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Preliminary Effectiveness of Auricular Point Acupressure on Chemotherapy-Induced Neuropathy: Part 1 Self-Reported Outcomes

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ABSTRACT

Purpose: To reduce chemotherapy-induced neuropathy (CIN)—a significant challenge among cancer patients following chemotherapy—we explored the effects of auricular point acupressure (APA), which involves needleless, acupuncture-like stimulation on specific ear points.
Design/Method: This pilot study examined the effects of a 4-week APA intervention in the management of CIN. Descriptive analysis was used to examine the changes in study outcomes.
Results: Fifteen participants were enrolled. Two participants dropped out because they developed new medical conditions. Thirteen participants completed the study (87% retention rate). Study participants had more severe symptoms in their lower extremities (i.e., toes, feet, soles) than in their upper extremities (i.e., fingers, wrists, elbows). After the 4–week APA intervention, the mean percentage change scores ranged from 38% (tingling) to 49% (numbness); compared to pre-intervention, the therapeutic effects of APA were sustained at the 1-month follow-up. Function in both upper and lower extremities improved after the APA intervention (≥28%) and continued to improve at the 1-month follow-up (≥36%).
Conclusions: Preliminary results from this small sample provide initial evidence of the effectiveness of APA on CIN. Future studies should confirm these results using a larger sample, a comparative sham control, and an examination of the underlying physiological mechanisms of the anti-CIN effects of APA.
Clinical Implications: APA may provide an inexpensive and effective complementary approach for the self-management of CIN. Once the seeds have been taped to the patient's ear by the provider, patients are empowered to self-manage their CIN in their own environment.

More than 60% of patients diagnosed with cancer experience chemotherapy-induced neuropathy (CIN), a severe side effect of chemotherapeutic agents (including platinum-based drugs, vinca alkaloids, taxanes, or bortezomib) (Seretny et al., 2014; Sisignano, Baron, Scholich, & Geisslinger, 2014). CIN may cause treatment delays, dose reductions, or discontinuation of therapy that can affect survival rates (Pike, Birnbaum, Muehlenbein, Pohl, & Natale, 2012). With improved cancer treatments and longer survival, the late effects of CIN continue to produce a significant burden on patients. Up to 50% of cancer survivors suffer from CIN 6 years after treatment completion, and there is a 1.8-fold increased risk for falls (Winters-Stone et al., 2017). CIN continues to cause significant

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functional disability, which significantly increases health care costs and resource use (Pike et al., 2012) and negatively affects quality of life (QOL) (Seretny et al., 2014; Staff, Grisold, Grisold, & Windebank, 2017).

Current treatment for CIN is limited; no uniformly effective treatment for CIN has been established (Hershman et al., 2014; Shah et al., 2018). Exercise and analgesics are commonly suggested to treat CIN. Although exercise can be helpful, it is burdensome (Irwin et al., 2014) and the effect size of exercise to reduce CIN is less than 0.50, which cannot effectively manage CIN (Kleckner et al., 2018). Opioids relieve neuropathic pain (Gilron et al., 2005; Gilron, Tu, Holden, Jackson, & DuMerton-Shore, 2015); however, long-term use is strongly discouraged because of opioid overuse (Dowell, Haegerich, & Chou, 2016) and addiction (Miller et al., 2015) and because it also brings adverse side effects such as constipation, nausea, somnolence (Benyamin et al., 2008; Candiotti & Gitlin, 2010; Poulsen, Brock, Olesen, Nilsson, & Drewes, 2015), opioid-induced hyperalgesia (Carullo, Fitz-James, & Delphin, 2015; Chen et al., 2014), and cognitive dysfunction (Dublin et al., 2015; Pergolizzi et al., 2008). Duloxetine (Bellingham & Peng, 2010), the only drug for CIN recommended by the American Society of Clinical Oncology (Hershman et al., 2014), was found to be superior to placebos, but it improved CIN by only 0.73 points (0-10 scale) (Smith et al., 2013).

Patients diagnosed with cancer already receive a combination of different drugs and are therefore exposed to various adverse effects. It would be ideal if patients diagnosed with cancer could quickly manage CIN without drugs, adverse side effects, prolonged effort, or frequent visits to a health care provider. A nonpharmacologic, noninvasive strategy called auricular point acupressure (APA) may be a solution to address the current shortcomings of CIN treatment. In APA, a skilled provider tapes small seeds on specific ear points. Patients press on the seeds to stimulate ear points three times daily, 3 minutes per time, for a total of 9 minutes per day. APA provides pain relief within 1-2 minutes after ear stimulation and pain relief is sustained for 1 month after 4 weeks of APA intervention (Yeh et al., 2013, 2014c, 2015a, 2017; Yeh, Chien, Chiang, & Huang, 2012; Yeh, Chien, Chiang, Suen, & Ren, 2015; Yeh, Chien, Lin, Bovbjerg, & van Londen, 2016).

APA, derived from auricular acupuncture, was developed from Chinese medicine. In 1980s, Dr. Paul Nogier mapped a somatotopic representation of the human body onto the ear that showed specific points corresponding to specific organs and areas of the body (Nogier, 1981, 1987, 2014). By stimulating these points, symptomatic parts of the body can be treated. The location of each point is confirmed by electrodermal responses using an electrical point finder (Oleson, 2014; Yeh & Huang, 2013), and, once identified, each point can be stimulated classically with acupuncture needles (Huang, 2005; Oleson, 2014) or, alternatively, with pressure by APA (Yeh et al., 2014c). Stimulation of specific points can lead to stimulation of specific areas of the brain, which in turn connect to particular areas of the body (Alimi, Geissmann, & Gardeur, 2002; Romoli et al., 2014). Preliminary results on healthy adults in brain imaging studies show connections between the ears and body locations (Alimi et al., 2002; Romoli et al., 2014). However, these results are based on healthy adults, and the translation of brain activity changes in patients with CIN needs to be further examined.

Compared with APA, which is sparsely used in the United States, acupuncture has gained interest in the United States and has been suggested as an adjuvant therapy for chronic pain (National Center for Complementary and Integrative Health, 2015; American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine, 2010) or CIN (Franconi, Manni, Schroder, Marchetti, & Robinson, 2013). The use of acupuncture is limited because of the high dropout rate as a result of the need for frequent treatments: two times per week for 3-6 weeks (Molsberger, Schneider, Gotthardt, & Drabik, 2010), limited insurance coverage (Nahin, Barnes, & Stussman, 2016), and fear of needles (Schapira et al., 2013).

Compared with acupuncture, the easy implementation of APA and its immediate and lasting pain relief may empower and motivate patients diagnosed with cancer to adhere to APA treatment and may allow patients to maintain or increase physical activity as a by-product of improved analgesia. However, only a limited number of clinical trials have supported APA in pain management (Asher et al., 2011; Yeh et al., 2014a). To our knowledge, there is no published study using APA to manage CIN yet. Thus the purpose of this study was to examine the feasibility of APA to manage CIN and to report the outcomes of preliminary studies of APA on CIN in patients diagnosed with cancer.

Study Framework

Guided by the National Institutes of Health Symptom Science Model (Cashion & Grady, 2015) and grounded in the biopsychosocial model of pain (Campbell & Edwards, 2009; Gatchel, Peng, Peters, Fuchs, & Turk, 2007; Lumley et al., 2011), the study framework (Fig. 1) posits that the effects of APA on CIN are mediated by endogenous inflammatory biomarkers and sensory function (Cashion & Grady, 2015; Markovitz, Drysdale, & Bettencourt, 2017; Otte, Carpenter, Russell, Bigatti, & Champion, 2010). Evidence suggests that pain, anxiety, depression (Brier, Chambless, Lee, & Mao, 2015; Laroche et al., 2014; Mao et al., 2014; Takei et al., 2012), fatigue, and sleep disturbance (Desai et al., 2013; Mao et al., 2014)—that is, the overall quality of life—are interrelated; therefore we also examine these symptoms in CIN patients. In addition to demographic characteristics, the comorbidity and chronic overlapping pain conditions are also investigated because of their impact on pain. In this study we assessed (1) the feasibility of recruiting CIN patients and (2) the descriptive characteristics of clinical outcomes and moderators including CIN symptoms, physical function, and quality of life.

Material and Methods

A waitlist control study design was conducted to examine the feasibility of a 4-week APA intervention to manage CIN. Waiting for 1 month before beginning the intervention allowed for verification of the chronicity of the CIN symptoms to ensure that those symptoms would not disappear because of the passing of time and to provide data for an untreated comparison group. After consent was obtained, baseline/control data were collected (hereafter, T0) and participants waited 1 month. After the 1-month wait, those participants completed the same data questionnaires as in T0 and then started receiving a 4-week APA intervention. Participants continued to receive their usual care from their primary health care providers such as through routine oncology appointments. Outcomes were assessed at T0, preintervention (T1), weekly during the intervention (selected measures, 1 week after the first APA intervention, T2; 1 week after the second APA intervention, T3; 1 week after the third APA intervention, T4), postintervention (T5), and at the 1-month follow-up (1 month after completion of the 4-week APA intervention, T6).

Participants

Eligible participants included (1) patients diagnosed with cancer who were aged 18 years or older; (2) able to read and write English; (3) diagnosed with CIN after receiving neurotoxic chemotherapy for cancer; (4) had an average intensity of CIN-

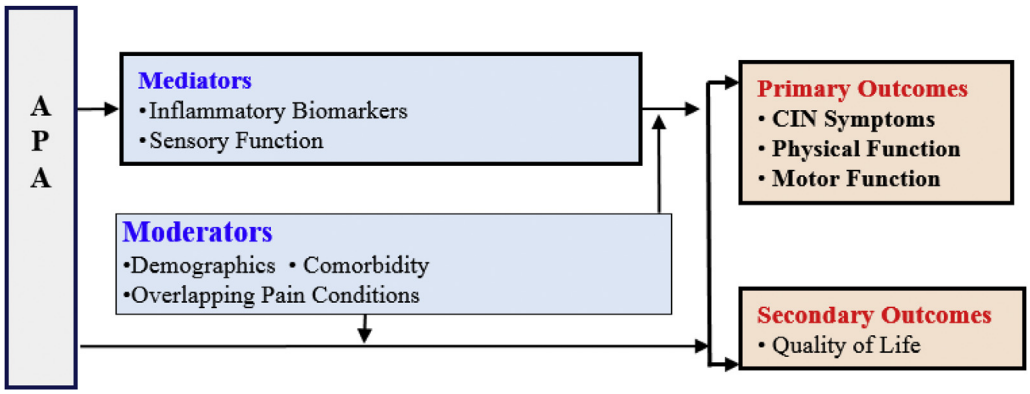

Figure 1. Framework of auricular point acupressure (APA) effects on chemotherapy-induced neuropathy (CIN).

related pain, such as pain, numbness, tingling, or stiffness of the extremities, of ≥4 on a 11-point numeric scale from the previous week; or (5) pain, numbness, tingling, or stiffness >3 months' duration attributed to CIN. Participants were excluded from the study if they reported any of the following: (1) use of an investigational agent for pain control concurrently or within the past 30 days; (2) prior celiac plexus block or other neurolytic pain control treatment; (3) other identified causes of painful paresthesia existing before chemotherapy, such as radiation or malignant plexopathy, lumbar or cervical radiculopathy, or preexisting peripheral neuropathy of another cause; and (4) allergy to latex (the tapes for APA include latex).

APA Intervention Protocol

The APA protocol was designed in accordance with the international revised STRICTA (Standards for Reporting Interventions in Clinical Trials of Acupuncture) guidelines (MacPherson et al., 2010). Auricular diagnosis, an objective method to locate ear points (Yeh & Huang, 2013), was used to identify reactive ear points correlating to symptomatic body areas for treatment. The ear points included (1) corresponding points located on the front and back of the ear, depending on the location of the participant's body pain complaints; (2) four points known for alleviating stress and pain: *shenmen*, sympathetic, cingulate gyrus, and nervous subcortex; and (3) two points related to the brain: brain and spinal cord sensory neurons (Fig. 2).

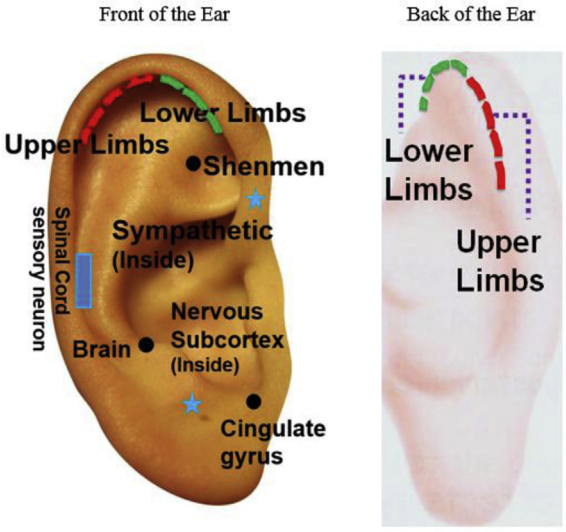

Figure 2. Auricular points for chemotherapy-induced neuropathy. Shenmen: Primary point for treatment. Cingulate gyrus: Helps to regulate autonomic motor function.

To identify the auricular points for treatment, an auricular point diagnosis was given. The first step of auricular diagnosis is to inspect the skin surface for changes on the outer ear to identify potential ear points corresponding to the symptomatic body (Huang & Huang, 2007; Yeh et al., 2014b). When a body disorder is present, the corresponding ear points may display discoloration, deformity, papules, or angiosclerosis. The second step is to use a probe to touch the corresponding ear points to locate points that are tender. An active ear point is identified if an ear point has increased tenderness during examination as determined by asking or observing the participant's subjective reaction at probing. The final step involves using an electrical point finder to confirm active ear points by assessing auricular cutaneous resistance. When body disorders are present, active corresponding ear points have a lower electrical resistance.

Bilateral ear points were identified and used for treatment. *Vaccaria* seeds—natural, nontoxic botanical seeds of no medicinal value, approximately 2 millimeters (mm) in diameter—were affixed to the ear points with waterproof tape. The size of the tape was approximately 6 mm^2. The waterproof tape covering the seeds remained on the ear for up to 5 days. Participants could shower and wash their hair during the treatment. All APA treatment points were affixed by the first author.

The first author demonstrated the pressing technique to the participants, instructing them to apply steady pressure on the taped seeds until either mild discomfort or tingling was felt. Participants were instructed to evenly press the tape and seeds covering each acupressure ear point without rubbing to avoid skin damage and infection, for 3 minutes per time, three times daily, even if they did not experience pain. A 2-second pause occurred between the two pressings. The optimal pressure was considered as achieved when the participant felt localized tingling or mild discomfort. Participants were instructed to remove both tape and seeds at the end of the fifth day. The treatment duration was 4 weeks with weekly cycles (Yeh et al., 2017; Yeh et al., 2015a). Each weekly cycle included one visit, 5 days of wearing the tape and seeds, and 2 days without, minimizing the risk of allergic reactions to the tape and allowing ear points to restore sensitivity for the next treatment.

Measures

A paperless data entry system installed on iPads was used to allow data to be directly entered into the database via REDCap.

CIN Symptoms (Pain, Numbness, Tingling, Stiffness)

The Short Form Brief Pain Inventory (BPI-sf) is a validated, widely used, self-administered questionnaire developed to assess pain location and multiple aspects of pain severity, including worst pain, least pain, average pain, and present pain, as well as the interference of pain with daily activities (Cleeland & Ryan, 1994). An 11-point numeric rating scale was used to measure severity (0, no pain; 10, pain as bad as you can imagine). To differentiate the APA effects on specific body location and different CIN symptoms, BPI-sf was modified for the present study by including body locations, such as fingers, wrists, elbows, toes, soles, feet, and ankles and four common CIN symptoms (i.e., pain, numbness, tingling, and stiffness), with different moments of severity, such as worst, least, average, and present. Scores for each symptom and body location ranged from 0 to 10 points, with higher scores indicating greater symptom intensity.

Additionally, the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group—Neurotoxicity Subscale (FACT/GOG-Ntx) was used to measure neurotoxic symptoms and concerns (Cella, 1997). FACT/GOG-Ntx is a validated tool developed to assess patient-reported platinum/paclitaxel–induced neurotoxic symptoms and concerns. It contains 11 items (scored from 0, not at all, to 4, very much), assessing sensory (7 items), hearing (2 items), motor (3 items), and dysfunction (2 items) symptoms. Only 9 items were used for the final analysis (2 items related to hearing were excluded because they were not relevant to the outcomes). The Cronbach's α coefficient for the 9-item FACT/GOG-Ntx was .87.

Physical Function

Physical function was assessed by four questionnaires, including (1) BPI–CIN Interference Subscale; (2) FACT/GOG-Ntx; (3) Quick Disabilities of the Arm, Shoulder and Hand score (QuickDASH); and (4) Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (Bellamy, 2002).

The BPI–CIN Interference subscale (wording was revised from the BPI-sf) was used to measure physical function caused by CIN. The seven items were rated from 0, does not interfere, to 10, completely interferes, in general activity, mood, walking ability, normal work, relations with other persons, sleep, and enjoyment of life. Scores were summed to determine the level of interference, ranging from 0 to 70. The Cronbach's α coefficient for the BPI-CN was .96.

QuickDASH was used to measure the upper extremity functional index (Beaton, Wright, & Katz, 2005). QuickDASH—an 11-item measure scored from 1, no difficulty, to 5, unable—was used to assess the perceived level of disability/symptom in participants' upper extremities, including shoulders, arms, or hands. QuickDASH has established reliability and validity (i.e., hypothesis testing) and moderate positive evidence for structural validity testing (Kennedy et al., 2013).

WOMAC was used to measure lower extremity function of pain, stiffness, and physical function (Bellamy, 2002). It is a 24-item tool, scored from 1, none, to 5, extreme, to assess pain (5 items), stiffness (2 items), and physical dysfunction (17 items). WOMAC has been widely used to assess lower extremity function with reported psychometrics (Pinsker, Inrig, Daniels, Warmington, & Beaton, 2015). The score of the Physical Dysfunction subscale was used to determine the level of physical dysfunction function, ranging from 0 to 85. The Cronbach's α coefficients ranged from .86 (Stiffness subscale) to .96 (Physical Dysfunction subscale).

Quality of Life

PROMIS-29 Version 2.0, a 29-item profile instrument, was used to measure seven subscales of health QOL on each domain: anxiety, depression, fatigue, sleep disturbance, pain interference, physical function, and satisfaction with participation in social roles. Each subscale includes 4 items of a 5-point Likert Scale plus a pain intensity scale using a 0-10 numeric rating item. PROMIS-29 has established reliability and validity (Hays et al., 2016; Hays, Spritzer, Schalet, & Cella, 2018) and is widely used in the United States. Scores were summed to determine each domain's health QOL, ranging from 0 to 20. The higher the score on a subscale, the better the quality of each domain. PROMIS-29 has been reported to have satisfactory reliability (Cronbach's α coefficients ranged from .86 in sleep disturbance to .96 fatigue).

Chronic Overlapping Pain Conditions

The listing of chronic overlapping pain conditions (Maixner, Fillingim, Williams, Smith, & Slade, 2016) was used to examine overlapping pain disorders, including the following: vulvodynia, temporomandibular disorders, myalgic encephalomyelitis/chronic fatigue syndrome, irritable bowel syndrome, interstitial cystitis/painful bladder syndrome, fibromyalgia, endometriosis, chronic tension-type and migraine headache, and chronic low back pain. This tool was rated as 1, yes, or 0, no, answers. The sum of the scores was used to determine the number of the overlapping pain disorders that participants had, ranging from 0 to 10.

The Charlson Comorbidity Index was used to examine comorbidities on 19 conditions (Charlson, Szatrowski, Peterson, & Gold, 1994). Conditions such as myocardial infarct, dementia, diabetes, and leukemia are included on this instrument. This tool was rated as 1, yes, or 0, no, answers. The sum of the scores was used to determine the number of comorbidities the participants had, ranging from 0 to 19.

Patient Global Impression of Change (PGIC) (Hurst & Bolton, 2004) was used to measure the participant's impression of change after completion of the trial (APA). The PGIC scores reflect a patient's belief about the efficacy of treatment. PGIC is a one-item instrument using a 7-point scale depicting a patient's rating of overall improvement, ranging from 1, very much improved, to 7, very much worse. PGIC has established psychometrics to identify clinically significant changes in patients' subjective outcome measures (Hurst & Bolton, 2004).

A survey of demographic characteristics included questions about ethnicity, socioeconomic status, comorbidities, body mass index (BMI), prior receipts of chemotherapy, and medication use for pain or sleep disturbances (Yeh et al., 2017).

Procedure

After Institutional Review Board approval, informed consents were obtained. Baseline data were collected by phone through a structured interview. After baseline assessments were collected,

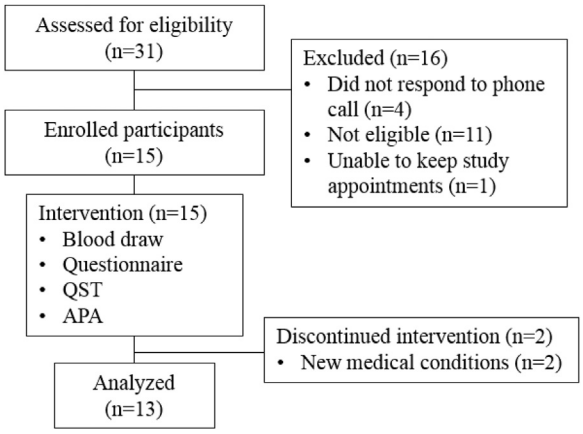

Figure 3. Participant recruitment flowchart. APA = auricular point acupressure; QST = quantitative sensory testing.

Table 1
Demographic and Clinical Characteristics (N = 15)

Characteristics	n (%)
Age	
Mean ± SD	60.20 ± 7.95
Body mass index (kg/m^2)	
Mean (range)	26.93 (21.95-38.64)
Race/ethnicity	
White	12 (80%)
Black/African American	3 (20%)
Marital status	
Currently married	9 (60%)
Divorced	3 (20%)
Widowed	2 (13%)
Never married	1 (7%)
Employment	
Working (full time, part time)	4 (26%)
On leave	1 (7%)
Not employed (unemployed, retired, homemaker)	10 (67%)
Education level	
High school graduate or equivalent	1 (7%)
Technical or vocational school	1 (7%)
Some college	2 (13%)
College graduate	2 (13%)
Postgraduate degree	9 (60%)
Type of cancer	
Breast	9 (60%)
Colon	2 (13%)
Leukemia	1 (7%)
Melanoma	1 (7%)
Non-Hodgkin's lymphoma	1 (7%)
Endometrial	1 (7%)

SD = standard deviation.

participants waited 1 month before they received the 4-week APA intervention. Participants received one treatment conducted by a trained therapist each week for 4 weeks. The first APA took about 15-20 minutes; the subsequent APA treatments took less than 10 minutes for the seed placement. Each weekly cycle included one office visit, followed by 5 days of wearing the tape and seeds on both ears and removing the tape and seeds for the last 2 days of the week to minimize the risk of allergic reactions. The removal of the tape and seeds also allowed the points on the ear to recover and restore sensitivity before the next treatment. After seed placement by the therapist, participants were instructed to apply pressure to the seeds on all ear points with the thumb and index finger three times per day (morning, noon, and evening) for 3 minutes each time to manage CIN.

Data Analysis

Descriptive statistics were used to present demographic characteristics and study measures. Data from two dropout participants were excluded from final analysis. To assess the adherence to APA practice, the adherence rate was defined by the number of participants who were able to follow at least two-thirds of the suggested pressing time (i.e., at least two times per day, 2 minutes per time) to determine the feasibility of practicing APA at home for the participants. The percentage change score was also calculated by dividing the raw change score by the T1 and multiplying by 100 to standardize the improved outcomes. A higher percentage means greater change. A cutoff point of 30% improvement for outcomes was used to

Table 2
Worst Intensity of Chemotherapy-Induced Neuropathy Symptoms at Control, Pre-post and 1-month Follow-Up After Auricular Point Acupressure

Symptoms	Study Visit (Mean ± SD)				Change (T5-T1)		Change (T6-T1)	
	Control (T0)	Pre (T1)	Post (T5)	1-M FU (T6)*	%	Effect Size	%	Effect Size
Pain								
Fingers	4.54 ± 3.46	4.54 ± 3.46	2.31 ± 2.72	1.90 ± 2.23†	−49	−0.64	−58	−0.76
Wrists	3.23 ± 3.09	3.23 ± 3.09	1.77 ± 3.17	1.60 ± 3.50	−45	−0.47	−50	−0.53
Elbows	2.77 ± 4.05	2.77 ± 4.05	1.00 ± 2.00	0.50 ± 1.58	−64	−0.44	−82	−0.56
Toes	6.46 ± 3.57	6.46 ± 3.57	3.46 ± 3.64	3.40 ± 3.53†	−46	−0.84	−47	−0.86
Soles	4.92 ± 3.66	4.92 ± 3.66	1.46 ± 2.18	2.00 ± 2.40†	−70	−0.95	−59	−0.80
Feet	5.85 ± 3.78	5.85 ± 3.78	2.54 ± 2.82	3.10 ± 3.00	−57	−0.88	−47	−0.73
Ankles	3.23 ± 3.96	3.46 ± 4.16	1.23 ± 2.62	0.70 ± 1.89	−64	−0.54	−80	−0.66
Numbness								
Fingers	4.85 ± 3.34	5.38 ± 3.15	2.31 ± 2.29	3.10 ± 2.51†	−57	−0.97	−42	−0.72
Wrists	2.00 ± 3.44	1.92 ± 3.48	1.15 ± 2.82	1.70 ± 3.65	−40	−0.22	−11	−0.06
Elbows	1.08 ± 2.50	1.08 ± 2.50	0.38 ± 0.96	0.60 ± 1.90	−65	−0.28	−44	−0.19
Toes	6.08 ± 3.43	6.08 ± 3.43	3.08 ± 2.93	3.50 ± 3.27*	−49	−0.87	−42	−0.75
Soles	4.23 ± 3.94	4.23 ± 3.94	2.38 ± 2.73	2.90 ± 3.35	−44	−0.47	−31	−0.34
Feet	5.46 ± 3.73	5.46 ± 3.73	3.00 ± 2.86	3.20 ± 3.26	−45	−0.66	−41	−0.61
Ankles	2.38 ± 3.38	2.77 ± 3.75	0.77 ± 1.36	0.90 ± 2.23	−72	−0.53	−68	−0.50
Tingling								
Fingers	3.77 ± 3.22	4.00 ± 3.27	2.54 ± 2.15	2.70 ± 2.16	−37	−0.45	−33	−0.40
Wrists	1.85 ± 3.16	1.77 ± 3.19	1.38 ± 2.79	1.20 ± 3.16	−22	−0.12	−32	−0.18
Elbows	1.08 ± 2.06	1.08 ± 2.06	0.54 ± 1.20	0.20 ± 0.63	−50	−0.26	−81	−0.43
Toes	5.69 ± 3.38	5.69 ± 3.38	3.54 ± 3.10	4.00 ± 3.30	−38	−0.64	−30	−0.50
Soles	4.08 ± 3.75	4.08 ± 3.75	2.00 ± 2.35	2.10 ± 2.51	−51	−0.55	−49	−0.53
Feet	5.08 ± 3.97	5.08 ± 3.97	3.00 ± 3.14	3.10 ± 3.35	−41	−0.52	−39	−0.50
Ankles	2.15 ± 3.29	2.54 ± 3.89	0.38 ± 0.96	0.10 ± 0.32	−85	−0.56	−96	−0.63
Stiffness								
Fingers	5.31 ± 3.30	5.31 ± 3.30	2.85 ± 2.58	2.20 ± 2.66	−46	−0.75	−59	−0.94
Wrists	3.62 ± 3.91	3.62 ± 3.91	1.92 ± 3.12	1.60 ± 3.50	−47	−0.43	−56	−0.52
Elbows	3.54 ± 4.22	3.54 ± 4.22	0.75 ± 1.14	0.67 ± 2.00	−79	−0.66	−81	−0.68
Toes	6.38 ± 3.55	5.85 ± 3.81	3.15 ± 3.34	2.90 ± 3.64	−46	−0.71	−50	−0.77
Soles	4.77 ± 4.27	4.23 ± 4.27	1.00 ± 1.47	1.10 ± 2.03	−76	−0.76	−74	−0.73
Feet	5.62 ± 4.09	5.08 ± 4.21	2.23 ± 2.68	1.80 ± 2.90	−56	−0.68	−65	−0.78

SD = standard deviation; 1-M FU = 1-month follow-up; (−%) decreasing from T1; (%) mean increasing from T1.
* Repeated measures one-way analysis of variance.
† $p \leq .05$.

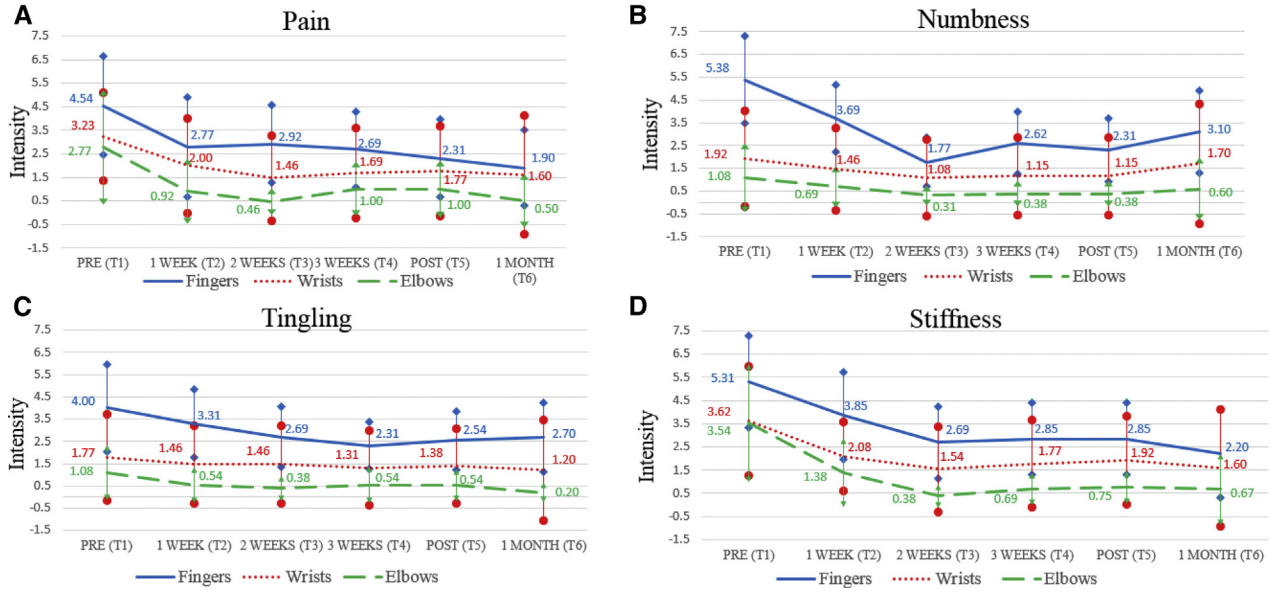

Figure 4. Mean worst pain, numbness, tingling, and stiffness intensity scores change over time in upper extremities. (A) Change in pain, (B) change in numbness, (C) change in tingling, and (D) change in stiffness from preintervention (T1), weekly during intervention (T2, T3, and T4), postintervention (T5), and at 1-month follow-up (T6). The diagram shows mean ± 1 standard error.

determine whether the mean score changes reached clinical significance (Dworkin et al., 2009).

Results

Feasibility of Recruitment and Adherence of APA Practice

For recruitment, we received 31 referrals from oncologists within 4 months. Sixteen participants were excluded because they did not respond to the study office's phone calls (n = 4), were not eligible for the study (n = 11), or were unable to keep a study appointment (n = 1). Of the 15 enrolled in the study, two dropped out because of new medical conditions. Thirteen participants completed the study (87% retention rate) (Fig. 3). The results indicate that the adherence rate—three times per day, 3 minutes per time—during the 4-week APA was high in week 1 (91%) and then gradually decreased (86% at week 4). Participants exhibited an 88% or greater adherence rate throughout the 4-week APA. All participants indicated that they would suggest APA to their family and friends. It took about 20-25 minutes to complete the self-reported questionnaires.

Participants' Characteristics

Table 1 presents the demographic characteristics of 15 participants. The average age of the participants was 60.27 years

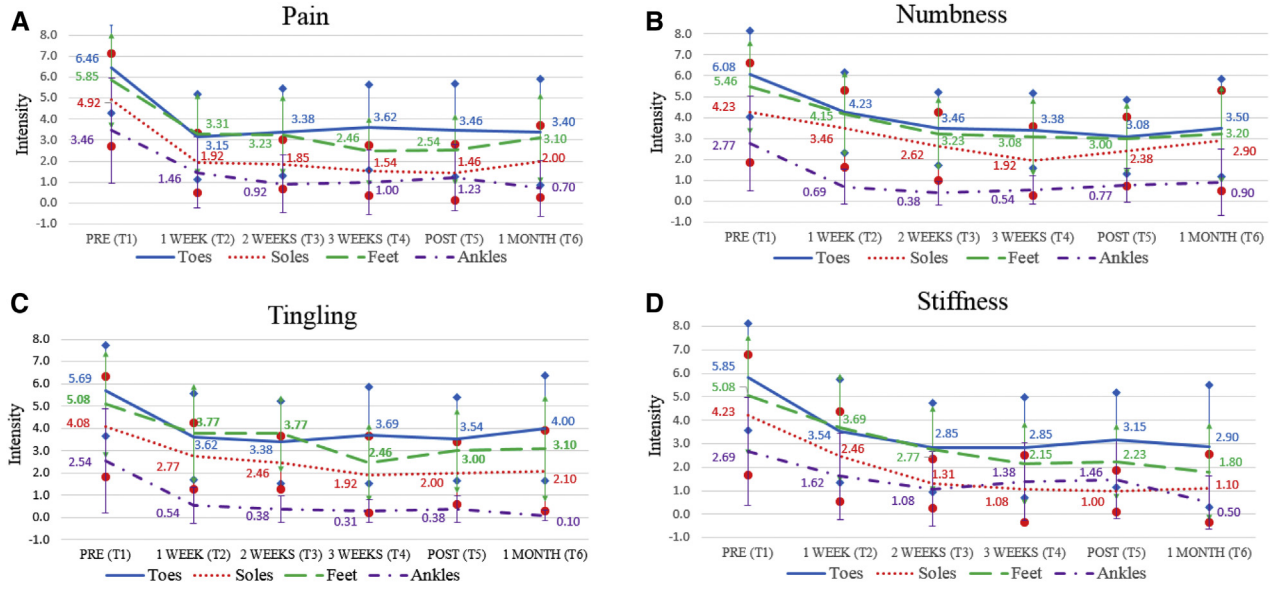

Figure 5. Mean worst pain, numbness, tingling, and stiffness intensity scores change over time in lower extremities. (A) Change in pain, (B) change in numbness, (C) change in tingling, and (D) change in stiffness from preintervention (T1), weekly during intervention (T2, T3, and T4), postintervention (T5), and at 1-month follow-up (T6). The diagram shows mean ± 1 standard error.

Table 3
Physical Function and Quality of Life at Control, Pre-post, and 1-Month Follow-Up After Auricular Point Acupressure

Other Outcomes	Study Visit (Mean ± SD)				Change (T5-T1)		Change (T6-T1)	
	Control (T0)	Pre (T1)	Post (T5)	1-M FU (T6)*	%	Effect Size	%	Effect Size
Physical function								
BPI-CIN-Interference	35.85 ± 24.13	34.92 ± 23.68	15.00 ± 16.45	11.90 ± 11.66†	−57	−0.84	−66	−0.97
QuickDASH	39.51 ± 24.52	36.01 ± 22.34	26.05 ± 17.15	22.05 ± 14.05	−28	−0.45	−39	−0.62
WOMAC Stiffness	3.85 ± 2.38	4.00 ± 2.36	4.00 ± 2.38	3.36 ± 2.54	−14	−0.23	−25	−0.42
Function	24.69 ± 16.83	26.26 ± 16.83	21.46 ± 16.84	14.65 ± 12.63	−29	−0.37	−36	−0.46
FACT/GOG-Ntx	21.62 ± 7.50	20.54 ± 7.60	17.69 ± 5.63	16.70 ± 5.81	−14	−0.38	−19	−0.51
Quality of life PROMIS-29								
Physical	33.29 ± 8.48	33.48 ± 7.72	31.85 ± 6.12	31.10 ± 6.22	−5	−0.21	−7	−0.31
Anxiety	55.68 ± 11.49	53.90 ± 10.65	50.54 ± 9.07	48.80 ± 9.02	−6	−0.32	−9	−0.48
Depression	53.41 ± 9.62	54.42 ± 8.82	52.18 ± 8.07	51.54 ± 6.35	−4	−0.25	−5	−0.33
Fatigue	55.93 ± 13.55	54.22 ± 12.77	52.18 ± 9.63	52.01 ± 9.24	−4	−0.16	−4	−0.17
Sleep	51.32 ± 9.08	50.88 ± 8.97	53.75 ± 9.05	52.25 ± 9.06	6	0.32	3	0.15
Satisfaction	42.35 ± 8.78	44.52 ± 7.53	45.56 ± 7.91	49.11 ± 8.86	2	0.14	10	0.61

SD = standard deviation; 1-M FU = 1-month follow-up; (−%) decreasing; (%) mean increasing; BPI-CIN = Brief Pain Inventory Chemotherapy-Induced Neuropathy; QuickDASH = The Quick Disabilities of the Arm, Shoulder and Hand score; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; FACT/GOG-Ntx = Functional Assessment of Cancer Therapy/Gynecologic Oncology Group—Neurotoxicity Subscale.
* Repeated measures one-way analysis of variance.
† $p \leq .05$.

(standard deviation [SD] = 7.95, range from 40 to 70), and the average BMI was 26.93 (SD = 4.77). Among the 15 participants, the majority were White (n = 12, 80%), women (n = 11, 73%), and had education beyond high school (n = 11, 73%). Cancer diagnoses included breast cancer (n = 9), colon cancer (n = 2), leukemia (n = 1), melanoma (n = 1), non-Hodgkin's lymphoma (n = 1), and endometrial cancer (n = 1). In addition to cancer diagnosis, the prevalence of comorbidity was 70% of the participants who had other types of chronic disease (mean [M] = 1.69, SD = 1.44). Approximately 60% of the participants had other chronic overlapping conditions (M = 2.13, SD = 1.13).

APA Treatment Outcomes

CIN Symptoms (Pain, Numbness, Tingling, and Stiffness)

Table 2 illustrates the mean severity and SD of CIN symptoms at control (T0), pretreatment (T1), posttreatment (T5), and 1-month follow-up (T6). The mean score of change on all the outcomes (worst pain, stiffness, physical function, disability, symptom severity, and symptom interferences) decreased over the 4-week APA intervention (Figs. 4 and 5). As shown in Table 2, there were no changes in CIN outcomes measured between control (T0, 1 month wait before first treatment) and pretreatment (T1, before the APA treatment), indicating that CIN symptoms and outcomes remained the same and that symptoms did not resolve as a result of time change.

For the upper extremities (finger, wrist, and elbow), the fingers had the most severe symptoms, including pain, numbness, tingling, and stiffness (M ≥ 4), compared with the wrist and elbow. For severity in the fingers, the mean percentage score changes from pretreatment (T1) to posttreatment (T5) ranged from 37% (tingling) to 57% (numbness) (Table 2). Figure 4 shows the trends of the change in pain (Fig. 4A), numbness (Fig. 4B), tingling (Fig. 4C), and stiffness (Fig. 4D) from the pretreatment (T1), weekly during intervention (T2, T3, and T4), posttreatment (T5), and 1-month follow-up (T6).

For lower extremities, toes had the most severe symptoms (pain, M = 6.46; numbness, M = 5.38; tingling, M = 5.69; stiffness, M = 5.85), followed by feet, soles, and ankles (Table 2). After the 4-week APA treatment, the mean percentage score changes ranged from 38% (tingling) to 49% (numbness); the effects maintained a similar degree at the 1-month follow-up (T6) (Table 2). Figure 5 shows the change in trend patterns of lower extremity symptoms, specifically pain (Fig. 5A), numbness (Fig. 5B), tingling (Fig. 5C), and stiffness (Fig. 5D). All CIN outcomes in the lower extremities decreased over the 4-week APA intervention and maintained a similar degree of improvement at the 1-month follow up (Fig. 5).

Physical Function

Table 3 presents the findings of APA effects on physical function. For CIN interference, compared with pretreatment (T1), the mean percentage score changes for the pain's interference with functions were 57% at posttreatment (T5) and 66% at the 1-month follow-up (T6), indicating that participants had better function after 4 weeks of receiving APA treatment (Table 3). There was a significant effect of the APA on CIN interferences. Function in the upper and lower extremities improved after the 4-week intervention (≥28%) and continued to improve at the 1-month follow-up (≥36%) (39% in QuickDASH and 36% in WOMAC). After the 4-week APA, neurotoxicity decreased 14% at post-APA assessment and decreased 19% at the 1-month follow-up.

QOL. As shown in Table 3, QOL measured by PROMIS 29 (including subscale of physical, anxiety, depression, and fatigue) was only slightly changed at posttreatment (T5) and at the 1-month follow-up (T6), compared with pretreatment (T1).

Patient's Impression of Change

The mean score for the participants' perception of treatment efficacy was 4.21 (SD = 1.37). A perception of "improved" ("much improved" or "very much improved") was reported in 60% of participants after the 4-week APA treatment.

Discussion

This is the first study to examine the feasibility and initial treatment effectiveness of a 4-week APA protocol to manage CIN in patients diagnosed with cancer. Our study findings indicate that APA is feasible for CIN patients in terms of recruitment, retention, and adherence and promising effectiveness for CIN outcomes. After the 4-week APA treatment, patients had improved CIN self-reported outcomes after APA, and the effectiveness was sustained at the 1-month follow-up. However, before interpreting the findings, several limitations of the study must be acknowledged: (1) study's sample size was small because of the nature of the pilot study; (2) the study lacked a placebo-control group and randomization and thus we were not able to differentiate the true effects of

APA from the possible psychological effects; (3) only 1 month of follow-up data were collected; therefore, we were not able to assess when the lasting effects of APA on CIN disappeared; and (4) the effect sizes of the study outcomes were reported to inform the sample size estimation for the future trial, but the interpretation should be taken with caution because of the sample size.

In recruiting participants, we received 37 referrals from a coauthor (T.J.S.) with minimal advertisements within 4 months. Fifteen participants enrolled in the study; only two dropped out for medical reasons; the retention rate was 87%. The participants seemed to be enthusiastic about the APA treatment, and exhibited an 88% or greater adherence rate throughout the 4-week APA. Except for one participant, who had an allergy to the latex on the tape, APA was a relatively well-tolerated treatment and minimal adverse effects were reported. No participant dropped out from the study because of adverse effects of APA.

To better assess CIN symptoms and to eliminate ambiguous questions, we revised the BPI by adding items to measure CIN symptoms such as pain, numbness, and tinging and affected areas such as fingers, wrist, elbow, toes, soles, feet, and ankles) (BPI-CIN). Overall, the participants thought that the revised BPI-CIN better captured the complexity of the CIN symptoms and the severity of these symptoms in different body locations.

Consistent with other studies (Miaskowski et al., 2017), patients diagnosed with cancer have a higher severity of symptoms in the lower extremities, such as toes and feet. The most severe lower extremity symptoms found in this study were numbness, followed by tingling. Our participants had higher BMIs (M = 26.93), which is consistent with a large study (n = 623) of CIN patients with higher BMIs (M = 26.56), compared with non-CIN patients (M = 24.85) (Miaskowski et al., 2017). High BMI is associated with increased risk of chronic illness; we found that 70% of our study participants had other coexisting chronic illnesses. These findings suggest that CIN management should also consider weight management and treating medical comorbidities.

Our study indicates the promising results that APA can reduce upper and lower extremity impairment and improve physical function. APA is a reproducible, standardized, and easy-to-perform intervention. Moreover, APA is a noninvasive, low-cost technique; relatively little training is required to learn how to deliver APA. We developed a systematic and objective APA treatment protocol to manage pain that can be replicated easily by researchers and clinicians. Our protocol featured standardized auricular nomenclature (World Health Organization, 1990), a systematic and objective method of identifying active points to treat (i.e., auricular diagnosis) (Yeh & Huang, 2013; Yeh et al., 2014b), and the use of seeds rather than needles, allowing treatment by nonacupuncturists. These systematic methods promote the wider utility of the APA patient-management model by overcoming difficulties in replicating individualized acupuncture/acupressure studies.

CIN persists as an important challenge because of the lack of an effective treatment to mitigate CIN's adverse effects. Our promising preliminary findings suggest that APA should be considered to help manage CIN. Randomized controlled trials with a sufficient sample size are warranted to determine the efficacy of APA in relieving CIN. Future studies should also control for possible placebo effects, including use of a sham control and nonspecific psychological factors such as treatment beliefs and expectations.

References

Alimi, D., Geissmann, A., & Gardeur, D. (2002). Auricular acupuncture stimulation measured on functional magnetic resonance imaging. *Medical Acupuncture, 13*(2), 18–21.

American Society of Anesthesiologists Task Force on chronic pain management and the American society of regional Anesthesia and pain medicine. (2010). practice guidelines for chronic pain management: an updated report by the American society of Anesthesiologists Task Force on chronic pain management and the American society of regional Anesthesia and pain medicine. *Anesthesiology, 112*, 810–833.

Asher, G. N., Jonas, D. E., Coeytaux, R. R., Reilly, A. C., Loh, Y. L., Motsinger-Reif, A. A., & Winham, S. J. (2011). Auriculotherapy for pain management: a systematic review and meta-analysis of randomized controlled trials. *Journal of Alternative and Complementary Medicine, 16*, 1097–1108.

Beaton, D. E., Wright, J. G., & Katz, J. N. (2005). Development of the QuickDASH: comparison of three item-reduction approaches. *J Bone Joint Surg Am, 87*, 1038–1046. https://doi.org/10.2106/jbjs.d.02060.

Bellamy, N. (2002). *WOMAC Osteoarthritis Index User Guide (Version V ed.)*. Brisbane, Australia: CONROD, The University of Queensland.

Bellingham, G. A., & Peng, P. W. (2010). Duloxetine: a review of its pharmacology and use in chronic pain management. *Regional Anesthesia and Pain Medicine, 35*, 294–303.

Benyamin, R., Trescot, A. M., Datta, S., Buenaventura, R., Adlaka, R., Sehgal, N., Glaser, S. E., & Vallejo, R. (2008). Opioid complications and side effects. *Pain Physician, 11*(2 Suppl), S105–S120.

Brier, M. J., Chambless, D. L., Lee, L., & Mao, J. J. (2015). Development and validation of the Penn Arthralgia Aging Scale among breast cancer survivors. *Cancer, 121*, 2808–2813.

Campbell, C. M., & Edwards, R. R. (2009). Mind-body interactions in pain: The neurophysiology of anxious and catastrophic pain-related thoughts. *Translational Research, 153*, 97–101.

Candiotti, K. A., & Gitlin, M. C. (2010). Review of the effect of opioid-related side effects on the undertreatment of moderate to severe chronic non-cancer pain: tapentadol, a step toward a solution? *Current Medical Research and Opinion, 26*, 1677–1684.

Carullo, V., Fitz-James, I., & Delphin, E. (2015). Opioid-induced hyperalgesia: a diagnostic dilemma. *Journal of Pain and Palliative Care Pharmacotherapy, 29*, 378–384.

Cashion, A. K., & Grady, P. A. (2015). The national Institutes of health/national Institutes of nursing research intramural research program and the development of the national Institutes of health symptom science model. *Nursing Outlook, 63*, 484–487.

Cella, D. (1997). *F.A.C.I.T. Manual. Manual of the functional assessment of chronic illness therapy (FACIT) scales (version 4)*. Evanston, IL: Northwestern Healthcare and Northwestern University Center on Outcomes, Research and Education (CORE).

Charlson, M., Szatrowski, T. P., Peterson, J., & Gold, J. (1994). Validation of a combined comorbidity index. *Journal of Clinical Epidemiology, 47*, 1245–1251.

Chen, L., Sein, M., Vo, T., Amhmed, S., Zhang, Y., Hilaire, K. S., Houghton, M., & Mao, J. (2014). Clinical interpretation of opioid tolerance versus opioid-induced hyperalgesia. *Journal of Opioid Management, 10*, 383–393.

Cleeland, C. S., & Ryan, K. M. (1994). Pain assessment: global use of the brief pain inventory. *Annals of the Academy of Medicine, Singapore, 23*(2), 129–138.

Desai, K., Mao, J. J., Su, I., Demichele, A., Li, Q., Xie, S. X., & Gehrman, P. R. (2013). Prevalence and risk factors for insomnia among breast patients diagnosed with cancer on aromatase inhibitors. *Support Care Cancer, 21*, 43–51.

Dowell, D., Haegerich, T. M., & Chou, R. (2016). CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA, 315*, 1624–1645.

Dublin, S., Walker, R. L., Gray, S. L., Hubbard, R. A., Anderson, M. L., Yu, O., Crane, K., & Larson, E. B. (2015). Prescription opioids and risk of dementia or cognitive decline: A prospective cohort study. *Journal of the American Geriatrics Society, 63*, 1519–1526.

Dworkin, R. H., Turk, D. C., McDermott, M. P., Peirce-Sandner, S., Burke, L. B., Cowan, P., Farrar, T. F., Hertz, S., Raja, N., Rappaport, B. A., Rauschkolb, C., & Sampaio, C. (2009). Interpreting the clinical importance of group differences in chronic pain clinical trials: IMMPACT recommendations. *Pain, 146*, 238–244.

Franconi, G., Manni, L., Schroder, S., Marchetti, P., & Robinson, N. (2013). A systematic review of experimental and clinical acupuncture in chemotherapy-induced peripheral neuropathy. *Evidence-Based Complementary and Alternative Medicine, 2013*, 516916.

Gatchel, R. J., Peng, Y. B., Peters, M. L., Fuchs, P. N., & Turk, D. C. (2007). The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychological Bulletin, 133*, 581–624.

Gilron, I., Bailey, J. M., Tu, D., Holden, R. R., Weaver, D. F., & Houlden, R. L. (2005). Morphine, gabapentin, or their combination for neuropathic pain. *The New England Journal of Medicine, 352*, 1324–1334.

Gilron, I., Tu, D., Holden, R. R., Jackson, A. C., & DuMerton-Shore, D. (2015). Combination of morphine with nortriptyline for neuropathic pain. *Pain, 156*, 1440–1448.

Hays, R. D., Revicki, D. A., Feeny, D., Fayers, P., Spritzer, K. L., & Cella, D. (2016). Using linear equating to map PROMIS((R)) global health items and the PROMIS-29 V2.0 profile measure to the health utilities index mark 3. *Pharmacoeconomics, 34*, 1015–1022.

Hays, R. D., Spritzer, K. L., Schalet, B. D., & Cella, D. (2018). PROMIS((R))-29 v2.0 profile physical and mental health summary scores. *Qual Life Res, 27*, 1885–1891.

Hershman, D. L., Lacchetti, C., Dworkin, R. H., Lavoie Smith, E. M., Bleeker, J., Cavaletti, G., Chauhan, C., Gavin, P., Lavino, A., Lustberg, M. B., Paice, J., Schneider, B., Smith, M. L., Smith, T., Terstriep, S., Wagner-Johnston, N., Bak, K., & Loprinzi, C. L. (2014). Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American society of clinical oncology clinical practice guideline. *Journal of Clinical Oncology, 32*, 1941–1967.

Huang, L. C. (2005). *Auricular medicine: a complete manual of auricular diagnosis and treatment*. Orlando, FL: Auricular International Research & Training.
Huang, L. C., & Huang, W. S. (2007). *Handbook of auricular treatment prescriptions & formulae*. Orlando, FL: Auricular International Research & Training.
Hurst, H., & Bolton, J. (2004). Assessing the clinical significance of change scores recorded on subjective outcome measures. *Journal of Manipulative and Physiological Therapeutics, 27*, 26–35.
Irwin, M. L., Cartmel, B., Gross, C. P., Ercolano, E., Li, F., Yao, X., Fiellin, M., Capozza, S., Rothbard, M., Zhou, Y., Harrigan, M., Sanft, T., Schmitz, K., Neogi, T., Hershman, D., & Ligibel, J. (2014). Randomized exercise trial of aromatase inhibitor-induced arthralgia in breast cancer survivors. *Journal of Clinical Oncology, 33*, 1104–1111.
Kennedy, C. A., Beaton, D. E., Smith, P., Van Eerd, D., Tang, K., & Inrig, T. (2013). Couban, R. Measurement properties of the QuickDASH (disabilities of the arm, shoulder and hand) outcome measure and cross-cultural adaptations of the QuickDASH: a systematic review. *Qual Life Res, 22*, 2509–2547. https://doi.org/10.1007/s11136-013-0362-4.
Kleckner, I. R., Kamen, C., Gewandter, J. S., Mohile, N. A., Heckler, C. E., Culakova, E., Fung, F., Janelsins, M. C., Asare, M., Lin, P. J., Reddy, P. S., Giguere, J., Berenberg, J., Kesler, S. R., & Mustian, K. M. (2018). Effects of exercise during chemotherapy on chemotherapy-induced peripheral neuropathy: a multicenter, randomized controlled trial. *Support Care Cancer, 26*, 1019–1028.
Laroche, F., Coste, J., Medkour, T., Cottu, P. H., Pierga, J. Y., Lotz, J. P., Beerblock, K., Tournigand, C., Decleves, X., de Cremoux, P., Bouhassira, D., & Perrot, S. (2014). Classification of and risk factors for estrogen deprivation pain syndromes related to aromatase inhibitor treatments in women with breast cancer: a prospective multicenter cohort study. *Journal of Pain, 15*, 293–303.
Lumley, M. A., Cohen, J. L., Borszcz, G. S., Cano, A., Radcliffe, A. M., Porter, L. S., Schubiner, H., & Keefe, F. J. (2011). Pain and emotion: a biopsychosocial review of recent research. *Journal of Clinical Psychology, 67*, 942–968.
MacPherson, H., Altman, D. G., Hammerschlag, R., Youping, L., Taixiang, W., White, A., & Moher, D. (2010). Revised STandards for reporting interventions in clinical trials of acupuncture (STRICTA): extending the CONSORT statement. *PLoS Medicine, 7*, e1000261.
Maixner, W., Fillingim, R. B., Williams, D. A., Smith, S. B., & Slade, G. D. (2016). Overlapping chronic pain conditions: implications for diagnosis and classification. *Journal of Pain, 17*(9 Suppl), T93–T107.
Mao, J. J., Farrar, J. T., Bruner, D., Zee, J., Bowman, M., Seluzicki, C., DeMichele, S. X., & Xie, S. X. (2014). Electroacupuncture for fatigue, sleep, and psychological distress in breast patients diagnosed with cancer with aromatase inhibitor-related arthralgia: a randomized trial. *Cancer, 120*, 3744–3751.
Markovitz, L. C., Drysdale, N. J., & Bettencourt, B. A. (2017). The relationship between risk factors and medication adherence among breast cancer survivors: what explanatory role might depression play? *Psychooncology, 26*, 2294–2299.
Miaskowski, C., Mastick, J., Paul, S. M., Topp, K., Smoot, B., Abrams, G., Chen, L. M., Kober, K. M., Conley, Y. P., Chesney, M., Bolla, K., Mausisa, G., Mazor, M., Wong, M., & Levine, J. D. (2017). Chemotherapy-induced neuropathy in cancer survivors. *Journal of Pain and Symptom Management, 54*, 204–218.e202.
Miller, M., Barber, C. W., Leatherman, S., Fonda, J., Hermos, J. A., Cho, K., & Gagnon, D. R. (2015). Prescription opioid duration of action and the risk of unintentional overdose among patients receiving opioid therapy. *JAMA Internal Medicine, 175*(4), 608–615.
Molsberger, A. F., Schneider, T., Gotthardt, H., & Drabik, A. (2010). German randomized acupuncture trial for chronic shoulder pain (GRASP) - a pragmatic, controlled, patient-blinded, multi-centre trial in an outpatient care environment. *Pain, 151*, 146–154.
Nahin, R. L., Barnes, P. M., & Stussman, B. J. (2016). Insurance coverage for complementary health approaches among adult users: United States, 2002 and 2012. *NCHS Data Brief*, (235), 1–8.
National Center for Complementary and Integrative Health. (2015). *Chronic pain*. Retrieved from https://nccih.nih.gov/health/pain/chronic.htm. (Accessed 25 April 2018).
Nogier, P. (1981). *Handbook to auriculotherapy Moulins-les-Metz*. France: Maisonneuve.
Nogier, P. (1987). *Points reflexes auricularis*. Moulin Les-Metz, France: Maisonneuve.
Nogier, R. (2014). How did Paul Nogier establish the map of the ear? *Medical Acupuncture, 26*(2), 76–83.
Oleson, T. (2014). *Auriculotherapy manual: Chinese and Western systems of ear acupuncture*. Edinburgh: Churchill Livingstone, Elsevier.
Otte, J. L., Carpenter, J. S., Russell, K. M., Bigatti, S., & Champion, V. L. (2010). Prevalence, severity, and correlates of sleep-wake disturbances in long-term breast cancer survivors. *Journal of Pain Symptom Management, 39*, 535–547.
Pergolizzi, J., Boger, R. H., Budd, K., Dahan, A., Erdine, S., Hans, G., Kress, H. G., Langford, R., Likar, R., Raffa, R. B., & Sacerdote, P. (2008). Opioids and the management of chronic severe pain in the elderly: consensus statement of an international expert panel with focus on the six clinically most often used World Health Organization step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). *Pain Practice, 8*, 287–313.
Pike, C. T., Birnbaum, H. G., Muehlenbein, C. E., Pohl, G. M., & Natale, R. B. (2012). Healthcare costs and workloss burden of patients with chemotherapy-associated peripheral neuropathy in breast, ovarian, head and neck, and nonsmall cell lung cancer. *Chemotherapy Research and Practice, 2012*, 913848.
Pinsker, E., Inrig, T., Daniels, T. R., Warmington, K., & Beaton, D. E. (2015). Reliability and validity of 6 measures of pain, function, and disability for ankle arthroplasty and arthrodesis. *Foot & Ankle International, 36*, 617–625.
Poulsen, J. L., Brock, C., Olesen, A. E., Nilsson, M., & Drewes, A. M. (2015). Evolving paradigms in the treatment of opioid-induced bowel dysfunction. *Therapy Advances in Gastroenterology, 8*, 360–372.
Romoli, M., Allais, G., Airola, G., Benedetto, C., Mana, O., Giacobbe, M., Pugliese, A. M., Battistella, G., & Fornari, E. (2014). Ear acupuncture and fMRI: a pilot study for assessing the specificity of auricular points. *Neurological Sciences, 35*(Suppl 1), 189–193.
Schapira, M. M., Mackenzie, E. R., Lam, R., Casarett, D., Seluzicki, C. M., Barg, F. K., & Mao, J. J. (2013). Breast cancer survivors willingness to participate in an acupuncture clinical trial: a qualitative study. *Supportive Care in Cancer, 22*, 1207–1215.
Seretny, M., Currie, G. L., Sena, E. S., Ramnarine, S., Grant, R., MacLeod, M. R., Colvin, L. A., & Fallon, M. (2014). Incidence, prevalence, and predictors of chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis. *Pain, 155*, 2461–2470.
Shah, A., Hoffman, E. M., Mauermann, M. L., Loprinzi, C. L., Windebank, A. J., Klein, C. J., & Staff, N. P. (2018). Incidence and disease burden of chemotherapy-induced peripheral neuropathy in a population-based cohort. *Journal of Neurology, Neurosurgery, and Psychiatry, 89*, 636–641.
Sisignano, M., Baron, R., Scholich, K., & Geisslinger, G. (2014). Mechanism-based treatment for chemotherapy-induced peripheral neuropathic pain. *Nature Reviews Neurology, 10*, 694–707.
Smith, E., Pang, H., Cirrincione, C., Fleishman, S., Paskett, E., Ahles, T., Bressler, C., Fadul, C., Knox, N., Le-Lindqwister, N., Gilman, P., Shapiro, C., & Alliance for Clinical Trials in Oncology. (2013). Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced painful peripheral neuropathy: A randomized clinical trial. *JAMA Internal Medicine, 309*, 1359–1367.
Staff, N. P., Grisold, A., Grisold, W., & Windebank, A. J. (2017). Chemotherapy-induced peripheral neuropathy: a current review. *Annals of Neurology, 81*, 772–781.
Takei, H., Ohsumi, S., Shimozuma, K., Takehara, M., Suemasu, K., Ohashi, Y., & Hozumi, Y. (2012). Health-related quality of life, psychological distress, and adverse events in postmenopausal women with breast cancer who receive tamoxifen, exemestane, or anastrozole as adjuvant endocrine therapy: National Surgical Adjuvant Study of Breast Cancer 04 (N-SAS BC 04). *Breast Cancer Research and Treatment, 133*, 227–236.
Winters-Stone, K. M., Horak, F., Jacobs, P. G., Trubowitz, P., Dieckmann, N. F., Stoyles, S., & Faithfull, S. (2017). Falls, functioning, and disability among women with persistent symptoms of chemotherapy-induced peripheral neuropathy. *Journal of Clinical Oncology, 35*, 2604–2612.
World Health Organization. (1990). *Report of the working group on auricular acupuncture nomenclature*. Lyons, France: World Health Organization.
Yeh, C. H., & Huang, L. C. (2013). Comprehensive and systematic auricular diagnosis protocol. *Medical Acupuncture, 25*, 423–436.
Yeh, C. H., Chien, L. C., Chiang, Y. C., & Huang, L. C. (2012). Auricular point acupressure for chronic low back pain: a feasibility study for 1-week treatment. *Evidence-Based Complement Alternative Medicine, 2012*, 383257.
Yeh, C. H., Chien, L. C., Balaban, D., Sponberg, R., Primavera, J., Morone, N. E., Glick, R., Albers, K. M., Cohen, S. M., Ren, D., Huang, L. C., & Suen, L. K. P. (2013). A randomized clinical trial of auricular point acupressure for chronic low back pain: a feasibility study. *Evidence-Based Complement Alternative Medicine, 2013*, 196978.
Yeh, C. H., Chiang, Y. C., Hoffman, S., Liang, Z., Klem, M. L., Tam, W. W. S., Chien, L. C., & Suen, L. K. P. (2014a). Efficacy of auricular therapy for pain management: a systematic review and meta-analysis. *Evidence-Based Complementary and Alternative Medicine, 2014*, 934670.
Yeh, C. H., Huang, L. C., & Suen, K. P. L. (2014b). The application of a comprehensive and systematic auricular diagnosis for musculoskeletal system disorder: a treatment protocol for chronic low back pain. *Medical Acupuncture, 26*, 148–153.
Yeh, C. H., Morone, N. E., Chien, L. C., Cao, Y., Lu, H., Shen, J., Margolis, L., Bhatnagar, S., Hoffman, S., Glick, R., & Suen, L. K. P. (2014c). Auricular point acupressure to manage chronic low back pain in older adults: a randomized controlled pilot study. *Evidence-Based Complementary and Alternative Medicine, 2014*, 375173.
Yeh, C. H., Suen, L. K. P., Chien, L. C., Margolis, L., Bhatnagar, S., Teika, T., Hoffman, Liang, Z., Glick, R., & Morone, N. E. (2015a). Day-to-day changes of auricular point acupressure to manage chronic low back pain: a 29-day randomized control study. *Pain Medicine, 16*, 1857–1869.
Yeh, C. H., Chien, L. C., Chiang, Y. C., Suen, L., & Ren, D. (2015b). Analgesic effect of auricular point acupressure as an adjunct treatment for patients diagnosed with cancer with pain. *Pain Management Nursing, 16*(3), 285–293.
Yeh, C. H., Chien, L. C., Lin, W. C., Bovbjerg, D. H., & van Londen, G. (2016). Pilot randomized controlled trial of auricular point acupressure to manage symptom clusters of pain, fatigue, and disturbed sleep in breast patients diagnosed with cancer. *Cancer Nursing, 39*, 402–410.
Yeh, C. H., Lin, W. C., Suen, L. K. P., Park, N. J., Wood, L. J., van Londen, G. J., & Bovbjerg, D. H. (2017). Auricular point acupressure to manage aromatase inhibitor-induced arthralgia in postmenopausal breast cancer survivors: a pilot study. *Oncology Nursing Forum, 44*, 476–487.