An Exploratory Prospective Trial of Rescue Acupuncture for the Treatment of Acute Migraine.

NCT02764996

June 29, 2016

PROTOCOL FOR CLINICAL INVESTIGATION – NON-EXEMPT HUMAN
(Wilford Hall Ambulatory Surgical Center – WHASC)
PROTOCOL SUMMARY

1. Title:

An Exploratory Prospective Trial of Rescue Acupuncture for the Treatment of Acute Migraine.
FWH20150084H

2.0. Principal Investigator (PI):	**WHASC PI:**
Name	Sarah Bobnick, D.O
Rank/Corps or Civilian Rating	Capt
Date of IRB Approved CITI Training & Date of Good Clinical Practice Training	07/09/15
Branch of Service	USAF
AD Mil/DoD Civilian/Ctr/Non-DoD Civ	AD MIL
Department & Base	Family Medicine Residency, Nellis AFB
Phone & Pager #	(702) 653-3298
E-Mail Address & AKO/DKO E-Mail Address	sarah.bobnick.1@us.af.mil

3.0. Research Plan:

3.1. Purpose:
To begin to determine if acupuncture is as effective as, or more effective than, rescue medication in the acute treatment of migraine.

3.2. Hypotheses, Research Questions or Objectives:
We will estimate the magnitude of effect that acupuncture has as an alternative to medication for treatment of acute migraine, as measured by change in headache pain severity 20-30 minutes, 2 hours, 4 hours 24 hours post treatment.

4. Brief Summary of the study:
This will be an exploratory observational trial of rescue acupuncture for the treatment of acute migraine in military beneficiaries to gain information to inform the power analysis of a larger, more definitive trial. We do not seek to definitively answer the question of whether this acupuncture protocol is effective; rather, we seek to estimate the proportion of migraine episodes that result in headache-free status 20-30 minutes, 2 hours, 4 hours, and 24 hours after an acupuncture treatment. Acupuncture treatments will be subject dependent, and points could include the N point (on scalp); various auricular points to include Shen Men, Point Zero, thalamus and Omega-2; body points to include Liver 2, Liver 3, Gall Bladder 20, bladder 10; and surface release over tense areas in the neck or shoulders. Researchers will document the points used, and data will be aggregated to determine overall effectiveness. Sub-group analysis by points will be performed to determine if there is more usefulness in 1 point or combination of points. These estimates will inform statistical power calculations for a future randomized controlled trial (RCT) that directly compares the effectiveness of Rescue Acupuncture with medical management of acute migraine with rescue medication. We will also assess the feasibility of this study protocol as well as patient receptivity and satisfaction.

5. Subjects:
Male and female DoD beneficiaries ages 18 years or older will be recruited at the Mike O'Callaghan Federal Medical Center (MOFMC). No special populations (e.g., pregnant women, children, military basic trainees, prisoners, detainees) will be recruited.

6. Inclusion/exclusion criteria:

Inclusion:
- Male and female DoD beneficiaries, age 18 years or older, who have been previously prescribed rescue medication to treat their acute migraine episodes.

Exclusion:
- Pregnant
- Absence of ear
- Active cellulitis of ear
- Ear anatomy precluding identification of acupuncture landmarks
- Use of Hearing Aids that preclude the insertion of needles

- Use of anticoagulants
- Unable to drive during rapid onset of migraine or inability to find someone to drive you

7. Number of Subjects: TOTAL NUMBER OF SUBJECTS (nation-wide/study-wide): 60

8. Use of an Investigational New Drug: N/A

9. Use of an Investigational Device: Seirin J-Type Acupuncture needles and Sedatelec ASP Original Gold Acupuncture needles, 510(k) exempt as Class II device under 21 CFR 880.5580

10. Use of a Placebo: N/A

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2.0. Principal Investigator (PI): **WHASC PI:**

Name	Sarah Bobnick, D.O
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Date of IRB Approved CITI Training & Date of Good Clinical Practice Training	07/09/15
Branch of Service	USAF
AD Mil/DoD Civilian/Ctr/Non-DoD Civ	AD MIL
Department & Base	Family Medicine Residency, Nellis AFB
Phone & Pager #	(702) 653-3298
E-Mail Address & AKO/DKO E-Mail Address	sarah.bobnick.1@us.af.mil

2.1. Associate Investigators (AI):

Name	AD/DoD Civ/Ctr/Non-DoD Civ	Rank/Corps or Civilian Rating/Title	Date of CITI Training	Phone #
Michael Kim, MD	AD	Capt	07/10/14	(702) 653-3298
David Moss, MD	AD	Maj	01/20/16	(702) 653-3298
Clinton Borchardt, MD	AD	Capt	06/04/14	(702) 653-3298
Katherine Reeve, MD	AD	Capt	12/14/15	(702) 653-3298
Matthew Hawks, MD	AD	Capt	09/13/13	(702) 653-3298
Stephen Cagle, MD	AD	Capt	01/09/14	(702) 653-3298
Carl Bryce, MD	AD	Capt	01/15/14	(702) 653-3298
Connor McKeown, MD	AD	Capt	05/22/14	(702) 653-3298
Travis Russell, MD	AD	Maj	07/03/15	(702) 653-3298
Garrett Huck, MD	AD	Capt	06/29/15	(702) 653-3298
Paul Crawford, MD	AD	Col	01/12/15	(702) 653-3298
Lee Church, MD	AD	Capt	09/03/14	(702) 653-3298
Cameron Shawver, DO	AD	Capt	07/10/15	(702) 653-3298
Rebecca Lauters, MD	AD	Capt	11/03/14	(702) 653-3298
Erik Clauson, DO	AD	Capt	07/26/15	(702) 653-3298
Charlie Collenborne, MD	AD	Capt	12/16/15	(702) 653-3298
Daniel Cieslak, MD	AD	Capt	12/14/15	(702) 653-3298
Michael Odom, MD	AD	Capt	11/30/15	(702) 653-3298

2.2. Research Assistants (RA) & Coordinators (RC):

Name	AD/DoD Civ/Ctr/Non-DoD Civ	Rank/Corps or Civilian Rating/Title	Date of CITI Training	Phone #
Tracy Bogdanovich, CCRC	CTR	Clinical Research Coordinator	03/31/14	(702) 653-2088
Jill Clark, MBA/HCM	CTR	Clinical Research Manager	03/19/14	(702) 653-3298
Daniel Shaffer, BSBA	CTR	Clinical Research Coordinator	06/29/15	(702) 653-2067
Jonathen Rowe, B.S.	CTR	Clinical Research Coordinator	10/27/15	(702) 653-2466
Jennie Moss, RN, M.S.	CTR	Senior Research Associate	09/01/15	(702) 653-2113

2.3. The research relevance of this protocol focuses on:
[ ] Diagnosis [x] Treatment [ ] Medical Utilization/Managed Care [ ] Prevention [ ] Medical Readiness [ ] Other

2.4. Location(s):

a. Collaborating Facilities: N/A
b. Air Force Sites seeking Regional IRB: Jill Clark, (702) 653-3298
c. List study sponsors: N/A

3. Research Plan:

3.1. Purpose:
To begin to determine if acupuncture is as effective as, or more effective than, rescue medication in the acute treatment of migraine.

3.2. Hypotheses, Research Questions or Objectives:
We will estimate the magnitude of effect that acupuncture has as an alternative to medication for treatment of acute migraine, as measured by change in headache pain severity 20-30 minutes, 2 hours, 4 hours, and 24 hours post treatment.

3.3. Significance:
Proof that acupuncture is superior to medication for treatment of migraine in military beneficiaries would result in less lost duty days, decreased medication use, and improved quality of life.

3.4. Military Relevance:
Migraine headaches are common in deployed US Army soldiers and exceed the expected prevalence. These headaches result in impaired duty performance and are a frequent cause of sick call visits. Migraine headaches tend to persist after deployment in many soldiers.[6] A survey of a cohort of returning US Army Iraqi war veterans revealed that Soldiers with migraine made a total of 490 sick call visits for headache over a 3-month period of which 90 were for possible migraine. In all, 75% of the soldiers with migraine used over-the-counter analgesics and only 4% used triptans. Soldiers with migraine contacted 3 months after returning from Iraq had a mean of 5.3 headache days per month and 36% had a Migraine Disability Assessment Scale grade of 3 or 4.

Furthermore, a recent analysis examined the impact of migraine headaches on US Army Trainees. An anonymous, voluntary migraine questionnaire was administered to 1389 consecutive US Army Reserve Officer Training Corps cadets upon completion of 5 weeks of military training. Headaches were classified as definite migraine or possible migraine. Migraine frequency, prior diagnosis, number of missed or suboptimal training days attributable to migraine, patterns of analgesic use, and trainee characteristics associated with impaired training performance were identified. "…54% of officer trainees completed the migraine questionnaire...The prevalence of definite migraine was 18% in all cadets...Migraines had been previously diagnosed in only 10% [of these]. During training, male trainees experienced a mean of 0.70 migraines/month compared with female trainees at 1.4 migraines/month. Only 3% of trainees meeting criteria for definite or possible migraine had ever been prescribed triptans. Eight percent of cadets experienced impaired training performance because of migraine resulting in 63 days of suboptimal or missed training. Characteristics associated with impaired training performance included a prior diagnosis of migraine, screening positive for definite migraine vs possible migraine, and a higher baseline frequency of migraine."[7] The conclusions from the study revealed that migraine is common yet under diagnosed and undertreated in US Army officer trainees which adversely impacted military training. This data could be extrapolated to include all DoD since the trainee population is generally similar between the services. Migraines may be a characteristic that could place military trainees at risk for impaired training performance. Improved treatment of migraine would result in improved training performance which obviously directly impacts readiness.

Various levels of acupuncture training have been taught to several hundred military physicians. A barrier to more widespread implementation has been lack of scientifically rigorous clinical trials to prove its worth in spite of the wide variety of anecdotal reports purporting its value in treating migraine. This trial will establish the efficacy acupuncture for acute migraine so that military beneficiaries can use less mind-altering medications. Additionally, many patients who have experienced traumatic brain injury develop chronic migraine that is refractory to medication, and acupuncture could be an important adjunct to this malady. Finally, management of medication side effects (i.e. chest pain in patients who take triptans) adds to costs that could be averted if acupuncture is effective. Proof that acupuncture is an effective treatment for acute migraine in military beneficiaries could result in fewer lost duty days, decreased medication use, and improved quality of life.

3.5. Background and Review of Literature:
Migraine is a recurring disorder characterized by attacks of severe headache generally associated with nausea, vomiting, and other neurologic symptoms. Duration is usually more than 4 hours and may last up to 72 hours with fluctuating intensity.[1] Migraine is commonly characterized as either episodic or chronic, depending on the frequency of attacks. Episodic migraine is more common, affecting up to 12% of the general population.[2] The direct medical costs of migraine headaches are approximately $1 billion per year in the U.S.,[3] with a national annual indirect burden of migraine estimated at $12 billion (mostly attributed to absenteeism).[3]

Management of migraine focuses both on the treatment of acute attacks and the prevention of such attacks.[4,5] The goals of migraine preventive therapy are to reduce attack frequency, severity, and duration; improve functional status/reduce disability; and improve response to acute treatments. The goal of acute treatment is typically to quickly eliminate or reduce the severity of migraine headache pain and associated symptoms. People who experience frequent migraine episodes often overuse

symptomatic medications. There are many "rescue medications" to choose from for the acute treatment of migraine, but side effects from pharmacologic approaches to migraine treatment can be considerable and often limit treatment options.

Acupuncture is a nonpharmacologic treatment approach that has been proven to significantly reduce the frequency and severity of episodic migraines.[6,7] However, there is (to our knowledge) only one published randomized controlled trial that evaluated the efficacy of acupuncture relative to a rescue medication for the acute treatment of migraine.[8] This represents a significant research and knowledge gap. We propose to fill this gap by conducting a large, carefully designed, phase III, randomized controlled trial that directly compares the efficacy of acupuncture with rescue medications in the acute treatment of episodic migraine.

The needles being used are Seirin No. 3(0.20)x30mm stainless steel J-type with tube acupuncture needles which are approved by the FDA for use in acupuncture and will be used in accordance with their FDA approved labeling. As part of this study, the acupuncture needles themselves are no the object of the investigation, the process of acupuncture and the effect it has is what we are studying. The needles are merely the avenue we use to perform the acupuncture. According to 21 CFR 880.5580, an acupuncture needle is a device intended to pierce the skin in the practice of acupuncture.[9] There are no known restrictions on the use of the acupuncture needles that prevent them from being used by qualified practitioners of acupuncture as they deem appropriate.

3.5.1. Bibliography:

1. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013; 33(9):629-80.
2. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology.* 2007;68(5):343-349.
3. Allais G, DeLorenzo C, Quirico PE, Lupi G, Airola G, Mana O. Non-Pharmacological approaches to chronic headaches: transcutaneous electrical nerve stimulation, laser therapy and acupuncture in transformed migraine treatment. Neurol Science. 2003; 24:S138-S142.
4. Silberstein SD. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology.[Erratum appears in Neurology 2000 Jan 9;56(1):142]. *Neurology.* 2000;55(6):754-762.
5. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology.* 2012;78(17):1337-1345.
6. Linde K, Allais G, Brinkhaus B, Manheimer E, Vickers A, White AR. Acupuncture for migraine prophylaxis. *Cochrane Database of Systematic Reviews* 2009, Issue 1. Art. No.: CD001218. DOI: 10.1002/14651858.CD001218.pub2.)
7. Wang Y, Xue CC, Helme R, Da Costa C, Zheng Z. Acupuncture for frequent migraine: a randomized, patient/assessor blinded, controlled trial with one-year follow-up. Evid Based Complement Alternat Med, 2015:920353, (Epub ahead of print), 2015.
8. Melchart D, Thormaehlen J, Hager S, Liao J, Linde K. Acupuncture versus placebo versus sumatriptan for early treatment of migraine attacks: a randomized controlled trial. *Journal of Internal Medicine.* 2003; 253:181-188.
9. U.S. Food and Drug Administration. General Hospital and Personal Use Therapeutic Devices. Retrieved July 17, 2015 from http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=880.5580.

3.6. Research Design and Methods:

Male and female (DoD beneficiaries). Age 18 years or older, who meet eligibility criteria will be offered an opportunity to participate via Primary Care Manager (PCM) referrals 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 the 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 patien will either be provide a contact number to the Research Staff, the Research Staff will be given the potential subjects contact information by the PCM, or the PCM will come and get the Research Staff to speak with the patient directly. We will administer acupuncture treatments for up to 6 different migraine episodes per subject over the course of 3 months. This type of Acupuncture for this indication is routinely done as part of standard-of-care in our Family Medicine and acupuncture clinics both in conjunction with rescue medications and as a stand-alone therapy.

<u>Screening Visit:</u>

- Obtain signed Informed Consent document and HIPAA Authorization. (research only)
- Review past medical history in Armed Forces Health Longitudinal Technology Application (AHLTA) to verify the inclusion/exclusion criteria including previous encounter, vital signs review, medication list, co-morbidities, demographics, problems list, and note any prior acupuncture received. (research only)
- Record: Date of birth, age, gender, race, ethnicity, last 4 of social security number, name of standard of care rescue medications (over-the-counter and prescription), current email address (to be used for scheduling only), height (in

inches), weight (in pounds), history of traumatic brain injury, concussion, or any mild to severe head trauma, medication use, history of acupuncture. (research only)
- We will ask what the subjects expectations are regarding acupuncture's effectiveness for migraine. (research only)
- We will instruct subjects not to take their over-the-counter and prescription headache medications until after their visit with the research staff. (Standard care)
- We will instruct subjects to bring their over-the-counter and prescription headache medications with them to each visit if their symptoms do not resolve from the acupuncture treatment. (research only)
- Patient will be instructed to contact the Research Coordinator, as soon as possible, after onset of migraine symptoms (including prodromal symptoms) to schedule an emergent visit with the research staff. (research only)
- Patient will be given a contact card with the names and phone numbers of the research staff to contact when they have a migraine episode.

Migraine Episode:

- Self-reported headache pain severity (0=no headache, 1=mild, 2=moderate, 3=severe) (Standard care)
- Record type and amount of rescue medications (over-the-counter and prescription) use in the past 7 days. (research only)
- Acupuncture treatments will be subject dependent, and points could include the N point (on scalp); various auricular points to include Shen Men, Point Zero, thalamus and Omega-2; body points to include Liver 2, Liver 3, Gall Bladder 20, bladder 10; and surface release over tense areas in the neck or shoulders. (Standard care)
- Researchers will document the points used. (Standard care)
  *If after 20-30 minutes these patients have not had resolution of their headache, they may take their standard of care rescue medication. (research only)
- The subject will sit for 20-30 minutes post-acupuncture(research only), and then the needles will be removed and the subject will be asked:
  - Self-reported headache pain severity (0=no headache, 1=mild, 2=moderate, 3=severe) (research only)
- Subject is allowed to leave and will be informed of the following telephone follow ups:
- 2 Hours post acupuncture:
  - Self-reported headache pain severity (0=no headache, 1=mild, 2=moderate, 3=severe) (research only)
- 4 Hours post acupuncture:
  - Self-reported headache pain severity (0=no headache, 1=mild, 2=moderate, 3=severe) (research only)
- 24 Hours post acupuncture:
  - Self-reported headache pain severity (0=no headache, 1=mild, 2=moderate, 3=severe)
  - Would you use acupuncture for future pain management? (Yes or no)
  - Would you prefer acupuncture or your rescue meds (both over-the-counter and prescription) for future episodes?
  - Record type and amount of rescue medications (over-the-counter and prescription) used since acupuncture. (research only)

Patients with missed phone calls will not be withdrawn from the study. If there is a missed call, we will mark as 'missed', including the reason and continue with the next phone call.

The Research Coordinator will record the name of the AI performing the acupuncture and also the placement of the acupuncture needles for each migraine episode.

Placement of Acupuncture:

Acupuncture treatments will be subject dependent, and points could include the N point (on scalp) (Figure 1); various auricular points to include Shen Men(Figure 2), Point Zero(Figure 3), thalamus(Figure 4) and Omega-2(Figure 5); body points to include Liver 2(Figure 6), Liver 3(Figure 6), Gall Bladder 20(Figure 7), bladder 10(Figure 7); and surface release over tense areas in the neck or shoulders. We will utilize the Seirin J-Type Acupuncture needles (Figure 98). Intermittent placement checks by the medical acupuncturist will be performed.

This study will follow all FDA requirements for the safe use of these devices.

Only the investigators listed on this study will perform the insertion of the acupuncture needles. All investigators are trained in this acupuncture technique and credentialed by the Credentials committees.

The Food and Drug Administration (FDA) regulates acupuncture needles 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 FDA regulates the acupuncture needles (see 21 CFR 880.5580), but not the practice of acupuncture itself.

The needles being used are Seirin J-Type Acupuncture needles (Figure 8), which are exempt from premarket notification by the FDA for use in acupuncture and will be used in accordance with their FDA approved labeling.

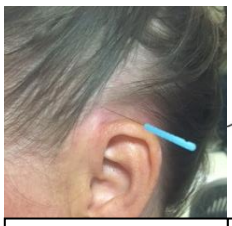

Figure 1: N Point

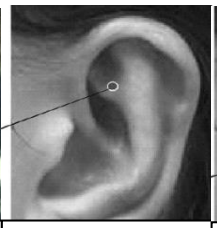

Figure 2: Shen Men

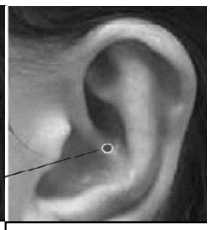

Figure 3: Point Zero

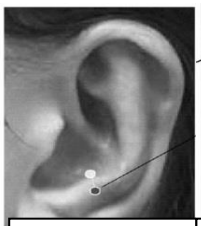

Figure 4: Thalamus

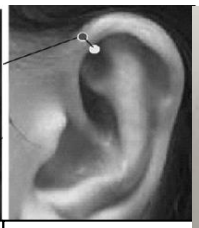

Figure 5: Omega 2

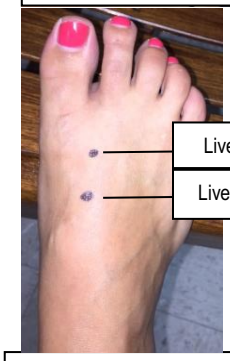

Figure 6: Liver 2 & Liver 3

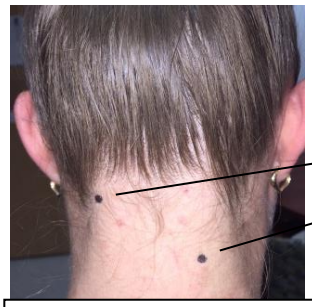

Figure 7: Gallbladder 20 & Bladder 10

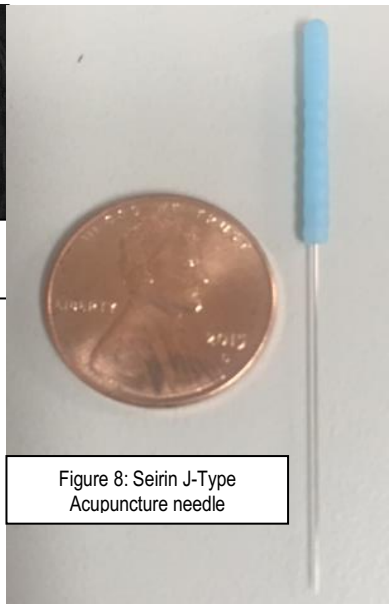

Figure 8: Seirin J-Type Acupuncture needle

3.6.1. Interventions, Observations, or Data Sought:
We will measure subject's migraine pain level, doses of analgesics taken before intervention and at 20-30 minutes, 2 hours, 4 hours, and 24 hours post treatment. Additionally, we will measure patient centered outcomes and receptivity to acupuncture. Acupuncture treatments will be subject dependent, and points could include the N point (on scalp); various auricular points to include Shen Men, Point Zero, thalamus and Omega-2; body points to include Liver 2, Liver 3, Gall Bladder 20, bladder 10; and surface release over tense areas in the neck or shoulders. Researchers will document the points used, and data will be aggregated to determine overall effectiveness. Sub-group analysis by points will be performed to determine if there is more usefulness in 1 point or combination of points.

3.6.2. Data Collection and Processing:
Data will be collected and recorded in a spreadsheet. At the conclusion of the study, all personally identifying information will be removed prior to analysis.

3.6.3. Setting:
Male and female (DoD beneficiaries). Age 18 years or older, who currently take rescue medication to treat their acute migraine episodes at the Mike O'Callaghan Federal Medical Center (MOFMC).

3.6.4. Date(s):
August 2015 through August 2017

3.6.5. Source of Research Material:

Source of Research Material per Migraine (Procedures)	# Routine Care	# Research Driven	# Total Procedures
Medical Record Review	0	1	1
Acupuncture	6	0	6
Questions: Pain Severity	12	18	30
Questions: Acupuncture for future pain management	0	6	6
Questions: Preference of acupuncture vs rescue meds	0	6	6
Questions: Rescue medication usage	0	12	12

3.6.6. Subjects:
Male and female (DoD beneficiaries). Age 18 years or older, who currently take rescue medication to treat their acute migraine episodes at the Mike O'Callaghan Federal Medical Center (MOFMC). No other special populations (e.g., children, military basic trainees, prisoners, detainees) will be recruited.

3.6.7. Inclusion/Exclusion Criteria:

Inclusion:

- Male and female DoD beneficiaries, age 18 years or older, who have been previously prescribed rescue medication to treat their acute migraine episodes.

Exclusion:

- Pregnant
- Absence of ear
- Active cellulitis of ear
- Ear anatomy precluding identification of acupuncture landmarks
- Use of Hearing Aids that preclude the insertion of needles
- Use of anticoagulants
- Unable to drive during rapid onset of migraine or inability to find someone to drive you

3.6.8. Instrumentation: N/A

4.0. Human Subject Protection:

4.1. Recruitment:

All potentially eligible patients will be offered an opportunity to participate. PCM referrals 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 the 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 patien will either be provide a contact number to the Research Staff, the Research Staff will be given the potential subjects contact information by the PCM, or the PCM will come and get the Research Staff to speak with the patient directly.

4.2. Consent Processes:

Informed Consent and HIPAA authorization will be sought in advance from each prospective 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 care 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 prior to making a decision. If the subject consents, a copy of the ICD 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 study-related PHI/PII into the "Nellis Acupuncture Research Data Repository (FWH20140048H)" for future research. If the subject does not give their authorization, then all PHI/PII will be destroyed no later than at the closure of the study.

4.3 Participation Compensation:

Subjects will not be paid for participation in this study.

4.4. Assent Process: N/A

4.5. Benefits:

There may be no direct benefits to the subjects for participating in this study.

4.6. Risks:

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

LIKELY: *Likely and not serious:*

- Pain
- Bleeding

LESS LIKELY: *Less Likely and not serious:*

- Infection

4.7. Costs: N/A

4.8. Safeguards for Protecting Information:
The research consents will be stored in a locked cabinet in a locked room. Medical records will be annotated with ICD-10 code Z00.6 to reflect the subject's participation in a research study. All research data including patient demographics will be kept in an electronic database, 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 will be destroyed as soon as the Final Report Approval has been obtained from the IRB with the exception of those that consent to place their study-related PHI/PII 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.

4.9. Safeguards for Protecting Subjects:
The principal investigator will be responsible for the protocol safety monitoring. The PI will make study documents (*e.g.*, consent forms, data pulls) and pertinent hospital or clinical records readily available for inspection by the local IRB and over sight staff for confirmation of the study data.

4.9.1. Minimizing Risks:
These risks 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.

4.9.2. Vulnerable Populations: N/A

4.9.3. 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.

4.9.4. Injury Compensation: N/A

4.9.5. Data Safety Monitoring:
The principal investigator will be responsible for the protocol safety monitoring. The PI will make study documents (*e.g.*, consent forms, data pulls) and pertinent hospital or clinical records readily available for inspection by the local IRB and over sight staff for confirmation of the study data.

5.0. Alternatives:
Acupuncture for migraine is done in the Family Medicine Residency as part of standard of care. Subjects may choose to get this type of acupuncture without participating in this study.

6.0. Data Analysis:

6.1. Outcome Measures:
Primary outcome: Reduction of migraine headache pain from mild, moderate or severe to pain free, 20-30 minutes, 2 hours, 4 hours and 24 hours post treatment. Secondary outcomes: patient global assessment of preference for trying acupuncture vs rescue medications; overall satisfaction and perceived effectiveness of the treatment; reduction of symptoms other than migraine headache pain; and use of rescue medication within 12 hours of the initial treatment (irrespective of which study treatment received). These standardized outcome measures are commonly used in comparative effective trials of migraine rescue medications. Researchers will document the points used, and data will be aggregated to determine overall effectiveness. Sub-group analysis by points will be performed to determine if there is more usefulness in 1 point or combination of points.

6.2. Sample size estimation/power analysis:
We will treat 30 subjects. We will administer up to 6 acupuncture treatments for up to 6 different migraine episodes per subject over the course of 3 months. We will not formally test a hypothesis. Rather, we will determine the proportion of migraines that resolve (as assessed by headache severity) 20-30 minutes, 2 hours, 4 hours, and 24 hours after the start of an acupuncture treatment. These data will be used to inform power calculations for future studies.

6.3. Statistical Analysis:
We will use descriptive statistics to characterize the clinical response of subjects after acupuncture treatments.

6.4 Number of Subjects:

Number of subjects planned for MOFMC	Enrolled in Study	60	to result in	30	completing the study.

TOTAL NUMBER OF SUBJECTS (nation-wide/study-wide): 60

7. Duration of Study: Approximate duration of the study: 2 years

8. Local and External Support Services: None

9. Intramural (GME) and Extramural Funding Support: None

10. Conflict of Interest: No financial, personal, or off duty employment conflicts of interest exist.

11. Use of an Investigational New Drug, use of a Drug for a non-FDA approved purpose, use of an investigative device or use of a placebo:

This research uses an Investigational New Drug	**[ ] YES [x] NO**
This research uses a FDA approved drug for a non-FDA approved purpose	**[ ] YES [x] NO**
This research uses an Investigational Device	**[x] YES [ ] NO**
This research uses a placebo.	**[ ] YES [x] NO**

12. Medical Research Area for the Study: (Pick as many as appropriate)

[] Analytical Chemistry	[] Anatomy	[] Anesthesiology	[] Biochemistry
[] Cardiovascular Surgery	[] Cardiology	[] Cell Biology	[] Dentistry
[] Dermatology	[] Dietetics	[] Electrophysiology	[] Endocrinology
[] Emergency medicine	[] Gastroenterology	[] General Surgery	[] Hematology
[] Histology	[] Immunology/Allergy	[] Infectious Disease	[] Microbiology
[] Molecular Biology	[] Neonatology	[x] Neurology	[] Neurosurgery
[] Nursing	[] OB/GYN	[] Occupational Medicine	[] Occupational Therapy
[] Oncology	[] Ophthalmology	[] Oral/Maxillofacial Surgery	[] Orthopedics
[] Pathology	[] Pediatrics	[] Pharmacology	[] Physical Therapy
[] Mental Health	[] Radiology/Imaging	[] Urology	[] Wellness
[x] Other (state): Family Medicine			

13. Attachments:

1. Contact Card
2. Certificate of Compliance
3. Informed Consent Document
4. HIPAA Authorization Document
5. Use of an Investigational Device in Research
6. Advertisement
7. Form A2 Study personnel
8. Application checklist