PROTOCOL FOR NON-EXEMPT RESEARCH INVOLVING HUMAN SUBJECTS

Title:	Acupuncture for vasectomy pre-procedural anxiety and pain control in the primary care setting: A randomized comparative effectiveness trial.
IRB #:	FWH20190062H

Principal Investigator (PI)	Rank / Civ Rating	Branch	AD/DoD Civ/ Ctr/Civilian	Dept/Base	Phone #	E-mail
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The research relevance of this protocol focuses on: ☒ Treatment

FOR 59 MDW PERSONNEL ONLY Individuals must be covered under 59 MDWI 40-404, *Managing Conflict of Interest in Research*			
CONFLICTS OF INTEREST:	**Do you or any of your research staff have a potential conflict of interest to disclose?** If unsure, read the below statement before proceeding.	☐Yes	☒No

Does the research fall under the purview of any other departments or committees?	Yes	No
Radiation Safety Committee		☒
Institutional Biosafety Committee or Biosafety Officer		☒
59th Medical Wing (59 MDW) Office of Research and Technology Applications (ORTA)		☒
59 MDW/SGARB Resource Management Office		☒

1. LOCATION AND SPONSOR

Collaborating Facilities: None

AF Sites Seeking Regional IRB:

Jill Clark, 99MDG, (702) 653-3298, jill.m.clark15.ctr@mail.mil

Study Sponsors: None

2. RESEARCH PLAN

Purpose of Study:

To compare auricular (ear) acupuncture and body acupuncture (Koffman protocol) versus clinic standardized pre-vasectomy medications to determine which has better outcomes at improving pre-procedural anxiety and procedural pain relief and medication usage in adult male patients following vasectomy.

Hypotheses, Research Questions, or Objectives:

We want to compare auricular (ear) and body acupuncture (Koffman protocol) versus clinic standardized pre-vasectomy medications to determine which has better outcomes at improving pre-procedural anxiety and procedural pain relief and medication usage in adult male patients following vasectomy. In this efficacy trial, we hypothesize that acupuncture will provide therapeutic anxiety and pain relief during and after vasectomy. We will measure anxiety immediately before and prior to the procedure and before and after the intervention via a standardized anxiety scale (comparative). We will also measure pain control immediately after the procedure using Defense and Veterans Pain Rating Scale (DVPRS). At the post op check (2-4 days after procedure) subjects will fill out a patient satisfaction survey. During the recovery period over 2 weeks, a medication usage diary will be kept by the subject including the time when the patient returns to full duties.

Significance:

Contraception is an important part of medical care and family planning. Vasectomy is a common, safe, effective contraceptive procedure. There are no established national standards of care regarding pre-vasectomy medication. In some clinics, benzodiazepines are commonly prescribed for pre-vasectomy anxiety management, and NSAIDs or opiates for procedural pain. However, these medications can have potentially harmful side effects and have a high risk of dependence and abuse. Acupuncture is a safe alternative with relatively few side effects and low risk of dependence or abuse.

Military Relevance:

Unwanted pregnancies can have a significant psychological, social, and financial burden for members of the armed services, distracting them from the mission especially during deployed operations. Furthermore, benzodiazepines and opiates are considered mind-altering medications and affecting the functionality and capability of the military member. Establishing acupuncture as a safe alternative to benzodiazepines and opiates could help to reduce the need for these medications and thereby support the military's objectives.

Several hundred active duty providers have received acupuncture training over the last decade. By investigating the effectiveness of this acupuncture protocol for the treatment of pre-procedural anxiety and procedural pain, we could potentially increase patient satisfaction during the procedure and decrease the recovery time. In addition, a similar protocol could be employed for other minor outpatient procedures. This should decrease profile duration and physical fitness exemptions, increase medical readiness, and improve quality of life for service members.

Background and Review of Literature:

Our review of the literature revealed no studies directly investigating the use of acupuncture in performing vasectomies. Nor did we reveal any studies directly comparing the using of acupuncture and benzodiazepines for pre-procedural anxiety. The subject is further complicated by the fact that there are many established acupuncture techniques and protocols for managing stress and anxiety, many of which (including the one which we are proposing for this study) have not yet been investigated for use in relation to small procedures. However, review of the literature did reveal several studies related to these topics. A nationally recognized standard of care does not exist recommending pre-vasectomy medication administration for anxiety or pain. Local clinic practice or provider preference dictates whether medications are prescribed.

Several studies have examined the effects of acupuncture on pre-procedure anxiety. A 2018 prospective non-randomized study (N=62) evaluated the effect of auricular acupuncture in the relief of anxiety prior to elective ambulatory gynecologic surgery.[1] Female patients (ages 19-55) presenting for elective ambulatory gynecologic surgery self-selected into an auricular acupuncture group (n=32) and a control group (n=30). The acupuncture group underwent treatment by an acupuncturist the night prior to the procedure and the control group hand no additional intervention. Patient anxiety was measured via the State Trait Anxiety Inventory (STAI) (range 20=no anxiety, 80=maximum imaginable anxiety) before acupuncture was performed, the evening prior to surgery, and immediately before surgery. Auricular acupuncture significantly decreased anxiety scores the night prior to surgery (42 vs. 47, $P<0.001$) as well as immediately prior to surgery (46 vs. 53, $P<0.01$) compared to no intervention. A 2001 RCT evaluated the effectiveness of acupuncture in management of pre-procedure anxiety. [2] Patients (ages 19-65) undergoing elective ambulatory surgery received either traditional Chinese acupuncture points (n=31), an auricular relaxation protocol (n=32), or no intervention (n=28) prior to the procedure. Auricular relaxation protocol resulted in improved anxiety scores on the STAI after 30 minutes compared to baseline versus control or traditional Chinese acupuncture (35 vs. 40 vs. 39, $P=0.014$). Anxiety in traditional Chinese acupuncture patients was not significantly different compared to auricular relaxation patients ($P=0.37$) or the control group ($P=0.28$). A similar 2004 RCT found that, compared to sham acupuncture, an auricular acupuncture relaxation protocol significantly reduced perceived pre-procedural Modified Yale Preoperative Anxiety Scale (MYPAS) scores in children (35 vs. 48, $P=0.03$) and STAI scores (43 vs. 50, $P=0.014$) in the mothers of those children prior to elective outpatient pediatric ENT surgery.[3]

A 1991 RCT (N=44) evaluated the effects of diazepam and acupuncture for the pain associated with osteoarthritis.[4] Patients (ages 42-77) with chronic cervical osteoarthritis received either diazepam (5mg PO), acupuncture, sham-acupuncture or placebo during a single treatment. However, all 44 patients received all four treatment options during the course of the study. Pain scores (based on a DVPRS) were assessed at before and two hours after treatment. Both diazepam and acupuncture significantly lowered pain scores within the groups (1.9 vs. 1.6, $P<0.05$ and 2.5 vs. 1.8, $P<0.005$) and compared to placebo ($P<0.05$). Data suggests acupuncture is at least as effective in managing pain as benzodiazepine drugs, but with less potential harmful side effects. Furthermore, a 2017 review of management options for post-vasectomy pain syndrome concluded that acupuncture was a useful part of multimodal pain management strategy, although clinical trials demonstrating effectiveness are lacking.[5]

Current research lacks a well-designed clinical trial to assess the comparative effectiveness of acupuncture therapy to pre-procedural medication for vasectomies. We propose a large randomized clinical trial that directly compares combined auricular (ear) acupuncture and body acupuncture (Koffman protocol) protocols to a standardized pre-procedural medication regimen for anxiety and pain control during elective vasectomies.

Bibliography:

1. Wunsch JK, Klausenitz C, Janner H, Hesse T, Mustea A, Hahnenkamp K, Petersmann A, Usichenko TI Auricular acupuncture for treatment of preoperative anxiety in patients scheduled for ambulatory gynaecological surgery: a prospective controlled investigation with a non-randomised arm. *Acupunct Med*. 2018;36:222-227.
2. Wang S, Peloquin C, Kain Z. The Use of Auricular Acupuncture to Reduce Preoperative Anxiety. *Anesthesia & Analgesia*. 2001 Nov; 93(5):1178–1180.
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4. Thomas M, Eriksson SV, Lundeberg T. A comparative study of diazepam and acupuncture in patients with osteoarthritis pain: a placebo controlled study. *Am J Chin Med*. 1991;19(2):95-100.
5. Sinha V, Ramasamy R. Post-vasectomy pain syndrome: diagnosis, management and treatment options. *Transl Androl Urol*. 2017 May; 6(Suppl 1): S44–S47. doi: 10.21037/tau.2017.05.33

SEE DATA ANALYSIS SECTION FOR REMAINING REFERENCES

6. Ingrid Djukanovic, Jörg Carlsson, Kristofer Årestedt. Is the Hospital Anxiety and Depression Scale (HADS) a valid measure in a general population 65–80 years old? A psychometric evaluation study. Health Qual Life Outcomes. 2017; 15: 193.
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15. 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/.

3. RESEARCH DESIGN AND METHODS

Research Design and Methods:

Male active duty members and DoD beneficiaries, 25 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 99MDG. No research-related procedures will be implemented without the subject first signing an Informed Consent and HIPAA Authorization Document. **All of the below items are research-related unless marked as 'standard of care':**

Telephone Eligibility review: We will obtain the potential subject's permission to be contacted prior to direct contact by study staff. Those subjects who respond to advertisements or from physician referrals with the subject's oral or written authorization have implicitly given their permission to be contacted. We will contact potential subjects over the telephone to determine their initial eligibility for and interest in this research study. We will use the attached "Telephone Eligibility Script". For those that are interested in participating, we will ask their DoD ID# so that we can book them a screening appointment in AHTLA/CHCS. The script does not contain any PHI/PII and will be placed in a shredding bin after we have booked an appointment with the subject or if they do not show up to their appointment.

Screening:

- Obtain and document signed Informed Consent document and HIPAA Authorization.
- Review past medical history in Armed Forces Health Longitudinal Technology Application (AHLTA) to verify the inclusion/exclusion criteria including previous encounter, vital signs review, co-morbidities, demographics, and problems list.
- Record: Date of birth, age, gender, race, ethnicity, DoD ID number, name of standard of care medications (over-the-counter and prescription), current email address (to be used for scheduling), height (in inches), weight (in pounds), history of prior injury to genital region.

Randomization: Subjects will be randomized into 1 of 2 **research treatment** groups using block randomization the day of their pre-vasectomy appointment:

- **Group 1:** Acupuncture involving the Koffman protocol (body acupuncture) for anxiety control (needles will be placed at bilateral LR-3, bilateral LI-4, GV 24.5 and GV 20) and Auricular ATP Plus (ear) for pain control (needles will be placed at points hippocampus, amygdala, hypothalamus, prefrontal cortex, Point Zero, Shen Men, vagus, insula, external

genitalia). Subjects who tolerate the auricular needles will be offered replacement with ASP acupuncture needles for continued pain management post-procedure. The subjects will receive local anesthetic during the vasectomy per standardized clinic protocol.

- **Group 2:** The clinic standardized pre-procedure medications alone (which include diazepam 5 mg by mouth (PO) x1 30 minutes prior to the procedure, an additional 5 mg PO x1 15 minutes later if desired effect is not achieved; and oxycodone/acetaminophen 5/325 mg PO x 1 30 minutes prior to the procedure. The subjects will receive local anesthetic during the vasectomy per standardized clinic protocol.

Pre-procedure (*before study intervention*):

- Provide clinic standardized pre-procedural vasectomy counseling and exam. (standard of care)
- Subjects will complete the Hospital Anxiety Scale.
- Subjects will complete the Defense and Veterans Pain Rating Scale (DVPRS).
- Subjects will be given a study diary to document the number of times they used post-procedure medications, as well as, reminded to complete the DVPRS every day for the 2 weeks following the procedure. Subjects will be informed that they have the option to either return it in paper format or input it into Survey Monkey or google forms at the last visit.

Study Intervention:

- **For the acupuncture group only:** Physicians performing acupuncture treatments will be provided standardized guides outlining the specific acupuncture points.
- Subjects will receive treatment according to their randomization group.

Post-procedure (*after study intervention but BEFORE the vasectomy*):

- Subjects will complete the Hospital Anxiety Scale.

Post-procedure (*after the vasectomy is completed*):

- Subjects will complete the Defense and Veterans Pain Rating Scale (DVPRS).
- **For the acupuncture group only:** Subjects who tolerate the auricular needles will be offered replacement with ASP acupuncture needles for continued pain management, in addition to the standard post-procedure ibuprofen as described below
  - If subjects have the ASP acupuncture needles placed, they will be instructed to have no heavy meals, no excessive hot or cold foods, no heavy exercise or intercourse, and no alcohol for 24 hours. The needles will fall out on their own within about one week.
- Subjects in both intervention groups will be prescribed ibuprofen 600-800 mg PO q8 hours as needed for pain.

2 Week Follow Up Visit (2 weeks from Post-Op Check Visit):

- Subjects will complete a questionnaire via paper, Survey Monkey, or Google Forms (whichever is most convenient for the patient) that includes patient satisfaction, the study diary, medication usage and the date they returned to normal duties.

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 Serin 0.25mm x 40mm (for body acupuncture) and Serin 0.25mm x 15 mm acupuncture needles (for auricular acupuncture), 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:

We will measure subject's anxiety level before and after the acupuncture/medication administration utilizing the standardized Hospital Anxiety Scale. Pain will be recorded before and after the procedure using the DVPRS. A patient satisfaction survey will be administered at the post op check (2-4 days after procedure). Subjects will be given a study diary to document the number of times they used post-procedure medications. Acupuncture (Koffman protocol + ATP Plus + external genitalia) vs. pre-procedure diazepam (Valium) plus oxycodone/acetaminophen (Percocet) will be compared for effectiveness.

b. Setting:

Male active duty members and DoD beneficiaries aged 25 years or older, who desire vasectomy, meet inclusion criteria and enrolled to the 99MDG.

c. Date(s):

04/15/19-04/15/21
d. Subjects:
Male (DoD beneficiaries). Age 25 years or older, who desire vasectomy, meet inclusion criteria and enrolled to the 99MDG. No other special populations (e.g., children, military basic trainees, prisoners, detainees) will be recruited.
e. Inclusion/Exclusion Criteria:

Inclusion Criteria	• Male active duty members and DoD beneficiaries aged 25 years or older • Scheduled for a vasectomy
Exclusion Criteria	• Repeat vasectomy • Chronic pain medication/benzodiazepine use • Current pain contract/pain management • Current anxiolytic medication • History of needle shock • Diagnosis of anxiety • Needle phobia • Blood/injury phobia • History of vasovagal reflex response

f. Source of Research Material:

Will you be using private information in this study?	☒Yes
If Yes,	☒protected health information (PHI) held by a covered entity

Use of identifiers 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
Names	☒	☒	☐	☐	☐	☐
Study codes linked to individuals' identities using a key only accessible by the researcher		☒	☒	☐	☐	☐
Phone	☒	☒	☐	☐	☐	☐
E-mails	☒	☒	☐	☐	☐	☐
DoD ID#	☒	☒	☐	☐	☐	☐

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. The code will be placed in a Master Key of identifiable PHI/PII for each subject.
Describe the method that will be used to create and assign unique study codes to specimens.	☒N/A, not collecting specimens
What is the format of the key?	☒Electronic
Who will have access to the key?	Research Staff
Where will the key be stored and how will it be protected?	Location(s): We will maintain a Master Key of identifiable PHI/PII that will be kept in an electronic database, which will be encrypted, password protected and the access will be restricted to the Research Coordinator. The Master Key will be electronically stored separately from the coded de-identified research data. The Master Key will not be stored on any non-government or personal computers or laptops. At the conclusion of the study, the data will be de-identified prior to review and analysis. 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.

Complete the table.

Source of Research Material per Participant (Procedures)	# Routine Care	# Research Driven	# Total Procedures
Acupuncture	0	1	1
Medication & Pain Diary	0	1	1
Hospital Anxiety Scale	0	2	2
DVPRS	0	15	15
Patient Satisfaction survey	0	1	1

g. Instrumentation: N/A

4. HUMAN SUBJECT PROTECTION

Recruitment and Consent Processes:

All potentially eligible patients will be offered an opportunity to participate. Some patients may be patients of the PI or AI, however, they will have the research team recruit their patients to prevent any misconception of coercion or undue influence. When a potential subject is identified by the treating physician, the Research Staff will be contacted to speak with the patient directly, with prior verbal or written authorization by the patient. Hospital staff will ask the patient if they are willing to speak with the research staff and, if they agree, then the research staff will be contacted to come to the clinic and discuss the study with the potential participant. Advertisements will be posted around the base.

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 through referral by their healthcare provider with oral or written authorization by the patient to be referred to the research team 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 3 years following the closure.

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 and physical function in both the treatment and control groups, however, this is not a guarantee.

Risks:

The potential risks to participate in this study are minimal. There is a risk of accidental breach of confidentiality. Other risks associated with participating in this research study include:

ACUPUNCTURE (Group 1):
LIKELY: *Likely and not serious:*

- Pain
- Bleeding

LESS LIKELY: *Less Likely and not serious:*

- Infection
- Muscle cramp
- Muscle spasm

RARE AND NOT SERIOUS*:*

- Needle Shock (extremely rare response which causes the subjects blood vessels to dilate and their blood pressure to suddenly drop. Usually subjects quickly recover without lasting effects when the needles are removed and the patient is placed in a supine position with their legs slightly raised so that they blood begins to flow back to the brain and heart)
  *Those subjects exhibiting symptoms of needle shock will immediately have the needles removed and the procedure completed as usual.

DIAZEPAM, OXYCODONE/ACETAMINOPHEN (Group 2-pre-procedure):
LIKELY: *Likely and not serious:*

- Lightheadedness
- Dizziness
- Sedation
- Dysphoria (state of unease)
- Nausea/vomiting

IBUPROFEN (Group 1 & 2-post-procedure):
LIKELY: *Likely and not serious:*

- Indigestion
- Nausea
- Abdominal pain

RARE AND SERIOUS*:*

- Gastrointestinal bleeding/ulcer

Costs: N/A

Safeguards for Protecting Information:		
Data and Specimen Storage Plan		
How will coded or identifiable data/specimens be stored?		
☒	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.
☒	Electronic data	Medical records will be annotated to reflect the subject's participation in a research study. All coded, de-identified research data will be electronically stored separately from the Master Key of identifiable patient demographics and PHI/PII at each site.
☒	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. Risks related to the acupuncture will be minimized by cleaning the acupuncture 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.

Categories of subjects	None

Clinical Care:

All subjects will receive national 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 the prescribed medication being used in this protocol can be performed in the Family Medicine Residency as standard of care outside of the subjects participation in this research study. The only reason they are considered "research" in this protocol is because we are randomizing the subjects into groups. Subjects may choose to get this type of treatment without participating in this study. Choosing not to participat in the study is another option for the subject.

6. DATA ANALYSIS

Data Analysis:

Outcome Measures:

The primary outcome measures are the Hospital Anxiety and Depression Scale (HADS) and the Defense and Veterans Pain Rating Scale (DVPRS).

The HADS is a self-rating scale developed to assess psychological distress in non-psychiatric patients. It consists of two subscales, Anxiety and Depression, each having seven items and a score range of 0 to 21. The HADS has been satisfactorily used in the general population and a number of clinical settings. A score less than 8 is considered as being normal, 8 to 10 as suggestive of anxiety or depression, and greater than 11 as being probable of anxiety or depression. The HADS score is ordinal and will be analyzed using nonparametric methods.[6,7,8]

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 VA health systems. The DVPRS has demonstrated linear scale qualities allowing parametric methods to be used.[9,10]

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 a vasectomy 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 treatment groups at the time of 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.[11] The median (interquartile range - IQR) HADS Anxiety score for a normal population is 2^4. A priori power for HADS Anxiety was assessed using the IQR as the minimal clinically important

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]. The minimal clinically important difference of an 11-point pain scale in post-operative patients has been determined to be a 35% percent change in the score.[12] This difference, mean and SD were used for the DVPRS effect size.
Two repeated measures (pre-procedure and post-procedure) will be taken of the HADS Anxiety scores for the two treatment groups. A priori power analysis of the HADS Anxiety variable under these conditions using the statistical method described below indicates 30 subjects will have a power of 0.951 to detect the minimal clinically important difference at alpha = 0.05. However, as the HADS scores will be assessed using a non-parametric method, 15% was added to the sample size to achieve the same power for the comparative parametric test to arrive at a final recommended sample size of 36 subjects.[13]

The DVPRS will be measured 15 times (1 post-procedure and 14 post-operative). A priori power analysis of the DVPRS variable under these conditions using the statistical method described below indicates 74 subjects will have a power of 0.953 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. Using this effect and sample size, post hoc tests will have a power of 0.773 at alpha = 0.057.

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 and ordinal variables. Frequency distributions will be produced for nominal and ordinal variables.

The null hypothesis for the HADS Anxiety outcome measure will be tested with a non-parametric longitudinal method for factorial experiments. The null hypotheses for the DVPRS outcome measure will be tested by a mixed effects repeated measures analysis of variance (rANOVA). In the event the null hypotheses are rejected, contrasts will be used to investigate effects and differences. The significance level of multiple comparison tests will be corrected to $\alpha = .05$ by the Holm method.[14]

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.[15]

Number of Subjects:

	# Planned to Enroll	# Enrolled	# Planned to Complete Study	TOTAL
Number of Subjects at 99MDG	85	0	74	85

7. STUDY DURATION

Duration of Study:

Approximate duration of the study: 2 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		☒No
A biologic		☒No
A compound intended to affect structure or any function of the body		☒No
A dietary supplement or substance *generally recognized as safe* that will be used to diagnose, cure, mitigate, treat, or prevent disease		☒No
A medical device	☒Yes	

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**
☒N/A, no FDA approved drugs being used according to the labeling
10C. List all **FDA approved drugs used for an unapproved use ("off-label")**
☒N/A, no FDA approved drugs being used "off-label"
10D. List all **biologics, compounds and dietary supplements**
☒N/A, no biologics, compounds and dietary supplements
10E. List all devices covered by an **Investigational Device Exemption (IDE)** from the **FDA** (approved or submitted)
☒N/A, an IDE has not been submitted to or approved by the FDA
10F. List all **FDA approved devices used for an unapproved use ("off-label")**
☒N/A, no FDA approved devices being used "off-label"
10G. List all **unapproved devices.**
☒N/A, no unapproved devices

10H. Device Storage Location(s):	N/A

Is this research an "applicable clinical trial" which must be registered on ClinicalTrials.gov?		
☒No		
Use of a placebo in place of standard therapy:		
Is a placebo being used in place of standard therapy?	☒No	☐Yes

11. MEDICAL RESEARCH AREA

☒Family Medicine Residency	☒ Family Medicine

12. ATTACHMENTS

1. Form A, Signature Sheet
2. Form A-2, Study Personnel Listing
3. Form D, Informed Consent Document
4. H15 Template, HIPAA Authorization Document
5. Application checklist
6. Hospital Anxiety Scale
7. DVPRS
8. Pre-eligibility Review Script
9. Study Diary (patient satisfaction, return to work, DVPRS, and medications)
10. Acupuncture Protocol for Study