


STUDY PROTOCOL

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Biomechanical effect of neurologic dance training (NDT) for breast cancer survivors with chemotherapy-induced neuropathy: study protocol for a randomized controlled trial and preliminary baseline data

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Abstract

Background Breast cancer (BC) is among the most common forms of cancer experienced by women. Up to 80% of BC survivors treated with chemotherapy experience chemotherapy-induced neuropathy (CIN), which degrades motor control, sensory function, and quality of life. CIN symptoms include numbness, tingling, and/or burning sensations in the extremities; deficits in neuromotor control; and increased fall risk. Physical activity (PA) and music-based medicine (MBM) are promising avenues to address sensorimotor symptoms. Therefore, we propose that we can combine the effects of music- and PA-based medicine through neurologic dance training (NDT) through partnered Adapted Tango (NDT-Tango). We will assess the intervention effect of NDT-Tango v. home exercise (HEX) intervention on biomechanically-measured variables. We hypothesize that 8 weeks of NDT-Tango practice will improve the dynamics of posture and gait more than 8 weeks of HEX.

Methods In a single-center, prospective, two-arm randomized controlled clinical trial, participants are randomly assigned (1:1 ratio) to the NDT-Tango experimental or the HEX active control intervention group. Primary endpoints are change from baseline to after intervention in posture and gait. Outcomes are collected at baseline, midpoint, post, 1-month follow-up, and 6-month follow-up. Secondary and tertiary outcomes include clinical and biomechanical tests of function and questionnaires used to compliment primary outcome measures. Linear mixed models will be used to model changes in postural, biomechanical, and PROs. The primary estimand will be the contrast representing the difference in mean change in outcome measure from baseline to week 8 between treatment groups.

Discussion The scientific premise of this study is that NDT-Tango stands to achieve more gains than PA practice alone through combining PA with MBM and social engagement. Our findings may lead to a safe non-pharmacologic intervention that improves CIN-related deficits.

Trial registration This trial was first posted on 11/09/21 at ClinicalTrials.gov under the identifier NCT05114005.

Keywords Chemotherapy-induced neuropathy, Oncology, Neurorehabilitation, Music, Dance, Biomechanics

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Introduction

Background and rationale

Breast cancer (BC) is among the most common forms of cancer experienced by women, second only to skin cancer [1]. Up to 80% of BC survivors treated with chemotherapy experience chemotherapy-induced neuropathy (CIN) [2, 3], a dose-limiting physiological effect of cancer treatment that degrades motor control [4, 5], sensory function [4], and quality of life [3]. Neurologically, CIN involves axonal dieback as well as central deficits [6] with even one cycle of chemotherapy altering cortical thickness in the sensorimotor regions of the brain [7]. Symptoms of CIN persist into survivorship as numbness, tingling, and/or burning sensations in the feet and hands [8]; measurable functional deficits in neuromotor control [4, 9–15]; and increased fall risk [16]. Pharmacologic treatment of CIN has failed to improve sensorimotor symptoms or remediate motor function directly while creating additional negative effects [17] and interactions with key treatment agents. Despite the high prevalence and debilitating consequences of neurotoxic chemotherapy exposure, treatment options remain limited [8].

Physical activity (PA) is a leading candidate to treat CIN non-pharmacologically [18–23], purportedly through inducing axonal regeneration [24], central plasticity [25], and other health benefits such as improved aerobic capacity [26] and reduced systemic inflammation [27]. However, more work is needed to motivate habitual participation and optimize neurorecovery potential. Music-based medicine (MBM) is another promising avenue through which to address sensorimotor symptoms [28]. Music triggers neurophenomena in humans and other species [29, 30] that manifest functionally as auditory-motor entrainment [31], functional neuromotor stabilization [32, 33], and pain reduction [28, 34–36]. We propose that we can combine the positive effects of music- and PA-based medicine through dance as neurologic training. Neurologic dance training (NDT) may optimize neurorecovery potential over and above MBM and PA, separately, by activating the neuropathic dynamic system [37] in the context of rhythmic auditory stimulation [32, 38], sensorimotor skill acquisition [39], creative engagement [40–42], and social engagement [43].

To test the hypothesis that NDT improves CIN symptoms more than PA, we propose to test the effect of NDT in the form of social dance versus (v.) PA in the form of home exercise training. Specifically, we will evaluate the effect of Adapted Argentine Tango practice (NDT-Tango), a light-moderate intensity social dance adapted for persons with mobility deficits [44, 45], on functional and patient-reported symptoms of chronic CIN among BC survivors. Research by the multiple principal investigators (MPIs) established NDT-Tango as feasible for

aging survivors (up to 82 years old) to engage in biweekly at a mean (SD) dose of 33 [4] min/session with high satisfaction and positive effects [43, 46]. We hypothesize that NDT-Tango will improve function and sensation among BC survivors who demonstrate CIN with balance dysfunction.

Objectives

The primary objective of this experiment is to assess the intervention effect of partnered NDT-Tango v. HEX intervention on biomechanically-measured functional variables that predict fall risk among BC survivors with CIN and postural control deficits. Secondary measures include functional and patient-reported outcomes (PROs) related to CIN symptom load and/or fall risk. Additionally, we will evaluate within-session effects of training on postural control and PROs. We hypothesize that 8 weeks of NDT-Tango practice (2×/week; 15–30 min dose of movement-to-music/session) will improve the dynamics of posture (Aim1) and gait (Aim2) more than 8 weeks of HEX (2×/week; 30–60 min dose of PA/session) among BC survivors with CIN and demonstrated balance dysfunction.

Methods

Study design

In a single-center, prospective randomized controlled study of superiority between two interventional arms, eligible participants who provide informed consent are randomly assigned to the NDT-Tango experimental or the HEX active control intervention group in a 1:1 ratio. The study primary endpoint evaluates change between baseline and 8 weeks of intervention in postural control variability, a measure of fall risk [47–50] (Aim1). As an exploratory endpoint, we will assess another biomechanical measure of fall risk: coefficient of variability for stride speed (CVspeed) [46, 51] (Aim2) after 8 weeks of intervention. Table 1 presents the data collection schedule, formatted per the Standard Protocol Items: Recommendations for Interventions Trials (SPIRIT) recommendations [52–54]. Figure 1 depicts the overall study design as a flow diagram. As detailed in Table 1, outcomes are assessed at baseline (i.e., repeatedly over 2 weeks prior to intervention), midpoint (i.e., after 4 weeks of intervention), endpoint (i.e., after 8 weeks of intervention), 1-month follow-up (i.e., 1 month after intervention completion), and weekly in the 6 months (mos) following intervention end. Secondary outcome measures include clinical and biomechanical tests of function that complement the primary outcome measures, patient-reported outcomes, and falls incidence. Tertiary outcome measures, depicted in Table 2, include within-session effects, satisfaction collected at session end, and surveys used to

Table 1 SPIRIT report of intervention effect outcome measures

Timepoints	Study period						
	Enrollment	Allocation	Post-allocation				6-month follow (assessed weekly)
	3 + months post last taxane exposure	0	Baseline	Midpoint (4 weeks)	Post (8 weeks)	1-month follow-up (12 weeks)	
Enrollment:							
Eligibility screen	x						
Informed consent	x						
Allocation		x					
Interventions:							
Tango group			x	x	x	x	x
HEX group			x	x	x	x	x
Assessments:							
Postural control dynamics during silence (primary outcome Aim1) (QEC)			x*	x	x	x	
Postural control dynamics during music listening (QECm)			x*	x	x	x	
TUG			x	x	x	x	
TUG-Cog			x	x	x	x	
Mini-BEST			x		x		
6mwt			x		x		
Gait dynamics (primary outcome Aim2)			x		x		
Co-contraction index (CCI)			x		x		
Satisfaction with Intervention				x	x		
Falls incidence				x	x	x	x
Ecological Momentary Assessment (EMA) of select symptoms			x*	x	x	x	x
CIPN-20			x*	x	x	x	
BPI			x*	x	x	x	
BFI			x*	x	x	x	
Intrinsic Motivation				x	x		

*measure repeated 4 times

inform monitoring and shaping of interventions including rating of perceived exertion (RPE; 6–20 scale) and Intrinsic Motivation Inventory (IMI). In addition, at the suggestion of participants, we repurposed the RPE to query mental exertion v. physical exertion and call this a Rating of Perceived Mental Exertion (RPME; 6–20 scale).

Repeated baseline schedule

Select measures, indicated in Table 1 with an asterisk, are collected repeatedly prior to intervention to characterize within-subject variability (WSV) in CIN-related deficits and symptoms at baseline. This is relevant for clinical decision-making because WSV represents the typical day-to-day means and variability per measure

that clinicians can expect to see among patients with CIN. Knowledge of WSV per measure enables longitudinal tracking of maintenance, improvement, or decline in function for individual patients [47]. Repeated baseline characterization of postural control is achieved through collection of the postural control dynamics during silence (QEC) test at the beginning of up to 5 visits, including the first screening test of postural control and 3–4 additional days. Within the current paper, we report results of this characterization of postural control variables known to predict future falls, [47] and results of our assessment regarding whether there is an effect of measuring postural dynamics repeatedly during this baseline period of testing. In addition to QEC, we collect postural control

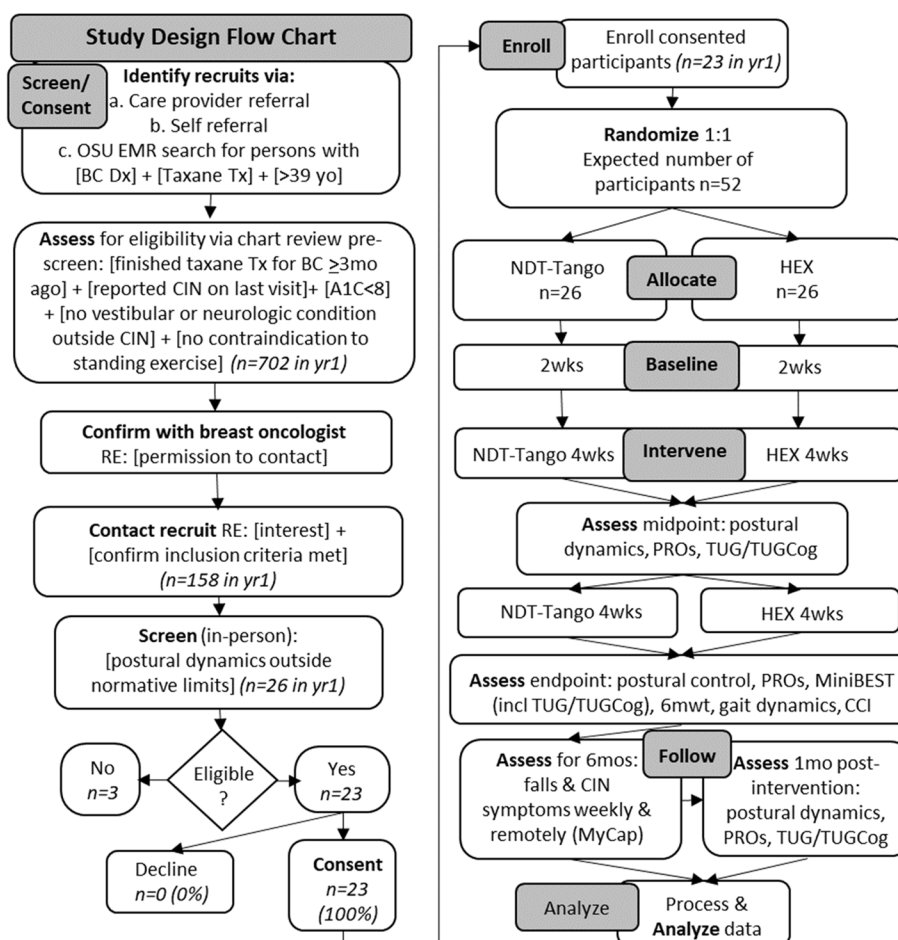


Fig. 1 Flow chart of study design from screening through enrollment, allocation, intervention, follow-up, and analysis with assessments indicated throughout

dynamics during music listening (QECm) and PROs at the beginning of baseline visits. At the end of baseline visits, we collect postural control and PROs again as well as rating of physical and mental exertion perceived during any activity involved in baseline testing (i.e., MiniBEST, 6mwt). To confirm the expected effect of no physical activity, we conduct at least one “resting” baseline test in which participants remain seated and engage in conversation with research staff for 20 min before re-testing QEC, QECm, and PROs. This extensive repeated baseline design allows us to compare intervention activity effects relative to outcome assessment activity (i.e., 6mwt, MiniBEST) and no physical activity (i.e., 20 min of conversing with research staff).

Study setting

The study is currently being conducted at The Ohio State University (OSU) and the research protocol has been approved by The OSU Institutional Review Board. Participants are recruited from the Stephanie Spielman

Comprehensive Breast Center (SSCBC) oncology outpatient facility as well as from the greater central Ohio (OH) community. Consent is obtained in a quiet and private setting prior to research activity either electronically, via REDCap, or using a paper version which is stored securely in a locked cabinet within a secure research-dedicated space at the host institution. Assessments (i.e., screening, repeated baseline, midpoint, post intervention, and 1-month follow-up assessments) are performed in an outpatient care clinic setting or within the volunteer’s home environment, as preferred by the survivor. The Tango intervention is performed at the outpatient care clinic in a group setting of up to 5 survivors at a time with their invited partners. The HEX intervention is performed by the participant in their own home environment. Participants are compensated \$20 per in-person assessment session that does not involve interventional instruction, with an additional \$20 compensated for sessions that require sensors to be applied to the skin (potential total of \$180 for participation in all assessments).

Table 2 SPIRIT report of within-session assessments

Session type	Baseline		NDT-Tango		HEX (remote in MyCap app)	
	Before beginning session (Beg)	After completing session (End)	Beg	End	Beg	End
Assessments:						
[QEC]	x	x	x	x		
[QECm]	x	x	x	x		
[CIPN-20]	X ^a	xb	X ^a	xb	X ^a	xb
[BPI]	X ^a		X ^a		X ^a	
[BFI]	X ^a		X ^a		X ^a	
[CTCAE (select symptoms)]	x	x	x	x	x	x
[EMA CIPN]	x	x	x	x	x	x
[EMA Pain]	x	x	x	x	x	x
[EMA Fatigue]	x	x	x	x	x	x
[Satisfaction with session activity as neuropathy Tx]				x		x
Collected to facilitate trial monitoring and intervention shaping:						
[Rating of Perceived Exertion (RPE)]		x		xb		xb
[Rating of Perceived Mental Exertion (RPME)]		x		xb		xb
[Intrinsic Motivation]				X ^c		X ^c

^a Recall period = during the last 2 weeks OR since we last saw you (if less than 2 weeks)

^b recall period = during the activity just performed

^c queried intermittently (i.e., every 2 weeks)

Eligibility criteria

Participants are eligible to join the study if they are ≥ 40 years old, diagnosed with BC (stage I–III), experiencing CIN (European Organization for Research and Treatment of Cancer, Chemotherapy-Induced Peripheral Neuropathy outcome measure (CIPN-20) sensorimotor score > 1), finished with taxane-based chemotherapy treatment for at least 3 months, able to understand and comply with directions associated with testing and study treatments, and if they demonstrate postural control measurements outside of normative values [47]. Participants are excluded from the study if they meet any of the following exclusion criteria: pre-existing vestibular disorders, history of motor deficits or neurological disease other than CIN-related, poorly controlled diabetes (HbA1c ≥ 8.0), non-ambulatory or lower extremity amputation (assistive devices allowed), participating in physical therapy during the study, or contraindicated to participate in unsupervised activity due to other issues (e.g., herniated vertebral disc).

We expect the study population to be representative of the demographics of the BC survivorship population. The CDC reports that 99% of BC cases occur among women and only 1% among men. Therefore, we anticipate that those who participate in this study will be almost exclusively women. The CDC census reports the rate of new BC cases in 2019 per 100,000 women by race as White/

non-Hispanic 132.5, Black/non-Hispanic 128.4, American Indian and Alaska Native/non-Hispanic 101.7, Asian and Pacific Islander/non-Hispanic 104.5, and Hispanic 101.9 [55].

Recruitment and screening

The research opportunity is posted on public-facing websites including ClinicalTrials.gov (NCT05114005), Research Match, and Study Search to allow volunteers to self-refer by calling a dedicated medical center phone line or emailing the secure address Tango@osumc.edu. Furthermore, advanced practice providers (APPs) refer eligible and interested clients to our research staff consisting of two clinical research assistants to complete screening. Clinical research assistants work onsite within the SSCBC outpatient facility at least 2 days per week to follow up with volunteers and referring APPs. In addition, queries are run within electronic medical records (EMR) to identify potentially eligible clients of the OSU academic medical center system. Reports are generated using the criteria of a taxane-based chemotherapy plan being entered in the EMR and filtered by age (> / = 40 years) and prescribing physician. Through chart review, we identify the subset of clients who meet these study inclusion criteria: (a) CIN symptoms reported within their last clinic visit on record, (b) no vestibular or neurologic disorder other than CIN, (c) no

uncontrolled diabetes (HbA1c < 8.0), and (d) not currently participating in physical therapy. Researchers are provided a list of potential recruits from a pharmacist on staff with SSCBC, which includes name, stage of breast cancer, whether they were exposed to taxane-based chemotherapy, and medical record number. Clinical research assistants pre-screen participants from this list using the previously mentioned criteria.

For those identified as eligible, we request approval from the treating oncologist to contact the client for recruitment purposes. Eligible clients who are approved for recruitment by their oncologist are contacted by phone to inquire whether CIN symptoms persist and, if so, to determine interest and availability in participating in this study. Those able and interested to participate are asked to schedule in-person screening of postural control, which involves attempting a short but challenging balance task reported to distinguish fallers from non-fallers by Maki et al. (1994) [48]. As previously reported [56], to perform this task volunteers stand quietly and bilaterally for 30 s on a balance plate (Bertec Corp, Columbus, OH) with eyes closed eyes (QEC). Center of pressure (COP) variables of interest are calculated per Prieto [57] and Roerdink [58]. Survivors are offered enrollment in the study if they demonstrate QEC postural control function that is outside of the estimated 70% confidence interval (CI) [47] of healthy, age-equivalent normative values in (1) COP ellipse area, (2) medial–lateral variability, (3) medial–lateral velocity or outside of the estimated 95% CI in terms of (4) COP complexity. Values corresponding to these inclusion thresholds are reported in Table 3.

Adequacy of the potential participant pool

Approximately 1200 new BC patients are seen annually at the OSU SSCBC, 240+ of whom will receive taxane-based cytotoxic chemotherapy annually. We expect at least 50% of BC patients treated with cytotoxic chemotherapy to experience persistent CIN and measurable postural control deficits [47] yielding an eligible patient pool that grows by approximately 120 BC survivors per year or 10 eligible individuals per month. Given the interest in non-pharmacologic options for survivorship treatment and lack of pharmacologic interventions to treat CIN [59], we anticipate that approximately 20% of eligible patients will be interested and consent to enroll in the study for a projected accrual rate of 2 new participants enrolled per month. In addition to this annual presentation of new individuals with BC, OSU houses an established survivorship program that serves thousands of BC survivors, including survivors not seen within our medical center, who have been living with chronic issues of survivorship such as CIN for years. Finally, these survivorship efforts are continually growing their reach by addressing and overcoming issues of access to survivorship programming.

Lastly, attending classes with an invited guest (partner) was found to affect engagement, by improving attendance of survivors [43]. Therefore, we encourage participants to invite a partner to attend training sessions with them and for those who prefer not to invite from their social circle, we provide partners from a pool of talented university students within the OSU Department of Dance and School of Health and Rehabilitation Sciences to activate social engagement for enrollees randomized to the Tango experimental intervention.

Table 3 Postural control norms among $n = 23$ breast cancer survivors with CIN and balance dysfunction

Variable of interest	Age	Years since last taxane exposure	COP Ellipse Area (COPa)	COP variability in medial–lateral direction (RMSx)		COP velocity in medial–lateral direction (Vel_x)		COP Complexity	
Mean	60.9	2.6	1012	5.66		11.1		0.474	
SD	9.8	2.0	846	2.19		5.2		0.159	
Min	40	0.25	230	1.95		4.5		0.207	
Max	78	6.2	3423	11.7		23.1		0.93	
Inclusion threshold	≥40	≥0.25	>400	>4.0		>9		<0.6	
% cohort who met inclusion criteria	100%	100%	75%	70%		57%		84%	
<i>Additional variables calculated that were not used for initial screening are reported below</i>									
Variable	Path length (PL)	PL Normalized	RMS_r	RMS_y	Vel_r	Vel_y	TUG(s)	TUGCog(s)	6mwt(m)
Mean	765	76.3	10.6	8.78	26.1	21.1	10.44	13.72	374.6
SD	358	33.1	4.27	3.97	11.1	9.51	2.29	4.06	67.2
Min	91	8.48	5.55	3.91	10.9	6.52	6.02	9.1	245.1
Max	1414	147	23.2	21.7	47.2	37.7	15.06	23.87	516.1

Interventions

Both interventions — NDT-Tango and HEX — occur over an 8-week period at a frequency of 2× per week. No intervention session in either arm will last longer than 1.5 h total.

Experimental intervention: NDT-Tango

The NDT-Tango intervention will consist of 16 Adapted Argentine Tango (Adapted Tango) sessions, adapted for neurorehabilitation by co-investigator (Co-I) Hackney [44, 60], and taught by the principal investigator (PI) Worthen-Chaudhari. Per session, we aim to deliver a NDT dose (defined as skilled movement-to-music) of at least 10 min and no more than 35 min, with breaks for water and rest offered at least every 10 min. Recommendations for implementation of Adapted Tango as a neurologic intervention focus on prevention of falls, use of implicit learning techniques to convey skilled movement goals, the structure of class (warm-up, lesson, cooldown), scaffolding and shaping lessons over time to establish competency in fundamentals, modifications deemed necessary for specific deficits, and music selection [44, 60]. Musical compositions (songs) used within this intervention are from the tango genre with a duration of 1.5 to 5 min. Participants may sit or rest as needed during or between songs. Instructors ensure appropriate activity wear choices (e.g., footwear, breast support). In addition, instructors ensure qualified volunteers are present to partner with participants. Instructors complete 16 h of training with Co-I Hackney as well as a certification exam to become qualified to teach the Adapted Tango technique. Volunteers who will partner participants for this study complete Co-I Hackney's 4 h Balance Management program plus an additional 3 h of training with PI Worthen-Chaudhari during which live instruction skills are evaluated by the PI before volunteers are cleared to partner participants.

The MPIs (Worthen-Chaudhari and Lustberg) previously demonstrated that an NDT-Tango dose of 32.9(3.9) min movement-to-music is feasible for cancer survivors with postural control deficits to participate in at a rate of 2× per week. To optimize factors mediating intrinsic motivation, instruction aims to achieve high Enjoyment and Perceived Competence among participants with low Pressure/Tension [61–63] as measured by IMI. We administer the IMI every 2 weeks to assess achievement of these instructional goals. To assure integrity of the training, Co-I Hackney assists MPIs Worthen-Chaudhari and Lustberg to monitor fidelity of the intervention. This subset of our team — representing 2 former professional dancers turned dance scientists and 1 oncology practitioner — monitor participant symptoms and

training progression and troubleshoot any issues that arise through weekly virtual meetings.

Active control intervention: home exercise

The active control intervention consists of an evidence-based, structured home exercise program (HEX) based on the 8-week PA intervention for CIN described by Zimmer et al. (2018) [22]. This PA design was modified for home exercise delivery among BC survivors with CIN in collaboration with OSU-based leaders in physical therapy who specialize in BC oncology rehabilitation (e.g., co-author Hock). This program combines endurance, resistance, and sensorimotor training for 45–60 min per session performed 2× per week [22]. Participants in the HEX group will be provided with a yoga mat and resistance bands with which to perform the interventional exercises. HEX participants will be prompted to report adverse events, symptoms, and barriers to participation 2× per week through the Research Electronic Database Capture (REDCap) MyCap application that is installed on participant smart phones. HEX instructional materials include (1) a manual with pictures and text descriptions per exercise that can be shared as a pdf document or paper binder and (2) short demonstration videos per exercise, viewable on a dedicated YouTube channel (i.e., @Tango_HomeExercise). HEX participants will be given the direct YouTube link and the channel will remain private, meaning only accessible by those with the link. Following completion of repeated baseline testing, research staff will work with HEX participants in a single 1:1 session to instruct in PA performance and modify exercises as needed in collaboration with the participant. Research staff with expertise in exercise instruction, including PI Worthen-Chaudhari who is certified through the American Council on Exercise (ACE) as a Medical Exercise Specialist (CMES), will determine what PA level HEX participants will start with: seated, beginning, moderate, or advanced. Research staff will contact HEX arm participants 2× per week to discuss potential required intervention shaping and modification as well as to offer social connection, a schedule designed to match social connection provided to participants of the experimental intervention group. If barriers to participation are identified, research staff will address by modifying the exercise form, challenge level, duration, and/or schedule of PA. For instance, participants who advance beyond the moderate challenge level of HEX exercise performance will be provided with the option of using a pair of 3-pound cuff weights to increase resistance challenge above what is provided by resistance bands. Participants who complete the 8-week HEX intervention will be offered participation in 16 Tango lessons after study completion.

Procedures/plans to ensure safety of interventions

Pain management

It will be critical to address the possibility that pain may interfere with training sessions [64]. While both music and movement have the potential to reduce cancer-related pain, and our prior work did not identify pain as a barrier to participation in the intervention, nevertheless, a structured plan is indicated for assessing and addressing the potential for pain in this population. Use of gabapentin, opiates, and/or duloxetine for neuropathic pain management will be allowed and addressed in statistical analysis as concurrent medications. We will monitor pain as we have previously [9], using question 6 from the Brief Pain Inventory, a visual analog scale (VAS) on which participants will rate how much pain they are in “right now” on a scale of 1 to 10 (10 being high). Pain ratings will be collected before and after each training session. Using a scheme the PI applied previously to guide intervention trials in neuropathic populations [65], if pain at the start of a session is more than 2 points above the start of the prior session, we will consider training to be contraindicated. If pain at the end of a session is more than 2 points above pain at the start of that session, we will require 2 days of rest before attempting the next training session and will not commence future training sessions until pain is within 2 points of the last training start. If pain remains elevated, or participation is not possible, for 4 sessions in a row then study participation will be terminated. Pain monitoring of NDT-Tango participants will occur at the time of each session and procedures will be carried out in-person by the PI via 1:1 discussion with the participant in a private setting. Pain monitoring of HEX participants will occur bi-weekly, via review of MyCap entries, and procedures will be carried out by research staff via phone contact.

Functional guarding

The Tango partner hold (aka “embrace” or “frame”) provides an opportunity to support participants in the upright position as well as to guard against falls during Tango movement practice. To train staff and volunteers in how to apply the Tango partner hold, and other techniques for best practices in functional guarding, Co-I Hackney conducts a 4-h standardized fall prevention (Balance Management) training program with each study personnel. This fall prevention training is in addition to Hackney’s 16-h certification program, with certifying exam, that prepares staff to teach Tango as a medically relevant activity for persons with neuropathology and is a standard offering from ACE.

Inclement weather

In the event of weather that creates unsafe driving conditions for planned in-person NDT-Tango intervention sessions, a video conference link (i.e., Zoom) will be sent to participants as an option through which to participate. Those who choose to participate will be instructed to position themselves in the corner of a room and/or near a stable surface (e.g., back of a stable chair that is not on wheels; countertop) such that the walls of the room and/or stable surface are available for support as needed. Participants will be instructed to aim the camera toward their position, enable video sharing, remain unmuted, and join with computer audio. No partner hold will be used; instead, participants will face the video display and mirror movement demonstrated by instructors in their camera view. At least one research staff person will monitor participant feeds to ensure safety throughout the video conference period.

Seated activity option

There is a chance that functional impairments or deconditioning may create challenges with prolonged standing (i.e., more than 1 min of standing at a time). Participants in both arms may stop to rest as desired. For the NDT-Tango arm, shorter compositions of 1.5 min or less will be used when participants are challenged with severe impairment or deconditioning. If we enroll a participant who cannot stand for longer than 1 min at a time, then that participant will be encouraged to sit as needed and to continue HEX or NDT-Tango movement from a seated position.

Depression and anxiety monitoring

The psychosocial state of participants is relevant to this project in terms of recruitment, retention, and effect. Depression and anxiety tend to be higher among cancer survivors than in the general population [66]; it is important to capture these aspects of the patient experience. The Patient-Reported Outcome (PRO) version of the *Common Terminology Criteria for Adverse Events v5 (CTCAE)*, developed by NCI, is a standard protocol in oncology to screen for signs of depression and anxiety associated with cancer treatment or progression [67]. We use the PRO-CTCAE to screen for sadness and anxiety per visit and will monitor and compare descriptive statistics between groups. Increases in the severity of sadness or anxiety of 2pts or greater between sessions are addressed by the MPIs. Monitoring of NDT-Tango participants occurs at the time of each session; the PI invites the participant to leave the group setting

to discuss. Monitoring of HEX participants occurs bi-weekly; MPIs reach out to the participant via phone contact.

COVID management plan

COVID vaccination was publicly available by the time of recruitment start in Aug 2021. Per medical center policy, we strongly encouraged COVID vaccination and maintained masking among all participants and staff during in-person visits. While COVID vaccination status was not codified as an inclusion criterion, we held separate Tango group sessions for vaccinated and unvaccinated participants as requested.

Outcome measure procedures and analysis

Primary outcome measures

Postural dynamics (Aim1) We measure postural dynamics as postural control or sway. The primary outcome, postural control variability, is measured through biomechanical data collection during a challenging 30-s balance task, that has been described previously [47, 56]. Briefly, participants are instructed to stand quietly and bilaterally for 30 s with eyes closed (QEC) on a portable balance plate (Bertec Corporation, Columbus, OH), with feet set apart (5 cm), and arms relaxed at their sides. To control for the effect of auditory stimulation [32], the test is performed in silence within a quiet environment. To control for known responses to vision obstruction, participants are asked to focus on a point approximately 8 ft in front of them at eye level prior to closing their eyes at the moment collection commenced [4, 9, 43, 47, 56] and in response to the researcher's countdown of "3.0.2.0.1.. close." Biomechanical data describing postural sway are acquired using custom software written in LabVIEW at a sampling frequency of 1000 Hz and consist of one channel of force data (Fz) and two channels of moment data (Mx, My) over time. From these data, we calculate the COP time series for the 30-s duration of QEC condition performance. We then calculate the primary outcome measures of COP variability in resultant and medial-lateral planes (RMSr, RMSml) for this 30-s duration per Prieto [57].

Gait dynamics (Aim2) We measure gait dynamics as gait variability [33, 51, 68] and stability [69–71] using data from inertial measurement units affixed to the foot, leg, thigh, pelvis, and/or lower cervical spine during the 6-min walk test (6mwt). The primary outcome measure for Aim2, CVspeed, will be calculated from acceleration data [72]. Steady-state walking epochs are detected from gyroscopic data.

Secondary and tertiary outcome measures

Postural dynamics Starting from the QEC COP time series data described in *postural dynamics (primary outcome measure)*, we calculate additional linear [57] and non-linear [58] secondary outcome measures. In addition to linear COP primary outcome measures (1) sway variability resultant (RMSr), (2) sway variability in the frontal plane (RMSml), and (3) variability in the anterior-posterior plane (RMSap), we calculate secondary outcome measures (4) 95% ellipse area (COPa), (5) path length (PL), and (6–8) mean velocity in resultant, medial-lateral, and anterior-posterior planes (COPvr, COPvml, COPvap). We analyze one non-linear COP measure: sample entropy of the resultant COP position using the increment calculation method (SEI) with constant values applied of $m=3$ and $r=0.3$ [58]. Entropy of postural responses represents the automatic complexity [73] of neuromotor control that is available to an individual and has been found sensitive to disease states such as brain injury [74] and neurodegenerative disease [75–78] as well as to skill mastery [79] and attentional focus [58, 80, 81]. Within this manuscript, we report descriptive statistics for these primary and secondary outcomes describing postural control and for select clinical measures of function among BC survivors enrolled to date ($n=23$). Within-subject variability at baseline as well as intervention effects will be reported in future publications.

Function We measure function using the following validated clinical tests, instrumenting some of them to accomplish biomechanical quantification of the motion performed during the tests. All functional tests are performed in a clinical space or the participant's home in an area that is distraction free. The *Timed Up-and-Go test (TUG)* is a timed test of a person's ability to stand from a chair, walk 10 feet, turn around, and return to sitting [82] with shorter times indicating better functional balance. Presence of CIN has been associated with longer TUG times [11–14]. To measure dual-task function, we use the TUG performed simultaneously with a cognitive task consisting of audibly counting backward by 3 s or 4 s (*TUGCog*). Blackwood and Rybicki (2021) reported that the TUGCog threshold of ≥ 11.32 s identified BC survivors at risk of falling (sensitivity=0.64 and specificity=0.8) [13]. To measure dynamic balance function we collect *Mini Balance Evaluation System Test (MiniBEST)*, which evaluates sensory organization, anticipatory and reactive postural control, and dynamic gait indices [5] and was found to discriminate BC survivors from controls in at least 1 prior study [12]. Finally, to measure physical function in terms of endurance and mobility we

collect 6mwt, in which shorter distances correlate with poorer function including among survivors with CIN [83]. Meta-analysis of 6mwt results among adults with pathology or fear of falling indicate that 14.0–30.5 m represents the minimum clinically-important difference (MCID) for improvement in this measure [84]. The 6mwt is performed within an oncology clinic, in a quiet area without distractions. Participants walk in a loop with the following configuration: a straight distance of 65 feet (ft) minimum marked by tape on the floor that participants turn around to their left; participants are cued to walk straight between tape marks and to turn comfortably at the end of each straightaway at the fastest pace they feel they can maintain for 6 min, resting as needed in a standing position before continuing.

Gait dynamics Measures of walking variability and stability have been found indicative of mild cognitive impairment [85], age [86], fall risk [51, 68, 87], and neuropathy [88, 89] regardless of age or type of cancer [90] including specifically in BC [10, 89, 91]. Using a portable inertial measurement unit (IMU) system while participants perform the 6mwt [92], stride-to-stride measures of variability previously found sensitive to health status will be calculated from the straight, steady-state sections of the 6mwt loop pattern [46, 51, 68]. Local dynamic stability [93–96] and orbital stability [10, 96, 97] will also be analyzed, as measures that have been shown sensitive to neuropathy and used previously by our team to measure intervention effect among BC survivors [98].

Co-contraction index (CCI) is a ratio of the activity produced in agonist v. antagonist muscles of the leg that provides unique insight into neuropathy effects [99]. We calculate this ratio from electromyographic (EMG) signals of the tibialis anterior, gastrocnemius, and soleus muscles. We calculate this muscle activity ratio during performance of select MiniBEST sensory organization tests as well as during QEC and QECm postural dynamics trials and the 6mwt.

Influence of music listening on postural dynamics We measure the influence of music listening on postural dynamics (QECm) per the protocol established by Ross et al. [32]. After completing the QEC trial (and always in this order), the participant is asked to step off the balance plate and walk or march in place for a few steps before being asked to step back on the plate into the QEC posture while we begin playing the musical composition "La Cumparsita" at a volume that is deemed loud but not uncomfortable by the participant. Participants are instructed to look at a defined spot approximately 8 feet away, during approximately, and no less than, 10 s

of acclimating to auditory stimulus, before being cued to close their eyes for collection of the QECm trial. Auditory acclimation is accomplished in the following way: we instruct participants to listen to the music, focusing specifically on the periodic rhythm (i.e., "beat"). To facilitate beat perception, we provide external cueing (i.e., snapping fingers or clapping hands to the musical beat) for approximately 4 s. We then extinguish external cueing over a 2-s period, by quieting then ceasing the cueing sound. Then participants are allowed to acclimate to auditory stimuli, without external cueing, for an additional 4 s before research staff verbalize the directions "3.0.2.0.1..close," speaking one word per beat for a measure of 4 counts and start of postural control data recording as participants close their eyes. COP-based variables of interest are calculated as described for the QEC trial.

Patient-reported outcomes (PROs) Patient self-report surveys are administered through The Ohio State University administered instance of the REDCap database for in-person visits and through the REDCap platform's MyCap mobile application (MyCap) for data entry that participants perform remotely (e.g., HEX activity, fall tracking in 6-month follow-up). Answers are reviewed manually by authorized research collaborators, who prompt participants to complete or clarify answers as needed and document their responsibility for review from a list of authorized data reviewers. Within this study, we collect the following PRO measures: (i.) *European Organization for Research and Treatment of Cancer's Quality of Life Questionnaire, Chemotherapy-Induced Peripheral Neuropathy (CIPN-20)*: is a validated 20-item patient-reported questionnaire instrument for longitudinal evaluation of neuropathy symptoms induced by chemotherapy(108). While validated for a recall period of "during the past week" we use modified forms of the CIPN-20 to query items for the recall periods of "during the activity just performed" (at the end of sessions) and "right now" (at the beginning and end of sessions). (ii.) *The Brief Pain Inventory (BPI)* is validated for ecological momentary assessment (EMA) of immediate and retrospective (prior 24 h) self-reported pain and relevant functional capacity in our target population [100]. (iii.) *The Brief Fatigue Inventory (BFI)* is validated for EMA of immediate and retrospective (prior 24 h) self-reported fatigue and relevant functional capacity in our target population. (iv.) *Ecological momentary assessment (EMA) of immediate symptomatology*. Using the Patient-Reported Outcome version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE), cancer-related symptoms such as balance problems, nausea or vomiting, dizziness, sensitivity to light or noise, feeling like "in a fog", confusion, sadness, and anxiety can be queried for the

recall period of the past 7 days [101]. This study requires query of symptomatology in the immediate moment, or “right now”: we capture these symptoms in this time-frame using an EMA tool that prompts for self-report of symptom severity “right now” called the Sports Concussion Assessment Tool (SCAT) symptom inventory [102]. The SCAT was created for and validated among individuals with mild traumatic brain injury, however, the SCAT symptom inventory queries the desired PRO-CTCAE items (i.e., 39–56) in the time frame of “right now” using a 7-point Likert scale (0 = no incidence; 6 = high severity), which affords greater sensitivity than the PRO-CTCAE 4 point Likert scale (1 = no incidence; 4 = high severity), and has been validated for use among individuals with known cognitive deficits. Therefore, we use the SCAT symptoms inventory in lieu of the PRO-CTCAE to query the desired subset of the PRO-CTCAE symptoms with regard to how participants feel “right now” with sensitivity and in a format appropriate for individuals who might have cognitive deficits associated with chemotherapy exposure. (v.) *Activity tracking*: Participants are asked if they have participated in the following activities: physical therapy, occupational therapy, fitness activity, other therapeutic or fitness activity. If any category of activity is checked as having occurred then participants are prompted to estimate the amount of time spent doing the activity since we last saw them (hours, minutes). (vi.) *Falls tracking*: Falling is defined as an unexpected loss of balance in which an individual comes to rest at a position lower than before the unexpected event [103]. We elicit self-report of falls and loss of balance using the question “How many times have you fallen or felt like you lost your balance since we last saw you?” Responses are typed by the participant and reviewed for incidence of falls, incidence of loss of balance, and details offered about either incidence. (vii.) *Barriers to participation*: Participants are asked “To help us understand barriers to participation, if you missed a session, please indicate the reason why you were unable to attend (e.g., schedule conflict, transportation, didn’t feel up to it, forgot).” (viii.) *Satisfaction with intervention* is measured after each class using a 7pt Likert scale and prompt for feedback about what did/did not work per class. Feedback is used to improve future sessions. (ix.) *The Intrinsic Motivation Inventory (IMI)* was developed from the perspective of Self Determination Theory to assess 7 dimensions of experience: Interest/Enjoyment, Perceived Competence, Effort/Importance, Pressure/Tension, and Choice [104]. We administer the 9-item short form of the IMI monthly to optimize instruction around low Pressure/Tension and high Interest/Enjoyment [61, 62] as well as to explore relationships between adherence, motor effects, and IMI dimensions including perceived benefit (i.e., Effort/Importance).

Power calculations

We targeted an effect size in postural control variability of 1.22 (Cohen’s *d*) based on pilot data from five cancer survivors with postural control deficits at baseline who participated in Tango practice [43]. Enrolling 26 participants per group (52 total) allows for a drop-out rate of up to 45% to yield full follow-up on 14 participants per arm and 85% power to detect the target effect size at the 5% significance level. This drop-out rate is conservative, corresponding to criteria that we used previously to assess an intervention’s feasibility [43, 105]. Regarding gait variability (i.e., CVspeed), primary outcome for Aim2, our pilot data [46] show an effect size of 0.73 (Cohen’s *d*) from seven survivors, not screened for CIN or postural control deficits, who completed the NDT-Tango intervention. The 26 enrolled participants per arm would yield 73% power to detect an effect of this magnitude.

Randomization

After a participant has both qualified and agreed to participate in this trial, researchers randomize them 1:1 into one of two groups: Tango or HEX. This is accomplished using a randomization schedule that was generated by the PI in Microsoft Excel prior to recruitment initiation, approved by the statistician, and stored as a password-protected text file. One member of the research team is blinded to the randomization schedule prior to allocation; this researcher schedules the potential participant throughout recruitment, screening, consenting, and group assignment. At the point of allocation, a second member of the research team accesses the randomization schedule, communicates group assignments, and documents allocation updates in the stored randomization schedule text file. Study participants cannot be blinded; they will inevitably know their group assignment as they are participating in one of two distinct styles of physical activity intervention.

Data management

Each study participant is assigned a unique six-digit identification number that cannot be traced to their protected health information. Participant data, coded using these identification numbers, are stored in a central database using REDCap. REDCap is a secure web-based platform that is designed for clinical trials which meets both HIPAA and 21 CFR. Clinical and biomechanical data are collected by study staff who input results into REDCap manually or via data upload. PRO data is manually entered into REDCap by study participants: Tango participants fill out questionnaires within REDCap before the start and at the end of each Tango session and HEX participants fill out questionnaires within MyCap, a mobile device application of REDCap, before the start and at the end of each home exercise session.

Statistical analysis

All outcome analyses will be performed on an intent-to-treat basis, and all hypothesis tests will be two-sided and at the 5% significance level. Linear mixed models will be used to model changes in postural, biomechanical, and PROs. Fixed effects will be included for time, treatment, treatment-by-time interactions, and baseline outcome measures. Random effects for subjects will be used to account for correlations between observations from the same subject. The primary estimand will be the contrast representing the difference in mean change in outcome measure from baseline to week 8 between treatment groups. While we expect balance between groups due to randomization, we will adjust for potential confounders including age, body mass index, concurrent medications, and other variables if an imbalance between groups occurs by chance. Pearson's *R* will be calculated to correlate postural control and balance outcomes and PROs. We use a longitudinal mixed effect model to analyze all outcomes and do not impute missing data. Subjects will be analyzed in the group to which they were randomized regardless of compliance with the assigned intervention. We will evaluate the effect of the number of intervention sessions completed on outcomes.

Visit effect (repeated baseline testing and intervention effects calculated separately)

Per participant, postural control data (QEC) are collected on 3–5 different days prior to intervention. Descriptive data are calculated. Log-transformed data are assessed regarding the effect of visit number. Results are presented below for the subset of participants who had completed repeated baseline testing at the time of this manuscript preparation ($n=23$).

Within-session effect

At the beginning and end of each in-person intervention session, we collect a subset of biomechanical and PRO data with which to evaluate the effect of the session. This subset includes the following biomechanical data, collected at the beginning and end of sessions unless otherwise indicated: postural control variables QEC and QECm. This protocol also includes the following EMA of PROs, collected at the beginning and end of sessions unless otherwise indicated: CIPN-20 since we last saw you (beginning only) or during the activity (end only); CIPN-20 momentary designed to assess the moment of instrument completion, BPI since we last saw you (beginning only); BPI “right now”; BFI since we last saw you (beginning only); BFI “right now”; SCAT as a generalized measure that covers neurocognitive physical and emotional symptoms impacted by neurotrauma; RPE (end only); RPME (end only); and satisfaction with

intervention (end only). Each measurement is collected using a computer, a touch screen tablet, or a cell phone.

Intervention effect

A linear mixed model will be applied to analyze the intervention effects for biomechanical outcomes (postural control in silence and to music, gait stability, and CCI); clinical outcomes (TUG, TUGCog, MiniBEST, 6-min walk test (6mwt)); and PROs.

Trial monitoring

No regular external trial auditing is scheduled. However, trial monitoring personnel include a safety officer (SO) appointed by the funding body (NIH) and the two PIs, Worthen-Chaudhari (PI) and Lustberg (MPI). Study staff and the PI will review information regarding safety, data quality, and validity on a biweekly basis, informing the MPI immediately of any concerns. All data related to recruitment, screening, enrollment, baseline measurement, and intervention measurement will be reviewed weekly by the PI. Data collected from enrolled participants will be reviewed weekly by the statistician with the PI. Additional investigators and study staff will be asked for their input or expertise as needs arise. If unforeseen hazards or risks are identified that may lead to serious adverse events, the PI consults the appropriate members of the team, including the NIH-appointed SO.

Adverse event monitoring and reporting

Both Tango and HEX participants answer a series of questions twice a week. Participants are asked to report adverse events at the beginning of each Tango or HEX session via REDCap or MyCap, respectively. Researchers review REDCap responses prior to the start of Tango lessons and if an adverse event is reported, the PI is notified. Researchers review MyCap responses once a week and if an adverse event is reported, the PI is notified.

Serious adverse events

All serious adverse events are immediately reported to the research team and PI and then reported to the IRB, sponsor, and SO within 24 h.

Nonserious adverse events

Any nonserious adverse events are reported to the SO in biannual meetings and are subject to review prior to receiving authorization for the continuation of the research.

Biannual reports

A biannual open report summarizing study progress and safety monitoring data is reviewed by the SO and representatives from the NIH/NIA. Approval of the SO is required for the trial to continue.

Post-trial care

Both Tango and HEX participants continue to report adverse events and CIPN-20 momentary for 6 months post-trial. Researchers monitor responses and check in with participants as needed. Upon completion of the 6-month follow-up period researchers communicate their appreciation for participation; HEX participants are invited to participate in up to 16 Tango sessions and Tango participants are offered access to HEX materials and offered one instruction session for the purpose of teaching safe performance of the HEX protocol.

Protocol amendments

Any changes to the protocol require written amendments that must be approved by the NIH and IRB. Upon acceptance from the sponsor and IRB, the PI makes updates to the study record published on ClinicalTrials.gov. If the PI determines that a protocol deviation is necessary for safety reasons, scheduling, recruitment, or personal accommodations for participants, the IRB will be notified immediately.

Confidentiality

Any physical documentation containing protected health information is stored in a locked cabinet located within research or clinical designated space that is locked and/or monitored when not occupied. Digital documentation is stored in REDCap and/or on secure servers requiring password authentication that are behind secure firewalls.

Access to data

Study staff, OSU IRB, and representatives of the NIH have access to study data. Study staff are trained in HIPAA standards for privacy protection and do not refer to confidential information with anyone outside of the study team.

Dissemination policy

The results of our research will be disseminated to (a) the scientific community; (b) breast cancer survivors; (c) persons with symptoms of neuropathy; and (d) the public. The results of this research will be presented at scientific conferences, including the American Congress of Rehabilitation Medicine and the American Society of Biomechanics. Additionally, results will be published in peer-reviewed journals.

Results

Results represent the first year of recruitment, enrollment, and baseline data collection for this trial.

Recruitment

Our search of EMR returned an average of 230 survivors ≥ 40 years old who had received taxane-based cytotoxic chemotherapy in 3 years prior to recruitment start. An additional 1 survivor/month self-referred or was referred to us by advanced practice providers. We performed pre-screen via chart review for these 702 individuals. The reasons for failing pre-screen are listed in order of most common: (1) neuropathy reported as resolved or not experienced ($n=96$ (14%)) and (2) lived too far from academic medical center (> 1 -h drive $n=15$ (2%)). After chart review, 158 of these survivors passed pre-screen. We attempted contact by phone for all 158 and succeeded in contacting approximately 33%. Of those contacted, approximately 50% refused for the following reasons, listed in order of most common: (1) too busy, (2) neuropathy resolved, (3) already on a physical activity program for neuropathy management, and (4) not interested. Twenty-six recruits volunteered for balance screening: 3 demonstrated postural control within normal limits and 23 demonstrated postural control that met our threshold for inclusion, thereby passing balance screening.

Enrollment

All individuals who passed screening then consented to participate in the study (22 females/1 male) and enrolled ($n=23$).

Baseline characteristics

Baseline characteristics from this cohort, representing the first year of recruitment of this study, are reported in Table 3 in terms of age, years since last taxane exposure, postural control at screening, and functional testing results.

Discussion

Despite extensive research, no pharmacologic intervention has significantly improved the neuromotor, functional, and patient-reported symptoms of chronic CIN, in concert, among breast cancer survivors. The rationale for this study stems from accumulating evidence that PA represents a non-pharmacologic avenue to treat chronic CIN. The scientific premise of this study is that NDT-Tango stands to achieve more gains than PA practice alone through combining PA with MBM and social engagement. On the basis of our preliminary data establishing safety, feasibility, and initial effect of NDT-Tango for survivors with CIN, we have designed a randomized controlled trial to compare the effectiveness of an active control arm that delivers PA for CIN [22] as home exercise v. an experimental arm that delivers NDT-Tango. We

assess comparative effectiveness in terms of neuromotor, functional, and patient-reported outcomes relevant to BC survivorship. Our findings may lead to a safe, effective, simple, economical, non-pharmacologic intervention that improves CIN-related deficits and symptoms through activity that can be performed with a friend or loved one. Adding small doses of NDT as standard of care (SOC) for survivors with CIN is a simple, cost-effective solution that can be implemented anywhere in the world without major regulatory hurdles. Better functional recovery for survivors with CIN will lead to better short- and long-term health and wellness outcomes for these individuals. Therefore, the risks that participants in this study might incur are minor relative to the potential benefits of improving function and symptoms for BC survivors with CIN and measurable balance deficits.

Trial status

The study has been active and open for enrollment since September 2021. Enrollment is expected to be completed in August 2023. Intervention delivery and follow-up are expected to be completed by May of 2024. The clinical trial number associated with this trial is NCT05114005.

Abbreviations

6mwt	6-Minute walk test
ACE	American Council on Exercise
Adapted Argentine Tango	Adapted Tango
Aim1	Dynamics of posture
Aim2	Dynamics of gait
APPs	Advanced practice providers
BC	Breast cancer
BFI	Brief Fatigue Inventory
BPI	Brief Pain Inventory
CCI	Co-contraction index
CI	Confidence interval
CIN	Chemotherapy-induced neuropathy
CIPN-20	European Organization for Research and Treatment of Cancer, Chemotherapy-Induced Peripheral Neuropathy outcome measure
CMES	Medical Exercise Specialist
Co-I	Co-investigator
COP	Center of pressure
COPa	COP Ellipse Area
CVspeed	Coefficient of variability for stride speed
EMA	Ecological Momentary Assessment
EMG	Electromyography
EMR	Electronic medical records
HEX	Home exercise
IMI	Intrinsic Motivation Inventory
IMU	Inertial measurement unit
MBM	Music-based medicine
MCID	Minimum clinically-important difference
MiniBEST	Mini Balance Evaluation System Test
MPIs	Multiple principal investigators
NDT	Neurologic dance training
NDT-Tango	Partnered, Adapted Argentine Tango practice
OH	Ohio
OSU	The Ohio State University
PA	Physical activity
partner	Invited guest

PI	Principal investigator
PL	Path length
PRO(s)	Patient-reported outcome(s)
PRO-CTCAE	Patient-Reported Outcome version of the Common Terminology Criteria for Adverse Events v5
QEC	Postural control dynamics during silence
QECm	Postural control dynamics during music listening
RMSmI	Sway variability
RMSap	Variability in the anterior–posterior plane
RMSr	COP variability resultant
RMSx	COP variability in the medial–lateral direction
RPE	Rating of perceived exertion
RPME	Rating of perceived mental exertion
SCAT	Sports Concussion Assessment Tool version 5
SEI	Sample entropy, calculated using the increment method
SO	Safety officer
SOC	Standard of care
songs	Musical composition
SPIRIT	Standard Protocol Items: Recommendations for Interventions Trails
SSCBC	Stephanie Spielman Comprehensive Breast Center
TUG	Timed Up-and-Go test
TUGCog	Timed Up-and-Go test with cognitive dual task
VAS	Visual analog scale
Vel_x	COP velocity in medial–lateral direction
WSV	Within-subject variability

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Authors' contributions

LWC and MBL conceived the project, which was developed with input from MEH and PS. PS developed the statistical analysis plan with input from LWC. KL and LWC prepared the first and subsequent drafts of this manuscript, following a co-author review. All authors reviewed and approved the submission of the final manuscript. All named authors adhere to the authorship guidelines of *Trials* and have agreed to publication.

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Availability of data and materials

The datasets used and/or established during the current study will be available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study obtained ethics approval by The Ohio State Cancer Institutional Review Board under The Ohio State University's OHRP Federalwide Assurance #00006378. All participants will provide informed and written consent before taking part.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

- Centers for Disease Control and Prevention. 2022 [cited 16 May 2023]. CDC: Basic Information About Breast Cancer. Available from: https://www.cdc.gov/cancer/breast/basic_info/index.htm
- Stubblefield M, Burstein H, Burton A, Custodio C, Deng G, Ho M, et al. NCCN task force report: management of neuropathy in cancer. *J Natl Compr Canc Netw*. 2009;7:51–26.
- Song SJ, Min J, Suh SY, Jung SH, Hahn HJ, Im SA, et al. Incidence of taxane-induced peripheral neuropathy receiving treatment and prescription patterns in patients with breast cancer. *Support Care Cancer*. 2017;25(7):2241–8.
- Monfort SM, Pan X, Patrick R, Singaravelu J, Loprinzi CL, Lustberg MB, et al. Natural history of postural instability in breast cancer patients treated with taxane-based chemotherapy: a pilot study. *Gait Posture*. 2016;48:237–42.
- Kneis S, Wehrle A, Dalin D, Wiesmeier IK, Lambeck J, Gollhofer A, et al. A new approach to characterize postural deficits in chemotherapy-induced peripheral neuropathy and to analyze postural adaptations after an exercise intervention. *BMC Neurol*. 2020;20(1):23.
- Kleckner I, Kleckner A, Belcher E, Xu H, Lin PJ, Dunne RF, et al. Brain correlates of chemotherapy-induced peripheral neuropathy (CIPN) during somatosensory and interoceptive attention: a functional MRI (fMRI) study. *J Clin Oncol*. 2021;39(15_suppl):e24095.
- Worthen-Chaudhari L, Monfort S, Chaudhari A, Lustberg M. Sensorimotor cortical thickness changes following taxane-based chemotherapy: support for a CNS role in CIPN? *Arch Phys Med Rehabil*. 2023;104(3):e51.
- Mezzanotte JN, Grimm M, Shinde NV, Nolan T, Worthen-Chaudhari L, Williams NO, et al. Updates in the treatment of chemotherapy-induced peripheral neuropathy. *Curr Treat Options in Oncol*. 2022;23(1):29–42.
- Monfort SM, Pan X, Patrick R, Ramaswamy B, Wesolowski R, Naughton MJ, et al. Gait, balance, and patient-reported outcomes during taxane-based chemotherapy in early-stage breast cancer patients. *Breast Cancer Res Treat*. 2017;164(1):69–77.
- Monfort SM, Pan X, Loprinzi CL, Lustberg MB, Chaudhari AM. Exploring the roles of central and peripheral nervous system function in gait stability: preliminary insights from cancer survivors. *Gait Posture*. 2019;71:62–8.
- Marshall TF, Zipp GP, Battaglia F, Moss R, Bryan S. Chemotherapy-induced-peripheral neuropathy, gait and fall risk in older adults following cancer treatment. *J Cancer Res Pract*. 2017;4(4):134–8.
- Morishita S, Hirabayashi R, Tsubaki A, Aoki O, Fu JB, Onishi H, et al. Assessment of the mini-balance evaluation systems test, timed up and go test, and body sway test between cancer survivors and healthy participants. *Clin Biomech*. 2019;69:28–33.
- Blackwood J, Rybicki K. Assessment of gait speed and timed up and go measures as predictors of falls in older breast cancer survivors. *Integr Cancer Ther*. 2021;20:15347354211006462.
- Evans ES, Ketcham CJ, Hibberd JC, Cullen ME, Basiliere JG, Murphy DL. Examination of clinical and laboratory measures of static and dynamic balance in breast cancer survivors. *Physiother Theory Pract*. 2021;37(11):1199–209.
- Wampler MA, Topp KS, Miaskowski C, Byl NN, Rugo HS, Hamel K. Quantitative and Clinical Description of Postural Instability in Women With Breast Cancer Treated With Taxane Chemotherapy. *Arch Phys Med Rehabil*. 2007;88(8):1002–8.
- Huang MH. Screening and examination of fall risk in older cancer survi...: rehabilitation oncology. *Rehabil Oncol*. 2019;37(2):E7–9.
- Loprinzi CL, Lacchetti C, Bleeker J, Cavaletti G, Chauhan C, Hertz DL, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: ASCO guideline update. *J Clin Oncol*. 2020;38(28):3325–48.
- Streckmann F, Kneis S, Leifert J, Baumann F, Kleber M, Ihorst G, et al. Exercise program improves therapy-related side-effects and quality of life in lymphoma patients undergoing therapy. *Ann Oncol*. 2014;25(2):493–9.
- Streckmann F, Zopf EM, Lehmann HC, May K, Rizza J, Zimmer P, et al. Exercise intervention studies in patients with peripheral neuropathy: a systematic review. *Sports Med*. 2014;44(9):1289–304.
- Wonders KY, Whisler G, Loy H, Holt B, Bohachek K, Wise R. Ten weeks of home-based exercise attenuates symptoms of chemotherapy-induced peripheral neuropathy in breast cancer patients. *Health Psychol Res*. 2013;1(3):e28.
- Vollmers PL, Mundhenke C, Maass N, Bauerschlag D, Kratzstein S, Röcken C, et al. Evaluation of the effects of sensorimotor exercise on physical and psychological parameters in breast cancer patients undergoing neurotoxic chemotherapy. *J Cancer Res Clin Oncol*. 2018;144(9):1785–92.
- Zimmer P, Trebing S, Timmers-Trebing U, Schenk A, Paust R, Bloch W, et al. Eight-week, multimodal exercise counteracts a progress of chemotherapy-induced peripheral neuropathy and improves balance and strength in metastasized colorectal cancer patients: a randomized controlled trial. *Support Care Cancer*. 2018;26(2):615–24.
- Patel AV, Friedenreich CM, Moore SC, Hayes SC, Silver JK, Campbell KL, et al. American college of sports medicine roundtable report on physical activity, sedentary behavior, and cancer prevention and control. *Med Sci Sports Exerc*. 2019;51(11):2391–402.
- English AW, Wilhelm JC, Ward PJ. Exercise, neurotrophins, and axon regeneration in the PNS. *Physiology*. 2014;29(6):437–45.
- Rajab AS, Crane DE, Middleton LE, Robertson AD, Hampson M, MacIntosh BJ. A single session of exercise increases connectivity in sensorimotor-related brain networks: a resting-state fMRI study in young healthy adults. *Front Hum Neurosci*. 2014;8:625. <https://doi.org/10.3389/fnhum.2014.00625/full>.
- Dimeo FC, Tilmann MHM, Bertz H, Kanz L, Mertelsmann R, Keul J. Aerobic exercise in the rehabilitation of cancer patients after high dose chemotherapy and autologous peripheral stem cell transplantation. *Cancer*. 1997;79(9):1717–22.
- Woods JA, Vieira VJ, Keylock KT. Exercise, inflammation, and innate immunity. *Immunol Allergy Clin North Am*. 2009;29(2):381–93.
- Rennie C, Irvine DS, Huang E, Huang J. Music therapy as a form of non-pharmacologic pain modulation in patients with cancer: a systematic review of the current literature. *Cancers*. 2022;14(18):4416.
- Janata P, Tomic ST, Haberman JM. Sensorimotor coupling in music and the psychology of the groove. *J Exp Psychol Gen*. 2012;141(1):54.
- Stupacher J, Hove MJ, Janata P. Audio features underlying perceived groove and sensorimotor synchronization in music. *Music Perception: An Interdisciplinary Journal*. 2016;33(5):571–89.
- Will U, Berg E. Brain wave synchronization and entrainment to periodic acoustic stimuli. *Neurosci Lett*. 2007;424(1):55–60.
- Ross JM, Warlaumont AS, Abney DH, Rigoli LM, Balasubramaniam R. Influence of musical groove on postural sway. *J Exp Psychol Hum Percept Perform*. 2016;42(3):308.
- Ravi DK, Marmelat V, Taylor WR, Newell KM, Stergiou N, Singh NB. Assessing the temporal organization of walking variability: a systematic review and consensus guidelines on detrended fluctuation analysis. *Front Physiol*. 2020;11:562. <https://doi.org/10.3389/fphys.2020.00562>. [cited 8 Mar 2023].
- Huang ST, Good M, Zauszniewski JA. The effectiveness of music in relieving pain in cancer patients: a randomized controlled trial. *Int J Nurs Stud*. 2010;47(11):1354–62.
- Nguyen TN, Nilsson S, Hellström AL, Bengtson A. Music therapy to reduce pain and anxiety in children with cancer undergoing lumbar puncture: a randomized clinical trial. *J Pediatr Oncol Nurs*. 2010;27(3):146–55.
- Nilsson U. The anxiety-and pain-reducing effects of music interventions: a systematic review. *AORN J*. 2008;87(4):780–807.

37. van Emmerik RE, Ducharme SW, Amado AC, Hamill J. Comparing dynamical systems concepts and techniques for biomechanical analysis. *J Sport Health Sci*. 2016;5(1):3–13.
38. de Dreu MJ, Van Der Wilk ASD, Poppe E, Kwakkel G, van Wegen EE. Rehabilitation, exercise therapy and music in patients with Parkinson's disease: a meta-analysis of the effects of music-based movement therapy on walking ability, balance and quality of life. *Parkinsonism Relat Disord*. 2012;18:S114–9.
39. Lakhani B, Borich MR, Jackson JN, Wadden KP, Peters S, Villamayor A, et al. Motor Skill Acquisition Promotes Human Brain Myelin Plasticity. *Neural Plasticity*. 2016; Article ID 7526135; 1–7. <https://www.ncbi.nlm.nih.gov/pmc/journals/478/>.
40. Wulf G, Chiviawosky S, Carodozo PL. Additive benefits of autonomy support and enhanced expectancies for motor learning. *Hum Mov Sci*. 2014;37:12–20.
41. Chiviawosky S, Wulf G, Lewthwaite R, Campos T. Motor learning benefits of self-controlled practice in persons with Parkinson's disease. *Gait Posture*. 2012;35(4):601–5.
42. Lewthwaite R, Chiviawosky S, Drews R, Wulf G. Choose to move: the motivational impact of autonomy support on motor learning. *Psychon Bull Rev*. 2015;22(5):1383–8.
43. Worthen-Chaudhari L, Lamantia MT, Monfort SM, Mysiw W, Chaudhari AMW, Lustberg MB. Partnered, adapted argentine tango dance for cancer survivors: a feasibility study and pilot study of efficacy. *Clin Biomech*. 2019;70:257–64.
44. Hackney ME, Earhart GM. Recommendations for implementing tango classes for persons with parkinson disease. *Am J Dance Ther*. 2010;32(1):41–52.
45. Hackney ME, Byers C, Butler G, Sweeney M, Rossbach L, Bozzorg A. Adapted tango improves mobility, motor-cognitive function, and gait but not cognition in older adults in independent living. *J Am Geriatr Soc*. 2015;63(10):2105–13.
46. Chaudhari A, Monfort S, Lamantia M, Lustberg M, Worthen-Chaudhari L. Effect of an argentine tango intervention on gait variability in cancer survivors: 2413 Board# 4 June 2 9. *Med Sci Sports Exerc*. 2017;49(5S):675–675.
47. Worthen-Chaudhari L, Monfort S, Bland C, Pan X, Chaudhari A. Characterizing within-subject variability in quantified measures of balance control: a cohort study. *Gait Posture*. 2018;64:141–6.
48. Maki BE, Holliday PJ, Topper AK. A prospective study of postural balance and risk of falling in an ambulatory and independent elderly population. *J Gerontol Med Sci*. 1994;49(2):72–84.
49. Thapa PB, Gideon P, Brockman KG, Fought RL, Ray WA. Clinical and biomechanical measures of balance fall predictors in ambulatory nursing home residents. *J Gerontol A Biol Sci Med Sci*. 1996;51A(5):M239–46.
50. Stel VS, Smit JH, Pluijij SM, Lips P. Balance and mobility performance as treatable risk factors for recurrent falling in older persons. *J Clin Epidemiol*. 2003;56(7):659–68.
51. Maki BE. Gait changes in older adults: predictors of falls or indicators of fear? *J Am Geriatr Soc*. 1997;45(3):313–20.
52. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med*. 2013;158(3):200–7.
53. Chan AW, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ*. 2013;2013:346.
54. Hopewell S, Boutron I, Chan AW, Collins GS, de Beyer JA, Hróbjartsson A, et al. An update to SPIRIT and CONSORT reporting guidelines to enhance transparency in randomized trials. *Nat Med*. 2022;28(9):1740–3.
55. Center for Disease Control and Prevention. United States Cancer Statistics Data Visualizations. Available from: <https://gis.cdc.gov/Cancer/USCS/#/Demographics/>. Accessed 16 May 2023.
56. Reed CA, Chaudhari AM, Worthen-Chaudhari LC, Bigelow KE, Monfort SM. A new perspective on transient characteristics of quiet stance postural control. *PLoS ONE*. 2020;15(8):e0237246.
57. Prieto TE, Myklebust JB, Hoffmann RG, Lovett EG, Myklebust BM. Measures of postural steadiness differences between healthy young and elderly adults. *Trans Biomed Eng*. 1996;43(9):965–6.
58. Roerdink M, Hlavackova P, Vuillerme N. Center-of-pressure regularity as a marker for attentional investment in postural control: a comparison between sitting and standing postures. *Hum Mov Sci*. 2011;30(2):203–12.
59. Li Y, Lustberg MB, Hu S. Emerging pharmacological and non-pharmacological therapeutics for prevention and treatment of chemotherapy-induced peripheral neuropathy. *Cancers*. 2021;13(4):766.
60. Hackney ME, McKee K. Community-based adapted tango dancing for individuals with Parkinson's disease and older adults. *JoVE (Journal of Visualized Experiments)*. 2014;94:e52066.
61. Ryan RM, Koestner R, Deci EL. Ego-involved persistence: When free-choice behavior is not intrinsically motivated. *Motiv Emot*. 1991;15(3):185–205.
62. Ryan RM, Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. *Am Psychol*. 2000;55(1):68.
63. McAuley E, Wraith S, Duncan TE. Self-efficacy, perceptions of success, and intrinsic motivation for exercise 1. *J Appl Soc Psychol*. 1991;21(2):139–55.
64. Paice JA, Ferrell B. The management of cancer pain. *CA Cancer J Clin*. 2011;61(3):157–82.
65. Faw TD, Lakhani B, Schmalbrock P, Knopp MV, Lohse KR, Kramer JLK, et al. Eccentric rehabilitation induces white matter plasticity and sensorimotor recovery in chronic spinal cord injury. *Exp Neurol*. 2021;346:113853.
66. Niedzwiedz CL, Knifton L, Robb KA, Katikireddi SV, Smith DJ. Depression and anxiety among people living with and beyond cancer: a growing clinical and research priority. *BMC Cancer*. 2019;19(1):943.
67. Colevas AD, Setser A. The NCI Common Terminology Criteria for Adverse Events (CTCAE) v 3.0 is the new standard for oncology clinical trials. *J Clin Oncol*. 2004;22(14_suppl):6098–6098.
68. Hausdorff J, Rios D, Edelberg H. Gait variability and fall risk in community-living older adults: a 1-year prospective study. *Archives of physical medicine and ...* 2001.
69. Kang HG, Dingwell JB. Intra-session reliability of local dynamic stability of walking. *Gait Posture*. 2006;24(3):386–90.
70. Dingwell JB, Kang HG. Differences between local and orbital dynamic stability during human walking. *J Biomech Eng*. 2007;129(4):586–93.
71. Stergiou N, Decker LM. Human movement variability, nonlinear dynamics, and pathology: is there a connection? *Hum Mov Sci*. 2011;30(5):869–88.
72. Zijlstra W, Hof AL. Assessment of spatio-temporal gait parameters from trunk accelerations during human walking. *Gait Posture*. 2003;18(2):1–10.
73. Haid T, Federolf P. Human postural control: assessment of two alternative interpretations of center of pressure sample entropy through a principal component factorization of whole-body kinematics. *Entropy*. 2018;20(1):30.
74. Quatman-Yates CC, Bonnette MS, Hugentobler JA, Médé MB, Kiefer AW, Kurowski BG, et al. Postconcussion postural sway variability changes in youth: the benefit of structural variability analyses. *Pediatr Phys Ther*. 2015;27(4):316.
75. Pelykh O, Klein AM, Bötzel K, Kosutzka Z, Ilmberger J. Dynamics of postural control in Parkinson patients with and without symptoms of freezing of gait. *Gait Posture*. 2015;42(3):246–50.
76. Kamięniarz A, Michalska J, Marszałek W, Stanią M, Słomka KJ, Gorzkowska A, et al. Detection of postural control in early Parkinson's disease: clinical testing vs. modulation of center of pressure. *PLOS ONE*. 2021;16(1):e0245353.
77. Pantall A, Del Din S, Rochester L. Longitudinal changes over thirty-six months in postural control dynamics and cognitive function in people with Parkinson's disease. *Gait Posture*. 2018;62:468–74.
78. Huisinga JM, Yentes JM, Filipi ML, Stergiou N. Postural control strategy during standing is altered in patients with multiple sclerosis. *Neurosci Lett*. 2012;524(2):124–8.
79. Kuczyński M, Szymańska M, Bieć E. Dual-task effect on postural control in high-level competitive dancers. *J Sports Sci*. 2011;29(5):539–45.
80. Rhea CK, Diekfuss JA, Fairbrother JT, Raisbeck LD. Postural Control Entropy Is Increased When Adopting an External Focus of Attention. *Motor Control*. 2019;23(2):230–42.
81. Potvin-Desrochers A, Richer N, Lajoie Y. Cognitive tasks promote automatization of postural control in young and older adults. *Gait Posture*. 2017;57:40–5.

82. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc*. 1991;39(2):142–8.
83. McCrary JM, Goldstein D, Wyld D, Henderson R, Lewis CR, Park SB. Mobility in survivors with chemotherapy-induced peripheral neuropathy and utility of the 6-min walk test. *J Cancer Surviv*. 2019;13(4):495–502.
84. Bohannon RW, Crouch R. Minimal clinically important difference for change in 6-minute walk test distance of adults with pathology: a systematic review. *J Eval Clin Pract*. 2017;23(2):377–81.
85. Mirelman A, Weiss A, Buchman AS, Bennett DA, Giladi N, Hausdorff JM. Association between performance on Timed Up and Go subtasks and mild cognitive impairment: further insights into the links between cognitive and motor function. *J Am Geriatr Soc*. 2014;62(4):673–8.
86. Vervoort D, Vuillerme N, Kosse N, Hortobágyi T, Lamothe CJ. Multivariate analyses and classification of inertial sensor data to identify aging effects on the Timed-Up-and-Go test. *PLoS ONE*. 2016;11(6):e0155984.
87. Toebes MJP, Hoozemans MJM, Furrer R, Dekker J, van Dieën JH. Local dynamic stability and variability of gait are associated with fall history in elderly subjects. *Gait Posture*. 2012;36(3):527–31.
88. Wright MJ, Twose DM, Gorter JW. Gait characteristics of children and youth with chemotherapy induced peripheral neuropathy following treatment for acute lymphoblastic leukemia. *Gait Posture*. 2017;58:139–45.
89. Hsieh KL, Trinh L, Sosnoff JJ. Gait variability is altered in cancer survivors with self-reported neuropathy. *Gait Posture*. 2019;72:206–10.
90. Gilchrist L, Tanner L. Gait patterns in children with cancer and vincristine neuropathy. *Pediatr Phys Ther*. 2016;28(1):16–22.
91. Vallabhajosula S, Deaterly CD, Madzima TA. Comparison of forward and backward gait characteristics between those with and without a history of breast cancer. *Gait Posture*. 2019;74:162–8.
92. Galiano-Castillo N, Arroyo-Morales M, Ariza-García A, Sánchez-Salado C, Fernández-Lao C, Cantarero-Villanueva I, et al. The six-minute walk test as a measure of health in breast cancer patients. *J Aging Phys Act*. 2016;24(4):508–15.
93. Dingwell JB, Cusumano JP, Sternad D, Cavanagh PR. Slower speeds in patients with diabetic neuropathy lead to improved local dynamic stability of continuous overground walking. *J Biomech*. 2000;33(10):1269–77.
94. Dingwell JB, Cavanagh PR. Increased variability of continuous overground walking in neuropathic patients is only indirectly related to sensory loss. *Gait Posture*. 2001;14(1):1–10.
95. Sloot LH, Van Schooten KS, Bruijn SM, Kingma H, Pijnappels M, van Dieën JH. Sensitivity of local dynamic stability of over-ground walking to balance impairment due to galvanic vestibular stimulation. *Ann Biomed Eng*. 2011;39:1563–9.
96. van Schooten KS, Sloot LH, Bruijn SM, Kingma H, Meijer OG, Pijnappels M, et al. Sensitivity of trunk variability and stability measures to balance impairments induced by galvanic vestibular stimulation during gait. *Gait Posture*. 2011;33(4):656–60.
97. Dingwell JB, Kang HG, Marin LC. The effects of sensory loss and walking speed on the orbital dynamic stability of human walking. *J Biomech*. 2007;40(8):1723–30.
98. Glover N, Wilder J, Hackney M, Lustberg M, Worthen-Chaudhari L. Case study in chemotherapy-induced neuropathy: tango dance improved over-ground local gait stability. *Arch Phys Med Rehabil*. 2023;104(3):e16.
99. Kneis S, Wehrle A, Freyler K, Lehmann K, Rudolphi B, Hildenbrand B, et al. Balance impairments and neuromuscular changes in breast cancer patients with chemotherapy-induced peripheral neuropathy. *Clin Neurophysiol*. 2016;127(2):1481–90.
100. Cleeland CS. Undertreatment of cancer pain in elderly patients. *JAMA*. 1998;279(23):1914–5.
101. Dueck AC, Mendoza TR, Mitchell SA, Reeve BB, Castro KM, Rogak LJ, et al. Validity and reliability of the US National Cancer Institute's patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE). *JAMA Oncol*. 2015;1(8):1051–9.
102. Hänninen T, Parkkari J, Howell DR, Palola V, Seppänen A, Tuominen M, et al. Reliability of the sport concussion assessment tool 5 baseline testing: a 2-week test–retest study. *J Sci Med Sport*. 2021;24(2):129–34.
103. Lamb SE, Jørstad-Stein EC, Hauer K, Becker C, Europe P of FN, Group OC. Development of a common outcome data set for fall injury prevention trials: the Prevention of Falls Network Europe consensus. *J Am Geriatr Soc*. 2005;53(9):1618–22.
104. Tsigilis N, Theodosiou A. Temporal stability of the intrinsic motivation inventory. *Percept Mot Skills*. 2003;97(1):271–80.
105. Worthen-Chaudhari L, McGonigal J, Logan K, Bockbrader MA, Yeates KO, Mysiw WJ. Reducing concussion symptoms among teenage youth: Evaluation of a mobile health app. *Brain Injury*. 2017;31(10):1279–86.

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