Akaishi et al., 2008). Acupuncture plays a role in regulating inflammation by modulating the expression of macrophages and pro-inflammatory cytokines and may therefore be a beneficial treatment for symptoms arising from neurogenic inflammation (Li et al., 2021).

Tissue response to injury – Proliferation and remodelling

The proliferation stage of healing is the platform for angiogenesis, re-epithelialization, and formation of granulation tissue (Cheret et al., 2013). Re-epithelialization begins early with epidermal keratinocyte migration occurring within 24 hours of wounding (Li et al., 2007). Granulation tissue fills the wound space and contains fibroblast cells which produce components of the extracellular matrix (ECM) such as type I and type III collagen fibres (Marieb & Hoehn, 2016). The fibroblasts differentiate into myofibroblasts in response to mechanical tension and growth factors as early as two-four days after wounding and contain actin and myosin which help pull the wound edges together (Gabbiani, 2003). In a normal healing response, once re-epithelialization is complete, myofibroblasts undergo apoptosis (Gabbiani, 2003; Lebonvallet et al., 2018), and fibroblast deposited type III collagen-fibres are slowly replaced by type I collagen phenotype fibres as the remodelling phase progresses (Cheret et al., 2013; Lebonvallet et al., 2018; Li et al., 2007). Substance P promotes fibroblast proliferation and inhibits apoptosis which is an important part of early wound healing and re-epithelisation (Jing et al., 2010). However, ongoing high concentrations of SP occurring during stimulation of mechanosensitive nociceptors (i.e., neurogenic inflammation) may contribute to reduced apoptosis and excessive scar tissue formation (Jing et al., 2010).

In normal skin type III collagen makes up 20% of the total collagen present but this increases to 50% during granulation tissue formation (van der Veer et al., 2009). The total amount of collagen in the healing tissue reaches maximal levels between two and three weeks following injury (for normal repair) and may take up to one year for the remodelling process to be complete (Li et al., 2007). Returning the pre-injury ratio of type I to type III collagen to normal is an important part of the remodelling phase, however, abnormal scars show increased amounts of type III collagen compared to normatrophic scars and uninjured skin (van der Veer et al., 2009). The proliferation and remodelling processes are modulated by several growth factors, including matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) (Gauglitz et al., 2011; Lebonvallet et al., 2018; Rohani & Parks, 2015). MMP's control the conversion of type III to type I collagen and are themselves regulated by TIMP's (Lebonvallet et al., 2018; Li et al., 2007). If the ratio of MMP's to TIMP's is decreased, this can result in excessive production of ECM

components such as collagen, which contributes to excessive scar tissue formation (Li et al., 2007; Ulrich et al., 2010).

As scars mature, they go through changes in sensory innervation. During normal healing, wound pain often increases in the 24 hours following tissue damage (Beldon, 2010). However, once the wound has closed and scar tissue has formed (by six weeks after wounding), pain should greatly reduce or disappear (Bijlard et al., 2017). In a mouse model it was shown that sensory nerve ingrowth for excisional cutaneous wounds had peak density of nociceptive C-fibres containing CGRP and SP between two-six weeks after wounding (Henderson et al., 2006). SP density remained at approximately twice the level of normal skin, but CGRP levels returned to normal by 12 weeks (demonstrating a mature scar) (Henderson et al., 2006). Following burn injury, sensory reinnervation in the mouse model has been shown to progress slowly (Morellini et al., 2012). In humans, depth and size of burn can affect reinnervation patterns, which can lead to scars that are hyper-innervated or have significantly reduced innervation (Morellini et al., 2012).

In summary, dysfunction in the wound healing process can lead to HTS which commonly begin to form within the first three months of wounding (Gauglitz et al., 2011; Mahdavian Delavary et al., 2012). A reduced inflammatory reaction within hours of wounding (Butzelaar et al., 2016) and prolonged (neurogenic) inflammation beyond two weeks (Akaishi et al., 2008) are two mechanisms contributing to HTS formation. Mechanical stimulation to the wound or scar (i.e., scratching an itch, stretching or acupuncture needle manipulation) activates mechanosensitive nerve endings/receptors and can negatively or positively influence neurogenic inflammation (Akaishi et al., 2008; Pavan et al., 2014; Perreault et al., 2019; Trento et al., 2021,) and may stimulate excessive collagen formation via down-regulation of cellular apoptosis (Aarabi et al., 2007). Tissue damage and resulting changes in nociceptive activity in the Dorsal Root Ganglia (DRG), thalamus, amygdala and anterior cingulate cortex can lead to central sensitisation (Lai et al., 2019). Central sensitisation refers to heightened reactivity of nociceptive afferents within the CNS (Lai et al., 2019). Chronically painful scars exhibit signs of central sensitisation such as allodynia and hyperalgesia and have increased ratios of nociceptive nerve fibres (Anderson et al., 2010; Hamed et al., 2011; Henderson et al., 2006).

The Anti-inflammatory and analgesic effects of acupuncture

Recently the term Western Medical Acupuncture has been used to describe acupuncture treatment based on the science of anatomy, physiology, and pathology (White, 2009). The anti-inflammatory actions of acupuncture contribute to pain relief via the Hypothalamus-Pituitary-Adrenal (HPA) axis, stimulation of sympathetic and parasympathetic (i.e., vagus nerve) autonomic nerve pathways and via stimulation of neuro-immune pathways in the local tissue (Dou et al., 2021; Jin et al., 2019; Lim et al., 2016; Trento et al., 2021).

Local tissue response to acupuncture

Acupuncture needle insertion causes local tissue injury and thereby stimulates a minor local inflammatory reaction (Zhang et al., 2012; Zhao, 2008). Usually, tissue damage is a controlled micro-trauma; hence the action of anti-inflammatory mediators is enhanced compared to that of pro-inflammatory mediators (Dou et al., 2021; Zhang et al., 2012). Acupuncture helps to regulate the actions of innate immune cells (i.e., macrophages, mast cells) and adaptive immune cells (i.e., lymphocytes) (Li et al., 2021). The overall effect in the local tissue is to down-regulate pro-inflammatory factors such as SP and CGRP, reduce sensitivity of peripheral nociceptors and promote the release of anti-inflammatory cytokines such as IL-10 (Dou et al., 2021; Li et al., 2021).

During acupuncture treatment, needle manipulation via rotation and/or up and down movements are performed to elicit sensation (deqi) and is considered vital to achieving acupuncture analgesia (Perreault et al., 2019). Conversion of mechanical signals into neural impulses occurs via the activation of mast cells located in the proximity of acupuncture needle insertion (Perreault et al., 2019). Acupuncture needle manipulation causes mast cell degranulation, and the release of histamine which activates afferent nerve fibres and sensitises them to respond to further stimuli (Perreault et al., 2019). In vitro studies found human mast cells released ATP in response to mechanical stress (Wang et al., 2013). Adenosine triphosphate is best known as an intracellular energy source, however once released into the extracellular space, quickly breaks down into adenosine (Burnstock, 2009; Burnstock, 2012). Adenosine has a local analgesic effect by binding to adenosine 1 receptors (Karst & Fink, 2016). Adenosine triphosphate and adenosine are key molecules involved in

purinergic signalling, the basis for intercellular communication throughout the nervous system (Burnstock, 2007). Mechanical deformation, hypoxia, heat, and electrical stimulation are now known to stimulate release of ATP from cells (keratinocytes, fibroblasts, and immune cells) without trauma or damage to cell membranes having occurred (Burnstock, 2009). Animal studies show that acupuncture stimulation leads to increased extracellular ATP (measured by interstitial fluid sampling) which breaks down to adenosine and binds to A1 receptors on sensory afferent nerve endings of Aδ and C-fibres (Goldman et al., 2010).

Langevin et al. (2001) demonstrated that needle manipulation caused a biomechanical response in the tissue via increased resistance to needle removal. They proceeded to demonstrate via in vivo ultrasonic imaging, that needle rotation causes winding of connective tissue fibres which then increases tissue displacement with up and down movement (Langevin et al., 2004). Bi-directional needle rotation was shown to stimulate fibroblast cytoskeletal remodelling in connective tissue (Langevin, et al., 2007), which was later shown to modulate the viscoelastic behaviour in connective tissue (Langevin et al., 2011). Adenosine triphosphate via purinergic signalling was shown to mediate the fibroblast activity when tissue stretch was applied (Langevin et al., 2013). Thus, acupuncture needle manipulation provides mechanical tissue stimulation, leading to ATP release which contributes to both the analgesic effect of acupuncture, and mediates fibroblast cytoskeletal remodelling (Langevin et al., 2007).

Segmental acupuncture analgesia

Segmental analgesia refers to inhibition of nociception at the segmental spinal cord level stimulated by acupuncture needle insertion and stimulation (White et al., 2008). Depending on the type, intensity and duration of needle stimulation, neuromodulators including adenosine, histamine, SP, CGRP, NO and norepinephrine are released in the acupoint region (Trento et al., 2021). Sensory nerve fibres including Aδ, Aβ and C fibres carry both excitatory (from histamine, SP, CGRP, NO and norepinephrine) and inhibitory (adenosine mediated) signals to the dorsal horn of the spinal cord (see appendix 1) (Trento et al., 2021; White et al., 2008; Zhang et al., 2012; Zhao, 2008). Via interactions with interneurons within the dorsal horn, nociceptive signals transmitted along ascending tracts (spinothalamic and spinoreticular tracts) to

the brainstem and cortex are inhibited and reduced (Bowsher, 1998; White, 1999; White et al., 2008; Zhao, 2008). Studies investigating pain relieving effects of acupuncture found that pain pressure threshold was increased following EA, within an area supplied by the same segmental nerve as the application of acupuncture treatment (Baeumler et al., 2015; Baeumler et al., 2014).

Carlsson (2002) proposed that different types of needle stimulation produce different physiological effects and therefore different outcomes. Therapeutic acupuncture for healing effects involves gentle manual or electrical stimulation whereas acupuncture for analgesia utilises high intensity manual or EA (Carlsson, 2002). Zhao reports that the sensations associated with acupuncture (heaviness, soreness – also referred to as deqi in TCM) are essential for acupuncture analgesia to occur (Zhao, 2008), which from a neurophysiological viewpoint, indicate activation of sensory nerve fibres and cortical recognition of the sensation.

Supraspinal effects of acupuncture

Additional analgesic effects of acupuncture arise from higher brain centres and provide more generalised analgesia via activation of the Periaqueductal Grey (PAG) in the midbrain (White et al., 2008). The PAG receives input from the arcuate nucleus of the hypothalamus where Aδ fibres activated by acupuncture terminate (via the spinothalamic tract), as well as the limbic system (White et al., 2008). It can have either an inhibitory or excitatory effect on nociceptive transmission in the dorsal horn, influenced by behavioural, emotional, and pathological states (Cortelli et al., 2013). Descending pathways from the PAG contribute to analgesia via release of serotonin and noradrenaline which have inhibitory actions on interneurons within the dorsal horn (White et al., 2008). Hence supraspinal mechanisms further inhibit nociceptive signal transmission at the spinal cord level and add to the analgesic effect of acupuncture.

Acupuncture for itch

The mechanisms for transmission and processing of the itch sensation continue to be poorly understood (Shah & Barik, 2022; Tang et al., 2022). Histamine is a common mediator of itch, as it is thought to activate a subset of pruritogenic C-fibres which terminate in the dorsal horn of the spinal cord (Goutos, 2013). Pruritogenic C-fibres have a slower conduction velocity, prolonged response to histamine and larger

receptive field/area of innervation than normal C-fibres (Goutos, 2013). Itch and pain impulses share ascending pathways (spinothalamic tract) and are both mediated by SP and CGRP in the periphery via the axon reflex (Goutos, 2013). A painful stimulus (i.e., scratching) can reduce itch, conversely opioid medication for pain can cause itch (Shah & Barik, 2022). Anti-histamines are commonly used for post-burn itch with reported benefits much greater in the early stages of healing, indicating that chronic itch may be more likely neuropathic in origin rather than peripherally mediatated histaminergic itch (Goutos, 2013). The neurogenic inflammation hypothesis supports this theory whereby increased afferent nerve signals from sensitised nociceptors provide increased pruriceptive input into the dorsal horn (Rosa & Fantozzi, 2013).

Although mechanisms of action are not clearly understood, it is thought that via its action on the neuroimmune system that acupuncture can inhibit the peripheral and central transmission of the itch sensation (Tang et al., 2022). A systematic literature review on acupuncture for dermatological conditions causing itch found three RCT's that met inclusion criteria (Yu et al., 2015) and provided weak evidence (as studies were under powered) to support the use of acupuncture for itch. A recent updated systematic review on acupuncture for dermatological conditions found positive results for uraemic pruritis relating to reduced histamine levels (Hwang & Lio, 2021). The same study found no benefit from prophylactic acupuncture for morphine induced post-caesarian section itch (Hwang & Lio, 2021). Dermatological conditions causing itch may have differing pruritogenic mechanisms than scar related itch and outcomes may not be reproducible in different populations.

There is limited research to support use of acupuncture in scar related pain and itch (Cuignet et al., 2015; Fang, 2014; Hunter, 2011; Song et al., 2011). However, these studies are of low quality and will be discussed further in the next chapter. Acupuncture has the potential to be a beneficial adjunct to other treatments in the management of scar tissue, especially via its proposed influence on neurally mediated symptoms such as pain and itch (Akaishi et al., 2008; Zhang et al., 2012). Acupuncture treatment has few side effects (White, 2004; Xu et al., 2013) making it relatively safe to use in many different patient populations (a register of reported adverse events as associated with acupuncture treatment in Australia is not readily available). Therefore, sufficient evidence to support treatment or establish treatment protocols for scar

symptoms has not been found. This project was designed to address this gap in the literature.

In conclusion, wound healing and consequent scar formation is a complex and tightly regulated process. There are many opportunities within this process for dysfunction to occur and lead to pathological scar formation and poor healing outcomes. Thus, the opportunity may exist to modulate the inflammatory process positively and influence tissue proliferation and remodelling via the application of acupuncture.

References

Aarabi, S., Bhatt, K. A., Shi, Y., Paterno, J., Chang, E. I., Loh, S. A., Holmes, J. W., Longaker, M. T., Yee, H., & Gurtner, G. C. (2007). Mechanical load initiates hypertrophic scar formation through decreased cellular apoptosis. *FASEB journal: official publication of the Federation of American Societies for Experimental Biology, 21*(12), 3250-3261. https://doi.org/10.1096/fj.07-8218com

Abali, A. E., Cabioglu, T., Bayraktar, N., Ozdemir, B. H., Moray, G., & Haberal, M. (2022). Efficacy of acupuncture on pain mechanisms, inflammatory responses, and wound healing in the acute phase of major burns: An experimental study on rats. *Journal of Burn Care and Research*. https://doi.org/10.1093/jbcr/irab142

Abali, A. E., Cabioglu, T., Ozdemir, H., & Haberal, M. (2015). Interactive effects of acupuncture on pain and distress in major burns: An experiment with rats. *Burns, 41*(4), 833-842. https://doi.org/10.1016/j.burns.2014.10.028

Akaishi, S., Ogawa, R., & Hyakusoku, H. (2008). Keloid and hypertrophic scar: neurogenic inflammation hypothesis. *Medical Hypotheses, 71*, 32-38. https://doi.org/10.1016/j.mehy.2008.01.032/c

Anderson, J. R., Zorbas, J. S., Phillips, J. K., Harrison, J. L., Dawson, L. F., Bolt, S. E., Rea, S. M., Klatte, J. E., Paus, R., Zhu, B., Giles, N. L., Drummond, P. D., Wood, F. M., & Fear, M. W. (2010). Systemic decreases in cutaneous

innervation after burn injury. *Journal of Investigative Dermatology, 130*(7), 1948-1951. https://doi.org/10.1038/jid.2010.47

Baeumler, P. I., Fleckenstein, J., Benedikt, F., Bader, J., & Irnich, D. (2015). Acupuncture-induced changes of pressure pain threshold are mediated by segmental inhibition-a randomized controlled trial. *Pain, 156*(11), 2245-2255. https://doi.org/10.1097/j.pain.0000000000000283

Baeumler, P. I., Fleckenstein, J., Takayama, S., Simang, M., Seki, T., & Irnich, D. (2014). Effects of acupuncture on sensory perception: A systematic review and meta-analysis. *PLOS ONE, 9*(12). https://doi.org/10.1371/journal.pone.0113731

Beldon, P. (2010). Basic science of wound healing. *Surgery (Oxford), 28*(9), 409-412. https://doi.org/10.1016/j.mpsur.2010.05.007

Bijlard, E., Uiterwaal, L., Kouwenberg, C. A. E., Mureau, M. A. M., Hovius, S. E. R., & Huygen, F. J. P. M. (2017). A systematic review on the prevalence, etiology, and pathophysiology of intrinsic pain in dermal scar tissue. *Pain Physician, 20*, 1-13.

Bowsher, D. (1998). Mechanisms of Acupuncture. In J. Filshie & A. White (Eds.), *Medical Acupuncture: A Western Scientific Approach* (pp. 69-82). Churchill Livingstone.

Brain, S. D. (1997). Sensory neuropeptides: their role in inflammation and wound healing. *Immunopharmacology, 37*(2-3), 133-152.

Brain, S. D., & Cox, H. M. (2006). Neuropeptides and their receptors: innovative science providing novel therapeutic targets. *British Journal of Pharmacology, 147 Suppl 1*, S202-211. https://doi.org/10.1038/sj.bjp.0706461

Burnstock, G. (2007). Physiology and pathophysiology of purinergic neurotransmission. *Physiological Reviews, 87*(2), 659-797. https://doi.org/10.1152/physrev.00043.2006

Burnstock, G. (2009). Acupuncture: a novel hypothesis for the involvement of purinergic signalling. *Medical Hypotheses, 73*(4), 470-472. https://doi.org/10.1016/j.mehy.2009.05.031

Burnstock, G. (2012). Discovery of purinergic signalling, the initial resistance and current explosion of interest. *British Journal of Pharmacology, 167*, 238-255. https://doi.org/10.1111/j.1476-5381.2012.02008.x

Butzelaar, L., Schooneman, D. P. M., Soykan, E. A., Talhout, W., Ulrich, M. M. W., van den Broek, L. J., Gibbs, S., Beelen, R. H. J., Mink van der Molen, A. B., & Niessen, F. B. (2016). Inhibited early immunologic response is associated with hypertrophic scarring. *Experimental Dermatology*, xx1-8. https://doi.org/10.1111/exd.13100

Carlsson, C. (2002). Acupuncture mechanisms for clinically relevant long-term effects -- reconsideration and a hypothesis. *Acupuncture in Medicine, 20*(2-3), 82-99.

Chen, W., Hsieh, C., Huang, C., Lin, T., Tzen, J., Ho, T., & Lin, Y. (2011). Acid-sensing ion channel 3 mediates peripheral anti-hyperalgesia effects of acupuncture in mice inflammatory pain. *Journal of Biomedical Science, 18*, 82-82. https://doi.org/10.1186/1423-0127-18-82

Chen, T. Y., Wen, T. K., & Dai, N. T. (2021). Cryogel/hydrogel biomaterials and acupuncture combined to promote diabetic skin wound healing through immunomodulation. *Biomaterials, 269*, Article 120608. https://doi.org/10.1016/j.biomaterials.2020.120608

Cheret, J., Lebonvallet, N., Carre, J., Misery, L., & Le Gall-Ianotto, C. (2013). Role of neuropeptides, neurotrophins, and neurohormones in skin wound healing. *Wound Repair and Regeneration, 21*, 772-788. https://doi.org/10.1111/wrr.12101

Chiu, I. M., Von Hehn, C. A., & Woolf, C. J. (2012). Neurogenic inflammation and the peripheral nervous system in host defense and immunopathology. *Nature Neuroscience, 15*(8), 1063-1067. https://doi.org/10.1038/nn.3144

Choi, Y. H., Kim, K. M., Kim, H. O., Jang, Y. C., & Kwak, I. S. (2013). Clinical and histological correlation in post-burn hypertrophic scar for pain and itching sensation. *Annals of Dermatology, 25*(4), 428-433. https://doi.org/10.5021/ad.2013.25.4.428

Cortelli, P., Giannini, G., Favoni, V., Cevoli, S., & Pierangeli, G. (2013). Nociception and autonomic nervous system. *Neurological Sciences, 34*, S41-S46. https://doi.org/10.1007/s10072-013-1391-z

Cuignet, O., Pirlot, A., Ortiz, S., & Rose, T. (2015). The effects of electroacupuncture on analgesia and peripheral sensory thresholds in patients with burn scar pain. *Burns, 41*(6), 1298-1305. https://doi.org/10.1016/j.burns.2015.03.002

da Silva, M. D., Bobinski, F., Sato, K. L., Kolker, S. J., Sluka, K. A., & Santos, A. R. S. (2015). IL-10 cytokine released from M2 macrophages is crucial for analgesic and anti-inflammatory effects of acupuncture in a model of inflammatory muscle pain. *Molecular Neurobiology, 51*(1), 19-31. https://doi.org/10.1007/s12035-014-8790-x

Dou, B., Yanan, L., Ma, J., Xu, Z., Fan, W., Tian, L., Chen, Z., Li, N., Gong, Y., Lyu, Z., Fang, Y., Liu, Y., Xu, Y., Wang, S., Chen, B., Guo, Y., Guo, Y., & Lin, X. (2021). Role of neuroimmune crosstalk in mediating the anti-inflammatory and analgesic effects of acupuncture on inflammatory pain. *Frontiers in Neuroscience, 15.695670*. https://doi.org/10.3389/fnins.2021.695670

Dunkelberger, J. R., & Song, W. C. (2010). Complement and its role in innate and adaptive immune responses. *Cell Research, 20*, 34-50. https://doi.org/10.1038/cr.2009.139

Fang, S. (2014). The successful treatment of pain associated with scar tissue using acupuncture. *Journal of Acupuncture and Meridian Studies, 7*(5), 262-264. https://doi.org/10.1016/j.jams.2014.05.001

Gabbiani, G. (2003). The myofibroblast in wound healing and fibrocontractive diseases. *The Journal of Pathology, 200*(4), 500-503. https://doi.org/10.1002/path.1427

Gauglitz, G. G., Korting, H. C., Pavicic, T., Ruzicka, T., & Jeschke, M. G. (2011). Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. *Molecular Medicine, 17*(1-2), 113-125. https://doi.org/10.2119/molmed.2009.00153

Gherardini, G., Gurlek, A., Milner, S. M., Matarasso, A., Evans, G. R. D., Jernbeck, J., & Lundeberg, T. (1998). Calcitonin gene-related peptide improves skin flap survival and tissue inflammation. *Neuropeptides 32*(3), 269-273.

Goldman, N., Chen, M., Fujita, T., Xu, Q., Peng, W., Liu, W., Jensen, T. K., Pei, Y., Wang, F., Han, X., Chen, J. -F., Schnermann, J., Takano, T., Bekar, L., Tieu, K., & Nedergaard, M. (2010). Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture. *Nature Neuroscience, 13*(7), 883-889. https://doi.org/10.1038/nn.2562

Goutos, I. (2013). Neuropathic mechanisms in the pathophysiology of burns pruritus: redefining directions for therapy and research. *Journal of Burn Care and Research, 34*(1), 82-93. https://doi.org/10.1097/BCR.0b013e3182644c44

Hamed, K., Giles, N., Anderson, J., Phillips, J. K., Dawson, L. F., Drummond, P., Wallace, H., Wood, F. M., Rea, S. M., & Fear, M. W. (2011). Changes in cutaneous innervation in patients with chronic pain after burns. *Burns, 37*, 631-637. https://doi.org/10.1016/j.burns.2010.11.010

Henderson, J., Terenghi, G., McGrouther, D. A., & Ferguson, M. W. J. (2006). The reinnervation pattern of wounds and scars may explain their sensory symptoms. *Journal of Plastic, Reconstructive & Aesthetic Surgery, 59*, 942-950. https://doi.org/10.1016/j.bjps.2005.11.038

Hunter, J. (2011). Acupuncture for keloid scar. *Acupuncture in Medicine, 29*(2). https://doi.org/10.1136/aim.2011.010011

Hwang, J., & Lio, P. A. (2021). Acupuncture in Dermatology: An Update to a Systematic Review. *Journal of Alternative and Complementary Medicine, 27*(1), 12-23. https://doi.org/10.1089/acm.2020.0230

Ishak, A., Jusuf, A. A., Simadibrata C.L., Barasila, A. C., & Novita, R. (2022). Effect of manual acupuncture and laser acupuncture on wound closure in rat with deep partial thickness burn injury. *Medical Acupuncture, 0*(0), 1-10. https://doi.org/10.1089/acu.2021.0083

Jin, B. X., Jin, L. L., & Jin, G.-Y. (2019). The anti-inflammatory effect of acupuncture and its significance in analgesia. *World Journal of Acupuncture - Moxibustion, 29*(1), 1-6. https://doi.org/10.1016/j.wjam.2019.03.003

Jing, C., Jia-Han, W., & Hong-Xing, Z. (2010). Double-edged effects of neuropeptide substance P on repair of cutaneous trauma. *Wound Repair and Regeneration, 18*, 319-324. https://doi.org/10.1111/j.1524-475X.2010.00589.x

Karst, M., & Fink, M. (2016). Acupuncture—A Biomedical Information Therapy: A Translational Analysis. *Medical Acupuncture, 28*(6), 308-315. https://doi.org/10.1089/acu.2016.1196

Kwak, I. S., Choi, Y. H., Jang, Y. C., & Lee, Y. K. (2014). Immunohistochemical analysis of neuropeptides (protein gene product 9.5, substance P and calcitonin gene-related peptide) in hypertrophic burn scar with pain and itching. *Burns, 40*(8), 1661-1667. https://doi.org/10.1016/j.burns.2014.04.004

Lai, H. C., Lin, Y. W., & Hsieh, C. L. (2019). Acupuncture-Analgesia-Mediated Alleviation of Central Sensitization. *Evidence-Based Complementary and Alternative Medicine, 2019*, Article 6173412. https://doi.org/10.1155/2019/6173412

Langevin, H. M., Bouffard, N. A., Churchill, D. L., & Badger, G. J. (2007). Connective tissue fibroblast response to acupuncture: Dose dependant effect of bidirectional needle rotation *The Journal of Alternative and Complementary Medicine, 13*(3), 355-360. https://doi.org/10.1089/acm.2007.6351

Langevin, H. M., Bouffard, N. A., Fox, J. R., Palmer, B. M., Wu, J., Iatridis, J. C., Barnes, W. D., Badger, G. J., & Howe, A. K. (2011). Fibroblast cytoskeletal remodeling contributes to connective tissue tension. *Journal Of Cellular Physiology, 226*(5), 1166-1175. https://doi.org/10.1002/jcp.22442

Langevin, H. M., Churchill, D. L., Fox, J. R., Badger, G. J., Garra, B. S., & Krag, M. H. (2001). Biomechanical response to acupuncture needling in humans. *Journal of Applied Physiology, 91*(6), 2471-2478.

Langevin, H. M., Fujita, T., Bouffard, N. A., Takano, T., Koptiuch, C., Badger, G. J., & Nedergaard, M. (2013). Fibroblast cytoskeletal remodeling induced by tissue stretch involves ATP signaling. *Journal Of Cellular Physiology, 228*(9), 1922-1926. https://doi.org/10.1002/jcp.24356

Langevin, H. M., Konofagou, E. E., Badger, G. J., Churchill, D. L., Fox, J. R., Ophir, J., & Garra, B. S. (2004). Tissue displacements during acupuncture using ultrasound elastography techniques. *Ultrasound In Medicine and Biology, 30*(9), 1173-1183.

Lebonvallet, N., Laverdet, B., Misery, L., Desmouliere, A., & Girad, D. (2018). New insights into the roles of myofibroblasts and innervation during skin healing and innovative therapies to improve scar innervation. *Experimental Dermatology, 27*, 950-958. https://doi.org/10.1111/exd.13681

Lee, J., Park, J., Min, S., Chae, Y., Lee, H., Lim, Y., & Park, H. (2014). Wound healing effect of acupuncture through activating angiogenesis in mice. *Oriental Pharmacy and Experimental Medicine, 14*(2), 93-101. https://doi.org/10.1007/s13596-014-0146-6

Lee, J. A., Jeong, H. J., Park, H. J., Jeon, S., & Hong, S. U. (2011). Acupuncture accelerates wound healing in burn-injured mice. *Burns 37*, 117-125. https://doi.org/10.1016/j.burns.2010.07.005

Li, J., Chen, J., & Kirsner, R. (2007). Pathophysiology of acute wound healing. *Clinics in Dermatology, 25*, 9-18. https://doi.org/10.1016/j.clindermatol.2006.09.007

Li, N., Guo, Y., Gong, Y., Zhang, Y., Fan, W., Yao, K., Chen, Z., Dou, B., Lin, X., Chen, B., Chen, Z., Xu, Z., & Lyu, Z. (2021). The anti-inflammatory actions and mechanisms of acupuncture from acupoint to target organs via neuro-

immune regulation. *Journal of Inflammation Research, 14*, 7191-7224. https://doi.org/10.2147/JIR.S341581

Lim, H., Kim, M., Lee, C., & Namgung, U. (2016). Anti-Inflammatory Effects of Acupuncture Stimulation via the Vagus Nerve. *PLOS ONE, 11*(3), Article e0151882-e0151882. https://doi.org/10.1371/journal.pone.0151882

Loskotova, A., & Loskotova, J. (2017). The use of acupuncture in first aid of burns-Clinical report. *Burns, 43*(8), 1782-1791. https://doi.org/10.1016/j.burns.2017.04.025

Mahdavian Delavary, B., van der Veer, W. M., Ferreira, J. A., & Niessen, F. B. (2012). Formation of hypertrophic scars: evolution and susceptibility. *Journal of Plastic Surgery and Hand Surgery, 46*(2), 95-101. https://doi.org/10.3109/2000656X.2012.669184

Marieb, E. N., & Hoehn, K. (2016). *Human Anatomy and Physiology* (10 ed.). Pearson.

Morellini, N. M., Fear, M. W., Rea, S. M., West, A. K., Wood, F. M., & Dunlop, S. A. (2012). Burn injury has a systemic effect on reinnervation of skin and restoration of nociceptive function. *Wound Repair and Regeneration, 20*(3), 367-377. https://doi.org/10.1111/j.1524-475X.2012.00787.x

Pavan, P. G., Stecco, A., Stern, R., & Stecco, C. (2014). Painful connections: densification versus fibrosis of fascia. *Current Pain and Headache Reports, 18*(8), 441. https://doi.org/10.1007/s11916-014-0441-4

Perreault, T., Grubb, M. T., Gendron, B. C., Perez-Santiago, J. C., & Flannagan, S. O. (2019). Mechanisms and dose parameters of manual needle stimulation: clinical considerations - Part 2. *Acupuncture in Physiotherapy, 31*(1), 9-23.

Rohani, M. G., & Parks, W. C. (2015). Matrix remodeling by MMPs during wound repair. *Matrix Biology, 44-46*, 113-121. https://doi.org/10.1016/j.matbio.2015.03.002

Rosa, A. C., & Fantozzi, R. (2013). The role of histamine in neurogenic inflammation. *British Journal of Pharmacology, 170*(1), 38-45. https://doi.org/10.1111/bph.12266

Shah, D. P., & Barik, A. (2022). The Spino-parabrachial pathway for itch. *Frontiers in Neural Circuits, 16,* Article 805831. https://doi.org/10.3389/fncir.2022.805831

Slominski, A. T., & Wortsman, J. (2000). Neuroendocrinology of the skin. *Endocrine reviews, 21*(5), 457-487.

Sluka, K. A. (2009). Peripheral mechanisms involved in pain processing. In K. A. Sluka (Ed.), *Mechanisms and management of pain for the physical therapist* (pp. 19-40). IASP Press.

Song, H., Jingping, M., & Jun, W. (2011). Clinical study on treatment of hypertrophic scar by acupuncture. *Journal of Acupuncture and Tuina Science, 9*(3), 159-161. https://doi.org/10.1007/s11726-011-0499-z

Sundman, E., & Olofsson, P. S. (2014). Neural control of the immune system. *Advances in Physiology Education, 38*, 135-139. https://doi.org/10.1152/advan.00094.2013

Tang, Y., Cheng, S., Wang, J., Jin, Y., Yang, H., Lin, Q., Xu, S., Hui, L., Yin, Q., Yang, Y., & Wu, X. (2022). Acupuncture for the treatment of itch: Peripheral and central mechanisms. *Frontiers in Neuroscience, 15,* Article 786892. https://doi.org/10.3389/fnins.2021.786892

Trento, M. M. S., More, A. O. O., Duarte, E. C. W., & Martins, D. F. (2021). Peripheral receptors and neuromediators involved in the antihyperalgesic effects of acupuncture: a state-of-the-art review. *Pflugers Archiv, 473*(4), 573-593. https://doi.org/10.1007/s00424-020-02503-0

Ulrich, D., Ulrich, F., Unglaub, F., Piatkowski, A., & Pallua, N. (2010). Matrix metalloproteinases and tissue inhibitors of metalloproteinases in patients with different types of scars and keloids. *Journal of Plastic Reconstructive and Aesthetic Surgery, 63*(6), 1015-1021. https://doi.org/10.1016/j.bjps.2009.04.021

van der Veer, W. M., Bloemen, M. C., Ulrich, M. M., Molema, G., van Zuijlen, P. P., Middelkoop, E., & Niessen, F. B. (2009). Potential cellular and molecular causes of hypertrophic scar formation. *Burns, 35*(1), 15-29. https://doi.org/10.1016/j.burns.2008.06.020

Wang, L., Sikora, J., Hu, L., Shen, X., Grygorczyk, R., & Schwarz, W. (2013). ATP release from mast cells by physical stimulation: a putative early step in activation of acupuncture points. *Evidence-Based Complementary And Alternative Medicine, 2013*, 350949-350949. https://doi.org/10.1155/2013/350949

White, A. (1999). Neurophysiology of acupuncture analgesia. In E. Ernst & A. White (Eds.), *Acupuncture: A scientific appraisal* (pp. 64-75). Butterworth-Heinemann.

White, A. (2004). A cummulative review of the range and incidence of significant adverse events associated with acupuncture. *Acupuncture in Medicine, 22*(3), 122-133.

White, A., Cummings, T. M., & Filshie, J. (2008). *An introduction to western medical acupuncture*. Churchill Livingstone.

White, A. (2009). Western Medical Acupuncture: a definition. *Acupuncture in Medicine, 27*(1), 33-35. https://doi.org/10.113B/aim,2006,000372

Widgerow, A. D., & Kalaria, S. (2012). Pain mediators and wound healing - Establishing the connection. *Burns, 38*, 951-959. https://doi.org/10.1016/j.burns.2012.05.024

Xu, S., Wang, L., Cooper, E., Zhang, M., Manheimer, E., Berman, B. M., Shen, X., & Lao, L. (2013). Adverse events of acupuncture: A systematic review of case reports. *Evidence-Based Complementary and Alternative Medicine, 2013*. https://doi.org/10.1155/2013/581203

Yu, C., Zhang, P., Lv, Z.-T., Li, J.-J., Li, H.-P., Wu, C.-H., Gao, F., Yuan, X.-C., Zhang, J., He, W., Jing, X.-H., & Li, M. (2015). Efficacy of Acupuncture in Itch: A Systematic Review and Meta-Analysis of Clinical Randomized Controlled

Trials. *Evidence-Based Complementary and Alternative Medicine, 2015*, 208690-208690. https://doi.org/10.1155/2015/208690

Zhang, D., Ding, G., Shen, X., Yao, W., Zhang, Z., Zhang, Y., . . . Gu, Q. (2008). Role of mast cells in acupuncture effect: a pilot study. *Explore (NY), 4*(3), 170-177. https://doi.org/10.1016/j.explore.2008.02.002

Zhang, Z. J., Wang, X. M., & McAlonan, G. M. (2012). Neural acupuncture unit: a new concept for interpreting effects and mechanisms of acupuncture. *Evidence-Based Complementary and Alternative Medicine, 2012*, 429412. https://doi.org/10.1155/2012/429412

Zhao, J., Wang, L., & Li, Y. (2017). Electroacupuncture alleviates the inflammatory response via effects on M1 and M2 macrophages after spinal cord injury. *Acupuncture in Medicine, 35*(3), 224-230. https://doi.org/10.1136/acupmed-2016-011107

Zhao, Z. Q. (2008). Neural mechanism underlying acupuncture analgesia. *Progress in Neurobiology, 85*, 355-375. https://doi.org/10.1016/j.pneurobio.2008.05.004

Zhu, Z., Ding, J., & Tredget, E. E. (2016). The molecular basis of hypertrophic scars. *Burns & Trauma, 4*(1). https://doi.org/10.1186/s41038-015-0026-4

Chapter 2 – Literature Review

This chapter presents a peer-reviewed, published systematic/comprehensive literature review on the current evidence to support the use of acupuncture/dry needling in the treatment of symptomatic scars. This review entitled “Efficacy of acupuncture in treating scars following tissue trauma” is included as published in 2019 (using Vancouver referencing as per journal requirements). Some text from the original article submission was omitted following the peer review process, to reduce word count and present findings in line with journal requirements.

Tuckey, C., Kohut, S., & Edgar, D. W. (2019). Efficacy of acupuncture in treating scars following tissue trauma. *Scars, Burns and Healing, 5*, 1-12. https://doi.org/10.1177/2059513119831911

Introduction

Acupuncture is the therapeutic insertion of fine needles into the body (1). It originated as one component of traditional Chinese Medicine (TCM), based on the vitalistic paradigm of qi (metaphysical vital energy force) (2, 3). Orthodox, medical use of acupuncture backdates to the early 1800’s (1, 3, 4). Subsequently Western health practitioners have adapted acupuncture into a conventional biomedical practice based on anatomy, neuroscience, pathology, and evidence-based medicine, rather than the Chinese qi-based paradigm (1, 5).

Empirically, acupuncture has been utilised for centuries to treat skin conditions including scars (6-8). Scar tissue is theorised to have the capacity to obstruct the circulation of qi and xue (nourishing of blood), with scar tissue demonstrating characteristics of stagnation of xue (6-8). In biomedical terms, scar tissue may cause adhesions between layers of skin and connective tissue (fascia) resulting in poor circulation around the scar and adjacent areas (9). Filshie & White (10) noted in 1998 that there was a scarcity of publications evaluating acupuncture treatment of scars. The first publication discussing acupuncture treatment of scars appeared in 1982 (11). Subsequently a limited number of case studies and controlled trials were published demonstrating the use of acupuncture for treating scars. However, a systematic review

of published scar and acupuncture-related material has not been undertaken until now. This systematic review reports on the low levels of methodological rigour, paucity of reporting of demographics, treatments, and other related details in the scar-related acupuncture literature. These issues align with early acupuncture research where the trials were poorly designed, executed and reported, despite reporting promising treatment outcomes (12, 13). Therefore, because of publication and methodological limitations, the findings of this critical appraisal do not support the efficacy of acupuncture in the treatment of scars. However, because empirical and clinical experience continue to suggest acupuncture is efficacious in the treatment of scars, this review will discuss current management, as well as acupuncture treatment recommendations for future acupuncture research of abnormal scars.

Normal skin healing processes in humans other than neonates, leaves a flattened scar that fades as it matures. However, abnormal, or prolonged healing responses can lead to the formation of abnormal scars such as hypertrophic scars (HTS) and keloid scars (14). Factors in burn injuries contributing to the formation of HTS include the severity of the trauma, time to heal, infection and inflammation prolonged beyond two weeks (15, 16). A reduced early inflammatory response demonstrated by low concentrations of inflammatory proteins at three hours after wounding, could be a factor in surgical scars becoming hypertrophic (17). In the first six months after tissue injury HTS rapidly develop and are often raised, red, itchy, and painful. They may take several years to reach maturity which is accompanied by progressive reduction of adverse symptoms (14, 16).

During wound healing, increased nerve density in and around the scar is normal in the first few weeks of healing. This gradually decreases to equal or lower than that of uninjured skin during scar maturation (18). However, chronically painful scars have been shown to have a higher density of nociceptive fibres than non-painful scars (19). The same authors described a correlation between increasing scar thickness and intensity of itch sensation ($p<0.05$), but there was no evidence that scar pain was associated in the same way in post-burn HTS (20). Itch is mediated by low level C-nociceptor stimulation for which high levels of stimulation result in pain (21). During movement a thicker scar may be more likely to activate mechanosensitive ergoreceptors due to pressure and stretch yet remain sub-threshold for pain.

Mechanical stimulation of sensory receptors induces neuropeptide release that further stimulates chemically sensitive nociceptors and leads to neurogenic inflammation of the scar tissue, disrupting and prolonging the healing process (22). Therefore, increased scar thickness, reduced pliability and greater density of nociceptors can be associated with abnormal tissue healing resulting in symptomatic, slow maturing scars (18, 23).

Current Treatments for HTS

Clinical evidence in the treatment of HTS has been driven by clinical experience, rather than gold standards or guidelines underpinned by research evidence (24). Current conservative scar treatment modalities such as pressure garments, silicone, topical ointments or gels and massage show positive effects on scar redness, thickness, and pliability. However, their ability to influence pain and itch is limited (25-31). Lu (26) reported that pressure garments are thought to control excess collagen synthesis by limiting supply of blood, oxygen, and nutrients to the scar. Moreover, by speeding up the maturation process and encouraging realignment of collagen bundles, scar thickness and colour are closer to that of normal skin. Silicone is believed to improve skin hydration and reduce overactivity of fibroblast cells associated with excess collagen formation (25, 30). Hence it may reduce scar thickness and improve elasticity. Combining pressure therapy with silicone gel sheeting produced the greatest reduction in scar thickness compared to either therapy applied alone (31). Potential effects of massage include mechanical disruption of scar tissue leading to improved pliability (25). The evidence in support of their long-term efficacy is lacking (28). Sidgwick et al (28) further comment on an unmet need of effective treatments for scar factors, such as inflammation and pruritis, that affect patients the most.

Medical management of HTS may include surgical excision, autologous fat grafting, percutaneous collagen induction (PCI), intralesional corticosteroid/other product (i.e., PRP) injections, radiotherapy, ablative and colour laser therapies, and antihistamine drugs (27, 32-37). Both PCI and fat grafting are invasive techniques performed under surgical conditions on large surface area, mature scars. PCI, also called medical needling has shown promising results in human and animal models (32, 38). The technique involves using a medical roller containing small needles to repetitively pierce the scar to the level of the dermis, while the skin is anaesthetised, promoting a healing

response. Such damage is thought to stimulate collagen fibre remodelling, resulting in reduced scar thickness and improved appearance of scarred skin (38). Acupuncture is similarly an invasive technique, however because it is specifically targeted treatment using fine gauge needles and a low number of needle insertions, it causes far less local tissue damage than the techniques listed above. Side effects such as pain, bruising, bleeding, and swelling are lesser with acupuncture treatment making it more tolerable and less expensive for the patient than other options.

Abbate (39) recommended inserting acupuncture needles into tender points around the scar and retaining them for 5-10 minutes to mechanically break up obstructions and re-establish energy pathways. In this context, acupuncture is applied in a manner theorised to access and modulate the flow of qi in meridian channels, to influence the spiritual and physical health and well-being of the individual (40). TCM practitioners believe that scars 'block' or alter qi flow along meridian channels, causing a systemic energy imbalance leading to dysfunction elsewhere in the body (11, 39). Hence by this reasoning, treatment for other conditions may be ineffective if the 'blockage' caused by the scar is not addressed (11, 39). An example of the TCM practitioner belief of scars leading to dysfunctions elsewhere in the body can be seen in a series of case reports published in 1982 by Rogers (11). Patients who had abdominal scars were treated for back pain, fatigue, weight gain, deafness, and headaches. Rogers reported that acupuncture treatment aimed at the scar as well as the presenting problem not only reduced sensitivity and abnormal colouring of scars, but in all except one case of deafness, the presenting problem was resolved or greatly improved following treatment.

Bradnam (41) discussed treatment of scars from a western medical perspective recommending local application of needles around the scar to stimulate sensory neuropeptide release and activate segmental inhibitory analgesic mechanisms. Another proposed local mechanism of effect is that of mechanotransduction. Manual acupuncture needle rotation within the connective tissue planes causes winding or local stretching of collagen fibres around the needle, generating mechanical signals (42-48). Potential effects include synthesis and release of growth factors, cytokines, enzymes, and structural components of the extracellular matrix (47). A survey of physiotherapists in New Zealand found that 70-75% of respondents used acupuncture

for treating scars (Luty, A., 2000 cited in Bradnam, 2001) (41). Physiotherapists who used acupuncture (applied in a Western medical context) to treat scars aimed to influence the scar itself, improving tissue pliability and to reduce symptoms such as pain and itch (41).

Studies on acupuncture for itch demonstrate that acupuncture applied locally to the itch or in the same neural segment (dermatome or myotome) reduced itch (49-51). Correspondingly, distant needle placement had minimal effect in both humans and animals (assessed by scratch responses). Local and segmental acupuncture stimulation will provide sensory input into the same segmental spinal nerves as the itch sensation (52, 53). Therefore, acupuncture may modulate signals at the level of the dorsal horn reducing intensity of noxious signals being sent to the central nervous system for processing (53).

Itch, induced in human skin via intradermal histamine injection, was reduced through the application of manual acupuncture (MA), and high frequency (80Hz) and low frequency (2Hz) electroacupuncture (EA) (the application of measured electrical current to acupuncture needles (49). Both MA and EA were applied either directly over the area of itch or proximally in the affected dermatome. Treatment applied outside of the affected dermatome demonstrated no significant effect on symptoms. This suggests that needle location plays an important role in itch reduction (49).

A reduction in scratch response in rats following serotonin induced itch was also shown following acupuncture treatment (50). It was demonstrated that acupuncture into the same or adjacent dermatome was more effective than stimulation elsewhere. High frequency EA (HFEA) and MA were both more effective than low frequency EA (LFEA), however HFEA was more effective than MA at reducing scratching responses.

Literature searches suggest that acupuncture may be used to reduce pain and itch in abnormal scars (54-56). Further, physical properties of scars including thickness and colour were reportedly improved following acupuncture treatment (11, 55). The aim of this review is to evaluate the current evidence for acupuncture treatment of HTS and recommend future possibilities for research for abnormal scars.

Methodology

The objective was to identify whether local acupuncture treatment is effective at reducing symptoms of abnormal scars such as pain and itch. The search strategy was based on guidelines from the Joanna Briggs Institute (JBI), aiming to find both published and unpublished studies.

An initial search on MEDLINE and CINAHL was undertaken using the following keywords:

Acupuncture OR dry needling OR needling AND

Scar OR cicatrix OR healing OR inflammation OR pruritus OR neurogenic

Text used in the title, abstract and keywords were analysed to assess whether search terms were sufficient. No further search terms were added after this initial search. The keyword ‘healing’ confounded the search and was removed from the list. The revised search terms were used across the following databases:

EBSCO Health databases, including: CINAHL, Medline, SportDiscus, Dentistry & Oral Sciences; Web of Science, Cochrane, Scopus, AMED, and PEDro.

Reference lists of all included articles were searched for further references, as were grey literature databases, relevant acupuncture textbooks and finally Google Scholar to ensure all available studies were identified. Clinical trials, mechanistic studies and case studies were included. Opinion articles and reviews were excluded, although searched for relevant references.

Studies published prior to February 2018 were considered for inclusion in this review. Non-English studies, with abstracts published in English, were translated and screened for inclusion. Inclusion criteria stipulated inclusion of human subjects with hypertrophic or abnormal scars treated by acupuncture interventions. This encompassed use of a filiform acupuncture needle and could be of the following modalities: acupuncture or dry needling. Following initial searching the following modalities were included: electroacupuncture and indwelling needle use. Interventions specifically excluded were bee venom acupuncture, dermarolling or PCI, moxibustion, cupping, cat gut embedding, plum blossom needling, scar injection needling,

prolotherapy and non-skin penetrating acupuncture e.g. laser acupuncture and acupressure.

Abstracts were obtained for articles that met the inclusion criteria and checked before obtaining full text copies. Screening was performed by two researchers CT and SK. Any discrepancies were resolved through discussion with a third researcher DE.

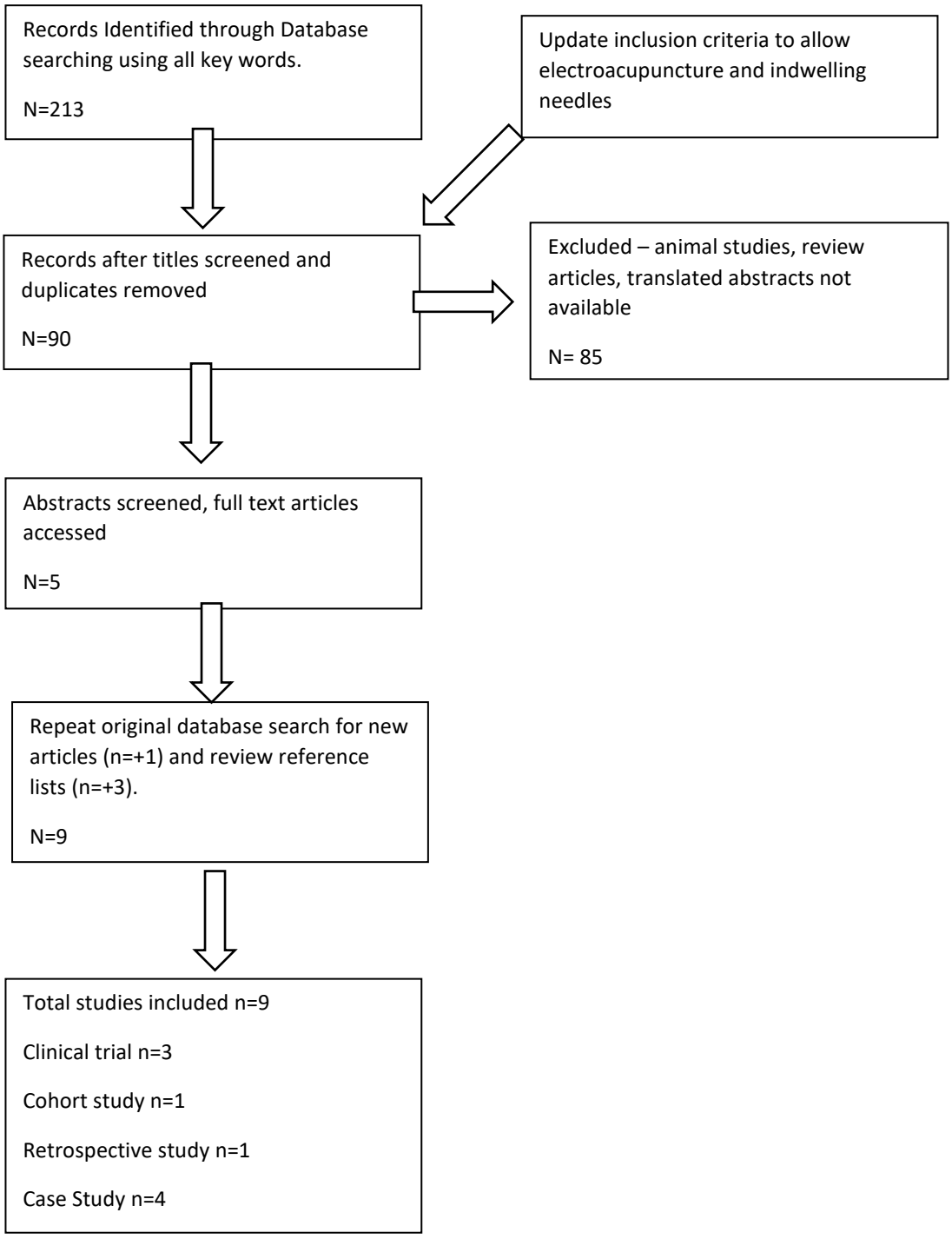
1. Data Analysis

The Oregon CONSORT STRICTA Instrument (OCSI); a tool combining CONSORT (57) and STRICTA (58) was used to rate study quality of randomised controlled trials in this review (13). The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for case reports (59) was applied to review and assess quality of case studies reporting on acupuncture treatment of scars. Studies were reviewed by CT and SK. Any disagreement was resolved by DE. Treatment data and protocol details were extracted by CT.

2. Results

Initial literature searching retrieved 213 citations. However, only one clinical trial and two case studies were found that met inclusion criteria, demonstrating a paucity of studies in this area of research. Hand searches revealed two further studies; one that used a combination of electroacupuncture and manual acupuncture, the other indwelling needles. As these are commonly used acupuncture modalities that elicit similar neuropeptide changes as manual acupuncture (60), therefore it was decided to expand the search to allow for both electroacupuncture and indwelling or intradermal needle use. Further relevant texts were not located. Review of reference lists of these articles found another two further case studies and one clinical trial (which was translated from Mandarin, prior to review by SK). Repetition of the search later identified one further retrospective study that had been published since the previous search was undertaken.

Figure 1. Results of literature review



None of the clinical trials reviewed scored above than 50% for methodological quality on the OCSI. The case studies fared equally poorly, scoring between 1-6 out of a total of eight points on the JBI checklist. All were missing significant information and data. Therefore, all clinical and case studies were considered to have a high risk of bias.

Three randomised trials were reviewed. Two were published prior to the publication of CONSORT and STRICTA (61, 62) and the third was published in English as a translation of the original paper from Mandarin (63). Further non-randomised studies reviewed and included were one cohort and one retrospective study (54, 64).

None of these studies provided information on practitioner training or acupuncture experience. Only one study specified that a single practitioner provided of all treatments, used blinded assessors, and provided enough detail on randomisation techniques, recruitment, adverse events and drop-outs (62). No studies provided evidence of patient or practitioner blinding.

Details on scar location, size, time since injury and spontaneous healing compared to skin graft were not adequately reported by two studies (61, 63) introducing potential confounding variables. Cuignet et al (54) provided this information revealing a heterogeneous patient cohort. Kotani et al (62) recruited subjects with intractable scar pain after failure of standard treatments, such as TENS, topical lidocaine and local anaesthetic injection. Although this limited diagnostic confounding factors, participant beliefs and expectations were not measured, which may be a particularly relevant confounding factor following multiple ineffective treatments.

A meta-analysis of results was not possible due to the limited numbers of studies located, variety of outcome measures used, conditions treated and heterogeneity in needling treatments provided. Two studies utilised different unvalidated scales based on practitioner assessment of colour, ‘hardness’ and itching with the treatment outcome assessed as either cure, effect, or failure. The Visual analogue scale (VAS) was used for pain measurement in two studies; however, study design and method of acupuncture treatment were dissimilar. Different methods of Quantitative Sensory Testing (QST) were utilised and applied. Pain pressure threshold was used to assess local scar tissue sensitivity and locate points for needle insertion along painful abdominal scars (62). Electrical stimulation along a shared meridian/dermatome to the

scar was hypothesised to assess systemic sensitivity when compared to the opposite and contralateral limb meridian/dermatome (54).

Adverse events and study completion were inadequately reported by most authors. Two studies reported that participants felt pain on needle insertion (62, 65) however the second of these was from the control intervention which included injection of local anaesthetic rather than the acupuncture treatment itself. Only one study reported the number and reason for dropouts (54), another study reported that they had no dropouts (62).

Two low quality case studies were published as brief reports (55, 66). A moderate-quality (6/8) case study report failed to gather final outcome measures as the patient declined further follow-up (56). Anderson (65) provided a moderate-quality (6/8) case study report where acupuncture was combined with other physical treatment modalities. Regrettably, details regarding treatment parameters were not provided. These included specific details of needle placement during each treatment, type and amount of needle stimulation, and whether the acupoints treated distant to the scar were on the ipsilateral or contralateral limb. Follow up data was not provided for any case study; hence it is unknown if improvements were maintained following treatment cessation.

Table 1. Clinical Trial Details: Part A

	Study Design	Type of Scar	Type of Control	Number of Participants	Type of Treatment	Needle Location
Cuignet et al. (2015)(54)	Cohort	HTS – burn	N/A	32	MA + EA	EA on extremity points of shared meridian and inner bladder line of nerve root supplying meridian of the scar. MA to TCM acupoints including some/all of: SP6, 9, 10, ST40, LI4, 11, BL13, 17
Huang et al. (1999)(61)	Clinical Trial (Quasi-experimental)	HTS – burn	Usual care	30 (?+30 control)	MA	3 main TCM points (SP10, ST36 & LI11), unclear whether local needles were also used
Kotani et al. (2001)(62)	Clinical Trial (RCT)	Abdominal surgery	Sham	70	Indwelling	Local tender points along scar.
Loskotova & Loskotova (2017)(64)	Retrospective	Acute Burns	Usual Care	1008 total subjects over 32 years. Comparison made for 198 with acu and 63 without acu	MA	TCM acupoints bilaterally, with combination of: LI4, LI11, & LU7 depending on access to unburnt skin.
Song et al. (2011)(63)	Clinical Trial (RCT)	HTS - burn	Ultrasound and Scareducer ointment	80	MA	Local around scar

Clinical Trial Details (Abbreviations: RCT – Randomised Controlled Trial, HTS – Hypertrophic scar, MA – manual acupuncture, EA – electroacupuncture, TCM – Traditional Chinese Medicine, VAS – visual analogue scale, QST – quantitative sensory testing, OCSI - Oregon CONSORT STRICTA Instrument). N/A – Details not available

Table 2. Clinical Trial Details: Part B

	Frequency of Treatment	Outcome Measures	Results	Statistical Analysis	OCSI Score	Risk of Bias
Cuignet et al. (2015)	30min, 1x week, duration 3 weeks	VAS pain and itch, QST	4/10-1/10 decrease in itch for all participants. Responders had decreased pain by 4 points, Non-responders had no change in pain scores. QST revealed difference between responders and non-responders.	Adequate use of statistical analysis, including use of p values	28%	High risk of Performance and Detection Bias.
Huang et al. (1999)	Unclear, differed between subjects	Unvalidated TCM diagnostic scale	Significant improvement in itch for all participants.	Use of p values, X^2	34%	High risk of Selection, Performance and Detection bias.
Kotani et al. (2001)	4 weeks, 20 sessions of 24hours indwelling needles in situ	VAS pain, QST	70% of participants in treatment group had good-excellent outcomes	Adequate statistical analysis including correlations and p values	50%	Low risk of Selection or Detection Bias. High risk of Performance bias.
Loskotova & Loskotova (2017)	Daily, 30 minutes. Unclear number of sessions.	Unclear, qualitative appearance of burn, colour and presence of HTS	Applying acupuncture within 48 hours resulted in complete healing without HTS in 6 weeks.	Some use of statistical analysis (X^2), poorly reported	13%	Risk of Detection and Reporting Bias.
Song et al. (2011)	30min, x 10 days, 7 day break, x4	Unvalidated 3 point scale – measuring pain, itch and scar pliability	Total effective rate was 93.9% for the treatment group and 77.8% for the control group after 1 year.	Unvalidated outcome measures, basic statistical analysis including p values	26%	High risk of Selection, Performance and Detection bias.

Clinical Trial Details (Abbreviations: HTS – Hypertrophic scar, MA – manual acupuncture, EA – electroacupuncture, TCM – Traditional Chinese Medicine, VAS – visual analogue scale, QST – quantitative sensory testing, OCSI - Oregon CONSORT STRICTA Instrument

Table 3. Case Report Details

	Type of Scar	Needle Location	Number of Treatments	Outcomes	Quality rating (JBI checklist)
Anderson (2014)(65)	Dupuytrens contracture surgery	Local plus LI4 and HT7	7 treatments over 3 months	Improved joint ROM, colour and numbness of skin	6/8
Fang (2014)(56)	Post-surgical on thigh	Local and distant – TCM diagnosis	8 treatments over 5 weeks	Pain decreased from 7/10 to 1-2/10	6/8
Hunter (2011)(55)	Post-surgical on wrist	Local Only	9 treatments over 4 months	Symptom free, flatter	2/8
McCowen (2006)(66)	Burns on hand	Local with EA	Unclear, could be just one.	Improved joint ROM, and appearance of scar, decreased pain	1/8

Case Studies (Abbreviations: TCM – Traditional Chinese Medicine, EA – electroacupuncture, ROM – range of motion)

Discussion

Despite rigorous search methods, very few articles were discovered that reported on the use of manual acupuncture for abnormal scars. Initial searching found only three references (one clinical trial and two case reports) hence additional inclusion criteria were added. Since acupuncture modalities; electrotherapy and indwelling needles use the same acupuncture needles and skin piercing technique as manual acupuncture, the authors decided to include these modalities and perform the search again. Further studies were discovered; however, this introduced the potential for confirmation bias (the tendency to search for information to confirm pre-existing beliefs or hypotheses) to this review. This is an understudied area of scar management with potential to enhance scar and HTS healing processes. The published studies are of very low quality, providing insufficient evidence to support the use of acupuncture for HTS. This review has highlighted the need for well-designed, methodologically rigorous research and case studies using validated outcome measures and clear reporting of results to

ascertain whether acupuncture is efficacious in the treatment of abnormal scars. However, empirically clinical results continue to be reported. Therefore, the findings of this review may be applied to providing an outline for future research in this field.

For the clinician treating abnormal scarring there are many physical treatment options to choose from. Practicing evidence-based medicine (EBM) means to integrate clinically relevant research with the practitioners' clinical expertise, in order to provide the best possible treatment (67). However, there is no consensus in the literature on treatment parameters when treating abnormal scars with acupuncture. The most commonly reported treatment method was to place acupuncture needles locally around the scar borders, also known in Chinese medicine as 'Surround the Dragon' (68). When discussing acupuncture for scar management; doctors (69), physiotherapists (41) and TCM practitioners (39) all recommend placing acupuncture needles locally around the scar, akin to 'surround the dragon'. Two of the three controlled trials and all four case reports in this review used local acupuncture as the primary type of treatment.

Loskotova and Loskotova (2017) (64) state that HTS formation in humans may be prevented or limited by early application of acupuncture treatment (64). This long-term retrospective series of case studies reported a significant reduction in scarring when acupuncture treatment was provided within 48 hours after burn injury. No other studies in human subjects have investigated using acupuncture as an early intervention treatment option following burn injury. Animal studies have demonstrated faster wound closure and less scarring following acupuncture treatment (70-72). Recommendations regarding scar prevention using acupuncture cannot be made without further clinical trials confirming these findings.

Studies reviewed noted between one and 40 treatments at daily, weekly or longer intervals. Hence, it unknown what the optimal treatment frequency, duration or placement of needles should be to achieve the best outcomes. Thus, there is not enough scientific evidence to make reliable conclusions at this stage, however clinicians may choose to be guided by the limited information available combined with their own clinical experience to inform treatment choices.

Recommendations and guidelines for future studies

There needs to be a comparison made between the use of local versus distant (extrasegmental, or TCM reasoned) acupuncture treatment. Available consensus suggests that local acupuncture application will have a greater influence on itch and connective tissue remodelling than distant acupuncture. Mechanistic studies demonstrate needle rotation, used to produce the sensation of deqi in acupuncture, can cause tissue displacement up to 4cm away from the needle (73), further informing the position of needles during locally applied acupuncture treatment for scars. Studies on itch found local dermatomal acupuncture treatment was more effective than that applied outside the segment, at reducing induced itch in human and animal models (49-51).

The use of distant or sham acupuncture in studies to date, have been based on TCM reasoning and point selection. All studies have used at least one acupoint with a shared dermatome/myotome to the affected area (74), including non-penetrating sham controls which may not be inert treatments (75, 76). The studies that used distal points for acupuncture tended to include points which are known as ‘big’ points in TCM theory (77). When these points are investigated from a neuroanatomical perspective, they demonstrate innervation from multiple segmental levels including dermatome, myotome, cutaneous and joint nerve supply, hence have input into the sensory nervous system via multiple segmental levels of spinal nerves (78). Thus, it could be argued that amount of sensory input rather than specific needle location could be a factor in results seen with acupuncture treatment.

Further investigation will help clarify whether itch and pain respond differently to treatment, as there is no evidence to suggest that locally applied acupuncture is more effective at reducing pain than distant acupuncture. Pragmatic trials comparing acupuncture to current best evidence will judge whether acupuncture should be considered as a primary intervention in scar management.

Table 4. Recommended Research Intervention Protocol – comparing local versus distant needle placement

Study Parameters	Recommendation
Age of Scar	Six weeks to one year. Pain associated with tissue damage fades as healing progresses and a scar is formed, usually around six weeks post-wounding (18). HTS develop in the first six months post- wounding (14, 16).
Needle Location	Local around the scar (same dermatome), compared with distant (no shared neuroanatomy to scar).
Number of Needles	To be calculated based on scar size/circumference to ensure equal stimulation between groups. Based on placing needles at 2cm intervals around the circumference of the scar.
Needle Stimulation	Bi-directional rotation as per Langevin (45), until moderate sensation is achieved and repeated at several intervals throughout treatment.
Treatment Duration	Acupuncture needles may be retained anywhere from 30 seconds to 30 minutes or more (i.e., indwelling) (68). An average time of 15 minutes duration is recommended.
Number of Treatments	Six treatments over four weeks.
Outcome Measures	Must be validated tools such as VAS and POSAS and include Quality of Life measures i.e., SF-36.

Reporting must follow STRICTA and CONSORT guidelines.

Conclusion

This review concludes that there is insufficient evidence to support the use of acupuncture in the management of abnormal scars due to the lack of quality, unbiased research trials. However, further investigation into acupuncture as a treatment for HTS is warranted, therefore recommendations for future research studies have been presented.

References

1. White A. Western Medical Acupuncture: a definition. Acupuncture in Medicine. 2009;27(1):33-5.

2. Rampes H, James R. Complications of Acupuncture. Acupuncture in Medicine. 1995;13(1):26-33.

3. Bivins R. The Needle and the Lancet: Acupuncture in Britain, 1683-2000. Acupuncture in Medicine. 2001;19(1):2-14.

4. Serejski E, Howard J. Early Essays on Acupuncture and Moxa -1. Acupunctura and Acupuncturation. USA: Eric Serejski and John Howard; 2017.

5. Cho ZH, Hwang SC, Wong EK, Son YD, Kang CK, Park TS, et al. Neural substrates, experimental evidences and functional hypothesis of acupuncture mechanisms. Acta neurologica Scandinavica. 2006;113(6):370-7.

6. Ching N. The Fundamentals of Acupuncture. London, UK: Jessica Kingsley Publishers; 2016.

7. Norris CM. Acupuncture: Treatment of Musculoskeletal Conditions. UK: Butterworth Heinemann; 2001.

8. Neal E. Introduction to Neijing Classical Acupuncture part III: Clinical Therapeutics. Journal of Chinese Medicine. 2014;104:5-23.

9. Stecco A, Stern R, Fantoni I, De Caro R, Stecco C. Fascial Disorders: Implications for Treatment. PM R. 2016;8(2):161-8.

10. Filshie J, White A. Medical Acupuncture: A Western Scientific Approach. 1 ed. London, UK: Churchill Livingstone; 1998.

11. Rogers C. Acupuncture therapy for postoperative scars. American Journal of Acupuncture. 1982;10(3):201-14.

12. MacPherson H, White A, Cummings M, Jobst K, Rose K, Niemtzow R. Standards for reporting interventions in controlled trials of acupuncture: the STRICTA recommendations. Complementary Therapies In Medicine. 2001;9:246-9.

13. Hammerschlag R, Milley R, Colbert A, Weih J, Yohalem-Ilsley B, Mist S, et al. Randomized controlled trials of acupuncture (1997-2007): An assessment of reporting quality with a CONSORT- and STRICTA-based instrument. Evidence - Based Complementary and Alternative Medicine. 2011.

14. Gauglitz GG, Korting HC, Pavicic T, Ruzicka T, Jeschke MG. Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. Molecular Medicine. 2011;17(1-2):113-25.

15. Butzelaar L, Ulrich MM, Mink van der Molen AB, Niessen FB, Beelen RH. Currently known risk factors for hypertrophic skin scarring: A review. J Plast Reconstr Aesthet Surg. 2016;69(2):163-9.

16. Zhu Z, Ding J, Tredget EE. The molecular basis of hypertrophic scars. Burns & Trauma. 2016;4(1).

17. Butzelaar L, Schooneman DPM, Soykan EA, Talhout W, Ulrich MMW, van den Broek LJ, et al. Inhibited early immunologic response is associated with hypertrophic scarring. Experimental Dermatology. 2016:xx1-8.

18. Bijlard E, Uiterwaal L, Kouwenberg CAE, Mureau MAM, Hovius SER, Huygen FJPM. A systematic review on the prevalence, etiology, and pathophysiology of intrinsic pain in dermal scar tissue. Pain Physician. 2017;20:1-13.

19. Hamed K, Giles N, Anderson J, Phillips JK, Dawson LF, Drummond P, et al. Changes in cutaneous innervation in patients with chronic pain after burns. Burns. 2011;37:631-7.

20. Choi YH, Kim KM, Kim HO, Jang YC, Kwak IS. Clinical and histological correlation in post-burn hypertrophic scar for pain and itching sensation. Annals of Dermatology. 2013;25(4):428-33.

21. Potenzieri C, Undem BJ. Basic Mechanisms of Itch. Clinical and Experimental Allergy. 2012;42(1):8-19.

22. Akaishi S, Ogawa R, Hyakusoku H. Keloid and hypertrophic scar: neurogenic inflammation hypothesis. Medical Hypotheses. 2008;71:32-8.

23. Cheng B, Liu H, Fu X. Update on pruitic mechanisms of hypertrophic scars in postburn patients: the potential role of opiods and their receptors. Journal of Burns Care Research. 2011;32:118-25.

24. Gold MH, McGuire M, Mustoe TA, Pusic A, Sachdev M, Waibel JS, et al. Updated International Clinical Recommendations on Scar Management: Part 2 - Algorithms for Scar Prevention and Treatment. Dermatologic Surgery. 2014;40:825-31.

25. Anthonissen M, Daly D, Janssens T, Van den Kerckhove E. The effects of conservative treatments on burn scars: A systematic review. Burns. 2016;42(3):508-18.

26. Lu J, Xu T, Liu Y, Yang M, Jiang X, Xu T. Pressure garment therapy for preventing hypertrophic and keloid scarring after a major burn injury. 2015.

27. Monstrey S, Middelkoop E, Vranckx JJ, Bassetto F, Ziegler UE, Meaume S, et al. Updated scar management practical guidelines: non-invasive and invasive measures. J Plast Reconstr Aesthet Surg. 2014;67(8):1017-25.

28. Sidgwick GP, McGeorge D, Bavat A. A comprehensive evidence-based review on the role of topicals and dressings in the management of skin scarring. Archives of Dermatological Research. 2014;307:461-77.

29. Linde K, Streng A, Jurgens S, Hoppe A, Brinkhaus B, Witt CM, et al. Acupuncture for patients with migrane: A randomised controlled trial. The Journal of the American Medical Association. 2005;293(17):2118-25.

30. Li-Tsang CW, Lau JC, Choi J, Chan CC, Jianan L. A prospective randomized clinical trial to investigate the effect of silicone gel sheeting (Cica-Care) on post-traumatic hypertrophic scar among the Chinese population. Burns. 2006;32(6):678-83.

31. Li-Tsang CW, Zheng YP, Lau JC. A randomized clinical trial to study the effect of silicone gel dressing and pressure therapy on posttraumatic hypertrophic scars. J Burn Care Res. 2010;31(3):448-57.

32. Zeitter S, Sikora Z, Jahn S, Stahl F, Strauss S, Lazaridis A, et al. Microneedling: Matching the results of medical needling and repetitive treatments to maximize potential for skin regeneration. Burns. 2014;40(5):966-73.

33. Issler-Fisher AC, Fisher OM, Smialkowski AO, Li F, van Schalkwyk CP, Haertsch P, et al. Ablative fractional CO2 laser for burn scar reconstruction: An extensive subjective and objective short-term outcome analysis of a prospective treatment cohort. Burns. 2017;43(3):573-82.

34. Aslser O, Goutos I. The evidence behind the use of platelet-rich plasma (PRP) in scar management: a literature review. Scars, Burns & Healing. 2018;4:1-15.

35. Issler-Fisher AC, Waibel JS, Donelan MB. Laser Modulation of Hypertrophic Scars: Technique and Practice. Clin Plast Surg. 2017;44(4):757-66.

36. Douglas H, Dunne JA, Rawlins JM. Management of Burns. Surgery. 2017;35(9).

37. Douglas H, Wood F. Burns Dressings. Australian Family Physician. 2017;46(3):94-7.

38. Aust MC, Knobloch K, Reimers K, Redeker J, Ipaktchi R, Altintas MA, et al. Percutaneous collagen induction therapy: An alternative treatment for burns scars. Burns. 2010;36(6):836-43.

39. Abbate S. A Simplified approach to the treatment of scars with oriental medicine. Acupuncture Today. 2001;2(11).

40. Hempen C-H, Chow V, W.,. Pocket atlas of acupuncture. New York: Thieme; 2012.

41. Bradnam L. The treatment of scars by acupuncture. [Unpublished Lecture notes]. In press 2001.

42. Fox JR, Gray W, Koptiuch C, Badger GJ, Langevin HM. Anisotropic Tissue Motion Induced by Acupuncture Needling Along Intermuscular Connective Tissue Planes. Journal of alternative and complementary medicine (New York, NY). 2014;20(4):29-294.

43. Langevin HM, Bouffard NA, Badger GJ, Churchill DL, Howe AK. Subcutaneous tissue fibroblast cytoskeletal remodeling induced by acupuncture: evidence for a mechanotransduction-based mechanism. Journal Of Cellular Physiology. 2006;207(3):767-74.

44. Langevin HM, Bouffard NA, Badger GJ, Iatridis JC, Howe AK. Dynamic fibroblast cytoskeletal response to subcutaneous tissue stretch ex vivo and in vivo. American Journal of Physiology - Cell Physiology. 2005;288(3):747-56.

45. Langevin HM, Bouffard NA, Churchill DL, Badger GJ. Connective tissue fibroblast response to acupuncture: Dose dependant effect of bidirectional needle rotation The Journal of Alternative and Complementary Medicine. 2007;13(3):355-60.

46. Langevin HM, Bouffard NA, Fox JR, Palmer BM, Wu J, Iatridis JC, et al. Fibroblast cytoskeletal remodeling contributes to connective tissue tension. Journal of cellular physiology. 2011;226(5):1166-75.

47. Langevin HM, Churchill DL, Cipolla MJ. Mechanical signaling through connective tissue: a mechanism for the therapeutic effect of acupuncture. FASEB Journal: Official Publication Of The Federation Of American Societies For Experimental Biology. 2001;15(12):2275-82.

48. Langevin HM, Fujita T, Bouffard NA, Takano T, Koptiuch C, Badger GJ, et al. Fibroblast cytoskeletal remodeling induced by tissue stretch involves ATP signaling. Journal of Cellular Physiology. 2013;228(9):1922-6.

49. Lundeberg T, Bondesson L, Thomas M. Effect of acupuncture on experimentally induced itch. The British journal of dermatology. 1987;117(6):771-7.

50. Han J-B, Kim CW, Sun B, Kim SK, Lee MG, Park DS, et al. The antipruritic effect of acupuncture on serotonin-evoked itch in rats. Acupuncture & Electro-Therapeutics Research. 2008;33(3-4):145-56.

51. Pfab F, Huss-Marp J, Gatti A, Fuqin J, Athanasiadis GI, Irnich D, et al. Influence of acupuncture on type I hypersensitivity itch and the wheal and flare

response in adults with atopic eczema a blinded, randomized, placebo-controlled, crossover trial. Allergy. 2010;65(7):903-10.

52. Kagitani F, Uchida S, Hotta H. Afferent nerve fibers and acupuncture. Auton Neurosci. 2010;157(1-2):2-8.

53. Bowsher D. Mechanisms of Acupuncture. In: Filshie J, White A, editors. Medical Acupuncture: A Western Scientific Approach. Edinburgh, United Kingdom: Churchill Livingstone; 1998. p. 69-82.

54. Cuignet O, Pirlot A, Ortiz S, Rose T. The effects of electroacupuncture on analgesia and peripheral sensory thresholds in patients with burn scar pain. Burns. 2015;41(6):1298-305.

55. Hunter J. Acupuncture for keloid scar. Acupuncture in Medicine. 2011;29(2).

56. Fang S. The successful treatment of pain associated with scar tissue using acupuncture. J Acupunct Meridian Stud. 2014;7(5):262-4.

57. Moher D, Hopewell S, Schulz KF, Montori V, Gotzsche PC, Devereaux PJ, et al. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials. Bmj. 2010;340:c869.

58. MacPherson H, Altman DG, Hammerschlag R., Youping L, Taixiang W, White A, et al. Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): Extending the CONSORT statement. PLoS Med. 2010;7(6):e1000261.

59. Moola S, Munn Z, Tufnaru C, Aromataris E, Sears K, Sfetcu R, et al. Systematic reviews of etiology and risk. In: Aromataris E, Munn Z, editors. Joanna Briggs Institute reviewers manual2017.

60. White A, Cummings M, Filshie J. Introduction. In: Filshie J, White A, Cummings M, editors. Medical Acupuncture: A western scientific approach. 2 ed. China: Elsevier; 2016.

61. Huang T, Wang L, Jin L. Clinical observation on using acupuncture to treat patients with burnt surface severe itching. Shanxi Nursing Journal. 1999;13(1):24-5.

62. Kotani N, Kushikata T, Suzuki A, Hashimoto H, Muraoka M, Matsuki A. Insertion of intradermal needles into painful points provides analgesia for intractable abdominal scar pain. Regional Anesthesia & Pain Medicine. 2001;26(6):532-8.

63. Song H, Jingping M, Jun W. Clinical study on treatment of hypertrophic scar by acupuncture. Journal of Acupuncture and Tuina Science. 2011;9(3):159-61.

64. Loskotova A, Loskotova J. The use of acupuncture in first aid of burns-Clinical report. Burns. 2017;43(8):1782-91.

65. Anderson F. Acupuncture in the treatment of scar tissue following surgery for Dupuytren's contracture. Journal of the Acupuncture Association of Chartered Physiotherapists. 2014;30:73-8.

66. McCowen SA, Liu G, Lee. M. Hypertrophic scar tissue modification using acupuncture on a burn patient: A case report. Archives of Physical Medicine and Rehabilitation. 2006;87:E34.

67. Sackett DL, Rosenberg WMC, Gray JAM, Haynes RB, Richardson WS. Evidence-based medicine: What it is and what it isn't. British Medical Journal (International Edition). 1996;312(7023):71-2.

68. White A, Cummings TM, Filshie J. An introduction to western medical acupuncture. New York, USA: Churchill Livingstone; 2008.

69. Gellman H. Acupuncture treatment for musculoskeletal pain: A textbook for orthopaedics, anesthesia and rehabilitation. USA: CRC Press; 2002.

70. Lee JA, Jeong HJ, Park HJ, Jeon S, Hong SU. Acupuncture accelerates wound healing in burn-injured mice. Burns 2011;37:117-25.

71. Park SI, Sunwoo YY, Jung YJ, Chang WC, Park MS, Chung YA, et al. Therapeutic effects of acupuncture through enhancement of functional angiogenesis and granulogenesis in rat wound healing. Evidence-Based Complementary and Alternative Medicine. 2012;2012.

72. Abali AE, Cabioglu T, Ozdemir H, Haberal M. Interactive effects of acupuncture on pain and distress in major burns: An experiment with rats. BURNS. 2015;41(4):833-42.

73. Langevin HM, Konofagou EE, Badger GJ, Churchill DL, Fox JR, Ophir J, et al. Tissue displacements during acupuncture using ultrasound elastography techniques. Ultrasound In Medicine & Biology. 2004;30(9):1173-83.

74. Langevin HM, Hammerschlag R, Lao L, Napadow V, Schnyder RN, Sherman KJ. Controversies in acupuncture research: selection of controls and outcome measures in acupuncture clinical trials. Journal of Alternative & Complementary Medicine. 2006;12(10):943-53.

75. Wu J, Qin Z, Lui Z. Pivotal factors concerned in design of acupuncture clinical research: From two articles in JAMA. Chinese Journal of Integrative Medicine. 2017;11:809-11.

76. Grillo CM, Zotelli VLR, Gil MLB, De Sousa MLR. Would a placebo acupuncture needle be able to induce Deqi? Journal of Acupuncture & Meridian Studies. 2018;11(5):273-9.

77. Bradnam L. A biopsychosocial clinical reasoning model for Western acupuncture. Physical Therapy Reviews. 2011;16(2):138-46.

78. Chapple W. Proposed catalogue of the neuroanatomy and the stratified anatomy for the 361 acupuncture points of 14 channels. Journal of Acupuncture & Meridian Studies. 2013;6(5):270e-4.

Chapter 3 – Methods – Study protocol

The following intervention protocol was developed based on acupuncture mechanisms (Chapter 1.) and guided by results from the published literature on acupuncture for scars in humans (Chapter 2.). The protocol was approved by the School of Physiotherapy Research Committee and The University of Notre Dame, Fremantle Human Research Ethics Committee (approval number #017029F). However, due to low recruitment, the focus of the study was changed to testing the clinical feasibility of the treatment protocol.

Study design

Randomised, clinical feasibility trial, with blinded patients, assessor (for self-report items) and statistical analysis of results.

Setting

Two treatment settings were initially proposed for this study to make it more accessible for a variety of participants. These were a private physiotherapy clinic in Cannington where the researcher worked, as well as the simulation laboratory in the School of Physiotherapy at the University of Notre Dame. During the recruitment period the researcher ceased working at the original private clinic location and thus her new workplace in Manning was approved to take over the private clinic treatment setting.

Randomisation

Prior to commencing recruitment, a physiotherapy student with no other involvement in the study used an online random number generator at http://www.graphpad.com/quickcalcs/randomize1.cfm to create a random allocation sequence of 86 numbers divided into two groups (A and B). The student placed (folded) paper printed with either A or B into opaque envelopes numbered from 1-86 as per the random allocation sequence. The numbered envelopes were opened in order of enrolment into the study and provided the participant ID number, following assessment of scar size and completing initial outcome measures.

Sample size

Sample size was calculated with the assistance of the statisticians at the Institute of Health Research, The University of Notre Dame Australia in Fremantle. The sample size calculation was based on the performance of the primary outcome measure, the Patient and Observer Scar Assessment Scale (POSAS) (patient response component). The POSAS contains seven categories for which the subject rates their symptoms from one to ten on individual numerical rating scales. A difference of two points on a numerical rating scale (NRS) for pain in adults is clinically relevant (Hawker et al., 2011). A previous study found that the response to acupuncture treatment for hypertrophic scars was normally distributed, with a standard deviation of three on a visual analogue scale (VAS) (Cuignet et al., 2015). Therefore, if the true difference between study and control participants is two points on each subscale of the POSAS, then 36 experimental and 36 control participants are required in order to reject the null hypothesis that the population means of both groups are equal with a probability (power) of 80%. The type I error probability of this experiment is 0.05. To allow for drop-out, 20% extra participants were planned to be recruited, totalling 43 participants per group (total n for study = 86).

Inclusion criteria

Participants were required to be aged 18 and over, with symptomatic scars from trauma or surgery. Accepted scar age ranged from six weeks to 12 months with pain and/or itch rated as 3/10 or higher on a numerical rating scale. Only one scar per participant received the study treatments, when multiple scars were present the participant was asked to choose the most irritable scar to receive treatment as part of this study.

Exclusion Criteria

- Scar currently receiving physical (hands on and/or equipment-based) treatment by another clinician.
- Atrophic scar (scar which is depressed or retracted below the line of the normal skin).
- Keloid scar (has extended beyond boundaries of original wound/has a shiny surface).

- Current pregnancy.
- Unstable medical conditions (such as uncontrolled blood pressure, or uncontrolled epilepsy).
- Allergies to stainless steel.
- Not consenting to receive acupuncture therapy or needle phobic.
- Other acupuncture related contraindications, i.e., lymphoedema in affected limb, loss of sensation in area to be treated (i.e., nerve injury, stroke, or diabetic neuropathy).
- Anyone who provides acupuncture treatment or has received significant training in this area (based on questioning of previous experience of acupuncture prior to enrolment).

Prior to assessment and subsequent enrolment into the study a phone interview was conducted with all respondents to exclude participants with either contraindications to receiving acupuncture or other exclusion criteria, as well as to answer any questions from potential participants. All participants consented to treatment prior to enrolment and indicated their ability/willingness to attend the prescribed treatment regimen. Participants were requested to avoid any other acupuncture treatment during the study period. For participants with previous acupuncture experience, a waiting period of a minimum one month following their last treatment was observed prior to study enrolment. Informed consent for acupuncture (Appendix 2) was given alongside consent to participate in a research study (Appendix 3).

Participant awareness of acupuncture

This study did not exclude participants with previous experience of acupuncture. Participants were advised that the study was comparing two different types of acupuncture. Perception is an important component of some types of placebo effects and can be influenced by the relationship between the therapist and the patient, and the use of verbal suggestions for pain relief (Vase et al., 2011). Hence the investigating therapist developed a standardised script (Appendix 4) which avoided discussing pain relief with each participant beyond the information contained in the study information sheet (Appendix 5) provided to potential participants prior to enrolment.

Recruitment

A flyer and information letter (see Appendix 7) was distributed (posted or hand-delivered) to GP clinics, plastic surgeons, and orthopaedic surgeons in the south of Perth region. Flyers were placed on noticeboards at the library, research office and School of Physiotherapy at the University of Notre Dame Australia (UNDA), Fremantle, and were displayed at the workplace of the researcher.

Social media was utilised via creation of a Facebook page with basic study information. Newspaper advertisements were placed in local area newspapers and a Freemantle newspaper published an article, including photo, about the study.

Potential participants were screened via phone or email for inclusion and exclusion criteria. The most common reason for exclusion was a scar older than 12 months.

Data Collection

This protocol was developed in 2019 and tested between 2019 -2021. All participants completed a personal information form (Appendix 6) which collected details on the event(s) that resulted in the scar including time since skin insult, current health conditions, current treatment regimens e.g., pressure garment use and demographic data e.g., age at the initial treatment session.

Outcome measures were given to participants when they arrived for their appointments by administration staff at each clinic. Participants were asked to fill out outcome measures at the prescribed times and place them in an envelope marked with the date and their participant ID. Patient data and results were stored together in a locked safe (as per university requirements and ethics approval), regardless of when and where they attended treatment. Envelopes stayed sealed until all participants treatment series were completed, then were unsealed, and entered into data spreadsheets. The therapist applying the treatment was blinded to the outcome measure results until all participants completed their treatment. Two attempts were made to follow-up participants who didn’t return outcome measures during the follow-up period, via email and SMS.

Outcome measures

Patient and Observer Scar Assessment Scale (POSAS)

The primary outcome measure was the patient response components of the POSAS. The scale consists of seven categories of scar symptoms for which the patient rates their scar on a scale from one to ten (Draaijers et al., 2004).

POSAS Questions

1. Has the scar been painful the past few weeks?
2. Has the scar been itchy the past few weeks?
3. Is the scar colour different from normal skin at present?
4. Is the scar stiffness different from normal skin at present?
5. Is the scar thickness different from normal skin at present?
6. Is the scar more irregular than normal skin at present?
7. What is your overall opinion of the scar compared to normal skin?

Participants performed the self-assessment part of the POSAS assessment at their initial enrolment into the study, midway, after their final treatment, and one- and two-months following treatment cessation. The POSAS has been demonstrated as a reliable and valid measure of both linear surgical scars as well as non-linear scars such as burns scars (Draaijers et al., 2004; van de Kar et al., 2005). The reliability of the observer scale completed by a single observer was acceptable ($r = 0.73$) and the internal consistency of the patient scale had a Cronbach's alpha of 0.76 (0.70 and above demonstrates consistency in a scale) (Draaijers et al., 2004). The POSAS was given to the participants upon arrival for each assessment appointment by administration staff, who were blinded to treatment allocation, and sealed in an envelope marked with their ID number and the date. During follow up, this was posted or emailed to the participant.

Numerical Rating Scale (NRS) for Pain and Itch

Participants were asked to rate average pain and itch on a scale from one to ten, for the period of 24 hours prior to attending treatment. This outcome measure was requested of participants upon arrival for each appointment by administration staff who were blinded to treatment allocation. Once completed results were sealed in an envelope marked with their ID number and the date.

Short form-36: Health related quality of life

A health-related quality-of-life measure the SF-36 was taken at recruitment, prior to beginning treatment, at the final treatment session, and one- and two-months after treatment cessation, along with the POSAS. These time points were selected so that QoL was measured monthly. It was not expected to see change in QoL over shorter time periods than this and was less taxing on the participants' time. The SF-36 is a non-disease specific quality of life measure that has been validated for various populations including burn injured patients (Edgar et al., 2010).

Responses to the SF-36 items are categorised into eight domains as follows:

1. Physical functioning (PF), measuring how health limits vigorous, moderate, and easy activities.
2. Role physical (RP), measuring how much health interferes with ability to perform daily activities and normal work.
3. Bodily pain (BP), measuring how much pain interferes with normal work.
4. General health (GH), measuring perception of health generally.
5. Vitality (V), measuring perceived personal energy level.
6. Social functioning (SF), measuring how health interferes with social activities.
7. Role emotional (RE), measuring how much emotional states of mind interfere with ability to perform daily activities and normal work.
8. Mental health (MH), measuring perceived mental (emotional) status.

Schedule of study measurements

One and two months following final treatment, participants were asked to complete the POSAS patient scale and SF-36 quality of life measures. These were sent to the patient via email or posted with a postage paid return envelope included.

Table 5. *Planned schedule of study measurements*

Outcome measure	Baseline	Prior to each session	Midway (4th session)	Final session	1 month (after final session)	2 months (after final session)
POSAS	√		√	√	√	√
NRS	√	√	√	√		
SF-36	√			√	√	√

POSAS – Patient and Observer Scar Assessment Scale (patient response component), NRS- Numerical Rating Scale, SF-36 – Health-related quality-of-life measure

Treatment provider

All treatment was provided by the same physiotherapist who had 11 years' experience in private practice physiotherapy at the beginning of this study period, including scar management post-surgery and trauma. The treating physiotherapist (who was also the research student), had a total of nine years' experience using dry needling as part of her management of a wide range of musculoskeletal conditions, including the use of local acupuncture needling of post-surgical and burns scars. This included introductory dry needling training in 2007 with ongoing clinical mentoring, additionally she completed post-graduate studies in western acupuncture in 2014, two years prior to commencing this research program.

Treatment

Routine care was provided to all study participants at the beginning of each treatment session prior to receiving acupuncture/dry needling treatment. Self-management advice in the form of a handout (see Appendix 8) was given to each participant at their first treatment session, recommending gentle stretching, cardiovascular exercises, and self-massage techniques.

Routine scar treatment consisted of soft tissue massage using techniques such as skin rolling, and effleurage. The aim of these techniques is to encourage the layers of skin and subcutaneous tissue to glide on each other. Sorbolene massage cream was used for all participants unless specific skin reactions were identified. The time of five minutes of massage therapy per scar was applied during the research session. Participants with multiple scars were advised to apply self-massage to all scars, however only the identified most irritable scar received treatment by the investigating therapist.

Treatment was performed twice weekly for two weeks, then once weekly for two weeks for a total of six treatments over four weeks. This treatment regimen was used by Chen et al. (2014) finding greater functional connectivity following verum acupuncture in central nervous system components such as the pre-frontal cortex and PAG which are involved in descending pain inhibitory pathways.

If participants found any of the acupuncture needles were too painful these were removed or re-positioned during treatment. Each treatment session was

considered complete if participants retained at least 80% of needles for at least 10 minutes per session. Participants were considered to have completed the treatment protocol if they attended five out of six sessions.

Local acupuncture

Treatment consisted of 30mm x 0.25μm Hwato brand acupuncture needles placed 2cm apart around the borders of the scar. Needles were inserted as close as possible to the margins of the scar (1-5mm away) to a depth of 5-10mm angling underneath the margins of the scar. In the case of local hypersensitivity, the needles were placed at a distance from the scar tolerable to the patient. Needles were left in situ for 15 minutes. Manual stimulation was applied via bidirectional rotation of the needle for 30 seconds or until moderate sensation (deqi) was described by the participant. This stimulation was repeated at five minute intervals at the time points of five and ten minutes, and immediately prior to needle removal.

Needle stimulation aims to produce an axon reflex response and affect local connective tissue around the scar. Zhang et al. (2012) state that the axon reflex response spreads from 1-3cm diameter from the needling site. Langevin et al. (2007) found that strong stimulation of the acupuncture needle can affect connective tissue up to 4cm away from the needle. Therefore, acupuncture needles were inserted at approximately 2cm apart. White et al. (2008) recommends leaving acupuncture needles in situ for 10-20 minutes per treatment session, hence each acupuncture treatment lasted 15 minutes. Scars were measured (in centimetres) during the initial treatment session (prior to randomisation) in order to calculate number of needles to be used for each treatment. Linear scars were measured, and the length doubled to give the scar circumference. Then this number was divided by two to calculate the number of needles to be placed every 2cm around both sides of the scar. For non-linear scars the circumference was measured and divided by two. The number of needles used was recorded for each patient, and the same number of needles used at each subsequent treatment session. No more than 20 needles were inserted per participant.

Distant Acupuncture/Dry Needling

As participants had scars in different body areas, they therefore required different needle placement between participants to avoid any neuroanatomical links to the scar being treated.

Treatment consisted of 30mm x 0.25μm Hwato needles inserted to a depth of 5-10mm perpendicular to the skin. The number of needles used was calculated as per the local treatment group depending on the size of the scar, so that the same number of needles was used relative to the size of the scar for each participant. No more than 20 needles were used per participant. Needles were left in situ for 15 minutes as per the local acupuncture group intervention. Manual stimulation via bidirectional rotation of the needle for 30 seconds or until moderate sensation was described by the participant, repeated at five-minute intervals was applied at the time points of five and ten minutes, and immediately prior to needle removal.

The therapist inserted acupuncture needles bilaterally to the following locations based on scar location. Points were recorded for each patient, along with number of needles to allow consistent treatment to be applied throughout the treatment series.

1. Scar located on upper limb, face, chest, or upper back – 2cm lateral to the spinous process of L3 and L4, midline of the posterior thigh 5cm and 10cm above the knee crease, 5cm below the knee crease.

2. Scar located on lower limb, lower back, or abdomen (below umbilicus) – 1cm lateral to the spinous process of C7 and T2, 5cm and 8cm above the elbow joint in the midline (posterior), midpoint of the forearm between the radius and ulna (dorsal surface).

These points were selected at a distance from one another, in order that this protocol seemed realistic to participants with previous acupuncture experience. They were also designed to avoid any neuroanatomical links to the scar being treated, based on segmental innervation theories which may confound results (Perreault et al., 2019). If extra needles were required based on scar size measurements, these were placed at 2cm intervals from the needles placed in the upper and lower limbs and recorded for consistent placement at each treatment session.

Data Analysis for Clinical Trial outcomes

Data was to be analysed with the assistance of the biostatisticians of The University of Notre Dame Australia, using an Intention to Treat (ITT) analysis of all participants regardless of protocol completion. A per protocol analysis of compliant participants was to be completed for comparison and sensitivity analysis. Descriptive statistics will be used to compare participant characteristics at baseline.

Linear mixed models will be used to compare treatments groups for each outcome of interest. This allows control of confounding variables (such as size of scar and previous acupuncture experience) and respects (clusters for) repeated observations taken per participant.

Hygiene and safety

A 70% alcohol-based hand wash was used by the treating therapist (Larmer et al., 2008). In the situation of compromised immunity or high infection risk for the participant a Povidone-Iodine Prep Pad was used to sterilise the skin two-minutes prior to needle insertion (Durani & Leaper, 2008). The therapist followed the Australian Society of Acupuncture Physiotherapists Guideline for Safe Acupuncture and Dry Needling, found at https://combinedhealth.com.au/wp-content/uploads/2018/01/ASAP-safety-guidelines-2007.pdf.

All participants were treated in a reclined position on a plinth to reduce any possibility of adverse events such as dizziness or fainting.

Adverse Events

Adverse events following acupuncture treatment are classified as mild, significant, and severe (White et al., 2008). Mild events are reversible and short-lived including faintness, nausea, drowsiness, bruising, pain, and symptom aggravation. Significant events require medical attention and include fainting, seizures, peripheral nerve injury and skin infections. Finally, serious events require hospital admission and include pneumothorax, vascular injuries, infection in the joints or brain, neuropathy, and paralysis.

Prior to each subsequent treatment session, participants were asked if there were any adverse events from the previous treatment. Minor adverse events such as

bleeding, bruising or short-term (<24 hours) increase in symptoms were recorded for each participant and reported in the final study summary. Had there been any significant or serious adverse events requiring medical attention, the researcher would have informed the Ethics committee. Post-treatment advice specific to acupuncture was provided to participants along with the general advice provided to all participants. This included advice on managing adverse events.

References

Chen, X., Spaeth, R., Retzepi, K., Ott, D., & Kong, J. (2014). Acupuncture modulates cortical thickness and functional connectivity in knee osteoarthritis patients. *Scientific Reports, 4*. https://doi.org/10.1038/srep06482

Cuignet, O., Pirlot, A., Ortiz, S., & Rose, T. (2015). The effects of electroacupuncture on analgesia and peripheral sensory thresholds in patients with burn scar pain. *Burns, 41*(6), 1298-1305. https://doi.org/10.1016/j.burns.2015.03.002

Draaijers, L. J., Tempelman, F. R. H., Botman, Y. A. M., Tuinebreijer, W. E., Middelkoop, E., Kreis, R. W., & van Zuijlen, P. P. M. (2004). The Patient and Observer Scar Assessment Scale: A Reliable and Feasible Tool for Scar Evaluation. *Plastic and Reconstructive Surgery, 113*(7), 1960-1965. https://doi.org/10.1097/01.prs.0000122207.28773.56

Durani, P., & Leaper, D. (2008). Povidone-iodine: use in hand disinfection, skin preparation and antiseptic irrigation. *International Wound Journal, 5*(3), 376-387.

Edgar, D., Dawson, A., Hankey, G., Phillips, M., & Wood, F. (2010, Nov). Demonstration of the validity of the SF-36 for measurement of the temporal recovery of quality of life outcomes in burns survivors. *Burns, 36*(7), 1013-1020. https://doi.org/10.1016/j.burns.2010.03.001

Hawker, G. A., Mian, S., Kendzerska, T., & French, M. (2011). Measures of Adult pain. *Arthritis Care and Research, 63*(S11), S240-252. https://doi.org/10.1002/acr.20543

Langevin, H. M., Bouffard, N. A., Churchill, D. L., & Badger, G. J. (2007). Connective tissue fibroblast response to acupuncture: Dose dependant effect of bidirectional needle rotation *The Journal of Alternative and Complementary Medicine, 13*(3), 355-360. https://doi.org/10.1089/acm.2007.6351

Larmer, P. J., Tillson, T. M., Scown, F. M., Grant, P. M., & Exton, J. (2008). Evidence-based recommendations for hand hygiene for health care workers in New Zealand. *The New Zealand Medical Journal, 121*(1272), 69-81.

Perreault, T., Grubb, M. T., Gendron, B. C., Perez-Santiago, J. C., & Flannagan, S. O. (2019). Mechanisms and dose parameters of manual needle stimulation: clinical considerations - Part 2. *Acupuncture in Physiotherapy, 31*(1), 9-23.

Van de Kar, A. L., Corion, L. U. M., Smeulders, M. J. C., Draaijers, L. J., van der Horst, C. M. A. M., & van Zuijlen, P. P. M. (2005). Reliable and Feasible Evaluation of Linear Scars by the Patient and Observer Scar Assessment Scale. *Plastic and Reconstructive Surgery, 116*(2), 514-522. https://doi.org/10.1097/01.prs.0000172982.43599.d6

Vase, L., Norskov, K. N., Petersen, G. L., & Price, D. D. (2011). Patients' direct experiences as central elements of placebo analgesia. *Philosophical Transactions of the Royal Society B, 366*, 1913-1921. https://doi.org/10.1098/rstb.2010.0402

White, A., Cummings, T. M., & Filshie, J. (2008). *An introduction to western medical acupuncture*. Churchill Livingstone.

Zhang, Z. J., Wang, X. M., & McAlonan, G. M. (2012). Neural acupuncture unit: a new concept for interpreting effects and mechanisms of acupuncture. *Evidence-Based Complementary and Alternative Medicine, 2012*, Article 429412. https://doi.org/10.1155/2012/429412

Chapter 4 – Case Study: Pilot test of the local acupuncture intervention for burn scars

The following case study was published to describe the application of the Methods as presented in the previous chapter (It is included here as published and uses the Vancouver referencing style required by the journal). This case study was performed concurrently to the participants participating in the randomised study design. The participant received the local acupuncture treatment protocol for a hypertrophic burn scar. This pilot study confirmed the feasibility of the treatment intervention and provided insight and recommendations for future research study design.

Tuckey, C. R., Kohut, S. H., & Edgar, D. W. (2022). Case study: Pilot testing of a local acupuncture intervention protocol for burn scars. Scars, Burns and Healing, 8. https://doi.org/:10.1177/20595131211058430

Introduction

Formation of hypertrophic scars following burn injury may contribute to loss of function and disfigurement in affected individuals (1-3). Skin grafting is used in acute burn injuries to restore the mechanical barrier and protect the excised damaged tissue. Although this minimises ongoing tissue damage and infection, it does not promote regeneration, and repair occurs with scar tissue formation (1). Several factors following burn injury can lead to scars becoming hypertrophic. These include severity (extent and depth) of the injury, infection, time to heal and prolonged inflammation beyond two weeks (4). The resulting hypertrophic scar may be painful, itchy and/or restrict mobility of the surrounding joints due to the contractile activity of collagen stimulated by inflammation (5). Following burn injury and subsequent skin transplantation, nerve ingrowth into the graft tissue occurs at different rates with unmyelinated fibres being most plentiful in the months immediately following injury (6). These unmyelinated fibres may cause increased sensitivity to noxious stimuli. This occurs through the release of neuropeptides including Substance P – consequently facilitating neurogenic inflammation in the tissue (6). Nociceptive input via the peripheral nervous system can trigger sensitisation of the central nervous system and lead to hyperalgesia (increased

sensitivity to painful stimuli) and allodynia (pain caused by non-nociceptive stimuli) (7). A systematic review found that intrinsic scar pain is most often reported in hypertrophic or burns scars (8). Furthermore, following burn injury, the size and depth of the burn was found to be predictive of the development of scar pain (8).

Standard conservative treatments often include the use of pressure garments, silicone, topical creams, gels, and massage (1, 2). Pressure garments have been used over many years and have been shown in some studies to reduce scar thickness (9, 10), however effectiveness has been questioned by other authors (11). Use of pressure garments combined with silicone gel sheets was shown to improve scar colour, thickness, vascularity, elasticity, and texture (12). However, use of a cohesive silicone bandage which applied compression as well as silicone added a significant improvement in scar itch compared to silicone gel sheeting and pressure garments (12). Neither silicone gel sheeting (13) or cohesive silicone bandages (12) have demonstrated a significant reduction in scar pain. Scar massage has shown promising results: however, studies are poor quality and use inconsistent treatment and assessment protocols (14). Although widely used and accepted as a treatment modality, use of specific categories of moisturisers or creams for scars has not been supported by research (15).

Previously published case studies reported positive outcomes for the use of acupuncture to reduce pain and itch in symptomatic scars (16-19). These case studies used manual or electroacupuncture for hypertrophic and keloid scars following surgery or burn injury. The number of treatments delivered along with treatment parameters (needle retention time, stimulation, number of needles) differed from case to case. However, the authors reported improved physical characteristics (colour, height, pliability), reduced pain and improved mobility in surrounding joints of scarred skin following acupuncture treatment.

Due the scarcity of data and consistent protocols for the use of acupuncture for treating symptomatic scars, the ideal treatment parameters to achieve optimal results is unknown (20). Acupuncture needles inserted locally into skin supplied by the same spinal segmental nerve level as the target tissue (also known as segmental needling) (21) targets local nociceptors and connective tissue. This is compared to extrasegmental or distant acupuncture, where needles are inserted into skin or muscle

without linked neuroanatomy through related dermatomes and myotomes (21). Extrasegmental needling is applied at a distance to the target tissue in order to prevent proximity related neural stimulation (21). Manual or electrical stimulation of acupuncture needles causes widespread activity in the cortical, subcortical, limbic and brainstem areas of the central nervous system (7, 22-24). These areas are involved in a diverse range of functions including sensory, locomotor, cognition, sleep, emotion, and visceral functions (23) and may contribute to non-specific acupuncture effects. As extrasegmental acupuncture is not an inert control treatment it may produce similar non-specific acupuncture effects as local segmental acupuncture (25, 26).

This case study aimed to pilot test a standardised methodology to explore the feasibility and sensitivity of clinical outcome measures to assess change associated with using local acupuncture. This standardised methodology is designed for use for a larger, future clinical trial, investigating acupuncture effect on both post-surgical and post-traumatic symptomatic scars. Specifically, this case study assessed patient tolerance and adherence to the treatment protocol, and compliance with outcome measures both during the treatment period and follow-up post treatment cessation.

Patient Demographics

This case study depicts the treatment journey of a 71-year-old otherwise healthy Caucasian male; A.B., previously employed fulltime as a mechanic in Western Australia.

Patient History

While using an oxyacetylene cutting torch at work, his shirt caught fire resulting in a third degree burn to his left lateral torso. He received minor burns to the fingers on his left hand, which he had used to try and extinguish the fire. A.B was admitted to Fiona Stanley Hospital (FSH) in Perth and underwent skin graft surgery using skin off his left anterior thigh to his left lateral torso. The grafted wound was assessed to be cellulitic in the first week after injury, however, this settled with a course of intra-venous antibiotics followed by oral antibiotics. He was discharged from hospital with compression garments and expected he would need to wear them for two years. A.B.

was referred by his General Practitioner (GP) for a gym-based exercise program under the supervision of an exercise physiologist early post-injury and commenced a gradual return to work program of light duties and reduced hours.

A.B.'s wife had been massaging his thoracic scar 1-2x daily for approximately ten minutes each day following hospital discharge. He reported that he was wearing his compression garment 23 hours per day (as per routine practice of State Adult Burn Unit at FSH) and attended the gym three times per week.

Three months after his burn and initial treatment, A.B. was referred by his GP (who had seen a recruitment flier for the author's clinical trial) for twelve sessions of massage and acupuncture treatment for the scar on his thorax. Throughout the course of his treatment, A.B. continued with his previous regimen of massage, stretching and exercise. All medical costs for his injury were covered by Workers Compensation Insurance.

Initial Clinical Presentation

During his initial appointment, A.B. reported that the burns on his left hand had healed and those skin changes were no longer symptomatic. The scar on his left lateral thorax was symptomatic (pain and itch), and he experienced some pulling during movement but had unrestricted shoulder and thoracic spine range of motion (ROM). Reduced sensation was noted around some sections of the thoracic scar.

Prior to commencing the acupuncture treatment protocol, A.B. reported that he remained working on reduced hours compared to normal and that these had been gradually increasing. At the start of this treatment protocol, he was working 75% of his usual hours and had restricted lifting capacity to a maximum of 5kg (approximately 15 % of his workplace maximum). A.B. was performing a combination of light cleaning tasks, administrative duties, and mechanical work, rather than full-time mechanical duties with no lifting restrictions.

Methods

<u>Standardised Local Acupuncture Treatment for Scars</u>

Prior to receiving treatment, A.B. was assessed for scar size and screened for medical conditions that may contraindicate treatment. He received a handout containing current World Health Organisation (WHO) recommendations regarding cardiovascular exercise and instructions for self-massage of his scar. The number of acupuncture needles used was calculated based on placing needles at 2-cm intervals surrounding the scar, limited to a maximum of 20-needles to avoid overstimulation. Outcome measures were assessed/requested based on the following schedule from the clinical trial protocol:

Table 6. Planned Schedule of Study Measurements

Outcome Measure	Baseline	Prior to each session	Midway	Final Session	1 Month post	2 Months post
POSAS	√		√	√	√	√
NRS	√	√	√	√		
SF-36	√			√	√	√

Patient and Observer Scar Assessment Scale (POSAS) – patient response component, Numerical Rating Scale for Pain and Itch (NRS), Quality of Life Measure (SF-36)

Each treatment involved five minutes of scar massage aimed at moving layers of connective tissue on each other, followed by 15-minutes of acupuncture. The needles were stimulated manually via bidirectional rotation until moderate deqi, or needling sensation was felt, three times over the course of each 15-minute treatment session. These parameters were chosen as it has been confirmed that the stimulation of needling sensation is vital for producing acupuncture analgesia and that the analgesic effects of acupuncture build slowly over the course of the treatment and continue following treatment cessation (27). Local acupuncture treatment aims at increasing blood flow and stimulating remodelling of collagen fibres (28).

Methods Applied to this case study

A.B. was referred for inclusion in a clinical trial (UNDA Ethics #017029F) and the methodology for the study was piloted with his consent. The opportunity arose because, he met the participant inclusion criteria, but he was unable to be randomly assigned to either treatment group as he had been referred by his doctor for a defined number of treatment sessions, under Workers Compensation Insurance provisions.

As his scar and symptoms met inclusion criteria, he gave permission for his data and photographs to be published as a separate pilot (case study). He received a total of 12 treatment sessions over seven weeks which is double the number of treatments in the clinical trial and this was specified in his referral from his doctor/case manager. Following scar massage as per the standard protocol A.B. received localised acupuncture treatment applied surrounding the entire skin graft area. Some needles were also inserted inside the grafted area adjacent to prominent red, raised bands of scar tissue. For each treatment 20-needles were inserted to a depth of 10-mm under the skin at a 45-degree angle so that 20-mm of the needle shaft was inserted at an angle underneath the edge of the scarred tissue.

On several occasions the patient reported greater sensitivity over his skin grafted area when he arrived for treatment coming straight from a day at work. This was postulated to be a combination of factors including heat and rubbing from work clothing and repetitive motion of his arm during work duties. Hence, needles were only placed around the entire scar border (into un-affected skin) to avoid overstimulation on these occasions, avoiding the central raised bands.

Outcome measures were taken prior to commencement of treatment, at his final treatment session and via a phone call follow-up 10 weeks after treatment completion. The phone call was undertaken following no reply to emails including requests for previously consented to post-treatment questionnaires. The three outcome measures were used. The Patient and Observer Scar Assessment Scale (POSAS) – patient rating component, was utilised at baseline, and at points following treatment cessation as this asks the patient about scar symptoms as well as the appearance and impact of the scar over the preceding few weeks (29). A short-term measure, the Numerical Rating Scale for pain and for itch was used at the beginning of each treatment session. This averages symptoms on a scale of 1-10 over the past 24 hours and was used to assess reaction to the previous treatment and scar sensitivity on the day of treatment and guide treatment intensity. Quality of Life was measured using the SF-36 which has been validated for use with burns survivors, as well as the general population (30). This was completed during his initial assessment with assistance of his wife due to language difficulties. Unfortunately, this measure was not able to be captured after his baseline measure. This outcome measure was included to test the ease of capture of

quality-of-life information, and to explore non-specific acupuncture effects. This was for the comparison between verum and control protocol in a future clinical trial.

Results

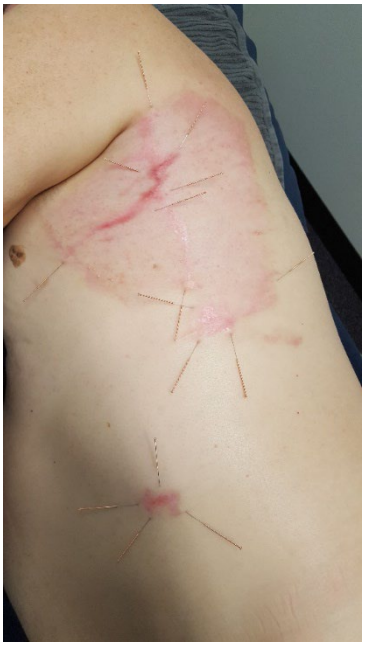
Table 7. Case Study Results

	Initial Assessment (3 months following burn injury)	At final Treatment (7 weeks after treatment commenced)	Follow-Up (10 weeks following Treatment cessation, 7 months post-injury)
NRS (pain)	7/10	4.5/10	6/10
NRS (itch)	5/10	4/10	5/10
POSAS	57/70 (81%)	27/70 (38%)	33/70 (47%)
SF-36	Summary Scores (%) PCS – 29, MCS – 46 Domain Scores (%) PF – 15 (74*) RP – 44 (71*) BP – 31 (75*) GH – 45 (81*) VT – 44 (60*) SF – 63 (91*) RE – 38 (88*) MH – 75 (87*)	Patient declined to complete	Unable to complete over the phone

(NRS – Numerical Rating Scale, POSAS – Patient and Observer Scar Assessment Scale (Patient response component), SF-36 – Quality of Life Measure, PCS – Physical Component Summary, MCS – Mental Component Summary, PF – Physical Functioning, RP – Physical Role Functioning, BP – Bodily Pain, GH – General Health, VT – Vitality, SF – Social Role Functioning, RE Emotional Role Functioning, MH – Mental Health Functioning) *with mean age and gender-based domain score for comparison (31)

On initial presentation, A.B.'s skin grafted area was pink with a dark red raised horizontal band and slightly raised pink vertical band of hypertrophic scarring (figure 2). Half-way through the treatment series (4-weeks following his initial treatment) the main grafted area of scar was lighter pink. The raised horizontal band was less raised and had lightened to red, with a section in the centre that had completely flattened and

changed colour to pink. The vertical band was barely distinguishable from the main section of the scar (figure 3a and 3b).

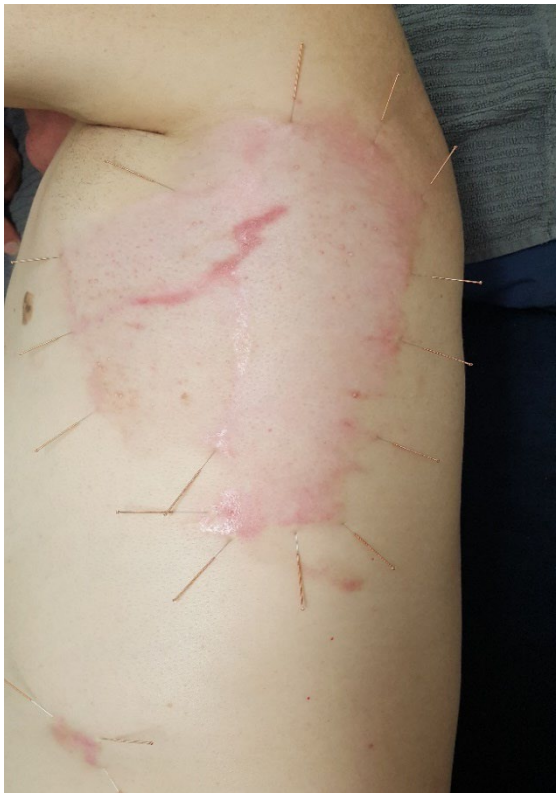


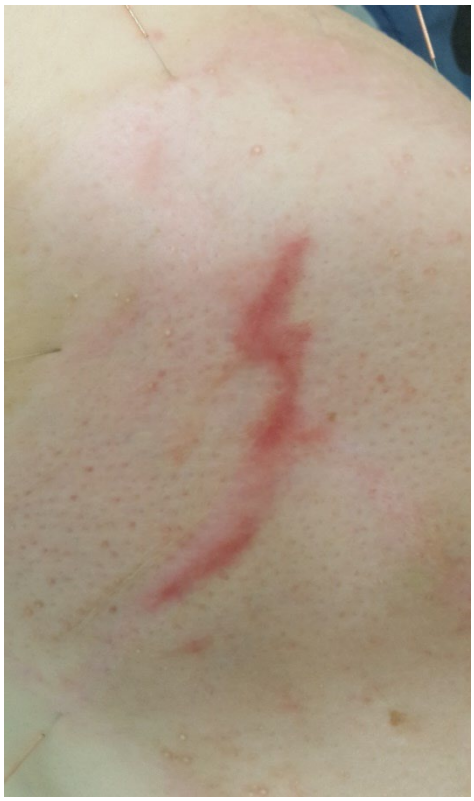
Seven weeks following initial treatment at his final (12th) session, the main section of scar was light pink. The horizontal band had reduced in size, with only a small section still raised and red, and the vertical band was no longer visible (figure 4).

At his final follow-up (via phone call) 7-months after his burn injury, the patient reported that he was working fulltime, performing all his normal duties. However, he reported that heat and repetitive arm movements were causing some scar irritation from the rubbing of clothing against his scar.

Figure 2. (left) Taken by and reproduced with consent of AB's wife

Figure 3a. and 3b. (below) Photo taken by the therapist and reproduced with consent of AB.





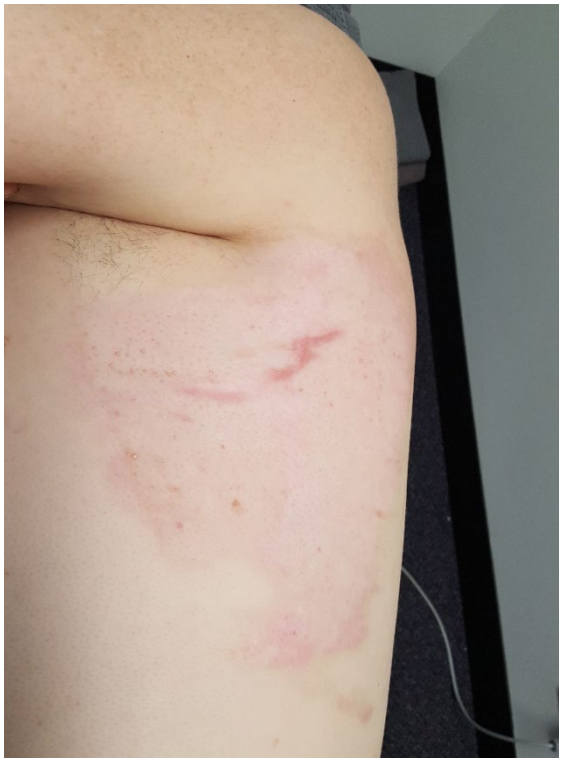


Figure 4. (left) Photo taken by the therapist and reproduced with consent of AB.

Adverse Events

The patient complained of some increased scar pain immediately following treatment, this required his usual pain medication, and settled within 12-hours post-treatment. Some irritation/pain following treatment was expected due to the increased neural sensitivity of his scar. A.B was asked to rate his pain and itch (on an NRS) at the beginning of each session and if he was already experiencing work-related symptom aggravation prior to treatment the needle stimulation intensity was reduced for that session. Future research could consider using less needles initially and increasing needle numbers throughout the course of treatment to increase stimulation intensity in line with patient tolerance.

Discussion

This case study related to the pilot testing of a local acupuncture treatment protocol for hypertrophic scars for an infected burn which received skin grafting. The treatment protocol was developed and based on the available evidence arising from the authors' recent review of the efficacy of acupuncture in treating scars (20). The clinical trial protocol involved random assignment to either an active group who received local acupuncture treatment or a control group who received distant, non-segmental acupuncture treatment. A.B. received the verum local acupuncture treatment protocol. The acupuncture needles were inserted into skin supplied by the same spinal segmental nerves as the target tissue, also known as segmental needling (21). No significant adverse effects were reported over the course treatment which is promising for a patient with such a large scar and history of skin graft and subsequent infection. The treatment methods were well tolerated by A.B., supporting its use in a larger

clinical trial. This case study also examined sensitivity and compliance with regards to outcome measures used and highlighted the challenge of using written questionnaires in participants with poor written English ability. In this case, initial measures were completed with the assistance of A.B.'s wife, then verbally with the treating therapist. Other potential methods for future data collection could include digital questionnaires or use of a translated version of the original questionnaire.

Clinically relevant symptom reduction was measured via POSAS and a Numerical Rating Scale (NRS) for pain and itch over the course of treatment supporting the use of these measures to assess treatment effect (32-34). Symptoms of pain and itch improved 10-15% over the course of treatment, however short-term symptom reduction was reported by the patient. Pain was reduced by 1.5/10 post treatment and 1/10 at follow-up. Itch reduced by 1/10 post-treatment, but this was not retained on 10-week follow-up. Significantly, the POSAS score dropped from 81% to 38% post treatment and remained at 47% on follow-up, indicating that self-perceived improvement of factors such as scar pigmentation, height and pliability were maintained over time. These measures were completed in person throughout the treatment series and via follow-up phone consultation. Regrettably, the symptom of itch did not reduce appreciably with treatment. There are several possible reasons for this. Due to the location of his scar, A.B complained that heat, sweat and rubbing from his clothing irritated it despite wearing either his compression garment or later a cotton singlet. Due to the location of his scar in the proximal axilla region and body contours, it is possible that his compression garment was less effective at maintaining consistent skin contact in this area during repetitive arm movements. Because he worked as a mechanic, his regular arm and trunk movements may have created friction between skin and clothing. This may have stimulated mechanosensitive nociceptors of histamine and other pro-inflammatory neuropeptides such as Substance P, therefore leading to neurogenic inflammation of the skin grafted region (35, 36). During treatment, acupuncture needle insertion and stimulation activates the same sensory neurons as does tissue damage, leading to local histamine release (23, 27). This may cause a short-term increase in symptoms (23). Further, due to lack of standardisation in measuring itch and applying acupuncture for itch, the published literature to date does not support its use in treating itch (37). It is currently unknown whether use of segmental (shared neuroanatomy) needle placement further away from the tissue

under consideration or extrasegmental needle placement (no shared neuroanatomy) influences itch. This requires further investigation; therefore the proposed clinical trial protocol compares the use of local segmental acupuncture with distant extrasegmental acupuncture. Extrasegmental acupuncture is not an inert control treatment, hence, it's use may produce non-specific acupuncture effects including potential effects on symptoms under investigation (25, 26).

Physical scar characteristics of pigmentation, height and pliability as measured by the POSAS (patient self-assessment) improved following treatment consisting of scar massage and local acupuncture. Bi-directional needle rotation is reported by Langevin and colleagues to influence fibroblast cellular activity in a dose-dependent manner via winding of collagen fibres around the needle (28, 38). This effect was demonstrated to occur up to 4-cm away from the shaft of the needle and is hypothesised to cause local collagen fibre remodelling (39, 40). Therefore, use of local acupuncture treatment with bidirectional rotation until moderate needling sensation (deqi) is felt, may contribute to physical changes in scar pigmentation, height, and pliability via stimulation of collagen remodelling within the scar tissue and warrants further investigation.

The SF-36 was validated for burns patients and provides valuable information that could be useful in understanding non-specific treatment effects of acupuncture (30). A.B scored significantly lower on all domains of the SF-36 compared to age matched controls, demonstrating both his physical and mental health had been affected by this injury. Unfortunately, this was only captured at baseline. A.B. declined to fill this in at his final appointment and follow up. Due to the length of the questionnaire, completion via telephone was not feasible. For these reasons, the use of a shortened quality of life measure might be beneficial when patients have difficulties with written language. The SF-36 can be mapped to the EQ5D-5L which only has five questions and was found to provide similar predictions with the exception of severe health states (41). This is an appropriate substitution for future clinical trial cohorts in order to provide some follow up data for comparison. However, the SF-36 provides valuable detail across multiple domains and is therefore the questionnaire of choice where logistically possible.

Whilst this case study showed promising results in a single patient, factors such as age may influence tissue healing and scar characteristics. It cannot be ascertained from a single case whether the improvement was more rapid than a normal healing response, nor can outcomes be generalised to other populations with burns or post-surgical scars. Further testing of this protocol is warranted to determine whether the recommendations arising from this case study should be applied.

Conclusion

This case and intervention applied was associated with a significant change in patient observed physical scar characteristics with a small but clinically relevant reduction in scar pain. The treatment protocol was well tolerated, and outcome measures sensitive to change. A larger trial with standardised treatment, as proposed below, is warranted to investigate the effect of acupuncture on hypertrophic scar symptoms in patients with post-surgical or burns scars, of various ages and stages of healing.

Appendix to case study – Proposed Comparison Groups for Clinical Trial

Group 1 – Local acupuncture (demonstrated in this case study)

Following standard scar massage, acupuncture treatment will consist of 30mm x 0.25μm acupuncture needles placed 2cm apart around the borders of the scar. Needles will be inserted as close as possible to the margins of the scar (1-5mm away) to a depth of 5-10mm angling underneath the margins of the scar. In the case of hypersensitivity, the needles will be placed at a distance from the scar tolerable to the patient. Needles will be left in situ for 15 minutes. Manual stimulation will be applied via bidirectional rotation of the needle for 30 seconds or until moderate sensation (deqi) has been described by the participant. This stimulation will be repeated at five-minute intervals at the time points of five and ten minutes, and immediately prior to needle removal.

Group 2 – Distant acupuncture (Control Condition #1)

As participants will have scars in different body areas, they will therefore require different needle placement between participants to avoid any segmental neuroanatomical links to the scar being treated.

Following standard scar massage, acupuncture treatment will consist of 30mm x 0.25μm acupuncture needles inserted to a depth of 5-10mm perpendicular to the skin. The number of needles used will be calculated as per the local treatment group depending on the size of the scar, so that the same number of needles will be used relative to the size of the scar for each participant. No more than 20 needles will be used per participant. Needles will be left in situ for 15 minutes as with the local acupuncture group. Manual stimulation via bidirectional rotation of the needle for 30 seconds or until moderate sensation (deqi) has been described by the participant, repeated at five-minute intervals will be applied at the time points of five and ten minutes, and immediately prior to needle removal.

The therapist will insert acupuncture needles bilaterally to the following locations based on using points extrasegmental to the scar location as segmental needling has been demonstrated to confound sham needling attempts in acupuncture clinical trials (21). Points used will be recorded for each patient, along with number of needles to allow consistent treatment to be applied throughout the treatment series.

1. Scar located on upper limb, face, chest or upper back – 2cm lateral to the spinous process of L3 and L4, midline of the posterior thigh 5cm and 10cm above the knee crease, 5cm below the knee crease.

2. Scar located on lower limb, lower back or abdomen (below umbilicus) – 1cm lateral to the spinous process of C7 and T2, 5cm and 8cm above the elbow joint in the midline (posterior), midpoint of the forearm between the radius and ulna (dorsal surface).

If extra needles are required based on scar size measurements, these will be placed at 2cm intervals from the needles placed in the upper and lower limbs and recorded for consistent placement at each treatment session.

These points have been selected at a distance from one another, in order that this protocol seems realistic to participants with previous acupuncture experience as they will not be excluded from participation in this trial. They are also designed to avoid any neuroanatomical links to the scar being treated, which would confound results (21).

Group 3 (Control Condition #2) – proposed as an additional group for future studies

Participants receive standard scar massage as per groups 1 and 2 but no acupuncture treatment.

References

1. Aarabi S, Longaker MT, Gurtner GC. Hypertrophic scar formation following burns and trauma: new approaches to treatment. PloS Med. 2007;4(9):e234.

2. Anthonissen M, Daly D, Janssens T, Van den Kerckhove E. The effects of conservative treatments on burn scars: A systematic review. Burns. 2016;42(3):508-18.

3. Franchitto N, Telmon N, Grolleau JL, Gavarri L, Laguerre J, Rouge D. Medicolegal evaluation of aesthetic impairment: particularities of post-burn scars. Burns. 2009;35(5):642-9.

4. Butzelaar L, Ulrich MM, Mink van der Molen AB, Niessen FB, Beelen RH. Currently known risk factors for hypertrophic skin scarring: A review. J Plast Reconstr Aesthet Surg. 2016;69(2):163-9.

5. Gauglitz GG, Korting HC, Pavicic T, Ruzicka T, Jeschke MG. Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. Molecular Medicine. 2011;17(1-2):113-25.

6. Ward RS, Tuckett RP, English KB, Johansson O, Saffle JR. Substance P axons and sensory threshold increase in burn-graft human skin. Journal of Surgical Research. 2004;118:154-60.

7. Lai HC, Lin YW, Hsieh CL. Acupuncture-Analgesia-Mediated Alleviation of Central Sensitization. Evidence-based complementary and alternative medicine : eCAM. 2019;2019:6173412.

8. Bijlard E, Uiterwaal L, Kouwenberg CAE, Mureau MAM, Hovius SER, Huygen FJPM. A systematic review on the prevalence, etiology, and pathophysiology of intrinsic pain in dermal scar tissue. Pain Physician. 2017;20:1-13.

9. Unal M. The Therapeutic Effects of Conservative Treatments on Burn Scars. 2017. In: Hot Topics in Burn Injuries [Internet]. IntechOpen. Available from: https://www.intechopen.com/books/hot-topics-in-burn-injuries/the-therapeutic-effects-of-conservative-treatments-on-burn-scars.

10. Anzarut A, Olson J, Singh P, Rowe BH, Tredget EE. The effectiveness of pressure garment therapy for the prevention of abnormal scarring after burn injury: a meta-analysis. J Plast Reconstr Aesthet Surg. 2009;62(1):77-84.

11. Atiyeh BS, El Khatib AM, Dibo SA. Pressure garment therapy (PGT) of burn scars: Evidence-based efficacy. Annals of Burns and Fire Disasters. 2013;26(4):205-12.

12. Moortgat P, Meirte J, Maertens K, Lafaire, C, De Cuyper L, Anthonissen M. Can a Cohesive Silicone Bandage Outperform an Adhesive Silicone Gel Sheet in the Treatment of Scars? A Randomized Comparative Trial. Plastic and Reconstructive Surgery. 2019;143(3):902-11.

13. Momeni M, Hafezi F, Rahbar H, Karimi H. Effects of silicone gel on burn scars. Burns. 2009;35(1):70-4.

14. Ault P, Plaza A, Paratz J. Scar massage for hypertrophic burns scarring-A systematic review. Burns. 2018;44(1):24-38.

15. Klotz T, Kurmis R, Munn Z, Heath K, Greenwood JE. The effectiveness of moisturizers in the management of burn scars following burn injury: a systematic review. JBI Database System Rev Implement Rep. 2015;13(10):291-315.

16. Hunter J. Acupuncture for keloid scar. Acupuncture in Medicine. 2011;29(2).

17. Fang S. The successful treatment of pain associated with scar tissue using acupuncture. J Acupunct Meridian Stud. 2014;7(5):262-4.

18. Anderson F. Acupuncture in the treatment of scar tissue following surgery for Dupuytren's contracture. Journal of the Acupuncture Association of Chartered Physiotherapists. 2014;30:73-8.

19. McCowen SA, Liu G, Lee. M. Hypertrophic scar tissue modification using acupuncture on a burn patient: A case report. Archives of Physical Medicine and Rehabilitation. 2006;87:E34.

20. Tuckey C, Kohut S, Edgar DW. Efficacy of acupuncture in treating scars following tissue trauma. Scars, Burns & Healing. 2019;5:1-12.

21. Ots T, Kandirian A, Szilagyi I, DiGiacomo SM, Sandner-Kiesling A. The selection of dermatomes for sham (placebo) acupuncture points is relevant for the outcome of acupuncture studies: a systematic review of sham (placebo) controlled randomized acupuncture trials. Acupuncture in Medicine. 2020;38(4):211-26.

22. Gong Y, Li N, Lv Z, Zhang K, Zhang Y, Yang T, et al. The neuro-immune microenvironment of acupoints-initiation of acupuncture effectiveness. J Leukoc Biol. 2020;108(1):189-98.

23. Zhang ZJ, Wang XM, McAlonan GM. Neural acupuncture unit: a new concept for interpreting effects and mechanisms of acupuncture. Evidence-based complementary and alternative medicine : eCAM. 2012;2012:429412.

24. Zhao J, Wang L, Li Y. Electroacupuncture alleviates the inflammatory response via effects on M1 and M2 macrophages after spinal cord injury. Acupuncture in medicine : journal of the British Medical Acupuncture Society. 2017;35(3):224-30.

25. Zhang CS, Tan HY, Zhang GS, Zhang AL, Xue CC, Xie YM. Placebo Devices as Effective Control Methods in Acupuncture Clinical Trials: A Systematic Review. PloS One. 2015;10(11):e0140825.

26. Chen ZX, Li Y, Zhang XG, Chen S, Yang WT, Zheng XW, et al. Sham Electroacupuncture Methods in Randomized Controlled Trials. Sci Rep. 2017;7:40837.

27. Zhao ZQ. Neural mechanism underlying acupuncture analgesia. Progress in Neurobiology. 2008;85:355-75.

28. Langevin HM, Bouffard NA, Badger GJ, Churchill DL, Howe AK. Subcutaneous tissue fibroblast cytoskeletal remodeling induced by acupuncture: evidence for a mechanotransduction-based mechanism. Journal Of Cellular Physiology. 2006;207(3):767-74.

29. van de Kar AL, Corion LUM, Smeulders MJC, Draaijers LJ, van der Horst CMAM, van Zuijlen PPM. Reliable and Feasible Evaluation of Linear Scars by the Patient and Observer Scar Assessment Scale. Plastic and Reconstructive Surgery. 2005;116(2):514-22.

30. Edgar D, Dawson A, Hankey G, Phillips M, Wood F. Demonstration of the validity of the SF-36 for measurement of the temporal recovery of quality of life outcomes in burns survivors. Burns. 2010;36(7):1013-20.

31. Kvannli L, Finlay V, Edgar DW, Wu A, Wood FM. Using the Burn Specific Health Scale-brief as a measure of quality of life after a burn-what score should clinicians expect? Burns. 2011;37(1):54-60.

32. Gallagher EJ, Liebman M, Bijur PE. Prospective validation of clinically important changes in pain severity measured on a visual analog scale. Annals of Emergencey Medicine. 2001;38:633-8.

33. Todd KH, Funk KG, Funk JP, Bonacci R. Clinical significance of reported changes in pain severity. Annals of Emergencey Medicine. 1996;27:485-9.

34. Kelly AM. The minimum clinically significant difference in visual analogue scale pain score does not differ with severity of pain. EMERGENCY MEDICINE JOURNAL. 2001;18(3):205-7.

35. Akaishi S, Ogawa R, Hyakusoku H. Keloid and hypertrophic scar: neurogenic inflammation hypotheses. Med Hypotheses. 2008;71(1):32-8.

36. Rosa AC, Fantozzi R. The role of histamine in neurogenic inflammation. British Journal of Pharmacology. 2013;170(1):38-45.

37. Kim KY, Kim J, Tsai AWW, Hsing WT. Acupuncture for the Treatment of Itch: Literature Review and Future Perspectives. Med Acupunct. 2021;33(2):137-43.

38. Langevin HM, Bouffard NA, Badger GJ, Churchill DL. Active connective tissue fibroblast response to acupuncture. Journal of Alternative & Complementary Medicine. 2006;12(2):208-9.

39. Langevin HM, Bouffard NA, Fox JR, Palmer BM, Wu J, Iatridis JC, et al. Fibroblast cytoskeletal remodeling contributes to connective tissue tension. Journal of cellular physiology. 2011;226(5):1166-75.

40. Langevin HM, Konofagou EE, Badger GJ, Churchill DL, Fox JR, Ophir J, et al. Tissue displacements during acupuncture using ultrasound elastography techniques. Ultrasound In Medicine & Biology. 2004;30(9):1173-83.

41. Rowen D, Brazier J, Roberts J. Mapping SF-36 onto the EQ-5D index: how reliable is the relationship? Health and Quality of Life Outcomes. 2009;7.

Chapter 5 – Pilot Study – Feasibility Testing of the Randomised Clinical Trial Protocol

Concurrent to the case study reported in Chapter 4, a pilot study was completed to test the randomised study protocol reported in Chapter 3. The aim of a pilot or feasibility study is to assess recruitment potential and process, assess the safety of a treatment intervention and to evaluate the treatment intervention and study design prior to use in a larger trial (Eldridge et al., 2016; Thabane et al., 2010).

Aim

To assess the feasibility of the treatment protocol in participants with surgical scars and to compare scar outcomes for local versus distant acupuncture treatment.

Methods

The detailed methodology for this pilot study is presented in Chapter 3 of this thesis.

Results

Participant demographics

Following enrolment into the study nine participants were randomly allocated to the local treatment group and six to the distant group (includes one drop-out). A random allocation sequence for 86 participants was created by a physiotherapy student, using an online random number generator. Random allocation was via numbered envelopes opened in order of enrolment into the study, hence there was uneven allocation between treatment groups. Scar age ranged from six weeks to 12 months. Most participants had post-surgical scars, one had fallen and received stitches, two had caesarean-sections and two had knee joint replacements. Six had had skin cancers or lipomas removed, two were following wrist surgery and two after lower limb surgery (compartment syndrome and Achilles repair). Most participants attended for treatment at the UNDA School of Physiotherapy (n=10), the remainder attended at the workplace of the researcher (n=5). Fourteen participants completed at least five of the six sessions of treatment. One participant did not complete treatment and withdrew from the study due to family and work commitments after attending the initial treatment session.

Table 8. *Participant details*

Group A (Local)	Group B (distant)
n=9 (4 males, 5 females)	n=6 (6 females)
Age range: 33-78 (mean:51.6years)	Age range: 20-72 (mean:44.2years)
All completed at least 5/6 sessions	5 completed at least 5/6 sessions, 1 drop out after 1 session – time/family reasons
Number of needles used, range:3-20 mean: 8.3	Number of needles used, range: 5-14 mean: 8.2
Scar age: 2-12 months, mean: 6.6 months	Scar age 6 weeks to 10 months, mean: 7.75 months
Location of needles/scar upper limb (n=2), lower limb (n=2), torso (n=4), face (n=1)	Location of needles upper body points (n=3), lower body points (n=3)

n – number of participants

Treatment intervention

Following completion of outcome measures at each session, participants received five minutes of scar massage followed by acupuncture applied either locally around the scar, or to distant points with no neuroanatomical links to the scar. The number of needles used was based on placing needles at 2cm intervals around the scar circumference (i.e., linear scar circumference = 2x length), with a maximum of 20 needles used per participant. Following needle insertion, needles were stimulated manually three times over the 15 minute treatment, via bi-directional rotation of the needle shaft until moderate needling sensation (deqi) was felt by the participant.

Group A – Local

Acupuncture needles were inserted as close as possible to the scar border, angled to aim the point of the needle underneath the scar tissue.

Group B – Distant

Acupuncture treatment was applied with the participant lying prone as all needles were placed on the dorsal surface of the trunk and limbs. Needle location was in the opposite half of the body to the scar as per the study protocol in Chapter 3. Three participants with scars below the umbilicus (includes one drop-out) received acupuncture in the upper limb and cervicothoracic region, the remaining three participants with scars above the umbilicus received acupuncture in the lower limbs and lumbar region.

Safety of treatment – Adverse events

There were no significant or serious adverse events requiring medical attention over this series of treatment. Patients were provided with an information sheet (Appendix 2) advising them that it is normal to experience increased symptoms following treatment, however, these should settle within 24 hours. They were advised to contact the researcher if they had any concerns, or if they experienced any unexpected symptoms (not listed on the information sheet). One participant in the local treatment group noted tenderness during scar massage at her first session, during her second session she reported that her scar was sensitive, but massage was tolerable. In this same participant, one needle was moved due to sensitivity during one treatment. A further five patients in the local acupuncture group (this included both patients with knee joint replacements) reported an increase in symptoms (pain and/or itch) for up to 12 hours post-treatment. One patient in the distant group noted scar pain following treatment (for less than 12 hours) and one patient in the distant group reported a small bruise at a needle site following treatment which had disappeared before her next treatment session. No participant required medical attention for adverse events over the study period.

Outcomes

Participants completed a NRS for pain and for itch at the beginning of every treatment session, the results of which are provided in Appendix 9. The POSAS, patient response component was completed at baseline (prior to receiving the first treatment), midway (fourth session), final session and at one- and two-months follow-up after treatment cessation. The SF-36 (health-related quality of life measure) was completed at baseline, final session and one- and two-months follow-up. The treating therapist was blinded to outcomes throughout the study, however, did collect data on adverse events.

The NRS measured pain and itch levels over the preceding 24 hours. The local acupuncture group had an average (mean) pain level of 2.5/10 at baseline, which improved to 1.6/10 (36% improvement) at their final treatment session four weeks later. In comparison the distant acupuncture group had an initial pain rating of 1.6/10 which improved to 1/10 (38% improvement) at their final treatment session. Concurrently, NRS measurements for itch reduced from and average (mean) 4/10 at

baseline to 1.4/10 (65% improvement) after four weeks of treatment for the local acupuncture group, and from an average (mean) 4.3/10 to 1.2/10 (72% improvement) for the distant acupuncture group.

The POSAS asked participants to rate their pain and itch over the preceding two weeks. Baseline average (mean) POSAS scores for pain were 3.7/10 for the local acupuncture group and reduced to 2.1/10 (43% improvement) at the final treatment. The average (mean) pain scores were 3.6/10 for the distant acupuncture group at baseline and 1.5/10 (58% improvement) at the final treatment. Concurrently, average (mean) itch scores on POSAS reduced from 3.8/10 to 2.8/10 (26% improvement) for the local acupuncture group, and 6/10 to 1.75/10 (71% improvement) for the distant acupuncture group.

Follow up POSAS questionnaires were returned by five participants in the local acupuncture group rating average (mean) pain as 1.8/10 and 1.6/10 and average (mean) itch as 2.6/10 and 2.4/10 at one and two months following treatment completion. In the same period, four participants in the distant acupuncture group reported average (mean) pain scores as 1/10 and 1.25/10, and average (mean) itch scores as 1.25/10 and 1.5/10.

The POSAS also measures scar physical characteristics of colour, stiffness, thickness, and irregularity. The local acupuncture group had an average (mean) combined score of 7.8/10 at baseline which improved 28% to 5.6/10 at their final treatment. In comparison the distant acupuncture group had a combined average (mean) score of 7.1/10 at baseline which improved 41% to 4.2/10 at the final treatment session. At one- and two-months follow-up after the final treatment session the local acupuncture group who returned questionnaires (n=5) had a combined average (mean) score of 7/10 and 7/10 respectively, which was an 11% improvement from baseline but had regressed compared to their final session. In comparison the distant acupuncture group (n=4) scored 3.2/10 and 3.3/10 respectively, which was a further 15% improvement from final treatment scores and a 55% improvement from baseline.

Finally, the participants gave their scar an overall rating on POSAS which at baseline was 7.8/10 for the local acupuncture group and 7.6/10 for the distant acupuncture group. At the final treatment, the local acupuncture group rated their scar as 6/10 (23%

improvement), and the distant acupuncture group rated theirs as 4.2/10 (45% improvement). As with the scar physical characteristics the local acupuncture group did not report continued improvements at one- and two-months following treatment cessation and rated their scar as 7.2/10 and 7.4/10 (5% improvement from baseline). The distant acupuncture group showed continued improvement of 3.5/10 and 3/10 (60% improvement from baseline). However, with only 55% of the local group providing completed follow-up questionnaires compared to 80% of the distant group, these results should be interpreted with caution.

The tables below give outcomes taken at baseline, the final treatment session and at one and two months post-treatment. Two participants who did not attend their final treatment have NRS scores included from their fifth treatment (three weeks from baseline) instead. Results from participant #3 are not included as they did not attend following their initial appointment. Full results for each participant are included in Appendix 9.

Table 9. *Pain rating on POSAS and NRS*

Participant # and group **Local/**Distant	Number of Needles per treatment	Pain (baseline) NRS	Pain (Final Treatment – 4 weeks later) NRS (compared to baseline)	Pain (baseline) POSAS	Pain (Final Treatment – 4 weeks later) POSAS, (compared to baseline)	Pain Follow-up scores (POSAS) 1 month, 2 months (compared to final treatment)
#2	20	7	8 (↑1)	8	6 (↓2)	n/c
#5	12	0	0=	0	1 (↑1)	1=,1 =
#7	3	1	0(↓1)	6	1 (↓5)	2 (↑1),1=
#8	4	1	2 (↑1)	2	2=	1 (↓1) ,2=
#10	3	4	3 (↓1)	4	3 (↓1)	4 (↑1),3=
#11	3	1	0 (↓1)	2	2=	n/c
#13	20	8	1 (↓7)	8	1 (↓7)	1=,1=
#14	3	0	1 (↑1) (5th session)	1	n/c	n/c
#15	7	1	0 (↓1)	2	1 (↓1)	n/c
#1	10	6	0 (↓6)	7	2 (↓5)	1 (↓1), 2 =
#4	7	0	2 (↑2) (5th session)	2	n/c	1(1↓), 1(↓1)
#6	8	2	2=	4	2 (↓2)	1 (↓1),1 (↓1)
#9	5	0	1 (↑1)	2	1 (↓1)	1=,1=
#12	5	0	0=	3	1 (↓2)	n/c

NRS – numerical rating scale, POSAS – patient and observer scar assessment scale (patient response component), n/c – not completed, ↓ score reduced (improved), ↑ score increased (worsened), = no change in score

Table 10. *Itch rating on POSAS and NRS*

Participant # and group **Local**/Distant	Number of Needles per treatment	Itch (baseline) NRS	Itch (Final Treatment – 4 weeks) NRS (compared to baseline)	Itch (baseline) POSAS	Itch (Final Treatment – 4 weeks) POSAS (compared to baseline)	Itch Follow-up scores (POSAS) 1 month, 2 months (compared to final treatment)
#2	20	7	8 (↑1)	8	6 (↓2)	n/c
#5	12	5	0 (↓5)	6	5 (↓1)	5=,3 (↓2)
#7	3	0	0=	1	1=	1=, 2 (↑1)
#8	4	3	0 (↓3)	3	2 (↓1)	1 (↓1), 2=
#10	3	5	2 (↓3)	5	2 (↓3)	5 (↑3),4 (↑2),
#11	3	6	0 (↓6)	7	2 (↓5)	n/c
#13	20	4	2 (↓2)	3	2 (↓1)	1 (↓1), 1 (↓1)
#14	3	2	1 (↓1) (5^{th} session)	2	n/c	n/c
#15	7	4	0 (↓4)	4	2 (↓2)	n/c
#1	10	3	0(↓1)	5	2 (↓3)	2=,1 (↓1)
#4	7	1	2 (↑1) (5^{th} session)	4	n/c	1 (↓3),1 (↓3)
#6	8	6	2 (↓4)	8	2 (↓6)	1 (↓1), 3 (↑1)
#9	5	4	1 (↓3)	6	1 (↓5)	1=,1=
#12	5	5	1 (↓4)	7	2 (↓5)	n/c

NRS – numerical rating scale, POSAS – patient and observer scar assessment scale (patient response component), n/c – not completed, ↓ score reduced (improved), ↑ score increased (worsened), = no change in score

Table 11. *Scar physical characteristics as measured by the POSAS self-reported component*

Participant # and group **Local**/Distant	Number of Needles per treatment	Physical Characteristics (POSAS) Baseline	Physical Characteristics (POSAS) Final Treatment – 4 weeks) (Compared to baseline)	Physical Characteristics (POSAS) Follow-up 1 month, 2 months (Compared to final treatment)
#2	20	Colour - 10 Stiffness - 7 Thickness - 10 Irregularity - 10 Overall -10	Colour – 7 (↓3) Stiffness – 7= Thickness – 10= Irregularity – 10= Overall – 8 (↓2)	n/c
#5	12	Colour - 9 Stiffness - 9 Thickness - 9 Irregularity - 9 Overall - 9	Colour – 8 (↓1) Stiffness – 8 (↓1) Thickness – 8 (↓1) Irregularity – 8 (↓1) Overall – 9=	Colour – 8=, 8= Stiffness – 8=,8= Thickness – 9 (↑1),8= Irregularity – 9(↑1),8= Overall – 9=,8 (↓1)
#7	3	Colour - 10 Stiffness - 10 Thickness - 10 Irregularity - 10 Overall - 10	Colour – 3 (↓7) Stiffness – 4 (↓6) Thickness – 5 (↓5) Irregularity – 4 (↓6) Overall – 4 (↓6)	Colour – 3=, 3= Stiffness – 3 (↓1), 3 (↓1) Thickness – 3 (↓2), 3 (↓2) Irregularity – 3 (↓1), 3 (↓1) Overall – 3 (↓1), 5 (↑1)
#8	4	Colour - 10 Stiffness - 10 Thickness - 10 Irregularity - 10 Overall - 10	Colour – 7 (↓3) Stiffness – 7 (↓3) Thickness – 7 (↓3) Irregularity – 7 (↓3) Overall – 7 (↓3)	Colour – 10 (↑3),10 (↑3) Stiffness – 10 (↑3),10 (↑3) Thickness – 10 (↑3),10 (↑3) Irregularity – 10 (↑3),10 (↑3) Overall – 10 (↑3),10 (↑3)
#10	3	Colour - 2 Stiffness - 9 Thickness - 9 Irregularity - 8 Overall - 8	Colour – 1 (↓1) Stiffness – 4 (↓5) Thickness – 4 (↓5) Irregularity – 4 (↓4) Overall – 5 (↓3)	Colour – 3 (↑2), 2 (↑1) Stiffness – 4=, 4= Thickness – 4=, 5 (↑1) Irregularity – 4=, 4= Overall – 4 (↓1), 5=
#11	3	Colour - 8	Colour – 3 (↓5)	n/c

		Stiffness - 10 Thickness - 10 Irregularity - 10 Overall - 10	Stiffness – 3 (↓7) Thickness – 5 (↓5) Irregularity – 5 (↓5) Overall – 4 (↓6)	
#13	20	Colour - 10 Stiffness - 10 Thickness - 10 Irregularity - 10 Overall - 10	Colour – 10= Stiffness – 8 (↓2) Thickness – 8 (↓2) Irregularity – 9 (↓1) Overall – 9 (↓1)	Colour – 10=,10= Stiffness – 10 (↑2), 10 (↑2) Thickness – 10(↑2),10 (↑2) Irregularity – 10 (↑1),10(↑1) Overall – 10(↑1), 9=
#14	3	Colour - 5 Stiffness - 2 Thickness - 5 Irregularity - 5 Overall - 2	n/c	n/c
#15	7	Colour - 1 Stiffness - 1 Thickness - 1 Irregularity - 1 Overall - 1	Colour – 1= Stiffness – 1= Thickness – 1= Irregularity – 2 (↑1) Overall – 2 (↑1)	n/c
#1	10	Colour - 5 Stiffness - 5 Thickness - 7 Irregularity - 7 Overall - 7	Colour – 3 (↓2) Stiffness – 2 (↓3) Thickness – 2 (↓5) Irregularity – 2 (↓5) Overall – 3 (↓4)	Colour – 2 (↓1), 2 (↓1) Stiffness – 1 (↓1), 1 (↓1) Thickness – 1 (↓1),1 (↓1) Irregularity – 2=, 2= Overall – 3=, 2 (↓1)
#4	7	Colour - 8 Stiffness - 7 Thickness - 7 Irregularity - 6 Overall - 7	n/c	Colour – 3 (↓5), 4 (↓4) Stiffness – 2 (↓5), 4 (↓3) Thickness – 1 (↓6), 4 (↓3) Irregularity – 2 (↓4), 4 (↓4) Overall – 3 (↓4), 4 (↓3)
#6	8	Colour - 8 Stiffness - 10 Thickness - 10	Colour – 4 (↓4) Stiffness – 4 (↓6) Thickness – 4 (↓6)	Colour – 3 (↓1), 5 (↑1) Stiffness – 4 =,3 (↓1) Thickness – 5 (↑1),5 (↑1)

		Irregularity - 10 Overall - 10	Irregularity – 4 (↓6) Overall – 4 (↓6)	Irregularity – 4 =,5 (↑1) Overall – 3 (↓1), 4=
#9	5	Colour - 4 Stiffness - 6 Thickness - 6 Irregularity - 6 Overall - 6	Colour – 1 (↓3) Stiffness – 2 (↓4) Thickness – 2 (↓4) Irregularity – 2 (↓4) Overall – 2 (↓4)	Colour – 1=, 1= Stiffness – 5 (↑3), 3 (↑1) Thickness – 6 (↑4), 5 (↑3) Irregularity – 6 (↑4), 3 (↑1) Overall – 5 (↑3), 2=
#12	5	Colour - 10 Stiffness - 4 Thickness - 8 Irregularity - 8 Overall - 8	Colour – 10 = Stiffness – 5 (↑1) Thickness – 10 (↑2) Irregularity – 10 (↑2) Overall – 10 (↑2)	n/c

POSAS – patient and observer scar assessment scale (patient response component), n/c – not completed, ↓ score reduced (improved), ↑ score increased (worsened), = no change in score

Table 12. *Quality of life – SF-36*

Participant # and group **Local**/Distant	Baseline **Above norm** *Below norm*	Final Treatment Compared to baseline	1 month Follow-up Compared to baseline	2 months Follow-up Compared to baseline	Age related Norms
#2 L	*PF- 25* *RF- 18.8* *BP- 10* *GH- 50* *V- 50* *SF- 25* **RE- 100** MH- 84	PF- 65 RF- 25 BP- 90 GH- 65 V- 20 SF- 25 RE- 100 MH- 72	n/c	n/c	PF- 90.9 RF- 85 BP- 76.8 GH- 76.6 V- 64.9 SF- 91.9 RE- 92.2 MH- 82.3
#5 L	**PF- 100** **RF- 100** **BP- 100** **GH- 95** **V- 65** SF- 87.5 **RE- 100** *MH- 64*	PF- 100 RF- 100 BP- 100 GH- 95 V- 65 SF- 87.5 RE- 100 MH- 64	PF- 100 RF- 100 BP- 100 GH- 95 V- 35 SF- 75 RE- 83.3 MH- 56	PF- 100 RF- 25 BP- 67.5 GH- 65 V- 35 SF- 25 RE- 50 MH- 48	PF- 92.3 RF- 80.4 BP- 79.6 GH- 78.7 V- 58.7 SF- 89.2 RE- 85.6 MH- 77.3
#7 L	**PF- 100** **RF- 100** BP- 90 GH- 80 **V- 70** **SF- 100** **RE- 100** **MH- 84**	PF- 100 RF- 100 BP- 90 GH- 80 V- 70 SF- 100 RE- 100 MH- 80	PF- 100 RF- 100 BP- 90 GH- 80 V- 75 SF- 100 RE- 100 MH- 80	PF- 100 RF- 100 BP- 100 GH- 80 V- 80 SF- 100 RE- 100 MH- 80	PF- 95.2 RF- 89.3 BP- 91.9 GH- 78.9 V- 65.4 SF- 93.8 RE- 91.7 MH- 81.2
#8 L	PF- 80 **RF- 87.5**	PF- 75 RF- 75	PF- n/c RF- 100	PF-95 RF- 100	PF- 80.3 RF- 77.8

	BP- 80 *GH- 35* **V- 70** **SF- 100** **RE- 100** MH- 80	BP- 57.5 GH- 40 V- 70 SF- 75 RE- 100 MH- 76	BP- 90 GH- n/c V- 60 SF- 100 RE- 100 MH- 64	BP- 90 GH- 60 V- 60 SF- 100 RE- 100 MH- 80	BP- 71.5 GH- 73.4 V- 61.4 SF- 90 RE- 88 MH- 80.8
#10 L	**PF- 100** RF- 87.5 BP- 77.5 **GH- 90** *V- 55* *SF- 87.5* **RE- 100** MH- 80	PF- 100 RF- 93.8 BP- 90 GH- 95 V- 70 SF- 100 RE- 100 MH- 80	PF- 100 RF- 100 BP- 90 GH- 90 V- 80 SF- 87.5 RE- 100 MH- 80	PF- 100 RF- 93.8 BP- 90 GH- 90 V- 80 SF- 100 RE- 100 MH- 80	PF- 90.9 RF- 85 BP- 76.8 GH- 76.6 V- 64.9 SF- 91.9 RE- 92.2 MH- 82.3
#11 L	**PF- 90** **RF- 100** **BP- 80** **GH- 85** **V- 70** **SF- 100** **RE- 100** *MH- 68*	PF- 90 RF- 100 BP- 80 GH- 70 V- 75 SF- 100 RE- 100 MH- 72	n/c	n/c	PF- 80.3 RF- 77.8 BP- 71.5 GH- 73.4 V- 61.4 SF- 90 RE- 88 MH- 80.8
#13 L	*PF- 40* *RF- 50* *BP- 67.5* **GH- 80** **V- 70** **SF- 100** **RE- 100** MH- 80	PF- 55 RF- 75 BP- 55 GH- 85 V- 70 SF- 87.5 RE- 100 MH- 80	PF- 45↓ RF- 68.8 BP- 55 GH- 85 V- 70 SF- 87.5 RE- 100 MH- 80	PF- 70 RF- 87.5 BP- 77.5 GH- 90 V- 75 SF- 100 RE- 100 MH- 80	PF- 58.2 RF- 67.1 BP- 73.1 GH- 71.2 V- 56.7 SF- 87.9 RE- 91.7 MH- 81.9
#14 L	**PF- 90** **RF- 68.8**	n/c	n/c	n/c	PF- 85.6 RF- 79.1

	BP- 100 **GH- 85** **V- 70** **SF- 100** **RE- 100** **MH- 84**				BP- 73.3 GH- 75.6 V- 59.5 SF- 88.9 RE- 85.2 MH-78.9
#15 L	**PF- 85** *RF- 68.8* *BP- 32.5* **GH- 75** *V- 45* *SF- 62.5* **RE- 100** *MH- 56*	PF- 90 RF- 81.3 BP- 90 GH- 75 V- 65 SF- 100 RE- 100 MH- 72	n/c	n/c	PF- 80.6 RF- 77.9 BP- 78.1 GH- 70.7 V- 65.1 SF- 93.7 RE- 94.2 MH- 85.6
#1 D	*PF- 80* RF- 81.3 *BP- 67.5* **GH- 80** *V- 45* **SF- 100** **RE- 91.7** *MH- 72*	PF- 65 RF- 25 BP- 90 GH- 65 V- 20 SF- 25 RE- 100 MH- 72	PF- 95 RF- 93.7 BP- 77.5 GH- 60 V- 50 SF- 100 RE- 100 MH- 76	PF- 85 RF- 75 BP- 77.5 GH- 55 V- 55 SF- 100 RE-100–MH - 100	PF- 90.8 RF- 80.5 BP- 76.4 GH- 77.7 V- 59.9 SF- 88.3 RE- 86.1 MH- 77.6
#4 D	PF- 95 *RF- 43.8* *BP- 35* *GH- 65* **V- 65** *SF- 37.5* **RE- 91.7** *MH- 68*	n/c	PF- 100 RF- 100 BP- 90 GH- 75 V- 70 SF- 50 RE- 83.3 MH- 60↓	PF- 100 RF- 100 BP- 100 GH- 85 V- 85 SF- 75 RE- 100 MH- 80	PF- 93.2 RF- 79.2 BP- 77.2 GH- 73.3 V- 58.5 SF- 84.2 RE- 81.8 MH- 75.6
#6 D	*PF-20* **RF- 100**	PF- 95 RF- 100	PF- 95 RF- 100	PF- 10 RF- 0	PF- 85.6 RF- 79.1

	BP- 67.5 **GH- 80** *V- 55* **SF- 100** **RE- 100** MH- 76	BP- 100 GH- 75 V- 55 SF- 100 RE- 100 MH- 76	BP- 100 GH- 80 V- 60 SF- 100 RE- 100 MH- 80	BP- 0 GH- 35 V- 45 SF- 62.5 RE- 100 MH- 84	BP- 73.3 GH- 75.6 V- 59.5 SF- 88.9 RE- 85.2 MH-78.9
#9 D	**PF- 85** **RF- 87.5** *BP- 67.5* *GH- 55* *V- 50* SF- 87.5 **RE- 100** *MH- 68*	PF- 85 RF- 93.8 BP- 57.5 GH- 65 V- 50 SF- 100 RE- 91.7 MH- 64	PF- 85 RF- 75 BP- 55 GH- 60 V- 45 SF- 100 RE- 100 MH- 60	PF- 90 RF- 93.8 BP- 90 GH- 45 V- 40 SF- 100 RE- 100 MH- 68	PF- 73.3 RF- 71.6 BP- 72 GH- 70.6 V- 59.6 SF- 88.9 RE- 84.8 MH- 80.4
#12 D	**PF- 100** **RF- 100** *BP- 67.5* **GH- 80** *V- 55* *SF- 75* **RE- 100** *MH- 60*	PF- 100 RF- 100 BP- 67.5 GH- 95 V- 55 SF- 100 RE- 100 MH- 60	n/c	n/c	PF- 85.6 RF- 79.1 BP- 73.3 GH- 75.6 V- 59.5 SF- 88.9 RE- 85.2 MH-78.9

Physical Function (PF), Role Physical (RF), Bodily Pain (BP), General Health (GH), Vitality (V), Social function (SF), Role Emotional (RE), Mental Health (MH), n/c – not completed, score increased (improved), score decreased (worsened),

Acupuncture Dosage

Participants received 3-20 needles per acupuncture treatment. The number of needles plus retention time constitutes acupuncture dosage and may influence outcomes via the amount of input into the central nervous system (i.e. greater number of needles provides a higher acupuncture dosage per treatment). Table 13 shows the percentage change in symptoms for pain and itch for low dose (three to six needles), medium dose (7-11 needles) and high dose (12-20 needles). The greatest response for both pain and itch was seen in participants receiving between seven and 11 acupuncture needles each treatment.

Table 13. *The influence of acupuncture dosage on pain and itch regardless of needle location*

Number of Needles	Pain (NRS)	Pain (POSAS)	Itch (NRS)	Itch (POSAS)
Low dose 3-6 (n=7)	No change	**41% decrease**	**80% decrease**	**61% decrease**
Medium dose 7-11 (n=4)	**55% decrease**	**55% decrease**	**71% decrease**	**62% decrease**
High dose 12-20 (n=3)	**40% decrease**	**49% decrease**	**38% decrease**	**23% decrease**

NRS – numerical rating scale, POSAS – patient and observer scar assessment scale (patient response component), n – number, decrease =improvement in symptoms

Discussion

Recruitment

Recruitment of sufficient participant numbers proved to be more challenging than anticipated. Although flyers and letters were distributed to local General Practitioner clinics, only one participant was referred as a result and his results were published as a separate case study (Chapter 4). Flyers placed around the University of Notre Dame were effective, as was an article published in a local Fremantle newsletter. However, although the newspaper article and paid advertisements stimulated enquiry, few respondents met inclusion criteria. Clients treated at either of the private physiotherapy clinics were either previous clients of the researcher or referred by colleagues. In order to increase participant numbers, additional treatment providers at other locations were approached to create a multi-centre trial. Additional treating therapists and locations received ethics approval by The University of Notre Dame Australia, Fremantle Ethics committee. These included a therapist in Melbourne

known to the researcher (who withdrew to family commitments prior to commencing recruitment) and a New Zealand-based therapist who was unable to obtain approval to provide treatment at her workplace.

Randomisation

Due to the initial goal of 86 participants, random number allocation was completed for the entire cohort, which due to low participant numbers, led to uneven numbers in each treatment group. In hindsight, block randomisation in groups of 10 would have prevented the group size discrepancy seen in this case series and been a more suitable type of randomisation.

Outcome measures

Both the NRS and POSAS were used as subjective measures of pain and itch. The POSAS also provided (self-reported) outcomes on physical scar characteristics, however this study lacked any objective scar measures which would be of benefit in future studies. DeJong et al. (2017) found the POSAS measures three independent dimensions of the patients' perception of the entire scar. These include a) the physical scar, b) pain and c) itch. The SF-36 was found to be time-consuming and complex, as noted in the discussion in Chapter 4 (case-study). The shorter EQ5D-5L is recommended and could be substituted for the SF-36 without affecting outcomes in participants without severe health conditions (Rowen, et al., 2009).

Compliance for completing outcome measures was high (100%) throughout the treatment series, however completion of follow-up (not completed in clinic) questionnaires proved inadequate. Only nine of fourteen (60%) of participants who completed the intervention protocol returned one and two month post-intervention outcome measures. Participants were advised of the follow-up questionnaires on enrolment to the study and asked their preference for providing outcomes (i.e., email or post). Follow-up questionnaires were either provided to participants along with a stamped envelope at their final treatment session or emailed to them a week prior to the due date. Non-respondents were contacted via email and phone/SMS to request a response, however 40% of participants did not respond. In future studies, use of electronic questionnaires and the shortened quality of life questionnaire should be

tested to improve adherence. Additionally follow-up could be limited to one follow-up questionnaire six weeks after the final treatment session to improve adherence.

Treatment intervention

Treatment was well tolerated with some participants experiencing short-term symptom aggravation post-treatment. A subgroup of participants (n=5) with high initial scores for both pain and itch (score of four or higher on NRS/POSAS) were identified as potentially hypersensitive (Table 13). Participants in this subgroup who received local treatment (n=3), reported mild-moderate (increase of 1-3/10 on NRS) post-treatment soreness (lasting less than 12 hours) after several treatment sessions, whereas only one participant who received distant acupuncture in this subgroup experienced one episode of mild (increase of 1/10 on NRS) post-treatment soreness. All participants in this subgroup had reduced symptoms at their final session as measured by POSAS, however, one reported a higher NRS score for both pain and itch, (participant outcomes for NRS at each session are included in Appendix 9 and show that this participant's pain/itch fluctuated from session to session). These findings suggest a subgroup of hypersensitive participants who may benefit from protocol modification to apply acupuncture treatment at a distance from the scar tissue to reduce likelihood of post-treatment soreness. In these participants who appear to have peripheral or central sensitisation, acupuncture treatment may be best applied extra-segmentally to reduce the occurrence of post-treatment soreness.

Table 14. *Participants identified as hypersensitive – Baseline score of 4 or higher on either POSAS or NRS for both pain and itch (excerpts from Table 9 & 10).*

Participant #, **L**/D, age of scar	Baseline scores Pain	Final Treatment Scores Pain	Baseline scores Itch	Final treatment score Itch
#13, **L**, 3 months	NRS = 8 POSAS = 8	NRS =1 POSAS = 1	NRS = 4 POSAS = 3	NRS = 2 POSAS = 2
# 10, **L**, 4 months	NRS = 4 POSAS = 4	NRS = 3 POSAS = 3	NRS = 5 POSAS = 5	NRS = 2 POSAS = 2
# 2, **L**, 5 months	NRS = 7 POSAS = 8	NRS = 8 POSAS = 6	NRS = 7 POSAS = 8	NRS = 8 POSAS = 6
#1, D, 8 months	NRS = 6 POSAS = 7	NRS = 0 POSAS = 2	NRS = 3 POSAS = 5	NRS = 0 POSAS = 2
#6, D, 10 months	NRS = 2 POSAS = 4	NRS = 2 POSAS = 2	NRS = 6 POSAS = 8	NRS = 2 POSAS = 2

L- local, D – distant, NRS – numerical rating scale, POSAS – patient and observer scar assessment scale (patient response component)

Local compared to distant acupuncture

Distant acupuncture was never considered by the research team to be an inert control intervention, especially as the same amount of needle manipulation and neuro-inflammatory stimulation was applied in both groups. Instead, the researchers hypothesised that local intervention would influence scar symptoms and physical characteristics via activation of local sensory nerve fibres and through direct connective tissue stimulation. As previously stated, research has shown that connective tissue winding that occurs during needle manipulation causes cytoskeletal remodelling of fibroblasts (Langevin et al., 2007) and that this involved ATP signalling (Langevin et al., 2013), but the therapeutic implications of this were unknown at the time. Hence, the hypothesis for this study, that local acupuncture may have an effect on the physical characteristics of scars via stimulation of local collagen fibres. The past few years have seen progression of research and understanding of needling-related acupuncture mechanisms, particularly in relation to the role of mast cells and histamine in acupuncture analgesia (Perreault et al., 2019). It has been confirmed that rotation of an acupuncture needle creates winding of connective tissue fibres, stimulating release of ATP from fibroblasts, keratinocytes, and mast cells (Perreault et al., 2019). This results in the release of endogenous opioids (enkephalin and beta-endorphin) at the spinal segmental level within the dorsal horn, that act to modulate nociceptive impulses (Baeumler et al., 2014). Additionally, mast cells have been identified as a key ingredient in acupuncture analgesia via the release of ATP, adenosine and histamine, and activation of A1 and H1 receptors (Huang et al., 2018). Some C-fibres contain H1 receptors and are activated by histamine, relaying sensory information from the periphery to the central nervous system (Perreault et al., 2019). Signals project along histaminergic fibres within the spinothalamic tract to supraspinal centres (including various areas within the brainstem (i.e., PAG), and hypothalamus) (Perreault et al., 2019). Histamine interacts with local neurons to trigger descending pain inhibitory mechanisms including the noradrenergic and serotonergic systems (Perreault et al., 2019). Hence, it could be postulated that both types of acupuncture used in this study provided sufficient stimulation of local mast cells to release histamine and therefore stimulate the central nervous system descending inhibitory mechanisms for pain and itch (Perreault et al., 2019).

Further conjecture to explain the distant acupuncture group results favouring the local acupuncture group in NRS and POSAS, could be linked to the neuro-antiflammatory effects of acupuncture via the autonomic nervous system (Jin et al., 2019; Trento et al., 2021). Downregulation of inflammatory cytokines and macrophages, with upregulation if anti-inflammatory cytokines such as IL10 and their precursor; the M2 macrophage, has been demonstrated with acupuncture to autonomically innervated acupoints such as ST36, SP6, GB30, GV6, GV9 (da Silva et al., 2015; Johnston & Webster, 2009; Pannell et al., 2016; Tracey, 2002; Wang et al., 2021). In both (upper body and lower body) distant acupuncture protocols the stimulation of the sympathetic and parasympathetic autonomic pathways could have been modulated with needling in the posterior leg and calf or the upper thoracic sympathetic outflow (Marieb & Hoehn, 2016). Additionally, humoral beta-endorphin and adrenocortiocotrophic (ATCH) hormone release is systemic via axes such as via the hypothalamic-pituitary-adrenal axis (Ulloa et al., 2017). Likewise, the cortico-trophic-factor (CRF) proopiomelanocortin corticosteroid axis in dermal fibroblasts produces ACTH and CRF in response to needling, causing corticosterone release from fibroblasts (Butts et al., 2016).

Another factor that remains elusive in acupuncture and dry needling research is how many needles are required and how long should they be left in situ? The protocol devised for this study utlised up to 20 needles per acupuncture treatment (based on scar size), with the needles remaining in situ for 15 minutes after the last needle was inserted. Each needle was stimulated three times over the course of each treatment sesison. Chen et al. (2014) found similar results from protocols using six needles (high dose) and two needles (low dose) during verum acupuncture, with a significant improvement compared to a placebo needle control group ($p=.025$). However, despite using different numbers of needles, this study protocol provided the same overall number of needle manipulations for both groups (i.e. the low dose group had more episodes of needle manipulation than the high dose group) hence the overall dosage was similar (Chen et al., 2014). Hence, it could be postulated that a larger central acupuncture effect occurred with greater numbers of needles inserted (when all individual needles received the same number of manipulations per needle). However, when outcomes were compared for participants based on number of inserted needles; results from the high dose (12-20 needles) group suggest that too

high a dosage becomes less effective, potentially due to overstimulation. All three participants receiving high dosage acupuncture were in the local acupuncture group, and two were identified as hypersensitive. Hence hypersensitivity rather than dosage may have contributed to overstimulation in this subgroup. Butts et al. (2021) found that multiple needles (5-20 depending on the musculoskeletal condition), left in situ for 20-30 minutes produced greater and longer lasting treatment effects than brief, single-needle interventions. Hence for future studies, it is recommended to use 5-20 needles, however, in the case of hypersensitive participants, an upper limit of 15 needles may be used to limit overstimulation.

Both the local and distant acupuncture treatment groups showed improvements in average score for all NRS and POSAS categories, at each time point compared to baseline. The greatest symptom reduction for both groups was reported for itch. The distant acupuncture group reported greater improvement than the local acupuncture group. Due to low numbers and uneven group sizes these findings must be interpreted with caution. However, these findings challenge the initial study hypothesis that local acupuncture would be more beneficial for scar symptoms and physical scar characteristics than distant acupuncture.

Routine care

Routine care consisting of scar massage and general advice was provided to all participants. The aim of scar massage is to reduce scar thickness, improve pliability and reduce symptoms such as pain and itch (Ault et al., 2018). As the treatment aim of scar massage is similar to that of the local acupuncture intervention, outcomes for acupuncture cannot be separated from potential benefits of scar massage. However, compliance with self-management advice was not measured and could therefore confound results. Future studies would benefit from separating massage and acupuncture interventions to compare outcomes and collecting data on adherence to self-massage and exercise advice.

Conclusion

The outcomes of this study supported that the protocol is feasible. However, recommendations have been made for modifications to the treatment groups so that outcomes for the effect of acupuncture for scars can be separated from the effects of massage therapy.

References

Ault, P., Plaza, A., & Paratz, J. (2018, Feb). Scar massage for hypertrophic burns scarring-A systematic review. *Burns, 44*(1), 24-38. https://doi.org/10.1016/j.burns.2017.05.006

Baeumler, P. I., Fleckenstein, J., Takayama, S., Simang, M., Seki, T., & Irnich, D. (2014). Effects of acupuncture on sensory perception: A systematic review and meta-analysis. *PLOS ONE, 9*(12), Article e113731. https://doi.org/10.1371/journal.pone.0113731

Butts, R., Dunning, J., & Serafino, C. (2021). Dry needling strategies for musculoskeletal conditions: Do the number of needles and needle retention time matter? A narrative literature review. *Journal of Bodywork and Movement Therapies, 26*, 353-363. https://doi.org/10.1016/j.jbmt.2020.12.003

Chen, X., Spaeth, R., Retzepi, K., Ott, D., & Kong, J. (2014). Acupuncture modulates cortical thickness and functional connectivity in knee osteoarthritis patients. *Scientific Reports, 4*. https://doi.org/10.1038/srep06482

da Silva, M. D., Bobinski, F., Sato, K. L., Kolker, S. J., Sluka, K. A., & Santos, A. R. S. (2015). IL-10 cytokine released from M2 macrophages is crucial for analgesic and anti-inflammatory effects of acupuncture in a model of inflammatory muscle pain. *Molecular Neurobiology, 51*(1), 19-31. https://doi.org/10.1007/s12035-014-8790-x

DeJong, H., Phillips, M., Edgar, D. W., & Wood, F. M. (2017). Patient opinion of scarring is multidimensional: An investigation of the POSAS with confirmatory factor analysis. *Burns,* 43(1), 56-68. https://doi.org/10.1016/j.burns.2016.06.026.

Eldridge, S. M., Chan, C. L., Campbell, M. J., Bond, C. M., Hopewell, S., Thabane, L., & Lancaster, G. A. (2016). CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *British Medical Journal 355*(i5239). https://doi.org/10.1136/bmj.i5239

Huang, M., Wang, X., Xing, B., Yang, H., Sa, Z., Zhang, D., Yao, W., Yin, N., Xia, Y., & Ding, G. (2018, Apr 25). Critical roles of TRPV2 channels, histamine H1 and

adenosine A1 receptors in the initiation of acupoint signals for acupuncture analgesia. *Sci Rep, 8*(1), 6523. https://doi.org/10.1038/s41598-018-24654-y

Jin, B. X., Jin, L. L., & Jin, G.-Y. (2019). The anti-inflammatory effect of acupuncture and its significance in analgesia. *World Journal of Acupuncture - Moxibustion, 29*(1), 1-6. https://doi.org/10.1016/j.wjam.2019.03.003

Johnston, G. R., & Webster, N. R. (2009). Cytokines and the immunomodulatory function of the vagus nerve. *British Journal of Anaesthesia, 102*(4), 453-462. https://doi.org/10.1093/bja/aep037

Langevin, H. M., Bouffard, N. A., Churchill, D. L., & Badger, G. J. (2007). Connective tissue fibroblast response to acupuncture: Dose dependant effect of bidirectional needle rotation *The Journal of Alternative and Complementary Medicine, 13*(3), 355-360. https://doi.org/10.1089/acm.2007.6351

Langevin, H. M., Fujita, T., Bouffard, N. A., Takano, T., Koptiuch, C., Badger, G. J., & Nedergaard, M. (2013). Fibroblast cytoskeletal remodeling induced by tissue stretch involves ATP signaling. *Journal Of Cellular Physiology, 228*(9), 1922-1926. https://doi.org/10.1002/jcp.24356

Marieb, E. N., & Hoehn, K. (2016). *Human Anatomy and Physiology* (10 ed.). Pearson.

Pannell, M., Labuz, D., Celik, M., Keye, J., Batra, A., Siegmund, B., & Machelska, H. (2016). Adoptive transfer of M2 macrophages reduces neuropathic pain via opioid peptides. *Journal of Neuroinflammation, 13*, 262. https://doi.org/10.1186/s12974-016-0735-z

Perreault, T., Grubb, M. T., Gendron, B. C., Perez-Santiago, J. C., & Flannagan, S. O. (2019). Mechanisms and dose parameters of manual needle stimulation: clinical considerations - Part 2. *Acupuncture in Physiotherapy, 31*(1), 9-23.

Rowen, D., Brazier, J., & Roberts, J. (2009). Mapping SF-36 onto the EQ-5D index: how reliable is the relationship? *Health and Quality of Life Outcomes, 7*. https://doi.org/10.1186/1477-7525-7-27

Thabane, L., Ma, J., Chu, R., Cheng, J., Ismaila, A., Rios, L. P., Robsob, R., Thabane, M., Giangregorio, L., & Goldsmith, C. H. (2010). A tutorial on pilot studies: the what, why and how. *BMC Medical Research Methodology, 10*.

Tracey, K. J. (2002). The inflammatory reflex. *Nature, 420*, 853-859. https://doi.org/10.1038/nature01321

Trento, M. M. S., More, A. O. O., Duarte, E. C. W., & Martins, D. F. (2021, Apr). Peripheral receptors and neuromediators involved in the antihyperalgesic effects of acupuncture: a state-of-the-art review. *Pflugers Archiv, 473*(4), 573-593. https://doi.org/10.1007/s00424-020-02503-0

Ulloa, L., Quiroz-Gonzalez, S., & Torres-Rosas, R. (2017). Nerve stimulation: Immunomodulation and control of inflammation. *Trends In Molecular Medicine, 23*(12), 1103-1120. https://doi.org/10.1016/j.molmed.2017.10.006

Wang, J., Lu, S., Yang, F., Guo, Y., Chen, Z., Yu, N., Yao, L., Huang, J., Fan, W., Xu, Z., & Gong, Y. (2021). The role of macrophage polarization and associated mechanisms in regulating the anti-inflammatory action of acupuncture: a literature review and perspectives. *Chinese Medicine, 16*, 56. https://doi.org/10.1186/s13020-021-00466-7

Chapter 6 – Discussion

On the journey to reach this endpoint, the researcher faced many challenges including juggling full-time employment and study. Changes in personal circumstances included purchase of a business, a first foray into parenthood and finally the impact of the global pandemic which extended and then curtailed the safe access to potential participants and the period of recruitment. The following chapter explores the opportunities to learn from the challenges that contributed to the inability to complete the full clinical trial that was originally planned. In addition, the researcher has added to the body of knowledge and evidence for using acupuncture as part of scar management via two peer-reviewed articles. Over the course of this research program, a comprehensive literature review (Chapter 2) guided the development of an acupuncture intervention protocol for hypertrophic scars (Chapter 3) which was then pilot tested on a participant with burn scarring (Chapter 4). This chapter provides an assimilation and discussion of the safety aspects, outcome measures and treatment adherence for the cases recruited.

Study design

The study protocol that was originally proposed compared the use of local acupuncture plus massage therapy to massage therapy (routine care) for irritable scars in a pragmatic clinical trial design. However, as part of the University of Notre Dame, Australia review and approval process the protocol was modified to include an acupuncture-based control group. It is becoming more and more apparent in the related literature, published prior to, and since this research program commenced, that sham and placebo acupuncture treatments in acupuncture research are not physiologically inert, and thus may lead to results underestimating the effect of acupuncture (Birch et al., 2021; Birch et al., 2022; Ots et al., 2020). The distant acupuncture control group method in this study was designed to avoid any neuroanatomical links to the scar being treated and although it was acknowledged to be an active treatment, it was hypothesised that local and segmental acupuncture effects would not occur, thereby reducing the effectiveness of the intervention. Secondly, as there would be less stimulation to collagen fibres local to the scar, it was hypothesised that participants receiving distant acupuncture may experience less change in scar physical characteristics. However, without an acupuncture only

treatment group, the effect of scar massage on symptoms, or scar physical characteristics cannot be separated from the effect of the acupuncture intervention. Since beginning this research program, acupuncture clinical trials and animal studies have progressed and refined previous knowledge of acupuncture mechanisms. Findings were consolidated and presented in a narrative literature review, highlighting the importance of needle manipulation for producing the analgesic effects of acupuncture (Perreault et al., 2019). Although segmentally applied acupuncture is considered to provide more effective analgesia to the area of pain than extra-segmental acupuncture (Baeumler et al., 2014), sufficient needle manipulation will (regardless of location), stimulate mast cell degranulation and histamine release, leading to activation of supraspinal and descending pain inhibitory mechanisms (Perreault et al., 2019). Furthermore the activation of axes enhancing humoral Beta-endorphin and ACTH release (Ulloa et al., 2017) and anti-inflammatory autonomic nervous system modulation of inflammatory cytokine production (Johnston & Webster, 2009). In this case series, the distant acupuncture group experienced fewer episodes of post-treatment soreness than the local group, whilst showing greater average improvements in outcomes. These findings suggest that extrasegmental acupuncture may be a beneficial treatment option for HTS symptoms. Future study design may benefit from including an acupuncture only group, as well as investigating the combination of acupuncture treatment types (i.e., use of local, segmental, extra-segmental and autonomically innervated acupoints).

Recruitment

Recruiting sufficient participant numbers was the greatest challenge faced during this project. Print media including flyers and newspaper advertisements generated some interest initially, however, this did not generate ongoing inquiries and could not target specific populations. For future study recruitment, the following strategies are recommended in addition or as an adjunct to protocols presented earlier:

- Social Media Campaign – Utilising Facebook, Instagram, and Twitter accounts to generate awareness of the study and provide the opportunity to ask questions via chat. Use monthly paid advertisements on these platforms targeting adults within a 15km radius of the treatment location(s).

- Attract referrals from local surgeons and medical centres – contact local medical providers with information about the study, provide them with print and digital flyers, request them to share via email and social media.
- Print Media – Create and print eye-catching flyers to place in high foot-traffic locations (with permission) such as medical centres, physiotherapy clinics, libraries (public and university), and local community noticeboards.
- Contact local newspapers regarding publishing a story in both print and online newspapers.

Participants and inclusion/exclusion criteria

Scar age greater than 12 months was the only reason potential participants were excluded from the study. As this information was collected during phone or email screening questions and no individual information collected, data was not recorded for the number of participants excluded. Future studies could investigate response rates in participants with scars older than 12 months, as 30% of all post-surgical scars were found to be hypertrophic at 12 months (Mahdavian Delavary et al., 2012).

Pregnant women were excluded from this study, however a recent review of the safety of acupuncture during pregnancy confirmed there was no difference in delivery outcomes (full-term, pre-term and still birth) between those who received acupuncture during pregnancy and those who did not (Moon et al., 2019). McDowell et al. (2019) recommends that acupuncture may be safely used to relieve symptoms such as pelvic girdle pain and lower back pain during the second and third trimester. Certain points are historically considered ‘forbidden’ during pregnancy by acupuncturists as they are used to induce labor or have the risk of penetrating the uterus (McDowell et al., 2019). Hence for future studies, pregnant women may be safely treated with acupuncture after the first trimester, provided the scar of interest is not in the abdominal region and lead maternity carer informed consent is sought in addition to participant consent.

One participant included in this study had high background pain levels from a complicated recovery after knee joint replacement surgery, and may have confounded results. His pain measured by NRS fluctuated between sessions as did his reported joint stiffness and swelling. A second participant who also had knee joint replacement surgery and an uncomplicated recovery, responded similarly to other participants receiving local scar acupuncture. The difference between these two participants was

the underlying joint-related pain, stiffness and inflammation, rather than scar age. These cases highlight the need to screen for other painful conditions in the area of the scar and either exclude them or wait until the other painful condition is resolved prior to enrollment in the scar study.

Adherence to the protocol

Only three patients deviated from protocol and follow up early. One participant dropped out after attending her initial assessment. This participant was returning to work after maternity leave and found it too hard to commit to attending as per the treatment protocol. Two participants did not attend their final treatment session (one was away and informed the researcher, the other did not return for her scheduled appointment), however as per the protocol they were considered to have completed treatment. Treatment reminders were sent via SMS the day before by the researcher. With one exception, this reminder was successful in helping participants comply with the treatment protocol.

There were challenges to scheduling appointments between the two locations which were multi-purpose rooms (i.e., the allocated space at The University of Notre Dame, Australia was the 'simulation lab' used for practical training of physiotherapy students and was only available at certain times). Additionally, the treating therapist worked full-time and had to work around the requirements of her employer. The treatment schedule that was used (totalling six sessions over four weeks) was chosen as it was effective at reducing pain associated with knee osteoarthritis (Chen et al., 2014). Previous acupuncture interventions for scars provided a variable number and frequency of treatment sessions as reported in Chapter 2. Hence this intervention tested the feasibility of the intervention schedule for both adherence and treatment outcomes. In this small sample, 93% of participants (14/15) completed the treatment protocol. Therefore, although treatment frequency and number of sessions are variables that could be manipulated in future studies, this protocol had satisfactory adherence during the active treatment phase.

All participants were taught self-scar massage and given general advice on exercise. There was no data collected about participants baseline exercise level, or

adherence to the self-massage or exercise advise. Considering that massage may have a positive benefit on scars, follow-up data on adherence to self-management strategies would be useful to compare with follow-up questionnaire responses to assess whether this correlates to maintenance of treatment effect over time. Nine out of 14 participants returned their follow-up questionnaires as requested. Potential methods to improve return of follow-up outcome measures includes the use of digital questionnaires and automated reminders.

Outcome measures

Outcome measures used have been supported in the scientific literature and included a numerical rating scale (NRS) for pain and itch, the POSAS (self-assessment component) and SF-36 quality of life questionnaire. Due to the length of the SF-36 and time taken to complete this, we suggest that the EQ5D-5L be substituted in as per discussion in Chapter 4 – published case study.

The POSAS was developed as a subjective outcome measure that has been validated for burn scars (Draaijers et al., 2004) as well as linear scars (van de Kar et al., 2005). Draaijers et al. (2004) reported that itch and scar thickness had the greatest impact on patient observations of burn scars compared to the importance placed on vascularisation, pigmentation, thickness, and skin surface relief by the observer. Patients and observers rate scar characteristics differently, with patients rating their scar as worse than the observer did which in turn influences their quality of life (van de Kar et al., 2005). This difference in patient and observer rating was suggested to be in part due to pain and itch which are invisible to the observer (van de Kar et al., 2005). This was highlighted by the following participant: a 34-year-old female with a caesarean section scar who received local treatment. This scar was just under 12 months old at the start of treatment and was observed to be raised and red by the treating therapist. The participant rated her itch as 5 on the NRS and 6 on POSAS (she reported 0 pain on POSAS and NRS). Over the course of her treatment the researcher/therapist noted changes to the physical appearance of the scar, at the final treatment session one third of the scar had become flattened and light pink and the participant scored a 0 on NRS and 5 on POSAS for itch – 2 months later she scored her itch as 3 on POSAS. Regardless of observations made by the treating researcher/therapist the participant still scored herself at 8 for all physical

characteristics on POSAS (compared to initial score of 9) at her final treatment session. In this study the decision was made not to use the observer part of the scale due to lack of training and experience in scar assessment scales by the researcher/therapist. However, un-trained observers were used in a reliability study of the POSAS for linear scars and found the observer scale was reliable for the total scar score for three observers as well as for a single observer (van de Kar et al., 2005). Thus, future studies would benefit from including a blinded assessor to perform the observer component (if logistically possible) as it has been shown that training and experience of the observer is not essential to achieve reliable measurements.

Control interventions

Massage – routine care

Massage therapy for scar management is a commonly used treatment modality which has low supporting evidence due to poor quality clinical trials, small sample sizes and inconsistent treatment methods (duration, frequency, use of cream and massage techniques) (Anthonissen et al., 2016; Ault et al., 2018; Shin & Bordeaux, 2012). In a review of 10 publications, Shin et al. (2012) found greater efficacy of massage for post-operative scars than traumatic or post-burn scars. They found 90% (27/30 surgical scars) showed improved physical characteristics or POSAS score compared to 45.7% of the total cohort (inclusive of burn or traumatic scars) showing improved outcomes. More recently two systematic reviews reported that massage therapy has a potential positive effect on pain, itch, and scar pliability in burn scars (Anthonissen et al., 2016; Ault et al., 2018). Only one study identified in both these reviews was considered of moderate to high quality. Cho et al. (2014) conducted a randomised controlled trial (RCT) of 146 participants with hypertrophic burn scars, comparing massage therapy combined with standard care, to standard care. A significant improvement in scar pain ($p=.001$) and itch ($p=.04$) were shown for patients receiving massage therapy. Objective measures of scar thickness (via ultrasound), elasticity (using Cutometer SEM 580) and trans-epidermal water loss (TEWL) showed significantly greater improvements ($p=.02$-$.04$) for the massage therapy group. This study had a moderately high level of methodological rigour as assessed by the CONSORT critiquing tool but was let down by lack of clarity on whether both groups received equal amounts of standard care treatment modalities. Therefore, this study and the weight of broadly accepted practice for post-burn scars, provides limited

evidence to support the use of massage therapy in burns and post-surgical scar management. However, outcomes included reduced pain, itch, and scar thickness, which are also targeted by acupuncture treatment.

Over the course of this research program, all participants received the same massage therapy with advice to perform self-massage at home. As massage therapy may help improve scar physical characteristics as well as modulate pain and itch sensations it is impossible to separate effects of acupuncture from massage. Additionally, it is unknown whether patients were compliant with recommended self-massage both during the treatment and follow-up periods, which in future studies a massage diary may contribute to a fuller understanding of treatment effects.

Distant acupuncture

In traditional Chinese Medicine, the use of specific points along meridians (channels) are used to treat a wide range of conditions. Under this framework, acupuncture points have specific functions, and this influences how control or sham acupoints are selected (Ots et al., 2020). Often control or sham treatment use points at a set distance from the “true” acupoint, or at acupoints that have no benefit for the condition being treated (Ots et al., 2020). Other trials have use specially designed non-penetrating acupuncture needles or toothpicks to simulate needle insertion without penetrating the skin to blind the patient and or therapist (Zhang et al., 2015). In Western Medical Acupuncture, acupuncture points are selected based on neuroanatomy as well as the goal of triggering the desired physiological response (White et al. 2008). Dermatomal and myotomal innervation is not considered in TCM, however many sham points used in clinical trials have been shown to share dermatomes and/or myotomes with the tissue or body area targeted by verum treatment. A correlation has been found between number of sham needles with shared dermatome and the difference between verum and sham treatment (Ots et al., 2020).

In such a small sample it was not possible to identify a difference in outcomes between distant and local acupuncture treatment groups. The distant acupuncture protocol was never intended to be an inert control treatment on the basis that stimulation of nociceptors anywhere in the body will elicit a physiological response. The intervention protocol provided the same needle stimulation (30 seconds bi-directional rotation or until needling sensation is felt) regardless of needle location.

Furthermore, one requirement for producing supraspinal effects and segmental analgesia is the stimulation of needling sensation (deqi) (Carlsson, 2002; Zhao, 2008). Hence, distant acupuncture treatment provided sufficient stimulation for supra-spinal, nociceptive, and autonomic mechanisms to contribute to modulation of symptoms such as pain and itch.

Local and systemic changes to scar innervation

There have been multiple studies demonstrating both local and systemic changes in sensory innervation following burn injury and subsequent healing. Burn injured rats had significantly reduced nerve fibre density two weeks post burn, in both injured and contralateral non-injured dermis, which was maintained at 12 weeks post burn (Anderson et al., 2010). Similarly in human subjects 18 months post burn, a pattern of reduced cutaneous innervation was observed in the scar and contralateral non-injured skin (Anderson et al., 2010). A pilot study found that three participants with post-burn HTS greater than one year duration, had significantly reduced nerve fibre density compared to normal, uninjured skin, but this was not observed in three participants with normotrophic burn scars. (Buhé et al., 2018). Another study investigated sensory function and sensory innervation in human participants with unilateral chronically painful scars compared to participants with unilateral normotrophic non-painful scars 24 months post-burn injury (Hamed et al., 2011). Sensory function of the scar compared to uninjured tissue was significantly diminished for both groups and there was no significant difference between groups. Total nerve density of both scar and uninjured skin showed no significant differences in either group or with a between group comparison. However, density of nociceptive nerve fibres was significantly higher in both scar and uninjured tissue in participants with chronic pain (Hamed et al., 2011). In a mouse burn injury model, cutaneous reinnervation in the dermis and epidermis occurred at different rates (Morellini et al., 2012). Dermal nerve fibres regenerated rapidly post burn, however, subsequently degenerated both in burned and distant unburnt skin (Morellini et al., 2012). In contrast, epidermal innervation was slower to regenerate but returned to normal levels in distant uninjured skin and wound periphery (but not wound centre) by eight weeks post wounding (Morellini et al., 2012).

It is less clear whether surgical scars show similar patterns of systemic sensory innervation changes. In mice with excisional wounds, SP immunoreactive nerve fibre

density dropped initially post-wounding then increased to more than double the initial amount after six weeks, and maintained this at 12 weeks (Henderson et al., 2006). Concurrently CGRP fibre density was elevated at two and six weeks post wounding, however was at normal levels at three and 12 weeks post wounding (Henderson et al., 2006). Finally, this study found that the proportion of nerve fibres that were not SP or CGRP reduced from 43% in unwounded skin to 11% at 12 weeks post wounding (Henderson et al., 2006). Systemic innervation was not investigated in this study, however the ratio of nociceptive to non-nociceptive fibres was altered and overall nerve fibre density reduced in the scar in a similar manner to that observed in burn scars. Hence, both burn and surgical HTS demonstrate locally reduced overall nerve fibre density along with altered ratios of nociceptive to non-nociceptive nerve fibres. Furthermore, these sensory changes occur systemically in individuals with chronically painful burn scars. Future studies would benefit from investigating whether painful surgical scars also exhibit systemic changes in sensory innervation.

Altered local sensory innervation of scar tissue may have implications for the effectiveness of locally applied acupuncture treatment, which relies on intact sensory nerve fibres to transmit signals from the periphery to the dorsal horn (White et al. 2008; Zhao, 2008). Reduced density and number of sensory nerve fibres may limit the analgesic potential of acupuncture via local, segmental and supraspinal mechanisms. Acupuncture needle manipulation is a mechanical stimulus relying on intact collagen fibres to convert mechanical stimuli into chemical and electrical signals via the action of mast cells (i.e., release of histamine, ATP and adenosine) (Perreault et al., 2019). Thickened HTS had thinner, more dense packed collagen fibres than normal tissue (Choi et al., 2013). Reduced scar innervation and altered collagen fibre structure may impact the effects of locally applied acupuncture treatment and explain the unexpected finding of greater reduction in pain and itch observed in the distant acupuncture group. Concurrently, higher than normal numbers of SP containing nerve fibres and an increased ratio of nociceptive nerve fibres, may contribute to neurogenic inflammation and increase scar sensitivity. This could explain why participants receiving local acupuncture experienced more episodes of post-treatment soreness.

Does scar age make a difference?

This study included participants from six weeks to 12 months post injury, as it was hypothesised to be the most active phase of scar recovery. However, acupuncture has been applied in a prophylactic manner prior to scar tissue formation indicating that the timing of treatment application impacted outcomes. In a retrospective case series, applying acupuncture (to specific TCM points) within 24 hours of burn injury, patients recovered with no sign of prior burn after 4-6 weeks (Loskotova & Loskotova, 2017). Mechanistic studies on mice (Lee et al., 2014; Lee et al., 2011) and rats (Abali et al., 2015) found local acupuncture helped accelerate wound healing and manage pain in the early phases post burn or excisional wounding. Following scar tissue formation and scar hypertrophy it is unclear whether the age of the scar impacts the effectiveness of treatment. In this research program, changes in both symptoms and scar characteristics were reported by participants with scars up to 12 months (Table 14). Hence, it may be appropriate in future studies to consider alternative measures to scar age, such as POSAS scores for symptoms and physical characteristics (i.e., redness and thickness) to determine appropriateness for treatment inclusion.

Table 15. *Pain, Itch and Physical Scar Characteristic change by Scar Age (post-injury) -taken from tables 9-11 (Chapter 5)*

Age of Scar (time post-wounding) **Local**	Change in Pain baseline to final treatment (4 weeks)	Change in Itch baseline to final treatment (4 weeks)	Change in Physical scar characteristics (colour, stiffness, thickness, irregularity) baseline to final treatment (4 weeks)
6 weeks	POSAS ↓1 NRS ↑1	POSAS ↓5 NRS ↓3	↓15
8 weeks	POSAS ↑1 (2 weeks) NRS ↑1 (5th session)	POSAS = (2 weeks) NRS ↓1 (5th session)	↓5 (2 weeks)
10 weeks	POSAS ↓5 NRS ↓1	POSAS = NRS =	↓24
3 months	POSAS ↓7 NRS ↓7	POSAS ↓1 NRS ↓2	↓5
4 months	POSAS ↓1 NRS ↓1	POSAS ↓3 NRS ↓3	↓15
5 months	POSAS ↓2 NRS ↑1	POSAS ↓2 NRS ↑1	↓3
7 months	POSAS = NRS ↓1	POSAS ↓5 NRS ↓6	↓22
8 months	POSAS ↓5 NRS ↓6	POSAS ↓3 NRS ↓3	↓15
9 months	POSAS ↑1 (2 weeks) NRS ↑2 (5th session)	POSAS ↓2 (2 weeks) NRS ↑1 (5th session)	↓12 (2 weeks)
10 months	POSAS ↓2 NRS =	POSAS ↓5 NRS ↓4	↑5
10 months	POSAS ↓2 NRS =	POSAS ↓6 NRS ↓4	↓22
12 months	POSAS = NRS ↑1	POSAS ↓1 NRS ↓3	↓12
12 months	POSAS ↓1 NRS ↓1	POSAS ↓2 NRS ↓4	↑1
12 months	POSAS ↑1 NRS =	POSAS ↓1 NRS ↓5	↓4

POSAS – Patient and Observer Scar assessment score (patient component), NRS – Numerical rating scale,
↑increased score (more pain/itch), ↓ decrease score (less pain/itch), = no change

Conclusion and Recommendations

Acupuncture combined with massage therapy was associated with beneficial outcomes for most participants with symptoms of pain or itch. The intervention protocol was well-tolerated, with no significant adverse events. Participant adherence to the active treatment phase was high (93%) and supported the intervention schedule (i.e., frequency and number of sessions). Compliance with returning follow-up questionnaires dropped to 60% requiring use of additional strategies to improve adherence in the future. This study was limited by small numbers and was therefore unable to demonstrate a difference in outcomes between acupuncture applied locally compared to distant acupuncture when combined with scar massage. Although the original intention was to perform a full RCT, circumstances led to changes which have still yielded results and recommendations for future studies.

Recommendations for clinical practice

Pilot testing has shown that both local and distant acupuncture were well-tolerated by participants, however those with high pain and itch scores (>4 POSAS/NRS) had more episodes of post-treatment soreness when treated with local acupuncture. Based on acupuncture mechanisms (Chapter 1), segmentally applied acupuncture has the greatest potential for achieving acupuncture analgesia based on stimulation of local collagen fibres and segmental nerve involvement. However, in chronic pain with potential central sensitisation mechanisms segmental acupuncture may initially aggravate the pain state (Dommerholt, 2011). Hence, when high levels of symptoms exist (hypersensitive participants), needle location should be modified to be further from the scar, but within a shared dermatome. Addition of extra-segmental (i.e., distant) needles may enhance the acupuncture analgesia effects by activation of supra-spinal mechanisms and descending pain inhibitory mechanisms. The use of parasympathetically innervated acupuncture points such as ST36 and SP6 could also be utilised bilaterally to enhance anti-inflammatory mechanisms (Chapple, 2013; da Silva et al., 2015; Jin et al., 2019).

Recommendations for future research

Future studies would benefit from separating the effect of massage from acupuncture by providing a massage-only group. Massage is often used as part of

routine scar management and may influence the same outcomes targeted by acupuncture.

Needle manipulation and sensation is an important factor in producing acupuncture analgesia via segmental and supra-spinal mechanisms. However, any control intervention that provides stimulation to the sensory nervous system is not an inert control and may therefore confound results. Hence the author recommends a pragmatic design comparing three treatment groups: routine care, routine care with acupuncture and acupuncture.

Proposed Study Protocol

The following protocol has been developed following the pilot-testing of the protocol described in Chapter 3.

Study Design

Pragmatic randomised clinical trial.

Setting

Where possible, include multiple locations and treatment providers to increase recruitment potential. Potential locations include private physiotherapy or medical centres, university clinics and hospital out-patient clinics.

Sample Size

Sample size calculations provided previously required 43 participants per treatment group (includes allowance for 20%) dropouts. These numbers would be re-assessed for future studies, based on up-to-date literature and altered outcome measures (i.e., use of EQ-5D rather than the SF-36).

Randomisation

Block randomisation in groups of twelve to be completed via a random number generator and placed in numbered envelopes by a student or person not involved in providing treatment. Following enrolment into the study and completion of initial outcome measures, the numbered envelope will be opened to inform the treating therapist of treatment group allocation.

Recruitment

Enlist the support of one or more surgeons or skin specialists to help promote awareness of the study. Initial contact to be made via letter or email, with follow-up conversations either face to face or via video conference.

Place flyers on local community noticeboards and at other high foot-traffic locations.

Utilise social media via creation of Facebook and Instagram accounts, use of stories and paid advertisements to gain awareness.

Approach local (to treatment location) newspapers to include a story about the study and include contact details.

Provide an online information and enrolment page, with eligibility questions that the potential participant can answer as part of their application for enrolment.

Questions include:

- How long have you had the scar?
- What was the cause of the scar (i.e., surgery, burn)?
- Has your scar spread beyond the original wound?
- Is your scar lower in height or pulled in more than the normal skin around it?
- Have you been receiving any other treatment for the scar? If yes please provide details_____
- Is your scar painful? If yes, please rate your average pain over the last 24 hours on a scale of 0-10 (10 being the worst pain you can imagine and 0 being no pain at all)_____
- Is your scar itchy? If yes, please rate your average itch over the last 24 hours on a scale of 0-10 (10 being the worst itch you can imagine and 0 being no itch at all)_____

Inclusion Criteria

Participants aged 18-years or older with symptomatic scars from trauma or surgery. To be considered symptomatic, scars must score higher than 2/10 for pain

and/or itch and demonstrate altered physical characteristics such as increased redness and/or thickness as reported on the patient response component of POSAS.

Exclusion Criteria

- Scar currently receiving physical (hands on) treatment by another clinician,
- Atrophic scar (scar which is depressed or retracted below the line of the normal skin),
- Keloid scar (has extended beyond boundaries of original wound/has a shiny surface),
- If there is significant pain from another structure within the same spinal segmental innervation level as the scar (i.e., following joint replacement surgery or fracture),
- During the first trimester of pregnancy,
- Abdominal scars during pregnancy
- Unstable medical conditions (such as uncontrolled blood pressure, or uncontrolled epilepsy),
- Allergies to stainless steel,
- Not consenting to receive acupuncture therapy, or needle phobic,
- Other acupuncture related contraindications, i.e., lymphoedema in affected limb, loss of sensation in area to be treated (i.e., nerve injury, stroke, or diabetic neuropathy).
- Anyone who provides acupuncture treatment or has received significant training in this area (based on questioning of previous experience of acupuncture prior to enrolment).

Prior to assessment and subsequent enrolment into the study a phone interview will be conducted with all respondents to exclude participants with either contraindications to receiving acupuncture or other exclusion criteria, as well as to answer any questions from potential participants. All participants must consent to treatment prior to enrolment and must indicate their ability/willingness to attend the prescribed treatment regimen. Participants will be requested to avoid any other acupuncture treatment during the study period. For participants with previous acupuncture experience, a waiting period of a minimum one month following their last treatment will be observed prior to study enrolment.

Participants will need to sign a consent form to participate in a research study (Appendix 3) and following group allocation, those receiving acupuncture will need to provide further consent to receive acupuncture (Appendix 2).

Participant Expectation

This study will not exclude participants with previous experience of acupuncture (but will record this in baseline demographic data).

A standardised script (Appendix 4) has been developed for use which avoids discussing pain relief with each participant beyond the information contained in the study information sheet (Appendix 5) provided to potential participants prior to enrolment.

Data Collection

Details will be collected on the event(s) that resulted in the scar including time since skin insult, current health conditions, current treatment regimens e.g., pressure garment use and demographic data e.g., age at the initial treatment session.

Outcome measures will be given to participants when they arrive for their appointments by administration staff or completed electronically prior to each session. For participants preferring paper questionnaires they will be asked to complete outcome measures at the prescribed times and place them in an envelope marked with the date and their participant ID. Administration staff will check that the questionnaires are completed correctly prior to sealing the envelope. Envelopes will stay sealed until all participants treatment series are completed, then will be unsealed, and data entered into spreadsheets. Electronic measures will be saved under the participant ID number and transferred to data spreadsheets on completion of the study. The therapist applying the treatment will be blinded to the outcome measure results until all participants have completed their treatment.

Outcome Measures
Patient and Observer Scar Assessment Scale (POSAS)

The primary outcome measure will be the patient response components of the POSAS. The scale consists of seven categories of scar symptoms for which the patient rates their scar on a scale from one to ten. Participants will perform the self-

assessment part of the POSAS assessment at initial enrolment into the study, after final treatment, and six weeks following treatment cessation.

The Observer subscale of the POSAS will be completed by a blinded assessor prior to the initial and final treatment session.

Numerical Rating Scale (NRS) for Pain and Itch

Participants will be asked to rate average pain and itch on a scale from one to ten, for the period of 24 hours prior to attending treatment.

Health-related Quality of Life (EQ5D-5L)

The EQ5D-5L has been substituted for the SF-36 to simplify and improve adherence to completion of the quality-of-life measurement. This should be completed at baseline, final treatment, and at six weeks follow-up.

Adherence to Self-management Advice

Data on adherence to self-management advice will be collected via an exercise diary or online app that measures adherence on a weekly basis, after obtaining baseline measures for exercise and scar massage. This will be continued over the follow-up period.

Questions to be asked include:

On how many days did you complete 30-minutes of cardiovascular exercise?

On how many days did you complete five-minutes of scar massage?

Planned Schedule of Study Measurements

Table 16. *Planned schedule of study measurements*

Outcome Measure	Baseline (1st treatment)	Prior to each session	Final Session (6th treatment)	Six weeks post
POSAS (self)	√		√	√
POSAS (observer)	√		√	
NRS	√	√	√	
EQ5D-5L	√		√	√
Self-management	√	√ (weekly)	√	√

Intervention Schedule

Participants will be requested to attend a total of six treatment sessions over four weeks. Sessions will be scheduled twice weekly for the first two weeks, then weekly for the final two weeks. Participants will be considered to have completed treatment if they attend five out of six sessions, follow up will be attempted for all dropouts to ascertain reason for drop-out. If participants find any of the acupuncture needles are too painful these will be removed during treatment. Treatment sessions will be considered complete if participants retain at least 80% of the needles for 10 minutes per session. Any deviation from protocol regarding needle number or retention time will be recorded.

Intervention Protocol

Group 1: Routine Care

Group 2: Routine Care plus Acupuncture

Group 3: Acupuncture

Routine Care

Participants will receive five minutes of scar massage using sorbolene cream each session. Massage is aimed at breaking up adhesions and improving gliding between layers of skin and fascia. They will be provided self-management advice (appendix 8) describing how to apply five minutes of self-massage daily, and general exercise advice to perform 30 minutes of cardiovascular exercise at least three times per week. Adherence will be monitored via a diary or an electronic app.

Acupuncture

Unlike the previously presented protocol that compared local and distant acupuncture, this updated protocol combines local/segmental and extrasegmental needling. The number of needles used will be calculated based on scar size (circumference divided by two). This number will be recorded for each participant and the same number used each session, however a minimum of five and maximum of 20 needles will be used. The majority (75-80%) of needles will be inserted within a shared dermatome to the scar receiving treatment. Local needles will be inserted at an angle underneath the margins of the scar to a depth of 5-10mm. For participants with high

levels of symptoms and sensitivity around the scar (>4 points on NRS or POSAS for both pain and itch), needles will initially be limited to a maximum of 15 and placed at a comfortable distance from the scar (i.e., between one and two centimetres away (as determined by participant tolerance of the treatment), but within the same dermatomes as the scar). This will ensure segmental stimulation of the affected tissue, and as sensitivity decreases the needles will be aimed closer to the scar margins. Additional extrasegmental needles will be placed in either upper or lower limb points (based on scar location). Use of extrasegmental points with known parasympathetic innervation such as ST36, GB30, GB34, SP6, BL60 and BL40 (Chapple, 2013), or that demonstrate vagal regulation such as auricular points, ST36, PC6, GV20 and GV14 (Jin et al., 2019; Ulloa et al., 2017) are recommended. Once inserted, the needles will be manipulated via bi-directional rotation until moderate sensation (deqi) is felt. Needle manipulation will be applied at five-minute intervals (three times) over the course of each 15 minute treatment session.

Data Analysis

Data will be analysed using an Intention to Treat (ITT) analysis of all participants regardless of protocol completion. A per protocol analysis of compliant participants will be completed for comparison and sensitivity analysis. Descriptive statistics will be used to compare participant characteristics at baseline.

Linear mixed models will be used to compare treatments groups for each outcome of interest. This allows control of confounding variables (such as size of scar and previous acupuncture experience) and respects (clusters for) repeated observations taken per participant.

Hygiene and safety

The treating therapist will follow hand-washing guidelines and use 70% alcohol-based hand sanitiser prior to each session. Participants' skin will be cleaned with soap and water between massage and acupuncture treatments. Extra precautions such as skin sterilisation are to be used in cases of participants with compromised immunity. Gloves are to be worn if the participant has any blood borne diseases such as hepatitis or HIV.

All participants will be treated in a reclined position on a plinth to reduce any possibility of adverse events such as dizziness or fainting.

Adverse Events

Prior to each subsequent treatment session, participants will be asked if there were any adverse events from the previous treatment. Minor adverse events such as bleeding, bruising, fatigue, or increased symptoms will be recorded for each participant and reported in the final study write-up. If any adverse events occur that require urgent medical attention, medical attention will be sought, if not already undertaken, and the Ethics committee will be informed immediately.

Post-treatment advice specific to acupuncture will be provided to participants along with general advice provided to all participants. This will include advice on managing adverse events.

References

Abali, A. E., Cabioglu, T., Ozdemir, H., & Haberal, M. (2015). Interactive effects of acupuncture on pain and distress in major burns: An experiment with rats. *Burns, 41*(4), 833-842. https://doi.org/10.1016/j.burns.2014.10.028

Anderson, J. R., Zorbas, J. S., Phillips, J. K., Harrison, J. L., Dawson, L. F., Bolt, S. E., Rea, S. M., Klatte, J. E., Paus, R., Zhu, B., Giles, N. L., Drummond, P. D., Wood, F. M . & Fear, M. W. (2010). Systemic decreases in cutaneous innervation after burn injury. *Journal of Investigative Dermatology, 130*(7), 1948-1951. https://doi.org/10.1038/jid.2010.47

Anthonissen, M., Daly, D., Janssens, T., & Van den Kerckhove, E. (2016). The effects of conservative treatments on burn scars: A systematic review. *Burns, 42*(3), 508-518. https://doi.org/10.1016/j.burns.2015.12.006

Ault, P., Plaza, A., & Paratz, J. (2018). Scar massage for hypertrophic burns scarring-A systematic review. *Burns, 44*(1), 24-38. https://doi.org/10.1016/j.burns.2017.05.006

Biljlard, E., Uiterwaal, L., Kouwenberg, C. A. E., Mureau, M. A. M., Hovius, S. E. R., & Huygen, F. J. (2017). A Systematic review on the prevalence, etiology, and pathophysiology of intrinsic pain in dermal scar tissue. *Pain Physician, 20*(1-13).

Birch, S., Lee, M. S., Kim, T.-H., & Alraek, T. (2021). Historical perspectives on using sham acupuncture in acupuncture clinical trials. *Integrative Medicine Research*. https://doi.org/10.1016/j.imr.2021.100725

Birch, S. J., Lee, M. S., Kim, T.-H., & Alraek, T. (2022). On defining acupuncture research and its techniques: a commentary on the problem of sham. *Integrative Medicine Research, 11*. https://doi.org/10.1016/j.imr.2022.100834

Buhé, V., Trimaille, A., Schollhammer, M., Morvan, F., Hu, W., Egles, C., Desmouliere, A., & Misery, L. (2018). Heterogeneity of skin re-innervation after burns and factors involved in its regulation: A pilot study. *Acta Dermato-Venerelogica, 98*, 280-281. https://doi.org/10.2340/00015555-2826

Carlsson, C. (2002). Acupuncture mechanisms for clinically relevant long-term effects -- reconsideration and a hypothesis. *Acupuncture in Medicine, 20*(2-3), 82-99.

Chapple, W. (2013). Proposed catalogue of the neuroanatomy and the stratified anatomy for the 361 acupuncture points of 14 channels. *Journal of Acupuncture & Meridian Studies, 6*(5), 270e-274. https://doi.org/10.1016/j.jams.2013.01.001

Chen, X., Spaeth, R., Retzepi, K., Ott, D., & Kong, J. (2014). Acupuncture modulates cortical thickness and functional connectivity in knee osteoarthritis patients. *Scientific Reports, 4*. https://doi.org/10.1038/srep06482

Cho, Y. S., Jeon, J. H., Hong, A., Yang, H. T., Yim, H., Cho, Y. S., . . . Seo, C. H. (2014). The effect of burn rehabilitation massage therapy on hypertrophic scar after burn: a randomized controlled trial. *Burns, 40*(8), 1513-1520. https://doi.org/10.1016/j.burns.2014.02.005

Choi, Y. H., Kim, K. M., Kim, H. O., Jang, Y. C., & Kwak, I. S. (2013). Clinical and histological correlation in post-burn hypertrophic scar for pain and itching sensation. *Annals of Dermatology, 25*(4), 428-433. https://doi.org/10.5021/ad.2013.25.4.428

da Silva, M. D., Bobinski, F., Sato, K. L., Kolker, S. J., Sluka, K. A., & Santos, A. R. S. (2015). IL-10 cytokine released from M2 macrophages is crucial for analgesic and anti-inflammatory effects of acupuncture in a model of inflammatory muscle pain. *Molecular Neurobiology, 51*(1), 19-31. https://doi.org/10.1007/s12035-014-8790-x

Dommerholt, J. (2011). Dry needling - peripheral and central considerations. *Journal of Manual and Manipulative Therapy, 19*(4), 223-237. https://doi.org/https://doi.org/10.1179/106698111X13129729552065

Draaijers, L. J., Tempelman, F. R. H., Botman, Y. A. M., Tuinebreijer, W. E., Middelkoop, E., Kreis, R. W., & van Zuijlen, P. P. M. (2004). The Patient and Observer Scar Assessment Scale: A Reliable and Feasible Tool for Scar Evaluation. *Plastic and Reconstructive Surgery, 113*(7), 1960-1965. https://doi.org/10.1097/01.prs.0000122207.28773.56

Gauglitz, G. G., Korting, H. C., Pavicic, T., Ruzicka, T., & Jeschke, M. G. (2011). Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. *Molecular Medicine, 17*(1-2), 113-125. https://doi.org/10.2119/molmed.2009.00153

Hamed, K., Giles, N., Anderson, J., Phillips, J. K., Dawson, L. F., Drummond, P., Wallace, H., Wood, F. M., Rea, S. M. & Fear, M. W. (2011). Changes in cutaneous innervation in patients with chronic pain after burns. *Burns, 37*, 631-637. https://doi.org/10.1016/j.burns.2010.11.010

Henderson, J., Terenghi, G., McGrouther, D. A., & Ferguson, M. W. J. (2006). The reinnervation pattern of wounds and scars may explain their sensory symptoms. *Journal of Plastic, Reconstructive & Aesthetic Surgery, 59*, 942-950. https://doi.org/10.1016/j.bjps.2005.11.038

Jin, B. X., Jin, L. L., & Jin, G.-Y. (2019). The anti-inflammatory effect of acupuncture and its significance in analgesia. *World Journal of Acupuncture - Moxibustion, 29*(1), 1-6. https://doi.org/10.1016/j.wjam.2019.03.003

Johnston, G. R., & Webster, N. R. (2009). Cytokines and the immunomodulatory function of the vagus nerve. *British Journal of Anaesthesia, 102*(4), 453-462. https://doi.org/10.1093/bja/aep037

Lee, J., Park, J., Min, S., Chae, Y., Lee, H., Lim, Y., & Park, H. (2014). Wound healing effect of acupuncture through activating angiogenesis in mice. *Oriental Pharmacy and Experimental Medicine, 14*(2), 93-101. https://doi.org/10.1007/s13596-014-0146-6

Lee, J. A., Jeong, H. J., Park, H. J., Jeon, S., & Hong, S. U. (2011). Acupuncture accelerates wound healing in burn-injured mice. *Burns 37*, 117-125. https://doi.org/10.1016/j.burns.2010.07.005

Loskotova, A., & Loskotova, J. (2017). The use of acupuncture in first aid of burns-Clinical report. *Burns, 43*(8), 1782-1791. https://doi.org/10.1016/j.burns.2017.04.025

Mahdavian Delavary, B., van der Veer, W. M., Ferreira, J. A., & Niessen, F. B. (2012). Formation of hypertrophic scars: evolution and susceptibility. *J Plast Surg Hand Surg, 46*(2), 95-101. https://doi.org/10.3109/2000656X.2012.669184

McDowell, J. M., Kohut, S. H., & Betts, D. (2019). Safe acupuncture and dry needling during pregnancy: New Zealand physiotherapists' opinion and practice. *Journal of Integrative Medicine, 17*, 30-37. https://doi.org/10.1016/j.joim.2018.11.006

Moon, H.-Y., Kim, M.-R., Hwang, D.-S., Jang, J.-B., Lee, J., Shin, J.-S., Ha, I., & Lee, Y. J. (2019). Safety of acupuncture during pregnancy: a retrospective cohort study in Korea. *Obstetrics and Gynaecology, 127*, 79-87. https://doi.org/10.1111/1471-0528.15925

Morellini, N. M., Fear, M. W., Rea, S. M., West, A. K., Wood, F. M., & Dunlop, S. A. (2012). Burn injury has a systemic effect on reinnervation of skin and restoration of nociceptive function. *Wound Repair and Regeneration, 20*(3), 367-377. https://doi.org/10.1111/j.1524-475X.2012.00787.x

Ots, T., Kandirian, A., Szilagyi, I., DiGiacomo, S. M., & Sandner-Kiesling, A. (2020). The selection of dermatomes for sham (placebo) acupuncture points is relevant for the outcome of acupuncture studies: a systematic review of sham (placebo) controlled randomized acupuncture trials. *Acupuncture in Medicine, 38*(4), 211-226. https://doi.org/10.1177/0964528419889636

Shin, T. M., & Bordeaux, J. S. (2012). The role of massage in scar management: a literature review. *Dermatol Surg, 38*(3), 414-423. https://doi.org/10.1111/j.1524-4725.2011.02201.x

Ulloa, L., Quiroz-Gonzalez, S., & Torres-Rosas, R. (2017). Nerve stimulation: Immunomodulation and control of inflammation. *Trends In Molecular Medicine, 23*(12), 1103-1120. https://doi.org/10.1016/j.molmed.2017.10.006

van de Kar, A. L., Corion, L. U. M., Smeulders, M. J. C., Draaijers, L. J., van der Horst, C. M. A. M., & van Zuijlen, P. P. M. (2005). Reliable and Feasible Evaluation of Linear Scars by the Patient and Observer Scar Assessment Scale. *Plastic and Reconstructive Surgery, 116*(2), 514-522. https://doi.org/10.1097/01.prs.0000172982.43599.d6

White, A., Cummings, T. M., & Filshie, J. (2008). *An introduction to western medical acupuncture*. Churchill Livingstone.

Zhang, C. S., Tan, H. Y., Zhang, G. S., Zhang, A. L., Xue, C. C., & Xie, Y. M. (2015). Placebo Devices as Effective Control Methods in Acupuncture Clinical Trials: A Systematic Review. *PLOS ONE, 10*(11), Article: e0140825. https://doi.org/10.1371/journal.pone.0140825

Zhao, Z. Q. (2008). Neural mechanism underlying acupuncture analgesia. *Progress in Neurobiology, 85*, 355-375. https://doi.org/10.1016/j.pneurobio.2008.05.004

Appendix

Appendix 1. Neural responses to Acupuncture needle insertion

Aδ fibres are activated by pin prick and heavy pressure to the skin (White, 1999). They travel to laminae I, II, and V in the dorsal horn, activating stalked cells between laminae I-II to release enkephalin (Bowsher, 1998). Enkephalin has an inhibitory effect on the transmission of nociceptive impulses from the Substantia Gelatinosa (SG) cells to the Wide Dynamic Range (WDR) neurons and therefore helps modulate pain transmission to higher brain centres (Bowsher, 1998).

Aβ and ergoreceptive Aδ (Type III) fibres respond to light touch and vibration and can therefore be stimulated by acupuncture and other electrical stimulation such as TENS (White, 1999). They send collateral branches to laminae II-V of the dorsal horn before entering the dorsal columns (ascending tracts) (White, 1999). Interneurons are stimulated to secrete γ-amino butyric acid (GABA) which acts on SG cells to inhibit nociceptive transmission (White, 1999).

C fibres give rise to poorly localised sensations including aching and burning when receptors on free nerve endings in the skin and deeper tissues are stimulated (Farquhar-Smith, 2007; Sluka, 2009; White, 1999). They terminate in laminae I-II of the dorsal horn into the SG cells and release neurotransmitters to react with receptors on the SG cells (White, 1999). Signals are transmitted via interneurons to the WDR neurons in lamina V prior to entering ascending tracts (White, 1999).

References

Bowsher, D. (1998). Mechanisms of Acupuncture. In J. Filshie & A. White (Eds.), *Medical Acupuncture: A Western Scientific Approach* (pp. 69-82). Edinburgh, United Kingdom: Churchill Livingstone.

Farquhar-Smith, W. P. (2007). Anatomy, physiology and pharmacology of pain. *Anaesthesia and Intensive Care Medicine, 9*(1), 3-7.

Sluka, K. A. (2009). Peripheral mechanisms involved in pain processing. In K. A. Sluka (Ed.), *Mechanisms and management of pain for the physical therapist* (pp. 19-40). Seattle: IASP Press.

White, A. (1999). Neurophysiology of acupuncture analgesia. In E. Ernst & A. White (Eds.), *Acupuncture: A scientific appraisal* (pp. 64-75). Oxford, United Kingdom: Butterworth-Heinemann.

Appendix 2. Acupuncture Information Sheet

Acupuncture therapy involves insertion of thin stainless steel needles into points on the body. It is often used for pain relief, stimulating the body's natural healing response, and improving general well-being. Before receiving acupuncture, you should be aware of the risks and benefits of treatment. Acupuncture is safe (less than one serious adverse reaction per 10,000 treatments), but there are some adverse reactions you should be aware of.

- Fainting – just like blood tests and injections some people may faint. Please let your therapist know if you feel dizzy, nauseous, or hot and sweaty and they will remove the needles straight away.
- Drowsiness – some people feel drowsy after treatment, if you experience this you are advised not to drive straight after treatment.
- Minor bleeding or bruising occurs in up to 3% of treatments.
- Pain during treatment – it is normal to feel some sensation during treatment, if the needle stings let your therapist know and they will remove the needle if this persists.
- Worsening of symptoms can occur initially after treatment, however this is a good sign that acupuncture will help you. This will generally settle on its own within 24 hours of treatment.

Although your therapist will have asked for your medical history, it is important that you make sure they are aware if:

- You have ever experienced a fit, faint, or funny turn.
- You have a pacemaker, or any other metal or electrical implants.
- You have a bleeding disorder or are on blood thinning medication, or are on anti-coagulants or other medication,
- You have damaged heart valves or any other particular risk of infection (ie. you have to go on antibiotics to go to the dentist).
- You have any diagnosed infections including HIV, hepatitis, or AIDS.
- You are pregnant or believe you may be.
- You have a poor immune system (due to illness or medication such as steroids).
- You have lymphoedema of any cause

These conditions will change the way your therapist applies your acupuncture treatment however your therapist will discuss any potential risks with you prior to treatment.

If you do have any unexpected reactions to treatment, please let your therapist know so they can help.

No treatment will be performed without your consent, and you always have the right to say no to treatment – even if you have previously said yes.

Appendix 3. Consent to Participate in Research

CONSENT FORM

Does acupuncture treatment reduce pain and itch in abnormal scars?

This Study will be undertaken by Cathy Smith (catherine.smith2@my.nd.edu.au) as part of her Masters of Science degree via The University of Notre Dame Australia, and co-supervised by Assoc Prof Dale Edgar (dale.edgar@nd.edu.au), and Susan Kohut (susan.kohut@aut.ac.nz). Please contact us if you have any questions before signing this consent form.

- I agree to take part in this research project.
- I consent to receiving acupuncture and physical treatment of my scar
- I have read the Information Sheet provided and been given a full explanation of the purpose of this study, the procedures involved and of what is expected of me.
- I understand that I will be asked to: attend regular treatment sessions to receive massage and acupuncture treatment for my scar, and fill in questionnaires regarding my symptoms.
- The researcher has answered all my questions and has explained possible problems that may arise as a result of my participation in this study.
- I understand that I may withdraw from participating in the project at any time without prejudice.
- I understand that all information provided by me is treated as confidential and will not be released by the researcher to a third party unless required to do so by law.
- I agree that any research data gathered for the study may be published provided my name or other identifying information is not disclosed. Further that data will be de-identified and kept for seven years in a secure location.
- I understand that this consent form will be kept by the researcher, but will be stored separately to other study data, and destroyed at the end of seven years.

Name of participant			
Signature of participant		Date	

- I confirm that I have provided the Information Sheet concerning this research project to the above participant, explained what participating involves and have answered all questions asked of me.

Signature of Researcher		Date	

Appendix 4. Standardised script for communication with study participants.

Commencing first treatment:

Acupuncture needle insertion stimulates sensory receptors in your skin and underlying tissue to send signals to your nerves. Various natural chemicals may be released from your nerves that may help control pain and itch in your scar.

For this study you will receive one of two different styles of acupuncture in addition to scar massage to compare responses to different treatment regimens. The number of needles used will depend on the size of your scar.

During each treatment:

I expect you may feel a slight stinging sensation when I insert the needles, however this should not last long – let me know if you feel stinging or sharp pain that doesn't ease within a few seconds. I will give you time to get used to the feeling, then I am going to stimulate (by rotating them back and forth) the needles three times over the treatment session. Please let me know if you feel unwell, experience too much pain/soreness or would like me to remove the needles for any reason.

I am going to rotate each needle, please let me know when you feel a moderate sensation, this should not be very painful or sharp, but may be a warm feeling or a dull ache.

I am going to remove the needles now you may feel a sharp sensation for a few seconds. I will use a cotton ball to compress each point for a few seconds in case of any bleeding.

If you have any concerns regarding treatment over the next few days, please get in contact with me.

Follow up at the beginning of subsequent treatments:

Do you have any concerns, questions, or comments regarding your last treatment? Ideally, I won't know your specific responses to treatment until after you have finished all your study treatments. However, if you are not happy then we should address this and adjust the treatment as able within the study. This is to help me be consistent in the treatment I provide to you. However, if you feel that treatment is making you worse or you have any concerns, please do let me know.

Appendix 5. Participant Information Sheet

PARTICIPANT INFORMATION SHEET– Does acupuncture treatment reduce pain and itch in abnormal scars?

Dear

You are invited to participate in the research project described below.

What is the project about?

This research project will investigate the effect of physiotherapy treatments massage and acupuncture/dry needling on the symptoms of scars such as pain and itch.

This study will provide treatment for symptomatic scars. It aims to assess change in scar symptoms over a four week period, with follow up at one- and two-months after that time. This will help us to evaluate these methods are for treating scar symptoms, and guide future treatment improvements.

Who is undertaking the project?

This project is being conducted by Cathy Smith and will form the basis for a Master of Science degree at The University of Notre Dame Australia, under the supervision of Assoc Prof Dale Edgar (The University of Notre Dame, Australia) and Susan Kohut (Auckland University of Technology, New Zealand).

Who can take part in this study?

Adults (18 years and over) with scars between 6 weeks and 1 year duration that are painful and/or itchy are able to take part in this study. If you have multiple scars, you will be asked to nominate the most symptomatic scar to receive treatment as part of this study.

Some people will not be eligible to participate based on medical grounds (unstable medical conditions), swelling in the affected area or loss of sensation in the affected area, current pregnancy or if you are allergic to stainless steel. Certain types of scars may also be excluded due to different pathology causing them. We will discuss these over the phone with you prior to enrolling you into this study. If you are not sure about something, please ask.

What will I be asked to do?

If you consent to take part in this research study, you will be asked to commit to being part of the study for three months. In that time, the first four weeks will involve attending the clinic once or twice per week. The final contacts will be by email, mail or phone, and will not require your physical attendance. Please feel free to ask any questions you may have, and ensure that all your questions have been answered to your satisfaction before you agree to participate.

Initially you will be asked for background information on health, how you got your scar(s), and what treatments you are currently undergoing for them.

During the study you will be asked to complete surveys regarding your scar, and general wellbeing. You will also be asked to complete these one and two months after completion of physical treatments, and return the surveys by post or email.

Participants will be randomly divided into two groups, both groups will receive scar massage, acupuncture and advice on self-massage, stretching and exercising. The only difference between the two groups will be the type of acupuncture. Sessions will take approximately 20-30 minutes to complete and will require attendance one to two times per week for four weeks (six sessions in total). There is no cost to you for this treatment, and all treatment will be focused on your scar. If you have more than one scar, please indicate the most painful/itchy scar to receive treatment as part of this study.

You can choose to attend your sessions either at Cannington Physiotherapy (20 Pattie Street, Cannington – 5 minutes walk from Carousel shopping centre) or at the School of Physiotherapy building of the university of Notre Dame in Fremantle.

Are there any risks associated with participating in this project?

It is possible that treatment may make your scar itch or pain increase. This is unlikely to last longer than a few hours, however you may try using cool wet towels, ice or taking your usual pain medication for relief. If at any time during the treatment program you wish to stop, you may do so without recourse.

Occasionally there may be minor bleeding when the needle is withdrawn but this is no worse than a blood test. Other common side effects include the possibility of minor bruising at the acupuncture site or feeling tired after treatment.

Acupuncture needles used in this study are made of sterile stainless steel, and are single person use only. If you have any increased risk of infection (i.e., damaged heart valves or have to take antibiotics to go to the dentist) extra hygiene precautions will be taken prior to acupuncture treatment. Please notify the investigator if you have any diagnosed health conditions.

Your therapist will collect information from you regarding your medical history to assess your level of risk for receiving treatment. It is important for your safety and your therapists' safety that you disclose any medical conditions or blood borne diseases you have. This doesn't necessarily exclude you from participation in this study, however, extra precautions may be taken, and you may be requested to get your doctors' consent before receiving any treatment.

What are the benefits of the research project?

The scar being treated may show changes in physical characteristics and symptoms, but this is not guaranteed as everyone responds differently to treatment. The outcomes of the research may guide treatment of future patients with scars.

What if I change my mind?

Participation in this study is completely voluntary. Even if you agree to participate, you can withdraw from the study at any time without discrimination or prejudice. If you withdraw, -all personal information you have provided will be erased. Survey results will be kept unless you request they be removed as these will not contain any identifiers for you.

Will anyone else know the results of the project?

Information gathered about you will be held in strict confidence. This confidence will only be broken if ordered by law.

Personal details will be kept separate to study data, and you will be identified by a number assigned to you on any data reviewed by any other researchers within the study team, including statisticians.

Once the study is completed, the data collected from you will be de-identified completely and stored securely in the School of Physiotherapy at The University of Notre Dame Australia for a period of seven years. The grouped results of the study will be published as a journal article.

Will I be able to find out the results of the project?

Once we have analysed the information from this study we can email you a summary of our findings, if you provide a current email address. You can expect to receive this feedback by December 2018.

Who do I contact if I have questions about the project?

If you have any questions about this project please feel free to contact either myself catherine.smith2@my.nd.edu.au or my supervisor, Assoc Prof Dale Edgar (dale.edgar@nd.edu.au or phone on 0413070384.). My supervisor and I are happy to discuss with you any concerns you may have about this study.

What if I have a concern or complaint?

The study has been approved by the Human Research Ethics Committee at The University of Notre Dame Australia (approval number 017029F). If you have a concern or complaint regarding the ethical conduct of this research project and would like to speak to an independent person, please contact Dr Natalie Giles, The University of Notre Dame's Ethics Officer at (+61 8) 9433 0943 or research@nd.edu.au. Any complaint or concern will be treated in confidence and fully investigated. You will be informed of the outcome.

How do I sign up to participate?

If you are happy to participate, please sign both copies of the consent form, keep one for yourself and mail the other to me in the envelope provided. I will be in contact with you shortly to organise a time for your first appointment and answer any questions you may have.

Thank you for your time. This sheet is for you to keep if you wish.

Yours sincerely,

Cathy Smith

Appendix 6. Participant Personal Details Form

Trial I.D. Number:_____

Surname_____ Name _____Title: Mr/Mrs/Ms/Miss

D.O.B___/____/_____ age_____

Contact Details: Phone_____ Email_____

Emergency Contact _____phone _____

Medical History:

Medications:_____
_____

Health conditions (circle any that apply):

- High or low Blood pressure
- Epilepsy
- Heart Condition_____
- Diabetes type 1/2
- Bleeding disorder
- Infectious condition: HIV/hepatitis
- Lymphoedema
- Stroke
- Nerve injury causing numbness or altered sensation
- Allergy to Stainless steel
- Allergy to skin cream
- Current pregnancy
- Other_____

How did you receive your scar?_____

How long have you had your scar?_____

Are you currently receiving treatment elsewhere for your scar? Y/N (if yes please provide details)_____

Are you using any creams/silicone or pressure garments for your scar?_____

Have you received acupuncture or dry needling treatment before?
Details_____

Appendix 7. Information Letter(a) and flyer(b)

a. Letter to Surgeon/Doctor

Dear _____

I am writing to you as a research student at The University of Notre Dame Australia. I am a qualified physiotherapist who has worked in private practice physiotherapy clinics for more than ten years, and am now undertaking a Master of Science degree.

My research involves conducting a clinical trial into the use of acupuncture/dry needling for managing pain and itch associated with hypertrophic scars. I aim to recruit participants who have developed hypertrophic scars, within one to six months following surgery, trauma or burns injury. During the study all participants will receive massage therapy and exercise recommendations in addition to either local acupuncture around the margins of their scar, or distant acupuncture away from the scar region.

I would be grateful of your assistance with recruiting participants by recommending this study to any of your clients who may benefit from this treatment. I have enclosed a flyer and information sheet for you and should you require more information I would be more than happy to discuss this further.

Yours Sincerely

Catherine Smith

BHSc (Physiotherapy)

b. Flyer

THE UNIVERSITY OF NOTRE DAME AUSTRALIA

DOES YOUR SCAR BOTHER YOU?

I am looking for people with itchy/painful scars to participate in a clinical trial using acupuncture/dry needling and massage to treat scars.

For more information email: catherine.smith2@my.nd.edu.au

This study has been approved by The University of Notre Dame Fremantle's Human Research Ethics Committee (HREC number 017029F)

Appendix 8. Post Treatment advice Handout for Participants

After your treatment, you may experience an initial increase in pain or itch in your scar – this is normal and should settle within 24 hours. As you progress through the course of treatment this reaction will become less and less. Please let your therapist know at your next appointment if you have any increased symptoms.

Some people will feel drowsy after treatment – please don't drive straight away if you are affected.

In between treatments:

Scar massage – you can do this yourself as demonstrated at your initial appointment. Use some cream on your fingers and massage your scar in a circular or side to side pattern. Aim for 3-5 minutes of massage per day.

Stretching – gentle stretching can be performed on the joints and muscles around your scar. Aim for a slow and gentle stretch, holding up to 30 seconds per stretch.

Other exercise – You should aim to maintain your usual exercise regimen while participating in this trial.

If you have any queries or concerns regarding treatment or your response to treatment, please don't hesitate to get in contact with me.

Catherine Smith

catherine.smith2@my.nd.edu.au

Appendix 9. Results of Pilot Study (case series)

Participant #1 – Distant Acupuncture

female, 47yrs, 8 months post-surgical, 10cm long scar

Needle placement: 2cm lat to SP of L3&4 bilaterally, 5+10cm above knee & 5cm below knee in Midline bilat

POSAS

	Baseline	Midway	Final Rx	1-month	2-month
Q1	7	3	2	1	2
Q2	5	3	2	2	1
Q3	5	3	3	2	2
Q4	5	2	2	1	1
Q5	7	2	2	1	1
Q6	7	3	2	2	2
Q7	7	3	3	3	2

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	6	4	5	0	1	0
NRS (Itch)	3	1	7	1	0	0

SF-36

	Baseline	Final Session	1-month	2-month		norms
Physical Function	80	65	95	85		90.82
Role Physical	81.3	25	93.8	75		80.53
Bodily Pain	67.5	90	77.5	77.5		76.39
General Health	80	65	60	55		77.69
Vitality	45	20	50	55		59.94
Social Function	100	25	100	100		88.26
Role Emotional	91.7	100	100	100		86.06
Mental Health	72	72	76	80		77.58

Participant #2 – Local Acupuncture

Male, 46yrs, 5 months post-surgical, 20cm long scar

Needle placement: local (knee)

POSAS

POSAS	Baseline	Midway	Final Treatment	1-month	2-months
Q1	8	8	6		
Q2	8	8	6		
Q3	10	3	7		
Q4	7	3	7		
Q5	10	8	10		
Q6	10	8	10		
Q7	10	4	8		

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	7	8	3	6	3	8
NRS (Itch)	7	4	2	6	1	8

SF-36

	Baseline	Final Treatment		norms
Physical Function	25	65		90.94
Role Physical	18.75	25		85
Bodily Pain	10	90		76.76
General Health	50	65		76.55
Vitality	50	20		64.86
Social Function	25	25		91.88
Role Emotional	100	100		92.16
Mental Health	84	72		82.32

Participant #3 – Distant Acupuncture

female, 34yrs, 8 months post-surgical, 14cm long scar

Needle placement: C7 & T1 bilateral, mid forearm bilateral 4,5,8,9cm above elbow

POSAS

POSAS	Baseline		
Q1	4		
Q2	8		
Q3	9		
Q4	9		
Q5	5		
Q6	7		
Q7	7		

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	2					
NRS (Itch)	2					

SF-36

	Baseline		norms
Physical Function	95		92.28
Role Physical	100		80.44
Bodily Pain	90		79.75
General Health	80		78.71
Vitality	50		58.67
Social Function	100		89.17
Role Emotional	100		85.62
Mental Health	64		77.27

Participant #4 – Distant Acupuncture

female, 20yrs, 9 months post-surgical, 7cm long scar

Needle placement: C6 & 7 bilateral 1cm, right & left mid arm, right mid forearm

POSAS

POSAS	Baseline	Midway	Final Treatment	1-month	2-months
Q1	2	3		1	1
Q2	4	2		1	1
Q3	8	5		3	4
Q4	7	2		2	4
Q5	7	5		1	4
Q6	6	4		2	4
Q7	7	5		3	4

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	0	0	2	1	2	
NRS (Itch)	1	1	4	1	2	

SF-36

	Baseline	Final Treatment	1-month	2-months		norms
Physical Function	95		100	100		93.16
Role Physical	43.75		100	100		79.17
Bodily Pain	35		90	100		77.23
General Health	65		75	85		73.3
Vitality	65		70	85		58.52
Social Function	37.5		50	75		84.19
Role Emotional	91.7		83.3	100		81.82
Mental Health	68		60	80		75.59

Participant #5 – Local Acupuncture

female, 34yrs, 12 months post-surgical, 12cm long scar

Needle placement: Abdomen

POSAS

POSAS	Baseline	Midway	Final Treatment	1-month	2-months
Q1	0	0	1	1	1
Q2	6	5	5	5	3
Q3	9	9	8	8	8
Q4	9	9	8	8	8
Q5	9	9	8	9	8
Q6	9	9	8	9	8
Q7	9	9	9	9	8

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	0	0	0	0	0	0
NRS (Itch)	5	5	3	4	6	0

SF-36

	Baseline	Final Treatment	1-month	2-months		norms
Physical Function	100	100	100	100		92.28
Role Physical	100	100	100	25		80.44
Bodily Pain	100	100	100	67.5		79.75
General Health	95	95	95	65		78.71
Vitality	65	65	35	35		58.67
Social Function	87.5	87.5	75	25		89.17
Role Emotional	100	100	83.3	50		85.62
Mental Health	64	64	56	48		77.27

Participant #6 – Distant Acupuncture

female, 47yrs, 10 months post-surgical, 8cm long scar

Needle placement: C6/T1 1cm bilateral, mid upper and lower arm bilateral

POSAS

POSAS	1	2	3	4	5
Q1	4	4	2	1	1
Q2	8	4	2	1	3
Q3	8	7	4	3	5
Q4	10	6	4	4	3
Q5	10	3	4	5	5
Q6	10	7	4	4	5
Q7	10	8	4	3	4

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	2	4	4	2	2	2
NRS (Itch)	6	5	3	2	2	2

SF-36

	Baseline	Final Treatment	1-month	2-months		norms
Physical Function	20	95	95	10		85.59
Role Physical	100	100	100	0		79.1
Bodily Pain	67.5	100	100	0		73.28
General Health	80	75	80	35		75.6
Vitality	55	55	60	45		59.51
Social Function	100	100	100	62.5		88.88
Role Emotional	100	100	100	100		85.2
Mental Health	76	76	80	84		78.93

Participant #7 – Local Acupuncture

Male, 33yrs, 10 weeks post-surgical, 2.5cm long scar

Needle placement: face

POSAS

POSAS	Baseline	Midway	Final Treatment	1-month	2-months
Q1	6		1	2	1
Q2	1		1	1	2

Q3	10		3	3	3
Q4	10		4	3	3
Q5	10		5	3	3
Q6	10		4	3	3
Q7	10		4	3	5

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	1	2	0	0	0	0
NRS (Itch)	0	0	0	0	0	0

SF-36

	Baseline	Final Treatment	1-month	2-months		norms
Physical Function	100	100	100	100		95.21
Role Physical	100	100	100	100		89.32
Bodily Pain	90	90	90	100		81.94
General Health	80	80	80	80		78.93
Vitality	70	70	75	80		65.4
Social Function	100	100	100	100		93.83
Role Emotional	100	100	100	100		91.68
Mental Health	84	80	80	80		81.26

Participant #8 – Local Acupuncture

female, 55yrs, 12 months post-surgical, 3.5cm long scar

Needle placement: Upper limb

POSAS

POSAS	Baseline	Midway	Final Treatment	1-month	2-months
Q1	2	3	2	1	2
Q2	3	2	2	1	2
Q3	10	10	7	10	10
Q4	10	10	7	10	10
Q5	10	10	7	10	10
Q6	10	10	7	10	10
Q7	10	10	7	10	10

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	1	1	2	2	1	2
NRS (Itch)	3	3	3	2	2	0

SF-36

	Baseline	Final Treatment	1-month	2-months		norms
Physical Function	80	75	n/a	95		80.31
Role Physical	87.5	75	100	100		77.79
Bodily Pain	80	57.5	90	90		71.47
General Health	35	40	n/a	60		73.42
Vitality	70	70	60	60		61.41
Social Function	100	75	100	100		90.03
Role Emotional	100	100	100	100		88.03
Mental Health	80	76	64	80		80.76

Participant #9 – Distant Acupuncture

female, 72yrs, 6 weeks post-surgical, 5cm long scar

Needle placement: L3+4 1cm lateral to Sp bilateral 10cm below knee on RHS

POSAS

POSAS	Baseline	Midway	Final Treatment	1-month	2-months
Q1	2	2	1	1	1
Q2	6	2	1	1	1
Q3	4	3	1	1	1
Q4	6	7	2	5	3
Q5	6	3	2	6	5
Q6	6	7	2	6	3
Q7	6	4	2	5	2

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	0	1	2	2	1	1
NRS (Itch)	4	3	2	1	1	1

SF-36

	Baseline	Final Treatment	1-month	2-months		norms
Physical Function	85	85	85	90		73.28
Role Physical	87.5	93.75	75	93.8		71.58
Bodily Pain	67.5	57.5	55	90		72.03
General Health	55	65	60	45		70.63
Vitality	50	50	45	40		59.64
Social Function	87.5	100	100	100		88.9
Role Emotional	100	91.66667	100	100		84.82
Mental Health	68	64	60	68		80.35

Participant #10 – Local Acupuncture

Male, 45yrs, 4 months post-surgical, 5cm long scar

Needle placement: Lumbosacral region

POSAS

POSAS	Baseline	Midway	Final Treatment	1-month	2-months
Q1	4	1	3	4	3
Q2	5	4	2	5	4
Q3	2	3	1	3	2
Q4	9	6	4	4	4
Q5	9	6	4	4	5
Q6	8	5	4	4	4
Q7	8	8	5	4	5

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	4	4	3	3	2	3
NRS (Itch)	5	4	4	4	2	2

SF-36

	Baseline	Final Treatment	1-month	2-months		norms
Physical Function	100	100	100	100		90.94

Role Physical	87.5	93.75	100	93.75		85
Bodily Pain	77.5	90	90	90		76.76
General Health	90	95	90	90		76.55
Vitality	55	70	80	80		64.86
Social Function	87.5	100	87.5	100		91.88
Role Emotional	100	100	100	100		92.16
Mental Health	80	80	80	80		82.32

Participant #11 – Local Acupuncture

Female, 58yrs, 7 months post-surgical, 3cm long scar

Needle placement: lower limb

POSAS

POSAS	Baseline	Midway	Final Treatment	1-month	2-months
Q1	2	9	2		
Q2	7	8	2		
Q3	8	8	3		
Q4	10	9	3		
Q5	10	6	5		
Q6	10	7	5		
Q7	10	7	4		

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	1	0	0	0	0	0
NRS (Itch)	6	0	1	0	1	0

SF-36

	Baseline	Final Treatment		norms
Physical Function	90	90		80.31
Role Physical	100	100		77.79
Bodily Pain	80	80		71.47
General Health	85	70		73.42
Vitality	70	75		61.41
Social Function	100	100		90.03

Role Emotional	100	100		88.03
Mental Health	68	72		80.76

Participant #12 – Distant Acupuncture

Female, 45yrs, 10 months post-surgical, 5cm long scar

Needle placement: L3,5 Bilateral , mid calf

POSAS

POSAS	Baseline	Midway	Final Treatment	1-month	2-months
Q1	3	1	1		
Q2	7	5	2		
Q3	10	10	10		
Q4	4	10	5		
Q5	8	10	10		
Q6	8	10	10		
Q7	8		10		

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	0	0	0	0	0	0
NRS (Itch)	5	5	3	2	2	1

SF-36

	Baseline	Final Treatment		norms
Physical Function	100	100		85.59
Role Physical	100	100		79.1
Bodily Pain	67.5	67.5		73.28
General Health	80	95		75.6
Vitality	55	55		59.51
Social Function	75	100		88.88
Role Emotional	100	100		85.2
Mental Health	60	60		78.93

Participant #13 – Local Acupuncture

Female, 78yrs, 3 months post-surgical, 20cm long scar

Needle placement: Lower limb

POSAS

POSAS	Baseline	Midway	Final Treatment	1-month	2-months
Q1	8	3	1	1	1
Q2	3	1	2	1	1
Q3	10	10	10	10	10
Q4	10	9	8	10	10
Q5	10	9	8	10	10
Q6	10	9	9	10	10
Q7	10	9	9	10	9

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	8	3	2	2	2	1
NRS (Itch)	4	4	2	1	1	2

SF-36

	Baseline	Final Treatment	1-month	2-months		norms
Physical Function	40	55	45	70		58.24
Role Physical	50	75	68.75	87.5		67.12
Bodily Pain	67.5	55	55	77.5		73.14
General Health	80	85	85	90		71.21
Vitality	70	70	70	75		56.67
Social Function	100	87.5	87.5	100		87.89
Role Emotional	100	100	100	100		91.66
Mental Health	80	80	80	80		81.94

Participant #14 – Local Acupuncture

Female, 54yrs, 2 months post-surgical, 3cm long scar

Needle placement: trunk (back)

POSAS

POSAS	Baseline	Midway
Q1	1	2
Q2	2	2
Q3	5	4
Q4	2	2
Q5	5	3
Q6	5	3
Q7	2	2

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	0	2	0	2	1	
NRS (Itch)	2	3	1	3	1	

SF-36

	Baseline			norms
Physical Function	90			85.59
Role Physical	68.75			79.1
Bodily Pain	100			73.28
General Health	85			75.6
Vitality	70			59.51
Social Function	100			88.88
Role Emotional	100			85.2
Mental Health	84			78.93

Participant #15 – Local Acupuncture

Male, 62yrs, 12 months post-surgical, 7cm long scar

Needle placement: Upper limb

POSAS

POSAS	Baseline	Midway	Final Treatment	1-month	2-months
Q1	2	1	1		
Q2	4	2	2		
Q3	1	2	1		
Q4	1	1	1		
Q5	1	1	1		
Q6	1	2	2		
Q7	1	2	2		

NRS

Session #	1	2	3	4	5	6
NRS (Pain)	1	1	1	1	0	0
NRS (Itch)	4	2	2	1	1	0

SF-36

	Baseline	Final Treatment		norms
Physical Function	85	90		80.61
Role Physical	68.75	81.25		77.89
Bodily Pain	32.5	90		78.14
General Health	75	75		70.73
Vitality	45	65		65.1
Social Function	62.5	100		93.66
Role Emotional	100	100		94.19
Mental Health	56	72		85.6