

**PROTOCOL FOR NON-EXEMPT RESEARCH INVOLVING HUMAN SUBJECTS**

<b>Title:</b>	A Comparison of Scar Infiltration, Scar Deactivation, and Standard of care for the Treatment of Chronic, Post-Surgical Pain after Cesarean Section in the Primary Care Setting: A comparative effectiveness trial.					
<b>IRB #:</b>	FWH20190005H					
<b>Principal Investigator (PI)</b>	<b>Rank / CIV Rating</b>	<b>Branch</b>	<b>AD/DoD CIV/ CTR/Civilian</b>	<b>Dept/Base</b>	<b>Phone #</b>	<b>E-mail</b>
Jennifer Loomis, DO	Capt	USAF	AD	Scott AFB/FMR	(570) 877-2078	jennifer.loomis2.mil@mail.mil

**The research relevance of this protocol focuses on:**

<input type="checkbox"/>	<b>Diagnosis</b>	<input checked="" type="checkbox"/>	<b>Treatment</b>	<input type="checkbox"/>	<b>Medical Utilization/Managed Care</b>
<input type="checkbox"/>	<b>Prevention</b>	<input type="checkbox"/>	<b>Medical Readiness</b>	<input type="checkbox"/>	<b>Other:</b>

**1. LOCATION AND SPONSOR**

<b>Collaborating Facilities:</b> None
<b>AF Sites Seeking Regional IRB:</b>
Jennifer Loomis, DO, Capt, Scott AFB, (570) 877-2078, jennifer.loomis2.mil@mail.mil Jill Clark, Nellis AFB, (702) 653-3298, jill.m.clark15.ctr@mail.mil
<b>Study Sponsors:</b> None

**2. RESEARCH PLAN**

<b>Purpose of Study:</b>
To compare scar infiltration with 0.5-1% Lidocaine at a dose of 3 mg/kg (max dose 300 mg) or scar deactivation with acupuncture surface release technique to determine which is more effective in reducing pain in adult patients with chronic, post-surgical pain related to the site of incision after low transverse Cesarean section compared to standard of care physical therapy with the McKenzie Method.
<b>Hypotheses, Research Questions, or Objectives:</b>
<ul style="list-style-type: none"> <li>• <u>Objective 1:</u> Compare whether a scar infiltration protocol with Lidocaine is more effective than scar deactivation with acupuncture surface release technique at improving pain in adults with chronic, post-surgical pain related to low transverse Cesarean section incision.</li> <li>• <u>Null Hypothesis 1:</u> 0.5-1% Lidocaine at a dose of 3 mg/kg (max dose 300 mg) does not reduce pain outcomes acutely and over time.</li> <li>• <u>Null Hypothesis 2:</u> Scar deactivation with acupuncture surface release technique does not reduce pain outcomes acutely and over time.</li> <li>• <u>Alternative Hypothesis 1:</u> 0.5-1% Lidocaine at a dose of 3 mg/kg (max dose 300 mg) reduces pain outcomes acutely and over time.</li> <li>• <u>Alternative Hypothesis 2:</u> Scar deactivation with acupuncture surface release technique reduces pain outcomes acutely and over time.</li> </ul>
<b>Significance:</b>
According to CDC 2015 data, 32% of all births are delivered via Cesarean section <sup>1</sup> . In patients who undergo Cesarean section, studies estimate 7-18% will experience chronic post-operative pain at the site of their incisional scar <sup>2</sup> . These statistics indicate that up to 1 in 6 out of every pregnancy is at risk of developing postoperative pain with an increased risk with each subsequent Cesarean section, and a significant portion of these members will seek care in the primary care clinic.
<b>Military Relevance:</b>
In 2016, the Department of Defense employed 1,288,596 active duty service members, of which 15.9% were women <sup>3</sup> . This age range is consistent with peak childbearing age, which extrapolates to a large portion of the female active duty force with the potential to have children during their military careers. Determining whether Scar infiltration or scar deactivation is more effective treatments for the reduction of chronic, post-surgical low transverse Cesarean section pain in military beneficiaries would result in less: lost duty days, profiles, and physical fitness testing exemptions in our active duty population, as well as an improved quality of life for all DoD beneficiaries. Scar infiltration is a technique using high dose and high volume lidocaine to infiltrate the scar. Scar infiltration uses 40cc to 60cc of 0.5% to 1% lidocaine, which is injected throughout the scar with a goal of 3-4mg/kg per injection. Typically a series of 4 to 5 injections. Scar deactivation is a technique when acupuncture needles are inserted into the skin surrounding the scar and are left in place for approximately 20 minutes and then removed. This can be repeated multiple times.

**Background and Review of Literature:**

**Existing Knowledge:** The etiology of chronic, post-surgical abdominal wall and/or pelvic pain after Cesarean section has multiple hypotheses. These possible sources include development of intra-peritoneal adhesions restricting fascial planes, anterior cutaneous nerve entrapment, and disruption of the autonomic nervous system within the intracellular fluid matrix known as an “interference field”<sup>2,4,5,6,7</sup>. While there is not a clearly established and widely accepted pathophysiological cause to this post-operative pain, studies have estimated that between 7-33% of patients experience chronic peri-incisional pain after Cesarean section with Pfannenstiel incision – a type of abdominal surgical incision that allows access to the abdomen and the most common method for performing Cesarean sections today – defined as pain persisting beyond the period of expected healing, approximately 3 months<sup>2,7</sup>.

**Gaps in Knowledge:** Management of chronic peri-incisional pain after Cesarean section requires an extensive workup including laboratory testing (CBC, ESR, Urinalysis, STI testing) and imaging (transvaginal ultrasonography and abdominal CT) to rule out organic causes<sup>5,6,8</sup>. Once a visceral etiology from postoperative pain has been excluded, there is not a well-established guideline dictating standard of care, however treatment can include analgesics such as Acetaminophen or Non-Steroidal Anti-inflammatory Drugs, and in refractory cases suggestive of neuropathic pain Tricyclic Antidepressants, Gabapentin, Pregabalin, and Serotonin-Norepinephrine Reuptake Inhibitors can be used<sup>5,6,8</sup>. If medicinal therapy fails to manage symptoms, consultation for pain management specialists and/or surgical evaluation is often considered<sup>5,6,8</sup>.

Scar deactivation is used as standard of care for treatment and resolution of scar associated pain in patients with a history of Cesarean section by medical acupuncturists, both abdominal and/or low back pain that began after the cesarean section. Scar infiltration with lidocaine has been used in numerous clinical settings, masquerading under different names. Referred to as “Neural Therapy” in Germany, the technique of injecting short-acting local anesthetic into the dermal subcutaneous junction of scar tissue has been widely applied; however there is limited readily available clinical trial evidence supporting its reported effectiveness<sup>9,10,11</sup>. Theoretically, it is postulated that the anti-inflammatory effects of local anesthetics play a role in mitigating the autonomic nervous system disruption of “interference fields” caused by scar tissue<sup>9,10,11</sup>. Local anesthetics promote anti-inflammatory activity through a variety of mechanisms including reversibly inhibiting leukocyte adhesion by interfering with the action of integrins and leukocyte adhesion molecule-1, limiting leukocyte migration, reversible inhibition of phagocytosis, inhibition of phospholipase A2, inhibition of prostaglandins, inhibition of thromboxane release, inhibition of leukotriene release, inhibition of histamine release, reduction in free radical formation, inhibition of cytokine release of IL-1 $\beta$ , IL-8 and TNF- $\alpha$ <sup>12,13</sup>. Additionally, Lidocaine injection is proposed to alleviate nerve entrapment within fascia through hydrodissection, a technique being effectively utilized in the management of carpal tunnel syndrome<sup>14</sup>.

Scar deactivation is the technique of inserting acupuncture needles at a 30-45 degree angle into the superficial fascia to surround a scar. It is postulated that needle insertion into connective tissue produces analgesia through a multifaceted process encompassing the disruption and remodeling of extracellular matrix in loose connective tissue, alterations in gene expression affecting neurotransmitter levels, and cellular signaling pathways impacted in response to fibroblast and mast-cell involvement (15). In traditional Chinese medicine, injuries resulting in scar tissue formation are thought of as areas of blood and subsequently Qi stagnation (16). Disruptions in the flow of Qi at the point of scar tissue can result in abnormal skin sensations such as pain, itching, and numbness in addition to systemic effects<sup>16</sup>. A case report has demonstrated effective pain relief in with an acupuncture protocol utilizing scar deactivation technique<sup>16</sup>.

**Bibliography:**

1. Martin, J, B Hamilton, M Osterman, et al “Births: Final data for 2015.” *National Vital Statistics Report*. 2017 Jan; 66(1):1-70.
2. Wasserman, JB, JL Steele-Thornborrow, JS Yuen, et al. “Chronic cesarean section scar pain treated with facial scar release techniques: A case series” *J of Bodywork & Movement Therapy* 2016; 20: 906-913.
3. 2016 Demographics Report. Department of Defense Military One Source website. <http://download.militaryonesource.mil/12038/MOS/Reports/2016-Demographics-Report.pdf>. Accessed April 3, 2018.
4. Okabayashi, K, H Ashrafian, E Zacharakis, et al. “Adhesions after abdominal surgery: a systematic review of the incidence, distribution, and severity” *Surg Today* 2014;44:405-420.
5. Suleiman, S and D Johnston. “The abdominal wall: an overlooked source of pain.” *Am Fam Physician*. 2001; 64:431-438.
6. Srinivasan, R and D Greenbaum. “Chronic abdominal wall pain: a frequently overlooked problem.” *American Journal of Gastroenterology*. 2002; 97(4):824-830
7. Loos, MJ, MR Scheltinga, LG Mulder, et al. “The Pfannenstiel incision as a source of chronic pain” *Obstet Gynecol*. 2008 Apr;111(4):839-46.
8. Speer, LM, S Mushkback, and T Erbele. “Chronic pelvic pain in women” *Am Fam Physician*. 2016 March; 93(5): 380-387.

9. Brobyn TL, MK Chung, and PJ LaRiccia "Neural therapy: An overlooked game changer for patients suffering chronic pain?" *J Pain Relief* 2015;4: 184.
10. Weinschenk S. "Neural therapy--A review of the therapeutic use of local anesthetics" *Acupuncture and Related Therapies* 2012.
11. Egli, S, M Pfister, SM Ludin, et al "Long-term results of therapeutic local anesthesia (neural therapy) in 280 referred refractory chronic pain patients" *BMC Complementary and Alternative Medicine* 2015;15:200.
12. Hollman MW, and ME Durieux "Local anesthetics and the inflammatory response: a new therapeutic indication?" *Anesthesiology* 2000;93(3):858-875.
13. Cassuto, J, R Sinclair, and M Bonderovic. "Anti-inflammatory properties of local anesthetics and their present and potential clinical implications" *Acta Anaesthesiol Scand* 2006; 50: 265—282.
14. Malone, D, T Clark, and N Wei. "Ultrasound-guided percutaneous injection, hydrodissection, and fenestration for carpal tunnel syndrome: description of a new technique." *Journal of Applied Research*. 2010;10(3):116-123.
15. Liddle, CE and RE Harris. "Cellular reorganization plays a vital role in acupuncture analgesia" *Medical Acupuncture* 2018 November; 30: 15-20.
16. Feng S. "The successful treatment of pain associated with scar tissue using acupuncture" *J of Acupunct Meridian Stud* 2014; 7(5): 262-264.

#### SEE DATA ANALYSIS SECTION FOR REMAINING REFERENCES

17. Fearmonti, R, J Bond, D Erdmann, et al. "The modified POSAS: A novel approach to defining pathologic and non-pathologic scarring" *Plast Reconstr Surg*. 2011 January ; 127(1): 242–247.
18. Polomano RC, Galloway KT, Kent ML, Brandon-Edwards H, Kwon KN, Morales C, Buckenmaier C' 3rd. Psychometric Testing of the Defense and Veterans Pain Rating Scale (DVPRS): A New Pain Scale for Military Population. *Pain Med*. 2016 Aug;17(8):1505-19.
19. Nassif TH, Hull A, Holliday SB, Sullivan P, Sandbrink F. Concurrent Validity of the Defense and Veterans Pain Rating Scale in VA Outpatients. *Pain Med*. 2015 Nov;16(11):2152-61.
20. Faul F, Erdfelder E, Lang A-G, Buchner A. G\*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*. 2007; 39 (2): 175-191.
21. Deck M, Kopriva D. Patient and observer scar assessment scores favour the late appearance of a transverse cervical incision over a vertical incision in patients undergoing carotid endarterectomy for stroke risk reduction. *Can J Surg*. 2015; 58 (4):245–249.
22. Kim HI, Kwak CY, Kim HY, Yi HS, Park EJ, Kim JH, Park JH. Correlation between dermal thickness and scar formation in female patients after thyroidectomy. *Arch Craniofac Surg*. 2018 Jun; 19(2): 120–126.
23. Sloman R, Wruble AW, Rosen G, Rom M. (2006). "Determination of clinically meaningful levels of pain reduction in patients experiencing acute postoperative pain." *Pain Manag Nurs* 7(4): 153-158.
24. Holm, S. 1979. A simple sequential rejective multiple test procedure. *Scand. J. Statistics*, 6: 65-70.
25. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2016 URL <http://www.R-project.org/> < Caution-<http://www.R-project.org/> > .

### 3. RESEARCH DESIGN AND METHODS

#### Research Design and Methods:

Active duty members and DoD beneficiaries, age 18 years of age or older, meeting the inclusion/exclusion criteria will be offered an opportunity to participate. They will be recruited from the clinics located at Nellis AFB and Scott AFB. All of the below items are research-related unless marked as 'standard of care':

**Pre-Eligibility review:** Subjects who responded to advertisements or recruitment letters or have given their permission to be contacted will be approached by a study staff member to discuss the subject's interest in the research study and to receive a pre-eligibility screening for study participation. The attached "Pre-Eligibility Review Script" will be used and response will be recorded. If the subject is interested in participating in the study, the study staff member will schedule a screening visit while the subject waits on the phone or in-person, in order to confirm the schedule appointment with the subject. Following the pre-screening procedure, the script will be shredded.

#### Screening Visit:

- Obtain and document signed Informed Consent document and HIPAA Authorization.
- Review past medical history to verify the inclusion/exclusion criteria including previous encounter, medication list (including analgesic medication currently taking), co-morbidities, demographics, and problems list.

- Record date of birth, age, gender, race, ethnicity, DoD ID, current email address, height (inches), weight (in pounds-not stated weight), obstetrical history, history of relevant pain and interventions.
- Instruct subjects to discontinue any current acupuncture treatment at the onset of entering the study. It is theorized that any acupuncture treatment can have a positive or a negative effect on treatment response regardless of the technique or treatment indication.
- If the subject is an active duty member, we will ask:
  - Have you or are you currently on a fitness restriction for this condition.
  - If so, what are/were the dates of the restriction?

**Randomization:**

- Subjects will be randomized into one of three research-related treatment groups using block randomization with repeated measures:
  - **Group 1: Scar Deactivation Surface Release Technique protocol:**
    - Alternating placement of Spring Ten (0.30x40 mm) acupuncture needles to surround scar left in place for a treatment duration of 20 minutes. Needles will be placed at intervals of 1cm to 1.5 cm and will surround the scar with a maximum of 20 needles per treatment.
  - **Group 2: Scar Infiltration with 0.25-1% Lidocaine:**
    - Will consist of calculation of 3 mg/kg dose of 0.5-1% Lidocaine and a dermal followed by subcutaneous injection using 1.5 inch 25 G needle and syringe appropriate for volume based on calculated dose.
  - **Group 3: Physical therapy:**
    - Will be a referral to physical therapy specifying McKenzie protocol treatment for the presenting complaint. The McKenzie protocol is a form of standard of care physical therapy in which the physical therapist tries to find a cause and effect relationship between the positions the patient usually assumes while sitting, standing, or moving, and the location of pain because of those positions or activities. The therapeutic approach requires a patient to move through a series of activities and test movement to gauge the patient's pain response. The approach then uses that information to develop an exercise program designed to centralize or alleviate the pain.

**Visit 1 (may be same day as screening visit) (visit window plus or minus 1 week):**

**Group 1: Scar Deactivation Surface Release Technique protocol (acupuncture):**

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- We will ask what the subjects' expectations are regarding acupuncture effectiveness for chronic, post-surgical pain related to low transverse Cesarean Section.
- The Research Coordinator will record the number of needles placed and the name of the provider performing the acupuncture.
- **Pre-Treatment:**
  - Defense and Veterans Pain Rating Scale (DVPRS)
  - Instruct patients to mark general area of scar on pictures provided on the Patient and Observer Scar Assessment Score (POSAS) Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.
- **Post-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.

**Group 2: Scar Infiltration with 0.25-1% Lidocaine:**

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- We will ask what the subjects' expectations are regarding lidocaine's effectiveness for chronic, post-surgical pain related to low transverse Cesarean Section.
- The Research Coordinator will document the total volume of 0.5-1% Lidocaine injection.
- **Pre-Treatment:**
  - DVPRS

- Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
- Instruct the PI or AI to complete the POSAS Observer Scale.
- **Post-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.

**Group 3: Physical Therapy:**

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- We will ask what the subjects' expectations are regarding physical therapy's effectiveness for chronic, post-surgical pain related to low transverse Cesarean Section.
- Subjects will be given a study diary and asked to track the dates and duration of their physical therapy treatments.
- DVPRS
- Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
- Instruct the PI or AI to complete the POSAS Observer Scale.

**Visit 2 (4 weeks after visit 1 (visit window plus or minus 1 week)):**

**Group 1: Scar Deactivation Surface Release Technique protocol (acupuncture):**

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- The Research Coordinator will record the number of needles placed and the name of the provider performing the acupuncture.
- **Pre-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.
- **Post-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.

**Group 2: Scar Infiltration with 0.25-1% Lidocaine:**

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- The Research Coordinator will document the total volume of 0.5-1% Lidocaine injection.
- **Pre-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.
- **Post-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.

**Group 3: Physical Therapy:**

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- We will record the information from the study diary and remind them to track the dates and duration of their physical therapy treatments.
- DVPRS
- Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.

- Instruct the PI or AI to complete the POSAS Observer Scale.

**Visit 3 (8 weeks after visit 1) (visit window plus or minus 1 week):**

***Group 1: Scar Deactivation Surface Release Technique protocol (acupuncture):***

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- The Research Coordinator will record the number of needles placed and the name of the provider performing the acupuncture.
- **Pre-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.
- **Post-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.

***Group 2: Scar Infiltration with 0.25-1% Lidocaine:***

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- The Research Coordinator will document the total volume of 0.5-1% Lidocaine injection.
- **Pre-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.
- **Post-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.

***Group 3: Physical Therapy:***

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- We will record the information from the study diary and remind them to track the dates and duration of their physical therapy treatments.
- DVPRS
- Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
- Instruct the PI or AI to complete the POSAS Observer Scale.

**Visit 4 (16 weeks after visit 1) (visit window plus or minus 1 week):**

***Group 1: Scar Deactivation Surface Release Technique protocol (acupuncture):***

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- The Research Coordinator will record the number of needles placed and the name of the provider performing the acupuncture.
- **Pre-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.
- **Post-Treatment:**
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided the POSAS Patient Scale.

- Instruct the PI or AI to complete the POSAS Observer Scale.

**Group 2: Scar Infiltration with 0.25-1% Lidocaine:**

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- The Research Coordinator will document the total volume of 0.5-1% Lidocaine injection.
- Pre-Treatment:
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.
- Post-Treatment:
  - DVPRS
  - Instruct patients to mark general area of scar on pictures provided the POSAS Patient Scale.
  - Instruct the PI or AI to complete the POSAS Observer Scale.

**Group 3: Physical Therapy:**

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- We will record the information from the study diary and remind them to track the dates and duration of their physical therapy treatments.
- DVPRS
- Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
- Instruct the PI or AI to complete the POSAS Observer Scale.

**Visit 5 (20 weeks after visit 1) (visit window plus or minus 1 week):**

**Group 1: Scar Deactivation Surface Release Technique protocol (acupuncture):**

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- DVPRS
- Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
- Instruct the PI or AI to complete the POSAS Observer Scale.
- We will record the subjects self-reported reduction in pain severity since the beginning of the study (reported a percentile (i.e. 10%, 20%, etc.).
- We will ask if the subjects' expectations were met regarding acupuncture's effectiveness for chronic, post-surgical pain related to low transverse Cesarean Section.

**Group 2: Scar Infiltration with 0.25-1% Lidocaine:**

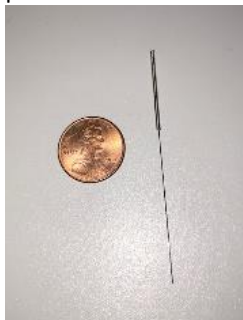
- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- DVPRS
- Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.
- Instruct the PI or AI to complete the POSAS Observer Scale.
- We will record the subjects self-reported reduction in pain severity since the beginning of the study (reported a percentile (i.e. 10%, 20%, etc.).
- We will ask if the subjects' expectations were met regarding lidocaine's effectiveness for chronic, post-surgical pain related to low transverse Cesarean Section.

**Group 3: Physical Therapy:**

- Study staff will reconcile medication list (including analgesic medication currently taking).
- Subjects will be weighed (in pounds-not stated weight).
- DVPRS
- Instruct patients to mark general area of scar on pictures provided on the POSAS Patient Scale.

- Instruct the PI or AI to complete the POSAS Observer Scale.
- We will record the subjects self-reported reduction in pain severity since the beginning of the study (reported a percentile (i.e. 10%, 20%, etc.).
- We will ask if the subjects' expectations were met regarding physical therapies effectiveness for chronic, post-surgical pain related to low transverse Cesarean Section.

This study will follow all FDA requirements for the safe use of the acupuncture needles. The Food and Drug Administration (FDA) regulates acupuncture needles (see 21 CFR 880.5580) as a class II medical device, because they are intended for use in the cure, mitigation, treatment, or prevention of disease in man or are intended to affect the structure or function of the body of man. The needles being used are Spring Ten 0.30x40mm Acupuncture needles (see figure 1 below), which are exempt from premarket notification by the FDA for use in acupuncture and will be used in accordance with their FDA approved labeling.



#### a. Interventions and Observations:

**Patient and Observer Scar Assessment Score (POSAS):** Scar evaluation tool which has been shown to be appropriate for evaluation of linear scars, such as the Pfannenstiel incision, with good reliability and internal consistency. This scale evaluates for pain and itching at the scar site, change in color of the skin, change in stiffness or thickness of the scar, change in irregularity of the scar and overall assessment of change in the scar.

#### Secondary Outcomes:

- Reduction in the POSAS score
- Reduction in related symptoms including
  - dyspareunia,
  - decreased libido, or
  - Seemingly unrelated symptoms.

#### b. Setting:

Female (DoD beneficiaries) age 18 years or older meeting the inclusion criteria will be offered an opportunity to participate at Scott AFB, Scott AFB O'Fallon Family Medicine Residency Clinic located at 3 St. Elizabeth's Blvd, Suite 4000, O'Fallon, IL and Nellis AFB.

#### c. Date(s):

March 2019-May 2022

#### d. Subjects:

Female DoD beneficiaries meeting the inclusion criteria will be offered an opportunity to participate at Scott AFB and Nellis AFB. No other special populations (e.g., children, military basic trainees, prisoners, detainees) will be recruited.

#### e. Inclusion/Exclusion Criteria:

Inclusion Criteria	<ul style="list-style-type: none"> <li>• Female DoD beneficiaries age 18 years or older</li> <li>• 3 months or greater postpartum with abdominal and/or back pain starting after low transverse Cesarean section scar.</li> <li>• If subject has had prior Scar Deactivation with Surface Release Technique for cesarean section scar they must have completed a washout period of 12 weeks or more.</li> </ul>
Exclusion Criteria	<ul style="list-style-type: none"> <li>• Pregnant</li> <li>• Prior Scar Deactivation with Surface Release Technique for cesarean section scar within the last 12 weeks.</li> <li>• Ever had Prior Scar Infiltration with Lidocaine for cesarean section.</li> <li>• Active cellulitis surrounding scar</li> </ul>



	<ul style="list-style-type: none"> <li>● Revision of Cesarean section scar</li> <li>● Vertical incision or emergent Cesarean section</li> </ul>
--	---

f. Source of Research Material:						
Will you be using <u>private information</u> in this study?			<input checked="" type="checkbox"/> Yes			
If Yes,	<input checked="" type="checkbox"/> protected health information (PHI) held by a covered entity					
Use of <u>identifiers</u> with private information						
Identifiers to be Used?	Column A Looked at by research team	Column B Recorded on enrollment log, subject list, or key list	Column C Recorded on data collection tool (survey, spreadsheet, etc.)	Column D Recorded on specimen containers	Column E Shared w/ others not on research team	Column F Stored after study ended
NONE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Names	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Study codes linked to individuals' identities using a key only accessible by the researcher		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Phone/Fax Numbers	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
E-mails	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
DoD ID#	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Coding Plan?						
Describe the method that will be used to create and assign unique study codes to data.	The unique study code will be assigned in sequential order beginning with 001 at each recruiting site. Subjects at Nellis AFB will be named such as NE001 and subjects at Scott AFB will begin with SC001. The code will be placed in a Master Key of identifiable PHI/PII for each subject at each collaborating site					
Describe the method that will be used to create and assign unique study codes to specimens.	<input checked="" type="checkbox"/> N/A, not collecting specimens					
What is the format of the key?	<input checked="" type="checkbox"/> Electronic					
Who will have access to the key?	Principal Investigator and/or Designated Research Coordinator at each study site					
Where will the key be stored and how will it be protected?	<p>Location(s): Each collaborating site will maintain a Master Key of identifiable PHI/PII that will be kept in an electronic database separate from the coded, de-identified research data, which will be encrypted, password protected and the access will be restricted to the PI and/or Designated Research Coordinator. The Master Key will not be stored on any non-government or personal computers or laptops. At the conclusion of the study, the data from each site will be de-identified prior to review and analysis.</p> <p>Confidentiality measures: The coded research data will be kept in a locked cabinet in a locked office and only the research department has the key. The coded research data will be retained until the conclusion of the research study. Once a Final Report has been approved by the IRB, all the paper records will be de-identified and any key linking the subject to their records will be destroyed, based on AFI 33-332, "The Air Force Privacy and Civil Liberties Program" and the National Institute of Standards and Technology Special Publication (NIST SP 800-88) for the approved methods to destroy PII. The anonymized research data will not be utilized for further research activity beyond the protocol stipulations without additional IRB approval.</p>					
Complete the table.						
Source of Research Material per Participant (Procedures)	# Routine Care	# Research Driven	# Total Procedures			
DVPRS	0	9	9			
POSAS	0	9	9			
Acupuncture	0	4	4			
Lidocaine	0	4	4			

McKenzie Protocol

0

4

4

**g. Instrumentation:** N/A**4. HUMAN SUBJECT PROTECTION****Recruitment and Consent Processes:**

All potentially eligible patients will be offered an opportunity to participate. Primary Care Manager (PCM) referrals, with the patient's oral or written authorization, and posted advertisements will be utilized for recruiting subjects to the study. Some patients may be patients of the PI or AI; however, they will have another study staff recruit their patients to prevent any misconception of coercion or undue influence. When a potential subject is identified by the treating PCM, the patient will either be provided a contact number to the Research Staff, the Research Staff will be given the potential subjects contact information by the PCM, or the Research Staff will speak with the patient directly. It is not standard of care to perform this type of acupuncture on pregnant women.

**Consent Processes:**

Informed Consent and HIPAA authorization will be sought in advance of any screening and study-related procedures from each prospective study subject and appropriately documented in accordance with 32 CFR 219.117. Potential candidates will be notified about the study either through posted advertisements or by their healthcare provider and will be given the opportunity to consent by one of the referred study coordinators. The study coordinator will provide a written copy of the Informed Consent Document (ICD). The subject may decline to consent without prejudice. At the subjects' discretion, they may take the ICD home to discuss further with family members or another physician, prior to making a decision. If they decide they are interested in participating in the study, they can contact the research department. If the subject consents, a copy of the signed ICD and HIPAA Authorization Document will be given to the subject. No vulnerable populations are included in this research study. Subjects who cannot provide Informed Consent will not be allowed to participate. No Legally Authorized Representatives (LAR) will be utilized. Each subject will be asked to place their de-identified research data into the "Nellis Acupuncture Research Data Repository (FWH20140048H) for future research. If the subject does not give their authorization, then the de-identified research data will be destroyed no later than at 3 years after closure of the study.

**Recruiting Service Members**

Will you be recruiting service members in a group setting?

☐ Yes☒ No**Participation Compensation:** ☒ Subjects will not be paid for participation in this study.**Assent Process:** N/A**Benefits:**

Subjects may experience an improvement in pain in both the treatment groups; however, this is not a guarantee.

**Risks:**

The potential risks to participate in this study are minimal. The risks associated with participating in this research study include:

**Acupuncture Risks:**

- Likely and not serious:
  - Pain
  - Bleeding
- Less Likely and not serious:
  - Infection
  - Muscle cramps/spasms
- Less Likely and serious:
  - Bowel Perforation
  - Transient vasovagal response to needling

**Lidocaine Risks:**

- Likely and not serious:
  - Pain
  - Bleeding

- Less Likely and not serious:
  - Infection
  - Lidocaine toxicity

These risks will be minimized by cleaning the treatment site with an alcohol swab prior to placement. If at any time the patient reports a side effect, they will be referred to one of the Investigators for care. There may be a risk of inadvertent breach of confidentiality.

**Costs:** N/A

#### **Safeguards for Protecting Information:**

The research consents and HIPAA Authorization Documents will be stored in a locked cabinet in a locked room with restricted access. All identifiable research data including patient demographics will be kept in an electronic database separate from the coded research data, which will be encrypted, double password protected and the access will be restricted. The research data will be coded and any links to identifiable data (i.e., Master Key) will be destroyed as soon as all data mergers have occurred, or no later than at the closure of the study, all identifiable patient information will be destroyed based on AFI 33-332, "The Air Force Privacy and Civil Liberties Program" and the National Institute of Standards and Technology Special Publication (NIST SP 800-88) for the approved methods to destroy PII. The anonymized research data will not be utilized for further research activity beyond the protocol stipulations without additional IRB approval. At the conclusion of the study, the data will be de-identified prior to review and analysis.

#### **Data and Specimen Storage Plan**

##### **How will coded or identifiable data/specimens be stored?**

<input checked="" type="checkbox"/>	Paper data, including completed consent forms	The research consents and HIPAA Authorization Documents will be stored in a locked cabinet in a locked room with restricted access.
<input checked="" type="checkbox"/>	Electronic data	Medical records will be annotated with ICD-10 code Z00.6 to reflect the subject's participation in a research study, in which they are receiving a research-related treatment intervention. All research data that includes the Master Key of identifiable patient demographics and PHI/PII will be kept in an electronic database at each site, separate from the coded research data, which will be encrypted, password protected and the access will be restricted.
<input checked="" type="checkbox"/>	Long-term storage (following completion of the study and inactivation of IRB approval)	The research data will be coded and any links to identifiable data will be destroyed (an approved shredding bin) as soon as possible or no later than at the closure of the study, with the exception of those study subjects that consent to place their de-identified research data into the "Nellis Acupuncture Research Data Repository (FWH20140048H)" for future research. The anonymized research data will not be utilized for further research activity beyond the protocol stipulations without additional IRB approval. All de-identified research data will be maintained for 3 years following study closure.

#### **Safeguards for Protecting Subjects Relative to Reasonably Expected Risks:**

Safeguards are in place for protecting subjects and their health data. The research consents and HIPAA Authorization Documents will be stored in a locked cabinet in a locked room. If at any time the patient reports a side effect, they will be referred to one of the Investigators for care.

**Categories of subjects:** None

**Clinical Care:**

All subjects will receive standard of care regardless of inclusion into this study. If at any time a subject experiences any injury or adverse effects, appropriate clinical care will be given or subject will be referred to appropriate provider.

**Injury Compensation:** N/A

**Data Safety Monitoring:**

☒ N/A – none of the situations listed above apply

## 5. ALTERNATIVES

**Alternatives:**

Acupuncture and lidocaine for scar infiltration are done in the Family Medicine Residency as part of standard of care. However, other medicinal therapies, such as Acetaminophen or Non-Steroidal Anti-inflammatory Drugs, Tricyclic Antidepressants, Gabapentin, Pregabalin, and Serotonin-Norepinephrine Reuptake Inhibitors can be used. If medicinal therapy fails to manage symptoms, consultation for pain management specialists and/or surgical evaluation is often considered. Subjects may choose to receive any of these types of treatment options without participating in this study.

## 6. DATA ANALYSIS

**Data Analysis:**

**Outcome Measures:**

The primary outcome measures are the Patient and Observer Scar Assessment Scale (POSAS), and the Defense and Veterans Pain Rating Scale (DVPRS).

The Patient and Observer Scar Assessment Scale consists of the total score of two numeric scales measured by the patient and a qualified observer. Each scale assesses the scar by six characteristics on 10-point scales with a 1 corresponding to normal skin and a 10 representing the worst imaginable condition for that characteristic. The Total Score of both scales is calculated by summing scores of the six items resulting in a range of 6 to 60. The POSAS is treated as an interval variable; therefore, parametric methods will be used for this outcome<sup>17</sup>.

The DVPRS consists of an 11-point numerical rating scale with 0 indicating no pain and 10 indicating severe pain. It has been confirmed for reliability and validity in measuring both acute and chronic pain, and is currently the standard for pain measurement throughout DoD and VHA health systems. The DVPRS has demonstrated linear scale qualities allowing parametric methods to be used.<sup>18, 19</sup>

**Outcome Measures:**

Primary outcome: Pain reduction and reduction of DVPRS score. The goal for pain reductions will be 50% as a primary outcome.

Secondary outcomes: Reduction of POSAS score, improvement in related and unrelated symptoms as identified by above mentioned questionnaire, and willingness to undergo further treatment.

**Sample Size Estimation/Power Analysis:**

The study is organized as a mixed effects, randomized complete block design with repeated measures. Subject is a random effect as subjects will have been randomly subjected to C-section from the population of patients obtaining similar care at these Air Force medical treatment facilities, randomly enrolled from this population of patients, and randomly assigned to 3 treatment groups at the time of study enrollment. Fixed effects are treatment group and time of repeated measure as these effects cannot be generalized to other treatments and times.

A priori power was assessed using G\*Power Version 3.1.9.2.<sup>20</sup> Mean (SD) Total POSAS scores for non-hypertrophic scars resulting from vertical incisions have been found to be 21.1 (8.3) and 21.4 (7.4).<sup>21,22,23</sup> Power for the Total POSAS score was assessed to detect a 1 SD difference. Mean (SD) DVPRS pain intensity for a broad sample consisting of inpatients and outpatients suffering from acute and chronic pain has been found to be 4.4 (2.4), and will serve as the effect size for this outcome.

A priori power analysis for a rANOVA for the POSAS indicates 24 subjects will have a power of 0.966 to detect the minimal clinically important difference at  $\alpha = 0.05$ . A priori power analysis for a rANOVA for the DVPRS indicates 33 subjects will have a power of 0.962 to detect the minimal clinically important difference at  $\alpha = 0.05$ . Post hoc tests within smaller subgroups may be required, such as differences due to time within a treatment group. Therefore, to achieve a power for post hoc tests of 0.95 at  $\alpha = 0.05$ , a sample size of 45 subjects will be required.

#### Statistical Analysis:

Sample and treatment group means and standard deviations will be calculated for normally distributed interval variables and medians and interquartile ranges (IQR) for non-normally distributed interval variables. Frequency distributions will be produced for nominal and ordinal variables.

The statistical hypotheses of null effects for POSAS and DVPRS outcome measures will be tested by a mixed effects repeated measures analysis of covariance (rANCOVA). In the event the rANCOVA null hypothesis is rejected, contrasts will be used to investigate effects and differences within time intervals.

In the event multiple comparison tests are used to investigate effects, the Holm method will be used to correct the significance level of  $\alpha$  to  $p = .05$ .<sup>24</sup>

Mr. Danny Sharon, Senior Research Biostatistician Subject Matter Expert for Clinical Research Management under contracts OMNI 0004 3-82 and OMNI 0005 3-126, is the statistical consultant supporting this study. Statistical analysis will be performed with R Version 3.5.1.<sup>25</sup>

#### Number of Subjects:

	# Planned to Enroll	# Enrolled	# Planned to Complete Study	TOTAL
Number of Subjects at Scott AFB	30	N/A	24	60
Number of Subjects at Nellis AFB	30	N/A	24	

*\*If one site recruits more than the other, then they will be able to continue recruitment until the accrual ceiling has been reached.*

### 7. STUDY DURATION

#### Duration of Study:

Approximate duration of the study: 5 years

### 8. LOCAL AND EXTERNAL SUPPORT SERVICES

Local and External Support Services: None

Describe the plan for training personnel who are not part of the research team and will be administering intervention(s).

☒ Not applicable – no training of non-study personnel required

### 9. INTRAMURAL (GME) AND EXTRAMURAL FUNDING SUPPORT

Intramural (GME) and Extramural Funding Support: None

### 10. DRUGS, BIOLOGICS, DIETARY SUPPLEMENTS, AND MEDICAL DEVICES

#### Does the study plan dictate the use of any of the following?

A drug (Lidocaine)	<input checked="" type="checkbox"/> Yes	<input type="checkbox"/> No
A biologic	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No
A compound intended to affect structure or any function of the body	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No
A dietary supplement or substance <i>generally recognized as safe</i> that will be used to diagnose, cure, mitigate, treat, or prevent disease	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No
A medical device (Acupuncture needles)	<input checked="" type="checkbox"/> Yes	<input type="checkbox"/> No

#### 10A. List all drugs covered by an Investigational New Drug (IND) from the FDA (approved or submitted)

☒ N/A, an IND has not been submitted to or approved by the FDA

#### 10B. List all FDA approved drugs being used in accordance with FDA approved labeling

<input checked="" type="checkbox"/> Lidocaine is an FDA approved drug being used according to the labeling	
<b>10C. List all FDA approved drugs used for an unapproved use ("off-label")</b>	
<input checked="" type="checkbox"/> N/A, no FDA approved drugs being used "off-label"	
<b>10D. List all biologics, compounds and dietary supplements</b>	
<input checked="" type="checkbox"/> N/A, no biologics, compounds and dietary supplements	
<b>10E. List all devices covered by an Investigational Device Exemption (IDE) from the FDA (approved or submitted)</b>	
<input checked="" type="checkbox"/> N/A, an IDE has not been submitted to or approved by the FDA	
<b>10F. List all FDA approved devices used for an unapproved use ("off-label")</b>	
<input checked="" type="checkbox"/> N/A, no FDA approved devices being used "off-label"	
<b>10G. List all unapproved devices.</b>	
<input checked="" type="checkbox"/> N/A, no unapproved devices	
<b>10H. Device Storage Location(s):</b>	

<b>Is this research an "<a href="#">applicable clinical trial</a>" which must be registered on ClinicalTrials.gov?</b>
<input checked="" type="checkbox"/> No

<b>Use of a placebo in place of standard therapy:</b>		
Is a placebo being used in place of standard therapy?	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Yes

**11. MEDICAL RESEARCH AREA**

<input checked="" type="checkbox"/> Other:	Family Medicine and Family Medicine Residency
--	---

**12. ATTACHMENTS**

1. Form A, Signature Sheet
2. Form A-2, Study Personnel Listing
3. Form D, Informed Consent Document
4. H16 Template
5. HIPAA Authorization Document
6. Advertisement
7. POSAS Patient Scale
8. POSAS Observer Scale
9. Procedure Instructions
10. DVPRS
11. Pre eligibility Review Script
12. Form O Use of a Drug in Research
13. Form P Use of an Investigational Device in Research