The Impact of Intrathecal Baclofen on Growth Among Children with Spasticity Ages 2-20 Years

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THE IMPACT OF INTRATHECAL BACLOFEN ON GROWTH AMONG CHILDREN WITH SPASTICITY AGES 2-20 YEARS

By
Amy Lynn Malmsberry Kaye

A DISSERTATION

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THE IMPACT OF INTRATHECAL BACLOFEN ON GROWTH AMONG CHILDREN
WITH SPASTICITY AGES 2-20 YEARS

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Spasticity is present in 80% of children experiencing Cerebral Palsy (CP) and 50% of those having sustained a Traumatic Brain Injury (TBI) (Tilton, 2015; O'Shea, 2008). Growth impairment among children with motor disabilities secondary to a Central Nervous System (CNS) insult is common and interferes with mobility, functioning, comfort, and Quality of Life (QOL) (Vles, 2011; Mullarkey, 2009; Krick, Murphy-Miller, Zeger, & Wright, 1996). Spasticity may range from mild to severe involving any body part (Mullarkey, 2009). There are a broad range of treatment modalities for managing spasticity impacting the child, parent or caregiver, and a multidisciplinary healthcare team (Brashear & Lambeth, 2009; Duff & Morton, 2007).

Historically, nutritional and hormonal abnormalities have been the key contributing factors for growth retardation in children exhibiting CP (Kuperminc & Stevenson, 2008; Thommessen, M. et al., 1991). Pediatric growth assessment is a standard of care for all children who seek medical care (Krick, Murphy-Miller, Zeger, & Wright, 1996). Monitoring growth parameters in children over time, while ensuring obtainment of expected standards set by the Centers for Disease Control (CDC) and the National Centers for Health Statistics, is imperative for managing deficiencies (CDC, 2000; Pryor & Thelander, 1967). Nutritional and non-nutritional treatment modalities are most effective for reducing the consequences of spasticity and growth impairment upon
discovery of abnormalities (Kuperminc, et al., 2013). Clinical observations have concluded a probable association of heightened caloric expenditure in association with spasticity (Andrew & Sullivan, 2010; Hemingway, McGrogan & Freeman, 2001). Oral antispasmodic medications and physiotherapy are the first line of treatment when managing spasticity. The use of Intrathecal Baclofen (ITB) therapy is a safe and effective method for controlling generalized spasticity (Gilmartin, et al., 2000; Penn, 1992).

The observed impact that ITB has on reducing spasticity has been demonstrated through numerous clinical trials; however, the association between the reduction of spasticity and subsequent growth lacks investigation (Awaad, et al., 2002; Shilt & Cabrera, 2005). Through the retrospective observation of growth measurements of height, weight, and Body Mass Index (BMI) over time, changes in growth of children receiving ITB was studied. The testing of the relation between spasticity management, growth, and ITB therapy through quantitative analysis was compromised due to lack of data. Case studies were additionally performed to observe the growth over time in six subjects who had the greatest documentation of growth measurements. Among the case studies, two males presented with normal growth compared to four females who had growth below that compared to their peers. All case studies demonstrated controlled spasticity with the implementation of ITB and reduced Ashworth spasticity scores.

Despite the lack of data, a linear regression analysis was conducted for random slopes and intercepts based upon z-scores. The results demonstrated a non-significant increase in height, a non-significant decrease in weight, and a significant decrease in BMI, among the sample group. These findings warrant the conduction of a study design
allowing for appropriate standards of measurements to be performed at specific times for children experiencing spasticity receiving ITB and those who are not receiving ITB. The literature review supports improvements in growth secondary to ITB administration for the reduction of spasticity and with the implementation of gastrostomy tube feedings (Henderson, et al., 2007). The implementation of standard of care for all children, specifically those with CNS disorders, is crucial to the early identification of growth retardation (Pin, McCartney, Lewis & Waugh, 2011).
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Chapter 1

Introduction

The etiology of growth retardation in children with Central Nervous System (CNS) disorders has been associated with both nutritional insufficiencies as well as hormonal abnormalities. Sufficient growth, development, and physiological function necessary for sustaining life is supported by adequate nutrition and maintenance of physiological integrity (Andrew & Sullivan, 2010). Insults to the CNS interfere with the normal growth process. The progression of growth may be interrupted or impacted by motor dysfunction, such as spasticity, commonly occurring in the presence of CNS disorders (Vles, 2011; Mullarkey, 2009). Research on the role of spasticity as a contributing factor on the impairment of growth is lacking. Therapeutic approaches to reduce spasticity may have the potential to ameliorate impairment of growth. The objective of this dissertation project is to determine if growth may be enhanced with the reduction of spasticity through the administration of Intrathecal Baclofen (ITB) therapy. Although ITB has been shown to be effective for the management of spasticity and concomitant mobility issues, it has not been determined if the effect of ITB on reducing spasticity exhibits an additional benefit of improving growth capability.

Spasticity is a motor disorder characterized by a velocity dependent increased resistance to passive movement of a muscle when stretched in the motion of extension (Lance, 1980). It is commonly observed in patients with damage to their upper motor neuron system (Pin, McCartney, Lewis, & Waugh, 2011; Lance, 1980). Spasticity of either cerebral or spinal origin is a symptom of neurological conditions having caused injury to the CNS (brain and spinal cord) where muscle function is regulated (Vles, 2011;
Spasticity of cerebral origin is associated with Cerebral Palsy (CP), Traumatic Brain Injury (TBI), anoxic brain damage, adrenaoleukodystrophy, phynylketonuria, and Cerebral Vascular Accidents (CVA; aka stroke). Spasticity of spinal origin involves any injury to the spinal cord as well as the autoimmune process of degenerating myelination of the spinal nerves associated with multiple sclerosis. Distribution of spasticity may be local or generalized, affecting any muscle group, with severity ranging from mild to severe (Mullarkey, 2009).

Spasticity, secondary to certain neurological conditions, is a symptom that affects a substantial number of children (Mullarkey, 2009). The number of children in the United States suffering from spasticity can be approximated by examining the prevalence of motor disorders that are most often associated with spasticity, i.e. CP and TBI (Zorowitz, et al., 2008). The prevalence of CP ranges from 1 to 4 of every 1,000 children or live births (Maenner, et al., 2012). Spasticity presents as the predominant symptom in approximately 80% of the pediatric CP population (Tilton, 2015). In 2012, 473,947 children between the ages of 0 and 14 years experienced a TBI. Of all the incidents of TBI in children, approximately 50% developed motor disorders in association with the development of spasticity (CDC, 2013; Zafonte & Srikrishnana, 2011; Greenwald & Rigg, 2009; Michaud, et al., 2007).

Children included in this retrospective chart review exhibited either paraparesis (paralysis effecting the lower limbs), spastic hemiplegia (increased tone in half of the body) or spastic quadriplegia (increased muscle tone in all extremities) (Taber’s Cyclopedic Medical Dictionary, 2014). A review of scientific literature involving growth in children with CP found that 35-40% of these children exhibit hemiplegia (Zonta et al., 2009).
the presence of hemiplegia, muscle mass has been observed to be of greater size on the side of the body unaffected by spasticity than that of the affected side with increasing tone over time considered a contributing factor (Zonta et al., 2009).

The etiology of CP is secondary to perinatal, prenatal, or postnatal complications (Tilton, 2015; Maenner et al., 2012; Pin, McCartney, Lewis & Waugh, 2011; Zonta et al., 2009; Centers for Disease Control (CDC), 2002). The development of an upper motor neuron lesion contributes to the development of a non-progressive encephalopathy with subsequent neurodevelopmental disabilities (Tilton, 2015; Samson-Fang & Bell, 2013; Maenner et al., 2012; Pin, McCartney, Lewis & Waugh, 2011; Zonta et al., 2009; CDC, 2002). Observations of large numbers of children over time support the scientific evidence that children with spastic CP grow more slowly. Unresolved contributing factors result in generally smaller body habitus with less body fat impacting total weight and muscle mass (Kuperminc et al., 2013; Samson-Fang & Bell, 2013; Zonta et al., 2009; Kuperminc & Stevenson, 2008; Henderson et al., 2007; Himmelmann et al., 2007).

Another leading cause of spasticity in children is TBI. Near-drowning, Shaken Baby Syndrome, and blunt head trauma are the associated causes of TBI in children (Richmond & Rogul, 2014). As observed in CP, CNS damage following a TBI results in the development of spasticity with varying degrees of disability and onset, impacting recovery and rehabilitation (Pin, McCartney, Lewis & Waugh, 2011; Greenwald & Rigg, 2009). Because of the prevalence of spasticity and consequences of growth impairment in individuals with CP and TBI, early intervention is the best possible treatment approach for both nutritional and non-nutritional related factors (Krick, Murphy-Miller, Zeger & Wright, 1996).
There are pharmacological, rehabilitative, and both orthopedic and neurosurgical interventions presently available to prevent movement and postural abnormalities observed in children with spasticity. The primary objective of treatment modalities is the reduction of muscle tone with improved range of motion, mobility, and comfort (Motta, Antonello, & Stignani, 2011; Pellegrino, 2007). One such pharmacological intervention used to reduce spasticity in children is ITB (Brashear & Lambeth, 2009). Through rigorous clinical research, ITB has been shown to be safe and effective for the treatment of spasticity in both children and adults with the diagnosis of CP or TBI (Guillame, et al., 2005; Gooch, et al., 2004; Awaad, et al., 2002; Bjornson, et al. 2001; Scheinberg, et al., 2001; Gerszten, et al., 1998, Gianino, et al., 1998).

**Spasticity and Growth**

Children with spasticity are at greater risk for experiencing growth deficiencies (Zonta, et al., 2009; Kuperminc & Stevenson, 2008; Henderson, et al., 2005). The timing of the brain insult, the type of movement disorder, and the severity of the motor dysfunction as it impacts the child’s ability to attain nutritional needs has the propensity to impact growth and development (Zonta, 2009). Further inquiries surrounding the causes of reduced linear growth and low Body Mass Index (BMI) among children with CP support both nutritional and non-nutritional contributing factors (Hamza, Ismail, & Hamed, 2011; Andrew & Sullivan, 2010; Stevenson, Roberts & Vogtle, 1995). Monitoring the potential impact of spasticity on growth and the status of the child’s overall well-being is key to the provision of quality care and a thorough health assessment.

Notably, spasticity has the capacity to impact oral-motor function and subsequent caloric intake affecting growth due to postural abnormalities necessary for sitting upright...

As nutrition is evaluated, it is necessary to recognize feeding as a social activity with greater risk for deficiency in children with special needs (Samson-Fang & Bell, 2013). While growth and development may be interpreted as a reflection of a parent or caregiver’s ability to nurture or care for a child, the presence of malnutrition in children with spasticity may be worrisome for the caregiver (Samson-Fang & Bell, 2013). One study has shown that despite institutionalization, children with disabilities who have full-time supportive services (such as nursing) grow better in a residential center rather than a private home (Henderson, et al., 2007). The assured delivery of nutrition to individuals with neurological deficits living in residential facilities contributes to improved growth patterns (Henderson, et al., 2007).

The non-nutritional factors associated with spasticity potentially impacting growth include lack of weight bearing activity (due to an inability to stand upright) and excessive caloric expenditure (due to continual muscle contraction) (Kuperminc, et al., 2013; Zonta, et al., 2013; Bell, et al., 2010; Kuperminc & Stevenson, 2008; Henderson, et al., 2007). Individuals experiencing spastic quadriplegia commonly have alterations in the muscle tone of the extremities and torso (Zonta, et al., 2009). Associated motor impairments
interfere with the ability to initiate movement and be physically active while standing upright (Zonta, et al., 2009; Kuperminc & Stevenson, 2008). The more severe spasticity a person presents with, the greater likelihood they will experience contractures and notable growth delay (Zonta, et al., 2009; Krick, Murphy-Miller, Zeger & Wright, 1996).

Scoliosis is common in children with spasticity due to truncal weakness and imbalance, as well as spastic paraspinal muscle tone (Scannell & Yaszay, 2015). The condition results in shorter stature secondary to spinal curvature and poor posture. The more generalized and severe the spasticity and functional limitations are, the more severe the scoliosis progresses (Koop, 2009).

Hormonal abnormalities impacting growth in children without insult to their CNS does occur. The focal and notable growth differences in children with CP and TBI who have not gone through the pubertal phase has prompted studies assessing the role of endocrinopathy upon growth. Despite the known significance of hormonal influences upon growth following TBI as well as growth hormone levels in children with CP, the association between the dynamics of growth and spasticity is lacking in the current literature (Kuperminc & Stevenson, 2008).

**Measurement of Spasticity**

Spasticity is measured through the implementation of an assessment tool known as the Modified Ashworth Scale (MAS) or Ashworth Scale score (Appendix 2). The stretch reflex elicited by individuals with spasticity reflects neuromotor function (Awaad, et al, 2002). Muscle tone is assessed objectively via the application of the standardized scoring system common to physiotherapists and other healthcare providers associated with neurorehabilitation (Awaad, et al., 2002). The Ashworth Scale was first presented in 1964
Presently the MAS score is a clinically accepted tool for measuring muscle tone due to a modification of the original Ashworth Scale in 1987 by Bohannon and Smith (Johnson, 2002). The MAS is commonly used for measuring outcomes following an intervention involving the elicitation of muscle tone. The primary purpose of using a standardized scale such as the MAS is to objectively document the degree of stretch found in specific disease entities associated with spasticity (Damiano, et al., 2002; Johnson, 2002). Severe spasticity is considered a score greater than (3) on the MAS. The description of the specific scores are noted in Appendix 2.

Measurement of Growth

The application of growth references for all children provides clinicians with the ability to make an accurate assessment of the severity of a child’s growth delay in comparison to the average pediatric population to age 20 (Krick, Murphy-Miller, Zeger & Wright 1996). Recorded anthropometric measurements allow for the observation and assessment of the growth parameters of height and weight obtained over time (Pryor & Thelander, 1967). Through statistical modeling of the growth patterns of thousands of children born in the United States, revisions to the 1977 CDC Growth charts resulted in set standards (CDC, 2000). The charts represent racial and ethnic diversity as well as encompassing a combination of breast and formula fed infants born at various gestational ages. These established parameters of normal growth specific for age and gender continue to be used to the present day (CDC, 2000). This research inquiry will utilize the growth charts developed by the National Center for Health Statistics, in conjunction with the CDC (2000), to plot anthropometric measurements obtained during the retrospective chart review.
Theoretical Framework for the Study

Based upon theory and concept synthesis, application of the Donabedian Model to the proposed research problem statement is useful in examining the effect of ITB therapy for the treatment of spasticity in children as it relates to their growth patterns. The issue of quality of care relative to the administration and management of ITB therapy in children with spasticity requires consistent, close, and collaborative monitoring by an interdisciplinary team of healthcare providers.

Structure, process, and outcomes are three defined categories comprising the framework of Donabedian’s Model (Donabedian, 1997) (Figure 1). The application of Donabedian’s Model aids in establishing the necessary components of a healthcare entity associated with the delivery of quality care. A review of the variables associated with a healthcare entity will reflect patient outcomes and the subsequent quality of care being provided within the healthcare institution.

*Structure* pertains to the context where the care occurs (Smitz-Naranjo & Kaimal, 2011). The primary component of *structure* allows for the assessment of the delivery of care including the location, staff, funding, and necessary equipment to provide care (Smitz-Naranjo & Kaimal, 2011). Having *structure* in place at any physical location involves specialty staff who are experienced in neurorehabilitation and capable of providing care to children with motor disorders. Financial reimbursement established through entities such as governmental programs, specifically Medicaid, or commercial insurance policies are needed to provide support and payment for the care of children. Obtainment of height, weight, and vital signs is common practice in pediatric medical offices. Having a skilled clinician is essential and crucial to the safety of the patient when managing a patient with
an ITB device. Specifically, the ability to implement the necessary MAS score to assess the level of spasticity, followed by subsequent dosing adjustments of the ITB device is imperative.

**Process** is the second concept of the model. Totaling the sum of diagnosis, treatment, preventive care, and patient education, *process* is the assessment of health care provision within the Donabedian Model (Donabedian, 2003). *Process* may be expanded to encompass compliance of patients and families, further enhancing the evaluation of the quality of care being delivered (Donabedian, 2003). The implementation of *process* is ascertained by medical, nursing, and physiotherapy staff allowing for each discipline to contribute to the sum of the diagnoses and relative treatment plans. The common goal involves the prevention of morbidities commonly observed in children with spasticity, specifically as they relate to growth impairment. Education to the patient and family may be provided by any member of a multidisciplinary team, to include nutritional and social services, encompassing all specialty recommendations involved in the care process. For the measurement of quality of care, appropriate documentation of the patient encounter including the history, physical exam, height, weight, vital signs, MAS score assessment, functional goals, and the attainment of such goals would be most beneficial and supportive of the *process* component. Direct observations, review of medical records, and interviews with healthcare team members are all modes of assessing the quality of care being delivered (Donabedian, 2003).

**Outcomes** are the final dimension of the Donabedian Model. Encompassing the ultimate indicator of the quality of care being provided, outcomes assess the effects of healthcare on patients or populations (Smitz-Naranjo & Kaimal, 2011). Relative to the
research objectives of this project, the assessment of patient outcomes includes the reduction of spasticity with subsequent growth measurement with the prospect of impacting mobility and functioning. Future health outcomes may benefit from the use of a patient/family-centered questionnaire useful in determining the impact of ITB on real-life and the reduction of spasticity as it relates to patient satisfaction, QOL, and performance of Activities of Daily Living (ADL).

The following observations make the application of Donabedian’s Model significant and relevant when assessing the provision of quality care. Reduction in spasticity, as measured by trained medical professionals using the MAS tool, has the potential to mediate changes in growth for those children who received ITB. Intrathecal baclofen use in children with spasticity has the potential to improve growth by alleviating muscle contractions interfering with normal gravitational bone growth. Children with CP and TBI commonly experience spasticity and have abnormal growth patterns.

**Purpose of Study**

The purpose of this study is to compare the direct effect of ITB on growth in children (ages 2-20) with spasticity to the growth of children of same ages, with spasticity, who are not receiving ITB. The subjects of interest will be further compared to children without spasticity, through the plotting of the obtained measurements on the CDC growth charts specific for age and gender (Figures 3-12). Growth as measured by height (assessed in centimeters), weight (measured in kilograms), and BMI (percentile) will be determined. A secondary aim is to examine whether changes in spasticity, as measured with the MAS, mediates changes in growth for those children who received ITB.
Research Hypotheses

The following research hypotheses will be tested in this study:

1) It is postulated that children (ages 2-20) who receive ITB for the treatment of spasticity will have improved growth, when compared to children not receiving ITB, as evidenced by increasing measurements of height, weight, and body mass index in comparison to expected parameters established by the CDC Growth Charts (2000).

2) Reduced spasticity partially mediates the effect of ITB on growth.

Assumptions

Based upon clinical research findings for ITB, the assumptions include:

1. Children with ITB pumps will have less spasticity. This notion is supported by multiple research findings, whereby thousands of individuals experienced statistically significant reductions in their MAS scores documented during the screening dose trial and with therapeutic use (Koman, Smith, Kolaski & Goodman, 2005; Gooch, et al., 2004; Scheinberg, et al., 2001). Furthermore, it is imperative to recognize this assumption to determine that growth will improve with the reduction of spasticity.

2. The children in this study receiving ITB will demonstrate growth changes through an assessment of height, weight, and BMI (Bell, et al., 2010; Day, et al. 2007).

3. Participants exhibiting spasticity are generally medically complex demonstrating impairments such as seizure disorders, mental retardation, gastric reflux, osteoporosis, and malnutrition (Henderson, et al., 2007).
4. Children in this comparative analysis will have similar types of spasticity.

To be a candidate for ITB therapy the subject’s spasticity will be generalized, severe, and of cerebral or spinal origin (Medtronic, 2017; Hoving, et al., 2009).

**Definition of Terms**

The definitions for the study variables are as follows:

**Spasticity**

*Definition:* Spasticity is the muscular resistance to passive range of motion observed or felt by the examiner as a limb is passed through the arc of motion. In patients with CP flexion of the arm and extension of the leg is common when sitting. Muscle overactivity, known as hypertonic tone, results in contractures or shortening of muscles when left untreated over time (Tilton, 2015). Weakness may subsequently occur impacting fine motor dexterity (Tilton, 2015). The assessment of spasticity is measured through application of findings to the MAS score (Awaad, 2002; Daminao, et al., 2002) (Appendix 2).

**Human Growth Assessment**

*Definition:* Human growth assessment is determined by collecting anthropometric measures which are comparative measures of the body, in this case, the height is obtained by a stadiometer or flexible tape measure. Weight may be obtained with the use of a standardized scale, ensuring accommodations for children in wheelchairs who are unable to stand upright. The calculation of the body mass index of humans is calculated with the use of the standardized formula requiring the numerical representation of both height and weight measurements.
**Cerebral Palsy**

*Definition:* Cerebral Palsy is a permanent disorder involving brain insult that may or may not be associated with perinatal complications, occurring before two years of age.

**Intrathecal Baclofen**

*Definition:* Intrathecal baclofen is a gamma aminobutyric acid (GABA) agonist which binds with primarily GABA-B receptors within the superficial layer of the dorsal aspect of the spinal cord, inhibiting monosynaptic extensor and polysynaptic flexor reflexes (Davidoff, 1985). Baclofen is delivered into the intrathecal space in measurements of microgram per hour, as determined by the pharmaceutical analysis of the solution per milliliter. This medication, when used in the form of tablets or intrathecal solution, is used for the primary purpose of managing spasticity by interfering with muscle contractions. The secondary benefits include improving ease of care (performance of ADL) and motor function in individuals displaying an upper motor neuron complex (Motta, Antonello, & Stignani, 2011).

**Conclusion**

The significance of growth impairments among individuals with spasticity are profound and complex. Secondary to multifactorial etiologies, the development of impairments that interfere with ambulation, associated motor functioning, performance of ADL, and possibly cognitive functioning all have the potential to impact the provision of self-care (Henderson, et al., 2007). There are many variables which may disrupt normal growth patterns, consisting of both nutritional and non-nutritional factors. Close monitoring of patient growth by healthcare providers is essential for prompt identification of delays, determination of etiology, and implementation of subsequent treatment.
modalities. The prevention of long term sequelae seen with both spasticity and growth impairments have the potential to impact physiological and psychological functioning, access to healthcare resources, motor function, survival, and overall well-being.

The effectiveness of ITB therapy through the identification of positive outcomes reported in scientific publications note generalized improvements in quality of life and functioning when administered. This research study will examine if there is a significant impact on the growth of children with spasticity receiving ITB therapy. Although there are noted improvements in the functioning, comfort, and ease of care associated with ITB therapy, there are few studies investigating growth with the reduction of spasticity. The review of literature will be provided in Chapter 2 with emphasis on physical growth, nutrition, hormones, scoliosis, psychosocial factors, and ITB administration.
Chapter 2
Review of Literature

Review of the scientific literature surrounding the issue of growth as it relates to spasticity observed in children between the ages of 2 to 20 will be presented in this chapter. Human growth assessment and the natural progression of growth patterns may be impacted by nutritional consumption, hormones, presence of scoliosis, or state of psychosocial being. A wide array of treatment modalities for spasticity management, ranging from conservative to invasive are available. Encompassing both pharmacological and non-pharmacological approaches, these interventions will be explored and described to identify secondary growth implications.

Spasticity

The impact of spasticity on quality of life and general health is evident through the investigation of lived experiences. When movement disorders are present, it is imperative to determine the specific type of motor disorder to ensure the most appropriate treatment modalities are implemented (Motta, Antonello, & Stignani, 2011). Optimization in this sense aids in improving the individual’s function as growth occurs over time (Gersten, et al., 1998). It is not uncommon for individuals with CNS damage to exhibit a combination of both spasticity and dystonia (O'Shea, 2008). Spasticity is the predominant symptom in the majority (approximately 80-90%) of children with CP and TBI (approximately 50%), resulting in motor dysfunction (Tilton, 2015; O'Shea, 2008).

The abstract definition of spasticity, as presented by Lance, is stated as: “a motor disorder characterized by a velocity dependent increase in tonic stretch reflexes (muscle
tone) with exaggerated tendon jerks, resulting from the hyper-excitability of stretch reflex, as one component of the upper motor neuron syndrome” (Lance, 1980). To fully appreciate the descriptive notion of spasticity, clinical observation of the condition and recognition of the relative cause are necessary. The elicitation and measurement of the various degrees of spasticity are found through several derived tools, the most notable for this inquiry is the application of the MAS scoring system (Mullarkey, 2009).

While spasticity may be of cerebral or spinal origin, there are distinct classifications associated with varying presentations of movement abnormalities. The degree of the severity of CP and resulting functionality is subsequently founded upon the level of motor impairment (O'Shea, 2008). The nature of the movement disorder may be classified as spasticity, dystonia, athetosis, chorea, or ataxia (O'Shea, 2008). The associated anatomical distribution of a motor disorder may be described as spastic diplegia, spastic hemiplegia, spastic quadriplegia, or quadriplegia (O'Shea, 2008; Korman & Smith, 2005).

The presence of an upper motor neuron lesion, observed with both CP and TBI, disrupts the pyramidal and corticospinal tract of the CNS, impacting voluntary movement (Zorowitz, et al., 2008). Rearrangements of movement may occur in variable amounts of time resulting in abnormal muscle contractions and reflex responses reflective of the actions of spasticity in conjunction with shortening of muscle fibers (Zorowitz, et al., 2008). The action of muscle contractions requires appropriate input from the CNS to ensure coordinated, controlled activity (Koman & Smith, 2005). The contractile and non-contractile properties of muscles are impacted by neurological, mechanical, and biological factors (Barrett & Barber, 2013). Increased muscle tone, characteristic of spasticity and CNS pathology of the brain (cerebral) and spinal cord, often results in an antagonist and
agonist muscle group synchronization (Barrett & Barber, 2013). When muscles contract simultaneously against one another, the outcome is that of stiffness or spasticity (Escolar, Tosi, Rocha and Kennedy, 2007; Korman & Smith, 2005). Although spasticity is the focus of this inquiry, it is imperative to recognize dystonia is associated with involuntary, sustained, muscle contractions, resulting in abnormal posturing secondary to twisting, repetitive motions (Tilton, 2015; Motta, Antonello, & Stignani, 2011). Muscle tone and strength, secondary to damage of the CNS, may be excessive (hypertonia) or deficient (hypotonia) (Barrett & Barber, 2013; Escolar, Tosi, Rocha, & Kennedy, 2007). The ability to walk, stand, or sit, is dependent upon the degree of involved muscle groups reflecting focal, regional, or generalized tone abnormalities associated with spasticity (Mullarkey, 2009). Spasticity may occur with rest or movement; spasticity may accompany dystonia, resulting in the descriptive term ‘spastic dystonia’ (Motta, Antonello, & Stignani, 2011).

Cerebral Palsy

Cerebral palsy is the most common physical disability among children with a prevalence ranging from 1.5 to 4 in 1000 live births (CDC, 2012; Bell, et al., 2010; Havong, et al., 2009; Shilt, 2008). Currently, boys with CP outnumber girls with CP by a factor of 1.2:1 (CDC, 2012). Fifty percent of individuals with CP are born premature (<32 weeks gestation), comprise neonatal risk factors of low birth weight (<2500 grams), intrauterine growth retardation, intraventricular hemorrhage, or trauma (neonatal or postnatal) (CDC, 2012). The remaining 50% of children who develop CP lack a known history of prenatal, perinatal or postnatal complications attributed to a developmental disability (Maenner, et al., 2012). Spastic quadriplegia involving all 4 extremities is reported in 27% of the total population of individuals with CP; however, more than 90% of all individuals with CP are
affected by spasticity (O’Shea, 2008; Zorowitz, 2008; Krick, Murphy-Miller, Zeger & Wright 1996; Stallings, et al., 1995).

Cerebral palsy comprises a group of neurological conditions affecting motor, cognitive, or sensory function secondary to brain injury or malformation with varying degrees of insult (Shilt, et al., 2008). The non-progressive, irreversible nature of CP often results in the distortion of posture secondary to abnormalities of motor functioning (Maenner, et al., 2012; O’Shea 2008). As spastic quadriplegia is the most common and severe form of CP, more prevalent and profound growth retardation is observed (Topp, et al., 2004; Reilly, et al., 1996). Other manifestations involving growth delay, oral motor dysfunction, comfort/pain, energy levels, performance of ADLs, and cognitive impairments are also observed among individuals with spastic quadriplegia (Walker, Bell, Boyd, & Davis, 2012; Bell et al, 2010; O’Shea, 2008; Zorowitz, et al., 2008; Stallings, Cronk, Zemel, & Charney, 1994). Observed in the presence of both spasticity and dystonia, “disturbances of sensation, cognition, communication, perception, and/or behavior and/or seizure disorders”, impact quality of life and level of autonomy (Tilton, 2015).

For the treatment of spasticity in children with CP, the predominant goal targets reduction of muscle tone, allowing for improved range of motion, function, comfort, and ease of care. Objectives aimed at improving motor function may be accomplished through the implementation of both pharmacological and non-pharmacological treatment modalities (Motta, Antonello, & Stignani, 2011). When spasticity associated with CP is not managed, the formation of joint deformities, contractures, and pain all have the propensity to interfere with the performance (active or passive) of ADLs necessary for feeding, bathing, hygiene, and positioning (Pin, McCartney, Lewis, & Waugh, 2011).
Treatment Modalities for Spasticity Management

Spasticity observed in both CP and TBI are comparable, resulting in mirrored treatment approaches (Pin, McCartney, Lewis & Waugh, 2011). It is imperative to manage spasticity in children exhibiting both cognitive and motor impairments associated with CP to maximize functioning and quality of life (Hadden & von Baeyer, 2002). The treatment of spasticity is individually tailored based on time since injury, severity of the spasticity, number of limbs involved, and preference of the patient and caregiver (Greenwald & Rigg, 2009). The most common conservative treatment interventions involve rehabilitative therapy and the provision of adaptive equipment to maximize functionality (Brashear & Lambeth, 2009; Goldstein, 2001).

The clinical presentation of spasticity manifests as both positive and negative factors. The negative factors impacting health are associated with a reduction in coordination, strength, and endurance (Tilton, 2015; Goldstein, 2001). Positive elements of spasticity impacting a child’s functioning include an increase in muscle tone, increased deep tendon reflexes, persistent primitive reflexes, clonus of the wrist or ankles, extensor plantar responses of the lower extremities, and discordant mass activation of muscles. The application of pharmacological agents and/or orthopedic surgery interventions are commonly used to treat these factors associated with spasticity (Motta, Antonello, & Stinanai, 2011; Goldstein, 2001).

Koman et al. (1994), suggest that physical and occupational therapy, combined with medication and/or surgical intervention, in conjunction with physical rehabilitation, reduces spasticity (Koman, et al., 1994). A key objective in treating individuals with
spasticity, regardless of the type of approach, is to prevent the development of secondary musculoskeletal deformities. These deformities include joint malformations, fixed contractures, and shortening of muscle fibers. These deformities significantly impact motor function, specifically, gait (Tilton, et al., 2017, Tilton, 2015; Barrett & Barber, 2013). Several studies have determined that orthopedic malformations of the pelvis and spine can develop as early as 1.5 years, emphasizing the importance of early intervention (Lai, et al., 2008; Duff & Morton, 2007). Options specific for spasticity management, ranging from least to most invasive, include oral agents, chemodenervation injections, surgical interventions, and ITB therapy. Patients, caregivers, and healthcare providers often collaborate to make the decision to initiate a specific intervention based upon patient needs and goals, most often guided by age or developmental issues (Duff & Morton, 2007).

**Oral Agents** The most conservative approach for the treatment of spasticity consists of the administration of oral medications, such as baclofen, dantrolene sodium, tizanidine, and diazepam. These agents have been used for decades for the treatment of generalized spasticity. Oral baclofen is approved by the U.S. Federal Drug Administration (FDA) for persons 2 years and older, whereas, dantrolene and tizanidine are approved for individuals over 18 years of age (U.S. Department of Health and Human Services, 2017). The molecular size prevents orally administered baclofen from achieving adequate CSF concentrations required to alleviate spasticity (Mullarkey, 2009). The associated side effects of oral agents are generally dose related (Brashear & Lambeth, 2009; Scheinberg, et al., 2001). The action of both oral baclofen and tizanidine demonstrate the ability to reduce muscle tone and provide similar benefits when administered to individuals with generalized spasticity (Mullarkey, 2009). Tizanidine administration has been noted to
provide better outcomes with regards to efficacy, tolerance, fewer side effects, and less muscle weakness when compared to oral baclofen and diazepam in a metanalysis (Mullarkey, 2009).

Approximately 4% of orally administered baclofen molecules cross the blood brain barrier and enter the cerebrospinal fluid (CSF) (Pin, McCartney, Lewis, & Waugh, 2011; Gooch, et al., 2004; Becker, Alberti, & Bauer, 1997). In addition, systemic exposure commonly results in the occurrence of adverse events (Penn & Kroin, 1984). Oral baclofen dosage is limited as side effects become more prevalent with increasing doses (Carera, Kolaski, & Shilt, 2005; Penn & Kroin, 1984). Adverse events include sedation, reduced seizure threshold, liver dysfunction, and various references to hypotonia (weakness, fatigue) (Brashear & Lameth, 2009). Abrupt withdrawal from baclofen, in any form, may lead to life threatening consequences (Brashear & Lambeth, 2009; Mullarkey, 2009).

**Chemodenervation** Chemodenervation involves targeting focal muscle groups with the clinical application of agents such as phenol or botulinumtoxin. The physiological mechanism of action of botulinumtoxin injections result in a significant reduction of muscle contractions. Toxins induce flaccid paralysis of the injected muscles due to partial, selective denervation (Koman, Smith, Kolaski & Goodman, 2005). Clostridium botulinum is found in seven different subtypes, designated as A, B, C, D, E, F, and G; however, only types A and B are approved for use in humans (Aoki, 2001; Schantz, 1992).

Children have historically been treated with botulinum toxin (types A and B) for various diagnostic entities; however, this has been off-label use, without FDA approval within the United States (US). Botulinumtoxin typeA injections are minimally invasive and considered the most notable, effective, and safe chemodenervation treatment option
for children above 2 years of age (Tilton, et al, 2017). Presently, abotulinumtoxinA (Dysport®, Ipsen Biopharmaceuticals, LLC.), approved by the US FDA in 2016, was attained following the review of the results of a double-blind, placebo-controlled, multicenter clinical trial (Delgado, et al., 2016). Presently, Dysport® is the only botulinum toxin approved for treating pediatric lower limb spasticity (Tilton, et al., 2017).

Although abobotulinumtoxinA (Dysport®) injections may be considered costly and the results transient, research has demonstrated effectiveness in reducing spasticity and improving mobility (Delgado, et al., 2016). With a reduction in the MAS score and improved equinus foot deformity, minimal side effects were reported in association with the delivery of the toxin (Tilton, et al., 2017). The effect of botulinum toxin type-A administration is less beneficial to children with severe, generalized spasticity secondary to the dosing limitations (Tilton, et al., 2017; Tilton, et al., 2015; Scheinberg, et al., 2001). The recently approved clinical trial demonstrated efficacy in the reduction of spasticity beyond 16 weeks following administration in 74% of patients, while 20% had relief beyond 28 weeks (Tilton, et al., 2017; Delgado, et al. 2016; Scheinbergh, et al., 2001). The use of botulinum toxin injections for children has a history of safety concerns in relation to the administration of high doses. A boxed warning for the class of botulinum toxin type-A products addresses potential for diffusion with resulting breathing and swallowing issues, as mandated by the US FDA (Delgado, et al, 2016; Goldstein, 2006).

Selective Dorsal Rhizotomy An invasive surgical treatment approach for spasticity treatment is the Selective Dorsal Rhizotomy (SDR) with limited advocacy among healthcare providers. The surgical procedure performed for a SDR involves surgical intervention aiming to reduce spasticity of the lower extremities, and to prevent the
progression of orthopedic deformities, which often occur in children with CP (Gersten, et al., 1998). The SDR procedure involves the division of anterior and posterior spinal rootlets (Koman & Shilt, 2005). The rootlets involved are instrumental in the facilitation of afferent nerve fibers’ sensory inhibitory input; subsequent dissection of the posterior rootlets results in the balancing of a damaged CNS (Koman & Shilt, 2005). Most often, 25-50% of the 50 to 70 rootlets, will be involved in the SDR process (Koman & Shilt, 2005). There are contrasting degrees of improvement shown in various studies on the effectiveness of SDR in children exhibiting spasticity (McLaughlin, et al., 2002; Scheinberg, et al., 2001). The most effective outcomes were observed through a comparative meta-analysis in children between the ages of 3 to 8 years with GMFC levels III-V (McLaughlin, et al., 2002). These children were more able to participate in the complex interventions of combined SDR procedure, recovery and physical therapy participation.

**Intrathecal Baclofen** The implantable, programmable device, manufactured by Medtronic®, includes the Synchromed II infusion device and catheter. The device is useful for the administration of ITB for the management of generalized, severe spasticity (Awaad, et al., 2002; Shilt & Cabrera, 2005). Intrathecal administration of baclofen use has been in practice since the 1980s (Haranhalli, et al., 2011). The use of ITB over time has withstood clinical trials validating long-term safety and efficacy in the treatment of spasticity of cerebral and spinal origin (Gilmartin, et al., 2000; Penn, 1992). Presently, ITB is approved by the US FDA for treatment of spasticity secondary to CP, TBI, Spinal Cord Injury (SCI), Multiple Sclerosis (MS), and CVAs, for both adults and children.
The intrathecal morphine pump, used for pain management through drug administration into the lumbar subarachnoid space, preceded the ITB administration. This provided a model which was duplicated with the administration of ITB for the treatment of spasticity (Penn & Kroin, 1985, 1984). The first instance of ITB administration occurred in 1984, with a bolus dose being administered by Penn and Kroin, to two SCI patients exhibiting both flexor and extensor spasms in the lower extremities (Penn & Kroin, 1985). The bolus administration of ITB into the subarachnoid space preceded the implantation of drug delivery via a programmable device. During the ITB screening test dose, the ITB provided a temporary reduction in the amount of spasticity within one hour, lasting 5 to 8 hours, depending on the dose (25 versus 50mcg) (Penn & Kroin, 1984). Subsequent indwelling ITB pumps were implanted in brain-injured patients exhibiting spasticity, leading to the US FDA approval in 1996, for those individuals with both CP and TBI (Gerszten, et al., 1998).

Adverse effects of ITB occur at a lower incidence when compared to oral baclofen (www.medtronic.com, 2017). The most common adverse events reported with the administration of ITB are hypotonia or weakness, nausea, vomiting, and seizures (Russman, 2009). In the event of side effects associated with ITB dosing, skilled clinicians may reduce the dose being administered to readily reverse undesired effects (Pin, McCartney, Lewis and Waugh, 2011). Occurring to a lesser extent (<5%) are surgical complications, including infections, CSF leaks, hematomas or seromas, and meningitis (Russman, 2009). Rare complications pertaining to the ITB drug delivery system are related to the hardware (pump and catheter) (Russman, 2009). Despite the occurrence of complications, most patients and families associated with the device are pleased with the
overall benefit (Kolaski, 2009, Russman, 2009; Gooch, et al., 2004). The high risk and
gain reported by Kolaski (2009) with the review of all reported adverse events did not
affect the desirability of ITB therapy use in patients with spasticity of cerebral origin.

Intrathecal administration of baclofen into the spinal column spares brain exposure
and subsequent neurological dysfunction associated with adverse events (Penn & Kroin,
1984). As ITB is placed directly into the intrathecal space, the amount of drug necessary
to achieve CSF concentrations sufficient to reduce spasticity is a fraction of that of oral
baclofen (Mullarkey, 2009; Cabrera, Kolaski, & Shilt, 2005). The intrathecal space is the
area of the spinal column within the sub-arachnoid space where the CSF, the fluid bathing
the brain and spinal cord, is found (Pellegrino, 2007). Intrathecal administration of
medication bypasses the blood-brain barrier, therefore, intrathecal medication preparations
must be free of preservatives as many of these ingredients are harmful to the CNS (Cabrera,
Kolaski, & Shilt, 2005).

Compared to oral baclofen, ITB therapy is more effective in replacing the
neurotransmitter, GABA, that would normally be released by the descending inhibitory
impulses in those individuals with normal neurological function (Gerszten, et al., 1998).
Intrathecal baclofen has been shown to decrease muscle tone, pain, and spasms, while
improving mobility (Mullarkey, 2009). Common drug and dose related side effects include
hypotonia, somnolence, seizures, and headache (Albright, et al., 2003).

Patient selection is the first step in the process of considering an appropriate
candidate for ITB therapy (Kolaski, 2005). Prior to the implantation of an ITB infusion
system, it is common practice to conduct a screening test dose of ITB to assess patient
response to the medication (Kolaski, 2005; Awaad, et al., 2002). The screening dose of ITB may be 50, 75, or 100 mcg bolus dose, administered through an epidural injection. The dosing is determined by the administering healthcare provider, with consideration of the child's weight, height, MAS, and response to previous treatment modalities (Gooch, et al., 2004; Awaad, et al., 2003). Prior to the administration of the bolus dose of ITB, a MAS score or Ashworth Scale assessment is performed, and later repeated at 1, 2, 4, 6, and/or 8 hours thereafter, by a physical and/or occupational therapist (Scheinberg, et al., 2001). An average decrease of at least 1 point in the Ashworth Scale score of the lower extremities is considered a positive trial response (Appendix 2) (Awaad, et al., 2002). Current standards suggest vital signs are to be monitored every 15 minutes for 2 hours, then hourly every 6 hours once the screening dose has been injected into the intrathecal space (Scheinberg, et al., 2001). After the screening trial, a plan is discussed between the patient and/or caregiver and physician and goals are established. Once the decision to consent to implant has taken place the patient is referred to the surgeon to discuss further the pump implantation process and risks (Shilt & Cabrera, 2005; Awaad, et al., 2002).

The implantation process of the ITB therapy system involves a pump and catheter insertion. The catheter is inserted into the intrathecal space at the level of the spine recommended by the healthcare practitioner. It is subsequently attached to the pump following a tunneling process occurring posteriorly to the spine (Gudesblatt & Koebel, 2011; Awaad, et al., 2002, Scheinberg, et al., 2001). The level of the catheter placement will influence the effectiveness of ITB on spasticity management (Pin, McCartney, Lewis & Waugh, 2011; Shiltz & Cabrera, 2005). ITB is molecularly heavy, and therefore, descends caudally once inside the spinal column. It is recommended that patients with
spastic diplegia undergo a catheter implantation at the level of T10-12 (Pin, McCartney, Lewis & Waugh, 2011). For individuals with spastic quadriplegia or quadriplegia, C5 to T2 is ideal (Pin, McCartney, Lewis & Waugh, 2011).

There are multiple dosing options for the titration of ITB delivery allowing for precise spasticity management and minimal adverse events. The software present within the device allows for multiple dosing options, conducive to the management of most forms and degrees of spasticity patterns (Gudesblatt & Koelbel, 2011). Baclofen is isotonic, hydrophilic and is excreted through the kidneys unchanged, caution is advised when using in patients with impaired renal function (Medtronic, 2017; Cabrera, Kolaski, & Shilt, 2005).

Many studies have been conducted to examine the clinical benefit of ITB use in children with spasticity (Chiodo & Saval, 2012; Gudesblatt & Koelbel, 2011; Haranhalli, et al., 2011; Miller, 2011; Motta, Antonello, & Stignani, 2011; Pin, McCartney, Lewis, & Waugh, 2011; Vles, 2011; Brashear & Lambeth, 2009; Hoving, et al., 2009; Ridgley & Rawlins, 2006; Gooch, et al., 2004; Scheinberg, et al., 2001). A retrospective analysis of 27 patients with CP or TBI exhibiting spastic diplegia, spastic quadriplegia, dystonic quadriplegia, and hemidystonia types, observed the impact of ITB on motor function assessed by the Gross Motor Function Classification System (GMFCS) (Motta, Antonello, & Stignani, 2011). The results of the research study found that children (mean age 13 years, 7 months) who received an ITB pump implant (all levels of spasticity) demonstrated improvement in the GMFCS, Ashworth scale scores (p<0.001 and p<0.05, respectively), and parent/caregiver reports of overall improvements in functionality (Motta, Antonello,
& Stignani, 2011). All subjects involved in this research inquiry received ITB for the management of their spasticity secondary to CP or a TBI.

The effectiveness of ITB in reducing spasticity was also evaluated in a study by Scheinberg, et al. (2001). This investigation found subjects greater than 4 years old with spasticity of cerebral origin to demonstrate a significant decrease in tone with ITB treatment (Scheinberg, et al., 2001). The greater than two-point reduction in Ashworth scores during the screening trial and 6-months post-implant, indicated a sustained reduction of spasticity (Scheinberg, et al., 2001). A similar trial performed by Gooch and colleagues (2004) involved 80 children less than 22 years of age (mean age 11 years). The study found positive caregiver responses relative to the delivery of ITB therapy in children with CP (Gooch, et al., 2004). Caregivers noted a greater improvement in ease of care and comfort secondary to tone reduction, with greater improvement in the lower extremities than the upper extremities. It is important to note that the reduction of spasticity in the lower extremities was observed with the implementation of ITB; however, no improvement in the range of motion occurred in the upper body (Gooch, et al., 2004). Ultimately, despite the imperfections of this therapy, 80% of caregivers reported that they (strongly felt) would have the procedure performed again, if given the opportunity (Gooch, et al., 2004). In the review of multiple publications, ITB is seen to generally reduce spasticity while improving quality of life in children with CP (Gooch, et al., 2004; Scheinberg, et al., 2001).

Despite the described effectiveness of ITB in improving the quality of the lives of both caregivers and patients affected by spasticity, there are limitations relative to the population of interest. It is essential to note that it is difficult to determine through measurement, the functional improvements experienced in children receiving ITB therapy
who have spastic quadraparesis or multi-limb spasticity as the available tools are too gross to evaluate performance (Miller, 2011; Motta, Antonello, & Stignani, 2011). Severe disabilities may prevent study participants from fully participating in motor skill assessments required of clinical trial participation. The selection of assessment tools often used for individuals with motor disabilities are essential in assessing the ability of the ITB to improve functioning, indirectly, through the reduction of spasticity (Motta, Antonello, & Stignani, 2011).

**Growth**

Previous research has evaluated the associations between CP, spasticity, growth, and ITB. However, not all causes of growth retardation in children with spasticity have been explored, specifically the observation of growth changes when spasticity is reduced. Literature reviews were repeatedly conducted between 2008-2017, using the search terms ‘spasticity’ and ‘growth’ and ‘ITB’. Due to limited findings, the search was expanded to include the terms ‘CP’ and/or ‘TBI’ and ‘growth’ and ‘ITB’, the primary etiologies for spasticity. There were many studies found with searching CP, TBI, spasticity, and growth. The following databases were explored, consisting of AcademicOneFile, CINAHL, Directory of Open-Access Journals, EBSCOhost Academic Research Premier, Elsevier Science Direct, OVID, Medscape, and Wiley Online Library.

The studies found in the review of the literature report that children with CP and spasticity experience growth issues more often than children exhibiting normal neurological functioning (Kuperminc, et al, 2013; Samson-Fang & Bell, 2013; Andrew & Sullivan, 2012; Walker, Bell, Boyd, & Davies, 2012; Krigger, 2006). Furthermore, the
impact of spasticity on growth, based upon a literature review of caloric expenditure associated with spasticity, suggests that the amount of energy expenditure exerted secondary to spasticity is approximately 10% of the total amount (Andrew & Sullivan, 2010).

Despite the limited findings with the literature review, a key case report supporting the research hypotheses and problem statement of this inquiry was derived from a publication by Hemingway, McGrogan, & Freeman (2001). The hallmark case study involved an evaluation of a 13-year-old boy with spastic quadriplegia, who underwent the implantation of an ITB pump, with documented, subsequent weight gain (Hemingway, McGrogan, & Freeman, 2001). The child reportedly experienced a 30-40% decrease in spasticity, with a weight gain from 20.86 to 24.49kg over a 9-month period (Hemingway, McGrogan, & Freeman, 2001). In support of validity and reliability, the child’s nutritional status was maintained with a constant ketogenic diet administered via a gastrostomy tube, ensuring his caloric intake and resting energy requirements were unchanged during the period of observation. In this case, the final analysis determined that the change in spasticity resulted in a reduction of caloric energy requirements following the implantation of an ITB pump (Hemingway, McGrogan, & Freeman, 2001). Despite the investigator’s failure to recognize the weight of the ITB device and medication, this finding presents the potential impact that ITB therapy can have on mediating the weight gain and growth potential in children with spastic quadriplegic CP by reducing spasticity.

The process of growth and development is a predictable biological process of expected patterns spanning from the time of fertilization to the closure of the epiphyseal plate after puberty (Hamza, Ismail, & Hamed, 2011; Wei & Gregory, 2009). Growth
maturation involves increases in height, weight, head size, and sexual development over
time (Pellegrino, 2007). From the time of birth, postnatal head circumference growth is
most predictive of neurodevelopmental outcomes (Andrew & Sullivan, 2010). Stunted
head circumference assessed at age 2 is often associated with a child who will experience
developmental delays (Andrew & Sullivan, 2010). For this reason, pediatricians exercise
standards of practice by plotting a child’s height, weight, and head circumference, specific
to age and gender, on the CDC Growth Charts (2000), allowing for direct comparison to
the expected progression (Day, et al., 2007).

**Nutrition** One of the greatest challenges reported in children with motor disorders
secondary to spasticity is related to the nutritional demands and caloric intake impacting
growth (Andrew & Sullivan, 2010; Bell, et al., 2010). Addressing the issues of oral motor
dysfunction and improvement of posture aid in preventing food aspiration during feeding
sessions (Kuperminc, et al., 2013; Thommessen, M. et al., 1991). Hypotonia (or lower
than normal muscle tone), poor oral motor coordination, tonic bite reflex, and hyperactive
gag reflex accompanied by tongue thrusting may prevent food from being swallowed.
Such mechanical issues impede caloric intake (Pellegrino, 2007). The presence of poor
appetite and food aversion may also result in negative feeding sessions. The resulting
discrepancy between caloric intake and the child’s metabolic demand may result in
malnutrition (Andrew & Sullivan, 2010).

Impaired muscle growth observed in children exhibiting spasticity has a
multifactorial etiology (Barrett & Barber, 2013). Muscle function, composition, and
energy are all impacted by nutrition and growth. It has been postulated that motor function
would improve as nutrition is normalized (Kuperminc & Stevenson, 2008). Evidence
demonstrates that malnutrition impacts one’s overall health and well-being, as all body systems are impacted (Kuperminc & Stevenson, 2008). Nutritional deficiencies may result in increasing cardiac circulation times, placing the child at risk for morbidity associated with congestive heart failure. Gastroesophageal reflux, immune dysfunction, reduced cerebral growth with impaired cognitive development, and behavioral issues may also accompany malnutrition (Kuperminc & Stevenson, 2008).

Kuperminc and colleagues (2013) developed a practical guide for nutritional management of children with CP. The program suggested close follow-up of repeated growth assessments, as frequent as once every 3 to 6 months, to ensure identification of early signs of growth retardation (Kuperminc, et al., 2013). The development of a tailored diet specific to the needs and ability of both child and family are essential to the success of a nutritional program (Kuperminc, et al., 2013). Demonstrating similar objectives, Samson-Fang and Bell (2013) also addressed monitoring growth and assessment of children with CP, while simultaneously recognizing the role of patient and family perspectives toward nutrition within the life of the child. The key to the development of a successful intervention is the conduction of regular assessments of height, weight, and head circumference. Feeding, dietary options, preferences, and nutritional plans are also most beneficial for growth when collaboration is conducted between the healthcare provider and child/family (Samson-Fang & Bell, 2013).

**Traumatic Brain Injury** Traumatic brain injury is one of the leading causes of death and disability in children. In children aged 0 to 4, the most common cause of trauma is attributable to falls (Richmond & Rogol, 2014). In older children, violence, child abuse, sports related injuries, and car accidents more often result in TBIs (Richmond & Rogol,
Brain injuries involving a change in the level of consciousness or anatomy of the brain occur in approximately 1 in 500 children per year, secondary to blunt head trauma (Michaund, et al., 2007). The duration and severity of a coma determine the extent of brain injury and subsequent physical and cognitive impairments (Michaund, et al., 2007).

Rehabilitation following a TBI should be guided by a comprehensive clinical assessment (Greenwald & Rigg, 2009). The goals developed to optimize function as well as to minimize impairments and complications involve a multidisciplinary approach from the rehabilitation team (Greenwald & Rigg, 2009). Two-year post-injury outcomes have shown that 75% of individuals have persistent cognitive, behavioral, or emotional deficits (Greenwald & Rigg, 2009). Spasticity is the most common disability observed, with a wide range of anatomical involvement with severe TBI. As with CP, spasticity that results from a TBI is of cerebral origin. Successful treatment requires an individualized management approach, recognizing the severity, time since injury, and patient/caregiver preference (Greenwald & Rigg, 2009).

Psychosocial Factors

Negative outcomes from inadequate social contact, emotional support, and intellectual deprivation occur when children lack human interaction (Sonuga-Barke, Scholtz & Rutter, 2010). The long-term effects of dysfunctional psychosocial circumstances are thought to impact the child more than the nutritional factors associated with the negative outcomes of growth (Sonuga-Barke, Scholtz & Rutter, 2010). The ability of the parent to provide feeding assistance impacts the relationship between the parent/caregiver and child. The characteristics of food selection, ingestion, and regulation are also influential in the process of feeding (Andrew & Sullivan, 2010; Thommassen, M.
et al., 1991; Satter, E.M., 1986). Special needs children with neurological insults are notorious for being resistant to new feeding approaches and oral experiences, contributing further to growth deficiencies (Satter, 1986). It is beneficial when a parent/caregiver identifies the child’s feedback of timing, amount, preference, pacing, and eating capability from the initial newborn period (Satter, 1986). The stimulation an infant receives during the process of attaining nutrition is also essential to the prevention of psychosocial risks.

In recognizing the potential impact of psychosocial and environmental stressors, the investigator will determine the residency of study participants. The impact of the child’s psychosocial situation, through observed differences in location of residency was determined to be a possible confounding factor influencing growth. A sentinel study compared individuals with CP living in homes with their family members to those living in residential facilities (Henderson, et al., 2007). The comparison was imperative as children without CP most often live in home situations with either parents or other family members. The growth variations between the two groups were examined, accounting for race, GMFCS, feeding modality, age, height, weight, skinfolds, and head circumference of children experiencing spastic quadriplegia (Henderson, et al., 2007). Seventy-five subjects of residential facilities and 205 subjects (aged 2-18) who lived at home were compared (Henderson, et al., 2007). More gastrostomy tube feedings were observed in the residential facility than the subjects living at home. Notable differences were observed despite the patients having been matched for their spasticity and diagnosis. The assessment of GMFCS, feeding modality, age, and living situation comparisons, in relation to growth and nutrition, required a multiple regression analysis. The conclusion reported that residential patients, although generally older, experienced more positive outcomes in relation to
growth and nutrition, with higher z-scores for height when compared to those children living in homes (-3.17±2.2, -2.68±0.12). The total differences were not fully clear. The gastrostomy tube feedings administered by healthcare personnel in a structured environment along with the availability of nurses, physicians, therapists, and dietician services, were noted to be factors most remarkably different from those identified within most home settings. This potentially impacts the “better health” seen among the subjects residing in residential facilities (Henderson, et al., 2007). This study is unique, and more of its kind would contribute to validity and value concerning patient outcomes, in association with care approach.

A second study found adverse early life events to be associated with environmental stressors, prompting puberty and early growth accelerations in children between the ages of 11 and 15 years who experienced puberty by age 11 years (Sonuga-Barke, Scholtz & Ritter, 2010). In this analysis, children sustained social isolation in an orphanage. Subsequent growth decelerations and psychological problems were observed in association with nutritional consumption (Sonuga-Barke, Scholtz & Ritter, 2010). Head circumference was observed to be smaller in those children experiencing psychosocial deprivation. Height and weight variables were not impacted when children experienced episodes of psychosocial stressors with intermittent periods of normalcy (Sonuga-Barke, Scholtz & Ritter, 2010).

Non-Nutritional Factors

**Spasticity** Although there are growth references previously defined for children with quadriplegic CP by the CDC and National Center for Health Statistics (1977), these
are no longer part of the pediatric assessment process for establishing therapeutic interventions relative to growth impairment (Samson-Fang & Bell, 2013). The current clinical application of the CDC established growth charts (2000) recognizes that healthcare providers often treat a broad range of children with CP and therefore, no differentiation is to be made. The observation of where a child plots on the growth charts compared to all children is key to initiating appropriate interventions (Samson-Fang & Bell, 2013). In this study, the researcher will use the recommended 2000 CDC growth charts specific for gender and age to determine the level children with spasticity compare to children with normal neurological status.

The calories exerted in the presence of spasticity may exceed that which is consumed through nutritional intake. Besides the energy over-utilization, growth may further be inhibited through the force exerted by muscles on the long bones during muscle contractions associated with spasticity. Normal gravitational bone growth of long bones, such as the humerus or femur, seem to be impacted most significantly by spasticity. This notion is supported by Day, et al. (2007) in their review of 141,961 measurements of height and weight of children with CP. The results noted muscle atrophy of affected limbs, independent of nutritional intake, with below average growth measurements when compared to peers through the plotting on the CDC growth charts. The conclusion gathered reports that children with spastic paresis, often associated with CP, are generally shorter, and comprise less body fat, muscle, and bone mass (Day, et al., 2007; Henderson, et al., 2007). As the age of a child with CP progresses, the deviation from the normal standards of growth set for healthy children is more marginal (Henderson, et al., 2007, Krick, Murphy-Miller, Zeger & Wright 1996).
Children with hemiplegia exhibit both poor linear growth and muscle bulk, worsening with age on the hemiplegic side (Stevens, Roberts & Vogtle, 1995). This finding has been observed in multiple studies since the 1950’s. Observations of children with either CP or TBI have demonstrated hemiplegia, growth retardation, and a reduction in skeletal growth on the hemiplegic side, despite normal nutrition and linear growth (on the unaffected side) (Andrew & Sullivan, 2012; Stevenson, Roberts, & Vogtle, 1995).

One research inquiry conducted on children with hemiplegia (n=20), compared to a neuronormal group, discovered that children with hemiplegic CP exhibited smaller measurements of breadth, circumference, and length on the affected side of the upper extremity, when aligned with the comparison group (Stevenson, Roberts, & Vogtle, 1995). The mean differences between the affected and unaffected side ranged from (-0.23 to -1.96%), demonstrating significance (Stevens, Roberts & Vogtle, 1995). This finding supports the idea that spasticity effects growth, as evident with greater growth measurements on the unaffected side of the body, compared to shorter length on the side of the body affected by spasticity. Additional research revealed 24% of individuals with CP, demonstrating either spastic hemiplegia or quadriplegia, exhibit more prevalent and profound growth and nutritional deviation from the norm than other types of CP (Reilly, et.al. 1996; Stallings, Cronk, Zemel, & Charney, 1994). In the population of children exhibiting hemiplegia, growth impairment has been more notable on the side affected by spasticity (Zonta, et al., 2009).

Weight bearing activity is essential to the growth and maintenance of both muscles and bones. Physical activity occurring during episodes of growth throughout childhood provides benefits to bone maturation into adulthood (Cameron & Bogin, 2012). The
occurrence of immobility in children with severe motor deficits, comprising spastic quadriplegia, results in reduced muscle bulk or atrophy associated with less weight-bearing activity (Andrew & Sullivan, 2010; Stevenson, Roberts, & Vogtle, 1995). There are multiple comorbidities affecting growth differences in children with CP, including: epileptic seizures, mental retardation, malnutrition, gastroesophageal reflux, osteoporosis, autism, blindness, deafness, and tremors associated with ataxia (Henderson, et al., 2007). Growth differences and other subsequent impairments associated with disease state result in an inability of affected individuals living with spasticity to ambulate or perform ADL, limiting autonomy and provision of self-care (Henderson, et al., 2007).

**Hormones**  Hormonal dysfunction following the occurrence of a TBI, secondary to damage of the hypothalamus and pituitary gland, is reflected in a wide range (5 to 90%) of individuals (Richmond & Rogol, 2014). The variation in prevalence is likely related to the timing of the assessment of hormone levels, in relation to the occurrence of the TBI with either a direct or indirect association (Richmond & Rogol, 2014). Irregular secretion of Growth Hormone (GH) is thought to be impacted by severe brain damage, evident by the overwhelming presence of growth retardation among children with brain insults, such as CP or TBI (Hamza, Ismail & Hamed, 2011). When addressing pubertal onset, specifically in females, multiple publications note the presence of adrenarche (later onset and longer lasting puberty) to potentially impact the final adult height. The growth spurt associated with the onset of puberty would be modified or extended in such cases (Kupermine & Stevenson, 2008; Day, et al., 2007; Sockalosky, Kriel, Krach & Sheehan, 1987).
A study conducted by Hamza, Ismail, & Hamed (2011), reported that children with CP showed deficient GH levels associated with a brain lesion or defect within the developing brain. As GH secretion occurs with acute stress, it is also suppressed with psychological deprivation (Wei & Gregory, 2009). A second study among 51 children sustaining a brain injury, observed 47.8% of children, (6 years and older) revealed hypopituitarism three-months following a TBI, while 34% were found to be deficient in GH one-year post injury (Cesano-Sancho, et al., 2013). With ongoing observation, all but 1 of the 23 children demonstrated growth within normal limits (Cesano-Sancho, et al., 2013). A more recent study revealed an association between hypopituitarism and growth in children >6 years who experienced a TBI (Richmond & Rogal, 2014). Results suggested that growth was not impacted in 23 children despite lower than normal levels of HGH (Richmond & Rogol, 2014). In summary, the role of hormone irregularities observed in children with both CP and TBI are significant as the onset and length of puberty impacts final adult height (Richmond & Rogol, 2014; Cesano-Sancho, et al., 2013). However, to the contrary, HGH levels don’t necessarily explain changes in the growth process when individuals with motor disabilities demonstrate insufficient growth (Richmond & Rogol, 2014; Cesano-Sancho, et al., 2013).

**Scoliosis** The average prevalence of scoliosis among the general population is 1-2 %; however, in individuals with CP it is reported to be 15 to 80% (Koop, 2009). In CP, neuromuscular scoliosis is typical, resulting in a C-shaped curve (Scannell & Yaszay, 2015). Literature relevant to the impact of scoliosis on growth is limited. From a practical standpoint, growth is presumed to be directly correlated to the level of scoliosis. When obtaining anthropometric measurements on a child with scoliosis, hip dysplasia and
contractures of the lower extremities are often observed in children with severe functional limitations, resulting in more complicated and questionable measurements (Koop, 2009).

A debate over the impact of ITB on the development of sagittal plane spinal deformities, such as those associated with scoliosis, is confounded by the complexity of scoliosis among youth with CP (Senaran, et al., 2007). A study by Senaran, et al. (2007), comprised a retrospective medical record and radiologic study review, comparing matched groups of children with quadriplegic CP according to age, GMFCS, and gender. The matching involved 26 subjects who received ITB and 25 who did not. Within the groups, the average curve per year was 16.3° in children receiving ITB and 16.1° for the control group. These results demonstrate that the curvatures progressed with growth in both groups (Senaran, et al., 2007). The impact that ITB has on spinal curvature, pelvic obliquity, or incidence of scoliosis has proven to be without cause among groups of children matched with and without pumps (Senaran, et al., 2007). The researchers of this study did not report changes in MAS; however, in the discussion of the publication, various modes of spasticity management were acknowledged.

A second study of 19 patients analyzed for scoliosis progression, were noted to have an 18° curvature per year before the ITB pump implant and an 11° per year after (Ginsburg & Lauder, 2007). Shilt and colleagues (2008) also compared 50 subjects with ITB pumps with 50 matched controls for age, sex, type of CP (diplegia or quadriplegia), and similarities of scoliosis within 10°. The study results determined that children receiving ITB had a mean curvature progress of 6.6° per year compared to 5.0° in children who were not receiving ITB. Although there was a 1.6° difference between the two groups, the difference was not statistically significant (p=0.39). In summary, ITB therapy does not
worsen the progression of scoliosis, as determined through repeated studies comparing radiologic findings among matched groups of children, with and without ITB pumps (Koop, 2009; Shilt, et al., 2008; Senaran, et al., 2007).

**Measurement of Spasticity**

The common clinical approach to the measurement of spasticity is founded in the MAS or Ashworth scale score (Appendix 2). There are several quantitative techniques available to subjectively assess the biomechanical features observed with spasticity. Spasticity is characterized by a ‘catch’ or velocity dependent increase in resistance when an extremity is passively stretched (Johnson, 2002). The Ashworth score was originally implemented in 1964 for use in multiple sclerosis (Johnson, 2002). A modification was made by Bohannon and Smith in 1987 (MAS) as they viewed the original scoring system as lacking documented duplication, precision and sensitivity (Johnson, 2002). Cross validation was exercised by the two practitioners and a correlation of >90% was established. The elbow and knee joints are involved in the assessments of the Ashworth scale scores, comprising an ordinal grading scale ranging from 0-4 (Johnson, 2002). Within this research inquiry, the spasticity could have been measured with either form of the Ashworth scale, it was unspecified with medical record reviews.

**Measurement of Growth**

The assessment of growth in children with spasticity is often challenging due to their posture and motor impairment (Andrew & Sullivan, 2010). For example, obtaining the weight of a child can be obtained with creative measures, such as weighing the wheelchair while the child is on an exam table, and then repeating the measurement once
the child returns to the wheelchair. Alternatively, the parent or caregiver can obtain their weight, and then hold child while being re-weighed, noting the change in weight to be that of the child. Regardless of how a measurement is obtained, it is imperative to keep the mode of measuring consistent (Andrew & Sullivan, 2010).

Expanding upon the anthropometric measurements, it is important to recognize that overwhelmingly, children with CP are noted to have poor growth and subsequent diminished adult height (Hamza, Ismail, & Hamed, 2011). Measurement of height is most accurate when measured with a stadiometer, requiring patients to stand upright. However, because children with spasticity often have difficulty standing, this option is not always ideal as expressed tone or spasticity interferes with complete extension of limbs (Andrew & Sullivan, 2010). The use of a flexible tape measure is the most suitable means of accurately measuring height when spinal or hip deformities exist (Samson-Fang & Bell, 2012).

Body mass index (BMI) is calculated as the weight in kilograms is divided by the height (m)² (Shahar, 2009). A BMI below 10th percentile in children with CP is indicative of under nourishment (Andrew & Sullivan, 2010). Early intervention is essential for treatment of poor growth as a child's deviation from the expected growth patterns is a serious indication of potential underlying health problems (Day, 2010).

**Donabedian Conceptual Model**

Based upon theory and concept synthesis, the application of the Donabedian Model to this research project involves the measurement of the quality of care relative to the treatment of growth delay and the assessment of growth indicators. The *structure*, *process*, and *outcome* variables comprising Donabedian’s Model were applied to the Florida
Department of Health (FDOH), Children’s Medical Services (CMS) program, the originally proposed healthcare program for children with special needs. By evaluating the structure of the healthcare system providing care to children, the process of both growth evaluation and spasticity management impact the outcomes within the system of interest (Donabedian, 1997) (Figure 1). The assessment of an institution, as it relates to the entire healthcare system, may be performed through the evaluation of established quality measures (Naranjo & Kaimal, 2011). The implementation of evidence based practice is founded through the collection of observed clinical outcomes within practice settings (Naranjo & Kaimal, 2011). Program modifications have the propensity to impact the lives of children with CP at both institutional and individual levels. Changes in the structure of an institution or department can ensure the provision of quality measures relevant to the use of ITB in improving growth in children with CP. The opportunity for children to receive the highest level of care for treatment of their spasticity impacts growth and attainment of wellness.

Summary of Literature Review

The management of growth in children with spasticity is a significant challenge for healthcare providers. There is a need for research data relevant to the impact of spasticity on growth, and the potential benefit that ITB may indirectly have on growth through the reduction of spasticity. In the case report titled: “Energy Requirements of Spasticity”, by Hemingway, McGrogan, & Freeman (2001), growth changes over time were observed in a child with CP receiving ITB. Through the reduction of spasticity and subsequent caloric energy requirements, the child's weight increased during a 9-month period. This research finding supports the notion that ITB therapy, with the reduction of spasticity and associated
reduced caloric expenditure, enhances the growth potential in children with spastic quadriplegic CP.

The literature review provided in this chapter explained factors impacting both Spasticity and Growth. Clinicians have various treatment options for the management of spasticity in children; however, ITB has been identified, through rigorous research, to be a safe and effective option for reducing generalized spasticity. A probable association has been observed between psychosocial factors, hormones, scoliosis and growth retardation, yet there is no mention of the role of spasticity. The absence of research and associated literature pertaining to ITB and growth necessitates this investigator’s inquiry. The supporting outcomes related to the ability of ITB to reduce spasticity and the resulting increase in height, weight, and BMI will be analyzed in this investigation, as presented in Chapter 3.
Chapter 3

Methods

Overview

Due to difficulties in collecting the data as initially planned, this chapter presents the originally intended methods as well as those procedures that were conducted. A description of the proposed study design, setting, data collection process, influencing variables, and data analysis plan will be provided. Research inquiry relevant to the variables of interest and the subsequent impact of ITB therapy on growth and spasticity among children, ages 2 to 20 was explored.

Purpose

The purpose of this study was to determine the impact of ITB on growth in children (ages 2-20) with spasticity. The research question stated: What is the impact of ITB on growth mediated by a reduction in spasticity? The study aimed at testing two hypotheses. The primary hypothesis being: It is postulated that children (ages 2-20) who receive ITB for the treatment of spasticity will have improved growth, as evident by increasing measurements of height, weight and body mass index in comparison to standard measurements established by the CDC Growth Charts (2000), representing children without spasticity exhibiting normal growth patterns. The secondary hypothesis is as follows: Reduced spasticity partially mediates the effect of ITB on growth.

Study Design

The original study design involved a retrospective medical record review comparing growth in two samples of children with spasticity (ages 2-20 years). One group would have undergone a Medtronic ITB pump implantation and the other sample would...
not possess an ITB pump. Height and weight measurements were to be collected from medical charts during the period of January 1\textsuperscript{st}, 2008 to January 1\textsuperscript{st}, 2014. Data was to be obtained at the following time points: pre-implantation of the device, 6, 12, 18 and 24 months (± 30 days) post-implantation. The data from the two samples were to be matched for Gross Motor Classification System (GMFCS) rating, level of spasticity (based upon their documented MAS score without ITB therapy), gender, and age. The third comparison was to be implemented as the data from the two groups were to be plotted on a standardized growth chart created by the CDC and the National Center for Health Statistics (2000) (http://www.cdc.gov/growthcharts/cdc_charts.htm). The growth charts are age and gender specific for all three variables of interest (height, weight, and BMI). The final analysis was designed to compare the subjects of interest against children without spasticity exhibiting normal growth parameters when plotted on the relative growth charts for age and gender.

Institutional Review Board (IRB) approval challenges occurred with the original submission of research inquiry, and subsequently, interrupted the conduction of the proposed study design. Alternative efforts to obtain approval from the University of Miami (UM) IRB resulted in a modification of the study design, as only children with ITB pumps could be identified and their records accessed. Once IRB approval from the UM was granted, the researchers initiated the modified study plan. The study design was changed to a one-group design, examining within-subject growth over time, as the subjects in the targeted sample all had undergone an ITB pump implantation. Data for the children who had over (5) measurement encounters were plotted on the CDC Growth Charts (2000). An indirect comparison (to peers) occurs when a child’s measurements are plotted on the CDC growth charts. The primary hypothesis was revised as follows: It is postulated that
children, ages 2-20 years, who receive ITB for the treatment of spasticity will have improved growth, as evidenced by increasing measurements of height, weight and body mass index in comparison to standard measurements established by the CDC Growth Charts (2000) representing children without spasticity, comprising normal growth patterns. The secondary hypothesis states that reduced spasticity partially mediates the effect of ITB on growth. The comparison plan involving children with spasticity without ITB devices had to be eliminated.

Setting

The original setting for this study involved a statewide, governmental program providing comprehensive, coordinated, pediatric care within a multi-disciplinary, interagency system, FDOH CMS. The program provides early intervention services and support to infants and toddlers with disabilities, as well as, their families in accordance with the Individuals with Disabilities Education Act. Children attending the CMS clinic underwent consultations and evaluations to determine the need for durable medical equipment to assist with transportation and mobility, secondary to movement disorders.

Since the IRB submission to conduct a chart review at the statewide agency was not approved, the actual setting for this study ultimately took place at the UM Miller School of Medicine. Through a retrospective chart review, information was gathered by the Medical Research Information Technology staff and the PhD candidate. Limited access to medical records of interest were provided through the Electronic Medical Record (EMR) system. Several record reviews (paper charts) were performed at the Medical Record Department by the researcher, as the data in the EMR was sparse.
The University of Miami is located near downtown Miami, Florida. The UM health system, known as UHealth, consists of three major hospitals, including the UM Hospital, Sylvester Cancer Center, and the Bascom Palmer/Ann Bates Leach Eye Hospital. Subjects were patients of UHealth and were being managed by three intrathecal therapy specialists. Clinicians, including neurologists and physiatrists specializing in neurorehabilitation, were trained by Medtronic Neuromodulation, Inc. to ensure safe and effective provision of ITB therapy.

**Inclusion/Exclusion Criteria**

The inclusion criteria as originally planned for this study was to include children between the ages of 2-20 who were patients of the FDOH CMS special needs program attending the Orthopedic Clinic. The presentation of spasticity, described as spastic diplegia, spastic hemiplegia, spastic quadriplegia, or quadriplegia, was required. The revised inclusion criteria consisted of children who sought medical care at the UM, Miller School of Medicine, between the ages of 2-20. The condition of spasticity was required, also described as spastic diplegia, spastic hemiplegia, spastic quadriplegia, or quadriplegia. Patients treated and assigned the ICD 9/10 codes specific for spasticity (ICD 9: 728.85), gait abnormality (ICD 10: R26.9), infantile cerebral palsy (ICD 9.0: 343.9), traumatic brain injury (ICD 9.0: 850.0, 859.9), or anoxic brain injury (ICD 9.0: 348.1) were of interest. The documented CPT codes, 62368 or 62370, found among medical records (EMR or paper) were used to identify subjects of interest, indicative of patients undergoing ITB pump management. Exclusion criteria for both study designs included children without evidence of spasticity, lacking the diagnostic codes associated with the inclusion criteria.
Additionally, subjects under 2 or older than 20 years of age were excluded from the study sample.

Measures

As supported in the literature review, variables of interest were chosen to assess the reduction of spasticity, speculated to impact growth in children with CP. The growth parameters, demographic variables, spasticity severity, and ITB dosing were of interest and will be expanded upon below.

Demographic and Condition-Related Variables The following demographic variables were expected to be gathered for this analysis: gender, date of birth, race (Caucasian, black, black-Hispanic, Hispanic), and location of residence (biological family, foster family, or skilled nursing facility where continuous 24-hour care is provided to the patient). The subject’s date of birth was used to calculate age at each time point. Gender, race, height, weight, and resulting BMI were all collected in accordance with the date of the ITB pump implantation. In addition, variables related to the child’s condition and treatment were to be collected to help explain growth patterns not caused by the independent variable of interest (covariates in the statistical analysis). These covariables included diagnoses related to the etiology of spasticity, GMFCS score reflecting motor function, nutrition mode (oral, gastrostomy tube or mixed), and any antispasmodic medications being administrated to participants at each time point. The GMFCS scores were not available in the medical record reviews.
**Independent Variable: ITB dose** The predictor variable was the ITB dose. The purpose of collecting ITB dosing was to conduct an exploratory analysis of dose effect on growth over time. The ITB dose was to be ascertained at multiple time points for patients receiving ITB therapy via the implanted device. The time points included the initial dose at the implantation date of the ITB pump, followed by additional documented ITB doses at 6, 12, 18, and 24-months post-implant.

**Mediator Variable: Spasticity** The proposed mediator variable in this study was spasticity. There is both an Ashworth Scale score and a MAS score (Appendix 2) useful in measuring the level of spasticity. In this analysis, there was not a specific mode of assessment score indicated in the documentation by the healthcare provider managing the spasticity (Table 5). The spasticity assessment was to be documented at each time point, including: the implantation date of the ITB pump, and at 6, 12, 18, and 24-months post-implant.

**Dependent Variable: Growth** The outcome variable was change in growth, consisting of measurements of height, weight, and calculated BMI at each time point. In this inquiry, height was collected in inches and weight was collected in pounds. The BMI was calculated by the researcher using an application embedded into the CDC Growth Chart software (2000) with ascertainment of the height (m²) and weight (kg) measurements. The BMI was further compiled from those measurements and transformed through statistical analysis into z-scores and percentiles (Table 3). The CDC Growth Charts (2000) are age and gender specific for all three variables of interest (height, weight,
and BMI), and therefore, measurements were readily compared to the normal growth parameters established.

**Protection of Human Subjects**

The data collection process initially involved the IRB application and submission to the FDOH for permission and plans to conduct medical record reviews of children with documented spasticity. All the subjects of interest were provided medical services at the FDOH, CMS special needs program. Following an 18-month period of review and consideration; a determination was made by the FDOH on June 16th, 2015. The decision to decline the request, secondary to concerns related to HIPPA compliance, was made despite stated plans by the researcher to de-identify all possible demographic information in alignment with regulatory requirements. Subsequently, the researcher was resolved to consult the UM IRB. The investigator was instructed to submit the proposed, revised research design and plan to the UM Human Subjects Research Office (HSRO). Approval for the research protocol was received from the University of Miami IRB on December 22nd, 2015.

**Data Collection Plan**

The study design was initiated following the IRB approval from the UM. Support was obtained from the Department of Research Information Technology for collection of the planned indicators from the existing EMR. Data captured from the period of January 1st, 2010 to October 1st, 2015 was reviewed in both electronic and paper form using the Data Collection Form (Figure 1). Revisions to the study design included the removal of the planned comparison groups, as the UM does not have an actual pediatric spasticity
program allowing for comparison between children with and without pumps. Subject parameters included: children with spasticity, aged 2-20, receiving ITB infusion as evidenced by the documented ICD 9 and 10 codes and CPT codes associated with spasticity, CP, and ITB pump management. In alignment with regulatory requirements, confidentiality was protected with assignment of individual study identification numbers (not linked to any patient identifiers), allocated to each subject of interest. Subject numbers were assigned sequentially based upon the patient list provided to the researcher by the Department of Research Information Technology.

Codes and formulas were assigned for each variable (Appendix 4), necessary for the analysis in conjunction with the Excel spreadsheet. The completed data collection forms for the study were organized numerically, by subject number, in a three-ring binder which file with all data collection forms.

A maximum of 150 records were expected to be reviewed from the EMR system at UHealth. Subject records were sorted according to medical record number as they were provided to the researcher from the Department of Research Information Technology. The random assignment of study numbers is in numerical order, starting with 001. Data time points may have included up to 3 observations prior to ITB implantation (at approximately 6, 12 and 18 months) and up to 4 observations post-implantation (approximately 6, 12, 18 and 24 months). The implant date of the Medtronic®, Synchromed II device for all patients being managed by the UM medical staff was imperative for the statistical analysis. Due to the lack of documented implantation dates, an IRB modification was submitted and approved for the request of pump implant dates, through a secured, shared list from Medtronic®.
Data Analysis Plan

The original analysis plan for the two-group design involved a general linear mixed model analysis, including fixed factors for group (ITB therapy and no ITB therapy), time points, and the interaction between group and time. Covariates for age, gender, race, and Ashworth spasticity score were to be included to control for possible independent influence on outcomes. Spasticity, the mediator variable, was proposed as a time-varying covariate. The random term was to be subject nested within group. A heterogeneous, autocorrelated covariance matrix was used to be the correlated data structure. Planned comparisons between groups at each time and between times within each group were proposed. The intention was to use the orthogonal polynomial contrasts to test for linear and quadratic trends overall and within each group. Plans to assess means and standard errors were stated. Software SAS 9.3 (SAS Institute, Inc., Cary, NC) was planned to be used for all analyses. Because the analyses were planned comparisons, the two-tailed 0.05 significance level was proposed to determine statistical significance for all tests.

To test the revised hypothesis: It is postulated that children, ages 2-20 years, who receive ITB for the treatment of spasticity will have improved growth as evidenced by increasing measurements of height, weight and body mass index in comparison to standard measurements established by the CDC Growth Charts (2000) encompassing children without spasticity, comprising normal growth patterns. The planned analysis was revised to be comprised of a within subjects repeated measures analysis of covariance. This hypothesis had no group within the model. While the covariates were unchanged, the significance tests were solely between times.
The implemented data analysis plan was considered appropriate for the proposed hypotheses. The collection of the data of interest, at multiple time points was not able to be retrieved upon the review of medical records. The absence of data did not allow for planned adjustments of the covariates. While each subject was missing data and the time points were not uniform, a mixed model regression analysis was conducted with random slopes and intercepts. With a mixed model regression analysis, each subject has their own intercept and slope. Subsequently, an intercept and slope was calculated for the sample group due to too few measurements of the individual subjects. The data documented on Excel comprised the information obtained from the medical record reviews (both paper and electronically). The data was further incorporated into the CDC Growth Chart (2000) analysis template accessed from the National Center for Health Statistics. Reflected changes in the measurements collected at random time points (height and weight values) were adjusted for age and gender according to the CDC Growth Chart software (2000). Data collection was reviewed twice for quality assurance after being collected by the research staff at the UM Department of Information Technology Research. Medical records were provided to the researcher via a password protected CD-ROM. Records were reviewed for clarification and inquiry pertinent to missing data. Values were entered in the investigator’s Excel document which was double password protected. Paper versions of the Data Collection Forms (Appendix 3) are kept in a three-ring binder in a locked cabinet possessed by the PhD candidate.

**Summary**

The original plan for this analysis was to determine the impact of ITB on the reduction of spasticity and the subsequent influence upon changes in height, weight, and
BMI among a double-cohort of subjects between the ages of 2-20 years. The analysis sought to identify changes in growth observed as spasticity is reduced or eliminated. A planned secondary analysis could be performed with the data obtained from a retrospective chart review of patient encounters occurring between January 1st, 2008 to January 1st, 2014. Demographic data and subsequent repeated measures of growth indicators for the double-cohort analysis were to be performed. However, due to denial of the original FDOH IRB request, this was not feasible.

The final statistical analysis included all children undergoing ITB pump management at UHealth between the period of January 1st, 2010 to October 1st, 2015. The sample included a single cohort of subjects (ages 2-20) who presented with spasticity. The variables of height and weight were not readily available within the review of medical records; therefore, modifications in the set plan for the statistical analysis was deemed necessary. The results section (Chapter 4) will provide an explanation of findings relative to five cases studies observed within the sample. These five subjects had at least five growth measurements recorded in the medical records.
Chapter 4

Results

As described in Chapter 3, the revised hypotheses include Hypothesis 1: It is postulated that children, ages 2-20 years, who receive ITB for the treatment of spasticity will have improved growth as evidenced by increasing measurements of height, weight, and body mass index in comparison to standard measurements established by the CDC Growth Charts (2000), encompassing children without spasticity, comprising normal growth patterns. Hypothesis 2 states: Reduced spasticity will partially mediate the effect of ITB on growth.

Missing Data

Secondary to missing data, the analysis for the primary hypothesis was revised. Table 1 presents the frequency of available data points in the clinical records. As shown, there is substantial missing data. The overall percent of valid measures for each variable (in order of most complete to least) include: age and gender (98%), race/ethnicity (91%), weight (86%), place of residence (85%), date of pump implant (73%), type of nutrition the child was receiving (70% each), height (67%), calculated BMI (64%), whether a nutritional consultation was performed (60% indicated the provision), baclofen dosing (50%), oral medications for treating spasticity (41%), measurement of MAS score for spasticity (41%), and type of supplemental oral antispasmodic medication (40%). An assessment of the amount of missing data determined that 68-86% of the data for the outcome measures of height, weight, and BMI were obtained (Table 1). Approximately 41% of the spasticity measures were valid (Table 1).
The amount of valid data supported testing the revised Hypothesis 1, using the general linear mixed model regression with random slopes and intercepts outlined in Chapter 3. The limited number of measurements of this sample of children with spasticity precluded the inclusion of pertinent covariates such as spasticity measurements and ITB dosing, limiting the conclusions of the intended analysis. A repeated, structured assessment using the same study design is suggested to support the implementation of the proposed hypothesis and analysis among a larger sample. There was insufficient data to test Hypothesis 2. Therefore, to supplement the results, case studies of five subjects were conducted using a qualitative approach, allowing for the use of all available data. Case studies provide a closer examination of growth patterns than those found with quantitative analysis. This form of an analysis allowed the researcher to explore other factors than age, affecting growth.

Subjects

Table 2 provides the descriptive statistics of the demographic and clinical variables. There were 16 subjects with usable data for at least five time points. Of the 16 subjects analyzed, 62% were male. For race, 47% of the subjects were black, 27% Caucasian, and 20% Hispanic. Additionally, approximately 92% of subjects lived with their biological parents. In addressing nutrition, 60% had documentation of receiving a nutritional consult, and of those, 40% ate by mouth and 60% received gastrostomy tube nourishment. Of the patients who received supplemental oral antispasmodics, only five had documentation of such. For the ITB pump implantation, the average age was 14.8 years (SD = 5.3), with a range of 4.9-19.8 years. The mean number of years since implantation was 4.9 (SD = 2.0), with a range from 1.1-9.0 years.
Test of the Hypotheses

Hypothesis 1  Hypothesis 1 stated: It is postulated that children, ages 2-20 years, who receive ITB for the treatment of spasticity will have improved growth as evidenced by increasing measurements of height, weight and body mass index in comparison to standard measurements established by the CDC Growth Charts (2000) encompassing children without spasticity, comprising normal growth patterns. In summary, neither hypotheses were not supported. Weight had a non-significant downward trend, indicating a decrease relative to weight in normal children. The BMI revealed a significant downward trend, and height had a non-significant upward trend in agreement with the hypothesized growth trend. In the conclusion, the projected height was still below the zero Z-score, indicating that the patients comprising the sample were still lower than normal height. For associated age intercept and trajectory, the Beta (regression coefficient) values are not significant for any of the weight measurements, as the values were uniformly less than 1 (Table 3).

The results of the random slopes and intercepts model for height, weight, and BMI of the entire sample are presented in Table 3. The plotting of the average predicted trajectories are presented in Figure 1. The findings from the regression analyses resulted in a negative average trajectory of weight (beta ± standard error: -0.19 ± 0.13, p = 0.169) and BMI (-0.16 ± 0.06, p = 0.020) (Table 3), indicating as subjects aged, they fell further below the expected weight and BMI on the CDC growth charts. The average trajectory height, however, had a positive trajectory (0.10 ± 0.11, p = 0.393) (Table 3, Figure 1).
Description of Measured Predictor Variables

**Intrathecal Baclofen** Table 4 provides an overview of the sample characteristics including age at baseline, age at implant and the number of years implanted. The average age of subjects at ITB device implantation was 14.8 years, while the average age at the time of the data collection was 20 years (Table 4). The mean number of years of implanted ITB devices was 4.9 (Table 4). The frequency of documented ITB dosing within the medical records declined over time is presented in Table 5. The ITB dose ranged from 826.5mcg at encounter (1) among (8) subjects, to 959mcg at encounter (3) among (7) subjects. The standard deviation had no set trend; however, the fourth and fifth encounters were the lowest at 205.3 and 296.6mcg at time points (4) and (5), respectively. The highest documented ITB dose was 940.9mcg at encounter (2). This analysis demonstrates the wide variability in the ITB dosing to achieve spasticity control among the sample being examined. Furthermore, the consideration of ITB dosing among this sample reflects a higher age at device implant reflecting this form of treatment may be considered a last resort option.

**Spasticity** The change in the subject’s level of spasticity, as measured by the assessment of the MAS, were tracked for all subjects noting the number of encounters documented. The number of encounters, the mean, and SD of the Ashworth scores for all subjects are noted in Table 5. The mean MAS score ranged from (1.0 to 1.7) with standard deviations ranging from (0 to 1.1). There appears to have been a slight reduction in spasticity from baseline to measurement five; however, the significance (p value) was not able to be calculated due to missing data.
Case Studies

Secondary to missing data resulting in limited power of the quantitative analysis, we are presenting five case studies describing the individual variables of interest. Subjects who had documentation of growth data (height, weight, and BMI) on at least five time points were individually assessed to explore their growth patterns.

Subject #8 was an 18-year-old Hispanic male with spastic quadripareisis associated with CP (non-ambulatory) (Figures 3 & 4). He lived with his biological mother and received nourishment via gastrostomy tube. The date of ITB pump implant was not available; however, the review of his records found increasing weight gain (from 92lbs to 116lbs) over an 8-month period (Figure 4). The sustained growth percentile for weight was below the 5th, with increases near the established 5th percentile with (6) measurements plotted over a 12-month period by 19 years of age (Figure 3). The height measurements on (2) recordings increased from below the 5th percentile to the 25th percentile, also during a 12-month period by age 19 (Figure 4). There were (2) BMI values plotted 12-months apart (Figure 3). The two values declined from the 5th percentile to below the 5th percentile, indicating that as he aged, his measurements fell further below the expected growth projections. This subject’s ITB doses ranged from (896-1055mcg) with no recorded changes noted in his spasticity (Modified Ashworth Score +1). Overall, this subject’s BMI for age percentile dropped over time, despite improvements in both height and weight, confirming previous research findings stating that as children with spasticity age, they fall further below the norm.
Subject #10 was a male with CP who underwent an ITB pump implantation at 17 years of age (Figures 5 & 6). He was Caucasian with spastic diparesis, the ability to walk, and resides with his parents. Subject #10 exhibited increases in height and weight over a 3.5-year time span (Figure 6). His height increased with (3) measurements (from 61 to 67 inches) from below the 5th percentile to the 5th percentile by age 20 years (Figure 6). Weight advancements occurred (from 142lbs. to 165lbs.) among (5) measurements, demonstrating an increase from the 50th to the 65th percentile by 20 years of age. The BMI trends were plotted above the 90th percentile for two of four measurements plotted over (3) years, with the last height assessment at 20 years above the 90th percentile (Figure 5). This patient ate by mouth; his ITB dosing ranged from (144mcg to 668mcg), and his MAS declined over time from +2 to +1, reflective of dosing specific for spasticity control. Overall, this subject’s measurements demonstrated growth measurements within normal parameters.

Subject #11, was a Caucasian female with transverse myelitis and subsequent diplegia of the lower extremities preventing her from ambulating (Figures 7 & 8). She had a pump implanted at 13.67 years of age which was managed at another clinic within an academic institution in the State of Florida. Over 2.5 years, her (5) measurements of height were documented as unchanged (66 inches) and within the 50th percentile (Figure 8). Her weight, relative to growth chart norms, decreased (105 to 100lbs) from the 10th to the 5th percentile, from ages 16 to 18 (Figure 8). Although her height was documented to be unchanged over three years, when plotted with weight changes, her resulting BMI fell well below the 5th percentile (Figure 7). Further inquiry into the onset age of the transverse myelitis would be beneficial in determining if her maximum growth was attained prior to
the development of myelitis. The time of onset of her spasticity was unknown. Her spasticity was well controlled with an ITB dose of 1021 to 1302mcg per day, supported by a MAS score of zero with repeated measures.

Subject #17 was a black female with bilateral spastic diplegia and known HIV seropositivity, secondary to perinatal transmission (Figures 9 & 10). Her records did not provide the original pump implantation date; however, the documents did note a pump implant at 19.3 years, which was most likely a replacement pump. The subject was non-ambulatory, lived with her biological family, and obtains her nourishment by mouth. Although she maintained her weight from age 18 to 20 (93 to 95 lbs., with a maximum weight of 101lbs), it plotted well below the 5th percentile on (5) occasions (Figure 10). The height of same subject was only measured once, plotting at approximately the 45th percentile (Figure 10). The measurements of her height and weight allowed for one BMI to be calculated, which was found to be well-below the 5th percentile (Figure 9). This patient’s MAS score was documented at +2 with an ITB dose ranging from 1051 to 1100mcg/day. The patient used a wheelchair for mobility. It is important to recognize from a clinical standpoint that this patient’s metabolic state may possibly have been impacted by the HIV diagnosis and the antiretroviral medication regimen she was taking.

Lastly, Subject #20, a female of unknown race who had her pump implanted at 19 years, experienced spasticity secondary to spina bifida (Figures 11 & 12). Although her spasticity was not secondary to CP or TBI, her results were examined due to the limited amount of data extracted for the sample. Her measurements were assessed over 3.5 years, no mode of nutrition was found with the medical record review. Her weight measurements demonstrated a decrease (from 115 to 100lbs) on three occasions with a range from the 45th
percentile to just below the 5th percentile (Figure 12). The height measurements remained below the 5th percentile over time with measurements occurring on (3) time points from 57 to 59 inches (Figure 12). Her BMI decreased markedly from over the 85th percentile to just above the 25th percentile during the 3.5-year time-period (Figure 11). The final BMI plotted at 19 years was in the 25th percentile when compared to her peers (Figure 11). The ITB dosing data points were sparse, with a range from 86 to 133mcg/d. No spasticity measurements were found in the medical record review. Noted MAS scores, reflecting the level of spasticity control in relation to ITB dosing, would provide vital information pertaining to the correlation between growth, spasticity severity, and her ITB dose.

Summary of Case Studies

The case studies reflected each subject’s growth tendencies, however, the findings when plotted, demonstrated that the males displayed normal growth tendencies. The case studies presented ranged in age from 15.5 to 20. Males had growth as evident by increasing measurements of height and weight over time, with the BMI value of one subject being normal and the other dropping just below the 5th percentile (only 2 values were plotted). The females, despite maintaining their individual height and weight parameters, had greater discrepancies when compared to their peers for all growth measurements. The female values all declined despite consistent measurements as they aged and were ultimately found to be below the 5th percentile for either height, weight, or both; indicative of being smaller than their peers.
Summary of Results

The overall lack of growth measurements for all subjects interfered with the conduction of the statistical analysis plan. The results of the regression analyses tested Hypothesis 1 (Table 3). With the focus of examining the impact of ITB, through the reduction of spasticity, on growth, Hypothesis 1 was not proven. To further explore the inquiry, a random slopes and intercepts model for height, weight, and BMI was conducted for z-scores. In review of the growth trajectories displayed in Figure 1, there was a non-significant weight decline, a significant BMI decline and a non-significant increase in the height. To ascertain more individual isolated changes in growth, case studies were conducted on subjects having growth measurements captured for at least five time points. Six subjects (2 males and 4 females) demonstrated differentiating outcomes in growth between genders. Subsequently, the males demonstrated more normal growth tendencies compared to their peers, evident with increasing measurements of height and weight over time, compared to the females observed. Overall, the outcomes associated with the action of ITB on the reduction of spasticity were not fully assessed due to the overabundance of undocumented data of interest.
CHAPTER 5

Discussion

This study was designed to answer the research question established in this inquiry: What is the impact of ITB on growth, as mediated by a reduction in spasticity? The first hypothesis postulated that children, ages 2-20 years, who receive ITB for the treatment of spasticity will have improved growth as evidenced by increasing measurements of height, weight, and body mass index, in comparison to a matched group of children who do not receive ITB. A secondary hypothesis postulated that reduced spasticity partially mediates the effect of ITB on growth. It has been determined in many clinical trials that ITB aids in reducing spasticity associated with prolonged muscle contractions. Furthermore, reduced spasticity is speculated to contribute to subsequent decreases in caloric expenditure.

The comparison to a matched group of children without spasticity could not be conducted because of the inability to access charts from the Department of Health as originally planned. The design was therefore changed to a one-group design and children with spasticity receiving ITB were compared to normative growth rates as represented by the established CDC growth charts (2000). Neither weight or BMI measurements for the sample were found to be near normal when plotted on the growth charts (2000). Although an increase in height was demonstrated in the sample of sixteen subjects, the lack of measurement encounters did not allow for an ongoing observation over time as the child aged. The BMI changes of the sample reflected a significant decline. The weight changes observed for the subjects of this study showed a non-significant decline with aging, in alignment with what has been established in the literature.
Due to the lack of sufficient data time points for a well-powered quantitative test of the hypotheses, a case-by-case review of six subjects who had at least five documented growth measurements was performed. The anthropometric measurements of these six subjects revealed differences between males and females who exhibited controlled spasticity. The case studies of this research inquiry resembled the key case study identified in the literature review by Hemmingway, McGrogan, and Freeman (2000). The case study of a 13-year-old male with spastic quadriplegia, through the reduction of spasticity with ITB administration and subsequent caloric energy requirements, demonstrated a weight increase during a 9-month period (Hemmingway, McGrogan, and Freeman, 2001). This research finding supports the notion that ITB therapy, with the reduction of spasticity and associated caloric expenditure may impact growth. The case studies of this inquiry similarly revealed greater growth outcomes in two male subjects with reduced spasticity.

Limitations of the Study

The lack of a comparison group and the amount of missing data were significant limitations of the study. All subjects did not have sufficient repeated measures available for the time points of interest, mandating that a modification in the data analysis process be implemented. The final sample size accounting for missing information not found with the retrospective medical record review was too small to support missing data. Insufficient data time points and growth measurements resulted in the conduction of a linear regression model to explore trajectories of height, weight and BMI standardized scores (z-scores).

Data obtained with this research inquiry supported Hypothesis 1 as an increase in height was observed; however, it was not sustained. Hypothesis 2 was not supported due to the lack of MAS measurements necessary for the evaluation of spasticity. Subsequently,
inadequate documentation of growth and spasticity management has interfered with the researcher’s attempt to document the potential benefits of continuous administration of ITB in children ages 2-20.

**Clinical Implications of Missing Data**

The quality of care being provided to children with special needs, based upon the failure to document growth parameters, was interpreted as being below satisfactory. When managing pediatric spasticity, it is imperative to recognize the need for diligent assessment of growth parameters. Measuring a child with spasticity presents challenges involving spinal abnormalities, involving the inability to stand upright, and the lack of measurement tools in various clinical settings (Kuperminc, et al., 2013). Standing height is best obtained using a stadiometer in children who are capable of standing. A flexible tape measure may be used, as patients with contractures, spasticity, scoliosis, and uncooperative behavior often provide unreliable measures of length or height (Samson-Fang & Bell, 2013). The researcher recognizes that spasticity often prevents a person from standing upright, in which case a wheelchair scale may be utilized for obtaining weight; a digital scale allows for more accuracy (Samson-Fang & Bell, 2013).

Due to the number of clinicians involved in caring for the subjects of this research inquiry, it can be inferred that the procedure for obtaining the height and weight was not standardized. Furthermore, the child’s inability to stand upright may have inhibited the measurement of height with the use of a stadiometer and the use of scales to obtain weight. The apparent outcomes identified may be isolated as the managing providers of those children receiving ITB therapy assumed the pediatricians (primary care providers) were monitoring the growth parameters. An assumption that endocrinologists and
gastroenterologists were monitoring the growth among the sample group may also have been exercised.

Based upon the lack of growth measurements within this study, a need for improved provision of the quality of care within the healthcare domain has been identified. The potential outcomes of appropriately monitoring growth can positively impact a child’s quality of life. Improving growth and strength, through early intervention, can positively support the performance of ADL (bathing, dressing, hygiene, feeding), in addition to, promoting independence of self-care, mobility, and overall functional improvements throughout the lifespan.

Due to the extent of missing growth measurements, spasticity assessment and documented interventions for both spasticity and growth issues, an evaluation of the structure of the network of services being provided warrants the implementation of standard operating procedures. Identification of administrative nursing staff who are equipped to implement the process of creating, educating, and implementing established standards of measurement, specifically for those individuals experiencing spasticity across departments, could have monumental benefits. These interventions, proven through evidenced based practice, have the propensity to impact outcomes, specifically those of growth, functioning, and QOL.

**Future Directions for Research**

Based on the results of the statistical analysis and the associated limitations, it is suggested that this study design be conducted as a prospective study with standardized repeated measurements to ensure the accuracy of data. A study comparing children with and without ITB pumps would be ideal to fully evaluate the effect of ITB on growth and
whether changes in spasticity mediate the effect of ITB on growth. The results of the case studies suggest that future research should focus on gender differences as it would be helpful to understand the role of testosterone in association with pubertal onset, the occurrence of the growth spurt, and the reduction of spasticity. In addition, a comparison of children with CP to those with TBI would be beneficial due to hormonal differences observed and documented in literature for those individuals with TBI that could possibly contribute to growth delay. The observation, assessment, and documentation of mode of nutrition for all children with spasticity would also provide useful data enhancing the usefulness of outcomes in relation to the regulation of caloric intake as it impacts growth progression.

The study design implemented may be duplicated in a healthcare setting, whereby the standard of care involving obtainment of growth indicators could be set. If growth patterns of children with spasticity receiving ITB could be analyzed in larger populations, the potential benefit could be assessed. Identification of healthcare providers managing the largest number of patients receiving ITB therapy would be ideal for obtaining the data of interest.

The findings of this research inquiry provided the researcher with additional concerns regarding the care and management of individuals exhibiting spasticity. From a global perspective, malnutrition has the propensity to impact children and their families with CP, unless modifications to the utilization of healthcare occurs in a timely manner. Future interventions for optimizing individual outcomes, as they relate to function, autonomy, mobility, and comfort with the potential to benefit many individuals experiencing motor disorders. The researcher plans to submit the research topic of this
dissertation for consideration of relevance to the National Institute of Health’s strategic 5-10-year plan for CP research. Through the National Institute of Neurological Disorders and Stroke and the Eunice Kennedy Shriver National Institute of Child Health and Human Development recommendations were derived for the establishment of CP research and improvement in clinical care, through collaboration with scientists, clinicians, and advocates in 2014 and 2016. It is the hope of this investigator that clinicians will exercise their clinical expertise and compassion to improve the lives of those who have been impacted neurologically by cerebral insults. The early implementation of the most innovative and effective treatment modalities is essential to the delivery of evidenced based practice to all who entrust their lives to us.
References


### APPENDICES

**Appendix 1: Gross Motor Function Classification System (Rosenbaum, et al., 2002)**

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I</td>
<td>Walks without restrictions; limitations in more advanced gross motor skills</td>
</tr>
<tr>
<td>Level II</td>
<td>Walks without assistive devices; limitations in walking outdoors and in the community</td>
</tr>
<tr>
<td>Level III</td>
<td>Walks with assistive mobility devices; limitations in walking outdoors and in the community</td>
</tr>
<tr>
<td>Level IV</td>
<td>Self-mobility with limitations; children are transported or use power mobility outdoors and in the community</td>
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<tr>
<td>Level V</td>
<td>Self-mobility is severely limited even with the use of assistive technology</td>
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### Appendix 2: Spasticity Scales (Awaad, 2002)

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<th>Modified Ashworth</th>
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<td>0</td>
<td>No increase in tone</td>
<td>No increase in tone</td>
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<tr>
<td>1</td>
<td>Slight increase in tone giving a catch when the limb was moved in flexion and extension</td>
<td>Slight increase in tone, manifested by a catch and release, or by minimal resistance at the end of the range of motion (ROM)</td>
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<tr>
<td>1+</td>
<td>Not applicable</td>
<td>Slight increase in tone, manifested by a catch, followed by minimal resistance throughout the remainder (&lt;50%) of the available ROM</td>
</tr>
<tr>
<td>2</td>
<td>More marked increase in tone, limb easily flexed</td>
<td>More marked increase in muscle tone through most of the ROM, but affected parts easily moved.</td>
</tr>
<tr>
<td>3</td>
<td>Considerable increase in tone, passive movement difficult</td>
<td>Considerable increase in tone, passive movement difficult</td>
</tr>
<tr>
<td>4</td>
<td>Limb rigid in flexion and extension</td>
<td>Affected parts rigid in flexion or extension</td>
</tr>
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</table>
Appendix 3: Data Collection Form

1. Date: _______________ D.O.B. _______________

2. Subject Number: _______________

3. Pump implant date: ___/___/_______

4. Gender: M / F

5. Race: Black / Black-Hispanic / Caucasian / Hispanic

6. Diagnosis ICD9 codes: 781.0, 355.9 CPT codes: 62368, 62370

7. Residence: Biological parents/ Residential facility/ SNIF/ Foster/ Other

8. Nutritional consult: YES / NO

9. GMFCS:

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<th></th>
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<tr>
<td>SCORE</td>
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10. Oral spasticity medications:

Date: ___/___/_______

Date: ___/___/_______

Date: ___/___/_______

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Appendix 3: Data Collection Form (con’t.)

13. BACLOFEN DAILY DOSING

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<th>12 months</th>
<th>18 months</th>
<th>24 months</th>
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14. ASHWORTH SCORE

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<th>12 months</th>
<th>18 months</th>
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<tbody>
<tr>
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</table>
### Variable Coding

**PUMP**
- YES: 1
- NO: 0

**D.O.B. (AGE):** XX/XX/XXXX

**RACE:**
- CAUCASIAN: 0
- BLACK: 1
- HISPANIC: 2
- OTHER: 3

**GENDER:**
- MALE: 0
- FEMALE: 1

**ASHWORTH SCORE:** 0-4

**HEIGHT:** Centimeters

**WEIGHT:** Kilograms

**BMI:** Numerical value

**DIAGNOSIS:**
- CP: 1
- TBI: 2
- ANOXIC BRAIN INJURY: 3

**DATE OF PUMP IMPLANT:** XX/XX/XXXX

**NUTRITION:**
- CONSULT: YES=1
  - NO=0

**NUTRITION TYPE:**
- GASTROSTOMY TUBE: 0
- ORAL: 1
- MIXED: 2

**RESIDENCE:**
- BIOLOGICAL: 0
- FOSTER: 1
- SKILLED NURSING FACILITY: 2

**GMFCS:** 1-5

**ORAL ANTISPASMODIC MEDICATIONS:**
- BACLOFEN: 0
- TIZANIDINE: 1
- KLOPONIN: 2
- ATIVAN: 3
Table 1: Variable Frequency

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<td>1</td>
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<td>1</td>
<td>25.0</td>
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</tr>
<tr>
<td>1</td>
<td>1</td>
<td>25.0</td>
<td></td>
</tr>
<tr>
<td>Variable</td>
<td>n</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Age</td>
<td>16</td>
<td>20.1</td>
<td>4.4</td>
</tr>
<tr>
<td>Age at Implant</td>
<td>12</td>
<td>14.8</td>
<td>5.3</td>
</tr>
<tr>
<td>Yrs Implanted</td>
<td>12</td>
<td>4.9</td>
<td>2.0</td>
</tr>
</tbody>
</table>
Table 3. Results of the random slopes and intercepts model for height, weight, and BMI Z-scores.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intercept</th>
<th>Trajectory over Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beta</td>
<td>SE</td>
</tr>
<tr>
<td>Weight</td>
<td>1.21</td>
<td>1.69</td>
</tr>
<tr>
<td>Height</td>
<td>-3.73</td>
<td>1.91</td>
</tr>
<tr>
<td>BMI</td>
<td>2.19</td>
<td>0.75</td>
</tr>
</tbody>
</table>
Table 4: Characteristic of Sample: Age at baseline, age at implant, & years implanted

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>16</td>
<td>20.1</td>
<td>4.4</td>
</tr>
<tr>
<td>Age Implant</td>
<td>12</td>
<td>14.8</td>
<td>5.3</td>
</tr>
<tr>
<td>Yrs Implant</td>
<td>12</td>
<td>4.9</td>
<td>2.0</td>
</tr>
</tbody>
</table>
Table 5: ITB Dose (mcg) and Ashworth scores over time.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITB (mcg)</td>
<td>1</td>
<td>8</td>
<td>826.5</td>
<td>887.9</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>7</td>
<td>954.0</td>
<td>940.8</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>7</td>
<td>959.1</td>
<td>882.7</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>4</td>
<td>936.5</td>
<td>205.3</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>3</td>
<td>874.7</td>
<td>296.6</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>0</td>
<td>------</td>
<td>-----</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>1</td>
<td>896.0</td>
<td>-----</td>
</tr>
<tr>
<td>Ashworth</td>
<td>1</td>
<td>7</td>
<td>1.4</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>5</td>
<td>1.0</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>4</td>
<td>1.7</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>3</td>
<td>1.3</td>
<td>0.6</td>
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<tr>
<td></td>
<td>6</td>
<td>0</td>
<td>------</td>
<td>-----</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0</td>
<td>------</td>
<td>-----</td>
</tr>
</tbody>
</table>
Figure 1: Donabedian’s Model (set for original study design/hypothesis)

<table>
<thead>
<tr>
<th>STRUCTURES OF CARE</th>
<th>PROCESSES OF CARE</th>
<th>OUTCOMES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children with Spasticity</td>
<td>Population Characteristics</td>
<td>Growth Changes</td>
</tr>
<tr>
<td>CMS Patients</td>
<td>ITB v. No ITB</td>
<td>Level of Spasticity</td>
</tr>
</tbody>
</table>

- **CHILDREN WITH SPASTICITY**
  - TBI
  - CP
  - NEAR DROWNING
  - SHAKEN BABY

- **INTRATHecal BACLOFEN PUMP**

- **GROWTH CHANGES**
  - BMI
  - HEIGHT
  - WEIGHT

- **POPULATION CHARACTERISTICS**
  - AGE
  - RACE
  - GENDER
  - NUTRITION
  - ORAL FEEDINGS
  - GASTIC TUBE FEEDINGS
  - MIXED
  - ASHWORTH SCORE
  - GMFCS

- **NO INTRATHecal BACLOFEN PUMP**

- **LEVEL OF SPASTICITY ASHWORTH SCORE**
Figure 2. Projected Trajectory of Growth Z-scores over age.
Figure 3: Subject 008 BMI
Figure 4: Subject 008 Stature
Figure 5: Subject 010 BMI

<table>
<thead>
<tr>
<th>Date</th>
<th>Age</th>
<th>Weight</th>
<th>Stature</th>
<th>BMI</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/24/10</td>
<td>75</td>
<td>140</td>
<td>5'8&quot;</td>
<td>25.1</td>
<td></td>
</tr>
<tr>
<td>2/25/10</td>
<td>75</td>
<td>142</td>
<td>5'8&quot;</td>
<td>24.9</td>
<td></td>
</tr>
</tbody>
</table>

To Calculate BMI: Weight (kg) = Stature (in) x Stature (in) x 703
Or Weight (kg) = Stature (in) x Stature (in) x 10,000

= Total Body Mass Index

kg/m²

AGE (YEARS) 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

BMI 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38

kg/m² 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30

Figure 23, Clinical growth chart 5th, 10th, 25th, 50th, 75th, 95th, 99th percentiles, 2 to 20 years: boys body mass index-for-age
Figure 6: Subject 010 Stature
Figure 7: Subject 011 BMI
Figure 8: Subject: 011 Stature

2 to 20 years: Girls
Stature-for-age and Weight-for-age percentiles

<table>
<thead>
<tr>
<th>Age</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>110</td>
<td>20</td>
</tr>
<tr>
<td>12</td>
<td>120</td>
<td>30</td>
</tr>
<tr>
<td>14</td>
<td>130</td>
<td>40</td>
</tr>
</tbody>
</table>

To calculate BMI: 
BMI = Weight (kg) / Height (m)²

Published May 26, 2010 (proposed July 1, 2000)

SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000)
http://www.cdc.gov/growthcharts

Figure 22: Clinical growth chart 5th, 10th, 25th, 50th, 75th, 90th, 95th percentiles. 2 to 20 years. Girls stature-for-age and weight-for-age
Figure 9: Subject 017 BMI
Figure 10: Subject 017 Stature

2 to 20 years: Girls
Stature-for-age and Weight-for-age percentiles

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Stature (cm)</th>
<th>Weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
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<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*To calculate BMI: Weight (kg) = Stature (cm) * Stature (cm) x 7,000
  or Weight (lb) = Stature (in) * Stature (in) x 703

Figure 20, Clinical growth chart 5th, 10th, 25th, 50th, 75th, 90th, 95th percentiles, 2 to 20 years. Girls stature-for-age and weight-for-age.
Figure 11: Subject 20 BMI
Figure 12: Subject 20 Stature

Figure 22. Clinical growth chart 5th, 10th, 25th, 50th, 75th, 95th, 99th percentiles, 2 to 20 years: Girls stature-for-age and weight-for-age.