Acupuncture Treatment of Chemotherapy-Induced Peripheral Neuropathy in Women with Breast or Gynecologic Cancers: Mechanisms of Action and Feasibility

IRB_00107709

NCT04067544

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Historical Protocol Versions

Version 1: 12/11/18
Version 2: 05/31/19
Version 3: 09/03/19
Version 4: 10/31/19
Version 5: 11/22/19

LIST OF ABBREVIATIONS

Abbreviation or Term[1]	Definition/Explanation
AE	Adverse Event
AT	Acupuncture Treatment
BPI	Brief Pain Inventory
CCAOM	Council of Colleges of Acupuncture and Oriental Medicine
CIPN	Chemotherapy-Induced Peripheral Neuropathy
CIPN-R-ODS	Chemotherapy-Induced Peripheral Neuropathy Rasch-built Overall Disability Scale
CNS	Central Nervous System
CNT	Clean Needle Technique
CRA	Clinical Research Associate
CTCAE	Common Terminology Criteria for Adverse Events (from National Cancer Institute)
CTRP	Clinical Trials Reporting Program
DAOM	Doctor of Acupuncture and Oriental Medicine
DSMC	Data and Safety Monitoring Committee
ECOG Status	Eastern Cooperative Oncology Group Performance Status
ERICA	Electronic Research Integrity and Compliance Administration
FDA	Food and Drug Administration
fMRI	Functional Magnetic Resonance Imaging

Abbreviation or Term[1]	Definition/Explanation
GB 34	Gall Bladder 34
GB 40	Gall Bladder 40
HCI	Huntsman Cancer Institute
INC	Imaging and Neuroscience Center
IND	Investigational New Drug
IRB	Institutional Review Board
KD 3	Kidney 3
LI 10	Large Intestine 10
MAIA-2	Multidimensional Assessment of Interoceptive Awareness Version 2
MRI	Magnetic Resonance Imaging
N/A	Not applicable
NCI	National Cancer Institute
PIs	Primary Investigators
RCO	Research Compliance Officer
SAE	Serious Adverse Event
SC	Study Coordinator
SPSS	Statistical Package for the Social Sciences
SSNRIs	Selective Serotonin and Norepinephrine Reuptake Inhibitors

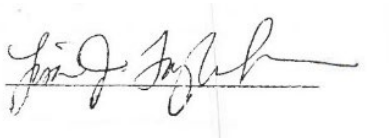
Abbreviation or Term[1]	Definition/Explanation
ST 36	Stomach 36
ST 41	Stomach 41
STRICTA	Standards for Reporting of Controlled Trials in Acupuncture
TNSc	Total Neuropathy Scale Clinical version

All of these abbreviations may or may not be used in protocol.

PROTOCOL SIGNATURE

I confirm that I have read this protocol, and I will conduct the study as outlined herein and according to the ethical principles stated in the latest version of the Declaration of Helsinki, the applicable ICH guidelines for good clinical practice, and the applicable laws and regulations of the federal government.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure that they are fully informed regarding the study treatment, the conduct of the study, and the obligations of confidentiality.



Signature of Principal Investigator — **Date**: **12/3/2019**

Lisa Jean Taylor-Swanson PhD, MAcOM, LAc
Principal Investigator Name

College of Nursing, University of Utah
Name of Institution

STUDY SUMMARY

Title	Acupuncture Treatment of Chemotherapy-Induced Peripheral Neuropathy (CIPN) in Women with Breast or Gynecologic Cancers: Feasibility and Mechanisms of Action
Short Title	CIPN Acu
Protocol Number	N/A
Phase	Clinical study phase: pilot phase II study
Design	Single arm, pilot feasibility study
Study Duration	18 months
Study Center(s)	Single-center: HCI/HCH
Objectives	This pilot study aims to demonstrate feasibility to recruit, retain and provide the study intervention and to identify potential mechanisms of action of acupuncture in CIPN management.
Number of Subjects	N=20
Diagnosis and Main Eligibility Criteria	This study will enroll female patients who have completed paclitaxel or docetaxel treatment at least 3 months prior with at least one month of altered sensation in feet (with or without presence in one or both hands) and/or pain with a score of greater than or equal to 20 for CIPN on the sensory subscale of the CIPN-20. Enrollment will be limited to patients with breast, ovarian, cervical, endometrial, or uterine cancer with CIPN and completed paclitaxel or docetaxel treatments.
Statistical Methodology	**Primary Endpoints:** Mean monthly enrollment, percentage completion rate of all study procedures, frequency count of serious adverse events, and percentage of enrolled participants completing questionnaires will be calculated. Data will be collected via REDCap and analyzed with SPSS. Analysis of demographic data will consist of calculating means, standard deviations, frequencies, and proportions. Analysis of feasibility data will consist of calculating frequencies and percentages. Analysis of questionnaires will consist of within-

	group pre/post analysis with student t-test and chi square with significance will be set at .05 and two-tailed hypotheses. **Sample Size Estimation:** A sample size of 25-30 participants is ideal for a pilot feasibility study[1]. However, we are recruiting only 20 participants due to funding constraints.

1 OBJECTIVES

This pilot study aims to evaluate the feasibility to conduct a study of acupuncture treatment (AT) for Chemotherapy-Induced Peripheral Neuropathy (CIPN) at Huntsman Cancer Institute and to investigate changes in physiological biomarkers when using acupuncture to treat CIPN.

1.1 Primary Objectives and Endpoints

To evaluate the feasibility to conduct a trial of AT for CIPN + standard of care therapy. Primary feasibility objectives will be evaluated in terms of recruitment (enrollment of 20 women, average of 2 eligible women per month to participate in the trial, identification of appropriate recruitment strategies, the appropriateness of eligibility criteria), retention (70% or more participants comply with 8 or more AT sessions and complete both fMRI scans), safety (zero serious adverse events directly related to AT) and questionnaire completion (70% or more enrolled participants comply with all data collection).

1.1.1 Primary outcome measures: Mean enrollment, completion rate of AT, fMRI, rate of serious adverse events, rate of questionnaire completion.

1.2 Secondary Objectives and Endpoints

To evaluate the impact of AT on the reported experience of CIPN.

1.2.1 To evaluate central pain processing and cortical connectivity in patients with CIPN treated by acupuncture by analyzing fMRI of all participants.

1.2.2 To evaluate if there is any change in patient-reported measures from before AT to after study completion.

2 BACKGROUND

Chemotherapy-induced peripheral neuropathy (CIPN) is one of the most common and disabling complications of cancer chemotherapy. CIPN is a major cause of morbidity and reduced quality of life among cancer survivors due to pain, gait instability, and fall related injury. Up to 60% of patients receiving potentially neurotoxic chemotherapeutics develop CIPN, 40% of whom have persistent neuropathy after termination of chemotherapy.[2,3] CIPN commonly necessitates dose reduction or cessation of therapy, potentially limiting treatment efficacy and likely impacting patient outcomes.[4] First-line treatments include anticonvulsants, tricyclic antidepressants, selective serotonin and norepinephrine reuptake inhibitors (SSNRIs) and topical lidocaine.[5]

Second-line treatments include opioids. Given the risk of abuse, overdose and addiction, treatments besides opioids are advised and warrant investigation. A multimodal approach may be most effective, with acupuncture being a safe option reporting low rates of adverse events[6]. Acupuncture treatment (AT) is a well-tolerated and safe treatment option frequently used for symptoms associated with cancer therapies such as nausea, vomiting, xerostomia and fatigue.[7] Several case series and small uncontrolled trials of AT for CIPN suggest potential efficacy, although well-designed and powered clinical trials are lacking and mechanisms underlying AT's potential efficacy are unknown.[8-14]

Although drug-induced damage to the peripheral nervous system is well recognized in CIPN, the central nervous system (CNS) also shows concomitant involvement. Much of our current understanding of the pathophysiology of central pain processing in chronic painful conditions such as diabetic neuropathy, trigeminal neuralgia, post-herpetic neuralgia and chronic low back pain has utilized functional magnetic resonance imaging (fMRI). Previous pain-related functional studies identified alterations in brain activation in multiple cortical and subcortical regions including the frontal lobe, insular cortex, somatosensory cortex, thalamus, periaqueductal grey and precuneus.[15]

While fMRI has not yet been used to evaluate mechanisms of action of AT in the context of CIPN, an increasing number of studies have applied fMRI to investigate AT over a wide range of pain disorders. Stimulation of acupuncture points is associated with overlapping activity in cortical and subcortical brain regions, including the insula, thalamus, anterior cingulate cortex, primary and secondary somatosensory cortices, and deactivation in limbic-paralimbic-neocortical network. Acupuncture can modulate activity within specific brain areas, many of which are known to be important to CIPN pain processing. We hypothesize that regions involved in pain perception will show decreased connectivity between the insula, amygdala and somatosensory cortex with successful pain treatment, with decreased task-related activation of the brain's salience network (anterior cingulate and frontal insula) during mental pain imagery. [13-15]

Additionally, neurological evidence indicates that some of the brain regions activated during pain perception are also activated when engaging in interoceptive awareness. [16] Acupuncture has been shown to alter pain processing regions but has not been evaluated regarding changes in mind-body awareness. The possible role of enhanced mind-body awareness as a mechanism of action of acupuncture has not yet been tested. This pilot study will provide a preliminary fMRI and questionnaire data for this topic. Clinical trials of interventions such as mindfulness-based cognitive therapy demonstrate increased interoceptive awareness[17] and decreased depression[18]. It seems plausible that AT may provide an opportunity for participants to increase their mind-body awareness while they lie on the treatment table and relax, as well as via neurologic changes in the insula, amygdala, and somatosensory cortex. These regions are known to affect pain processing as well as interoceptive (or mind-body) awareness.

This pilot feasibility study aims to determine if conducting a trial of AT for CIPN is feasible at HCI. We aim to enroll and retain twenty participants who will undergo fMRI during the baseline visit, receive up to 10 sessions of AT, and undergo fMRI after completion of AT. We will examine fMRI for potential neurologic mechanisms of action of AT in CIPN management.

The ultimate objective of this pilot project is to lay the foundation for a future randomized controlled clinical trial of AT for CIPN. Specifically, we will be able to demonstrate that we have the team and location in place to conduct a successful trial.

3 DRUG INFORMATION

N/A

4 STUDY DESIGN

4.1 Description

We propose a pilot feasibility trial. Oncologists at Huntsman Cancer Institute (HCI) will be informed of the trial and asked to refer female patients diagnosed with breast or gynecologic cancer and CIPN who have completed all paclitaxel or docetaxel treatments three or more months previously. All referred patients will be informed of the study and voluntarily recruited by the Study Coordinator (SC). The SC will call the individual after sending a recruitment letter, inform them of the study, screen them for eligibility, and if consent is obtained, enroll the participant. Standard oncological care is defined as care the participant was already receiving and that care will not be interrupted in any way for any study participant.

4.2 Dose Limiting Toxicity

N/A

4.3 Number of Patients

Twenty participants will be enrolled. Sample size for this pilot feasibility study is determined by budgetary constraints. While a sample of 25-30 would be ideal for the aims of this study[1], we are limited by our study budget to twenty participants.

4.4 Number of Study Centers

All participants will be recruited from HCI and AT will be delivered onsite at HCI in the Linda B. and Robert B. Wiggins Wellness and Integrative Health Center. This is a single-center pilot phase II trial.

4.5 Study Duration

Eighteen months.

5 ELIGIBILITY CRITERIA

This eligibility checklist is used to determine patient eligibility and filed with signature in the patient research chart.

Patient No. _____
Patient's Initials: (L,F,M) _____

5.1 **Inclusion Criteria**
Yes/No (Response of "no" = patient ineligible)

5.1.1 _____ Female age 18 or older.

5.1.2 _____ Histologically proven breast, uterine, cervical or ovarian cancer of any stage.

5.1.3 _____ Received either (1) a Paclitaxel treatment dose of at least 480 mg/m^2 paclitaxel as a single or combination agent **or** (2) a Docetaxel treatment dose of at least 150 mg/m^2 docetaxel as a single or combination agent. Treatment must be completed at least 3 months prior to enrollment.

5.1.4 _____ Eligible patients report at least 1 month of altered sensation and/or pain in the feet (with or without presence in one or both hands) with a score of greater than or equal to 20 for CIPN on the sensory subscale of the CIPN-20 (scale 0-100).

5.1.5. _____ Able to provide informed consent and willing to sign an approved consent form that conforms to federal and institutional guidelines.

5.1.6. _____ ECOG status of 0 (asymptomatic), 1 (symptomatic but completely ambulatory) or 2 (symptomatic, <50% in bed during the day).

5.2 **Exclusion Criteria**
Yes/No (Response of "yes" = patient ineligible)

5.2.1 _____ Preexisting neuropathy due to other identified etiologies includes diabetes, vitamin B12 deficiency, or alcoholism.

5.2.2 _____ Having received more than 6 acupuncture treatments for any condition in the last six months.

5.2.3 _____ Patients with claustrophobia, pacemakers, non-MRI compatible breast expanders or port-a-caths, neurostimulator devices, current or expected pregnancy, exposure to shrapnel, left-handedness, recent tattoos or otherwise unsafe for MRI scanning.

I certify that this patient meets all inclusion and exclusion criteria for enrollment onto this study.

_____ _____
Investigator Signature **Date**

6 STRATIFICATION FACTORS

N/A

7 TREATMENT PLAN

7.1 Administration Schedule

Twenty participants will be enrolled. The manualized acupuncture treatment (AT) intervention will be designed by Dr. Budhathoki and Dr. Taylor-Swanson and administered by Dr. Budhathoki and members of Huntsman acupuncture team. Ten sessions of AT will be delivered: twice per week for 2 weeks, thereafter once per week for six weeks, with a total of 10 treatments during a two-month course. Each session will last 45-60 minutes, with acupuncture needles retained 30-40 minutes. A minimum of 8 treatments must be received within the acupuncture treatment window. Concurrent medications are allowed as prescribed and will be tracked in the study and analyzed as potential confounders.

Participants in the study will undergo study interview and fMRI at the following two time points: within 9 days after baseline following enrollment and within one week of acupuncture treatment completion. Clinical data including current medications and medical history and fall rates will be gathered during the baseline and study conclusion. Questionnaires will be completed in person or emailed to patients via REDCap at baseline and study conclusion, as well as at a 3-month follow-up. Reminder calls and AT appointments will be scheduled by HCI Wellness and Integrative Health Center personnel in coordination with the study coordinator (SC). The SC will aid participants in scheduling fMRI with an online scheduling system.

7.2 Acupuncture treatment and ongoing standard care Treatment

7.2.1 How Supplied, Stored, Packaged and Labeled

Acupuncture needles arrive labeled, sealed and boxed from the manufacturer and are stored in a secured cabinet. All acupuncture needles remain unopened until use.

7.2.2 Preparation and Administration

Acupuncture will be provided according to standard procedure and will include use of Clean Needle Technique.

Clean Needle Technique

In the United States, Clean Needle Technique (CNT) is governed by the CCAOM, the Council of Colleges of Acupuncture and Oriental Medicine. This study will follow the CNT outlined by the CCAOM, 6th ed. (2009)
CNT helps to ensure participant and practitioner safety in the acupuncture process

General CNT Guidelines

Clean needle technique requires the following:
Hand washing before and after patient contact, and before setting up a clean field
Set up a clean field with equipment and supplies
Locate the acupuncture point

Uni-directional swabbing of the acupuncture point with alcohol
Needling with guide tube and adjust needle to desired depth
At end of session, remove and immediately isolate acupuncture needles into approved sharps containers

Acupuncture Needles
Acupuncture needles are regulated as medical devices by the United States Food and Drug Administration. The acupuncture needles to be used in this clinical trial will be single-use, sterile acupuncture needles.

Acupuncture Needles: DBC™ Spring Ten needle .16 x 30mm, 40-gauge (manufactured by DBC Made in Korea; distributed by Lhasa OMS, Inc. Weymouth, MA)
Auricular Acupuncture Needles: DBC™ Sooji Chim Korean Hand Needles .18x30mm, 42-gauge DBC needles (manufactured by DBC Made in Korea; distributed by Lhasa OMS, Inc. Weymouth, MA)
Scalp Acupuncture Needles: Nano Tech™.16 x 30mm, 40-gauge (manufactured by DBC Made in Korea; distributed by Lhasa OMS, Inc. Weymouth, MA)

Note: if these specific needles are unavailable for use, whichever brand is used clinically by the staff will also be used for study participants.

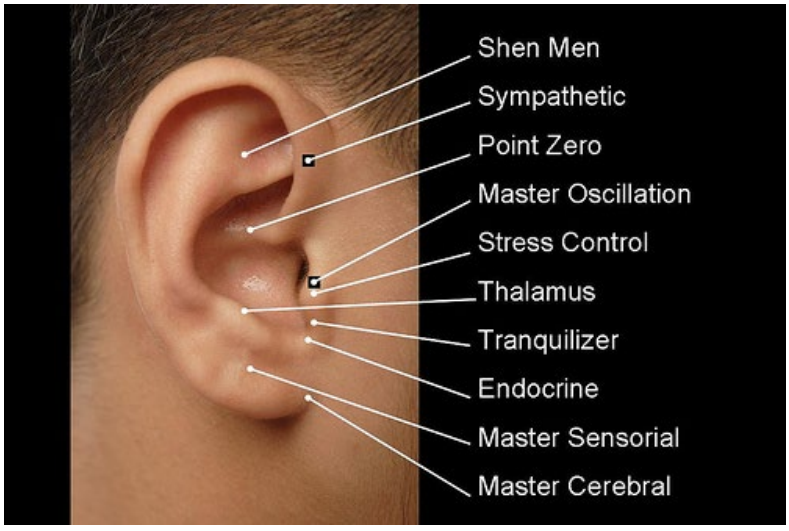
The acupuncture protocol and procedures employed have been devised with adherence to the Standards for Reporting of Controlled Trials in Acupuncture (STRICTA) recommendations. The point prescription in this study is a manualized protocol (i.e., a protocol that is standardized but allows the Study Acupuncturist to modify treatments based on the patient's current symptoms).

Manualized Protocol
A manualized protocol was chosen, as opposed to a fixed acupuncture point protocol, in order to facilitate a standardization of treatments and because it was shown to be effective in a number of other acupuncture clinical trials. Acupuncture points relevant to an individual patient will be selected from the list below.

ACUPUNCTURE POINTS ALLOWED IN THE MANUALIZED PROTOCOL

Point Name	Location – from Chinese Acupuncture and Moxibustion, Foreign Languages Press, Beijing (2010, Xinnong, C., 3rd ed.)
Full body acupuncture points (given at each visit, bilaterally)	
LI 10	On the line joining Yangxi (LI-5) and Quchi (LI-11), 2 cun below the cubital crease.
GB 40	Anterior and inferior to the external malleolus, in the depression on the lateral side of the tendon of m. extensor digitorum longus.
GB 34	In the depression anterior and inferior to the head of the fibula.

ST 41	On the dorsum of the foot, at the midpoint of the transverse crease of the ankle joint, in the depression between the tendons of m. extensor digitorum longus and hallucis longus, approximately at the level of the tip of the external malleolus.
ST 36	3 cun below Dubi (ST-35), one finger-breadth (middle finger) from the anterior border of the tibia.
KD 3	In the depression between the tip of the external malleolus and the anterior side of the tendon Achilles.
Ba Xie	When the hand is made into a fist, six of these points lie in the depressions between the metacarpal heads, proximal to the web margins. The remaining two points lie equidistant between the thumb and index metacarpals, proximal to the web margins.
Ba Feng	On the dorsum of the foot, between the toes, 0.5 cun proximal to the margin of the web.
Auricular acupuncture points: Shen Men, Thalamus, Endocrine, Point Zero, Sympathetic	



Standard care will be delivered according to the participants' healthcare team.

7.2.3 Accountability and Compliance

The Licensed Acupuncturists in this study are licensed in the state of Utah under the Utah Code Title 58 Chapter 72 Acupuncture Licensing Act. Licensed Acupuncturists are also credentialed through the University of Utah medical credentialing department as advance practice clinicians to provide acupuncture treatments in the Huntsman Cancer Hospital and throughout University of Utah healthcare system.

The Licensed Acupuncturists in this study comply with all state and federal regulations for acupuncture and the scope of practice set forth at the Huntsman Cancer Hospital and University of Utah.

7.3 Prohibited Concomitant Medications

No concomitant medications are prohibited in this study.

7.4 Duration of Therapy

Ten sessions of AT will be delivered: twice per week for 2 weeks, thereafter once per week for six weeks, with a total of 10 treatments during a two-month course. Each session will last 45-60 minutes, with acupuncture needles retained 30-40 minutes. A minimum of 8 treatments must be received by each participant with no more than 10 days' gap between treatments permitted. Participants who do not complete 8 or more acupuncture sessions will be dropped from the study. All participants will be educated as to the importance of completion of the study after baseline.

Subjects must be withdrawn from the study treatment for the following reasons:

- Subject withdraws consent from the study treatment and/or study procedures. A subject must be removed from the trial at his/her own request or at the request of his/her legally acceptable representative. At any time during the trial and without giving reasons, a subject may decline to participate further. The subject will not suffer any disadvantage as a result.
- Subject is lost to follow-up.
- Death.

Subjects may be withdrawn from the study for the following reasons:

- The subject is non-compliant with trial procedures.
- If, in the investigator's opinion, continuation of the trial would be harmful to the subject's well-being.
- The development of an additional cancer.
- Development of an intercurrent illness or situation which would, in the judgment of the investigator, significantly affect assessments of clinical status and trial endpoints.
- Deterioration of ECOG performance status to 4.

8 TOXICITIES AND DOSEAGE MODIFICATION

N/A

This study will utilize the CTCAE (NCI Common Terminology Criteria for Adverse Events) Version 5.0 for adverse event and serious adverse event reporting.

8.1 Dose Modifications

N/A

8.2 Supportive Care

8.2.1 All supportive measures consistent with optimal patient care will be given throughout the study.

9 STUDY CALENDAR

			Week (+/- 2 days)										Week (+/- 7 days)
Examination	**Screening[1]**	**Baseline[1, 2] Day 1**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**End of study[5]**	**22**
Informed consent	**X**												
Eligibility criteria	**X**												
Concomitant medications	**X**											**X**	
Questionnaires[3]													
• CIPN-20	**X**											**X**	**X**
• BPI		**X**										**X**	**X**
• CIPN-R-ODS		**X**										**X**	**X**
• MAIA-2		**X**										**X**	**X**
• Demographics		**X**											
Acupuncture treatment (AT)[4]				**X X**	**X X**	**X**	**X**	**X**	**X**	**X**	**X**		
fMRI[6]			**X**									**X**	

[1] Screening visit and Baseline visit can occur on the same day.

[2] Day 1 (Baseline) should occur within 2 weeks of the screening visit.

[3] Questionnaires include: (See Appendices).

[4] Acupuncture treatment (AT) will occur at the Wellness & Integrative Health Center at HCI. Twice a week treatments will occur within 4 business days.

[5] End of study visit should occur within one week of final acupuncture treatment.

[6] Must be within 9 days of baseline visit. If participant prefers, first study fMRI can be same day as first AT treatment.

10 STUDY PROCEDURES

This study will enroll female patients who have completed treatment with either paclitaxel or docetaxel at least three months prior. Paclitaxel is a neurotoxic chemotherapy known to cause CIPN. Docetaxel is also a neurotoxic chemotherapy known to cause CIPN. Patients must have experienced at least one month of altered sensation in feet (with or without

presence in one or both hands) and/or pain with a score of greater than or equal to 20 for CIPN on the sensory subscale of the CIPN-20. We will commence recruitment 3 months after patients have completed their last chemotherapy dose.

Patients will be recruited from the Huntsman Cancer Center Oncology Clinics in collaboration with their oncologists.

For this study, enrollment will be limited to patients with breast, ovarian, cervical, endometrial, or uterine cancer with CIPN and completed chemotherapy treatments.

Visits:

Screening Visit:

Potentially eligible subjects will be scheduled for a screening visit. After informed consent is obtained, the SC will review and confirm inclusion/exclusion criteria. The SC will take a brief medical, history and administer the CIPN-20 questionnaire. If all inclusion and exclusion criteria are fulfilled, the subject will be scheduled for a baseline visit. This visit may occur on the same day as screening, but must occur within 2 weeks of study screening visit. If the participant has received treatment outside of University of Utah Health a medical record release form will be initiated and submitted as appropriate.

Baseline Visit:

Patients diagnosed with breast, ovarian, cervical, endometrial, or uterine cancer who will be treated with paclitaxel or docetaxel chemotherapy associated with CIPN will undergo a number of questionnaires. The patient will then be enrolled in the study and scheduled in the Wellness Center for acupuncture therapy (AT). All participants will be scheduled for fMRI , which must occur within nine days after baseline.

Participants will undergo study interview and fMRI within 9 days after baseline following enrollment.

Clinical data including current medications and medical history and fall rates will be gathered. Questionnaires (BPI, CIPN-20, CIPN-R-ODS, MAIA-2, Demograhpics) will be completed in person or emailed to patients via REDCap. Reminder calls and AT appointments will be scheduled by HCI Wellness and Integrative Health Center personnel in conjunction with a SC. The SC will aid participants in scheduling fMRI appointments online. AT treatments will occur within 7 days/4 business days in general. If participant prefers the first study fMRI and first AT appointment can occur same day, with the fMRI procedure occurring prior to AT treatment.

Follow up Visits:

Participants will receive 10 sessions of AT: twice per week for 2 weeks, thereafter once per week for six weeks, with a total of 10 treatments during a two-month course. Each session will last 45-60 minutes, with acupuncture needles retained 30-40 minutes. A minimum of 8 treatments must be received by each participant with no more than 9 days' gap between weekly treatments permitted (sessions 5-10). Concurrent medications are allowed as prescribed and will be tracked in the study and analyzed as potential confounders.

Final Visit:

Participants will undergo examination within one week of AT completion. This will include the fMRI scan and questionnaires. Compensation for participation will be offered at this visit.

***Procedures*:**

Measures: Questionnaires will be completed in person or emailed to patients via REDCap at baseline and study conclusion, as well as at a 3-month follow-up. *Primary Endpoints:* Mean enrollment, percentage completion rate of all study procedures, frequency count of serious adverse events, and percentage of enrolled participants completing questionnaires will be calculated. Data will be collected via REDCap, stored in the Research Subject Registry (RSR) and analyzed with SPSS.

Additional measures to be collected: CIPN-20: This measure includes questions about tingling, numbness, painful numbness, cramps, balance, temperature intolerance, grasping items, ankle flexion weakness and leg weakness. CIPN-R-ODS (a validated measure of quality of life specific to CIPN), will be used to assess impact on function, BPI to assess pain and Multidimensional Assessment of Interoceptive Awareness (MAIA-2) to assess mind-body awareness. We will also collect *demographic* information including age, marital status, race and ethnicity. Related medical history and current medications information will be collected.

Acupuncture therapy (AT): AT will be delivered onsite at HCI in the Linda B. and Robert B. Wiggins Wellness & Integrative Health Center. AT will be delivered twice per week for two weeks and then weekly for six weeks by Annie Budhathoki, DAOM, a Licensed Acupuncturist who has over five years' clinical experience treating persons with cancer, or another Licensed Acupuncturist in the Wellness & Integrative Health Center. Each session will last 45-60 minutes, with acupuncture needles retained 30-40 minutes. A minimum of 8 treatments must be received by each participant.

Functional MRI (fMRI) to be conducted within 9 days after baseline and within 1 week of final AT session. fMRI scans will be conducted at Imaging and Neuroscience Center (INC) in Research Park. Imaging will consist of structural brain imaging (MP2RAGE), task fMRI, and resting-state fMRI connectivity. Task fMRI will consist of a mental imagery task with a 20-second block design wherein patients will alternate between concentration on a part of their body where they experience pain and a part of their body where they do not experience pain, prompted by visual cues. We will provide gift cards for $25 after the completion of the second fMRI.

11 CRITERIA FOR EVALUATION AND ENDPOINT

11.1 **Feasibility**

To evaluate the feasibility to conduct a trial of AT for CIPN + standard of care therapy. Primary feasibility objectives will be evaluated in terms of recruitment (enrollment of 20, average of 2 eligible women per month to participate in the trial, identification of appropriate

recruitment strategies, the appropriateness of eligibility criteria), retention (70% or more participants comply with AT attendance defined as 8 or more of 10 AT sessions, and complete both fMRI scans), safety (zero serious adverse events directly related to AT) and questionnaire completion (70% or more enrolled participants comply with data collection).

Primary outcome measures: Mean enrollment, completion rate of AT and fMRI, rate of serious adverse events, rate of questionnaire completion.

11.2 **Safety**

The DSMC will consist of the appropriate Huntsman Cancer Institute (HCI) DSMC members.

Overall safety of this study will be assessed using the CTCAE (NCI Common Terminology Criteria for Adverse Events) version 5.0 and the following safety and tolerability endpoints will be used:

-incidence of treatment-emergent adverse events associated (TEAE's) with acupuncture- known TEAE's detailed below.

Patients will be instructed to disclose all study-related side-effects, symptoms or AEs.
Potential adverse effects of acupuncture treatment include:
Bruising
Bleeding
Needle shock
Pre-syncope (Dizziness)
Diaphoresis (Sweating)
Nausea and Vomiting
Loss of consciousness

The main side effects of acupuncture include a slightly increased risk of minor bruising and bleeding and rarely infection. Needle shock, a vaso-vagal response to needle insertion, occurs about 5% of the time usually during the first or second treatment. Patients may become faint, diaphoretic, nauseated and occasionally lose consciousness. These are often reversible by removing the acupuncture needles and laying the patient supine.

-incidence of procedure-related adverse events associated with fMRI (source: FDA)

MR images are made without using any ionizing radiation, so patients are not exposed to the harmful effects of ionizing radiation. But while there are no known health hazards from temporary exposure to the MR environment, the MR environment involves a strong, static magnetic field, a magnetic field that changes with time (pulsed gradient field), and radiofrequency energy, each of which carry specific safety concerns:

- The strong, static magnetic field will attract magnetic objects (from small items such as keys and cell phones, to large, heavy items such as oxygen tanks and floor buffers) and may cause damage to the scanner or injury to the patient or medical professionals if those objects

become projectiles. Careful screening of people and objects entering the MR environment is critical to ensure nothing enters the magnet area that may become a projectile.

- The magnetic fields that change with time create loud knocking noises which may harm hearing if adequate ear protection is not used. They may also cause peripheral muscle or nerve stimulation that may feel like a twitching sensation.
- The radiofrequency energy used during the MRI scan could lead to heating of the body. The potential for heating is greater during long MRI examinations.

Acupuncture Schedule Adjustments

The main toxic effects of acupuncture include a slightly increased risk of minor bruising and bleeding and rarely infection. Needle shock, a vaso-vagal response to needle insertion, occurs about 5% of the time usually during the first or second treatment. Patients may become pre-syncopal, diaphoretic, nauseated and occasionally lose consciousness. These symptoms are easily reversible by removing the acupuncture needles and laying the patient supine. There are no universal guidelines in patients with lymphoedema however there may be hospital, academic medical center, or department specific guidelines. These concerns can adequately be addressed by the Study Acupuncturist as toxic effects of acupuncture are taught in all acupuncture schools.

Reporting adverse events and referrals for patient care

During the study, all study patients will be under the care of either a medical oncologist or a surgical oncologist. If any abnormalities or problems, including possible study related adverse events (AE) or reportable serious adverse events(SAEs), are detected during screening, subsequent measurements, or study activities, the patient will be referred back to their medical provider for appropriate care. The SC and study primary investigators (PIs) will be responsible for recording and reporting any intervention related AEs and reportable SAEs. The possible routes of referral are as follows:

a. Abnormality/problem detected during screening and subsequent clinic visits: The SC will notify and discuss with the study PIs. The responsible site investigator as appropriate will refer the patient to their medical provider. The SC and study PIs will record and report any study-related AEs and reportable SAEs as appropriate.

b. Abnormality/problem detected during telephone contact: The SC will refer the patient to their medical provider and the responsible site investigator as appropriate. The SC and study PIs will record and report AEs and reportable SAEs as appropriate.

c. Abnormality/problem detected during acupuncture session: The Study Acupuncturist will notify and discuss with the responsible site investigator. The SC will be notified and the SC and the responsible site investigator as appropriate will refer the patient to their medical provider. The SC and study investigators will record and report as appropriate.

More on adverse event procedures are outlined in section **16.4.1**

11.3 **Stopping Rules**

Conditions that may lead to reasonable cause and warrant termination of this study include, but are not limited to:

-Subject or investigator noncompliance

-Unsatisfactory subject enrollment

-Lack of adherence to protocol procedures

-Lack of valuable and/or complete data

-Potentially unacceptable risk to study subjects

12 STATISTICAL CONSIDERATIONS

Data will be collected via REDCap and analyzed with SPSS. Missing data will be handled with imputation of the median value of all available data for each individual item.[19]

Demographics: Analysis of demographic data will consist of calculating means, standard deviations, frequencies, and proportions. Demographic information to include: age, marital status, race and ethnicity, current medications and medical history.

Feasibility data: will be analyzed by calculating frequency and percentages, specifically:

- **Recruitment** – frequency count (enrollment of 20 women, average of 2 eligible women per month to participate in the trial, identification of appropriate recruitment strategies, the appropriateness of eligibility criteria),
- **Retention** – frequency and percentage (70% or more participants comply with 8 or more AT sessions and complete both fMRI scans)
- **Safety** – frequency count (zero serious adverse events directly related to AT)
- **Questionnaire completion** – frequency and percentage (70% or more enrolled participants complete at least 80% of questions at all protocol-directed time points).

Questionnaires: analyses will consist of student t-test and chi square computations according to the type of data.

- CIPN-20
- CIPN-R-ODS
- BPI
- Multidimensional Assessment of Interoceptive Awareness (MAIA-2)

Functional MRI quantification: Volume and Surface preprocessing pipelines from the Human Connectome Project will be executed for each resting sequence on completion of structural preprocessing. MultiEcho ICA Cleaning: All resting state data will additionally be processed using MultiEcho ICA pipeline (AFNI) allowing removal of non-neural components in the BOLD data. Head motion: Rigorous control of head motion begins before acquisition with subject

training and instruction, continues during scanning with repeated reminders to hold still and analysis of image quality after each scan with repetition as possible, and postprocessing including voxelwise despiking, motion parameter estimation and correction, physiologic waveform regression, Multiecho ICA cleaning, and volume censoring (scrubbing). Post-hoc mean and maximal root-mean-square head motion estimates will be used as covariates for all biomarkers. Connectivity: Time series will be estimated FreeSurfer-defined subject-specific regions of interest in somatosensory cortex, anterior cingulate, anterior insula, amygdala, thalamus, medial prefrontal cortex, orbitofrontal cortex, and precuneus, as well as at 361 ROIs for graph-theoretic and network analyses (modularity and clustering coefficient) comprising 333 cortical ROIs strategically positioned at network hubs, 14 cerebellar ROIs, and 14 subcortical gray matter ROIs defined from Freesurfer segmented subject specific nuclei.

Functional MRI Analysis: *We will analyze functional connectivity using a parcellation covering the cortical and subcortical gray matter at 5 mm resolution. Brain parcellation will be constructed by assessing regions of interest (ROIs) and measuring each voxel, which can represent a million brain cells. Each voxel will be tested in sequence beginning with the inferior left voxel in the cerebellum. If a voxel is greater than 5 mm distant to voxels already selected, then this voxel will be included in the set of ROI center coordinates.*

13 REGISTRATION GUIDELINES

N/A

Patients must meet all of the eligibility requirements listed in Section 5 prior to study procedures.

14 DATA SUBMISSION SCHEDULE

N/A

15 SPECIAL INSTRUCTIONS

15.1 Pathology review

N/A

15.2 Pharmacokinetic

N/A

15.3 Correlative Studies

N/A

16 ETHICAL AND REGULATORY CONSIDERATIONS

16.1 Informed consent

Informed consent will be obtained from all research participants prior to performing any study procedures using the most recent Institutional Review Board (IRB) approved version.

16.2 **Institutional Review**

Study will be approved by the IRB of University of Utah.

16.3 **Data and Safety Monitoring Plan**

A Data and Safety Monitoring Committee (DSMC) is established at Huntsman Cancer Institute (HCI) and approved by the NCI to assure the well-being of patients enrolled on Investigator Initiated Trials that do not have an outside monitoring review. Roles and responsibilities of the DSMC are set forth in the NCI approved plan. The activities of this committee include a quarterly review of adverse events including SAEs, important medical events, significant revisions or amendments to the protocol, and approval of cohort/dose escalations. If the DSMC and/or the PI have concerns about unexpected safety issues, the study will be stopped and will not be resumed until the issues are resolved. The DSMC also reviews and approves audit reports generated by the Research Compliance Office.

This study is a low risk trial. All low risk studies are audited no less than annually by the Research Compliance Office and audit reports will be reviewed and approved by the full DSMC. The DSMC will also review all reportable Serious Adverse Events for patients on this study.

16.4 **Adverse Events / Serious Adverse Events**

This study will utilize the CTCAE (NCI Common Terminology Criteria for Adverse Events) Version 5.0 for AE and SAE reporting. An electronic copy can be downloaded from: **https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf**

16.4.1 Adverse Events (AE)

There is no protocol-directed administration of systemic therapy in this non-pharmacologic study; patients will be taking standard of care anti-cancer therapy prescribed by their treating oncologist. The study-specific AE reporting plan detailed below will be followed. The PI will determine the attribution/relatedness of each AE. Any AEs with a *causal* relation to the research will be graded for severity and seriousness, and followed to either resolution or until the 3-month post follow-up (whichever comes first).

Subjects will receive a systemic treatment regimen for their cancer during study participation. Since such routine interventions and treatment may influence the study results, information regarding the concomitant medications will be collected but not reported to the IRB.

Potential AEs of acupuncture treatment include:

- Excessive and/or unusual bruising
- Excessive and/or unusual bleeding
- Needle shock
- Pre-syncope (Dizziness)
- Diaphoresis (Sweating)
- Nausea and Vomiting

- Loss of consciousness

16.4.2 Serious Adverse Event (SAE)

AE's which are determined by the PI to be both attributable to study intervention and serious will be reported to the DSMC and/or the IRB as appropriate (refer to section 16.5 for reporting requirements). An AE is considered serious when it results in one or more of the following:

- Death
- Initial or prolonged hospitalization
- Life threatening event
- Disability or permanent damage
- Congenital Anomaly/Birth defect
- Other important medical event which is deemed serious by the PI

16.5 **SAE Reporting Requirements**

SAEs must be reported to the DSMC and/or the IRB according to the requirements described below:

DSMC Notifications:

- All SAEs which are attributable to study intervention will be reported to the DSMC.
- A MedWatch 3500A form* must be completed and submitted to compliance@hci.utah.edu as soon as possible, but no later than 24 hours from first knowledge.
- An HCI Research Compliance Officer (RCO) will process and submit the MedWatch form to the proper DSMC member as necessary for each individual study.
- The RCO will summarize and present all reported SAEs according to the Data and Safety Monitoring Plan at the quarterly DSMC meeting.

IRB Notification:

- Events meeting the University of Utah IRB reporting requirements (http://www.research.utah.edu/irb/) will be submitted through the IRB's electronic reporting system within 10 working days.

*Medwatch 3500A form can be found at http://www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/ucm082728.pdf

16.6 **Reporting of Pregnancy**

Although pregnancy is not considered an adverse event, it is the responsibility of investigators or their designees to report any pregnancy or lactation in a subject as an SAE. Pregnancies or lactation that occurs during the course of the trial or with 30 days of completing the trial or starting another new anticancer therapy, whichever is earlier, must be

reported to the DSMC, and IRB. All subjects and female partners who become pregnant must be followed to the completion/termination of the pregnancy. Pregnancy outcomes of spontaneous abortion, missed abortion, fetal death, intrauterine death, miscarriage and stillbirth must be reported as serious events.

16.7 **Protocol Amendments**

Any amendments or administrative changes in the research protocol during the period, for which the IRB approval has already been given, will not be initiated without submission of an amendment for IRB review and approval.

These requirements for approval will in no way prevent any immediate action from being taken by the investigator in the interests of preserving the safety of all patients included in the trial.

16.8 **Protocol Deviations**

A protocol deviation (or violation) is any departure from the defined procedures and treatment plans as outlined in the protocol version submitted and previously approved by the IRB. Protocol deviations have the potential to place participants at risk and can also undermine the scientific integrity of the study thus jeopardizing the justification for the research. Protocol deviations are unplanned and unintentional events.

Because some protocol deviations pose no conceivable threat to participant safety or scientific integrity, reporting is left to the discretion of the PI within the context of the guidelines below. The IRB requires the **prompt reporting** of protocol deviations which are:

- Exceptions to eligibility criteria.
- Intended to eliminate apparent immediate hazard to a research participant or
- Harmful (caused harm to participants or others, or place them at increased risk of harm - including physical, psychological, economic, or social harm), or
- Possible serious or continued noncompliance

16.9 **FDA Annual Reporting**

This study is Investigational New Drug (IND) exempt therefore there are no annual reporting requirements to the FDA.

16.10 **Clinical Trials Data Bank**

The study will be registered on **http://clinicaltrials.gov**

16.11**Record Keeping**

Investigator records shall be kept until 2 years after the investigation is discontinued .

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Appendix A: CIPN-20

20 Items are scored 1 to 4 with 1 representing “not at all” and 4 “very much.” Maximum score is 100. Higher scores indicate worse CIPN.

EORTC QLQ-CIPN20

Sensory symptoms and problems
1. Tingling fingers or hands?
2. Tingling toes or feet?
3. Numbness in fingers or hands?
4. Numbness in toes or feet?
5. Aching or burning pain in fingers or hands?
6. Aching or burning pain in toes or feet?
9. Trouble standing or walking?
10. Trouble distinguishing hot and cold water?
18. Trouble hearing?

Motor scale
7. Cramps in hands?
8. Cramps in feet?
11. Trouble holding a pen making writing difficult?
12. Trouble handling small objects (e.g. buttoning a blouse)?
13. Trouble opening jar/bottle due to loss of strength in hands?
14. Trouble walking because your feet come down to hard?
15. Trouble walking stairs or standing up from a chair due to weakness in legs?
19. Only for those driving cars: trouble driving due to use of pedals?

Autonomic scale
16. Dizziness after standing up?
17. Blurry vision?
20. Only for males; Trouble getting or maintaining an erection?

Appendix B: CIPN-R-ODS

Each item is rated on a scale of 0-5:

Item
Get out of the bed
Visit family/friends
Dress your lower body
Run laundry washing machine
Use knife/fork (spoon)
Sit down from standing
Go to a hospital
Rub lotion on body
Move a chair
Get money from cash point (ATM)
Bend and pick up something
Do the cooking
Throw object (e.g. ball)
Use both dustpan and brush
Do the shopping
Clean a toilet
Vacuum
Get in or get out of the bathtub
Walk upstairs with bag
Walk on uneven ground
Walk up hill
Walk up 3 stairs
Stand from squat
Stand on 1 leg
Walk outdoors >1km
Lift heavy objects (10kg)
Stand for hours
Run

Appendix C: Brief Pain Inventory (BPI)

4 Items are scored from 0 ‘no pain’ to 10 ‘pain as bad as you can imagine’
1 item is scored 0% ‘no relief’ to 100% ‘complete relief’ regarding how much relieve pain treatments or meications provided.
7 items ar rated from 0 ‘does not interfere’ to 10 ‘completely interferes’ regarding pain interference.

1903

Date: ☐☐ / ☐☐ / ☐☐ (month) (day) (year)

Subject's Initials : _____

Study Subject #: ☐☐☐☐

Study Name: _____

Protocol #: _____

PI: _____

Revision: 07/01/05

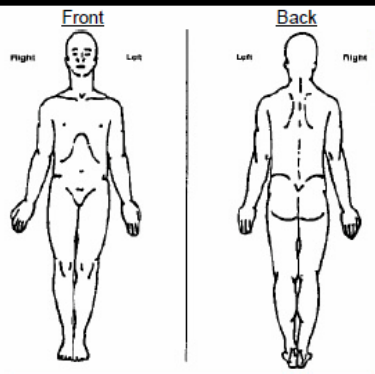
PLEASE USE BLACK INK PEN

Brief Pain Inventory (Short Form)

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

☐ Yes ☐ No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by marking the box beside the number that best describes your pain at its worst in the last 24 hours.

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

No Pain — Pain As Bad As You Can Imagine

4. Please rate your pain by marking the box beside the number that best describes your pain at its least in the last 24 hours.

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

No Pain — Pain As Bad As You Can Imagine

5. Please rate your pain by marking the box beside the number that best describes your pain on the average.

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

No Pain — Pain As Bad As You Can Imagine

6. Please rate your pain by marking the box beside the number that tells how much pain you have right now.

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

No Pain — Pain As Bad As You Can Imagine

Page 1 of 2

1903

Date: (month) / (day) / (year)

Subject's Initials : _____

Study Subject #:

PLEASE USE BLACK INK PEN

Study Name: _____

Protocol #: _____

PI: _____

Revision: 07/01/05

7. What treatments or medications are you receiving for your pain?

8. In the last 24 hours, how much relief have pain treatments or medications provided? Please mark the box below the percentage that most shows how much relief you have received.

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
☐ No Relief	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Complete Relief

9. Mark the box beside the number that describes how, during the past 24 hours, pain has interfered with your:

A. General Activity

☐ 0 Does Not Interfere ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Completely Interferes

B. Mood

☐ 0 Does Not Interfere ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Completely Interferes

C. Walking ability

☐ 0 Does Not Interfere ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Completely Interferes

D. Normal Work (includes both work outside the home and housework)

☐ 0 Does Not Interfere ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Completely Interferes

E. Relations with other people

☐ 0 Does Not Interfere ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Completely Interferes

F. Sleep

☐ 0 Does Not Interfere ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Completely Interferes

G. Enjoyment of life

☐ 0 Does Not Interfere ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Completely Interferes

Page 2 of 2

Appendix D: Multidimensional Assessment of Interoceptive Awareness (MAIA-2)
37 items are rated from 0 ‘never to 5 ‘always’

Below you will find a list of statements. Please indicate how often each statement applies to you generally in daily life.

	Circle one number on each line					
	Never					Always
1. When I am tense I notice where the tension is located in my body.	0	1	2	3	4	5
2. I notice when I am uncomfortable in my body.	0	1	2	3	4	5
3. I notice where in my body I am comfortable.	0	1	2	3	4	5
4. I notice changes in my breathing, such as whether it slows down or speeds up.	0	1	2	3	4	5
5. I ignore physical tension or discomfort until they become more severe.	0	1	2	3	4	5
6. I distract myself from sensations of discomfort.	0	1	2	3	4	5
7. When I feel pain or discomfort, I try to power through it.	0	1	2	3	4	5
8. I try to ignore pain	0	1	2	3	4	5
9. I push feelings of discomfort away by focusing on something	0	1	2	3	4	5
10. When I feel unpleasant body sensations, I occupy myself with something else so I don’t have to feel them.	0	1	2	3	4	5
11. When I feel physical pain, I become upset.	0	1	2	3	4	5
12. I start to worry that something is wrong if I feel any discomfort.	0	1	2	3	4	5
13. I can notice an unpleasant body sensation without worrying about it.	0	1	2	3	4	5
14. I can stay calm and not worry when I have feelings of discomfort or pain.	0	1	2	3	4	5
15. When I am in discomfort or pain I can’t get it out of my mind	0	1	2	3	4	5
16. I can pay attention to my breath without being distracted by things happening around me.	0	1	2	3	4	5
17. I can maintain awareness of my inner bodily sensations even when there is a lot going on around me.	0	1	2	3	4	5
18. When I am in conversation with someone, I can pay attention to my posture.	0	1	2	3	4	5

How often does each statement apply to you generally in daily life? Circle one number on each line

	Never					Always
19. I can return awareness to my body if I am distracted.	0	1	2	3	4	5
20. I can refocus my attention from thinking to sensing my body.	0	1	2	3	4	5
21. I can maintain awareness of my whole body even when a part of me is in pain or discomfort.	0	1	2	3	4	5
22. I am able to consciously focus on my body as a whole.	0	1	2	3	4	5
23. I notice how my body changes when I am angry.	0	1	2	3	4	5
24. When something is wrong in my life I can feel it in my body.	0	1	2	3	4	5
25. I notice that my body feels different after a peaceful experience.	0	1	2	3	4	5
26. I notice that my breathing becomes free and easy when I feel comfortable.	0	1	2	3	4	5
27. I notice how my body changes when I feel happy / joyful.	0	1	2	3	4	5
28. When I feel overwhelmed I can find a calm place inside.	0	1	2	3	4	5
29. When I bring awareness to my body I feel a sense of calm.	0	1	2	3	4	5
30. I can use my breath to reduce tension.	0	1	2	3	4	5
31. When I am caught up in thoughts, I can calm my mind by focusing on my body/breathing.	0	1	2	3	4	5
32. I listen for information from my body about my emotional state.	0	1	2	3	4	5
33. When I am upset, I take time to explore how my body feels.	0	1	2	3	4	5
34. I listen to my body to inform me about what to do.	0	1	2	3	4	5
35. I am at home in my body.	0	1	2	3	4	5
36. I feel my body is a safe place.	0	1	2	3	4	5
37. I trust my body sensations.	0	1	2	3	4	5