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The Impact of Chemotherapy on the Neuromuscular Components of Gait

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ABSTRACT

Background and Purpose: Pediatric cancers affect over ten thousand children in the United States each year. Although survival rates continue to climb, debilitating long-term side effects from cancer treatment are surfacing. The purpose of this study was to investigate the effects of chemotherapy on selected gait characteristics in children ages five to twenty-two.

Methods: This was a prospective, cross-sectional study that investigated the differences found in and between children undergoing cancer treatment for non-central nervous system cancers and children without cancer. The data was collected in the oncology program of the two campuses of Children's Hospitals and Clinics of Minnesota. Sixty children with cancer and thirty-six children without cancer (controls) participated in this study. Each participant completed impairment testing including: ankle range of motion, ankle strength, and neuropathy rating using the ped-mTNS. Their gait pattern was recorded using the GaitRite Gait Analysis System and then each subject completed a 6 minute walk test.

Results: Using MANOVA procedures, we found that subjects with cancer demonstrated significantly slower walking velocity, decreased cadence, and shorter step length ($\alpha \leq .05$) compared to controls. No significant gait differences were found between cancer patients who received vincristine and those who received IT methotrexate in addition to vincristine ($\alpha \geq .05$). Within the cancer group, significant correlations were found between underlying impairments of ankle dorsiflexion strength, and neuropathy with selected gait characteristics ($\alpha \leq .05$). Significant correlations were also found between

the distance walked in six minutes with velocity and step length ($\alpha \leq .05$).

Conclusions: Children who received chemotherapy treatment had significantly slower velocities, decreased cadence and shorter step lengths when compared to controls. However, adding IT methotrexate in addition to vincristine did not significantly impact gait characteristics. Underlying impairments, such as ankle strength, significantly affected gait characteristics. Finally, the distance children with cancer walked in six minutes was negatively impacted by their decreased velocity and step length. Overall, this study gives insight into the debilitating effects chemotherapy has on selected gait characteristics. Physical therapy may benefit this population by working to improve gait patterns and overall function.

The undersigned certify that they have read, and recommended approval of the research project entitled...

THE IMPACT OF CHEMOTHERAPY ON THE NEUROMUSCULAR COMPONENTS OF GAIT

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in partial fulfillment of the requirements for the Doctor of Physical Therapy Program

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Chapter I: INTRODUCTION

Pediatric cancers, although rare, still affect over ten thousand children in the United States each year. Healthcare has extensively progressed and survival rates continue to improve, but cancer is still the second leading cause of death in children under the age of fifteen.[1] Today, children that become cancer survivors exceed 80% of the pediatric cancer population. These children will very likely become long-term survivors and will have to learn to live with the inevitable side effects following treatment.[2]

Although chemotherapeutic drugs have been successful in treating pediatric cancers and an increase in cure rates has been seen, the side effects of treatment may be extensive and debilitating.[3,4] Many body systems are adversely affected by such drugs, including the cardiovascular, pulmonary and sensory systems.

Chapter II: REVIEW OF RELEVANT RESEARCH

Chemotherapeutic Agent Side Effects:

Chemotherapeutic drugs are designed to destroy rapidly dividing cells; however, at this time these drugs are not specific enough to target only cancerous cells. Unfortunately, other healthy cells in the body that also divide rapidly are affected as well. For example, healthy rapidly dividing cells are found in the endothelial layer of the gastrointestinal tract, in the blood, and in lymph nodes. Chemotherapeutic agents involve adverse gastrointestinal effects, immunity suppression, and low production of red and white blood cells and platelets.

Although neurons in the peripheral nervous system are not rapidly dividing cells, they can be negatively affected by chemotherapeutic drugs. Sensory and autonomic neurons and the cells that support them are nourished by highly permeable capillaries that allow for easy diffusion of toxins.[5] Chemotherapy drugs alter axonal transport and also hinder the metabolic needs of neurons, thus leading to impaired motor and sensory function.[5]

Two such drugs utilized in chemotherapy for the treatment of common childhood cancers are methotrexate (MTX) and vincristine(VCR). MTX is widely used to treat leukemias and solid tumors in children, and is known to lead to neurotoxicity of the central nervous system when administered intrathecally or in conjunction with radiation therapy.[5] The side effects of central neurotoxicity may also have a part in contributing to overall neurotoxicity.[6] VCR in conjunction with other agents has been effective in treating many children with cancer in the United States.[7] However, this treatment has

multiple toxic side effects which limit the dosage at which it can be administered. These effects often present as peripheral neuropathy, with progressive involvement of motor, sensory, and autonomic systems.[7] The symptoms that accompany the neurotoxic side effects are pain, numbness and tingling of the hands and feet, and weakness in both upper and lower extremities.[8,5] Within the first five months of treatment, children are at risk of developing weakness and experiencing a decrease in functional mobility.[6] Other long term impairments include slowed motor nerve conduction velocity, diminished or absent deep tendon reflexes, decreased ankle range of motion, further weakness in distal musculature, which have a negative impact on functional mobility.[9,5]

To date, there are studies that demonstrate that children treated with VCR and MXT perform significantly poorer on functional outcome measures for playing activities and mobility when compared to healthy children.[10] Research has also indicated decreased walking efficiency in adult survivors of pediatric cancer.[9] However, the impact of neurotoxic chemotherapy on neuromuscular gait characteristics in children and adolescents undergoing treatment has yet to be described.

Gait Analysis in Children:

There has been a variety of research, as described above, regarding the effects of chemotherapy on many different aspects of function. However, limited research has been conducted connecting these effects to changes in pediatric gait patterns. There are a variety of techniques used to measure temporal and spatial gait characteristics that have the potential to change with chemotherapy treatment.

Visual observation and video analysis with a stopwatch are two inexpensive techniques to measure gait characteristics with moderate to high reliability, but only determine temporal gait characteristics. Paper walkway is a technique used to measure temporal characteristics through visual observation and some aspects of spatial characteristics from footprints on the paper. Although this method can be used to measure both temporal and spatial aspects of gait, it can be time consuming to set up and analyze data. In more recent years, the GaitRite system was developed as a simplified data collection system for temporal and spatial gait analysis. This system uses a flat walkway with multiple pressure sensors, which record a variety of gait characteristics on a computer. Several research studies have focused on determining the validity and reliability of the GaitRite system with a wide variety of subjects ranging from children to adults and healthy to impaired subjects. Overall, high validity and reliability have been established for this system.[11,12]

The GaitRite system has also been utilized to analyze pediatric and adult gait patterns in populations that present with impaired gait. These studies obtained normative and impaired temporal-spatial gait characteristics in children, young adults, and adults using the GaitRite walkway system, which has been reported to have moderate to high validity and reliability. The data obtained is able to be utilized as a comparison for future studies and is beneficial in recognizing pathologic gait characteristics.[13,14,15,16] For these reasons the GaitRite system was chosen for gait data collection of the present study.

The purpose of this study was to investigate the effects of chemotherapy on selected gait characteristics in children and adolescents ages five to twenty-two years.

This study is part of a larger, on-going study of the impact of chemotherapy on physical function in school-aged children and adolescents.

We generated multiple hypotheses based on the available literature for this study:

1. The gait characteristics of children/adolescents with cancer will differ from children/adolescents without cancer.
2. The gait characteristics of subjects treated with different types of chemotherapy (that is vincristine vs. vincristine with MTX) will be similar.
3. Select neuromuscular impairments will be significantly related to changes observed in the gait pattern of children/adolescents with cancer.
4. Children/adolescents without cancer will walk farther in six minutes compared to children/adolescents with cancer.
5. Selected gait characteristics will be significantly related to the distance subjects walked in six minutes.

Chapter III: METHODS

Study Design

The study had a prospective and cross-sectional design that used a descriptive technique to analyze gait characteristics and is quasi-experimental in estimating the impacts of chemotherapy on selected gait characteristics. All the data collected for each participant was completed in one day and included a chart review or health history and impairment, gait, and functional measurements.

Subjects

Participants were recruited through the oncology program at the two campuses of the Children's Hospitals and Clinics of Minnesota. Subjects and their parents were approached in either the hospital or outpatient clinic during a routine visit. One of the investigators invited the subjects and any siblings meeting the criteria to participate. After recruitment, the patient population included sixty children, between the ages of five and twenty-two, who fit within the inclusion and exclusion criteria. The inclusion criteria included having a diagnosis of either ALL, a type of lymphoma, or a solid tumor; at the appropriate point in treatment based on diagnosis and treatment regime (see appendix A); subjects who gave assent according to institutional guidelines and parental consent to participate. Exclusion criteria included a diagnosis of CNS cancer; a lower extremity amputation or limb salvage surgery; an antecedent neurological, developmental, or genetic disorder; or an ICU stay longer than 48 hours in the previous two weeks. The control population included thirty-six children, between the ages of five and twenty-one,

who were siblings of the patient population or children of clinical staff at Children's Hospitals and Clinics of Minnesota. After completing all the testing, each participant received a ten-dollar gift card.

Procedures

Initially, general health information was collected through a chart review for the patient population and a health history form for the control population. The information gathered from both groups included the following: age, gender, height, weight, leg length, co-morbid conditions, and current medications. Additionally, cancer type and treatment parameters were collected by medical record abstraction for the patient population.

Impairment measures included a neuropathy scale and ankle dorsiflexion range of motion (ROM) and strength. These impairments were chosen based on previous literature, which states these impairments have impacts on the functional mobility of individuals after chemotherapy treatment. [5,6,9] The neuropathy scale used was the pediatric-modified total neuropathy scale (ped-mTNS), which is a scale adapted by Dr. Laura Gilchrist for the use in the pediatric population. This scale uses clinical assessment tools including deep tendon reflexes, pin sensibility, vibration sensation, light touch, and manual muscle testing.[20,21] Based on the score in all five areas, an overall score is generated. (see appendix B)

Ankle dorsiflexion ROM was measured with subject positioned in prone with the knee extended and the foot over the edge of the table. The knee extended position has

been found to correlate best with available ROM of the ankle during heel strike phase of gait (a point in the gait cycle that the greatest amount of ankle dorsiflexion is required). When a standardized approach is used by trained clinicians, the inter-rater reliability has been reported to be high (0.88).[22] The last impairment measure was ankle dorsiflexion strength, which was measured in standard manual muscle testing position. Reliability for manual muscle testing has been reported to be good (0.63).[23]

The GaitRITE gait analysis system was used to collect the gait measures used in this study. This system involves an electronic walkway that contains sensor pads that are connected to a computer for data acquisition. The spatiotemporal parameters of gait focused on in this study included velocity, cadence, step length, single limb support, double limb support, and base of support. The GaitRITE was used instead of observational gait analysis since the GaitRITE has been proved to be reliable and valid among a multitude of populations as discussed earlier, whereas; observational gait analysis has questionable validity and reliability.[24,25] Each subject completed two trials and the gait variables were averaged for the two trials. All subjects were instructed to walk at their "normal" speed. Additionally, velocity, cadence, and step length were normalized to account for the varying height differences amongst the participants.

Lastly, the functional measure used was the six minutes walk test (6MWT), which is a measure of sub-maximal functional capacity and endurance of the cardiorespiratory system. Guidelines for administration from American Thoracic Society[26] were followed. The 6MWT demonstrated strong concurrent validity to the VO2 max during the treadmill test and strong test-retest reliability.[27] Recently, height-specific reference standards for

the 6MWT were constructed using a sample of 1,445 healthy children aged 7 to 16 years.[28]

Statistical Analysis

After the data collection, the data was entered into an Excel spreadsheet by two researchers. Two different researchers performed a spot check of the data to ensure accurate entry and removed extreme values determined to be likely due to measurement error and subjects with missing data.

In order to account for unequal stature between participants, various methods of normalization that have been previously established in other studies was investigated. These methods include scaling data to leg length, height, velocity, and body mass.[29] In literature, Hof discussed non-dimensional forms as methods of normalizing data such as by leg length. Hof described dividing data by the normalization variable or using ratios to obtain dimensionless data.[29] In addition, a study by Standsfield et al. reported semi-dimensional and non-dimensional normalized data in a seven year longitudinal study of gait in 16 children ages 5-12 years old. In this study, the children walked over the GaitRite system and the researchers collected ground reaction forces, motion data, weight, height and leg length. Semi-dimensional normalization was used for velocity, cadence, and step length based on description in the literature. Non-dimensional normalization was utilized for weight, length and time. The gait data was normalized to height and leg length. These authors recommended use of non-dimensional normalization

rather than semi-dimensional for comparing the development of children's gait patterns.[18,29]

Based on the literature stated above, selected gait characteristics including velocity, cadence, and left and right step length were normalized in order to account for size differences amongst participants per the protocol described by Strandsfield et al. The formula used for normalization was (leg length/height) x variable, where the variable was either velocity, cadence, or step length.[18] Stride length was not analyzed for our purposes as it is not directly addressed in clinic practice.

SPSS version 19 was used for statistical analysis of the results. ANOVA and MANOVA procedures were used to analyze variance between groups. MANOVA was used when multiple variables were included in the analysis in order to minimize experiment-wise error rate. Pearson R correlation was used to verify relationships between selected variables.

Chapter IV: RESULTS

Demographics

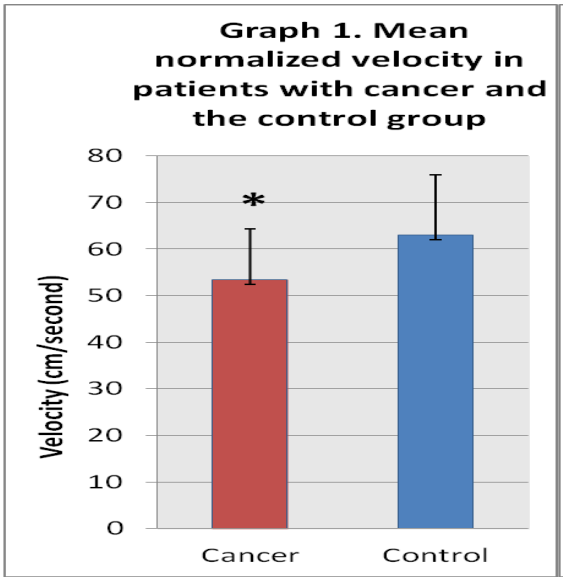
Table 1 shows the means +/- 1 standard deviation of age and height and percentage for gender and cancer type as well as the percentages for gender and cancer type. Based on the MANOVA analysis, no statistical significance difference was found between the two groups ($\alpha > 0.05$). A MANOVA analysis revealed that there was no significant difference in age, height, and gender between the cancer and control group.

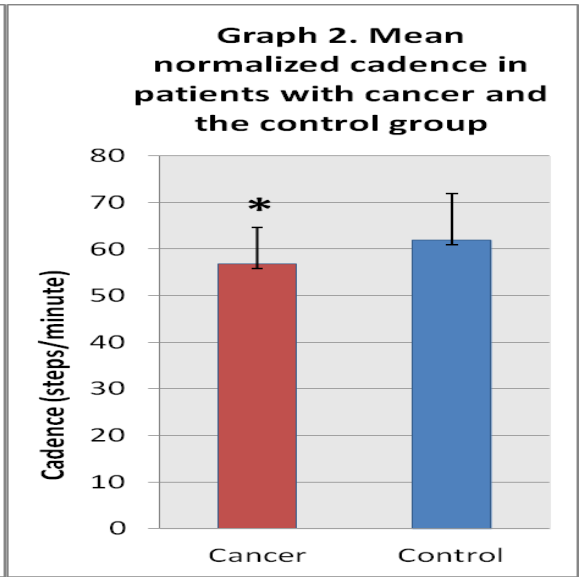
Table 1. Baseline characteristics of patients with cancer and the control group

	Cancer Group (n=60) **Mean** ± 1 SD			**Control Group (n=36)** **Mean** ± 1 SD
Age (years)	11.6 ± 4.6			11.2 ± 3.4
Height (cm)	147.4 ± 23.2			149.3 ± 18.7
Gender (%M)	43			53
Diagnosis (%)	48.3 ALL	30.0 Lymph	21.7 ST	NA

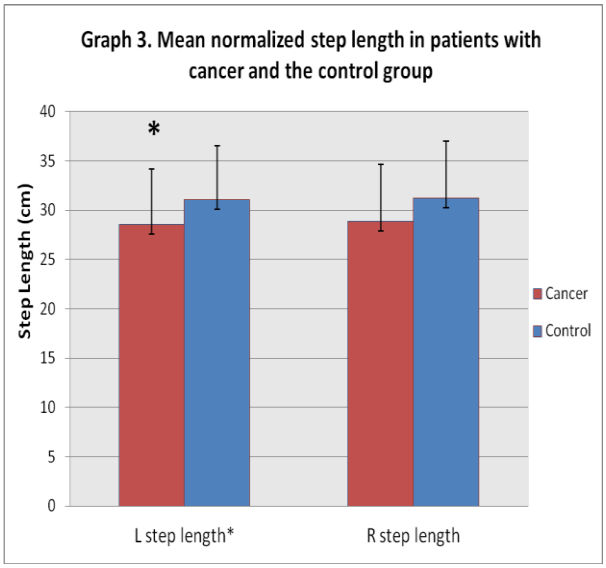
Our first hypothesis was that the gait characteristics of children/adolescents with cancer will differ from children/adolescents without cancer. A MANOVA analysis using Wilks' Lambda between the cancer (n=60) and the control group (n=36) was run to determine differences between the groups for the following gait characteristics: mean normalized velocity, cadence, left and right step length, and right and left base of support, and single limb support time. The analysis revealed significant differences between the cancer and control group for mean normalized velocity, cadence and left step length ($p \leq .05$). Subjects with cancer demonstrated significantly slower walking velocity ($p=.001$), decreased cadence ($p=.007$) and shorter left step length ($p=.034$) compared to controls. Mean normalized right step length approached significance at $p=.056$, however,

was not statistically significant. In addition, there was no significant difference in mean left and right base of support and single limb support time between the groups ($p \geq .05$). This analysis yielded sufficient power at 0.860.



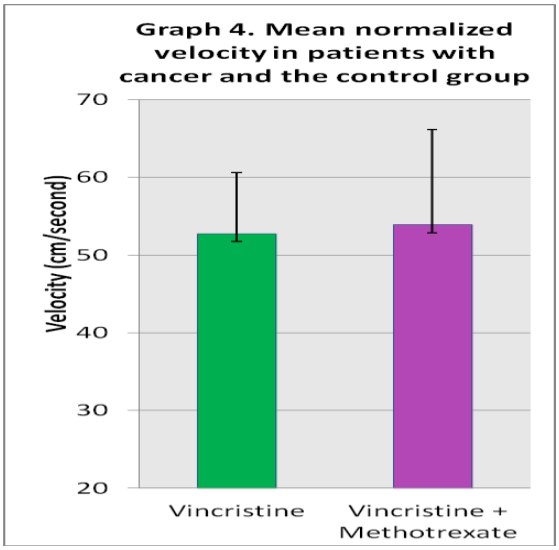


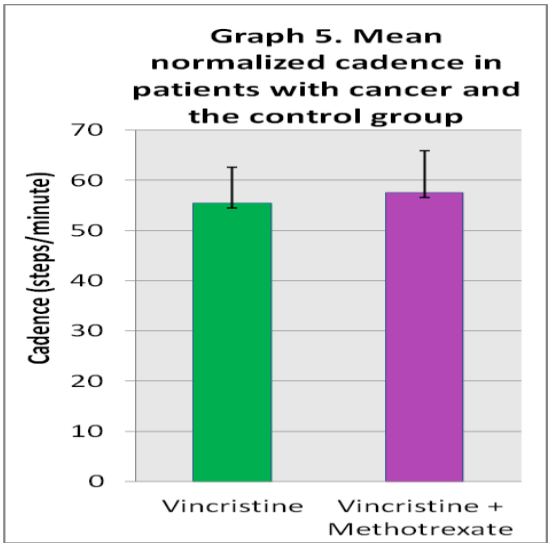
Graph 1 and 2 show the significant differences in mean normalized velocity and cadence between the cancer and control group ($p \leq 0.05$). These graphs demonstrate that subjects with cancer had significantly reduced velocity and cadence.



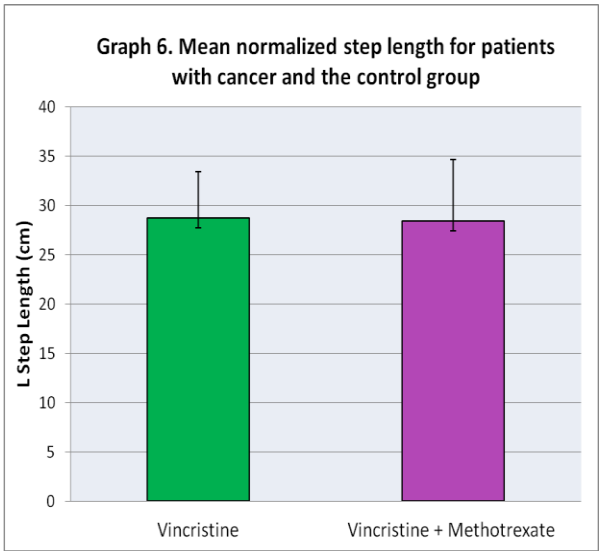
Graph 3 shows differences in mean normalized left and right step length between the cancer and control group. Left step length was found to be significantly different between the groups ($p \leq 0.05$) and although right step length approached significance at 0.056, it was not significant.

Our second hypothesis was that the gait characteristics of children treated with different types of chemotherapy regimes will be similar. A MANOVA analysis using Wilks' Lambda between subjects who received only vincristine (n=22) and those who received vincristine with intrathecal (IT) methotrexate (n=38) was run to determine differences between the chemotherapy treatment groups for the following selected gait characteristics: mean normalized velocity, cadence, left and right step length, and right and left base of support, and single limb support time. The MANOVA analysis showed that no significant differences were found in gait characteristics when adding IT methotrexate to vincristine treatment for normalized velocity, cadence, left and right step length, and- left and right base of support and single limb support time (Wilks' Lambda=.932; F8-51=.467;p=.873). The power analyses yielded a power of 0.195 suggesting that there was an- insufficient sample size to detect a- difference between groups.





Graphs 4 and 5 illustrates the effect of Vincristine and Vincristine with IT Methotrexate on the mean normalized velocity and cadence in patients with cancer. These graphs show that no significant differences were found between treatments for these gait variables ($p \geq 0.05$).



Graph 6 illustrates the effect of Vincristine and Vincristine with IT Methotrexate on the mean normalized left step length. Similarly, there was no difference in left step length between the chemotherapy treatment groups ($p \geq 0.05$).

Our third hypothesis was that select neuromuscular impairments will be significantly related to changes observed in the gait pattern of children with cancer. The Pearson R correlation analysis was used to determine relationships between impairment and gait variables. Explored impairment variables included neuropathy, left and right dorsiflexion strength, and left and right active dorsiflexion range of motion. Explored gait variables included normalized velocity, cadence, and left and right step length. Other gait variables such as right and left base of support and single limb support were not included in the correlation analysis as they were not statistically significant between the cancer and control groups. Mean normalized cadence was significantly inversely correlated with mean neuropathy ($r = -.280$, $p \leq .05$). Also, mean left dorsiflexion strength was positively correlated with mean normalized left step length ($r = .306$, $p \leq .05$). Lastly, mean right dorsiflexion strength was significantly positively related to normalized mean right step length ($r = .263$, $p \leq .05$). Based on the correlation analysis we found that patients with higher neuropathy scores demonstrated lower cadence. In addition, patients with greater

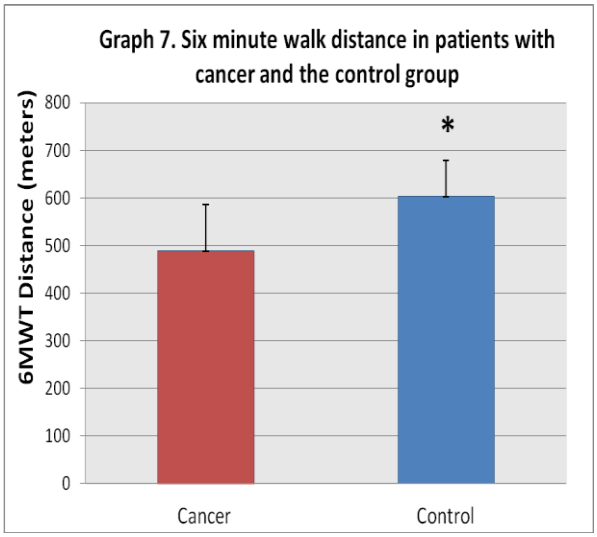
left and right dorsiflexion strength had longer left step length. No other correlations between neuromuscular impairments and gait characteristics were statistically significant.

Table 2. Significant Correlations Between Impairments and Gait Characteristics

Gait Variables	**Impairments**				
	Neuropathy	**L DF Strength**	**R DF Strength**	**L DF ROM**	**R DF ROM**
Velocity	-.100	.217	.209	.069	.058
Cadence	**-.280***	-.055	-.040	.159	.176
L Step Length	.111	**.306***	**.263***	-.084	-.093
R Step Length	.149	.246	.218	-.052	-.036

Table 2 demonstrates the significant correlations between impairments and gait characteristics. The correlation (r) value is listed between impairment variables and gait variables. Significant correlations are bolded in the table. * Indicates significance of $p \leq 0.05$.

Our fourth hypothesis was that children without cancer will walk farther in six minutes compared to children with cancer. An ANOVA analysis using Wilks' Lambda between the cancer (n=60) and the control group (n=36) was run to determine if a difference existed in the 6 minute walk distance between the groups. The 6 minute walk distance was chosen for analysis as it is a functional measure of the efficiency of ones' gait. The analysis revealed significant differences in the distance children were able to walk in 6 minutes between children with cancer compared to controls ($p \leq .001$). Our results suggest that patients without cancer walker farther in 6 minutes when compared to children with cancer.



Graph 7 demonstrates the 6 minute walk distance in meters between the cancer and control group. This graph demonstrates that patients without cancer walked farther in 6 minutes when compare to children with cancer ($p \leq 0.05$).

Our fifth hypothesis was that selected gait characteristics will be significantly related to the distance cancer patients walked in six minutes. Pearson R analysis was used to determine relationships between gait characteristics and the 6 minute walk distance. Variables that were included in Pearson R analysis were the 6 minute walk distance, left and right single limb support and normalized velocity, cadence, and left and right step length. Significant positive correlations were found between the distance walked in 6 minutes and normalized velocity and step length in cancer patients. Mean normalized velocity was positively correlated with mean 6 minute walk distance ($r=.354$, $p \leq .05$). Mean normalized right step length demonstrated a positive relationship with mean 6 minute walk distance ($r=.347$, ,$p \leq .05$). Lastly, mean normalized left step length demonstrated a positive relationship with mean 6 minute walk distance ($r=.321$, $p \leq .05$). No other significant correlations were found. These results suggest that with increased speed and step length (right greater than left), children demonstrated increased walking

distance in 6 minutes. In addition, we did not find a significant relationship between single limb support, and normalized cadence with 6 minute walk distance.

Table 3. Significant correlations between selected gait variables and 6 minute walk distance

	Significant Correlation Values
Normalized Velocity	.354*
Normalized R Step Length	.347*
Normalized L Step Length	.321*

Table 3 demonstrates significant correlations between selected gait variables and the 6 Minute Walk Distance($p \leq 0.05$).

Chapter V: DISCUSSION

The results of the current study indicate children who have gone through a chemotherapy treatment of vincristine or vincristine with IT methotrexate have impaired gait characteristics and functional mobility compared to children without cancer. Significant differences were found both at the impairment and functional levels, with significant correlations between the two. Children treated with chemotherapy had significantly slower velocities, decreased cadence and left step length when compared to the control group, suggesting that chemotherapy has a negative impact on gait characteristics.

Although differences between the groups were found, no significant results were found as a function of the type of chemotherapy received within the cancer group. The addition of IT methotrexate to the vincristine regimen did not significantly affect any of the children's gait characteristics. These results are somewhat consistent with what Hartman and colleagues found in 2006[8] when investigating the motor performance in children with cancer and whether this performance was based on cumulative vincristine dosage. Using the Movement Assessment Battery for Children scale (m-ABC), they measured differences in 128 children between ages of 4 and 12 who had completed treatment at least one year prior. Results of that study found no significant differences on the functional measures between children who received pulses of vincristine and steroids during treatment compared to those who did not. This literature, in addition to our results, suggests the addition of IT methotrexate does not further influence the effect on gait characteristics.

Investigation into the impact of impairments on gait characteristics in this study revealed significant associations within the cancer group. As hypothesized, worse neuropathy was associated with a reduced cadence, as well as stronger left and right dorsiflexion strength correlated with increased left step length. Comparison of these results to previous literature found changes in ankle dorsiflexion and peripheral muscle strength as long-term side effects of chemotherapy treatment in children. A study done by Hartman and colleagues[10] examined these deficiencies in ankle dorsiflexor and wrist extensor strength and ROM pinch grip, as well as their association with motor performance. When comparing these impairments to functional measures, ankle dorsiflexion ROM was not significantly correlated with functional movement on the m-ABC. Although this study investigated functional movement and not specific gait characteristics, it was similar to our findings of a lack of correlation between ankle ROM and gait characteristics.

Another result of this study found children without cancer walked farther distances in six minutes than those in the cancer group. This was consistent with what we anticipated and is congruent with the literature Ness and colleagues[9] performed that found walking efficiency was the most common physical performance limitation seen in cancer survivors, with 46.5% of participants scoring in the lowest 10th percentile, compared to age, sex, height, and weight matched normative values. While in this analysis we did not normalize the data for height or gender, the demographic analysis of the two groups yielded no significant differences. Thus, we feel comfortable that the differences between groups on the six minute walk distance are due to cancer and

treatment variables and not height or gender. Overall, these findings demonstrate the negative impact cancer and chemotherapy have on functional activities such as community ambulation.

Our final hypothesis studied the impact of gait characteristics on the six-minute walk test results. Consistent with our prediction, we found that six minute walk distance was significantly correlated with self-selected "normal" velocity on the GaitRite mat as well as left and right normalized step lengths for their "normal" walking velocity. Ankle dorsiflexion strength was positively correlated with step length and step length was also positively correlated with velocity. These relationships suggest variables such as these can impact the ability to walk efficiently. It is important to take into consideration, however, the toxicity chemotherapy has on other systems, such as the cardiovascular and pulmonary systems, which also affect the distance one can walk in six minutes. The analysis of the impact of impairments of other body structures and systems on walking distance is beyond the scope of this study.

Collectively, these outcomes uncover the potential for physical therapy in this population and suggest therapists should take into consideration the power of improving ankle dorsiflexion strength and delegating time to perform gait interventions. It is also important for therapists to examine the barriers to treating this population. A study by Jones and colleagues[19] found the barriers for exercise recommendations by physicians included not being aware of the benefit in this population and being unsure of referral options. It is crucial that therapists strive to educate physicians on the available literature

and potential for physical therapy as well as provide a referral option for cancer survivors.

The results from this study should be interpreted while taking into consideration possible limitations. These include a limited number of participants and diagnoses as well as no intentional age or gender matching between groups at this time. The impairments and gait characteristics were only measured once, compared to examining the changes over time. The impact of the two agents vincristine and IT methotrexate were analyzed; however, children did receive other medications that could potentially impact gait variables. The GaitRite system was used to measure the gait characteristics and therefore there was no kinematic record or EMG data to examine. All of these limitations have to potential to be addressed in follow up studies of this population.

There are many future opportunities for research on this topic. It would be beneficial to measure the changes in gait characteristics before and after performing the six-minute walk test in order to evaluate the impact of fatigue on these parameters. It would also be important to recruit more participants, match the control and cancer group by age and gender and further evaluate the impact of differing chemotherapy doses of vincristine and IT methotrexate as well as the influence of other medications. It would be valuable to track changes in impairments over time and research needs to be conducted to investigate the impact physical therapy interventions may have on improving gait characteristics in this population.

Chapter VI: CONCLUSION

In conclusion, this study gives insight into the impact of chemotherapy on selected gait characteristics in children and young adults. Physical therapy may benefit this population by working to improve impairments, gait patterns, and overall function.

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APPENDICES

Appendix A: Timing of Measurement

***** Indicates Time of Physical Impairment and Motor Performance Measurement

Diagnosis	Month 1	2	3	4	5	6	7	8	9	10	11	12
ALL	Intensive Chemotherapy → *						Maintenance Chemo 2-3 years →					
Lymphoma												
Hodgkins Low Risk	Chemotherapy → *			Follow-up								
Hodgkins Int/High Risk	Chemotherapy → *					Follow-up						
Non-Hodgkins	Chemotherapy → *			Maintenance Chemo →			Follow-up					
Solid Tumors												
Ewings Sarcoma	Chemotherapy →			S ± R	Chemotherapy → *			Follow-up				
EwingsSarcoma /alt protocol	Chemotherapy →			S ± R	Chemotherapy → *				Follow-up			
Neuroblastoma	Chemotherapy (up to 1 year) → * (or within 1 month of end if treatment > 6 mo)											
Rhabdomyo-sarcoma Low risk	Chemotherapy →		S± R	Chemotherapy → *			Follow-up					
Rhabdomyo-sarcoma Int. Risk	Chemo →	S ± R	Chemotherapy → *				Follow-up					
Wilm's Tumor	S± R	Chemotherapy → *							Follow-up			
Wilm's Tumor Alt. Protocol	Chemotherapy →			S± R	Chemotherapy → *				Follow-up			

S = Surgery, R = Radiation

Appendix B:
Pediatric - Modified Total Neuropathy Scale

Sensory Symptoms: _____ (record worst score for the three sensations)
" Do you have any parts of your body that are tingly, numb (can hardly feel), or hurt?"
_____ Tingly _____ Numb _____ Hurt (record number for each)
If yes, "Where you have those feelings?"

0 None
1 Symptoms limited to fingers or toes
2 Symptoms extend to ankles or wrists
3 Symptoms extend to knee or elbow
4 Symptoms above knee or elbow

Functional Symptoms: _____ (record worst score of the three questions)
"Do you have trouble buttoning shirts or tying your shoes?" _____
"Do you have trouble walking such as tripping frequently?" _____
"Do you have trouble going up or down stairs?" _____
If yes to any, "Is it…..(read choices)" and record after each question

0 Not Difficult
1 A little difficult
2 Somewhat difficulty
3 I need help
4 I can't do that at all

Autonomic Symptoms: _____ (record worst score of the three questions)
"Do you feel dizzy or light-headed when you get up out of bed?"
"Do your hands or feet feel hotter or colder than normal?"

0 Never
1 A little bit
2 Sometimes
3 Very much
4 Almost always

Clinical Testing:
Light Touch Sensation: _____

0 Normal
1 Reduced in fingers/toes
2 Reduced up to wrist/ankle
3 Reduced up to elbow/knee
4 Reduce to above elbow/knee

	Semmes		Semmes	Bumps
Toes R		Finger R		
L		L		
Med Mal R		Wrist R		XXX
L		L		XXX
Knee R		Elb R		XXX
L		L		XXX

Pin Sensibility: _____

0 Normal
1 Reduced in fingers/toes
2 Reduced up to wrist/ankle
3 Reduced up to elbow/knee
4 Reduce to above elbow/knee

Vibration Sensibility: _____ (worst score)

0 Normal
1 Reduced in fingers/toes
2 Reduced up to wrist/ankle
3 Reduced up to elbow/knee
4 Reduce to above elbow/knee

	Bioesth	R-S TF		Bioes	R-S TF
Toes R	/		Finger R	/	
L	/		L	/	
Med Mal R	/		Wrist R	/	
L	/		L	/	
Knee R	/		Elb R	/	
L	/		L	/	

Strength: _____ Worst Score (MRC Score R / L)

MRC level: Great Toe ___/___ ankle DF___/___ finger abd___/___ wrist ext___/___

0 Normal
1 Mild weakness (MRC 4)
2 Moderate weakness (MRC 3)
3 Severe weakness (MRC 2)
4 Paralysis (MRC 1-0)

Deep Tendon Reflexes: _____ (Achilles, Patellar)

0 Normal
1 Ankle reflex reduced (Achilles +1)
2 Ankle reflex absent (Achilles 0, others +2)
3 Ankle reflex absent, others reduced (Achilles 0, others +1)
4 All reflexes absent (all 0)