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TITLE: Comparative Effectiveness of Acupuncture for Chronic Pain & Co-Morbid Conditions in Veterans

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14. ABSTRACT

Building on identified scientific gaps in the literature and our promising preliminary data, we will conduct a randomized controlled trial (RCT) of Electro-acupuncture (EA) vs. Battle Field Acupuncture (BFA) vs. Waitlist Control usual care (WLC) on 360 patients with chronic musculoskeletal pain. We will also examine the effects of baseline outcome expectancy and genetic polymorphisms on pain reduction. The overarching goal of the Personalized Electro-acupuncture vs. Auricular-acupuncture Comparative Effectiveness (PEACE) trial is to investigate EA and BFA (a form of auricular acupuncture) to guide the personalized delivery of treatment to improve pain and co-morbid symptoms. To achieve the overarching goal, the specific aims are:

Specific Aim 1: To compare the effects of Electro-acupuncture (EA) vs. Battle Field Acupuncture (BFA) vs. Waitlist Control usual care (WLC) on patient-reported pain (primary outcome), physical functions, and co-morbid symptoms [fatigue, sleep disturbance, anxiety, depression, and post-traumatic stress disorder (PTSD)] among patients experiencing chronic musculoskeletal pain for three months or greater.

Specific Aim 2: To determine the interaction between outcome expectancy and type of needling delivery (EA vs. BFA) on pain reduction.

Specific Aim 3: To evaluate the association between specific genetic polymorphisms and patients' responses to acupuncture.

15. SUBJECT TERMS
Acupuncture; Electro-Acupuncture; Auricular-Acupuncture; Clinical Trial; Pain; Musculoskeletal Pain; Chronic Pain; Sleep Disturbance; Fatigue; Anxiety; Depression; Post-traumatic Stress Disorder; Physical Functioning; Genetics; Expectancy; Comparative Effectiveness

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INTRODUCTION:

Building on identified scientific gaps in the literature and our promising preliminary data, we will conduct a randomized controlled trial (RCT) of Electro-acupuncture (EA) vs. Battle Field Acupuncture (BFA) vs. Waitlist Control usual care (WLC) on 360 patients with chronic musculoskeletal pain. We will also examine the effects of baseline outcome expectancy and genetic polymorphisms on pain reduction. The overarching goal of the Personalized Electro-acupuncture vs. Auricular-acupuncture Comparative Effectiveness (PEACE) trial is to investigate EA and BFA (a form of auricular acupuncture) to guide the personalized delivery of treatment to improve pain and co-morbid symptoms.

1. KEYWORDS:

- Acupuncture
- Electro-Acupuncture
- Auricular-Acupuncture
- Clinical Trial
- Pain
- Musculoskeletal Pain
- Chronic Pain
- Sleep Disturbance
- Fatigue
- Anxiety
- Depression
- Post-traumatic Stress Disorder
- Physical Functioning
- Genetics
- Expectancy
- Comparative Effectiveness

2. ACCOMPLISHMENTS:

What were the major goals of the project?

To achieve the overarching goal described above, the specific aims are:

Specific Aim 1: To compare the effects of Electro-acupuncture (EA) vs. Battle Field Acupuncture (BFA) vs. Waitlist Control usual care (WLC) on patient-reported pain (primary outcome), physical functions, and co-morbid symptoms [fatigue, sleep disturbance, anxiety, depression, and post-traumatic stress disorder (PTSD)] among patients experiencing chronic musculoskeletal pain for three months or greater.

Specific Aim 2: To determine the interaction between outcome expectancy and type of needling delivery (EA vs. BFA) on pain reduction.

Specific Aim 3: To evaluate the association between specific genetic polymorphisms and patients' responses to acupuncture.

Table I. Work Plan to Accomplish Specific Aims 1, 2, & 3:

	Timeline from Award Date 9/15/2016 (Months)	Completion Progress as of 9/14/2018
Major Task 1: Plan & Prepare	**1-6**	**In Progress**
Review and confirm protocol and procedure, incorporating input from co-investigators	1	Done
Submit & obtain Approval from IRB at MSKCC	2-4	Done
Submit & obtain Approval from HRPO	4-6	Done
Submit amendments, adverse events and protocol deviations as needed	As Needed	
Build procedure for annual IRB report (continuing review)	2	Done
Hire Staff as needed	1-3	Done
Train Staff as needed	2-4	Done
Develop database	2-4	Done
Pilot data collection with staff to ensure success	4-6	Done
Pilot recruitment process with staff to ensure success	4-6	Done
Major Task 2: Launch Study	**7**	Done
Coordinate with facilities to kickoff recruitment	7	Done
Major Task 3: Conduct Trial	**7-54**	**In progress**
Enroll subjects (40 patients) and randomly distribute patients between EA, BFA, & WLC – perform designated treatment, collecting data as needed	7-12	50/360 patients enrolled
Enroll subjects (120 patients) and randomly distribute patients between EA, BFA, & WLC – perform designated treatment, collecting data as needed	13-24	185/360 patients enrolled
Enroll subjects (140 patients) and randomly distribute patients between EA, BFA, & WLC – perform designated treatment, collecting data as needed	25-36	330/360 patients enrolled
Enroll subjects (60 patients) and randomly distribute patients between EA, BFA, & WLC – perform designated treatment, collecting data as needed	37-42	
Extract necessary data from bio-samples and catalogue in the database	7-42	
Perform ongoing data entry and data verification – preemptively managing missing data	7-42	In progress
Follow up with subjects at defined intervals to collect surveys and understand delayed effects of treatment	10-45	In progress
Expand to recruitment regional network sites in New Jersey or New York affiliated with MSK if necessary to meet recruitment milestones	As Needed	In progress
Major Task 4: Conduct Analysis	**12-48**	
Genotype DNA extracted from patients to address Specific Aim 3	36-48	

Complete all analyses according to specifications, share output and finding with all investigators	36-48	
Write manuscript based on findings, prepare for submission to peer- reviewed clinical trial journal	12-48	In progress
Major Task 5: Share Results	**48+**	
Submit to peer-reviewed clinical trial journal		
Present Interim & final findings at DOD Conference		

What was accomplished under these goals?

- The protocol was approved by MSK's review committees (primary department, biostatistics, research council, etc.) and IRB on November 25, 2016.
- On February 7, 2017, we received notice that the US Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), and Human Research Protection Office (HRPO) reviewed the protocol and found that it complies with applicable DOD, US Army, and USAMRMC human subjects protection requirements and that "no greater than minimal risk study was approved for the enrollment of 360 subjects".
- Research staff and acupuncturists have been trained.
- The study data collection materials and database have been developed and pilot tested.
- The recruitment and enrollment of subjects has begun.
- As of 9/20/2019, 330 patients have been enrolled and randomly distributed into the EA, BFA, & WLC groups and data collection has begun. Patients in the EA and BFA groups are receiving designated treatment.
- We are on track with accomplishing our stated goals outlined in Table 1.

What opportunities for training and professional development has the project provided?

- Kevin Liou, MD, who was a clinical research fellow had been promoted to instructor, he will continue to train under Dr. Mao to learn about conducting acupuncture research and clinical trial management.
- Sally Romero, PhD, a postdoctoral research fellow, completed a 6-week Genomics workshop hosted through Weill Cornell Medical College to gain a better understanding of contemporary genomics technologies and their applications in the biomedical field to apply to the project's Specific Aim 3. She also attended the following relevant seminars/workshops/conferences: Responsible Conduct of Research Reproducibility research ethics course; Replication, Rigor and Transparency seminar; Transform How You Present Your Science workshop; Stress and Resilience: The Science of Adapting to a Challenging World symposium; ASCO's 2017 Cancer Survivorship Symposium; the Society for Integrative Oncology 14th annual conference; and the Dissemination and Implementation 10th annual conference.
- Jason Bussell, PhD, a postdoctoral research fellow, trained under Dr. Mao to learn about conducting acupuncture research and clinical trial management. He also attended the following relevant seminars/workshops: Responsible Conduct of Research Reproducibility research ethics course; Replication, Rigor and Transparency seminar; and the Society for Integrative Oncology 14th annual conference.
- The research staff and study acupuncturists underwent a Battle Field Acupuncture (BFA) training session led by Colonel (Ret) Richard C. Niemtzow, MD.

How were the results disseminated to communities of interest?

- Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

- During this next year, we will continue to accomplish the Major Tasks outlined in Table 1.
- We plan to have recruited and randomized all 360 MSK patients to the RCT by September 2020 (Major Task 3).
- We will continue to perform designated treatment of study participants and collect data per protocol (Major Task 3).
- We will continue to perform ongoing data entry and data verification (Major Task 3).
- We will prepare a protocol manuscript to be submitted to a peer-reviewed clinical trial journal (Major Task 4).

3. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

- Nothing to report.

What was the impact on other disciplines?

- Nothing to report.

What was the impact on technology transfer?

- Nothing to report.

What was the impact on society beyond science and technology?

- Nothing to report.

4. CHANGES/PROBLEMS:

Changes in approach and reasons for change

- Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them

- Nothing to report.

Changes that had a significant impact on expenditures

- Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

- **Significant changes in use or care of human subjects:** Nothing to report.
- **Significant changes in use or care of vertebrate animals:** Not applicable.
- **Significant changes in use of biohazards and/or select agents:** Not applicable.

5. PRODUCTS:

- **Publications, conference papers, and presentations:** Nothing to report.

- **Journal publications:** Nothing to report.
- **Books or other non-periodical, one-time publications:** Nothing to report.
- **Other publications, conference papers, and presentations:** Nothing to report.
- **Website(s) or other Internet site(s)***:* Nothing to report.
- **Technologies or techniques**: Nothing to report.
- **Inventions, patent applications, and/or licenses**: Nothing to report.
- **Other Products**: Nothing to report.

6. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Jun J. Mao
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	ORCID ID: 0000-0001-9229-0380
Nearest person month worked:	5
Contribution to Project:	Dr. Mao responded to clarification questions posed by the HRPO and MSK IRB committees as the protocol moved through the approval process. Dr. Mao trained acupuncturists assigned to the study. He also oversaw the training of the research staff as well as the development of the study database, data collection materials, recruitment materials, and recruitment and retention plans. Dr. Mao oversees all aspects of the trial. Dr. Mao has conducted study visits to confirm the eligibility of potential study participants.
Funding Support:	DoD

Name:	Ting Bao
Project Role:	Medical Director
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	3
Contribution to Project:	Dr. Bao is a practicing physician acupuncturist. She serves as the medical director to assist the PI with evaluating eligibility criteria for research participants and handling adverse events during the course of the study.
Funding Support:	DoD

Name:	Sally A. D. Romero
Project Role:	Post-doctoral Researcher
Researcher Identifier (e.g. ORCID ID):	ORCID ID: 0000-0001-6028-4111
Nearest person month worked:	9
Contribution to Project:	Dr. Romero is a post-doctoral researcher serving as the overall research project manager. She assists the PI with preparing the protocols for the MSK IRB and HRPO committees and quarterly progress reports to DoD. Additionally, she works with the PI to oversee the development of the study database, data collection materials, recruitment materials, and recruitment and retention plans.
Funding Support:	NIH - T32; Byrne Fund; DoD

Name:	Kevin Liou
Project Role:	Instructor
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	3
Contribution to Project:	Dr. Liou is an instructor at MSKCC. He assists the PI with overseeing patient recruitment, eligibility visits, and acupuncture treatment protocols and procedures.
Funding Support:	DoD

Name:	Jason Bussell
Project Role:	Post-doctoral Researcher
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	8
Contribution to Project:	Dr. Bussell was a post-doctoral research fellow serving as the acupuncture project manager. He assisted the PI with overseeing patient recruitment, eligibility visits, and acupuncture treatment protocols and procedures.

Funding Support:	DoD

Name:	Qing Susan Li
Project Role:	Data / Regulatory Manager
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	13
Contribution to Project:	Ms. Li worked with Drs. Mao and Romero to prepare the data collection materials and study database, including piloting the data collection and data entry processes. She manages the study database and data entry processes.
Funding Support:	DoD

Name:	Melissa Assel
Project Role:	Data Analyst
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	1
Contribution to Project:	Ms. Ansel was a master-level biostatistical analyst who worked with Drs. Vickers and Satagopan for data analyses/programming as related to specific aims 1 and 2.
Funding Support:	DoD

Name:	Raymond Baser
Project Role:	Data Analyst
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	3
Contribution to Project:	Mr. Baser is a master-level biostatistical analyst who will work with Drs. Mao and Satagopan for data analyses/programming as related to specific aims 1-3.
Funding Support:	DoD

Name:	Lauren Piulson
Project Role:	Clinical Research Supervisor
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	3
Contribution to Project:	Ms. Piulson assists the PI with regulatory tasks, including preparing and submitting protocol amendments to the MSK IRB. She also works with the PI to oversee the study research assistants and their tasks, including patient recruitment, data collection and data entry.
Funding Support:	DoD

Name:	Janice DeRito
Project Role:	Regional Research Coordinator
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	1
Contribution to Project:	Ms. DeRito assists the PI and research team to oversee research tasks in the regional clinical sites.
Funding Support:	DoD

Name:	Jamie Green
Project Role:	Research Assistant
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	27
Contribution to Project:	Ms. Green has been trained to help with patient recruitment, preparing patient binders, performing data collection, and completing data entry. She screens, enrolls and follows patients in the trial.
Funding Support:	DoD; PCORI

Name:	Mary Shea
Project Role:	Research Assistant
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	18
Contribution to Project:	Ms. Shea has been trained to screen and recruit patients, perform data collection, and complete data entry into the study database. She screens, enrolls and follows patients in the trial.
Funding Support:	DoD, PCORI

Name:	Stephanie Pearson
Project Role:	Research Assistant
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	5
Contribution to Project:	Ms. Pearson was trained to screen and recruit patients, perform data collection, and complete data entry into the study database. She screened and enrolled patients to the study.
Funding Support:	DoD; PCORI

Name:	Yi Lily Zhang
Project Role:	Acupuncturist
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	5
Contribution to Project:	Ms. Zhang is an acupuncturist for the study. She conducts patient eligibility visits and acupuncture treatment procedures.
Funding Support:	DoD; Byrne Fund

Name:	Yi Chan
Project Role:	Acupuncturist
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	4
Contribution to Project:	Mr. Chan is an acupuncturist for the study. He conducts acupuncture treatment procedures.
Funding Support:	DoD

Name:	Matthew Weitzman
Project Role:	Acupuncturist
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	2
Contribution to Project:	Mr. Weitzman is an acupuncturist for the study. He conducts acupuncture treatment procedures.
Funding Support:	DoD

Name:	Jonathan Siman
Project Role:	Acupuncturist
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	3
Contribution to Project:	Mr. Siman was an acupuncturist for the study. He conducted acupuncture treatment procedures.
Funding Support:	DoD

Name:	Christina Seluzicki

Project Role:	Assistant Editor
Researcher Identifier (e.g. ORCID ID):	Not applicable
Nearest person month worked:	2
Contribution to Project:	Ms. Seluzicki is an assistant editor for the study. She assists the PI with the preparation of study-related documents and manuscripts.
Funding Support:	DoD

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

- Nothing to report.

What other organizations were involved as partners?

- Nothing to report.

7. SPECIAL REPORTING REQUIREMENTS

- **COLLABORATIVE AWARDS:** Not applicable.
- **QUAD CHARTS:** Not applicable.

8. APPENDICES: None.