PROTOCOL TITLE: The effect of a collaborative art therapy and physical therapy intervention on children undergoing a hematopoietic cell transplant: a randomized clinical trial

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Objectives / Specific Aims

Aim 1: In children undergoing HCT during in-patient care, does a randomized group receiving a combination of PT plus AT have improved functional activity level outcomes of selfcare and mobility as measured by the Pediatric Evaluation of Disability Inventory Computerized Adaptive Test (PEDI CAT) and the 6-Minute Walk Test (6MWT), compared with a group receiving PT only.
Hypothesis 1: Children receiving the combined intervention of PT plus AT will demonstrate greater improvements in selfcare and mobility skills.

Aim 2: Do children receiving PT plus AT have different physiological (sympathetic or parasympathetic) and emotional responses to oil pastels and gouache as measured by respiratory sinus arrhythmia (RSA) derived from heart rate variability (HRV) and Self-Assessment Manikin (SAM) scores during each of the daily AT sessions.
Hypothesis 2: Oil pastels or gouache AT will generate a greater RSA value in the direction of needed parasympathetic activity and balance in the emotions of valence, arousal, and dominance.

Aim 3: In children receiving PT plus AT, determine if there is a stronger association between the RSA values of oil pastels or gouache AT and an increased walking distance as measured by accelerometry during daily PT sessions.
Hypothesis 3: The media that best generates a parasympathetic RSA value and emotional balance will be associated with a greater walking distance.

2.0 Background

Overview: For the 13,000 children with hematological disease undergoing allogeneic hematopoietic cell transplant (HCT) in the United States1, art therapy (AT) and physical therapy (PT) are prescribed at a rate of approximately 50%2 to minimize negative treatment consequences. Anxiety, pain, loss of control as well as reductions in physical conditioning, functional mobility, selfcare, and motor skills are common consequences associated with HCT in children and will inform this proposed research project's outcomes and aims.3

As we consider the impact of AT and PT on children undergoing HCT, the AT literature generally emphasizes AT's effect on emotional health (e.g., pain, anxiety) and PT's on physical health (e.g., mobility, selfcare). The Model of Art Therapy in Management of Pediatric Chronic Pain4,5 fosters improvements in anxiety and pain following AT that then promote greater compliance with medical treatments.4,5 (Appendix 1). It is this theoretical premise that supports our proposed project's suggestion that a collaborative treatment of AT and PT would be more effective than only providing AT or PT or providing both independent of each other. We believe the interconnected use of AT to reduce emotional distress prior to PT would not only enhance PT compliance, but also provide greater opportunity for improvements in physical performance and overall health.

Art Therapy Evidence in Pediatric HCT
The American Art Therapy Association (AATA) defines AT as an integrative mental health and human services profession that enriches the lives of individuals, families, and communities through active art-

making, creative process, applied psychological theory, and human experience within a psychotherapeutic relationship.6 This AT process involves three important components: 1) patient, 2) art therapist, and 3) art making materials that interact collectively to impact emotional and health outcomes. In a 2019 review entitled Effectiveness of Art Therapy with Pediatric Populations Affected by Medical Health Conditions: A Systematic Review, Clapp acknowledges that the goals of AT interventions focused on enhancing emotional understanding and promoting symptom management.5 Similarly, yet specific to pediatric oncologic health conditions, the efficacy for AT is drawn from descriptive qualitative studies that support: 1) emotional communication in response to anxiety, fear of death, loss of control, 2) a strategy by which to distract and/or cope, and 3) symptoms, anxiety, and pain amelioration.7,8 It is clearly stated in this systematic review that the majority of AT research findings are based on qualitative methods and, although this qualitative work is informative and guiding, the need to objectively quantify the effectiveness of AT and its impact on health outcomes has been noted and acknowledged within the literature.9 In fact, direct calls for more robust studies to examine AT's impact on health outcomes have been documented5,10 and are necessary, not only to increase the uptake of AT in children undergoing HCT, but other pediatric populations as well.

Physical Therapy in Pediatric HCT

The American Physical Therapy Association defines physical therapy as the promotion, maintenance, and restoration of health through physical examination, diagnosis, prognosis, patient education, physical intervention, rehabilitation, disease prevention and health promotion.11 Physical therapists are consider movement experts11 and address illnesses or injuries that interfere with individuals' ability to move and perform functional activities in their daily lives such a mobility and selfcare. The efficacy of physical therapy interventions using a variety of therapeutic exercise in pediatric populations has been well demonstrated in children with juvenile idiopathic arthritis12, having chronic pain13, and with hemiparetic cerebral palsy.14,15 Although efficacy is not yet supported, the implementation of exercise programming by physical therapists in the area of pediatric HCT is becoming more common to mitigate deconditioning and functional losses during the treatment course.16,17 For the children who receive PT, evidence indicates that exercise interventions across the continuum of HCT improve functional mobility, abilities of daily living, strength and endurance17, and promotes a reintegration into everyday participation. Yet in spike of these positive gains, prolonged motor delays following HCT remain common.18-25

While a few PT studies have incorporated the use of emotional wellbeing education into exercise interventions to improve strength and endurance in patients during HCT17,26, in the reality of clinical settings where HCT take place, the primary focus of PT is therapeutic exercise and activities geared toward physical health. Knowing that emotional health is as important as physical health and with evidence of AT's positive impact on emotional health for children undergoing HCT, it seems logical that collaborative interventions incorporating AT and PT would boost health outcomes. As such, we broadly hypothesize that children undergoing HCT in an in-patient setting receiving AT immediately prior to PT will display greater improvement in the body function (i.e., physiologic and emotional) and activity level (i.e., mobility and selfcare) outcomes across the International Classification of Functioning, Disability and Health27 (Appendix 2) than children only receiving PT. By exploring this broad hypothesis, we create an excellent opportunity to also investigate in greater depth the impact of AT media on body function and activity level outcomes.

Motivation 1: Innovative use of quantifiable RSA/HRV to examine the impact of art therapy on the Autonomic Nervous System (ANS) in children undergoing HCT.

Our first motivation for this research is believing that AT can physiologically improve the state of the ANS which can lead to better health outcomes for children with health conditions and disability and specific to this proposed study- children undergoing HCT. The Children's Hospital at MUSC has an active in-patient HCT program and for that reason, we have an opportunity and are proposing that the use

a collaborative treatment of AT and PT, as compared to PT only, will improve mobility and selfcare outcomes in children undergoing HCT. Because of emotional impairments (i.e., pain and anxiety) that are associated with hematopoietic disease and HCT in children28, the ANS demonstrates a dominance toward fight or flight or unstable homeostasis.29,30

To better understand this ANS dysfunction, a basic review is provided. The ANS consists of two systems: sympathetic (SNS) and parasympathetic nervous systems (PNS) that shape vagal tone by exerting influence upon the vagus nerve. The SNS creates a fight or flight state while the PNS fosters a rest and digest condition. Homeostasis is created when the two systems work in unison to create balanced vagal tone upon the vagal nerve. Intrinsic (e.g., hydration, body temperature) and extrinsic factors (e.g., bone marrow biopsy, chemotherapy treatment) can facilitate or interrupt this homeostasis. It is important to recognize that the although the SNS and PNS are interconnected, the SNS provides dominant and steady stimulation to the vagus nerve while the PNS providing ongoing, yet variable, braking to the SNS. It is this relationship that promotes either homeostatic stability or instability as intrinsic and extrinsic factors demand.

Porges' Polyvagal theory31 provides a more in depth understanding of the relationship between vagal tone and ANS. He proposes that 3 phylogenetic stages exist within the human ANS that are ordered to allow for 1) social communication, 2) mobilization or fight-flight, and 3) dissociation or immobilization. (Appendix 3.) Activation of the myelinated ventral vagus, in which the SNS and PNS are providing stimulation and braking to the vagal nerve, allows for homeostasis and social communication. This is the desired and more healthy state for human beings including children undergoing HCT. When intrinsic or extrinsic factors trigger the SNS with vagal braking inhibited, sympathetic dominance or a fight-flight responses manifest. Because of medical interventions (extrinsic) as well as anxiety and pain (intrinsic), this is this stage in which most children having HCT dwell.29,30

Respiratory sinus arrhythmia is a direct measure of this vagal tone31 and is derived from HRV across the respiratory cycle. Heart rate variability is defined as the variation between consecutive heartbeats33 or beat to beat variability32. It is considered a validated physiological mechanism for evaluating the state of the ANS and more specifically emotional responsivity. In a systematic review, Kirizawa and colleagues29 have advocated for the use of HRV as a physiological marker to evaluate ANS function in individuals with leukemia. The heart's ability to demonstrate high variability is considered advantageous, but often undesirable intrinsic and extrinsic factors decrease variability. One such factor is the treatment of HCT in children with hematopoietic disease. Because RSA/vagal tone/HRV has been successfully used to investigate the ANS in pediatric traumatic brain injury34, premature babies35, and children with autism spectrum disorders36,37, we believe its use with children undergoing HCT in our study is promising. An additional advantage is the fact that the collection of RSA/HRV is non-invasive and improved technological development has led to the delivery of reliable, portable HRV monitors. Again, making its use appealing with children undergoing HCT.

Motivation 2: Exploring the effect AT media on RSA/HRV, emotional state, and the health outcome of mobility in children undergoing HCT.
Recognizing that AT and certain aspects of AT media have promoted changes in the ANS as measured by HRV in children and adults3, and that calls have been made for the use of HRV in studies exploring AT interventions5,9,10, we arrive at our second research motivation: to capture RSA/HRV during AT interventions in order determine if one type of media leads to improved changes in the ANS as captured by HRV/RSA, emotional ratings, and daily mobility.

Understanding the relationship between patient, therapist, and the art making material is critical to generate effective patient outcomes. Much of the AT evidence discusses the important bond developed

between patient and therapist; however, awareness considering the qualities of the art making material has had limited examination. Despite the known interactive role of media through kinesthetic, tactile, perceptual, and symbolic input, media make play a more important than has previously been suggested. Kramer cleverly has described the media as the third hand, which contributes to an art therapist's ability to steer the creative and restorative process.38,39 The Expressive Therapies Continuum (ETC) provides a conceptual model with developmental hierarchical levels that guide the assessment and application of art making materials during art therapy. (Appendix 4). It consisted of four levels:
1) kinesthetic/sensory: sensory motor experience gained through the body's interaction with the material
2) perceptual/affective: emotional connection established by interaction with materials and creation of form/product
3) cognitive/symbolic: emergence of symbolic or abstract thought centered about the product/form allowing for sophisticated, formative thought
4) creative: communication or expressive interaction between the individual and the product/form promoting personal well-being whether by providing closure to a false sense of self or elation to restoration of an authentic sense of self.40-43
These levels often interactive or overlap, but advancing through each of these levels over one art therapy session may not be achieved. This is especially the true for creative, the highest level.43

Art therapy literature provides some degree of prescription for the use of specific media. Across an ordinal scale and based on fluidity, rankings for media from least to most emotionally engaging are pencils, oil pastels, and gouache.39 The use of markers and pencils is said to offer structure, control, and a limited emotional response that does not generate anxiety. Oil pastels or chalk are noted to afford moderate fluidity and tactical enrichment through touching and smearing, thereby resulting in greater emotional arousal (moderate anxiety) than pencils.42,44 When not using a brush, the fluidity offered by gouache painting yields high levels of emotional engagement and anxiety; however, use of a brush decreases emotional engagement. It is important to consider that gouache painting has also being described as liberating.45,46

As has been encouraged by AT literature and organizations, several studies have examined the impact of media. The first study looked at media's impact on the outcome of emotional responses and the second on HRV. Pesso-Aviv and colleagues explored the effects of pencils, oil chalks, and gouache paint on anxiety and self-control using survey data on 41 males between the ages of 7 to 9 years, who although not reported within the narrative appear to have been healthy, typically developing youth. Ten intervention session were provided for each of the three different media groups. Surprisingly, the results indicated no change in anxiety and self-control outcomes. This may be possibly explained by the youth being healthy and typically developing with little to no impairments in anxiety and self-control, thus, creating a ceiling effect with little space for documenting improvement. For children undergoing HCT, we know that emotional engagement and anxiety are problematic so media's impact may be more detectable in this group. In the second study, Haiblum-Itskovitch and researchers hypothesized that emotional and ANS responses as measured by RSA/HRV values would be more reflective of PNS activity as fluidity of the media decreases in a normative sample of adult participants; thus, pencils would offer the greatest PNS activity followed by oil pastel and then gouache with brush. Surprisingly, results indicated that oil pastels resulted in the greater PNS activation than gouache while also corresponded to more meaningful emotional engagement. Thirty-five percent of the variance in the PNS value was explained by the media with a change in the RSA value of 1 representing the effect size needed for detecting a meaningful difference between materials. The author offered the possibility that the oil pastels facilitated greater tactile input which like fluidity may also played a role in ANS activity and emotional engagement. Based on the above information and considering that no study has explored the use of RSA/HRV as a physiological measure by which to evaluate a media's impact on a population of children with a health

condition, our proposed study seeks to accomplish this by evaluating 2 media's impact on physiological (RSA/HRV), emotional (SAM), and health outcomes (mobility) of in children undergoing HCT.

3.0 Intervention to be studied (if applicable)

Side-by-side integration of AT and PT has not been examined and we propose to conduct a clinical trial in which for two weeks daily (Monday-Friday), 20 children between the ages of 3 ~~5~~-18 years with be randomly assigned into one of two groups: 1) collaborative intervention: 45 minutes of AT immediately followed by 30 minutes of PT or 2) PT only intervention: 30 minutes. During the collaborative intervention of week 1, oil pastels will be the media and week 2 gouache painting without brush.

Treatment: 45 minutes of AT closely followed by 30 minutes of PT OR 30 minutes of PT.

AT treatments will seek to reduce sympathetic dominance/physiological and emotional distress. Oil pastels will be used for Days 1-5 and gouache painting for days 6-10. Art therapy is a collaborative, interactive, and iterative process that evolves across the session between the child and art therapist, as such, outside of the actual change in medium, there is no study specific art therapy prescription or protocol. Art therapy sessions will occur in the child's room.

PT treatments will seek to prevent physical deconditioning and encourage mobility, ambulation, and selfcare participation based on participant's ability. Physical therapy sessions will occur in the child's room and on the HCT unit.

The same art and physical therapist and art therapist will conduct children's session across the 2-week study duration. This art and physical therapist commonly work on the HCT unit. The coordinator again will monitor all sessions to ensure the following of study procedures.

4.0 Study Endpoints (if applicable)

Aim 1: Pre and post-test data collection, storage, and scoring calculations will be carried on by study coordinator/PhD student.
Pediatric Evaluation of Disability Computerized Adaptive Test (PEDI CAT) using a study iPad: The PEDI CAT measures 0 to 18-year-old children's abilities across three domains of mobility, selfcare and social function. It can be used with all pediatric diagnosis, across settings, and measures change following an intervention. It demonstrates excellent reliability48, good validity49,50 with a minimal detectable change ranging between 2.2 to 3.3 across domains.51 Our study will measure only selfcare and mobility domains, which takes approximately 20 minutes to administer. Scaled (criteria referenced) and Standard (normative referenced) PEDI-CAT scores will be calculated.

6-Minute Walk Test (6MWT)
The 6MWT has demonstrated good reliability and validity in various pediatric populations.52,53 It has also been found to be predictive of cardiovascular fitness in survivors of children with pediatric cancers.54 The 6MWT takes 6 minutes to administer.

Aim 2: Daily data collection by art and physical therapists during or after sessions, but data will be managed by study coordinator/PhD student following the sessions.
The Self-Assessment Manikin (SAM): The SAM is an image-based tool used to evaluate affective change in pleasure, arousal, and dominance in response to an object or event.55-57 (Appendix 6) Good reliability and validity of the SAM has been demonstrated.58 Suggestions are that it perform similarly across diverse cultures and ages.59-61 The SAM has been collected in studies involving exercise in which large

effect sizes were noted.62 We plan to use the computerized application of the SAM, which will take seconds to administer before and after daily AT and PT interventions.

Respiratory Sinus Arrhythmia derived from Heart Rate Variability: HRV measures short-term R-to-R intervals, which is reflective of the autonomic nervous system. The portable, non-invasive Firstbeat Bodyguard 2 (Appendix 7) will be worn to gather HRV. The monitor will be placed on the chest of the child 10 minutes prior to the beginning of AT and worn by the child until removal following PT. We will evaluate the first and last 5-minute of HRV data during the AT session. Using Cardio Batch software, RSA will be calculated from the HRV data. The Firstbeat Bodyguard 2 accurately measures 99.95% of the heartbeats compared to standard EKG.63 Placement and removal of the HRV monitor requires only seconds. The study coordinator/PhD student will clean all HRV files for artifact and calculate RSA values using Cardio Batch software. At the end of each day, the coordinator/PhD student will be responsible for collecting, cleaning, scoring, and storing all daily data.

Aim 3: Daily collection: Daily data collection by art and physical therapists during or after sessions, but data will be managed by study coordinator/PhD following the sessions.
Walking distance during PT session as measured by accelerometer: The ActiGraph GT9X Link (Appendix 8) will collect walking distance as measures by distance and steps during PT. It is similar in looks and wear to an iWatch. It has demonstrated good reliability and validity.64,65 It can collect a variety of outcomes (e.g., energy expenditure, body position, sleep), but for aim 3, we will be most interested in walking distance and number of steps. At the end of each day, the study coordinator/PhD student will be responsible for collecting, calculating distance and step values using Actigraphy software, and storing accelerometry data.

5.0 Inclusion and Exclusion Criteria/ Study Population

Inclusion criteria: Children between the ages of 4 and 18 years undergoing HCT in response to hematological disease during the in-patient hospital treatment phase.

Exclusion criteria: Children with central nervous system impairments (e.g., cerebral palsy), other genetic diseases (e.g., Down syndrome), and cognitive impairment will be excluded from study participation.

Children undergoing HCT were chosen as this study's population because they often receive intermittent and stand-alone AT or PT. We believe more daily PT and/or AT as well as the collaboration between PT and AT will improve health outcomes. Because children display continual cognitive, behavior, and motor development changes, this study chose not to involve adults undergoing HCT. The outcomes for children and adults undergoing HCT cannot be validly compared. This study has no exclusions for any specific sex/gender or racial/ethnic group.

6.0 Number of Subjects

20

Approximately 30 children undergo HCT at MUSC Children's Hospital annually for which 50% are male and female, 10% considered Hispanic, 55% Caucasian, and 35% African American.

7.0 Setting

MUSC Shawn Jenkins Children's Hospital.

8.0 Recruitment Methods

Participants will be recruited prior to and at the time of admission for the HCT. A flyer will be provider to the HCT team members to share with participants. Members of the HCT team will be made aware of the inclusion criteria and can approach all potential participants for possible study enrollment. While any team member may recruit a study participant, the study art therapist and physical therapist, who commonly associated with the HCT team, will especially be important for recruitment. In the majority of case, they are aware of dates that children will be transiting into the hospital for HCT. The study art therapist and physical therapist have a developed relation with the study PI. The art therapist and PI serve together as leaders within the MUSC Office of Humanities. The art therapist has also provided instruction within the PIs' DPT and IP courses. The physical therapist is a graduate of the DPT program in which that the PI teaches. The physical therapist and PI have carried out national presentations together and the physical therapist also instructs within the PI's courses. Participants and HCT team members will contact the PI when interest in enrollment is expressed. Parents will be welcome to contact the PI as well. The PI will contact parents of participants and seek informed consent and assent for study participation.

9.0 Consent Process

Informed consent will be sought upon each child's admission to MUSC Shawn Jenkins Children's Hospital. It will occur approximately on or before Day 13 of the HCT. Day 14 will be for pre-testing and day 15 for start of intervention. Children's authorized representative will have at least 24 hours prior to study intervention initiation.

Consent may be obtained in person at the hospital or using an electronic consent.

For in person consents, the PI will obtain informed consent from parents or legal guardians at the MUSC Shawn Jenkins Children's Hospital.

The PI will communicate by phone or email with the parent or legal guardian to establish a time to seek informed consent at the hospital OR discuss the use of an electronic consent. If an electronic consent is used, the PI will email the consent to the parent or legal guardian using secure MUSC email. Then the PI will contact the parent or legal guardian by phone to review the informed consent and answer any questions. If the parent or legal guardian wishes to enroll in the study, they will sign the informed consent and return to the PI through the MUSC email system.

Assent will be obtained from each individual child or adolescent at the same time that the informed consent is obtained from parents. If informed consent is carried out electronically, the parent will be asked to document the child or adolescent's assent using MUSC email communication.

If a child withdraws assent prior to a study session, parents will be notified. If the child withdraws assent for a session for 3 days in a row, the child will be withdrawn from the study. If assent is less than 3 days, then missed days will be added to the study duration until 10 days are completed.

10.0 Study Design / Methods

Design: Randomized clinical trial to compare collaborative AT and PT to only PT in children undergoing HCT.

Using excel, the study coordinator will randomize each participant to either the PT and AT or PT only group. Each group will be assigned 10 participants.

<u>Power</u>

With a recruitment expectation of 30 participants, we expect a 30% drop out rate leaving 20 enrolled participants and feel confident that this study's aim 2 and 3 will be successfully power to identify statistical significance ($p<0.05$) in outcomes. For Aims 2 and 3 which involve the collection of clustered data for HRV, SAM, and walking distance, in order to identify a medium effect, 80% or 90% power will be achieved with 61 or 82 measurement points respectively.54,55,66,67 Accounting for a dropout rate of 30%, the expected number of participants is 20. With 10 participants in the intervention group, 100 measurement points for HRV, SAM, and walking distance each are expected; thus, ensuring adequate power for aim 2 and 3.

For the PEDI CAT and 6MWT, to achieve 80% power, the projected sample size in each group is estimated to be 16 and 20; therefore, we proposed that we may not be adequately powered for aim 1.51,68 However, findings attributed to aim 1 will provide pilot data to inform a larger randomized control trial. Although aim 1 may not be adequately power, the published minimal detectable change (MDC) for the PEDI CAT selfcare and mobility domains are 2.2 and 2.5 respectively while the Minimally Clinically Important Difference (MCID) for the 6MWT is 7%.69,70 Although, power to find a statistically significant difference may be inadequate, we expect to observe this level/magnitude of improvement in our proposed study. Variation values from this aim will provide data that are essential to guide future research.

Data Analyses

Aim 1: In children undergoing HCT during in-patient care, do a randomized group receiving a combination of Physical Therapy (PT) plus Art Therapy (AT) have improved functional activity level outcomes of self care and mobility as measured by the Pediatric Evaluation of Disability Inventory Computerized Adaptive Test and the 6-Minute Walk Test, compared with a group receiving PT only.
Hypothesis 1: Children receiving the combined intervention of PT plus AT will demonstrate greater improvements in self care and mobility skills.
Statistical Test: Independent sample t-tests

Aim 2: Do children receiving PT plus AT have physiological (sympathetic or parasympathetic) and emotional responses to oil pastels and gouache as measured by respiratory sinus arrhythmia derived from heart rate variability and Self-Assessment Manikin scores during each of the daily AT sessions.
Hypothesis 2: Oil pastels or gouache AT will generate a RSA value in the direction of needed parasympathetic activity and balance the emotions of valence, arousal, and dominance.
Statistical Test: Repeated measures generalized linear regression

Aim 3: In children receiving PT plus AT, determine if there is a stronger association between the RSA values of oil pastels or gouache AT and an increased walking distance as measured by accelerometry during daily PT sessions.
Hypothesis 3: The media that best generates a parasympathetic RSA value and emotional balance will be associated with a greater walking distance.
Statistical Test: Repeated measures generalized linear regression

Data Collection

The 10-day intervention will begin on approximately Day 15 of HCT. Pre-test (Pediatric Evaluation of Disability Inventory and 6-Minute Walk Test) will be collected on Day 14. The same post-test data will be collected the day following the tenth day of intervention.

During the 10 days of intervention, the Self Assessment Manikin, heart rate variability, and walking distance will be collected daily.

The study coordinator will be responsible for storing all data. All documentation and data concerning each participant will be coded to protect confidentiality. All data collection and storage processes and locations will use study equipment (i.e., heart rate variability monitors, computers, College of Health Professions DA server) that is password protected, encrypted, and behind the MUSC firewall. All study related equipment will be locked in the office of the PI when not in use. There will be no transfer of data to a third party.

Procedures
1) IRB approval
2) Begin participant enrollment
3) Collaborate with HCT team to initiate recruitment and share study flyer
4) PI will obtain informed consent from participants in the hospital or electronically through MUSC secure email.
5) Randomize participant to AT and PT or PT only
6) Approximately Day 14 of HCT complete pre-test (Pediatric Evaluation of Disabilities Inventory and 6-Minute Walk Test)
7) Day 15-24 of HCT: 45 minutes of AT and 30 minutes of PT OR 30 minutes of PT only. Heart rate variability, Self Assessment Manikin, accelerometry collected across sessions.
8) Approximately Day 25 of HCT complete post-test (Pediatric Evaluation of Disabilities Inventory and 6-Minute Walk Test)
9) Data analyses and dissemination.

11.0 Specimen Collection and Banking (if applicable)
Not applicable.

12.0 Data Management
All documentation and data concerning each participant will be coded to protect confidentiality. All data collection and storage processes and locations will use study equipment (i.e., heart rate variability monitors, computers, College of Health Professions DA server) that is password protected, encrypted, and behind the MUSC firewall. All study related equipment will be locked in the office of the PI when not in use. There will be no transfer of data to a third party.

13.0 Provisions to Monitor the Data to Ensure the Safety of Subjects (if applicable)
All documentation and data concerning each participant will be coded to protect confidentiality. All data collection and storage processes and locations will use study equipment (i.e., heart rate variability monitors, computers, College of Health professions DA server) that is password protected, encrypted, and behind the MUSC firewall. All study related equipment will be locked in the office of the PI when not in use. There will be no transfer of data to a third party.

Children undergoing HCT will experience symptoms related to the HCT and may experience additional medical complications. Our study involving art and physical therapy interventions will only be carried out during the in-patient phase, which will be helpful when considering adverse effects because a variety of

healthcare professionals will be at hand to possibly prevent and ameliorate any adverse events. For example, prior to each daily session, the art and/or physical therapist will ask the child's nurse if the patient is medical stable to participate. If the nurse, reports that the child is not medically stable, then the child's session will be postponed until stable.

Common symptoms following transplant include fatigue and deconditioning which is associated with lower strength and endurance. We believe children' participation in this study will lead to temporary reports of elevations in fatigue, weakness, and poorer endurance symptoms; however, we will not view these as adverse events since these symptoms are also common to increases in activity level that will be generated by art and physical therapy.

Unanticipated adverse events that might be possible are falls secondary to possibly osteostatic hypotension or clumsiness. If an unanticipated event were to occur, the intervention therapists would immediately report the incident to the child's nurse and attending physician so that appropriate assessment and treatment can begin. The intervention therapist would then report the event to the PI, who would contact the IRB and complete an adverse event report. To avoid experiencing an adverse event, before each intervention session, study team members will communicate with each child's nurse concerning child's medical status that day. If nursing agrees the child's statue is stable, the intervention will proceed. If nursing reports that the child's status is not stable, the intervention will be postponed. If the child experiences a change in medical status that requires transferred to a more complicated medical environment, such as the ICU, study intervention will be postponed until return to the HCT unit. If a child's medical status improves and they are transferred to a "regular" hospital room, the study intervention will continue. Once the child is discharge to home, the study intervention will be stopped even if 10 days of the study intervention have not been provided.

We consider this study to be low risk however our data and safety monitoring plan will be continuous, close monitoring by the study investigator/co-investigators of all participants. The PI (Dodds) and Co-I's (Hinson) will meet once a month discuss data and safety monitoring. During these meetings we will look for any negative trends in the data we have collected (Self Assessment Manikin, PEDI, 6-Minute Walk Test, heart rate variability, accelerometry) that could indicate adverse events and provide a timely summary report of adverse events to the IRB.

Any reportable safety events that are unexpected, serious or may be related to the subjects' participation in this research will be reported to the MUSC IRB and NEA in accordance with their policies.

14.0 Withdrawal of Subjects (if applicable)

Not applicable.

15.0 Risks to Subjects

As with any study there is a risk of loss in confidentiality. All documentation and data concerning each participant will be coded to protect confidentiality. All data collection, storage processes, and storage locations will use study specific equipment (i.e., heart rate variability monitors, computers, College of Health professions DA server) that is password protected, encrypted, and behind the MUSC firewall.

Secondary to undergoing HCT, children often experience sympathetic dominance/physiological and emotional distress (increased heart rate, decreased HR variability, fear) and physical deconditioning (fatigue, atrophy, weakness, decreased endurance) in the short and long term. This study seeks to ameliorate these symptoms by providing AT and PT; however, during AT and PT, children may experience an increase in these symptoms in the short term. Since this study is being carried out during an

in-patient phase of treatment, the HCT care and study team will be able to easily monitor and manage any adverse events.

Unanticipated adverse events that might be possible are falls secondary to possibly orthostatic hypotension or clumsiness during physical therapy and/or all walking type activities.

The treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.

16.0 Potential Benefits to Subjects or Others

Potential benefits to children in the study may include reduced and/or improved sympathetic dominance/ physiological and/or emotional distress and reduced and/or improved physical deconditioning in the short and long-term as a consequence of HCT. If daily AT and PT during the in-patient stay of improves outcomes, the support for daily AT and PT over the course of HCT may be improved.

17.0 Sharing of Results with Subjects

Results will be publicly disseminated through peer-review processes, which will be available to participating families and all interested others through the NEA website and other journals.

18.0 Drugs or Devices (if applicable)

Not applicable.

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