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Acupuncture for treatment of uncontrolled pain in cancer patients: a pragmatic pilot study

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ABSTRACT

Purpose: Pain control is an ongoing challenge in the oncology setting. Prior to implementing a large randomized trial at our institution, we investigated the feasibility, safety and initial efficacy of acupuncture for uncontrolled pain among cancer patients.

Hypotheses: Our hypotheses were that the acupuncture treatments provided would be: 1) feasible, 2) safe, and 3) a beneficial adjunct to pain management.

Study Design: This was a single arm, non-randomized pragmatic pilot study.

Methods: Participants experiencing pain ≥ 4 on a 0-10 numeric rating scale received a maximum of 10 treatments on an individualized basis. Recruitment, attrition, compliance, and adverse events (AEs) were assessed. Pain (Brief Pain Inventory – Short Form), quality of life (MD Anderson Symptom Inventory [MDASI]), and patient satisfaction were assessed at baseline and at the end of treatment.

Results: Of 115 patients screened, 52 (45%) were eligible and agreed to participate. Eleven (21%) were lost to follow-up, leaving 41 who completed all study procedures. No AEs were reported. Mean pain *severity* was 6.0±1.3 at baseline and 3.8±2.0 at follow-up ($p<0.0001$). Pain *interference* was 6.2±2.3 at baseline and 4.3±2.8 at follow-up ($p<0.0011$). On the MDASI, the mean symptom *severity* was 4.6±1.8 at baseline and 3.2±1.9 at follow-up ($p<0.0001$), and mean symptom *interference* was 5.8±2.4 at baseline and 4.1±2.9 at follow-up ($p<0.002$). Prescribed pain medications decreased across the course of the study. Patient satisfaction was high: 87% reported that their expectations were met “very well” or “extremely well”; 90% said they were likely to participate again; 95% said they were likely to recommend acupuncture to others; and 90% reported they found the service to be “useful” or “very useful.”

Conclusions: Acupuncture was feasible, safe, and a helpful treatment adjunct for cancer patients experiencing uncontrolled pain in this study. Randomized placebo-controlled trials are needed to confirm these results.

Key words: acupuncture, pain, cancer, complementary medicine, integrative medicine, symptom management

INTRODUCTION

Pain is a common symptom among cancer patients and can be caused by disease or side effects of treatment.[1] Pain control is an ongoing challenge in the oncology setting and has important implications for patient's emotional, social, and physical well-being. For many, traditional pain management approaches such as opioid treatment are not an optimal choice,[2] and studies have shown acupuncture has fewer side effects than pharmacological treatments.[3-8]

Several systematic reviews and meta-analyses[9-12] evaluating acupuncture for pain management in cancer patients have been published. Three of these studies[9-11] concluded the evidence was insufficient to support the use of acupuncture because of methodological limitations in the randomized controlled trials (RCTs) that were included. Interestingly, a recent meta-analysis by Choi and colleagues[12] reported that, although acupuncture was not more effective than drug therapy, acupuncture plus drug therapy was significantly more effective than drug therapy alone (n=437; RR, 1.36; 95% CI 1.13 to 1.64; p=0.003), implying there is a synergistic effect of acupuncture when added to conventional care.

Although not involving cancer patients, robust evidence supporting the use of acupuncture for multiple chronic pain conditions was recently published by Vickers and colleagues.[13] An analysis of patient-level data from 29 high quality RCTs including 17,922 patients found acupuncture was superior to both sham and no-acupuncture for back pain, neck pain, shoulder pain, osteoarthritis, and chronic headaches (p<0.001 for all comparisons). In this study, one of the largest ever conducted on acupuncture, the investigators found modest, but statistically significant, effect size differences between acupuncture and sham (shoulder pain 0.62, spinal pain 0.37, osteoarthritis 0.26, and chronic headache 0.15) and considerably larger effect size differences between acupuncture and no-acupuncture controls (spinal pain 0.55, osteoarthritis 0.57, and chronic headache 0.42). No trials evaluating shoulder pain compared acupuncture to a no-acupuncture treatment group. This study provides strong evidence that acupuncture for chronic pain management is more than a placebo.

Functional magnetic resonance imaging (fMRI) studies also suggest stimulation of acupuncture points can initiate multiple pathways of analgesia through the modulation of neurotransmitter and pain control systems at various levels of the central nervous system (CNS). Huang and colleagues[14] characterized acupuncture stimuli in a recent systematic review and meta-analysis of fMRI data and reported the response to acupuncture involves a broad network of brain regions consistent with affective, cognitive and somatosensory processing. Specific areas found to be involved were the somatosensory cortices, limbic system, basal ganglia, brain stem, and cerebellum. Differences in CNS activity between active and sham acupuncture were also noted.

Electroacupuncture, adding an electrical current between two needles, is often used for pain management, and according to Han and colleagues,[16] specific frequencies of electrical stimulation induce the gene expression of specific neuropeptides in the CNS. The release of opioid peptides evoked by electroacupuncture depends on the frequency of current delivered.[16] For example, a frequency of 2 Hz induces the gene expression of endorphins in the diencephalons, 2-15 Hz causes the release of endorphins and enkephalin in the brain and dynorphin in the spinal cord, and a frequency of 100 Hz causes the release of dynorphin in the spinal cord alone.[16] When alternating frequencies are used, these three opioids are likely to have a synergistic effect.[17] Genetic factors may also play a role in individual response to acupuncture, and multiple molecules, in addition to opioid peptides (i.e,, glutamate [NMDA and AMPA/KA receptors], 5-hydroxytryptamine, and cholecystokinin octapeptide), may help mediate analgesia.[19]

Auricular acupuncture, also applied in this study, involves the placement of needles in ear points and is often used for pain management.[20] Alimi and colleagues[21,22] evaluated the efficacy of auricular acupuncture for decreasing pain intensity among cancer patients in two randomized, placebo-controlled trials and concluded there was a clear benefit.

A recent systematic review of acupuncture in cancer care[23] confirmed that few studies with rigorous scientific methodology have examined its role for pain management in this population. As the overall

safety of acupuncture is well established in other populations,[3-8] and there are data suggesting a benefit,[24] clinical trials evaluating the use of acupuncture for pain management in cancer patients are warranted. Prior to embarking on a randomized trial at our institution, we conducted a single-arm study to examine the feasibility, initial efficacy, and level of patient satisfaction with acupuncture treatment.

METHODS

Participants

Potential participants in this pilot study were identified by faculty in the Pain Management Center at our institution and were referred to the research nurse for assessment of eligibility and to obtain informed consent. Approval from the Institutional Review Board was obtained.

Patients were recruited for participation regardless of gender, age, ethnicity, type of cancer, stage of disease, or previous cancer treatment received. Specific inclusion criteria were (1) ability to understand English; (2) Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2; and (3) pain score ≥ 4 on a 0-10 numerical rating scale (NRS). Patients were excluded if they had any of the following: (1) local infection at or near acupuncture sites used for pain control; (2) deformities that could interfere with accurate acupuncture point location; or (3) known coagulopathy or warfarin or heparin use, including low-molecular-weight heparins. Patients were allowed to participate if they were taking clopidogrel, aspirin, or other non-steroidal anti-inflammatory agents. Other exclusion criteria included mental incapacitation or significant emotional or psychological disorder that would interfere with the ability to cooperate during this slightly invasive procedure; planned changes in the pain medication regimen, and pregnancy. Finally, patients were excluded if they had a platelet count <100,000 K/μL or a white blood cell count < 3000 K/μL, which were conservative institutional guidelines in place for acupuncture at the time the study was conducted.

As the purpose of this study was to examine the initial effects of acupuncture on the management of uncontrolled pain and to examine the logistics of running this type of protocol, participants were not

excluded if they were receiving concomitant chemotherapy or investigational anticancer therapies; however, eligible patients had to remain on a stable course of pain medication throughout the treatment period, although minor changes and reductions in dosage were permitted. No specific prior pain treatment regimen was required for participation.

Patients' medical records were reviewed, and the following baseline characteristics were recorded: primary cancer diagnosis; stage of disease at time of study entry; presence or absence of metastasis; history of cancer treatment; pain management history; type and location of pain and its suspected etiology. Prescribed pain medications at the time of study entry and at the end of treatment were also recorded.

Treatment and Procedures

After baseline measures for pain and quality of life were obtained, patients received individualized acupuncture treatments 1-3 times per week, depending on the acupuncturists' recommendation as well as the patient's scheduling preferences. Two licensed and experienced acupuncturists (over 30 years combined), who were credentialed by the hospital, provided all treatments. Both practitioners graduated from the same standardized masters' degree program in Houston, Texas; thus, variability in treatment approach and methods was limited.

Patients received a maximum of 10 treatments in the acupuncture clinic at our institution. On the first visit, patients who had no contraindications were given the option of undergoing a single treatment consisting of the insertion of gold-plated stainless steel ear studs (Aiguille Semi-Permanent [ASP] auricular acupuncture needles; SEDATELEC, Lyon, France) placed consecutively and bilaterally into the following points: Cingulate gyrus (CG), Shenmen, Point zero, and Subcortex.[25] Patients were eligible for this initial session if they did not have allergies to gold or other dermatologic issues and were capable of safely maintaining the retention needles. They were instructed that the ear studs would remain in place for 3-5 days and told they should remove them with an alcohol swab or tweezers if any evidence of redness or irritation developed. Patient-reported pain scores were

recorded on a 0-10 NRS before and after this initial treatment.

During subsequent treatment sessions, patients were assisted into a comfortable position and assessed by the acupuncturist to determine the most appropriate treatment approach. Points were selected on an individualized basis according to the theory of traditional Chinese medicine,[26] patient's medical history, location and type of pain, and concomitant symptoms. All treatments were given using needles (32-40 gauge and 15-40mm length) manufactured by Seirin Corporation (Shizuoka, Japan). A list of the most common points used, by location, is provided in Table 1.

Standardized techniques for point location were utilized.[26,27] As documented in the patient's electronic medical record, if there was active disease, needles were not placed in the same anatomical region as tumor. After the skin was prepped with 70% alcohol, the needles were placed at the selected body points and left in place for approximately 25 minutes. Needle insertion endpoints were the standardized recommended depth of insertion[26,27] or achievement of *de qi* sensation. *De qi* sensation is defined as the sensation of numbness, tingling, or warmth at the needle insertion site. It may also be experienced by the acupuncturist as the needle being "grabbed" by underlying tissues. The recommended depth of insertion[26,27] ranged from 0.5-1.5 inches for body points and 1-2mm for ear points.

Electrical Stimulation

At each visit, patients were assessed by the acupuncturist to determine whether or not electrical stimulation should be added. No electrical stimulation was applied if the patient had a cardiac pacemaker or a history of prior negative response or intolerance to electrical stimulation. Electrical stimulation was added after *de qi* sensation was elicited and was applied to acupoints by placing lead wires on the needles connected to an electro-acupuncture stimulator (IC-1107; ITO Co., LTD, Tokyo, Japan). The electrical stimulation was applied to points along the same channel with the leads attached from negative to positive in the same direction as channel flow.[26] The stimulator was

programmed to alternate between high and low frequencies (2-100 Hz) using a continuous (dense-disperse) waveform for 20 minutes.

Measures

Patients completed self-report questionnaires at baseline and after the last acupuncture session. Data collected shortly after the last treatment included assessment of current pain, average pain, worst/least pain within the last 24 hours, and the *interference* of pain with daily activities and quality of life (QOL) within the last 24 hours.

Brief Pain Inventory-Short Form (BPI-SF): The BPI-SF is a validated, widely used, self-administered questionnaire to assess the *severity* of pain and its impact on daily functioning.[28] Item 1 assesses whether or not patients are currently experiencing pain other than minor headache, sprain, or toothache. The second item asks patients to indicate on a whole body diagram the exact location of their pain, and items 3-6 measure pain *severity* on a 0-10 numeric scale (worst, least, and average pain in the last 24 hours and current pain level). Items 7-8 assess treatments and pain relief from treatments or medications within the last 24 hours. Finally, item 9 includes seven subratings that determine the degree to which pain has *interfered* with the patient's QOL within the previous 24 hours. Assessment of "pain at its worst in the last 24 hours" (item 3 on the BPI-SF) satisfies the United States Food and Drug Administration (FDA) guidelines for measuring a pain reduction treatment effect, and a reduction of at least two points on a 0-10 scale indicates a clinically significant improvement.[29] For this study, patients, therefore, had be experiencing pain >4/10 on the NRS.

MD Anderson Symptom Inventory (MDASI): The MDASI is a brief questionnaire that measures on a scale of 0-10 the *severity* and impact of cancer-related symptoms on the patient's QOL over the previous 24 hours.[30] Thirteen core items ask about symptoms common to cancer and cancer treatment. An additional 6 items evaluate the extent to which cancer-related symptoms interfere with the patient's daily activities.

Participant Feedback Form (PFF): The PFF is a standard departmental form used to assess patient satisfaction with services offered. It consists of 6 questions that evaluate on a scale of 0-3 whether or not the service met the patient's expectations and whether or not they would recommend it to others. An additional 3 items are open-ended and allow patients to make recommendations for future program or service offerings. The PFF was administered to all study participants at the end of the treatment period.

Statistical Considerations

Our criteria for determining study feasibility were that half of the patients screened would be eligible, at least 80% of eligible patients would agree to participate, and we would have a drop-out rate ≤ 25%. Additionally, three different methods of analysis were conducted to measure the treatment effect. First, paired *t*-tests were performed to evaluate differences from baseline to the end of treatment for patients who completed all prescribed acupuncture treatment sessions and study procedures. For additional comparison, data were analyzed with simple imputation by replacing missing data with group means at the corresponding time point. Furthermore, intent-to-treat procedures with multiple imputations were utilized to evaluate all patients who consented to participate and completed at least one treatment session using the *SAS* V9.2 MI procedure with the Markov Chain Monte Carlo method to impute 10 times and then using the MIANALYZE procedure to generate statistical inferences.[31]

RESULTS

Of the 115 patients screened, 56 (49%) met all eligibility requirements. Of the eligible patients, 52 agreed to participate, with four declining either because of scheduling conflicts, transportation problems, or because they stated, "I don't like needles." Participant characteristics are shown in Table 2. The average length of time patients had been receiving treatment for pain management was 31 months (range, 0.25-107 months). Most participants (67%) reported pain in multiple locations as follows: back (40%), neck/shoulders (23%), trunk/thorax (15%), lower extremities (15%), upper extremities (13%), abdomen (8%), joints (6%), peripheral neuropathy (4%), rectum/genitals (4%), general body pain (4%), headache (2%), and orofacial pain (2%). All patients received acupuncture

1-2 times per week. Thirty-nine (75%) patients received auricular ASP needles on their first visit and electroacupuncture stimulation on subsequent visits

Patient flow throughout the study is presented in Figure 1. Eleven (21%) patients who entered the study were lost to follow-up owing to difficulty in scheduling treatments, changes in pain medications, or disease progression. For these 11 patients, the average number of treatments received was five (range, 2-10) over an average of 4 weeks (range, 1-13). One patient failed to complete the second page of one questionnaire. Therefore, 41 patients completed all study procedures and the prescribed acupuncture treatment regimen (average number of treatments = 8; range, 2-10) over an average of 5 weeks (range, 1-14). Of these, 71% (29/41) received auricular ASP needles on their first visit. On subsequent visits, 71% (29/41) received electroacupuncture at body points, although not necessarily the same 29 patients who received auricular acupuncture.

Paired *t*-tests revealed significant differences in symptom *severity* scores and *interference* scores on both the BPI-SF and the MDASI between baseline and the end of the study for the 41 evaluable patients (see Figure 2 and Table 3). For the BPI-SF, there were significant reductions in both the pain *severity* score and the *interference* score from baseline to follow-up ($p<0.0001$ and $p<0.0011$, respectively). Reduction in “worst pain in the last 24 hours” was 2.4 points ($p<0.0001$). For the MDASI, there were also significant reductions in both the symptom *severity* ($p<0.0001$) and *interference* ($p<0.002$) scores from baseline to follow-up. When the analyses were repeated using intent-to-treat procedures with either simple imputation (i.e., replacing missing values with group means at the corresponding time point) or multiple imputations, all findings remained highly significant.

Subset analyses were performed comparing the 29 patients who received both ear and body point acupuncture with electrical stimulation versus the 12 who received body point acupuncture only with no electrical stimulation. No significant differences between the two groups were found on either the BPI-SF or MDASI. Additionally, examination of pre- and post-treatment pain scores (0-10 NRS)

immediately before and after the auricular acupuncture given on the first visit in this subset of 29 patients revealed significant reductions in pain (mean change in scores: -1.3±1.1; p<0.0001).

For 34% (14/41) of patients, prescribed medications for pain were reduced by the end of treatment, and their BPI-SF pain *severity* scores and *interference* scores were also significantly reduced compared with baseline (p=0.0003 and 0.07, respectively). Among these patients, worst pain (p=0.006), least pain (p=0.003), average pain (p=0.01), and pain "right now" (p=0.0002) were also significantly lower at the end of treatment, as were their MDASI symptom *severity* and *interference* scores (p=0.02 and 0.01, respectively). For 10% (4/41) of patients, prescribed pain medications were increased. Among these patients, only the BPI-SF and MDASI *interference* scores were significantly lower at follow-up (p=0.02 for both).

For 44% (18/41) of patients, the prescribed pain medications were unchanged, yet the BPI-SF pain *severity* and *interference* scores were significantly reduced from baseline (p=0.0002 and 0.01, respectively). Among these patients, worst pain (p=0.007), least pain (p=0.003), average pain (p=0.002), and pain "right now" (p=0.0008) were also significantly lower at the end of treatment, as were MDASI symptom *severity* and *interference* scores (p=0.004 and 0.007, respectively). For 12% (5/41) of patients, changes in prescribed pain medications were unclear due to missing data. Among these patients, the BPI-SF pain *severity* and *interference* scores were significantly reduced from baseline (p=0.02 and 0.04, respectively). Although a significant reduction from baseline was found for worst pain (p=0.009), least pain, average pain, and pain "right now" were not significantly improved. Likewise, no significant improvement was found for MDASI symptom *severity* or *interference* scores.

Changes in pain medication prescription were as follows: 81% (34/42) of patients had opioids prescribed at baseline, with only 52% (22/42) at follow-up; 43% (18/42) had non-opioid analgesics prescribed at baseline, with 31% (13/42) at follow-up; 12% (5/42) had tricyclic anti-depressants prescribed at baseline, with 2% (1/41) at follow-up; 29% (12/42) had other anti-depressants prescribed at baseline, with 17% (7/42) at follow-up; 52% (22/42) had gabapentin prescribed at

baseline, with 40% (17/42) at follow-up; 7% (3/42) had steroids prescribed at baseline, with 5% (2/42) at follow-up; 12% (5/42) had muscle relaxants prescribed at baseline, with 17% (7/42) at follow-up; and 14% (6/42) had benzodiazepines prescribed at baseline, with 0% (0/42) at follow-up. Additionally, 2/42 (5%) patients had electronic pain pumps at baseline, and 1/42 (2%) had a pain pump at follow-up.

In terms of patient satisfaction, 87% stated that the course of acupuncture met their expectations "very well" or "extremely well", 90% said they were likely to have acupuncture again, 95% said they were likely to recommend acupuncture to others, and 90% said they found the acupuncture to be "useful" or "very useful."

DISCUSSION

Pain among cancer patients takes many forms and is often difficult to manage. Furthermore, the logistics of providing acupuncture service in the setting of a busy clinic are challenging. This study was, therefore, designed to determine the feasibility, safety, and initial efficacy of acupuncture to treat uncontrolled pain in a cancer patient population in order to inform a future larger randomized trial. Although only 49% of patients screened were eligible for acupuncture therapy, all other feasibility criteria were met: of eligible patients, 93% agreed to participate, and the drop-out rate was 21% during the study period. The treatment was safe and there were no adverse events reported by the patients.

In terms of an initial assessment of effect, there was a highly significant reduction in pain *severity* and *interference* scores between baseline and the end of treatment. Similar improvements were seen in overall QOL and *interference* scores. It is also notable that 78% of patients had either a reduction or no change in their pain medications, yet their pain outcomes and QOL improved. Importantly, the reduction in "worst pain in the last 24 hours" for all patients was 2.4 points, which represents a clinically significant reduction in pain scores.[29]

Although changes in pain medications should be interpreted with caution, as patients who took less medication may have experienced more pain and vice versa, 34% of patients had fewer pain medications prescribed at the end of treatment compared with baseline. Furthermore, the percentage of patients who were prescribed opioids was reduced from 81% at baseline to 52% at the end of treatment. Moreover, there were also reductions in the percentages of all other categories of pain medications, except for muscle relaxers, which were prescribed at a slightly higher rate. The reason for this small increase in use of muscle relaxers is unclear, however, it was due to only two patients out of 42 and should be interpreted with caution. Overall, most patients reported a benefit from acupuncture treatment, with no adverse events reported.

Even though the study found significant improvement in pain and QOL outcomes, the specific effects of acupuncture needling are not well understood, and it is important to remember that the natural history of pain is to decline over time. The use of acupuncture for pain control in a cancer population also likely has a large placebo effect,[32] which needs to be controlled for in future studies. However, it is important to note that on average these patients had been experiencing pain for more than 2 years and were on pain medications that did not seem to bring them adequate pain relief, and for which there is also a substantial placebo effect. Other limitations of the study were that there was no long-term follow-up; for patient convenience, data were collected shortly after the last treatment session. However, the questionnaires evaluated average symptoms and symptoms over the past 24 hours, and according to the FDA, assessment of “pain at its worst in the last 24 hours” on the BPI-SF is sufficient for measuring a pain reduction treatment effect.[29] An additional limitation was that the acupuncture treatments (i.e., point selection as well as number and frequency of treatments) were individualized. Although individualized treatments are representative of actual clinical practice, for research purposes, using a non-fixed treatment approach makes interpretation of the results difficult, as the specific effects of acupuncture remain unknown.

CONCLUSION(S)

Acupuncture was found to be a feasible, safe, and helpful adjunct for treating uncontrolled pain among cancer patients in this preliminary trial. Randomized placebo-controlled trials are needed to confirm the efficacy of acupuncture for pain management in a cancer population.

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Table 1. Most common acupuncture points used by location.

Location	Acupuncture Points*
Head	Yintang, DU 20, ST 8, GB 8, GB 20, B 10
Neck/shoulders	Huatojiaji, GB 21, LI 15, SJ 14, SI 9-12
Upper extremities	Baxie, LI 4, LI 11, LI 14, SI 3
Lower extremities	Bafeng, Heding, Xiyan, LV 3, SP 6, ST 36, GB 34, GB 39,
Upper-mid back	DU 14, B 11-21, B 41-50
Lower back	Yaoyan, B 22-35, B 51-54
Chest	LU 1-2, CV 17
Abdomen	CV 4, CV 6, CV 12, St 25
Hips/thighs	GB 27-30
General body pain	SP 21

*The average number of points used per treatment was 14 (range 8-23).

Table 2. Patient characteristics.

CHARACTERISTICS	Number of Patients (%), n=52	
Age: Mean (SD)	54 (11.9)	Range: 33-88
Gender	37 (71)	Female
	15 (29)	Male
Race/Ethnicity	41 (78.8)	White
	5 (9.6)	Black
	3 (5.8)	Asian
	3 (5.8)	Hispanic
Primary Cancer	16 (30.8)	Breast
	8 (15.4)	Genitourinary
	8 (15.4)	Lymphoma/Myeloma
	4 (7.7)	Melanoma/Skin
	4 (7.7)	Oro/Nasopharyngeal
	4 (7.7)	Unknown
	3 (5.8)	Brain/Spine
	2 (3.8)	Gastrointestinal
	2 (3.8)	Sarcoma
	1 (1.9)	Lung
Stage of Disease	9 (17)	Stage I
	18 (35)	Stage II
	12 (23)	Stage III
	13 (25)	Stage IV
	7 (13.5)	Remission
	26 (50)	NED*
Location of Pain†	20 (38.5)	Low Back
	12 (23.1)	Neck/Shoulder
	8 (15.4)	Trunk/Thorax
	8 (15.4)	Lower Extremity
	7 (13.5)	Upper Extremity
	4 (7.7)	Abdomen
	3 (5.8)	General joint
	2 (3.8)	CIPN‡
	2 (3.8)	Rectum/genitals
	2 (3.8)	General Body
	1 (1.9)	Headache
	1 (1.9)	Orofacial
	1 (1.9)	Upper Back
# Months of Pain Management: Mean(SD)	31.1 (28.8)	Range: 0.25-107

* NED indicates no evidence of cancer at the time of study entry.
† Some patients experienced pain at multiple locations.
‡ CIPN indicates chemotherapy-induced peripheral neuropathy in all four extremities.

Table 3. Comparison of patient outcomes.

Measure	Baseline (N=41)	Follow-up (N=41)	Difference from Baseline	% Change from Baseline	P Values*		
					t-tests N=41	SI† N=52	MI‡ N=52
BPI-SF							
Severity	6.0±1.3	3.8±2.0	-2.1±1.7	35	<0.0001	<0.0001	<0.0001
Worst	8.1±1.4	5.6±2.7	-2.4±2.8	30	<0.0001	<0.0001	<0.0001
Least	4.5±1.8	2.6±2.2	-1.8±1.9	40	<0.0001	<0.0001	<0.0001
Average	5.7±1.4	4.2±2.1	-1.5±2.0	26	<0.0001	<0.0001	<0.0001
Current	5.5±1.9	2.8±2.4	-2.6±2.4	47	<0.0001	<0.0001	<0.0001
Interference	6.2±2.3	4.3±2.8	-1.6±2.9	26	<0.0011	<0.0001	0.0003
MDASI							
Severity	4.6±1.8	3.2±1.9	-1.4±2.0	30	<0.0001	<0.0001	<0.0001
Interference	5.8±2.4	4.1±2.9	-1.5±2.9	26	0.002	<0.0001	0.0008

* Three different methods of analysis were conducted to measure treatment effect. First, paired *t*-tests were performed to evaluate differences from baseline to the end of treatment for patients who completed all prescribed acupuncture treatment sessions and study procedures.
† For additional comparison, data were analyzed with simple imputation (SI) by replacing missing data with group means at the corresponding time point.
‡ Finally, intent-to-treat procedures with multiple imputations (MI) were utilized to evaluate all patients who consented to participate and completed at least one treatment session using the *SAS* V9.2 MI procedure with the Markov Chain Monte Carlo method to impute 10 times and then using the MIANALYZE procedure to generate statistical inferences.[31]

Figure 1. Patient flow diagram.

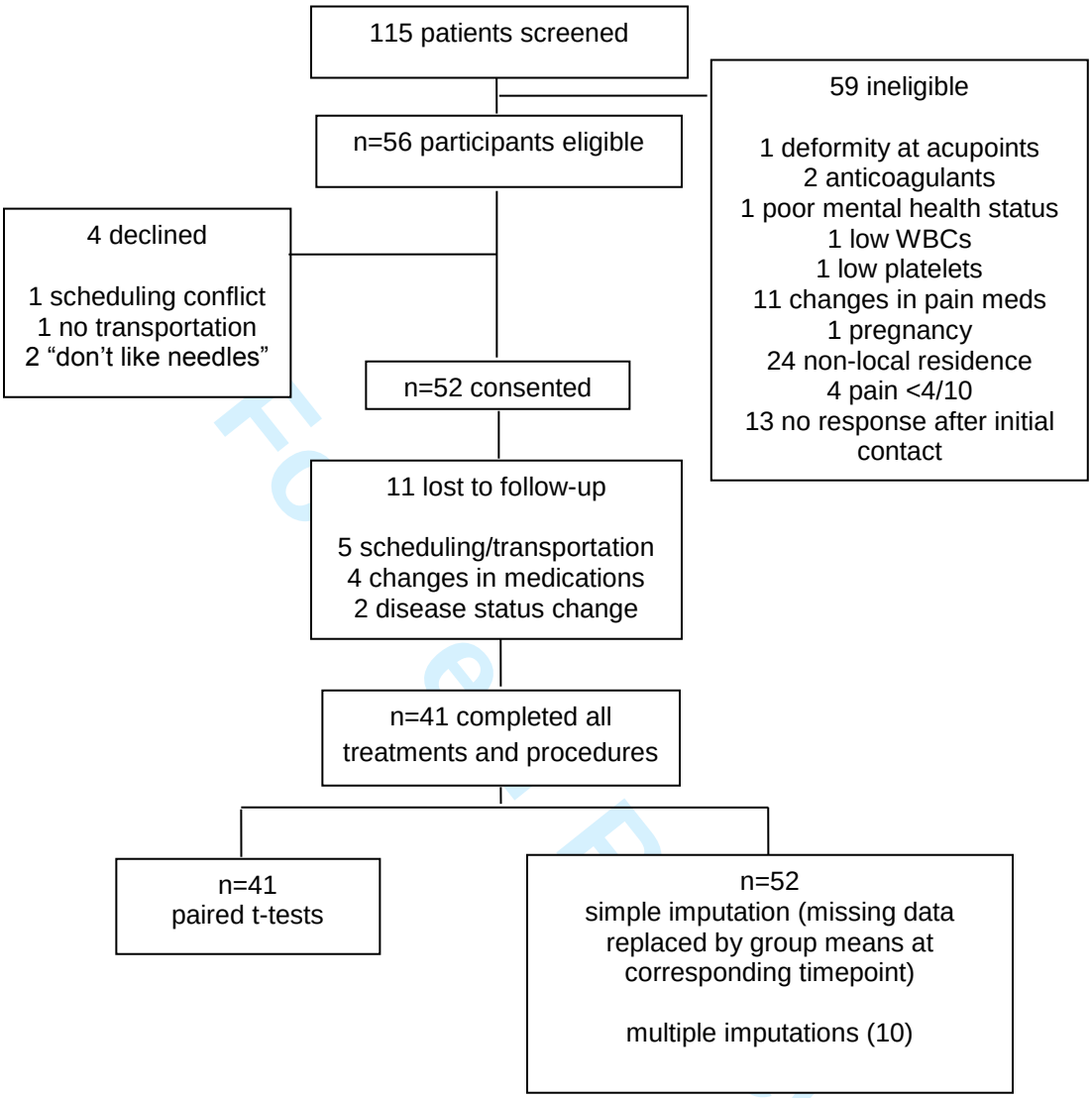
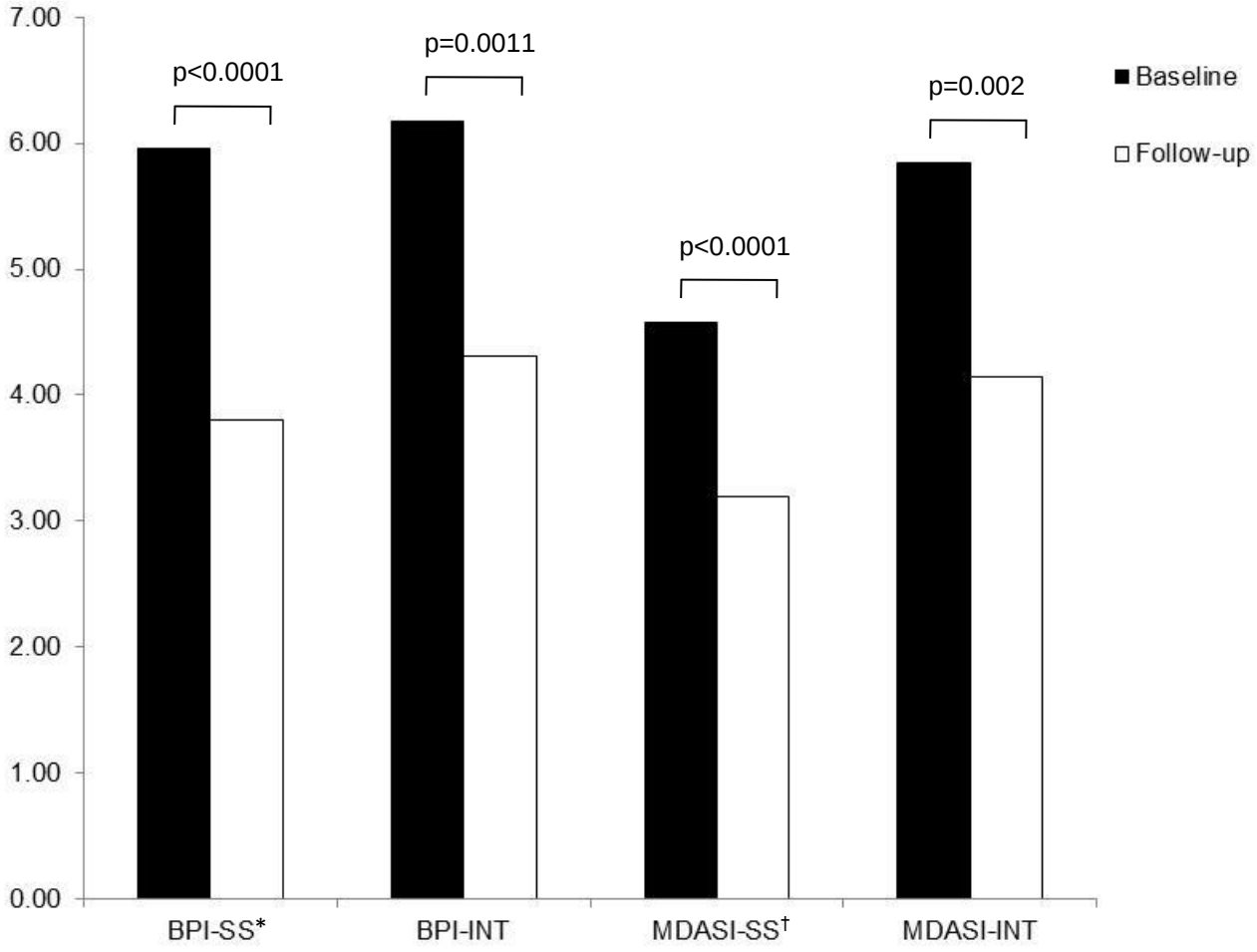


Figure 2. Brief Pain Inventory – Short Form and MD Anderson Symptom Inventory scores.



* BPI-SS=Brief Pain Inventory-Short Form, Symptom Severity; BPI-INT=Brief Pain Inventory-Short Form, Interference

† MDASI-SS=M.D. Anderson Symptom Inventory, Symptom Severity; MDASI-INT=M.D. Anderson Symptom Inventory, Interference