Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

Appendix: Acupuncture Intervention

Description of the Intervention:

i. **Electro-Acupuncture (EA) procedure**: The following acupuncture treatment was developed by Dr. Mao and based on classic acupuncture text books in both Chinese and English in consultation with acupuncturists both in China and U.S. to treat musculoskeletal pain. The protocol has been piloted in our prior research to demonstrate adequate safety and efficacy in pain reduction.

The delivery of EA will be administered in the following steps:

1. History/tongue diagnosis/pulse diagnosis
2. Assist patient to lie comfortably on a table
3. Identify one focal body area that the patient considers to be the most painful (i.e. knee, ankle, low back). This area will be the primary focus during the entire treatment course.
4. Choose at least four acupuncture points from Table 1 to address the pain in the most severe joint/area. The acupuncturist may choose additional acupuncture points or a trigger (ashi/tender point) that may not be located on the meridian, however, please specify on the case report form.
5. Identify constitutional complaints of the patient (e.g., general aching, anxiety, depression, fatigue, or poor sleep)
6. Choose at least four acupuncture points using the table below, or your own clinical judgment to address the patient's general constitutional symptoms. Please specify points used on the case report form.
7. Limit the total number of points to 10-20.
8. Clean the skin at needle insertion sites following aseptic technique
9. Insert needle to appropriate depth with brief stimulation to achieve "De Qi" sensation
10. Connect the four local needling points to a TENS unit at 2 Hz frequency stimulation. Increase electrical stimulation intensity to appropriate level. The patient should feel the stimulation but it should not be painful.
11. Set timer for 30 minutes
12. Document acupuncture procedure
13. Check patient in 15 minutes for comfort
14. Turn off electrical stimulation and remove leads. Remove needles and wipe any blood with a sterile cotton-tipped applicator
15. Assist patient to slowly get up from the examination table
16. Complete documentation of the case report form

Table 1: Electro-Acupuncture Point Selection Guide

Joint Pain Location	Acupuncture Points					
Shoulder	Jianyu (L.I.15)	Jianliao (S.J.14)	Jianzhen (S.I.9)	Naoshu (S.I.10)	Houxi (S.I 3)	
Scapula	Tianzong (S.I.11)	Bingfeng (S.I.12)	Jianwaishu (S.I.14)	Gaohuangshu (U.B.43)		
Elbow	Quchi (L.I.11)	Chize (Lu. 5)	Tianjing (S.J.10)	Waiguan (S.J.5)	Hegu (L.I.4)	
Hand / Finger	Houxi (S.I.3)	Sanjian (L.I.3)	Baxie (Extra)	Hegu (L.I.4)		
Hip	Huantiao (G.B.30)	Yinmen (U.B.37)	Juliao (G.B.29)	Quixu (G.B.40)		
Knee	Lianqiu (St.34)	Dubi (St. 35)	Xiyan (Extra)	Yanlingquan (G.B.34)	Xiangguan (G.B. 35)	Yinlingquan (Sp. 9)
Leg	Chengshan (U.B. 57)	Feiyang (U.B. 58)				
Ankle	Jiexi (St.41)	Shangqui (Sp. 5)	Quixu (G.B.40)	Kunlun (U.B.60)	Taixi (K.3)	
Foot / Toe	Gongsun (Sp.4)	Shugu (U.B.65)	Bafeng (Extra)	Taixi (Liv. 3)		
Low Back Pain	Shenshu (U.B 23)	Dachangshu (U.B.25)	Weizhong (U.B. 40)	Chengshan (U.B. 57)	Huatuo (Extra)	Kunlun (U.B. 60)
Neck Pain	Jianjing (G.B.21)	Huatuo (Extra)	Luozhen (Extra)	Dazhui (GV14)	Fengchi (G.B. 20)	
General Symptoms						
General Aching	Houxi (S.I. 3)	Shenmai (U.B. 62)	Dabao (Sp.21)	Geshu (U.B.17)	Yinlingquan (Sp. 9)	Hegu/Taixi (L.I.4/Liv3)
Generalized Anxiety	Neiguan (P.C. 6)	Taixi (Liv. 3)	Yin Tang (Extra)			
Generalized Fatigue	Sanxinjiao (Sp. 6)	Zusanli (St.36)	Qihai (CV6)			
Sleep	Shenmen (Ht.7)	Anmian (Extra)				
Depression	Baihui (Du.20)	Ganshu (U.B.18)	Taixi (Liv. 3)			

ii. **Battle Field Acupuncture (BFA) Procedure**: The BFA procedure involves placing tiny (2.5 mm) ASP auricular acupuncture needles into ten well-defined and studied auricular acupuncture points (five points in each ear – See Figure 1). The delivery of BFA is simple and not dependent on specific pain location or diagnoses. The auricular needles are stainless steel, semi-permanent needles, and are designed to stay in the ear for 3-4 days. They fall out naturally as the ear re-epithelizes the site. Since the needles are tiny and the ear is not adjacent to any vulnerable structures, the technique is extremely safe with no significant complications ever reported. ASP needles should be removed after 4 days. Patients are instructed to remove needles before undergoing an MRI

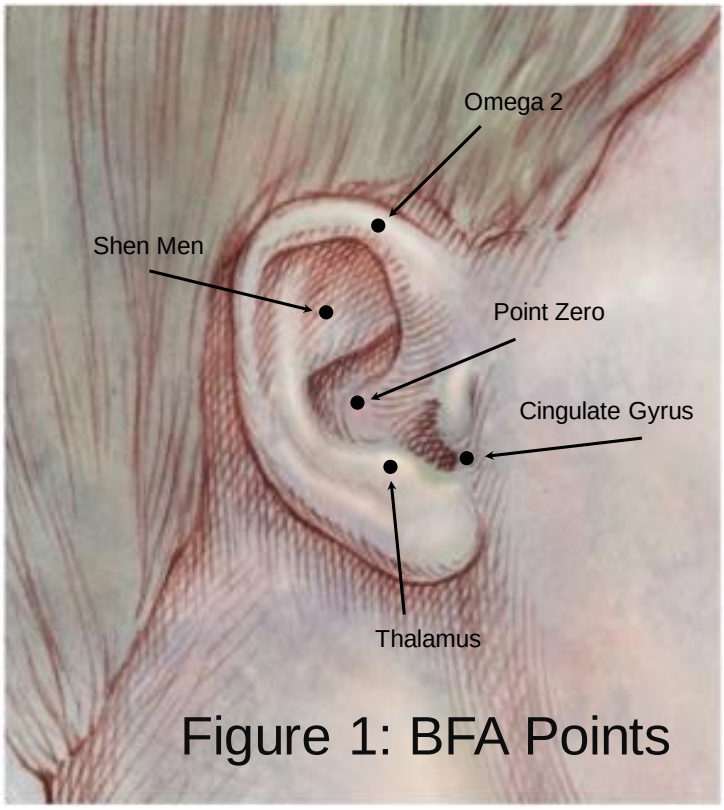

Figure 1: BFA Points

The delivery of BFA will be administered in the following steps:

1. The practitioner will direct the patient to sit and ensure that he or she is comfortable, with his or her back well supported.
2. The practitioner will clean the right ear using an alcohol pad.
3. The practitioner will place the needle in the Cingulate Gyrus point on the clean right ear, making sure to position and insert the needle with the proper technique.
4. The practitioner will assist the patient in rising, and guide them in walking for one minute.
5. Should the patient feel light-headed, the practitioner will assist them in sitting down.
6. Once one minute has transpired, the practitioner will assess the patient's pain level, taking note of the reported pain level.
7. If the pain is greater than 0-1, and the patient is willing, practitioner will continue, repeating steps 2-4 on the left ear for the Cingulate Gyrus point.
8. If pain has decreased below 1, patient requests the practitioner stop due to discomfort, or the practitioner observes significant vaso-vagal reaction, practitioner will stop inserting needles.
9. If patient continues to report pain greater than 0-1 and is willing, practitioner will continue inserting needles following steps 3-4, first in the right ear, then in the left ear at the Thalamus point, the Omega 2 point, Point Zero, and Shen Men point.

10. The practitioner will once again assess the patient's pain level, ensure they are feeling well, and release the patient.

eTable 1: Descriptive Statistics of Pain Outcome Measures, by Week and Arm

		Usual Care		Auricular Acupuncture		Electroacupuncture	
Outcome Measure	**Week**	**n**	**Mean (SD)**	**n**	**Mean (SD)**	**n**	**Mean (SD)**
BPI Pain Severity	**0**	71	5.6 (1.5)	141	5.0 (1.7)	145	5.2 (1.8)
	12	66	5.0 (2.0)	135	3.1 (2.1)	133	2.7 (2.0)
	24	--	--	126	3.0 (2.1)	134	3.0 (2.2)
BPI Pain Interference	**0**	71	5.3 (2.2)	141	4.7 (2.2)	145	5.1 (2.4)
	12	66	4.4 (2.4)	133	2.3 (2.0)	133	2.2 (2.1)
	24	--	--	125	2.2 (2.1)	133	2.5 (2.5)
BPI Worst Pain Item	**0**	71	7.1 (1.8)	141	6.6 (1.8)	145	6.9 (1.7)
	12	66	6.1 (2.1)	135	4.4 (2.5)	133	3.9 (2.5)
	24	--	--	126	4.0 (2.5)	134	4.0 (2.7)
BPI Average Pain Item	**0**	71	6.1 (1.6)	141	5.4 (1.7)	145	5.6 (1.7)
	12	66	5.4 (1.9)	135	3.2 (2.1)	133	2.9 (2.1)
	24	--	--	126	3.2 (2.0)	134	3.1 (2.2)
Pain Medication QAQ Score	**0**	69	1.7 (2.2)	136	1.6 (2.2)	142	1.6 (2.1)
	12	68	1.7 (2.8)	125	1.1 (1.7)	133	1.1 (1.8)
	24	--	--	122	1.1 (1.6)	128	1.1 (1.8)

eTable 2. Primary and Secondary Outcomes (extended version of manuscript Table 2)[a]

		Usual Care (UC)		Electroacupuncture (EA)			Auricular Acupuncture (AA)			
Outcome	Week	Mean (95% CI)	Change from Baseline, Mean (95% CI)	Mean (95% CI)	Change from Baseline, Mean (95% CI)	Difference from UC in Change from Baseline, Mean (95% CI)	Mean (95% CI)	Change from Baseline, Mean (95% CI)	Difference from UC in Change from Baseline, Mean (95% CI)	Difference in Change From Baseline, AA - EA, Mean (95% CI)
Primary Outcome:										
BPI Pain Severity	**0**	5.23 (5.03, 5.43)	--	5.23 (5.03, 5.43)	--	--	5.23 (5.03, 5.43)	--	--	
	12	4.75 (4.37, 5.14)	-0.48 (-0.85, -0.10)	2.84 (2.55, 3.13)	-2.39 (-2.66, -2.12)	-1.92 (-2.43, -1.40)[b]	3.20 (2.91, 3.49)	-2.03 (-2.30, -1.76)	-1.56 (-2.07, -1.04)[b]	0.36 (∞, 0.665)[c]
	24	--	--	3.04 (2.76, 3.33)	-2.19 (-2.46, -1.92)	--	3.24 (2.95, 3.53)	-1.99 (-2.27, -1.72)	--	0.20 (∞, 0.51)[d]
Secondary Outcomes:[e]										
BPI Pain Interference	**0**	4.96 (4.74, 5.19)	--	4.96 (4.74, 5.19)	--	--	4.96 (4.74, 5.19)	--	--	
	12	4.10 (3.67, 4.53)	-0.86 (-1.28, -0.45)	2.20 (1.88, 2.52)	-2.76 (-3.06, -2.46)	-1.90 (-2.40, -1.40)	2.44 (2.12, 2.76)	-2.52 (-2.82, -2.22)	-1.66 (-2.16, -1.16)	0.24 (-0.17, 0.64)
	24	--	--	2.49 (2.17, 2.81)	-2.47 (-2.77, -2.17)	--	2.49 (2.17, 2.82)	-2.47 (-2.78, -2.16)	--	0.00 (0.41, -0.41)
BPI Worst Pain	**0**	6.85 (6.61, 7.09)	--	6.85 (6.61, 7.09)	--	--	6.85 (6.61, 7.09)	--	--	
	12	5.90 (5.40, 6.40)	-0.95 (-1.45, -0.45)	3.90 (3.54, 4.27)	-2.94 (-3.31, -2.58)	-2.00 (-2.59, -1.40)	4.48 (4.12, 4.84)	-2.37 (-2.73, -2.00)	-1.42 (-2.01, -0.82)	0.58 (0.09, 1.06)
	24	--	--	4.00 (3.64, 4.36)	-2.85 (-3.21, -2.49)	--	4.26 (3.89, 4.63)	-2.58 (-2.96, -2.21)	--	0.27 (-0.22, 0.76)
BPI Average Pain	**0**	5.60 (5.40, 5.80)	--	5.60 (5.40, 5.80)	--	--	5.60 (5.40, 5.80)	--	--	
	12	5.14 (4.75, 5.53)	-0.46 (-0.84, -0.07)	3.07 (2.78, 3.35)	-2.53 (-2.81, -2.25)	-2.07 (-2.53, -1.61)	3.32 (3.03, 3.61)	-2.28 (-2.55, -2.00)	-1.82 (-2.28, -1.36)	0.25 (-0.12, 0.63)
	24	--	--	3.22 (2.93, 3.51)	-2.38 (-2.65, -2.10)	--	3.42 (3.13, 3.72)	-2.17 (-2.46, -1.89)	--	0.20 (-0.17, 0.58)
PROMIS Physical Health	**0**	40.68 (39.93, 41.42)	--	40.68 (39.93, 41.42)	--	--	40.68 (39.93, 41.42)	--	--	
	12	41.09 (39.80, 42.37)	0.41 (-0.76, 1.58)	44.99 (44.01, 45.98)	4.32 (3.48, 5.15)	3.91 (2.49, 5.32)	45.17 (44.17, 46.17)	4.50 (3.64, 5.35)	4.09 (2.66, 5.51)	0.18 (-0.98, 1.34)
	24	--	--	44.28 (43.29, 45.26)	3.60 (2.77, 4.43)	--	45.28 (44.26, 46.30)	4.60 (3.73, 5.48)	--	1.00 (-0.18, 2.18)
PROMIS Mental Health	**0**	45.75 (44.82, 46.69)	--	45.75 (44.82, 46.69)	--	--	45.75 (44.82, 46.69)	--	--	
	12	45.02 (43.53, 46.52)	-0.73 (-2.04, 0.58)	47.60 (46.42, 48.78)	1.85 (0.92, 2.78)	2.58 (0.99, 4.16)	48.47 (47.27, 49.66)	2.71 (1.76, 3.67)	3.44 (1.84, 5.04)	0.87 (-0.44, 2.17)
	24	--	--	47.20 (46.02, 48.38)	1.45 (0.52, 2.38)	--	48.67 (47.46, 49.88)	2.92 (1.94, 3.89)	--	1.47 (0.15, 2.79)
Pain Medication QAQ Scc	**0**	1.58 (1.38, 1.78)	--	1.58 (1.38, 1.78)	--	--	1.58 (1.38, 1.78)	--	--	
	12	1.71 (1.37, 2.04)	0.13 (-0.17, 0.43)	1.14 (0.88, 1.40)	-0.44 (-0.66, -0.23)	-0.57 (-0.94, -0.21)	1.19 (0.92, 1.46)	-0.39 (-0.61, -0.17)	-0.52 (-0.88, -0.15)	0.05 (-0.25, 0.35)
	24	--	--	1.15 (0.88, 1.41)	-0.43 (-0.65, -0.21)	--	1.30 (1.03, 1.57)	-0.28 (-0.50, -0.06)	--	0.15 (- 0.15, 0.46)

a. For each outcome, estimates are derived from a linear mixed model with baseline means constrained to be equal across study arms. The dependent variable vector included the pre-randomization baseline (week 0) assessment, as well as all post-randomization assessments at weeks 4, 10, 12, 16, and 24. The independent variables were the randomization stratification variables (accrual site and baseline opioid use), treatment arm, week (categorical), and the arm-by-week interaction. A patient-level random intercept was included in the model to account for the repeated outcome measurements within patients.

b. Primary endpoint. Point estimates with 97.5% confidence intervals (adjusted for 2 comparisons) are presented. P<0.001 for both comparisons of treatment arms with UC for differences in BPI Pain Severity change from baseline to week 12.

c. Primary endpoint comparison of non-inferiority of AA to EA at Week 12. Point estimate with one-sided 95% confidence interval is presented. The non-inferiority margin was 0.657. The one-sided 95% confidence interval contains the non-inferiority margin; therefore, we cannot conclude that AA is non-inferior to EA at our prespecified $p < 0.05$ threshold. The p-value for the non-inferiority test was $p = 0.055$.

d. Secondary endpoint comparison of non-inferiority of AA to EA at Week 24. Point estimate with one-sided 95% confidence interval is presented. The non-inferiority margin was 0.657. The one-sided 95% confidence interval did not contain the non-inferiority margin, supporting the non-inferiority of AA to EA at Week 24 at the $p < 0.05$ threshold. The p-value for the non-inferiority test was $p = 0.007$. This test was not prespecified as part of our primary endpoint comparisons and was conducted post-hoc as an exploratory analysis.

e. Secondary outcomes were not adjusted for multiple comparisons. Results are presented as point estimates with 95% confidence intervals.

Abbreviations: CI, confidence interval; BPI, Brief Pain Inventory; PROMIS, Patient-Reported Outcomes Measurement Information System; QAQ, Quantitative Analgesic Questionnaire.