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Quantification of standing balance in survivors of childhood posterior fossa brain tumour

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Résumé

Malgré un intérêt grandissant pour la question du devenir des survivants de tumeur cérébrale pédiatrique, l'évaluation de leur équilibre est souvent négligée. Les objectifs de nos travaux étaient de 1) examiner les écrits portant sur l'équilibre chez les survivants de tumeur cérébrale pédiatrique; 2) comparer l'équilibre debout et la qualité de vie entre les survivants et un groupe d'enfants témoins; et 3) examiner l'association entre l'équilibre debout et qualité de vie chez les survivants.

Notre recension des écrits démontra que les survivants de tumeur cérébrale présentent des troubles de l'équilibre, mais les limites méthodologiques des études nous empêchent de conclure de manière définitive. Ensuite, nous avons recruté un groupe d'enfants survivants d'une tumeur cérébrale de la fosse postérieure et un groupe d'enfants sains. Leur équilibre était évalué à l'aide du *Bruininks-Oseretsky Test of Motor Proficiency-2nd edition* (BOT-2) et du *Pediatric Balance Scale* (PBS). Certains participants ont aussi été évalués avec une plate-forme de force où les limites de stabilité étaient documentées. Finalement, tous les enfants et leurs parents remplissaient le *Pediatric Quality of Life Inventory* (PedsQL4.0).

Nos résultats démontrent que les survivants présentent une diminution de l'équilibre mise en évidence par le BOT-2, mais que leur qualité de vie est similaire aux enfants sains. La performance au BOT-2 est associée à la dimension physique du PedsQL4.0, suggérant une relation entre l'équilibre et la qualité de vie. Nos résultats suggèrent qu'une évaluation de l'équilibre pourrait être bénéfique chez cette clientèle afin de mieux cerner ses besoins de réadaptation.

Mots clés: Tumeur cérébrale, pédiatrie, équilibre, qualité de vie, survivant

Abstract

There is growing interest in studying outcomes in survivors of pediatric brain tumours. Physical outcomes, especially balance abilities, are less investigated. Objectives of this thesis are to: 1) examine the literature for balance outcomes in survivors of pediatric brain tumours, 2) compare standing balance and health-related quality of life (HRQOL) between survivors of pediatric posterior fossa brain tumours (PFBT) and typically-developing controls and 3) explore the association between balance and HRQOL.

A comprehensive review demonstrated that although the literature suggests that survivors of pediatric brain tumours display ongoing balance deficits, studies have limitations, emphasizing the need for further research.

Survivors of pediatric PFBT and typically-developing children were recruited and their balance assessed with the Bruininks-Oseretsky Test of Motor Proficiency-2nd edition (BOT-2) and Pediatric Balance Scale (PBS). Dynamic balance was also evaluated for some participants using a force platform. The Pediatric Quality of Life Inventory measured HRQOL. Statistical analyses included Mann-Whitney U tests to compare results between groups and Spearman's rank correlation coefficient to determine the association between balance and HRQOL.

Balance abilities were significantly worse in survivors as measured by the BOT-2. The PBS displayed a ceiling effect. Certain laboratory outcome measures suggested balance difficulties. All participants' HRQOL scores were within normative values. In survivors, an association was found between BOT-2 scores and the physical dimension of HRQOL.

Survivors of PFBT demonstrate persistent balance difficulties, best assessed by the BOT-2; however, they report normal HRQOL. Future research should be collaborative and focus upon the best ways to manage balance deficits.

Keywords: Brain tumour, pediatrics, balance, health-related quality of life, survivor

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List of Abbreviations

ALL	Acute Lymphoblastic Leukemia
APA	Anticipatory postural adjustment
BOS	Base of support
BOT-2	Bruininks-Oseretsky Test of Motor Proficiency – 2nd edition
BOTMP	Bruininks-Oseretsky Test of Motor Proficiency
CBTRUS	Central Brain Tumor Registry of the United States
CCSS	Childhood Cancer Survivor Study
CNS	Central nervous system
COM	Centre of mass
COP	Centre of pressure
CSAPPA	Child's Self-Perceptions of Adequacy In and Predilection for Physical Activity Scale
EMG	Electromyography
fMRI	Functional magnetic resonance imaging
FRT	Functional Reach Test
HRQOL	Health-related quality of life
HUI	Health Utilities Index
ICCC	International Classification of Childhood Cancer
IQ	Intelligence quotient
LOS	Limits of stability
mABC	Movement Assessment Battery for Children
MDRT	Multidirectional Reach Test
OCEBM	Oxford Centre for Evidence-Based Medicine
PBS	Pediatric Balance Scale
PCTSIB	Pediatric Clinical Test of Sensory Interaction for Balance

PedsQL4.0	Pediatric Quality of Life Inventory
PFBT	Posterior fossa brain tumour
PRT	Pediatric Reach Test
ROM	Range of motion
WHO	World Health Organization

Dedications

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Chapter 1: Introduction

With recent progress made in the treatment of pediatric brain tumours, children and adolescents are surviving longer than before, with 5-year survival rates reaching 71%.[1] Consequently, there has been increasing interest in studying the long-term outcomes of this growing population of survivors to better understand secondary impairments and associated disabilities as well as to establish how best to serve this population from a rehabilitation perspective. To date, many different areas have been explored such as cognitive, medical, social and educational outcomes.[2-5] On the other hand, physical outcomes have been less frequently investigated in survivors of pediatric brain tumours.

The most frequent location of pediatric brain tumours is the posterior fossa, a region of the brain that includes the cerebellum and brainstem.[6,7] The cerebellum is known to play a crucial role in the control of balance.[8,9] Other areas, including the basal ganglia, brainstem, thalamus and neocortex, and their inter-connections may also influence postural control.[8] One can expect that a brain tumour, especially one located within the posterior fossa, could have deleterious consequences on postural and motor control. Therefore, it is surprising that there is not more research conducted into the physical outcomes, including balance, of survivors of pediatric brain tumours.

From a clinical standpoint, physiotherapists working with this population may observe that they demonstrate difficulties in maintaining standing balance but there has been a lack of studies interested in balance abilities in this population. Furthermore, although there may be a growing need for ongoing physiotherapy follow-up in survivors of pediatric brain tumours, it is not always available or provided due to a lack of evidence emphasizing the need for continued rehabilitation services. Another difficulty physiotherapists face is not having any information regarding how well the available clinical assessment tools actually measure standing balance in survivors of pediatric brain tumours. This is due to the fact that there are few studies that utilize clinical outcome measures to assess whether or not these survivors show ongoing quasi-static and dynamic standing balance difficulties. To

date, most of the studies conducted with this population use laboratory based measures but these tools are often not available in the clinical setting.[10-14]

Another issue surrounding the lack of continued rehabilitation in survivors of pediatric brain tumours is that the association between balance abilities and quality of life remains unknown. It can be postulated that difficulty in maintaining quasi-static or dynamic standing balance may lead to difficulty performing certain motor tasks or functions that could in turn affect quality of life. This could further emphasize the need for continued physiotherapy follow-up of these patients. It would be interesting to verify if there exists a relationship between balance abilities, as assessed by the tools regularly used in physiotherapy, and health-related quality of life as this is very rarely measured in the clinical setting.

This thesis will hopefully shed some light into these issues that physiotherapists working with survivors of pediatric brain tumours face. I will begin with a review of the literature on pediatric brain tumours, long-term outcomes in survivors and the control of balance followed by the first manuscript presenting a structured review on balance abilities in survivors of pediatric cancers. Chapter 4 will outline the objectives and hypotheses of the research study while Chapter 5 will provide the methodology. In Chapters 6 and 7, I will present two other manuscripts, one that will present some key results while the second will highlight a specific part of the methods used for this research project. Additional results will be provided in Chapter 8 followed by a discussion in Chapter 9. The final chapter of the thesis will be a conclusion.

Chapter 2: Literature Review

2.1 Brain Tumours in Children and Adolescents

2.1.1 Definitions and Trends

Tumours of the central nervous system (CNS) represent the second most common form of pediatric cancer, after leukemia, and the most common solid tumour in children and adolescents.[15-19] CNS tumours can be described as a "*heterogeneous collection of neoplasms of different histology, behaviour and prognosis*".[19] In children and adolescents, nearly all CNS tumours are primary in origin, meaning that they arise in the CNS.[20] The causes of brain tumours are not well known. There is some evidence that certain brain tumours may be attributed to a genetic predisposition and the only known risk factor for brain tumours is previous exposure to ionizing radiation.[18,21,22] However, these factors account for only a small percentage of all brain tumours in the pediatric population.[6]

There are several trends that emerge with regards to pediatric brain tumour characteristics. The literature tends to suggest that males are slightly more affected than females as noted in several studies looking specifically at incidence rates. Bauchet et al. (2009) found that 52.4% of primary CNS tumours occur in males while Johannesen et al. (2004) found that 55.8% of CNS tumours occur in males.[15,23] Some studies have also reported gender differences in incidence rates: Dreifalt et al. (2004) found an incidence rate of 5.26 cases/100 000 person-years for boys versus 4.5 cases/100 000 person-years for girls.[16] Kohler et al. (2011) report a less striking difference of 48.8/1 000 000 person-years for boys and 48.12/ 1 000 000 person-years for girls.[24] Furthermore, various studies involving participants with pediatric brain tumours, a higher percentage of subjects tend to be male.[20]

Another trend that emerges from the literature is that a majority of pediatric brain tumours occur in the infratentorial region of the brain. This region, also known as the posterior fossa, is defined as the area of the brain that lies below the tentorium cerebelli and contains important structures such as the cerebellum and brainstem.[25] The Central Brain Tumor Registry of the United States (CBTRUS), the largest, highest-quality, population-based database on brain tumours, reports that 28% of all

pediatric CNS tumours occur in the cerebellum (17%) or brainstem (11%).[7] Arora et al. (2009) report similar findings of 30% of brain tumours in children aged 0-14 years old occur in the posterior fossa.[6] A few studies report even higher percentages of pediatric tumours occurring in the posterior fossa: Bauchet et al. (2009) report approximately 50%; Kadri et al. (2005) report 53% while Cho et al. (2002) report 39.1%.[15,26,27]

2.1.2 Incidence

Examining the literature, one notes that incidence rates vary by country and even by geographic regions within a given country. Comparison of incidence rates between studies can be difficult as specific registries have different requirements and methods of collecting data.[22] For example, some registries include benign tumours while others only consider malignant brain tumours. Furthermore, the classification systems used by the various registries to categorize brain tumours are not always the same.

The Canadian Cancer Society reports that between the years 2003-2007, 1039 CNS tumours were diagnosed in children and youth aged 0-19 years old, which represents the third most common form (16%) of pediatric cancer behind leukemia (26%) and lymphoma (17%).[1] Incidence rates from the Canadian Cancer Society are reported to be 27/1 000 000 per year.[1] The most recent report from CBTRUS, dated 2012, reports the incidence of CNS tumours to be 5.05/100 000 person-years in children and adolescents aged 0-19.[7] Incidence rates are highest in the 0-4 age group with an incidence of 5.46/100 000 person-years.[7] This peak is similar to findings in other studies that show a greater incidence in the 0-4 age range.[19,21,23,28] The incidence rates reported by CBTRUS are slightly higher than those reported by several studies on European incidence rates. For example, Peris-Bonet et al. (2006) found an incidence rate of 29.9/1 000 000 children using the Automated Childhood Cancer Information System, a large European database.[19]

An area that is garnering lots of attention is whether or not the incidence rates of pediatric brain tumours are increasing. Several studies report an escalation in the incidence rates of CNS tumours in the pediatric population.[16,22,23,28,29] Some reports highlight a sharp rise in incidence of tumours during the mid-80s, which they attribute to the introduction of magnetic resonance imaging.[16,30] These studies appear to be comprehensive as they analyze trends over several decades with data stemming from multiple sources. Others report that this increase is due to the changing of classification systems as well as the inclusion of benign brain tumours in registries.[22,30] To date, there is little consensus as to whether or not the incidence of pediatric brain tumours is actually rising and no study has been able to empirically explain why these increases may be occurring.

2.1.3 Presenting Signs and Symptoms

The presenting signs and symptoms of brain tumours in the pediatric population vary according to the nature and location of the tumour, as well as the age of the child or adolescent.[31-35] Often signs are related to increased intracranial pressure, which can be attributed either to mass effect of the tumour on the brain or the tumour itself.[32,34] A systematic review and meta-analysis done by Wilne et al. in 2007 found that the most frequent signs or symptoms upon presentation, regardless of tumour location, are headache (33%), nausea and/or vomiting (32%) and abnormal gait or coordination (27%).[36] Several subsequent studies not included in the systematic review have also shown that these three symptoms are among the most common but also include visual problems such as papilloedema or abnormal eye movements.[31,33,37] Many studies also show that the vast majority of children and adolescents will exhibit at least two of these symptoms upon diagnosis of the brain tumour.[37-40] Other reported signs and symptoms from the meta-analysis include seizures, unspecified signs of increased intracranial pressure, squint, change in behaviour or school performance, macrocephaly, cranial nerve palsy, lethargy, hemiplegia, weight loss, focal motor weakness or altered level of consciousness.[36]

Because signs and symptoms of brain tumours vary according to location, tumours occurring in the posterior fossa tend to present in the same manner. Tumours affecting the cerebellum often present with increased intracranial pressure and/or hydrocephalus, causing headaches and vomiting or even macrocephaly.[32,33,41] Other commonly reported signs and symptoms of cerebellar tumours include ataxia, incoordination, head tilt, cranial nerve palsy, gait changes or nystagmus.[32-34,41] Brainstem tumours may additionally present with swallowing difficulties, hemiplegia or upper motor neuron signs.[34,41]

2.1.4 Classification and Most Common Types

A general classification system used, particularly in cancer incidence and survival studies, to categorize pediatric cancer is the International Classification of Childhood Cancer (ICCC). A separate system from adults was deemed necessary as it is believed that tumours in children and adolescents should be categorized by their morphology and not their location.[42] In 2005, a third edition of the ICCC, the ICCC-3, was released.[42] The ICCC-3 includes all types of cancer found in children and adolescents including leukemia, lymphoma and CNS tumours. One shortcoming of the ICCC-3 is that the subdivision of CNS tumours is quite limited with only 6 categories; however, these categories comply with World Health Organization (WHO) classification of tumours of the CNS, which is based on the pathology and genetics of tumours.[42]

The WHO classification of CNS tumours was initially established in 1979, with the most recent 4th edition published in 2007.[43] This extensive classification system, based on tumour histology, is accepted and used worldwide, making international collaboration possible.[43] Certain tumours are further graded into more benign or malignant categories, with low-grade tumours generally classified as WHO grade I or II, while WHO grades III and VI denote high-grade tumours.[43]

Many epidemiological studies have been conducted in order to establish what the most frequent pediatric CNS tumours are and results between the studies are similar. Astrocytomas are the

most common, reportedly accounting for 25.7-47% of all brain tumours in childhood.[1,15,16,26,27,41,44] This is followed by embryonal tumours (16-27.5%) and ependymal tumours (4.8-11.4%).[1,15,16,26,41,44] Based on WHO histological classification, the most common specific type of brain tumours found in children and adolescents varies by age but overall, the most common are pilocytic astrocytomas followed by medulloblastomas, craniopharyngiomas and ependymomas.[6,7,21,26-28,38] Interestingly, three of these four tumours are commonly located in the posterior fossa. Medulloblastomas occur exclusively in the cerebellum and are the most common malignant tumours in children and adolescents.[45] Although not exclusively found in the cerebellum, pilocytic astrocytomas and ependymomas arise primarily in the posterior fossa.[46,47]

2.1.5 Treatment and Acute Side Effects

Treatment of pediatric brain tumours is dependent upon several factors including age, tumour histology and location and may include one or a combination of neurosurgical procedure, radiation therapy or chemotherapy.[20,48-50] Treatment protocols for pediatric brain tumours are constantly evolving as many children and adolescents with CNS tumours are enrolled in clinical trials.[20,48] Groups such as the Children's Oncology Group, a large conglomerate of international centres treating pediatric brain tumours, conduct various trials in order to design effective therapies for tumours where survival is less than optimal or to design treatment protocols that minimize long-term effects on survivors.[20,48] As pediatric brain tumours overall remain rare, these consortiums exist in order to pool patient populations to have more substantial sample sizes.

Often the first step in treatment of pediatric brain tumours is a neurosurgical procedure. Surgery may be necessary on an urgent basis if there is acute deterioration in a child or adolescent's status due to either hydrocephalus or mass effect of the brain tumour itself.[20,48] If the tumour is located in an area amenable to resection, the goal of neurosurgery is to determine histology and to reduce tumour volume, often referred to as "debulking".[20,35,51] Gross total resection of the tumour done as

safely as possible (i.e. without injuring normal brain tissue) is another aim as the extent of resection is highly prognostic.[48,49,52-56] For certain tumours, such as pilocytic astrocytomas or other low-grade gliomas, surgery may be the only necessary treatment.[34,35,49-51,54,56,57]

Complications may arise following neurosurgical resection of a brain tumour. Post-operative complications may include focal neurological deficits including weakness or sensory problems, perioperative stroke (hemorrhage or infarct), brain swelling or cerebrospinal fluid leak.[34,48,57,58] Hydrocephalus may also occur following resection of a brain tumour and may require more permanent solutions such as a third ventriculostomy or insertion of a ventriculoperitoneal shunt.[57,58] Another significant sequela of neurosurgery, specifically after surgery involving the posterior fossa, is the development of posterior fossa syndrome also known as cerebellar mutism.[34,48,57,58] Posterior fossa syndrome is characterized by delayed onset (1-6 days post-operative) of mutism that is often accompanied by emotional lability and other neurologic signs such as hypotonia, ataxia or hemiparesis.[59,60] It has been reported to occur in up to 29% of those having undergone resection of a posterior fossa tumour.[59] Posterior fossa syndrome can resolve in a matter of days or months and recovery is often spontaneous as there is little evidence supporting specific medical or therapeutic treatment; however, children and adolescents can be left with long-term speech difficulties such as dysarthria.[59,60]

With regards to adjuvant treatment, radiation therapy is often used in the treatment of malignant brain tumours as well as unresectable benign tumours.[48,52,56] Radiation therapy involves the delivery of high-energy beams to either a specific area of the brain or to the whole craniospinal axis.[20,48,52,61] Recent improvements in technology have allowed for treatment to better target affected areas, minimizing damage to normal brain tissue.[20,35,48,50,52,61] Medulloblastoma and ependymoma are examples of tumours where radiation therapy is part of the standard of care; however, for some younger children (i.e. those under the age of three years old) all efforts are made to delay radiation as there are well documented long-term effects on the developing brain that will be discussed later.[48-

[51,56,62] Acute side effects of radiation therapy are often short lived and subside within a few days or weeks after radiation has stopped. These acute side effects include local skin reactions, anorexia, nausea, fatigue, local alopecia, otitis, myelosupression, low-grade headaches or acute encephalopathy.[34,48,61,63]

The use of chemotherapy in the treatment of pediatric brain tumours is one that is continuously evolving as researchers attempt to establish the most effective protocols. A major challenge of chemotherapy for CNS tumours is the fact that agents used must be able to overcome the blood-brain barrier.[20,48] There are several indications for the use of chemotherapy in the treatment of brain tumours including: attempting to slow the growth of low-grade tumours, use as an adjuvant to enhance surgery and/or radiation, to delay radiation in infants or young children or to be used concomitantly during radiation therapy to augment effectiveness.[20,51] For some high-grade tumours, chemotherapy in conjunction with radiation therapy remains one of the best ways to prolong survival.[48,50-52] The most commonly used chemotherapy agents are vincristine, etoposide, cisplatin, carboplatin, cyclophosphamide, lomustine, carmustine, methotrexate and temozolomide.[48,49,52] There are many systemic side effects of chemotherapy including nausea, constipation, alopecia, encephalopathy and myelosupression.[34,48,58] Some more focal side effects include peripheral neuropathy caused by vincristine, which can be either motor or sensory or mixed and is usually reversible once treatment is stopped.[34,48,64] Another common focal side effect is irreversible ototoxicity and hearing loss caused by cisplatin or carboplatin.[34,48,64]

2.2 Surviving a Brain Tumour

2.2.1 Survival and Recurrence Rates

According to the most recent statistics from the Canadian Cancer Society, the overall five-year survival rate for primary CNS tumours in Canadian children and adolescents is 71%.[1] These rates are comparable to those reported by larger scale databases in Europe and the United States where overall

survival rates range from 64% to over 70%.[19,30,65] In the literature there is a tendency for studies to show that children diagnosed under the age of three or four years old have a less favourable prognosis, although this is not always statistically significant, with those diagnosed in infancy (i.e. < one year old) having the worst prognosis.[19,30,66,67] With regards to time trends, there has been an unquestionable improvement in overall survival rates of children and adolescents with CNS tumours.[19,24,30,67]

Tumour type, along with age, plays a significant role in survival rates and reports demonstrate a marked difference in survival among various diagnostic groups.[22] In order to simplify the discussion, only the most common forms of pediatric CNS tumours as described above (i.e. astrocytoma, medulloblastoma and ependymoma) will be focused on. Even within a given tumour histology, outcome varies. For example, low-grade astrocytomas such as pilocytic astrocytoma have been described as having very successful 5-year survival rates ranging from 81-97%.[1,24,66,68-71] On the other hand, high-grade astrocytomas, such as glioblastoma, have more abysmal survival that is frequently described in the literature as 2-year (as opposed to 5-year) rates ranging from 29-32%.[66,71-73] Survival rates for medulloblastoma, the most common malignant pediatric brain tumour, have greatly improved over the last decade, now ranging from 41.4-80%.[24,30,66,68,71,74] This variability in rates can likely be attributed to the fact that patients with medulloblastoma are divided into two different risk groups for therapy: standard risk (age>3 years old, residual tumour <1.5 cm^2, no metastatic disease) or high risk (age<3 years, residual tumour >1.5cm^2 and signs of disseminated disease) and not all reports make the distinction between the two groups when reporting survival.[45] Finally, for the third most common tumour histology, ependymoma, survival rates also vary depending on sub-type but are generally reported to be between 64.9-72%.[1,66,75,76]

It is more challenging to find literature reporting specific recurrence rates for pediatric CNS tumours. Many reports are case studies or series and/or focus on treatment of recurrent CNS tumours without noting actual percentages. There is no mention of recurrence rates in the larger reports stemming from the more extensive databases such as CBTRUS. Furthermore, many studies report

progression-free survival, defined as "*time from diagnosis to the date of progression or date of death*".[77] Although the definition does vary slightly depending on the report, progression-free survival may not reflect true recurrence as the cause of death for each subject is generally not established in studies and cannot be directly attributed to tumour recurrence or progression.

Even though the literature is sparse, there are several reports looking at recurrence rates in low-grade glioma and astrocytoma. This is likely owing to the fact that survival rates are higher in these tumours and medical teams need to know how frequently to monitor these children and adolescents for recurrence once their treatment is completed. One study describing outcomes in 361 children diagnosed with low-grade glioma between 1985-2007 reports progression of primary tumour in 38% of patients.[77] Two other studies report recurrence rates of 7% and 44% for low-grade astrocytoma, demonstrating inconsistent rates.[69,78] Direct comparison of these rates is problematic owing to the differing practices in various centers regarding treatment protocols and information maintained in their databases, which likely contributes to the variability of the rates reported in the literature. However, one commonality between many studies is that recurrence tends to occur more frequently in those with only partially resected tumours as compared to those where gross total resection is achieved.[69,70,79]

2.2.2 Long-term Outcomes

As survival continues to improve after diagnosis of pediatric CNS tumours, there is a growing interest in studying the long-term outcomes of this population. Late-effects may be due to the tumours themselves or to the effects of its treatment on the developing brain. Much effort in recent years has gone into investigating what domains may be affected in the long-term in these survivors.

2.2.2.1 Physical Outcomes

Late-effects of treatment on physical and functional outcomes of survivors of pediatric CNS tumours is an area where there is a smaller amount of literature available compared to other domains such as cognitive status. Many of the available studies report physical and functional deficits based on physician assessment or via subjective questionnaires. In fact, very few studies use standardized, objective outcome measures to assess physical functioning in survivors of pediatric CNS tumours. Nonetheless, it remains interesting to examine the available literature.

Of the studies that employ subjective reports, three of the four reports stem from the Childhood Cancer Survivor Study (CCSS).[2,3,80] The CSSS is a large-scale epidemiological follow-up study of survivors (five years or longer) of childhood cancer, consisting of 26 collaborating institutions in the United States and Canada.[81] All three of these studies utilized a 24-page questionnaire to collect data and compared results to a randomly selected group of siblings, who are also included in the CCSS cohort as a control group. Therefore, it is quite likely that these three studies present data with the same participants. One of these studies investigated late-effects in physical performance in survivors of all forms of childhood cancer and found that survivors of CNS tumours had the greatest risk for performance limitations as well as the highest prevalence of participation restrictions compared to both the control groups of siblings and survivors of other forms of pediatric cancer.[80] Both of these concepts (performance limitations and participation restrictions) are abstract and although there was an attempt to quantify them in a systematic manner, neither is well defined in the article. The other two studies specifically investigated survivors of pediatric CNS tumours and found that participants were more likely to report new onset of weakness in arms and legs and coordination or motor problems than the sibling control group.[2,3] The final study using subjective reports to obtain data on physical outcomes in 21 participants found that 8 (38%) had limb ataxia (with 5 of the 8 participants reporting that it limits their daily life), 6 (28.5%) had truncal ataxia (with 3 out of 6 participants reporting that it limits their daily life) and 4 (19%) complained about frequent headaches.[82] But there is no information on how

ataxia was described to participants and what their understanding of ataxia is. So although all these studies report that survivors of pediatric CNS tumours have some deficits in physical functioning, the results are very general in terms of the severity and types of impairments.

Studies utilizing physician-reported outcomes may not be better at providing information on the long-term effects of CNS tumours and their treatment in this population. Very few standardized measures are reported; therefore, the methods for describing the impairments are liable to vary between physicians. For example, in the studies where physicians assessed ataxia in survivors, methods of assessing and classifying ataxia are not presented.[83-85] Although comparison may be inappropriate, rates of ataxia range from 14.5-30.4% in these studies where the sample sizes are small and the timing of the evaluations post-treatment is not the same. Similarly, another abstract concept physicians assess is motor problems. There is no widely accepted definition of what constitutes a motor problem or deficit and often studies utilize a self-made classification system where criteria are quite general. For example, in a study by Macedoni-Lukšič et al. (2003), they attempted to grade motor impairment into categories based on the presence of hemiparesis or ataxia (either graded as mild, moderate or severe) and on cranial nerve function.[86] Other studies use broader categories such as motor problem or abnormal gait without noting any specific criteria used.[75,84,87] Nonetheless, these studies report that motor dysfunction is found in 20.3-56% of their study samples but, as was the problem with the subjectively reported studies, sample sizes are small and time post-treatment that participants are evaluated is not always specified.[75,84,86,87] Although not well defined, according to these studies, it does appear that survivors of pediatric CNS tumours continue to show some form of motor or neurological impairment even up to 30 years after treatment.

Reports that make use of standardized outcome measures to quantify physical outcomes may be more meaningful in that they can objectively describe level of functioning. But studies are very variable and direct comparison becomes impossible owing to different inclusion criteria and the assortment of measures used. One of the most comprehensive studies found, conducted by Ness et al.

(2010), evaluated 78 survivors of pediatric brain tumours compared to a control group matched for age, gender and zip code.[88] Although no specific conceptual framework was elaborated, the study participants were evaluated on a multitude of objective measurements comprising what the authors felt were different facets of physical functioning including: touch sensation using a 5.07 Semmes-Weinstein monofilament (the threshold for loss of protective sensation), hand grip and knee extensor strength using hand-held myometry and several standardized tests: Physical Performance Test, Berg Balance Test and Functional Status Index.[88] They found significant differences between the two groups on all these measures, indicating poorer physical functioning in the multiple areas assessed.[88]

Conversely, the other studies used only one objective measure. Two studies used the Karnofsky Performance Status Scale, a tool that quantifies the functional status of cancer patients on a scale from 0 (dead) to 100 (normal functioning).[89] In both of these studies, 73% of participants had no complaints, functioned normally and were considered independent for daily life.[78,90] Another study investigating motor function using the Bruininks-Oseretsky Test of Motor Proficiency - 2nd edition (BOT-2) in 15 participants with cerebellar tumours diagnosed before the age of five years old, found that 47% showed significant impairment in at least one of the subcategories on the BOT-2 and 40% showed significant impairment in the overall score.[91] However, none of the participants' scores were in the range denoting clinical impairment though they were very close.[91] Rueckriegel et al. (2009) used two fine motor tasks examined via kinematic analysis in a group of 41 survivors with cerebellar tumour (25 with medulloblastoma and 16 with pilocytic astrocytoma) as compared to a control group matched for age and gender.[92] Results showed that survivors of medulloblastoma demonstrated impairment in the parameters of speed, automation and variability in the tasks of writing a sentence and drawing circles while survivors of pilocytic astrocytoma showed impairments only for the writing task in the speed and automation parameters.[92] A final study using the Finger Tapping Test, which measures motor speed, found impairments in 69-77% of 16 10-year survivors of childhood medulloblastoma.[93] Although we cannot directly compare results of these studies, they tend to

demonstrate that survivors of pediatric CNS tumours have multiple areas of difficulty in physical functioning.

Several studies, regardless of how data was collected, try to link certain patient characteristics and tumour or treatment variables to physical outcomes in order to predict who may have difficulties. Results are conflicting. For example, a pair of studies finds a significant association between adjuvant treatments received and motor performance.[3,91] One found that poorer motor performance was associated with both chemotherapy and radiation therapy while the other found poorer results only in those survivors treated with radiation therapy.[3,91] Other studies do not find any significant associations between either of these factors.[78,90] Similar contrasting results are shown when looking at the associations between age at diagnosis and motor performance, with certain studies showing poorer performance in those diagnosed at a younger age.[88,90,92] Other studies demonstrate no significant correlation between age at diagnosis and motor outcomes.[78,91] One reason that some of these studies may not show significant results could be attributed to the small sample sizes of many of the reports. Thus, there may be actual associations between patient characteristics and treatment or tumour variables and physical impairments in survivors of pediatric CNS tumours, but the literature at this time does not provide sufficient empirical evidence to support this.

2.2.2.2 Cognitive and Academic Outcomes

Contrarily to physical outcomes, long-term cognitive outcomes are well documented in survivors of pediatric CNS tumours. There is so much literature that a large-scale meta-analysis was done in 2010 describing neurocognitive sequelae in survivors of pediatric CNS tumours.[4] A total of 39 studies, published between 1992-2009, combining data from 1 318 children were used for the calculations in several domains of neurocognitive functioning.[4] Survivors showed significant deficits compared to normative data in the areas of overall cognitive ability, verbal intelligence, non-verbal intelligence, academic achievement, attention, psychomotor skill, visual-spatial skill, verbal memory

and language as assessed by various standardized tests.[4] Effect sizes varied from small to large depending on the domain.[4] The authors stated that they were unable to analyze for potential predictors or moderating factors as they relate to cognitive performance due to the differing inclusion criteria of the studies.[4] Sample sizes of the included studies varied from 4 to 133 participants as did the time post diagnosis or treatment for survivors although the majority of studies evaluated participants three years after diagnosis.[4]

Studies that were not included in the meta-analysis or that were published after the time period for the search, demonstrate similar results. Most studies investigating cognitive outcomes use a version of the Wechsler Intelligence Scale for Children, which has been translated into several languages, available for different age ranges, undergone several revisions and is available in an abbreviated version. Many of the studies will describe several domains of the test but all of them will report an intelligence quotient (IQ) derived from this tool. Several studies demonstrate that the IQ for survivors of pediatric CNS tumours tends to be significantly lower than the normative range but not at levels where they would be classified as having an intellectual impairment.[77,94,95] Further studies showed that their sample had lower IQ scores (or a greater proportion scored in the lower range compared to the normal population) but was not statistically significant.[90,96,97] It would be interesting to add these studies to the aforementioned meta-analysis to help strengthen the results.

There is further interest in evaluating cognitive function over time to determine whether there is an overall decrease, as is hypothesized by many researchers. Only three studies were found that specifically look at neurocognitive function over several time periods after treatment for pediatric CNS tumours. Sample sizes of these studies are small, ranging from 26-35 participants, each study investigates a different tumour type and all studies use a version of the Wechsler Intelligence Scale for Children.[98-100] One study reveals a decline in overall age-adjusted IQ over time since administration of radiotherapy.[99] On the other hand, the two other studies reveal stable IQs in survivors of CNS tumours over time.[98,100] Another commonly held belief is that children who are diagnosed and treated at a

younger age are more at risk of cognitive deficits. Two studies were found that specifically investigated neurocognitive function in survivors of pediatric CNS tumours who were diagnosed before age three in one study and before age five in the other.[87,91] In the study done by Fouladi et al. (2005) involving participants diagnosed with malignant CNS tumours before age three, significant declines in IQ were found over time, notably in participants who had undergone craniospinal irradiation.[87] Davis et al. (2010) demonstrated that children diagnosed with cerebellar tumours under the age of five had lower overall cognitive scores compared to normative data but that these scores did not fall within the range denoting significant clinical impairment.[91]

Overall, it would appear that neurocognitive function, most often reported as IQ, is significantly impaired in survivors of pediatric CNS tumours regardless of age at diagnosis or tumour type. The question then becomes, what impact does this have on their academic outcomes? Several studies investigate this question. One indicator of academic proficiency these studies employ is the use of specialized educational services. Multiple studies examine this and report that 22-90% of survivors of pediatric CNS tumours require specialized educational services.[2,86,87,93,96,97] Although this represents a large range, it still appears to be a significant proportion of survivors that require additional support. To further highlight educational outcomes, some studies also explore the highest level of education attained by survivors of pediatric CNS tumours. Two studies report that 75% and 54% receive their high school diploma.[86,96] The numbers significantly drop off for those who finish community college or university, reported in two studies as 3% and 20%, which is much lower than general population norms (53% in Canada).[86,96,101] Vinchon et al. (2011) noted that 58% of survivors of pediatric CNS tumours completed high school or higher education without distinguishing between the levels of education.[90] In the only study employing a control group, Armstrong et al. (2009) found that siblings of survivors of pediatric CNS tumours were more likely to graduate from college.[102] Even though most will require special assistance along the way, it appears that many survivors of pediatric CNS tumours are able to obtain a high school diploma and some attain higher levels of post-secondary education.

2.2.2.3 Behavioural and Social Outcomes

When describing behavioural and social outcomes in survivors of pediatric CNS tumours, constructs that are not always well defined, it becomes difficult to separate the two as they are inextricably related. The Child Behavior Checklist, a parent-report measure of psychosocial functioning in children between the ages of 4-18 years appears to be the most widely used outcome measure to evaluate these constructs.[103] There is also a self-report version called the Youth Self-Report.[103] A review article written by Schulte & Barrera (2010) discussed social outcomes in survivors of pediatric CNS tumours, focusing on reports published between 2000-2009.[5] Half of the twenty studies included in the review use the Child Behavior Checklist while three more use the Youth Self-Report.[5] Overall, most studies demonstrate compromised social competence, specifically in what the authors describe as social adjustment, in survivors as compared to normative data or to a control group when used.[5] The review article also investigated if any of the included studies evaluated associations between participant characteristics and treatment to social outcomes and found that the evidence supports that disease recurrence and longer time since diagnosis are related to lower social competence.[5] Additional studies found in the literature that were not included in the review did not demonstrate the same behavioural and social difficulties. For example, a study by Zuzak et al. (2008) found that 4 out of 15 participants (26%) evaluated by the Youth Self-Report had clinically significant deficits and 1 out of 9 survivors (11%) had clinically significant deficits as reported by parents using the Child Behavior Checklist.[82] Similarly, another study evaluating 54 survivors of pediatric CNS tumours found significant deficits in only the internalizing sub score of the Child Behavior Checklist as compared to normative values but did not discuss how this related to social competence.[104]

Another assessment tool found in the literature that is used to quantify behaviour in survivors of pediatric CNS tumours is the Behavioral Assessment System for Children, a questionnaire with self-, parent- and teacher-report versions.[105] This tool does not appear to be as widely used as only two studies employ it to quantify social competence and behavioural problems. One study used the

Behavioral Assessment System for Children in 32 adolescents who were at least one year off treatment for a brain tumour and found that they were not at a greater risk for problems compared to normative values.[105] Similarly, the other study employing this questionnaire with parents of 25 children treated for malignant brain tumours found all scores to be within normal limits.[106] The Behavioural Assessment System for Children may be less widely used as its psychometric properties have not been evaluated in this population so it may be less sensitive to difficulties in social competence in survivors of pediatric CNS tumours.

Interestingly, the only two studies found that employ a control group when investigating social and behavioural outcomes in survivors of pediatric CNS tumours do not use typically-developing children and adolescents but a patient control group. One study uses children and adolescents with juvenile rheumatoid arthritis as a control group when evaluating facial expression recognition.[107] Results of this study showed that survivors of pediatric CNS tumours made significantly more errors in recognizing facial expressions than children with juvenile rheumatoid arthritis.[107] The authors feel this method may be an objective way to evaluate social competence but do not suggest that it fully assesses the construct.[107] The other study used a group of survivors of leukemia as the control group and found that CBCL scores were within normal limits compared to norms and there were no significant differences between survivors of pediatric CNS tumours and survivors of leukemia.[108] Overall, it seems that social and behavioural difficulties may be present in survivors of pediatric CNS tumours, but as these constructs are very vague, definitions need to be standardized and more objective outcome measures need to reflect this definition.

2.2.2.4 Health-Related Quality of Life

There is a growing body of literature on health-related quality of life (HRQOL) in survivors of pediatric CNS tumours. This can be attributed to the fact that the medical community is interested in the impact that increased survival rates in this population have had on HRQOL. The current literature

does not offer any conclusive results. Most of the studies compare their participants' scores to published norms as opposed to using a control group. Furthermore, of the ten studies retrieved that report HRQOL, nine different outcome measures are used. Some of these measures have had their psychometric properties tested while others have not as they were specifically developed for that particular study. Therefore, before researchers begin assessing HRQOL in survivors of pediatric CNS tumours, it may become more important to establish valid and reliable tools.

Results from studies are highly variable. Some report significantly lower HRQOL in survivors of pediatric CNS tumours.[75,109] An additional study, that did not provide statistical analysis, demonstrated a trend for lower HRQOL scores in survivors compared to normative data.[2] There are some studies that show that survivors of CNS tumours rate their HRQOL similar to published norms.[93,106,110] One of these, conducted by Cardarelli et al. (2006), is one of the few that employs a control group.[110] They used the Health Utilities Index to assess HRQOL and the control group consisted of survivors of either acute lymphoblastic leukemia (ALL) or solid tumours located outside the CNS.[110] Results showed no significant differences in HRQOL between any of the groups.[110] Divergent to all the above mentioned results, there are two studies that demonstrate that survivors of pediatric CNS tumours rated their HRQOL higher than published norms.[82,111] This is completely counter-intuitive; however, neither of these studies proposed a clear explanation for this phenomenon. Interestingly, both focused exclusively on survivors of low-grade tumours.[82,111]

Unfortunately, it is difficult to draw specific conclusions from some of the studies with regards to HRQOL. One such study conducted by Reimers et al. (2009) evaluated 126 survivors of pediatric CNS tumours with no control group using a HRQOL tool, the Minneapolis-Manchester Quality of Life questionnaire.[112] The authors used an early version of the tool that had not been fully developed and had been translated to Danish without any norms or testing of its psychometric properties.[112] The aim of their study was to look for potential risk factors related to HRQOL but they did not report or comment upon overall scores.[112] They concluded that lower IQ is a strong determinant for HRQOL,

but this may not necessarily be meaningful if HRQOL was not compromised in their participants.[112] Another study by Odame et al. (2006) evaluated osteopenia, physical activity and HRQOL in a group of 25 survivors of pediatric CNS tumours with no control group.[113] They were primarily interested in the prevalence of osteopenia in their sample and tried to see how the outcomes listed associated with radiation therapy treatment.[113] Results of HRQOL were not compared to norms and although not significant, they found a trend that HRQOL was higher in those participants who had not received radiation therapy.[113] But as with the above study, as there was no mention of how their scores compared to norms or a control group, it is difficult to draw specific and meaningful conclusions.

To conclude, the evidence is conflicting with regards to HRQOL in survivors of pediatric CNS tumours. Studies demonstrate either worse, the same or better HRQOL as compared to published norms or to a control group when used. As previously mentioned, it will likely be necessary to develop tools that are valid and reliable to measure HRQOL in this population. This is the only way to truly assess how the improved medical management and survival rates in children and adolescents with CNS tumours affect their HRQOL.

2.3 Balance

2.3.1 Definitions

The two main functions of the postural control system are to maintain postural orientation and postural stability.[114] On one hand, postural orientation can be thought of as sustaining the alignment of body segments in relation to a one's environment.[114,115] On the other hand, postural stability, more commonly referred to as balance, is defined as "*the ability to maintain the centre of mass (COM) within the limits of the base of support (BOS)*".[114]

2.3.1.1 Quasi-Static Postural Stability

Quasi-static postural stability refers to a person's ability to maintain a stationary position.[114,115] Although the body is stationary, many studies have demonstrated that during quiet standing there are many small oscillations of the COM.[114] This is known as body sway and is often estimated from the centre of pressure (COP), which is described as the location of the vertical ground reaction force acting upon the COM.[114,116] One mechanism proposed for the control of upright posture is the inverted pendulum model, whereby the body sways about the ankle joints.[117] In this model, Winter et al. state that the difference between the location of the COM and the COP is proportional to the acceleration of the COM, which oscillates during quiet standing.[117] This model forms the basis of many studies involving kinetic analysis of balance or dynamic posturography, which will be discussed later.

2.3.1.2. Dynamic Balance

Dynamic balance refers to how a person maintains their postural stability either during movement or in response to perturbations.[114] In these circumstances a person may use both feedback and feed-forward mechanisms in order to maintain balance.[114,115,118,119] Feedback mechanisms, sometimes referred to as reactive postural adjustments, are thought to be the only ones available when dealing with unexpected postural perturbations.[115,118-120] These reactive postural adjustments include reactions such as the ankle, hip and stepping strategies.[114] On the other hand, feed forward control, also known as anticipatory postural adjustments (APA), refers to the preparations to postural control that occur prior to expected movements or perturbations.[114,115] It is believed that feedback information from previous experiences also contribute to these APAs.[118,120]

2.3.2 Neuroanatomy and Systems Involved

The exact way in which balance is controlled in humans is not completely understood. It involves many different parts of the human anatomy as well as the multiple connections between them.

Three of the most important and well-known peripheral systems for balance are the visual, vestibular and somatosensory systems.[114] These systems provide information about where a person's body is in space thereby giving direction as to whether postural adjustments need to be made.[114,121] A very brief overview of each system will be provided. Studies have demonstrated that the visual system is heavily relied upon by children in order to maintain balance.[122-125] Vision allows for people to know the orientation of their head and body within their environment.[114,126] Although vision is heavily relied upon, it not always necessary, as demonstrated by the fact that people can maintain their balance even in the absence of visual input. The parts of the vestibular system that contribute to balance are the semicircular canals and otoliths.[114,121,126] These sensors provide information regarding the acceleration and linear position of the head.[114,121] Finally, the somatosensory system, comprised of proprioceptive and cutaneous sensors including muscle spindles, Golgi tendon organs, joint receptors, nociceptors and thermal receptors, provides additional information regarding body position and movement.[114,121,126] The control of balance requires the integration of all the information provided by these sensory systems. Under differing balance conditions, the reliance on each system varies and these multiple inputs are integrated.

Several areas of the brain are thought to be involved in the control of balance; none more extensively studied than the cerebellum.[8,9] Many studies have shown that different areas of the cerebellum assist in different aspects of balance.[9,127-129] For example, the more medial parts of the cerebellum are thought to the most important for the control of balance.[127,129,130] This is due to the fact that multiple afferent connections arrive from the visual and vestibular systems as well as the dorsal and ventral spinocerebellar tracts, so it is believed that sensory information is integrated there.[8,9,127] To further support this, studies investigating cerebellar lesions in patients have found that those with midline lesions demonstrate worse balance abilities than those with lesions in other areas of the cerebellum.[9,10,131,132] Furthermore, an emerging concept with regards to the role of the cerebellum is its

importance to the motor learning aspect of balance control.[9,128,129] It is believed that the cerebellum, together with the motor cortex, helps finesse APAs based on trial-and-error practice.[9,128,129,133]

Other brain structures involved in the control of balance are the basal ganglia.[8,128,133-135] Less studied than the cerebellum, the exact mechanisms as to how the basal ganglia contribute to balance are unknown. Much of what is known stems from studies involving patients with lesions of the basal ganglia, notably those with Parkinson's disease.[8,135] Visser et al. (2005) suggest that the basal ganglia play a role in the fine tuning of responses to postural perturbations, the running of simultaneous motor programs and sensorimotor integration.[135] Furthermore, after conducting a literature review, Ioffe et al. (2007) assert that the basal ganglia play an important role in the learning of postural control, although no mechanism is clearly proposed.[128] It is known that the basal ganglia receive inputs from the cerebral cortex, including the motor cortex, with projections to the brainstem and spinal cord, which may support these suggestions.[8,135] A study by Goble et al. (2011) utilizing functional magnetic resonance imaging (fMRI) demonstrated activation in different areas of the basal ganglia when healthy participants were performing various tasks wherein balance was challenged.[134]

Lastly, an emerging area of research pertains to the role of the cerebral cortex in the control of balance but, as was the case with the basal ganglia, the mechanisms are not well understood. Various areas of the cortex contribute in differing ways. For example, the visual cortex is involved in the processing of visual information, therefore assisting in maintaining balance.[8,130] Several studies using either fMRI or other similar imaging techniques have shown activation in the parietal, sensory and motor cortices during different balance tasks.[134,136,137] Recent research has also focused upon the role of the pre-frontal cortex in the control of balance. It is believed that the pre-frontal cortex is involved in the regulation of postural responses, notably APAs.[8,133] This is supported by a study by Mihara et al. (2008) where functional imaging showed early activation of the pre-frontal cortex in response to "warned" perturbations.[136] This has led to increased interest of studying the effects of attentional demand on balance, what is also known as dual-task performance.[138] These studies often employ

different balance tasks combined with cognitive ones and several have been conducted in typically-developing children and adolescents.[139-142] All studies demonstrate in one form or another that postural control is decreased when a cognitive task is added in all age groups.[139-142] From the available literature, it does appear that cognitive tasks alter the control of balance in typically-developing children and adolescents, which would support the notion that the pre-frontal cortex plays a role.

2.3.3 Development of Balance

One of the earliest papers on the development of balance was written by Forssberg and Nashner in 1982.[143] Based on their study using kinetic analysis and electromyography (EMG), they found that younger children produced larger and more variable APAs than older children and adults and that younger children demonstrated larger postural sway under altered sensory input.[143] They suggested that the age of 7 ½ years old represents a turning point in balance control, whereby after this age it becomes similar to an adult's.[143] This assertion has been supported by other researchers. For example, in several papers, Assaiante et.al (2005, 2012) discuss previous research conducted by their group where children around the ages of 7-8 years old begin to adopt a head stabilization strategy similar to adults when balance becomes more difficult.[144,145] They also assert that children at age 7 begin to be more selective in terms of the postural strategies that they use.[145] However, they do admit that adolescence is a period where balance mechanisms are still undergoing a maturation process, notably in the integration of sensory information.[144] Similarly, Barela et al. (2003) found that although the coupling of sensory information from visual and proprioceptive systems is adult-like in children at age 6, it has not matured to adult levels by 8 year old (the oldest age investigated).[146] Another study by Girolami et al. (2010) investigating APAs in reaching tasks using kinetic analysis and EMG data found that COP displacement and timing of muscle activation patterns were similar between children older than 7 years old and adults but only had a sample size of 10 participants.[147]

There is literature that challenges this assertion that 7 years old represents a turning point in the development of balance, many of them investigating sensory systems. Hirabayashi and Iwasaki (1995), investigated 112 typically-developing children and adolescents and found that various sensory systems matured at different times.[148] Notably, they found that visual function reached adult levels at 14-15 years old and that vestibular function had not yet reached adult levels at 15 years of age, the oldest age included in the study.[148] Similarly, based on their results, Nolan et al. (2005) suggest that the visual control of balance is still undergoing maturation at 15-16 years of age.[149] Interestingly, Viel et al. (2009), from results of their study comprising of 20 participants between the ages of 14-15 years old, propose a theory where adolescents neglect proprioceptive information during balance tasks.[125] This theory was based on the fact that adults were better able to stabilize various body segments in response to postural perturbations and that adolescents relied mostly on vision.[125] Finally, Sparto et al. (2006) more specifically investigated the integration of sensory information in a group of children between the ages of 7-12 years old and found that the weighting of the information does not reach adult levels.[124]

Other studies refuting that the age of 7 years old represents a turning point in balance control report data on COP parameters. Two studies investigated static balance with trials of eyes open and eyes closed.[150,151] Both studies found that children at age 10 years old have higher maximal excursion of COP and COP velocity as compared to adults.[150,151] Furthermore, Schmid et al. (2005) propose that the transition period for balance control occurs between 9 -11 years old.[151] Finally, another study investigated responses to postural perturbations leading to a fall noted differences in the activation pattern of muscles between adolescents aged 14 years old and adults.[152] Therefore, although all studies tend to agree that the control of balance continues to mature throughout childhood and adolescence, the turning point where responses become similar to adults is still debated.

The literature also seems to support the notion that the control of balance continues to mature as a child gets older and is subjected to different environments that challenge balance. However,

directly comparing studies investigating the development of balance can be challenging. This is due to the fact that the aims and subsequent study designs, tasks and variables, vary immensely between studies as well as the ages represented by the sample.

With regards to sensory integration, studies have shown that children as young as 4 years old are able to take multiple sensory inputs and place differing importance on each one in order to control balance.[146,148,153] However, these studies also demonstrated that this sensory reweighting is not refined at this age and continues to improve throughout childhood and adolescence.[124,146,153] It is not known at exactly what age this sensory integration becomes adult-like.[124,148]

In terms of development of the control of balance, several studies investigate how static balance evolves in children and all utilize COP parameters to describe balance abilities.[149,150,154] Two of these studies, with similar methodology, found that older children and adolescents demonstrated decreased COP excursion and velocity, indicating improved control of balance.[149,150] However, Lebiedowska and Syczewska (2000) found contrasting results.[154] They evaluated children aged 7-18 years old in quiet standing with eyes open and found no changes in any COP parameters over the age groups.[154] This difference could be attributed to the fact that the first two include an eyes closed condition and may offer more of a challenge to balance than the eyes open condition.[149,150] However, Nolan et al. (2005) did report differences in sway parameters in the eyes open as well as the eyes closed conditions.[149]

Studies investigating the development of the control of dynamic balance mostly examine responses to postural perturbations. Two studies, by the same group of researchers, included infants as young as 9 months old among their sample and both had the children stand on a force platform that was subjected to unexpected backwards translations.[155,156] One of these studies examined COP parameters as well as EMG data and divided participants both by developmental level (i.e. stander, new walkers, etc...) and by age group.[156] They found that younger children had stronger distal activation patterns and delayed activation of more proximal muscles (i.e. hip abductors and

hamstrings).[156] As they get older, children show increased activation of proximal muscles as well as the paraspinals.[156] Finally, they concluded that developmental level may be a more appropriate way to predict balance improvement as compared to chronological age.[156] The other study including 9 month old infants, undertook kinematic and kinetic analysis of their participants, whom they divided into groups based on developmental level.[155] They found that even the most developmentally immature participants were able to maintain balance under minimally disturbing perturbations, indicating some rudimentary form of balance skills.[155] Furthermore, they found that the various developmental levels displayed differing patterns of torque adjustments to perturbations and concluded that as a child gains motor skills and interacts with their environment, they refine their balance responses.[155]

The next set of studies investigated children beginning at ages 3-4 years old. Do and Chong (2008) compared responses in children between the ages of 4-14 years old and in adults in a situation where a fall was triggered using EMG and kinetic data.[152] They found that children showed co-activation of soleus and tibialis anterior muscles in response to fall initiation while adults showed alternating contraction of these muscles.[152] Unfortunately, they did not report responses between the various age groups to investigate how they evolved.[152] Another study investigated APAs under either self-initiated or externally imposed perturbations.[118] They found that all participants shifted their COP backwards after the postural disturbance, more so in the externally generated perturbations and that this difference between the two conditions decreased as participants got older.[118] They concluded that feed-forward postural control is present in children as young as 3 years old and that the process refines as children age.[118] Similarly, Girolami et al. (2010) found that children and adolescents between 7-16 years old show direction-specific shifts in COP during specific arm movement tasks.[147] However, the younger children in the study had less consistency in their EMG activation when compared to older children and adolescents but there were only 10 participants in this study so not all ages were represented in the same manner.[147]

Only one study was retrieved that attempted to longitudinally evaluate the same cohort of children and their development of balance control.[116] They followed seventeen children beginning at age 5-6 years old and evaluated them at intervals of 3-4 months until the age of 8 years old.[116] Static balance was assessed in the eyes open condition only and COP parameters were compared. Based on their results, notably changes in COP velocity, they suggest that balance develops in a non-linear fashion between the ages of 5-8 years old.[116] So, although there is a plethora of literature describing the development of balance in children and adolescents, it appears to lack consensus. Furthermore, very few studies attempt to longitudinally assess participants, which may provide more meaningful insight into development trajectories of balance control.

2.3.4 Evaluation of Balance in Pediatrics

2.3.4.1 Clinical Balance Measures

Evaluation of balance in the pediatric population can be challenging as tools need to be applicable to a variety of ages and developmental levels. They need to be easily understood by younger children and the items need to be challenging enough for the older children and adolescents. Unfortunately there is no gold standard for the evaluation of standing balance in the pediatric population. It is important for clinicians to have valid and reliable outcome measures in order to quantify standing balance in survivors of pediatric CNS tumours. However, there are no tools that have been specifically developed or that have had their psychometric properties tested in these children and adolescents. Several measures exist that have been developed for use in other patient groups with brain injury. For example, the Community Balance and Mobility Scale has demonstrated excellent reliability for children and adolescents who have sustained an acquired brain injury.[157] The Balance Error Scoring System was developed for assessment of postural stability after concussions.[158] Neither of these tests is recommended for use in other patient groups so they should not yet be administered to survivors of pediatric CNS tumours.

Some standardized outcome measures were developed for specific age brackets within childhood and therefore would not be applicable for use in all children and adolescents. The Ghent Developmental Test was created to evaluate the progression of balance abilities in children aged 18 months to 5 years.[159] Similarly, the Maastricht's Motor Test was created to qualitatively and quantitatively assess movement in 5 to 6 year olds and includes both a dynamic and static balance subtest.[160] Neither of these tests can be used in children older than the suggested ages as the balance items would not be challenging enough for older children and adolescents.

A few tests that were originally developed for adults have been modified for use in the pediatric population. The Functional Reach Test (FRT) was initially developed for use in the elderly and has been studied extensively in this group and found to be a reliable tool that assesses balance in a dynamic and functional way.[161] Donahoe et al. (1994) were the first to propose the use of the FRT in the pediatric population.[162] Subsequent studies revealed poor test-retest reliability.[163] Owing to this low reliability, Bartlett and Birmingham (2003) modified the FRT to create the Pediatric Reach Test (PRT).[164] They proposed using the FRT in the sitting and standing positions as well as adding a side reach position.[164] Key features of the PRT as well as its psychometric properties are summarized in Table I (p.33). Volkman et al. (2007) also proposed modifications to the FRT in both the way that the reach was performed and measured.[165] Their results demonstrated that a two-arm reach and measuring the distance from finger to toes was more reliable than traditional methods.[165] No data exists on the use of the FRT or PRT in children and adolescents with CNS tumours.

Another test that was modified for use in the pediatric population is the Berg Balance Test. As with the FRT, the Berg Balance Test was originally designed to evaluate balance abilities and risk of falls in an elderly population.[166] Franjoine et al. (2003) modified this test to create the Pediatric Balance Scale (PBS) after examining use of the Berg in children and found that many of them had difficulty completing items due to their behaviour and attention span.[167] They pilot tested the PBS, which re-ordered the items of the Berg and lowered the time standards for certain tasks.[167] Table I

(p.33) presents psychometric properties of this tool. A follow-up study tested the PBS in 643 typically-developing children between the ages of 2 and 13 years and found a ceiling effect in children over the age of 7 years old.[168] Therefore it was recommended that the PBS be used to assess balance abilities in children aged 3 to 7 years old and in those with mild to moderate motor impairments.[168]

Finally, the Pediatric Clinical Test of Sensory Interaction for Balance (PCTSIB) was created as a more objective and standardized version of the adult one.[169] In this test, children are asked to maintain standing balance under six different sensory conditions with their feet placed in two different positions, feet together and tandem.[169] Scores are obtained from the duration that the stance is maintained and the amount of sway. A second evaluator is necessary in order to accurately calculate sway, which is measured by placing a backdrop with lines denoting various angles behind the participant.[169] Reliability of the PCTSIB is summarized in Table I (p.33). A study investigating the use of the PCTSIB in children aged 4 and 5 years old suggested using only the feet together position in this age group as the tandem position was too difficult and few children could maintain it.[170] Another found concurrent validity to be lacking and was unable to establish construct validity of the PCTSIB with a slight modification in typically-developing children aged 5 through 16 years old.[171] As validity is questionable and there is no consensus on which positions to use as well as the fact that two evaluators are required to properly administer the PCTSIB, it may not yet be a feasible tool to use to assess standing balance in the pediatric population.

There also exist a number of standardized outcome measures that assess motor development or ability in the pediatric population that include balance items. However, only two report balance subtest scores separately. One is the Movement Assessment Battery for Children (mABC)[172]. This test underwent a recent revision but reliability and validity data for this updated version is lacking.[173] Furthermore, the manual accompanying the revised mABC reports information based on the original version.[173,174] Certain features of the mABC and its psychometric properties are summarized in Table I

(p.33). It may be difficult to recommend the use of the mABC until further studies are conducted to investigate its psychometric properties, especially for the balance subtest as there are only 3 items.

Another pediatric test with a separately reported balance subtest is the Bruininks-Oseretsky Test of Motor Proficiency – 2nd edition (BOT-2). This test is a recent revision of an earlier version and is a test of both fine and gross motor skills.[175] For each subtest, including the balance subtest, point scores can be converted into standard scores and into descriptive categories of performance (well-above average, above average, average, below average and well-below average).[175] Psychometric properties of the BOT-2 balance subtest are summarized in Table I (p.33).The BOT-2 may be better suited to fully evaluate balance in the pediatric population as both static and dynamic tasks are used and a wide range of ages can be tested. Furthermore, the balance subtest can be independently administered and provide meaningful information without the need to combine the results into a total score.

Overall, there are several seemingly well-developed outcome measures to test standing balance in the pediatric population; however, reliability and validity has not always been extensively investigated especially for the revised versions of some tests. Furthermore, none of the measures have had their psychometric properties evaluated in survivors of pediatric CNS tumours. Several of the existing tools could be applicable as they include normative data from large samples of children and adolescents. Future studies are warranted to fully validate these outcome measures for use in survivors of pediatric CNS tumours.

Table I: Summary of select pediatric balance outcome measures

Test Name	Modified from	Recommended Age	Number of Items	Validity	Reliability	Normative Data	Conditions Evaluated In
PRT[164]	Functional Reach Test	Not specified	6 items	Concurrent[164] Construct[164]	Intra-rater (ICC = 0.54-0.88)[164] Inter-rater (ICC = 0.50-0.93)[164]	Not available	-Cerebral Palsy[176] -Down's Syndrome[177]
PBS[167]	Berg Balance Scale	3-7 years	14 items	Not established	Test-retest (ICC = 0.998)[167] Inter-rater (ICC = 0.997)[167]	Not available	-Mild to moderate motor impairments[167]
PCTSIB[169]	Modified from adult version	4-9 years	6 sensory conditions tested in two standing positions (feet together and tandem)	Not established	Test-retest (Spearman = 0.51-0.88)[163] Inter-rater (Spearman = 0.69-0.92)[169]	Yes	-Cerebral Palsy[163] -Learning disabilities[163]
mABC[172]	Revised in 2007	3-16 years	3 items in balance subtest	Content[172]	Test-retest (Pearson = 0.73)[173]	Yes	-Developmental Coordination Disorder[178,179]
BOT-2[175]	Revised in 2005	4-21 years	9 items in balance subtest	Not specifically evaluated for balance subtest	Inter-rater (Pearson = >0.90)[180]	Yes	-Intellectual disabilities[178,179]

Abbreviations used: PRT = Pediatric Reach Test, ICC = Intraclass correlation coefficient, PBS = Pediatric Balance Scale, PCTSIB = Pediatric Clinical Test of Sensory Interaction for Balance, mABC = Movement Assessment Battery for Children, BOT-2 = Bruininks-Oseretsky Test of Motor Proficiency – 2nd edition

2.3.4.2 Laboratory Balance Measures

Standing balance can also be evaluated using various biomechanical approaches that require more sophisticated equipment. Among those, the use of a force platform appears to be one of the more popular options. The majority of the literature describing these methods is focused upon the control of quasi-static standing balance. As previously mentioned, the force platform is used to measure the COP, which is thought to reflect the oscillations of the COM during quiet standing.[117] This technique has been used in clinical and research settings for various pediatric patient groups including children and adolescents with cerebral palsy and ALL.[181-184] However, all of the research investigating the best ways to analyze data obtained on a force platform has been conducted with healthy young adults or the elderly.

There are many different ways in which the trajectory of the COP can be analyzed during standing. A lack of consensus stems from the fact that there is no normal pattern for COP movement and that there exists a plethora of COP variables that are inter-related and often redundant.[185] It has been suggested that COP parameters be grouped into categories measuring different aspects of the COP trajectory and only select variables from each grouping be chosen for analysis.[185-187] It has also been suggested that parameters which include both anteroposterior and mediolateral components are preferable.[186] Some of the more commonly used COP parameters are the mean velocity and sway area as represented by the 95% confidence ellipse area.[186,188,189] The mean velocity of the COP has been found to be the most reliable of all parameters and is thought to be related to the amount of regulatory activity associated with maintaining a quiet standing position.[185,186,189,190] The 95% confidence ellipse area is defined as the area that is expected to contain 95% of the points of the COP path, which in turn provides information of the size of the COP oscillations.[185,186] Results of a systematic review of the literature regarding COP parameters suggest that the selection of variables should include both distance and time-distance variables, highlighted by both the 95% confidence ellipse area and the mean velocity.[189]

Reliability testing for these COP parameters has been conducted almost exclusively in healthy adults.[189] A systematic review by Ruhe et al. (2010) attempting to examine the reliability of various COP variables found that comparison of results between studies is impossible.[189] This is due to the fact that the methodology, for example trial length, number of trials, positions tested and statistical methods for analyzing data, of each study is different.[189] Another set of studies use the Generalizability Theory to assess the reliability of COP parameters in quiet standing.[188,191] Overall, these studies found low to moderate reliability of the various COP parameters in young healthy adults but sample sizes were quite small.[188,191] Unfortunately, little is known about the reliability of these COP parameters in general, let alone in the pediatric population. It thus becomes difficult to extrapolate the results of reliability studies to the population of pediatric CNS tumour survivors.

Because the methodology is highly variable between studies, there is a lack of consensus as to the best procedures for collecting data regarding quasi-static standing balance using a force platform. As was the case with reliability, studies investigating this have been conducted primarily in healthy adults. One area where there are definite discrepancies is with regards to the length of individual trials. A few studies have found that different trial lengths are required to optimize reliability of individual COP variables.[192,193] Studies have suggested trials from as little as 20-30 seconds up to 600 seconds.[192-194] The systematic review by Ruhe et al. (2010) found that reliability improved as the length of the trial increased and that a 90-second trial should be used as this appears to provide the best compromise between reliability and what is clinically feasible.[189] However, this is based primarily on samples from a healthy adult population and 90-second trials are likely impractical in a pediatric setting due to their lower attention spans. Therefore, this suggested trial length needs to be validated in the pediatric population. There is also lack of consensus on the number of trials to use as protocols in individual studies vary. In their systematic review, Ruhe et al. (2010) suggest taking the average of 3-5 trials; however, there is no empirical evidence to support this.[189] Moreover, there are many other factors that have been shown to shape performance on individual trials of standing balance on a force platform.

For example, one study demonstrated that different verbal instructions influenced outcomes.[195] Additional factors that have been found to affect data collection are the size of visual feedback provided as well as foot placement.[196,197] It has been suggested that in order to better compare results, foot placement be standardized between participants.[197] Thus there exist no optimal protocols for the use of a force platform to assess the control of quasi-static standing balance in any population.

There are extremely few studies specifically investigating how to best assess dynamic aspects of standing balance using a force platform and they have used diverse methodological approaches. Some researchers utilize procedures where the force platform itself moves causing externally driven perturbations but this type of testing requires specially-designed and expensive force platforms.[187] Other methods described to evaluate the dynamic aspect of standing balance have been based on self-initiated perturbations. For example, several studies utilize a method known as the limits of stability (LOS).[198,199] These studies require the participants to trace a circle with the largest radius possible by leaning as far as they can while maintaining both feet in contact with the force platform.[198,199] This may not be feasible in children as the concept and instructions could be difficult for them to understand. An additional approach to evaluating dynamic standing balance is the multi-directional reach test (MDRT), whereby the distance a person is able to reach in various directions is measured by a ruler. A study investigating the validity of the MRDT found that although it appears to measure the same construct of balance as the LOS, only fair correlations exist between the centre of pressure (COP) displacements calculated by these two methods.[200] Using COP data to analyze MDRT may provide meaningful information on the strategies participants use to complete the tasks. Reaching in various directions while data is collected via a force platform has been used in several studies to evaluate sitting balance in participants with spinal cord injury.[201,202] This technique may be useful to assess standing balance in children and adolescents as well as survivors of pediatric CNS tumours as instructions are simple for children to understand and represent a goal-oriented task. Unfortunately, none of the above mentioned methods have been tested for validity and reliability in children and

adolescents. Overall, there is no gold standard to assess quasi-static and dynamic standing balance using laboratory measures in the pediatric population.

Chapter 3: Manuscript 1

Title: Effect of treatment for paediatric cancers on balance: What do we know? A review of the evidence.

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Abstract:

This review aims to explore the literature investigating balance outcomes in survivors of childhood cancer. A structured search of five databases resulted in sixteen articles included in this review. Nearly all were classified as Level 4 evidence using the updated Oxford Centre for Evidence-Based Medicine Levels of Evidence. Balance abilities have been investigated solely in survivors of acute lymphoblastic leukaemia or central nervous system tumours. The literature tends to support the idea that survivors present with balance difficulties but the results need to be closely scrutinized. Several studies report results using the same experimental group, while other studies use balance outcome measures that have not had their psychometric properties assessed with this population. There are also few studies that evaluate dynamic balance abilities in survivors of paediatric cancers, which may be more influential on functional tasks. Furthermore, very few of the included studies investigate how the found balance deficits affect this population's daily lives, which would be necessary in order to determine if intervention should be geared towards this area. Directions for future research should also include multi-centred, clinically-oriented trials to evaluate balance abilities in survivors of childhood cancers compared to healthy control subjects in order to strengthen the literature.

Keywords: cancer, children, adolescents, survivor, posture, balance

Introduction:

With progress made in the treatment of paediatric cancers, children and adolescents are surviving longer than before. Although incidence rates appear to be rising, so has prognosis.[65,203] In Europe, 5 year survival rates for all forms of paediatric cancer are reported between 72%-83%.[65,203-205] These survival rates are similar to those in North America.[1,30] As the population of survivors continues to grow, so too has the interest in studying the long-term outcomes in this group. There have been several recent systematic reviews or meta-analyses done describing the health-related quality of life, neurocognitive status and social functioning in survivors of childhood cancers.[4,5,206,207] Physical functioning has been less extensively investigated.

The studies that have been conducted in this area have focused on only one aspect of the physical domain such as writing tasks, range of motion and strength, visuomotor deficits, or gait analysis.[208-212] For example, Fiorillo et al. analyzed gait in survivors of posterior fossa brain tumours and found that survivors demonstrated increased stance phase and wider step width than controls.[209] The wider step length may imply balance difficulties as the subjects may be using a wider step width to enlarge their base of support but balance, nor the relationship between balance abilities and gait, were not explicitly investigated in this particular study.

Physiotherapists working with paediatric cancer survivors may observe that this population demonstrates difficulties in maintaining balance. Balance or postural stability can be defined as the ability to maintain one's centre of mass within the limits of their base of support and requires the proper functioning and interaction of the visual, somatosensory and vestibular systems.[114] Treatments received for paediatric cancers may impact one or more of these systems. For example, the use of certain chemotherapeutic agents, such as vincristine, have been known to cause sensory or mixed sensorimotor peripheral neuropathies.[213] Long-term effects of treatments may also lead to other body changes in survivors; for example, children having undergone radiation therapy are at higher risk for obesity which has been shown to lead to decreased balance abilities when performing more complex

tasks.[214,215] One could postulate that survivors of paediatric cancers may be at risk for developing balance deficits due to their treatment.

A better understanding of balance abilities in survivors of paediatric cancers is important in order to inform professionals on the extent to which they may need to address this issue in the management of their patients. The primary aim of this paper is to present findings of a structured review of the available literature focusing on the balance outcomes of survivors of childhood cancer.

Methods:

A search of the literature was conducted using the following databases: Medline, CINAHL, PsycINFO, EMBASE and PEDro. The search terms entered were: "neoplasm", "psychomotor performance", "postural balance" and the corresponding MESH words were used to perform individual queries. The resultant searches were combined as follows: "neoplasm" AND "psychomotor performance" OR "postural balance". The inclusion criteria for the retrieved studies were: 1) the primary outcome must be of motor interest (i.e. not quality of life, cognitive outcomes, etc...), 2) studies with human subjects, 3) the use of standardized outcome measures to quantify balance, 4) the majority of subjects included were diagnosed and treated <18 years old for any form of paediatric cancer and 5) any type of published article or abstract found in peer reviewed journals after 1990 until July 2011 including case reports, retrospective studies, cross-sectional studies and abstracts or posters presented at conferences with published proceedings. Exclusion criteria were: 1) studies using only questionnaires to assess balance, 2) studies including subjects who had ongoing treatment, 3) studies in languages other than English or French and 4) studies that included subjects with secondary neurological conditions or other medical conditions that could influence postural control.

In order to compare the results of the retained articles, certain information regarding the subjects and methodology was extracted and recorded. For each study, the diagnoses of the subjects as well as their age at diagnosis were noted. Also, the subjects' ages at evaluation and the time post-

treatment that the evaluation took place were extracted. If a control group was used, information such as what the matching criteria were, if any, was documented. Finally, it was noted exactly what balance outcome measures were used in each study and the primary results obtained regarding these measures.

Additionally, the included articles/abstracts were classified into levels of evidence using the updated Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence.[216] The primary reason for using this classification system is that it is applicable to a broader range of clinical questions and the organization of levels has been simplified from the original version.[217] The row used to rate the retained articles was the first one that considers the question: How common is the problem? (See Table II (p.42)). This row offers four different levels of classification based on where the information comes from.

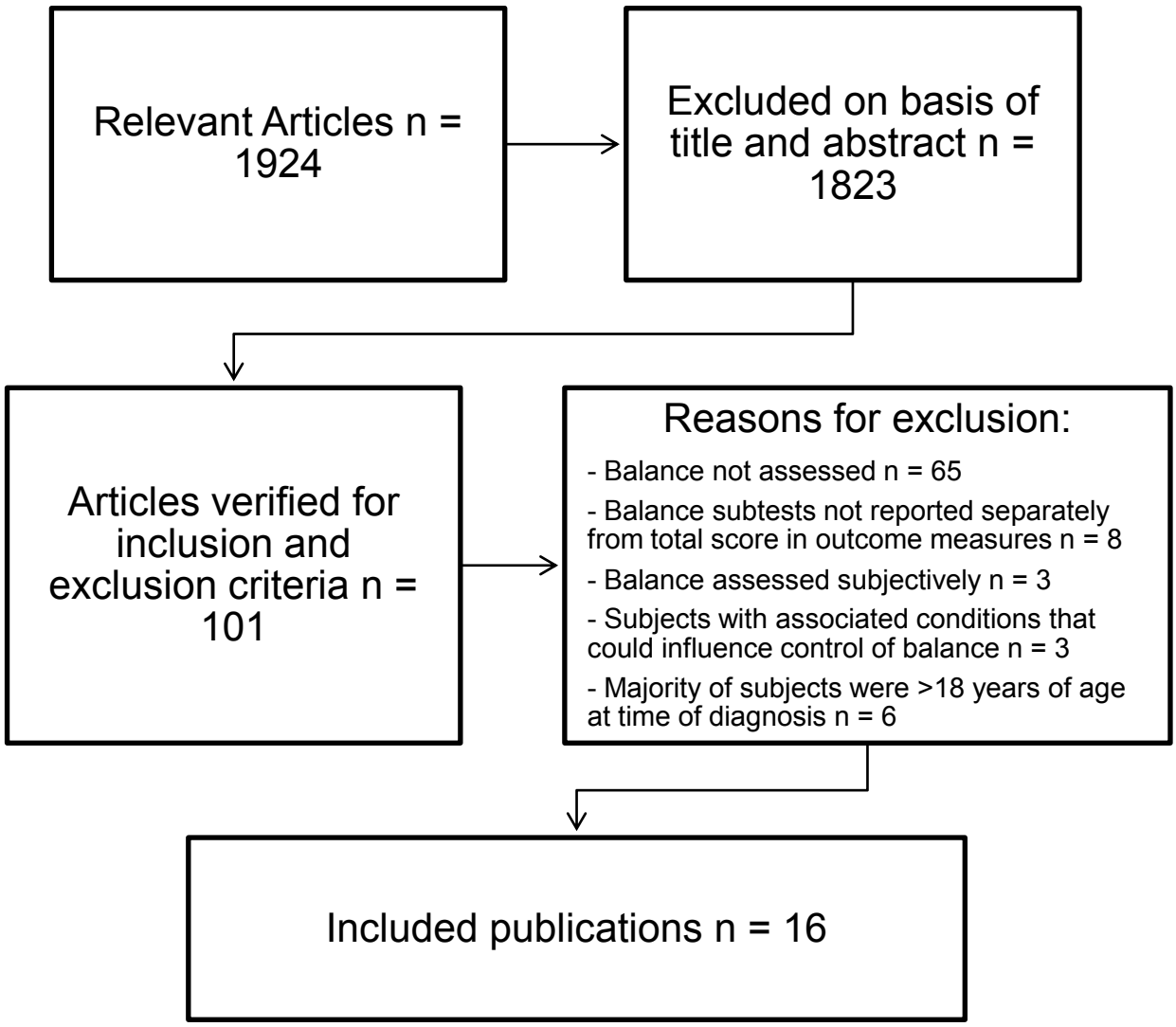
Table II: Oxford Centre of Evidence-Based Medicine 2011 Levels of Evidence – Question: How common is the problem?[216]

Level 1	Local and current random sample surveys (or censuses)
Level 2	Systematic reviews of surveys that allow matching to local circumstances
Level 3	Local non-random sample
Level 4	Case-Series
Level 5	Not Applicable

Results:

After searching all five databases, a total of 1924 articles were retrieved. After duplicate results were removed and titles and abstracts scanned, 88 articles were read in their entirety. The reference lists of read articles were scanned leading to another 41 abstracts consulted and 13 more articles read. Overall, 101 articles were verified for fulfilment of inclusion and exclusion criteria. A total of 16 articles were included in this review. Articles were excluded for reasons presented in the flow chart in Figure 1 (p.43).

Figure 1: Flow chart for retrieved articles including reasons for exclusion



The majority of the articles retained for this review had subjects that were diagnosed with either acute lymphoblastic leukaemia or central nervous system tumours and could be classified as Level 4 evidence based on the OCEBM 2011 Levels of Evidence. Information extracted from each article is summarized in Table III (p.45).

Discussion:

The primary aim of this paper is to present findings of a structured review of the available literature focusing on the balance outcomes of survivors of childhood cancer. Of the sixteen articles included, five focus on survivors of acute lymphoblastic leukaemia (ALL) while the remaining eleven focus on central nervous system (CNS) tumours. This is not surprising as ALL and CNS tumours represent the most common forms of paediatric cancer.[65,205]

If one is to examine the quality of evidence regarding studies investigating balance abilities in survivors of paediatric cancers, according the OCEBM Levels of Evidence 2011, most included studies would be classified as Level 4 evidence.[216] In fact, two articles would not be classifiable as they are case reports. Higher quality studies would be necessary in order to ascertain balance abilities in survivors of paediatric cancers. According to the OCEBM, higher levels of evidence require local random surveys or systematic reviews that allow for comparison be conducted.[216] This may prove difficult to achieve as the population of paediatric cancer survivors although growing remains a limited one, as represented by the small sample sizes in each of the included studies, which range from 5-99 subjects in the experimental groups. To achieve more comprehensive results, multi-centred studies would likely be necessary in the future.

The included studies demonstrate that many survivors of childhood cancers present with balance difficulties; however, these results need to be more profoundly dissected. If we first look at the studies investigating balance in survivors of ALL, all studies include subjects that are at least one year post-treatment. Four of the five studies are conducted by the same group of researchers where the

Table III: Data extraction table for retained articles

Article	Level of Evidence	Diagnosis + number of subjects	Age at Diagnosis	Age at Evaluation	Time post-treatment at evaluation	Control Group	Balance Outcome Measure(s) used	Primary Results
Wright et al., 1996[218]	Level 4	ALL n=36 Wilms' Tumour n=9	Not specified	Not specified	Not specified	Yes n=36 comparable healthy children	BOTMP Balance Subtest	-Balance scores worse in ALL than other groups ($p<0.001$) -No difference between controls and Wilms' tumour group
Wright et al., 1998[219]	Level 4	ALL n=36	0.3-8.8 years	5.5-14.5 years	>12 months	Yes n=36 healthy children matched for age and gender	BOTMP Balance Subtest	-Balance scores worse in ALL group ($p<0.001$)
Bastian et al., 1998[131]	Level 4	Brain tumour: 4th ventricle tumour n=5	> 4 years old	6-15 years	1-24 months	Yes n=5 healthy children matched for age, gender, and handedness	Tandem gait Hopping on one leg (kinematic analysis of tasks)	-Tandem gait: subjects took fewer steps ($p\leq0.01$) than controls -Hopping: subjects showed more variation in height (no statistical information) than controls
Galea et al., 2004[182]	Level 4	-ALL n=79	0.3-17 years	5.7-25.2 years	>1 year	Yes n=83 healthy children matched for age	Force platform: COP displacements, velocity, RMS of excursion (6 conditions tested: normal surface eyes open + eyes closed,	-No statistically significant differences between controls and subjects except: 1) youngest group of subjects lower displacement and

							Romberg eyes open + eyes closed, foam surface eyes open + eyes closed)	velocity of COP 2) 32% of subjects vs. 2% of controls could not perform Romberg eyes closed task ($p<0.01$)
Wright et al., 2005[220]	Level 4	ALL n=99	0.3-17 years	5.1-25.2 years	1.0-13.6 years	Yes n=89 healthy children matched for age and gender	BOTMP Balance Subtest	-Balance scores worse in ALL group ($p<0.001$) -Cranial irradiation, overweight and longer time off treatment were predictors of poorer balance (but explained only 18.7% of variability)
Konczak et al., 2005[10]	Level 4	Brain Tumour: cerebellar tumour n=22	1-17 years	10-28 years	>3 years post-surgery	Yes n=14 healthy controls	Force platform: total sway area of COG, length of sway path, (6 conditions tested: stable platform with eyes open + closed + sway-referenced, sway-referenced platform with eyes open + closed + sway-referenced)	-64% of subjects had enlarged sway areas and sway path lengths that exceeded control group in conditions with sway-referenced platform and altered visual input
Toy et al., 2006[221]	N/C	Medullo-blastoma and posterior fossa syndrome (case	Not specified	12 years	19 months post-surgery	No	PBS BOTMP Balance Subtest Outcomes assessed at 1,4 and 8 weeks post physical therapy	Initial PBS score=50/56 – final score 54/56 Initial BOTMP Balance scale score=5 – final scale score=9

		report, n=1)					intervention	
Van Brussel et al., 2006[222]	Level 4	-ALL n=13 (including 1 with non-Hodgkin lymphoma)	Not specified	8.6-23.7 years	46-73 months	No	Movement ABC	-Reported Static and Dynamic Balance Subset: only 1 subject scored between 5-15th percentile (indicating risk for motor delay), the rest scored >15th percentile
Schoch et al., 2006[12]	Level 4	Brain Tumour: Cerebellar Tumour n=22 (post-hoc analysis of previous study)	1-17 years (age at surgery)	10-28 years	3-25 years (based on data in table)	Yes n=14 healthy controls	Force platform: total sway area of COG (6 conditions tested: stable platform with eyes open + closed + sway-referenced, sway-referenced platform with eyes open + closed + sway-referenced)	-64% of subjects had enlarged sway areas and sway path lengths that exceeded control group in conditions with sway-referenced platform and altered visual input -Damage to cerebellar nuclei has greater impact on balance function than adjuvant treatment
Syczewska et al., 2006[14]	Level 4	CNS tumours n=41	Not specified	6-17 years	Not specified	No	Force platform: maximum medio-lateral and antero-posterior displacements, mean radius of sway and total path covered by COP (2 conditions tested: standing eyes open + eyes closed)	-20 subjects' balance did not differ from healthy subjects -21 subjects had balance deficits (no definition provided), 75% had increased total COP path only -No statistical information
Rorke-Adams and Portnoy,	N/C	gliomatosis cerebelli (case	13 months	18 years old	17 years	No	Romberg test	-Positive Romberg on left monopedal stance with eyes closed

2008[223]		report, n=1)						
Ilg et al., 2008[132]	Level 4	Brain Tumour: Cerebellar Tumour n=12	Not specified	13-39 years	10-133 months post-surgery	Yes n=12 healthy children matched for age	-Kinematic analysis: step width and lateral body sway during gait	-6 subjects classified with impaired balance: cut off criteria defined by control group results -Lesion of medial zone of cerebellum more common in impaired balance group
Syczewska et al., 2008[13]	Level 4	CNS tumours n=88	1-19 years	5-24 years	1-23 years	No	Force platform: COP sway parameters: max radius of sway, mean radius of sway, total sway path, max left + right displacements, max fore + aft displacements (2 conditions tested: standing eyes open + eyes closed) Subjects were also scored on a scale created by authors based on COP variables to compare to reference values for healthy subjects	-No statistical difference in any COP variables in either condition between groups based on location of tumour -Using the scoring system developed by the authors, only in the eyes open condition was there a significant difference between subjects and reference values, but only in group of subjects with tumours located in the posterior fossa
Yissar et al., 2010[224]	Level 4	Brain Tumour: Posterior Fossa Tumour n=13	Not specified	Mean age = 10.47	>3 months	No	BOT-2 Balance Subtest	-Balance scores significantly lower in children after posterior fossa tumour removal (no statistical information)

		Moderate-Severe brain injury n=11						
Ness et al., 2010[88]	Level 4	Brain Tumour n=78	<21 years	18.4-58.3 years	>5 years post-diagnosis	Yes n=78 matched for age, gender and zip code	Berg Balance Test	-Significantly lower balance scores in subjects ($p<0.001$) -Radiation to the posterior fossa or occipital/parietal lobe, treatment with platinum or vincristine and age <5 years at diagnosis associated with lower balance scores (explained 26% of the variance)
Schoch et al., 2010[11]	Level 4	Brain Tumour: Cerebellar Tumour n=16	3.2-38.3 years (age at surgery)	11.3-39.1 years	9.9-133.4 months post-surgery	Yes n=16 healthy controls	Kinematic analysis: total body sway, shoulder sway, sagittal trunk angle (10 conditions tested: sitting eyes open + closed, sitting on cushion eyes open + closed, standing eyes open + closed, standing on cushion eyes open + closed, tandem standing eyes open + closed)	1)Sitting: -On cushion eyes closed, 50% subjects demonstrated abnormal shoulder sway -With eyes closed, 31.3% of subjects had higher shoulder sway -on cushion eyes open, 18.8% subjects had abnormal shoulder sway -Mean trunk angle and mean trunk angular velocity showed little differences between

								groups 2)Standing: -On cushion with eyes closed, 68.8% subjects values above normal (shoulder sway and lumbar sway) -Tandem with eyes open, 75.5% subjects had higher shoulder and lumbar sway values -Tandem with eyes closed, 62.5% had higher shoulder and lumbar sway values -Mean trunk angle showed little difference between the groups -Mean trunk angular velocity was higher in subjects

Abbreviations used: ALL = acute lymphoblastic leukaemia, BOTMP = Bruininks-Oseretsky Test of Motor Proficiency 1st ed., COP = centre of pressure, RMS = root mean square, COG = centre of gravity, N/C = Not classifiable, PBS = Pediatric Balance Scale, CNS = central nervous system, BOT-2 = Bruininks-Oseretsky Test of Motor Proficiency 2nd ed.

sample population and the control groups are recruited from the same hospital setting/area and could potentially include the same subjects.[182,218-220] So although there appears to be literature investigating balance in survivors of childhood ALL, it may not be as extensive as it initially seems. Three of their studies use a clinical measure of gross motor function that includes a balance subtest – the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP) and all found significantly lower scores in survivors of ALL compared to the control group.[218-220] However, in a subsequent study where they used a force platform to measure centre of pressure (COP) displacements in static standing under various conditions (eyes open, eyes closed, Romberg, on foam, etc...), no statistically significant differences were found between groups other than the fact that more ALL survivors could not perform a Romberg test with eyes closed.[182] If some of their study subjects do overlap, a given subject may be classified as having a balance deficit on one study using the BOTMP but their balance has been scored as normal when assessed by the force platform. Therefore, caution must be used when drawing conclusions from these studies. Similarly, the other study investigating balance in ALL survivors concluded that survivors of ALL do not present with balance difficulties. In this study, the Movement Assessment Battery for Children (Movement ABC test), a screening tool of motor performance that includes a balance subset, was used.[222] Only one of thirteen subjects scored in the range that would place him/her at risk of difficulties. Again, we must be cautious in interpreting these results as there was no control group and the median age of their subjects was 15.5 years old while this clinical test was designed for use in children between the ages of 4-12 years old. From the results of these five studies, we may not have conclusive answers into the balance abilities of survivors of childhood ALL.

Similarly, although the literature tends to support the idea that survivors of paediatric CNS tumours present with balance difficulties, the results of these studies need to be more closely scrutinized. It is interesting to note that eight of the eleven studies investigate only tumours that could be classified as posterior fossa tumours (i.e. located in the cerebellum and 4th ventricle areas). If we first examine the articles that have used more clinically-based outcome measures we note that two of

them are case reports, which according to the OCEBM levels of evidence are not classifiable.[216] One report focuses on the long-term survival of an infant with a cerebellar tumour and found that at the age of 18 years old, the subject demonstrated what the authors call a positive Romberg in left single leg stance with eyes closed, which could indicate some extent of balance difficulties.[223] The other case report focuses on a 12 year old boy with a medulloblastoma who underwent physiotherapy intervention for balance issues approximately 19 months post-surgical intervention.[221] The selected outcome measure was the BOTMP and showed that even post physiotherapy intervention, the subject's score was in the range that suggests persistent balance difficulties.

Similarly, the three remaining studies that utilize more clinically-based outcome measures, all demonstrate that survivors of CNS tumours present with balance difficulties.[88,131,224] Bastian et al. investigated five children with prior surgical intervention for posterior fossa brain tumours using tandem gait and found that subjects took significantly fewer steps than controls.[131] Likewise, Yissar et al. found that children having undergone resection of posterior fossa brain tumours had significantly impaired balance compared to published norms of the balance subtest of the second edition of the Bruininks-Oseretsky Test of Motor Proficiency (BOT-2) and compared to a group of children who had sustained moderate to severe traumatic brain injury.[224] But, as this was published in the proceedings of a conference, there is neither statistical information provided nor data regarding individual subjects. The final study utilizing clinically-based outcome measures is a large cohort study done by Ness et al in 2010. Using the Berg Balance Scale, they found that survivors of childhood brain tumours at least five years post-diagnosis presented with significantly lower scores compared to controls, indicating a balance deficit.[88]

Overall it would seem that studies and case reports using more clinically based outcome measures have shown that survivors of paediatric CNS tumours exhibit balance difficulties; however, one major consideration when interpreting these results is that none of the outcome measures used: BOTMP, BOT-2, tandem gait, Berg Balance Scale and Romberg test, have had their psychometric

properties specifically investigated in the population of children and adolescents with CNS tumours or any other form of childhood cancer. This may be overcome with certain tools such as the BOTMP and the most recent version, the BOT-2. Both are norm-referenced tools, with normative values based on a large sample of healthy children and adolescents.[180] Nonetheless, as the population of survivors of paediatric cancers continues to grow, it will become essential to ascertain whether the available outcome measures that assess balance are valid and reliable for use in this population in order to better evaluate long-term outcomes.

Contrarily to the clinical-based outcome measures, many of the studies using more laboratory-based outcome measures (i.e. force platform and/or kinematic analysis) show mixed results. It also becomes difficult to directly compare the results from the various studies as subject inclusion criteria differ as well as the parameters measured and testing positions. One set of studies conducted by Syczewska et al. utilize a force platform to record the COP in two conditions: bipodal standing with eyes open and eyes closed.[13,14] There are no control groups used; however, the subjects' values are compared to those obtained with healthy children in a previous study by the lead author.[154] In the preliminary report they conclude that twenty-one (of forty-one) subjects show a balance deficit and all of those subjects show an increase in total COP path.[14] There is no clear definition of what constitutes a balance deficit. In the follow-up study, the authors further divided subjects into groups based on tumour location and they also developed their own 4-point (0-3) balance scoring system based on the results from the COP sway data.[13] The only statistically significant result was that subjects with posterior fossa brain tumours had worse scores on the author-created balance scoring system in the eyes closed position only. It becomes problematic to draw conclusions into the balance abilities of survivors of childhood CNS tumours from only these two studies as the testing positions were extremely limited and there were no control subjects.

In another set of three studies done by a different group of researchers, we may be able to gain better insight. Two of the articles report data on the exact same group of subjects – the later study a

post-hoc analysis on previous results obtained.[10,12] So, as was the case with survivors of ALL, there may less literature than there initially appears when reviewing balance abilities in survivors of CNS tumours. These two articles report that 64% of their twenty-two cerebellar brain tumour subjects at least three years post-surgery have enlarged centre of gravity sway areas and sway path lengths when compared to a group of fourteen healthy controls in conditions where their proprioceptive and/or visual input was altered.[10,12] This is a similar finding to the above mentioned study by Syczewska et al. where they reported an increased total COP path in their subjects.[14] A later study, and the only one included in this review to assess sitting balance, aimed to kinematically analyze sitting and standing balance in sixteen subjects with benign cerebellar tumours compared to sixteen healthy controls.[11] The tasks that were analyzed were ones that could easily be performed in a clinical setting with minimal equipment. They found that 56% of subjects in sitting and 87.5% of subjects in standing displayed abnormal performance, characterized by shoulder sway above the normal range or by falls, as compared to their control group. This group of researchers was also particularly interested in where surgical lesions were present in the cerebellum and how that would explain balance difficulties. Overall it would seem that their research supports the notion that children and adolescents treated for cerebellar tumours present with persistent balance deficits.

A final study utilizing laboratory measures conducted by Ilg et al. focuses primarily on gait control in twelve subjects with benign cerebellar brain tumours.[132] This was the only study utilizing laboratory measures that evaluated balance during a more functional and dynamic task. Using kinematic analysis and based on the parameters of step width and lateral sway, half of the subjects were classified into the impaired balance during gait group.[132] These parameters were classified as abnormal based on the data obtained from the control group. In the future, more research should focus on the evaluation of dynamic balance abilities in this population as this may give us more information on their functional capabilities.

One interesting point from this review is the fact that there seems to be little correlation between treatment type (surgery, chemotherapy, radiotherapy) and balance abilities. This becomes more of an issue with CNS tumour subjects, compared to ALL subjects, as treatment can be either surgery alone or combined therapy. It is difficult to directly compare studies as inclusion criteria regarding treatments are variable; however, most results demonstrate some degree of balance difficulties regardless of whether they include subjects with only benign tumours or only malignant tumours. There are two studies that directly address this question and both deal with survivors of CNS tumours. One study, the post-hoc analysis by Schoch et al, concludes that the area of the cerebellum that is lesioned during surgery has more of an impact on balance deficits than adjuvant therapy for cerebellar tumours.[12] On the other hand, the other study found an association between lower balance scores and radiation treatment and treatment with platinum or vincristine, although these variables along with tumour location and age of less than five years old at diagnosis explained only 26% of the variance on the Berg Balance Scale.[88]

Overall it does seem that balance appears to be impaired to some extent in survivors of paediatric cancer but one important concept that is not addressed is if and how these deficits interfere with this population's daily life. Of the articles retained for this review, only one attempted to gain some insight into this question. In one of their studies, Wright et al. used the Child's Self-perceptions of Adequacy in and Predilection for Physical Activity Scale (CSAPPA) and the Health Utilities Index (HUI) in their study with children who had been treated for ALL.[220] They found that there was no statistically significant relationship between CSAPPA scores and balance scores (from the BOTMP) but did find that balance scores associated positively with HUI scores.[220]

Strengths of this review article include a 20 year time frame for the search, making certain that articles are relevant to the current population of survivors (i.e. keeping with modern medical management of paediatric cancers). Similarly, broad inclusion and exclusion criteria ensured that any potentially relevant articles were not overlooked. Finally, the extracted data regarding the outcome

measures from the retained articles was extremely detailed thereby making it easier to compare the various studies. One major limitation of this review article was the quality of the studies included. Most studies were classified Level 4, the lowest level, while two were not classifiable according to the Oxford Centre of Evidence-Based Medicine 2011 Levels of Evidence. This highlights that further studies are necessary in order to get a clear idea of balance abilities in the population of paediatric cancer survivors.

Conclusion:

The aim of this paper was to review the available literature on balance outcomes in survivors of paediatric cancers. Although at first glance it may seem that there is extensive literature in this area, several of the studies have overlapping subjects and discuss results from the same experimental group. All the articles discuss survivors of either acute lymphoblastic leukaemia or central nervous system tumours, which is unsurprising as these are the most common forms of paediatric cancer. Overall, the few studies available seem to suggest that balance abilities in survivors are decreased when compared to healthy controls; however, not all studies included control groups. The quality of the studies supporting this conclusion is of a low level and this may only be overcome by collaborative, multi-centred studies in the future. Some of the studies are more clinically-oriented than others but few explicitly investigate dynamic balance tasks. Future studies should evaluate dynamic balance abilities in survivors of paediatric cancer as this may be more related to functional tasks. Furthermore, studies should focus on investigating the relationship between balance abilities and quality of life as it would guide health care professionals on whether or not balance would be an important area to focus their interventions on.

Chapter 4: Objectives and Hypothesis

4.1 Objectives

The general objective of this study is to describe balance abilities in survivors of pediatric posterior fossa brain tumour (PFBT) using a variety of methods.

The specific objectives are:

1) To quantify quasi-static and dynamic standing balance in survivors of pediatric PFBT using clinical outcome measures (the balance subtest of the Bruininks-Oseretsky Test of Motor Proficiency, 2nd edition and the Pediatric Balance Scale) and laboratory measures and to compare their performance to that of matched healthy children and adolescents:
2) To evaluate quality of life in survivors of pediatric PFBT and to compare their results to the matched control group:
3) To determine the association between standing balance and quality of life in children and adolescent survivors of PFBT.

4.2 Hypotheses:

The hypotheses of this research study were that:

1) PFBT survivors will show decreased balance capabilities when compared to healthy controls.
2) Quality of life will be lower in survivors of pediatric PFBT as compared to controls.
3) Better quasi-static and dynamic balance abilities will be associated with improved quality of life in survivors of pediatric PFBT.

Chapter 5: Methodology

The following section will elaborate on the methods used for this research study. First, the process for obtaining approval from the ethics committee is described. Then, the procedures for participant recruitment with the inclusion and exclusion criteria are explained. This is followed by an explanation of the various aspects of the data collection: the clinical evaluation, the clinical balance assessment and the HRQOL evaluation. Finally methods regarding statistical analysis and sample size justification will be provided.

5.1 Ethics Approval

Ethical approval was obtained from the Research and Ethics Committee of the Montreal Children's Hospital of the McGill University Health Centre (Appendix A). Informed consent was obtained for all participants and their parents, for those under the age of 18 years old, and informed consent and assent forms were signed prior to participation in this study (Appendix B).

5.2 Study Design

This is an analytical cross-sectional study comparing standing balance between survivors of pediatric posterior fossa brain tumour (PFBT) and healthy children and adolescents.

5.3 Participant Recruitment

The experimental group, consisting of survivors of pediatric PFBT were recruited from the neuro-oncology clinic of the Montreal Children’s Hospital of the McGill University Health Centre. A control group of age- and gender-matched healthy children and adolescents was also recruited via publicity placed throughout the hospital and word of mouth.

5.3.1 Inclusion and Exclusion Criteria

The following inclusion and exclusion criteria were used when recruiting participants for this study.

Inclusion criteria for experimental group:

- Having received the diagnosis of PFBT at the age of 4 years or older
- To be at least 6 months post-completion of treatment for the brain tumour (either neurosurgical intervention, radiotherapy and/or chemotherapy)
- To be English or French speaking
- To possess the ability to maintain a standing position independently without the use of an assistive device for at least one minute

The inclusion criteria for the control group were as per the experimental group except for the diagnosis and treatment of brain tumours.

Exclusion criteria for all participants were as follows:

- Other pre-existing musculoskeletal or neurological diagnoses that would affect standing balance.
- Any visual field deficits that have been diagnosed by an ophthalmologist.
- Severe cognitive impairments that would make them unable to follow simple directions or to concentrate on a task.

5.4 Data Collection Procedures

The following section will outline all aspects of the data collection procedures for the participants with the exception of the dynamic balance assessment using the laboratory procedures. This will be outlined in the second manuscript, which directly follows the methodology chapter.

5.4.1 Clinical Evaluation

Testing was done in a quiet room by an experienced pediatric physiotherapist. Participant's height and weight was measured. Lower extremity range of motion (ROM) (hip flexion, knee flexion/extension, ankle dorsiflexion/plantarflexion) was assessed using an Accumar Inclinometer[*] while strength of key lower extremity muscle groups (hip extensors, hip abductors, knee extensors, ankle dorsiflexors) was tested using a hand-held dynamometer[†]. The procedure for dynamometry used was the one described by van den Beld et al. (2006), which showed high test-retest reliability in children.[225] Ankle plantarflexor strength was assessed using standing single leg heel raises as it cannot be accurately measured with a hand-held dynamometer.[226] Sensation was assessed in two ways: light touch and proprioception. Although the psychometric properties of the monofilaments are disputed, light touch was measured in the foot and ankle using select monofilaments[‡] with the following delineations: 2.83(0.07g) normal, 3.61(0.4g) normal, 4.31(2.0g) diminished light touch, 4.56(4.0g) diminished protective sensation, 5.07(10g) loss of protective sensation, 6.65(300g) deep pressure sensation only. Proprioception was assessed, as described by Thibault et al. (1994), by passively moving the subject's ankle while they were blinded and asking them to identify the position. This method has demonstrated excellent test-retest reliability in children.[227]

5.4.2 Clinical Balance Assessment

Clinical measures of quasi-static and dynamic standing balance were done with a rest given in between tests. The two tools that were used were the balance subtest of the BOT-2 and the PBS. Both of these tools were described in the literature review chapter. The order of the tools was reversed for half the subjects. These two tools were chosen as they are the most widely used by physiotherapists to assess balance in the pediatric population.

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[*] Accumar single digital inclinometer, Lafayette Instrument Company, Lafayette, Indiana.
[†] MicroFET2 Muscle Tester, Hoggan Scientific LLC, Salt Lake City, Utah.
[‡] Touch-Test Sensory Evaluators – Foot Screening Kit, North Coast Medical Inc, Gilroy, California

5.4.3 Health-Related Quality of Life Evaluation

The Pediatric Quality of Life Inventory (PedsQL4.0) Generic Core Scales is a patient or parent-reported HRQOL measure for use in all children.[228] There exists multiple versions for various age groups; young child 5-7 years old, child 8-12 years old and teen 13-18 years old. Separate parental proxy versions are also available for each age group. The questionnaire incorporates 23 items in areas such as physical, emotional, social and school functioning. Each item is scored on a 5-point Likert scale from 0-4 except for the young child version, which is scored on a 3-point scale. Total point scores can then be converted to a scale ranging from 0-100. All versions are available in both English and French. Psychometric analysis has revealed construct validity and internal consistency in both healthy children and children with brain tumours.[228-230]

5.5 Statistical Analysis

Data for all variables and outcome measures were summarized and descriptive statistics were compiled for both the experimental and control groups. In order to compare standing balance abilities on all the clinical measures and to compare HRQOL between the two groups, Mann-Whitney U tests were used. Due to the non-parametric nature of the test scores, a Spearman's rank correlation coefficient (ρ) was used to determine the association between balance abilities and HRQOL for the experimental group. The level of statistical significance was set at an alpha of 0.05 and all data was analyzed using SPSS® statistical analysis software.

5.6 Sample Size Justification

As there had been no prior studies using the primary outcome measure in survivors of PFBT, calculations were based on two prior studies done in pediatric survivors of ALL.[219,220] This was deemed a comparable population as chemotherapy agents used in the treatment of leukemia patients are also used in brain tumour patients. In these studies an effect size of 6 and standard deviation of 5 were found using the BOT-2 balance subtest (our primary outcome measure). If a similar effect size

was to be found in our study, sample size was fixed at 20 subjects per group, with a power greater than 80%. Unfortunately, due to slow recruitment, this number has not yet been reached for the experimental group.

Chapter 6: Manuscript 2

Title: Standing balance and quality of life in survivors of childhood posterior fossa brain tumours: An exploratory study

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Abstract:

BACKGROUND: The most frequent location of childhood brain tumours is the posterior fossa, which includes the cerebellum that plays a crucial role in balance. Few studies assess standing balance in this population. Standing balance difficulties may interfere with motor functions, in turn affecting health-related quality of life (HRQOL). **OBJECTIVES:** To compare standing balance and HRQOL between survivors of childhood posterior fossa brain tumours and a control group and to explore any associations between balance and HRQOL. **METHODS:** 6 males aged 7-18 years having completed treatment for a posterior fossa brain tumour and six healthy controls were recruited. Balance was assessed using the Bruininks-Oseretsky Test of Motor Proficiency–2nd ed. (BOT-2) and the Pediatric Balance Scale (PBS). HRQOL was measured using the Pediatric Quality of Life Inventory (PedsQL4.0). **RESULTS:** BOT-2 scores were significantly lower ($p=0.004$) in survivors (mean=9.5) versus controls (mean=15.67). The PBS demonstrated a ceiling effect and HRQOL was similar in both groups. In survivors, an association ($\rho=0.715$) was found between the BOT-2 and physical dimension of the PedsQL4.0. **CONCLUSIONS:** Survivors of childhood posterior fossa brain tumours demonstrate significant balance deficits after ending treatment; however, they report relatively normal HRQOL. In survivors, better balance abilities may contribute to better HRQOL.

Key Words: postural control, health-related quality of life, brain tumour, pediatrics, survivor

Introduction:

As survival continues to improve after the diagnosis of childhood brain tumours, there is a growing interest in studying the long-term outcomes in this population. Late-effects may be due to the tumours themselves or to the effects of treatment on the developing brain. Although a large amount of literature is available for certain areas like cognitive and social outcomes, there are fewer studies that explore the late-effects of treatment on physical and functional outcomes.[4,5] Many of the available studies report physical and functional deficits based on physician assessment or via subjective questionnaires.[3,80] In fact, very few studies use standardized, objective outcome measures to assess physical functioning in survivors of childhood brain tumours.

The most frequent location of childhood brain tumours is the posterior fossa, a region of the brain that includes the cerebellum and brainstem.[7] The cerebellum is known to play a crucial role in the control of balance.[9] One can expect that a brain tumour, especially one located within the posterior fossa, could have deleterious consequences on postural and motor control. Therefore, it is surprising that there is not more research conducted into the physical outcomes, including postural control and balance in standing, of survivors of childhood brain tumours.

On the other hand, there is a growing body of literature on health-related quality of life (HRQOL) in survivors of childhood brain tumours. Some studies report significantly lower HRQOL while others demonstrate that survivors of brain tumours rate their HRQOL similar to published norms.[106,231] It can be postulated that difficulty in maintaining standing balance may lead to difficulty performing certain motor tasks or functions that could in turn affect quality of life. It would be interesting to verify if there exists a relationship between balance abilities and HRQOL since quality of life may not be routinely measured in the clinical setting for survivors of childhood brain tumours.

The primary objective of this exploratory study was to describe standing balance abilities in survivors of childhood posterior fossa brain tumours and to compare their results to those of age- and gender-matched controls. Secondary objectives were to compare HRQOL between survivors of

childhood posterior fossa brain tumours and controls and to explore any associations between balance scores and HRQOL in the experimental group.

Methods:

Subjects

A group of 6 males aged between 7-18 years old were recruited from the neuro-oncology clinic of the Montreal Children's Hospital of the McGill University Health Centre. Individual characteristics regarding age at diagnosis, tumour pathology and adjuvant treatment received are summarized in IV (p.69). Inclusion criteria were: 1) the diagnosis of posterior fossa brain tumour at ≥ 4 years of age; 2) to be ≥ 6 months post-completion of treatment; and 3) to have the ability to maintain a standing position independently, without the use of an assistive device, for one minute. Participants were excluded if they had any other conditions that could affect their balance (i.e. visual field deficits) or their ability to follow directions. A convenience sample of volunteers recruited through publicity placed in the hospital and through word of mouth formed a control group of age- and gender-matched healthy children or adolescents. Informed consent was obtained from all participants and their parents and ethical approval was granted from the Research and Ethics Committee of the Montreal Children's Hospital.

Data Collection

Testing was done in a quiet room by an experienced pediatric physiotherapist. Two clinical balance tests were administered, as described below, and the order of the tests was reversed for half the participants. Finally, the HRQOL questionnaire was administered to the participants and their parents separately. The testing session lasted approximately 30 minutes.

Outcome Measures

Bruininks-Oseretsky Test of Motor Proficiency – 2nd edition (BOT-2)

The BOT-2 is a test of both fine and gross motor skills developed for children, adolescents and young adults between the ages of 4-21 years old.[175] The balance subtest comprises 9 tasks that assess both static and dynamic standing balance and point scores can be converted into standard scores. Standard scores can be divided into the following descriptive categories (based on the standard deviation (SD) from the mean standard score of 15): well-below average 0-5, below average 6-10, average 11-19, above average 20-24, well-above average ≥25.[175] Good inter-rater and test-retest reliability have been found as well as adequate content and construct validities.[180]

Pediatric Balance Scale (PBS)

The PBS is comprised of 14 items that assess both quasi-static and dynamic balance and is a modified version of the Berg Balance Scale.[167] The PBS re-orders the items of the Berg and lowers the time standards for certain tasks. Extremely high test-retest reliability has been reported as well as high test-retest and inter-rater reliability in children with mild to moderate motor impairments.[167]

Pediatric Quality of Life Inventory (PedsQL4.0) Generic Core Scales

The PedsQL4.0 is a self and/or parent-reported HRQOL measure for use in all children.[228] There exists multiple versions for various age groups; young child 5-7 years old, child 8-12 years old and teen 13-18 years old. The questionnaire incorporates 23 items in areas such as physical, emotional, social and school functioning. Each item is scored on a 5-point Likert scale from 0-4 except for the young child version, which is scored on a 3-point scale. Total point scores can then be converted to a scale ranging from 0-100. Psychometric analysis has revealed construct validity and internal consistency in both healthy children and children with brain tumours.[228,229]

Statistical Analysis

In order to compare both balance abilities and HRQOL between survivors of childhood posterior fossa brain tumours and healthy controls, descriptive statistics (i.e. mean and standard deviation) were first calculated and then Mann-Whitney U tests were applied. Due to the non-parametric nature of the test scores, a Spearman's rank correlation coefficient (ρ) was used to determine the association between balance abilities and HRQOL for the experimental group. All data was analyzed using SPSS® statistical analysis software.

Results:

Balance abilities

The mean scale scores for the balance subtest of the BOT-2 were 9.50 (SD=3.94) for the experimental group and are indicative of a balance deficit, as they fall in the below average category. Performances of the experimental group were significantly worse than those of the control group, who had a mean of 15.67 (SD=4.55), placing them in the average category (p=0.004) (Figure 2 (p.68)). On the PBS, mean scores for the experimental group (mean=55.67, SD=0.82) were similar to those of the control group (mean=55.83, SD=0.41) (Figure 2 (p.68)). All but two subjects obtained the maximum score of 56 for the PBS. Scores for all participants are noted in Table IV (p.69).

Figure 2: Mean balance scores in both groups

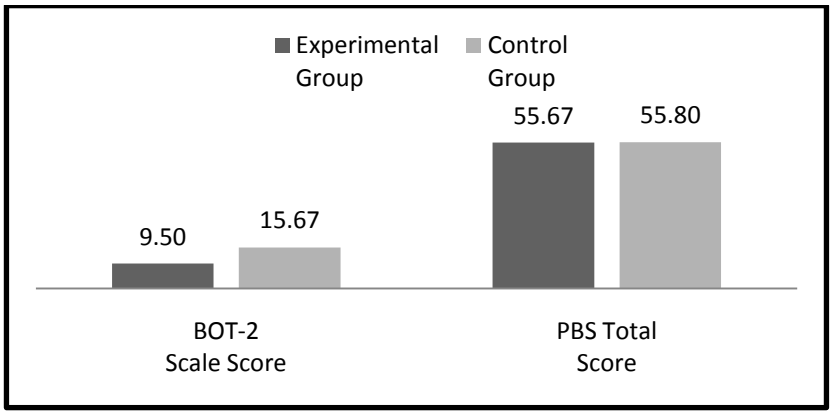


Table IV: Subject characteristics and individual scores for all participants

Experimental Group

Characteristics						Balance Scores		PedsQL4.0 Self-Report Scores		PedsQL4.0 Parent-Report Scores	
Subject	**Age at Evaluation**	**Age at Diagnosis**	**Pathology**	**Chemo-therapy**	**Radiation Therapy**	**BOT-2**	**PBS**	**Total Score**	**Physical Domain**	**Total Score**	**Physical Domain**
E01	14y10m	5y2m	MB	Y	Y	3	54	78.3	75	79.4	78.6
E02	8y2m	6y5m	JPA	N	N	13	56	97.8	100	83.7	100
E03	10y3m	5y6m	MB	Y	Y	8	56	84.8	87.5	80.4	84.4
E04	7y11m	4y4m	EPY	N	Y	12	56	67.4	87.5	80.4	100
E05	15y2m	11y3m	JPA	N	N	13	56	96.7	100	97.9	100
E06	18y0m	8y1m	JPA	N	N	8	56	85.9	100	87	100
					Mean	9.50	55.67	85.15	91.67	84.80	93.83
					SD	3.94	0.82	11.46	10.21	7.01	9.73

Control Group

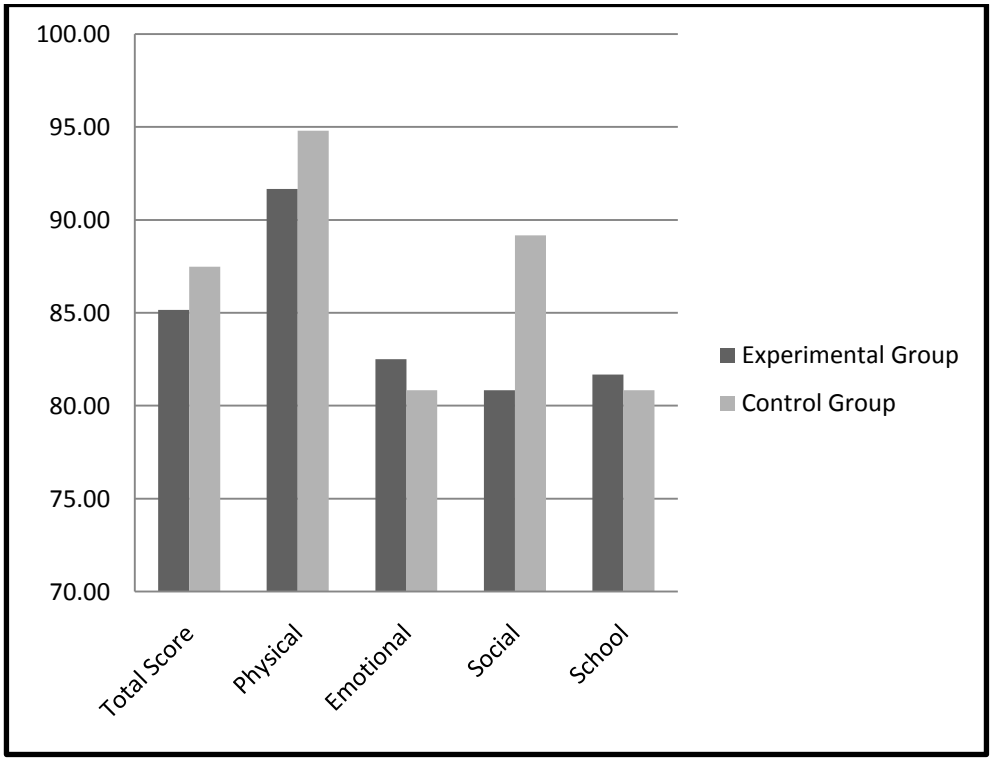
		Balance Scores		PedsQL4.0 Self-Report Scores		PedsQL4.0 Parent-Report Scores	
Subject	**Age at Evaluation**	**BOT-2**	**PBS**	**Total Score**	**Physical Domain**	**Total Score**	**Physical Domain**
C01	15y10m	22	56	85.9	96.9	93.5	100
C02	8y11m	11	56	90.2	96.9	82.6	87.5
C03	9y8m	20	55	93.5	100	94.6	100
C04	8y11m	15	56	81.5	84.4	93.5	93.8
C05	16y9m	15	56	80.4	90.6	66.3	84.4
C06	17y1m	11	56	93.4	100	95.7	100
	Mean	15.67	55.83	87.48	94.80	87.70	94.28
	SD	4.55	0.41	5.78	6.14	11.51	6.96

Abbreviations used: MB = medulloblastoma, JPA = juvenile pilocytic astrocytoma, EPY = ependymoma, BOT-2 = Bruininks-Oseretsky Test of Motor Proficiency (2nd ed.), PBS = Pediatric Balance Scale, PedsQL4.0 = Pediatric Quality of Life Inventory Generic Core Scales

Quality of Life

Mean total scores on the PedsQL4.0 Generic Core Scales self-report were 85.15 (SD=11.46) for the experimental group and 87.48 (SD=5.78) for the control group. Mean parent-report total scores were 84.80 (SD=7.00) for the experimental group and 87.70 (SD=11.51) for the control group. The mean physical dimension scores on the self-report versions were 91.67 (SD=10.21) for the experimental group and 94.80 (SD=6.14) for the control group. Mean parent-reported physical scores were 93.83 (SD=9.73) for the experimental group and 94.28 (SD=6.96) for the control group. Scores for each dimension are presented in Figure 3 (p.70).

Figure 3: Mean PedsQL4.0 scores in both groups



Association between quality of life and balance abilities

Due to the ceiling effect of the PBS, a Spearman rank correlation coefficient was calculated for the BOT-2 balance subtest scale scores and the physical dimension score of the PedsQL4.0. For the experimental group, it was found to be $\rho=0.715$ denoting an association.

Discussion:

The first objective of this exploratory study was to determine the balance abilities of survivors of childhood posterior fossa brain tumours and compare them to age- and gender-matched controls. Based on normative values, survivors' balance scores are indicative of a deficit while the control group's balance abilities are not. Although the sample size is small, the difference between the two groups is significant and clinically meaningful. This supports the notion that survivors demonstrate poorer balance abilities. These results are similar to the only other brief report found in the literature investigating balance among a group of thirteen survivors of childhood brain tumour using the BOT-2.[224] Thus it would seem that the balance subtest of the BOT-2 is sensitive to detect differences in balance abilities between survivors of childhood posterior fossa brain tumour and healthy controls.

Evaluation of balance abilities using the PBS demonstrates a ceiling effect for both groups as all but two subjects achieved the maximum score of 56. The PBS does not appear to be sensitive enough to detect balance differences in these groups. Ceiling effects have also been reported in typically-developing children older than 7 years old.[168] The developers of the PBS recommend that the BOT-2 be used when investigating balance in children over the age of 6 years old.[168] In the present study, the balance subtest of the BOT-2 does reflect balance difficulties in survivors of childhood posterior fossa brain tumours. The results of the present exploratory study suggest that the BOT-2 is a more appropriate tool to use in clinical practice and in research protocols to assess balance abilities in survivors of childhood posterior fossa brain tumours than the PBS.

The second objective of this study was to compare HRQOL in survivors of childhood posterior fossa brain tumours to age- and gender-matched controls. All self-report and parent-report total scores and all dimension scores for survivors fall within the published norms and scores were quite similar between self- and parent-report versions.[228] This is similar to other studies that report survivors score their HRQOL using the PedsQL4.0 Generic Core Scales similarly to their parents.[82,231] In the present study, scores between survivors of childhood posterior fossa brain tumours and controls denote no major differences in HRQOL despite differences in standing balance abilities. This is compatible with another study that reported that survivors of low-grade cerebellar astrocytoma ranked their HRQOL the same or higher as controls.[82] However, some other studies have documented lower HRQOL in survivors of all forms of brain tumours.[231] This difference could be attributed to the fact that the present study includes subjects with tumours in a specific region of the brain whereas other studies include a broader range of brain tumours, which may reflect a more heterogeneous group.

The third objective was to investigate any associations between balance scores and HRQOL. To this end, as the PBS demonstrated a ceiling effect, only the balance subtest score of the BOT-2 was compared to the physical dimension score of the PedsQL4.0. In the experimental group, there appears to be an association between balance scores and the physical HRQOL indicating better balance can contribute to better HRQOL. These results need to be interpreted with caution due to our very small sample size but definitely warrant further investigation. To the best of our knowledge, no other studies have investigated the relationship between balance scores and HRQOL.

One of the major limitations of this study is the small sample size which restricts the generalizability of the present results. However, as this was an exploratory study with some interesting results, future research is warranted to further elucidate balance abilities in survivors of childhood posterior fossa brain tumours. Another limitation of this study was the fact that the evaluator was not blinded to which group the participant belonged. However, owing to the standardized nature of the tests used, this may not have been too much of a confounding factor.

Conclusion:

This exploratory study showed a statistically and clinically meaningful balance deficit in a small group of survivors of childhood posterior fossa brain tumours as compared to an age- and gender-matched control group. This difference was best demonstrated using the balance subtest of the BOT-2. Future studies should be geared towards evaluating the psychometric properties of this tool in this population. This study also demonstrated that quality of life scores, using the PedsQL4.0 Generic Core Scales, were very similar between the two groups and that for all subjects the self-report and parent-report scores were comparable. For survivors, higher balance scores on the BOT-2 reflected higher scores in the physical dimension of the PedsQL4.0.This would need to be more deeply investigated before any specific conclusion can be drawn.

Chapter 7: Manuscript 3

Title: Quantifying the comfortable limits of stability in standing among children who have survived a brain tumour: A proof of concept.

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PREFACE:

In order to quantify dynamic standing balance utilizing laboratory measures in survivors of childhood brain tumours, we needed to develop a new approach. As mentioned in the literature review, there exist few methods to evaluate dynamic standing balance using a force platform in children. Therefore, it is unknown which set-up, tasks or parameters are best suited to fully describe dynamic balance abilities in survivors of childhood brain tumours. In the present study, a new method had to be assessed. The concept for the method and tasks stems from previous studies into the limits of stability conducted by several researchers, including Dr. Dany Gagnon, on sitting and standing balance in individuals with a spinal cord injury and able-bodied controls. Although the population of survivors of childhood brain tumours is extremely different from that of spinal cord injured people, the task of reaching was thought to be simple enough for children to follow.

The programs that were used to collect and analyze the data were already available at the Pathokinesiology laboratory at the Institut de réadaptation Gingras-Lindsay-de-Montréal. The testing protocol (i.e. testing position, instructions, visual feedback, etc...) attempted to combine any recommendations found in the literature. What required further development was the data analysis. Although some parameters used in the spinal cord injured population were applicable, as our testing was done in a standing position, additional outcome measures needed to be developed in order to more completely analyze the COP movements.

Unfortunately, due to circumstances with the equipment, we were unable to test a large number of participants with the force platform. Only four of the experimental group were tested and owing to a variety of reasons, much of their data was incomplete and could not be analyzed. Some of these reasons included, inconsistencies in when the recording of the trial was started, inconsistent positioning of the feet, difficulty standardizing the reaching method, calibration difficulties and inability to properly construct the base of support. After all the testing had been completed, only one participant's data could be easily and completely analyzed. Therefore it was decided to present the

laboratory evaluation of dynamic balance as a proof of concept paper in order to elaborate the methods and outcome measures.

Abstract:

Few studies have attempted to quantify standing balance in survivors of childhood posterior fossa tumours via use of force platforms. Most evaluate balance under quasi-static standing conditions only. *Objective:* This proof of concept aims to describe a novel method for quantifying the comfortable limits of stability (LOS) in standing in a survivor of childhood posterior fossa tumour. *Methods:* The participant stood at the centre of a force platform and reached as far as possible along eight different directions, separated by 45° intervals. The main outcome measures were: Precision Index-Angle, Precision Index-Distance, Direction-Specific Index of Stability and Overall Stability Index. *Results:* The results for the precision indices were contradictory with the participant demonstrating relatively precise displacements in the required direction but less precise trajectories toward their maximal displacement. The Overall Stability Index confirmed that the participant's COP excursions remained within 30% of their BOS. It is difficult to assert if the laboratory measures highlight balance difficulties as no normative data exists for the outcome measures. *Conclusion:* Although requiring further development, the comfortable LOS offers a promising new method to evaluate dynamic standing balance in survivors of childhood posterior fossa tumours that could be used as a complement to traditional quasi-static techniques.

Keywords: dynamic postural control, limits of stability, evaluation, pediatrics

Introduction:

Tumours of the central nervous system represent the second most common form of pediatric cancer and the most common solid tumour found in children and adolescents.[15] It has been reported that up to 50% of these tumours occur in the posterior fossa, a region of the brain that includes the cerebellum.[15] The cerebellum plays a critical role in the control of balance.[9] Therefore, damage to the cerebellum and surrounding structures could lead to balance deficits. To date, only a few studies have attempted to quantify standing balance in survivors of childhood posterior fossa tumours via use of force platforms in laboratory or clinical environments.

Standing balance commonly refers to a person's ability to maintain their centre of pressure (COP) within the limits of the base of support (BOS), defined as the contours of their feet, when maintaining a bipodal standing position.[114] The location of the COP reflects where the vertical ground reaction force acts upon the centre of mass (COM) within the BOS to control standing balance.[114] The height of the COM and the dimension of the BOS are closely linked within the concept of postural stability. It is recognized that the larger the BOS, for a constant height of the COM, the larger the area in which the COP can oscillate safely. Consequently, this minimizes the risk of losing balance. These COP oscillations are proportional to inertial effects and to the change in position of the COM when a person moves in standing.[117]

An alternative way to explain the relationship between the COM and COP is the inverted pendulum model proposed by Winter et al. This model states that the difference between the location of the COM and the COP is proportional to the acceleration of the COM.[117] Therefore, the COP trajectory provides information about the oscillations of the COM within the BOS and can be characterized using different methodological approaches in standing.[186,187] A lack of consensus in these approaches stems from the fact that there is no normative pattern for COP movement and that there exists a plethora of COP variables that are inter-related and often redundant.[185-187] Nonetheless, force platforms are essential to measure the COP, especially when no kinematic data is recorded. Force

platforms may also offer the capability to quantify more subtle standing balance deficits or those not detected by clinical outcome measures.

Most of the studies investigating balance in survivors of childhood posterior fossa tumours using force platforms evaluate balance under quasi-static standing conditions only.[11,13,14] Others attempt to introduce a postural perturbation component by tilting the force platform in the anterior and posterior directions while requiring that the participant maintain a steady standing position.[10] All of these methods for evaluating quasi-static and dynamic balance abilities may not translate into functional tasks, which often require self-initiated movements in a multitude of directions while maintaining a fixed BOS.

Another method used to incorporate a dynamic component to standing balance assessment with a force platform is the limits of stability (LOS). The LOS can be described as the maximum possible displacement of the COP without having to modify the BOS.[114] To measure the LOS, some studies employ an approach requiring the participants to trace a circle with the largest radius possible with their head/arm/trunk segment by leaning as far as they can in standing while maintaining both feet in contact with the force platform.[198,199] This may not be feasible in children as the concept could be difficult to understand especially when no visual feedback is provided. An additional method proposed for evaluating dynamic standing balance is the multi-directional reach test, whereby the distance a person is able to reach in various directions (forwards, backwards, right and left) is measured.[232] Using COP data to analyze the multi-directional reach test may provide complementary and meaningful information on the neuromotor strategies a person uses to complete the tasks. A previous study investigated the multi-directional reach test while healthy adult participants stood on a force platform and found that it appears to measure the same construct of balance as the LOS.[200] In fact, the COP excursions were correlated with the distance reached in all directions except for backwards.[200] Reaching in various directions while data is collected via a force platform has also been used in a few studies to evaluate sitting balance in healthy adults as well as in adults with neurological

impairment.[201,202,233] This technique may be useful to assess standing balance in children and adolescents as well as survivors of childhood posterior fossa tumours as instructions appear relatively simple for children to understand. Providing real-time visual feedback of the COP may also facilitate comprehension as children rely heavily on their visual system in order to maintain balance.[123]

To the best of our knowledge, utilizing a multi-directional reach test to assess dynamic standing balance abilities while providing visual feedback has not yet been done in survivors of childhood posterior fossa brain tumour. Thus, this proof of concept aims to describe a method used to quantify the comfortable LOS in standing and to report results computed in a survivor of childhood posterior fossa tumour.

Methods:

Participant:

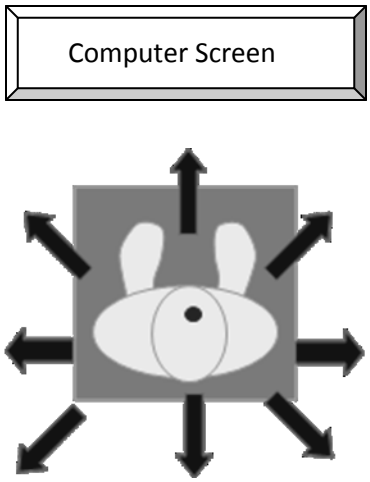
A male survivor of childhood posterior fossa tumour (age=ten years, three months; height=146.3cm; weight=39.4kg; right handed) participated in this study. He was diagnosed with a medulloblastoma, which was surgical resected, at the age of five years, six months, which was followed by radiation therapy and chemotherapy. His lower extremity range of motion as measured with an inclinometer showed some limitations in ankle dorsiflexion (right=3°; left=2°) and hyperextension in both knees (10° bilaterally). Evaluation of lower extremity strength and sensation confirmed the sensorimotor integrity of the lower extremities. The participant's balance abilities were assessed by the nine item balance subtest of the Bruininks-Oseretsky Test of Motor Proficiency - second edition (BOT-2), a commonly used pediatric clinical balance measure. This test includes tasks such as standing on one foot with eyes open and closed, walking along a line and standing tandem on a balance beam. As the participant obtained a normalized scale score of 8, his balance abilities would be classified as below average based on the fact that the mean normalized scale score is established at 15 (SD=5).

This study was approved by the research ethics board of the Montreal Children's Hospital of the McGill University Health Centre and both informed consent and assent were obtained prior to participation in this study.

Procedure:

The participant stood barefoot at the centre of a portable Bertec force platform (FP-4060-05-PT; Bertec Corporation, Columbus, OH) used to continuously record the tri-axial components of the ground reactions forces at 600Hz. The outlines of his feet were traced over the force platform with a dry-erase marker to ensure consistency in position between trials after the participant had self-selected his comfortable and habitual foot placement. From this steady starting position, the participant reached as far as possible with one arm flexed/abducted to 90° along eight different directions, separated by 45° intervals while maintaining his balance (Figure 4 (p.82)). For the posterior directions, the participant crossed his arms over his chest. The participant bent his head/arm/trunk segment from the hips and ankles at a self-selected velocity while keeping his heels down. The expected direction of displacement of the COP and the real-time COP position were displayed in front of the participant on a computer screen to provide visual feedback and to ensure movement was performed along the proper direction. Two repetitions were randomly recorded in each direction for a total of sixteen trials. Each trial had to be completed within a 15 second period. Upon completion of the test, a minimum of 50 pressure points were digitized (from the traced outlines) while the evaluator applied a vertical force with a rigid and heavy metallic rod (20kg) to compute the boundary of the BOS. The sixteen COP time series recorded in the horizontal plane, reflecting a combination of the anteroposterior (Fx) and mediolateral (Fz) ground reaction force directions within the platform referential, were filtered with a fourth-order Butterworth zero-lag low pass digital filter with a cut-off frequency of 10Hz and then down-sampled at 300Hz for analysis.

Figure 4: Position of the participant on the force platform and reach directions



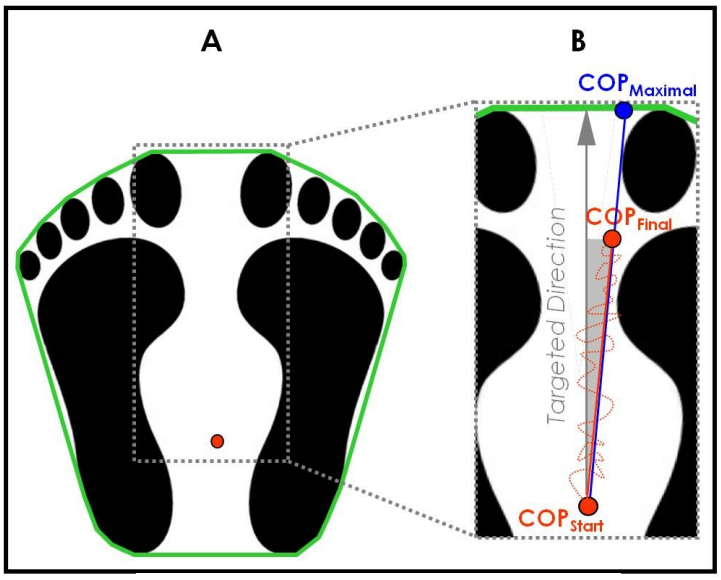
Main Outcome Measures:

The main outcome measures, computed with a MATLAB program developed for the study are described below and illustrated in Figure 5 (p.83):

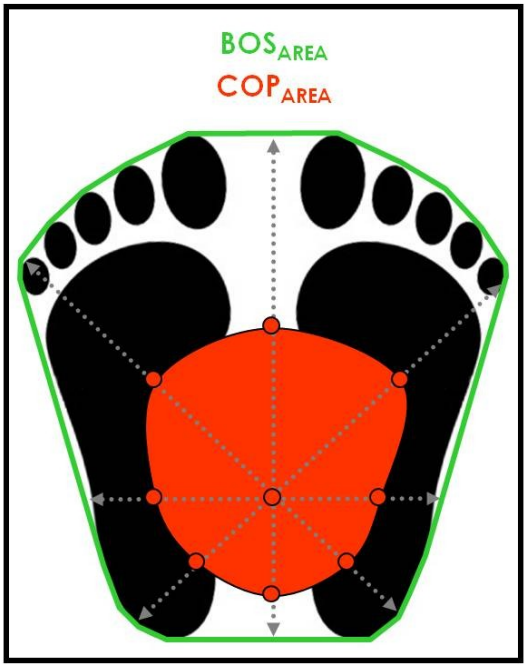
Precision Index - Angle: For each of the eight directions tested, this represents the absolute difference in degrees between the targeted direction versus the actual direction of the COP displacements, as determined using the initial and maximal COP positions. This can be interpreted as the angle error for each direction tested and values exceeding ±10° are defined as demonstrating insufficient precision.

Precision Index - Distance: For each of the eight directions tested, this represents a COP displacement ratio between the minimal mathematical distance separating the initial COP position from the maximal COP displacement (numerator) and the actual distance travelled by the COP between these two points (denominator). Described as a percentage, a value of 100% corresponds to a perfectly linear displacement of the COP between the two COP positions whereas a value closer to 0% reflects an extremely arbitrary displacement.

Figure 5: Main outcome measures for comfortable limits of stability



5A: Precision Indices



5B: Stability Indices

Direction-Specific Index of Stability: For each of the eight directions tested, the initial position of the COP (COP_{Start}), the furthest position reached by the COP in the indicated direction (COP_{Final}) and the maximal theoretical potential position the COP could have reached to attain the boundary of the BOS in the indicated trajectory ($COP_{Maximal}$) were computed. Then, the direction-specific stability index, expressed as a percentage, was calculated for each of the eight directions (Eq.1):

$$\text{Eq.1: Direction} - \text{Specific Index of Stability (\%)}$$

$$= \left[\frac{COP_{Final} - COP_{Start}}{COP_{Maximal} - COP_{Start}}\right] \text{x } 100$$

Overall Stability Index: Incorporating all directions tested, an overall stability index representing the area defined by an ellipse (COP_{Area}) convexly fitting the mean furthest position reached by the COP in each of the eight directions tested, normalized against the area of the BOS (BOS_{Area}), was calculated and expressed as a percentage (Eq.2):

$$\text{Eq. 2: Overall Stability Index (\%)}$$

$$= \left[\frac{COP_{Area}}{BOS_{Area}}\right] \text{x } 100$$

Results:

A tracing of the COP displacements in each of the eight directions are shown in Figure 6 (p.85). All outcome measures computed for the participant in each of the eight directions tested and the overall means for each index are presented in Table V (p.86). With regards to the Precision Index-Angle, the participant showed fairly precise displacements, as his deviations were less than 10° for all directions. Conversely, for the Precision Index-Direction, the participant's displacements lack precision in most directions with values ranging between 23.2 and 38.8 for all directions. The Direction-Specific Stability Index reached values ranging between 53% and 77%. Finally, the Overall Stability Index confirmed that the participant's overall COP excursions remained within 30% of their BOS.

Figure 6: Tracing of COP displacements

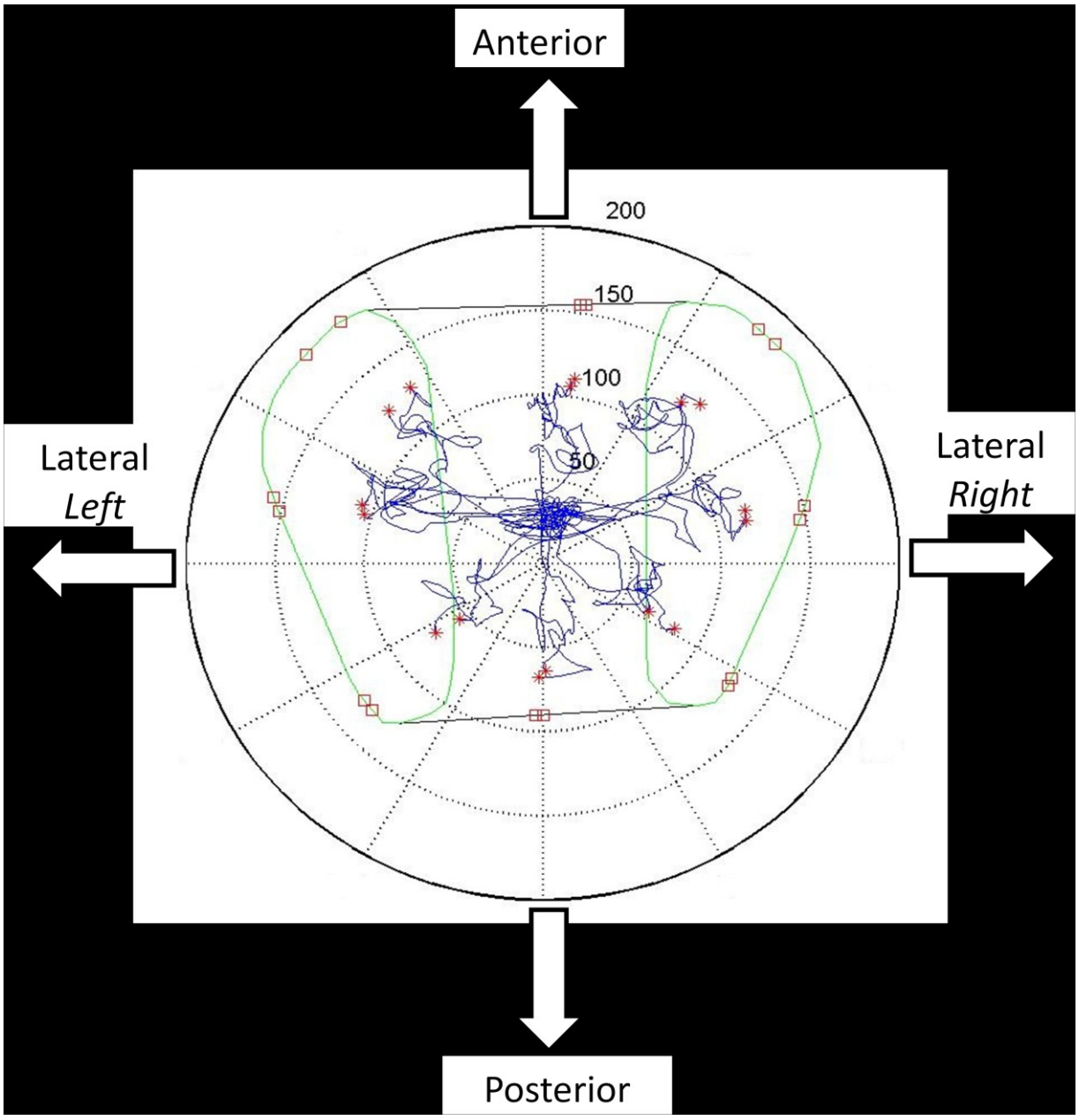


Table V: Results for main outcome measures on comfortable limits of stability

Main Outcome Measures	**Directions of COP displacement**								
	Ant	Right Ant-Lat	Right Lat	Right Post-Lat	Post	Left Post-Lat	Left Lat	Left Ant-Lat	Overall Mean
Precision Index- Angle (º)	7.3	2.3	3.9	1.2	3.9	1.3	4.0	4.7	3.6
Precision Index-Distance(%)	26.6	24.7	27.5	27.9	38.8	36.1	26.1	23.2	28.9
Direction-Specific Stability Index(%)	58.1	59.5	64.4	53.6	77.0	55.4	66.2	63.7	62.3
Overall Stability Index	Area $COP_{Maximal}$ (cm^2)	Area BOS (cm^2)	Overall Stability Index (%)						
	19.1	64.4	29.7						

Abbreviations used: COP=Centre of pressure, Ant=Anterior, Lat=Lateral, Post=Posterior, BOS=Base of support

Discussion:

The objective of this exploratory study was to present a novel way to quantify the comfortable LOS in standing in a survivor of childhood posterior fossa tumour. This technique could be used as a complement to the quasi-static tests that are routinely conducted on a force platform in order to have a more comprehensive assessment of balance abilities. In our participant, the clinical tool the BOT-2 revealed below-average balance abilities. It is difficult to assert if the laboratory measures also highlight difficulties as this is a new method and no normative data exists for our outcome measures. Future studies would be necessary to establish how the outcome measures quantify balance in a pediatric population.

The testing of this new method revealed several ways that it could be improved in the future. Firstly, the tasks in the present study may not be challenging enough as the participant remained in their comfortable LOS. Also, the outcome measures may not reflect how difficult the participant found the task as there was no way to gauge what level of effort they were using. A participant's level of effort could potentially reveal how confident they are in their balance abilities. Had the instructions included the command to not only displace the COP as far as possible but to go as fast as possible too, this could reveal how confident they are in their balance abilities. Furthermore, this information on COP velocity in conjunction with maximal excursion for a given direction (i.e. Direction-Specific Index of Stability), may provide an idea of how much balance reserve is available for a participant. This could translate into how a participant is able to perform in response to perturbations (i.e. reactive postural adjustments) and may offer a better assessment of dynamic balance abilities, especially in a more functional context. It appears that refinement is needed to these new outcome measures of the comfortable LOS.

A limitation of this exploratory study was that foot placement was self-selected and not standardized so starting points on the platform would not be identical between subjects if we would like to compare performances in future studies. Along with standardizing foot placement, pressure

switches may be fixed under participants' heels in order to ensure that they remain in contact with the platform at all times. This would ensure that no compensation would be allowed, thereby reflecting the participant's true comfortable LOS. Adding an instrumented pressure mat to the set up would allow for more precise measurement of the BOS and weight distribution, in turn providing more accurate analysis of the weight shifting during reaching. Other possible improvements to the comfortable LOS could include adding a measure to account for COP velocity as this would provide extra information on stability, as previously discussed. Additional practice trials may also be required as children and adolescents may not necessarily understand what is asked of them right away. Finally, adding a target placed at shoulder height in each of the tested reaching directions may provide another method of feedback to ensure movement is in the expected directions.

To conclude, although requiring further development, the comfortable multidirectional LOS offers a promising new method to evaluate standing balance in survivors of childhood cerebellar tumours. This technique could be used as a complement to traditional quasi-static outcome measures frequently used in clinical practice in order to have a more comprehensive picture of balance abilities. In addition to refinement of the technique, future research should be geared to testing the psychometric properties of the comfortable LOS in the pediatric population.

Chapter 8: Additional Results

8.1 Clinical Variables

Mean scores for both groups' lower extremity ROM and strength are presented in Table VI (p.89). Visual inspection of these results, as well as those for distal lower extremity sensation, denotes no major differences between the groups. Although it was intended that these variables possibly be used to explain differences in balance abilities, our small sample size limited their use in analysis.

Table VI: Mean lower extremity range of motion and strength

	ROM (in degrees)			**Strength (in N)**	
	Exp. Group	Cont. Group		Exp. Group	Cont. Group
Right Hip Flexion	128.7	118.8	**Right Hip Extensors**	103.6	117.5
Left Hip Flexion	130.7	118.0	**Left Hip Extensors**	96.7	110.5
Right Knee Flexion	143.5	135.7	**Right Hip Abductors**	98.5	137.6
Left Knee Flexion	146.5	141.5	**Left Hip Abductors**	93.8	143.8
Right Knee Extension	4.7	0.7	**Right Knee Extensors**	122.2	137.2
Left Knee Extension	3.7	0.0	**Left Knee Extensors**	127.9	117.2
Right Ankle Dorsiflexion	9.8	7.7	**Right Ankle Dorsiflexors**	136.6	121.6
Left Ankle Dorsiflexion	10.3	6.5	**Left Ankle Dorsiflexors**	130.3	117.1
Right Ankle Plantarflexion	50.0	51.7	**Heel Raises (number)**	26.3	28.5
Left Ankle Plantarflexion	54.2	51.5			

Abbreviations used: ROM=Range of Motion, N=Newton, Exp=Experimental, Cont=Control

Chapter 9: Discussion

In this section, the main findings of this thesis will be summarized and further discussed. This will be followed by the clinical implications and limitations of this study as well as future directions for research in the area of rehabilitation for survivors of pediatric CNS tumours.

9.1 Summary of Key Results

A structured literature review was conducted in order to elucidate what is known with regards to balance outcomes in survivors of pediatric cancers. This was done to guide the present research study where the main objective was to quantify quasi-static and dynamic standing balance in survivors of PFTB using clinical and laboratory balance outcomes measures and to compare them to healthy, matched controls. Secondary objectives were to quantify and compare HRQOL between the groups and to explore the association between standing balance abilities and HRQOL in the experimental group. The results pertaining to these objectives are described below.

9.1.1 Literature Review

The main finding of the literature review into balance outcomes of survivors of pediatric cancers, consisting of only ALL and pediatric CNS tumours, was that balance deficits seem to persist once treatment has been completed. Based on the OCEBM Levels of Evidence, these studies were of low quality. Some limitations of the available literature were the lack of clinically-oriented studies, the assessment of dynamic balance was limited and how the balance deficits affect everyday lives was not addressed.

9.1.2. Experimental Group Characteristics

A highly interesting observation was that all participants in the experimental group were male. Their age at diagnosis of a PFBT ranged from 4 years and 3 months to 11 years and 3 months

(median=6 years) and their time since completion of treatment ranged from 20 to 119 months (median=44.5 months). Based on the WHO classification of CNS tumours, two were diagnosed with medulloblastoma, three with juvenile pilocytic astrocytoma and one with ependymoma. All participants received surgical intervention, while the subject with ependymoma received additional radiotherapy and the two with medulloblastoma received both adjuvant radiotherapy and chemotherapy.

9.1.3. Balance Abilities

Using the clinical outcome measures, the scores on the PBS were similar for both the experimental and control groups and demonstrated a strong ceiling effect. Scores on the balance subtest of the BOT-2 were found to be significantly different between the groups. This difference was a clinically meaningful one as each groups' scores were classified in two distinct descriptive categories.

In order to calculate the power of the present study the following points were considered: 1) our primary outcome measure was the balance subtest of the BOT-2; 2) there were 6 participants per group; 3)the experimental group had a mean of 9.50 (SD=3.94) and the control group had mean of 15.67 (SD=4.55) on the balance subtest of the BOT-2 and; 4) the desired sign level was 0.05. Based on these considerations, the power of the research study was calculated at 75.2.

A new method was utilized to assess dynamic standing balance using laboratory outcome measures and the comfortable LOS. With regards to the Precision Index-Angle, the participant showed fairly precise displacements. Conversely, for the Precision Index-Direction, the participant's displacements lack accuracy in most directions. The Direction-Specific Stability Index values varied depending on the direction and the Overall Stability Index demonstrated that the participant's COP excursions remained within 30% of their BOS.

9.1.4. Health-Related Quality of Life

All scores on the PedsQL4.0 Generic Core Scales were within the normative ranges for the experimental and control groups for both the self- and parent-reported versions.[228] Comparisons of scores on the self- and parent-reported versions for all participants were quite similar.

9.1.5. Association Between Balance Abilities and Health-Related Quality of Life

In order to determine the association between balance abilities and HRQOL, only the BOT-2 was used as the PBS demonstrated a ceiling effect. Furthermore, only the physical dimension scores of the PedsQL4.0 were used as this was felt to be the most pertinent domain to relate to balance abilities. A Spearman's rank correlation coefficient was calculated for the experimental group and found to be $\rho = 0.715$ denoting an acceptable association.

9.2 Discussion of Key Results

9.2.1. Experimental Group Characteristics

With regards to the experimental group, it is noteworthy that only male participants were recruited. Although the literature suggests that males are more often diagnosed with CNS tumours than females in the pediatric population, the difference is only slight.[15] However, the fact that the study sample is only male, the results may not be readily applied to all PFBT survivors as some studies do find differences in balance abilities between genders in typically-developing children and adolescents.[148,149,234,235] Another interesting feature of the experimental group is the fact that the most common pathologies are all represented: juvenile pilocytic astrocytoma, medulloblastoma and ependymoma.[7] This makes the present research study more generalizable to all PFBT tumours as no particular pathology is more prominent. Likewise, the treatments received by the experimental group correspond to the standards described in the literature, assisting the applicability of the results.[20,48]

9.2.2. Balance Abilities

Although sample size was small, the power of the study was fairly good. There is a significant difference in balance abilities as measured by the BOT-2 between survivors of pediatric PFBT and healthy controls. Moreover, this difference is a clinically meaningful one as the score for PFBT survivors places them in the below average category based on the normative data while the controls scored in the average range. Interestingly these deficits can persist for years after treatment is completed as in our sample, time off treatment varied from just under 2 years to almost 10 years post-treatment (Median = 3.7 years). This highlights the fact that standing balance can remain affected long after treatment is completed. As mentioned previously in the review article, literature is sparse investigating balance outcomes in survivors of pediatric CNS tumours using clinical outcome measures.[236] Nonetheless, the results of the present study are comparable to the only other study found in the literature that investigated standing balance using the BOT-2 in children having undergone resection of PFBT.[224]

On the other hand, the PBS demonstrated a ceiling effect for all participants as most achieved a maximal score of 56/56. For that reason, the PBS is likely not sensitive enough to detect balance difficulties in survivors of pediatric PFBT. In the present study, it was thought that PFBT survivors' could have greater balance difficulties than what was found so the PBS was initially chosen in order to be able to measure varying levels of balance abilities. The developers of this tool also found a ceiling effect in typically-developing children over the age of 7 years old and therefore recommend the PBS be used to assess balance abilities in children aged 3 to 6 years old.[168] The youngest participant in the present research study was aged 7 years and 11 months.

When using laboratory measures to assess dynamic standing balance, the results of the comfortable LOS were contradictory for certain parameters. This could be due to the fact that the outcome measures may not reflect how difficult a participant found the task. There was no way to gauge what level of effort they were using. As discussed in the review article, there is only one other

study that attempts to assess dynamic standing balance in survivors of pediatric CNS tumours utilizing laboratory measures.[132] It is impossible to compare results of the study by Ilg et al. (2008) to the present study's comfortable LOS as kinematic analysis was used in the evaluation of step width and lateral sway during gait. Although the comfortable LOS attempts to assess balance in a dynamic manner, it may not automatically reflect the anticipatory and reactive postural adjustments required when undertaking functional tasks, such as gait.

9.2.3. Health-Related Quality of Life

In the present research study, overall HRQOL appears to be similar between the survivors of pediatric PFBT and controls. This is analogous to several other studies that have found no differences in HRQOL for survivors of pediatric CNS tumour, using a variety of tools, as compared to normative values.[82,93,106] One study even demonstrated that survivors reported their HRQOL as higher than a group of typically-developing children.[111] On the other hand, there are reports that demonstrate the opposite; that survivors rate their HRQOL as lower.[75,109,214,231] These conflicting findings are likely due to the fact that pediatric CNS tumour survivors are a very heterogeneous group and participant characteristics vary widely between studies in terms of types and locations of the tumours as well as types of treatment received by the participants. If we focus upon only the studies investigating HRQOL in survivors of tumours located exclusively in the posterior fossa, it is noted that this disagreement in the results still exists as two studies report similar HRQOL while another reports lower HRQOL.[82,93,109]

Additionally, both participants and their parents express very similar scores on the PedsQL4.0. This would imply that the parents of survivors of pediatric PFBT in this study have good insight into how their child is doing. Other studies that investigated this generally found good agreement between parent and proxy reports of the PedsQL4.0.[82,231] In future studies, should a survivor not be able to

answer the questionnaire due to decreased cognitive abilities, which is quite possible as cognitive deficits have been established in this group, parent-reports can be relied upon to assess HRQOL.

Overall, from the present study, it can be believed that survivors of pediatric PFBT have a relatively normal quality of life in all spheres, which is an encouraging picture. However, this study only included participants that were able to stand independently without the use of an assistive device. This represents a potential selection bias as survivors with more severe physical disabilities and potentially lower HRQOL were excluded.

9.2.4. Association Between Balance Abilities and Health-Related Quality of Life

Based on the very preliminary results of this study, there appears to be an association between balance scores and physical HRQOL in survivors of pediatric PFBT. This may possibly indicate that better balance can contribute to better HRQOL. To the best of our knowledge, no other studies have investigated the relationship between balance scores and HRQOL. Nevertheless, these results need to be interpreted with great caution especially due to the small sample size and that the physical summary scores of survivors of pediatric PFBT fell within the normative values.

9.3 Clinical Implications

This study, along with the review article presented in this thesis, has shown that some survivors of pediatric PFBT demonstrate balance difficulties but have relatively normal quality of life when compared to matched controls. Various outcome measures were used to establish these findings; however, none have their psychometric properties substantiated in this population. The clinical implications of this are discussed below.

Although the incidence of CNS tumours in the pediatric population remains low in Canada, medical management has improved and survival is increasing with 5-year survival rates currently

reaching 71%.[1] While literature remains sparse with regards to long-term physical outcomes in this population, physiotherapists working with this group may notice persistent balance deficits. This is especially true in those with tumours occurring in the posterior fossa, which represents the most common location of pediatric CNS tumours.[6,7,15,26,27] It will become imperative to document the impact of these improved medical outcomes and new treatment regimens on long-term outcomes in survivors of pediatric CNS tumours. This research study may be a step towards recognizing the persistent physical difficulties faced by survivors.

That survivors of pediatric PFBT demonstrate ongoing balance deficits in the present study, in some cases for years after treatment has been completed, likely supports the need for continued physiotherapy follow-up in this population. It could be recommended that all survivors of PFBT, and possibly all other CNS tumours, be screened for their balance abilities. At the Montreal Children's Hospital, this would imply having a physiotherapist present in the neuro-oncology clinics along with the medical and nursing professionals, in order to make this clinic truly interdisciplinary. There is a growing trend in many centres across North America, where special clinics are being implemented to evaluate and manage long-term difficulties in survivors of all forms of pediatric cancer, including CNS tumours. A more comprehensive evaluation of physical, cognitive and psychosocial outcomes in survivors would be achieved if the Montreal Children's Hospital had such a clinic that included not only physiotherapists but occupational therapists, social workers and psychologists as well.

Should a physiotherapist more proactively evaluate standing balance in survivors of PFBT in the neuro-oncology clinic, from the results of the present study, it would appear the balance subtest of the BOT-2 would be the most appropriate tool to use in order to screen for balance difficulties. Although little is known with regards to psychometric properties of the BOT-2 in this population, it remains quick to perform, requires little equipment or space and as such could easily be incorporated into the clinic visit. There are possibly other tools that could be used to screen for balance deficits in survivors of pediatric PFBT such as those discussed in the literature review that would warrant further

investigation. If screening reveals difficulties, a more thorough balance assessment would be indicated and could include items such as gait analysis or dual-task balance and cognitive activities, which is currently an emerging area of research in postural control. Although it is likely more efficient to screen only those survivors of pediatric PFBT that may be at higher risk for developing balance deficits, the small sample size in the present study did not allow for this analysis. The literature does not further clarify this matter as the two studies investigating associations between clinical and treatment variables and balance abilities offer contradictory conclusions.[12,88] Nevertheless, should screening reveal significant balance deficits, survivors of pediatric PFBT should be referred for appropriate rehabilitation services.

Unfortunately this group is often not accepted for intensive in- or out-patient functional rehabilitation for a variety of reasons. The fact that survivors of pediatric PFBT demonstrate relatively normal quality of life in the present study, although encouraging, would likely substantiate the rehabilitation centres' refusal to provide services for this population. But this study also suggests that better balance abilities are correlated with better scores in the physical dimension of HRQOL. Therefore, it appears beneficial to improve balance abilities in survivors of pediatric PFBT. If rehabilitation centres are not planning to develop specialized rehabilitation programs for this population, there may be other ways to address these issues. For example, as there are more survivor clinics appearing in hospital centres, it will likely fall to them to offer survivor rehabilitation programs where groups of survivors, not only of CNS tumours but all forms of pediatric cancers, can participate in structured exercise. Unfortunately, the likelihood of this happening is limited by budgetary and staffing constraints; therefore, solutions must be found in the community. For example, exercise programs could be provided and individualized for survivors of pediatric PFBT. These programs should be tailored to the individual survivor and based on their interests so that the exercises could be performed either at home possibly via a web-based exercise group, in a gym or incorporated into any other physical activity they already participate in.

9.4 Limitations

The most obvious limitation of the present study is with regards to the sample size. Overall, only six participants were recruited to the experimental group and of those, only four were able to be assessed using the force platform. There were several contributing factors to this. Firstly, there was an unfortunate administrative delay in having the project approved by the Research Ethics Committee that was beyond our control. As a consequence, instead of receiving ethics approval at the beginning of the summer of 2011, as was originally planned to optimize recruitment as many neuro-oncology clinics were being held due to summer holidays, ethical approval was obtained only at the end of August 2011. Furthermore, there were many cancelled neuro-oncology clinics over the last year due to absences by the neurosurgeons. Finally, the clinical nurse specialist who was assisting with recruitment took a leave of absence in January 2012, resulting in the need to find an alternate person to assist with recruitment. These difficulties coupled with the fact that the force platform had to be returned to its owner for use in another project in June 2012, lead to only a few participants being evaluated with this equipment. Due to the novel approach used, procedures for collecting the data with the force platform may not have been optimal and as previously mentioned, only one participant's data could be easily and completely analyzed. This small sample size limited possible statistical analysis and generalizability of the results. Be that as it may, the power of the study was fairly good and some relevant results were still obtained in this research study and the need to more extensively study using the proposed approach was established.

Another limitation of this study was the fact that the evaluator was not blinded to which group a participant belonged to. Although the outcome measures used were objective and standardized, this could always be a potentially confounding factor. Finally, the cross-sectional nature of the study does not enable us to investigate how balance abilities evolve over time in survivors of pediatric PFBT.

9.5 Future Directions

Owing to the improved survival rates, it will become essential to continue investigating long-term physical outcomes, especially balance, in survivors of all forms of pediatric CNS tumours as this is a growing group. Balance may be a crucial place to begin as implications for potential deficits on functional tasks are evident (e.g. increased risk of falls and slower gait speed). An interesting and obvious next step is to conduct longitudinal research in order to see how balance abilities change over time. This would help to elucidate as to whether or not there exists a critical time point (or specific level of balance ability) to intervene.

Following this, the next logical step in research, is to investigate ways to treat these balance difficulties in survivors of pediatric PFBT. Is it possible for physiotherapists to improve balance outcomes and when should they intervene? Future research could be geared into examining the timing of physiotherapy interventions and the most effective methods to improve balance abilities in survivors of pediatric PFBT. This would help to expand and further define some of the proposals mentioned above with regards to programs developed for improving balance abilities in survivors of PFBT. Furthermore, should physiotherapists become more formally involved in the follow-up clinics for these patients, future research should be geared to measuring the implications of their involvement. Do those survivors that are screened by physiotherapy and then provided with intervention have better outcomes than those who are not?

But in order to make sure physiotherapists properly assess balance abilities in survivors of pediatric CNS tumours, tools must be examined for psychometric properties (i.e. validity, reliability, responsiveness and minimal detectable change) for use in this population. It is likely easier to begin by evaluating existing tools or possibly by combining specific items of the available tools in order to have a more comprehensive picture of balance abilities. With regards to laboratory measures, further investigation is warranted into the use of comfortable LOS as this is a novel approach to quantifying dynamic standing balance not only in survivors of pediatric CNS tumours but in typically-developing

children and adolescents as well. LOS outside the comfortable zone may also deserve attention as they may be more relevant to balance requirements encountered in daily life.

Finally, more collaborative efforts are required in order to improve sample sizes of studies involving survivors of pediatric CNS tumours. Much of the literature describing balance outcomes in this population, including the present research study, suffers from small sample sizes. This can make finding significant results difficult and can possibly lead to hesitation when ones are found. Additionally, it is challenging to establish what, if any, associations exist between patient, tumour or treatment characteristics and balance abilities. As mentioned above, this could help identify those survivors that are more at risk for balance difficulties and would allow physiotherapists to better target the screening and the follow-up of their patients. Collaboration between centres, clinicians and researchers would drastically improve the quality and quantity of the research conducted in the area of not only balance outcomes but also physical outcomes in survivors of pediatric CNS tumours.

Chapter 10: Conclusion

There is a growing need to investigate the long-term outcomes in survivors of pediatric CNS tumours as medical management of these patients has become more intense in order to improve outcomes. Long-term effects of these treatments are currently an emerging area of research. This includes any outcomes with regards to physical functioning, which is where physiotherapists are most interested. However, this is an area where there has been little investigation using objective, standardized outcome measures.

This study confirms the fact that many survivors of pediatric PFBT have persistent balance deficits, even greater than a year post-treatment regardless of the type of intervention, as noted using the BOT-2. This tool appears to be the most able to identify differences between the experimental and control groups. The PBS demonstrates a ceiling effect in all participants. For the comfortable LOS, only certain outcomes measures suggested balance difficulties.

Finally, HRQOL for survivors of pediatric PFBT appears to be within the normative range. Higher balance scores were associated with higher scores on the physical dimension of HRQOL in survivors of PFBT. This could imply that if balance is improved, for example with continued rehabilitation, this could lead to improved quality of life, at least in the physical dimension. Future research should focus upon the best ways to screen and manage these balance difficulties, including the timing of interventions. More collaborative and longitudinal studies are required.

This research study contributes to the expanding literature investigating the long-term outcomes in survivors of pediatric CNS tumours. Over the last few decades, the medical management and survival outcomes have been the strict focus of research in this population. Excitingly, we are on the cusp of a shift of that focus away from solely the medical aspect to a more comprehensive, patient-centred point of view that includes rehabilitation and societal participation.

Bibliography

1. Canadian Cancer Society. *Canadian Cancer Statistics 2011*. Toronto, ON: Canadian Cancer Society's Steering Committee on Cancer Statistics.;2011.

2. Armstrong GT. Long-term survivors of childhood central nervous system malignancies: the experience of the Childhood Cancer Survivor Study. *European Journal of Paediatric Neurology.* 2010;14(4):298-303.

3. Packer RJ, Gurney JG, Punyko JA, et al. Long-Term Neurologic and Neurosensory Sequelae in Adult Survivors of a Childhood Brain Tumor: Childhood Cancer Survivor Study. *Journal of Clinical Oncology.* 2003;21(17):3255-3261.

4. Robinson KE, Kuttesch JF, Champion JE, et al. A quantitative meta-analysis of neurocognitive sequelae in survivors of pediatric brain tumors. *Pediatr Blood Cancer.* 2010;55(3):525-531.

5. Schulte F, Barrera M. Social competence in childhood brain tumor survivors: a comprehensive review. *Supportive Care in Cancer.* 2010;18(12):1499-1513.

6. Arora RS, Alston RD, Eden TOB, Estlin EJ, Moran A, Birch JM. Age-incidence patterns of primary CNS tumors in children, adolescents, and adults in England. *Neuro-oncol.* 2009;11(4):403-413.

7. Central Brain Tumour Registry of the United States. CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2004-2008. 2012; www.cbtrus.org. Accessed March 20, 2012.

8. Lalonde R, Strazielle C. Brain regions and genes affecting postural control. *Progress in Neurobiology.* 2007;81(1):45-60.

9. Morton SM, Bastian AJ. Cerebellar Control of Balance and Locomotion. *The Neuroscientist.* 2004;10(3):247-259.

10. Konczak J, Schoch B, Dimitrova A, Gizewski E, Timmann D. Functional recovery of children and adolescents after cerebellar tumour resection. *Brain.* 2005;128(Pt 6):1428-1441.

11. Schoch B, Hogan A, Gizewski ER, Timmann D, Konczak J. Balance control in sitting and standing in children and young adults with benign cerebellar tumors. *The Cerebellum.* 2010;9(3):324-335.

12. Schoch B, Konczak J, Dimitrova A, Gizewski ER, Wieland R, Timmann D. Impact of surgery and adjuvant therapy on balance function in children and adolescents with cerebellar tumors. *Neuropediatrics.* 2006;37(6):350-358.

13. Syczewska M, Dembowska-Baginska B, Perek-Polnik M, Kalinowska M, Perek D. Postural sway in children and young adults, survivors of CNS tumours. *Advances in Medical Sciences.* 2008;53(2):256-262.

14. Syczewska M, Dembowska-Baginska B, Perek-Polnik M, Perek D. Functional status of children after treatment for a malignant tumour of the CNS: a preliminary report. *Gait & Posture.* 2006;23(2):206-210.

15. Bauchet L, Rigau V, Mathieu-Daudé H, et al. Clinical epidemiology for childhood primary central nervous system tumors. *J Neurooncol.* 2009;92(1):87-98.

16. Dreifaldt AC, Carlberg M, Hardell L. Increasing incidence rates of childhood malignant diseases in Sweden during the period 1960-1998. *European Journal of Cancer.* 2004;40(9):1351-1360.

17. Li J, Thompson TD, Miller JW, Pollack LA, Stewart SL. Cancer incidence among children and adolescents in the United States, 2001-2003. *Pediatrics.* 2008;121(6):e1470-e1477.

18. McKinney PA. Brain tumours: incidence, survival, and aetiology. *Journal of Neurology, Neurosurgery & Psychiatry.* 2004;75 Suppl 2:ii12-17.

19. Peris-Bonet R, Martinez-Garcia C, Lacour B, et al. Childhood central nervous system tumours--incidence and survival in Europe (1978-1997): report from Automated Childhood Cancer Information System project. *European Journal of Cancer.* 2006;42(13):2064-2080.

20. Fleming AJ, Chi SN. Brain Tumors in Children. *Current Problems in Pediatric and Adolescent Health Care.* 2012;42(4):80-103.

21. Wohrer A, Waldhor T, Heinzl H, et al. The Austrian Brain Tumour Registry: a cooperative way to establish a population-based brain tumour registry. *J Neurooncol.* 2009;95(3):401-411.

22. Wrensch M, Minn Y, Chew T, Bondy M, Berger MS. Epidemiology of primary brain tumors: current concepts and review of the literature. *Neuro-oncol.* 2002;4(4):278-299.

23. Johannesen TB, Angell-Andersen E, Tretli S, Langmark F, Lote K. Trends in incidence of brain and central nervous system tumors in Norway, 1970-1999. *Neuroepidemiology.* 2004;23(3):101-109.

24. Kohler BA, Ward E, McCarthy BJ, et al. Annual report to the nation on the status of cancer, 1975-2007, featuring tumors of the brain and other nervous system. *J Natl Cancer Inst.* 2011;103(9):714-736.

25. Nolte J. *The human brain : an introduction to its functional anatomy.* 6th ed. Philadelphia, PA: Mosby/Elsevier; 2009.

26. Kadri H, Mawla AA, Murad L. Incidence of childhood brain tumors in Syria (1993-2002). *Pediatr Neurosurg.* 2005;41(4):173-177.

27. Cho KT, Wang KC, Kim SK, Shin SH, Chi JG, Cho BK. Pediatric brain tumors: statistics of SNUH, Korea (1959-2000). *Child's Nervous System.* 2002;18(1-2):30-37.

28. Caldarella A, Crocetti E, Paci E. Is the incidence of brain tumors really increasing? A population-based analysis from a cancer registry. *J Neurooncol.* 2011;104(2):589-594.

29. Van Der Horst M, Winther JF, Olsen JH. Cancer incidence in the age range 0-34 years: Historical and actual status in Denmark. *International Journal of Cancer.* 2006;118(11):2816-2826.

30. Smith MA, Seibel NL, Altekruse SF, et al. Outcomes for Children and Adolescents With Cancer: Challenges for the Twenty-First Century. *Journal of Clinical Oncology.* 2010;28(15):2625-2634.

31. Ansell P, Johnston T, Simpson J, Crouch S, Roman E, Picton S. Brain Tumor Signs and Symptoms: Analysis of Primary Health Care Records From the UKCCS. *Pediatrics.* 2010;125(1):112-119.

32. Duffner PK. Diagnosis of brain tumors in children. *Expert review of neurotherapeutics.* 2007;7(7):875-885.

33. Reulecke BC, Erker CG, Fiedler BJ, Niederstadt T-U, Kurlemann G. Brain Tumors in Children: Initial Symptoms and Their Influence on the Time Span Between Symptom Onset and Diagnosis. *Journal of Child Neurology.* 2008;23(2):178-183.

34. Ullrich NJ. Neurologic Sequelae of Brain Tumors in Children. *Journal of Child Neurology.* 2009;24(11):1446-1454.

35. Pollack IF. Pediatric brain tumors. *Seminars in Surgical Oncology.* 1999;16(2):73-90.

36. Wilne S, Collier J, Kennedy C, Koller K, Grundy R, Walker D. Presentation of childhood CNS tumours: a systematic review and meta-analysis. *The Lancet Oncology.* 2007;8(8):685-695.

37. Hayashi N, Kidokoro H, Miyajima Y, et al. How do the clinical features of brain tumours in childhood progress before diagnosis? *Brain and Development.* 2010;32(8):636-641.

38. Dobrovoljac M, Hengartner H, Boltshauser E, Grotzer M. Delay in the diagnosis of paediatric brain tumours. *European Journal of Pediatrics.* 2002;161(12):663-667.

39. Wilne S, Collier J, Kennedy C, et al. Progression from first symptom to diagnosis in childhood brain tumours. *European Journal of Pediatrics.* 2012;171(1):87-93.

40. Wilne SH, Ferris RC, Nathwani A, Kennedy CR. The presenting features of brain tumours: a review of 200 cases. *Archives of Disease in Childhood.* 2006;91(6):502-506.

41. Keene DL, Hsu E, Ventureyra E. Brain tumors in childhood and adolescence. *Pediatric Neurology.* 1999;20(3):198-203.

42. Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International Classification of Childhood Cancer, third edition. *Cancer.* 2005;103(7):1457-1467.

43. Louis DN, International Agency for Research on Cancer. *WHO classification of tumours of the central nervous system.* 4th ed. Lyon: International Agency for Research on Cancer; 2007.

44. Makino K, Nakamura H, Yano S, Kuratsu J-I, Kumamoto Brain Tumor G. Population-based epidemiological study of primary intracranial tumors in childhood. *Child's Nervous System.* 2010;26(8):1029-1034.

45. Massimino M, Giangaspero F, Garrè ML, et al. Childhood medulloblastoma. *Critical Reviews in Oncology/Hematology.* 2011;79(1):65-83.

46. Dubuc A, Northcott P, Mack S, Witt H, Pfister S, Taylor M. The Genetics of Pediatric Brain Tumors. *Current Neurology and Neuroscience Reports.* 2010;10(3):215-223.

47. Grill J, Bergthold G, Ferreira C. Pediatric ependymomas: will molecular biology change patient management? *Current Opinion in Oncology.* 2011;23(6):638-642.

48. Levy AS. Brain Tumors in Children: Evaluation and Management. *Current Problems in Pediatric and Adolescent Health Care.* 2005;35(6):230-245.

49. Mueller S, Chang S. Pediatric Brain Tumors: Current Treatment Strategies and Future Therapeutic Approaches. *Neurotherapeutics.* 2009;6(3):570-586.

50. Pollack IF, Jakacki RI. Childhood brain tumors: epidemiology, current management and future directions. *Nature Reviews Neurology.* 2011;7(9):495-506.

51. Pollack IF, Jakacki R, Deutsch M, Hamilton RL. Current management of pediatric brain tumors. *Seminars in Neurosurgery.* 2002;13(1):5-18.

52. Bouffet E, Tabori U, Huang A, Bartels U. Possibilities of new therapeutic strategies in brain tumors. *Cancer Treatment Reviews.* 2010;36(4):335-341.

53. Merchant TE, Pollack IF, Loeffler JS. Brain Tumors Across the Age Spectrum: Biology, Therapy, and Late Effects. *Seminars in Radiation Oncology.* 2010;20(1):58-66.

54. Nejat F, El Khashab M, Rutka JT. Initial Management of Childhood Brain Tumors: Neurosurgical Considerations. *Journal of Child Neurology.* 2008;23(10):1136-1148.

55. Reddy A. Advances in biology and treatment of childhood brain tumors. *Current Neurology and Neuroscience Reports.* 2001;1(2):137-143.

56. Pollack IF. Multidisciplinary management of childhood brain tumors: a review of outcomes, recent advances, and challenges. *Journal of Neurosurgery: Pediatrics.* 2011;8(2):135-148.

57. Muzumdar D, Ventureyra EC. Treatment of posterior fossa tumors in children. *Expert review of neurotherapeutics.* 2010;10(4):525-546.

58. Vazquez E, Delgado I, Sanchez-Montanez A, Barber I, Sanchez-Toledo J, Enriquez G. Side effects of oncologic therapies in the pediatric central nervous system: update on neuroimaging findings. *Radiographics : a review publication of the Radiological Society of North America, Inc.* 2011;31(4):1123-1139.

59. Gudrunardottir T, Sehested A, Juhler M, Schmiegelow K. Cerebellar mutism. *Child's Nervous System.* 2011;27(3):355-363.

60. Küpeli S, Yalçın B, Bilginer B, Akalan N, Haksal P, Büyükpamukçu M. Posterior fossa syndrome after posterior fossa surgery in children with brain tumors. *Pediatr Blood Cancer.* 2011;56(2):206-210.

61. Hoffman KE, Yock TI. Radiation Therapy for Pediatric Central Nervous System Tumors. *Journal of Child Neurology.* 2009;24(11):1387-1396.

62. Merchant TE, Conklin HM, Wu S, Lustig RH, Xiong X. Late Effects of Conformal Radiation Therapy for Pediatric Patients With Low-Grade Glioma: Prospective Evaluation of Cognitive, Endocrine, and Hearing Deficits. *Journal of Clinical Oncology.* 2009;27(22):3691-3697.

63. Behin A, Delattre JY. Complications of radiation therapy on the brain and spinal cord. *Seminars in neurology.* 2004;24(4):405-417.

64. Monje M, Fisher PG. Neurological complications following treatment of children with brain tumors. *Journal of pediatric rehabilitation medicine.* 2011;4(1):31-36.

65. Kaatsch P. Epidemiology of childhood cancer. *Cancer Treatment Reviews.* 2010;36(4):277-285.

66. Lannering B, Sandstrom PE, Holm S, et al. Classification, incidence and survival analyses of children with CNS tumours diagnosed in Sweden 1984-2005. *Acta paediatrica.* 2009;98(10):1620-1627.

67. Magnani C, Aareleid T, Viscomi S, Pastore G, Berrino F. Variation in survival of children with central nervous system (CNS) malignancies diagnosed in Europe between 1978 and 1992: the EUROCARE study. *European Journal of Cancer.* 2001;37(6):711-721.

68. de Araujo OL, da Trindade KM, Trompieri NM, Fontenele JB, Felix FHC. Analysis of survival and prognostic factors of pediatric patients with brain tumor. *Jornal de Pediatria.* 2011;87(5):425-432.

69. Fisher PG, Tihan T, Goldthwaite PT, et al. Outcome analysis of childhood low-grade astrocytomas. *Pediatr Blood Cancer.* 2008;51(2):245-250.

70. Wisoff JH, Sanford RA, Heier LA, et al. Primary neurosurgery for pediatric low-grade gliomas: A prospective multi-institutional study from the children's oncology group. *Neurosurgery.* 2011;68(6):1548-1554.

71. Tseng JH, Tseng MY. Survival analysis of children with primary malignant brain tumors in England and Wales: a population-based study. *Pediatr Neurosurg.* 2006;42(2):67-73.

72. Perkins SM, Rubin JB, Leonard JR, et al. Glioblastoma in Children: A Single-Institution Experience. *International Journal of Radiation Oncology*Biology*Physics.* 2011;80(4):1117-1121.

73. Song KS, Phi JH, Cho BK, et al. Long-term outcomes in children with glioblastoma. *Journal of neurosurgery. Pediatrics.* 2010;6(2):145-149.

74. Johannesen TB, Langmark F, Lote K. Cause of death and long-term survival in patients with neuro-epithelial brain tumours: a population-based study. *European Journal of Cancer.* 2003;39(16):2355-2363.

75. Aarsen FK, Paquier PF, Reddingius RE, et al. Functional outcome after low-grade astrocytoma treatment in childhood. *Cancer.* 2006;106(2):396-402.

76. Phi JH, Wang KC, Park SH, et al. Pediatric infratentorial ependymoma: prognostic significance of anaplastic histology. *J Neurooncol.* 2012;106(3):619-626.

77. Armstrong GT, Conklin HM, Huang S, et al. Survival and long-term health and cognitive outcomes after low-grade glioma. *Neuro-oncol.* 2011;13(2):223-234.

78. Due-Tonnessen BJ, Helseth E, Scheie D, Skullerud K, Aamodt G, Lundar T. Long-term outcome after resection of benign cerebellar astrocytomas in children and young adults (0-19 years): report of 110 consecutive cases. *Pediatr Neurosurg.* 2002;37(2):71-80.

79. Vassilyadi M, Shamji M, Tataryn Z, Keene D, Ventureyra E. Postoperative Surveillance Magnetic Resonance Imaging for Cerebellar Astrocytoma. *The Canadian Journal of Neurological Sciences.* 2009;36(6):707-712.

80. Ness KK, Mertens AC, Hudson MM, et al. Limitations on Physical Performance and Daily Activities among Long-Term Survivors of Childhood Cancer. *Annals of Internal Medicine.* 2005;143(9):639-647.

81. St Jude Children's Research Hospital. The Childhood Cancer Survivor Study. 2012; http://ccss.stjude.org. Accessed July 2, 2012, 2012.

82. Zuzak T, Poretti A, Drexel B, Zehnder D, Boltshauser E, Grotzer M. Outcome of children with low-grade cerebellar astrocytoma: long-term complications and quality of life. *Child's Nervous System.* 2008;24(12):1447-1455.

83. Aarsen FK, Van Dongen HR, Paquier PF, Van Mourik M, Catsman-Berrevoets CE. Long-term sequelae in children after cerebellar astrocytoma surgery. *Neurology.* 2004;62(8):1311-1316.

84. Benesch M, Lackner H, Sovinz P, et al. Late sequela after treatment of childhood low-grade gliomas: a retrospective analysis of 69 long-term survivors treated between 1983 and 2003. *J Neurooncol.* 2006;78(2):199-205.

85. Sonderkaer S, Schmiegelow M, Carstensen H, Nielsen LB, Muller J, Schmiegelow K. Long-term neurological outcome of childhood brain tumors treated by surgery only. *Journal of Clinical Oncology.* 2003;21(7):1347-1351.

86. Macedoni-Lukšič M, Jereb B, Todorovski L. Long-Term Sequelae in Children Treated for Brain Tumors: Impairments, Disability, and Handicap. *Pediatric Hematology-Oncology.* 2003;20(2):89-101.

87. Fouladi M, Gilger E, Kocak M, et al. Intellectual and Functional Outcome of Children 3 Years Old or Younger Who Have CNS Malignancies. *Journal of Clinical Oncology.* 2005;23(28):7152-7160.

88. Ness KK, Morris EB, Nolan VG, et al. Physical performance limitations among adult survivors of childhood brain tumors. *Cancer.* 2010;116(12):3034-3044.

89. Karnofsky DA, Abelmann WH, Craver LF, Burchenal JH. The use of the nitrogen mustards in the palliative treatment of carcinoma. With particular reference to bronchogenic carcinoma. *Cancer.* 1948;1(4):634-656.

90. Vinchon M, Baroncini M, Leblond P, Delestret I. Morbidity and tumor-related mortality among adult survivors of pediatric brain tumors: a review. *Child's Nervous System.* 2011;27(5):697-704.

91. Davis EE, Pitchford NJ, Jaspan T, McArthur D, Walker D. Development of cognitive and motor function following cerebellar tumour injury sustained in early childhood. *Cortex; a journal devoted to the study of the nervous system and behavior.* 2010;46(7):919-932.

92. Rueckriegel SM, Blankenburg F, Henze G, Baqué H, Driever PH. Loss of fine motor function correlates with ataxia and decline of cognition in cerebellar tumor survivors. *Pediatr Blood Cancer.* 2009;53(3):424-431.

93. Maddrey AM, Bergeron JA, Lombardo ER, et al. Neuropsychological performance and quality of life of 10 year survivors of childhood medulloblastoma. *J Neurooncol.* 2005;72(3):245-253.

94. Hardy KK, Willard VW, Watral MA, Bonner MJ. Perceived Social Competency in Children With Brain Tumors: Comparison Between Children on and off Therapy. *Journal of Pediatric Oncology Nursing.* 2010;27(3):156-163.

95. Reimers TS, Mortensen EL, Schmiegelow K. Memory deficits in long-term survivors of childhood brain tumors may primarily reflect general cognitive dysfunctions. *Pediatr Blood Cancer.* 2007;48(2):205-212.

96. Edelstein K, Spiegler BJ, Fung S, et al. Early aging in adult survivors of childhood medulloblastoma: Long-term neurocognitive, functional, and physical outcomes. *Neuro-oncol.* 2011;13 (5):536-545.

97. Turner CD, Chordas CA, Liptak CC, et al. Medical, psychological, cognitive and educational late-effects in pediatric low-grade glioma survivors treated with surgery only. *Pediatr Blood Cancer.* 2009;53(3):417-423.

98. Mabbott DJ, Monsalves E, Spiegler BJ, et al. Longitudinal evaluation of neurocognitive function after treatment for central nervous system germ cell tumors in childhood. *Cancer.* 2011;117(23):5402-5411.

99. Palmer SL, Goloubeva O, Reddick WE, et al. Patterns of Intellectual Development Among Survivors of Pediatric Medulloblastoma: A Longitudinal Analysis. *Journal of Clinical Oncology.* 2001;19(8):2302-2308.

100. Sands SA, Oberg JA, Gardner SL, Whiteley JA, Glade-Bender JL, Finlay JL. Neuropsychological functioning of children treated with intensive chemotherapy followed by myeloablative consolidation chemotherapy and autologous hematopoietic cell rescue for newly diagnosed CNS tumors: An analysis of the Head Start II survivors. *Pediatr Blood Cancer.* 2010;54(3):429-436.

101. Human Resources and Skills Development Canada. Learning - Educational Attainment. 2012; http://www4.hrsdc.gc.ca/.3ndic.1t.4r@-eng.jsp?iid=29#M_1. Accessed Sept 3rd, 2012, 2012.

102. Armstrong GT, Liu Q, Yasui Y, et al. Long-Term Outcomes Among Adult Survivors of Childhood Central Nervous System Malignancies in the Childhood Cancer Survivor Study. *J Natl Cancer Inst.* 2009;101(13):946-958.

103. Achenback TM, Achenback TM. *Manual for the Youth Self-Report and 1991 profile.* Burlington, VT: Dept. of Psychiatry, University of Vermont; 1991.

104. Schulte F, Bartels U, Bouffet E, Janzen L, Hamilton J, Barrera M. Body weight, social competence, and cognitive functioning in survivors of childhood brain tumors. *Pediatr Blood Cancer.* 2010;55(3):532-539.

105. Carpentieri SC, Meyer EA, Delaney BL, et al. Psychosocial and behavioral functioning among pediatric brain tumor survivors. *J Neurooncol.* 2003;63(3):279-287.

106. Sands S, Pasichow K, Weiss R, et al. Quality of life and behavioral follow-up study of Head Start I pediatric brain tumor survivors. *J Neurooncol.* 2011;101(2):287-295.

107. Bonner MJ, Hardy KK, Willard VW, Anthony KK, Hood M, Gururangan S. Social Functioning and Facial Expression Recognition in Survivors of Pediatric Brain Tumors. *Journal of Pediatric Psychology.* 2008;33(10):1142-1152.

108. Holmquist LA, Scott J. Treatment, Age, and Time-Related Predictors of Behavioral Outcome in Pediatric Brain Tumor Survivors. *Journal of Clinical Psychology in Medical Settings.* 2002;9(4):315-321.

109. Pompili A, Caperle M, Pace A, et al. Quality-of-life assessment in patients who had been surgically treated for cerebellar pilocytic astrocytoma in childhood. *Journal of Neurosurgery.* 2002;96(2):229-234.

110. Cardarelli C, Cereda C, Masiero L, et al. Evaluation of health status and health-related quality of life in a cohort of Italian children following treatment for a primary brain tumor. *Pediatr Blood Cancer.* 2006;46(5):637-644.

111. Musial-Bright L, Panteli L, Hernáiz Driever P. Pediatric low-grade glioma survivors experience high quality of life. *Child's Nervous System.* 2011;27(11):1895-1902.

112. Reimers TS, Mortensen EL, Nysom K, Schmiegelow K. Health-related quality of life in long-term survivors of childhood brain tumors. *Pediatr Blood Cancer.* 2009;53(6):1086-1091.

113. Odame I, Duckworth J, Talsma D, et al. Osteopenia, physical activity and health-related quality of life in survivors of brain tumors treated in childhood. *Pediatr Blood Cancer.* 2006;46(3):357-362.

114. Shumway-Cook A, Woollacott MH. *Motor control : theory and practical applications.* 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2001.

115. Massion J. Postural Control Systems in Developmental Perspective. *Neuroscience & Biobehavioral Reviews.* 1998;22(4):465-472.

116. Kirshenbaum N, Riach C, Starkes J. Non-linear development of postural control and strategy use in young children: a longitudinal study. *Experimental Brain Research.* 2001;140(4):420-431.

117. Winter DA, Patla AE, Prince F, Ishac M, Gielo-Perczak K. Stiffness Control of Balance in Quiet Standing. *Journal of Neurophysiology.* 1998;80(3):1211-1221.

118. Hay L, Redon C. Feedforward versus feedback control in children and adults subjected to a postural disturbance. *Experimental Brain Research.* 1999;125(2):153-162.

119. Westcott SL, Burtner P. Postural Control in Children. *Physical & Occupational Therapy in Pediatrics.* 2004;24(1-2):5-55.

120. Frank JS, Earl M. Coordination of Posture and Movement. *Physical Therapy.* 1990;70(12):855-863.

121. Kuo AD. An optimal state estimation model of sensory integration in human postural balance. *Journal of neural engineering.* 2005;2(3):S235-249.

122. Casselbrant ML, Mandel EM, Sparto PJ, Redfern MS, Furman JM. Contribution of vision to balance in children four to eight years of age. *Annals of Otology, Rhinology & Laryngology.* 2007;116(9 part 1):653-657.

123. Hatzitaki V, Zlsi V, Kollias I, Kioumourtzoglou E. Perceptual-Motor Contributions to Static and Dynamic Balance Control in Children. *Journal of motor behavior.* 2002/06/01 2002;34(2):161-170.

124. Sparto P, Redfern M, Jasko J, Casselbrant M, Mandel E, Furman J. The influence of dynamic visual cues for postural control in children aged 7–12 years. *Experimental Brain Research.* 2006;168(4):505-516.

125. Viel S, Vaugoyeau M, Assaiante C. Adolescence: a transient period of proprioceptive neglect in sensory integration of postural control. *Motor control.* 2009;13(1):25-42.

126. Chen Y-S, Zhou S. Soleus H-reflex and its relation to static postural control. *Gait & Posture.* 2011;33(2):169-178.

127. Cerminara N, Apps R. Behavioural Significance of Cerebellar Modules. *The Cerebellum.* 2011;10(3):484-494.

128. Ioffe M, Chernikova L, Ustinova K. Role of cerebellum in learning postural tasks. *The Cerebellum.* 2007;6(1):87-94.

129. Morton S, Bastian A. Mechanisms of cerebellar gait ataxia. *The Cerebellum.* 2007;6(1):79-86.

130. Ouchi Y, Okada H, Yoshikawa E, Nobezawa S, Futatsubashi M. Brain activation during maintenance of standing postures in humans. *Brain.* 1999;122(Pt 2):329-338.

131. Bastian AJ, Mink JW, Kaufman BA, Thach WT. Posterior vermal split syndrome. *Annals of Neurology.* 1998;44(4):601-610.

132. Ilg W, Giese M, Gizewski E, Schoch B, Timmann D. The influence of focal cerebellar lesions on the control and adaptation of gait. *Brain: A Journal of Neurology.* 2008;131(11):2913-2927.

133. Jacobs JV, Horak FB. Cortical control of postural responses. *Journal of Neural Transmission.* 2007;114(10):1339-1348.

134. Goble DJ, Coxon JP, Van Impe A, et al. Brain Activity during Ankle Proprioceptive Stimulation Predicts Balance Performance in Young and Older Adults. *The Journal of Neuroscience.* 2011;31(45):16344-16352.

135. Visser JE, Bloem BR. Role of the Basal Ganglia in Balance Control. *Neural Plasticity.* 2005;12(2-3):161-174.

136. Mihara M, Miyai I, Hatakenaka M, Kubota K, Sakoda S. Role of the prefrontal cortex in human balance control. *NeuroImage.* 2008;43(2):329-336.

137. Slobounov S, Wu T, Hallett M. Neural basis subserving the detection of postural instability: an fMRI study. *Motor control.* 2006;10(1):69-89.

138. Woollacott M, Shumway-Cook A. Attention and the control of posture and gait: a review of an emerging area of research. *Gait & Posture.* 2002;16(1):1-14.

139. Blanchard Y, Carey S, Coffey J, et al. The influence of concurrent cognitive tasks on postural sway in children. *Pediatric Physical Therapy.* 2005;17(3):189-193.

140. Olivier I, Cuisinier R, Vaugoyeau M, Nougier V, Assaiante C. Age-related differences in cognitive and postural dual-task performance. *Gait & Posture.* 2010;32(4):494-499.

141. Palluel E, Nougier V, Olivier I. Postural control and attentional demand during adolescence. *Brain Research.* 2010;1358(0):151-159.

142. Schmid M, Conforto S, Lopez L, D'Alessio T. Cognitive load affects postural control in children. *Experimental Brain Research.* 2007;179(3):375-385.

143. Forssberg H, Nashner L. Ontogenetic development of postural control in man: adaptation to altered support and visual conditions during stance. *The Journal of Neuroscience.* 1982;2(5):545-552.

144. Assaiante C. Action and representation of action during childhood and adolescence: A functional approach. *Neurophysiologie Clinique/Clinical Neurophysiology.* 2012;42(1–2):43-51.

145. Assaiante C, Mallau S, Viel S, et al. Development of Postural Control in Healthy Children: A Functional Approach. *Neural Plasticity.* 2005;12(2-3):109-118.

146. Barela JA, Jeka JJ, Clark JE. Postural control in children. *Experimental Brain Research.* 2003;150(4):434-442.

147. Girolami G, Shiratori T, Aruin A. Anticipatory postural adjustments in children with typical motor development. *Experimental Brain Research.* 2010;205(2):153-165.

148. Hirabayashi S-i, Iwasaki Y. Developmental perspective of sensory organization on postural control. *Brain and Development.* 1995;17(2):111-113.

149. Nolan L, Grigorenko A, Thorstensson A. Balance control: sex and age differences in 9- to 16-year-olds. *Developmental Medicine & Child Neurology.* 2005;47(7):449-454.

150. Rival C, Ceyte H, Olivier I. Developmental changes of static standing balance in children. *Neuroscience Letters.* 2005;376(2):133-136.

151. Schmid M, Conforto S, Lopez L, Renzi P, D'Alessio T. The development of postural strategies in children: a factorial design study. *Journal of neuroengineering and rehabilitation.* 2005;2:29.

152. Do M-C, Chong RK-Y. Balance recovery from a forward fall: Developmental aspects of sensorimotor organization and the role of supraspinal control. *Neuroscience Letters.* 2008;442(3):300-304.

153. Bair W-N, Kiemel T, Jeka J, Clark J. Development of multisensory reweighting for posture control in children. *Experimental Brain Research.* 2007;183(4):435-446.

154. Lebiedowska MK, Syczewska M. Invariant sway properties in children. *Gait & Posture.* 2000;12(3):200-204.

155. Roncesvalles MN, Woollacott MH, Jensen JL. Development of lower extremity kinetics for balance control in infants and young children. *Journal of motor behavior.* 2001;33(2):180-192.

156. Sundermier L, Woollacott M, Roncesvalles N, Jensen J. The development of balance control in children: comparisons of EMG and kinetic variables and chronological and developmental groupings. *Experimental Brain Research.* 2001;136(3):340-350.

157. Wright FV, Ryan J, Brewer K. Reliability of the Community Balance and Mobility Scale (CB&M) in high-functioning school-aged children and adolescents who have an acquired brain injury. *Brain Injury.* 2010;24(13-14):1585-1594.

158. Riemann BL, Guskiewicz KM, Shields EW. Relationship between clinical and forceplate measures of postural stability. *Journal of Sport Rehabilitation.* 1999;8:71-82.

159. De Kegel A, Baetens T, Peersman W, Maes L, Dhooge I, Van Waelvelde H. Ghent Developmental Balance Test: A New Tool to Evaluate Balance Performance in Toddlers and Preschool Children. *Physical Therapy.* 2012;92(6):841-852.

160. Kroes M, Vissers YLJ, Sleijpen FAM, et al. Reliability and validity of a qualitative and quantitative motor test for 5- to 6-year-old children. *European Journal of Paediatric Neurology.* 2004;8(3):135-143.

161. Duncan PW, Weiner DK, Chandler J, Studenski S. Functional Reach: A New Clinical Measure of Balance. *The Journal of Gerontology.* 1990;45(6):M192-M197.

162. Donahoe B, Turner D, Worrell T. The Use of Functional Reach as a Measurement of Balance in Boys and Girls Without Disabilities Ages 5 to 15 Years. *Pediatric Physical Therapy.* 1994;6:189-193.

163. Westcott SL, Lowes LP, Richardson PK. Evaluation of Postural Stability in Children: Current Theories and Assessment Tools. *Physical Therapy.* 1997;77(6):629-645.

164. Bartlett D, Birmingham T. Validity and reliability of a pediatric reach test. *Pediatric Physical Therapy.* 2003;15(2):84-92.

165. Volkman KG, Stergiou N, Stuberg W, Blanke D, Stoner J. Methods to improve the reliability of the functional reach test in children and adolescents with typical development. *Pediatric Physical Therapy.* 2007;19(1):20-27.

166. Berg K. Measuring balance in the elderly: preliminary development of an instrument. *Physiotherapy Canada.* 1989;41(6):304-311.

167. Franjoine MR, Gunther JS, Taylor MJ. Pediatric balance scale: a modified version of the berg balance scale for the school-age child with mild to moderate motor impairment. *Pediatric Physical Therapy.* 2003;15(2):114-128.

168. Franjoine MR, Darr N, Held SL, Kott K, Young BL. The performance of children developing typically on the Pediatric Balance Scale. *Pediatric Physical Therapy.* 2010;22(4):350-359.

169. Crowe TK, Deitz JC, Richardson PK, Atwater SW. Interrater Reliability of the Pediatric Clinical Test of Sensory Interaction for Balance. *Physical & Occupational Therapy in Pediatrics.* 1991;10(4):1-27.

170. Richardson PK, Atwater SW, Crowe TK, Deitz JC. Performance of preschoolers on the Pediatric Clinical Test of Sensory Interaction for Balance. *The American Journal of Occupational Therapy.* 1992;46(9):793-800.

171. Gagnon I, Swaine B, Forget R. Exploring the Comparability of the Sensory Organization Test and the Pediatric Clinical Test of Sensory Interaction for Balance in Children. *Physical & Occupational Therapy in Pediatrics.* 2006;26(1-2):23-41.

172. Henderson SE, Sugden DA, Barnett AL. *Movement assessment battery for children-2 second edition [Movement ABC-2]*. London, UK: The Psychological Corporation; 2007.

173. Brown T, Lalor A. The Movement Assessment Battery for Children—Second Edition (MABC-2): A Review and Critique. *Physical & Occupational Therapy in Pediatrics.* 2009;29(1):86-103.

174. Wiart L, Darrah J. Review of four tests of gross motor development. *Developmental Medicine & Child Neurology.* 2001;43(4):279-285.

175. Bruininks RH, Bruininks BD. *BOT2: Bruininks-Oseretsky Test of Motor Proficiency : Manual.* Minneapolis, Minn: Pearson Assessments; 2005.

176. Gan S-M, Tung L-C, Tang Y-H, Wang C-H. Psychometric Properties of Functional Balance Assessment in Children With Cerebral Palsy. *Neurorehabilitation and Neural Repair.* 2008;22(6):745-753.

177. Villamonte R, Vehrs PR, Feland JB, Johnson AW, Seeley MK, Eggett D. Reliability of 16 Balance Tests in Individuals with Down Syndrome. *Perceptual and Motor Skills.* 2010;111(2):530-542.

178. Wuang Y-P, Su C-Y. Reliability and responsiveness of the Bruininks–Oseretsky Test of Motor Proficiency-Second Edition in children with intellectual disability. *Research in Developmental Disabilities.* 2009;30(5):847-855.

179. Wuang Y-P, Su J-H, Su C-Y. Reliability and responsiveness of the Movement Assessment Battery for Children–Second Edition Test in children with developmental coordination disorder. *Developmental Medicine & Child Neurology.* 2012;54(2):160-165.

180. Deitz JC, Kartin D, Kopp K. Review of the Bruininks-Oseretsky Test of Motor Proficiency, Second Edition (BOT-2). *Physical & Occupational Therapy in Pediatrics.* 2007;27(4):87-102.

181. Cherng RJ, Su FC, Chen JJ, Kuan TS. Performance of static standing balance in children with spastic diplegic cerebral palsy under altered sensory environments. *American Journal of Physical Medicine & Rehabilitation.* 1999;78(4):336-343.

182. Galea V, Wright MJ, Barr RD. Measurement of balance in survivors of acute lymphoblastic leukemia in childhood. *Gait & Posture.* 2004;19(1):1-10.

183. Harris GF, Riedel SA, Matesi D, Smith P. Standing postural stability assessment and signal stationarity in children with cerebral palsy. *IEEE Transactions on Rehabilitation Engineering.* 1993;1(1):35-42.

184. Rose J, Wolff DR, Jones VK, Bloch DA, Oehlert JW, Gamble JG. Postural balance in children with cerebral palsy. *Developmental Medicine & Child Neurology.* 2002;44(1):58-63.

185. Rocchi L, Chiari L, Cappello A. Feature selection of stabilometric parameters based on principal component analysis. *Medical & Biological Engineering & Computing.* 2004;42(1):71-79.

186. Prieto TE, Myklebust JB, Hoffmann RG, Lovett EG, Myklebust BM. Measures of postural steadiness: differences between healthy young and elderly adults. *IEEE Transactions on Biomedical Engineering.* 1996;43(9):956-966.

187. Prieto TE, Myklebust JB, Myklebust BM. Characterization and modeling of postural steadiness in the elderly: a review. *IEEE Transactions on Rehabilitation Engineering.* 1993;1(1):26-34.

188. Doyle RJ, Hsiao-Wecksler ET, Ragan BG, Rosengren KS. Generalizability of center of pressure measures of quiet standing. *Gait & Posture.* 2007;25(2):166-171.

189. Ruhe A, Fejer R, Walker B. The test-retest reliability of centre of pressure measures in bipedal static task conditions--a systematic review of the literature. *Gait & Posture.* 2010;32(4):436-445.

190. Lin D, Seol H, Nussbaum MA, Madigan ML. Reliability of COP-based postural sway measures and age-related differences. *Gait & Posture.* 2008;28(2):337-342.

191. Santos BR, Delisle A, Lariviere C, Plamondon A, Imbeau D. Reliability of centre of pressure summary measures of postural steadiness in healthy young adults. *Gait & Posture.* 2008;27(3):408-415.

192. Carpenter MG, Frank JS, Winter DA, Peysar GW. Sampling duration effects on centre of pressure summary measures. *Gait & Posture.* 2001;13(1):35-40.

193. van der Kooij H, Campbell AD, Carpenter MG. Sampling duration effects on centre of pressure descriptive measures. *Gait & Posture.* 2011;34(1):19-24.

194. Le Clair K, Riach C. Postural stability measures: what to measure and for how long. *Clinical Biomechanics (Bristol, Avon).* 1996;11(3):176-178.

195. Zok M, Mazza C, Cappozzo A. Should the instructions issued to the subject in traditional static posturography be standardised? *Medical Engineering & Physics.* 2008;30(7):913-916.

196. Cawsey RP, Chua R, Carpenter MG, Sanderson DJ. To what extent can increasing the magnification of visual feedback of the centre of pressure position change the control of quiet standing balance? *Gait & Posture.* 2009;29(2):280-284.

197. Chiari L, Rocchi L, Cappello A. Stabilometric parameters are affected by anthropometry and foot placement. *Clinical Biomechanics (Bristol, Avon).* 2002;17(9-10):666-677.

198. Forth KE, Fiedler MJ, Paloski WH. Estimating functional stability boundaries for bipedal stance. *Gait & Posture.* 2011;33(4):715-717.

199. Haibach P, Slobounov S, Slobounova E, Newell K. Virtual time-to-contact of postural stability boundaries as a function of support surface compliance. *Experimental Brain Research.* 2007;177(4):471-482.

200. Holbein-Jenny MA, McDermott K, Shaw C, Demchak J. Validity of functional stability limits as a measure of balance in adults aged 23–73 years. *Ergonomics.* 2007;50(5):631-646.

201. Kerr HM, Eng JJ. Multidirectional measures of seated postural stability. *Clinical Biomechanics.* 2002;17(7):555-557.

202. Preuss RA, Popovic MR. Quantitative analysis of the limits of stability in sitting. *Journal of applied biomechanics.* 2010;26(3):265-272.

203. Magnani C, Pastore G, Coebergh JW, Viscomi S, Spix C, Steliarova-Foucher E. Trends in survival after childhood cancer in Europe, 1978–1997: Report from the Automated Childhood Cancer Information System project (ACCIS). *European Journal of Cancer.* 2006;42(13):1981-2005.

204. Gatta G, Zigon G, Capocaccia R, et al. Survival of European children and young adults with cancer diagnosed 1995-2002. *European Journal of Cancer.* 2009;45(6):992-1005.

205. Johnston WT, Lightfoot TJ, Simpson J, Roman E. Childhood cancer survival: A report from the United Kingdom Childhood Cancer Study. *Cancer Epidemiology.* 2010;34(6):659-666.

206. Cantrell MA. A narrative review summarizing the state of the evidence on the health-related quality of life among childhood cancer survivors. *Journal of Pediatric Oncology Nursing.* 2011;28(2):75-82.

207. McDougall J, Tsonis M. Quality of life in survivors of childhood cancer: a systematic review of the literature (2001-2008). *Supportive Care in Cancer.* 2009;17(10):1231-1246.

208. Buizer AI, De Sonneville LM, van den Heuvel-Eibrink MM, Njiokiktjien C, Veerman AJ. Visuomotor control in survivors of childhood acute lymphoblastic leukemia

treated with chemotherapy only. *Journal of the International Neuropsychological Society.* 2005;11(5):554-565.

209. Fiorillo A, Rinaldi M, Foggia L. Gait analysis in children treated by surgery followed by adjuvant therapy for posterior fossa tumors. *Acta Neurologica Belgica.* 2010;110(4):306-310.

210. Gocha Marchese V, Chiarello LA, Lange BJ. Strength and functional mobility in children with acute lymphoblastic leukemia. *Med Pediatr Oncol.* 2003;40(4):230-232.

211. Hartman A, Van Den Bos C, Stijnen T, Pieters R. Decrease in peripheral muscle strength and ankle dorsiflexion as long-term side effects of treatment for childhood cancer. *Pediatric Blood and Cancer.* 2008;50 (4):833-837.

212. Reinders-Messelink HA, Schoemaker MM, Hofte M, et al. Fine motor and handwriting problems after treatment for childhood acute lymphoblastic leukemia. *Med Pediatr Oncol.* 1996;27(6):551-555.

213. Quasthoff S, Hartung HP. Chemotherapy-induced peripheral neuropathy. *J Neurol.* 2002;249(1):9-17.

214. Armstrong GT, Stovall M, Robison LL. Long-term effects of radiation exposure among adult survivors of childhood cancer: results from the childhood cancer survivor study. *Radiation Research.* 2010;174(6):840-850.

215. Wearing SC, Hennig EM, Byrne NM, Steele JR, Hills AP. The impact of childhood obesity on musculoskeletal form. *Obesity Reviews.* 2006;7(2):209-218.

216. Howick J, Chalmers I, Glasziou P, et al. The Oxford 2011 Levels of Evidence. 2011; http://www.cebm.net/index.aspx?o=5653. Accessed August 15th, 2011, 2011.

217. Howick J, Chalmers I, Glasziou P, et al. Explanation of the 2011 Oxford Center for Evidence-Based Medicine (OCEBM) Levels of Evidence (Background Document). 2011; http://www.cebm.net/index.aspx?o=5653. Accessed August 15th, 2011, 2011.

218. Wright MJ, Halton JM, Barr RD. Musculoskeletal and gross motor function in survivors of acute lymphoblastic leukemia and Wilms' tumor. *J Pediatr Hematol Oncol.* 1996;18(4):461.

219. Wright MJ, Halton JM, Martin RF, Barr RD. Long-term gross motor performance following treatment for acute lymphoblastic leukemia. *Med Pediatr Oncol.* 1998;31(2):86-90.

220. Wright MJ, Galea V, Barr RD. Proficiency of balance in children and youth who have had acute lymphoblastic leukemia. *Physical Therapy.* 2005;85(8):782-790.

221. Toy SL, Senesac C, Trombini A. Postural control and balance training in a pediatric patient status-post medulloblastoma removal. *Pediatric Physical Therapy.* 2006;18(1):107-108.

222. Van Brussel M, Takken T, Van Der Net J, et al. Physical function and fitness in long-term survivors of childhood leukaemia. *Pediatric Rehabilitation.* 2006;9(3):267-274.

223. Rorke-Adams LB, Portnoy H. Long-term survival of an infant with gliomatosis cerebelli: Case report. *Journal of Neurosurgery: Pediatrics.* 2008;2 (5):346-350.

224. Yissar T, Eisenstein E, Wachtel S, et al. The use of the bruininks-oseretsky test of motor proficiency (second edition) as a tool to document motor performance in children with brain injury. *Brain Injury.* 2010;Conference: 8th World Congress on Brain Injury of the International Brain Injury Association Washington, DC United States. Conference Start: 20100310 Conference End: 20100314. Conference Publication: (var.pagings). 24 (3):332.

225. van den Beld WA, van der Sanden GA, Sengers RC, Verbeek AL, Gabreels FJ. Validity and reproducibility of hand-held dynamometry in children aged 4-11 years. *Journal of Rehabilitation Medicine.* 2006;38(1):57-64.

226. Maurer C, Finley A, Martel J, Ulewicz C, Larson CA. Ankle plantarflexor strength and endurance in 7-9 year old children as measured by the standing single leg heel-rise test. *Physical & Occupational Therapy in Pediatrics.* 2007;27(3):37-54.

227. Thibault A, Forget R, Lambert J. Evaluation of cutaneous and proprioceptive sensation in children: a reliability study. *Developmental Medicine & Child Neurology.* 1994;36(9):796-812.

228. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL™* 4.0 as a Pediatric Population Health Measure: Feasibility, Reliability, and Validity. *Ambulatory Pediatrics.* 2003;3(6):329-341.

229. Palmer SN, Meeske KA, Katz ER, Burwinkle TM, Varni JW. The PedsQL Brain Tumor Module: initial reliability and validity. *Pediatr Blood Cancer.* 2007;49(3):287-293.

230. Varni JW, Limbers CA. The pediatric quality of life inventory: measuring pediatric health-related quality of life from the perspective of children and their parents. *Pediatric clinics of North America.* 2009;56(4):843-863.

231. Bhat SR, Goodwin TL, Burwinkle TM, et al. Profile of daily life in children with brain tumors: an assessment of health-related quality of life. *Journal of Clinical Oncology.* 2005;23(24):5493-5500.

232. Newton RA. Validity of the Multi-Directional Reach Test: A Practical Measure for Limits of Stability in Older Adults. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences.* 2001;56(4):M248-M252.

233. Gauthier C, Gagnon D, Grangeon M, et al. Comparison of multidirectional seated postural stability between individuals with spinal cord injury and able-bodied individuals. *Journal of rehabilitation medicine : official journal of the UEMS European Board of Physical and Rehabilitation Medicine.* Nov 9 2013;45(1):47-54.

234. Holm I, Vøllestad N. Significant Effect of Gender on Hamstring-to-Quadriceps Strength Ratio and Static Balance in Prepubescent Children From 7 to 12 Years of Age. *The American Journal of Sports Medicine.* 2008;36(10):2007-2013.

235. Humphriss R, Hall A, May M, Macleod J. Balance ability of 7 and 10 year old children in the population: Results from a large UK birth cohort study. *International Journal of Pediatric Otorhinolaryngology.* 2011;75(1):106-113.

236. Turner M, Gagnon D, Lagace M, Gagnon I. Effect of treatment for paediatric cancers on balance: what do we know? A review of the evidence. *European Journal of Cancer Care.* 2013;22(1):3-11.

APPENDIX A:

ETHICS APPROVAL

L'Hôpital de Montréal pour enfants
The Montreal Children's Hospital

Centre universitaire de santé McGill
McGill University Health Centre

August 29, 2011

Ms. Isabelle Gagnon, PhD
Pediatric Physiotherapy,Trauma/Child Development
Montreal Children's Hospital
Room D-292

Re: ***10-363-PED Quantification of Quasi-Static and Dynamic Standing Balance in Survivors of Pediatric Posterior Fossa Brain Tumours***
Funded by: ***Internal funds***

Dear Ms. Gagnon,

The above-named research proposal received Full Board review at the convened meeting of the Montreal Children's Hospital Research Ethics Board on August 8, 2011 and was found to be within ethical guidelines for conduct at the McGill University Health Centre, and was entered accordingly into the minutes of the Research Ethics Board (REB) meeting. At the MUHC, sponsored research activities that require US federal assurance are conducted under Federal Wide Assurance (FWA) 00000840.

We are pleased to inform you that final approval was provided on August 23, 2011 for the following:

- MUHC Initial Review form
- MCH science approval letter (dated 5th May 2011)
- Protocol, revised version May 16, 2011
- Consent, English & French version August 17, 2011
- Assent, English & French version August 17, 2011

All research involving human subjects requires review at a recurring interval and the current study approval is in effect until August 22, 2012 (anniversary of initial approval). It is the responsibility of the principal investigator to submit an Application for Continuing Review to the REB prior to the expiration of approval to comply with the regulation for continuing review of "at least once per year".

The Research Ethics Boards (REBs) of the McGill University Health Centre are registered REBs working under the published guidelines of the Tri-Council Policy Statement, in compliance with the "Plan d'action ministériel en éthique de la recherche et en intégrité scientifique" (MSSS, 1998) and the Food and Drugs Act (7 June, 2001), acting in conformity with standards set forth in the (US) Code of Federal Regulations governing human subjects research, and functioning in a manner consistent with internationally accepted principles of good clinical practice.

We wish to advise you that this document completely satisfies the requirement for Research Ethics Board Attestation as stipulated by Health Canada.

The project was assigned MUHC Study Number **10-363-PED** that is required as MUHC reference when communicating about the research. Should any revision to the study, or other unanticipated development occur prior to the next required review, you must advise the REB without delay. Regulation does not permit initiation of a proposed study modification prior to REB approval for the amendment.

Jane McDonald, M.D., F.R.C.P.C
Chairperson, Research Ethics Board

APPENDIX B:

CONSENT AND ASSENT FORMS

L'Hôpital de Montréal pour enfants
The Montreal Children's Hospital
Centre universitaire de santé McGill
McGill University Health Centre

INFORMED CONSENT

Title: Quantification of quasi-static and dynamic standing balance in survivors of pediatric posterior fossa brain tumours

Principal Investigator: Dr Isabelle Gagnon, PhD
Researcher, Trauma & Child Development Programs
Montreal Children's Hospital
Assistant Professor
School of Physical and Occupational Therapy
McGill University

Co-Investigators: Dr Dany Gagnon, PhD,
Researcher, Centre de Recherche Interdisciplinaire en Réadaptation du Grand Montréal
Assistant Professor
School of Rehabilitation
Université de Montréal

Melissa Turner, pht
Physiotherapist
Montreal Children's Hospital

PARENT CONSENT FORM

Purpose and General information

You/your child are invited to participate in a research study about standing balance abilities in children and adolescents who have had a brain tumour and how it compares to that of other children who have not had a brain tumour.

The purpose of the study is to evaluate standing balance abilities, using two different ways, in children and adolescents who have had treatment for a certain type of brain tumour. Their balance will be compared to those of other children who have not had a brain tumour. We would like to be able to see which way of testing balance is better and we will be able to see if balance abilities are different between those children who have had a brain tumour and those who have not. Finally, we would like to see if balance affects a child's quality of life.

Your participation will involve one visit lasting approximately 90 minutes where your child will be assessed by a physiotherapist. We would also like you and/or your child to fill out a simple questionnaire.

In total, we would like to have 40 children participate in this study, with 20 in each group (20 children who have had a brain tumour and 20 children who have not).

Study Procedures

This study will be done in a quiet room at the Montreal Children's Hospital by a qualified physiotherapist, who will not know, if possible, what group you child belongs to. First, they will assess the movement, strength and sensation of your child's legs. This will be followed by the balance testing, which will be done several ways. There

will be two different physiotherapy tests that ask your child to perform a variety of tasks such as standing on one leg or standing on a balance beam. Next, an evaluation of standing balance using a special platform that is connected to a computer will be done and will require similar tasks as the physiotherapy tests. Breaks will be given at different times during the testing. This part should last approximately 90 minutes.

During one of the breaks, you and your child will be asked to fill out a simple questionnaire regarding their quality of life. The questionnaires should take no longer than 15 minutes to complete.

Your child's hospital records will also be looked at by the investigators to get information needed for the study.

Possible Risks and Discomforts

There are no risks associated with your child's participation in this study other than the possible frustration and upset by your child if they cannot perform the tasks.

Possible Benefits

There are no direct benefits to your child for participating in this study, but he/she may contribute to new medical knowledge that may help other children in the future.

Voluntary participation

Your child's participation is voluntary and you should not feel any obligation to join the study. You may agree now but are free to withdraw your child from this study at any time. Refusal to join or withdrawal from the study will not affect your child's medical care.

During the course of the study you will be informed of any new information which may affect your willingness to have your child continue in this study.

Confidentiality

All information obtained during the study will be kept confidential as required or permitted by law and will be kept for 5 years. Your child's personal identity will remain confidential, as your child will only be identified by a subject identification number.

Your child's name and other personal identifying information will not be used in any reports, presentations or publications. Representatives from Health Canada, the Montreal Children's Hospital Research Institute and the McGill University Health Centre's Research Ethics Office Quality Assurance, may have access to your child's records as it pertains to this study. The research team will have access to your child's hospital records.

Contact person

For any questions you may have regarding the research project at any time, you may contact the principal investigator, **Isabelle Gagnon,** at (514) 412-4400 ext. 22001 or the co-investigator, **Melissa Turner,** at (514) 412-4400 ext. 22109.

For additional information regarding your child's rights as a research subject, you may contact the hospital's Patient Representative (ombudsman), Patricia Boyer (514) 412-4400 ext. 22223, who is independent of the investigators, and works to protect patients' rights.

Consent

I have read this information and consent form and have had the opportunity to ask questions which have been answered to my satisfaction before signing my name. I acknowledge that I will receive a copy of the Information and Consent Form for future reference. I agree to have my child participate in the research study.

_____

Participant's name:

_____

Parent or guardian's printed name:

_____

Parent or guardian's signature:

_____

Relationship to child:

_____

Date: (dd/month/yy)

_____

Name of the person who obtained consent

_____

Signature of the person who obtained consent

_____

Date: (dd/month/yy)

L'Hôpital de Montréal pour enfants
The Montreal Children's Hospital
Centre universitaire de santé McGill
McGill University Health Centre

ASSENT FORM (for 7-17 year olds)

Title: Quantification of quasi-static and dynamic standing balance in survivors of pediatric posterior fossa brain tumours

Principal Investigator: Dr Isabelle Gagnon, PhD
Researcher, Trauma & Child Development Programs
Montreal Children's Hospital
Assistant Professor
School of Physical and Occupational Therapy
McGill University

Co-Investigators: Dr Dany Gagnon, PhD,
Researcher, Centre de Recherche Interdisciplinaire en Réadaptation du Grand Montréal
Assistant Professor
School of Rehabilitation
Université de Montréal

Melissa Turner, pht
Physiotherapist
Montreal Children's Hospital

You are invited to participate in a research study about standing balance.

What is this study about?
The reason we are doing this study is to compare the standing balance of children and teenagers who have had a brain tumour to other children who have not.

What will I have to do?
You will be tested by a physiotherapist at the hospital only one time. The test will last about 90 minutes. The physiotherapist will look at how strong your legs are and if you can feel when your foot is touched. Then they will test your balance by asking you to do things like stand on one foot or stand on a balance beam. You and your parents will also answer some questions about your daily life.

What are the possible risks and discomforts?
There are no risks involved with taking part in this study, but you may feel frustrated if you have trouble with some of the tests.

What are the possible benefits?
You will not receive any direct benefits but we may learn from the information you provide and we may be able to help other children in the future.

What are my options?
You have the choice to be in this study or not and you should not feel any pressure to agree. You can agree now and are always free to change your mind. No one will be mad at you. Your doctor will still continue to give you the care you need, even if you don't want to be in the study.

During this study you will be told of any new information which may affect you wanting to continue.

Who will know what I did?
All information we get during the study will be kept secret. Your personal identity will remain secret, and your name will not be written on any papers. Your name and personal information will not be used in any presentations.

There may be certain people who are allowed to look at the information but it is only to check and make sure we are doing the study properly. The research team will be able to look at your hospital records.

Who can I contact if I have questions?
Any questions you may have about the research project will be answered. You can call Isabelle Gagnon, the principal investigator, at (514) 412-4400 ext. 22001 or Melissa Turner, the co-investigator, at (514) 412-4400 ext. 22109 at any time.

Assent

I have read this information and have had the opportunity to ask questions which have been answered to my satisfaction before signing my name. I agree to participate in the research study.

_____
Participant's name:

_____
Participant's signature:

_____
Date: (dd/month/yy)

APPENDIX C:

PEDIATRIC QUALITY OF LIFE INVENTORY GENERIC CORE SCALES

*In the past **ONE month**, how much of a **problem** has this been for you …*

About My Health and Activities ***(PROBLEMS WITH…)***	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. It is hard for me to walk more than one block	0	1	2	3	4
2. It is hard for me to run	0	1	2	3	4
3. It is hard for me to do sports activity or exercise	0	1	2	3	4
4. It is hard for me to lift something heavy	0	1	2	3	4
5. It is hard for me to take a bath or shower by myself	0	1	2	3	4
6. It is hard for me to do chores around the house	0	1	2	3	4
7. I hurt or ache	0	1	2	3	4
8. I have low energy	0	1	2	3	4

About My Feelings ***(PROBLEMS WITH…)***	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. I feel afraid or scared	0	1	2	3	4
2. I feel sad or blue	0	1	2	3	4
3. I feel angry	0	1	2	3	4
4. I have trouble sleeping	0	1	2	3	4
5. I worry about what will happen to me	0	1	2	3	4

How I Get Along with Others ***(PROBLEMS WITH…)***	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. I have trouble getting along with other kids	0	1	2	3	4
2. Other kids do not want to be my friend	0	1	2	3	4
3. Other kids tease me	0	1	2	3	4
4. I cannot do things that other kids my age can do	0	1	2	3	4
5. It is hard to keep up when I play with other kids	0	1	2	3	4

About School ***(PROBLEMS WITH…)***	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. It is hard to pay attention in class	0	1	2	3	4
2. I forget things	0	1	2	3	4
3. I have trouble keeping up with my schoolwork	0	1	2	3	4
4. I miss school because of not feeling well	0	1	2	3	4
5. I miss school to go to the doctor or hospital	0	1	2	3	4

APPENDIX D:

ARTICLE SUBMITTED TO L'ORDRE PROFESSIONNEL DE LA PHYSIOTHÉRAPIE DU QUÉBEC (REQUIRMENT FOR BURSARY RECEIVED)

Quantification de l'équilibre debout chez les enfants et adolescents ayant survécu à une tumeur cérébrale de la fosse postérieure

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École de Réadaptation, Faculté de Médecine
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Physiothérapeute
Hôpital de Montréal pour Enfants
Centre universitaire de santé McGill

Directeurs de recherche: Dr Dany Gagnon, pht, PhD et Dre Isabelle Gagnon, pht, PhD

Introduction:

Suite au progrès du traitement des tumeurs cérébrales pédiatriques, les enfants et les adolescents survivent plus longtemps suite à l'annonce de ce diagnostic (1). C'est pourquoi l'on s'intéresse de plus en plus au devenir à long terme de cette population. Plusieurs domaines tels que la cognition, les besoins médicaux, la performance académique et dans une moindre mesure, la performance motrice ont été explorés chez les enfants et adolescents survivants suite à une tumeur cérébrale (2, 3). Dans la pratique clinique en physiothérapie, nous observons que le maintien de l'équilibre en position debout représente un défi pour plusieurs de ces enfants et adolescents, sans pouvoir s'appuyer sur des données empiriques claires. Malgré un intérêt grandissant pour la question du devenir des survivants de tumeur cérébrale pédiatrique, l'évaluation de leur équilibre est souvent négligée.

Les objectifs de nos travaux étaient de 1) examiner les écrits portant sur l'équilibre chez les survivants de tumeur cérébrale pédiatrique; 2) comparer l'équilibre debout et la qualité de vie entre les survivants et un groupe d'enfants témoins; et 3) examiner l'association entre l'équilibre debout et la qualité de vie chez les survivants.

Méthodologie:

Pour répondre au premier objectif, une analyse structurée des écrits a été complétée. Les mots clés: "*neoplasm*", "*psychomotor control*" et "*postural balance*", ont été combinés pour une recherche dans cinq bases de données différentes (Medline, CINAHL, PschyINFO, EMBASE et PEDro). Les titres et abrégés des articles ont été examinés pour leur pertinence selon des critères prédéterminés. Les articles inclus dans l'analyse ont été classés selon les critères du *Oxford Centre for Evidence-Based Medicine Levels of Evidence* (4).

Une étude transversale comparant l'équilibre debout et la qualité de vie entre un groupe de survivants de tumeur cérébrale pédiatrique de la fosse postérieure et un groupe d'enfants et adolescents sains a ensuite été réalisée avec l'approbation du Comité d'éthique de la recherche de l'Hôpital de Montréal pour Enfants du Centre Universitaire de Santé McGill. *Participants:* Un groupe expérimental de 6 enfants ou adolescents ayant survécu à une tumeur cérébrale ont été recrutés à la Clinique de neuro-oncologie de l'Hôpital de Montréal pour Enfants. Les participants, âgés de 5 à 18 ans, ayant complété avec succès, depuis au moins 6 mois, un traitement neurochirurgical, radio-oncologique ou de chimiothérapie pour une tumeur cérébrale de la fosse postérieure et ayant la capacité à se maintenir debout sans aide pendant une minute étaient éligible pour cette étude. Une groupe contrôle a été apparié selon l'âge et le genre aux enfants et adolescents survivants. Le consentement et l'assentiment des participants et de leurs parents ont été obtenus avant le début de l'étude. *Collecte de données:* Lors de l'évaluation, le poids et la taille des enfants même que leurs amplitudes articulaires, la force musculaire des membres inférieurs ainsi que la sensibilité des pieds furent mesurés. L'évaluation de l'équilibre fut effectuée à l'aide du *Bruininks-Oseretsky Test of Motor Proficiency-2nd edition* (BOT-2) et du *Pediatric Balance Scale* (PBS) (5, 6). Finalement, tous les enfants et leurs parents ont rempli le *Pediatric Quality of Life Inventory* (PedsQL4.0) (7). *Analyses statistiques :* Pour comparer les résultats de l'équilibre debout ainsi que la qualité de vie entre les deux groupes, mesurés à partir des outils cliniques, des tests

U de Mann-Whitney ont été complétés. L'association entre les différentes mesures d'équilibre et celles de la qualité de vie a été vérifiée avec des coefficients de corrélation de Spearman.

Résultats:

Notre recension des écrits a démontré que les survivants d'une tumeur cérébrale pédiatrique présentent des troubles de l'équilibre. Cependant, les limites méthodologiques des études nous empêchent de conclure de manière définitive sur l'impact de ces difficultés. Certaines limites des écrits disponibles sont: l'insuffisance de recherches axées dans le cadre clinique, l'absence d'évaluations de l'équilibre dynamique et finalement, le manque d'études visant à expliquer comment les troubles d'équilibre affectent la vie quotidienne des survivants. (Pour davantage des détails, veuillez consulter l'article publié dans le *European Journal of Cancer Care* (8)).

Le projet de recherche clinique a démontré plusieurs résultats intéressants. Six survivants de tumeurs cérébrales de la fosse postérieure (tous des garçons et diagnostiqués entre 4 et 11 ans) ont été recrutés pour participer dans cette étude. En ce qui concerne la performance lors des mesures cliniques de l'équilibre, les scores au PBS étaient similaires pour les deux groupes et ont démontré un effet plafond important. Par contre, la sous-échelle d'équilibre du BOT-2 a révélé une différence significative dans les capacités d'équilibre debout entre les deux groupes ($p=0.004$). Les survivants présentaient des capacités d'équilibre sous la moyenne comparativement au groupe de contrôle qui se retrouve dans la moyenne selon les normes proposées par ce test.

La qualité de vie, mesurée par le PedsQL4.0, se situait parmi les valeurs normatives pour les deux groupes d'enfants et adolescents (7). De plus, les participants et leurs parents ont coté la qualité de vie de manière similaire. Pour explorer l'association entre les capacités d'équilibre et la qualité de vie, le BOT-2 a été utilisé car le PBS a démontré un effet plafond. Une bonne association ($\rho= 0.715$) a été quantifiée entre les scores dans le domaine physique du PedsQL4.0 et le BOT-2.

Retombées cliniques:

Les résultats de cette étude démontrent que les enfants et adolescents ayant survécu à une tumeur cérébrale de la fosse postérieure présentent des troubles d'équilibre persistants. Cela suggère qu'un suivi à long terme en physiothérapie de cette population pourrait être nécessaire. Il pourrait par exemple être recommandé que tous les survivants de tumeurs cérébrales pédiatriques subissent un dépistage de leurs habilites équilibre une fois leur traitement complété. Selon les résultats de la présente étude, la sous-échelle d'équilibre de BOT-2 pourrait être un outil sensible à utiliser. Même si les qualités psychométriques n'ont pas été étudiées avec cette population, le BOT-2 est un outil facile à administrer avec des valeurs normatives. Si ce dépistage révèle des difficultés au niveau de l'équilibre pour un patient, une évaluation clinique ou en laboratoire plus complète et un plan d'intervention individualisé seraient indiqués.

Bien que les enfants et adolescents ayant survécu à une tumeur cérébrale de la fosse postérieure rapportent une qualité de vie comparable aux normes, les résultats de la présente étude suggèrent que de meilleures capacités d'équilibre debout pourraient être reliées à de plus hauts scores du domaine physique de la PedsQL4.0. Ceci suggère que l'amélioration de l'équilibre debout des survivants serait bénéfique à leur qualité de vie. Il serait probablement utile de développer des programmes locaux et interdisciplinaires qui visent à suivre tous les survivants de tumeurs cérébrales pédiatriques afin de répondre à leurs besoins en réadaptation à plus long terme.

Limites:

La limite la plus évidente de cette étude est le petit nombre de sujets recrutés. Plusieurs facteurs entrent en ligne de compte, mais de toute façon, des résultats significatifs ont été retrouvés. D'autres limites sont que l'évaluateur n'était pas aveugle à quel groupe appartenaient les participants et l'ébauche de cette 'étude transversale ne permettait pas d'étudier l'évolution des capacités d'équilibre des survivants dans le temps.

Conclusions:

Avec les améliorations dans la survie des enfants et adolescents diagnostiqués avec une tumeur cérébrale, le devenir à long terme de cette population est un domaine émergent dans la recherche en réadaptation. Il existe peu d'écrits dans le domaine de la physiothérapie pour ces survivants. La présente étude confirme que les survivants des tumeurs cérébrales de la fosse postérieure possèdent des troubles d'équilibre après que leurs traitements soient terminés. Malgré cela, leur qualité de vie demeure normale lorsque comparée aux normes et les capacités d'équilibre semblent reliés à ces scores. Dans le futur, il serait essentiel d'entreprendre des études longitudinales et multicentriques pour avoir un portrait plus complet des effets secondaires des traitements médicaux pour les enfants et adolescents ayant survécu à une tumeur cérébrale. L'ajout des mesure obtenues à l'aide d'une plateforme de force dans un contexte clinique (ex: Balance Master, Biodex, console WiiFit, etc.) mériterait également d'être considéré.

Remerciements:

Je souhaite remercier l'Ordre Professionnel de la Physiothérapie du Québec, ainsi que le Faculté de Médecine de L'Université de Montréal pour leur soutien financier en forme de bourse.

Références:

1. Canadian Cancer Society. Canadian Cancer Statistics 2011. Toronto, ON: Canadian Cancer Society's Steering Committee on Cancer Statistics., 2011.

2. Armstrong GT. Long-term survivors of childhood central nervous system malignancies: the experience of the Childhood Cancer Survivor Study. European Journal of Paediatric Neurology. 2010;14(4):298-303. PubMed PMID: 20110182. Pubmed Central PMCID: 2885448. eng.

3. Packer RJ, Gurney JG, Punyko JA, Donaldson SS, Inskip PD, Stovall M, et al. Long-Term Neurologic and Neurosensory Sequelae in Adult Survivors of a Childhood Brain Tumor: Childhood Cancer Survivor Study. Journal of Clinical Oncology. 2003;21(17):3255-61.

4. Howick J, Chalmers I, Glasziou P, Greenhalgh T, Heneghan C, Liberati A, et al. The Oxford 2011 Levels of Evidence: Oxford Center for Evidence-Based Medicine; 2011 [cited 2011 August 15th, 2011]. Available from: http://www.cebm.net/index.aspx?o=5653.

5. Bruininks RH, Bruininks BD. BOT2: Bruininks-Oseretsky Test of Motor Proficiency : Manual. Minneapolis, Minn: Pearson Assessments; 2005.

6. Franjoine MR, Gunther JS, Taylor MJ. Pediatric balance scale: a modified version of the berg balance scale for the school-age child with mild to moderate motor impairment. Pediatric Physical Therapy. 2003;15(2):114-28.

7. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL™* 4.0 as a Pediatric Population Health Measure: Feasibility, Reliability, and Validity. Ambulatory Pediatrics. 2003;3(6):329-41.

8. Turner M, Gagnon D, Lagace M, Gagnon I. Effect of treatment for paediatric cancers on balance: what do we know? A review of the evidence. European Journal of Cancer Care. 2013;22(1):3-11.

APPENDIX E:

POSTER PRESENTED AT THE CANADIAN PHYSIOTHERAPY ASSOCIATION CONGRESS - MAY 2013, MONTREAL

STANDING BALANCE AND QUALITY OF LIFE IN SURVIVORS OF CHILDHOOD POSTERIOR FOSSA BRAIN TUMOURS: AN EXPLORATORY STUDY

Melissa Turner, B.Sc.PT[1,2], Dany Gagnon, PT PhD[1,3] & Isabelle Gagnon, PT PhD[2,4]

1. École de Réadaptation, Faculté de Medecine, Université de Montréal, 2. Physiotherapy Department, Montreal Children's Hospital, McGill University Health Centre, 3. Centre de recherche interdisciplinaire en réadaptation du Grand Montréal, 4. School of Physical and Occupational Therapy, Faculty of Medicine, McGill University

PURPOSE:

- To compare standing balance and health-related quality of life (HRQOL) between survivors of pediatric posterior fossa brain tumours and healthy controls
- To explore any associations between balance abilities and HRQOL

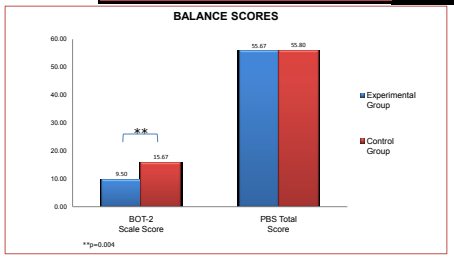
RELEVANCE:

- The most frequent location of childhood brain tumours is the posterior fossa, a region that includes the cerebellum[1]
- Few studies assess standing balance in a clinically-oriented way in this population[2]
- The available literature demonstrates poorer balance abilities in this group[2]
- Standing balance difficulties may interfere with motor functions, in turn affecting health-related quality of life (HRQOL)

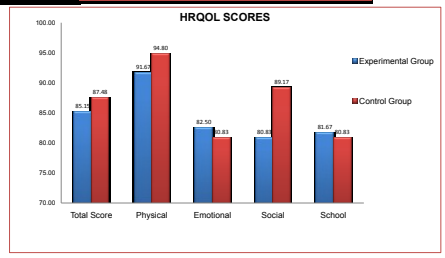
METHODS:

- PARTICIPANTS: 6 survivors of pediatric posterior fossa brain tumours (all male, aged 7-18 years old) were recruited and 6 age- and gender-matched controls
- OUTCOME MEASURES:
  - Balance: balance subtest of the Bruininks-Oseretsky Test of Motor Proficiency (BOT-2) and the Pediatric Balance Scale (PBS)
  - HRQOL: Pediatric Quality of Life Inventory Generic Core Scales (PedsQL4.0)
- STATISTICAL ANALYSIS: Mann Whitney U tests to compare results between groups and Spearman's rank correlation coefficient to determine association between balance abilities and HRQOL

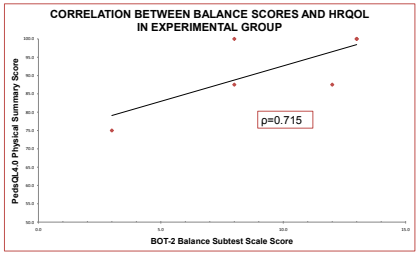
RESULTS:



- PBS demonstrates a ceiling effect
- BOT-2 balance subtest scores significantly lower in survivors
- Based on normative values of the BOT-2:
  - The experimental groups' balance abilities fall into the below average range
  - The control groups' balance abilities are in the average category



- HRQOL similar in both groups (self-report scores)
- HRQOL scores fall into the normative range for all participants in all domains
- No significant differences found likely owing to the small sample size



- Scores on BOT-2 were used as PBS demonstrated a ceiling effect
- Correlated with the physical domain summary score of the PedsQL4.0

CONCLUSIONS:

- Survivors of posterior fossa brain tumours demonstrate significant balance deficits after ending treatment but report relatively normal HRQOL
- Better balance abilities may contribute to higher HRQOL in this group
- The balance subtest of the BOT-2 may be the most appropriate tool to use to screen for balance difficulties in this population
- This research study may be a step towards recognizing the persistent physical difficulties faced by survivors and likely supports the needs for continued physiotherapy follow-up in this population

ACKNOWLEDGMENTS:

This project was supported by bursaries from the Ordre Professionnel de la Physiothérapie du Québec (OPPQ) and the Faculté de Medecine de l'Université de Montréal

REFERENCES:

1. Central Brain Tumor Registry of the United States. CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2004-2008, March 20, 2012. Available from www.cbtrus.org
2. Turner, M et al. Effect of treatment for paediatric cancers on balance: What do we know? A review of the evidence. *European Journal of Cancer Care*. 2013; 22(1):3-11.